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# Non-Enzymatic RNA Backbone Proofreading by Energy-Dissipative Recycling

A. Mariani[1] and J. D. Sutherland[1*]
[1]MRC Laboratory of Molecular Biology,
Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge CB2 0QH, UK
amariani@mrc-lmb.cam.ac.uk, *johns@mrc-lmb.cam.ac.uk

Non-enzymatic oligomerization of activated ribonucleotides leads to ribonucleic acid that contains a mixture of 2′,5′- and 3′,5′-phosphodiester linkages, and overcoming this backbone heterogeneity has long been considered one of the greatest limitations to the prebiotic emergence of RNA[1]. We present and experimentally demonstrate a model in which non-enzymatic chemistry progressively converts 2′,5′-linkages to 3′,5′-linkages by iterative degradation and repair. With multiple rounds of this energy-dissipative recycling[2], we show that all 3′,5′-linked duplex RNA can emerge from a backbone heterogeneous mixture, thereby delineating a route that could have driven RNA evolution on the early Earth.

**References:** [1] Bowler FR et al. (2013) *Nat. Chem.* 5:383-389. [2] Sutherland JD (2017) *Nat. Rev. Chem.* DOI 10.1038/s41570-016-0012.

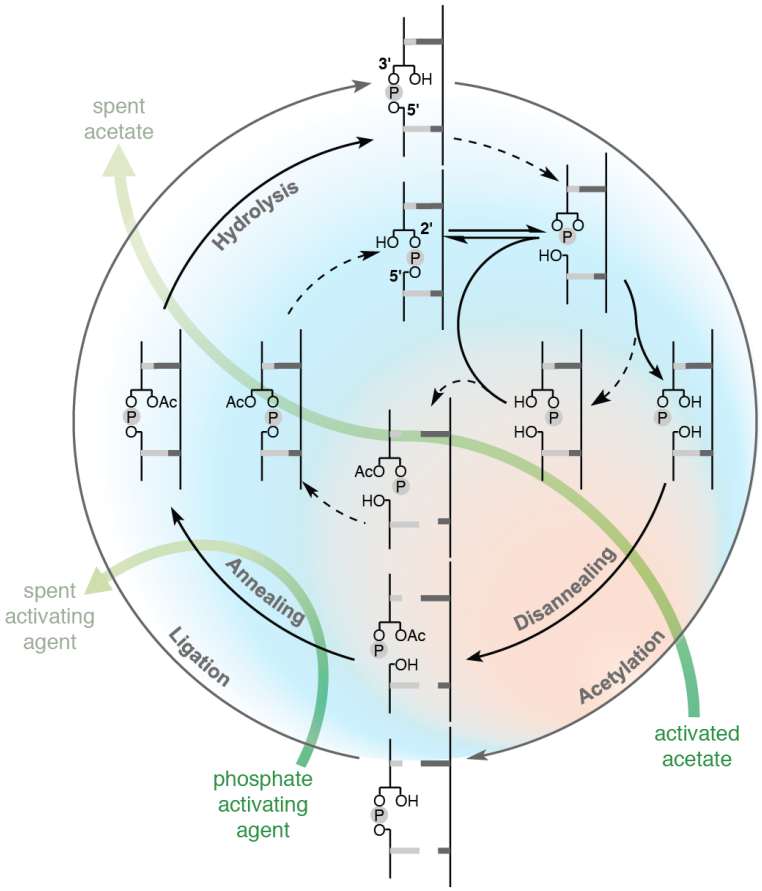


**Figure 1** –Proposed model for the recycling of backbone heterogeneous ribonucleic acid. Favored (bold lines) and unfavored (dashed lines) pathways resulting in the conversion of 2′,5′-bonds to 3′,5′-bonds.