

Evolution of Cooperation in an RNA world

Walter de Back^{1,2} and Sergio Branciamore^{1,3}

¹Collegium Budapest
Institute for Advanced Study
Budapest, Hungary

²Department of Innovative Methods of Computing
Center for High Performance Computing
Technische Universität Dresden, Germany

³Department of Molecular Biology
Beckman Research Institute
City of Hope, Duarte, USA

walter@deback.net

Coupling an informational to a metabolic system is one of the essential steps towards a living system *sensu* Gánti (2003)(Fernando et al., 2005). The metabolic model proposed by Czárán and Szathmáry (2000) provides a prebiotic scenario in which such a coupling might have been realized in an RNA world (Gilbert, 1986). They show coexistence of multiple enzymatic replicators that contribute to a metabolism, from which all replicators benefit. Cooperation among replicators to the common metabolism persists, provided the population is spatially structured by adsorption on a surface (or in an open chaotic flow (Károlyi et al., 2002; Scheuring et al., 2003)). The system is ecologically stable, even in the presence of strong parasites. Parasites may even enhance the system by evolving a replicase (Könnyű et al., 2008). However, it remains unclear whether this metabolic cooperation is attainable by natural selection from a pool of nonfunctional RNA molecules. Here, we investigate the evolutionary origins of the metabolic model for template coexistence.

In order to find an evolutionary route towards the emergence of metabolic cooperation, we have extended the original cellular automaton model (Czárán and Szathmáry, 2000). Since catalytic activity of RNA enzymes (ribozymes) typically depends on the folded structure, we model the replicators in our model as RNA-like molecules specified by a sequence and the secondary structure (calculated using the **Vienna RNA package** (Hofacker et al., 1994)). The population evolves under low replication fidelity, where erroneous base substitutions lead to mutations. Molecules with the correct structure can catalyze a particular reaction in a metabolic pathway (see figure 1). We model the metabolic network as a simple linear pathway and account for the adsorption, reaction and diffusion of small metabolites over the surface.

As a starting condition, we assume a population of RNA self-replicators without catalytic activity. This system is an extreme heterotroph in that it fully depends on the availability of compounds from the external environment (Szathmáry, 2006). The evolution towards a metabolic system thus involves the appearance of active ribozymes, the establishment of cooperation, and subsequent complexification (elongation) of the system by progressively adding ribozymes. The appearance of a specific ribozyme from a pool of nonfunctional RNA seems unlikely given the vast sequence space, especially as no selective gradients exist towards enzymatic function. Moreover, good catalysts are typically bad replicators. As demonstrated *in vitro*, evolution

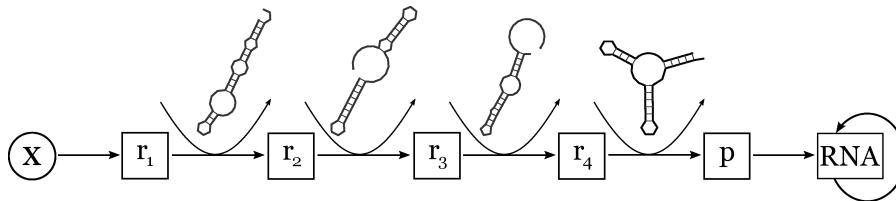


Figure 1: Metabolic pathway. The product p is required for RNA replication. Reactions are catalyzed by ribozymes with the structures shown.

of RNA replicators tends towards short and fast replicators (Kacian et al., 1972), not towards catalysts.

If ribozymes do appear that contribute to the common metabolism, their activity is an altruistic act (Maynard-Smith, 1979). Giving catalysis aids their own replication, but benefits replication of other molecules including parasites as well. The increase in system complexity requires cooperative interactions between various ribozymes catalyzing different reactions. The success of an enzymatic replicator therefore critically depends on the catalysis provided by the other ribozymes in the pathway. The evolution of cooperation thus implies that ribozymes sacrifice their replicatory autonomy.

These difficulties notwithstanding, our simulations demonstrate the emergence of the metabolically coupled templates. Starting with a random population of noncatalytic RNA, the templates rapidly evolve to optimize fecundity, as expected. Because resources are consumed during replication, the external environment is slowly depleted. When the resource concentration decreases beyond a critical point, the direction of the selective pressure reverses. Selection for structural stability results in a high diversity of near-neutral structures. This transient phenomenon enables the chance appearance of specific ribozymes.

Parasites appear simultaneously with active ribozymes. Stable coexistence of catalytic RNA with parasites is due to the fact that metabolism (hence replication) slows down in areas where parasites are abundant, while regions with less parasites continue to produce ribozymes. Interestingly, because parasites can evolve more freely as ribozymes, they play a key role in the complexification of the metabolic network. They provide a genetic pool out of which new ribozymes can be recruited. Through progressive depletion of resources and discovery of ribozymes, the metabolic pathway is enzymatized in a way akin to the retrograde evolution model (Horowitz, 1945). A limit to the evolvability of complexity arises due to an increasingly stringent Allee effect (Allee, 1931). Our simulations show the evolution of a metabolic system consisting of four ribozymes and a parasite and is ecologically and evolutionarily stable.

The evolutionary route sketched above presents an example of the formation of a new level of organization. The initial selfish replicator population is transformed into a cooperative system whose resistance against parasites is facilitated by group level selection, favouring metabolically active trait groups. A clear division of labor among molecular species arises, and the organization of heredity has shifted from the replicator level to the group level, allowing for further information integration. Thus, the qualitative changes observed in our model carry the hallmarks of a major evolutionary transition (Maynard-Smith and Szathmary, 1997). Our results emphasize the

importance of the interplay between genetic information, the ecological organization and the external environment as the driving force in the evolution of complexity.

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