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Core–shell–corona macromolecular architectures *via* electrostatic co-assembly

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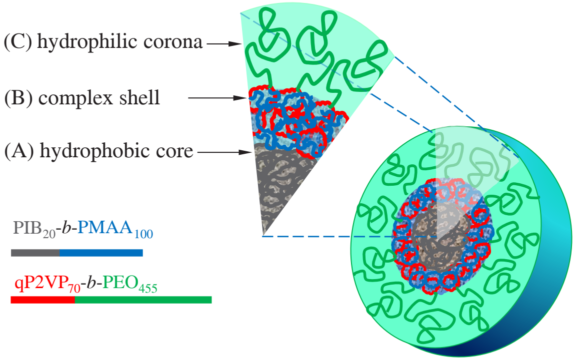
Water-soluble macromolecular complexes are prepared *via* electrostatic co-assembly of a micelle-forming (non-ionic hydrophobic/ionic) diblock copolymer, polyisobutylene-*block*-poly(sodium methacrylate), with a double hydrophilic (ionic/non-ionic hydrophilic) diblock copolymer, exhaustively quaternized poly(2-vinylpyridine)-*block*-poly(ethylene oxide), taken at the equimolar (1 : 1) ratio of their ionic groups. The original micelles appear to act as templates, leading to compartmentalized (core–shell–corona) nanosized macromolecular architectures with a hydrophobic polyisobutylene core, an interpolyelectrolyte complex polymethacylate/poly(2-vinylpyridinium) shell, and a hydrophilic poly(ethylene oxide) corona.



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Interpolyelectrolyte complexes (IPECs), which are also referred to in the literature as polyion (polycation–polyanion) complexes or complex coacervates, are formed when oppositely charged macromolecules interact with each other in a cooperative manner.[1–9] It is generally accepted that the formation of such co-assembled architectures is mainly driven by the entropic gain due to a favorable release of small counterions that were previously associated with the interacting components, although some enthalpic contributions might also play a role.[10]

Advantageous and sometimes even unique properties of IPECs make them attractive and promising for many important applications, *e.g.*, drug delivery,[11] non-viral gene transfection,[11,12] surface modification and flocculation,[13,14] *etc*. It is worth noting that application potential of the co-assembled species is ever-increasing along with enhancing the structural diversity and functionalities of their components, which have become available over last decades due to considerable progress achieved in controlled polymerization techniques.

So far, a vast number of publications are related to IPECs based on oppositely charged linear polyions, although non-linear polyionic species are currently also in focus of close attention as inherently structured components, which can be used to obtain complex products with a higher level of structural organization. In this context, the co-assembled architectures based on ionic dendrimers, polyelectrolyte stars, and molecular polyelectrolyte brushes, which nowadays become in-demand for rapidly developing nanotechnologies, are to be mentioned.[15]

Importantly, IPECs based on oppositely charged homopolyelectrolytes become insoluble and lose their solubility (or colloidal stability) in aqueous media when the charge of a ‘host’ component is sufficiently compensated by a ‘guest’ one.[1,3] This limits the application potential of such co-assembled species, *e.g.*, as nanocontainers or nanoreactors. At the same time, macroscopic phase separation in such polycation–polyanion systems can be avoided even at full charge compensation if double hydrophilic (ionic/non-ionic hydrophilic) diblock copolymers, which comprise a polyelectrolyte block and a hydrophilic but non-ionic block, are used instead of homopolyelectrolytes.[2,6]

Self-assembled architectures such as polymeric micelles, which possess a core–corona structure with a non-polar core and a polyelectrolyte corona, can also be considered as polyionic species of non-linear (*e.g.*, star-like) topology. Their electrostatic co-assembly with double hydrophilic diblock copolymers is of interest in the context of preparation of novel multi-compartment architectures, wherein considerable (or even full) charge compensation of the polyelectrolyte corona can be achieved without loss of solubility (or colloidal stability) of the formed IPECs.

Despite the formation and some properties of such co-assembled species have been described elsewhere,[16,17] there is certain lack of their structural characterization. In this context, we have examined for the first time the electrostatic interaction of the anionic star-like micelles of a polyisobutylene-*block*-poly(methacrylic acid) (PIB-*b*-PMAA) diblock copolymer with a cationic exhaustively quaternized poly(2-vinylpyridine)-*block*-poly(ethylene oxide) (qP2VP-*b*-PEO) diblock copolymer, and highlight herein the formation of compartmentalized (core–shell–corona or onion-like) IPECs, wherein the parent PIB-*b*-PMAA micelles act as templates.

