

“Relaxed clocks” were developed in response to observations that variation in the rate of molecular evolution is widespread (e.g., Drummond et al. 2006; Kishino et al. 2001; Sanderson 2002). So, at first glance, these new methods seem to be a more realistic approach to molecular dating, because they allow rate variation and they get the “right answer” for the metazoan radiation. But, like traditional molecular clock analyses, relaxed clocks must make very strong assumptions about the way that rates change over the tree (Welch and Bromham 2005). Typically this involves specifying not only models of rate change (usually favouring many small rate changes over fewer large ones), but also the distribution of speciation and extinction events in time. Given that these important assumptions concern aspects of a lineage’s evolutionary history about which we often know little, the parameter estimates used are usually chosen for reasons of statistical expedience, not because they are accurate reflections of the processes of molecular evolution (Welch et al. 2005).

For example, some methods use a model of rate change borrowed from descriptions of physical processes. The Ornstein-Uhlenbeck process (OUP) was formulated to describe the motion of a particle retarded by friction, and as such it is biased towards decreases in rate. What is reasonable for a moving particle is not necessarily reasonable for molecular rates, for which there is no a priori reason to believe that decreases in rate are more likely than increases. Unlike the motion of a particle, rates of molecular change are not expected to ever decrease to zero. An alternative model assumes an exponential distribution of rate changes. Exponential models are widely used in biology, but their use in relaxed clocks once again favours decreases in rates over rate increases (see Welch and Bromham 2005; Welch et al. 2005).

While the overall approach of relaxed clocks may seem more biologically appealing, the core assumptions of many of these methods are not necessarily a more realistic description of the data. This is not necessarily bad, but two things need to be ascertained: (1) the robustness of the methods to violations of these assumptions; (2) an empirical appreciation of how often we expect real data to violate these assumptions. The effect of these assumptions on date estimates can be seen in published data studies that present estimates obtained under several different models. For example, Peterson et al. (2004) demonstrated the sensitivity of date estimates to the assumption of variation in rates across sites: when all sites were assumed to evolve at the same rate, they obtained

date estimates for the metazoan diversification broadly compatible with the appearance of the Ediacaran fauna (573 Myr ago), but allowing rates to vary between sites gave a much older date estimate (656 Myr). Several studies have demonstrated that choosing between alternative models of rate variation or branch length estimation can dramatically change the date estimates obtained (Ho et al. 2005; Welch et al. 2005).

So, as molecular dating methods have become more sophisticated, it has become possible to arrive at a very wide range of possible date estimates by varying the assumptions made in the estimation process. This means that any reasonable position, and quite a few unreasonable ones, can now be supported by molecular date estimates. The most obvious conclusion to be drawn from this array of estimates is that molecular dates cannot be taken at face value: the data and the methods employed can dramatically change the date estimates gained. So how do we know which molecular dates are right, and which are wrong? The most attractive solution is to select the molecular dates most compatible with other lines of evidence. In effect, this makes molecular date estimates redundant – if we, quite sensibly, opt to believe only those molecular date estimates that match our prior expectations, then this is equivalent to saying that we gain no extra information from using molecular data. So it can be argued that we should ignore molecular dates altogether: if we know that we cannot take molecular dates at face value, and if the only way of determining which dates we can trust is to compare them to the fossil record, then why not just forget about molecular dates and use the fossils on their own?

Of course, it is also possible to make this kind of argument about many sources of historical data. For example, at a recent Royal Society conference (“Major Steps in Cell Evolution”, September 2005), many eminent scientists presented reasonable interpretations of the same data that enabled them to reach entirely contradictory opinions. The same rock sections were labelled as containing cells or abiotic inclusions. Phylogenetic trees were interpreted as evidence both for and against a late origin of methanogenesis. Geochemical analysis provided evidence of early eukaryotes, or for their late arrival. Snowball Earth episodes were short or long, thick or thin. There were many vigorous debates. But nobody claimed that, because two knowledgeable palaeontologists can look at the same rock and draw different conclusions, we should therefore scrap the fossil record altogether. Instead, these sometimes passionate exchanges generally ended with an agreement that more data

is needed, and more work needs to be done on its interpretation.

I would argue that we should take the same attitude to the development of molecular clocks. Molecular dates can be misleading. There are examples where they are clearly wrong, and there are cases where they are evidently imprecise. But to give up on molecular data altogether would be equivalent to rejecting all fossil evidence on the basis that the existence of Lazarus taxa demonstrates the unreliability of the geological record. The surprising history of the coelacanth, "extinct" in the fossil record since the Cretaceous, yet happily swimming the oceans today, does not mean the vertebrate fossil record is worth nothing.

There is historical information in DNA. Genomes change as organisms evolve. The longer two lineages have been separated in evolutionary time, the greater the difference between their genomes will be. But the relationship between genetic distance and time is complex, and its predictive power may be limited in many cases. The molecular clock is unlikely ever to replace the fossil record as the primary source of information on evolution in deep time. But it has a critical role to play as an alternative historical narrative, potentially complementing the biases and gaps of the palaeontological record.

The amount of genetic divergence between modern animals is far greater than we would expect from half a billion years of evolution, given what we know about rates of molecular evolution in the Phanerozoic. This observation suggests either that the animal kingdom has a deep hidden history, or that the rates of molecular evolution in the early part of the metazoan radiation were somehow must faster than they have been for most of the Phanerozoic. Just as the astounding burst of animal diversity in the early Cambrian needs to be explained (whether due to rapid evolution or palaeontological artefact), the molecular data for the metazoan radiation also requires explanation (whether deep divergence, fast early rates, or measurement artefact). I find that the more I learn about molecular clocks, the more I despair that they can ever be trusted. But the reason I keep working in the field of molecular clocks, rather than giving up, is this: wouldn't it be great if we could make them work?

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