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The Center for
Molecular Life Sciences

Master Project in Nanoscience: Formation Kinetics of Liquid-Liquide Phase Separation by Microfluidics

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Liquid-Liquid phase separation (LLPS) is a recently emerging and fascinating concept of cellular organization. LLPS describes the physical principle of spontaneous de-mixing of a multi-component system (solution) into multiple spatially separated liquid phases of high respectively low density. Cellular structures formed by LLPS are commonly referred as membrane-less organelles (MLOs) and are thought to play a key role in the spatial-temporal orchestration of complex biochemical reactions in cells. Our Lab tries to understand how a particular group of proteins, the Dead-Box ATPases (DDXs), regulates LLPS and the formation of MLOs from a bio-physical/chemical and cellular point of view.[1]

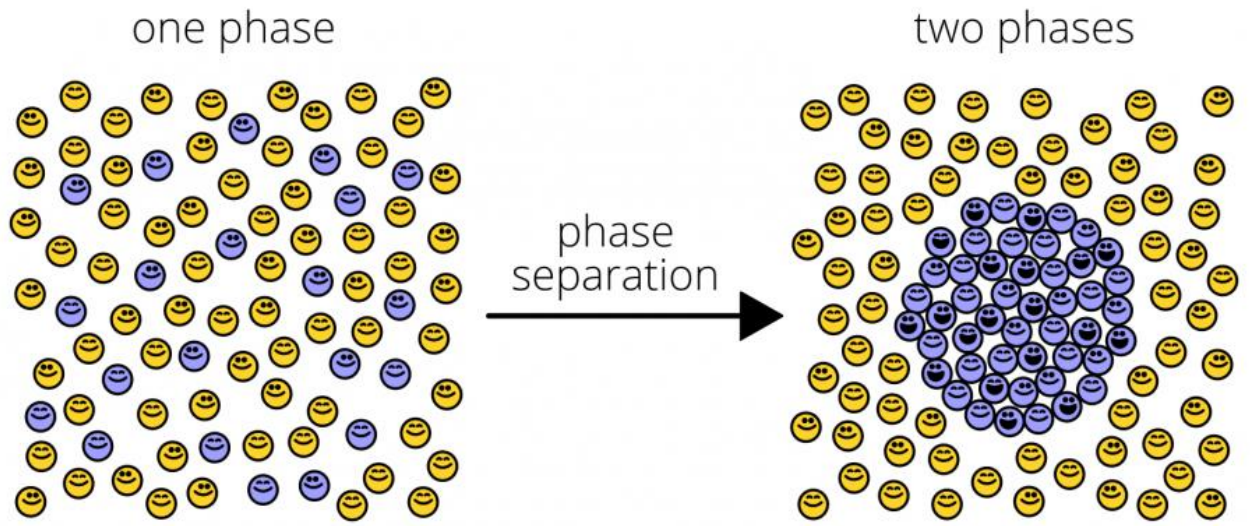

Figure 1: Liquid-Liquid Phase Separation in a Nutshell: This schematic depiction illustrates the most basic principle of liquid-liquid phase separation. A multi-component system (two components) maintains a homogeneous distribution if the interaction strength of all the components is similar. Spontaneous demixing is observed when one of the components prefers to interact with each self. [2]

We are offering a highly interdisciplinary project for a master thesis or research project + Master Thesis for Nanoscience students. The Hondele Lab was formed two years ago and currently consists – besides Maria as group leader – of 6 PhD students, 2 postdocs and a labmanager that together have broad expertise ranging from structural biology, biophysics, biochemistry, cell biology and light microscopy. The highly motivated and dynamic research group provides an ideal environment for enthusiastic students to work on their own projects under proper supervision and to learn the methods / soft skills required to work independently in a scientific Lab.

The Project

The goal of the project is to established a microfluidics system in the lab according to guidance and information provided by our collaborators (Arosio Lab, ETH Zürich) for quantitative analysis of the formation of protein droplets (LLPS). The second phase of the project will be to analyze the yeast DDXs Dhh1 and Ded1 with this microfluidics setup and to compare different variants (mutants) of the proteins with respect to their condensate forming ability (kinetics, thermodynamics, miscibility). This will constitute one of the first quantitative studies of condensate formation kinetics in the field of LLPS and the data generated in the scope of this master project will be extremely valuable independent of the overall outcome. In addition, you will get the chance to actively shape the future of the lab by implementing a new method which will be used constantly.

