

**The Ribosome and the RNA World.** Loren Dean Williams and Jessica Bowman, School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, Georgia, 30332 (loren.williams@chemistry.gatech.edu).

An RNA World that predated the modern world of polypeptide and polynucleotide is one of the most widely accepted models in origin of life research. The defining ribozyme of the RNA World, which unites all RNA World models, performed template-directed synthesis of RNA: in the RNA World, RNA self-replicated.

One essential element of a RNA World Hypothesis is a feasible pathway out of the RNA World into the extant DNA/RNA/protein World. Life on earth is bi-phasic under RNA World scenarios (Figure 1). The origin and evolution of the ribosome marks the boundary between the two phases. It has been proposed that ribozyme-based biology gradually transitioned to extant biology as ribozymes incrementally relinquished catalytic function first to ribonucleoprotein enzymes, then to protein-based enzymes that lack RNA components entirely. In this model, the translation system shepherded the RNA World into the extant biology of DNA, RNA and protein.

Here, we examine the RNA World Hypothesis in the context of increasingly detailed information available about the origins, evolution, functions and mechanisms of the translation system. We conclude that the translation system presents critical challenges to RNA World Hypotheses.

Firstly, a timeline of the RNA World is problematic when the ribosome is fully incorporated. The mechanism of peptidyl transfer within the ribosome appears anomalous when compared to mechanisms of evolved enzymes, signaling origins in a chemical rather than biological milieu. The ribosome seems to be an early addition to life on earth, not a midstream correction.

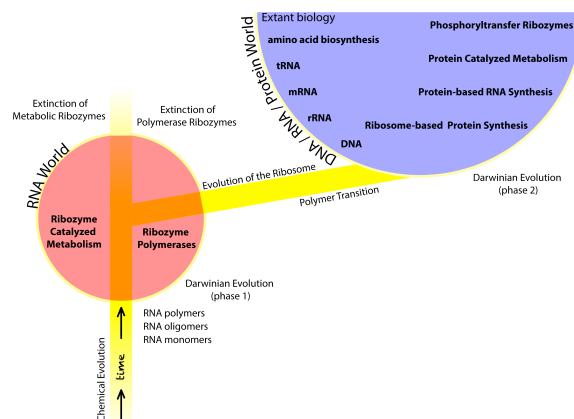
Secondly, we do not see specific evidence in biological systems of takeover of ribozyme function by protein enzymes. The catalytic portions of known ribozymes are cleanly excluded from replacement processes. None of the rRNA in or immediately surrounding the PTC or the decoding center has been replaced by protein in any system. RNase P, a universally distributed ribozyme originating in LUCA, shows a pattern similar to the ribosomes.

Thirdly, we see no evidence that the basic biochemical toolset of life is subject to substantive change by Darwinian evolution, as required for the transition from the RNA world to extant biology. During the putative Polymer Transition, which would have occurred in the context of Darwinian evolution, translation took root, gained utility and assumed its current status of centrality, preeminence and universality (Figure 1). An entirely new type of biopolymer (coded

polypeptide) was invented and took catalytic control. New biochemistries, including biosynthesis of amino acids, charging of tRNAs and synthesis of coded polypeptide, were introduced and became fundamental and essential. However, biopolymer backbones in extant biology are not observed to change by Darwinian evolutionary processes. Evolution, as observed, improvises by altering sequences of pre-existing biopolymers.

Finally, we can find no basis for preservation of the ribosome as ribozyme if other information transducing ribozymes, such as ribozyme polymerases, were replaced by protein analogs and erased from the phylogenetic record. In the RNA World Hypothesis, most ribozymes were rendered redundant and went extinct. All traces of ribozyme RNA polymerases, the defining catalytic systems of the RNA World, have been erased from the phylogenetic record. Yet the ribosome remains, permanent and universal.

We suggest that an updated model of the RNA World should address the current state of knowledge of the translation system.



**Figure 1.** Timeline of the RNA World. In the RNA World Hypothesis, life on earth passed through a phase in which chemical transformations were catalyzed and regulated by RNA, and RNA-based genetic material was replicated by a ribozyme polymerase. The ribosome and other components of the translation system were absent from the first phase of Darwinian evolution. Biology underwent a Polymer Transition, and entered a second phase, adopting coded protein as the primary enzymatic biopolymer. The origins and evolution of the ribosome mark the boundary between the two limiting phases of biology. During and after the polymer transition, core ribozymes of the RNA World went extinct and were washed out of the phylogenetic record.