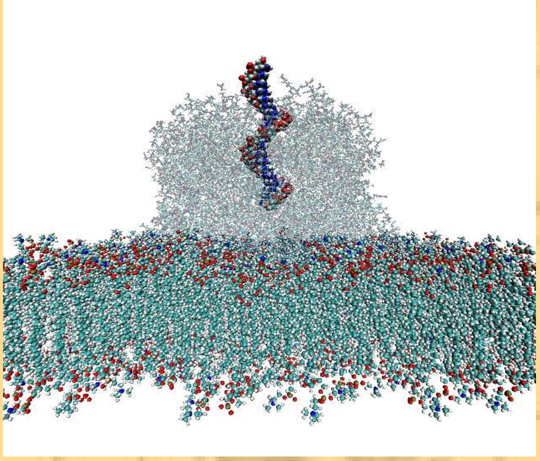
SPICE: Simulated Pore Interactive Computing Environment

Using Grid computing to understand DNA translocation across nanopores embedded in lipid membranes

HPC ANALYTICS CHALLENGE FINALIST

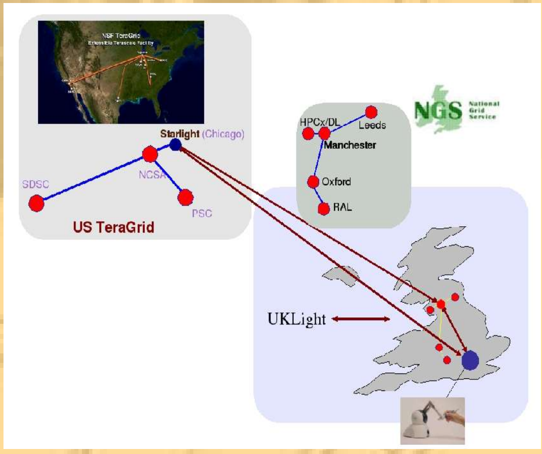


The figure above shows a single-strand of DNA entering an alpha hemolysim protein pore. The pore is typically found embedded in lipid membranes. Biomolecules, such as DNA and mRNA translocate through the wide pore formed by the barrel of the protein.

An understanding of the translocation of biomolecules like messenger-RNA and DNA is critical to successfully address both fundamental and applied problems, ranging from genetic information transfer to the design of high-throughput DNA screening devices. The details of translocation are not well understood.

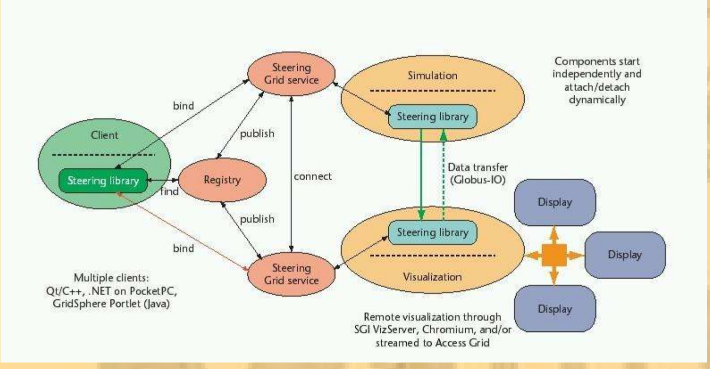
SPICE is a joint UK/US high-end computing project funded by the EPSRC and the US NSF that uses sophisticated grid infrastruture, along with advanced networking capabilities, to effectively utilise the computational resources of a federated trans-Atlantic Grid. Designed to facilitate novel analysis techniques, the scientific aim of the project is to advance the understanding of the vital translocation process of biomolecules across membrane channel pores in biological cells.

Using a Single Federated Grid: As shown in the network diagram on the right, SPICE exploits high performance resources on adminstratively-distinct Grids – the UK NGS and the US TeraGrid – to form a single federated Grid. The federated grid provides unparalleled computational power in a coordinated and coherent fashion; this enables the heterogenous and geographically distributed resources to be marshalled in service of a single scientific problem. For example, the federated grid enables multiple steered simulations and simultaneous high-end compute and visualization resources. The use of advanced optically switched lightpaths, for both intra and inter-Grid transfer, makes such federation worthwhile. UKLight [3] provides a persistent connection from UCL (steering & visualization) to the HPC resources (simulations) in the UK. It also provides a direct link from UCL, Manchester and HPCx to TeraGrid nodes via Starlight (Chicago).



