Polymer-Protein Assembly via Fast Mixing to Fabricate Homogeneous Functional Nanoparticles

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Functional polymer-protein nanoparticles (NPs) *via* co-assembly have broad applications in biotechnology and nanotechnology. In principle, controllable and vigorous mixing is required to fabricate homogeneous NPs, which, however, remains a challenge via conventional bulk synthetic methods. Herein, an electrokinetics (EK) based microfluidic reactor with fast mixing was explored to assemble a variety of functional proteins with poly(4-vinylpyridine) (P4VP) polymers in an ethanol/water co-solvent system. A micro mixer with a quasi T-shaped microchannel with electrically conductive sidewalls was fabricated. Teflon was used to avoid clotting issue in the micro mixer. Bovine serum albumin (BSA), N-oxygenase CmlI, florescence proteins EGFP and mCherry were used to co-assemble with P4VP polymer with this micro mixer. The resultant NPs showed significantly improved size distribution by comparison with the ones prepared using conventional bulk method, while the NPs size could be tuned by adjusting the mass ratio of polymer to protein. More importantly, the structure and functionality of the assembled proteins were sustained upon the EK based microfluidic mixing.

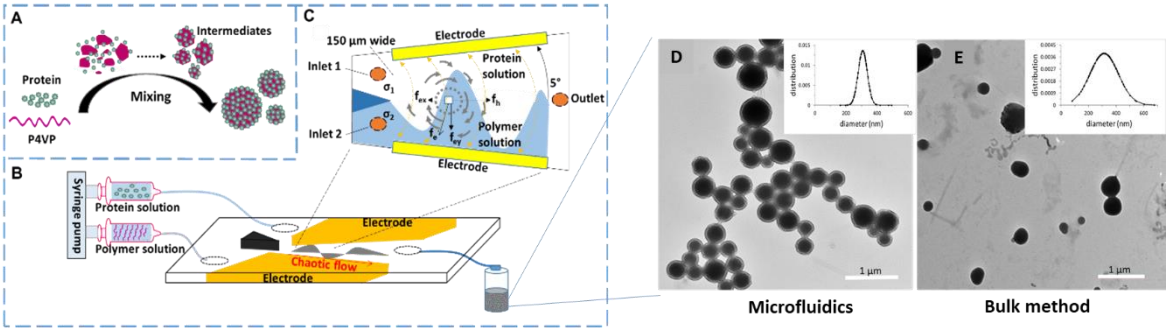

Fig. 1 (A) Schematic illustration of proposed polymer-protein co-assembly process. (B) Scheme of the microfluidics assisted polymer protein co-assembly to form core shell NPs. (C) Illustration of the microchannel near the entrance. The flows with different conductivity (σ_1 & σ_2) in the non-parallel microchannel are driven by the hydrodynamic force f_h and the electrical body force f_e which can be divided into f_{ex} and f_{ey}. The f_{ex} at different points along the electric line can be either negative or positive related to f_h. The big difference between the force in x-direction ($f_h + f_{ex}$) and the force in y-direction f_{ey} can generate a shear stress and produce a micro vertex effect,[5] resulting in ultrafast mixing. (D) TEM image of P4VP-BSA NPs fabricated from microfluidics (E) TEM image of P4VP-BSA NPs fabricated from conventional stirring method in bulk reactors.

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