NORTHWESTERN UNIVERSITY'S DEPARTMENT OF MATERIALS SCIENCE AND ENGINEERING PRESENTS:

2021 MSE SPRING SEMINAR SERIES

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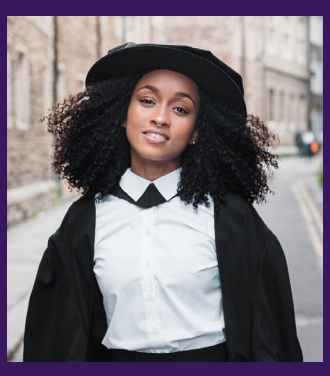

Jerelle A Joseph is an independent Research Fellow in Physical and Chemical Sciences at King's College, Cambridge, and collaborates closely with the groups of Dr Rosana Collepardo, Prof. Tuomas Knowles, and Prof. Daan Frenkel, at the University of Cambridge. Her research encompasses developing multiscale approaches to study how cells organise their contents via liquid–liquid phase separation. She has published over 18 peer-reviewed articles and one book chapter in the fields of chemical physics and biophysics. Jerelle has over 10 years of teaching experience. Jerelle holds a PhD in Chemistry from the University of Cambridge. For her PhD work, under the supervision of Prof David Wales FRS and as a Gates Cambridge Scholar, Jerelle developed computational methods to study large-scale structural changes in proteins. Originally from the Caribbean, Jerelle is an avid advocate for Caribbean-based mentorship and is actively involved in efforts aimed at alleviating underrepresentation of Black Scientists in academia. In 2017, she founded CariScholar; an organisation that connects Caribbean students to established professionals and academics in their field of study.

Robust multiscale modelling toolkits for probing cellular compartmentalization via liquid–liquid phase separation

When we consider intracellular organisation, we often picture different regions of the cell forming tiny membrane-bound compartments, like ribosomes and mitochondria. However, there are several important micro-environments inside the cell that are not enclosed by membranes. For decades, scientists have wondered how do these "membrane-less" organelles arise, and how are their structures maintained without physical membranes? Over the last two decades, ground-breaking experiments have proposed the transformative paradigm of liquid-liquid phase separation (LLPS), which suggests that the physical chemistry of phase separation of multicomponent mixtures sustains such micro-environments: Analogous to the separation of oil and water into distinct liquid phases, macromolecules in the cytoplasm and nucleoplasm exhibit weak attractive interactions with each other that drive them to condense and then undergo LLPS, forming "oil-like droplets" inside cells (formally termed biomolecular condensates). The formation of biomolecular condensates via LLPS provides a mechanism for spatiotemporal control of vital cellular processes, including RNA processing and stress signalling. Furthermore, aberrant LLPS has been implicated in several age-related disorders. Hence, elucidating the precise molecular interactions that sustain LLPS, as well as the physical determinants governing the composition, structural, and kinetic properties of biomolecular condensates, is attracting significant attention. Resolving the behaviour of biomolecules inside liquid droplets and describing the phenomenon leading to their condensation is challenging, both experimentally and computationally. Impressive advances in experimental techniques, particularly microfluidic analysis methods and single-molecule fluorescence microscopy, hold great potential for characterising biomolecular condensates and visualising molecules within liquid droplets. The availability of such techniques necessitates the development of computational models to determine the underlying physical mechanisms leading to the observed structural and dynamical features. From a modelling point of view, the computational costs of simulating large numbers of biomolecules for the long timescales involved in LLPS would be prohibitively expensive. In this talk, I will discuss the development of robust multiscale modelling strategies for probing biomolecular LLPS. This discussion includes: the design of minimal coarse-grained models that allow for simulating thousands of interacting biomolecules in an efficient manner, and delineating physical parameters that dictate stability and composition of condensates (1,2); the use of use of atomistic calculations and residue-level coarse-grained simulations to shed light on the molecular grammar and mechanisms underlying LLPS (3,4); the development of an innovative multiscale strategy that extracts atomistic condensates from pre-equilibrated coarse-grained ones and can be used to rationalize trends in stability against fusion of condensates (5). Finally, I will propose how such multiscale toolkits can be used for rational design of novel LLPS systems.

References:
(1) Joseph*, Espinosa*, Sanchez-Burgos, Garaizar, Frenkel, Collepardo-Guevara. Biophys. J (2021).
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J A Joseph, Computational Chemist/Biophysicist, University of Cambridge
(3) Krainer*, Welsh*, Joseph*, Espinosa, de Csilléry, Wittmann, Sridhar, Toprakcioglu, Gudiškytė, Czekalska, Arter, Guillén-Boixet, Franzmann, Qamar, St George-Hyslop, Hyman, Collepardo-Guevara, Alberti, Knowles. Nat. Commun. (2021).
(4) Farr, Woods, Joseph, Garaizar, Collepardo-Guevara. Nat. Commun. (2021, in press; preprint).
(5) Welsh*, Krainer*, Espinosa*, Joseph, Sridhar, Jahnel, Arter, Saar, Alberti, Collepardo-Guevara, Knowles. bioRxiv (2020).

Monday, May 17 • 4 PM CDT • Zoom

Registration is required. RSVP link.

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