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Pre-LUCA cells: life but not alive

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Introduction: The early evolution of life included a series of transition from non-living matter, through prebiotic organic synthesis, towards the assembly of first evolvable protocells and the Last Universal Common Ancestor of all life (LUCA). Prebiotic chemistry and the simplest, prebiotically plausible stages of protocell evolution have been studied for many years. On the other end of the origin of life timeline, the state and properties of the first live cell, LUCA, have been inferred from phylogenetic analysis and ancient protein reconstitiution. Relatively less effort was focused on the non-living, yet immediately pre-life stages of origins. Our work focuses on that immediately-pre-life stage of evolution. Using liposome bioreactors we create synthetic minimal cells that exhibit some key properties of life without being entirely alive.

Synthetic minimal cells express proteins inside phospholipid liposomes using cell-free protein expression systems and DNA templates. This system represents the latest stage of prebiotic evolution, after the establishment of the Central Dogma. The minimal cells do not undergo spontaneous division, so they're not alive. The cells do not have active homeostasis, but they can maintain a separate internal environment due to relative impermeability of phospholipid membrane. The controllability and modular designeability of cell-free protein expression system and simple phospholipid membranes allow studying major transitions in evolution. They can be used to study heaviliy deoptimised biological processes, and recreate the assembly of basic live cell systems from ancestral components.

In our work, we create synthetic minimal cells expressing complex genetic pathways, with membrane proteins facilitating communication with external environment, and we use combinatorial and programmable fusion to control synthetic cell populations. Together, this creates a comprehensive system to study the advent of cellular processes on the boundary between prebiotic and Darwinian evolution.

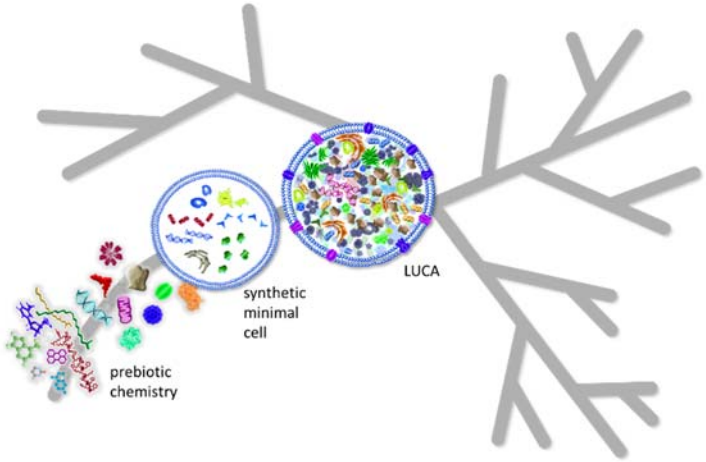

Figure 1 – Synthetic minimal cells are liposome bioreactors mimicking late pre-LUCA stage of prebiotic evolution. The liposome of synthetic minimal cells is made of phospholipids, the cells contain ribosomes, express proteins from DNA, contain membrane channel proteins and maintain some level of homeostasis. The synthetic cells do not spontaneously divide and do not undergo Darwinian evolution.