Department of Physics Colloquium:

Physics of Protein Evolutionary Switches and Phase Separation in Membraneless Organelles

Hue Sun Chan
Biochemistry, University of Toronto

Host: Paul Whitford

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How might new protein folds evolve without detrimental effects on the biological function performed by the original structural fold? Recent studies indicate that selection of latent traits can be an efficient route to new function, and that the "adaptive conflict" between the old fold and the new fold can be resolved by gene duplication [1]. Intense research in the past 1.5 decades has also demonstrated that not all proteins function as folded structures. Intrinsically disordered proteins (IDPs) perform critical functions, especially for the regulation of cellular processes in higher organisms [2]. Remarkably, some IDPs function not only as individual molecules, but also collectively by undergoing liquid-liquid phase separation in the living cell. The resulting high-IDP phase forms a major component of membraneless organelles that, by creating their own IDP-rich compartments, stimulate critical biological functions [3]. To gain physical insight into these fascinating phenomena of Life, I will discuss our recent advances in using simple computational models and analytical theory to elucidate how new protein folds might have arisen in evolution [1,4] and how biologically functional phase separation of IDPs is governed by their genetically coded amino acid sequences [5].

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References:

[1] Sikosek & Chan (2014) *J Royal Soc Interface* **11:**20140419

[2] Chen, Song & Chan (2015) *Curr Opin Struct Biol* **30:**32

[3] Brangwynne, Tompa & Pappu (2015) *Nature Physics* **11:**899

[4] Sikosek, Krobath & Chan (2016) *PLoS Comput Biol* **12(6):**e1004960

[5] Lin, Forman-Kay & Chan (2016) *Phys Rev Lett* **117:**178101