ID de Contribution: **19** Type: **Non spécifié**

Poster : Mechanism of bacterial DNA segregation: LLPS behavior, beyond trend and reality.

In bacteria, low-copy-number replicons carry self-specific partition systems to ensure their faithful segregation. Among these systems, ParABS partition systems, consisting of a Walker-type ATPase (ParA) and a DNA-binding protein (ParB) along with parS centromere sites, are the most prevalent on plasmids and the only one present on chromosomes. ParB proteins, recently shown to belong to a novel class of CTP-dependent molecular switches, self-assemble into partition complexes nucleated from parS sites, with over 90% of intracellular ParB concentrated within these clusters. It has been proposed that partition complexes behave as bio-molecular condensates through liquid-liquid phase separation (LLPS). This physical principle describes the behavior of biomolecules in solution that auto-assemble in condensates, with general properties such as a spherical shape, a different mobility of molecules inside and outside the droplet and the ability of the droplets to fuse.

To elucidate the assembly dynamics of partition complexes/condensates, we investigated the fusion behavior of ParB condensates in vivo. Such fusion behavior is hindered by the intrinsic function of partition, through ParA ATPases, which separate and localize ParB condensates. To observe ParB condensates fusion, we disrupted ParA activity by removing the matrix over which ParA is mediating their anchoring, i.e. the nucleoid. We developed an inducible, chromosome specific DNA degradation system that occurs rapidly. We showed that in absence of nucleoid, ParB condensates still form on plasmids carrying parS centromere sites, and rapidly fuse, irrespective of the initial number of complexes present in cells. In addition, we found that fusion strictly depends on ParB proteins and conservatively clusters all ParB proteins in a single condensate per cell. Moreover, we have shown that hexanediol, a disruptor of weak hydrophobic protein–protein interactions, rapidly induces the disassembly of ParB condensates within tens of seconds. This effect is reversible. It thus indicates that weak ParB-ParB interactions are central to the assembly of ParB condensates.

Lastly, we further characterized the fusion/fission dynamics of some condensates and found that fusions occur within seconds, independently of the presence of ParA. These rapid dynamics reinforce the notion that the assembly of partition complexes is mediated by LLPS. Our results underscore the critical role of ParA activity in counteracting the intrinsic merging properties of the LLPS-driven ParB condensates.

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