

# Molecular Rate Variation (Molecular Clocks)

## Molecular Rate Variation

The rate of molecular evolution is the rate at which substitutions accumulate in an organism's genome. Rates of molecular evolution can vary dramatically, for example, the rate of molecular evolution in some viruses is around one substitution per base pair per 1,000 years (Pagán et al. 2010), while in mammals the rate is around one substitution per base pair per 1,000 million years (Nabholz et al. 2008). Even closely related plants and animals can have rates of molecular evolution that vary by more than an order of magnitude (Thomas et al. 2006; Smith and Donoghue 2008; Welch et al. 2008; Lanfear et al. 2013). Accounting for molecular rate variation is important in methods that use molecular sequence data to date the divergences between species (molecular dating).

There has been a great deal of research into the causes of variation in rates of molecular evolution. This research has identified a range of factors which may cause variation in the rate of molecular evolution (Bromham 2011), and these factors can be broken up into those that affect the mutation rate and those that affect the rate at which new mutations are fixed in a population (the fixation rate). An increase in either the mutation rate or the fixation rate can potentially increase the overall rate of molecular evolution, although there are some situations in which these increases will leave the rate of molecular evolution unchanged (de Visser et al. 1999).

Many factors have been suggested to increase mutation rates in DNA sequences, including temperature, UV radiation, oxygen radicals, recombination, genome copying, and natural selection (Martin and Palumbi 1993; Davies et al. 2004; Wright et al. 2006; Lanfear et al. 2007; Thomas et al. 2010; Hodgkinson and Eyre-Walker 2011; Wright et al. 2011; Lourenço et al. 2013; Lanfear et al. 2013). In principle, variation in any of these factors could cause variation in the rates of molecular evolution between species, although the evidence for this is weak for UV radiation and oxygen radicals in particular (Davies et al. 2004; Lanfear et al. 2007; Joyner-Matos et al. 2011; Lanfear et al. 2013). However, there is good evidence that the many mutations occur during genome-copying events (meiosis and mitosis) and that variation in long-term rates of genome copying may explain much of the variation in the rates of molecular evolution between species (Smith and Donoghue 2008; Welch et al. 2008; Thomas et al. 2010; Lanfear et al. 2013). Intriguingly, it has also been suggested that natural selection may play a role in determining mutation rates and rates of molecular evolution, either through selection for increased longevity (Nabholz et al. 2008; Welch et al. 2008; Galtier et al. 2009) or through the reduced efficacy of natural selection in small populations (Lynch 2010, 2011).

Anything that increases the fixation rate of new mutations can also increase the substitution rate. Two factors combine to determine the fixation rate of a new mutation: the effect of that mutation on the carrier's fitness and the effective population size of the host population. As fitness effects become more beneficial and effective population sizes get larger, fixation rates increase (Woolfit 2009). This is because a population's effective population size determines the balance of power between natural selection and genetic drift. The larger the effective population size, the stronger natural selection is relative to genetic drift, and the faster beneficial mutations are fixed in the population, and deleterious mutations removed. Because we expect most mutations to be deleterious, it is generally thought that organisms with smaller effective population size should have faster rates of molecular evolution. Some studies have supported this idea and have shown that organisms with smaller effective population sizes tend to evolve more quickly, at least by some measure of the rate of molecular evolution (Moran 1996; Woolfit and Bromham 2003, 2005). However, other results suggest that the relationship between population size and the rate of molecular evolution can be much more complex than this simple model suggests (Charlesworth and Eyre-Walker 2007; Wright et al. 2009).

We have a fairly good understanding of the most important causes of variation in rates of molecular evolution. But despite this, we can often explain less than half of the variation that we can measure, suggesting that we still have a lot to learn. A better understanding of molecular rate variation is important because it can help improve molecular dating methods. Perhaps the best example of this is the development of new methods which leverage what we know about the causes and correlates of molecular rates to directly improve our estimates of divergence dates from DNA sequence data (Lartillot and Poujol 2011; Lartillot and Delsuc 2012). As our understanding of molecular rate variation continues to increase, we will be able to continue to improve the accuracy of molecular dating methods.

