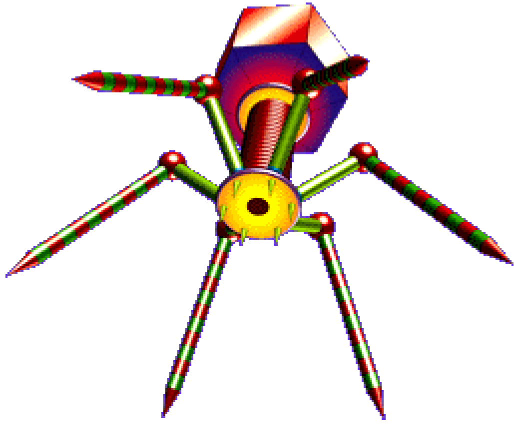

Bacteriophage Ecology Group News

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@ www.phage.org

by Stephen T. Abedon (editor)

December 1, 2006 issue (#25)

Phage Ecology on Wikipedia

Stephen T. Abedon, The Ohio State University

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In this day of search engines—and increasing expectation by students, the public, and academics alike for finding answers to questions online—an effective, dynamic, and permanent presence on the World Wide Web is important, if not crucial, for the maintenance of coherence, efficiency, effectiveness, and outreach by academic disciplines. Phage ecology is one such discipline, and toward establishing a web presence we have BEG and *BEG News*. Unfortunately, as the absence of *BEG News* from your lives for over a year and a half is testament, maintaining a web presence, especially by one person, is pretty difficult and time consuming. It also places the online "defining" of a discipline into too few hands, plus lacks a certain permanence that academics prefer, and should demand. Who, after all, is going to keep BEG alive after I'm gone?

In effect, every discipline faces these problems, and some no doubt have solved them. Solutions, however, tend to be *ad hoc*. Should every academic discipline re-invent the wheel to develop their own, personal online presence? Should we all be hiring IT people to produce technologically effective web sites that we then endow and seek to maintain for eternity? Should we all just sit on information that might otherwise be useful to our colleagues—knowledge of patents, interesting web sites, obscure references, laboratory subtleties, etc.—just because they are not readily published in traditional venues? To all these questions I say, "No!". Publishing is (very) important but still is a very limited means of disseminating information. Combinations of mailing and photocopying (or mimeographing) have been employed in the past to transcend the problem that we can't publish everything, and that we can accomplish only so much in terms of information dissemination through travel, such as to meetings. Personal web pages, or even those of societies, have supplanted earlier, paper-based attempts at self publishing, and are hugely powerful due to modern search engines. Nevertheless, personal web pages suffer from the problems outlined above: Too few people are responsible for maintaining (too-little) information that is too labile and otherwise impermanent.

The next generation of online-information generators, whether you realize it or not, is you. The future of online information dissemination, especially from the perspective of public outreach, but also in terms of student access and exchange among academics, is user-modifiable publishing. Imagine a world in which every publication in an academic discipline was listed online, perhaps in an annotated form, with links to full-text versions? A page that you or anybody else could use. A page that you or anybody else could update, with new publications, or new recipes, or with the addition of an (ideally) improved perspective. Imagine a seamless flow of information, a way of combining all of those many course sites (Bio 101!) that so many of us have worked so hard to develop. Imagine not having to develop *ad hoc* the technology to make all of this possible. Imagine a place where 10s or more hours of work toward improving the public face of your discipline aren't destined to be lost at the whims of your department's computer tech consultant!

All of the technology and great ideas which address many of the problems outlined above are, in principle, solvable. Wikipedia, an online, user-updateable and editable encyclopedia points the way toward the future of less-formal (i.e., other than traditionally published) online scholarship. Technology that is preexisting and easy to use. Unfortunately, its power is damped, enormously, by its strength: Everybody can add information (which, given sufficient volume, can be overwhelming if that information is garbage) and, perhaps more importantly, whole entries can be irretrievably deleted. Nevertheless, I am an optimist and, so far, am of the opinion that these problems, grave as they may be, in fact can be

surmounted. Therefore, this essay—and this issue of *BEG News*— is more about a realistic push for using and contributing to Wikipedia, rather than a call for snubbing it. Thus, I encourage you to visit and contribute to a number of Wikipedia pages that have phage-, phage ecology-, or, more generally, microbial population biology-related themes, which may be found through these Wikipedia "Category" pages:

http://en.wikipedia.org/wiki/Category:Bacteriophage
http://en.wikipedia.org/wiki/Category:Phage_workers
http://en.wikipedia.org/wiki/Category:Microbial_population_biology

Farther down in this issue of *BEG News* I also present earlier (though slightly updated) copies of some of the pages that may be reached via the above list, ones for which I was either nearly entirely responsible for creating or did in collaboration outside of Wikipedia (and therefore feel reasonably secure in my right to reproduce them):

Page presented here	Wikipedia link
Phage Ecology	http://en.wikipedia.org/wiki/Phage_ecology
Phage Monographs	http://en.wikipedia.org/wiki/Phage_monographs
Phage Experimental Evolution	http://en.wikipedia.org/wiki/Phage_experimental_evolution
Cyanophage	http://en.wikipedia.org/wiki/Cyanophage

I place copies of these pages here, in this issue of *BEG News*, so that you will be able to get a sense of what Wikipedia is all about without having to actually click on a link (or two!) to get there. But please, do go to the Wikipedia versions. In fact, if only for the sake of assuring its survival, if you do nothing else, please go to (and contribute to) this page:

http://en.wikipedia.org/wiki/Phage_meetings

It is crazy that academia has not developed an effective, universal means of disseminating information via the World Wide Web, or maybe we have. Movement is afoot to create a Wikipedia "fork", called Citizendium (www.citizendium.org), which just may succeed in addressing this lapse while simultaneously subduing Wikipiedia's more anti-academic tendencies (though, of course, we shall see). Already in existence are a number "private" Wiki-like sites such as those provided by OpenWetWare, where by "private" I mean that these are not open to modification by everybody (that is, of course, not by *you*). OpenWetWare in particular exists more as a means of within-group communication rather than for the sake of widespread information dissemination to the general public (the latter, of course, is what I and BEG are all about). So please support the phage and phage-ecology presence on Wikipedia—as the best user-modifiable phage web site that we currently have—by using, contributing to, and expanding upon the existing phage and phage ecology entries.

Only you can help create and maintain an effective online phage presence.

Other items found in this issue of *BEG News*
are a list of new BEG members
and a list of new phage ecology references (with abstracts).

Phage Ecology

Stephen T. Abedon[1], The Ohio State University
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The following is my first Wikipedia effort. Feel free to add to the Wikipedia version, found at:

http://en.wikipedia.org/wiki/Phage_ecology.

(equivalent to Wikipedia version as of Saturday, October 21, 2006)

Bacteriophage (phage) are the viruses of bacteria (more generally, of prokaryotes[1]), and **phage ecology** is the study of the interaction of bacteriophage with their environments.[2]

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- Phage "organismal" ecology (suggested reading)
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- Aquatic phage ecology (suggested reading
- Other environments (suggested reading)

8 Notes

Introduction to phage ecology

Vastness of phage ecology

Phage are obligate intracellular parasites meaning that they are able to reproduce only while infecting bacteria. Phage therefore are found only within environments that contain bacteria. Most environments contain bacteria, including our own bodies (there called normal flora). Often these bacteria are found in large numbers[1]. As a consequence, phage are found almost everywhere.

As a rule of thumb, many phage biologists expect that phage population densities will exceed bacterial densities by a ratio of 10-to-1 or more (VBR or virus-to-bacterium ratio; see [2] for a summary of actual data). As there exist estimates of bacterial numbers on Earth of approximately 10^{30}[3], there consequently is an expectation that 10^{31} or more individual virus (mostly phage[4]) particles exist[5], making phage the most numerous category of "organisms" on our planet.

Bacteria (along with archaeabacteria) appear to be highly diverse and there likely are millions of species[6]. Phage-ecological interactions therefore are quantitatively vast: huge numbers of intereactions. Phage-ecological interations are also qualitatively diverse: There are huge numbers of environment types, bacterial-host types[7], and also individual phage types[8]).

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[1] With the help of various Wikipedia editors.

Studying phage ecology

The scale of phage ecology is at once both exhilarating and intimidating. As a guiding principle toward understanding phage ecology we therefore seek generalizations, plus look to more established scientific disciplines for guidance, the most obvious being general ecology. Toward that end we can speak of phage "organismal" ecology, population ecology, community ecology, and ecosystem ecology. Phage ecology from these perspectives will be described in turn (re: links in previous sentence).

Phage ecology also may be considered (though mostly less well formally explored) from perspectives of phage behavioral ecology, evolutionary ecology, functional ecology, landscape ecology, mathematical ecology, molecular ecology, physiological ecology (or ecophysiology), and spatial ecology. Phage ecology additionally draws (extensively) from microbiology, particularly in terms of environmental microbiology, but also from an enormous catalog (90 years) of study of phage and phage-bacterial interactions in terms of their physiology and, especially, their molecular biology.

Suggestions for further reading are provided below.

Phage "organismal" ecology

Phage "organismal" ecology is primarily the study of the evolutionary ecological impact of phage growth parameters:

- latent period, plus
  - eclipse period (or simply "eclipse")
  - rise period (or simply "rise")
- burst size, plus
  - rate of intracellular phage-progeny maturation
- adsorption constant, plus
  - rates of virion diffusion
  - virion decay (inactivation) rates
- host range, plus
  - resistance to restriction
  - resistance to abortive infection
- various temperate-phage properties, including
  - rates of reduction to lysogeny
  - rates of lysogen induction
- the tendency of at least some phage to enter into (and then subsequently leave) a not very well understood state known (inconsistently) as pseudolysogeny

Another way of envisioning phage "organismal" ecology is that it is the study of phage adaptations that contribute to phage survival and transmission to new hosts or environments. Phage "organismal" ecology is the most closely aligned of phage ecology disciplines with the classical molecular and molecular genetic analyses of bacteriophage.

From the perspective of ecological subdisciplines, we can also consider phage behavioral ecology, functional ecology, and physiological ecology under the heading of phage "organismal" ecology. However, as noted, these subdisciplines are not as well developed as more general considerations of phage "organismal" ecology. Phage growth parameters often evolve over the course of phage experimental adaptation studies.

Suggestions for further reading are provided below.

Historical overview

In the mid 1910s, when phage were first discovered, the concept of phage was very much a whole-culture phenomenon (like much of microbiology[3]), where various types of bacterial cultures (on solid media, in broth) were visibly cleared by phage action. Though from the start there was some sense, especially by Félix d'Hérelle, that phage consisted of individual "organisms", in fact it wasn't until the late 1930s through the 1940s that phage were studied, with rigor, as individuals, e.g., by electron microscopy and single-step growth experiments (example of latter). Note, though, that for practical reasons much of "organismal" phage study is of their properties in bulk culture (many phage) rather than the properties of individual phage virions or or individual infections.

This somewhat whole-organismal view of phage biology saw its heyday during the 1940s and 1950s, before giving way to much more biochemical, molecular genetic, and molecular biological analyses of phage, as seen during the 1960s and

onward. This shift, paralleled in much of the rest of microbiology[9], represented a retreat from a much more ecological view of phages (first as bacterial killers, and then as organisms unto themselves). However, the organismal view of phage biology lives on as a foundation of phage ecological understanding. Indeed, it represents a key thread that ties together the ecological thinking on phage ecology with the more "modern" considerations of phage as molecular model systems.

Methods

The basic experimental toolkit of phage "organismal" ecology consists of the single-step growth (or one-step growth; example) experiment and the phage adsorption curve (example). Single-step growth is a means of determining the phage latent period (example), which is approximately equivalent (depending on how it is defined) to the phage period of infection. Single-step growth experiments also are employed to determine a phage's burst size, which is the number of phage (on average) that are produced per phage-infected bacterium.

The adsorption curve is obtained by measuring the rate at which phage virion particles (see [10]) attach to bacteria. This is usually done by separating free phage from phage-infected bacteria in some manner so that either the loss of not currently infecting (free) phage or the gain of infected bacteria may be measured over time.

Suggestions for further reading are provided below.

Phage population ecology

A population is a group of individuals which either do or can interbreed or, if incapable of interbreeding, then are recently derived from a single individual (a clonal population). Population ecology considers characteristics that are apparent in populations of individuals but either are not apparent or are much less apparent among individuals. These characteristics include so-called intraspecific interactions, that is between individuals making up the same population, and can include competition as well as cooperation. Competition can be either in terms of rates of population growth (as seen especially at lower population densities in resource-rich environments) or in terms of retention of population sizes (seen especially at higher population densities where individuals are directly competing over limited resources). Respectively, these are population-density independent and dependent effects.

Phage population ecology considers issues of rates of phage population growth, but also phage-phage interactions as can occur when two or more phage adsorb an individual bacterium.

Suggestions for further reading are provided below.

Phage community ecology

A community consists of all of the biological individuals found within a given environment (more formally, within an ecosystem), particularly when more than one species is present. Community ecology studies those characteristics of communities that either are not apparent or which are much less apparent if a community consists of only a single population. Community ecology thus deals with interspecific interactions. Interspecific interactions, like intraspecific interactions, can range from cooperative to competitive but also to quite antagonistic (as are seen, for example, with predator-prey interactions). An important consequence of these interactions is coevolution.

The interaction of phage with bacteria is the primary concern of phage community ecologists. Phage, however, are capable of interacting with species other than bacteria, e.g., such as phage-encoded exotoxin interaction with animals[11]. Phage therapy is an example of applied phage community ecology.

Suggestions for further reading are provided below.

Phage ecosystem ecology

An ecosystem consists of both the biotic and abiotic components of an environment. Abiotic entities are not alive and so an ecosystem essentially is a community combined with the non-living environment within which that ecosystem exists. Ecosystem ecology naturally differs from community ecology in terms of the impact of the community on these abiotic entities, and *vice versa*. In practice, the portion of the abiotic environment of most concern to ecosystem ecologists is inorganic nutrients and energy.

Phage impact the movement of nutrients and energy within ecosystems primarily by lysing bacteria. Phage can also impact abiotic factors via the encoding of exotoxins (a subset of which are capable of solubilizing the biological tissues of

living animals[12]). Phage ecosystem ecologists are primarily concerned with the phage impact on the global carbon cycle, especially within the context of a phenomenon know as the microbial loop.

Suggestions for further reading are provided below.

External links

- The Bacteriophage Ecology Group (BEG): Home of Phage Ecology and Phage Evolutionary Biology (www.phage.org)
- The Virus Ecology Group (VEG)

Further reading

Provided are suggested readings gleaned mostly from the secondary literature, presented by category. When available, links are being provided to full text, online versions of articles, or to abstracts if full text versions are not available. Avoided are linking directly to PDFs or to materials posted on personal web sites, unless the latter is where an article was "published". An approximation of ASM (American Society for Microbiology) conventions are used throughout. Some articles may be found online on personal web pages[4]. An extensive list of phage monographs also exists, though these do not by and large have a strong phage ecology emphasis.

General Reviews

These are articles that provide a good overview of general aspects phage ecology.

Abedon, S. T. 2006. **Phage ecology,** p. 37-46. In R. Calendar and S. T. Abedon (eds.), The Bacteriophages. Oxford University Press, Oxford. ISBN 0-195-14850-9

Breitbart, M., F. Rohwer, and S. T. Abedon. 2005. **Phage ecology and bacterial pathogenesis,** p. 66-91. In M. K. Waldor, D. I. Friedman, and S. L. Adhya (eds.), Phages: Their Role in Bacterial Pathogenesis and Biotechnology. ASM Press, Washington DC. ISBN 1-555-81307-0

Brüssow, H., and E. Kutter. 2005. **Phage ecology,** p. 129-164. In E. Kutter and A. Sulakvelidze (eds.), Bacteriophages: Biology and Application. CRC Press, Boca Raton, Florida. ISBN 0-849-31336-8

Chibani-Chennoufi, S., A. Bruttin, M. L. Dillmann, and H. Brüssow. 2004. **Phage-host interaction: an ecological perspective.** J. Bacteriol. 186:3677-3686. full text

Weinbauer, M. G. 2004. **Ecology of prokaryotic viruses.** FEMS Microbiol. Rev. 28:127-181. abstract

Paul, J. H., and C. A. Kellogg. 2000. **Ecology of bacteriophages in nature,** p. 211-246. In C. J. Hurst (ed.), Viral Ecology. Academic Press, San Diego. ISBN 0-123-62675-7

Levin, B. R., and Richard Lenski. 1985. **Bacteria and phage: A model system for the study of the ecology and co-evolution of hosts and parasites,** p. 227-242. In D. Rollinson and R. M. Anderson (eds.), Ecology and Genetics of Host-Parasite Interactions. Academic Press, London. ISBN 0-125-93690-7

Anderson, E. S. 1957. **The relations of bacteriophages to bacterial ecology,** p. 189-217. In R. E. O. Williams and C. C. Spicer (eds.), Microbial Ecology. Cambridge University Press, London.

Books

A handful of books provide a good (if in many cases dated) overview of various aspects of phage ecology.

Abedon, S. T. (2007=scheduled publication date, and we are on schedule!). **Bacteriophage Ecology: Population Growth, Evolution, and Impact of Bacterial Viruses.** Cambridge University Press, Cambridge, UK.

Ackermann, H.-W., and M. S. DuBow. 1987. **Viruses of Prokaryotes, Volume 1, General Properties of Bacteriophages.** CRC Press, Boca Raton, Florida. ISBN 0-849-36056-0

Ackermann, H.-W., and M. S. DuBow. 1987. **Viruses of Prokaryotes, Volume 2, Natural Groups of Bacteriophages.** CRC Press, Boca Raton, Florida. ISBN 0-849-36056-0

Goyal, S. M., C. P. Gerba, and G. Bitton. 1987. **Phage Ecology.** CRC Press, Boca Raton, Florida. ISBN 0-471-82419-4

Phage "organismal" ecology (suggested reading)

None of these reviews are devoted exclusively to issues of phage "organismal" ecology, but of those reviews of phage ecology, these cover that subject most extensively. See virulence evolution, etc., on the phage experimental evolution page for additional references. Return to phage "organismal" ecology.

Abedon, S. T. 2006. **Phage ecology**, p. 37-46. In R. Calendar and S. T. Abedon (eds.), The Bacteriophages. Oxford University Press, Oxford. ISBN 0-195-14850-9

Breitbart, M., F. Rohwer, and S. T. Abedon. 2005. **Phage ecology and bacterial pathogenesis**, p. 66-91. In M. K. Waldor, D. I. Friedman, and S. L. Adhya (eds.), Phages: Their Role in Bacterial Pathogenesis and Biotechnology. ASM Press, Washington DC. ISBN 1-555-81307-0

Brüssow, H., and E. Kutter. 2005. **Phage ecology**, p. 129-164. In E. Kutter and A. Sulakvelidze (eds.), Bacteriophages: Biology and Application. CRC Press, Boca Raton, Florida. ISBN 0-849-31336-8

Chibani-Chennoufi, S., A. Bruttin, M. L. Dillmann, and H. Brüssow. 2004. **Phage-host interaction: an ecological perspective.** J. Bacteriol. 186:3677-3686. full text

Weinbauer, M. G. 2004. **Ecology of prokaryotic viruses**. FEMS Microbiol. Rev. 28:127-181. abstract

Paul, J. H., and C. A. Kellogg. 2000. **Ecology of bacteriophages in nature**, p. 211-246. In C. J. Hurst (ed.), Viral Ecology. Academic Press, San Diego. ISBN 0-123-62675-7

Robb, F. T., and R. T. Hill. 2000. **Bacterial viruses and hosts: Influence of culturable state**, p. 199-208. In R. R. Colwell and D. J. Grimes (eds.), Nonculturable Microorganisms in the Environment. ASM Press, Washington, D.C. ISBN 1-555-81196-5

Schrader, H. S., J. O. Schrader, J. J. Walker, N. B. Bruggeman, J. M. Vanderloop, J. J. Shaffer, and T. A. Kokjohn. 1997. **Effects of host starvation on bacteriophage dynamics**, p. 368-385. In R. Y. Morita (ed.), Bacteria in Oligotrophic Environments. Starvation-Survival Lifestyle. Chapman & Hall, New York. ISBN 0-412-10661-2

Kutter, E., E. Kellenberger, K. Carlson, S. Eddy, J. Neitzel, L. Messinger, J. North, and B. Guttman. 1994. **Effects of bacterial growth conditions and physiology on T4 infection**, p. 406-418. In J. D. Karam (ed.), The Molecular Biology of Bacteriophage T4. ASM Press, Washington, DC. ISBN 1-555-81064-0

Herskowitz, I., and F. Banuett. 1984. **Interaction of phage, host, and environmental factors in governing the λ lysis-lysogeny decision**, p. 59-73. In V. L. Chopra, B. C. Joshi, R. P. Sharma, and H. C. Bansal (eds.), Genetics, New Frontier: Proceedings of the XV International Congress of Genetics. Oxford and I.B.H., New Delhi.

Lwoff, A. 1953. **Lysogeny**. Bacteriol. Rev. 17:269-337. full text

Phage "organismal" experimental protocols (suggested reading)

It is important to characterize phages "organismally". A number of protocols have been published. Additional phage protocols should be available before the end of 2007. Return to phage "organismal" ecology methods.

Carlson, K. 2005. **Working with bacteriophages: common techniques and methodological approaches**, p. 437-494. In E. Kutter and A. Sulakvelidze (eds.), Bacteriophages: Biology and Application. CRC Press, Boca Raton, Florida. ISBN 0-849-31336-8

Carlson, K., and E. S. Miller. 1994. **Enumerating phage: the plaque assay**, p. 427-429. In J. D. Karam (ed.), Molecular Biology of Bacteriophage T4. ASM Press, Washington, DC. ISBN 1-555-81064-0

Carlson, K., and E. S. Miller. 1994. **General procedures**, p. 427-437. In J. D. Karam (ed.), Molecular Biology of Bacteriophage T4. ASM Press, Washington, DC. ISBN 1-555-81064-0

Carlson, K. 1994. **Single-step growth**, p. 434-437. In J. D. Karam (ed.), Molecular Biology of Bacteriophage T4. ASM Press, Washington. ISBN 1-555-81064-0

Snustad, D. P., and D. S. Dean. 1971. **Genetics Experiments with Bacterial Viruses.** W. H. Freeman and Co., San Francisco. ISBN 0-716-70161-8

Eisenstark, A. 1967. **Bacteriophage techniques.** Methods in Virology 1:449-524.

Adams, M. H. 1959. **Bacteriophages.** Interscience, New York.

Phage population ecology (suggested reading)

There are very few reviews on phage ecology that spend much time emphasizing phage population ecology, published at least. Anticipate better than a doubling of the number before the end of 2007. Return to phage population ecology.

Abedon, S. T. 2006. **Phage ecology**, p. 37-46. In R. Calendar and S. T. Abedon (eds.), The Bacteriophages. Oxford University Press, Oxford. ISBN 0-195-14850-9

Bull, J. J., D. W. Pfening, and I.-W. Wang. 2004. **Genetic details, optimization, and phage life histories.** Trends Ecol. Evol. 19:76-82. abstract & pay article

Phage community ecology (suggested reading)

Having received the most attention from both experimentalists and theoreticians among the various phage ecologies, a relatively large number of phage ecology reviews exist. Note that much of this literature has been motivated more from the bacterial rather than explicitly the phage perspective. See coevolution on the phage experimental evolution page for additional references. Return to phage community ecology.

Abedon, S. T. 2006. **Phage ecology**, p. 37-46. In R. Calendar and S. T. Abedon (eds.), The Bacteriophages. Oxford University Press, Oxford. ISBN 0-195-14850-9
Abedon, S. T., and J. T. LeJeune. 2005. **Why bacteriophage encode exotoxins and other virulence factors.** Evolutionary Bioinformatics Online 1:97-110. full text
Comeau, A. M., and H. M. Krisch. 2005. **War is peace--dispatches from the bacterial and phage killing fields.** Curr. Opin. Mirobiol. 8:488-494. abstract & pay article
Weinbauer, M. G., and F. Rassoulzadegan. 2004. **Are viruses driving microbial diversification and diversity?** Environmental Microbiology 6:1-11. abstract
Levin, B. R., and J. J. Bull. 2004. **Population and evolutionary dynamics of phage therapy.** Nat. Rev. Microbiol. 2:166-173. abstract
Sutherland, I. W., K. A. Hughes, L. C. Skillman, and K. Tait. 2004. **The interaction of phage and biofilms.** FEMS Microbiol. Lett. 232:1-6. abstract
Bohannan, B. J. M., and R. E. Lenski. 2000. **Linking genetic change to community evolution: insights from studies of bacteria and bacteriophage.** Ecol. Lett. 3:362-377. full text
Suttle, C. A. 1994. **The significance of viruses to mortality in aquatic microbial communities.** Microb. Ecol. 28:237-243. abstract & pay article
Miller, R. V., and G. S. Sayler. 1992. **Bacteriophage-host interactions in aquatic systems,** p. 176-193. In E. M. H. Wellington and J. D. van Elsas (eds.), Genetic Interactions among Microorganisms in the Natural Environment. Pergamon Press, Oxford. ISBN 0080420001
Lenski, R. E. 1988. **Dynamics of interactions between bacteria and virulent bacteriophage.** Adv. Microbial. Ecol. 10:1-44.
Levin, B. R., and R. E. Lenski. 1985. **Bacteria and phage: A model system for the study of the ecology and co-evolution of hosts and parasites,** p. 227-242. In D. Rollinson and R. M. Anderson (eds.), Ecology and Genetics of Host-Parasite Interactions. Academic Press, London. ISBN 0-125-93690-7
Krüger, D. H., and T. A. Bickle. 1983. **Bacteriophage survival: Multiple mechanisms for avoiding deoxyribonucleic acid restriction systems of their hosts.** Microbiol. Rev. 47:345-360. full text
Levin, B. R., and R. E. Lenski. 1983. **Coevolution in bacteria and their viruses and plasmids,** p. 99-127. In D. J. Futuyama and M. Slatkin (eds.), Coevolution. Sinauer Associates, Inc., Sunderland, Massachusetts. ISBN 0-878-93229-1
Barksdale, L., and S. B. Ardon. 1974. **Persisting bacteriophage infections, lysogeny, and phage conversions.** Ann. Rev. Microbiol. 28:265-299. abstract & pay article
Anderson, E. S. 1957. **The relations of bacteriophages to bacterial ecology,** p. 189-217. In R. E. O. Williams and C. C. Spicer (eds.), Microbial Ecology. Cambridge University Press, London.

Phage ecosystem ecology (suggested reading)

The majority (if not all!) reviews with a phage ecosystem ecology emphasis also emphasize aquatic phage ecology. The following are examples. Return to phage ecosystem ecology.

Weinbauer, M. G. 2004. **Ecology of Prokaryotic Viruses.** FEMS Microbiol. Rev. 28:127-181. abstract
Wommack, K. E., and R. R. Colwell. 2000. **Virioplankton: viruses in aquatic ecosystems.** Microbiol. Mol. Biol. Rev. 64:69-114. full text
Suttle, C. A. 2000. **Cyanophages and their role in the ecology of cyanobacteria,** p. 563-589. In B. A. Whitton and M. Potts (eds.), The Ecology of Cyanobacteria: Their Diversity in Time and Space. Kluwer Academic Publishers, Boston. ISBN 0-792-34735-8
Suttle, C. A. 2000. **The ecology, evolutionary and geochemical consequences of viral infection of cyanobacteria and eukaryotic algae,** p. 248-286. In C. J. Hurst (ed.), Viral Ecology. Academic Press, New York. ISBN 0-123-62675-7
Fuhrman, J. A. 1999. **Marine viruses and their biogeochemical and ecological effects.** Nature 399:541-548. abstract & pay article
Wilhelm, S. W., and C. A. Suttle. 1999. **Viruses and nutrient cycles in the sea.** BioScience 49:781-788. full text
Bratbak, G., T. F. Thingstad, and M. Heldal. 1994. **Viruses and the microbial loop.** Microb. Ecol. 28:209-221. abstract & pay article
Fuhrman, J. A., R. M. Wilcox, R. T. Noble, and N. C. Law. 1993. **Viruses in marine food webs,** p. 295-298. In R. Guerrero and C. Pedros-Alio (eds.), Trends in microbial ecology. Spanish Society for Microbiology, Barcelona.
Thingstad, T. F., M. Heldal, G. Bratbak, and I. Dundas. 1993. **Are viruses important partners in pelagic food webs?** Trends Ecol. Evol. 8:209-213. abstract
Fuhrman, J. A. 1992. **Bacterioplankton roles in cycling of organic matter: the microbial food web,** p. 361-383. In P. G. Falkowski and A. D. Woodhead (eds.), Primary Productivity and Biogeochemical Cycles in the Sea. Plenum, New York. ISBN 0-306-44192-6

Terrestrial phage ecology (suggested reading)

Not nearly as well developed as aquatic phage ecology, due to the complexity and heterogensity of solid phase versus liquid phage, terrestrial phage ecology has been explored in a number of reviews. The following are suggested readings.

Gill, J. J., and S. T. Abedon. 2003. **Bacteriophage ecology and plants.** APSnet feature. full text

Williams, S. T., A. M. Mortimer, and J. Eccleston. 1994. **Bacteriophages in soil,** p. 121R. Webster and A. Granoff (eds.), Encyclopedia of Virology. Academic Press.

Williams, S. T., A. M. Mortimer, and L. Manchester. 1987. **Ecology of soil bacteriophages,** p. 157-179. In S. M. Goyal, C. P. Gerba, and G. Bitton (eds.), Phage Ecology. John Wiley & Sons, New York. ISBN 0-471-82419-4

Williams, S. T., and S. Lanning. 1984. **Studies of the ecology of streptomycete phage in soil,** p. 473-483. In L. Ortiz-Ortiz, L. F. Bojalil, and V. Yakoleff (eds.), Biological, Biochemical and Biomedical Aspects of Actinomycetes. Academic Press, London. ISBN 0-125-28620-1

Anderson, E. S. 1957. **The relations of bacteriophages to bacterial ecology,** p. 189-217. In R. E. O. Williams and C. C. Spicer (eds.), Microbial Ecology. Cambridge University Press, London.

The following deals more with phage (and other virus) retention in soils more than phage ecology per se.

Duboise, S. M., B. E. Moore, C. A. Sorber, and B. P. Sagik. 1979. **Viruses in soil systems,** p. 245-285. In H. D. Isenberg (ed.), CRC Critical Reviews in Microbiology. CRC Press, Boca Raton, FL.

Aquatic phage ecology (suggested reading)

Aquatic phage ecology came to dominate phage ecology stemming from the seminal publication by Bergh *et al.* in 1989 (Bergh, O., K. Y. Børsheim, G. Bratbak, and M. Heldal. 1989. **High abundance of viruses found in aquatic environments.** Nature 340:467-468.). A large number of publications, and a large number reviews followed. The latter are listed below, exclusive of those listed above under the heading of Phage ecosystem ecology (suggested reading). See also cyanophage for additional references.

Mann, N. H. 2006. **Phages of cyanobacteria,** p. 517-533. In R. Calendar and S. T. Abedon (eds.), The Bacteriophages. Oxford University Press, Oxford. ISBN 0-471-82419-4

Miller, R. V. 2006. **Marine phages,** p. 534-544. In R. Calendar and S. T. Abedon (eds.), The Bacteriophages. Oxford University Press, Oxford. ISBN 0-471-82419-4

Brüssow, H., and E. Kutter. 2005. **Phage ecology,** p. 129-164. In E. Kutter and A. Sulakvelidze (eds.), Bacteriophages: Biology and Application. CRC Press, Boca Raton, Florida. ISBN 0-849-31336-8

Paul, J. H., and M. B. Sullivan. 2005. **Marine phage genomics: what have we learned?** Curr. Opin. Biotechnol. 16:299-307. abstract & pay article

Fuhrman, J. A., and M. Schwalbach. 2003. **Viral influence on aquatic bacterial communities.** Biol. Bull. 204:192-195. full text

Paul, J. H., M. B. Sullivan, A. M. Segall, and F. Rohwer. 2002. **Marine phage genomics.** Comparative Biochemistry and Physiology 133:463-476.

Suttle, C. A. 2002. **Community structure: viruses,** p. 364-370. In C. J. Hurst, G. R. Knudson, M. J. McInerney, L. D. Stezenbach, and M. V. Walter (eds.), Manual of Environmental Microbiology (2nd Edition). ASM Press, Washington, DC.

Fuhrman, J. A. 2000. **Impact of viruses on bacterial processes,** p. 327-350. In D. L. Kirchman (ed.), Microbial Ecology of the Oceans. Wiley & Sons, New York.

Martin, E. L., and T. A. Kokjohn. 1999. **Cyanophages,** p. 324-332. In A. Granoff and R. G. Webster (eds.), Encyclopedia of Virology second edition. Academic Press, San Diego.

Suttle, C. A. 1999. **Do viruses control the oceans?** Nat. His. 108:48-51.

Proctor, L. M. 1998. **Marine virus ecology,** p. 113-130. In S. E. Cooksey (ed.), Molecular Approaches to the Study of the Ocean. Chapman & Hall, London.

Proctor, L. M. 1997. **Advances in the study of marine viruses.** Microscopy Research and Technique 37:136-161.

Suttle, C. A. 1997. **Community structure: viruses,** p. 272-277. In C. J. Hurst, G. R. Knudson, M. J. McInerney, L. D. Stezenbach, and M. V. Walter (eds.), Manual of Environmental Microbiology. ASM Press, Washington DC.

Paul, J. H., C. A. Kellogg, and S. C. Jiang. 1996. **Viruses and DNA in marine environments,** p. 119-128. In R. R. Colwell, U. Simidu, and K. Ohwada (eds.), Microbial Diversity in Time and Space. Plenum Press, New York, N.Y.

Suttle, C. A. 1994. **The significance of viruses to mortality in aquatic microbial communities.** Microb. Ecol. 28:237-243.

Bratbak, G., M. Heldal, A. Naess, and T. Roeggen. 1993. **Viral impact on microbial communities,** p. 299-302. In R. Guerrero and C. Pedros-Alio (eds.), Trends in Microbial Ecology. Spanish Society for Microbiology, Barcelona.

Fuhrman, J. A., and C. A. Suttle. 1993. **Viruses in marine planktonic systems.** Oceanography 6:50-62.
Thingstad, T. F., M. Heldal, G. Bratbak, and I. Dundas. 1993. **Are viruses important partners in pelagic food webs?** Trends Ecol. Evol. 8:209-213.
Miller, R. V., and G. S. Sayler. 1992. **Bacteriophage-host interactions in aquatic systems,** p. 176-193. In E. M. H. Wellington and J. D. van Elsas (eds.), Genetic Interactions among Microorganisms in the Natural Environment. Pergamon Press, Oxford.
Cannon, R. E. 1987. **Cyanophage ecology,** p. 245-265. In S. M. Goyal, C. P. Gerba, and G. Bitton (eds.), Phage Ecology. John Wiley & Sons, New York.
Farrah, S. R. 1987. **Ecology of phage in freshwater environments,** p. 125-136. In S. M. Goyal, G. P.
Moebus, K. 1987. **Ecology of marine bacteriophages,** p. 137-156. In S. M. Goyal, G. P. Gerba, and G. Bitton (eds.), Phage Ecology. John Wiley & Sons, New York.
Cannon, R. E., M. S. Shange, and E. DeMichele. 1974. **Ecology of blue-green algal viruses.** J. Environ. Eng. Div. , ASCE 100:1205-1211.
Shilo, M. 1972. **The ecology of cyanophages.** Bamidgeh 24:76-82.
Spencer, R. 1963. **Bacterial viruses in the sea,** p. 350-365. In C. H. Oppenheimer (ed.), Symposium on Marine Microbiology. Charles C. Thomas, Publisher, Springfield, IL.

Other environments (suggested reading)

Bogosian, G. 2006. **Control of bacteriophage contamination in commercial microbiology and fermentation facilities,** p. 667-673. In R. Calendar and S. T. Abedon (eds.), The Bacteriophages. Oxford University Press, Oxford. ISBN 0-195-14850-9
Sanders, M. E. 1987. **Bacteriophages of industrial importance,** p. 211-244. In S. M. Goyal, G. P. Gerba, and G. Bitton (eds.), Phage Ecology. John Wiley & Sons, New York. ISBN 0-471-82419-4

Notes

^ The term "prokaryotes" is useful to mean the sum of the bacteria and archaeabacteria but otherwise can be controversial, as discussed by Woese, 2004; see also pp. 103-104 of Woese, C. R. 2005. Evolving biological organization, p. 99-118. In J. Sapp (ed.), Microbial Phylogeny and Evolution Concepts and Controversies. Oxford University Press, Oxford.
^ This article on phage ecology was expanded from a stub during the writing of the first chapter of the edited monograph, *Bacteriophage Ecology* (forecasted publication date: 2007, Cambridge University Press), in order to be cited by that chapter especially as a repository of phage ecology review chapters and articles.
^ Summers, W. C. 1991. From culture as organisms to organisms as cell: historical origins of bacterial genetics. J. Hist. Biol. 24:171-190.
^ Many PDF- (or, alternatively, html-) based articles are online through PubMed or via the web sites of open access journals such as those published by BioMed Central. Alternatively, they may be posted on "private" web sites (perhaps in copyright violation) by authors or other individuals. Consequently, it is often possible to find an article by doing a Google search on article titles. You can sometimes increase useful hits by placing titles in quotes, adding author names (outside of quotes), or by limiting searches to PDF documents only.

Phage Monographs

Stephen T. Abedon[2], The Ohio State University
Bacteriophage Ecology Group News (*BEG News*) 25

The following is my second Wikipedia effort. Feel free to add to the Wikipedia version, found at:

http://en.wikipedia.org/wiki/Phage_monographs

(equivalent to Wikipedia version as of Saturday, October 21, 2006)

Bacteriophage (phage) are viruses of bacteria. The history of this discipline is captured, in part, in the books published on the topic. Presented is a list of 100-plus phage or phage-related monographs

Contents

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- Books published in the 2000s
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- Books published in the 1950s
- Books published in the 1940s
- Books published in the 1930s

Books published in the 1920s

History of list

Scientific disciplines often are not defined by their books but, rather, are reflected by them: A book is an author's or editor's sense of what is important in one subdiscipline, or an entire field, at one particular moment — within the constraints of whatever limitations have been placed on content, typically as by the publisher. Important limitations include such things as space, color plates, merit, etc. With the advent of the World Wide Web, many of these old limits no longer exist, though potentially at the cost of permanence. An author (or authors) today (as of September, 2006) can write anything they want, and reach a wide audience. But they will stay in "print" only so long as their web host stays in business and/or appropriate fees are paid. Wikipedia suggests a compromise, where, contrasting to one's own web page, content, in principle, may last "forever". Of course "forever" will be in a mutable form, but that also means that both error correction and updating are possible. Indeed, are encouraged!

Within this context, this article consists of a list of phage monographs (as loosely defined) dating back to 1921 (phage are viruses of bacteria). The list was created — because of the space limitations of traditional print — during the writing of the first chapter of the edited monograph, *Bacteriophage Ecology* (forcasted publication date: 2007, Cambridge University Press) and in order to be cited by that chapter. A forerunner of this list can be found in the January 1, 2005, issue (#23) of the *Bacteriophage Ecology Group News*, an online newsletter of the Bacteriophage Ecology Group. See phage ecology for more on that subdiscipline of phage biology and ecology.

Editing list

An approximation of ASM (American Society for Microbiology) conventions are used throughout. Titles (or English translations) have been presented in bold to allow for rapid scanning, and italics have been avoided both to improve readability and as consistent with ASM conventions. OCLC refers to a monograph's WorldCat accession number. ASIN is the Amazon Standard Identification Number (shown if ISBN is not known).

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[2] With the help of various Wikipedia editors.

Bullets indicate uncertainty about the appropriateness of an entry for this list. If you feel that a monograph should be removed from this list then please indicate why in brackets at the end of the entry (in italics), e.g., *[this entry should be removed from this list because...]*

Help with cyrillic lettering, transliterations, translations, missing information, uncited monographs, etc. is much appreciated. Please contact Dr. Stephen T. Abedon (through www.phage.org) with suggested changes or, of course, feel free to make changes (including updating) as appropriate.

List of phage monographs (descending date order)

Books published in the 2000s

Cairns, J., G. Stent, and J. D. Watson. 2007. **Phage and the Origins of Molecular Biology (40th anniversary edition).** Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY. OCLC ???, ISBN 0-879-69800-4

Holmes, F. L., and W. C. Summers. 2006. **Reconceiving the Gene: Seymour Benzer's Adventures in Phage Genetics.** Yale University Press, New Haven, CT. OCLC 62342731, ISBN 0-300-11078-2

Calendar, R., and S. T. Abedon. 2006. **The Bacteriophages.** 2nd edition. Oxford University Press, Oxford. OCLC 65192869, ISBN 0-195-14850-9

Häusler, T. 2006. **Viruses vs. Superbugs: A Solution to the Antibiotic Crisis.** Macmillan, OCLC 62804701, ISBN 1-403-98764-5

Birge, E. A. 2006. **Bacterial and Bacteriophage Genetics.** Springer-Verlag, New York. OCLC 17838673, ISBN 0-387-23919-7

Yartseva, A. 2006. **Modeling of λ Phage Genetic Switch.** Lulu Press. OCLC ???, ISBN 1-411-69545-3

Kutter, E., and A. Sulakvelidze. 2005. **Bacteriophages: Biology and Application.** CRC Press, Boca Raton, FL. OCLC 56880238, ISBN 0-849-31336-8

Sidhu, S. S. 2005. **Phage Display In Biotechnology and Drug Discovery.** CRC Press, OCLC 60311940, ISBN 0-824-75466-2

Waldor, M. K., D. Friedman, and S. Adhya. 2005. **Phages: Their Role in Bacterial Pathogenesis and Biotechnology.** ASM Press, Washington, DC. OCLC 57557385, ISBN 1-555-81307-0

Clackson, T., and H. B. Lowman. 2004. **Phage Display: A Practical Approach.** Oxford University Press, Oxford. OCLC 54904081, ISBN 0-19963-874-8

Ptashne, M. 2004. **Genetic Switch: Phage Lambda Revisited.** Cold Spring Harbor, New York, Cold Spring Harbor Laboratory Press. OCLC 54035585, ISBN 0-879-69716-4

Häusler, T. 2003. Gesund durch Viren — Ein Ausweg aus der Antibiotika-Krise. Piper, München, Germany. [German; **Healthy through Viruses - A Way Out of the Antibiotic-Resistance Crisis**] OCLC 53098607

O'Brien, P. M., and R. Aitken. 2002. **Antibody Phage Display: Methods and Protocols.** Humana Press, Totawa, NJ. OCLC 50175105, ISBN 0-896-03906-4

Burton, D. R., J. K. Scott, G. J. Silverman, and C. F. Barbas. 2001. **Phage Display: A Laboratory Manual.** Cold Spring Harbor Laboratory Press, Cold Spring Harbor,NY. OCLC 43903550, ISBN 0-879-69740-7

Birge, E. A. 2000. **Bacterial and Bacteriophage Genetics.** Springer-Verlag, New York. OCLC 41273243, ISBN 0-387-23919-7

Stahl, F. W. 2000. **We can sleep later: Alfred D. Hershey and the Origins of Molecular Biology.** Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY. OCLC 43185885, ISBN 0-879-69567-6

The following have not yet been sufficiently scrutinized to ascertain that they technically are books (e.g., are not theses), are generally available, and are sufficiently about phage to be included in the above list:

Catalano, C. E. 2005. **Viral Genome Packaging Machines: Genetics, Structure, and Mechanism.** Eurekah.Com Inc , ??? OCLC 57731385, ISBN 0-306-48227-4

Jacob, F., N. Peyrieras, and M. Morange. 2002. Travaux Scientifiques de François Jacob. Odile Jacob, Paris. [French; **Scientific work of François Jacob**] OCLC 49567654

Rasool, S. A. 2002. **Bacterial Viruses: Basic and Applied Concepts.** University Grants Coommission, Islamabad. OCLC 62340547

Jia, P. X. 2001. **Molecular Biology of Bacteriophage.** Science Press, Beijing. OCLC ???

Kutter, E. 2001. **Phage Therapy: Bacteriophage as Natural, Self-limiting Antibiotics.** AstraZeneca Research Foundation India , India. OCLC ???, ISBN 8-190-12383-1

Books published in the 1990s

Summers, W. C. 1999. **Felix d'Herelle and the Origins of Molecular Biology.** Yale University Press, New Haven, Connecticut. OCLC 47011823, ISBN 0-300-07127-2

Kay, B. K., J. Winter, and J. McCafferty. 1996. **Phage Display of Peptides and Proteins: A Laboratory Manual.** Academic Press, San Diego, CA. OCLC 34409484, ISBN 0-124-02380-0

Rothman-Denes, L., and R. Weisberg. 1995. **Recent developments in bacteriophage virology.** Academic Press, London. OCLC 34099713

Birge, E. A. 1994. **Bacterial and Bacteriophage Genetics.** Springer-Verlag, New York. OCLC 29791890, ISBN 3-540-94270-X

Jacob, F. 1995. **The Statue Within: An Autobiography.** Cold Spring Harbor Laboraotory Press, Cold Spring Harbor, New York. OCLC 17353378, ISBN 0-879-69476-9

Karam, J. D. 1994. **Molecular Biology of Bacteriophage T4.** ASM Press, Washington, DC. OCLC 30028892, ISBN 1-555-81064-0

Twort, A. 1993. **In Focus, Out of Step: A Biography of Frederick William Twort F.R.S. 1877-1950.** A. Sutton, Dover, NH. OCLC 28025779, ISBN 0-750-90327-9

Klaus, S., W. Krüger, and J. Meyer. 1992. Bakterienviren. Gustav Fischer, Stuttgart. [German; **Bacterioviruses**] OCLC 26765458

Ptashne, M. 1992. **A Genetic Switch: Phage λ and Higher Organisms.** Blackwell, Cambridge, MA. OCLC 25713934, ISBN 0-865-42209-5

Cairns, J., G. Stent, and J. D. Watson. 1992. **Phage and the Origins of Molecular Biology (expanded edition).** Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY. OCLC 25872929

The following have not yet been sufficiently scrutinized to ascertain that they technically are books (e.g., are not theses), are generally available, and are sufficiently about phage to be included in the above list:

Anonymous. 1991. **Practical Phage Control.** International Dairy Federation. OCLC ???

Ho, N. B., Z. T. Si, and M. X. Yu. 1991. **Bacteriophages from China, an electron microscopical atlas.** Science Press, Beijing. OCLC ???

Books published in the 1980s

Birge, E. A. 1988. **Bacterial and Bacteriophage Genetics: An Introduction.** Springer-Verlag, New York. OCLC 17838673, ISBN 0-387-96696-X

Hobom, G., and R. Rott. 1988. **The Molecular Biology of Bacterial Virus Systems.** Springer-Verlag, Berlin. OCLC 18590320, ISBN 0-387-18513-5

Jacob, F. 1988. **The Statue Within: An Autobiography.** Basic Books, New York. OCLC 17353378, ISBN 0-465-08222-X

Fischer, E. P., and C. Lipson. 1988. **Thinking About Science: Max Delbrück and the Origins of Molecular Biology.** W.W. Norton & Co., New York. OCLC 16277429, ISBN 0-393-02508-X

Calendar, R. 1988. **The Bacteriophages. Volume I** Plenum Press, New York. OCLC 18686137

Calendar, R. 1988. **The Bacteriophages. Volume II** Plenum Press, New York. OCLC 17675040

Goyal, S. M., C. P. Gerba, and G. Bitton. 1987. **Phage Ecology.** CRC Press, Boca Raton, Florida. OCLC 15654933, ISBN 0-471-82419-4

Symonds, N., A. Toussaint, P. van de Putte, and W. V. Howes. 1987. **Phage Mu.** Cold Spring Harbor Press, Cold Spring Harbor, N.Y. OCLC 16089280, ISBN 0-879-69306-1

Ackermann, H.-W., and M. S. DuBow. 1987. **Viruses of Prokaryotes, Volume 1, General Properties of Bacteriophages.** CRC Press, Boca Raton, Florida. OCLC 15518646, ISBN 0-849-36056-0

Ackermann, H.-W., and M. S. DuBow. 1987. **Viruses of Prokaryotes, Volume 2, Natural Groups of Bacteriophages.** CRC Press, Boca Raton, Florida. OCLC ???, ISBN 0-849-36056-0

Ptashne, M. 1986. **A Genetic Switch: Gene Control and Phage λ.** Blackwell, Cambridge, MA. OCLC 14719427, ISBN 0-865-42315-6

Mendzhul, M. I. 1985. Tsianofagi: Virusy Tsianobakterii. Nauk. dumka, Kiev. [Russian; **Cyanophages**] OCLC 16131273

Luria, S. E. 1984. **A Slot Machine, a Broken Test Tube: An Autobiography.** Harper & Row, Publishers, New York. OCLC 9758798, ISBN 0-060-91213-8 (1985 paperback ISBN 0-465-07831-1)

Lin, E. C. C., R. Goldstein, and M. Syvanen. 1984. **Bacteria, Plasmids, and Phages: An Introduction to Molecular Biology.** Harvard University Press, Cambridge, MA . OCLC 10182998, ISBN 0-674-58166-0

Mathews, C. K., E. M. Kutter, G. Mosig, and P. B. Berget. 1983. **Bacteriophage T4.** American Society for Microbiology, Washington, DC. OCLC 9622410, ISBN 0-914-82656-5

Hendrix, R. W., J. W. Roberts, F. W. Stahl, and R. A. Weisberg. 1983. **Lambda II.** Cold Spring Harbor Laboratory, Cold Spring Harbor, New York. OCLC 9556019, ISBN 0-879-69150-6

Birge, E. A. 1981(or 1980?). **Bacterial and Bacteriophage Genetics: An Introduction.** Springer-Verlag, New York. OCLC 7248504, ASIN B000ICBYWI

DuBow, M. 1981. **Bacteriophage Assembly:** Proceedings of the Seventh Biennial Conference on Bacteriophage Assembly, Asilomar, California, September 14-17, 1980. A.R. Liss, New York. OCLC 7555738, ISBN 0-845-10064-5

Randall, L. L., and L. Philipson. 1980. **Virus Receptors part 1 Bacterial Viruses.** Chapman and Hall, London and New York. OCLC 8409813

The following have not yet been sufficiently scrutinized to ascertain that they technically are books (e.g., are not theses), are generally available, and are sufficiently about phage to be included in the above list:

Smith-Keary, P. F. 1988. **Genetic Elements in *Escherichia coli*.** MacMillan Education Ltd., London. OCLC ???, ISBN 0-333-44268-7

Sorber, C. A., and S. W. Funderburg. 1983. **Bacteriophages as Indicators of Human Enteric Viruses in Activated Sludge Wastewater Treatment.** Univ of Texas at Austin Center. OCLC ???, ISBN 9-993-06064-X

??? 1983. **Cloning with Bacteriophage.** ???, ??? OCLC ???

??? 1982. Bakteriofagi: Sbornik Nauchnykh Trudov. ???, ??? [language; **title in English**] OCLC 18836533

Desjardins, P. R., and G. B. Olson. 1983. **Viral Control of Nuisance Cyanobacteria (Blue-Green Algae). II. Cyanophage Strains, Stability on Phages and Hosts, and Effects of Environmental Factors on Phage-Host Interactions.** California Water Resource Center, University of California, Davis, CA. OCLC ???

