Inheritance and selection in RNA autocatalytic sets with self-organisation properties

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Nucleic acids possess remarkable potential for self-organization to form higher-order complex structures. This self-organization property has been shown to be a driving force for producing first life-like conditions on Earth [1]. In this regard, RNA is of special interest as it has been hypothesized that in prebiotic world RNA acted both as an information carrier and a catalyst [2]. However, the origin of life based on RNA must have required a system for the replication of RNA to allow molecular evolution to begin. One view would be that reproduction could be ensured by self-assembly of small RNA fragments in an autocatalytic manner to overcome the problem of error-catastrophe in a pure replication-based origin-of-life system. In a recent work, the benefits of cooperative autocatalytic sets have been experimentally demonstrated using small RNA fragments derived from Azoarcus group I intron [3, 4]. However, it is not immediately clear how such a collective system formed of RNA networks could evolve. Indeed, several ingredients in addition to material amplification need to be fulfilled to start a Darwinian mode of evolution : reproduction with inheritance, variation and selection.

We have developed a high-throughput experimental platform where we combine droplet microfluidics and next-generation sequencing to address these main questions : 1) Inheritance : addressing inheritance requires to map effect of different initial input or seed on the respective outputs. In particular we are interested in whether self-assembly of these small RNA fragments leads to a common universal final output or whether there is a strong dependence on initial input. 2) Selection : for Darwinian-like selection, one requires a measure of fitness and selection should be based on that. To address this in the self-assembly of small RNA fragments, we are developing a fluorescence assay where amount of self-assembly can be co-related with the fluorescent signal. Then based on microfluidic-system [5], selection pressure can be applied in order to select for the RNA self-assemblies with the higher fitness.

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