Research on drug targeting of the early processes of bimolecular condensate formation

Understanding dynamic liquid-liquid phase separation (LLPS) processes by observing the formation and size distribution of the proteins as they change over time.

Challenge

Distortions of biomolecular condensates are hallmarks of a plethora of age-related diseases, such as cancers and neurodegenerative diseases. Prof. Tobias Madl investigates the (dys)regulation and drug targeting of the early processes of condensate formation, when condensates are small. He used BRAVE B-Curious to study the size and dynamics of biomolecular condensates.
His challenges were:

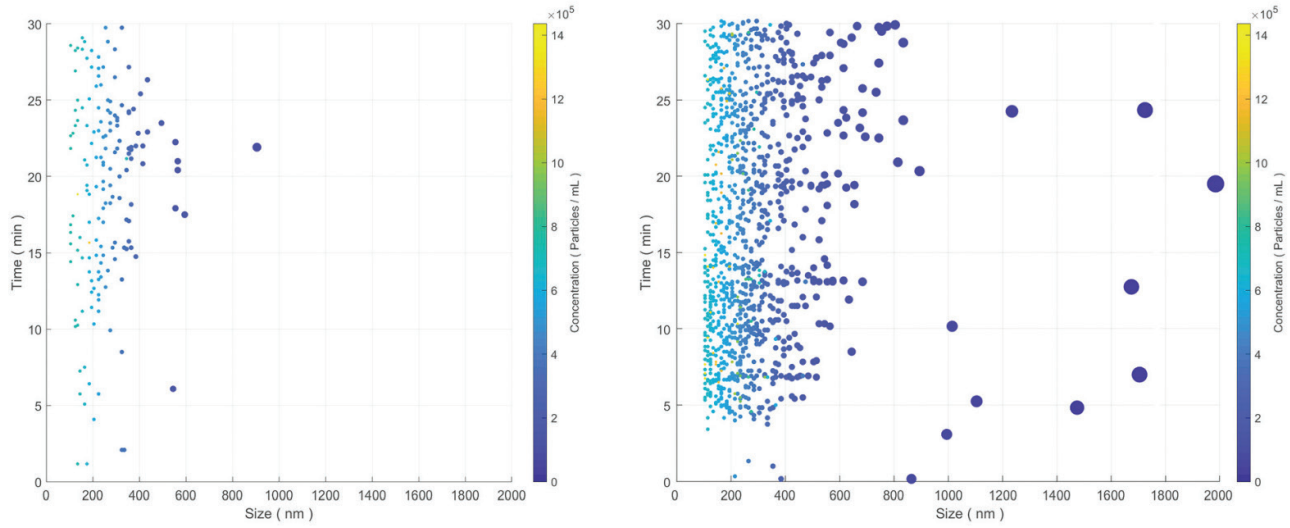
- Other methods did not allow live/time-resolved measurements to monitor changes of molecular condensates and PSD as they happen.
- Only small sample amounts are available (patient samples); high protein and RNA concentrations are required to obtain results.
- Particle size is very small; size distribution range is wide.
- Microscopy does not resolve the formation processes in the early stages when condensates start to form and proteins start to interact with RNA.

Application highlights

Prof. Madl carried out time-resolved measurements on different concentrations of proteins and RNA. The measuring results clearly showed the kinetics of LLPS processes and allowed comparison of the formation of particles in the presence of different RNA concentrations.

Benefits of OF2i:

- Visualizing the formation and size distribution of proteins as they change over time in one seamless and complete measurement.
- Results with single-particle sensitivity, even for condensate particles in the size range 10 nm to 2000 nm.
- Measurements on low-volume samples of 80 µL to 100 µL and at concentrations relevant for drug discovery.



Time-resolved PSD: Particle formation processes during liquid-liquid phase separation (LLPS) with low (left) and high (right) RNA concentrations over 30 minutes. © BRAVE Analytics & Marko Šimić