Books published in the 1970s

Stahl, F. W. 1979. **Genetic Recombination: Thinking About it in Phage and Fungi.** W.H. Freeman, San Francisco. OCLC 4956846, ISBN 0-716-71037-4

Pulverer, G., P. B. Heczko, and G. Peters. 1979. **Phage-Typing of Coagulase-Negative Staphylococci**: Proceedings of the 1st International Conference, Cologne, September 16-18, 1977. G. Fischer, Stuttgart. OCLC 5105577

Denhardt, D. T., D. Dressler, and D. S. Ray. 1978. **The Single-Stranded DNA Phages.** Cold Spring Harbor Laboratory, Cold Spring Harbor, NY. OCLC 4491528, ISBN 0-879-69122-0

Fraenkel-Conrat, H., and R. R. Wagner. 1976. **Comprehensive Virology: Reproduction of Bacterial DNA Viruses.** Plenum Press, New York. OCLC 2331482, 0-306-35147-1

Primrose, S. B. 1976. **Bacterial Transduction.** Meadowfield Press Ltd., Durham, England. OCLC 3857517, ISBN 0-904-09523-1

Winkler, U., W. Rüger, and W. Wackernagel. 1976. **Bacterial, Phage and Molecular Genetics. An Experimental Course.** Springer, Berlin. OCLC 2121428, ISBN 0-387-07602-6

Fraenkel-Conrat, H., and R. R. Wagner. 1976. **Comprehensive Virology: Regulation and Genetics of Bacterial DNA Viruses.** Plenum Press, New York. OCLC 35284451, ISBN 0-306-35148-X

Douglas, J. 1975. **Bacteriophages.** p.77-133. Chapman and Hall, London. OCLC 1176725

Zinder, N. D. 1975. **RNA Phages.** Cold Spring Harbor Laboratory, Cold Spring Harbor, NY. OCLC 1582488, ISBN 0-879-69109-3

King, R. C. 1974. **Handbook of Genetics: Bacteria, Bacteriophages, and Fungi.** Plenum Press, New York. OCLC ???, ISBN 0-306-37611-3

Krzywy, T., and T. Slopek. 1974. Morfologia i ultrastruktura bakteriofagów Shigella i Klebsiella. Polish Medical Publishers, Warsaw. [Polish; **Morphology and Ultrastructure of Shigella and Klebsiella bacteriophages**] OCLC 6943982

Champe, S. P. 1974. **Phage.** Dowden, Hutchinson & Ross, Stroudsburg, PA. OCLC 980240

Poglazov, B. F. 1973. **Morphogenesis of T-Even Bacteriophages.** Karger, New York. OCLC ???, ISBN 3-805-51645-2

Dalton, A. J., and F. Haguenau. 1973. **Ultrastructure of Animal Viruses and Bacteriophages. An Atlas.** Academic Press, New York. OCLC 762216, ASIN B0006C4EEA

Mathews, C. K. 1971. **Bacteriophage Biochemistry.** Van Nostrand Reinhold Co., New York. OCLC 136326, ISBN 0-841-20288-5

Hershey, A. D. 1971. **The Bacteriophage Lambda.** Cold Spring Harbor Laboratory, OCLC 220264

Snustad, D. P., and D. S. Dean. 1971. **Genetics Experiments with Bacterial Viruses.** W. H. Freeman and Co., San Fransisco. OCLC 333991, ISBN 0-716-70161-8

Tomizawa, J.-I. 1971. **Virulent Phage (Selected Papers in Biochemistry).** University of Tokyo Press, Tokyo. OCLC 208390, ISBN 0-839-10612-2

Hayes, W. 1970. **The Genetics of Bacteria and their Viruses: Studies in Basic Genetics and Molecular Biology.** Wiley, New York. OCLC 4655740, ASIN B000H5C8WG

Tikhonenko, A. S. 1970. **Ultrastructure of Bacterial Viruses.** Plenum Press, New York. [Russian; Bacterial Virus Ultrastructure] OCLC 14492588, ISBN 0-306-30421-X

The following have not yet been sufficiently scrutinized to assertain that they technically are books (e.g., are not theses), are generally available, and are sufficiently about phage to be included in the above list:

??? 1979. Matematicheskie Modeli Molekuliarno-Geneticheskikh Sistem Upravleniia. ???, ??? [Russian; **Mathematical Models of Molecular Genetic Regulatory Systems**] OCLC 7733759
Desjardins, P. R., M. B. Barkley, S. A. Swiecki, and S. N. West. 1978. **Viral Control of blue-green algae.** California Water Resource Center, University of California, OCLC ???
??? 1978. Bakteriofagi i Ikh Ispol'zovanie v Veterinarnoi Praktike. ???, ??? [Russian; **Bacteriophages and Their Utilization in Veterinary Practice**] OCLC 4111249
??? 1977. **Gene Expression V. 3 Plasmids and Phages.** ???, ??? OCLC 13187199
??? 1974. Bactéries. **Bactériophages.** ???, ??? [French; Bacteria. Bacteriophages] OCLC ???
??? 1974. Lysotypie und Andere Spezielle Epidemiologische Laboratoriumsmethoden. ???, ??? [German & English; **Lysotyping and Other Special Epidemiological Laboratory Methods**] OCLC ???
??? 1972. Bakterien-, Phagen- und Molekulargenetik. ???, ??? [German; **Bacteria-, Phage- and Molecular Genetics**] OCLC 692617
??? 1972. Saikin Faji Iden Jikkenho. ???, ??? [Japanese; **Experimental Methods in Bacteriophage Genetics**] OCLC 14420642
Tomizawa, J. 1971. **Bacterial Genetics and Temperate Phage (Selected Papers in Biochemistry).** University Park Press, Baltimore, MD. OCLC 200390, ISBN 0-839-10611-4

Books published in the 1960s

Hayes, W. 1968. **The Genetics of Bacteria and their Viruses.** Wiley, New York. OCLC 5628
Tikhonenko, A. S. 1968. Ultrastruktura Virusov Bakterii. ???, ??? [Russian; **Ultrastructure of Bacterial Viruses**] OCLC 14492588
Raettig, H. 1967. **Bakteriophagie 1957-1965 (Bacteriophagy 1957-1965).** G. Fischer, Stuttgart. [German and English] OCLC 14503598
Cairns, J., G. Stent, and J. D. Watson. 1966. **Phage and the Origins of Molecular Biology.** Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY. OCLC 712215
Stent, G. S. 1965. Molekuliarnaia Biologiia Virusov Bakterii. Izd.-vo "MIR",; Russia (Federation); Moscow, Moskva. [Russian; **Molecular Biology of Bacterial Viruses**] OCLC 55892813
Gani, J. 1965. **Stochastic Models For Bacteriophage.** Methuen & Co. Ltd., London. OCLC 279694
Hayes, W. 1964. **The Genetics of Bacteria and their Viruses.** Wiley, New York. OCLC 559954
Stent, G. S. 1963. **Molecular Biology of Bacterial Viruses.** WH Freeman and Co., San Francisco, CA. OCLC 268815
Geissler, E. 1962. Bakteriophagen, Objekte der Modernen Genetik. Akademie-Verlag, Berlin. [German; **Bacteriophages, Objects of the Modern Genetics**] OCLC 14607452
Pekhov, A. P. 1962. Elektronnomikroskopicheskoe issledovanie bakterii i fagov. ???, ??? [Russian; **Electron Microscopic Study of Bacteria and Phage**] OCLC 14607218
Stent, G. S. 1960. **Papers on Bacterial Viruses.** Little, Brown and Co., Boston. OCLC 485853

The following have not yet been sufficiently scrutinized to assertain that they technically are books (e.g., are not theses), are generally available, and are sufficiently about phage to be included in the above list:

??? 1961. Bakteriofagi. ???, ??? [language; **Bacteriophage**] OCLC 18358144

Books published in the 1950s

Adams, M. H. 1959. **Bacteriophages.** Interscience, New York. OCLC 326505
Ho, N. B., Z. T. Si, and M. X. Yu. 1959. **Bacteriophages from China. An Electron Microscopical Atlas.** Science Press, Beijing. OCLC ???
Hercik, F. 1959. Biophysik der Bakteriophagen. VEB Deutscher Verlag der Wissenschaften, Berlin. [German; **Biophysics of Bacteriophages**] OCLC 15258981
Burnet, F. M., and W. M. Stanley. 1959. **The Viruses: Biochemical, Biological and Biophysical Properties: Plant and Bacterial Viruses.** Academic Press, New York. OCLC 326764
Raettig, H. 1958. Bakteriophagie, 1917 bis 1956; Zugleich en Vorschlag zur Dokumentation Wissenschaftlicher Literatur. G. Fischer, Stuttgart. [German; **Bacteriophagy 1917 to 1956; At the Same Time a suggestion on the Documentation of Scientific Literature**] OCLC 4309311
Terada, M. 1956. **Studies on Bacterial Viruses.** Naya Publishing Co., Tokyo. OCLC 1064505
Jacob, F. 1954. Les bactéries lysogènes et la notion de provirus. Masson, Paris. [French; The Lysogenic Bacteria and the Concept of the Provirus] OCLC 5780525

International Union of Biological Sciences. 1953. Le Bactériophage: Premier Colloque International. Institut Pasteur, Paris. [French; **The Bacteriophage: First International Conference**] OCLC 11662838

Evans, E. A. 1952. **Biochemical Studies of Bacterial Viruses.** University of Chicago Press, Chicago. OCLC 3195879

Hedén, C.-G. 1951. **Studies of the infection of *E. coli* B with the bacteriophage T2.** Acta. Path. Microbiol. Scand. supplement 8:1-126. OCLC 14670314

Lederberg, J. 1951. **Papers in Microbial Genetics: Bacteria and Bacterial Viruses.** University of Wisconsin Press, Madison. OCLC 2472829

The following have not yet been sufficiently scrutinized to assertain that they technically are books (e.g., are not theses), are generally available, and are sufficiently about phage to be included in the above list:

??? 1958. Bakteriofagi i ikh primenenie v meditsinskoi praktike. ???, ??? [language; **title in English**] OCLC 14614699

??? 1950. Biologicheskie Antiseptiki: Bakteriofagi, Antitela, Antibiotik. ???, ??? [language; **title in English**] OCLC 14672517

Adams, M. H., J. H. jr. Comroe, and E. H. Venning. 1950. **Methods of Study of Bacterial Viruses.** Year Book Publishers, Chicago. OCLC 67599839

Books published in the 1940s

Hammarström, E. 1949. **Phage-Typing of *Shigella sonnei*.** Stockholm. OCLC 5140885

Lilleengen, K. 1948. **Typing of *Salmonella typhimurium* by means of bacteriophage.** The Bacteriological Hygenical Department of the Royal Veterinary College, Stockholm. OCLC 14665054

Steinmann, J. 1946. Le Bactériophage: Sa Nature et son Emploi Thérapeutique. K, Bâle. [French; The **Bacteriophage: Its Nature and its Therapeutic Employment**] OCLC 14735726

Flu, P. C. 1946. **The Bacteriophage: A Historical and Critical Survey of 25 Years Research.** Universitaire Pers Leiden, Leiden. OCLC 14744384

The following have not yet been sufficiently scrutinized to assertain that they technically are books (e.g., are not theses), are generally available, and are sufficiently about phage to be included in the above list:

??? 1948. Ultravirusi, rikecie i bakteriofagi. ???, ??? [language; **title in English**] OCLC 14661068

??? 1945. Anaerobnye Bakteriofagi. ???, ??? [language; **title in English**] OCLC 14736765

Raiga, A. 1941. Traitement des Plaies de Guerre par le Bactériophage de d'Hérelle . Legrand & Bertrand, Paris. [French; **Treatment of the wounds of war by the bacteriophage of Hérelle**] OCLC 14725592

Books published in the 1930s

Northrop, J. H. 1939. **Crystalline Enzymes. The Chemistry of Pepsin, Trypsin, and Bacteriophage.** Columbia University Press, New York. OCLC 2387455

d'Hérelle, F. 1938. Le Phénomène de la Guérison dans les Maladies Infectieuses. Masson et cie, Paris. [French; The phenomenon of the Cure in the Infectious Diseases] OCLC 5784382

d'Hérelle, F. 1933. Le Bactériophage et ses Applications Thérapeutiques. Doin, Paris. [French; **The Bacteriophage and its Therapeutic Applications**] OCLC 14749145

Gardner, A. D. 1931. **Microbes and Ultramicrobes: An Account of Bacteria, Viruses and the Bacteriophage.** Methuen & Co. Ltd., London. OCLC 3180401

d'Hérelle, F., and G. H. Smith. 1930. **The Bacteriophage and its Clinical Application.** p.165-243. Charles C. Thomas, Publisher, Springfield, Illinois. OCLC 347451

Books published in the 1920s

d'Hérelle, F. 1929. Études sur le Choléra. Impr. A. Serafini, Alexandrie. [French; **Studies on Asiatic Cholera**] OCLC 15864352

Schuurman, C. J. 1927. Der Bakteriophage, eine Ultramikrobe; das D'Herellesche Phänomen. Rohrmoser, Bonn. [German; **The Bacteriophage, an Ultramicrobe: the D'Hérelle phenomenon**] OCLC 14743783

d'Hérelle, F. 1926. Le Bactériophage et son Comportement. Masson et Cie, Paris. [French; **The Bacteriophage and its Behavior**] OCLC 11981307

d'Hérelle, F., and G. H. Smith. 1926. **The Bacteriophage and Its Behavior.** The Williams &Wilkins Co., Baltimore. OCLC 2394374

Hauduroy, P. 1925. Le Bactériophage de d'Hérelle. Librairie Le François, Paris. [French; **The Bacteriophage of d'Hérelle**] OCLC 17294190

d'Hérelle, F. 1924. Drie Voordrachten over het Verschijnsel der Bacteriophagie. J.B. Wolters, Groningen. [Dutch; **Three presentations concerning the phenomenon of the bacteriophage**] OCLC 17864544

d'Hérelle, F., and G. H. Smith. 1924. **Immunity in Natural Infectious Disease.** Williams & Wilkins Co., Baltimore. OCLC 586303

d'Hérelle, F. 1922. Der Bakteriophage und seine Bedeutung für die Immunität; nach einem erweiterten und verbesserten. F. Vieweg & Sohn, Braunschweig. [German; **The Bacteriophage and its Meaning for Immunity: toward an extended and improved text of the author's translation**] OCLC 36920828

d'Hérelle, F. 1922. **The Bacteriophage: Its Role in Immunity.** Williams and Wilkins Co./Waverly Press, Baltimore. OCLC 14789160, ASIN B000H6G02O, B000H6EK2G

d'Hérelle, F. 1921. Le Bactériophage: Son Rôle dans l'Immunité. Masson et cie, Paris. [French; **The Bacteriophage: Its Role in Immunity**] OCLC 14794182

The following have not yet been sufficiently scrutinized to assertain that they technically are books (e.g., are not theses), are generally available, and are sufficiently about phage to be included in the above list:

d'Hérelle, F., R. H. Malone, and M. N. Lahiri. 1930. **Studies on Asiatic Cholera.** Thacker, Spink & Co., Calcutta. OCLC 25936856

d'Hérelle, F. 1923. Les Défenses de l'Organisme. Flammarion, Paris. [French; **The Defenses of the Organism**] OCLC 11127665

Phage Experimental Evolution

Siobain Duffy, Yale University and
Stephen T. Abedon[3], The Ohio State University
Bacteriophage Ecology Group News (*BEG News*) 25

This was my first collaborative Wikipedia project. Feel free to add to the Wikipedia version, found at:

http://en.wikipedia.org/wiki/Phage_experimental_evolution

(equivalent to Wikipedia version as of Saturday, October 21, 2006)

Bacteriophage (phage) are the viruses of bacteria. Provided is an annotated bibliography of modern phage experimental evolution studies. Phage experimental evolution is part of the broader field of virus evolution.

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2.5 Coevolution
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Instructions and history

Editing instructions (of references) as well as tips for finding references online can be found here.
Reviews, purely theoretical studies, etc. are presented as footnotes within introductions to subtopics.

Tentatively added references should be presented using a bullet rather than a number.

This table is an expansion of a table presented by Breitbart *et al.* (2005)[1] and was created during the writing of the chapters 1 and 6 of the edited monograph, *Bacteriophage Ecology* (forecasted publication date: 2007, Cambridge University Press), in order to be cited by chapter 1.

We invite further editing, additions, categories, discussion, introduction, updating, etc. For a primer on the early phage literature, see phage monographs.

Experimental studies, by category

Laboratory phylogenetics

Phylogenetics is the study of the evolutionary relatedness of organisms. Laboratory phylogenetics is the study of the evolutionary relatedness of laboratory-evolved organisms.

[3] With the help of various Wikipedia editors.

Hahn, M. W., M. D. Rausher, and C. W. Cunningham, 2002. **Distinguishing between selection and population expansion in an experimental lineage of bacteriophage T7.** Genetics 161:11-20. full text
Oakley, T. H., and C. W. Cunningham, 2000. **Independent contrasts succeed where ancestor reconstruction fails in a known bacteriophage phylogeny.** Evolution 54:397-405. abstract
Cunningham, C.W., K. Jeng, J. Husti, M. Badgett, I.J. Molineux, D.M. Hillis and J.J. Bull, 1997. **Parallel molecular evolution of deletions and nonsense mutations in bacteriophage T7.** Mol. Biol. Evol. 14:113-116. full text
Bull, J. J., C. W. Cunningham, I. J. Molineux, M. R. Badgett, and D. M. Hills, 1993. **Experimental molecular evolution of bacteriophage T7.** Evolution 47:993-1007. abstract
Hillis, D.M., J.J. Bull, M.E. White, M.R. Badgett and I.J. Molineux, 1992. **Experimental phylogenetics: generation of a known phylogeny.** Science. 255:589-592. abstract & pay article
Studier, F. W., 1980. **The last of the T phages,** p. 72-78. In N. H. Horowitz and E. Hutchings, Jr. (eds.), Genes, Cells, and Behavior: A View of Biology Fifty Years Later. W.H. Freeman & Co., San Fransisco. ISBN 0-716-71217-2
Studier, F. W., 1979. **Relationships among different strains of T7 and among T7-related bacteriophages.** Virology 95:70-84.

Epistasis

Epistasis is the dependence of the effect of one gene or mutation on the presence of another gene or mutation.

Burch, C.L., and L. Chao. 2004. **Epistasis and its relationships to canalization in the RNA virus Φ6.** Genetics. 167:559-567. full text
You, L., and J. Yin. 2002. **Dependence of epistasis on environment and mutation severity as revealed by in silico mutagenesis of phage T7.** Genetics. 160:1273-1281. full text
Schuppli, D., J. Georgijevic, and H. Weber. 2000. **Synergism of mutations in bacteriophage Qβ RNA affecting host factor dependence of Qβ replicase.** J. Mol. Biol. 295:149-154.

The phage literature provides many examples of epistasis which are not studied under the context of experimental evolution nor necessarily described as examples of epistasis.

Experimental adaptation

Experimental adaptation involves selection of organisms either for specific traits or under specific conditions...

Bull, J. J., J. Millstein, J. Orcutt and H.A. Wichman. 2006. **Evolutionary feedback mediated through population density, illustrated with viruses in chemostats.** Am. Nat. 167:E39-E51. abstract
Bull, J. J., M. R. Badgett, R. Springman, and I. J. Molineux. 2004. **Genome properties and the limits of adaptation in bacteriophages.** Evolution 58:692-701. abstract
Bull, J. J., M. R. Badgett, D. Rokyta, and I. J. Molineux. 2003. **Experimental evolution yields hundreds of mutations in a functional viral genome.** J. Mol. Evol. 57:241-248. abstract & pay article
Bull, J. J., M.R. Badgett, H.A. Wichman, J.P. Hulsenbeck, D.M. Hillis, A. Gulati, C. Ho and I.J. Molineux. 1997. **Exceptional convergent evolution in a virus.** Genetics. 147:1497-1507. full text

The reader should be aware that numerous phage experimental adaptations were performed in the early decades of phage study.

…to usual hosts

Wichman, H. A., J. Wichman, and J. J. Bull. 2005. **Adaptive molecular evolution for 13,000 phage generations: A possible arms race.** Genetics 170:19-31. full text
Rokyta, D., M. R. Badgett, I. J. Molineux, and J. J. Bull. 2002. **Experimental genomic evolution: extensive compensation for loss of DNA ligase activity in a virus.** Mol. Biol. Evol. 19:230-238. full text
Burch, C. L., and L. Chao. 2000. **Evolvability of an RNA virus is determined by its mutational neighbourhood.** Nature 406:625-628. abstract & pay article
Wichman, H. A., L. A. Scott, C. D. Yarber, and J. J. Bull. 2000. **Experimental evolution recapitulates natural evolution.** Philos. Trans. R. Lond. ,B 355:1677-1684. abstract
Wichman, H. A., M. R. Badgett, L. A. Scott, C. M. Boulianne, and J. J. Bull. 1999. **Different trajectories of parallel evolution during viral adaptation.** Science 285:422-424. abstract & pay article

…to new or modified hosts

Duffy, S., P. E. Turner, and C. L. Burch. 2006. **Pleiotropic Costs of Niche Expansion in the RNA Bacteriophage Φ6.** Genetics 172:751-757. full text

Pepin, K. M., M. A. Samuel, and H. A. Wichman. 2006. **Variable Pleiotropic Effects From Mutations at the Same Locus Hamper Prediction of Fitness From a Fitness Component.** Genetics 172:2047-2056. full text

Crill, W. D., H. A. Wichman, and J. J. Bull. 2000. **Evolutionary reversals during viral adaptation to alternating hosts.** Genetics 154:27-37. full text

Bull, J. J., A. Jacoboson, M. R. Badgett, and I. J. Molineux. 1998. **Viral escape from antisense RNA.** Mol. Microbiol. 28:835-846. full text

Hibma, A. M., S. A. Jassim, and M. W. Griffiths. 1997. **Infection and removal of L-forms of *Listeria monocytogenes* with bred bacteriophage.** Int. J. Food Microbiol. 34:197-207. abstract & pay article

Jassim, S. A. A., S. P. Denyer, and G. S. A. B. Stewart. 1995. **Virus breeding.** International Patent Application. WO 9523848. full text (under tab labeled "documents")

Schuppli, D., G. Miranda, H. C. T. Tsui, M. E. Winkler, J. M. Sogo, and H. Weber. 1997. **Altered 3'-terminal RNA structure in phage Qβ adapted to host factor-less *Escherichia coli.*** Proc. Natl. Acad. Sci. USA 94:10239-10242. full text

Hashemolhosseini, S., Z. Holmes, B. Mutschler, and U. Henning. 1994. **Alterations of receptor specificities of coliphages of the T2 family.** J. Mol. Biol. 240:105-110. abstract & pay article

The older phage literature, e.g., pre-1950s, contains numerous examples of phage adaptations to different hosts. We invite interested individuals to track down and include these references in the above list.

…to modified conditions

Bacher, J. M., J. J. Bull, and A. D. Ellington. 2003. **Evolution of phage with chemically ambiguous proteomes.** BMC Evol. Biol. 3:24 full text

Bull, J. J., A. Jacoboson, M. R. Badgett, and I. J. Molineux. 1998. **Viral escape from antisense RNA.** Mol. Microbiol. 28:835-846. full text

Merril, C. R., B. Biswas, R. Carlton, N. C. Jensen, G. J. Creed, S. Zullo, and S. Adhya. 1996. Long-circulating bacteriophage as antibacterial agents. Proc. Natl. Acad. Sci. USA 93:3188-3192. full text

Gupta, K., Y. Lee and J. Yin. 1995. **Extremo-phage: in vitro selection of tolerance to a hostile environment.** J. Mol. Evol. 41:113-114. abstract & pay article

The older phage literature, e.g., pre-1950s, also contains examples of phage adaptations to different culture conditions, such as phage T2 adaptation to low salt conditions. We invite interested individuals to track down and include these references in the above list.

…to high temperatures

Knies, J.L., R. Izem, K.L. Supler. J.G. Kingsolver, and C.L. Burch. 2006. **The genetic basis of thermal reaction norm evolution in lab and natural phage population.** PLoS Biology. 4:e201. full text

Poon, A., and L. Chao. 2005. **The rate of compensatory mutation in the DNA bacteriophage ΦX174.** Genetics. 170:989-999. full text

Poon, A., and L. Chao. 2004. **Drift increases the advantage of sex in RNA bacteriophage Φ6.** Genetics 166:19-24. full text

Holder, K. K., and J. J. Bull. 2001. **Profiles of adaptation in two similar viruses.** Genetics 159:1393-1404. full text

Bull, J. J., M. R. Badgett, and H. A. Wichman. 2000. **Big-benefit mutations in a bacteriophage inhibited with heat.** Mol. Biol. Evol. 17:942-950. full text

…as compensation for deleterious mutations

Poon, A., and L. Chao. 2005. **The rate of compensatory mutation in the DNA bacteriophage ΦX174.** Genetics. 170:989-999. full text

Heineman, R. H., I. J. Molineux, and J. J. Bull. 2005. **Evolutionary robustness of an optimal phenotype: re-evolution of lysis in a bacteriophage deleted for its lysin gene.** J. Mol. Evol. 61:181-191. abstract & pay article

Hayashi, Y., H. Sakata, Y. Makino, I. Urabe, and T. Yomo. 2003. **Can an arbitrary sequence evolve towards acquiring a biological function?** J. Mol. Evol. 56:162-168. abstract & pay article

Rokyta, D., M. R. Badgett, I. J. Molineux, and J. J. Bull. 2002. **Experimental genomic evolution: extensive compensation for loss of DNA ligase activity in a virus.** Mol. Biol. Evol. 19:230-238. full text

Burch, C. L., and L. Chao. 1999. **Evolution by small steps and rugged landscapes in the RNA virus Φ6.** Genetics 151:921-927. full text

Klovins, J., N. A. Tsareva, M. H. de Smit, V. Berzins, and D. Van. 1997. **Rapid evolution of translational control mechanisms in RNA genomes.** J. Mol. Biol. 265:372-384. abstract & pay article

Olsthoorn, R. C., and J. van Duin. 1996. **Evolutionary reconstruction of a hairpin deleted from the genome of an RNA virus.** Proc. Natl. Acad. Sci. USA 93:12256-12261. full text

Nelson, M. A., M. Ericson, L. Gold, and J. F. Pulitzer. 1982. **The isolation and characterization of TabR bacteria: Hosts that restrict bacteriophage T4 rII mutants** Mol. Gen. Genet. 188:60-68. abstract & pay article

Nelson, M.A. and L. Gold. 1982. **The isolation and characterization of bacterial strains (Tab32) that restrict bacteriophage T4 gene 32 mutants** Mol. Gen. Genet. 188:69-76.

There are many examples in the early phage literature of phage adapting and compensating for deleterious mutations, and we especially invite additions of such papers to this section.

…as toward change in phage virulence

Virulence is the negative impact that a pathogen (or parasite) has on the Darwinian fitness of a harboring organism (host). For phage, virulence results either in reduction of bacterial division rates or, more typically, in the death (via lysis) of individual bacteria. A number of theory papers exist on this subject, especially as it applies to the evolution of phage latent period: Abedon, 1989[2], Wang *et al.*, 1996[3], Abedon *et al.*, 2001[4], Bull *et al.*, 2004[5], and Abedon, 2006[6].

Kerr, B., C. Neuhauser, B. J. M. Bohannan, and A. M. Dean. 2006. **Local migration promotes competitive restraint in a host–pathogen 'tragedy of the commons'.** Nature 442:75-78. abstract & pay article

Wang, I.-N. 2006. **Lysis timing and bacteriophage fitness.** Genetics 172:17-26. full text

Abedon, S. T., P. Hyman, and C. Thomas. 2003. **Experimental examination of bacteriophage latent-period evolution as a response to bacterial availability.** Appl. Environ. Microbiol. 69:7499-7506. full text

Messenger, S. L., I. J. Molineux, and J. J. Bull. 1999. **Virulence evolution in a virus obeys a trade-off.** Proc. R. Soc. Lond. B Biol. Sci. 266:397-404. abstract

Bull, J. J., and I. J. Molineux. 1992. **Molecular genetics of adaptation in an experimental model of cooperation.** Evolution 46:882-895.

Bull, J. J., I. J. Molineux, and W. R. Rice. 1991. **Selection for benevolence in a host-parasite system.** Evolution 45:875-882.

The older phage literature contains numerous references to phage virulence, and phage virulence evolution. However, the reader should be warned that virulence is often used as a synonym for "not temperature", a usage which is neither employed here nor to be encouraged generally.

Impact of sex/coinfection

More than one phage can coinfect the same bacterial cell. When this happens, the phage can exchange genes, which is equivalent to "sex." Note that a number of the immediately following studies employ sex to overcome Muller's ratchet while papers that demonstrate Muller's ratchet (i.e., without employing sex to overcome the result) are instead presented under that heading.

Froissart, R., C. O. Wilke, R. Montville, S. K. Remold, L. Chao, and P. E. Turner. 2004. **Co-infection weakens selection against epistatic mutations in RNA viruses.** Genetics 168:9-19. full text

Montville, R., R. Froissart, S. K. Remold, O. Tenaillon, and P. E. Turner. 2005. **Evolution of mutational robustness in an RNA virus.** PLoS Biology 3:e381 full text

Sachs, J.L. and J. J. Bull. 2005. **Experimental evolution of conflict mediation between genomes.** Proc. Natl. Acad. Sci. 102:390-395. full text

Poon, A., and L. Chao. 2004. **Drift increases the advantage of sex in RNA bacteriophage Φ6.** Genetics 166:19-24. full text

Turner, P. E., and L. Chao. 1998. **Sex and the evolution of intrahost competition in RNA virus Φ6.** Genetics 150:523-532. full text

Chao, L., T. T. Tran, and T. T. Tran. 1997. **The advantage of sex in the RNA virus Φ6.** Genetics 147:953-959. full text

Malmberg, R. L. 1977. **The evolution of epistasis and the advantage of recombination in populations of bacteriophage T4.** Genetics 86:607-621. full text

Muller's ratchet

Muller's ratchet is the gradual, but irreversible accumulation of deleterious mutations in asexual organisms. Asexual organisms do not undergo gene exchange and therefore can't recreate mutation-free genomes. Chao, 1997[7], provides a phage-emphasizing review of the subject.

1. de la Peña, M., S. F. Elena, and A. Moya. 2000. **Effect of deleterious mutation-accumulation on the fitness of RNA bacteriophage MS2.** Evolution 54:686-691. abstract
2. Chao, L. 1990. **Fitness of RNA virus decreased by Muller's ratchet.** Nature 348:454-455. abstract

Prisoner's Dilemma

Prisoner's dilemma is a part of game theory which involves two individuals choosing to cooperate or defect, reaping differential rewards. During phage coinfection, it pertains to viruses which produce more protein products than they use (cooperators) and viruses which use more protein products than they produce (defectors). For theoretical treatment, see Brown, 2001[8].

1. Turner, P. E., and L. Chao. 2003. **Escape from Prisoner's Dilemma in RNA phage Φphi6.** Am. Nat. 161:497-505. abstract
2. Turner, P. E., and L. Chao. 1999. **Prisoner's dilemma in an RNA virus.** Nature 398:441-443. abstract

Coevolution

Coevolution is the study of the evolutionary influence that two species have upon each other. Phage-bacterial coevolution is typically studied within the context of phage community ecololgy and reviews of phage coevolution are found at this link.

1. Buckling, A., Y. Wei, R. C. Massey, M. A. Brockhurst, and M. E. Hochberg. 2006. **Antagonistic coevolution with parasites increases the cost of host deleterious mutations.** Proc. R. Soc. Lond. B Biol. Sci. 273:45-49. abstract
2. Morgan, A. D., S. Gandon, and A. Buckling. 2005. **The effect of migration on local adaptation in a coevolving host-parasite system.** Nature 437:253-256. abstract & pay article
3. Forde, S. E., J. N. Thompson, and B. J. M. Bohannan. 2004. **Adaptation varies through space and time in a coevolving host–parasitoid interaction.** Nature 431:841-844. abstract
4. Mizoguchi, K., M. Morita, C. R. Fischer, M. Yoichi, Y. Tanji, and H. Unno. 2003. **Coevolution of bacteriophage PP01 and Escherichia coli O157:H7 in continuous culture.** Appl. Environ. Microbiol. 69:170-176. full text
5. Buckling, A., and P. B. Rainey. 2002. **Antagonistic coevolution between a bacterium and a bacteriophage.** Proc. R. Soc. Lond. B Biol. Sci. 269:931-936. full text
6. Buckling, A., and P. B. Rainey. 2002. **The role of parasites in sympatric and allopatric host diversification.** Nature 420:496-499. abstract & pay article
7. Lenski, R.E. and B.R. Levin. 1985. **Constraints on the coevolution of bacteria and virulent phage – a model, some experiments and predictions for natural communities.** Am. Nat. 125:585-602.
8. Chao, L., B.R. Levin, and F.M. Stewart. 1977. **A complex community in a simple habitat: an experimental study with bacteria and phage.** Ecology. 58:369-378. abstract

Historical considerations

The following is quoted from d'Hérelle and Smith, 1924[9]:

> ADAPTATION AND THE BACTERIOPHAGE
>
> All authors admit that the virulence of the bacteriophage may increase for a given bacterium, or that it may diminish, according to the condition of the moment. This is then a phenomenon of adaptation analogous to that observed with all parasites.
>
> The fact of attenuation and of exaltation of virulence is sufficient by itself to show that the badteriophage is an autonomous parasite. Certain authors (Seiffert) while admitting the fact, have tried to maintain that it is not the bateriophage which adapts itself, but rather the bacterium. An obvious reply would be that it is not the bacterium with which the passages are made, since each passage involves the action of the filtrate of a preceding lysed culture upon a fresh normal suspension of bacteria. By virtue of the fact that

only the filtrate is concerned in the passages the adaptation must be something which is found in the filtrate.

But this is not all. It is certain that the bacterium, which is also a living being, must react, must likewise undergo adaptation. Constant experience shows that this is just what happens, but the adaptation which takes place, far from tending toward a destructive action, as would be the case if the bacterium adapted itself to the secretion of a lytic substance, reacts against the bacteriophage by a process of adaptation tending to hinder the action of the bacteriophage. The bacterium acquires a resistance. This resistance may, indeed, reach to a completely refractory condition, and, in such a case, it is the bacterium which destroys the bacteriophage (d'Herelle, Flu).

The bacteriophage adapts itself to a more and more vigorous attack against the bacterium, and the bacterium accustoms itself to resist this attack. Considering only experimental facts this is clearly evident when no pretense is made to interpret these facts to make them fit into a preconceived theoretical scheme.

But there are still other points. The bacteriophage adapts itself to harmful effects of the medium. I have shown that the bacteriophage can gradually adapt itself to the harmful action of glycerol and of acids. Asheshov has habituated a bacteriophage, originally unable to effect bacteriophagy in an acid medium, to act very strongly after a number of passages in a medium of increasing acidity. Wolff and Janzen have succeeded in adapting it to different antiseptics.

We have already seen that the bacteriophage functions as an antigen and that the serum of an animal which has received serial injections of a bacteriophage possesses the property of inhibiting bacteriophagous actions. Prausnitz has shown further that it is possible to adapt the bacteriophage to resist the inhibiting action of an antiserum. Once this adaptation is accomplished bacteriophagy takes place in any quantity of antiserium, although prior to the adaptation, an amount of a thousandth of a cubic centimeter or even less paralyzed bacteriophagy completely.

The proofs are then multiple: The bacteriophage possesses the power of adaptation. We have seen that it also possesses that of assimilation. It possesses likewise the two corollaries of these powers; the faculties of multiplication and variability as everyone admits. (pp. 267-268)

The bacteriophagous corpuscles are endowed with the powers of assimilation and adaptation, the faculties of multiplication and of variation. They are this necessarily living beings since they possess all of the characteristics of other living things.

A single bacteriophage is usually virulent, at the same time, for a certain number of bacterial species. This virulence is variable and is subject to increase or attenuation. Increase may always be secured in vitro by the method of passages at the expense of the bacterium for which it is desired to inrease the virulence.
The bacterium does not remain passive before the attack of the bacteriophage. It is capable of resistance. It is even able, when the conditions for it are favorable, to acquire a complete immunity. (pp. 269-270)

Notes

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Cyanophage

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Bacteriophage Ecology Group News (*BEG News*) 25

Long-time readers will recognize this as having come from a BEG News article
Please help with the maintenance of the Wikipedia version, found at:

http://en.wikipedia.org/wiki/Cyanophage

(equivalent to Wikipedia version as of Saturday, October 21, 2006)

Cyanophage are viruses of cyanobacteria. Because of the important role of cyanobacteria as producers in the world's oceans, the study of the ecology of cyanophage, as cyanobacterium predators/antagonists, is important toward understanding global carbon cycling.

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[4] With the help of various Wikipedia editors.

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External links

- the Virus Ecology Group (VEG)
- the Bacteriophage Ecology Group (BEG)

Cyanophage publications

The following is an unannotated list of cyanophage publications. Effort has been made to provide a complete list of these publications, though likely not all older publications are present, and without question the latest cyanophage publications will be missing, at least temporarily. We invite further editing, additions, updating, etc.

- Tentatively added references should be presented using a bullet rather than a number, and should be placed at the end of the lists otherwise spanning individual years. Theses or meeting abstracts should be entered using bullets rather than numbered.

Editing instructions (of references) as well as tips for finding references online can be found here. For a primer on the more-general phage literature, see phage monographs.
This list is an expansion of a list presented as the cyanophage literome in *BEG News* in 2004. *BEG News* is an online newsletter published by the Bacteriophage Ecology Group.

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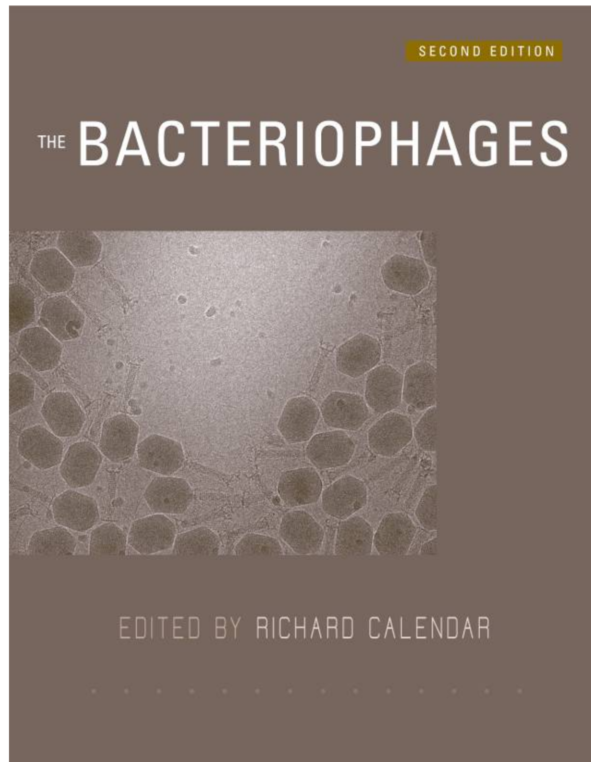
name		address/research interests
Angus Buckling (BEG link)	PI	Department of Zoology, University of Oxford, Oxford OX1 3PS, UK
	Interests:	Bacteria-phage antagonistic coevolution; phage as drivers of bacterial diversity; evolution of phage life histories.
Zehua Chen (BEG link)		Bldg 469 Room 215, NCI-Frederick, Frederick, MD 21702
	Interests:	Molecular information theory based T7-like promoter models and SD models; Evolutionary analysis and classification of T7-like phages and their transcription systems; Analysis of T7-like promoter containing regions in microbial genomes.
Siobain Duffy (BEG link)		Department of Ecology and Evolutionary Biology, Yale University, Osborn Memorial Laboratories, 165 Prospect Street, PO Box 208106, New Haven, CT 06520-8106
	Interests:	Phage as model viral systems; Experimental evolution; Disease ecology and evolution.
Juan Jofre (BEG link)	PI	Department of Microbiology, Faculty of Biology, University of Barcelona, Diagonal 645. 08028 Barcelona. (Spain.)
	Interests:	Use of phages as indicators of faecal pollution in the environment (specifically water and compost models). Establishments of different methodologies (ISO) for the enumeration of phages as indicators. Development of the ISO method for enumeration of Bacteroides fragilis phages. Research on bacteriophages as elements for horizontal genetic transfer.
Matt Jones (BEG link)		OmniLytics, Inc., 5450 W. Wiley Post Way, Salt Lake City, UT 84116
	Interests:	Development and optimization of commercial bacteriophage applications in agriculture, food & water safety, industrial, pharmaceutical, and defense.
Kate Newton (BEG link)		Department of Microbiology, University of Liverpool John Moores, L3 3AF. England
	Interests:	Interactions between phage as competitors in environments similar to that of sewage. In particular, comparisons of host range, replication speeds, structure, and attachment.
Aldwin Ong (BEG link)		Department of Biology, Ateneo de Manila University, Loyola Heights, Quezon City, Philippines
	Interests:	Use of mitomycin-C for lytic cycle induction of temperate bacteriophage in *Escherichia coli* MH2700 and some other pathogenic bacteria.
Andrzej Piekarowicz (BEG link)	PI	Institut of Microbiology, Warsaw University, Miecznikowa 1

	Interests:	Bacteriophages of *Haemophilus influenzae*.
Ramesh Prakash (BEG link)	PI	OmniLytics, Inc., 5450 W. Wiley Post Way, Salt Lake City, UT 84116
	Interests:	Development and optimization of commercial bacteriophage applications in agriculture, food & water safety, industrial, pharmaceutical, and defense.
Randy Scott (BEG link)	PI	OmniLytics, Inc., 5450 W. Wiley Post Way, Salt Lake City, UT 84116
	Interests:	Development and optimization of commercial bacteriophage applications in agriculture, food & water safety, industrial, pharmaceutical, and defense.
Télesphore Sime-Ngando (BEG link)	PI	Laboratoire de Biologie des Protistes, Université Blaise Pascal, F - 63177 Aubière Cedex, France
	Interests:	Phage-bacteria community ecology in freshwaters ecosystems.
Shanmuga Sozhamannan (BEG link)	PI	Biological Defense Research Directorate, Naval Medical Research Center, BDRD Annex, 12300 Washington Avenue, Rockville, MD 20852
	Interests:	I am interested in the biology of phages infecting bacterial pathogens relevant to biodefense and the use of phages in various biodefense applications such as bacterial detection, vaccine development and therapeutics.
Constantinos A. Vorkas (BEG link)	PI	1, Ouralion Street, P.O. Box 53321 CY-3302 Limassol, CYPRUS
	Interests:	Wastewater treatment and disposal, Water treatment, Appropriate technologies in water and wastewater treatment, Pollution control and water resources management, Environmental health, Wastewater reuse, Water supply surveillance & quality control, Environmental and catchment surveillance (GIS, Remote surveillance, Biotic monitoring), New methods in microbiological and environmental monitoring.

New Phage-Ecology References

(see www.phage.org/beg_mission_statement.htm for
why papers covering more than just bacteriophages are included)



Bacteriophages: Biology and Applications

Richard Calendar
plus Stephen T. Abedon (eds)

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www.TheBacteriophages.org

1. Abedon,S.T. (2006). **Phage ecology.** pp. 37-46 In Calendar,R. and Abedon,S.T. (eds.), *The Bacteriophages*. Oxford University Press, Oxford. **Abstract:** Phages are found nearly everywhere bacteria are found and phage ecology is the study of the interactions between phages and their environments. These interactions are consequential, particularly to the extent that they affect bacteria. During the molecular characterization of phages, however, traditionally only minimal consideration of their ecology is made. Bucking these trends, here I consider, *from a phage's perspective*, organismal, population, community, and ecosystem ecology (Table 1). For additional approaches to the review of phage ecology as well as the related field of phage environmental microbiology see [REFS] plus various recent reviews of aquatic and ecosystem phage ecology [REFS]. Visit www.phage.org for additional phage-ecology resources.

2. Attoui,H.**,** Jaafar,F.M.**,** Belhouchet,M.**,** de Micco,P.**,** de Lamballerie,X.**,** Brussaard,C.P. (2006). **Micromonas pusilla reovirus: a new member of the family Reoviridae assigned to a novel proposed genus (Mimoreovirus).** *J. Gen. Virol.* 87:1375-1383. **Abstract:** *Micromonas pusilla* reovirus (MpRV) is an 11-segmented, double-stranded RNA virus isolated from the marine protist *Micromonas pusilla*. Sequence analysis (including conserved termini and presence of core motifs of reovirus polymerase), morphology and physicochemical properties confirmed the status of MpRV as a member of the family Reoviridae. Electron microscopy showed that intact virus particles are unusually larger (90-95 nm) than the known size of particles of viruses belonging to the family Reoviridae. Particles that were purified on caesium chloride gradients had a mean size of 75 nm (a size similar to the size of intact particles of members of the family Reoviridae), indicating that they lost outer-coat components. The subcore particles had a mean size of 50 nm and a smooth surface, indicating that MpRV belongs to the non-turreted Reoviridae. The maximum amino acid identity with other reovirus proteins was 21 %, which is compatible with values existing between distinct genera. Based on morphological and sequence findings, this virus should be classified as the representative of a novel genus within the family Reoviridae, designated Mimoreovirus (from *Micromonas pusilla* reovirus). The topology of the phylogenetic tree built with putative polymerase sequences of the family Reoviridae suggested that the branch of MpRV could be ancestral. Further

analysis showed that segment 1 of MpRV was much longer (5792 bp) than any other reovirus segment and encoded a protein of 200 kDa (VP1). This protein exhibited significant similarities to O-glycosylated proteins, including viral envelope proteins, and is likely to represent the additional outer coat of MpRV.

3. Avsaroglu,M.D.**,** Buzrul,S.**,** Alpas,H.**,** Akcelik,M.**,** Bozoglu,F. (2006). **Use of the Weibull model for lactococcal bacteriophage inactivation by high hydrostatic pressure.** *Int. J. Food Microbiol.* 108:78-83. **Abstract:** Four lactococcal bacteriophages (ϕLl6-2, ϕLl35-6, ϕLd66-36 and ϕLd67-42) in M17 broth were pressurized at 300 and 350 MPa at room temperature and their survival curves were determined at various time intervals. Tailing (monotonic upward concavity) was observed in all survival curves. The resulting non-linear semi-logarithmic survival curves were described by the Weibull model and goodness of fit of this model was investigated. Regression coefficients (R2), root mean square error (RMSE), residual and correlation plots strongly suggested that Weibull model produced a better fit to the data than the traditional linear model. Hazard plots suggested that the Weibull model was fully appropriate for the data being analyzed. These results have confirmed that the Weibull model, which is mostly utilized to describe the inactivation of bacterial cells or spores by heat and pressure, could be successfully used in describing the lactococcal bacteriophage inactivation by high hydrostatic pressure.

4. Bettarel,Y.**,** Bouvy,M. **,** Dumont,C.**,** Sime-Ngando,T. (2006). **Virus-bacterium interactions in water and sediment of West African inland water system.** *Appl. Environ. Microbiol.* 72:5274-5282. **Abstract:** The ecology of virioplankton in tropical aquatic ecosystems is poorly documented, and in particular, there are no references concerning African continental waters in the literature. In this study, we examined virusbacterium interactions in the pelagic and benthic zones of seven contrasting shallow inland waters in Senegal, including one hypersaline lake. SYBR Gold-stained samples revealed that in the surface layers of the sites, the numbers of viruses were in the same range as the numbers of viruses reported previously for productive temperate systems. Despite high bacterial production rates, the percentages of visibly infected cells (as determined by transmission electron microscopy) were similar to the lowest percentages (range, 0.3 to 1.1%; mean, 0.5%) found previously at pelagic freshwater or marine sites, presumably because of the local environmental and climatic conditions. Since the percentages of lysogenic bacteria were consistently less than 8% for pelagic and benthic samples, lysogeny did not appear to be a dominant strategy for virus propagation at these sites. In the benthic samples, viruses were highly concentrated, but paradoxically, no bacteria were visibly infected. This suggests that sediment provides good conditions for virus preservation but ironically is an unfavorable environment for proliferation. In addition, given the comparable size distributions of viruses in the water and sediment samples, our results support the paradigm that aquatic viruses are ubiquitous and may have moved between the two compartments of the shallow systems examined. Overall, this study provides additional information about the relevance of viruses in tropical areas and indicates that the intensity of virus-bacterium interactions in benthic habitats may lower than the intensity in the adjacent bodies of water.

5. Bordenstein,S.R.**,** Marshall,M.L.**,** Fry,A.J.**,** Kim,U.**,** Wernegreen,J.J. (2006). **The tripartite associations between bacteriophage, *Wolbachia*, and arthropods.** *PLoS Pathog.* 2:e43. **Abstract:** By manipulating arthropod reproduction worldwide, the heritable endosymbiont *Wolbachia* has spread to pandemic levels. Little is known about the microbial basis of cytoplasmic incompatibility (CI) except that bacterial densities and percentages of infected sperm cysts associate with incompatibility strength. The recent discovery of a temperate bacteriophage (WO-B) of *Wolbachia* containing ankyrin-encoding genes and virulence factors has led to intensifying debate that bacteriophage WO-B induces CI. However, current hypotheses have not considered the separate roles that lytic and lysogenic phage might have on bacterial fitness and phenotype. Here we describe a set of quantitative approaches to characterize phage densities and its associations with bacterial densities and CI. We enumerated genome copy number of phage WO-B and *Wolbachia* and CI penetrance in supergroup A- and B-infected males of the parasitoid wasp *Nasonia vitripennis*. We report several findings: (1) variability in CI strength for A-infected males is positively associated with bacterial densities, as expected under the bacterial density model of CI, (2) phage and bacterial densities have a significant inverse association, as expected for an active lytic infection, and (3) CI strength and phage densities are inversely related in A-infected males; similarly, males expressing incomplete CI have significantly higher phage densities than males expressing complete CI. Ultrastructural analyses indicate that approximately 12% of the A *Wolbachia* have phage particles, and aggregations of these particles can putatively occur outside the *Wolbachia* cell. Physical interactions were observed between approximately 16% of the *Wolbachia* cells and spermatid tails. The results support a low to moderate frequency of lytic development in *Wolbachia* and an overall negative density relationship between bacteriophage and *Wolbachia*. The findings motivate a novel phage density model of CI in which lytic phage repress *Wolbachia* densities and therefore reproductive parasitism. We conclude that phage,

Wolbachia, and arthropods form a tripartite symbiotic association in which all three are integral to understanding the biology of this widespread endosymbiosis. Clarifying the roles of lytic and lysogenic phage development in Wolbachia biology will effectively structure inquiries into this research topic.

6. Buckling,A., Wei,Y., Massey,R.C., Brockhurst,M.A., Hochberg,M.E. (2006). **Antagonistic coevolution with parasites increases the cost of host deleterious mutations.** *Proc. R. Soc. Lond. B Biol. Sci.* 273:45-49. **Abstract:** The fitness consequences of deleterious mutations are sometimes greater when individuals are parasitized, hence parasites may result in the more rapid purging of deleterious mutations from host populations. The significance of host deleterious mutations when hosts and parasites antagonistically coevolve (reciprocal evolution of host resistance and parasite infectivity) has not previously been experimentally investigated. We addressed this by coevolving the bacterium *Pseudomonas fluorescens* and a parasitic bacteriophage in laboratory microcosms, using bacteria with high and low mutation loads. Directional coevolution between bacterial resistance and phage infectivity occurred in all populations. Bacterial population fitness, as measured by competition experiments with ancestral genotypes in the absence of phage, declined with time spent coevolving. However, this decline was significantly more rapid in bacteria with high mutation loads, suggesting the cost of bacterial resistance to phage was greater in the presence of deleterious mutations (synergistic epistasis). As such, resistance to phage was more costly to evolve in the presence of a high mutation load. Consistent with these data, bacteria with high mutation loads underwent less rapid directional coevolution with their phage populations, and showed lower levels of resistance to their coevolving phage populations. These data suggest that coevolution with parasites increases the rate at which deleterious mutations are purged from host populations.