The diblock copolymer PIB-*b*-PMAA with the number-average degrees of polymerization of the polysiobutylene (PIB) and the poly(methacrylic acid) (PMAA) blocks of $DP_n^{PIB} = 20$ and $DP_n^{PMAA} = 100$, respectively, and a polydispersity index of 1.16 was used. Being dissolved in alkaline solutions, it formed well-defined star-like micelles, each having a small (a few nm in radius) non-polar (PIB) core and a considerably (by a factor of ~5–6) larger polyelectrolyte (PMAA) corona.[18]

The diblock copolymer qP2VP-*b*-PEO with the number-average degrees of polymerization of the exhaustively quaternized poly(2-vinylpyridine) (qP2VP) and the poly(ethylene oxide) (PEO) blocks of $DP_n^{qP2VP} = 70$ and $DP_n^{PEO} = 455$, respectively, and a polydispersity index of 1.03 was taken as a cationic component. Being a double hydrophilic, it exists in aqueous solutions in the molecularly dispersed state, that is, as individual cationic macromolecules.

Importantly, qP2VP-*b*-PEO, which apart from a cationic (qP2VP) block also contains a non-ionic hydrophilic (PEO) block, prevents macroscopic phase separation of its aqueous mixtures with the PIB-*b*-PMAA micelles even at the equimolar (1 : 1) ratio Z of their ionic groups, $Z = [N^+]/[(COO^- + COOH)]$, (Figure S1, see Online Supplementary Materials). This behavior is in drastic contrast to the interaction of linear cationic homopolyelectrolytes, *e.g.*, exhaustively quaternized poly(vinylpyridine)s with the same micelles, wherein the macroscopic phase separation is observed when Z exceeds a certain threshold value[19] (see Figure S1 in Online Supplementary Materials). It is worth mentioning that the absence of the macroscopic phase separation has been already reported for other systems containing double hydrophilic diblock copolymers as one or both components,[20–23] being attributed to stabilization of the co-assembled species by non-ionic hydrophilic blocks of the copolymers.

The formation of an IPEC in the aqueous mixtures of the PIB-*b*-PMAA micelles and qP2VP-*b*-PEO can be followed by means of analytical ultracentrifugation, wherein sedimentation of cationic macromolecules can be detected in the scanning mode at $\lambda = 280$ nm. At this wavelength, qP2VP-*b*-PEO efficiently absorbs light due to the presence of chromophoric pyridinium groups in each monomer unit of the cationic block, while the PIB-*b*-PMAA micelles demonstrate only weak light scattering. Figure 1 presents a typical sedimentation pattern (curve *1*) for the aqueous mixture of PIB-*b*-PMAA micelles and qP2VP-*b*-PEO ($Z = 1$) at pH 7 when the components are oppositely charged. As is seen, only one type of the species is detected, and their sedimentation velocity is pronouncedly higher than that of the individual cationic macromolecules (curve *2*) under the same conditions. This finding demonstrates that qP2VP-*b*-PEO quantitatively binds to PIB-*b*-PMAA micelles. In other words, no free cationic macromolecules are present in the system and qP2VP-*b*-PEO sediments as a component of the co-assembled species.

The hydrodynamic and molecular weight characteristics of the IPECs formed in the aqueous mixtures of the PIB-*b*-PMAA micelles and qP2VP-*b*-PEO at $Z = 1$ were obtained by means of dynamic and static light scattering. As is seen, the hydrodynamic size distribution of the scattering species is in the nanometer range and appears to be essentially monomodal (Figure 2). Their apparent mean hydrodynamic radius R_h (obtained *via* CONTIN analysis) and weight-average molecular mass M_w are expectedly larger (by a factor of ~1.4 and ~5, respectively) than those measured for the original PIB-*b*-PMAA micelles under the same conditions (Table 1). These findings indicate the binding of qP2VP-*b*-PEO by PIB-*b*-PMAA micelles (this process is naturally accompanied by the increase in their mass and size) and therefore are in line with the results obtained for this system by means of analytical ultracentrifugation (Figure 1).

Importantly, the aggregation number N_{agg} of PIB-*b*-PMAA micelles does not change when they bind qP2VP-*b*-PEO (Table 1), although these self-assemblies are dynamic as we have reported previously.[24] In other words, the PIB-*b*-PMAA micelles act as templates for the formation of IPECs, which was also observed upon their interaction with linear cationic homopolyelectrolytes such as exhaustively quaternized poly(vinylpyridine)s.[18] In this aspect, the PIB-*b*-PMAA micelles despite being star-like behave differently from the star-shaped polyelectrolytes [*e.g.*, poly(acrylic acid) stars], which were typically shown to yield multi-star rather than mono-star co-assembled species when they bind the same qP2VP-*b*-PEO.[25,26]

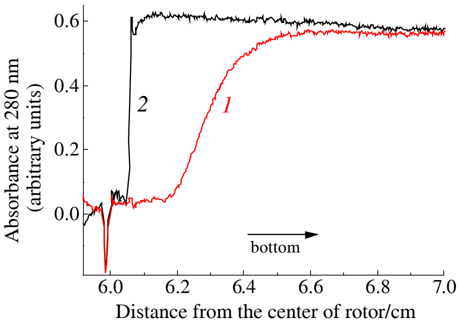

Figure 1 Sedimentation patterns obtained for (*1*) the aqueous mixture of PIB-*b*-PMAA micelles and qP2VP-*b*-PEO at $Z = 1$ (red) and (*2*) the aqueous solution of qP2VP-*b*-PEO (black). Conditions: 0.1 M NaCl, pH 7 (0.01 M Tris/Tris·HCl), 25 °C. The speed and time of rotor rotation were 20 000 rpm and 32 min, respectively.

