SEMINARIO
DEPARTAMENTO DE QUÍMICA FÍSICA

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Sala de Grados de la Biblioteca

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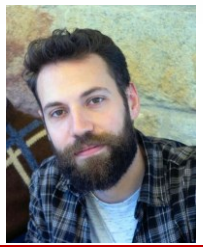
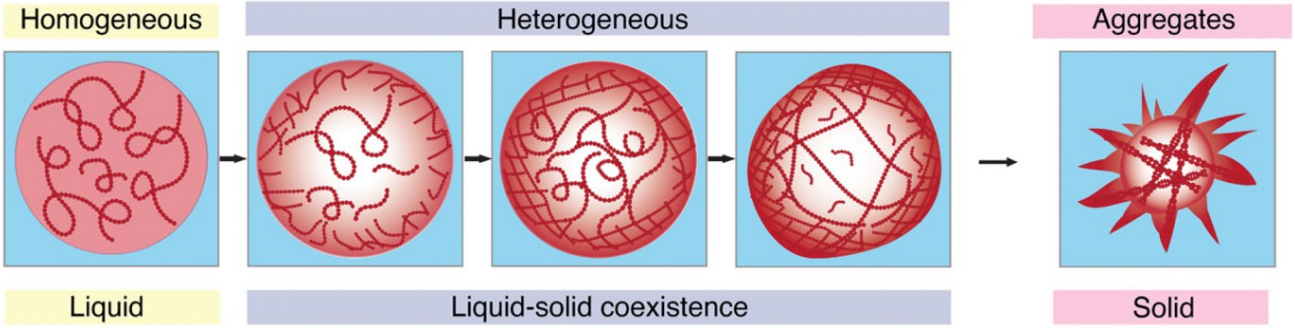


Organelles *sans frontières*: A new phase in cell biology

The eukaryotic cell consists of an organized collection of billions of biomolecules exquisitely coordinated to carry out biological function. Compartmentalization represents a key feature in such coordination and enables the spatiotemporal organization of the cell material. Over the past decade, transformative experiments have revealed that most intracellular compartments are, surprisingly, not enclosed by membranes [1]. Instead, membraneless assemblies, known as biomolecular condensates, are formed via liquid-liquid phase separation and execute a myriad of biological functions including control of biochemical reactions, gene regulation, or cell signalling, among many others [2,3]. Nevertheless, a potential risk underlying these functions is the strengthening of intermolecular interactions achieved by locally concentrating biomolecules to high levels. Accumulating evidence points to condensate misregulation as a major source of irreversible biomolecule aggregation and formation of pathological solid-like assemblies associated to multiple neurodegenerative and age-related disorders [4]. In this talk, we will explore how the main biomolecular building blocks forming intracellular condensates–i.e., proteins and nucleic acids–can give rise to multi-component assemblies with varying surface tensions, viscosities, and internal molecular architectures, which over time, can (or not) drift their material properties into aberrant solid aggregates. To this end, we shall make use of a multiscale modelling approach combining coarse-grained potentials, residue-resolution sequence-dependent models, and all-atom simulations [5-7]. Uncovering the mechanistic and molecular pathway underlying liquid-to-solid transitions of functional condensates into pathological aggregates (see Fig.) is one of the first steps required for guiding the prediction, rationalization, and eventually modulation of protein/RNA solidification within biomolecular organelles.



Liquid to solid transition pathway of FUS protein condensates through β-sheet fibrillation [5].

[1] C. P. Brangwynne, *et al*, *Science*, vol. 324, no. 5935, pp. 1729, 2009.
[2] S. Alberti, A. Gladfelter, and T. Mittag, *Cell*, vol. 176, no. 3, pp. 419, 2019.
[3] A. G. Larson, *et al*, *Nature*, vol. 547, pp. 236, 7 2017.
[4] S. Alberti and A. A. Hyman, *Nature Reviews Molecular Cell Biology*, vol. 22, no. 3, pp. 196, 2021.
[5] A. Garaizar, *et al*, *Proceedings of the National Academy of Sciences*, vol. 119, no. 26, p. e2119800119, 2022.
[6] A. R. Tejedor, *et al*, *Nature Communications*, vol. 13, no. 5717, pp. 1–15, 2022.
[7] S. Blazquez, *et al*, *Advanced Science*, vol. 10, p. 2207742, 2023.