7. Bull,J.J., Millstein,J., Orcutt,J., Wichman,H.A. (2006). **Evolutoinary feedback mediated through population density, illustrated with viruses in chemostats.** *Am. Nat.* 167:E39-E51. **Abstract:** A cornerstone of evolutionary ecology is that population density affects adaptation: *r* and *K* selection is the obvious example. The reverse is also appreciated: adaptation impacts population density. Yet, empirically demonstrating a direct connection between population density and adaptation is challenging. Here, we address both evolution and ecology of population density in models of viral (bacteriophage) chemostats. Chemostats supply nutrients for host cell growth, and the hosts are prey for viral reproduction. Two different chemostat designs have profoundly different consequences for viral evolution. If host and virus are confined to the same chamber, as in a predator-prey system, viral regulation of hosts feeds back to maintain low viral density (measured as infections per cell). Viral adaptation impacts host density but has a small effect on equilibrium viral density. More interesting are chemostats that supply the viral population with hosts from a virus-free refuge. Here, a type of evolutionary succession operates: adaptation at low viral density leads to higher density, but high density then favors competitive ability. Experiments support these models with both phenotypic and molecular data. Parallels to these designs exist in many natural systems, so these experimental systems may yield insights to the evolution and regulation of natural populations.

8. Bull,J.J. (2006). **Optimality models of phage life history and parallels in disease evolution.** *J. Theor. Biol.* 241:928-938. **Abstract:** Optimality models constitute one of the simplest approaches to understanding phenotypic evolution. Yet they have shortcomings that are not easily evaluated in most organisms. Most importantly, the genetic basis of phenotype evolution is almost never understood, and phenotypic selection experiments are rarely possible. Both limitations can be overcome with bacteriophages. However, phages have such elementary life histories that few phenotypes seem appropriate for optimality approaches. Here we develop optimality models of two phage life history traits, lysis time and host range. The lysis time models show that the optimum is less sensitive to differences in host density than suggested by earlier analytical work. Host range evolution is approached from the perspective of whether the virus should avoid particular hosts, and the results match optimal foraging theory: there is an optimal "diet" in which host types are either strictly included or excluded, depending on their infection qualities. Experimental tests of both models are feasible, and phages provide concrete illustrations of many ways that optimality models can guide understanding and explanation. Phage genetic systems already support the perspective that lysis time and host range can evolve readily and evolve without greatly affecting other traits, one of the main tenets of optimality theory. The models can be extended to more general properties of infection, such as the evolution of virulence and tissue tropism.

9. Capparelli,R., Ventimiglia,I., Roperto,S., Fenizia,D., Iannelli,D. (2006). **Selection of an *Escherichia coli* O157:H7 bacteriophage for persistence in the circulatory system of mice infected experimentally.** *Clin. Microbiol. Infect.* 12:248-253. **Abstract:** A bacteriophage lytic for *Escherichia coli* O157:H7 was isolated from bovine manure. Following in-vivo selection, the phage acquired the capacity to persist in the

circulatory system of mice for at least 38 days. When mice were infected experimentally with *E. coli* O157:H7 (10(7) CFU/mouse), simultaneous injection of the mice with phage (10(8) PFU/mouse) cleared *E. coli* O157:H7 from the mice within 48 h.

10. Chen,Z.**,** Schneider,T.D. (2006). **Comparative analysis of tandem T7-like promoter containing regions in enterobacterial genomes reveals a novel group of genetic islands.** *Nucleic Acids Research* 34:1133-1147. **Abstract:** Based on molecular information theory, 10 T7-like promoter models were built for the T7 group of phages and used to scan their host genomes and closely related genomes. 38 genomes were scanned and 12 clusters of tandem promoters were identified in nine enteropathogens. Comparative analysis of these tandem promoter-bearing regions reveals that they are similar to each other, forming prophage-like islands of 4-13 kb. Each island appears to contain two or three tandem T7-like promoters within a stretch of 150-620 bases, but there are no corresponding RNA polymerase (RNAP) genes. The promoters would transcribe two to five putative phage-related proteins, but none of these resemble known phage structural proteins. An integrase belonging to the Int family of site-specific recombinases is encoded upstream of the tandem promoters. A direct repeat of 17-24 bases was found on the ends of all 12 islands. Comparative analysis of the islands shows that these islands appear to have recombined with each other. These results suggest that the islands could encode a group of satellite phages. Activation and function of the islands may depend on transcription by a T7-like RNAP after infection by a T7-like phage or foreign DNA that encodes a T7-like RNAP.

11. Clokie,M.R.J.**,** Shan,J.**,** Bailey,S.**,** Jia,Y.**,** Krisch,H.M.**,** West,S.**,** Mann,N.H. (2006). **Transcription of a 'photosynthetic' T4-type phage during infection of a marine cyanobacterium.** *Environ. Microbiol.* 8:827-835. **Abstract:** The transcription of S-PM2 phage following infection of *Synechococcus* sp. WH7803, a marine cyanobacterium, was analysed by quantitative real-time PCR. Unlike the distantly related coliphage T4, there were only two (early and late) instead of three (early, middle and late) classes of transcripts during the developmental cycle of the phage. This difference is consistent with the absence from the S-PM2 genome of T4-like middle mode promoter sequences and the transcription factors associated with their recognition. Phage S-PM2 carries the 'photosynthetic' genes psbA and psbD that encode homologues of the host photosystem II proteins D1 and D2. Transcripts of the phage psbA gene appeared soon after infection and remained at high levels until lysis. Throughout the course of infection, the photosynthetic capacity of the cells remained constant. A considerable transient increase in the abundance of the host psbA transcripts occurred shortly after infection, suggesting that the host responds to the trauma of phage infection in a similar way as it does to a variety of other environmental stresses. The very substantial transcription of the phage psbA gene during the latter phase of phage infection suggests that S-PM2 has acquired this cellular gene to ensure that D1 levels and thus photosynthesis are fully maintained until the infected cell finally lyses. Unexpectedly, transcripts of a phage-encoded S-layer protein gene were among the earliest and most abundant detected, suggesting that this partial homologue of a host protein plays an important role in the S-PM2 infection process.

12. Curtin,J.J.**,** Donlan,R.M. (2006). **Using bacteriophages to reduce formation of catheter-associated biofilms by *Staphylococcus epidermidis*.** *Antimicrob. Agents Chemother.* 50:1268-1275. **Abstract:** Use of indwelling catheters is often compromised as a result of biofilm formation. This study investigated if hydrogel-coated catheters pretreated with a coagulase-negative bacteriophage would reduce *Staphylococcus epidermidis* biofilm formation. Biofilms were developed on hydrogel-coated silicone catheters installed in a modified drip flow reactor. Catheter segments were pretreated with the lytic *S. epidermidis* bacteriophage 456 by exposing the catheter lumen to a 10-log-PFU/ml culture of the bacteriophage for 1 h at 37 degrees C prior to biofilm formation. The untreated mean biofilm cell count was 7.01+/-0.47 log CFU/cm2 of catheter. Bacteriophage treatment with and without supplemental divalent cations resulted in log-CFU/cm2 reductions of 4.47 (P<0.0001) and 2.34 (P=0.001), respectively. Divalent cation supplementation without bacteriophage treatment provided a 0.67-log-CFU/cm2 reduction (P=0.053). Treatment of hydrogel-coated silicone catheters with an *S. epidermidis* bacteriophage in an in vitro model system significantly reduced viable biofilm formation by *S. epidermidis* over a 24-h exposure period, suggesting the potential of bacteriophage for mitigating biofilm formation on indwelling catheters and reducing the incidence of catheter-related infections.

13. Dabrowska,K.**,** Switala-Jelen,K.**,** Opolski,A.**,** Gorski,A. (2006). **Possible association between phages, Hoc protein, and the immune system.** *Arch. Virol.* 151:209-215. **Abstract:** Mammals have become "an environment" for enterobacterial phage life cycles. Therefore it could be expected that bacteriophages adapt to them. This adaptation must comprise bacteriophage proteins. Gp Hoc seems to have significance neither for phage particle structure nor for phage antibacterial activity. It is evidently not necessary for the "typical" antibacterial actions of bacteriophages. But the rules of evolution make it

improbable that gp Hoc really has no function, and non-essential genes of T4-type phages are probably important for phages' adaptation to their particular lifestyle. More interesting is the eukaryotic origin of gp Hoc: a resemblance to immunoglobulin-like proteins that reflects their evolutionary relation. Substantial differences in biological activity between T4 and a mutant that lacks gp Hoc were observed in a mammalian system. Hoc protein seems to be one of the molecules predicted to interact with mammalian organisms and/or modulate these interactions.

14. Danelishvili,L., Young,L.S., Bermudez,L.E. (2006). **In vivo efficacy of phage therapy for *Mycobacterium avium* infection as delivered by a nonvirulent mycobacterium.** *Microb. Drug Res.* 12:1-6. **Abstract:** The emergence of mycobacteria resistant to currently available antimicrobial agents has become an important problem in modern medicine. *Mycobacterium avium* and *M. tuberculosis* are intracellular pathogens that replicate and survive within the mononuclear phagocytes. TM4 is a lytic mycobacteriophage that kills both extracellular *M. avium* and *M. tuberculosis*. When delivered by *M. smegmatis* transiently infected with TM4, it kills both *M. avium* and *M. tuberculosis* within RAW 264.7 macrophages. To evaluate the treatment of *M. avium* infection with phage in vivo, C57 BL/6 mice were infected with *M. avium* 109 and, 7 days later, treated either once or twice with TM4 phage (7.9 x 10(10) PFU/ml), *M. smegmatis* (4 x 10(8) cFU/ml), or *M. smegmatis* with TM4 phage delivered intravenously (i.v.). Treatment with TM4 phage alone or *M. smegmatis* without TM4 did not show a significant decrease in number of intracellular bacteria in the spleen compared with untreated control. In contrast, administration of *M. smegmatis*-TM4 resulted in a significant decrease in the number of *M. avium* in the spleen. However, 23% of bacteria recovered from treated mice were resistant to TM4. These in vivo studies confirmed the in vitro findings that an avirulent mycobacterium can be used as a carrier to deliver antimycobacterial phage intracellularly.

15. de Paepe,M., Taddei,F. (2006). **Viruses' life history: Towards a mechanistic basis of a trade-off between survival and reproduction among phages.** *PLoS Biol.* 4:e193. **Abstract:** Life history theory accounts for variations in many traits involved in the reproduction and survival of living organisms, by determining the constraints leading to trade-offs among these different traits. The main life history traits of phages—viruses that infect bacteria—are the multiplication rate in the host, the survivorship of virions in the external environment, and their mode of transmission. By comparing life history traits of 16 phages infecting the bacteria *Escherichia coli*, we show that their mortality rate is constant with time and negatively correlated to their multiplication rate in the bacterial host. Even though these viruses do not age, this result is in line with the trade-off between survival and reproduction previously observed in numerous aging organisms. Furthermore, a multiple regression shows that the combined effects of two physical parameters, namely, the capsid thickness and the density of the packaged genome, account for 82% of the variation in the mortality rate. The correlations between life history traits and physical characteristics of virions may provide a mechanistic explanation of this trade-off. The fact that this trade-off is present in this very simple biological situation suggests that it might be a fundamental property of evolving entities produced under constraints. Moreover, such a positive correlation between mortality and multiplication reveals an underexplored trade-off in host–parasite interactions.

16. Dennehy,J.J., Friedenberg,N.A., Yang,Y.W., Turner,P.E. (2006). **Bacteriophage migration via nematode vectors: host-parasite-consumer interactions in laboratory microcosms.** *Appl. Environ. Microbiol.* 72:1974-1979. **Abstract:** Pathogens vectored by nematodes pose serious agricultural, economic, and health threats; however, little is known of the ecological and evolutionary aspects of pathogen transmission by nematodes. Here we describe a novel model system with two trophic levels, bacteriophages and nematodes, each of which competes for bacteria. We demonstrate for the first time that nematodes are capable of transmitting phages between spatially distinct patches of bacteria. This model system has considerable advantages, including the ease of maintenance and manipulation at the laboratory bench, the ability to observe many generations in short periods, and the capacity to freeze evolved strains for later comparison to their ancestors. More generally, experimental studies of complex multispecies interactions, host-pathogen coevolution, disease dynamics, and the evolution of virulence may benefit from this model system because current models (e.g., chickens, mosquitoes, and malaria parasites) are costly to maintain, are difficult to manipulate, and require considerable space. Our initial explorations centered on independently assessing the impacts of nematode, bacterium, and phage population densities on virus migration between host patches. Our results indicated that virus transmission increases with worm density and host bacterial abundance; however, transmission decreases with initial phage abundance, perhaps because viruses eliminate available hosts before migration can occur. We discuss the microbial growth dynamics that underlie these results, suggest mechanistic explanations for nematode transmission of phages, and propose intriguing possibilities for future research.

17. Duffy,S.**,** Turner,P.E.**,** Burch,C.L. (2006). **Pleiotropic costs of niche expansion in the RNA bacteriophage φ6.** *Genetics* 172:751-757. **Abstract:** Natural and experimental systems have failed to universally demonstrate a trade-off between generalism and specialism. When a trade-off does occur it is difficult to attribute its cause to antagonistic pleiotropy without dissecting the genetic basis of adaptation, and few previous experiments provide these genetic data. Here we investigate the evolution of expanded host range (generalism) in the RNA virus φ6, an experimental model system allowing adaptive mutations to be readily identified. We isolated 10 spontaneous host range mutants on each of three novel *Pseudomonas* hosts and determined whether these mutations imposed fitness costs on the standard laboratory host. Sequencing revealed that each mutant had one of nine nonsynonymous mutations in the φ6 gene P3, important in host attachment. Seven of these nine mutations were costly on the original host, confirming the existence of antagonistic pleiotropy. In addition to this genetically imposed cost, we identified an epigenetic cost of generalism that occurs when phage transition between host types. Our results confirm the existence in φ6 of two costs of generalism, genetic and environmental, but they also indicate that the cost is not always large. The possibility for cost-free niche expansion implies that varied ecological conditions may favor host shifts in RNA viruses.

18. Forterre,P. (2006). **The origin of viruses and their possible roles in major evolutionary transitions.** *Virus Res.* 117:5-16. **Abstract:** Viruses infecting cells from the three domains of life, Archaea, Bacteria and Eukarya, share homologous features, suggesting that viruses originated very early in the evolution of life. The three current hypotheses for virus origin, e.g. the virus first, the escape and the reduction hypotheses are revisited in this new framework. Theoretical considerations suggest that RNA viruses may have originated in the nucleoprotein world by escape or reduction from RNA-cells, whereas DNA viruses (at least some of them) might have evolved directly from RNA viruses. The antiquity of viruses can explain why most viral proteins have no cellular homologues or only distantly related ones. Viral proteins have replaced the ancestral bacterial RNA/DNA polymerases and primase during mitochondrial evolution. It has been suggested that replacement of cellular proteins by viral ones also occurred in early evolution of the DNA replication apparatus and/or that some DNA replication proteins originated directly in the virosphere and were later on transferred to cellular organisms. According to these new hypotheses, viruses played a critical role in major evolutionary transitions, such as the invention of DNA and DNA replication mechanisms, the formation of the three domains of life, or else, the origin of the eukaryotic nucleus.

19. Fouts,D.E.**,** Rasko,D.A.**,** Cer,R.Z.**,** Jiang,L.**,** Fedorova,N.B.**,** Shvartsbeyn,A.**,** Vamathevan,J.J.**,** Tallon,L.**,** Althoff,R.**,** Arbogast,T.S.**,** Fadrosh,D.W.**,** Read,T.D.**,** Gill,S.R. (2006). **Sequencing *Bacillus anthracis* typing phages gamma and cherry reveals a common ancestry.** *J. Bacteriol.* 188:3402-3408. **Abstract:** The genetic relatedness of the *Bacillus anthracis* typing phages Gamma and Cherry was determined by nucleotide sequencing and comparative analysis. The genomes of these two phages were identical except at three variable loci, which showed heterogeneity within individual lysates and among Cherry, Wbeta, Fah, and four Gamma bacteriophage sequences.

20. Gorski,A.**,** Kniotek,M.**,** Perkowska-Ptasinska,A.**,** Mroz,A.**,** Przerwa,A.**,** Gorczyca,W. **,** Dabrowska,K.**,** Weber-Dabrowska,B.**,** Nowaczyk,M. (2006). **Bacteriophages and transplantation tolerance.** *Transplant. Proc.* 38:331-333. **Abstract:** Our recent findings suggest that bacteriophages (phages) may not only eliminate bacteria, but also modulate immune functions. In this communication, we demonstrate that phages may strongly inhibit human T-cell activation and proliferation as well as activation of the nuclear transcription factor NF-kappaB in response to a viral pathogen. Phage administration in vivo can diminish cellular infiltration of allogeneic skin allografts. Thus, phage treatment should be considered in antibiotic-resistant posttransplantation infections. Furthermore, phages could find a broader application in clinical transplantation.

21. Häusler,T. (2006). ***Viruses vs. Superbugs: A Solution to the Antibiotic Crisis.*** Macmillan, 22. Jensen,M.A.**,** Faruque,S.M.**,** Mekalanos,J.J.**,** Levin,B.R. (2006). **Modeling the role of bacteriophage in the control of cholera outbreaks.** *Proc. Natl. Acad. Sci. USA* 103:4652-4657. **Abstract:** Cholera is a waterborne diarrheal disease that continues to plague the developing world. Individuals become infected by consuming water from reservoirs contaminated by virulent strains of the bacterium *Vibrio cholerae*. Epidemiological and environmental observations of a cholera outbreak in Dhaka, Bangladesh, suggest that lytic bacteriophage specific for *V. cholerae* may limit the severity of cholera outbreaks by killing bacteria present in the reservoir and in infected individuals. To quantify this idea and generate testable hypotheses, we analyzed a mathematical model that combines the

epidemiology of cholera with the population dynamics of the bacteria and phage. Under biologically reasonable conditions, we found that vibriophage can ameliorate cholera outbreaks. If phage predation limits bacterial density before an outbreak, a transient reduction in phage density can disrupt that limitation, and subsequent bacterial growth can initiate a cholera outbreak. The severity of the outbreak depends on the density of phage remaining in the reservoir. If the outbreak is initiated instead by a rise in bacterial density, the introduction of phage can reduce the severity of the outbreak and promote its decline. In both situations, the magnitude of the phage effect depends mainly on vibrio growth and phage mortality rates; the lower the rates, the greater the effect. Our analysis also suggests that either bacteria in the environmental reservoir are hyperinfectious or most victims ingest bacteria amplified in food or drinking water contaminated by environmental water carrying few viable *V. cholerae*. Our theoretical results make a number of empirically testable predictions.

23. Khemayan,K.**,** Pasharawipas,T.**,** Puiprom,O.**,** Sriurairatana,S.**,** Suthienkul,O.**,** Flegel,T.W. (2006). **Unstable lysogeny and pseudolysogeny in *Vibrio harveyi* siphovirus-like phage 1.** *Appl. Environ. Microbiol.* 72:1355-1363. **Abstract:** Exposure of *Vibrio harveyi* (strain VH1114) to *V. harveyi* siphovirus-like phage 1 (VHS1) resulted in the production of a low percentage of lysogenized clones of variable stability. These were retrieved most easily as small colonies within dot plaques. Analysis revealed that VHS1 prophage was most likely carried by VH1114 as an episome rather than integrated into the host chromosome. In the late exponential growth phase, lysogenized VH1114 continuously produced VHS1 but also gave rise to a large number of cured progeny. The absence of phage DNA in the cured progeny was confirmed by the absence of VHS1 DNA in Southern blot and PCR assays. Curiously, these very stable, cured subclones did not show the parental phenotype of clear plaques with VHS1 but instead showed turbid plaques, both in overlaid lawns and in dot plaque assays. This phenotypic difference from the original parental isolate suggested that transient lysogeny by VHS1 had resulted in a stable genetic change in the cured clones. Such clones may be called pseudolysogens (i.e., false lysogens), since they have undergone transient lysogeny and have retained some resistance to full lytic phage development, despite the loss of viable or detectable prophage.

24. Khies,J.L.**,** Izem,R.**,** Supler,K.L.**,** Kingsolver,J.G.**,** Burch,C.L. (2006). **The genetic basis of thermal reaction norm evolution in lab and natural phage population.** *PLoS Biol.* 4:e207. **Abstract:** Two major goals of laboratory evolution experiments are to integrate from genotype to phenotype to fitness, and to understand the genetic basis of adaptation in natural populations. Here we demonstrate that both goals are possible by re-examining the outcome of a previous laboratory evolution experiment in which the bacteriophage G4 was adapted to high temperatures. We quantified the evolutionary changes in the thermal reaction norms—the curves that describe the effect of temperature on the growth rate of the phages—and decomposed the changes into modes of biological interest. Our analysis indicated that changes in optimal temperature accounted for almost half of the evolutionary changes in thermal reaction norm shape, and made the largest contribution toward adaptation at high temperatures. Genome sequencing allowed us to associate reaction norm shape changes with particular nucleotide mutations, and several of the identified mutations were found to be polymorphic in natural populations. Growth rate measures of natural phage that differed at a site that contributed substantially to adaptation in the lab indicated that this mutation also underlies thermal reaction norm shape variation in nature. In combination, our results suggest that laboratory evolution experiments may successfully predict the genetic bases of evolutionary responses to temperature in nature. The implications of this work for viral evolution arise from the fact that shifts in the thermal optimum are characterized by tradeoffs in performance between high and low temperatures. Optimum shifts, if characteristic of viral adaptation to novel temperatures, would ensure the success of vaccine development strategies that adapt viruses to low temperatures in an attempt to reduce virulence at higher (body) temperatures.

25. Lacqua,A.**,** Wanner,O. **,** Colangelo,T.**,** Martinotti,M.G.**,** Landini,P. (2006). **Emergence of biofilm-forming subpopulations upon exposure of *Escherichia coli* to environmental bacteriophages.** *Appl. Environ. Microbiol.* 72:956-959. **Abstract:** Exposure of *Escherichia coli* MG1655 to environmental bacteriophages results in rapid selection for phage-tolerant subpopulations displaying increased biofilm formation. Analysis of one phage-tolerant strain revealed large amounts of the DNA-binding Dps protein in the outer membrane protein and production of fimbria-like structures. In dps and fimA mutant derivatives of MG1655, no selection of phage-tolerant bacteria upon exposure to bacteriophages occurred, suggesting a role for Dps and type I pili in bacteriophage tolerance.

26. Liu,J.**,** Glazko,G.**,** Mushegian,A. (2006). **Protein repertoire of double-stranded DNA bacteriophages.** *Virus Res.* 117:68-80. **Abstract:** The complexity and diversity of phage gene sets, which are produced by rapid evolution of phage genomes and rampant gene exchanges among phages, hamper the efforts to

decipher the evolutionary relationships between individual phage proteins and reconstruct the complete set of evolutionary events leading to the known phages. To start unraveling the natural history of phages, we built the phage orthologous groups (POGs), a natural system of phage protein families that includes 6378 genes from 164 complete genome sequences of double-stranded DNA bacteriophages. Phage proteomes have high POG coverage: on average, 39 genes per phage genome belong to POGs, which is close to half of all genes in most phages. In an agreement with the notion of phage role in horizontal gene transfer, we see many cases of likely gene exchange between phages and their microbial hosts. At the same time, about 80% of all POGs are highly specific to phage genomes and are not commonly found in microbial genomes, indicating coherence and large degree of evolutionary independence of phage gene sets. The information on orthologous genes is essential for evolutionary classification of known bacteriophages and for reconstruction of ancestral phage genomes.

27. Pavesi,A. (2006). **Origin and evolution of overlapping genes in the family Microviridae.** *J. Gen. Virol.* 87:1013-1017. **Abstract:** The possibility of creating novel genes from pre-existing sequences, known as overprinting, is a widespread phenomenon in small viruses. Here, the origin and evolution of gene overlap in the bacteriophages belonging to the family Microviridae have been investigated. The distinction between ancestral and derived frames was carried out by comparing the patterns of codon usage in overlapping and non-overlapping genes. By this approach, a gradual increase in complexity of the phage genome--from an ancestral state lacking gene overlap to a derived state with a high density of genetic information--was inferred. Genes encoding less-essential proteins, yet playing a role in phage growth and diffusion, were predicted to be novel genes that originated by overprinting. Evaluation of the rates of synonymous and non-synonymous substitution yielded evidence for overlapping genes under positive selection in one frame and purifying selection in the alternative frame.

28. Pepin,K.M.**,** Samuel,M.A.**,** Wichman,H.A. (2006). **Variable pleiotropic effects from mutations at the same locus hamper prediction of fitness from a fitness component.** *Genetics* 172:2047-2056. **Abstract:** The relationship of genotype, fitness components, and fitness can be complicated by genetic effects such as pleiotropy and epistasis and by heterogeneous environments. However, because it is often difficult to measure genotype and fitness directly, fitness components are commonly used to estimate fitness without regard to genetic architecture. The small bacteriophage ϕX174 enables direct evaluation of genetic and environmental effects on fitness components and fitness. We used 15 mutants to study mutation effects on attachment rate and fitness in six hosts. The mutants differed from our lab strain of ϕX174 by only one or two amino acids in the major capsid protein (gpF, sites 101 and 102). The sites are variable in natural and experimentally evolved ϕX174 populations and affect phage attachment rate. Within the limits of detection of our assays, all mutations were neutral or deleterious relative to the wild type; 11 mutants had decreased host range. While fitness was predictable from attachment rate in most cases, 3 mutants had rapid attachment but low fitness on most hosts. Thus, some mutations had a pleiotropic effect on a fitness component other than attachment rate. In addition, on one host most mutants had high attachment rate but decreased fitness, suggesting that pleiotropic effects also depended on host. The data highlight that even in this simple, well-characterized system, prediction of fitness from a fitness component depends on genetic architecture and environment.

29. Prangishvili,D.**,** Garrett,R.A.**,** Koonin,E.V. (2006). **Evolutionary genomics of archaeal viruses: Unique viral genomes in the third domain of life.** *Virus Res.* 117:52-67. **Abstract:** In terms of virion morphology, the known viruses of archaea fall into two distinct classes: viruses of mesophilic and moderately thermophilic Eueryarchaeota closely resemble head-and-tail bacteriophages whereas viruses of hyperthermophilic Crenarchaeota show a variety of unique morphotypes. In accord with this distinction, the sequenced genomes of euryarchaeal viruses encode many proteins homologous to bacteriophage capsid proteins. In contrast, initial analysis of the crenarchaeal viral genomes revealed no relationships with bacteriophages and, generally, very few proteins with detectable homologs. Here we describe a re-analysis of the proteins encoded by archaeal viruses, with an emphasis on comparative genomics of the unique viruses of Crenarchaeota. Detailed examination of conserved domains and motifs uncovered a significant number of previously unnoticed homologous relationships among the proteins of crenarchaeal viruses and between viral proteins and those from cellular life forms and allowed functional predictions for some of these conserved genes. A small pool of genes is shared by overlapping subsets of crenarchaeal viruses, in a general analogy with the metagenome structure of bacteriophages. The proteins encoded by the genes belonging to this pool include predicted transcription regulators, ATPases implicated in viral DNA replication and packaging, enzymes of DNA precursor metabolism, RNA modification enzymes, and glycosylases. In addition, each of the crenarchaeal viruses encodes several proteins with prokaryotic but not viral homologs, some of which, predictably, seem to have been scavenged from the crenarchaeal

hosts, but others might have been acquired from bacteria. We conclude that crenarchaeal viruses are, in general, evolutionarily unrelated to other known viruses and, probably, evolved via independent accretion of genes derived from the hosts and, through more complex routes of horizontal gene transfer, from other prokaryotes.

30. Pride,D.T.**,** Wassenaar,T.M.**,** Ghose,C.**,** Blaser,M.J. (2006). **Evidence of host-virus co-evolution in tetranucleotide usage patterns of bacteriophages and eukaryotic viruses.** *BMC Genom.* 7:8. **Abstract:** BACKGROUND: Virus taxonomy is based on morphologic characteristics, as there are no widely used non-phenotypic measures for comparison among virus families. We examined whether there is phylogenetic signal in virus nucleotide usage patterns that can be used to determine ancestral relationships. The well-studied model of tail morphology in bacteriophage classification was used for comparison with nucleotide usage patterns. Tetranucleotide usage deviation (TUD) patterns were chosen since they have previously been shown to contain phylogenetic signal similar to that of 16S rRNA. RESULTS: We found that bacteriophages have unique TUD patterns, representing genomic signatures that are relatively conserved among those with similar host range. Analysis of TUD-based phylogeny indicates that host influences are important in bacteriophage evolution, and phylogenies containing both phages and their hosts support their co-evolution. TUD-based phylogeny of eukaryotic viruses indicates that they cluster largely based on nucleic acid type and genome size. Similarities between eukaryotic virus phylogenies based on TUD and gene content substantiate the TUD methodology. CONCLUSION: Differences between phenotypic and TUD analysis may provide clues to virus ancestry not previously inferred. As such, TUD analysis provides a complementary approach to morphology-based systems in analysis of virus evolution.

31. Rokyta,D.R.**,** Burch,C.L.**,** Caudle,S.B.**,** Wichman,H.A. (2006). **Horizontal gene transfer and the evolution of microvirid coliphage genomes.** *J. Bacteriol.* 188:1134-1142. **Abstract:** Bacteriophage genomic evolution has been largely characterized by rampant, promiscuous horizontal gene transfer involving both homologous and nonhomologous source DNA. This pattern has emerged through study of the tailed double-stranded DNA (dsDNA) phages and is based upon a sparse sampling of the enormous diversity of these phages. The single-stranded DNA phages of the family Microviridae, including ϕX174, appear to evolve through qualitatively different mechanisms, possibly as result of their strictly lytic lifestyle and small genome size. However, this apparent difference could reflect merely a dearth of relevant data. We sought to characterize the forces that contributed to the molecular evolution of the Microviridae and to examine the genetic structure of this single family of bacteriophage by sequencing the genomes of microvirid phage isolated on a single bacterial host. Microvirids comprised 3.5% of the detectable phage in our environmental samples, and sequencing yielded 42 new microvirid genomes. Phylogenetic analysis of the genes contained in these and five previously described microvirid phages identified three distinct clades and revealed at least two horizontal transfer events between clades. All members of one clade have a block of five putative genes that are not present in any member of the other two clades. Our data indicate that horizontal transfer does contribute to the evolution of the microvirids but is both quantitatively and qualitatively different from what has been observed for the dsDNA phages.

32. Shutt,T.E.**,** Gray,M.W. (2006). **Bacteriophage origins of mitochondrial replication and transcription proteins.** *Trends Genet.* 22:90-95. **Abstract:** Mounting evidence suggests that key components of the mitochondrial transcription and replication apparatus are derived from the T-odd lineage of bacteriophage rather than from an alpha-Proteobacterium, as the endosymbiont hypothesis would predict. We propose that several mitochondrial replication genes were acquired together from an ancestor of T-odd phage early in the evolution of the eukaryotic cell, at the time of the mitochondrial endosymbiosis. We further propose that at a later stage the single-subunit RNA polymerase, originally acquired for mitochondrial DNA replication, was co-opted to serve in mitochondrial transcription.

33. Skurnik,M.**,** Strauch,E. (2006). **Phage therapy: facts and fiction.** *Int. J. Med. Microbiol.* 296:5-14. **Abstract:** Recent examples of the use of bacteriophages in controlling bacterial infections are presented, some of which show therapeutic promise. The therapeutic use of bacteriophages, possibly in combination with antibiotics, may be a valuable approach. However, it is also quite clear that the safe and controlled use of phage therapy will require detailed information on the properties and behavior of specific phage-bacterium systems, both in vitro and especially in vivo. In vivo susceptibility of bacterial pathogens to bacteriophages is still largely poorly understood and future research on more phage-bacterium systems has to be undertaken to define the requirements for successful phage treatments.

34. Sonenshein,A.L. (2006). **Bacteriophages: how bacterial spores capture and protect phage DNA.** *Curr. Biol.* 16:R14-R16. **Abstract:** A recent study explains how bacterial spores capture and protect phage DNA, which remains free in the host cytoplasm but is unable to initiate the virulence pathway that leads to lysis of actively growing bacterial cells.

35. Stewart,J.R., Vinje,J., Oudejans,S.J.G., Scott,G.I., Sobsey,M.D. (2006). **Sequence variation among group III F-specific RNA coliphages from water samples and swine lagoons.** *Appl. Environ. Microbiol.* 72:1226-1230. **Abstract:** Typing of F-specific RNA (FRNA) coliphages has been proposed as a useful method for distinguishing human from animal fecal contamination in environmental samples. Group II and III FRNA coliphages are generally associated with human wastes, but several exceptions have been noted. In the present study, we have genotyped and partially sequenced group III FRNA coliphage field isolates from swine lagoons in North Carolina (NC) and South Carolina (SC), along with isolates from surface waters and municipal wastewaters. Phylogenetic analysis of a region of the 5' end of the maturation protein gene revealed two genetically different group III FRNA subclusters with 36.6% sequence variation. The SC swine lagoon isolates were more closely related to group III prototype virus M11, whereas the isolates from a swine lagoon in NC, surface waters, and wastewaters grouped with prototype virus Qβ. These results suggest that refining phage genotyping systems to discriminate M11-like phages from Qβ-like phages would not necessarily provide greater discriminatory power in distinguishing human from animal sources of pollution. Within the group III subclusters, nucleotide sequence diversity ranged from 0% to 6.9% for M11-like strains and from 0% to 8.7% for Qβ-like strains. It is demonstrated here that nucleotide sequencing of closely related FRNA strains can be used to help track sources of contamination in surface waters. A similar use of phage genomic sequence information to track fecal pollution promises more reliable results than phage typing by nucleic acid hybridization and may hold more potential for field applications.

36. Sturino,J.M., Klaenhammer,T.R. (2006). **Engineered bacteriophage-defence systems in bioprocessing.** *Nature reviews. Microbiology* 4:395-404. **Abstract:** Bacteriophages (phages) have the potential to interfere with any industry that produces bacteria as an end product or uses them as biocatalysts in the production of fermented products or bioactive molecules. Using microorganisms that drive food bioprocesses as an example, this review will describe a set of genetic tools that are useful in the engineering of customized phage-defence systems. Special focus will be given to the power of comparative genomics as a means of streamlining target selection, providing more widespread phage protection, and increasing the longevity of these industrially important bacteria in the bioprocessing environment.

37. Takao,Y., Mise,K., Nagasaki,K., Okuno,T., Honda,D. (2006). **Complete nucleotide sequence and genome organization of a single-stranded RNA virus infecting the marine fungoid protist *Schizochytrium* sp.** *J. Gen. Virol.* 87:723-733. **Abstract:** The complete nucleotide sequence of the genomic RNA of a marine fungoid protist-infecting virus (Schizochytrium single-stranded RNA virus; SssRNAV) has been determined. The viral RNA is single-stranded with a positive sense and is 9,018 nt in length [excluding the 3' poly(A) tail]. It contains two long open reading frames (ORFs), which are separated by an intergenic region of 92 nt. The 5' ORF (ORF1) is preceded by an untranslated leader sequence of 554 nt. The 3' large ORF (ORF2) and an additional ORF (ORF3) overlap ORF2 by 431 nt and are followed by an untranslated region of 70 nt [excluding the 3' poly(A) tail]. The deduced amino acid sequences of ORF1 and ORF2 products show similarity to non-structural and structural proteins of dicistroviruses, respectively. However, Northern blot analysis suggests that SssRNAV synthesizes subgenomic RNAs to translate ORF2 and ORF3, showing that the translation mechanism of downstream ORFs is distinct from that of dicistroviruses. Furthermore, although considerable similarities were detected by using a blast genome database search, phylogenetic analysis based on both the nucleotide and amino acid sequences of the putative RNA-dependent RNA polymerase (RdRp) and the RNA helicase suggests that SssRNAV is phylogenetically distinct from other virus families. Therefore, it is concluded that SssRNAV is not a member of any currently defined virus family and belongs to a novel, unrecognized virus group.

38. Wang,I.-N. (2006). **Lysis timing and bacteriophage fitness.** *Genetics* 172:17-26. **Abstract:** The effect of lysis timing on bacteriophage (phage) fitness has received little theoretical or experimental attention. Previously, the impact of lysis timing on phage fitness was studied using a theoretical model based on the marginal value theorem from the optimal foraging theory. An implicit conclusion of the model is that, for any combination of host quantity and quality, an optimal time to lyse the host would exist so that the phage fitness would be the highest. To test the prediction, an array of isogenic λ-phages that differ only in their lysis times was constructed. For each phage strain, the lysis time, burst size, and fitness (growth

rate) were determined. The result showed that there is a positive linear relationship between lysis time and burst size. Moreover, the strain with an intermediate lysis time has the highest fitness, indicating the existence of an optimal lysis time. A mathematical model is also constructed to describe the population dynamics of phage infection. Computer simulations using parameter values derived from phage λ-infection also showed an optimal lysis time. However, both the optimum and the fitness are different from the experimental result. The evolution of phage lysis timing is discussed from the perspectives of multiple infection and life-history trait evolution.

39. Wang,J.**,** Hu,B.**,** Xu,M.**,** Yan,Q.**,** Liu,S.**,** Zhu,X.**,** Sun,Z.**,** Reed,E.**,** Ding,L.**,** Gong,J.**,** Li,Q.Q.**,** Hu,J. (2006). **Use of bacteriophage in the treatment of experimental animal bacteremia from imipenem-resistant *Pseudomonas aeruginosa*.** *International journal of molecular medicine* 17:309-317. **Abstract:** The emergence of antibiotic-resistant bacterial strains still remains a significant problem for antimicrobial chemotherapy in the clinic. Bacterial viruses (bacteriophages or phages) have been suggested to be used as alternative therapeutic agents for bacterial infections. However, the efficacy of phage therapy in treating drug-resistant infections in humans is uncertain. Therefore in the present study, we examined the effectiveness of phages in the treatment of imipenem-resistant *Pseudomonas aeruginosa* (IMPR-Pa) infection in an experimental mouse model. Twenty-nine strains of phage were isolated from our hospital sewage, and phage OA392 was representatively used for all testing because it has lytic activity against a wide range of clinical isolates of IMPR-Pa. We found that intraperitoneal (i.p.) injections of one IMPR-Pa strain (3 x 10(7) CFU) caused bacteremia and all mice died within 24 h. A single i.p. inoculation of the phage strain (MOI > or =0.01) at up to 60 min after the bacterial challenge was sufficient to rescue 100% of the animals. This lifesaving effect coincided with the rapid appearance of OA392 in the circulation (within 2 h after i.p. injection), which remained at substantially higher levels for up to 48 h until the bacteria were eradicated. However, the survival rates of the mice dropped to approximately 50% and 20% when the same dose of this purified phage preparation was administered at 180 min and 360 min, respectively, after IMPR-Pa infections. In addition, we demonstrated that the ability of this phage to rescue bacteremic animals was due to the functional capabilities of the phage and not to a non-specific immune effect. The protection from death occurred only in animals inoculated with bacteria-specific virulent phage strains. When the heat-inactivated phages were used, the survival rate of the infected mice was dramatically reduced to 20% or lower. Moreover, the levels of the antibody against the phage were not significantly changed at the time when the bacteremic animals were protected by the active phages. Finally, our observations revealed that the inoculation of the mice with high-doses of OA392 alone produced no adverse effects attributable to the phage. These data indicate that phages can save animals from pernicious *P. aeruginosa* infections and suggest that phage therapy may be potentially used as a stand-alone therapy for patients with IMPR-Pa infections.

40. Yee,S.Y.F.**,** Fong,N.Y.**,** Fong,G.T.**,** Tak,O.J.**,** Hui,G.T.**,** Su Ming,Y. (2006). **Male-specific RNA coliphages detected by plaque assay and RT-PCR in tropical river waters and animal fecal matter.** *International Journal of Environmental Health Research* 16:59-68. **Abstract:** Male-specific RNA coliphages (FRNA) have been recommended as indicators of fecal contamination and of the virological quality of water. In this study, 16 river water and 183 animal fecal samples were examined for the presence of FRNA coliphages by a plaque assay using Salmonella typhimurium WG49 and WG25 to differentiate between male-specific and somatic phages, a RNase spot test to differentiate between DNA and RNA phages and a reverse transcriptase-polymerase chain reaction (RT-PCR) for the specific identification of FRNA phages. The overall recovery rate for F-specific coliphages was 8.0%. (4.4% from animal fecal matter and 50% from river water samples). Plaque counts were generally low (< 6 x 10(2) pfu per g feces or ml water), with FRNA (6.5%) and Male-specific DNA coliphages (FDNA) (7.0%) phages occurring at almost equal frequencies. The RT-PCR was positive in all FRNA plaques and was able to identify FRNA phages in mixed populations of FRNA, FDNA and somatic phages.

41. Yoshida,T.**,** Takashima,Y.**,** Tomaru,Y.**,** Shirai,Y.**,** Takao,Y.**,** Hiroishi,S.**,** Nagasaki,K. (2006). **Isolation and characterization of a cyanophage infecting the toxic cyanobacterium *Microcystis aeruginosa*.** *Appl. Environ. Microbiol.* 72:1239-1247. **Abstract:** We isolated a cyanophage (Ma-LMM01) that specifically infects a toxic strain of the bloom-forming cyanobacterium *Microcystis aeruginosa*. Transmission electron microscopy showed that the virion is composed of anisometric head and a tail complex consisting of a central tube and a contractile sheath with helical symmetry. The morphological features and the host specificity suggest that Ma-LMM01 is a member of the cyanomyovirus group. Using semi-one-step growth experiments, the latent period and burst size were estimated to be 6 to 12 h and 50 to 120 infectious units per cell, respectively. The size of the phage genome was estimated to be ca. 160 kbp using pulse-field gel electrophoresis; the nucleic acid was sensitive to DNase I, Bal31, and all 14

restriction enzymes tested, suggesting that it is a linear double-stranded DNA having a low level of methylation. Phylogenetic analyses based on the deduced amino acid sequences of two open reading frames coding for ribonucleotide reductase alpha- and beta-subunits showed that Ma-LMM01 forms a sister group with marine and freshwater cyanobacteria and is apparently distinct from T4-like phages. Phylogenetic analysis of the deduced amino acid sequence of the putative sheath protein showed that Ma-LMM01 does not form a monophyletic group with either the T4-like phages or prophages, suggesting that Ma-LMM01 is distinct from other T4-like phages that have been described despite morphological similarity. The host-phage system which we studied is expected to contribute to our understanding of the ecology of Microcystis blooms and the genetics of cyanophages, and our results suggest the phages could be used to control toxic cyanobacterial blooms.

42. Abedon,S.T.**,** LeJeune,J.T. (2005). **Why bacteriophage encode exotoxins and other virulence factors.** *Evol. Bioinf. Online* 1:97-110. **Abstract:** This study considers gene location within bacteria as a function of genetic element mobility. Our emphasis is on prophage encoding of bacterial virulence factors (VFs). At least four mechanisms potentially contribute to phage encoding of bacterial VFs: (i) Enhanced gene mobility could result in greater VF gene representation within bacterial populations. We question, though, why certain genes but not others might benefit from this mobility. (ii) Epistatic interactions—between VF genes and phage genes that enhance VF utility to bacteria—could maintain phage genes via selection acting on individual, VF-expressing bacteria. However, is this mechanism sufficient to maintain the rest of phage genomes or, without gene co-regulation, even genetic linkage between phage and VF genes? (iii) Phage could amplify VFs during disease progression by carrying them to otherwise commensal bacteria colocated within the same environment. However, lytic phage kill bacteria, thus requiring assumptions of inclusive fitness within bacterial populations to explain retention of phage-mediated VF amplification for the sake of bacterial utility. Finally, (iv) phage-encoded VFs could enhance phage Darwinian fitness, particularly by acting as ecosystem-modifying agents. That is, VF-supplied nutrients could enhance phage growth by increasing the density or by improving the physiology of phage-susceptible bacteria. Alternatively, VF-mediated break down of diffusion-inhibiting spatial structure found within the multicellular bodies of host organisms could augment phage dissemination to new bacteria or to environments. Such phage-fitness enhancing mechanisms could apply particularly given VF expression within microbiologically heterogeneous environments, ie, ones where phage have some reasonable potential to acquire phage-susceptible bacteria.

43. Aertsen,A.**,** Faster,D.**,** Michiels,C.W. (2005). **Induction of Shiga toxin-converting prophage in *Escherichia coli* by high hydrostatic pressure.** *Appl. Environ. Microbiol.* 71:1155-1162. **Abstract:** Since high hydrostatic pressure is becoming increasingly important in modern food preservation, its potential effects on microorganisms need to be thoroughly investigated. In this context, mild pressures (<200 MPa) have recently been shown to induce an SOS response in *Escherichia coli* MG1655. Due to this response, we observed a RecA- and LexA-dependent induction of lambda prophage upon treating *E. coli* lysogens with sublethal pressures. In this report, we extend this observation to lambdoid Shiga toxin (Stx)-converting bacteriophages in MG1655, which constitute an important virulence trait in Stx-producing *E. coli* strains (STEC). The window of pressures capable of inducing Stx phages correlated well with the window of bacterial survival. When pressure treatments were conducted in whole milk, which is known to promote bacterial survival, Stx phage induction could be observed at up to 250 MPa in *E. coli* MG1655 and at up to 300 MPa in a pressure-resistant mutant of this strain. In addition, we found that the intrinsic pressure resistance of two types of Stx phages was very different, with one type surviving relatively well treatments of up to 400 MPa for 15 min at 20°C. Interestingly, and in contrast to UV irradiation or mitomycin C treatment, pressure was not able to induce Stx prophage or an SOS response in several natural Stx-producing STEC isolates.

44. Aleem,A.**,** Malik,A. (2005). **Genotoxicity of the Yamuna River water at Okhla (Delhi), India.** *Ecotoxicology and Environmental Safety* 61:404-412. **Abstract:** Water samples from the Yamuna River at Okhla (Delhi), India, were concentrated using XAD resins (XAD-4 and XAD-8) and liquid-liquid extraction procedures. Gas chromatographic analysis of liquid-liquid extracted water samples revealed the presence of the pesticides DDT, BHC, dieldrin, endosulfan, aldrin, 2,4-D, dimethoate, methyl parathion, and malathion at concentrations of 14, 25, 2.1, 114, 0.9, 0.6, 0.9, 1.7, and 1.9 ng/L, respectively. The genotoxicity of the extracted water samples was evaluated with the Ames Salmonella/mammalian microsome test, DNA repair-defective mutants, and bacteriophage λ systems. The results of the Salmonella test demonstrated that the XAD-concentrated water samples had maximum mutagenicity with the TA98 strain both with and without metabolic activation. However, the liquid-liquid-extracted water samples were also found to be mutagenic with one or more of the Ames tester strains, but to a lesser extent as compared with XAD

extracts. The damage brought about in the DNA repair-defective mutants in the presence of XAD-concentrated water samples was found to be markedly high as compared with that liquid-liquid-extracted water samples at the dose level of 20 μl/mL culture. All mutants invariably exhibited significant declines in their colony-forming units as compared with their isogenic wild-type counterparts. Survival decreased by 86.3 and 75.5% in the polA- strain after 6 h of treatment with XAD-concentrated and liquid-liquid-extracted water samples, respectively. A significant decrease was also observed in the survival of bacteriophage λ when treated with the test samples. Mutagenic responses of the liquid-liquid-extracted water samples may not necessarily reflect the mutagenicity of existing pesticides in the test water, because some other organic pollutants might accompany the pesticides in the extract.

45. Arraj,A.**,** Bohatier,J.**,** Laveran,H.**,** Traore,O. (2005). **Comparison of bacteriophage and enteric virus removal in pilot scale activated sludge plants.** *J. Appl. Microbiol.* 98:516-524. **Abstract:** AIMS: The aim of this experimental study was to determine comparatively the removal of two types of bacteriophages, a somatic coliphage and an F-specific RNA phage and of three types of enteric viruses, hepatitis A virus (HAV), poliovirus and rotavirus during sewage treatment by activated sludge using laboratory pilot plants. METHODS AND RESULTS: The cultivable simian rotavirus SA11, the HAV HM 175/18f cytopathic strain and poliovirus were quantified by cell culture. The bacteriophages were quantified by plaque formation on the host bacterium in agar medium. In each experiment, two pilots simulating full-scale activated sludge plants were inoculated with viruses at known concentrations, and mixed liquor and effluent samples were analysed regularly. In the mixed liquor, liquid and solid fractions were analysed separately. The viral behaviour in both the liquid and solid phases was similar between pilots of each experiment. Viral concentrations decreased rapidly following viral injection in the pilots. Ten minutes after the injections, viral concentrations in the liquid phase had decreased from 1.0 +/- 0.4 log to 2.2 +/- 0.3 log. Poliovirus and HAV were predominantly adsorbed on the solid matters of the mixed liquor while rotavirus was not detectable in the solid phase. In our model, the estimated mean log viral reductions after 3-day experiment were 9.2 +/- 0.4 for rotavirus, 6.6 +/- 2.4 for poliovirus, 5.9 +/- 3.5 for HAV, 3.2 +/- 1.2 for MS2 and 2.3 +/- 0.5 for ϕX174. SIGNIFICANCE AND IMPACT OF THE STUDY: This study demonstrates that the pilots are useful models to assess the removal of infectious enteric viruses and bacteriophages by activated sludge treatment. Our results show the efficacy of the activated sludge treatment on the five viruses and suggest that coliphages could be an acceptable indicator of viral removal in this treatment system.

46. Atterbury,R.J.**,** Dillon,E.**,** Swift,C.**,** Connerton,P.L.**,** Frost,J.A.**,** Dodd,C.E.R.**,** Rees,C.E.D.**,** Connerton,I.F. (2005). **Correlation of *Campylobacter* bacteriophage with reduced presence of hosts in broiler chicken ceca.** *Appl. Environ. Microbiol.* 71:4885-4887. **Abstract:** *Campylobacter jejuni* and *Campylobacter*-specific bacteriophage were enumerated from broiler chicken ceca selected from 90 United Kingdom flocks (n = 205). *C. jejuni* counts in the presence of bacteriophage (mean log(10) 5.1 CFU/g) were associated with a significant (P < 0.001) reduction compared to samples with *Campylobacter* alone (mean log(10) 6.9 CFU/g).

