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Novel mathematical modeling of ribosomal RNA sequence data suggests a new way of looking at evolution

A team of scientists, led by a faculty member of the Scientific Computing and Imaging (SCI) Institute at the University of Utah, have used novel mathematical modeling of ribosomal RNA (rRNA) sequence data to uncover two previously unknown coexisting evolutionary relationships, a convergence and a divergence between the major taxonomic groups of Archaea and Microsporidia, which cannot be described by a single tree of life. This suggests a new way of looking at evolution as a composition of changes rather than a hierarchy of changes.

In an article published in the journal *PLoS One* on April 29, 2011, Orly Alter, USTAR associate professor of bioengineering and human genetics at SCI, and her colleagues, propose that even on the level of a single rRNA molecule, an organism's evolution is composed of multiple changes due to concurrent forces that act independently upon different degrees of freedom of the rRNA molecule. Using a novel mathematical decomposition, a framework for modeling composite data, Alter, her students Chaitanya Muralidhara and Andrew M. Gross, and colleague Robin R. Gutell, find that insertions and deletions of prominent structural motifs are correlated, possibly even causally coordinated, with the relationships of convergence and divergence between the taxonomic groups. They identify these motifs, which are involved in rRNA folding and function, as evolutionary degrees of freedom.

Ribosomal RNA is an essential component of the ribosome, the cellular organelle that translates the cell's genotype into its phenotype by catalyzing protein synthesis in all known organisms, and therefore also underlies cellular evolution. The diversity of life is commonly evaluated by using rRNA sequence comparisons to classify living things into a hierarchical tree of life. Hierarchies built from different types of rRNAs, however, often disagree, and the quest for a universal tree of life remains elusive.

Alter and colleagues find that viewing evolution as a composition of changes rather than a hierarchy of changes appears to give a consistent picture of life. The mathematical models they created from small-subunit 16S rRNAs and large-subunit 23S rRNAs uncover qualitatively the same relationships among the taxonomic groups, and identify correlations with the same structural motifs.

In her Genomic Signal Processing Lab, Alter creates mathematical models from large-scale molecular biological data, the output of recent sequencing or DNA microarray hybridization technologies, by arranging the data in multidimensional tables known as tensors. She then develops algorithms, inspired by the mathematical frameworks that underlie theoretical physics, to uncover patterns in these data structures.

Alter is able to relate some of these patterns to known biological modes of regulation, and that is why she is able to use her models to computationally predict new ones. She believes that future discovery and control in biology and medicine will come from such mathematical modeling of large-scale molecular biological data, where the mathematical variables and operations can be related to biological reality, just as Kepler discovered the laws of planetary motion by using mathematics to describe trends in astronomical data.

Recent experimental results in collaboration with John F. X. Diffley, deputy director of the London Research Institute of Cancer Research UK, published in the journal *Molecular Systems Biology* in 2009, demonstrate that Alter's mathematical modeling of DNA microarray data can

be used to correctly predict previously unknown cellular mechanisms. This brings biologists a step closer to one day being able to understand and control the inner workings of the cell as readily as NASA engineers plot the trajectories of spacecraft today.

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<https://doi.org/10.1371/journal.pone.0018768>

To read the October 13, 2009 report in *Molecular Systems Biology* visit:

<https://doi.org/10.1038/msb.2009.70>