

## CODON USAGE BIAS IS EVOLUTIONARILY CONSERVED

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### ABSTRACT

Codon usage bias (CUB) reflects the frequency distribution of codons usage in the genome. Several studies suggest that CUB is based on the combinations, which are most chemically efficient and minimise translational error, show that amongst closely related species, CUB is similar. However, previous studies were mainly carried out on a limited number of related species. This study tests the hypothesis that CUB is evolutionarily conserved, and examines CUB over a large set of organisms. Codon usage distributions from 18 organisms across a diversity of classes were examined. The correlations of codon usage frequencies were calculated between and within classes. Our results demonstrated that Pearson's correlation between CUBs of different organisms within the same class is significantly higher than random. The correlation between the CUBs of mammals, birds, insects, yeast, and bacteria also corresponded to evolutionary distance. This suggests that CUB is evolutionarily conserved and the degree of conservation corresponds to evolutionary distance.

**Keywords:** codon usage bias, CUB, evolutionary distance

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## REFERENCES

- Aravind, L., Walker, D. R., & Koonin, E. V. (1999). Conserved domains in DNA repair proteins and evolution of repair systems. *Nucleic acids research*, 27(5), 1223-1242.
- Bejerano, G., Pheasant, M., Makunin, I., Stephen, S., Kent, W. J., Mattick, J. S., & Haussler, D. (2004). Ultraconserved elements in the human genome. *Science*, 304(5675), 132-1325.
- Bourque, G., Pevzner, P. A., & Tesler, G. (2004). Reconstructing the genomic architecture of ancestral mammals: lessons from human, mouse, and rat genomes. *Genome research*, 14(4), 507-516.
- Brandão, P. E. (2013). The evolution of codon usage in structural and non-structural viral genes: The case of Avian coronavirus and its natural host *Gallus gallus*. *Virus research*, 178(2), 264-271.
- Chamary, J. V., & Hurst, L. D. (2004). Similar rates but different modes of sequence evolution in introns and at exonic silent sites in rodents: evidence for selectively driven codon usage. *Molecular biology and evolution*, 21(6), 1014-1023.
- Chen, J. Y., Huang, D. Y., & Li, C. W. (1999). An early Cambrian craniate-like chordate. *Nature*, 402(6761), 518-522.
- Coleman, J. R., Papamichail, D., Skiena, S., Futcher, B., Wimmer, E., & Mueller, S. (2008). Virus attenuation by genome-scale changes in codon pair bias. *Science*, 320(5884), 1784-1787.
- Comeron, J. M., & Aguadé, M. (1998). An evaluation of measures of synonymous codon usage bias. *Journal of molecular evolution*, 47(3), 268-274.
- Das, S., Roymondal, U., & Sahoo, S. (2009). Analyzing gene expression from relative codon usage bias in Yeast genome: A statistical significance and biological relevance. *Gene*, 443(1), 121-131.
- Das, S., Roymondal, U., Chottopadhyay, B., & Sahoo, S. (2012). Gene expression profile of the cyanobacterium *Synechocystis* genome. *Gene*, 497(2), 344-352.
- Dass, J., & Sudandiradoss, C. (2012). Insight into pattern of codon biasness and nucleotide base usage in serotonin receptor gene family from different mammalian species. *Gene*, 503(1), 92-100.
- De Curtis, I. (2011). Host-Pathogen Interactions: Cheating the Host by Making New Connections. *Current Biology*, 21(5), R192-R194.
- dos Reis, M., Wernisch, L., & Savva, R. (2003). Unexpected correlations between gene expression and codon usage bias from microarray data for the whole *Escherichia coli* K-12 genome. *Nucleic acids research*, 31(23), 6976-6985.
- Gustafsson, C., Govindarajan, S., & Minshull, J. (2004). Codon bias and heterologous protein expression. *Trends in biotechnology*, 22(7), 346-353.
- Hedges, S. B., Parker, P. H., Sibley, C. G., & Kumar, S. (1996). Continental breakup and the ordinal diversification of birds and mammals. *Nature*, 381(6579), 226-229.
- Higgs, P. G., & Ran, W. (2008). Coevolution of codon usage and tRNA genes leads to alternative stable states of biased codon usage. *Molecular biology and evolution*, 25(11), 2279-2291.
- Iriarte, A., Baraibar, J. D., Romero, H., Castro-Sowinski, S., & Musto, H. (2013). Evolution of optimal codon choices in the family Enterobacteriaceae. *Microbiology*, 159(Pt 3), 555-564.