47. Aziz,R.K.**,** Edwards,R.A.**,** Taylor,W.W.**,** Low,D.E.**,** McGeer,A.**,** Kotb,M. (2005). **Mosaic prophages with horizontally acquired genes account for the emergence and diversification of the globally disseminated M1T1 clone of *Streptococcus pyogenes*.** *J. Bacteriol.* 187:3311-3318. **Abstract:** The recrudescence of severe invasive group A streptococcal (GAS) diseases has been associated with relatively few strains, including the M1T1 subclone that has shown an unprecedented global spread and prevalence and high virulence in susceptible hosts. To understand its unusual epidemiology, we aimed to identify unique genomic features that differentiate it from the fully sequenced M1 SF370 strain. We constructed DNA microarrays from an M1T1 shotgun library and, using differential hybridization, we found that both M1 strains are 95% identical and that the 5% unique M1T1 clone sequences more closely resemble sequences found in the M3 strain, which is also associated with severe disease. Careful analysis of these unique sequences revealed three unique prophages that we named M1T1.X, M1T1.Y, and M1T1.Z. While M1T1.Y is similar to phage 370.3 of the M1-SF370 strain, M1T1.X and M1T1.Z are novel and encode the toxins SpeA2 and Sda1, respectively. The genomes of these prophages are highly mosaic, with different segments being related to distinct streptococcal phages, suggesting that GAS phages continue to exchange genetic material. Bioinformatic and phylogenetic analyses revealed a highly conserved open reading frame (ORF) adjacent to the toxins in 18 of the 21 toxin-carrying GAS prophages. We named this ORF paratox, determined its allelic distribution among different phages, and found linkage disequilibrium between particular paratox alleles and specific toxin genes, suggesting that they may move as a single cassette. Based on the conservation of paratox and other genes flanking the toxins, we propose a recombination-based model for toxin dissemination among prophages. We also

provide evidence that a minor population of the M1T1 clonal isolates have exchanged their virulence module on phage M1T1.Y, replacing it with a different module identical to that found on a related M3 phage. Taken together, the data demonstrate that mosaicism of the GAS prophages has contributed to the emergence and diversification of the M1T1 subclone.

48. Baker,M.L., Jiang,W. , Rixon,F.J., Chiu,W. (2005). **Common ancestry of herpesviruses and tailed DNA bacteriophages.** *J. Virol.* 79:14967-14970. **Abstract:** Comparative analysis of capsid protein structures in the eukaryote-infecting herpesviruses (Herpesviridae) and the prokaryote-infecting tailed DNA bacteriophages (Caudovirales) revealed a characteristic fold that is restricted to these two virus lineages and is indicative of common ancestry. This fold not only serves as a major architectural element in capsid stability but also enables the conformational flexibility observed during viral assembly and maturation. On the basis of this and other emerging relationships, it seems increasingly likely that the very diverse collection of extant viruses may have arisen from a relatively small number of primordial progenitors.

49. Balding,C., Bromley,S.A., Pickup,R.W., Saunders,J.R. (2005). **Diversity of phage integrases in Enterobacteriaceae: development of markers for environmental analysis of temperate phages.** *Environ. Microbiol.* 7:1558-1567. **Abstract:** Viruses are the most abundant biological entities in aquatic systems. Temperate bacteriophages have enormous influences on microbial diversity, genetic exchange and bacterial population dynamics. However, development of molecular tools for their detection in the environment has been problematic. The integrase gene is used here as a molecular marker to analyse the diversity of temperate bacteriophages in a population of freshwater bacteria. Interrogation of the GenBank database revealed 32 non-cryptic enteric phage integrase sequences, leading to the development of a suite of 11 degenerate primer sets specific to the extant sequences elucidated. Application of these primer sets to enterobacterial isolates recovered from a freshwater pond and the temperate phages induced from them revealed a number of diverse integrase genes, including novel integrase-like sequences not represented in the databases. This highlights the potential of utilizing the integrase gene family as a marker for phage diversity.

50. Bettarel,Y., Sime-Ngando,T., Amblard,C., Bouvy,M. (2005). **Low consumption of virus-sized particles by heterotrophic nanoflagellates in two lakes of the French Massif central.** *Aquat. Microb. Ecol.* 39:205-209. **Abstract:** Seasonal and depth-related variability in the grazing activity of heterotrophic nanoflagellates (HNF) on viruses was examined in the oligo-mesotrophic Lake Pavin and in the eutrophic Lake Aydat, French Massif Central, between May and November 2000. Ingestion rates (IR) were determined using 50 nm diameter fluorescent microspheres, as virus analogues. In both lakes, highest grazing activities on virus-sized particles were recorded in the metalimnion, at the beginning and the end of the thermal stratification period. Estimated IRs in Lake Pavin (mean = 0.4 viruses HNF[-1] h^{-1}, CV = 38.0%) and in Lake Aydat (mean = 0.3 viruses HNF[-1] h^{-1}, CV = 35.6%) were not significantly different, in contrast to clearance rates (CR), which were significantly higher in the oligomesotrophic (2.3 x 10^{-2} nl HNF[-1] h^{-1}) than in the eutrophic lake (0.7 × 10^{-2} nl HNF[-1] h^{-1}). CRs for viruses were correlated with CRs for bacteria in Lake Aydat but not in Lake Pavin, suggesting a greater abundance within the HNF assemblages of virus-sized particle feeders in the less productive lake. We estimated that 4.1 and 0.8% of viral production were grazed by HNF in Lake Pavin and Lake Aydat, respectively. Finally, although viruses seem to represent a minor food source for HNF (i.e. compared to bacteria), they may not be inconsequential in their diet, especially in oligotrophic lakes.

51. Beumer,A., Robinson,J.B. (2005). **A broad-host-range, generalized transducing phage (SN-T) acquires 16S rRNA genes from different genera of bacteria.** *Appl. Environ. Microbiol.* 71:8301-8304. **Abstract:** Genomic analysis has revealed heterogeneity among bacterial 16S rRNA gene sequences within a single species; yet the cause(s) remains uncertain. Generalized transducing bacteriophages have recently gained recognition for their abundance as well as their ability to affect lateral gene transfer and to harbor bacterial 16S rRNA gene sequences. Here, we demonstrate the ability of broad-host-range, generalized transducing phages to acquire 16S rRNA genes and gene sequences. Using PCR and primers specific to conserved regions of the 16S rRNA gene, we have found that generalized transducing phages (D3112, UT1, and SN-T), but not specialized transducing phages (D3), acquired entire bacterial 16S rRNA genes. Furthermore, we show that the broad-host-range, generalized transducing phage SN-T is capable of acquiring the 16S rRNA gene from two different genera: Sphaerotilus natans, the host from which SN-T was originally isolated, and Pseudomonas aeruginosa. In sequential infections, SN-T harbored only 16S rRNA gene sequences of the final host as determined by restriction fragment length polymorphism analysis. The frequency of 16S rRNA gene sequences in SN-T populations was determined to be 1 x 10(-9) transductants/PFU. Our findings further implicate transduction in the horizontal transfer of 16S rRNA genes between different species or genera of bacteria.

52. Bille,E., Zahar,J.R. , Perrin,A., Morelle,S., Kriz,P., Jolley,K.A., Maiden,M.C.J., Dervin,C., Nassif,X., Tinsley,C.R. (2005). **A chromosomally integrated bacteriophage in invasive meningococci.** *J. Exp. Med.* 201:1905-1913. **Abstract:** Cerebrospinal meningitis is a feared disease that can cause the death of a previously healthy individual within hours. Paradoxically, the causative agent, *Neisseria meningitidis*, is a common inhabitant of the human nasopharynx, and as such, may be considered a normal, commensal organism. Only in a small proportion of colonized people do the bacteria invade the bloodstream, from where they can cross the blood-brain barrier to cause meningitis. Furthermore, most meningococcal disease is caused by bacteria belonging to only a few of the phylogenetic groups among the large number that constitute the population structure of this genetically variable organism. However, the genetic basis for the differences in pathogenic potential remains elusive. By performing whole genome comparisons of a large collection of meningococcal isolates of defined pathogenic potential we brought to light a meningococcal prophage present in disease-causing bacteria. The phage, of the filamentous family, excises from the chromosome and is secreted from the bacteria via the type IV pilin secretin. Therefore, this element, by spreading among the population, may promote the development of new epidemic clones of *N. meningitidis* that are capable of breaking the normal commensal relationship with humans and causing invasive disease.

53. Blanford,W.J., Brusseau,M.L., Jim Yeh,T.C., Gerba,C.P., Harvey,R. (2005). **Influence of water chemistry and travel distance on bacteriophage PRD-1 transport in a sandy aquifer.** *Water Res.* 39:2345-2357. **Abstract:** Experiments were conducted to evaluate the impact of groundwater chemistry and travel distance on the transport and fate behavior of PRD-1, a bacteriophage employed as a surrogate tracer for pathogenic enteric viruses. The experiments were conducted in the unconfined aquifer at the United States Geological Survey Cape Cod Toxic-Substances Hydrology Research Site in Falmouth, Massachusetts. The transport behavior of bromide (Br(-)) and PRD-1 were evaluated in a sewage-effluent contaminated zone and a shallower uncontaminated zone at this site. Several multilevel sampling devices located along a 13-m transect were used to collect vertically discrete samples to examine longitudinal and vertical variability of PRD-1 retardation and attenuation. The concentration of viable bacteriophage in the aqueous phase decreased greatly during the first few meters of transport. This decrease is attributed to a combination of colloid filtration (attachment) and inactivation. The removal was greater (10(-12) relative recovery) and occurred within the first meter for the uncontaminated zone, whereas it was lesser (10(-9) relative recovery) and occurred over 4m in the contaminated zone. The lesser removal observed for the contaminated zone is attributed to the influence of sorbed and dissolved organic matter, phosphate, and other anions, which are present in higher concentrations in the contaminated zone, on PRD-1 attachment. After the initial decrease, the aqueous PRD-1 concentrations remained essentially constant in both zones for the remainder of the tests (total travel distances of 13 m), irrespective of variations in geochemical properties within and between the two zones. The viable, mobile PRD-1 particles traveled at nearly the rate of bromide, which was used as a non-reactive tracer. The results of this study indicate that a small fraction of viable virus particles may persist in the aqueous phase and travel significant distances in the subsurface environment.

54. Bongiorni,L., Magagnini,M., Armeni,M., Noble,R., Danovaro,R. (2005). **Viral production, decay rates, and life strategies along a trophic gradient in the North Adriatic Sea.** *Appl. Environ. Microbiol.* 71:6644-6650. **Abstract:** Although the relationships between trophic conditions and viral dynamics have been widely explored in different pelagic environments, there have been few attempts at independent estimates of both viral production and decay. In this study, we investigated factors controlling the balance between viral production and decay along a trophic gradient in the north Adriatic basin, providing independent estimates of these variables and determining the relative importance of nanoflagellate grazing and viral life strategies. Increasing trophic conditions induced an increase of bacterioplankton growth rates and of the burst sizes. As a result, eutrophic waters displayed highest rates of viral production, which considerably exceeded observed rates of viral decay (up to 2.9 x 10(9) VLP liter(-1) h(-1)). Viral decay was also higher in eutrophic waters, where it accounted for ca. 40% of viral production, and dropped significantly to 1.3 to 10.7% in oligotrophic waters. These results suggest that viral production and decay rates may not necessarily be balanced in the short term, resulting in a net increase of viruses in the system. In eutrophic waters nanoflagellate grazing, dissolved-colloidal substances, and lysogenic infection were responsible together for the removal of ca. 66% of viral production versus 17% in oligotrophic waters. Our results suggest that different causative agents are primarily responsible for the removal of viruses from the water column in different trophic conditions. Factors other than those considered in the past might shed light on processes responsible for the removal and/or decay of viral particles from the water column.

55. Borysowski,J., Weber-Dabrowska,B., Gorski,A. (2005). **[The potential use of bacteriophages in view of the current antibiotic therapy crisis].** *Polskie Archiwum Medycyny Wewnetrznej* 113:73-78.

56. Brabban,A.D., Hite,E., Callaway,T.R. (2005). **Evolution of foodborne pathogens via temperate bacteriophage-mediated gene transfer.** *Foodborne Pathog. Dis.* 2:287-303. **Abstract:** Temperate bacteriophages have always been central to the evolution of bacteria, although their importance has been consistently underestimated compared to transformation and conjugation. In the last 20 years, as more gene and genome sequences have become available and researchers have more accurately determined bacteriophage populations in the environment, we are gaining a clearer picture of their role in the past and potential role in the future. The transductive and lysogenic capacities of this class of bacteriophages have contributed to the evolution and shaping of emerging foodborne pathogenic bacteria through the dissemination of virulence and antibiotic resistance genes. For example, the genome sequences of *Shigella dysenteriae*, *Escherichia coli* O157:H7, and the Stx encoding bacteriophages demonstrate the critical role bacteriophage-mediated gene transfer events played in the evolution of these high-profile human pathogens. In this review, we describe the basic genetic exchange mechanisms mediated by temperate bacteriophages and how these mechanisms have been central to the dissemination of virulence genes, such as toxins and antibiotics from one species to another (the shiga-like toxins, and multiple antibiotic resistance dissemination in *Salmonella* are used as specific examples). Data demonstrating the role of bacteriophages in the spread of antimicrobial resistance in bacteria, including interspecies transduction, are also presented. That temperate bacteriophages play a role in the on-going evolution of emerging pathogenic bacteria is obvious, but it is also clearly an on-going process with a breadth that must be appreciated as well as studied further if we are to be able to foresee what new challenges will arise to imperil food safety.

57. Braquart-Varnier,C., Greve,P., Felix,C., Martin,G. (2005). **Bacteriophage WO in *Wolbachia* infecting terrestrial isopods.** *Biochem. Biophys. Res. Com.* 337:580-585. **Abstract:** *Wolbachia* are maternally inherited intracellular alpha-proteobacteria that infect a wide range of arthropods. They are associated with a number of different reproductive phenotypes in arthropods and nematodes. In isopod crustacean, *Wolbachia* are responsible for feminization of genetic males in many species, and for cytoplasmic incompatibility in two species. In this paper, we report the first detection of phage WO from *Wolbachia* infecting terrestrial isopods. All *Wolbachia* strains tested in this study were infected with phage WO. Based on the orf7 phage sequence, we identified three different phage sequences in four *Wolbachia* strains. The phage of *Wolbachia* infecting *Armadillidium vulgare* seems to be not active, unlike other phages WO previously described in arthropods.

58. Breitbart,M., Rohwer,F. (2005). **Here a virus, there a virus, everywhere the same virus?** *Trends Microbiol.* 13:278-284. **Abstract:** There are an estimated 10(31) viruses on Earth, most of which are phages that infect bacteria. Metagenomic analyses have shown that environmental viral communities are incredibly diverse. There are an estimated 5000 viral genotypes in 200 liters of seawater and possibly a million different viral genotypes in one kilogram of marine sediment. By contrast, some culturing and molecular studies have found that viruses move between different biomes. Together, these findings suggest that viral diversity could be high on a local scale but relatively limited globally. Also, by moving between environments, viruses can facilitate horizontal gene transfer.

59. Breitbart,M., Rohwer,F., Abedon,S.T. (2005). **Phage ecology and bacterial pathogenesis.** pp. 66-91 In Waldor,M.K., Friedman,D.I., and Adhya,S.L. (eds.), *Phages: Their Role in Bacterial Pathogenesis and Biotechnology*. ASM Press, Washington DC. **Abstract:** [first paragraph] Bacteriophages (phages) are the virues of bacteria. The impact of phages on bacterial pathogenesis may be divided into two major themes, transduction and predation. (i) Phages can move genes, including genes encoding bacterial virulence factors (VFs), between bacteria. This movement can occur via generalized or specialized transduction. (ii) Phages can also virulently attack bacteria. This predation can modify the structure of bacterial communities, selecting for bacteria that are resistant to phage infection. Depending on the nature of a phage infection-e.g., lytic versus lysogenic infection or infection of a bacterial pathogen versus infection of a competitor in the normal flora-phages may either negatively or positively affect bacterial pathogenicity. An understanding of the phage impact on bacterial pathogenesis consequently requires not just knowledge of VF expression but also an understanding of phage transduction and propagation in the environment. In this chapter, we take a phage-centered view of the ecology of the phage-bacterium relationship, looking in particular for unappreciated subtleties that might impact pathogen formation, disease progression, or the phage-induced destruction of bacterial populations.

60. Brion,G., Viswanathan,C., Neelakantan,T.R., Lingireddy,S., Girones,R., Lees,D., Allard,A., Vantarakis,A. (2005). **Artificial neural network prediction of viruses in shellfish.** *Appl. Environ. Microbiol.* 71:5244-5253.

Abstract: A database was probed with artificial neural network (ANN) and multivariate logistic regression (MLR) models to investigate the efficacy of predicting PCR-identified human adenovirus (ADV), Norwalk-like virus (NLV), and enterovirus (EV) presence or absence in shellfish harvested from diverse countries in Europe (Spain, Sweden, Greece, and the United Kingdom). The relative importance of numerical and heuristic input variables to the ANN model for each country and for the combined data was analyzed with a newly defined relative strength effect, which illuminated the importance of bacteriophages as potential viral indicators. The results of this analysis showed that ANN models predicted all types of viral presence and absence in shellfish with better precision than MLR models for a multicountry database. For overall presence/absence classification accuracy, ANN modeling had a performance rate of 95.9%, 98.9%, and 95.7% versus 60.5%, 75.0%, and 64.6% for the MLR for ADV, NLV, and EV, respectively. The selectivity (prediction of viral negatives) was greater than the sensitivity (prediction of viral positives) for both models and with all virus types, with the ANN model performing with greater sensitivity than the MLR. ANN models were able to illuminate site-specific relationships between microbial indicators chosen as model inputs and human virus presence. A validation study on ADV demonstrated that the MLR and ANN models differed in sensitivity and selectivity, with the ANN model correctly identifying ADV presence with greater precision.

61. Brnakova,Z., Farkasovska,J., Godany,A. (2005). **The use of bacteriophages in eliminating polyresistant strains of *Staphylococcus aureus* and *Streptococcus agalactiae*.** *Folia Microbiol (Praha)* 50:187-194. **Abstract:** Temperate bacteriophages were induced in and released from isolates of *Staphylococcus aureus* and *Streptococcus agalactiae* using mitomycin C. Various specific indicator cultures were tested for providing clear plaques after phage infection. Specific lytic mixture of bacteriophages was prepared using the induced, modified and laboratory variants of phages. Under laboratory conditions, the mixture eliminated all isolates from the tested collection of microorganisms. The restriction barrier of some bacterial isolates to bacteriophage infection was overcome either by UV irradiation or in vitro modification of bacteriophage DNA with specific methyltransferases. Conjugative R plasmids, capable of replication in G+ and G- bacteria, were detected and isolated from *S. aureus* and *S. agalactiae* antibiotic-resistant strains.

62. Brockhurst,M.A., Buckling,A., Rainey,P.B. (2005). **The effect of a bacteriophage on diversification of the opportunistic bacterial pathogen, *Pseudomonas aeruginosa*.** *Proc. Roy. Soc. Lond. B* 272:1385-1391. **Abstract:** *Pseudomonas aeruginosa* is an opportunistic human pathogen that colonizes the lungs of cystic fibrosis (CF) patients. CF lungs often contain a diverse range of *P. aeruginosa* phenotypes, some of which are likely to contribute to the persistence of infection, yet the causes of diversity are unclear. While the ecological heterogeneity of the lung environment and therapeutic regimes are probable factors, a role for parasitic bacteriophage cannot be ruled out. Parasites have been implicated as a key ecological variable driving the evolution of diversity in host populations. PP7 drove cycles of morphological diversification in host populations of *P. aeruginosa* due to the de novo evolution of small-rough colony variants that coexisted with large diffuse colony morph bacteria. In the absence of phage, bacteria only displayed the large diffuse colony morphology of the wild-type. Further assays revealed there to be two distinct types of resistant bacteria; these had very different ecological phenotypes, yet each carried a cost of resistance.

63. Brookes,J.D., Hipsey,M.R., Burch,M.D., Regel,R.H., Linden,L.G., Ferguson,C.M., Antenucci,J.P. (2005). **Relative value of surrogate indicators for detecting pathogens in lakes and reservoirs.** *Environ. Sci. Technol.* 39:8614-8621. **Abstract:** This study investigated the relative behavior of pathogens, fecal indicator organisms, and particles of varying size during transport through a reservoir following a storm event inflow in Myponga Reservoir, South Australia. During the inflow, samples were collected from the river and at various locations within the reservoir to determine the fate and transport of microroganisms as they progressed through the water body. Microbiological analysis included the indicator organisms *Escherichia coli*, enterococci, *Clostridium perfringens*, aerobic spores, and somatic coliphages, the protozoan pathogens *Cryptosporidium* spp. and *Giardia* spp., and the potential physical surrogates of pathogen contamination including particle size and turbidity. Of the microbial indicator groups, *C. perfringens* spores were the most highly correlated with *Cryptosporidium* spp. concentrations (Spearman Rho = 0.58), closely followed by enterococci (Spearman Rho = 0.57). *Cryptosporidium* spp. oocysts were predominantly associated with small sized particles (range of 14.3-27.7 microm). All of the microbial indicator groups tested were associated with larger sized particle ranges (> 63.3 microm) except *C. perfringens* spores which were associated with particles in the size range of 45.5-63.3 microm. Although indicators may rank correlate with *Cryptosporidium* spp., the variation in settling rates of different microorganisms has significant implications for the use of surrogates to estimate pathogen attenuation

within reservoirs. For example, concentrations of *Cryptosporidium* spp. oocysts were reduced by a factor of 3 on reaching the dam wall, whereas enterococci were reduced by a factor of 10.

64. Brussow,H. (2005). **Phage therapy: the *Escherichia coli* experience.** *Microbiology (Reading)* 151:2133-2140. **Abstract:** Phages have been proposed as natural antimicrobial agents to fight bacterial infections in humans, in animals or in crops of agricultural importance. Phages have also been discussed as hygiene measures in food production facilities and hospitals. These proposals have a long history, but are currently going through a kind of renaissance as documented by a spate of recent reviews. This review discusses the potential of phage therapy with a specific example, namely *Escherichia coli*.

65. Bruttin,A.**,** Brüssow,H. (2005). **Human volunteers receiving *Escherichia coli* phage T4 orally: a safety test of phage therapy.** *Antimicrob. Agents Chemother.* 49:2874-2878. **Abstract:** Fifteen healthy adult volunteers received in their drinking water a lower *Escherichia coli* phage T4 dose (10(3) PFU/ml), a higher phage dose (10(5) PFU/ml), and placebo. Fecal coliphage was detected in a dose-dependent way in volunteers orally exposed to phage. All volunteers receiving the higher phage dose showed fecal phage 1 day after exposure; this prevalence was only 50% in subjects receiving the lower phage dose. No fecal phage was detectable a week after a 2-day course of oral phage application. Oral phage application did not cause a decrease in total fecal *E. coli* counts. In addition, no substantial phage T4 replication on the commensal *E. coli* population was observed. No adverse events related to phage application were reported. Serum transaminase levels remained in the normal range, and neither T4 phage nor T4-specific antibodies were observed in the serum of the subjects at the end of the study. This is, to our knowledge, the first safety test in the recent English literature which has measured the bioavailability of oral phage in humans and is thus a first step to the rational evaluation of phage therapy for diarrheal diseases.

66. Carlton,R.M.**,** Noordman,W.H.**,** Biswas,B.**,** de Meester,E.D.**,** Loessner,M.J. (2005). **Bacteriophage P100 for control of *Listeria monocytogenes* in foods: genome sequence, bioinformatic analyses, oral toxicity study, and application.** *Regulatory toxicology and pharmacology : RTP* 43:301-312. **Abstract:** *Listeria monocytogenes* is an opportunistic foodborne pathogen responsible for Listeriosis, a frequently fatal infection. This investigation represents a comprehensive approach to characterize and evaluate the broad host range, strictly virulent phage P100, which can infect and kill a majority of *Listeria monocytogenes* strains. First, the complete nucleotide sequence (131,384 basepairs) of the genome of P100 was determined, predicted to encode 174 gene products and 18 tRNAs. Bioinformatic analyses revealed that none of the putative phage proteins has any homologies to genes or proteins of *Listeria* or any other bacteria which are known or suspected to be toxins, pathogenicity factors, antibiotic resistance determinants, or any known allergens. Next, a repeated dose oral toxicity study in rats was conducted, which did not produce any abnormal histological changes, morbidity or mortality. Therefore, no indications for any potential risk associated with using P100 as a food additive were found. As proof of concept, and to determine the parameters for application of P100 to foods sensitive to *Listeria* contamination, surface-ripened red-smear soft cheese was produced. Cheeses were contaminated with low concentrations of *L. monocytogenes* at the beginning of the ripening period, and P100 was applied to the surface during the rind washings. Depending on the time points, frequency and dose of phage applications, we were able to obtain a significant reduction (at least 3.5 logs) or a complete eradication of Listeria viable counts, respectively. We found no evidence for phage resistance in the *Listeria* isolates recovered from samples. Taken together, our results indicate that P100 can provide an effective and safe measure for the control of *Listeria* contamination in foods and production equipment.

67. Casjens,S.R. (2005). **Comparative genomics and evolution of the tailed-bacteriophages.** *Curr. Opin. Mirobiol.* 8:451-458. **Abstract:** The number of completely sequenced tailed-bacteriophage genomes that have been published increased to more than 125 last year. The comparison of these genomes has brought their highly mosaic nature into much sharper focus. Furthermore, reports of the complete sequences of about 150 bacterial genomes have shown that the many prophage and parts thereof that reside in these bacterial genomes must comprise a significant fraction of Earth's phage gene pool. These phage and prophage genomes are fertile ground for attempts to deduce the nature of viral evolutionary processes, and such analyses have made it clear that these phage have enjoyed a significant level of horizontal exchange of genetic information throughout their long histories. The strength of these evolutionary deductions rests largely on the extensive knowledge that has accumulated during intensive study into the molecular nature of the life cycles of a few 'model system' phages over the past half century. Recent molecular studies of phages other than these model system phages have made it clear that much remains to be learnt about the variety of lifestyle strategies utilized by the tailed-phage.

68. Chavan,M., Rafi,H., Wertz,J., Goldstone,C., Riley,M.A. (2005). **Phage associated bacteriocins reveal a novel mechanism for bacteriocin diversification in *Klebsiella*.** *J. Mol. Evol.* 60:546-556. **Abstract:** Ninety-six isolates of *Klebsiella pneumoniae* and *K. oxytoca* were recovered from wild mammals in Australia. 14.6% of these bacteria produce killing phenotypes that suggest the production of bacteriocin toxins. Cloning and sequencing of the gene clusters encoding two of these killing phenotypes revealed two instances of a bacteriocin associated with a bacteriophage gene, the first such genetic organization described. The newly identified klebicin C gene cluster was discovered in both *K. pneumoniae* and *K. oxytoca*. The newly identified klebicin D gene cluster was detected in *K. oxytoca*. Protein sequence comparisons and phylogenetic inference suggest that klebicin C is most closely related to the rRNase group of colicins (such as colicin E4), while klebicin D is most closely related to the tRNase group of colicins (such as colicin D). The klebicin C and D gene clusters have similar genetic and regulatory organizations. In both cases, an operon structure is inferred consisting of a phage-associated open reading frame and klebicin activity and associated immunity genes. This novel bacteriophage/bacteriocin organization may provide a novel mechanism for the generation of bacteriocin diversity in *Klebsiella*.

69. Chen,Y., Golding,I., Sawai,S., Guo,L., Cox,E.C. (2005). **Population fitness and the regulation of *Escherichia coli* genes by bacterial viruses.** *PLoS Biol.* 3:e229. **Abstract:** Temperate bacteriophage parasitize their host by integrating into the host genome where they provide additional genetic information that confers higher fitness on the host bacterium by protecting it against invasion by other bacteriophage, by increasing serum resistance, and by coding for toxins and adhesion factors that help the parasitized bacterium invade or evade its host. Here we ask if a temperate phage can also regulate host genes. We find several different host functions that are down-regulated in lysogens. The pckA gene, required for gluconeogenesis in all living systems, is regulated directly by the principal repressor of many different temperate prophage, the cI protein. cI binds to the regulatory region of pckA, thereby shutting down pckA transcription. The pckA regulatory region has target sequences for many other temperate phage repressors, and thus we suggest that down-regulation of the host pckA pathway increases lysogen fitness by lowering the growth rate of lysogens in energy-poor environments, perhaps as an adaptive response to the host predation system or as an aspect of lysogeny that must be offset by down-regulating pckA.

70. Chen,Z., Schneider,T.D. (2005). **Information theory based T7-like promoter models: classification of bacteriophages and differential evolution of promoters and their polymerases.** *Nucleic Acids Research* 33:6172-6187. **Abstract:** Molecular information theory was used to create sequence logos and promoter models for eight phages of the T7 group: T7, φA1122, T3, φYeO3-12, SP6, K1-5, gh-1 and K11. When these models were used to scan the corresponding genomes, a significant gap in the individual information distribution was observed between functional promoter sites and other sequences, suggesting that the models can be used to identify new T7-like promoters. When a combined 76-site model was used to scan the eight phages, 108 of the total 109 promoters were found, while none were found for other T7-like phages, φKMV, P60, VpV262, SIO1, PaP3, Xp10, P-SSP7 and Ppu40, indicating that these phages do not belong to the T7 group. We propose that the T7-like transcription system, which consists of a phage-specific RNA polymerase and a set of conserved T7-like promoters, is a hallmark feature of the T7 group and can be used to classify T7-like phages. Phylogenetic trees of the T7-like promoter models and their corresponding RNA polymerases are similar, suggesting that the eight phages of the T7 group can be classified into five subgroups. However the SP6-like polymerases have apparently diverged from other polymerases more than their promoters have diverged from other promoters.

71. Cho,M., Chung,H., Choi,W., Yoon,J. (2005). **Different inactivation behaviors of MS-2 phage and *Escherichia coli* in TiO2 photocatalytic disinfection.** *Appl. Environ. Microbiol.* 71:270-275. **Abstract:** Despite a wealth of experimental evidence concerning the efficacy of the biocidal action associated with the TiO(2) photocatalytic reaction, our understanding of the photochemical mechanism of this particular biocidal action remains largely unclear. It is generally accepted that the hydroxyl radical (.OH), which is generated on the surface of UV-illuminated TiO(2), plays the main role. However, our understanding of the exact mode of action of the hydroxyl radical in killing microorganisms is far from complete, and some studies report that other reactive oxygen species (ROS) (H(2)O(2) and O(2).(-), etc.) also play significant roles. In particular, whether hydroxyl radicals remain bound to the surface or diffuse into the solution bulk is under active debate. In order to examine the exact mode of action of ROS in inactivating the microorganism, we tested and compared the levels of photocatalytic inactivation of MS-2 phage and *Escherichia coli* as representative species of viruses and bacteria, respectively. To compare photocatalytic microbial inactivation with the photocatalytic chemical degradation reaction, para-chlorobenzoic acid, which rapidly reacts with a hydroxyl radical with a diffusion-limited rate, was used as a probe compound. Two different hydroxyl radical scavengers, tert-butanol and methanol, and an activator of the bulk phase hydroxyl

radical generation, Fe(2+), were used to investigate their effects on the photocatalytic mode of action of the hydroxyl radical in inactivating the microorganism. The results show that the biocidal modes of action of ROS are very different depending on the specific microorganism involved, although the reason for this is not clear. It seems that MS-2 phage is inactivated mainly by the free hydroxyl radical in the solution bulk but that *E. coli* is inactivated by both the free and the surface-bound hydroxyl radicals. *E. coli* might also be inactivated by other ROS, such as O(2).(-) and H(2)O(2), according to the present results.

72. Chopin,M.C.**,** Chopin,A.**,** Bidnenko,E. (2005). **Phage abortive infection in lactococci: variations on a theme.** *Curr. Opin. Mirobiol.* 8:473-479. **Abstract:** Abortive infection (Abi) systems, also called phage exclusion, block phage multiplication and cause premature bacterial cell death upon phage infection. This decreases the number of progeny particles and limits their spread to other cells allowing the bacterial population to survive. Twenty Abi systems have been isolated in *Lactococcus lactis*, a bacterium used in cheese-making fermentation processes, where phage attacks are of economical importance. Recent insights in their expression and mode of action indicate that, behind diverse phenotypic and molecular effects, lactococcal Abis share common traits with the well-studied *Escherichia coli* systems Lit and Prr. Abis are widespread in bacteria, and recent analysis indicates that Abis might have additional roles other than conferring phage resistance.

73. Comeau,A.M.**,** Krisch,H.M. (2005). **War is peace--dispatches from the bacterial and phage killing fields.** *Curr. Opin. Mirobiol.* 8:488-494. **Abstract:** Large-scale sequence analyses of phage and bacteria have provided new insights into the diverse and multifaceted interactions of these genomes. Such interactions are important because they determine the partitioning of a large fraction of global biomass. Furthermore, the struggle between phage and bacteria has had a significant impact on the evolution of the biosphere. This competition for resources has created an enormous pool of genetic diversity. Eons of horizontal genetic transfer have permitted the entire biosphere to directly benefit from a bargain-basement source of evolutionary innovation.

74. Comeau,A.M.**,** Buenaventura,E.**,** Suttle,C.A. (2005). **A persistent, productive, and seasonally dynamic vibriophage population within Pacific oysters (*Crassostrea gigas*).** *Appl. Environ. Microbiol.* 71:5324-5331. **Abstract:** In an effort to understand the relationship between *Vibrio* and vibriophage populations, abundances of *Vibrio* spp. and viruses infecting *Vibrio parahaemolyticus* (VpVs) were monitored for a year in Pacific oysters and water collected from Ladysmith Harbor, British Columbia, Canada. Bacterial abundances were highly seasonal, whereas high titers of VpVs (0.5 x 10(4) to 11 x 10(4) viruses cm(-3)) occurred year round in oysters, even when *V. parahaemolyticus* was undetectable (< 3 cells cm(-3)). Viruses were not detected (<10 ml(-1)) in the water column. Host-range studies demonstrated that 13 VpV strains could infect 62% of the *V. parahaemolyticus* strains from oysters (91 pairings) and 74% of the strains from sediments (65 pairings) but only 30% of the water-column strains (91 pairings). Ten viruses also infected more than one species among *V. alginolyticus*, V. natriegens, and *V. vulnificus*. As winter approached and potential hosts disappeared, the proportion of host strains that the viruses could infect decreased by approximately 50% and, in the middle of winter, only 14% of the VpV community could be plated on summer host strains. Estimates of virus-induced mortality on *V. parahaemolyticus* indicated that other host species were required to sustain viral production during winter when the putative host species was undetectable. The present study shows that oysters are likely one of the major sources of viruses infecting *V. parahaemolyticus* in oysters and in the water column. Furthermore, seasonal shifts in patterns of host range provide strong evidence that the composition of the virus community changes during winter.

75. Davies-Colley,R.J.**,** Craggs,R.J.**,** Park,J.**,** Sukias,J.P.S.**,** Nagels,J.W.**,** Stott,R. (2005). **Virus removal in a pilot-scale 'advanced' pond system as indicated by somatic and F-RNA bacteriophages.** *Water Sci. Technol.* 51:107-110. **Abstract:** Advanced pond systems (APS), incorporating high-rate ponds, algal settling ponds, and maturation ponds, typically achieve better and more consistent disinfection as indicated by *Escherichia coli* than conventional waste stabilisation ponds. To see whether this superior disinfection extends also to enteric viruses, we studied the removal of somatic phages ('model' viruses) in a pilot-scale APS treating sewage. Measurements through the three aerobic stages of the APS showed fairly good removal of somatic phage in the summer months (2.2 log reduction), but much less effective removal in winter (0.45 log reduction), whereas *E. coli* was removed efficiently (> 4 logs) in both seasons. A very steep depth-gradient of sunlight inactivation of somatic phage in APS pond waters (confined in silica test tubes) is consistent with inactivation mainly by solar UVB wavelengths. Data for F-RNA phage suggests involvement of longer UV wavelengths. These findings imply that efficiency of virus removal in APS will vary seasonally with variation in solar UV radiation.

76. Dickerson,T.J., Kaufmann,G.F., Janda,K.D. (2005). **Bacteriophage-mediated protein delivery into the central nervous system and its application in immunopharmacotherapy.** *Expert Opin. Biol. Ther.* 5:773-781. **Abstract:** Cocaine addiction continues to be a major health and social problem in spite of governmental efforts devoted towards educating the public in the dangers of illicit drug use. A variety of pharmacotherapies and psychosocial programmes have been proposed in an effort to provide a method for alleviating the physical and psychological symptoms of cocaine abuse. Unfortunately, these methods have been met with limited success, illustrating a critical need for new effective approaches for the treatment of cocaine addiction. The authors have recently disclosed an alternative cocaine abuse treatment strategy using intranasal administration of an engineered filamentous bacteriophage displaying cocaine-sequestering antibodies on its surface. These phage particles are an effective vector for central nervous system penetration and are capable of binding cocaine, thereby blocking its behavioural effects in a rodent model.

77. El Shibiny,A., Connerton,P.L., Connerton,I.F. (2005). **Enumeration and diversity of campylobacters and bacteriophages isolated during the rearing cycles of free-range and organic chickens.** *Appl. Environ. Microbiol.* 71:1259-1266. **Abstract:** Campylobacters and *Campylobacter*-specific bacteriophages were isolated and enumerated during the rearing cycle of free-range (56 days) and organic chickens (73 days) at 3-day intervals from hatching until slaughter. In both flocks *Campylobacter jejuni* was the initial colonizer but *Campylobacter coli* was detected more frequently from 5 weeks of age. The diversity of the *Campylobacter* isolates was examined by pulsed-field gel electrophoresis of SmaI-digested genomic DNA and antimicrobial resistance typing. Bacteriophages were isolated from 51% (19 of 37 birds) of *Campylobacter*-positive organic birds (log10 2.5 to log10 5.7 PFU/g of cecal contents). The bacteriophages were all typical group III Campylobacter bacteriophages in terms of genomic size but could be characterized in terms of their host range and placed into five different groups. In contrast to the organic birds, anti-*Campylobacter* activity (bacteriocin-like) was observed in 26% (10 of 38 birds) of *Campylobacter*-positive free-range birds, and only one bacteriophage was isolated. Appearance of either bacteriophages or anti-*Campylobacter* activity was associated with changes in the levels of colonization and the predominant genotypes and species isolated. The frequency and potential influence of naturally occurring bacteriophages and/or inhibitory substances on the diversity and fluctuations of populations of campylobacters have not previously been reported in either free-range or organic chickens.

78. Faruque,S.M., Naser,I.B., Islam,M.J., Faruque,A.S.G., Ghosh,A.N., Nair,G.B., Sack,D.A., Mekalanos,J.J. (2005). **Seasonal epidemics of cholera inversely correlate with the prevalence of environmental cholera phages.** *Proc. Natl. Acad. Sci. USA* 102:1702-1707. **Abstract:** The relationship among (i) the local incidence of cholera, (ii) the prevalence in the aquatic environment of *Vibrio cholerae*, and (iii) bacterial viruses that attack potentially virulent O1 and O139 serogroup strains of this organism (cholera phages) was studied in Dhaka, Bangladesh. Over nearly a 3-year period, we found that significantly more environmental water samples contained either a phage or a phage-susceptible *V. cholerae* strain than both ($P < 0.00001$). The number of cholera patients varied seasonally during this period and frequently coincided with the presence of pathogenic V. cholerae strains in water samples that otherwise lacked detectable cholera phages. Interepidemic periods were characterized by water samples containing cholera phages but no viable bacteria. Our data support the conclusion that cholera phages can influence cholera seasonality and may also play a role in emergence of new *V. cholerae* pandemic serogroups or clones.

79. Faruque,S.M., Islam,M.J., Ahmad,Q.S., Faruque,A.S.G., Sack,D.A., Nair,G.B., Mekalanos,J.J. (2005). **Self-limiting nature of seasonal cholera epidemics: Role of host-mediated amplification of phage.** *Proc. Natl. Acad. Sci. USA* 102:6119-6124. **Abstract:** Phage predation of Vibrio cholerae has recently been reported to be a factor that influences seasonal epidemics of cholera in Bangladesh. To understand more about this phenomenon, we studied the dynamics of the *V. cholerae*-phage interaction during a recent epidemic in Dhaka. Because the outbreak strain causing this epidemic was resistant to multiple antibiotics, including streptomycin, we used a selective medium containing streptomycin to monitor accurately the abundance of this strain in the environment. The changing prevalence in the environment of the epidemic *V. cholerae* O1 strain and a particular lytic cholera phage (JSF4) to which it was sensitive was measured every 48-72 h for 17 weeks. We also monitored the incidence of phage excretion in stools of 387 cholera patients during the epidemic. The peak of the epidemic was preceded by high *V. cholerae* prevalence in the environment and was followed by high JSF4 phage levels as the epidemic ended. The buildup to the phage peak in the environment coincided with increasing excretion of the same phage in the stools of cholera patients. These results suggest that patients toward the end of the epidemic ingested both JSF4 phage and the outbreak *V. cholerae* strain. Host-mediated phage amplification during the cholera epidemic likely contributed to increased environmental phage abundance, decreased load of

environmental *V. cholerae* and, hence, the collapse of the epidemic. Thus, in vivo phage amplification in patients and subsequent phage predation in the environment may explain the self-limiting nature of seasonal cholera epidemics in Bangladesh.

80. Filee,J., Tetart,F., Suttle,C.A., Krisch,H.M. (2005). **Marine T4-type bacteriophages, a ubiquitous component of the dark matter of the biosphere.** *Proc. Natl. Acad. Sci. USA* 102:12471-12476. **Abstract:** Tailed bacteriophages are the most abundant biological entities in marine environments. However, most of these marine phages are uncharacterized because few of their hosts have been cultivated. To learn more about such phages, we designed a set of degenerate PCR primers for phage T4 g23, which encodes the major capsid protein in all of the T4-type phages, an important family of the tailed phage. These primers were used to amplify g23-related sequences from diverse marine environments (fjords and bays of British Columbia, the eastern Gulf of Mexico, and the western Arctic Ocean) revealing a remarkable level of molecular diversity, which in some cases was correlated with morphological variation of the virions. Phylogenetic analysis showed that although some of these sequences were closely related to well studied subgroups of the T4-type phage, such as the T-evens, the majority of them belong to five previously uncharacterized subgroups. These data indicate that the host range of T4-type phages is much broader than previously imagined and that the laboratory isolate T4 belongs to a phage family that is extraordinarily widespread and diverse in the biosphere.

81. Fiorentin,L., Vieira,N.D., Barioni,W.J. (2005). **Oral treatment with bacteriophages reduces the concentration of *Salmonella Enteritidis* PT4 in caecal contents of broilers.** *Avian pathology : journal of the W. V. P. A* 34:258-263. **Abstract:** Bacteriophages isolated from free-range chickens were tested as a therapeutic agent for reducing the concentration of *Salmonella enterica* serovar Enteritidis phage type 4 (*S. Enteritidis* PT4) in caeca of broilers. One-day-old broilers infected with *S. Enteritidis* PT4 by a seeder bird method were orally treated on the seventh day of age with a mixture of 10(11) plaque-forming units of each of three bacteriophages. Five days after treatment the bacteriophage-treated group showed a reduction of 3.5 orders of magnitude on colony-forming units of *S. Enteritidis* PT4 per gram of caecal content. Samples collected at 10, 15, 20 and 25 days after treatment revealed that treated birds still had lower colony-forming units of *S. Enteritidis* PT4 per gram of caecal content. These data gave us compelling evidence that a mixture of bacteriophages may be efficacious in reducing *S. Enteritidis* PT4 concentration in broilers' caeca and therefore reducing contamination of poultry products by this food-borne pathogen.

82. Fokine,A., Leiman,P.G., Shneider,M.M., Ahvazi,B., Boeshans,K.M., Steven,A.C., Black,L.W., Mesyanzhinov,V.V., Rossmann,M.G. (2005). **Structural and functional similarities between the capsid proteins of bacteriophages T4 and HK97 point to a common ancestry.** *Proc. Natl. Acad. Sci. USA* 102:7163-7168. **Abstract:** Gene product (gp) 24 of bacteriophage T4 forms the pentameric vertices of the capsid. Using x-ray crystallography, we found the principal domain of gp24 to have a polypeptide fold similar to that of the HK97 phage capsid protein plus an additional insertion domain. Fitting gp24 monomers into a cryo-EM density map of the mature T4 capsid suggests that the insertion domain interacts with a neighboring subunit, effecting a stabilization analogous to the covalent crosslinking in the HK97 capsid. Sequence alignment and genetic data show that the folds of gp24 and the hexamer-forming capsid protein, gp23*, are similar. Accordingly, models of gp24* pentamers, gp23* hexamers, and the whole capsid were built, based on a cryo-EM image reconstruction of the capsid. Mutations in gene 23 that affect capsid shape map to the capsomer's periphery, whereas mutations that allow gp23 to substitute for gp24 at the vertices modify the interactions between monomers within capsomers. Structural data show that capsid proteins of most tailed phages, and some eukaryotic viruses, may have evolved from a common ancestor.

83. Gnanou Besse,N., Audinet,N., Kerouanton,A., Colin,P. , Kalmokoff,M. (2005). **Evolution of *Listeria* populations in food samples undergoing enrichment culturing.** *Int. J. Food Microbiol.* 104:123-134. **Abstract:** The isolation of *Listeria monocytogenes* from food is carried out using a double enrichment. It is believed that the double enrichment can allow the overgrowth of *Listeria* innocua in samples where both species are present. In this study, we have evaluated the impact of overgrowth between *Listeria* species and strains during each step of the enrichment process. The effect of factors minimizing interactions between strains or phage inhibitory effects has also been estimated. In an artificially contaminated food undergoing enrichment, overgrowth could result from competitive interactions between *Listeria* spp. resulting from the production of bacteriocins and bacteriophage at high initial contamination levels (>10(4) cfu/g), but not at lower levels (50-100 cfu/g) as generally found in contaminated foods. At high levels of inoculation, the competitive effect could be reduced by solidification of the selective broths, to limit the diffusion of the inhibitors. Overgrowth resulting from differences in growth rate occurred independent of the initial contamination level. However, in naturally contaminated foods undergoing enrichment, there were no

absolute correlations between growth rates or inhibitory profiles in terms of strain evolution during enrichment. In fact, *Listeria* strains which were predominant in the original sample in most cases remained the dominant strains at the end of the enrichment, although the relative proportion of any given strain could change significantly over the enrichment process. Additional factors which have yet to be identified impact on the evolution of *Listeria* in the two-step enrichment process. Analysis of strain evolution in eight naturally contaminated foods has indicated that the second enrichment step in Fraser broth can be reduced from 48 to 24 h without impacting on the recovery of *L. monocytogenes*. Our limited survey of naturally contaminated foods also demonstrated that maximum recovery of *L. monocytogenes* and other *Listeria* strains was found following 24 h incubation in 1/2 Fraser Broth. This finding suggests that it may be possible to shorten the current two-step isolation method further without reducing method sensitivity.

84. Goh,S.**,** Riley,T.V.**,** Chang,B.J. (2005). **Isolation and characterization of temperate bacteriophages of *Clostridium difficile*.** *Appl. Environ. Microbiol.* 71:1079-1083. **Abstract:** The lack of information on bacteriophages of *Clostridium difficile* prompted this study. Three of 56 clinical *C. difficile* isolates yielded double-stranded DNA phages ϕC2, ϕC5, ϕC6, and ϕC8 upon induction. Superinfection and DNA analyses revealed relatedness between the phages, while partial sequencing of ϕC2 showed nucleotide homology to the sequenced C. difficile strain CD630.

85. Greer,G.G. (2005). **Bacteriophage control of foodborne bacteria.** *J. Food Prot.* 68:1102-1111. **Abstract:** Bacteriophages are measurable components of the natural microflora in the food production continuum from the farm to the retail outlet. Phages are remarkably stable in these environments and are readily recovered from soil, sewage, water, farm and processing plant effluents, feces, and retail foods. Purified high-titer phage lysates have been used for the species-specific control of bacteria during the pre- and postharvest phases of food production and storage. For example, the inhibition of the phytopathogens *Erwinia amylovara* and *Xanthomonas campestris* has reduced the incidence of diseases such as fire blight in apples and bacterial spot of tomato and peaches. Research on preslaughter treatment of food animals has demonstrated phage control of salmonellosis in chickens, enteropathogenic *Escherichia coli* infections in calves, piglets, and lambs, and *E. coli* O157:H7 shedding by beef cattle. Phages have also been applied to control the growth of pathogens such as *Listeria monocytogenes*, *Salmonella*, and *Campylobacter jejuni* in a variety of refrigerated foods such as fruit, dairy products, poultry, and red meats. Phage control of spoilage bacteria (e.g., *Pseudomonas* spp. and *Brochothrix thermosphacta*) in raw chilled meats can result in a significant extension of storage life. Phage biocontrol strategies for food preservation have the advantages of being self-perpetuating, highly discriminatory, natural, and cost-effective. Some of the drawbacks of biopreservation with phages are a limited host range, the requirement for threshold numbers of the bacterial targets, phage-resistant mutants, and the potential for the transduction of undesirable characteristics from one bacterial strain to another. Most research to date has involved experimentally infected plants and animals or artificially inoculated foods. This technology must be transferred to the field and to commercial environments to assess the possibility of controlling natural contaminants under more realistic production and processing conditions.

86. Halgasova,N.**,** Majtan,T.**,** Ugorcakova,J.**,** Timko,J. **,** Bukovska,G. (2005). **Resistance of corynebacterial strains to infection and lysis by corynephage BFK 20.** *J. Appl. Microbiol.* 98:184-192. **Abstract:** AIMS: Defence mechanisms of the corynebacterial strains against corynephage BFK 20, which causes lysis of *Brevibacterium flavum* CCM 251. METHODS AND RESULTS: We tested adsorption of the phage BFK 20 to the corynebacterial cell surface. We observed strong adsorption ranging from ca 79 to 93% on the cells of B. flavum ATCC strains, but only ca 76% for *B. flavum* CCM 251. Minor adsorption for *Brevibacterium lactofermentum* BLOB (ca 13%) and no adsorption for *Corynebacterium glutamicum* RM3 were determined. BFK 20 infection had no significant effect on growth and viability of *C. glutamicum* and *B. lactofermentum*, but significantly influenced growth and viability of *B. flavum* ATCC 21127, 21128 and 21474. Cell growth stopped in short time after infection but with no lysis. *Brevibacterium flavum* CCM 251 cell growth was arrested too and lysis occurred. The Southern hybridization confirmed the presence of significant amount of BFK 20 DNA in samples from *B. flavum* CCM 251 and *B. flavum* ATCC strains after BFK 20 infection. Only weak hybridization signal was detected for DNA from infected cells of *B. lactofermentum* BLOB and no signal for *C. glutamicum* RM3. CONCLUSIONS: Based on the above results we suggest presence of a mechanism leading to abortive infection in *B. flavum* ATCC 21127, 21128 and 21474. In *B. lactofermentum* BLOB and *C. glutamicum* RM3 the adsorption barrier is more likely. SIGNIFICANCE AND IMPACT OF THE STUDY: This study increases the knowledge on defence mechanisms of corynebacteria against bacteriophages.

87. Hambly,E.**,** Suttle,C.A. (2005). **The viriosphere, diversity, and genetic exchange within phage communities.** *Curr. Opin. Mirobiol.* 8:444-450. **Abstract:** Natural phage communities are reservoirs of the greatest uncharacterized genetic diversity on Earth. Yet, identical phage sequences can be found in extremely different environments, which implies that there is wide circulation of viral genes among distantly related host populations. Further evidence of genetic exchange among phage and host communities is the presence in phage of genes coding for proteins that are essential for photosynthesis. These observations support the idea that a primary role of host populations in phage ecology and evolution is to serve as vectors for genetic exchange.

