

I find it exciting that we are discovering biomolecular condensates have complex properties. An increasing number of condensates are reported to be multiple components or organized into sub-compartments. While some condensates are formed via liquid-liquid phase separation, others seem not. Classic liquid-like condensates are found to be more than simple liquids: nucleoli are viscoelastic, and surface fluctuation of stress granules cannot be explained by surface tension only. With emerging tools to characterize condensates in cells, e.g., super-resolution microscopy for substructures, proximity labeling for composition, and quantitative approaches for material properties, I think more complexity in condensate properties will be revealed. Such complexity will promote the development of new physical models to understand how condensate properties arise from complicated interactions that do not exist for non-biological molecules.

Equally exciting is that causal relations between phase separation and cellular functions start to emerge, mainly using mutations that disrupt phase separation. However, it is often challenging to differentiate phase separation from other functions that can arise from the same interactions. An alternative approach is using chemical or optogenetic tools to control phase separation and compare functional differences between the condensed and non-condensed states. For example, the ability of condensates to restructure chromatin and promote enzymatic reaction has been elegantly demonstrated with inducible condensates by Clifford Brangwynne's lab and Michael Rosen's lab, respectively. This approach can also be used to mimic ectopic condensates that occur in diseased cells to study their assembly and function. For example, we used chemical inducers of protein phase separation to create aberrant PML body formation on telomeres in telomerase-free cancer cells and demonstrate its role in telomere clustering for homology-directed telomere DNA synthesis. I envision more sophisticated condensates with controlled chemical, structural, and material properties will be engineered to help reveal how property complexity arises from and contributes to cellular functions. Designer condensates can also be used as synthetic tools to manipulate cellular processes, as shown in cell proliferation and division control via the sequestration of endogenous proteins by Matthew Good's lab. I look forward to seeing novel applications emerge in the coming years as we learn more about condensates' diverse properties and functions.