Non-equilibrium statistical mechanics of biomolecular condensates

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(Theoretical & numerical internship, possibly leading to a Ph.D.)

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Lieu du stage: Saclay/Paris
Stage uniquement : OUI
Thèse uniquement: NON
Stage pouvant déboucher sur une thèse : OUI
Financement proposé : OUI (stage)

In a nutshell: Understanding theoretically how surface tension is affected by non-equilibrium processes in biological condensates.
Expected skills: Some knowledge of statistical mechanics.
Techniques used: Analytical and numerical work on minimal models of biological condensates.

Biomolecular condensates are compartments found within cells and enriched in specific types of biomolecules. Many of these are membraneless, as they lack any membrane protecting them from the environment; they are thus believed to form because of liquid-liquid phase separation. A very intense research activity in the biophysics community, both at experimental and theoretical level, is currently investigating the properties of biomolecular condensates, their biological function and their role in diseases [1,2]. Recently, quantitative measurements of the physical properties of biomolecular condensates became possible both in vivo and in vitro, see for example [3,4] for recent works.

Biomolecular condensates are non-equilibrium (otherwise called *active*) systems, in the fact that there is a continuous energy consumption in the cell. While several models have been developed [6], it remains largely open what their minimal description should be. This is partially because most of the quantitative experimental studies on condensates is currently performed in vitro, in setups in which strictly no activity is present. Furthermore, so far, in-vivo observations failed to clearly identify non-equilibrium physics taking place at the scale of the condensate, which instead is predicted by standard models of *active* phase separation [5,6]. As such, it is so far unclear what properties of biomolecular condensates are crucially due to activity.

A likely fingerprint of activity at the scale of the condensate is that it can result – at variance with what happens in equilibrium – in different surface tensions determining different physical processes. This is indeed what we have been showing to happen in other active contexts describing systems of self-propelled particles, where the interfacial tension determining the rate of relaxation of capillary waves does not coincide with the one determining the Laplace pressure [7]. While a biomolecular condensates might show qualitative similar features to phase separating fluids, it is likely that the concept of interfacial tension needs activity to be defined properly. It is also likely that measuring time-correlations and the entropy production in biological condensates will allow to decipher whether activity is relevant at the scale of the condensate.

In this internship we will investigate theoretically how to assess the role of activity in biological condensates. We will work both analytically and numerically on their field-theoretical descriptions. These are extensions of Model B or Cahn-Hilliard model [6] which describes phase separation in equilibrium fluids or the ferromagnetic transition in the Ising model. We will attempt at generalising the concepts of interfacial tension for these theories and corroborate our analytical investigations with numerical analysis. If successful, this work will pave the way to understand how to measure the impact of activity into the macroscopic properties of biological condensates and, as such, might impact both the theoretical and experimental communities working in the field. The project is suitable to be continued in a Ph.D.

[1] AA Hyman et al., Annual review of cell and developmental biology **30**, 39 (2014); [2] Y Shin et al., Science **357** eaaf4382 (2017); [3] DSW Lee et al., Nature Physics **14**, 586 (2023); [4] JO Law et al., **9**, eadg0432 (2023) [5] E. Tjhung et al., PRX, **8**, 031080 (2018); [6] CA Weber et al., Rep. Progr. in Phys. **82**, 064601 (2019); [7] G Fausti et al., PRL **127**, 068001 (2021).