88. Harcombe,W.R.**,** Bull,J.J. (2005). **Impact of phages on two-species bacterial communities.** *Appl. Environ. Microbiol.* 71:5254-5259. **Abstract:** A long history of experimental work has shown that addition of bacteriophages to a monoculture of bacteria leads to only a temporary depression of bacterial levels. Resistant bacteria usually become abundant, despite reduced growth rates relative to those of phage-sensitive bacteria. This restoration of high bacterial density occurs even if the phages evolve to overcome bacterial resistance. We believe that the generality of this result may be limited to monocultures, in which the resistant bacteria do not face competition from bacterial species unaffected by the phage. As a simple case, we investigated the impact of phages attacking one species in a two-species culture of bacteria. In the absence of phages, *Escherichia coli* B and *Salmonella enterica* serovar Typhimurium were stably maintained during daily serial passage in glucose minimal medium (M9). When either of two E. coli-specific phages (T7 or T5) was added to the mixed culture, *E. coli* became extinct or was maintained at densities that were orders of magnitude lower than those before phage introduction, even though the *E. coli* densities with phage reached high levels when *Salmonella* was absent. In contrast, the addition of a phage that attacked only *Salmonella* (SP6) led to transient decreases in the bacterial number whether *E. coli* was absent or present. These results suggest that phages can sometimes, although not always, provide long-term suppression of target bacteria.

89. Heineman,R.H.**,** Molineux,I.J.**,** Bull,J.J. (2005). **Evolutionary robustness of an optimal phenotype: re-evolution of lysis in a bacteriophage deleted for its lysin gene.** *J. Mol. Evol.* 61:181-191. **Abstract:** Optimality models are frequently used to create expectations about phenotypic evolution based on the fittest possible phenotype. However, they often ignore genetic details, which could confound these expectations. We experimentally analyzed the ability of organisms to evolve towards an optimum in an experimentally tractable system, lysis time in bacteriophage T7. T7 lysozyme helps lyse the host cell by degrading its cell wall at the end of infection, allowing viral escape to infect new hosts. Artificial deletion of lysozyme greatly reduced fitness and delayed lysis, but after evolution both phenotypes approached wild-type values. Phage with a lysis-deficient lysozyme evolved similarly. Several mutations were involved in adaptation, but most of the change in lysis timing and fitness increase was mediated by changes in gene 16, an internal virion protein not formerly considered to play a role in lysis. Its muralytic domain, which normally aids genome entry through the cell wall, evolved to cause phage release. Theoretical models suggest there is an optimal lysis time, and lysis more rapid or delayed than this optimum decreases fitness. Artificially constructed lines with very rapid lysis had lower fitness than wild-type T7, in accordance with the model. However, while a slow-lysing line also had lower fitness than wild-type, this low fitness resulted at least partly from genetic details that violated model assumptions.

90. Higgins,J.P.**,** Higgins,S.E.**,** Guenther,K.L.**,** Huff,W.**,** Donoghue,A.M.**,** Donoghue,D.J.**,** Hargis,B.M. (2005). **Use of a specific bacteriophage treatment to reduce *Salmonella* in poultry products.** *Poult Sci* 84:1141-1145. **Abstract:** Bacteriophages represent a group of viruses that specifically infect and replicate in bacteria and could potentially be used to reduce recovery of *Salmonella* from poultry carcasses. Bacteriophages were isolated from municipal wastewater in the presence of *Salmonella enteritidis* phage type 13A (SE). In the first 2 experiments, commercially processed broiler carcass rinse water was pooled and divided. The addition of 10(10) pfu/mL of a single bacteriophage (PHL 4) with selected concentrations of SE reduced ($P < 0.05$) frequency of SE recovered as compared with the control rinse water sample. In experiments 3 and 4, broiler carcasses were intentionally inoculated with SE, sprayed with selected concentrations of PHL 4, and rinsed for SE enrichment and isolation. Application of 5.5 mL of 10(8) or 10(10) pfu/mL of PHL 4 reduced ($P < 0.05$) the frequency of SE recovery as compared with controls. In experiments 5 and 6, commercially processed turkeys were rinsed with water containing 72 wild-type bacteriophages isolated against SE, which were amplified in SE, or the *Salmonella* isolated antemortem from drag swabs from the flock selected for in-plant treatment, or a combination of bacteriophages amplified by each bacterial host. All bacteriophage treatments reduced ($P < 0.05$) frequency of *Salmonella* recovery as compared with controls. Sufficient concentrations of an appropriate bacteriophage, or a bacteriophage mixture, can significantly reduce recoverable Salmonella from carcass rinses.

91. Hornak,K., Masin,M., Jezbera,J., Bettarel,Y., Nedoma,J., Sime-Ngando,T., Simek,K. (2005). **Effects of decreased resource availability, protozoan grazing and viral impact on a structure of bacterioplankton assemblage in a canyon-shaped reservoir.** *FEMS Microbiol. Ecol.* 52:315-327. **Abstract:** We conducted a transplant experiment to elucidate the effects of different levels of grazing pressure, nutrient availability, especially phosphorus, and the impact of viruses on the changes in the structure of bacterioplankton assemblage in a meso-eutrophic reservoir. A sample taken from the nutrient-rich inflow part of the reservoir was size-fractionated and incubated in dialysis bags in both inflow and dam area. The structure of bacterial assemblage was examined by fluorescence *in situ* hybridization using oligonucleotide probes with different levels of specificity. In terms of the relative proportions of different bacterial groups, we found very few significant changes in the bacterioplankton composition after transplanting the treatments to the nutrient-poor dam area. However, we observed marked shifts in morphology and biomass towards the development of filaments, flocs and "vibrio-like" morphotypes of selected probe-defined groups of bacteria induced by increased grazing pressure. Despite the very high abundances of viruses in all the treatments, their effects on bacterioplankton were rather negligible.

92. Huff,W.E., Huff,G.R. , Rath,N.C., Balog,J.M., Donoghue,A.M. (2005). **Alternatives to antibiotics: utilization of bacteriophage to treat colibacillosis and prevent foodborne pathogens.** *Poult Sci* 84:655-659. **Abstract:** Bacteriophages are viruses that infect and kill bacteria. Bacteriophage do not infect animal and plant cells, which makes them a potentially safe alternative to antibiotics. We have been conducting research on the efficacy of bacteriophage to prevent and treat colibacillosis in poultry. Bacteriophages that were lytic to a non-motile, serotype 02 isolate of *Escherichia coli* were isolated from municipal wastewater treatment plants and poultry processing plants. This *E. coli* isolate is pathogenic to poultry, causing severe respiratory and systemic infections. Two bacteriophage isolates were selected for use in studies designed to determine the efficacy of these bacteriophage to prevent and treat severe colibacillosis in poultry. Colibacillosis was induced by injecting 6 x 10(4) cfu of *E. coli* into the thoracic air sac when birds were 1 wk of age. Initial studies demonstrated that mortality was significantly reduced from 85 to 35% when the challenge culture was mixed with equal titers of bacteriophage, and the birds were completely protected when the challenge culture was mixed with 10 pfu of bacteriophage. In subsequent studies, we have shown that an aerosol spray of bacteriophage given to birds prior to this *E. coli* challenge could significantly reduce mortality even when given 3 d prior to the *E. coli* challenge. Our research on treating colibacillosis in poultry has demonstrated that an intramuscular injection of bacteriophage given 24 or 48 h after the birds were challenged rescued the birds from this severe *E. coli* infection. We have demonstrated that bacteriophage can be used to prevent and treat colibacillosis in poultry and may provide an effective alternative to antibiotic use in animal production.

93. Islam,M.S., Rahman,M.Z., Khan,S.I., Mahmud,Z.H., Ramamurthy,T., Nair,G.B., Sack,R.B., Sack,D.A. (2005). **Organization of the CTX prophage in environmental isolates of *Vibrio mimicus*.** *Microbiology and Immunology* 49:779-784. **Abstract:** The organization of the CTX prophage in environmental strains of *Vibrio mimicus* was investigated. Sixteen hundred non-sucrose fermenting vibrios were examined for ctx gene by hybridization. Out of 1,600 isolates, 6 *V. mimicus* isolates contained ctxA gene. The organization of CTX prophage was determined by RFLP using ctxA probe. The CTX prophage integrated at a single site in *V. mimicus* genome which was present as a single copy flanked by at least a single RS element. Ribotype pattern revealed that a particular clone of *V. mimicus* acquired the CTXPhi in the aquatic environment. This study demonstrated that *V. mimicus* could act as a reservoir of CTXPhi in the aquatic environment.

94. Jacquet,S., Domaizon,I., Personnic,S., Pradeep Ram,A.S., Hedal,M., Duhamel,S., Sime-Ngando,T. (2005). **Estimates of protozoan- and viral-mediated mortality of bacterioplankton in Lake Bourget (France).** *Freshw. Biol.* 50:627-645. **Abstract:** 1. We performed three, 1-week *in situ* experiments in March-April (expt 1), May (expt 2) and August (expt 3) 2003 in order to assess protozoan and virus-induced mortality of heterotrophic bacteria in a French lake. Viral and bacterial abundances were obtained using flow cytometry (FCM) while protozoa were counted using epifluorescence microscopy (EFM). ¶ 2. A dilution approach, applied to pretreated grazer-free samples, allowed us to estimate that viral lysis could be responsible for 60% (expt 1), 35% (expt 2) and 52% (expt 3) of daily heterotrophic bacterial mortality. Flagellate (both mixotrophic and heterotrophic) grazing in untreated samples, was responsible for 56% (expt 1), 63% (expt 2) and 18% (expt 3) of daily heterotrophic bacteria removal. ¶ 3. These results therefore suggest that both viral lysis and flagellate grazing had a strong impact on bacterial mortality, and this impact varied seasonally. ¶ 4. From parallel transmission electron microscopy (TEM) analysis, we found that the burst size (i.e. the number of viruses potentially released per lysed cell) ranged from nine to 25 (expt 1), 10 to 35 (expt 2) and eight to 25 (expt 3). The percentage of infected

heterotrophic bacteria was 5.7% (expt 1), 3.4% (expt 2) and 5.7% (expt 3) so that the calculated percentage of bacterial mortality induced by viruses was 6.3% (expt 1), 3.7% (expt 2) and 6.3% (expt 3). ¶ 5. It is clear that the dilution-FCM and TEM methods yielded different estimates of viral impact, although both methods revealed an increased impact of viruses during summer.

95. Jikia,D., Chkhaidze,N., Imedashvili,E., Mgaloblishvili,I., Tsitlanadze,G., Katsarava,R., Glenn Morris,J.J., Sulakvelidze,A. (2005). **The use of a novel biodegradable preparation capable of the sustained release of bacteriophages and ciprofloxacin, in the complex treatment of multidrug-resistant *Staphylococcus aureus*-infected local radiation injuries caused by exposure to Sr90.** *Clinical and experimental dermatology* 30:23-26. **Abstract:** In December 2001, three Georgian lumberjacks from the village of Lia were exposed to a strontium-90 source from two Soviet-era radiothermal generators they found near their village. In addition to systemic effects, two of them developed severe local radiation injuries which subsequently became infected with *Staphylococcus aureus*. After hospitalization in Tbilisi, Georgia, the patients were treated with various medications, including antibiotics and topical ointments; however, wound healing was only moderately successful, and their *S. aureus* infection could not be eliminated. Approximately 1 month after hospitalization, treatment with PhagoBioDerm (a wound-healing preparation consisting of a biodegradable polymer impregnated with ciprofloxacin and bacteriophages) was initiated. Purulent drainage stopped within 2-7 days. Clinical improvement was associated with rapid (7 days) elimination of the aetiologic agent, a strain of *S. aureus* resistant to many antibiotics (including ciprofloxacin), but susceptible to the bacteriophages contained in the PhagoBioDerm preparation.

96. John,D.E., Rose,J.B. (2005). **Review of factors affecting microbial survival in groundwater.** *Environ. Sci. Technol.* 39:7345-7356. **Abstract:** This review quantitatively examines a number of published studies that evaluated survival and inactivation of public-health-related microorganisms in groundwater. Information from reviewed literature is used to express microbial inactivation in terms of log10 decline per day for comparison to other studies and organisms. The geometric mean value for inactivation rates for coliphage, poliovirus, echovirus, coliform bacteria, enterococci, and Salmonella spp. were similar at approximately 0.07-0.1 log10 day(-1), while geometric mean inactivation rates for hepatitis A virus, coxsackievirus, and phage PRD-1 were somewhat less at 0.02-0.04 log10 day(-1). Viruses show a temperature dependency with greater inactivation at greater temperatures; however this occurs largely at temperatures greater than 20 degrees C. Coliform bacteria die off in groundwater does not show the temperature dependency that viruses show, likely indicating a complex interplay of inactivation and reproduction subject to influences from native groundwater organisms, temperature, and water chemistry. The presence of native microorganisms seems to negatively impact *E. coli* survival more so than viruses, but in most cases, nonsterile conditions led to a greater inactivation for viruses also. The effect of attachment to solid surfaces appears to be virus-type-dependent, with PRD-1 more rapidly inactivated as a result of attachment and hepatitis A and poliovirus survival prolonged when attached.

97. Kalantri,S., Pai,M., Pascopella,L., Riley,L., Reingold,A. (2005). **Bacteriophage-based tests for the detection of *Mycobacterium tuberculosis* in clinical specimens: a systematic review and meta- analysis.** *BMC Infect. Dis.* 5:59. **Abstract:** BACKGROUND: Sputum microscopy, the most important conventional test for tuberculosis, is specific in settings with high burden of tuberculosis and low prevalence of non tuberculous mycobacteria. However, the test lacks sensitivity. Although bacteriophage-based tests for tuberculosis have shown promising results, their overall accuracy has not been systematically evaluated. METHODS: We did a systematic review and meta-analysis of published studies to evaluate the accuracy of phage-based tests for the direct detection of *M. tuberculosis* in clinical specimens. To identify studies, we searched Medline, EMBASE, Web of science and BIOSIS, and contacted authors, experts and test manufacturers. Thirteen studies, all based on phage amplification method, met our inclusion criteria. Overall accuracy was evaluated using forest plots, summary receiver operating (SROC) curves, and subgroup analyses. RESULTS: The data suggest that phage-based assays have high specificity (range 0.83 to 1.00), but modest and variable sensitivity (range 0.21 to 0.88). The sensitivity ranged between 0.29 and 0.87 among smear-positive, and 0.13 to 0.78 among smear-negative specimens. The specificity ranged between 0.60 and 0.88 among smear-positive and 0.89 to 0.99 among smear-negative specimens. SROC analyses suggest that overall accuracy of phage-based assays is slightly higher than smear microscopy in direct head-to-head comparisons. CONCLUSION: Phage-based assays have high specificity but lower and variable sensitivity. Their performance characteristics are similar to sputum microscopy. Phage assays cannot replace conventional diagnostic tests such as microscopy and culture at this time. Further research is required to identify methods that can enhance the sensitivity of phage-based assays without compromising the high specificity.

98. Kao,C.C., Green,S., Stein,B., Golden,S.S. (2005). **Diel infection of a cyanobacterium by a contractile bacteriophage.** *Appl. Environ. Microbiol.* 71:4276-4279. **Abstract:** Light was found to strongly influence the infection of a freshwater cyanobacterium (*Synechococcus elongatus* PCC 7942) by a contractile DNA phage named AS-1. Phage progeny production was correlated with the amount of light in the laboratory and occurred in a diel pattern under natural light. At least one effect of light on AS-1 infection is at the level of adsorption.

99. Karlsson,F., Malmborg-Hager,A.C., Albrekt,A.S., Borrebaeck,C.A.K. (2005). **Genome-wide comparison of phage M13-infected vs. uninfected *Escherichia coli*.** *Can. J. Microbiol.* 51:29-35. **Abstract:** To identify *Escherichia coli* genes potentially regulated by filamentous phage infection, we used oligonucleotide microarrays. Genome-wide comparison of phage M13-infected and uninfected *E. coli*, 2 and 20 min after infection, was performed. The analysis revealed altered transcription levels of 12 *E. coli* genes in response to phage infection, and the observed regulation of phage genes correlated with the known *in vivo* pattern of M13 mRNA species. Ten of the 12 host genes affected could be grouped into 3 different categories based on cellular function, suggesting a coordinated response. The significantly upregulated genes encode proteins involved in reactions of the energy-generating phosphotransferase system and transcription processing, which could be related to phage transcription. No genes belonging to any known *E. coli* stress response pathways were scored as upregulated. Furthermore, phage infection led to significant downregulation of transcripts of the bacterial genes *gadA*, *gadB, hdeA, gadE, slp,* and *crl*. These downregulated genes are normally part of the host stress response mechanisms that protect the bacterium during conditions of acid stress and stationary phase transition. The phage-infected cells demonstrated impaired function of the oxidative and the glutamate-dependent acid resistance systems. Thus, global transcriptional analysis and functional analysis revealed previously unknown host responses to filamentous phage infection.

100. Kurtboke,D.I. (2005). **Actinophages as indicators of actinomycete taxa in marine environments.** *Antonie van Leeuwenhoek J. Microbiol.* 87:19-28. **Abstract:** It is necessary to continue to screen for new metabolites and evaluate the potential of less known and new bacterial taxa so that new and improved compounds for future use against drug-resistant bacteria or for chemical modification may be developed. There has been considerable interest in the detection and identification of marine microorganisms since they have been reported to produce bioactive compounds ranging from antitumour to antibacterial and antiviral agents. In this study, an improved technique that involves the exploitation of marine actinophages as indicators of the marine actinomycete taxa and uses marine bacteriophages as tools to reduce the numbers of common marine bacteria, which impedes the growth of rare actinomycetes on isolation plates, has been applied. This technique reduced the numbers of colony forming units of unwanted bacteria on isolation plates and hence increased the chances of detecting novel marine actinomycete genera for isolation and subsequent screening for antiviral activity.

101. Lacroix-Gueu,P., Briandet,R., leveque-Fort,S., Bellon-Fontaine,M.N., Fountaine-Aupart,M.P. (2005). **In situ measurements of viral particles diffusion inside mucoid biofilms.** *C. R. Biol.* 328:1065-1072. **Abstract:** Fluorescence correlation spectroscopy (FCS) under two-photon excitation was used successfully to characterize the diffusion properties of model virus particles (bacteriophages) in bacterial biofilm of *Stenotrophonas maltophilia*. The results are compared to those obtained with fluorescent latex beads used as a reference. The FCS data clearly demonstrated the possibility for viral particles to penetrate inside the exopolymeric matrix of mucoid biofilms, and hence to benefit from its protective effect toward antimicrobials (antibiotics and biocides). Microbial biofilms should hence be considered as potential reservoirs of pathogenic viruses, and are probably responsible for numerous persistent viral infections.

102. Langmark,J., Storey,M.V., Ashbolt,N.J., Stenstrom,T.A. (2005). **Accumulation and fate of microorganisms and microspheres in biofilms formed in a pilot-scale water distribution system.** *Appl. Environ. Microbiol.* 71:706-712. **Abstract:** The accumulation and fate of model microbial "pathogens" within a drinking-water distribution system was investigated in naturally grown biofilms formed in a novel pilot-scale water distribution system provided with chlorinated and UV-treated water. Biofilms were exposed to 1-mum hydrophilic and hydrophobic microspheres, *Salmonella* bacteriophages 28B, and *Legionella pneumophila* bacteria, and their fate was monitored over a 38-day period. The accumulation of model pathogens was generally independent of the biofilm cell density and was shown to be dependent on particle surface properties, where hydrophilic spheres accumulated to a larger extent than hydrophobic ones. A higher accumulation of culturable legionellae was measured in the chlorinated system compared to the UV-treated system with increasing residence time. The fate of spheres and fluorescence in situ hybridization-positive legionellae was similar and independent of the primary disinfectant applied and water residence

time. The more rapid loss of culturable legionellae compared to the fluorescence in situ hybridization-positive legionellae was attributed to a loss in culturability rather than physical desorption. Loss of bacteriophage 28B plaque-forming ability together with erosion may have affected their fate within biofilms in the pilot-scale distribution system. The current study has demonstrated that desorption was one of the primary mechanisms affecting the loss of microspheres, legionellae, and bacteriophage from biofilms within a pilot-scale distribution system as well as disinfection and biological grazing. In general, two primary disinfection regimens (chlorination and UV treatment) were not shown to have a measurable impact on the accumulation and fate of model microbial pathogens within a water distribution system.

103. Lindell,D., Jaffe,J.D., Johnson,Z.I., Church,G.M., Chisholm,S.W. (2005). **Photosynthesis genes in marine viruses yield proteins during host infection.** *Nature* 438:86-89. **Abstract:** Cyanobacteria, and the viruses (phages) that infect them, are significant contributors to the oceanic 'gene pool'. This pool is dynamic, and the transfer of genetic material between hosts and their phages probably influences the genetic and functional diversity of both. For example, photosynthesis genes of cyanobacterial origin have been found in phages that infect *Prochlorococcus* and *Synechococcus*, the numerically dominant phototrophs in ocean ecosystems. These genes include psbA, which encodes the photosystem II core reaction centre protein D1, and high-light-inducible (hli) genes. Here we show that phage psbA and hli genes are expressed during infection of *Prochlorococcus* and are co-transcribed with essential phage capsid genes, and that the amount of phage D1 protein increases steadily over the infective period. We also show that the expression of host photosynthesis genes declines over the course of infection and that replication of the phage genome is a function of photosynthesis. We thus propose that the phage genes are functional in photosynthesis and that they may be increasing phage fitness by supplementing the host production of these proteins.

104. Little,J.W. (2005). **Lysogeny, prophage induction, and lysogenic conversion.** pp. 37-54 In Waldor,M.K., Friedman,D.I., and Adhya,S.L. (eds.), *Phages: Their Role in Bacterial Pathogenesis and Biotechnology*. ASM Press, Washington DC. **Abstract:** Temperate phages can carry genes that affect the phenotype and behavior of their bacterial host. These genes can be considered extra genetic material in that they are not necessarily for viral lytic growth or for the lysogenic lifestyle. In this chapter, these extra genes will be termed "foreign genes" for ease of reference. Foreign genes include genes for various toxins that have pathogenic effects. The expression of toxin genes has been documented to occur in two different phases of the viral life cycle. The primary goal of this chapter is to describe circumstances under which foreign genes can be expressed. We will first consider the life cycle of temperate phages. With this background, we will then describe how foreign genes can be expressed in the lysogenic state. We will then turn to a more detailed description of a particular temperate phage, λ, with an emphasis on the regulatory mechanisms that are best understood for this phage. This description will facilitate an understanding of how foreign genes can be expressed during the process of prophage induction, and a particular example will be descrbed.

105. Loc Carrillo,C., Atterbury,R.J., El Shibiny,A., Connerton,P.L., Dillon,E., Scott,A. , Connerton,I.F. (2005). **Bacteriophage therapy to reduce *Campylobacter jejuni* colonization of broiler chickens.** *Appl. Environ. Microbiol.* 71:6554-6563. **Abstract:** Colonization of broiler chickens by the enteric pathogen *Campylobacter jejuni* is widespread and difficult to prevent. Bacteriophage therapy is one possible means by which this colonization could be controlled, thus limiting the entry of campylobacters into the human food chain. Prior to evaluating the efficacy of phage therapy, experimental models of *Campylobacter* colonization of broiler chickens were established by using low-passage *C. jejuni* isolates HPC5 and GIIC8 from United Kingdom broiler flocks. The screening of 53 lytic bacteriophage isolates against a panel of 50 *Campylobacter* isolates from broiler chickens and 80 strains isolated after human infection identified two phage candidates with broad host lysis. These phages, CP8 and CP34, were orally administered in antacid suspension, at different dosages, to 25-day-old broiler chickens experimentally colonized with the *C. jejuni* broiler isolates. Phage treatment of *C. jejuni*-colonized birds resulted in *Campylobacter* counts falling between 0.5 and 5 log10 CFU/g of cecal contents compared to untreated controls over a 5-day period postadministration. These reductions were dependent on the phage-*Campylobacter* combination, the dose of phage applied, and the time elapsed after administration. Campylobacters resistant to bacteriophage infection were recovered from phage-treated chickens at a frequency of <4%. These resistant types were compromised in their ability to colonize experimental chickens and rapidly reverted to a phage-sensitive phenotype in vivo. The selection of appropriate phage and their dose optimization are key elements for the success of phage therapy to reduce campylobacters in broiler chickens.

106. Loisy,F., Atmar,R.L., Le Saux,J.C., Cohen,J., Caprais,M.P., Pommepuy,M., Le Guyader,F.S. (2005). **Use of rotavirus virus-like particles as surrogates to evaluate virus persistence in shellfish.** *Appl. Environ. Microbiol.* 71:6049-6053. **Abstract:** Rotavirus virus-like particles (VLPs) and MS2 bacteriophages were bioaccumulated in bivalve mollusks to evaluate viral persistence in shellfish during depuration and relaying under natural conditions. Using this nonpathogenic surrogate virus, we were able to demonstrate that about 1 log10 of VLPs was depurated after 1 week in warm seawater (22 degrees C). Phage MS2 was depurated more rapidly (about 2 log10 in 1 week) than were VLPs, as determined using a single-compartment model and linear regression analysis. After being relayed in the estuary under the influence of the tides, VLPs were detected in oysters for up to 82 days following seeding with high levels of VLPs (concentration range between 10(10) and 10(9) particles per g of pancreatic tissue) and for 37 days for lower contamination levels (10(5) particles per g of pancreatic tissue). These data suggest that viral particles may persist in shellfish tissues for several weeks.

107. Los,M., Los,J.M., Blohm,L., Spillner,E., Grunwald,T., Albers,J., Hintsche,R., Wegrzyn,G. (2005). **Rapid detection of viruses using electrical biochips and anti-virion sera.** *Lett. Appl. Microbiol.* 40:479-485. **Abstract:** AIMS: Rapid detection and quantification of viruses is crucial in clinical practice, veterinary medicine, agriculture, basic research as well as in biotechnological factories. However, although various techniques were described and are currently used, development of more rapid, more sensitive and quantitative methods seems to be still important. METHODS AND RESULTS: Here we describe a method for rapid detection of viruses (using bacteriophages as model viruses), based on electrical biochip array technology with the use of antibodies against capsid proteins. CONCLUSIONS: Using the procedure developed in this work, we were able to detect 2 x 10(4) virions on the chip. The whole assay procedure takes c. 50 min and the assay is quantitative. SIGNIFICANCE AND IMPACT OF THE STUDY: This procedure may be useful in various approaches, including detection of bacteriophage contamination in bioreactors and possibly detection of toxin gene-bearing phages or other viruses in food samples.

108. Lunde,M., Aastveit,A.H., Blatny,J.M., Nes,I.F. (2005). **Effects of diverse environmental conditions on φLC3 prophage stability in *Lactococcus lactis*.** *Appl. Environ. Microbiol.* 71:721-727. **Abstract:** The effects of various growth conditions on spontaneous φLC3 prophage induction in *Lactococcus lactis* subsp. *cremoris* IMN-C1814 was analyzed with a half fraction of a 4(4) factorial experimental design. The four factors included in the study were nutrient availability, acidity, osmolarity, and temperature, each applied at four levels. These environmental factors are related to the fermentation processes in the dairy industry, in which bacteriophage attacks on sensitive starter strains are a constant threat to successful fermentation processes. The frequency of spontaneous φLC3 induction was determined by quantitative analyses of restored DNA attachment sites (attB) on the bacterial chromosomes in a population of lysogenic cells. Statistical analysis revealed that all four environmental factors tested affected φLC3 prophage stability and that the environmental factors were involved in interactions (interactions exist when the effect of one factor depends on the level of another factor). The spontaneous φLC3 induction frequency varied from 0.08 to 1.76%. In general, the induction frequency remained at the same rate or decreased when level 1 to 3 of the four environmental factors was applied. At level 4, which generally gave the least favorable growth conditions, the induction frequency was either unchanged, decreased, or increased, depending on the type of stress. It appeared that the spontaneous induction frequency was independent of the growth behavior of the host. It was the environmental growth conditions that were the decisive factor in induction frequency.

109. Malek,W., Sajnaga,E., Wdowiak-Wrobel,S., Studzinska,B., Icka,I.S., Nosalewicz,I., Slomka,M., Tatara,A., Gawron,A. (2005). **Characterization of phages virulent for *Sarothamnus scoparius bradyrhizobia*.** *Curr. Microbiol.* 51:244-249. **Abstract:** Four virulent phages--φDI, φTI, φCYT21, and φOS6, infective on *Sarothamnus scoparius rhizobia*--were isolated from the soil and characterized for morphology, host range, rate of adsorption to bacterial cells, and genome size. New phages were separated into two morphological families: Siphoviridae with long, noncontractile tails (φDI, φTI) and Myoviridae with long, contractile tails (φCYT21, φOS6). They were also classified into two groups by a host specificity. One of them included viruses (φDI and φTI) that lysed *S. scoparius bradyrhizobia* and *Bradyrhizobium* sp. (Lupinus) strain DI, and the second one comprised phages (φCYT21 and φOS6) that parasitized only Scotch broom native microsymbionts. Phages specific for *S. scoparius rhizobia* were differentiated not only by morphology and host range but also by a genome size that was in the range from 47,583 to 60,098 b.p.

110. Mann,N.H. (2005). **The third age of phage.** *PLoS Biol.* 3:e182. **Abstract:** The third age of phage has begun with the recognition that phages may be key to the great planetary biogeochemical cycles and represent the greatest potential genetic resource in the biosphere.

111. Matsuda,T.**,** Freeman,T.A.**,** Hilbert,D.W.**,** Duff,M.**,** Fuortes,M.**,** Stapleton,P.P.**,** Daly,J.M. (2005). **Lysis-deficient bacteriophage therapy decreases endotoxin and inflammatory mediator release and improves survival in a murine peritonitis model.** *Surgery* 137:639-646. **Abstract:** BACKGROUND: Lysis-deficient (LyD) bacteriophages (phages) kill bacteria without endotoxin (Et) release. This may minimize systemic cytokine responses and limit inflammation in bacterial sepsis. We determined the effects of t amber A3 T4 LyD and virulent wild-type (WT) phages on mouse bacterial peritonitis. METHODS: Balb/c mice were injected with B40sul *Escherichia coli*, treated intraperitoneally with LyD, WT, or a beta-lactam antibiotic [latamoxef sodium (LMOX)], and followed for survival. We measured Et release, tumor necrosis factor (TNF)-alpha and interleukin (IL)-6, as well as bacterial counts and peritoneal exudative cells (PECs) in peritoneal lavage fluid at 6 and 12 hours after infection. RESULTS: LyD mice showed significantly greater survival compared with other groups. Et levels were significantly lower in the LyD mice at 6 and 12 hours after infection. TNF-alpha and IL-6 levels were lower in LyD mice compared with control (untreated) mice at 12 hours. Compared with controls, bacteria counts in peritoneal lavage fluid were lower in all treatment groups (LyD, WT, or LMOX) at 6 and 12 hours. PEC counts were highest in LyD mice at 6 hours but significantly lower than that in WT phage- and LMOX-treated mice at 12 hours. CONCLUSIONS: LyD phage therapy significantly improves survival and attenuates the systemic effects of bacterial sepsis by minimizing Et release and pro-inflammatory mediators in murine bacterial peritonitis. Further studies may find phage therapy useful in treating peritonitis and multidrug-resistant bacterial infections.

112. Matsuzaki,S.**,** Rashel,M.**,** Uchiyama,J.**,** Sakurai,S. **,** Ujihara,T.**,** Kuroda,M.**,** Ikeuchi,M.**,** Tani,T.**,** Fujieda,M.**,** Wakiguchi,H.**,** Imai,S. (2005). **Bacteriophage therapy: a revitalized therapy against bacterial infectious diseases.** *Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy* 11:211-219. **Abstract:** Bacteriophage (phage) therapy involves using phages or their products as bioagents for the treatment or prophylaxis of bacterial infectious diseases. Much evidence in support of the effectiveness of phage therapy against bacterial infectious diseases has accumulated since 1980 from animal model studies conducted in Western countries. Reports indicate that appropriate administration of living phages can be used to treat lethal infectious diseases caused by gram-negative bacteria, such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Vibrio vulnificus*, and *Salmonella* spp., and gram-positive bacteria, such as *Enterococcus faecium* and *Staphylococcus aureus*. The phage display system and genetically modified nonreplicating phages are also effective for treatment of *Helicobacter pylori* and *P. aeruginosa*, respectively. In addition to phage particles per se, purified phage-encoded peptidoglycan hydrolase (lysin) is also reported to be effective for the treatment of bacterial infectious diseases caused by gram-positive bacteria such as *Streptococcus pyogenes*, *S. pneumoniae*, *Bacillus anthracis*, and group B streptococci. All phage lysins that have been studied to date exhibit immediate and strong bacteriolytic activity when applied exogenously. Furthermore, phage-coded inhibitors of peptidoglycan synthesis (protein antibiotics), search methods for novel antibacterial agents using phage genome informatics, and vaccines utilizing phages or their products are being developed. Phage therapy will compensate for unavoidable complications of chemotherapy such as the appearance of multidrug resistance or substituted microbism.

113. McDaniel,L.**,** Paul,J.H. (2005). **Effect of nutrient addition and environmental factors on prophage induction in natural populations of marine *Synechococcus* species.** *Appl. Environ. Microbiol.* 71:842-850. **Abstract:** A series of experiments were conducted with samples collected in both Tampa Bay and the Gulf of Mexico to assess the impact of nutrient addition on cyanophage induction in natural populations of *Synechococcus* sp. The samples were virus reduced to decrease the background level of cyanophage and then either left untreated or amended with nitrate, ammonium, urea, or phosphate. Replicate samples were treated with mitomycin C to stimulate cyanophage induction. In five of the nine total experiments performed, cyanophage induction was present in the non-nutrient-amended control samples. Stimulation of cyanophage induction in response to nutrient addition (phosphate) occurred in only one Tampa Bay sample. Nutrient additions caused a decrease in lytic (or control) phage production in three of three offshore stations, in one of three estuarine experiments, and in a lysogenic marine *Synechococcus* in culture. These results suggest that the process of cyanophage induction as an assay of *Synechococcus* lysogeny was not inorganically nutrient limited, at least in the samples examined. More importantly, it was observed that the level of cyanophage induction (cyanophage milliliter(-1)) was inversely correlated to *Synechococcus* and cyanophage abundance. Thus, the intensity of the prophage induction response is

defined by ambient population size and cyanophage abundance. This corroborates prior observations that lysogeny in *Synechococcus* is favored during times of low host abundance.

114. McNerney,R., Traore,H. (2005). **Mycobacteriophage and their application to disease control.** *J. Appl. Microbiol.* 99:223-233. **Abstract:** The resurgence of tuberculosis and emergence of drug resistant disease has stimulated fresh research into mycobacteriophage. Studies are currently underway to develop phage-based tools for therapeutic and diagnostic use. Previous attempts at mycobacteriophage therapy in experimentally infected animals were not successful and alternative strategies of phage delivery that enable killing of intracellular bacteria are required. Replication of mycobacteriophage provides a simple means of detecting viable bacteria and good progress has been made towards the development of new phage-based diagnostic tools. When screening isolates for resistance to the major antituberculosis drug rifampicin phage-based tests have been shown to have high sensitivity. For the diagnosis of pulmonary tuberculosis evaluation studies indicate that current phage tests are not as sensitive as traditional culture methods. Further trials are needed to determine whether they might have a role in the detection of smear negative tuberculosis. A second generation of phage tests are under development following the construction of luciferase reporter phage. Preliminary data suggests they may offer rapid detection of mycobacteria and simple screening for drug resistance. The potential of mycobacteriophage to detect and treat other mycobacterial diseases remains largely unexplored. The resurgence of tuberculosis and emergence of drug resistant disease has stimulated fresh research into mycobacteriophage. Studies are currently underway to develop phage-based tools for therapeutic and diagnostic use. Previous attempts at mycobacteriophage therapy in experimentally infected animals were not successful and alternative strategies of phage delivery that enable killing of intracellular bacteria are required. Replication of mycobacteriophage provides a simple means of detecting viable bacteria and good progress has been made towards the development of new phage-based diagnostic tools. When screening isolates for resistance to the major antituberculosis drug rifampicin phage-based tests have been shown to have high sensitivity. For the diagnosis of pulmonary tuberculosis evaluation studies indicate that current phage tests are not as sensitive as traditional culture methods. Further trials are needed to determine whether they might have a role in the detection of smear negative tuberculosis. A second generation of phage tests are under development following the construction of luciferase reporter phage. Preliminary data suggests they may offer rapid detection of mycobacteria and simple screening for drug resistance. The potential of mycobacteriophage to detect and treat other mycobacterial diseases remains largely unexplored.

115. Moce-Llivina,L., Lucena,F., Jofre,J. (2005). **Enteroviruses and bacteriophages in bathing waters.** *Appl. Environ. Microbiol.* 71:6838-6844. **Abstract:** A new procedure for detecting and counting enteroviruses based on the VIRADEN method applied to 10 liters of seawater was examined. It improved the efficiency of detection by taking into account both the number of positive isolations and numbers found with traditional methods. It was then used to quantify viruses in bathing waters. A number of bacterial indicators and bacteriophages were also tested. Cultivable enteroviruses were detected in 55% of the samples, most of which complied with bacteriological criteria. In contrast, viral genomes were only detected in 20% of the samples by reverse transcription-PCR. Somatic coliphages outnumbered all other indicators. F-specific RNA phages were detected in only 15% of the samples, whereas phages infecting Bacteroides thetaiotaomicron were detected in 70% of samples. A numerical relationship between the numbers of enteroviruses and the numbers of enterococci and somatic coliphages was observed. In situ inactivation experiments showed that viruses persisted significantly longer than the bacterial indicators. Only somatic coliphages and bacteriophages infecting Bacteroides persisted longer than the viruses. These results explain the numbers of enteroviruses and indicators in bathing waters attending the numbers usually found in sewage in the area. Somatic coliphages show a very good potential to predict the risk of viruses being present in bathing waters.

116. Montville,R., Froissart,R., Remold,S.K., Tenaillon,O., Turner,P.E. (2005). **Evolution of mutational robustness in an RNA virus.** *PLoS Biol.* 3:e381. **Abstract:** Mutational (genetic) robustness is phenotypic constancy in the face of mutational changes to the genome. Robustness is critical to the understanding of evolution because phenotypically expressed genetic variation is the fuel of natural selection. Nonetheless, the evidence for adaptive evolution of mutational robustness in biological populations is controversial. Robustness should be selectively favored when mutation rates are high, a common feature of RNA viruses. However, selection for robustness may be relaxed under virus co-infection because complementation between virus genotypes can buffer mutational effects. We therefore hypothesized that selection for genetic robustness in viruses will be weakened with increasing frequency of co-infection. To test this idea, we used populations of RNA phage ϕ6 that were experimentally evolved at low and high

levels of co-infection and subjected lineages of these viruses to mutation accumulation through population bottlenecking. The data demonstrate that viruses evolved under high co-infection show relatively greater mean magnitude and variance in the fitness changes generated by addition of random mutations, confirming our hypothesis that they experience weakened selection for robustness. Our study further suggests that co-infection of host cells may be advantageous to RNA viruses only in the short term. In addition, we observed higher mutation frequencies in the more robust viruses, indicating that evolution of robustness might foster less-accurate genome replication in RNA viruses.

117. Morgan,A.D.**,** Gandon,S.**,** Buckling,A. (2005). **The effect of migration on local adaptation in a coevolving host-parasite system.** *Nature* 437:253-256. **Abstract:** Antagonistic coevolution between hosts and parasites in spatially structured populations can result in local adaptation of parasites; that is, the greater infectivity of local parasites than foreign parasites on local hosts. Such parasite specialization on local hosts has implications for human health and agriculture. By contrast with classic single-species population-genetic models, theory indicates that parasite migration between subpopulations might increase parasite local adaptation, as long as migration does not completely homogenize populations. To test this hypothesis we developed a system-specific mathematical model and then coevolved replicate populations of the bacterium *Pseudomonas fluorescens* and a parasitic bacteriophage with parasite only, with host only or with no migration. Here we show that patterns of local adaptation have considerable temporal and spatial variation and that, in the absence of migration, parasites tend to be locally maladapted. However, in accord with our model, parasite migration results in parasite local adaptation, but host migration alone has no significant effect.

118. Moxon,E.R.**,** Jansen,V.A. (2005). **Phage variation: understanding the behaviour of an accidental pathogen.** *Trends Microbiol.* 13:563-565. **Abstract:** Understanding why carriers of meningococci occasionally develop invasive disease is a major challenge. Individual strains of meningococci are extremely variable and undergo dynamic changes in DNA content and organization. This heterogeneity of meningococcal populations might enhance the fitness of this human-restricted bacterium. The recent discovery of a meningococcal bacteriophage and its associations to disease is an intriguing example of this variability and could contribute to a better understanding of microbial commensal and virulence behaviour.

119. Muhling,M.**,** Fuller,N.J.**,** Millard,A.**,** Somerfield,P.J.**,** Marie,D.**,** Wilson,W.H.**,** Scanian,D.J.**,** Post,A.F.**,** Joint,I.**,** Mann,N.H. (2005). **Genetic diversity of marine *Synechococcus* and co-occurring cyanophage communities: evidence for viral control of phytoplankton.** *Environ. Microbiol.* 7:499-508. **Abstract:** Unicellular cyanobacteria of the genus *Synechococcus* are a major component of the picophytoplankton and make a substantial contribution to primary productivity in the oceans. Here we provide evidence that supports the hypothesis that virus infection can play an important role in determining the success of different *Synechococcus* genotypes and hence of seasonal succession. In a study of the oligotrophic Gulf of Aqaba, Red Sea, we show a succession of *Synechococcus* genotypes over an annual cycle. There were large changes in the genetic diversity of *Synechococcus* , as determined by restriction fragment length polymorphism analysis of a 403- bp *rpoC1* gene fragment, which was reduced to one dominant genotype in July. The abundance of co-occurring cyanophage capable of infecting marine *Synechococcus* was determined by plaque assays and their genetic diversity was determined by denaturing gradient gel electrophoresis analysis of a 118-bp *g20* gene fragment. The results indicate that both abundance and genetic diversity of cyanophage covaried with that of *Synechococcus* . Multivariate statistical analyses show a significant relationship between cyanophage assemblage structure and that of *Synechococcus* . These observations are consistent with cyanophage infection being a major controlling factor in picophytoplankton succession.

120. Muller-Merbach,M.**,** Neve,H.**,** Hinrichs,J. (2005). **Kinetics of the thermal inactivation of the *Lactococcus lactis* bacteriophage P008.** *J. Dairy Res.* 72:281-286. **Abstract:** The thermal resistance of the lactococcal bacteriophage P008 was investigated between 55 and 80 degrees C. Inactivation kinetics revealed an order of reaction above 1 and could be determined by a non-1st-order regression model. Phage inactivation was influenced by the medium (milk and Ca-M17-broth). Within the investigated temperature range, milk had a protective effect on phage P008. This was reflected in the rate constant and in the activation energy. Thermal phage inactivation studies reported in literature were re-analysed using non-1st-order regression. The obtained kinetic parameters showed that phage P008 belongs to the most heat resistant lactococcal phages investigated so far.

121. Muniesa,M.**,** Blanch,A.R.**,** Lucena,F.**,** Jofre,J. (2005). **Bacteriophages may bias outcome of bacterial enrichment cultures.** *Appl. Environ. Microbiol.* 71:4269-4275. **Abstract:** Enrichment cultures are widely used for the isolation of bacteria in clinical, biotechnological, and environmental studies. However,

competition, relative growth rates, or inhibitory effects may alter the outcome of enrichment cultures, causing the phenomenon known as enrichment bias. Bacteriophages are a major component in many microbial systems, and it abounds in natural settings. This abundance means that bacteriophages are likely to be present in many laboratory enrichment cultures. Our hypothesis was that bacteriophages present in the sample might bias the enriched subpopulation, since it can infect and lyse the target bacteria during the enrichment step once the bacteria reach a given density. Here we show that the presence of bacteriophages in *Salmonella* and *Shigella* enrichment cultures produced a significant reduction (more than 1 log unit) in the number of these bacteria compared with samples in which bacteriophages had been reduced by filtration through 0.45-microm non-protein-binding membranes. Furthermore, our data indicate that the *Salmonella* biotypes isolated after the enrichment culture change if bacteriophages are present, thus distorting the results of the analysis.

122. Nagasaki,K., Takao,Y., Shirai,Y., Mizumoto,H., Tomaru,Y. (2005). **[Molecular ecology of microalgal viruses] [text in Japanese].** *Uirusu* 55:127-132. **Abstract:** A great amount of virus particles exist in natural waters. Each virion is considered to have its own ecological role, affecting the maintenance and fluctuation of aquatic ecosystems. We have been studying viruses infectious to micro-plankton, especially those infecting phytoplankton. Red tides are caused by drastic increase in abundance of plankton. We succeeded in elucidating that viral infection is one of the most important factors determining the dynamics and termination of algal blooms by means of field survey and molecular experiments. In addition, we demonstrated that the interrelationship between viruses and their hosts are highly complicated, and might be determined by the molecular-structural difference of viral capsids among distinct virus ecotypes. Furthermore, in the process of our investigation on various aquatic algal viruses, their importance as genetic sources has also been suggested. In order to deeply understand the mechanism of aquatic ecosystem, more intensive studies as for aquatic viruses are urgently required.

123. Nunez,M.E., Martin,M.O., Chan,P.H., Spain,E.M. (2005). **Predation, death, and survival in a biofilm: *Bdellovibrio* investigated by atomic force microscopy.** *Colloids and surfaces. B, Biointerfaces* 42:263-271. **Abstract:** Biofilms are complex microbial communities that are resistant to attack by bacteriophages and to removal by drugs and chemicals. Here we use atomic force microscopy (AFM) to image the attack on *Escherichia coli* biofilms by *Bdellovibrio bacteriovorus* 109J. *Bdellovibrio* is a small, predatory bacterium that invades and devours other Gram-negative bacteria. We demonstrate that under dilute nutrient conditions, bdellovibrios can prevent the formation of simple bacterial biofilms and destroy established biofilms; under richer conditions the prey bacteria persist and are not eradicated, but may be shifted toward solution populations. Using AFM we explore these bacterial interactions with more detail and accuracy than available by more traditional staining assays or optical microscopy. AFM also allows us to investigate the nanoscale morphological changes of the predator, especially those related to motility. This demonstration of *Bdellovibrio*'s successful predation in a biofilm inspires us to consider ways that it might be used productively for industrial, medical, agricultural, and biodefensive purposes.

124. O'Flaherty,S., Ross,R.P., Meaney,W., Fitzgerald,G.F., Elbreki,M.F., Coffey,A. (2005). **Potential of the polyvalent anti-*Staphylococcus* bacteriophage K for control of antibiotic-resistant staphylococci from hospitals.** *Appl. Environ. Microbiol.* 71:1836-1842. **Abstract:** The increasing prevalence of antibiotic-resistant staphylococci has prompted the need for antibacterial controls other than antibiotics. In this study, a lytic bacteriophage (phage K) was assessed in vitro for its ability to inhibit emerging drug-resistant *Staphylococcus aureus* strains from hospitals and other species of *Staphylococcus* isolated from bovine infections. In in vitro inhibitory assays, phage K lysed a range of clinically isolated methicillin-resistant *S. aureus* (MRSA) strains, *S. aureus* with heterogeneous vancomycin resistance and vancomycin resistance, and teicoplanin-resistant strains. In these assays, 14 of the MRSA strains were initially only weakly sensitive to this phage. However, propagation of phage K on these less-sensitive strains resulted in all 14 being sensitive to the modified phages. The results enforce the principle that, while certain target bacteria may be relatively insensitive to lytic phage, this can be overcome by obtaining modified phage variants from passage of the phage through the insensitive strains. Model in situ hand wash studies using a phage-enriched wash solution resulted in a 100-fold reduction in staphylococcal numbers on human skin by comparison with numbers remaining after washing in phage-free solution. Infusion of the phage into a nonimmunogenic bismuth-based cream resulted in strong anti-*Staphylococcus* activity from the cream on plates and in broth.

125. O'Flaherty,S., Coffey,A., Meaney,W.J., Fitzgerald,G.F., Ross,R.P. (2005). **Inhibition of bacteriophage K proliferation on *Staphylococcus aureus* in raw bovine milk.** *Lett. Appl. Microbiol.* 41:274-279. **Abstract:** AIMS: To assess the ability of staphylococcal bacteriophage K to inhibit *Staphylococcus aureus* in raw milk. METHODS AND RESULTS: The ability of bacteriophage (phage) to replicate in milk is

important in situations where phage might be used as a therapeutic for bovine mastitis. Phage K was able to replicate normally, leading to elimination of the host culture in milk, which had been previously heat-treated. When raw milk was used under identical conditions, the phages were unable to replicate. Phage adsorption assays were performed and these demonstrated that adsorption of phage was significantly reduced in the raw milk while it was restored in the heat-treated sample (86.50% compared with 99.96% adsorption respectively). When confocal microscopy with a Live/Dead Bac light staining system was employed, it was observed that in raw milk *S. aureus* formed clusters associated with fat globules, while in heat-treated milk, bacterial agglutination had not occurred. CONCLUSIONS: Raw milk inhibits staphylococcal phage K proliferation. Significance and Impact of the Study: This observation has implications for the exploitation of staphylococcal therapeutic phage in milk.

126. Olson,M.R.**,** Axler,R.P.**,** Hicks,R.E.**,** Henneck,J.R.**,** McCarthy,B.J. (2005). **Seasonal virus removal by alternative onsite wastewater treatment systems.** *Water Hlth.* 3:139-155. **Abstract:** Viral contamination of public waters is a leading health concern around the world, including in Minnesota where cold climate, abundant onsite systems on poor or thin soils, and abundant surface water resources present a significant risk of wastewater pathogens reaching sensitive water sources. Three alternative onsite treatment systems, a sand filter, peat filter and subsurface-flow constructed wetland (CW) at a field research site were evaluated for seasonal virus removal by seeding each with MS2 bacteriophage. The sand and peat filters and CW removed 2.7, 7.0, and 1.4 log10 of MS2, respectively, during summer and 1.8 and 6.9 log for the sand and peat filter during winter (CW not seeded). Somatic coliphage reductions for the sand filter, peat filter and CW were 2.9, 3.5, 1.0 log10 in summer, and 1.5, 2.8, 0.7 log10 during winter, respectively over a 3 year period. During this period, fecal coliform log10 reductions were 2.9, 4.6, 2.0 in summer for the sand and peat filters and CW, and 2.0, 4.6, 1.6 in winter. The peat filter was the most effective system for removing MS2, somatic coliphage and fecal coliforms during both winter and summer but all systems removed > 90% of viruses throughout the year.

127. Ottoson,J.**,** Norstrom,A.**,** Dalhammar,G. (2005). **Removal of micro-organisms in a small-scale hydroponics wastewater treatment system.** *Lett. Appl. Microbiol.* 40:443-447. **Abstract:** Aims: To measure the microbial removal capacity of a small-scale hydroponics wastewater treatment plant. Methods and Results: Paired samples were taken from untreated, partly-treated and treated wastewater and analysed for faecal microbial indicators, i.e. coliforms, *Escherichia coli*, enterococci, *Clostridium perfringens* spores and somatic coliphages, by culture based methods. *Escherichia coli* was never detected in effluent water after >5.8-log removal. Enterococci, coliforms, spores and coliphages were removed by 4.5, 4.1, 2.3 and 2.5 log respectively. Most of the removal (60-87%) took place in the latter part of the system because of settling, normal inactivation (retention time 12.7 d) and sand filtration. Time-dependent log-linear removal was shown for spores (k = -0.17 log d(-1), r(2) = 0.99). Conclusions: Hydroponics wastewater treatment removed micro-organisms satisfactorily. Significance and Impact of the Study: Investigations on the microbial removal capacity of hydroponics have only been performed for bacterial indicators. In this study it has been shown that virus and (oo)cyst process indicators were removed and that hydroponics can be an alternative to conventional wastewater treatment.