- Lake, J. A. (1990). Origin of the Metazoa. *Proceedings of the National Academy of Sciences*, 87(2), 763-766.
- Jordan, I.K., Marino-Ramirez, L., & Koonin, E.V. (2005). Evolutionary significance of gene expression divergence. *Gene*, 345:119-126.
- Kaper, J. B., Nataro, J. P., & Mobley, H. L. (2004). Pathogenic *Escherichia coli*. *Nature Reviews Microbiology*, 2(2), 123-140.
- Kjeldsen, K. U., Bataillon, T., Pinel, N., De Mita, S., Lund, M. B., Panitz, F., ... & Schramm, A. (2012). Purifying selection and molecular adaptation in the genome of *Verminephrobacter*, the heritable symbiotic bacteria of earthworms. *Genome biology and evolution*, 4(3), 307-315.
- Ling, M.H.T., Ban, Y., Wen, H., Wang, SM, Ge, SX. (2013). Conserved Expression of Natural Antisense Transcripts in Mammals. *BMC Genomics*, 14(1): 243.
- Moriyama, E.N., & Powell, J.R. (1998). Gene length and codon usage bias in *Drosophila melanogaster*, *Saccharomyces cerevisiae* and *Escherichia coli*. *Nucleic acids research*, 26(13), 3188-3193.
- Moura, G.R., Pinheiro, M., Freitas, A., Oliveira, J. L., Frommlet, J. C., Carreto, L., & Santos, M.A. (2011). Species-specific codon context rules unveil non-neutrality effects of synonymous mutations. *PLoS one*, 6(10), e26817.
- Moya, A., Latorre, A., Sabater-Muñoz, B., & Silva, F. J. (2002). Comparative molecular evolution of primary (*Buchnera*) and secondary symbionts of aphids based on two protein-coding genes. *Journal of molecular evolution*, 55(2), 127-137.
- Pal, A., Mondal, U.K., Mukhopadhyay, S., & Bothra, A.K. (2011). Genomic heterogeneity within conserved metabolic pathways of *Arthrobacter* species - a bioinformatic approach. *Bioinformatics*, 5(10), 446.
- Philippe, H., Adoutte, A., Coombs, G. H., Vickerman, K., Sleigh, M. A., & Warren, A. (1998). The molecular phylogeny of Eukaryota: solid facts and uncertainties. *Evolutionary relationships among protozoa*, 25-56.
- Piovesan, A., Vitale, L., Pelleri, M.C., & Strippoli, P. (2013). Universal tight correlation of codon bias and pool of RNA codons (codonome): The genome is optimized to allow any distribution of gene expression values in the transcriptome from bacteria to humans. *Genomics*, 101(5), 282-289.
- Porceddu, A., Zenoni, S., & Camiolo, S. (2013). The signatures of selection for translational accuracy in plant genes. *Genome biology and evolution*, 5(6), 1117-1126.
- Potter, S., Orgeig, S., Donnellan, S., & Daniels, C.B. (2007). Purifying selection drives the evolution of surfactant protein C (SP-C) independently of body temperature regulation in mammals. *Comparative Biochemistry and Physiology Part D: Genomics and Proteomics*, 2(2), 165-176.
- Ran, W., & Higgs, P.G. (2012). Contributions of speed and accuracy to translational selection in bacteria. *PLoS one*, 7(12), e51652.
- Rocha, E.P. (2004). Codon usage bias from tRNA's point of view: redundancy, specialization, and efficient decoding for translation optimization. *Genome research*, 14(11), 2279-2286.
- Roymondal, U., Das, S., & Sahoo, S. (2009). Predicting gene expression level from relative codon usage bias: an application to *Escherichia coli* genome. *DNA research*, 16(1), 13-30.

- Sbisà, E., Tanzariello, F., Reyes, A., Pesole, G., & Saccone, C. (1997). Mammalian mitochondrial D-loop region structural analysis: identification of new conserved sequences and their functional and evolutionary implications. *Gene*, 205(1), 125-140.
- Siepel, A., Bejerano, G., Pedersen, J.S., Hinrichs, A.S., Hou, M., Rosenbloom, K., Clawson H., Spieth J., Hillier L.W., Richards S., Weinstock G.M., Wilson R.K., Gibbs R.A., Kent W. J., Miller W. & Haussler, D. (2005). Evolutionarily conserved elements in vertebrate, insect, worm, and yeast genomes. *Genome research*, 15(8), 1034-1050.
- Thiele, I., Fleming, R.M., Que, R., Bordbar, A., Diep, D., & Palsson, B.O. (2012). Multiscale modeling of metabolism and macromolecular synthesis in *E. coli* and its application to the evolution of codon usage. *PLoS one*, 7(9), e45635.
- Vogt, P. (1990). Potential genetic functions of tandem repeated DNA sequence blocks in the human genome are based on a highly conserved "chromatin folding code". *Human genetics*, 84(4), 301-336.
- Wang, Y., Huang, X.L., & Qiao, G.X. (2013). Comparative Analysis of Mitochondrial Genomes of Five Aphid Species (Hemiptera: Aphididae) and Phylogenetic Implications. *PLoS one*, 8(10), e77511.
- Webster, R.G., Bean, W.J., Gorman, O.T., Chambers, T.M., & Kawaoka, Y. (1992). Evolution and ecology of influenza A viruses. *Microbiological reviews*, 56(1), 152-179.
- Wong, E.H., Smith, D.K., Rabadan, R., Peiris, M., & Poon, L.L. (2010). Codon usage bias and the evolution of influenza A viruses. Codon Usage Biases of Influenza Virus. *BMC evolutionary biology*, 10(1), 253.
- Yang, Z., & Nielsen, R. (2008). Mutation-selection models of codon substitution and their use to estimate selective strengths on codon usage. *Molecular biology and evolution*, 25(3), 568-579.
- Zhou, Y., Chen, X., Ushijima, H., & Frey, T.K. (2012). Analysis of base and codon usage by rubella virus. *Archives of virology*, 157(5), 889-899.