Theoretical design of drug carrying block copolymer micelles

One of the challenges of next generation drugs is the design of target-specific delivery of pharmaceutical agents to the cancerous tumors or diseased cells. Polymer micelles and hydrogels have been traditional candidates for drug-delivery purposes. Poorly soluble therapeutic molecules are encapsulated within the hydrophobic cores while the hydrophilic segments provide solubility and efficient delivery. Diffusive nature of the drug release, from the three-dimensional structure of hydrogels, provides controlled release of the therapeutic agents. On-site drug delivery and release require utilization of stimuli-responsive polymer micelles and hydrogels. Human body can experience significant changes of pH, which can be used to direct therapeutic agents to a specific body area. pH-sensitive polymer carriers require to embody charged moieties within their chemical structure. In this study, we carry out the theoretical design of hydrophobic-capped triblock polymers solutions with intrinsic pH-sensitive behaviour and switchable micelle-hydrogel properties. We use molecular dynamics (MD) method in which the interactions of involved species are treated according to Newton’s equation of motion.

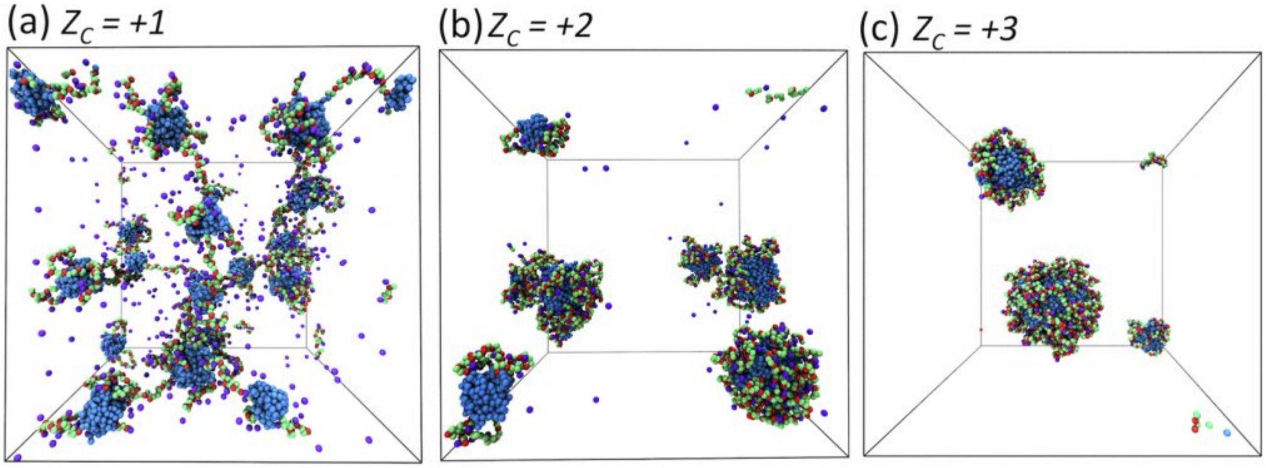

Fig. 1. Simulation snapshots showing the copolymer micellar solution at different counterion valences.

We have employed coarse-grained description of the copolymer chains in which the fine chemical details are dumped into a group of interaction beads. Our main goal is to capture the effects of midblock charge fraction (resembling the pH-sensitivity), valency of the neutralizing counterions, and rigidity of hydrophobic endblocks on the self-organization of the copolymer solutions. Interconnected network of hydrophobic aggregates cross-linked by stretched midblock chains are captured through gradual increase in the charge content of midblock chains. In the case of introducing multivalent counterions (Fig. 1) we can see the collapse of interconnected hydrogel into bulky spherical aggregates. More stiff endblocks yield a hydrogel network with bundle-like motifs. Outcomes can be rationalized as invoking the fine interplay of the minimization of the surface energy of hydrophobic chains, configurational entropy of the midblocks, and the translational entropy of mobile counterions.

The discussed results can shed light on the fundamental association mechanisms of these stimuli-responsive micelles/hydrogels that are otherwise challenging to capture experimentally. Understandings at this level are vital for the design of novel smart copolymers with tailor-made properties.

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