**Governing Principles of Condensate-Membrane Interactions in Biological Cells**
**Supervisors:** Dr Mark Miller (DU Chemistry) and Prof Halim Kusumaatmaja (DU Physics)

The emerging role of biomolecular condensates formed through a liquid-liquid phase separation process inside biological cells is driving a paradigm change in our understanding of cellular organisation. They are critical for development and function, and their dysregulation plays a critical role in ageing and disease. Several groups, including us and our collaborators, have further recognised that these biomolecular condensates can interact with other cellular components, including lipid membranes. Fig. 1 illustrates several key functional examples of condensate-membrane interactions [1], such as for the formation of protein storage vacuoles in Arabidopsis plant (panel a), and for the degradation of harmful cytosolic cargoes during a process called autophagy (panel b). Our overall aim in this project is to identify and develop governing principles of condensate-membrane interactions inside biological cells, which we broadly term as intracellular wetting.

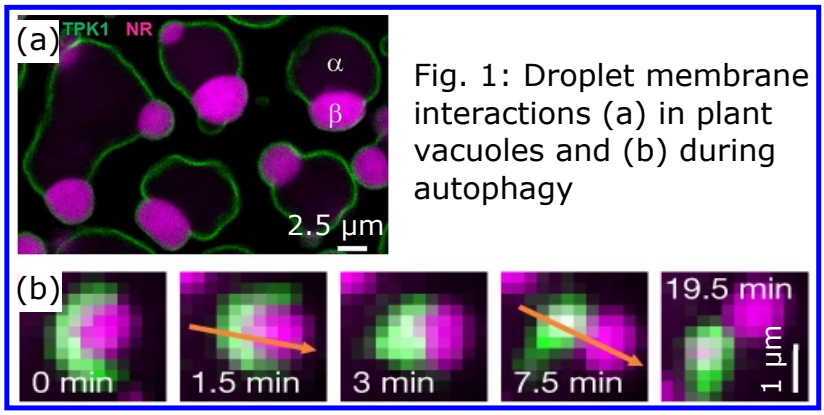

Fig. 1: Droplet membrane interactions (a) in plant vacuoles and (b) during autophagy

Key concepts we will address in this project may include:

1. **Phase separation and nucleation under soft confinement:** We will investigate how these processes can be enhanced or inhibited due to confinement by lipid membranes.
2. **Capillary adhesion between membranes:** Such capillary forces may provide a novel non-specific and reversible adhesion mechanism between closely apposing membranes.
3. **Membrane mediated interactions:** Membrane deformations can provide long-range elastic interactions that influence how the condensates coalesce.

The PhD student will use a multiscale modelling approach, taking advantage of recent advances in coarse-grained molecular dynamics [2] and continuum approaches (analytical calculations [3] and lattice Boltzmann [4]) developed by Dr Miller and Prof Kusumaatmaja. They will also benefit from close interactions with several experimental collaborators.

**References:**

[1] Kusumaatmaja et al., J. Cell Biol. 220, e202103175, 2021
[2] Potter et al., JCTC 17, 5777, 2021
[3] Kusumaatmaja et al., PNAS 118, e2024109118, 2021
[4] Pepona et al., PRE 103, 022112, 2021