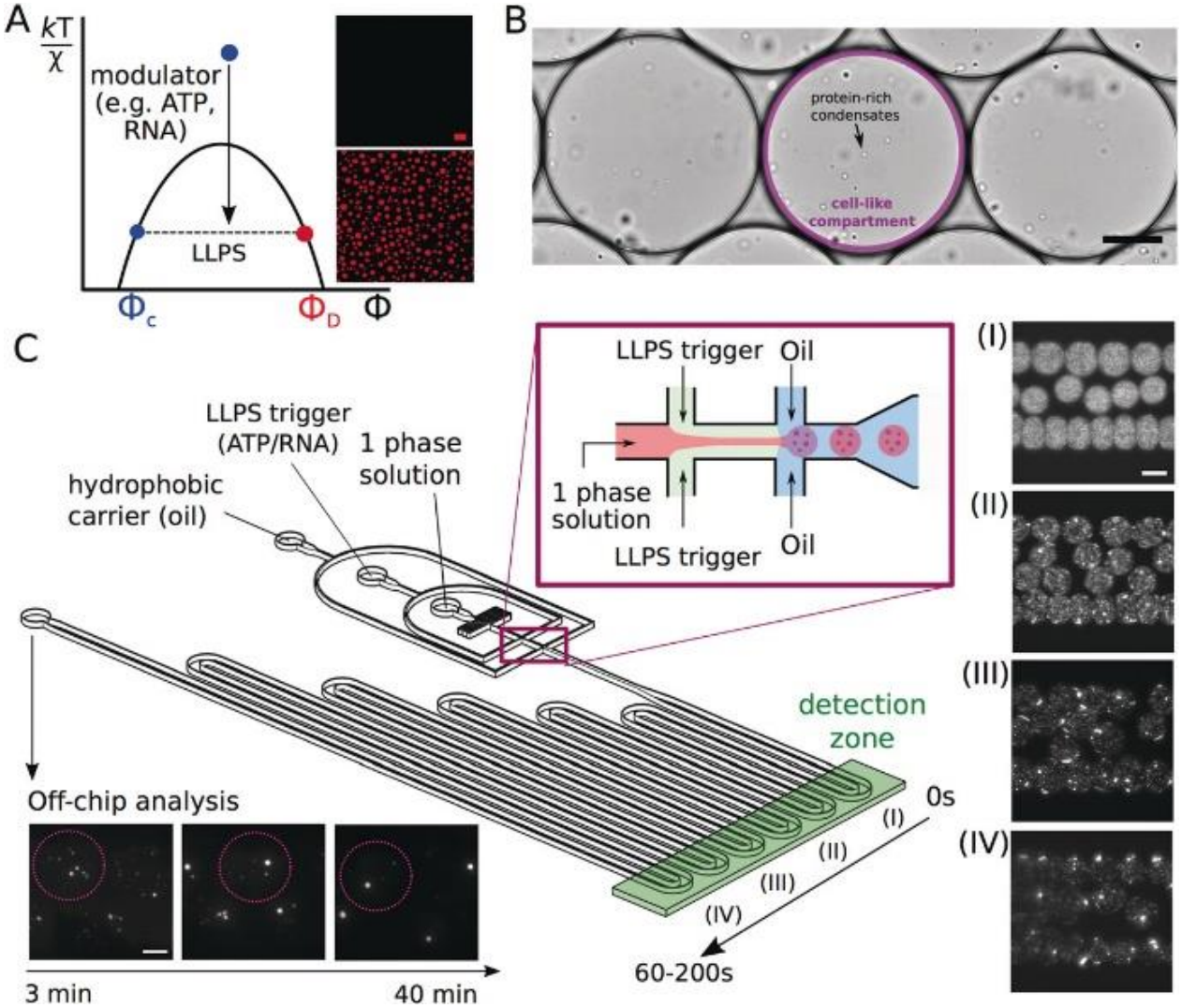

Figure 2: Microfluidics for Analyzing LLPS: The provided microfluidics setup allows to trigger LLPS under precisely controlled conditions and to monitor the formation of the protein droplets in real-time. This approach will provide more reproduceable results and reduce the material needed for an experiment. [3]

What Am I Going to Learn?

In the scope of this project you will learn the basic methods used in a biological 'wet lab' (cloning, SDS Page, Western Blots, PCR,…) and how to express and purify recombinant proteins from bacteria. You will learn the entire workflow of producing and designing your own PDMS microfluidics chips and how to operate the system. You will have daily interactions for advice with a highly experienced PhD student, but you are also encouraged to work independently and to tackle upcoming problems analytically. This solution-oriented approach will prepare you optimally for your future career in scientific research.

Who are you?

We are looking for highly motivated and curiosity-driven master student who finds motivation in challenging tasks. The candidate should have an open personality and be able to work independently. In addition, experience in image analysis and programming is beneficial, but not mandatory. The highly interdisciplinary nature of the project makes Nanoscience student predestinated for this project due to their broad and excellent scientific education in the fields of biology, chemistry & physics.

How to Apply?

If we you are interested in our research and looking for and interesting master thesis don't hesitate to contact us. We are more than happy to show you our lab and answer your questions!!!!

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References

[1] M. Hondele *et al.*, "DEAD-box ATPases are global regulators of phase-separated organelles," *Nature*, vol. 573, no. 7772, Art. no. 7772, Sep. 2019, doi: 10.1038/s41586-019-1502-y.
[2] "phase-separation-cartoon-900x386.png (WEBP Image, 900 × 386 pixels)." https://bioscope.faculty.ucdavis.edu/wp-content/uploads/sites/490/2019/11/phase-separation-cartoon-900x386.png (accessed Oct. 11, 2022).
[3] M. Linsenmeier, M. R. G. Kopp, S. Stavrakis, A. de Mello, and P. Arosio, "Analysis of biomolecular condensates and protein phase separation with microfluidic technology," *Biochim. Biophys. Acta BBA - Mol. Cell Res.*, vol. 1868, no. 1, p. 118823, Jan. 2021, doi: 10.1016/j.bbamcr.2020.118823.