Reviewer: Jake Hanson
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Title: Information Processing in Cooperative RNA Networks

General Strengths:

The paper is well motivated and the purpose for the study is easily understood both in its own right and in its application to broader questions.

General Weaknesses:

I was a bit hindered in understanding what is being simulated in the model. I'm aware that you start with fragments, but what are these fragments made of? I know they evolve kinetically over time, but I'm not sure what is evolving so its hard for me to understand the final output. This information is surely all contained in the paper but without being explicitly stated I was not able to figure it out.

Abstract

It is of particular interest to understand how chemical species can cooperate in such a way that each species promotes the growth of others.

- A reference here would strengthen this point.

Introduction

The origin of life is the greatest unsolved mystery in the history of science.

- This is a strong opinion! Depending on where this is published, this may or may not be highly controversial.

Accordingly, there has been and continues to be an exhaustive search for a self replicating RNA molecule. However, to date, a self-replicating ribozyme remains elusive.

- Why does self-replicating matter? Explicitly stating it here would be informative.

Models and Methods

The IGS is always associated with the 'W' segments, while 'W', 'X', and 'Y' may contain tags.

- So W can be used as an IGS or a tag?

First, a selfish genotype, labeled with 'S,' and also cooperative one, labeled

with 'E.' The different assemblies can be labeled as 'E1,' 'E2,' 'E3,' 'S1, 'S2,' and 'S3.' in accordance with figure ().

- I'm unsure how genotype plays into the model. Namely, the model seems set up to talk about WXYZ, and I don't know how genotype connects to the WXYZ framework.

Therefore such that all fragments have an equal initial abundance which was set to 500…and it is assumed h = 5 unless otherwise stated.

- Why these values? Even if they are arbitrary it would help to state them as such.

This numerical model is completely specified by the catalytic rate constants (table 1), the spontaneous formation rate constant (h), and the initial abundance of fragments.

- Missing Table 1

A kinetic Monte-Carlo algorithm was used to simulate the chemical kinetics 4. For each experiment, all assemblies were initialized as fragments, with each genotype represented equally. Therefore such that all fragments have an equal initial abundance.

- What assemblies are being referred to here?

The quantities of interest in this system are the abundances of each of the assembled genotypes.

- This helps clarify what is evolving in the model. However, I am still unsure how genotype maps to WXYZ framework.

There are six distinct genotypes, each of which can take on real positive integer values, on the interval [0;500] (because the initial number of fragments is 500).

- How does genotypes relate to the number of fragments?

Fig. 1 The dynamics of the system are shown here. In green the total number of covalently assembled cooperative molecules are shown while the total number of the covalently assembled selfish molecules are shown in red.

- What defines a molecule in this sense? i.e. is a molecule a certain size?

Results

However, in contrast to the results presented in 1, it should be noted that the cooperative molecules do not always out compete the selfish ones.

- Is there an interpretation for why this may be the case?

Discussion

The source of this failure could be due to one of two distinct factors. First, the coarse-grainning chosen here may not capture the relevant system dynamics. Alternatively, it is possible that the information measures chosen are ill-suited to measure the types of correlations relevant to the system dynamics.

- Is it also possible that the system and the model operate in a fundamentally different manner regardless of course-graining?

Regardless of the interpretation, information theory provides a coherent way of comparing biological and chemical evolution. In this light, the use the study of information dynamics should be extended in the study of both biological and chemical evolution. This would allow more direct comparisons between theory of experiments and may provide new insights into the origin of life on earth.

- Good summary of the scope of this work.