128. Pang,L.**,** Close,M.**,** Goltz,M.**,** Noonan,M.**,** Sinton,L. (2005). **Filtration and transport of *Bacillus subtilis* spores and the F-RNA phage MS2 in a coarse alluvial gravel aquifer: implications in the estimation of setback distances.** *J Contam Hydrol* 77:165-194. **Abstract:** Filtration of *Bacillus subtilis* spores and the F-RNA phage MS2 (MS2) on a field scale in a coarse alluvial gravel aquifer was evaluated from the authors' previously published data. An advection-dispersion model that is coupled with first-order attachment kinetics was used in this study to interpret microbial concentration vs. time breakthrough curves (BTC) at sampling wells. Based on attachment rates (katt) that were determined by applying the model to the breakthrough data, filter factors (f) were calculated and compared with f values estimated from the slopes of log (cmax/co) vs. distance plots. These two independent approaches resulted in nearly identical filter factors, suggesting that both approaches are useful in determining reductions in microbial concentrations over transport distance. Applying the graphic approach to analyse spatial data, we have also estimated the f values for different aquifers using information provided by some other published field studies. The results show that values of f, in units of log (cmax/co) m(-1), are consistently in the order of 10(-2) for clean coarse gravel aquifers, 10(-3) for contaminated coarse gravel aquifers, and generally 10(-1) for sandy fine gravel aquifers and river and coastal sand aquifers. For each aquifer category, the f values for bacteriophages and bacteria are in the same order-of-magnitude. The f values estimated in this study indicate that for every one-log reduction in microbial concentration in groundwater, it requires a few tens of meters of travel in clean coarse gravel aquifers, but a few hundreds of meters in contaminated coarse gravel aquifers. In contrast, a one-log reduction generally only requires a few meters of travel in sandy fine gravel aquifers and sand aquifers. Considering the highest concentration in human effluent is

in the order of 10(4) pfu/l for enteroviruses and 10(6) cfu/100 ml for faecal coliform bacteria, a 7-log reduction in microbial concentration would comply with the drinking water standards for the downgradient wells under natural gradient conditions. Based on the results of this study, a 7-log reduction would require 125-280 m travel in clean coarse gravel aquifers, 1.7-3.9 km travel in contaminated coarse gravel aquifers, 33-61 m travel in clean sandy fine gravel aquifers, 33-129 m travel in contaminated sandy fine gravel aquifers, and 37-44 m travel in contaminated river and coastal sand aquifers. These recommended setback distances are for a worst-case scenario, assuming direct discharge of raw effluent into the saturated zone of an aquifer. Filtration theory was applied to calculate collision efficiency (alpha) from model-derived attachment rates (katt), and the results are compared with those reported in the literature. The calculated alpha values vary by two orders-of-magnitude, depending on whether collision efficiency is estimated from the effective particle size (d10) or the mean particle size (d50). Collision efficiency values for MS-2 are similar to those previously reported in the literature (e.g.) [DeBorde, D.C., Woessner, W.W., Kiley, QT., Ball, P., 1999. Rapid transport of viruses in a floodplain aquifer. Water Res. 33 (10), 2229-2238]. However, the collision efficiency values calculated for Bacillus subtilis spores were unrealistic, suggesting that filtration theory is not appropriate for theoretically estimating filtration capacity for poorly sorted coarse gravel aquifer media. This is not surprising, as filtration theory was developed for uniform sand filters and does not consider particle size distribution. Thus, we do not recommend the use of filtration theory to estimate the filter factor or setback distances. Either of the methods applied in this work (BTC or concentration vs. distance analyses), which takes into account aquifer heterogeneities and site-specific conditions, appear to be most useful in determining filter factors and setback distances.

129. Payan,A., Ebdon,J., Taylor,H., Gantzer,C., Ottoson,J., Papageorgiou,G.T., Blanch,A.R., Lucena,F., Jofre,J., Muniesa,M. (2005). **Method for isolation of *Bacteroides* bacteriophage host strains suitable for tracking sources of fecal pollution in water.** *Appl. Environ. Microbiol.* 71:5659-5662. **Abstract:** Bacteriophages infecting *Bacteroides* are potentially a good tool for fecal source tracking, but different *Bacteroides* host strains are needed for different geographic areas. A feasible method for isolating *Bacteroides* host strains for phages present in human fecal material is described. Useful strains were identified for application in Spain and the United Kingdom. One strain, GA-17, identified as *Bacteroides thetaiotaomicron*, was tested in several locations in Europe with excellent performance in Southern Europe.

130. Phulpoto,M.A., Qayyum,S., Rizvi,N., Khuhawar,S.M. (2005). **Diagnostic yield of fast plaque TB test for rapid detection of *Mycobacterium* in tuberculosis suspects.** *Journal of the Pakistan Medical Association* 55:57-60. **Abstract:** OBJECTIVE: To compare the diagnostic yield of FAST Plaque TB test with the conventional methods for detection of *Mycobacterium tuberculosis* in sputum of Tuberculosis suspects at Jinnah Postgraduate Medical Center Karachi Pakistan. METHODS: A comparative study of diagnostic yield of FAST Plaque TB test with the culture and ZN staining, conducted from January to June 2004. RESULTS: The study was completed on 48 samples, 31 (64.58%) male and 17 females (35.42%). Half of the cases were sputum positive. Culture positive was in 17 (35.41%) and negative in 28 (58.3%) wereas 3 (6.25%) were contaminated. FAST Plaque TB test was positive in 16 (33.33%) and negative in 32 (66.6%) specimens. Out of 17 culture positive, 2 (11.7%) were negative and in 28 culture negative, 1 (3.57%) specimen was positive for FAST Plaque TB test. Out of 24 smear positive, 11 (45.83%) were negative and in 24 smear negative, 3 (12.5%) were positive, for FAST Plaque TB test. Compared to culture it has sensitivity of 86.23% and specificity of 96.42%, positive predictive value of 93.75% and negative predictive value of 93.1%. CONCLUSION: FAST Plaque TB test is a simple test that can detect viable mycobacterium in 2 days. It has a good sensitivity and specificity. The cost is three times less than the other available tests like PCR. Thus it can be useful in the diagnosis of tuberculosis as an adjunct to sputum microscopy in endemic countries.

131. Poon,A., Chao,L. (2005). **The rate of compensatory mutation in the DNA bacteriophage φX174.** *Genetics* 170:989-999. **Abstract:** A compensatory mutation occurs when the fitness loss caused by one mutation is remedied by its epistatic interaction with a second mutation at a different site in the genome. This poorly understood biological phenomenon has important implications, not only for the evolutionary consequences of mutation, but also for the genetic complexity of adaptation. We have carried out the first direct experimental measurement of the average rate of compensatory mutation. An arbitrary selection of 21 missense substitutions with deleterious effects on fitness was introduced by site-directed mutagenesis into the bacteriophage φX174. For each deleterious mutation, we evolved 8-16 replicate populations to determine the frequency at which a compensatory mutation, instead of the back mutation, was acquired to recover fitness. The overall frequency of compensatory mutation was approximately 70%. Deleterious mutations that were more severe were significantly more likely to be compensated for. Furthermore,

experimental reversion of deleterious mutations revealed that compensatory mutations have deleterious effects in a wild-type background. A large diversity of intragenic compensatory mutations was identified from sequencing fitness-recovering genotypes. Subsequent analyses of intragenic mutation diversity revealed a significant degree of clustering around the deleterious mutation in the linear sequence and also within folded protein structures. Moreover, a likelihood analysis of mutation diversity predicts that, on average, a deleterious mutation can be compensated by about nine different intragenic compensatory mutations. We estimate that about half of all compensatory mutations are located extragenically in this organism.

132. Pradeep R.,A.S., Boucher,D., Sime-Ngando,T., Debroas,D., Romagoux,J.C. (2005). **Phage bacteriolysis, protistan bacterivory potential, and bacterial production in a freshwater reservoir: coupling with temperature.** *Microb. Ecol.* 50:64-72. **Abstract:** Phage abundance and infection of bacterioplankton were studied from March to November 2003 in the Sep Reservoir (Massif Central, France), together with temperature, chlorophyll, bacteria (abundance and production), and heterotrophic nanoflagellates (abundance and potential bacterivory). Virus abundance (VA) ranged from 0.6 to 13 x 10(10) viruses l(-1), exceeding bacterial abundance (BA) approximately sixfold on average. In terms of carbon, viruses corresponded to up to 25% of bacterial biomass. A multiple regression model indicated that BA was the best predictor for VA (R(2) = 0.75). The frequency of infected bacteria (estimated from the percentage of visibly infected cells) varied from 1% to 32% and was best explained by a combination of temperature (R(2) = 0.20) and bacterial production (R(2) = 0.25). Viruses and flagellates contributed about equally to bacterial mortality. Both factors destroyed 55% of bacterial production, with a shift from phage bacteriolysis in early spring to protistan bacterivory in late summer. The vertical differences in most of the biological variables were not significant, contrasting with the seasonal differences (i.e., spring vs. summer-autumn). All biological variables under study were indeed significantly coupled to temperature. We regarded this to be the consequence of the enhanced discharge of the reservoir in 2003 (compared to previous years). This substantially weakened the stability and the thermal inertia of the water column, thereby establishing temperature as a stronger forcing factor in setting the conditions for optimal metabolic activity of microbial communities.

133. Rakonjac,J., O'Toole,P.W., Lubbers,M. (2005). **Isolation of lactococcal prolate phage-phage recombinants by an enrichment strategy reveals two novel host range determinants.** *J. Bacteriol.* 187:3110-3121. **Abstract:** Virulent lactococcal prolate (or c2-like) phages are the second most common phage group that causes fermentation failure in the dairy industry. We have mapped two host range determinants in two lactococcal prolate phages, c2 and 923, for the host strains MG1363 and 112. Each phage replicates on only one of the two host strains: c2 on MG1363 and 923 on 112. Phage-phage recombinants that replicated on both strains were isolated by a new method that does not require direct selection but rather employs an enrichment protocol. After initial mixed infection of strain 112, two rotations, the first of which was carried out on strain MG1363 and the second on 112, permitted continuous amplification of double-plating recombinants while rendering one of the parent phages unamplified in each of the two rotations. Mapping of the recombination endpoints showed that the presence of the N-terminal two-thirds of the tail protein L10 of phage c2 and a 1,562-bp cosR-terminal fragment of phage 923 genome overcame blocks of infection in strains MG1363 and 112, respectively. Both infection inhibition mechanisms act at the stage of DNA entry; in strain MG1363, the infection block acts early, before phage DNA enters the cytoplasm, and in strain 112, it acts late, after most of the DNA has entered the cell but before it undergoes cos-end ligation. These are the first reported host range determinants in bacteriophage of lactic acid bacteria required for overcoming inhibition of infection at the stage of DNA entry and cos-end ligation.

134. Repik,A., Pincus,S.E., Ghiran,I., Nicholson-Weller,A., Asher,D.R., Cerny,A.M., Casey,L.S., Jones,S.M., Jones,S.N., Mohamed,N., Klickstein,L.B., Spitalny,G., Finberg,R.W. (2005). **A transgenic mouse model for studying the clearance of blood-borne pathogens via human complement receptor 1 (CR1).** *Clinical and experimental immunology* 140:230-240. **Abstract:** Complement receptor 1 (CR1) on the surface of human erythrocytes facilitates intravascular clearance of complement-opsonized pathogens. The need for complement activation can be circumvented by directly coupling the organism to CR1 using a bispecific monoclonal antibody heteropolymer (HP). Lack of a functional homologue to CR1 on mouse erythrocytes has made it difficult to study HP-dependent clearance of pathogens in small animals. We have developed a transgenic mouse that expresses human CR1 on erythrocytes. CR1 antigen is of appropriate size and in a clustered distribution as confirmed by immunoblotting and fluorescence microscopy, respectively. HP that immobilized bacteriophage ϕX174 prototype pathogen to erythrocyte CR1 of the transgenic mice increased the rate of clearance of the virus compared with HP that bound

bacteriophage, but not CR1. This transgenic mouse model will allow evaluation of different HPs for their in vivo efficacy and potential as human therapeutics.

135. Resch,A., Fehrenbacher,B., Eisele,K., Schaller,M., Gotz,F. (2005). **Phage release from biofilm and planktonic *Staphylococcus aureus* cells.** *FEMS Microbiol. Lett.* 252:89-96. **Abstract:** The ability of pathogenic staphylococci to form biofilms facilitates colonization and the development of chronic infections. Therapy is hampered by the high tolerance of biofilms towards antibiotic treatment and the immune system. We found evidence that lysogenic *Staphylococcus aureus* cells in a biofilm and in planktonic cultures spontaneously release phages into their surroundings. Phages were detected over a much longer period in biofilm cultures than in planktonic supernatants because the latter were degraded by secreted proteases. Phage release in planktonic and biofilm cultures was artificially increased by adding mitomycin C. Two morphologically distinct phages in the *S. aureus* strain used in this work were observed by electron microscopy. We postulate that phage-release is a frequent event in biofilms. The resulting lysis of cells in a biofilm might promote the persistence and survival of the remaining cells, as they gain a nutrient reservoir from their dead and lysed neighboring cells. This might therefore be an early differentiation and apoptotic mechanism.

136. Robins,H., Krasnitz,M., Barak,H., Levine,A.J. (2005). **A relative-entropy algorithm for genomic fingerprinting captures host-phage similarities.** *J. Bacteriol.* 187:8370-8374. **Abstract:** The degeneracy of codons allows a multitude of possible sequences to code for the same protein. Hidden within the particular choice of sequence for each organism are over 100 previously undiscovered biologically significant, short oligonucleotides (length, 2 to 7 nucleotides). We present an information-theoretic algorithm that finds these novel signals. Applying this algorithm to the 209 sequenced bacterial genomes in the NCBI database, we determine a set of oligonucleotides for each bacterium which uniquely characterizes the organism. Some of these signals have known biological functions, like restriction enzyme binding sites, but most are new. An accompanying scoring algorithm is introduced that accurately (92%) places sequences of 100 kb with their correct species among the choice of hundreds. This algorithm also does far better than previous methods at relating phage genomes to their bacterial hosts, suggesting that the lists of oligonucleotides are "genomic fingerprints" that encode information about the effects of the cellular environment on DNA sequence. Our approach provides a novel basis for phylogeny and is potentially ideally suited for classifying the short DNA fragments obtained by environmental shotgun sequencing. The methods developed here can be readily extended to other problems in bioinformatics.

137. Saren,A.M., Ravantti,J.J., Benson,S.D., Burnett,R.M., Paulin,L., Bamford,D.H., Bamford,J.K.H. (2005). **A snapshot of viral evolution from genome analysis of the tectiviridae family.** *J. Mol. Biol.* 350:427-440. **Abstract:** The origin, evolution and relationships of viruses are all fascinating topics. Current thinking in these areas is strongly influenced by the tailed double-stranded (ds) DNA bacteriophages. These viruses have mosaic genomes produced by genetic exchange and so new natural isolates are quite dissimilar to each other, and to laboratory strains. Consequently, they are not amenable to study by current tools for phylogenetic analysis. Less attention has been paid to the Tectiviridae family, which embraces icosahedral dsDNA bacterial viruses with an internal lipid membrane. It includes viruses, such as PRD1, that infect Gram-negative bacteria, as well as viruses like Bam35 with Gram-positive hosts. Although PRD1 and Bam35 have closely related virion morphology and genome organization, they have no detectable sequence similarity. There is strong evidence that the Bam35 coat protein has the "double-barrel trimer" arrangement of PRD1 that was first observed in adenovirus and is predicted to occur in other viruses with large facets. It is very likely that a single ancestral virus gave rise to this very large group of viruses. The unprecedented degree of conservation recently observed for two Bam35-like tectiviruses made it important to investigate those infecting Gram-negative bacteria. The DNA sequences for six PRD1-like isolates (PRD1, PR3, PR4, PR5, L17, PR772) have now been determined. Remarkably, these bacteriophages, isolated at distinctly different dates and global locations, have almost identical genomes. The discovery of almost invariant genomes for the two main Tectiviridae groups contrasts sharply with the situation in the tailed dsDNA bacteriophages. Notably, it permits a sequence analysis of the isolates revealing that the tectiviral proteins can be dissected into a slowly evolving group descended from the ancestor, the viral self, and a more rapidly changing group reflecting interactions with the host.

138. Sarma,T.A., Kaur,S.P. (2005). **Growth of cyanophage N-1 under the influence of heavy metal ions.** *Acta virologica. English ed* 49:23-28. **Abstract:** The growth of cyanophage N-1 in the cyanobacterium *Nostoc muscorum* under the influence of heavy metal ions, namely Co2+, Cr6+, Cu2+, Mn2+ and Ni2+ has been studied. One-step growth experiments revealed that heavy metal ions extended the latent period by 1-2 hrs with a concomitant decrease in the phage burst size. The latter was reduced in the order Cu2/Mn2+, Ni2+, Co2+ and Cr6+. The treatment of the phage-infected bacteria with heavy metal ions did not induce

mutations affecting either the phage plaque morphology or burst size. The final phage titer after such a treatments was lowest with Co2+, Cu2+ and Cr6+. The inhibition of the phage growth under the influence of heavy metal ions is discussed in context with the interaction of cyanophage N-1 with the photosynthetic reactions in the host bacteria.

139. Scholl,D.**,** Adhya,S. **,** Merril,C. (2005). ***Escherichia coli* K1's capsule is a barrier to bacteriophage T7.** *Appl. Environ. Microbiol.* 71:4872-4874. **Abstract:** *Escherichia coli* strains that produce the K1 polysaccharide capsule have long been associated with pathogenesis. This capsule is believed to increase the cell's invasiveness, allowing the bacteria to avoid phagocytosis and inactivation by complement. It is also recognized as a receptor by some phages, such as K1F and K1-5, which have virion-associated enzymes that degrade the polysaccharide. In this report we show that expression of the K1 capsule in *E. coli* physically blocks infection by T7, a phage that recognizes lipopolysaccharide as the primary receptor. Enzymatic removal of the K1 antigen from the cell allows T7 to adsorb and replicate. This observation suggests that the capsule plays an important role as a defense against some phages that recognize structures beneath it and that the K1-specific phages evolved to counter this physical barrier.

140. Scholl,D.**,** Merril,C. (2005). **The genome of bacteriophage K1F, a T7-like phage that has acquired the ability to replicate on K1 strains of *Escherichia coli*.** *J. Bacteriol.* 187:8499-8503. **Abstract:** Bacteriophage K1F specifically infects *Escherichia coli* strains that produce the K1 polysaccharide capsule. Like several other K1 capsule-specific phages, K1F encodes an endo-neuraminidase (endosialidase) that is part of the tail structure which allows the phage to recognize and degrade the polysaccharide capsule. The complete nucleotide sequence of the K1F genome reveals that it is closely related to bacteriophage T7 in both genome organization and sequence similarity. The most striking difference between the two phages is that K1F encodes the endosialidase in the analogous position to the T7 tail fiber gene. This is in contrast with bacteriophage K1-5, another K1-specific phage, which encodes a very similar endosialidase which is part of a tail gene "module" at the end of the phage genome. It appears that diverse phages have acquired endosialidase genes by horizontal gene transfer and that these genes or gene products have adapted to different genome and virion architectures.

141. Seed,K.D.**,** Dennis,J.J. (2005). **Isolation and characterization of bacteriophages of the *Burkholderia cepacia* complex.** *FEMS Microbiol. Lett.* 251:273-280. **Abstract:** The *Burkholderia cepacia* complex consists of nine phenotypically similar but genotypically distinct beta-proteobacteria that are metabolically diverse and highly antibiotic resistant. Because of this exceptional intrinsic antibiotic resistance, infections with *B. cepacia* complex members are difficult to treat clinically and new alternative therapies are required. One strategy that holds some promise is the use of naturally occurring antibacterial bacteriophages that could potentially bind to and lyse *B. cepacia* complex cells in vivo. Towards that end, we used enrichment techniques to isolate lytic and lysogenic bacteriophages specific to the *B. cepacia* complex. The newly isolated bacteriophages were characterized by host range analysis, electron microscopy, genome restriction analysis, and partial DNA sequencing. These isolates include a bacteriophage with one of the broadest host ranges yet identified for any bacteriophage specific to the *B. cepacia* complex, and the first description of bacteriophages capable of lysing *B. ambifaria*.

142. Shang,C.**,** Wong,H.M. **,** Chen,G. (2005). **Bacteriophage MS-2 removal by submerged membrane bioreactor.** *Water Res.* 39:4211-4219. **Abstract:** A membrane bioreactor (MBR) may serve as a pre-disinfection or disinfection unit, in addition to its solid/liquid separation and biological conversion functions, to produce sewage effluent of high quality. This bench-scale pilot study focuses on investigating the performance of a submerged MBR in pathogen removal and the factors affecting the removal, using a 0.4-microm hollow-fiber membrane module submerged in an aeration tank and bacteriophage MS-2 as the indicator organism. Removal of the MS-2 phage was found to be contributed by physical filtration by the membrane itself, biomass activity in the aeration tank and bio-filtration achieved by the biofilm developed on the membrane surface. The membrane alone gave poor virus removal (0.4+/-0.1 log) but the overall removal increased substantially with the presence of biomass and the membrane-surface-attached biofilm. The contributions of the suspended biomass and attached biofilm to the phage removal are dependent on the inter-related parameters including the concentration of mixed liquor suspended solids (MLSS), the sludge retention time (SRT) and the food to mass (F/M) ratio. The correlations between effluent flux/trans-membrane pressure and virus removal give evidence that phage removal in the MBR is most likely susceptible to both biological and physical factors including the quantity and property of the biomass and the biofilm and the membrane pore size reduction.

143. Sharma,M.**,** Ryu,J.H. **,** Beuchat,L.R. (2005). **Inactivation of *Escherichia coli* O157:H7 in biofilm on stainless steel by treatment with an alkaline cleaner and a bacteriophage.** *J. Appl. Microbiol.* 99:449-459.

Abstract: AIMS: To determine the effectiveness of an alkaline cleaner used in food-processing plants and a lytic bacteriophage specific for *Escherichia coli* O157:H7 in killing wild type and rpoS-deficient cells of the pathogen in a biofilm. METHODS AND RESULTS: Wild type and rpoS-deficient cells were attached to stainless steel coupons (c. 7-8 log CFU per coupon) on which biofilms were developed during incubation at 22 degrees C for 96 h in M9 minimal salts media (MSM) with one transfer to fresh medium. Coupons were treated with 100 and 25% working concentrations of a commercial alkaline cleaner (pH 11.9, with 100 microg ml(-1) free chlorine) used in the food industry, chlorine solutions (50 and 100 microg ml(-1) free chlorine), or sterile deionized water (control) at 4 degrees C for 1 and 3 min. Treatment with 100% alkaline cleaners reduced populations by 5-6 log CFU per coupon, a significant (P < or = 0.05) reduction compared with treatment with water. Initial populations (2.6 log CFU per coupon) of attached cells of both strains were reduced by 1.2 log CFU per coupon when treated with bacteriophage KH1 (7.7 log PFU ml(-1)) for up to 4 days at 4 degrees C. Biofilms containing low populations (2.7-2.8 log CFU per coupon) of wild type and rpoS-deficient cells that had developed for 24 h at 22 degrees C were not decreased by more than 1 log CFU per coupon when treated with KH1 (7.5 log PFU ml(-1)) at 4 degrees C. CONCLUSIONS: Higher numbers of cells of *E. coli* O157:H7 in biofilms are killed by treatment with an alkaline cleaner than with hypochlorite alone, possibly through a synergistic mechanism of alkaline pH and hypochlorite. Populations of cells attached on coupons were reduced by treating with bacteriophage but cells enmeshed in biofilms were protected. SIGNIFICANCE AND IMPACT OF THE STUDY: The alkaline pH, in combination with hypochlorite, in a commercial cleaner is responsible for killing *E. coli* O157:H7 in biofilms. Treatment with bacteriophage KH1 reduces populations of cells attached to coupon surfaces but not cells in biofilms.

144. Sierra,O.E.**,** Gaona de Hernandez,M.A.**,** Rey,G.J. (2005). **[Permeability to phi chi 174 bacteriophages in polyolephin membrane condoms].** *Biomedica : revista del Instituto Nacional de Salud* 25:603-608. **Abstract:** Membranes used for the manufacture of condoms eventually can develop tiny pores, thereby decreasing dramatically their effectiveness as a physical barrier against the transmission of infectious agents. A technique was designed that was based on the ability of bacteriophage viruses to trespass membranes and to infect certain bacteria species, and then developing lysis plaques in the colonies of the host bacteria. The effectiveness of 60 polyolefin condoms in preventing the diffusion of the bacteriophage phi chi 174(ATCC13706-B1), 27 nm diameter, was compared to 20 latex condoms. Physiological conditions such as pressure, pH, superficial tension, length, time of exposure and viral titre were simulated. A pressurization system was designed, in which compressed air was injected simultaneously to ten condoms. Four of the 60 polyolefin condoms and one of the 20 latex condoms were permeable to the virus. Therefore, at least 93% of the condoms evaluated were able to contain the virus. The difference in permeability between the two types of membranes was not statistically significant (P = 0.79).

145. Silander,O.K.**,** Weinreich,D.M.**,** Wright,K.M.**,** O'Keefe,K.J.**,** Rang,C.U.**,** Turner,P.E.**,** C.,L. (2005). **Widespread genetic exchange among terrestrial bacteriophages.** *Proc. Natl. Acad. Sci. USA* 102:19009-19014. **Abstract:** Bacteriophages are the most numerous entities in the biosphere. Despite this numerical dominance, the genetic structure of bacteriophage populations is poorly understood. Here, we present a biogeography study involving 25 previously undescribed bacteriophages from the Cystoviridae clade, a group characterized by a dsRNA genome divided into three segments. Previous laboratory manipulation has shown that, when multiple Cystoviruses infect a single host cell, they undergo (i) rare intrasegment recombination events and (ii) frequent genetic reassortment between segments. Analyzing linkage disequilibrium (LD) within segments, we find no significant evidence of intrasegment recombination in wild populations, consistent with (i). An extensive analysis of LD between segments supports frequent reassortment, on a time scale similar to the genomic mutation rate. The absence of LD within this group of phages is consistent with expectations for a completely sexual population, despite the fact that some segments have >50% nucleotide divergence at 4-fold degenerate sites. This extraordinary rate of genetic exchange between highly unrelated individuals is unprecedented in any taxa. We discuss our results in light of the biological species concept applied to viruses.

146. Song,I.**,** Choi,C.Y.**,** O'Shaughnessy,S.**,** Gerba,C.P. (2005). **Effects of temperature and moisture on coliphage PRD-1 survival in soil.** *J. Food Prot.* 68:2118-2122. **Abstract:** The goal of this study was to quantitatively assess the effects of temperature and soil moisture on the survival of coliphage PRD-1 in soil. PRD-1 was added to sandy loam soil at five different soil moisture levels. The soil seeded with PRD-1 was packed into sterile polyethylene jars and exposed to eight different temperatures in an oven. Samples were collected over 14 to 25 days depending on the temperature. The inactivation rate of PRD-1 increased linearly with increased temperature. The inactivation rate gradually decreased when the soil moisture level decreased from 20.9 to 8.9%. However, the inactivation rate increased when the soil

moisture content reached 5.1%, suggesting the existence of an optimal soil moisture condition for PRD-1 survival. It is also possible that there is a threshold soil moisture level below which the inactivation of PRD-1 suddenly increases. Marked reductions in recoveries were observed as the soil moisture approached or fell below 5.0% as a result of evaporation. The increased inactivation of PRD-1 due to strong association with soil particles may have caused rapid reductions in recoveries. The evaporation process appeared to affect PRD-1 survival substantially at higher temperatures whereas little effect was observed at lower temperatures. A model developed from this study predicted PRD-1 survival in subsurface soil in field conditions with an average error of 11.0%.

147. Springman,R., Badgett,M.R., Molineux,I.J., Bull,J.J. (2005). **Gene order constrains adaptation in bacteriophage T7.** *Virology* 341:141-152. **Abstract:** The order of genes in the genome is commonly thought to have functional significance for gene regulation and fitness but has not heretofore been tested experimentally. We adapted a bacteriophage T7 variant harboring an ectopically positioned RNA polymerase gene to determine whether it could regain the fitness of the wild type. Two replicate lines maintained the starting gene order and showed only modest recovery of fitness, despite the accumulation of over a dozen mutations. In both lines, a mutation in the early terminator signal is responsible for the majority of the fitness recovery. In a third line, the phage evolved a new gene order, restoring the wild-type position of the RNA polymerase gene but also displacing several other genes to ectopic locations. Due to the recombination, the fitness of this replicate was the highest obtained but it falls short of the wild type adapted to the same growth conditions. The large benefits afforded by the terminator mutation and the recombination are explicable in terms of T7 biology, whereas several mutations with lesser benefits are not easily accounted for. These results support the premise that gene order is important to fitness and that wild-type fitness is not rapidly re-evolved in reorganized genomes.

148. Stone,G.P., Mernaugh,R., Haselton,F.R. (2005). **Virus detection using filament-coupled antibodies.** *Biotech. Bioeng.* 91:699-706. **Abstract:** Two attractive features of ELISA are the specificity of antibody-antigen recognition and the sensitivity achieved by enzymatic amplification. This report describes the development of a non-enzymatic molecular recognition platform adaptable to point-of-care clinical settings and field detection of biohazardous materials. This filament-antibody recognition assay (FARA) is based on circumferential bands of antibody probes coupled to a 120 microm diameter polyester filament. One advantage of this design is that automated processing is achieved by sequential positioning of filament-coupled probes through a series of 25-60 μL liquid filled microcapillary chambers. This approach was evaluated by testing for the presence of M13KO7 bacterial virus using anti-M13KO7 IgG(1) monoclonal antibody coupled to a filament. Filament motion first positioned the antibodies within a microcapillary tube containing a solution of M13KO7 virus before moving the probes through subsequent chambers, where the filament-coupled probes were washed, exposed to a fluorescently labeled anti-M13K07 antibody, and washed again. Filament fluorescence was then measured using a flatbed microarray scanner. The presence of virus in solution produced a characteristic increase in filament fluorescence only in regions containing coupled antibody probes. Even without the enzymatic amplification of a typical ELISA, the presence of 8.3 x 10(8) virus particles produced a 30-fold increase in fluorescence over an immobilized negative control antibody. In an ELISA comparison study, the filament-based approach had a similar lower limit of sensitivity of approximately 1.7 x 10(7) virus particles. This platform may prove attractive for point-of-care settings, the detection of biohazardous materials, or other applications where sensitive, rapid, and automated molecular recognition is desired.

149. Sullivan,M.B., Coleman,M., Weigele,P., Rohwer,F., Chisholm,S.W. (2005). **Three *Prochlorococcus* cyanophage genomes: Signature features and ecological interpretations.** *PLoS Biol.* 3:e144. **Abstract:** The oceanic cyanobacteria *Prochlorococcus* are globally important, ecologically diverse primary producers. It is thought that their viruses (phages) mediate population sizes and affect the evolutionary trajectories of their hosts. Here we present an analysis of genomes from three *Prochlorococcus* phages: a podovirus and two myoviruses. The morphology, overall genome features, and gene content of these phages suggest that they are quite similar to T7-like (P-SSP7) and T4-like (P-SSM2 and P-SSM4) phages. Using the existing phage taxonomic framework as a guideline, we examined genome sequences to establish "core" genes for each phage group. We found the podovirus contained 15 of 26 core T7-like genes and the two myoviruses contained 43 and 42 of 75 core T4-like genes. In addition to these core genes, each genome contains a significant number of "cyanobacterial" genes, i.e., genes with significant best BLAST hits to genes found in cyanobacteria. Some of these, we speculate, represent "signature" cyanophage genes. For example, all three phage genomes contain photosynthetic genes (psbA, hliP) that are thought to help maintain host photosynthetic activity during infection, as well as an aldolase family gene (talC) that could facilitate alternative routes of carbon metabolism during

infection. The podovirus genome also contains an integrase gene (int) and other features that suggest it is capable of integrating into its host. If indeed it is, this would be unprecedented among cultured T7-like phages or marine cyanophages and would have significant evolutionary and ecological implications for phage and host. Further, both myoviruses contain phosphate-inducible genes (phoH and pstS) that are likely to be important for phage and host responses to phosphate stress, a commonly limiting nutrient in marine systems. Thus, these marine cyanophages appear to be variations of two well-known phages—T7 and T4—but contain genes that, if functional, reflect adaptations for infection of photosynthetic hosts in low-nutrient oceanic environments.

150. Tanji,Y., Shimada,T., Fukudomi,H., Miyanaga,K., Nakai,Y., Unno,H. (2005). **Therapeutic use of phage cocktail for controlling *Escherichia coli* O157:H7 in gastrointestinal tract of mice.** *Journal of Bioscience and Bioengineering* 100:280-287. **Abstract:** To investigate the therapeutical use of phage mixture for controlling gastrointestinal *Escherichia coli* O157:H7 cells, in vitro and in vivo experiments were conducted. Three phages, SP15, SP21, and SP22 were selected from 26 phage stock screened from feces of stock animals and sewage influent. Addition of single or binary phage to the *E. coli* cell batch-culture reduced the turbidity of the culture. However, reascend of the turbidity due to the appearance of phage resistance cell was observed. On the other hand, addition of three phage mixture (SP15-21-22) did not produce reascend of culture turbidity under aerobic condition. Under anaerobic condition, slight reascend of culture turbidity was observed after SP15-21-22 addition. Chemostat continuous culture was operated under anaerobic condition to optimize the titer of phage cocktail and frequency of the addition for controlling *E. coli* cells. Five-log decrease of *E. coli* cell concentration after addition of phage cocktail of 10(9) Plaque forming unit (PFU)/ml was observed. However, reascend of cell concentration was observed after 1 d incubation. Repeated addition of phage cocktail was effective to reduce the cell concentration. Suspension of phage cocktail in the buffer containing 0.25% CaCO3 neutralized 9 times much more buffer of pH 2. Based on this *in vitro* experiment, phage cocktail (SP15-21-22) suspended in the buffer containing 0.25% CaCO3 was orally administrated to the mice in which *E. coli* O157:H7 cells was administrated in 2-d advance. *E. coli* and phage concentration in the feces was monitored for 9 d after phage addition. High titer of phage was detected in the feces when the phage cocktail administrated daily. *E. coli* O157:H7 concentration in the feces has been reduced according to the time period. However, difference of *E. coli* concentration in the feces of mice administrates with phage and in the control mice without phage addition became slight after 9-d test period. High titer of the phage settled down in the gastrointestinal tracts and reduced the concentration of *E. coli* cell. Repeated oral administration of SP15-21-22 was effective for rapid evacuation of *E. coli* O157:H7 from the feces and gastrointestinal tract of mice.

151. Tanner,B.D., Brooks,J.P., Haas,C.N., Gerba,C.P., Pepper,I.L. (2005). **Bioaerosol emission rate and plume characteristics during land application of liquid class B biosolids.** *Environ. Sci. Technol.* 39:1584-1590. **Abstract:** This study investigated bioaerosol emission rates and plume characteristics of bioaerosols generated during land application of liquid Class B biosolids. In addition, it compared the rate of aerosolization of coliphages and total coliform bacteria during land application of liquid Class B biosolids to the rate of aerosolization during land application of groundwater inoculated with similar concentrations of Escherichia coli and coliphage MS2. Air samples were taken immediately downwind of a spray applicator as it applied liquid (approximately 8% solids) biosolids to farmland near Tucson, Arizona. Air samples were also collected immediately downwind of groundwater seeded with MS2 and *E. coli* applied to land in an identical manner. Air samples, collected with liquid impingers, were taken in horizontal and vertical alignment with respect to the passing spray applicator. Vertical and horizontal sample arrays made it possible to calculate the flux of microorganisms through a virtual plane of air samplers, located 2 m downwind of the passing spray applicator. Neither coliphages nor coliform bacteria were detected in air downwind of spray application of liquid Class B biosolids. Based on limits of detection for the methodology, the rate of aerosolization during land application of liquid biosolids was calculated to be less than 33 plaque forming units (PFU) of coliphage and 10 colony forming units (CFU) of coliform bacteria per meter traveled by the spray applicator. The rate of aerosolization during land application of seeded groundwater was found to be, on average, 2.02 x 10(3) CFU *E. coli* and 3.86 x 10(3) PFU MS2 aerosolized per meter traveled by the spray applicator. This is greater aerosolization than was observed during land application of biosolids. Because concentrations of coliphages and coliforms were similar in the liquid biosolids and the seeded water, it was concluded that some property of biosolids reduces aerosolization of microorganisms relative to groundwater. Additional experiments utilizing a novel air sampling protocol showed that the duration of bioaerosol exposure immediately (2 m) downwind of biosolids spray application is brief and the plume of bioaerosols generated is discrete. Additional air samples showed that aerosolization of coliphages and coliform bacteria after liquid biosolids have been applied to land does not occur at detectable levels.

152. Thurston-Enriquez,J.A., Gilley,J.E., Eghball,B. (2005). **Microbial quality of runoff following land application of cattle manure and swine slurry.** *Water Hlth.* 3:157-171. **Abstract:** Concentrations of human health-related microorganisms in runoff from agricultural plots (0.75 m x 2 m) treated with fresh and aged cattle manure, swine slurry and no manure (control) were determined. Three consecutive simulated rainfall events, producing 35 mm rainfall and separated by 24 h, were carried out for each plot. Fecal indicator (*Escherichia coli*, enterococci, Clostridium perfringens and coliphage) loads released in rainfall runoff from plots treated with fresh cattle manure, aged cattle manure and swine slurry treatments ranged from 5.52 x 10(5) to 4.36 x 10(9), 3.92 x 10(4) to 4.86 x 10(8), and 9.63 x 10(5) to 3.05 x 10(8), respectively. Plot runoff concentrations of protozoa (*Cryptosporidium* oocysts and *Giardia* cysts) ranged from 1.65 x 10(5) to 1.04 x 10(6), 2.93 x 10(3) to 2.75 x 10(5), and 9.12 x 10(4) to 3.58 x 10(6) for fresh cattle manure, aged cattle manure and swine slurry plot treatments, respectively. These results suggest that large microbial loads could be released via heavy precipitation events that produce runoff from livestock manure-applied agricultural fields, of even modest size, and could have a significant impact on water bodies within the watershed. Because of the lack of multiplication in the environment, highly elevated concentrations in manured land runoff, and correlation to protozoan parasite presence, Clostridium may be an alternative indicator for livestock manure contamination.

153. Toro,H., Price,S.B. , McKee,A.S., Hoerr,F.J., Krehling,J., Perdue,M., Bauermeister,L. (2005). **Use of bacteriophages in combination with competitive exclusion to reduce *Salmonella* from infected chickens.** *Avian Diseases* 49:118-124. **Abstract:** *Salmonella*-spedfic bacteriophages (BP) and competitive exclusion (CE) were used to reduce *Salmonella* colonization in experimentally infected chickens. A "cocktail" of distinct phage (i.e., phage showing different host ranges and inducing different types of plaques on *Salmonella* Typhimurium [ST] cultures) was developed. The killing activity of the selected BPs on ST cultures differed significantly, as determined in in vitro killing assays. BPs were administered orally to the chickens several days prior and after ST challenge but not simultaneously. BPs were readily isolated from the feces of the BP-treated chickens approximately 48 hr after administration. A CE product consisting of a defined culture of seven different microbial species was used either alone or in combination with BP treatment. CE was administered orally at hatch. *Salmonella* counts in intestine, ceca, and a pool of liver/spleen were evaluated in *Salmonella*-challenged chickens treated with BP or with BP and CE. In both trials 1 and 2, a beneficial effect of the phage treatment on weight gain performance was evident. A reduction in *Salmonella* counts was detected in cecum and ileum of BP-, CE-, and BP+CE-treated chickens as compared with nontreated birds. In trial 1, BP treatment reduced ST counts to marginal levels in the ileum and reduced counts sixfold in the ceca. A reduction of *Salmonella* counts with BP, CE, and BP+CE treatments was evident in chickens from trial 2. Both CE and BP treatments showed differences in the reduction of *Salmonella* counts after challenge between spedmens obtained at days 4 and 14 postchallenge in ceca, liver/spleen, and ileum. The preliminary data presented in this report show that isolation and characterization of *Salmonella*-specific BP is uncomplicated and feasible on a larger scale. Results indicate a protective effect of both *Salmonella*-specific BPs and a defined competitive exclusion product against *Salmonella* colonization of experimentally infected chickens. These results are encouraging for further work on the use of BP as an effective alternative to antibiotics to reduce *Salmonella* infections in poultry.

154. Tucker,S., Pollard,P. (2005). **Identification of cyanophage Ma-LBP and infection of the cyanobacterium *Microcystis aeruginosa* from an Australian subtropical lake by the virus.** *Appl. Environ. Microbiol.* 71:629-635. **Abstract:** Viruses can control the structure of bacterial communities in aquatic environments. The aim of this project was to determine if cyanophages (viruses specific to cyanobacteria) could exert a controlling influence on the abundance of the potentially toxic cyanobacterium *Microcystis aeruginosa* (host). *M. aeruginosa* was isolated, cultured, and characterized from a subtropical monomictic lake-Lake Baroon, Sunshine Coast, Queensland, Australia. The viral communities in the lake were separated from cyanobacterial grazers by filtration and chloroform washing. The natural lake viral cocktail was incubated with the *M. aeruginosa* host growing under optimal light and nutrient conditions. The specific growth rate of the host was 0.023 h-1; generation time, 30.2 h. Within 6 days, the host abundance decreased by 95%. The density of the cyanophage was positively correlated with the rate of *M. aeruginosa* cell lysis (*r*2 = 0.95). The cyanophage replication time was 11.2 h, with an average burst size of 28 viral particles per host cell. However, in 3 weeks, the cultured host community recovered, possibly because the host developed resistance (immunity) to the cyanophage. The multiplicity of infection was determined to be 2,890 virus-like particles/cultured host cell, using an undiluted lake viral population. Transmission electron microscopy showed that two types of virus were likely controlling the host cyanobacterial abundance. Both viruses displayed T7-like morphology and belonged to the *Podoviridiae* group (short tails) of viruses that we called cyanophage Ma-LBP. In Lake Baroon, the

number of the cyanophage Ma-LBP was 5.6 x 104 cyanophage · ml-1, representing 0.23% of the natural viral population of 2.46 x 107 · ml-1. Our results showed that this cyanophage could be a major natural control mechanism of *M. aeruginosa* abundance in aquatic ecosystems like Lake Baroon. Future studies of potentially toxic cyanobacterial blooms need to consider factors that influence cyanophage attachment, infectivity, and lysis of their host alongside the physical and chemical parameters that drive cyanobacterial growth and production.

155. Vantarakis,A.C.**,** Tsibouxi,A.**,** Venieri,D.**,** Komninou,G.**,** Athanassiadou,A.**,** Papapetropoulou,M. (2005). **Evaluation of microbiological quality of coastal waters in Greece.** *Water Hlth.* 3:371-380. **Abstract:** To evaluate the microbiological water quality of bathing sites along the Achaia coastline (south western Greece), a survey was conducted to determine the concentration of faecal bacterial and phage indicators as well as the presence of human viruses. Seawater samples (234) were collected from nine bathing sites on the Achaia coastline and were analysed for the presence of: total coliforms, faecal coliforms, faecal streptococci, *Escherichia coli*, somatic coliphages, F-RNA bacteriophages, bacteriophages infecting *Bacteroides fragilis*, enteroviruses, adenoviruses and hepatitis A viruses. Most of the bacteriological analysis results were in accordance with the European Union standards. In all sites, bacteriophages were detected occasionally. Enteroviruses and adenoviruses were detected in 24 samples (10.26%) and 37 samples (15.81%) respectively. No samples were positive for the presence of hepatitis A virus. The overall data indicates that bathing sites are impacted by human faecal material. Both bacterial indicators and phages have low predictive capability for the presence of human viruses in coastal waters. None of the environmental parameters analysed was strongly related to the presence of the indicator organisms and viruses. Appropriate and effective administrative measures that should be taken into account may be considered in order to improve water quality and reduce public health risk.

156. Vega,E.**,** Smith,J.**,** Garland,J.**,** Matos,A.**,** Pillaii,S.D. (2005). **Variability of virus attachment patterns to butterhead lettuce.** *J. Food Prot.* 68:2112-2117. **Abstract:** Enteric viruses account for most foodborne illness in the United States. The objective of this study was to determine whether the isoelectric point (pI) of viruses such as feline calicivirus (FCV), echovirus 11, and bacteriophages ϕX174 and MS2 had any effect on their attachment to butterhead lettuce. The adsorption of virus particles to the lettuce was variable. Bacteriophage MS2 was the only virus that fit the current Derjaguin-Landau-Verway-Overbeek model of virus attachment. Echovirus 11 had the highest affinity to lettuce surface. Echovirus 11 appeared to exhibit reversible attachment above its pI, whereas below its pI strong adsorption was observed. Adsorption of FCV was at its maximum above its pI. Bacteriophage ϕX174 exhibited the most complex adsorption pattern, with attachment occurring only at the pH extremes (pH 3.0 and 8.0). These results suggest the current model for virus adsorption to sediment does not adequately explain the attachment of virus to lettuce. Importantly, the results indirectly suggest that current sample processing methods to recover viruses from lettuce may differentially select for the recovery of only certain virus types.

157. Vinodkumar,C.S.**,** Neelagund,Y.F.**,** Kalsurmath,S. (2005). **Bacteriophage in the treatment of experimental septicemic mice from a clinical isolate of multidrug resistant *Klebsiella pneumoniae*.** *J. Commun. Dis.* 37:18-29. **Abstract:** Drug resistance is the major cause of increase in morbidity and mortality in neonates. The emergence of antibiotic-resistant bacterial strains requires the exploration of alternative antibacterial therapies and the concern that human kind in re-entering the 'pre-antibiotic era' has become very real and the development of alternative anti-infection modalities has become one of the highest priorities of modern medicine and biotechnology. This has spurred biomedical researchers to expand their efforts to identify new technologies and products that employ novel mechanism of action against the "super-bugs". One of such alternatives stems up from an old idea is the bacteriophage therapy, which led our group to study the ability of bacterial viruses (bacteriophages or phages) to rescue septicemic mice with multidrug resistant (MDR) *Klebsiella pneumoniae* isolated from neonatal septicemia. The phage strain used in this study had lytic activity against a wide range of clinical isolates of MDR *Klebsiella pneumoniae*. One of these MDR *Klebsiella* strain was used to induce septicemia in mice by intraperitoneal (i.p.) injection of 10(9) CFU. The resulting bacteremia was fatal within 48 h. A single i.p. injection of 3x10(8) PFU of the phage strain administered 45 min after the bacterial challenge, was sufficient to rescue 100% of the animals. Even when treatment was delayed to the point where all animals were moribund, approximately 50% of them were rescued by a single injection of this phage preparation. The ability of this phage to rescue septicemic mice was demonstrated to be due to the functional capabilities of the phage and not to a nonspecific immune effect. The rescue of septicemic mice could be affected only by phage strains able to grow in vitro on the bacterial host used to infect the animals and when such strains are heat inactivated they lose their ability to rescue the infected mice.

158. Wagenaar,J.A., Van Bergen,M.A.P., Mueller,M.A., Wassenaar,T.M., Carlton,R.M. (2005). **Phage therapy reduces *Campylobacter jejuni* colonization in broilers.** *Vet Microbiol* 109:275-283. **Abstract:** The effect of phage therapy in the control of *Campylobacter jejuni* colonization in young broilers, either as a preventive or a therapeutic measure, was tested. A prevention group was infected with *C. jejuni* at day 4 of a 10-day phage treatment. A therapeutic group was phage treated for 6 days, starting 5 days after *C. jejuni* colonization of the broilers had been established. Treatment was monitored by enumerating *Campylobacter* colony forming units (CFU) and phage plaque forming units (PFU) from caecal content. Counts were compared with control birds not receiving phage therapy. A clear 3 log decline in *C. jejuni* counts was initially observed in the therapeutic group, however, after 5 days bacterial counts stabilized at a level 1 log lower than that of the control group. Colonization of *C. jejuni* in the prevention group was delayed by the treatment and after an initial 2 log reduction, colonization stabilized within a week at levels comparable to the therapeutic group. The CFU and PFU counts displayed opposing highs and lows over time, indicative of alternating shifts in amplification of bacteria and phages. There were no adverse health effects from the phage treatment. Two different phages were combined as therapeutic treatment of *Campylobacter* positive chickens challenged at the age approaching broiler harvest. This again resulted in a significant decrease in *Campylobacter* colonization. We conclude that phage treatment is a promising alternative for reducing *C. jejuni* colonization in broilers.

159. Weitz,J.S., Hartman,H., Levin,S.A. (2005). **Coevolutionary arms races between bacteria and bacteriophage.** *Proc. Natl. Acad. Sci. USA* 102:9535-9540. **Abstract:** We propose a computational and theoretical framework for analyzing rapid coevolutionary dynamics of bacteriophage and bacteria in their ecological context. Bacteriophage enter host cells via membrane-bound surface receptors often responsible for nutrient uptake. As such, a selective pressure will exist for the bacteria to modify its receptor configuration and, in turn, for the phage to modify its tail fiber. A mathematical model of these trait adaptations is developed by using the framework of adaptive dynamics. Host strains differ in their efficiency of resource uptake and resistance to phage, whereas phage strains differ in their host preference for adsorption. We solve the evolutionary ecology model and find the conditions for coevolutionary branching and relevant dimensionless parameters leading to distinct quasispecies. We confirm these calculations using stochastic Monte Carlo simulations of populations evolving in a chemostat with fixed washout rate and inflow resource density. We find that multiple quasispecies of bacteria and phage can coexist in a homogeneous medium with a single resource. When diversification occurs, quasispecies of phage adsorb effectively to only a limited subset of the total number of quasispecies of bacteria, i.e., functional differences between quasispecies arise endogenously within the evolutionary ecology framework. Finally, we discuss means to relate predictions of this model to experimental studies in the chemostat, using the model organisms *Escherichia coli* and the virulent strain of λ phage.

160. Williamson,K.E., Radosevich,M., Wommack,K.E. (2005). **Abundance and diversity of viruses in six Delaware soils.** *Appl. Environ. Microbiol.* 71:3119-3125. **Abstract:** The importance of viruses in marine microbial ecology has been established over the past decade. Specifically, viruses influence bacterial abundance and community composition through lysis and alter bacterial genetic diversity through transduction and lysogenic conversion. By contrast, the abundance and distribution of viruses in soils are almost completely unknown. This study describes the abundance and diversity of autochthonous viruses in six Delaware soils: two agricultural soils, two coastal plain forest soils, and two piedmont forest soils. Viral abundance was measured using epifluorescence microscopy, while viral diversity was assessed from morphological data obtained through transmission electron microscopy. Extracted soil virus communities were dominated by bacteriophages that demonstrated a wide range of capsid diameters (20 nm to 160 nm) and morphologies, including filamentous forms and phages with elongated capsids. The reciprocal Simpson's index suggests that forest soils harbor more diverse assemblages of viruses, particularly in terms of morphological distribution. Repeated extractions of virus-like particles (VLPs) from soils indicated that the initial round of extraction removes approximately 70% of extractable viruses. Higher VLP abundances were observed in forest soils (1.31 x 10(9) to 4.17 x 10(9) g(-1) dry weight) than in agricultural soils (8.7 x 10(8) to 1.1 x 10(9) g(-1) dry weight). Soil VLP abundance was significantly correlated to moisture content (r = 0.988) but not to soil texture. Land use (agricultural or forested) was significantly correlated to both bacterial (r = 0.885) and viral (r = 0.812) abundances, as were soil organic matter and water content. Thus, land use is a significant factor influencing viral abundance and diversity in soils.