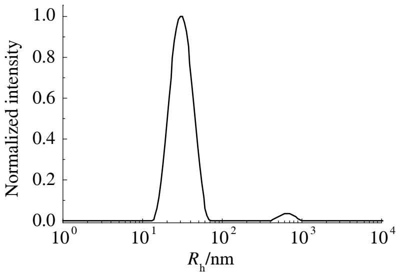

Figure 2 Intensity distribution (obtained *via* CONTIN analysis) of apparent hydrodynamic radii of the IPECs formed in the aqueous mixture of PIB-*b*-PMAA micelles and qP2VP-*b*-PEO at $Z = 1$ measured at a scattering angle of 90°. The corresponding normalized intensity autocorrelation function is given in Figure S2 (Online Supplementary Materials). Conditions: 0.1 M NaCl, pH 7 (0.01 M Tris/Tris·HCl), 25 °C.

We reasonably suppose that the formed IPECs have a core–shell–corona (also referred to as onion-like) structure (Figure 3), wherein a hydrophobic (PIB) core (A) of the original PIB-*b*-PMAA micelle is wrapped by a water-insoluble complex shell (B) assembled from the oppositely charged PMA and qP2VP fragments, and stabilized as a whole by a hydrophilic (PEO) corona (C) built up from non-ionic blocks of qP2VP-*b*-PEO. The hydrophilic corona imparts solubility to the co-assembled species in aqueous media and protects them from aggregation. The remarkable feature of this macromolecular architecture is pronounced compartmentalization, which results from incompatibility of the different nanosized domains (core, shell and corona).

Thus, we highlight a peculiar type of IPECs with a core–shell–corona (onion-like) structure, which can be built up *via* facile bottom-up strategy. Specifically, they result from the electrostatic interaction of anionic star-like PIB-*b*-PMAA micelles with cationic qP2VP-*b*-PEO diblock copolymer,

Table 1 Hydrodynamic and molecular weight characteristics of PIB-*b*-PMAA micelles and their IPECs with qP2VP-*b*-PEO formed at $Z = 1$ as determined by means of dynamic and static light scattering. Conditions: 0.1 M NaCl, pH 7 (0.01 M Tris/Tris·HCl), 25 °C.

Sample	$R_h{}^a$/nm	M_w/g mol^{-1}	$N_{agg}{}^b$
PIB-*b*-PMAA micelles	21 ± 2	748 000	76 (84)^c
IPEC (PIB-*b*-PMAA micelles + qP2VP-*b*-PEO at $Z = 1$)	30 ± 2	3 830 000	77

[a] Measured at a scattering angle of 90°. [b] N_{agg} is the number of macromolecules of the PIB-*b*-PMAA diblock copolymer in the self- or co-assembled species. [c] N_{agg} of the PIB-*b*-PMAA micelles determined at 0.1 M NaCl and pH 10 (0.01 M Tris) by means of small-angle neutron scattering.[18]

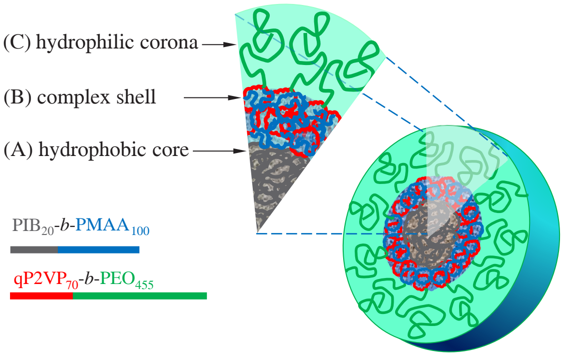

Figure 3 Schematic representation of a core–shell–corona (onion-like) macromolecular architecture formed in an aqueous mixture of PIB-*b*-PMAA micelles and qP2VP-*b*-PEO at $Z = 1$.

wherein the above micelles act as templates and dictate morphology of the resultant co-assembled species. The different domains within such IPECs: a hydrophobic (PIB) core, a complex (PMA/qP2VP) shell, and a hydrophilic (PEO) corona, which can be selectively loaded, for example, with various (even non-compatible or antagonistic) payloads (*e.g.*, drugs, dyes, nanoparticles, *etc.*), combined with easy preparation of such IPECs (*via* simple mixing of aqueous solutions of the oppositely charged components) make the described macromolecular architectures the promising prototypes of nanocontainers/nanoreactors for potential applications in medicine, biotechnology, and catalysis.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.71267/mencom.7640.

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