Cooperation in an All-RNA Network

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The discovery of catalytic RNA molecules (ribozymes) capable of catalyzing a significant number of diverse chemical reactions suggests that an RNA world preceded the DNA-RNA-Protein world we know today. The self-replication of RNA molecules would be the central process of the RNA world. However, a single self-replicating RNA would not sustain information on its own if it surpassed the “error threshold” leading to an error catastrophe (1). On the other hand, a cooperative network of RNA replicators would be able to accumulate, preserve and process information. In the current work, we used a collection of RNA fragments that covalently assemble into an *Azoarcus* group I ribozyme (2) to explore the ability of RNA replicators to form a cooperative catalytic network. Three different constructs of the *Azoarcus* ribozyme with different internal guide sequences (IGS) – GUG (canonical), GAG, and GCG – were designed that are capable of a minimal amount of self-assembly when broken into two fragments. Here, self-assembly depends on a mismatch with non-complementary sequences, CGU, CAU and CUU, respectively, to be recognized by IGS via autocatalysis. Yet when all three constructs are present in the same reaction vessel, concomitant assembly of all three covalent ribozymes is enhanced through an interdependent reaction network. Analysis of these reactions indicates that each system is capable of guiding its own reproduction weakly, along with providing enhanced catalytic support for the reproduction of other constructs through matched and mismatched IGS-tag interactions. The resulting RNA population was observed to evolve over time based on genotyping of more than 50 individual RNAs for various time-points. The unequal catalytic rates of various assembly reactions favor the assembly of one construct over the others. However, the cooperation among all three constructs help all constructs to assemble demonstrating that this RNA network meets many of the requirements of an all RNA hypercycle as envisioned by Eigen (1). Also, when co-incubated with non-interacting (i.e., selfish) yet efficient self-assembly systems, the cooperative assembly outcompetes the selfish self-assembly systems, demonstrating the ability of a cooperative organization to possess an evolutionary advantage (3).

References

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