## Bibliography

- Bromham, L., 2011. The genome as a life-history character: why rate of molecular evolution varies between mammal species. *Philosophical Transactions of the Royal Society, B: Biological Sciences*, 366, 2503-2513.
- Charlesworth, J., and Eyre-Walker, A., 2007. The other side of the nearly neutral theory, evidence of slightly advantageous back-mutations. *Proceedings of the National Academy of Sciences of the United States of America*, 104, 16992-16997.
- Davies, T. J., Savolainen, V., Chase, M. W., Moat, J., and Barraclough, T. G., 2004. Environmental energy and evolutionary rates in flowering plants. *Proceedings of the Biological Sciences*, 271, 2195-2200.
- de Visser, J. A. G. M., Zeyl, C. W., Gerrish, P. J., Blanchard, J. L., and Lenski, R. E., 1999. Diminishing returns from mutation supply rate in asexual populations. *Science*, 283, 404-406.
- Galtier, N., Blier, P. U., and Nabholz, B., 2009. Inverse relationship between longevity and evolutionary rate of mitochondrial proteins in mammals and birds. *Mitochondrion*, 9, 51-57.
- Hodgkinson, A., and Eyre-Walker, A., 2011. Variation in the mutation rate across mammalian genomes. *Nature Reviews. Genetics*, 12, 756-766.
- Joyner-Matos, J., Bean, L. C., Richardson, H. L., Sammeli, T., and Baer, C. F., 2011. No evidence of elevated germline mutation accumulation under oxidative stress in *Caenorhabditis elegans*. *Genetics*, 189, 1439-1447.
- Lanfear, R., Thomas, J. A., Welch, J. J., Brey, T., and Bromham, L., 2007. Metabolic rate does not calibrate the molecular clock. *Proceedings of the National Academy of Sciences of the United States of America*, 104, 15388-15393.
- Lanfear, R., Ho, S. Y. W., Jonathan Davies, T., Moles, A. T., Aarssen, L., Swenson, N. G., Warman, L., Zanne, A. E., and Allen, A. P., 2013. Taller plants have lower rates of molecular evolution. *Nature Communications*, 4, 1879.
- Lartillot, N., and Delsuc, F., 2012. Joint reconstruction of divergence times and life-history evolution in placental mammals using a phylogenetic covariance model. *Evolution*, 66, 1773-1787.
- Lartillot, N., and Poujol, R., 2011. A phylogenetic model for investigating correlated evolution of substitution rates and continuous phenotypic characters. *Molecular Biology and Evolution*, 28, 729-744.
- Lourenço, J. M., Glémin, S., Chiari, Y., Galtier, N., 2013. The determinants of the molecular substitution process in turtles. *Journal of Evolutionary Biology*, 26(1), 38-50.
- Lynch, M., 2010. Evolution of the mutation rate. *Trends in Genetics*, 26, 345-352.
- Lynch, M., 2011. The lower bound to the evolution of mutation rates. *Genome Biology and Evolution*, 3, 1107-1118.
- Martin, A. P., and Palumbi, S. R., 1993. Body size, metabolic rate, generation time, and the molecular clock. *Proceedings of the National Academy of Sciences of the United States of America*, 90, 4087-4091.
- Moran, N. A., 1996. Accelerated evolution and Muller's ratchet in endosymbiotic bacteria. *Proceedings of the National Academy of Sciences of the United States of America*, 93, 2873-2878.
- Nabholz, B., Glémin, S., and Galtier, N., 2008. Strong variations of mitochondrial mutation rate across mammals - the longevity hypothesis. *Molecular Biology and Evolution*, 25, 120-130.
- Pagán, I., Firth, C., and Holmes, E. C., 2010. Phylogenetic analysis reveals rapid evolutionary dynamics in the plant RNA virus genus Tobamovirus. *Journal of Molecular Evolution*, 71, 298-307.
- Smith, S. A., and Donoghue, M. J., 2008. Rates of molecular evolution are linked to life history in flowering plants. *Science*, 322, 86-89.
- Thomas, J. A., Welch, J. J., Woolfit, M., and Bromham, L., 2006. There is no universal molecular clock for invertebrates, but rate variation does not scale with body size. *Proceedings of the National Academy of Sciences of the United States of America*, 103, 7366-7371.
- Thomas, J. A., Welch, J. J., Lanfear, R., and Bromham, L., 2010. A generation time effect on the rate of molecular evolution in invertebrates. *Molecular Biology and Evolution*, 27, 1173-1180.
- Welch, J. J., Bininda-Emonds, O. R. P., and Bromham, L., 2008. Correlates of substitution rate variation in mammalian protein-coding sequences. *BMC Evolutionary Biology*, 8, 53.
- Woolfit, M., 2009. Effective population size and the rate and pattern of nucleotide substitutions. *Biology Letters*, 5, 417-420.
- Woolfit, M., and Bromham, L., 2003. Increased rates of sequence evolution in endosymbiotic bacteria and fungi with small effective population sizes. *Molecular Biology and Evolution*, 20, 1545-1555.
- Woolfit, M., and Bromham, L., 2005. Population size and molecular evolution on islands. *Proceedings of the Biological Sciences*, 272, 2277-2282.

- Wright, S., Keeling, J., and Gillman, L., 2006. The road from Santa Rosalia: a faster tempo of evolution in tropical climates. *Proceedings of the National Academy of Sciences of the United States of America*, 103, 7718-7722.
- Wright, S. D., Gillman, L. N., Ross, H. A., and Keeling, D. J., 2009. Slower tempo of microevolution in island birds: implications for conservation biology. *Evolution*, 63, 2275-2287.
- Wright, S. D., Ross, H. A., Keeling, D. J., McBride, P., and Gillman, L. N., 2011. Thermal energy and the rate of genetic evolution in marine fishes. *Evolutionary Ecology*, 25, 525-530.

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