

Biomimetic nanotechnology: conformational behavior of polypeptides

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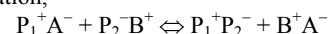
Introduction: Novel multilayer films and capsules can be formed based on the interactions between polyanions and polycations. These multilayers can be manipulated at the molecular level with a wide range of applications, including biomedical device, pharmaceuticals, and food science. Understanding of polyanion-polycation interactions is critical for the design, synthesis and fabrication of coatings on biomedical devices.

Methods: Polypeptides were synthesized using Fmoc chemistry. Polypeptide solutions at three pHs (i.e. 3.9, 7.4, and 11.7) were prepared with the same concentration, under which no turbidity was visible. Polypeptide complexes in solution were obtained by mixing same amount of two polypeptide solutions of same pH. 20-layer polypeptide films were formed on negatively-charged quartz microscope slides by alternate immersion of the slides for 20 min in the prepared solutions of two oppositely-charged polypeptides. More details about the electrostatic self-assembly process refer to reference [1]. CD spectra were recorded using a Jasco J-810 spectropolarimeter to study polypeptide secondary structure.

Results: Two *de novo* polypeptides, [(KVKGKCKV)₃KVKGKCKY] and [(EVEGECEV)₃EVEGECEY], have been designed. K, E, V, G, C, Y represent, respectively, the amino acids lysine, glutamic acid, valine, glycine, cysteine, and tyrosine. These two polypeptides are oppositely-charged, possessing a strong tendency to form complex due to electrostatic attraction. It has been found that pH and temperature influence the structure of these polypeptides, and each polypeptide is mainly in random coil structure at neutral pH at ambient temperature (Fig. 1a). β -sheet is favorable upon complexation of these two polypeptides,

more β -sheet has been found in polypeptide complex than in each polypeptide, and predominant β -sheet has been observed in the resulted films (Fig. 1c).

Discussion: The dominant driving force for the formation of polypeptide complexes/films in the electrostatic self-assembly process is the release into solution of counterions. The mechanism of interaction can be schematically described by the following equation,



where P_1^+ represents a protonated lysine site having an A^- counterion; P_2^- represents a dissociated glutamic site having a B^+ counterion; $P_1^+P_2^-$ is the corresponding complexed form.

That's to say, the oppositely-charged polypeptides interact with each other mainly through electrostatic attraction, and hydrogen bonding induces the conformational change of polypeptides from disordered coil structure (Fig. 1a) before self-assembly to a highly ordered structure, a typical β -sheet structure (Fig. 1c), after self-assembly. Electrostatic self-assembly (Fig. 1b) is a very useful tool in developing supramolecular architectures based on polyanion-polycation interactions. The results presented indicate that very specific structures can be achieved in polypeptide complex which can be quite different from the structures of the pure polypeptides under identical conditions.

Conclusions: Novel polypeptides were synthesized for electrostatic self-assembly of nanobiofilms. The secondary structure of polypeptides changes from random coil in solution to β -sheet in the biofilms.

References: 1. Li, B; Haynie, D. *Biomacromolecules* 2004;5:1667-1670.

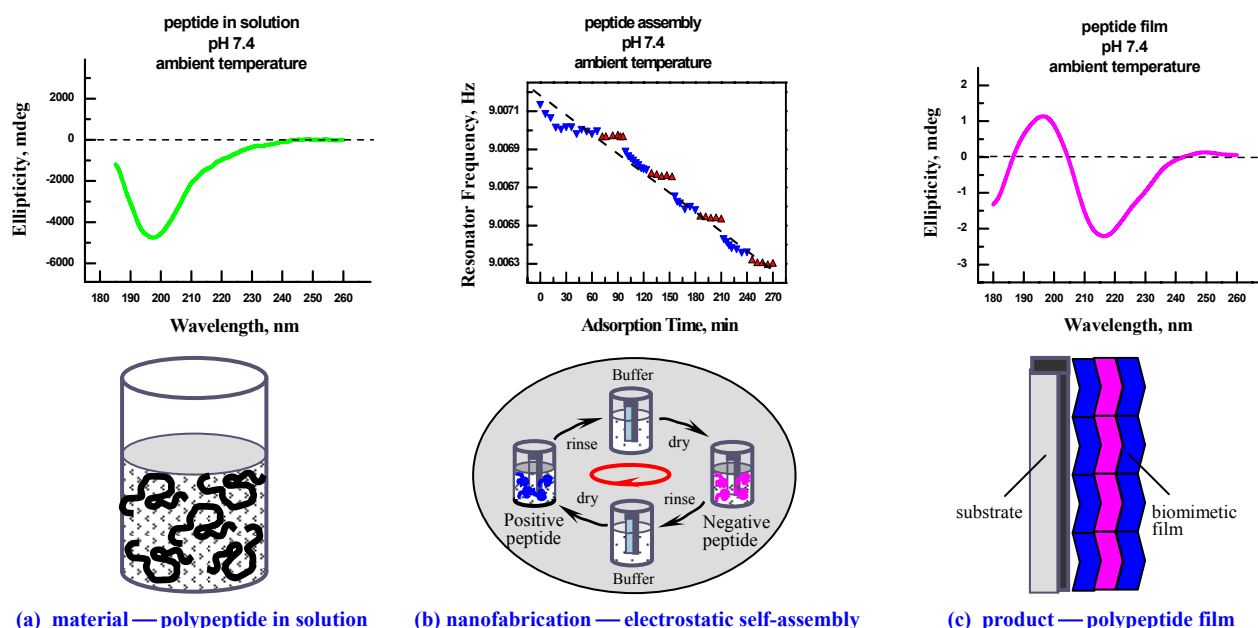


Fig. 1. The *de novo* designed polypeptides undergo a conformational change from random coil in solution (a) to β -sheet in films (c) upon electrostatic self-assembly (b).