161. Wills,Q.F., Kerrigan,C., Soothill,J.S. (2005). **Experimental bacteriophage protection against *Staphylococcus aureus* abscesses in a rabbit model.** *Antimicrob. Agents Chemother.* 49:1220-1221. **Abstract:** In a

rabbit model of wound infection caused by *Staphylococcus aureus*, 2 x 10(9) PFU of staphylococcal phage prevented abscess formation in rabbits when it was injected simultaneously with *S. aureus* (8 x 10(7) CFU) into the same subcutaneous site. Phage multiplied in the tissues. Phages might be a valuable prophylaxis against staphylococcal infection.

162. Yoichi,M.**,** Abe,M.**,** Miyanaga,K.**,** Unno,H.**,** Tanji,Y. (2005). **Alteration of tail fiber protein gp38 enables T2 phage to infect *Escherichia coli* O157:H7.** *J Biotechnol* 115:101-107. **Abstract:** Artificial control of phage specificity may contribute to practical applications, such as the therapeutic use of phages and the detection of bacteria by their specific phages. To change the specificity of phage infection, gene products (gp) 37 and 38, expressed at the tip of the long tail fiber of T2 phage, were exchanged with those of PP01 phage, an *Escherichia coli* O157:H7 specific phage. Homologous recombination between the T2 phage genome and a plasmid encoding the region around genes 37-38 of PP01 occurred in transformant *E. coli* K12 cells. The recombinant T2 phage, named T2ppD1, carried PP01 gp37 and 38 and infected the heterogeneous host cell E. coli O157:H7 and related species. On the other hand, T2ppD1 could not infect *E. coli K12*, the original host of T2, or its derivatives. The host range of T2ppD1 was the same as that of PP01. Infection of T2ppD1 produced turbid plaques on a lawn of *E. coli* O157:H7 cells. The binding affinity of T2ppD1 to *E. coli* O157:H7 was weaker than that of PP01. The adsorption rate constant (ka) of T2ppD1 (0.17 x 10(-9)(ml CFU(-1) min(-1)) was almost 1/6 that of PP01 (1.10 x 10(-9)(ml CFU(-1) min(-1))). In addition to the tip of the long tail fiber, exchange of gene products expressed in the short tail fiber may be necessary for tight binding of recombinant phage.

163. Alimova,A.**,** Katz,A. **,** Podder,R.**,** Minko,G.**,** Wei,H.**,** Alfano,R.R.**,** Gottlieb,P. (2004). **Virus particles monitored by fluorescence spectroscopy: a potential detection assay for macromolecular assembly.** *Photochem Photobiol* 80:41-46. **Abstract:** Native fluorescence spectroscopy was used for in situ investigations of two lipid-containing bacteriophages from the cystovirus family as well as their Pseudomonad host cells. Both the viruses ϕ6 and ϕ12 and their bacterial host proteins contain the amino acid tryptophan (trp), which is the predominant fluorophore in UV. Within proteins, trp's structural environment differs, and the differences are reflected in their spectroscopic signatures. It was observed that the peak of the trp emission from both viruses was at 330 nm, a significantly shorter wavelength than trp in either the Pseudomonad host cells or the amino acid's chemical form. This allowed us to monitor the viral attachment process and subsequent lytic release of progeny virus particles by measurement of the trp emission spectra during the infection process. This work demonstrates that fluorescence may offer a novel tool to detect viruses and monitor viral infection of cells and may be part of a biodefense application.

164. Bettarel,Y.**,** Sime-Ngando,T.**,** Amblard,C.**,** Dolan,J. (2004). **Viral activity in two contrasting lake ecosystems.** *Appl. Environ. Microbiol.* 70:2941-2951. **Abstract:** For aquatic systems, especially freshwaters, there is little data on the long-term (i.e., >6-month period) and depth-related variability of viruses. In this study, we examined virus-induced mortality of heterotrophic bacteria over a 10-month period and throughout the water column in two lakes of the French Massif Central, the oligomesotrophic Lake Pavin and the eutrophic Lake Aydat. Concurrently, we estimated nonviral mortality through heterotrophic nanoflagellate and ciliate bacterivory. Overall, viral infection parameters were much less variable than bacterial production. We found that the frequency of visibly infected cells (FVIC), estimated using transmission electron microscopy, peaked in both lakes at the end of spring (May to June) and in early autumn (September to October). FVIC values were significantly higher in Lake Pavin (mean [M] = 1.6%) than in Lake Aydat (M = 1.1%), whereas the opposite trend was observed for burst sizes, which averaged 25.7 and 30.2 virus particles bacterium(-1), respectively. We detected no significant depth-related differences in FVIC or burst size. We found that in both lakes the removal of bacterial production by flagellate grazing (M(Pavin) = 37.7%, M(Aydat) = 18.5%) was nearly always more than the production removed by viral lysis (M(Pavin) = 16.2%, M(Aydat) = 19%) or ciliate grazing (M(Pavin) = 2.7%, M(Aydat) = 8.8%). However, at specific times and locations, viral lysis prevailed over protistan grazing, for example, in the anoxic hypolimnion of Lake Aydat. In addition, viral mortality represented a relatively constant mortality source in a bacterial community showing large variations in growth rate and subject to large variations in loss rates from grazers. Finally, although viruses did not represent the main agent of bacterial mortality, our data seem to show that their relative importance was higher in the less productive system.

165. Boratynski,J.**,** Syper,D.**,** Weber-Dabrowska,B.**,** Lusiak-Szelachowska,M.**,** Pozniak,G.**,** Gorski,A. (2004). **Preparation of endotoxin-free bacteriophages.** *Cellular & molecular biology letters* 9:253-259. **Abstract:** Bacteriophages (phages) are bacterial viruses that interact with bacterial walls and invade bacterial cells. Moreover, they disturb bacterial metabolism and lead to bacteria lysis. In the case of

Gram-negative bacteria crude phage cultures, apart from the phages themselves, the bacterial debris, bacterial proteins and nucleic acids contain endotoxins. These endotoxins (lipopolysaccharides) posses a high degree of toxicity in vitro and in vivo, and their removal is essential for safety in antibacterial bacteriophage therapy. An effective, scaleable purification of bacteriophages from endotoxins was accomplished by sequential ultrafiltration through polysulfone membrane (30 nm) followed by chromatography on sepharose 4B and Matrex Cellulofine Sulfate. The phage fraction after gel filtration chromatography routinely contained endotoxins in the 150-2500 EU/ml range. The procedure yielded bacteriophages contaminated with as little as 0.4-7 EU/ml (Limulus assay). This value lies within the permitted level for intravenous applications (5 EU/kg/h by European Pharmacopoeia, 1997).

166. Brockhurst,M.A.**,** Rainey,P.B.**,** Buckling,A. (2004). **The effect of spatial heterogeneity and parasites on the evolution of host diversity.** *Proc. R. Soc. Lond. B Biol. Sci.* 271:107-111. **Abstract:** Both spatial heterogeneity and exploiters (parasites and predators) have been implicated as key ecological factors driving population diversification. However, it is unclear how these factors interact. We addressed this question using the common plant-colonizing bacterium *Pseudomonas fluorescens*, which has been shown to diversify rapidly into spatial niche-specialist genotypes when propagated in laboratory microcosms. Replicate populations were evolved in spatially homogeneous and heterogeneous environments (shaken and static microcosms, respectively) with and without viral parasites (bacteriophage) for approximately 60 bacterial generations. Consistent with previous findings, exploiters reduced diversity in heterogeneous environments by relaxing the intensity of resource competition. By contrast, exploiters increased diversity in homogeneous environments where there was little diversification through resource competition. Competition experiments revealed this increase in diversity to be the result of fitness trade-offs between exploiter resistance and competitive ability. In both environments, exploiters increased allopatric diversity, presumably as a result of divergent selection for resistance between populations. Phage increased total diversity in homogeneous environments, but had no net effect in heterogeneous environments. Such interactions between key ecological variables need to be considered when addressing diversification and coexistence in future studies.

167. Brüssow,H.**,** Canchaya,C.**,** Hardt,W.D. (2004). **Phages and the evolution of bacterial pathogens: from genomic rearrangements to lysogenic conversion.** *Microbiol. Mol. Biol. Rev.* 68:560-602, table. **Abstract:** Comparative genomics demonstrated that the chromosomes from bacteria and their viruses (bacteriophages) are coevolving. This process is most evident for bacterial pathogens where the majority contain prophages or phage remnants integrated into the bacterial DNA. Many prophages from bacterial pathogens encode virulence factors. Two situations can be distinguished: *Vibrio cholerae*, Shiga toxin-producing *Escherichia coli*, *Corynebacterium diphtheriae*, and *Clostridium botulinum* depend on a specific prophage-encoded toxin for causing a specific disease, whereas *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Salmonella enterica* serovar Typhimurium harbor a multitude of prophages and each phage-encoded virulence or fitness factor makes an incremental contribution to the fitness of the lysogen. These prophages behave like "swarms" of related prophages. Prophage diversification seems to be fueled by the frequent transfer of phage material by recombination with superinfecting phages, resident prophages, or occasional acquisition of other mobile DNA elements or bacterial chromosomal genes. Prophages also contribute to the diversification of the bacterial genome architecture. In many cases, they actually represent a large fraction of the strain-specific DNA sequences. In addition, they can serve as anchoring points for genome inversions. The current review presents the available genomics and biological data on prophages from bacterial pathogens in an evolutionary framework.

168. Burch,C.L.**,** Chao,L. (2004). **Epistasis and Its relationship to canalization in the RNA virus ϕ6.** *Genetics* 167:559-567. **Abstract:** Although deleterious mutations are believed to play a critical role in evolution, assessing their realized effect has been difficult. A key parameter governing the effect of deleterious mutations is the nature of epistasis, the interaction between the mutations. RNA viruses should provide one of the best systems for investigating the nature of epistasis because the high mutation rate allows a thorough investigation of mutational effects and interactions. Nonetheless, previous investigations of RNA viruses by S. Crotty and co-workers and by S. F. Elena have been unable to detect a significant effect of epistasis. Here we provide evidence that positive epistasis is characteristic of deleterious mutations in the RNA bacteriophage 6. We estimated the effects of deleterious mutations by performing mutation-accumulation experiments on five viral genotypes of decreasing fitness. We inferred positive epistasis because viral genotypes with low fitness were found to be less sensitive to deleterious mutations. We further examined environmental sensitivity in these genotypes and found that low-fitness genotypes were also less sensitive to environmental perturbations. Our results suggest that even random mutations impact the degree of canalization, the buffering of a phenotype against genetic and environmental

perturbations. In addition, our results suggest that genetic and environmental canalization have the same developmental basis and finally that an understanding of the nature of epistasis may first require an understanding of the nature of canalization.

169. Chibani-Chennoufi,S.**,** Dillmann,M.L.**,** Marvin-Guy,L.**,** Rami-Shojaei,S.**,** Brüssow,H. (2004). ***Lactobacillus plantarum*** **Bacteriophage LP65: a New Member of the SPO1-Like Genus of the Family Myoviridae.** *The Journal of Bacteriology* 186:7069-7083. **Abstract:** The virulent *Lactobacillus plantarum* myophage LP65 was isolated from industrial meat fermentation. Tail contraction led to reorganization of the tail sheath and the baseplate; a tail tube was extruded. In ultrathin section the phage adsorbed via its baseplate to the exterior of the cell, while the tail tube tunneled through the thick bacterial cell wall. Convoluted membrane structures were induced in the infected cell. Progeny phage was detected 100 min postinfection, and lysis occurred after extensive digestion of the cell wall. Sequence analysis revealed a genome of 131,573 bp of nonredundant DNA. Four major genome regions and a large tRNA gene cluster were observed. One module corresponded to DNA replication genes. Helicase/primase and two replication/recombination enzymes represented the only links to T4-like Myoviridae from gram-negative bacteria. Another module corresponded to the structural genes. Sequence relatedness identified links with *Listeria* phage A511, *Staphylococcus* phage K, and *Bacillus* phage SPO1. LP65 structural proteins were identified by two-dimensional proteome analysis and mass spectrometry. The putative tail sheath protein showed a shear-induced change in electrophoretic migration behavior. The genome organization of the structural module in LP65 resembled that of Siphoviridae from the lambda supergroup.

170. Chibani-Chennoufi,S.**,** Canchaya,C.**,** Bruttin,A.**,** Brüssow (2004). **Comparative genomics of the T4-Like *Escherichia coli* phage JS98: implications for the evolution of T4 phages.** *J. Bacteriol.* 186:8276-8286. **Abstract:** About 130 kb of sequence information was obtained from the coliphage JS98 isolated from the stool of a pediatric diarrhea patient in Bangladesh. The DNA shared up to 81% base pair identity with phage T4. The most conserved regions between JS98 and T4 were the structural genes, but their degree of conservation was not uniform. The head genes showed the highest sequence conservation, followed by the tail, baseplate, and tail fiber genes. Many tail fiber genes shared only protein sequence identity. Except for the insertion of endonuclease genes in T4 and gene 24 duplication in JS98, the structural gene maps of the two phages were colinear. The receptor-recognizing tail fiber proteins gp37 and gp38 were only distantly related to T4, but shared up to 83% amino acid identity to other T6-like phages, suggesting lateral gene transfer. A greater degree of variability was seen between JS98 and T4 over DNA replication and DNA transaction genes. While most of these genes came in the same order and shared up to 76% protein sequence identity, a few rearrangements, insertions, and replacements of genes were observed. Many putative gene insertions in the DNA replication module of T4 were flanked by intron-related endonuclease genes, suggesting mobile DNA elements. A hotspot of genome diversification was located downstream of the DNA polymerase gene 43 and the DNA binding gene 32. Comparative genomics of 100-kb genome sequence revealed that T4-like phages diversify more by the accumulation of point mutations and occasional gene duplication events than by modular exchanges.

171. Clokie,M.R.**,** Millard,A.D.**,** Wilson,W.H.**,** Mann,N.H. (2004). **Encapsidation of host DNA by bacteriophages infecting marine *Synechococcus* strains.** *FEMS Microbiol. Ecol.* 46:349-352. **Abstract:** It has been speculated that horizontal gene transfer might be important in the evolution of strains of the marine cyanobacterium *Synechococcus* and that phages might mediate this process, but until now there has been no direct evidence to support this idea. We have rigorously purified bacteriophages (cyanomyoviruses) from their *Synechococcus* host and performed a series of experiments on phage encapsidated DNA to reveal the presence of chromosomal *Synechococcus* DNA. Quantitative polymerase chain reaction has shown that V1 in 105 *Synechococcus* phage particles contain a host marker gene in their capsids. This is the first study that has shown that phages infecting marine *Synechococcus* strains can package host DNA and this provides evidence for the potential importance of these phage in horizontal gene transfer.

172. Dabrowska,K.**,** Opolski,A.**,** Wietrzyk,J.**,** Switala-Jelen,K.**,** Boratynski,J.**,** Nasulewicz,A.**,** Lipinska,L.**,** Chybicka,A.**,** Kujawa,M.**,** Zabel,M.**,** Dolinska-Krajewska,B.**,** Piasecki,E.**,** Weber-Dabrowska,B.**,** Rybka,J.**,** Salwa,J.**,** Wojdat,E.**,** Nowaczyk,M.**,** Gorski,A. (2004). **Antitumor activity of bacteriophages in murine experimental cancer models caused possibly by inhibition of β3 integrin signaling pathway.** *Acta virologica. English ed* 48:241-248. **Abstract:** Bacteriophages (phages) as bacterial viruses are generally believed to have no intrinsic tropism for mammalian cells. In this study the interactions between phages and various eukaryotic cells were investigated. Binding of phages to the membranes of cancer and normal blood cells was observed. Moreover, it was shown that the wild-type phage T4 (wtT4) and its

substrain HAP1 with enhanced affinity for melanoma cells inhibit markedly and significantly experimental lung metastasis of murine B16 melanoma cells by 47% and 80%, respectively. A possible molecular mechanism of these effects, namely a specific interaction between the Lys-Gly-Asp motif of the phage protein 24 and β 3-integrin receptors on target cells is proposed. It was also shown that anti-β3 antibodies and synthetic peptides mimicking natural β3 ligands inhibit the phage binding to cancer cells. This is in line with the well-described β3 integrin-dependent mechanism of tumor metastasis. It is concluded that the blocking of β3 integrins by phage preparations results in a significant decrease in tumor invasiveness.

173. Day,M. (2004). **Bacterial sensitivity to bacteriophage in the aquatic environment.** *Sci. Prog.* 87:179-191. **Abstract:** There are several unusual features about phage when you first encounter them as a biologist. They are small, but conform to one of a few morphological types. Next their genomes can be composed of DNA or RNA and be single or double stranded. Finally they are numerically more abundant than prokaryotes and a significant proportion of them form an association in their microbial host populations termed lysogeny. The latter findings indicate that they are numerically significant in microbial populations. Since bacterial and phage abundance or lack of it is related in environments, this implies that the phage populations 'titrate' their hosts, and more probably the host's physiological status. Microbial populations wax and wane with nutritional inputs and there is a dynamic relationship between phage population sizes and host numbers and physiology. Overlay this with the different phage life cycle strategies, exemplified at the extremes by phage lambda (temperate) and phage T4 (virulent), then it becomes apparent that phage are a component in nutrient cycling in ecology. But their contribution does not stop there. Many are capable of transduction, moving DNA from one cell into another. So they can also aid the evolutionary progress of microbial populations by allowing them to share genes, just as gene exchange via plasmids and transformation does. Our perception of bacteria has been derived from pure culture studies and we are just being able to appreciate how subtle their ecological interactions are. This is no less true of the studies on bacteriophage, which are almost all based on laboratory experimentation, where the hosts are physiologically stressed by growing in 'high nutritional and optimum conditions'. The natural environment is naturally discontinuous and life evolved in this. Thus our perceptions of bacteriophage and their life cycle patterns derived from laboratory experimentation may be a little off the mark when we come to understand how they and their hosts interact in the niches available to them. It is worth just considering this as you read the article, as I suspect phage behaviours are more intimately involved in, and moderated by the physiological stresses in the life cycle of bacteria than we currently believe.

174. Emery,D.L., Whittington,R.J. (2004). **An evaluation of mycophage therapy, chemotherapy and vaccination for control of *Mycobacterium avium* subsp. paratuberculosis infection.** *Vet Microbiol* 104:143-155. **Abstract:** The control of ovine Johne's disease (OJD) is important for domestic trade, the viability of farming units and possibly also for public health. Current strategies in Australia have included quarantine and pasture spelling to decrease prevalence and shedding rates and reduce numbers of *Mycobacterium paratuberculosis* (Mptb) ingested by susceptible sheep. However, alternative procedures are needed and vaccination with Gudair has recently commenced. This review examines prospects for the control of OJD by chemotherapy, vaccination and mycophages. Current chemotherapeutic regimes for treatment of *M. paratuberculosis* in ruminants are prohibitively expensive and of dubious efficacy, and apart from environmental concerns, mycophage therapy lacks a track record of success against intracellular bacteria. There is substantial evidence that live and killed mycobacterial vaccines reduce the incidence of clinical disease and shedding rates in OJD. An appraisal of recent experimental results suggests that neonatal vaccination with a defined dose of *M. paratuberculosis* offers the best prospects for the induction of protective Th1-type immunity.

175. Fischer,C.R., Yoichi,M., Unno,H., Tanji,Y. (2004). **The coexistence of *Escherichia coli* serotype O157:H7 and its specific bacteriophage in continuous culture.** *FEMS Microbiol. Lett.* 241:171-177. **Abstract:** For the development of phage therapy, systematic understanding mechanisms of bacteriophage resistance will be required. We describe a new strain of *Escherichia coli* O157:H7, named Mu(L), which stably co-exists with the O157:H7-specific lytic bacteriophage PP01. Chemostat cultures of *E. coli* O157:H7 infected with PP01 showed unchanging cell concentration, but phage concentrations which increased by approximately 10(8) PFU mL(-1). However, the latent period, burst size, and growth rate of Mu(L) were the same as in a PP01-susceptible strain. The binding rate of PP01 to the cell surface was diminished 8.5-fold in Mu(L). By observation of the binding of fluorescently labeled O157:H7-specific phage to individual Mu(L) cells, we found that clonal Mu(L) cultures were heterogeneous in their ability to bind bacteriophage. 15% of the Mu(L) population was completely resistant to PP01 infection. Mu(L) also co-existed with bacteriophages unrelated to PP01. Broad-range phage resistance by clonal heterogeneity represents a new class of bacteria-phage interactions.

176. Forde,S.E., Thompson,J.N., Bohannan,B.J.M. (2004). **Adaptation varies through space and time in a coevolving host–parasitoid interaction.** *Nature* 431:841-844. **Abstract:** One of the central challenges of evolutionary biology is to understand how coevolution organizes biodiversity over complex geographic landscapes. Most species are collections of genetically differentiated populations, and these populations have the potential to become adapted to their local environments in different ways. The geographic mosaic theory of coevolution incorporates this idea by proposing that spatial variation in natural selection and gene flow across a landscape can shape local coevolutionary dynamics(1, 2, 3, 4, 5, 6, 7). These effects may be particularly strong when populations differ across productivity gradients, where gene flow will often be asymmetric among populations(8). Conclusive empirical tests of this theory have been particularly difficult to perform because they require knowledge of patterns of gene flow, historical population relationships and local selection pressures(2). We have tested these predictions empirically using a model community of bacteria and bacteriophage (viral parasitoids of bacteria). We show that gene flow across a spatially structured landscape alters coevolution of parasitoids and their hosts and that the resulting patterns of adaptation can fluctuate in both space and time.

177. Gabrielian,N.I., Gorskaia,E.M., Spirina,T.S., Darbeeva,O.S., Maiskaia,L.M. (2004). **[Sensitivity of nosocomial microflora circulating in a transplantation clinic to medicinal bacteriophages].** *Zhurnal mikrobiologii, epidemiologii, i immunobiologii* 6-10. **Abstract:** The sensitivity of 239 isolates obtained from patients with postoperative infectious complications to phagolysis was determined. *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Escherichia coli* were found to have the highest sensitivity to phages. Variations in the sensitivity of the same cultures to phages from different producers and even from the same producer were established. The sensitivity of cultures to phages may serve as an additional criterion of the biological properties of strains and their marker.

178. Gelman,F., Lewis,K. , Klibanov,A.M. (2004). **Drastically lowering the titer of waterborne bacteriophage PRD1 by exposure to immobilized hydrophobic polycations.** *Biotechnology Letters* 26:1695-1700. **Abstract:** Decrease in the titer of bacteriophage PRD1 (a model of animal adenoviruses) in aqueous solutions caused by the presence of systematically chemically derivatized surfaces was kinetically investigated. The greatest loss of infectivity--up to a 4-log reduction in the titer--was observed with immobilized hydrophobic polyethylenimine-based and dendrimer-based polycations.

179. Greco,K.M., McDonough,M.A., Butterton,J.R. (2004). **Variation in the Shiga toxin region of 20th-century epidemic and endemic *Shigella dysenteriae* 1 strains.** *J. Infect. Dis.* 190:330-334. **Abstract:** The Shiga toxin (Stx) region of *Shigella dysenteriae* 1 lies on a defective prophage homologous to lambdoid bacteriophages in Stx-producing *Escherichia coli*. *S. dysenteriae* 1 strains obtained in locations throughout the world over the course of the past 60 years were assessed for variations in the Stx region by use of polymerase chain reaction and sequence analysis. The defective prophage was present in all strains examined, suggesting that all *S. dysenteriae* 1 isolates derive from a clone that resulted from a single phage-integration event. All western-hemisphere strains have an additional iso-IS1 insertion element upstream of stxAB, implying that there has been minimal exchange of strains between hemispheres in recent decades.

180. Greub,G., Raoult,D. (2004). **Microorganisms resistant to free-living amoebae.** *Clin. Microbiol. Rev.* 17:413-433. **Abstract:** Free-living amoebae feed on bacteria, fungi, and algae. However, some microorganisms have evolved to become resistant to these protists. These amoeba-resistant microorganisms include established pathogens, such as *Cryptococcus neoformans*, *Legionella* spp., *Chlamydophila pneumoniae*, *Mycobacterium avium*, *Listeria monocytogenes*, *Pseudomonas aeruginosa*, and *Francisella tularensis*, and emerging pathogens, such as *Bosea* spp., *Simkania negevensis*, *Parachlamydia acanthamoebae*, and *Legionella*-like amoebal pathogens. Some of these amoeba-resistant bacteria (ARB) are lytic for their amoebal host, while others are considered endosymbionts, since a stable host-parasite ratio is maintained. Free-living amoebae represent an important reservoir of ARB and may, while encysted, protect the internalized bacteria from chlorine and other biocides. Free-living amoebae may act as a Trojan horse, bringing hidden ARB within the human "Troy," and may produce vesicles filled with ARB, increasing their transmission potential. Free-living amoebae may also play a role in the selection of virulence traits and in adaptation to survival in macrophages. Thus, intra-amoebal growth was found to enhance virulence, and similar mechanisms seem to be implicated in the survival of ARB in response to both amoebae and macrophages. Moreover, free-living amoebae represent a useful tool for the culture of some intracellular bacteria and new bacterial species that might be potential emerging pathogens.

181. Hazan,R., Engelberg-Kulka,H. (2004). ***Escherichia coli* mazEF-mediated cell death as a defense mechanism that inhibits the spread of phage P1.** *Mol. Gen. Genom.* 272:227-234. **Abstract:** The *Escherichia coli* gene pair mazEF is a regulatable chromosomal toxin-antitoxin module: mazF encodes a stable toxin and mazE encodes for a labile antitoxin that overcomes the lethal effect of MazF. Because MazE is labile, inhibition of mazE expression results in cell death. We studied the effect of mazEF on the development of bacteriophage P1 upon thermoinduction of the prophage P1CM c1ts and upon infection with virulent phage particles (P1vir). In several *E. coli* strains, we showed that the Delta mazEF derivative strains produced significantly more phages than did the parent strain. In addition, upon induction of K38(P1CM c1ts), nearly all of the Delta mazEF mutant cells lysed; in contrast, very few of the parental mazEF + K38 cells underwent lysis. However, most of these cells did not remain viable. Thus, while the Delta mazEF cells die as a result of the lytic action of the phage, most of the mazEF+ cells are killed by a different mechanism, apparently through the action of the chromosomal mazEF system itself. Furthermore, the introduction of lysogens into a growing non-lysogenic culture is lethal to Delta mazEF but not for mazEF+ cultures. Thus, although mazEF action causes individual cells to die, upon phage growth this is generally beneficial to the bacterial culture because it causes P1 phage exclusion from the bacterial population. These results provide additional support for the view that bacterial cultures may share some of the characteristics of multicellular organisms.

182. Koch,S., Hufnagel,M., Huebner,J. (2004). **Treatment and prevention of enterococcal infections--alternative and experimental approaches.** *Expert Opinion on Biological Therapy* 4:1519-1531. **Abstract:** Enterococci are one of the leading types of organisms isolated from infections of hospitalised patients and the third most common cause of nosocomial bloodstream infections. They contribute significantly to patient mortality and morbidity, as well as healthcare costs. The emergence of resistance against virtually all clinically available antibiotics and the ability to transfer these resistance determinants to other pathogens demonstrates the urgency for an improved understanding of enterococcal virulence mechanisms, and the development of alternative treatment and prevention options. This article reviews new antimicrobials, vaccine targets, bacteriophage therapy, as well as treatments targeting virulence factors and biofilm, for their potential to treat and/or prevent enterococcal infections. Although clinical isolates often cause serious infections, so-called 'non-pathogenic' strains are used as therapeutics in the form of probiotics. Understanding the differences between true pathogens and beneficial commensals may help to evaluate future treatment and prophylactic options.

183. Larsen,A., Fonnes,G.A., Sandaa,R.A., Castberg,T., Thyrhaug,R., Erga,S.E., Jacquet,S., Bratbak,G. (2004). **Spring phytoplankton bloom in Norwegian coastal waters: Microbial community dynamics, succession and diversity.** *Limnol. Oceanogr.* 49:180-190. **Abstract:** Most studies of spring bloom succession in Norwegian waters have employed light microscopy and accounted for species composition of phyto- and zooplankton. Flow cytometry and molecular tools enable us to extend such investigations to include smaller organisms like bacterio- and virioplankton. Here, we describe succession and diversity of algae, bacteria, and viruses in relation to environmental changes from 15 February to 27 April. The spring succession started with an increase in autotrophic picoeukaryotes and *Synechococcus* sp. The diatoms bloomed around the middle of March and caused nutrient depletion in the upper part of the water column. Upwelling in the beginning of April gave rise to a second bloom, consisting of diatoms and *Phaeocystis pouchetii*. Numerically, autotrophic picoeukaryotes and *Synechococcus* sp. dominated the periods between and after these two major blooms. Heterotrophic bacterial abundance increased throughout the experimental period and reached peak values during and after phytoplankton blooms. These bacteria were succeeded by viruses having low DNA fluorescence, whereas viruses with medium DNA fluorescence bloomed during or after blooms of autotrophic picoeukaryotes. High-DNA fluorescence viruses reached maximum concentrations during and after the diatom and Phaeocystis blooms. The diversity of the bacterial community remained relatively stable, whereas viral diversity varied more and increased after major phytoplankton blooms. Our investigation thus demonstrates how virioplankton are important elements of the total microbial diversity and how they are intimately linked to the rest of the microbial community and possibly act as an internal driving force in spring bloom successions.

184. Lee,S., Kriakov,J., Vilcheze,C., Dai,Z., Hatfull,G.F., Jacobs,W.R.J. (2004). **Bxz1, a new generalized transducing phage for mycobacteria.** *FEMS Microbiol. Lett.* 241:271-276. **Abstract:** We have isolated and characterized a new generalized transducing phage, Bxz1, from soil sampling at a neighboring Wildlife Preservation Park. The hosts of the phage, measured by the formation of plaques, include fast growing *Mycobacterium smegmatis* and *Mycobacterium vaccae*. Bxz1 is capable of transducing chromosomal markers, point mutations, and plasmids at frequencies ranging from 10(-8) to 10(-6) per plaque forming unit between strains of *M. smegmatis*. We also demonstrated cotransduction of a transposon insertion linked to a point mutation of the ndh gene.

185. Morgan,A.D., Buckling,A. (2004). **Parasites mediate the relationship between host diversity and disturbance frequency.** *Ecol. Lett.* 7:1029-1034. **Abstract:** Patterns of community and population diversity are likely to be dependent on interactions between ecological variables. Here we address how two important ecological variables - extrinsic periodic mortality events (disturbances) and the presence of obligate-killing parasites - interact to affect the diversity of niche-specialist genotypes in laboratory populations of the bacterium *Pseudomonas fluorescens*. Consistent with previous studies, diversity was maximized at intermediate frequencies of disturbance in the absence of parasitic bacteriophages (phages). By contrast, no relationship was found between diversity and disturbance frequency in the presence of phage. The results can be explained in part by differential effects of phage on bacterial densities, and hence resource competition, under different disturbance regimes.

186. Nelson,D. (2004). **Phage taxonomy: we agree to disagree.** *J. Bacteriol.* 186:7029-7031. **Abstract:** [first paragraph] Bacteriophage (phage) researchers are in universal agreement that phage biology has undergone a renaissance in recent years. No longer just tools of molecular biology, phage are now recognized to play critical roles in bacterial pathogenesis (3, 29) and bacterial population dynamics (5, 10). Likewise, phage therapy is enjoying renewed interest in Western medicine (24). Phage-derived proteins are currently being used as molecular machines (23), diagnostic agents (22), and therapeutic agents (15, 17, 22) and for drug discovery (14). However, the resurgence in phage popularity has only fanned the flames of an ongoing debate, namely, that of phage taxonomy. Many phage biologists feel that the current taxonomic classification scheme, devised over 3 decades ago by the International Committee on Taxonomy of Viruses (ICTV), is outdated and in need of revision in light of the postgenomic age. However, choosing one methodology on the basis of which to classify all known and yet to be discovered phage is an area where phage researchers agree to disagree. In this issue of the Journal of Bacteriology, Chibani-Chennoufi et al. provide support for a comparative genomics-based alternative classification scheme (6).

187. Obradovic,A., Jones,J.B., Momol,M.T., Balogh,B., Olson,S.M. (2004). **Management of tomato bacterial spot in the field by foliar applications of bacteriophages and SAR inducers.** *Plant Dis.* 88:736-740. **Abstract:** Various combinations of the harpin protein, acibenzolar-*S*-methyl, and bacteriophages were compared for controlling tomato bacterial spot in field experiments. Harpin protein and acibenzolar- *S*-methyl were applied every 14 days beginning twice before transplanting and then an additional four applications throughout the season. Formulated bacteriophages were applied prior to inoculation followed by twice a week at dusk. A standard bactericide treatment, consisting of copper hydroxide plus mancozeb, was applied once prior to inoculation and then every 7 days, while untreated plants served as an untreated control. Experiments were conducted in north and central Florida fields during fall 2001, spring 2002, and fall 2002. In three consecutive seasons, acibenzolar-*S*-methyl applied in combination with bacteriophage or bacteriophage and harpin significantly reduced bacterial spot compared with the other treatments. However, it did not significantly affect the total yield compared with the standard or untreated control. Application of host-specific bacteriophages was effective against the bacterial spot pathogen in all three experiments, providing better disease control than copper-mancozeb or untreated control. When results of the disease severity assessments or harvested yield from the bacteriophage-treated plots were grouped and compared with the results of the corresponding nonbacteriophage group, the former provided significantly better disease control and yield of total marketable fruit.

188. Ortega-Cejas,V., Fort,J., Méndez,V., Campos,D. (2004). **Approximate solution to the speed of spreading viruses.** *Phys. Rev. E* 69:031909-1-031909-4. **Abstract:** Recently, it has been shown that the speed of virus infections can be explained by time-delayed reactiondiffusion [J. Fort and V. Méndez, Phys. Rev. Lett. **89**, 178101 (2002)], but no analytical solutions were found. Here we derive formulas for the front speed, valid in appropriate limits. We also integrate numerically the evolution equations of the system. There is good agreement with both numerical and experimental speeds.

189. Sauer,K., Cullen,M.C., Rickard,A.H., Zeef,L.A.H., Davies,D.G., Gilbert,P. (2004). **Characterization of nutrient-induced dispersion in *Pseudomonas aeruginosa* PAO1 biofilm.** *J. Bacteriol.* 186:7312-7326. **Abstract:** The processes associated with early events in biofilm formation have become a major research focus over the past several years. Events associated with dispersion of cells from late stage biofilms have, however, received little attention. We demonstrate here that dispersal of *Pseudomonas aeruginosa* PAO1 from biofilms is inducible by a sudden increase in carbon substrate availability. Most efficient at inducing dispersal were sudden increases in availability of succinate > glutamate > glucose that led to approximately 80% reductions in surface-associated biofilm biomass. Nutrient-induced biofilm dispersion was associated with increased expression of flagella (fliC) and correspondingly decreased expression of

pilus (pilA) genes in dispersed cells. Changes in gene expression associated with dispersion of *P. aeruginosa* biofilms were studied by using DNA microarray technology. Results corroborated proteomic data that showed gene expression to be markedly different between biofilms and newly dispersed cells. Gene families that were upregulated in dispersed cells included those for flagellar and ribosomal proteins, kinases, and phage PF1. Within the biofilm, genes encoding a number of denitrification pathways and pilus biosynthesis were also upregulated. Interestingly, nutrient-induced dispersion was associated with an increase in the number of Ser/Thr-phosphorylated proteins within the newly dispersed cells, and inhibition of dephosphorylation reduced the extent of nutrient-induced dispersion. This study is the first to demonstrate that dispersal of *P. aeruginosa* from biofilms can be induced by the addition of simple carbon sources. This study is also the first to demonstrate that dispersal of *P. aeruginosa* correlates with a specific dispersal phenotype.

190. Sillankorva,S.**,** Oliveira,R.**,** Vieira,M.J.**,** Sutherland,I.W.**,** Azeredo,J. (2004). **Bacteriophage Φ S1 infection of *Pseudomonas fluorescens* planktonic cells versus biofilms.** *Biofouling* 20:133-138. **Abstract:** This communication focuses on the efficacy of a specific lytic phage, phage Φ S1, as a control agent of *Pseudomonas fluorescens* biofilms. The effect of phage infection temperature and the host growth temperature were evaluated. The results obtained showed that the phage infection process was temperature dependent and that the optimum temperature of infection of planktonic cells and biofilms was 26 degrees C. At this temperature, bacteriophage Φ S1, at a multiplicity of infection (MOI) of 0.5 infected both planktonic cells and biofilms causing a biomass reduction of about 85% in both cases.

191. Smarda,J.**,** Slovackova,H. (2004). **Ten new temperate bacteriophages of *Citrobacter youngae*.** *Folia Microbiol (Praha)* 49:671-678. **Abstract:** In a cross-test, we examined 55 strains of *Citrobacter youngae* against each other as potential producers of temperate bacteriophages and as potential sensitive indicators for them. Ten strains (18.2 %) showed the production of phages. Seven different strain-specific spectra of activity (from 1 to 11 strains each) were found. Phage production by 6 strains was inducible with mitomycin C, in 4 strains it was not inducible. The plaques of the phages were more or less turbid, without a lytic halo, tiny to small, 0.2-1.3 mm in diameter. Using a polyclonal, specific anti-lambda serum, all 10 phages were found to be clearly distinct from *E. coli* lambda phage, the phage 31/47 showing the highest neutralization titre of all. Interspecific tests with 15 strains of 8 species of Enterobacteriaceae revealed not a single case of activity of Citrobacter phages towards any of them. Five phage-immune clones lysogenized with 5 of the phages kept their remaining phage sensitivity spectra, though extended by sensitivity to 1-3 phages; 2 of these strains acquired also sensitivity to phage lambda. The phages belong to the morphotypes of Myoviridae (6 phages) and Siphoviridae (4 phages), with head diameters of 51-58 nm and tail length of 97-173 nm. Three strains produced corpuscular bacteriocins.

192. Snyder,J.C.**,** Spuhler,J.**,** Wiedenheft,B.**,** Roberto,F.F.**,** Douglas,T.**,** Young,M.J. (2004). **Effects of culturing on the population structure of a hyperthermophilic virus.** *Microb. Ecol.* 48:561-566. **Abstract:** The existence of a culturing bias has long been known when sampling organisms from the environment. This bias underestimates microbial diversity and does not accurately reflect the most ecologically relevant species. Until now no study has examined the effects of culture bias on viral populations. We have employed culture independent methods to assess the diversity of Sulfolobus spindle-shaped viruses (SSVs) from extremely hyperthermal environments. This diversity is then compared to the viral diversity of cultured samples. We detected a clear culturing bias between environmental samples and cultured isolates. This is the first study identifying a culture bias in a viral population.

193. Sockett,R.E.**,** Lambert,C. (2004). **Bdellovibrio as therapeutic agents: a predatory renaissance?** *Nature Rev. Microbiol.* 2:669-675. **Abstract:** *Bdellovibrio* are predatory bacteria that invade the periplasm of other Gram negative bacteria where they undergo a complex developmental cycle that culminates in killing of the prey cell. Their intracellular niche allows *Bdellovibrio* to feed without competition and their lytic action can rapidly reduce bacterial populations, including pathogens, making these predatory bacteria interesting potential candidates for therapeutic applications. With the complete genome sequence for one *Bdellovibrio* strain now available, researchers now have an opportunity to evaluate the therapeutic potential of these predatory bacteria.

194. Srivastava,A.S.**,** Chauhan,D.P.**,** Carrier,E. (2004). **In utero detection of T7 phage after systemic administration to pregnant mice.** *BioTechniques* 37:81-83. **Abstract:** The phage is used as a scaffold to display recombinant libraries of peptides, which provides the means to rescue and amplify peptides that bind target macromolecules. Many reports showed that the T7 phage display method can be used to obtain a ligand-binding peptidefor tissue-targeted therapies in adult animals. In utero tissue targeting of

fetal tissues may help in the correction of many genetic and metabolic diseases. Here we demonstrate the distribution and detection of T7 phage displaying the C-X7-C peptide library in mouse fetal tissues after systemic injection of T7 phage into pregnant mouse tail vein. T7 phage was recovered from fetal tissues 15 min after injection of T7 phage. Our results suggest that T7 phage may be a useful tool in selecting the tissue-specific ligand-binding peptide for fetal tissues. This approach may be helpful in designing in utero tissue-targeted therapies.

195. Strauch,E.**,** Schaudinn,C.**,** Beutin,L. (2004). **First-time isolation and characterization of a bacteriophage encoding the Shiga toxin 2c variant, which Is globally spread in strains of *Escherichia coli* O157 .** *Infect. Immun.* 72:7030-7039. **Abstract:** A bacteriophage encoding the Shiga toxin 2c variant (Stx2c) was isolated from the human *Escherichia coli* O157 strain CB2851 and shown to form lysogens on the *E. coli* K-12 laboratory strains C600 and MG1655. Production of Stx2c was found in the wild-type *E. coli* O157 strain and the K-12 lysogens and was inducible by growing bacteria in the presence of ciprofloxacin. Phage 2851 is the first reported viable bacteriophage which carries an stx_{2c} gene. Electron micrographs of phage 2851 showed particles with elongated hexagonal heads and long flexible tails resembling phage lambda. Sequence analysis of an 8.4-kb region flanking the stx_{2c} gene and other genetic elements revealed a mosaic gene structure, as found in other Stx phages. Phage 2851 showed lysis of *E. coli* K-12 strains lysogenic for Stx phages encoding Stx1 (H19), Stx2 (933W), Stx (7888), and Stx1c (6220) but showed superinfection immunity with phage lambda, presumably originating from the similarity of the *c*I repressor proteins of both phages. Apparently, phage 2851 integrates at a different chromosomal locus than Stx2 phage 933W and Stx1 phage H19 in *E. coli*, explaining why Stx2c is often found in combination with Stx1 or Stx2 in *E. coli* O157 strains. Diagnostic PCR was performed to determine gene sequences specific for phage 2851 in wild-type *E. coli* O157 strains producing Stx2c. The phage 2851 *q* and *o* genes were frequently detected in Stx2c-producing *E. coli* O157 strains, indicating that phages related to 2851 are associated with Stx2c production in strains of *E. coli* O157 that were isolated in different locations and time periods.

196. Sturino,J.M.**,** Klaenhammer,T.R. (2004). **Bacteriophage defense systems and strategies for lactic acid bacteria.** *Advances in Applied Microbiology* 56:331-378. **Abstract:** Bacteriophages (phages) have the potential to interfere with any industry that produces bacteria as an end product or uses them as biocatalysts in the production of fermented products or bioactive molecules. Using microorganisms that drive food bioprocesses as an example, this review will describe a set of genetic tools that are useful in the engineering of customized phage-defence systems. Special focus will be given to the power of comparative genomics as a means of streamlining target selection, providing more widespread phage protection, and increasing the longevity of these industrially important bacteria in the bioprocessing environment.

197. Walkerpeach,C.R.**,** Pasloske,B.L. (2004). **DNA bacteriophage as controls for clinical viral testing.** *Clinical chemistry* 50:1970-1971. **Abstract:** In the mid- to late-1980s, a revolution in molecular diagnostics began with the introduction of innovative methods for the detection of nucleic acids. In retrospect, the appearance of these technologies roughly coincided with the debuts of new pathogenic viruses, such as human immunodeficiency virus (HIV) and hepatitis C virus (HCV). Techniques such as PCR, transcription-mediated amplification (TMA), and branched DNA (bDNA) were applied to the detection and quantification of these viruses. Eventually, these tests were integrated into routine clinical laboratories for diagnosing and monitoring the treatment of patients infected with these viruses. Quantification data ("viral load") indicated whether the current drug cocktail was having the desired effect on the virus (i.e., lowering the viral load). If not, then another drug course could be prescribed. Today, the main advantages of these assays are great sensitivity (measuring as few as 50 copies/mL of plasma), ease of use for quantification, and early detection of viral nucleic acid in the peripheral blood before an antibody response develops, an application that has proven to be especially important in screening of human blood products. ¶ These technologies were focused not only on the newly emerging RNA viruses but also on the better-known hepatitis B virus (HBV), cytomegalovirus (CMV), herpes simplex virus (HSV), varicella zoster virus (VZV), human papillomavirus (HPV), and Epstein-Barr virus (EBV). In developing DNA-based tests for these viruses, laboratories incorporated positive controls from one of three potential sources: plasmid DNA, positive patient specimens, or commercially available viral preparations. None of these formats is ideal. Plasmid DNA cannot be used until after the specimen analyte has been extracted. Patient specimens have become more difficult to use in the US after the introduction of new "HIPAA" regulations for protection of patient privacy. Moreover, viral nucleic acids in patient specimens are degraded during multiple freeze-thaw cycles. Lastly, the...

198. Wang,K., Chen,F. (2004). **Genetic diversity and population dynamics of cyanophage communities in the Chesapeake Bay.** *Aquat. Microb. Ecol.* 34:105-116. **Abstract:** In order to understand the genetic diversity and population dynamics of cyanophages in estuarine waters, the viral capsid assembly (g20) gene was used as a gene marker to monitor genetic variations of natural cyanomyovirus communities in the Chesapeake Bay, USA. Unique and diverse g20 sequences were found. Only 1 of 15 g20 genotypes was closely related to the known cyanomyovirus isolates. Most of the g20 genotypes in the bay were not related to the g20 clonal sequences recovered from open-ocean waters. Terminal-restriction fragment length polymorphism (T-RFLP) based on the g20 gene was developed to investigate spatial and temporal distribution of cyanomyovirus communities in the bay. The T-RFLP profiles of the g20 gene demonstrated that the cyanomyovirus population structures in the bay were more dynamic seasonally than spatially. Seasonal variation in the cyanophage community appeared to correspond to changes in host-cell density, which in turn was mainly affected by water temperature. This study represents the first effort to monitor both cyanophage titer and genetic diversity over time and space. The results of our study suggest that cyanophages could play a significant role in regulating *Synechococcus* biomass and population structure in the Chesapeake Bay.

199. Ackermann,H.-W. (2003). **Bacteriophage observations and evolution.** *Res. Microbiol.* 154:245-251. **Abstract:** Bacteriophages are classified into one order and 13 families. Over 5100 phages have been examined in the electron microscope since 1959. At least 4950 phages (96%) are tailed. They constitute the order *Caudovirales* and three families. *Siphoviridae* or phages with long, noncontractile tails predominate (61% of tailed phages). Polyhedral, filamentous, and pleomorphic phages comprise less than 4% of bacterial viruses. Bacteriophages occur in over 140 bacterial or archaeal genera. Their distribution reflects their origin and bacterial phylogeny. Bacteriophages are polyphyletic, arose repeatedly in different hosts, and constitute 11 lines of descent. Tailed phages appear as monophyletic and as the oldest known virus group.

200. Balogh,B., Jones,J.B., Momol,M.T., Olson,S.M., Obradovic,A., Jackson,L.E. (2003). **Improved efficacy of newly formulated bacteriophages for management of bacterial spot on tomato.** *Plant Dis.* 87:949-954. **Abstract:** Bacteriophages are currently used as an alternative method for controlling bacterial spot disease on tomato incited by *Xanthomonas campestris* pv. *vesicatoria* . However, the efficacy of phage is greatly reduced due to its short residual activity on plant foliage. Three formulations that significantly increased phage longevity on the plant surface were tested in field and greenhouse trials: (i) PCF, 0.5% pregelatinized corn flour (PCF) + 0.5% sucrose; (ii) Casecrete, 0.5% Casecrete NH-400 + 0.5% sucrose + 0.25% PCF; and (iii) skim milk, 0.75% powdered skim milk + 0.5% sucrose. In greenhouse experiments, the nonformulated, PCF-, Casecrete-, and skim milk– formulated phage mixtures reduced disease severity on plants compared with the control by 1, 30, 51, and 62%, respectively. In three consecutive field trials, nonformulated phage caused 15, 20, and 9% reduction in disease on treated plants compared with untreated control plants, whereas plants treated with PCF- and Casecrete-formulated phage had 27, 32, and 12% and 30, 43, and 24% disease reduction, respectively. Plants receiving copper–mancozeb treatments were included in two field trials and had a 20% decrease in disease in the first trial and a 13% increase in the second one. Skim milk–formulated phage was tested only once and caused an 18% disease reduction. PCF-formulated phage was more effective when applied in the evening than in the morning, reducing disease on plants by 27 and 13%, respectively. The Casecrete formulated phage populations were over 1,000-fold higher than the nonformulated phage populations 36 h after phage application.

201. Bettarel,Y., Amblard,C., Sime-Ngando,T., Carrias,J.F., Sargos,D., Garabetian,F., Lavandier,P. (2003). **Viral lysis, flagellate grazing potential and bacterial production in Lake Pavin.** *Microb. Ecol.* 45:119-127. **Abstract:** Abundances of different compartments of the microbial loop (i.e., viruses, heterotrophic bacteria, nonpigmented nanoflagellates, and pigmented nanoflagellates), bacterial heterotrophic production (BHP), viral lysis, and potential flagellate grazing impacts on the bacterial assemblages were estimated during a short-term study (24 h) conducted in June 1998 in the epilimnion (5 m) and metalimnion (10 m) of a moderate-altitude oligomesotrophic lake (Lake Pavin, France). Viral and bacterial abundances were higher in the metalimnion than in the epilimnion, whereas pigmented and nonpigmented nanoflagellates were more numerous in the epilimnion. The control of the BHP due to viral lysis (determined by examination of viral-containing bacteria using a transmission electron microscope) was significantly higher in the meta- (range = 6.0-33.7%, mean = 15.6%) than in the epilimnion (3.5-10.3%, 6.4%). The same was for the losses of BHP from the potential predation by nanoflagellates which ranged from 0.5 to 115.4% (mean = 38.7%) in the epilimnion, and from 0.7 to 97.5% (mean = 66.7%) in the metalimnion. Finally, estimated viral mediated mortality rates from the percentage of visibly infected

cells and potential nanoflagellate grazing rates based on assumed clearance rates suggest that flagellates consumed a larger proportion of bacterial production than was lost to viral lysis.

202. Bettarel,Y.**,** Sime-Ngando,T.**,** Amblard,C.**,** Carrias,J.F.**,** Portelli,C. (2003). **Virioplankton and microbial communities in aquatic systems: a seasonal study in two lakes of differing trophy.** *Freshw. Biol.* 48:810-822. **Abstract:** 1. The seasonal and vertical distribution of the abundance of virus-like particles (VLPs), together with the abundances of other microbial organisms (bacteria, unpigmented and pigmented nanoflagellates and ciliates), were determined in an oligomesotrophic lake (Pavin, France) and in a eutrophic lake (Aydat, France) between March and December 2000. ¶ 2. The abundance of the viral plankton and those of other microbial taxa were significantly higher in the more productive system. The same was for the virus-to-bacteria quotient (VBQ), which averaged seven in Lake Pavin and nine in Lake Aydat. ¶ 3. The abundance of viruses increased during the period of thermal stratification in both lakes, with the highest values being recorded at the end of summer/early autumn in the epi- and the metalimnion. The seasonal pattern of abundance of viruses in both lakes in the surface layer was similar, indicating that the dynamics of viruses may be controlled by environmental factors such as light conditions. ¶ 4. There was no correlation between the abundance of viruses and protists. We found correlations between viruses and heterotrophic bacteria in the whole water column in Lake Pavin, but only in the dark bottom waters in Lake Aydat. ¶ 5. Overall, the empirical findings in this study lead us to speculate that the weaker correlation between bacteria and viruses in Lake Aydat than in Lake Pavin, as well as the higher VBQ in the former, is a consequence of the increasing relative abundance of non-bacteriophage VLPs along the trophic gradient of aquatic systems.

