

Constructive neutral evolution cannot explain current kinetoplastid panediting patterns

In their stimulating article, Lukeš et al. (1) discuss the origins of unexpected molecular processes in protists. They argue that similarities among independently evolved complex processes—in Alveolata and Euglenozoa—result from selectively neutral molecular changes and their concomitant epistatic constraints (2). The three examples are as follows:

- (i) Transsplicing and polycistronic messengers in dinoflagellates and kinetoplastids.
- (ii) “Three-membrane” plastids and extra hydrophobic stretches following transit sequences in dinoflagellates and euglenophytes.
- (iii) Mitochondrial gene fragmentation and RNA editing in dinoflagellates and kinetoplastids.

Only the first example of “convergent” (somewhat confusingly describing the result of epistatic constraints only) evolution, in which transsplicing allows translation of all cistrons, seems convincing. The third example is especially problematic, as these systems just seem to have gene fragmentation in common: Editing mechanisms differ and whereas kinetoplastid mRNAs need extra guide RNAs to restore reading frames, the split rRNA fragments in dinoflagellates probably regain functionality by base pairing.

Importantly, can constructive neutral evolution (2) explain these elaborate idiosyncrasies? Obviously, evolution results from the interplay between variation (chance processes) and selection. Contributions of neutral processes, such as random mutation, genetic drift, and chance fixation have long been underestimated. Theoretically, slight differences in likelihoods of molecular occurrences and their reversals (such as nucleotide deletion vs. insertion in genes having to be restored at the RNA level) could lead to accumulation of widespread

instances of “useless” processes. However, there are some problems:

- (i) Neutral changes have to take over the complete population by chance alone. It is highly unlikely but has to occur again, and again . . .
- (ii) Changes that individually can be considered “neutral” will upon accumulation cease to be so (every extra editing instance will make the organism more error prone, costs ATP, and increases coding DNA).
- (iii) The model categorically states that reversal must be almost impossible. In kinetoplastid editing reverse transcription of one edited mRNA can nullify hundreds of editing instances (3), making retention of panediting incomprehensible. In fact, current patterns of panediting levels nicely seem to correlate with life cycle complexity (4) as predicted by a model in which panediting and its inherent fragmentation function as a mechanism against loss of genes temporarily relieved of selection pressure (5).

The reconstruction of the relative contributions of chance (neutral changes) and necessity (selection pressures) to the evolution of panediting in kinetoplastids is still too difficult, but saying it is all just chance is way too easy.

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