IMPRS on Multiscale Biosystems

Title: Artificial organelle life: compartmentalization of enzymatic reactions in lipid vesicles

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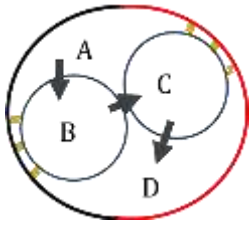
Project description: A common definition of cellular life is "a self-sustaining chemical system capable of Darwinian evolution". In order to understand the origin of biological life on Earth, we must first be able to comprehend how simple cellular life could emerge from prebiotic chemistry. A key requirement of the early cell, or protocell, was the ability to compartmentalize basic polymers needed for encoding genetic information. Later on, the formation of complex sub-cellular organelles allowed more functionality and diversity.

Our aim is to understand how the protocell was able to develop complex organelles by creating artificial vesicle structures. Vesicles composed of synthetic lipid membranes can easily be produced and used to encapsulate various biomolecules such as proteins, peptides, saccharides, or DNA. Such lipid compartments can even contain protein expression systems or enzymatic reactions. Furthermore, it is possible to prepare vesicles with multiple sub-populations of vesicles.



We will dissect the role of compartmentalization of biosynthetic pathways in eukaryotes by studying the first steps of the biosynthesis of the molybdenum cofactor (Moco). While in prokaryotes all steps for Moco biosynthesis are localized in the cytosol, in eukaryotes the first step is localized in the mitochondria and a stable intermediate is transported to the cytosol where all further steps proceed. We are planning to separate the steps using the bacterial proteins for Moco biosynthesis and will encapsulate them into vesicles. This will enable studies of the transported intermediate in detail and will give insights into the role of mitochondria for Moco biosynthesis in humans.

A successful candidate will first work in a biophysics lab to learn how to produce lipid vesicles with multiple compartments. Fluorescence microscopy to image and characterize these structures will be used, as well as microfluidic platforms designed to handling them. Once established, these compartments will be used to encapsulate proteins to initiate and monitor enzymatic reactions (See Figure) which will be performed in a biochemistry lab. The aim is to understand the compartmentalization of biosynthetic pathways during evolution.

The project is highly interdisciplinary requiring close collaboration between biophysics and biochemistry labs. It is a unique opportunity to mimic cellular enzyme cascades in a controlled artificial membrane system that will gain valuable insights into the origin of life.

Required background:
We are looking for a student with a practical lab experience and a background preferably in biotechnology, biochemistry, or chemistry. Practical experience with microfluidics, membrane

biophysics, protein purification, and fluorescence microscopy would be ideal. Good working knowledge of English is required.

Paper to read before the interview:

1. T. Robinson, P. Kuhn, K. Eyer and P. S. Dittrich, Microfluidic trapping of giant unilamellar vesicles to study transport through a membrane pore, Biomicrofluidics, 7, 4 (2013) 044105.
2. Fräsdorf B., Radon C., Leimkühler S. Characterization and interaction studies of two isoforms of the dual localized 3-mercaptopyruvate sulfurtransferase TUM1 from humans. J Biol Chem. (2014) 289:34543-56.
3. Mendel RR, Leimkühler S. The biosynthesis of the molybdenum cofactors. J Biol Inorg Chem. (2015) 20:337-47.

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