EPSRC Centre for Doctoral Training (CDT) in Molecular Sciences for Medicine (MoSMed)

Multiscale Simulations of Droplet-Membrane Mutual Remodelling

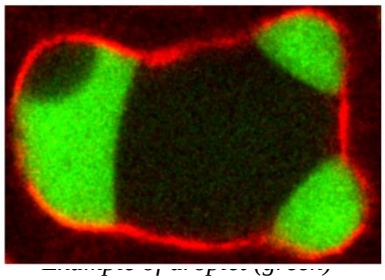
Durham University, Department of Physics

Supervisory Team	• **Prof Halim Kusumaatmaja, Durham University (Lead Academic)** • **Dr Agnieszka Bronowska, Newcastle University** • **Prof Wolfram Antonin, RWTH Aachen University**

Overview

Phase separation is a familiar concept in the physical sciences, ranging from the common observation of water and oil demixing, to its use to create advanced materials for food, energy and photonic applications. In cellular biology, intracellular phase separation has now garnered much attention as a means to organize intracellular solutions through the formation of droplet-like sub-compartments [1]. Examples of such droplet compartments include the stress granules and P-bodies.

Key to this project is the recent recognition that these droplets interact with biological membranes inside cells, and as a result, the droplets and the membranes can mutually remodel their shapes and morphologies [2]. For example, such interplay has been demonstrated during autophagy [3,4]. Here, membrane sheets remodel into double-membrane organelles called autophagosomes, and they can selectively isolate cargoes for elimination, including harmful cytosolic droplets. Excitingly, a growing number of physiological processes can be identified with similar membrane morphologies, suggesting that these droplet-membrane interactions are a general cellular mechanism.



membrane (red) remodelling observed in vivo.

Research Project

The aim of this interdisciplinary PhD project, therefore, is to develop the much-needed understanding of these droplet-membrane interactions, and their mutual remodelling. Here, we will use a multiscale modelling approach. At the molecular level, we will employ molecular dynamics simulations to study the formation of the droplets via a liquid-liquid phase separation mechanism and the affinity between the droplet and membrane. These results will inform a continuum modelling approach based on elasticity theory for studying the droplet and membrane shapes. The theoretical/computational work will also provide an important framework to rationalise and guide ongoing in vitro and in vivo experiments. Our long-term goal is to provide new insights into processes inside cells exploiting this novel physical mechanism based on droplet-membrane interactions.

References

[1] Y. Shin and C. P. Brangwynne, *Science* **357**, eaaf4382 (2017).
[2] H. Kusumaatmaja and R. Lipowsky, *Soft Matter* **7**, 6914 (2011).
[3] Y. Fujioka et al., *Nature* **578**, 301-305 (2020).
[4] J. Agudo-Canalejo et al., *Nature*, 10.1038/s41586-020-2992-3 (2021).

Training & Skills

The student will work at an exciting interface between physics, chemistry and biology, and will be rigorously trained in computational biophysics methods, covering both atomistic molecular dynamics simulations and continuum modelling methods. The student will have access to High Performance Computing facilities at Durham and Newcastle.

The student will also collaborate and interact actively with the experimental partners in Germany. Furthermore, to achieve our long-term strategic vision, our groups have developed a broad network of collaborators in Japan, Norway, Germany, France, UK and USA. The student will have access to this network.

Further Information

The start date for this project is October 2021 as part of Cohort 3 of EPSRC Centre for Doctoral Training (CDT) in Molecular Sciences for Medicine (MoSMed). Applicants should have an excellent first degree with relevant experience or a Master's degree in physics, mathematics, chemistry, engineering or another related subject.

Please note that due to pre-existing funding commitments associated with this project application is open to UK students only.

Informal enquiries are welcome and should be addressed to Prof. Halim Kusumaatmaja (halim.kusumaatmaja@durham.ac.uk).

Further details about MoSMed CDT can be found at https://research.ncl.ac.uk/mosmed and about Prof Kusumaatmaja's group at https://sites.google.com/site/kusumaatmaja.

How to Apply

To apply for this project please visit the Durham University application portal to be found at: https://www.dur.ac.uk/study/pg/apply/**.** Please select the course code F1A201 for a PhD in Molecular Sciences for Medicine and indicate the reference MoSMed 21_14 in the 'Field of Study' section of the application form. Should you have any queries regarding the application process at Durham University please contact the Durham MoSMed CDT Manager, Emma Worden at: emma.worden@durham.ac.uk.

Please note that the deadline to apply for this project is **Monday 29th March 2021 at 5pm GMT.**

Newcastle University Durham University UKRI Engineering and Physical Sciences Research Council