THE EMERGENCE OF BIOLOGICAL RNA FROM THE PREBIOTIC CHEMICAL MIXTURE

Paul G Higgs, Andrew S Tupper and Kevin Shi. Origins Institute, McMaster University, Hamilton, Ontario L8S4M1, Canada. (higgsp@mcmaster.ca, tuppea2@mcmaster.ca, shik6@mcmaster.ca).

Introduction: Biological RNA shows three kinds of ordered properties - it uses only 'right-handed' nucelotides rather than a mixture of both chiralities, it uses a specific set of four nucleotides rather than a mixture of many other similar molecules, and it uses regular 3'-5' bonds between ribose sugars rather than a mixture of different bond types. We will show that if template-directed replication is important, we can explain the emergence of all these ordered properties by the same mechanism in terms of symmetry breaking phase transitions.

Chiral Symmetry Breaking: There are many previous models that show how chiral biopolymers can arise when there is asymmetric autocatalysis - see references in [1]. These models assume that the formation of nucleotides of a given handedness (D or L) is catalyzed by nucleotides of the same handedness, or by RNA strands of the same handedness. Here we propose that the asymmetric autocatalysis comes from template-directed synthesis of complementary strands, rather than from catalysis of nucleotide synthesis.

We studied a computational model where nucleotides can spontaneously polymerise to form oligomers of all lengths and oligomers can be hydrolyzed to shorter oligomers and monomers. This generates an exponential distribution of oligomer lengths (as shown in [2]). Additionally, uniform oligomers (all D or all L) can act as templates that catalyze the ligation of shorter oligomers of the same handedness. Mixed oligomers cannot act as templates. The rate of the ligation reaction is controlled by rate constant k_{lig}. If k_{lig} is small, most monomers end up in mixed oligomers, and the concentration of D and L oligomers is equal (Fig. 1). If k_{lig} is large, chiral symmetry breaking occurs, uniform oligomers of one handedness become dominant, while strands of the opposite handedness and mixed strands become rare.

Selection of RNA relative to alternatives: Many alternative "XNA" nucleotides with different bases or different sugars could have been formed by prebiotic chemistry at the same time as standard ribonucleotides. We studied a model in which R and X monomers can polymerize and hydrolyze, and uniform R or X oligomers can act as templates for strands of the same kind. If the rate constants for R and X are identical, the problem is identical to the chiral symmetry breaking problem (circles in Fig. 2 are the same as Fig. 1). If R is a better template than X, then the phase transition is rounded out (triangles in Fig. 2). The polymer with the best template ability is dominant when k_{lig} is large.

We also studied a very similar model in which strands with regular 3'-5' bonds emerge from a mixture of 3'-5' and 2'-5' bonds. We therefore propose that all three ordered properties of RNA emerge by essentially the same mechanism - uniform oligomers are better templates than mixed oligomers.

References:

[1] Wu M, Walker SI, Higgs PG (2012) *Astrobiology* 12: 818-829.

[2] Higgs PG. (2016) *Life* 6: 24.

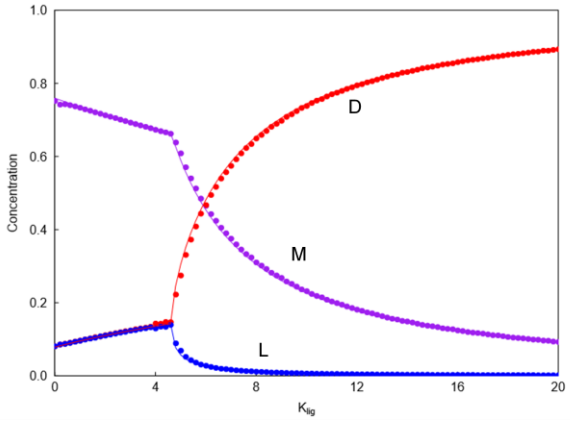

Fig. 1 - Relative concentrations of nucleotides contained in uniform right and left-handed oligomers (D and L) and in mixed oligomers (M) as a function of the the rate constant k_{liq} for template-directed ligation.

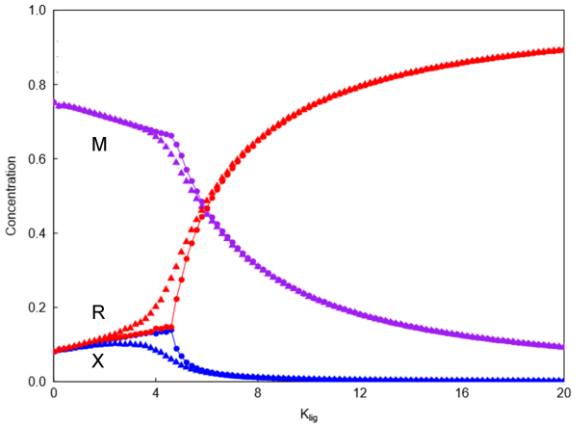

Fig. 2 - Relative concentrations of nucleotides contained in oligomers of uniform RNA (R), uniform XNA (X), and in mixed oligomers (M) as a function of the the rate constant k_{lig} for template-directed ligation.