O-11.3 Short talk

Multi-component phase separation of postsynaptic density is controlled by membrane geometry via valency and volume effects

Risa Yamada [1], Giovanni Brandani [1], Shoji Takada [1]

[1] Kyoto University, Kyoto, Japan

Biomolecular condensates across cellular compartments form multi-component structures with distinct phase morphologies, such as core-shell droplets, implicating their functional roles. Their organization depends on competitive molecular interactions and location. Recent studies revealed an intriguing reversal in postsynaptic density component morphology between solubilized construct and sub-membrane system. We investigated this puzzling phenomenon by examining condensate behaviour in both solution (3D) and beneath the membrane (2D). Our mesoscale molecular simulations reproduced the core-shell structure in solution with AMPAR/PSD-95 forming the core and NMDAR/CaMKII forming the shell after CaMKII activation, while showing reversed arrangement on the membrane. This reversal stems from competitive properties of CaMKII: high valency and large volume. We found environment-dependent interaction behaviour: in solution, its non-specific volume interactions predominate, while on membranes, specific multivalent interactions overcome the volume repulsion. The layered membrane arrangement diminishes volume effects of CaMKII on receptors, allowing multivalent interactions to predominate. These findings highlight fundamental differences between condensates in solution and those on membrane, influenced by their spatially layered organization.