The figure above shows the federated grid – UK NGS and US TeraGrid and the various point-to-point connections available using UKLight/GLIF.

This grid-of-grids enables novel usage of powerful supercomputers. In order to enable use in scientifically productive ways and to seamlessly couple these heterogenous, distributed resources requires sophisticated middleware. SPICE builds upon the successful RealityGrid Steering Library and associated middleware to federate the UK National Grid Service and US TeraGrid. The architecture diagram of the steering infrastructure and associated middleware is shown (left).



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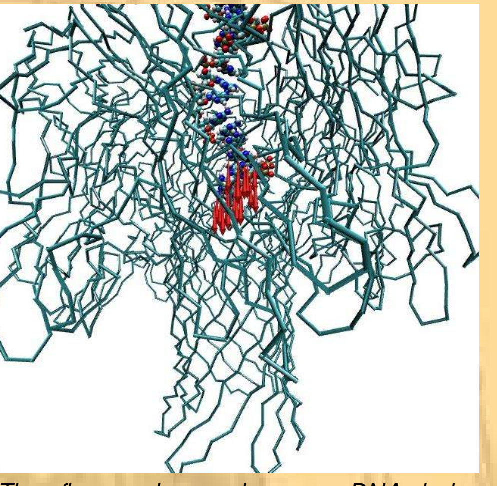
Grid Computing Using Novel Algorithms

The size and complexity of the problem, along with the timescale of translocation, makes computing free energies computationally very expensive. We use Steered Molecular Dynamics to *"pull DNA through the pore"* along with Jarzynski's Equation. This approach introduces new "variables" and "optimal" values for these parameters need to be determined which require interactive simulations – where the visualization is used to steer the simulation. Our approach reduced the computational cost by a factor of 50-100 and thus make feasible an otherwise computationally intractable problem. This reduces the computational cost by a factor of 50-100! The solution, however, not only exploits grid infrastructure but also requires it.



The figure above shows ss-DNA being pulled through the alpha-hemolysin pore during an interactive simulation.

Grid Computing – A suitable computing paradigm: The RealityGrid steering framework permits the integration of numerical simulations and instruments to the same grid middleware. This is utilized to introduce haptic devices into the computational loop – so as to use new analysis and intution building approaches. Algorithmic advances permit the decomposition of a single long problem into several shorter problems, which when coupled with the capabilities to launch, monitor and steer high-end simulations, enable an efficient solution of this problem on the Grid. UKLight/GLIF ensure schedulable capacity for high rate/high volume communication and well-bounded QoS in terms of packet latency, jitter and loss. For interactive simulations, the use of UKLight/GLIF as opposed to regular production networks for communication between the simulation and a visualizer [4,5], leads to signficant improvement in simulation performance.

Although SPICE aims to solve a specific real scientific problem of interest, the methodology however, can be adopted to study a broad-range of scientific problems, e.g. simulating "real" immunological systems as well as characterising drug-binding properties for systems that are otherwise too large to be approached using routine computational approaches.

References:

1. The RealityGrid Project http://www.realitygrid.org
2. Simulated Pore Interactive Computing Environment, *Proceedings of the ACM/IEEE Supercomputing Conference 2005*. S. Jha, et al http://sc05.supercomputing.org/schedule/pdf/ana109pdf
3. UKLight http://www.uklight.ac.uk
4. S. Jha *et al Proceedings of the UK eScience AHM 2005*. http://www.nesc.ac.uk/talks/ahm2005/455.pdf
5. The ESLEA Project http://www.eslea.ac.uk

SPICE Schedule at SC05:

- Manchester Computing	:Mon,14 Nov 19:00-20:00
-PSC Stand	:Tue, 15 Nov 11:00-12:00
- HPC Analytics [611-614]	:Tue, 15 Nov 14:30-15:00
- UK eScience	:Tue, 15 Nov 15:00-15:30
- SC Global [618-620]	:Wed,16 Nov 10:30-11:05
- NCSA Stand	:Thu, 17 Nov 11:00-11:30
- ANL [TG/GIG] Booth	:Thu, 17 Nov 12:00-13:00

SPICE is built upon work from projects in the RealityGrid and ELSEA.

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