MAJOR EVOLUTIONARY TRANSITIONS IN THE RNA WORLD Paul G Higgs. McMaster University, Hamilton, Ontario. higgsp@mcmaster.ca

Introduction: The RNA World is a period thought to have existed in the early evolution of life on Earth when RNA sequences acted as both genes and catalysts. A key component of the RNA world would have been a polymerase that acts on a template strand to make a complementary strand to the template. Sustained replication is possible by this means if the polymerase is able to deal with templates that are at least as long as itself and if the accuracy of replication is sufficient to preserve the sequence against accumulation of mutations.

Co-operation in Spatial Models: A polymerase is a co-operator in the sense that it copies other strands and requires other strands to copy it [1]. As in many areas of evolutionary biology, co-operators are vulnerable to being destroyed by parasites. In the RNA World, any strand that can act as a template is potentially a parasite of the polymerase. A polymerase would first arise in a prebiotic world that must have already contained many random non-functional sequences, so it would be born into a world full of parasites.

In previous studies using mathematical and computational models, we have shown that a polymerase can survive and spread if diffusion is relatively slow and spatial clustering of strands arises [2]. In this case, co-operative strands tend to interact with other co-operative strands and help one another. In contrast, if the system is well mixed, encounters between strands occur at random, and parasites tend to invade and destroy the polymerases.

The origin of life is the first of the major transitions in evolution. Spatial clustering greatly facilitates the origin of life in models that consider the transition from a non-living to a living state [3]. When diffusion is slow, small patches arise with high concentration of replication molecules. These patches then spread across the rest of the surface. In contrast, well-mixed systems tend to remain stuck in a non-living state.

Evolving Increasing Complexity: Another major transition involves the evolution of a single component polymerase system towards a modern genetic system in which many genes of different functions are all replicated by the same mechanism. As a first step in this increasing complexity, we are currently developing spatial models of RNA replication to investigate the conditions in which other ribozymes having useful functions can coexist with a polymerase.

A nucleotide synthase could help a polymerase by increasing the monomer concentration but it would be dependent on the polymerase for its own replication. However, a synthase also takes time and resources away from the polymerase itself. In well mixed systems, we find that the synthase either replicates more slowly than the polymerase, in which case it dies out, or it replicates faster than the polymerase, in which case it behaves like a parasite and destroys the system. However, in spatial models there is a possibility of stable coexistence of the two catalysts, and there are parameter ranges where the two can survive together but neither could survive on its own. Thus, once again, the spatial structure plays an essential role.

Evolving a Genome: In modern organisms, it is clear that the genome (DNA) is separate from the catalytic molecules (proteins). In the RNA World, if every sequence acts both as a template and a catalyst, there is no separate genome. The first step in the major transition towards creating a genome may have been the establishment of an RNA replication system involving double stranded RNA. Double strands would have functioned as a genome, and single strands as catalysts. Many single strands could potentially be transcribed from the same double strand. We are studying the way that the separation of the roles of gene and catalyst affects the accumulation of mutations and the error threshold.

There is an interesting parallel with double stranded RNA viruses that exist today. If transcription is conservative, a new single strand is produced and the double strand retains two old strands. If transcription is semi-conservative, one of the old strands becomes single stranded and the double strand contains one old and one new strand. These two mechanisms are identical if there are no errors, but they are different in the way that mutations accumulate. We are using mathematical models to compare these two mechanisms with each other and with the simpler system involving only single strands.

References:

[1] P.G. Higgs, and N. Lehman (2015) Nature Rev. Genet. 16: 7-17.
[2] J.A. Shay, C. Huynh and P.G. Higgs (2015) J. Theor. Biol. 364: 249-259.
[3] M. Wu and P.G. Higgs (2012) Biol. Direct 7: 42.