July 16-21, 2017 at UC San Diego, CA, USA

Autocatalytic sets of RNA replicators in origin of life

Ameta S.[1], Arsene S.[1], Nghe P.[1], Lehman N.[2], Griffiths A.D.[1]*
[1]Laboratory of Biochemistry, ESPCI Paris, UMR 8231 ESPCI-CNRS, Paris, France,
[2]Department of Chemistry, Portland State University, Portland OR, USA
*andrew.griffiths@espci.fr

Introduction: Autocatalytic sets must have been an intriguing feature of prebiotic molecules to generate first life-like scenarios on Earth [1-3]. Such autocatalytic sets brings a network-based perspective in origin-of-life where ideas of cooperativity between earlier molecules [1], collective fitness [2,4] and storing information in group of molecules [5] can be applied. Though there is considerable theoretical work promoting the network-based approach in origin-of-life [2,3,6], empirical studies targeting different properties of network in context of origin-of-life are still scarce. Recently, small RNA fragments of *Azoarcus* group I intron have been shown to spontaneously recombine to generate fully-functional ribozymes by forming cooperative and autocatalytic networks [7,8]. Such RNA recombination system have potential of overcoming the hurdle of error-catastrophe in a pure replication-based origin-of-life system [9]. However, here individual networks in isolation were not studied. In the current work, we are exploiting RNA networks formed by *Azoarcus* group I intron ribozyme to assess different network-level parameters [4,6] with an ultimate goal of demonstrating Darwinian-like evolution with such rudimentary RNA system. In order to explore the total network space, we have developed a high-throughput experimental set-up by combining droplet-microfluidics[10] with next-generation sequencing by which RNA networks can be sequenced in each droplet at an unprecedented resolution (Figure1).

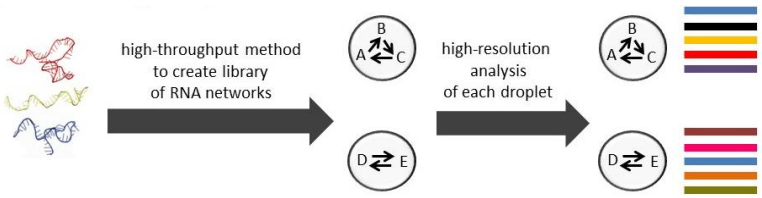

Figure 1 – Schematic representation of a high-throughput method to create a diverse library of RNA networks from the fragments of *Azoarcus* group I intron ribozyme. Using droplet-based microfluidics each of the network from the library can be analyzed at high-resuloution.

Using this set-up, we have analyzed a diverse RNA network library containing between 2-12 membered networks. Initial analysis revealed that network topology could be a strong determinant for growth of a network. More efforts are now focused on evaluating the relation between network topology and 'fitness' and future experiment will also address robustness and evolvability of such networks.

References:

[1] Higgs PG, Lehman N (2015) *Nature Reviens Genetics* 16:7-17. [2] Vasas V, Fernando C, Santos M, Kauffman S, Szathmáry E (2012) *Biology Direct* 7:1-14. [3] Hordijk W, Steel (2017) *BioSystems* 152:1-10. [4] Nghe P, Hordijk W, Kauffman SA, Walker SI, Schmidt FJ, Kemble H, Yeates JAM, Lehman N (2015) *Molecular BioSystems* 11: 3206-3217. [5] Segré D, Ben-Eli D, Lancet D (200) *Proceedings of the National Academy of Sciences USA* 97: 4112-4117. [6] Jain S, Krishna S (2001) *Proceedings of the National Academy of Sciences USA*, 98: 543-47. [7] Hayden EJ, Lehman N (2006) *Chemistry and Biology* 13:909-918. [8] Vaidya N, Manapat ML, Chen IA, Xulvi-Brunet R, Hayden EJ, Lehman N (2012) *Nature* 491:72-77. [9] Eigen M, Schuster P (1977) *Die Naturwissenschaften* 64:541-565. [10] Matsumura S, Kun A, Ryckelynck M, Coldren F, Szilagyi A, Jossinet F, Rick C, Nghe P, Szathmáry E, Griffiths AD (2016) *Science* 354: 1293-1296.