

Molecular engineering of polymersomes: design principles and applications

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Among the different biomimetic efforts, we have focussed our attention in possibly one of the few that encompasses polymerisation, compartmentalisation and positional self-assembly in the same unit; Polymersomes. These are vesicles formed by the self-assembly of amphiphilic block copolymers in water. Copolymers can be fully synthetic and/or derived from biomolecules and their sequence can be engineered to control both interactions with water and among each other. In analogy to natural vesicles (typically formed by phospholipids), polymersomes can house controlled aqueous volumes to create chemical potentials across the membranes. However, the macromolecular nature of the polymersome building blocks allows the design of vesicle membranes with control over their thickness, brush density, mechanical properties, and permeability. Furthermore, copolymers can be designed with tunable solubility, and hence, polymersomes can be made responsive to a large plethora of environmental stimuli such as pH, ionic strength, enzymatic degradation, hydrolysis, light, temperature, and many others.

We can summarise this into three steps process, at the molecular level (0.1-1nm) we can select appropriate molecules and use them as monomers for controlled polymerisation to form macromolecules with defined chemical signature to control supramolecular interactions (Macromolecular Engineering). These are then used to control the formation of larger structures (1-100nm) via a two-step processes (nucleation + growth) whose final topology is defined by the combination of the different supramolecular forces (Supramolecular Engineering). Polymersomes can be formed using either bottom-up or top-down approaches. The former involves a total solubilisation of the membrane-forming copolymers typically using organic solvents or exploiting pH, temperature or other stimuli that control the copolymer solubility. Once dissolved, the solution conditions are changed (e.g. solvent exchange of environmental changes) so to makes the copolymer amphiphilic and hence triggering the self-assembling. Polymersomes requires a minimum radius to be stable and hence a number of aggregates in order of thousands. This means that at the early stages of self-assembly, membrane forming copolymers nucleate into frustrated micelles and they further grow into enclosed vesicles. Similarly, as we hydrate a given amphiphilic copolymers, its internal structure evolve according to the different phase diagram discussed above and the final size and shape of the vesicles is given by the kinetics of hydration. We have been studying these kinetic for several years and learned how to control both bottom-up or top-down approaches to engineering the polymersome shape topology as showed in the Figure above. On a different level of complexity, we can also engineer the polymersome surface topology by combining different polymersome-forming copolymers and, in doing so, tuning the interaction between them. The resulting structures can be as simple as phase-separated bimodal or spinodal domains or more complex super-symmetric arrangements. Similarly, the same approach can be used to control the polymersome topography mixing different size copolymers and controlling line tension. Finally, the asymmetry of the polymersome can be further controlled pushing the phase separations to full coarsening (see the structure showed in Figure above).

References

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