203. Brockhurst,M.A.**,** Morgan,A.D.**,** Rainey,P.B.**,** Buckling,A. (2003). **Population mixing accelerates coevolution.** *Ecol. Lett.* 6:975-979. **Abstract:** Theory predicts that mixing in spatially structured populations of hosts and parasites can increase the rate of antagonistic coevolution. We experimentally tested this prediction by allowing populations of bacteria (*Pseudomonas fluorescens*) and parasitic bacteriophage to coevolve in mixed and unmixed microcosms. Coevolution proceeded at approximately twice the rate in mixed populations compared with unmixed populations and caused the evolution of more resistant hosts and more infective parasites.

204. Bull,J.J.**,** Badgett,M.R.**,** Rokyta,D.**,** Molineux,I.J. (2003). **Experimental evolution yields hundreds of mutations in a functional viral genome.** *J. Mol. Evol.* 57:241-248. **Abstract:** Two lines of the bacteriophage T7 were grown to fix mutations indiscriminately, using a combination of population bottlenecks and mutagenesis. Complete genome sequences revealed 404 and 299 base substitutions in the two lines, the largest number characterized in functional microbial genomes so far. Missense substitutions outnumbered silent substitutions. Silent substitutions occurred at similar rates between essential and nonessential genes, but missense substitutions occurred at a higher rate in nonessential genes than in essential genes, as expected if they were less deleterious in the nonessential genes. Viral fitness declined during this protocol, and subsequent passaging of each mutated line in large population sizes restored some of the lost fitness. Substitution levels during these recoveries were less than 6% of those during the bottleneck phase, and only two changes during recovery were reversions of the original mutations. Exchanges of genomic fragments between the two recovered lines revealed that fitness effects of some substitutions were not additive-that interactions were accumulating which could lead to incompatibility between the diverged genomes. Based on these results, unprecedented high rates of nucleotide and functional divergence in viral genomes should be attainable experimentally by using repeated population bottlenecks at a high mutation rate interspersed with recovery.

205. Casjens,S. (2003). **Prophages and bacterial genomics: what have we learned so far?** *Mol. Microbiol.* 49:277-300. **Abstract:** Bacterial genome nucleotide sequences are being completed at a rapid and increasing rate. Integrated virus genomes (prophages) are common in such genomes. Fifty-one of the 82 such genomes published to date carry prophages, and these contain 230 recognizable putative prophages. Prophages can constitute as much as 10-20% of a bacterium's genome and are major contributors to differences between individuals within species. Many of these prophages appear to be defective and are in a state of mutational decay. Prophages, including defective ones, can contribute important biological properties to their bacterial hosts. Therefore, if we are to comprehend bacterial genomes fully, it is essential that we are able to recognize accurately and understand their prophages from nucleotide sequence analysis. Analysis of the evolution of prophages can shed light on the evolution of both bacteriophages and their hosts. Comparison of the Rac prophages in the sequenced genomes of three *Escherichia coli* strains and the Pnm prophages in two *Neisseria meningitidis* strains suggests that some prophages can lie in residence for very long times, perhaps millions of years, and that recombination events have occurred between related prophages that reside at different locations in a bacterium's

genome. In addition, many genes in defective prophages remain functional, so a significant portion of the temperate bacteriophage gene pool resides in prophages.

206. Edelman,D.C., Barletta,J. (2003). **Real-time PCR provides improved detection and titer determination of bacteriophage.** *BioTechniques* 35:368-375. **Abstract:** The plaque assay is the traditional method for the quantification of bacteriophage, particularly for λ cloning vectors. Unfortunately, this technique is fraught with procedural difficulties, and the quality of the data obtained from this gold standard assay may be inaccurate due to the subjective interpretation of the results. The application of quantitative real-time PCR (QPCR) technology can address these issues and be a more accurate platform to evaluate phage growth conditions and quantify viral titers in phage preparations. QPCR, with an improved primer set specific for λ phage and coupled with fluorescent dye detection of PCR products, was used to detect and quantify phages in lysates with no prior DNA purification. Phages were detected below one plaque-forming unit, and at least 89 viral copies were detected from a purified DNA sample. When unknown concentrations of various phage preparations were assessed using QPCR, they were attained more efficiently, with greater sensitivity and precision, and the method produced more accurate quantitative data spanning a wider linear range than those obtained by the plaque assay (six logs vs. one log, respectively). Finally, QPCR for the detection of phage has multiple applications, including conventional cloning and in alternative fields of study such as environmental sciences.

207. Faruque,S.M., Mekalanos,J.J. (2003). **Pathogenicity islands and phages in *Vibrio cholerae* evolution.** *Trends Microbiol.* 11:505-510. **Abstract:** The identification of accessory genetic elements (plasmids, phages and chromosomal 'pathogenicity islands') encoding virulence-associated genes has facilitated our efforts to understand the origination of pathogenic microorganisms. Toxigenic *Vibrio cholerae*, the etiologic agent of cholera, represents a paradigm for this process in that this organism evolved from environmental nonpathogenic *V. cholerae* by acquisition of virulence genes. The major virulence genes in *V. cholerae*, which are clustered in several chromosomal regions, appear to have been recently acquired from phages or through undefined horizontal gene transfer events. Evidence is accumulating that the interactions of phages with each other can also influence the emergence of pathogenic clones of *V. cholerae*. Therefore, to track the evolution of pathogens from their nonpathogenic progenitors, it is also crucial to identify and characterize secondary genetic elements that mediate lateral transfer of virulence genes in trans. Understanding the evolutionary events that lead to the emergence of pathogenic clones might provide new approaches to the control of cholera and other infectious diseases.

208. Gamage,S., Strasser,J.E., Chalk,C.L., Weiss,A.A. (2003). **Nonpathogenic *Escherichia coli* can contribute to the production of Shiga toxin.** *Infect. Immun.* 71:3107-3115. **Abstract:** The food-borne pathogen, *Escherichia coli* O157:H7, has been associated with gastrointestinal disease and the life-threatening sequela hemolytic uremic syndrome. The genes for the virulence factor, Shiga toxin 2 (Stx2), in *E. coli* O157:H7 are encoded on a temperate bacteriophage under the regulation of the late gene promoter. Induction of the phage lytic cycle is required for toxin synthesis and release. We investigated the hypothesis that nonpathogenic *E. coli* could amplify Stx2 production if infected with the toxin-encoding phage. Toxin-encoding phage were incubated with *E. coli* that were either susceptible or resistant to the phage. The addition of phage to phage-susceptible bacteria resulted in up to 40-fold more toxin than a pure culture of lysogens, whereas the addition of phage to phage-resistant bacteria resulted in significantly reduced levels of toxin. Intestinal *E. coli* isolates incubated with Shiga toxin-encoding phage produced variable amounts of toxin. Of 37 isolates, 3 produced significantly more toxin than was present in the inoculum, and 1 fecal isolate appeared to inactivate the toxin. Toxin production in the intestine was assessed in a murine model. Fecal toxin recovery was significantly reduced when phage-resistant *E. coli* was present. These results suggest that the susceptibility of the intestinal flora to the Shiga toxin phage could exert either a protective or an antagonistic influence on the severity of disease by pathogens with phage-encoded Shiga toxin. Toxin production by intestinal flora may represent a novel strategy of pathogenesis.

209. Sandaa,R.-A., Skjoldal,E., Bratbak,G. (2003). **Virioplankton community structure along a salinity gradient in a solar saltern.** *Extremophiles* 7:347-351. **Abstract:** The virioplankton community structure along a salinity gradient from near seawater (40‰) to saturated sodium chloride brine (37‰) in a solar saltern was investigated by pulsed-field gel electrophoresis. Viral populations with genome sizes varying from 10 kb to 533 kb were detected. The viral community structure changed along the salinity gradient. Cluster analysis of the viral genome-banding pattern resulted in two main clusters. The virioplankton diversity within the samples with salinity from 40‰ to 15‰ was on the same cluster of a cladogram. The other group consisted of virioplankton from samples with salinity above 220‰. The virioplankton diversity in the

different samples was calculated using the Shannon index. The diversity index demonstrated an increase in diversity in the samples along the gradient from 40‰ to 15‰ salinity, followed by a decrease in the diversity index along the rest of the salinity gradient. These results demonstrate how viral diversity changes from habitats that are considered one of the most common (seawater) to habitats that are extreme in salt concentrations (saturated sodium brine). The diversity index was highest in the environments that lie in between the most extreme and the most common.

210. Sato,T., Shimizu,T. , Watarai,M., Kobayashi,M., Kano,S., Hamabata,T., Takeda,Y., Yamasaki,S. (2003). **Genome analysis of a novel Shiga toxin 1 (Stx1)-converting phage which Is closely related to Stx2-converting phages but not to other Stx1-converting phages.** *J. Bacteriol.* 185:3966-3971. **Abstract:** Two Stx-converting phages, designated Stx1ϕ and Stx2ϕ-II, were isolated from an *Escherichia coli* O157:H7 strain, Morioka V526, and their entire nucleotide sequences were determined. The genomes of both phages were similar except for the *stx* gene-flanking regions. Comparing these phages to other known Stx-converting phages, we concluded that Stx1ϕ is a novel Stx1-converting phage closely related to Stx2-converting phages so far reported.

211. Selas,B., Lakel,A., Andres,Y., Le Cloirec,P. (2003). **Wastewater reuse in on-site wastewater treatment: bacteria and virus movement in unsaturated flow through sand filter.** *Water Sci. Technol.* 47:59-64. **Abstract:** In on-site wastewater treatment plants, effluents are pre-treated by septic tank and treated by soil infiltration or sand filtration systems, with unsaturated flow conditions. These systems remove efficiently carbon, nitrogen and suspended solids. But for microbial pollution, the treatment efficiency depends on the hydrodynamic behaviour and filtering media characteristics. Contamination of superficial water and groundwater due to pathogenic viruses and pathogenic bacteria is responsible for many diseases. The objective of this study is to approach the mechanisms and operating conditions to control bacteria and virus release in the environment. Experiments were carried out on reactors of different length packed with sand. Hydraulic load of 90 cm x d(-1) with a pulse periodic flow was used. The influence of chemical composition of the solution on the treatment efficiency has also been studied. For the first time, the residence time distribution (RTD) has been studied using a conservative tracer (KI), to determine the main hydrodynamic parameters. For the second time, the RTD with bacterial and viral tracers (*E. coli*, bacteriophage MS2) was applied, with the aim to define microbial behaviour in filtering media, including adsorption and filtration phenomena. This work allowed us to determine retardation factors according to the hydraulic loads and chemical composition.

212. Vrede,K., Stensdotter,U., Lindstrom,E.S. (2003). **Viral and bacterioplankton dynamics in two lakes with different humic contents.** *Microb. Ecol.* 46:406-415. **Abstract:** Viral and bacterioplankton dynamics were investigated, together with the temporal variation of phage-infected bacterioplankton in two oligotrophic lakes, one humic and the other clearwater. Bacterial abundance was significantly higher in the humic lake, while the abundance of virus-like particles (VLP) was significantly higher in the clearwater lake. There were no differences in either the frequency of infected bacterial cells (FIC), or in burst size between the lakes. Because of the higher bacterial abundance in the humic lake, a larger number of bacteria were lyzed in this lake. FIC showed large seasonal changes, varying between 9 and 43%, which covers almost the entire range of previously published data from both lacustrine and marine environments. The temporal changes in VLP abundance and FIC were slow in both the humic and clearwater lakes. The burst size was low in both lakes (average value, nine in each case), probably because of the oligotrophic status of the lakes. The chlorophyll a concentrations were higher and positively correlated with VLP numbers in the clearwater lake, indicating that a significant proportion of the viruses in this lake may be phytoplankton viruses.

213. Anonymous (2002). **[Bacteriophages in the milk industry (they are no small enemy)] Los bacteriofagos en la industria láctea (no hay enemigo pequeño) [Spanish].** *Industrias Lácteas Españolas* 32-35. 214. Bettarel,Y., Sime-Ngando,T., Amblard,C., Carrias,J.F., Sargos,D., Garabetian,F., Lavandier,P. (2002). **The functional importance of bacteriophages in the microbial loop of an oligomesotrophic lake over a diel cycle.** *Annales de Limnology - International Journal of Limnology* 38:263-269. **Abstract:** The abundances of the different compartments of the microbialloop (i.e., viruses, heterotrophic bacteria, heterotrophic nanoflagellates, and pigmented nanoflagellates), total (TPP) and excreted (EPP) primary production, bacterial production (BP), viral lytic activity (LA), and bacterivory by nanoflagellates (FG) were measured on lune 15 and 16, 1998, in a moderate-altitude oligomesotrophic lake (Lac Pavin, France), at 5 and 10 m depths. At both depths, losses of the bacterial community by virallysis (LA5m = 1.7 X 106 cells.l-1.h-1, LAC = 2.0 X 106 cells.l-1.h-1) were, on average, lower than those due to the grazing activity of flagellates (FG5m = 10.3 X 106 cells.l-1.h-1, FG10m= 8.4 X 106 cells.l-1.h-1). A carbon budget

exercise indicated that, for the sampling period and depths, 17.8 % of C from TPP (= 38.1 % of EPP) was used by bacteria. On the other hand, 52.7 % of BP (= 2.15% of TPP) was grazed by nanoflagellates, while 11.0% of BP (= 0.45% of TPP) was lysed by viruses.

215. Castberg,T., Thyrhaug,R., Larsen,A., Sandaa,R.-A. , Heldal,M., Bratbak,G. (2002). **Isolation and characterization of virus infecting *Emiliania huxleyi* (Haptophyceae).** *Phycology* 38:767-774. **Abstract:** The isolation and characterization of a virus (designated EhV) that infects the marine coccolithophorid *Emiliania huxleyi* (Lohmann) Hay & Mohler are described. Three independent clones of EhV were isolated from Norwegian coastal waters in years 1999 and 2000. EhV is a double-stranded DNA-containing virus with a genome size of ~415 kilo-base pairs. The viral particle is an icosahedron with a diameter of 160-180 nm. The virus particle contains at least nine proteins ranging from 10 to 140 kDa; the major capsid protein weighs ~54 kDa. EhV has a latent period of 12-14 h and a burst size of 400-1000 (mean, 620) viral particles per cell. A phylogenetic tree based on DNA polymerase amino acid sequences indicates EhV should be assigned to the Phycodnaviridae virus family and that the virus is most closely related to viruses that infect *Micromonas pusilla* and certain *Chlorella* species.

216. Fields,B.S., Benson,R.F., Besser,R.E. (2002). **Legionella and Legionnaires' disease: 25 years of investigation.** *Clin. Microbiol. Rev.* 15:506-526. **Abstract:** There is still a low level of clinical awareness regarding Legionnaires' disease 25 years after it was first detected. The causative agents, legionellae, are freshwater bacteria with a fascinating ecology. These bacteria are intracellular pathogens of freshwater protozoa and utilize a similar mechanism to infect human phagocytic cells. There have been major advances in delineating the pathogenesis of legionellae through the identification of genes which allow the organism to bypass the endocytic pathways of both protozoan and human cells. Other bacteria that may share this novel infectious process are *Coxiella burnetti* and *Brucella* spp. More than 40 species and numerous serogroups of legionellae have been identified. Most diagnostic tests are directed at the species that causes most of the reported human cases of legionellosis, *L. pneumophila* serogroup 1. For this reason, information on the incidence of human respiratory disease attributable to other species and serogroups of legionellae is lacking. Improvements in diagnostic tests such as the urine antigen assay have inadvertently caused a decrease in the use of culture to detect infection, resulting in incomplete surveillance for legionellosis. Large, focal outbreaks of Legionnaires' disease continue to occur worldwide, and there is a critical need for surveillance for travel-related legionellosis in the United States. There is optimism that newly developed guidelines and water treatment practices can greatly reduce the incidence of this preventable illness.

217. Martin,M.O. (2002). **Predatory prokaryotes: an emerging research opportunity.** *J. Mol. Microbiol. Biotechnol.* 4:467-477. **Abstract:** Predatory prokaryotes have evolved a unique strategy of obtaining energy and biosynthetic materials from their surroundings: acquiring them from other living bacterial cells. These types of microbes have been found in a diverse variety of environments, and may play an important role in modulating microbial population structure and dynamics, as has been hypothesized for marine viruses and possibly protists. Only one genus of predatory bacterium, *Bdellovibrio*, has been extensively described and studied, though several other examples have been reported in the literature. In this review, the four basic strategies used by currently described predatory prokaryotes will be discussed: "wolfpack" group predation, epibiotic attachment, direct cytoplasmic invasion, and periplasmic invasion. Special adaptations to each approach will be considered, and compared overall to the genetic and biochemical characteristics of symbiotic or pathogenic prokaryotes living within eukaryotic cells. Two specific examples of predatory microbes, *Bdellovibrio* and *Ensifer*, will be described in terms of predation strategy, association with host cells, and host range. The prospects for bringing to bear the tools of molecular microbial genetics to the study of predatory prokaryotes will be explored, using current research with *Bdellovibrio* and *Ensifer* as examples.

218. Tait,K., Skilmman,L.C., Sutherland,I.W. (2002). **The efficacy of bacteriophage as a method of biofilm eradication.** *Biofouling* 18:305-311. **Abstract:** The ability of bacteriophage and their associated polysaccharide depolymerases to control enteric biofilm formation was investigated. Bacteriophages specific for *Enterobacter* strains were isolated from primary effluent sewage. Combinations of three phages were required before complete eradication of single species biofilms of *Enterobacter cloace* occurred. Attempts to eliminate a susceptible bacterial population within a dual species biofilm were unsuccessful. It was thought that the structural heterogeneity of the biofilm produced pockets of unattainable, susceptible bacteria. These results suggest that phage and bacteria can co-exist stably within a biofilm. Bacteriophage, would, therefore, make poor tools for the control of biofilm formation. However, the results suggest that combined treatment with bacteriophage polysaccharide depolymerases and disinfectant may provide an alternative control strategy.

219. Wagner,P.L., Livny,J., Neely,M.N., Acheson,D.W.K., Friedman,D.I., Waldor,M.K. (2002). **Bacteriophage control of Shiga toxin 1 production and release by *Escherichia coli*.** *Mol. Microbiol.* 44:957-970. **Abstract:** The stx genes of many Shiga toxin-encoding *Escherichia coli* (STEC) strains are encoded by prophages of the λ bacteriophage family. In the genome of the Stx1-encoding phage H-19B, the stx(1)AB genes are found approximately 1 kb downstream of the late phage promoter, p(R)', but are known to be regulated by the associated iron-regulated promoter, p(Stx1). Growth of H-19B lysogens in low iron concentrations or in conditions that induce the prophage results in increased Stx1 production. Although the mechanism by which low iron concentration induces Stx1 production is well understood, the mechanisms by which phage induction enhances toxin production have not been extensively characterized. The studies reported here identify the factors that contribute to Stx1 production after induction of the H-19B prophage. We found that replication of the phage genome, with the associated increase in stx(1)AB copy number, is the most quantitatively important mechanism by which H-19B induction increases Stx1 production. Three promoters are shown to be involved in stx(1)AB transcription after phage induction, the iron-regulated p(Stx1) and the phage-regulated p(R) and p(R)' promoters, the relative importance of which varies with environmental conditions. Late phage transcription initiating at the p(R)' promoter, contrary to previous findings in the related Stx2-encoding phage ϕ361, was found to be unnecessary for high-level Stx1 production after phage induction. Finally, we present evidence that phage-mediated lysis regulates the quantity of Stx1 produced by determining the duration of Stx1 accumulation and provides a mechanism for Stx1 release. By amplifying stx(1)AB copy number, regulating stx(1)AB transcription and allowing for Stx1 release, the biology of the Stx-encoding phages contributes greatly to the production of Stx, the principal virulence factor of STEC.

220. Wilson,W.H., Tarran,G.A., Schroeder,D., Cox,M., Oke,J., Malin,G. (2002). **Isolation of viruses responsible for the demise of an *Emiliania huxleyi* bloom in the English Channel.** *Journal of the Marine Biological Association of the UK* 82:369-377. **Abstract:** This study used analytical flow cytometry (AFC) to monitor the abundance of phytoplankton, coccoliths, bacteria and viruses in a transect that crossed a high reflectance area in the western English Channel. The high reflectance area, observed by satellite, was caused by the demise of an *Emiliania huxleyi* bloom. Water samples were collected from depth profiles at four stations, one station outside and three stations inside the high reflectance area. Plots of transect data revealed very obvious differences between Station 1, outside, and Stations 2-4, inside the high reflectance area. Inside, concentrations of viruses were higher; *E. huxleyi* cells were lower; coccoliths were higher; bacteria were higher and virus:bacteria ratio was lower than at Station 1, outside the high reflectance area. This data can simply be interpreted as virus-induced lysis of *E. huxleyi* cells in the bloom causing large concentrations of coccoliths to detach, resulting in the high reflectance observed by satellite imagery. This interpretation was supported by the isolation of two viruses, EhV84 and EhV86, from the high reflectance area that lysed cultures of *E. huxleyi* host strain CCMP1516. Basic characterization revealed that they were lytic viruses approximately 170 nm-190 nm in diameter with an icosahedral symmetry. Taken together, transect and isolation data suggest that viruses were the major contributor to the demise of the *E. huxleyi* population in the high reflectance area. Close coupling between microalgae, bacteria and viruses contributed to a large organic carbon input. Consequent cycling influenced the succession of an *E. huxleyi*-dominated population to a more characteristic mixed summer phytoplankton community.

221. Brakmann,S., Grzeszik,S. (2001). **An error-prone T7 RNA polymerase mutant generated by directed evolution.** *Chembiochem : a European journal of chemical biology* 2:212-219. **Abstract:** Viruses replicate their genomes at exceptionally high mutation rates. Their offspring evolve rapidly and therefore, are able to evade common immunological and chemical antiviral agents. In parallel, virus genomes cannot tolerate a further increase in mutation rate: Experimental evidence exists that even few additional mutations are sufficient for the extinction of a viral population. A future antiviral strategy might therefore aim at increasing the error-producing capacity of viral replication enzymes. We employed the principles of directed evolution and developed a scheme for the stringent positive selection of error-prone polymerase activity. A mutant T7 RNA polymerase with a nucleotide substitution error rate at least 20-fold greater than that of the wild-type was selected. This enzyme synthesized highly heterogeneous RNA products in vitro or in vivo and also decreased the replication efficiency of wild-type bacteriophage T7 during infection.

222. Brüssow,H. (2001). **Phages of dairy bacteria.** *Ann. Rev. Microbiol.* 55:283-303. **Abstract:** Bacteriophages of lactic acid bacteria are a threat to industrial milk fermentation. Owing to their economical importance, dairy phages became the most thoroughly sequenced phage group in the database. Comparative

genomics identified related cos-site and pac-site phages, respectively, in lactococci, lactic streptococci and lactobacilli. Each group was represented with closely related temperate and virulent phages. Over the structural genes their gene maps resembled that of lambdoid coliphages, suggesting distant evolutionary relationships. Despite a lack of sequence similarity, a number of biochemical characteristics of these dairy phages are λ-like (genetic switch, DNA packaging, head and tail morphogenesis, and integration, but not excision). These dairy phages thus provide interesting variations to the phage λ paradigm. The structural gene cluster of Lactococcus phage r1t resembled that of phages from mycobacteria. Virulent lactococcal phages with prolate heads (c2-like genus of Siphoviridae), in contrast, have no known counterparts in other bacterial genera.

223. Entis,P., Fung,D.Y.C., Griffiths,M.W., McIntyre,L., Russell,S., Sharpe,A.N., Tortello,M.L. (2001). **Rapid methods for detection, identification, and enumeration.** pp. 89-126 In Downes,F.P. and Ito,K. (eds.), *Compendium of Methods for the Microbiological Examination of Foods*. American Public Health Association, Washington, DC. **Abstract:** [first paragraph of section 10.7: phage probes] The existence of bacterial viruses known as bacteriophages-eaters of bacteria-was first reported by the British scientist F.W. Twort in 1915, and somewhat controversially in 1917 by the Canadian bacteriologist F d'Herelle. Twort's publication in the Lancet documented the phenomenon of "glassy transformation" observed in colonies of micrococci grown on agar in the presence of small pox vaccine. He postulated that the "transparent dissolving material" might be caused by: i) an enzyme; ii) could be part of the life cycle of the bacterium; or iii) was caused by a virus, a term first used vaguely by Jenner in 1796 and used more specifically in 1898 by the Dutch botanist Martinus Beijerinck in his study of Tobacco Mosaic Virus.[114].

224. Khan,A.U., Ajamaluddin,M., Ahmad,M. (2001). **A unique group of self-splicing introns in bacteriophage T4.** *Indian journal of biochemistry & biophysics* 38:289-293. **Abstract:** We describe in this review, the salient splicing features of group I introns of bacteriophage T4 and propose, a hypothetical model to fit in the self-splicing of nrdB intron of T4 phage. Occurrence of non-coding sequences in prokaryotic cells is a rare event while it is common in eukaryotic cells, especially the higher eukaryotes. Therefore, T4 bacteriophage can serve as a good model system to study the evolutionary aspects of splicing of introns. Three genes of T4 phage were found to have stretches of non-coding sequences which belonged to the group IA type introns of self-splicing nature.

225. Murga,R., Forster,T.S., Brown,E., Pruckler,J.M. , Fields,B.S., Donlan,R.M. (2001). **Role of biofilms in the survival of *Legionella pneumophila* in a model potable-water system.** *Microbiology (Reading)* 147:3121-3126. **Abstract:** Legionellae can infect and multiply intracellularly in both human phagocytic cells and protozoa. Growth of legionellae in the absence of protozoa has been documented only on complex laboratory media. The hypothesis upon which this study was based was that biofilm matrices, known to provide a habitat and a gradient of nutrients, might allow the survival and multiplication of legionellae outside a host cell. This study determined whether Legionella pneumophila can colonize and grow in biofilms with and without an association with *Hartmannella vermiformis*. The laboratory model used a rotating disc reactor at a retention time of 6.7 h to grow biofilms on stainless steel coupons. The biofilm was composed of *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and a *Flavobacterium* sp. The levels of *L. pneumophila* cells present in the biofilm were monitored for 15 d, with and without the presence of *H. vermiformis*, and it was found that, although unable to replicate in the absence of *H. vermiformis*, *L. pneumophila* was able to persist.

226. Noble,R., Steward,G. (2001). **Estimating viral proliferation in aquatic samples.** *Meth. Microbiol.* 30:67-84. **Abstract:** [first paragraph] It is only within the last decade that marine viruses were determined to be consistently the most abundant biological entities in the sea (Fuhrman, 1999). Since then, many advances have been made in understanding viral ecology (Fuhrman, 1999, Wilhelm and Suttle, 1999). Initial discoveries showed that viruses are both abundant in the ocean and that many bacteria are infected with viruses (Bergh *et al.*, 1989; Proctor and Fuhrman, 1990). These data led researchers to believe that viruses are an important source of mortality in marine microbial food webs, but only provided a static picture. Subsequent studies have shown that virus populations are extremely dynamic, and can change quickly over short time scales (Bratbak *et al* 1990, 1996). Estimates of viral production and decay rates provided the valuable confirmation that viruses are active members of the marine community (Heldal and Bratbak, 1991; Steward *et al.*, 1992b). The production of viruses implies the lysis of host cells and the release of cellular material as dissolved and colloidal organic carbon. Therefore, measurements of viral replication rates are also useful for assessing the contribution of viruses to bacterial mortality and organic matter cycling in the ocean. By assuming a burst size, viral productivity can be used to estimate rates of bacterial lysis. This approach provides an additional means to assess bacterial mortality along

with the original electron microscopy-based method of Proctor and Fuhrman (1990). Accurate measurements of viral productivity and turnover are required if we are to properly model their dynamics and impact within the microbial food web. So far, however, there is no standard method for measuring viral productivity. A wide variety of different approaches have been used each with associated advantages and disadvantages. These methods include:

1. Quantifying net increases in viral abundance over time (Bratbak *et al*., 1990)
2. Measuring rates of viral decay (Heldal and Bratbak, 1991)
3. Estimating viral DNA synthesis rates by radiolabeling (Steward *et al*., 1992a,b)
4. Calculating expected viral release rates from estimated rates of bacterial lysis and an assumed burst size (Weinbauer *et al.,* 1993)
5. Measuring tracer dilution rates using fluorescently labeled viruses (FLV) as tracers (Noble and Fuhrman, submitted).

227. Paul,J.H.**,** Jiang,S.C. (2001). **Lysogeny and transduction.** *Meth. Microbiol.* 30:105-125. **Abstract:** [first paragraph] Lysogeny and transduction describe a type of phage/host interaction and a method of bacterial gene transfer (procaryotic sex), respectively. Although they are often reviewed together, these topics are linked only in that one type of transduction (specialized) has an obligate requirement for a lysogenic interaction. In this chapter we describe the background for understanding both of these processes, and give methods that we have found useful in studying lysogeny and transduction in the marine environment.

228. Puig,A.**,** Arujo,R.**,** Jofre,J.**,** Frias-Lopez,J. (2001). **Identification of cell wall proteins of *Bacteroides fragilis* to which bacteriophages B40-8 binds specifically.** *Microbiology (Reading)* 147:281-288. **Abstract:** Bacteriophage infecting *Bacteroides fragilis*, one of the most abundant bacteria in the human colon, have been proposed as indicators of virological faecal pollution. The first identification of a receptor for a bacteriophage in *B.fragilis* is reported here. First, resistant mutants were characterized following phage inactivation, and it was shown that cell wall proteins are involved in phage binding. Then the proteins involved were identified by various approaches: (i) comparison of the protein profiles of wild-type *B.fragilis* HSP40 and phage-resistant mutants; (ii) application of a modification of the virus overlay protein blot assay (VOPBA). At least two proteins of *B.fragilis*, with apparent molecular masses of 35 ± 5kDa and 65 ± 5kDa, bind to B40-8. This result was later confirmed by running a complex consisting of this phage bound to radiolabelled proteins of *B. fragilis* on an immunoaffinity column loaded with a specific antibody against the phage. Cell proteins retained in the column also coincided with the proteins that differed in the profiles of resistant mutants. Finally, to identify the potential function of these two proteins, their N-terminal sequences were determined and compared to published sequences, but no homologies were found.

229. Sandaa,R.-A.**,** Heldal,M.**,** Castberg,T.**,** Thyrhaug,R.**,** Bratbak,G. (2001). **Isolation and characterization of two viruses with large genome size infecting *Chrysochromulina ericina* (Prymnesiophyceae) and *Pyramimonas orientalis* (Prasinophyceae).** *Virology* 290:272-280. **Abstract:** Two lytic viruses specific for *Chrysochromulina ericina* (Prymnesiophyceae) and for *Pyramimonas orientalis* (Prasinophyceae) were isolated from Norwegian coastal waters in June 1998. The lytic cycle was 14-19 h for both viruses; the burst size was estimated at 1800-4100 viruses per host cell for the *Chrysochromulina* virus and 800-1000 for the *Pyramimonas* virus. Thin sections of infected cells show that both viruses replicate in the cytoplasm and that they have a hexagonal cross section, indicating icosahedral symmetry. The Chrysochromulina virus had a particle size of 160 nm and a genome size of 510 kbp; the size of the major polypeptide was 73 kDa. The Pyramimonas virus had a particle size of 220 x 180 nm and a genome size of 560 kbp; the size of the major polypeptide was 44 kDa. The genome sizes of these viruses are among the largest ever reported for viruses and they are larger than the minimum required for cellular life. The Chrysochromulina virus clone CeV-01B and the Pyramimonas virus clone PoV-01B described in this study have several properties in common with other viruses infecting microalgae, suggesting that they belong to the Phycodnaviridae.

230. Steward,G.F. (2001). **Fingerprinting viral assemblages by pulsed field gel electrophoresis.** pp. 85-102 In Paul,J.H. (ed.), *Marine Microbiology*. Academic Press, London. **Abstract:** Viruses are the most abundant microorganisms in marine and freshwater environments and perhaps the most genetically diverse (Fuhrman and Suttle, 1993). Counting viruses in aquatic samples is now a routine matter, but assessing the diversity and dynamics within complex assemblages is still a challenge. DNA-based fingerprinting approaches which rely on amplification of rRNA gene fragments by PCR have facilitated analyses of bacterial community composition. These approaches have more restricted application when analyzing viral assemblages, because of the extreme genetic diversity among viruses. Unlike in bacteria, there are no gene sequences conserved in all viruses which can serve as universal primer sites for PCR

amplification. PCR-based analyses of viral assemblages must therefore target specific subsets of the total viral assemblage. For example, PCR amplification of specific genes has recently been used to examine the genetic diversity among cyanophages (Fuller *et al.*, 1998) and among phycodnaviridae (Chen *et al.*, 1996; Short and Suttle, 1999). A more general fingerprinting approach, which encompasses the total viral assemblage, is a valuable complement to these more specific, higher resolution analyses. The approach described here uses variation in genome size as the basis for obtaining a fingerprint of a viral assemblage (Klieve and Swain, 1993). A whole genome fingerprinting approach is possible, because viral genomes can vary greatly in length (a few thousand to hundreds of thousands of base pairs) yet they fall within a range that is easily resolved using pulsed field gel electrophoresis (PFGE). The PFGE fingerprinting technique provides a quick and relatively simple means of visualizing differences in the composition of viral assemblages (Swain *et al.*, 1996; Wommack *et al.*, 1999a; Steward and Azam, 2000). As a supplement to the more specific treatment of PFGE provided in this chapter, the reader is encouraged to consult the excellent introductory text to PFGE by Birren and Lai (1993).

231. Wilhelm,S.W.**,** Poorvin,L. (2001). **Quantification of algal viruses in marine samples.** *Meth. Microbiol.* 30:53-65. **Abstract:** [first paragraph] Phycoviruses (viruses that infect either cvanobacteria or eukaryotic algae) impart significant mortality on their hosts in aquatic environments. Microorganisms (both eukaryotic and prokaryotic) in marine systems are thought to be responsible for as much as 50% of the photosvnthetic carbon fixation on the planet (Field *et al.,* 1988). It is therefore apparent that agents of mortality that act directly to reduce primary production in marine environments will alter carbon and energy flux through these systems (Willielm and Suttle, 1999; Fuhrman, 1999). This has, in part, led to the increased interest in the ecology of marine viruses that has occurred through the last decade.

232. Wilson,W.H.**,** Francis,I.**,** Ryan,K.**,** Davy,S.K. (2001). **Temperature induction of viruses in symbiotic dinoflagellates.** *Aquat. Microb. Ecol.* 25:99-102. **Abstract:** Bleaching manifests itself as a loss of symbiotic dinoflagellates (zooxanthellae) and/or chlorophyll from a variety of symbiotic hosts, including corals and sea anemones. Bleaching is known to result from a range of environmental stresses, the most significant of which is elevated temperature; how these stresses elicit a bleaching response is currently the focus of intense research. One consequence of environmental stress that has yet to be considered is viral attack. Here, we have isolated a transferable infectious agent believed to be a virus, from zooxanthellae of the temperate sea anemone *Anemonia viridis*. The infectious agent is induced by elevated temperature. Once induced, the filterable agent can be further propagated without heat induction, thus fulfilling Koch's postulates. We propose that zooxanthellae harbor a latent viral infection that is induced by exposure to elevated temperatures. If such a mechanism also operates in the zooxanthellae harbored by reef corals, and these viruses kill the symbionts, then this could contribute to temperature- induced bleaching.

233. Budzik,J.M. (2000). **Phage isolation and investigation.** *Dartmouth Undergraduate Journal of Science* III:37-43. **Abstract:** A novel bacteriophage, named phage #3, that infects several major strains of *Pseudomonas aeruginosa* has been discovered. The phage has a lambdoid morphology as seen by electron microscopy. Its nucleic acid is double stranded DNA and is 10-15 kb in length. Phage immunity tests have shown that the phage is temperate. The phage has been used to mediate transduction in the reconstruction of mutants. A pilot experiment has been developed to screen for mutant phages with a higher efficiency to mediate transduction.

234. Gindreau,E.**,** Lopez,R.**,** Garcia,P. (2000). **MM1, a temperate bacteriophage of the type 23F Spanish/USA multi-drug resistant epidemic clone of *Streptococcus pneumoniae*: structural analysis of the site-specific integration system.** *J. Virol.* 74:7803-7813. **Abstract:** We have characterized a temperate phage (MM1) from a clinical isolate of the multiply antibiotic-resistant Spanish/American 23F *Streptococcus pneumoniae* clone (Spain23F-1 strain). The 40-kb double-stranded genome of MM1 has been isolated as a DNA-protein complex. The use of MM1 DNA as a probe revealed that the phage genome is integrated in the host chromosome. The host and phage attachment sites, *attB* and *attP*, respectively, have been determined. Nucleotide sequencing of the attachment sites identified a 15-bp core site (5*-TTATA ATTCATCCGC-3*) that has not been found in any bacterial genome described so far. Sequence information revealed the presence of an integrase gene (*int*), which represents the first identification of an integrase in the pneumococcal system. A 1.5-kb DNA fragment embracing *attP* and the *int* gene contained all of the genetic information needed for stable integration of a nonreplicative plasmid into the *attB* site of a pneumococcal strain. This vector will facilitate the introduction of foreign genes into the pneumococcal chromosome. Interestingly, DNAs highly similar to that of MM1 have been detected in several clinical pneumococcal isolates of different capsular types, suggesting a widespread distribution of these phages in relevant pathogenic strains.

235. Golovlev,E.L. (2000). **[General and molecular ecology of Legionella].** *Mikrobiologiia* 69:5-12. **Abstract:** The review is devoted to the general and molecular ecology of bacteria of the genus Legionella in natural and anthropogenic environments. Invasion of amoebae and infusoria by legionellae and their replication in these protozoa can be considered to be a pre-adaptation for invasion of the human immune system. Symbiosis of bacteria and protozoa as a promising model of cellular microbiology and the conception of bacterial ecological niches are discussed in relation to the low fidelity of most bacterial species to their habitats (biotopes). The necessity of elaboration of a similar conception for microbial consortia and associations is emphasized.

236. McShan,W.M. (2000). **The bacteriophages of group A streptococci.** pp. 105-116 In Fischetti,V.A., Novick,R.P., Ferreti,J.J., Portnoy,D.A., and Rood,J.I. (eds.), *Gram Positive Pathogens*. ASM Press, Washington DC. **Abstract:** Bacteriophages (or phages), the ubiquitous viruses infecting almost all known species of bacteria, were discovered early in the twentieth century, apparently independently, by Twort in Britain and d'He´relle in France (1). The ensuing years saw numerous studies in the new phenomenon of bacterial viruses, finding that phages could be isolated from water and soil as well as from the exterior and interior surfaces of humans and animals. With few exceptions, phages could be isolated that infected virtually all pathogenic and nonpathogenic bacteria. In those preantibiotic days, the idea of viruses that could kill many human pathogens attracted considerable attention in the scientific community, and much of the first work on the phages of the genus *Streptococcus* involved attempts to use these agents therapeutically to cure streptococci-associated diseases (reviewed by Evans [23]). The study of bacteriophages of streptococci and the related genera has maintained a consistent level of interest by the scientific community for a number of reasons, both medical and industrial. This chapter focuses on the influence that the phages of *Streptococcus pyogenes* (group A streptococci; GAS), both lytic and lysogenic, have on the biology and dissemination of virulence factors of this important gram-positive pathogen.

237. Robb,F.T., Hill,R.T. (2000). **Bacterial viruses and hosts: Influence of culturable state.** pp. 199-208 In Colwell,R.R. and Grimes,D.J. (eds.), *Nonculturable Microorganisms in the Environment*. ASM Press, Washington,D.C. **Abstract:** [conclusion] It is concluded that phage growth occurs on stationary-phase cells, with separate pathways for phage development operating in logarithmically growing and stationary-phase bacterial cells. Preliminary evidence indicates that transcriptional template selection may be critical in deciding which pathway is operative. ¶ It is tempting to speculate that many oligotrophic environments, including oceanic marine waters, may yield evidence of similar pathways for phage development. Indeed, it would be surprising if alternative pathways (such as the bacteriophage a3a System) did not exist as an alternative to lysogeny, ensuring the propagation of phage under conditions of nutrient starvation and/or declining bacterial populations.

238. Swanson,M.S.**,** Hammer,B.K. (2000). ***Legionella pneumophila* pathogesesis: a fateful journey from amoebae to macrophages.** *Ann. Rev. Microbiol.* 54:567-613. **Abstract:** *Legionella pneumophila* first commanded attention in 1976, when investigators from the Centers for Disease Control and Prevention identified it as the culprit in a massive outbreak of pneumonia that struck individuals attending an American Legion convention (). It is now clear that this gram-negative bacterium flourishes naturally in fresh water as a parasite of amoebae, but it can also replicate within alveolar macrophages. *L. pneumophila* pathogenesis is discussed using the following model as a framework. When ingested by phagocytes, stationary-phase *L. pneumophila* bacteria establish phagosomes which are completely isolated from the endosomal pathway but are surrounded by endoplasmic reticulum. Within this protected vacuole, *L. pneumophila* converts to a replicative form that is acid tolerant but no longer expresses several virulence traits, including factors that block membrane fusion. As a consequence, the pathogen vacuoles merge with lysosomes, which provide a nutrient-rich replication niche. Once the amino acid supply is depleted, progeny accumulate the second messenger guanosine 3',5'-bispyrophosphate (ppGpp), which coordinates entry into the stationary phase with expression of traits that promote transmission to a new phagocyte. A number of factors contribute to *L. pneumophila* virulence, including type II and type IV secretion systems, a pore-forming toxin, type IV pili, flagella, and numerous other factors currently under investigation. Because of its resemblance to certain aspects of Mycobacterium, Toxoplasma, Leishmania, and Coxiella pathogenesis, a detailed description of the mechanism used by *L. pneumophila* to manipulate and exploit phagocyte membrane traffic may suggest novel strategies for treating a variety of infectious diseases. Knowledge of *L. pneumophila* ecology may also inform efforts to combat the emergence of new opportunistic macrophage pathogens.

239. Wilson,W.H.**,** Lane,D.**,** Pearce,D.**,** Ellis-Evans,J.C. (2000). **Transmission electron microscope analysis of viruses in the freshwater lakes of Signy Island, Antarctica.** *Polar Biology* 23:657-660. **Abstract:**

Water samples from a range of fresh-water Antarctic lakes on Signy Island (South Orkney Islands: 60°45'S, 45 °38'W) were examined for the presence of virus-like particles (VLPs) during the 1998/1999 field season. It was discovered that VLPs were ubiquitous, morphologically diverse and abundant, with high concentrations ranging from 4.9 x 10^6 ml^-1 to 3.1 × 10^7 ml^-1. Likely hosts include bacteria, cyanobacteria and eukaryotic algae. In addition, an unusually large virus morphotype was observed with a head diameter 370 x 330 nm and a tail 1.3 μm long.

240. Engelberg-Kulka,H.**,** Glaser,G. (1999). **Addiction modules and programmed cell death and antideath in bacterial cultures.** *Ann. Rev. Microbiol.* 53:43-70. **Abstract:** In bacteria, programmed cell death is mediated through "addiction modules" consisting of two genes. The product of the second gene is a stable toxin, whereas the product of the first is a labile antitoxin. Here we extensively review what is known about those modules that are borne by one of a number of *Escherichia coli* extrachromosomal elements and are responsible for the postsegregational killing effect. We focus on a recently discovered chromosomally borne regulatable addiction module in *E. coli* that responds to nutritional stress and also on an antideath gene of the *E. coli* bacteriophage λ. We consider the relation of these two to programmed cell death and antideath in bacterial cultures. Finally, we discuss the similarities between basic features of programmed cell death and antideath in both prokaryotes and eukaryotes and the possibility that they share a common evolutionary origin.

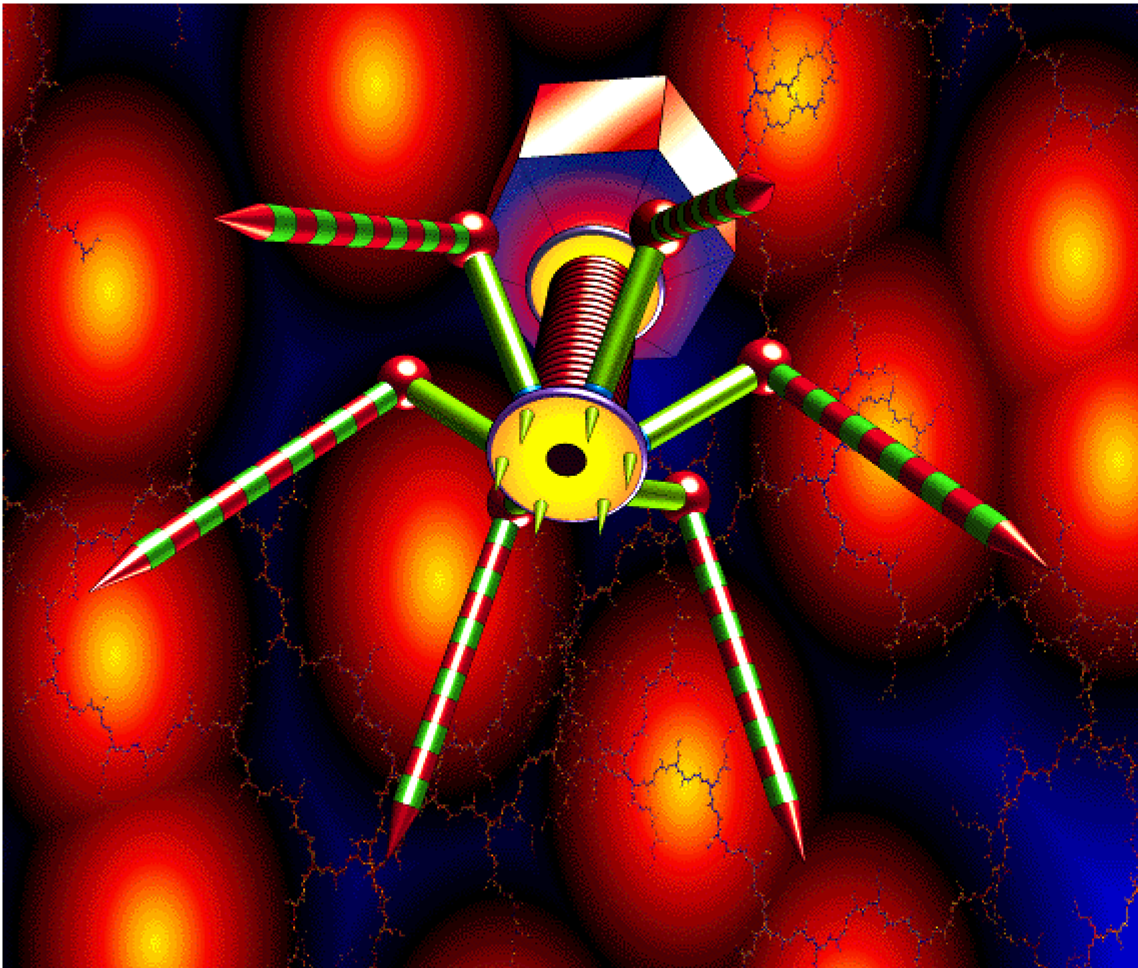
241. Fuchs,S.**,** Muhldorfer,I.**,** Donohue-Rolfe,A.**,** Kerenyi,M.**,** Emody,L.**,** Alexiev,R.**,** Nenkov,P.**,** Hacker,J. (1999). **Influence of RecA on in vivo virulence and Shiga toxin 2 production in *Escherichia coli* pathogens.** *Microb. Pathog.* 27:13-23. **Abstract:** The enterohemorrhagic *Escherichia coli* (EHEC) O157:H7 strains 933 and 86-24 as well as the uropathogenic *E. coli* (UPEC) strain 536 were compared with their isogenic rec A mutants and rec A trans -complemented strains in intravenous lethality and lung toxicity assays in mice. While the wild-type EHEC strains were fully virulent, the virulence of the rec A mutants was strongly reduced. Complementation of the EHEC rec A mutants with the cloned *E. coli* recA gene restored their virulence capacity. The stx2EHEC mutant TUV86-2 as well as its isogenic rec A mutant were completely avirulent in both assays. In contrast, RecA had no influence on the virulence of UPEC strain 536. We conclude that the lethality observed with EHEC is presumably mainly due to Shiga toxin, which is severely down-regulated in the rec A mutants as a result of lacking spontaneous phage induction. Therefore, the EHEC rec A+strains 933 and 86-24 were compared for their Shiga toxin 2 (Stx2) production with the respective rec A-counterparts. The rec A mutants of the EHEC strains were significantly reduced in toxin synthesis and were devoid of Stx2 specific phage production. Complementation of the EHEC rec A mutants with the cloned rec A gene enabled the rec A mutants to restore toxin and phage production. These results suggest that the higher level of Stx2 synthesis in the EHEC strains is the result of a higher level of spontaneous Stx2 specific phage induction, which is controlled by RecA.

242. Newsome,A.L.**,** Scott,T.M.**,** Benson,R.F.**,** Fields,B.S. (1998). **Isolation of an amoeba naturally harboring a distinctive Legionella species.** *Appl. Environ. Microbiol.* 64:1688-1693. **Abstract:** There are numerous in vitro studies documenting the multiplication of Legionella species in free-living amoebae and other protozoa. It is believed that protozoa serve as host cells for the intracellular replication of certain Legionella species in a variety of environmental settings. This study describes the isolation and characterization of a bacterium initially observed within an amoeba taken from a soil sample. In the laboratory, the bacterium multiplied within and was highly pathogenic for Acanthamoeba polyphaga. Extracellular multiplication was observed on buffered charcoal yeast extract agar but not on a variety of conventional laboratory media. A 16S rRNA gene analysis placed the bacterium within the genus Legionella. Serological studies indicate that it is distinct from previously described species of the genus. This report also describes methods that should prove useful for the isolation and characterization of additional Legionella-like bacteria from free-living amoebae. In addition, the characterization of bacterial pathogens of amoebae has significant implications for understanding the ecology and identification of other unrecognized bacterial pathogens.

243. Steinert,M.**,** Birkness,K.**,** White,E.**,** Fields,B.**,** Quinn,F. (1998). ***Mycobacterium avium* grow saprozoically in co-culture with *Acanthamoeba polyphaga* and survive within cyst walls.** *Appl. Environ. Microbiol.* 64:2256-2261. **Abstract:** Protozoans are gaining recognition as environmental hosts for a variety of waterborne pathogens. We compared the growth of *Mycobacterium avium*, a human pathogen associated with domestic water supplies, in coculture with the free-living amoeba *Acanthamoeba polyphaga* with the growth of *M. avium* when it was separated from amoebae by a 0.1-µm-pore-size polycarbonate membrane (in a parachamber). Although viable mycobacteria were observed within amoebal vacuoles,

there was no significant difference between bacterial growth in coculture and bacterial growth in the parachamber. This suggests that *M. avium* is able to grow saprozoically on products secreted by the amoebae. In contrast, *Legionella pneumophila*, a well-studied intracellular parasite of amoebae, multiplied only in coculture. A comparison of amoebae infected with *L. pneumophila* and amoebae infected with *M. avium* by electron microscopy demonstrated that there were striking differences in the locations of the bacteria within amoebal cysts. While *L. pneumophila* resided within the cysts, *M. avium* was found within the outer walls of the double-walled cysts of *A. polyphaga*. These locations may provide a reservoir for the bacteria when environmental conditions become unfavorable.

(see www.phage.org/beg_mission_statement.htm for
why papers covering more than just bacteriophages are included)



This is the BEG mascot phage with new background. I don't know who generated the background.