Copolymer-stabilized coacervate microdroplets as multicompartmentalized artificial cells

Block-copolymers self-assemble into a myriad of fascinating structures. These systems have been instrumental to direct the organization of superstructures of many types of inorganic materials spanning bio-minerals, semiconductors, and even superconductor materials. The traditional approach to stabilize nanostructures of block-copolymers is tuning the chemistry and/or volume fraction of the blocks. In this presentation, we will show that a single block-copolymer type that *per se* is only stable in 1D multilayers can organize into multiple nanostructures, when physically hybridized by a lipid template. Polymer-lipid physical hybrids adopt tunable and remarkably well-ordered 1D lamellar, 2D hexagonal, and 3D bicontinuous cubic structures in air. Importantly, the unit cell sizes are one order of magnitude smaller than attained with pure block-copolymer systems allowing superior packing density of inorganic materials.

10:30 AM BM09.12.07
Copolymer-Stabilized Coacervate Microdroplets as Multicompartmentalized Artificial Cells Alex Mason[1], Loai Abdelmohsen[1], N. Amy Yewdall[1], Bastiaan Buddingh[1], David Williams[2] and Jan van Hest[1]; [1]Technische Universiteit Eindhoven, Eindhoven, Netherlands; [2]Chemistry, Swansea University, Swansea, United Kingdom.

Complex coacervates are a membrane-free, solution-phase material that are formed by the electrostatic interactions between oppositely-charged macromolecules. They are interesting from an artificial cell perspective because they resemble the cell cytosol, particularly as a crowded and charged environment. However, due to their inherently membrane-free nature, they are unstable, with coacervate droplets prone to coalescence on relatively short time scales, which inhibits their use in longer experiments. This work describes the development of a triblock copolymer that self-assembles on the surface of an amylose-based complex coacervate, forming a robust, passivating layer that prevents droplet coalescence and content mixing. These discrete, cell-sized, polymer-stabilized coacervate droplets are capable of encapsulating macromolecular cargo, which remain in an active conformation. In addition, the polymer membrane is semi-permeable, enabling the incorporation of a simple enzymatic cascade in different protocell populations, a rudimentary demonstration of protocellular communication.

This robust scaffold has now been utilized to demonstrate the formation of a multicompartment system. Through the encapsulation within the coacervate protocell of nanometre-sized polymer vesicles containing functional enzymes, it is possible to generate assemblies reminiscent of organelles within a eukaryotic cell. This structural motif was used to incorporate enzymatic cascades, demonstrating increased rates of reaction and control over the reaction pathway depending on the spatial organization of enzymes within the artificial organelles. These polymer-stabilized coacervate droplets already offer many characteristics that are interesting to the artificial cell community, while also being modular and open to further polymer engineering, paving the way for the incorporation of more complex biomimetic systems and behaviours.

10:45 AM BM09.12.08
Redox-Responsive Disassembly of Dual Diselenide Containing Triblock Copolymer Nanocarriers Based on Poly(ethylene glycol)-b-PCL-b-poly(ethylene glycol) for Triggered Anticancer Drug Release Balkew Z. Hailemeskel, Kefyalew Dagnew Addisu, Abegaz T. Andrgie, Hsiao-Ying Chou and Hsieh Chih Tsai1; Graduate Institute of Applied Science and Technology, National Taiwan University of Science and Technology (NTUST), Taipei, Taiwan.

In recent years, different kinds of nanoparticles (NPs) have been synthesized with the aim of being utilized as drug delivery system for anticancer drugs. In this study, diselenide containing biodegradable triblock copolymer, poly(ethylene glycol)-b-poly(caprolactone)-b-poly(ethylene glycol) (mPEG-SeSe)$_2$PCL was carefully prepared through the reaction of ditosylated polycaprolactone and poly(ethylene glycol) methyl ether tosylate in the presence of disodium diselenide. The diselenide containing triblock copolymer allowed the formation of selfassembled aggregates which revealed response to glutathione (GSH) and Hydrogen peroxide (H_2O_2) because of the redox-stimuli cleavable property of diselenide bond. Such redox response confirmed an increased release of Dox from the nanoparticles in tumor microenvironments. The cytotoxicity of (mPEGSeSe)$_2$PCL triblock copolymer was tested by cell viability assay using HeLa and HaCaT cells. The in vitro drug release studies exhibited that above 62 % and 56 % of Dox was released in 72 h at 37^{o}C from the nanoparticles in the presence of 6.5 mM GSH and 0.1% H_2O_2 respectively, whereas only about 30 % of Dox was released from the nanoparticles without stimuli under the same conditions. The MTT assay studied using HeLa cells and HaCaT cells showed that the Dox-loaded (mPEGSeSe)$_2$PCL nanoparticles have high antitumor activity in HeLa cells and low antitumor activity in HaCaT within 24h incubation. Furthermore, the confocal laser scanning microscopy (CLSM) measurements confirmed that the Dox-loaded nanoparticles could be localized efficiently by HeLa cells and release Dox inside the tumor cells. However, the internalization of Dox-loaded nanoparticles and release of Dox inside HaCaT cells was very less. The results indicated that the synthesized material (mPEGSeSe)$_2$PCL was biocompatible and it could be an alternative candidate for anticancer drug delivery system.

11:00 AM BM09.12.09
Highly-Crystalline Peptoid-Based Nanomaterials Assembled from Short Peptoid Oligomers Peng Mu[2, 1], Guangwen Zhou[2] and Chun-Long Chen[1]; [1]Pacific Northwest National Laboratory, Richland, Washington, United States; [2]Mechanical Engineering, Binghamton University, The State University of New York, Binghamton, New York, United States.

Peptoid (N-substituted glycines), as one of the unique sequence-defined synthetic “foldamers that mimic proteins and peptides for functions, - have recently received increasing attention for building biomimetic nanomaterials with hierarchical structures. Due to the unique proteinase-resistance, chemical and thermal stabilities of the peptoids, peptoid-based nanomaterials are promising for applications under the hostile environment where protein- or peptide-based materials are vulnerable and easy to degrade or lose functions. Recently, by designing amphiphilic oligomers that contain aromatic hydrophobic domains, our group recently reported their self-assembly into highly crystalline membrane-mimetic 2D nanomaterials and 1D nanotubes. We demonstrated that these peptoid-based nanomaterials are highly stable and a wide range of functional groups can be precisely placed within these materials as peptoid side chains. Furthermore, our mechanistic studies indicate that the packing of hydrophobic side chains is the key for the stabilization of these biomimetic nanomaterials. To gain the atomic level of understanding the self-assembly of these 2D and 1D nanomaterials, herein, we report the design and synthesis of short peptoid oligomers for self-assembly of biomimetic nanomaterials with similar structures. X-ray diffraction data indicate that nanomaterials assembled from these short sequences are highly crystalline and the change of one side-chain group at the N-terminal can significantly influence the materials formation process. By analyzing the XRD data of a number of biomimetic materials assembled from peptoids with similar chemistries, and the assistance of CryoEM and AFM characterizations, we gained a better understanding of peptoid assembly process and the structures of 2D and 1D peptoid-based nanomaterials.

11:15 AM BM09.12.10
Self-Assembly and Supramolecular Chirality Reversal of a Sophorolipid-Functionalized Chromophore Kyle C. Peters[1], Shekar Mekala[2], George Heidbreder[1], Richard A. Gross[2] and Kenneth Singer[1]; [1]Physics, Case Western Reserve University, Cleveland, Ohio, United States; [2]Center for Biotechnology and Interdisciplinary Studies, Rensselaer Polytechnic Institute, Troy, New York, United States.