Biodegradable segmented nanostructures for controlled drug delivery

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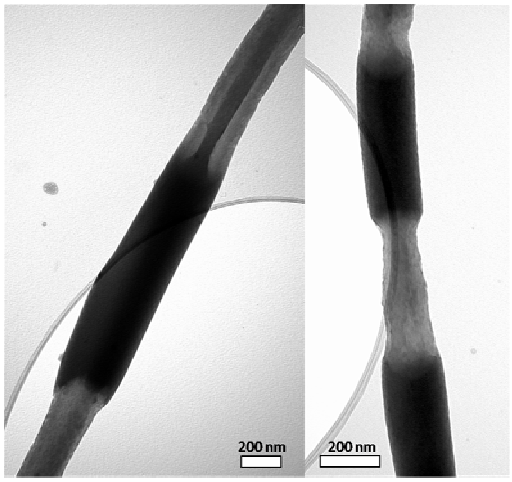
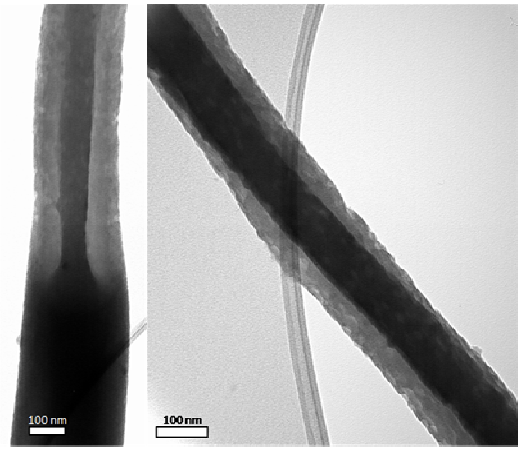
Heterogeneous, segmented one-dimensional (1D) nanomaterials, such as nanorods and nanowires, have been utilized for a variety of different biomedical applications because they offer a unique combination of properties and provide a material platform for integrating multiple functions. These multifunctional 1D nanomaterials are commonly fabricated from metals or semiconductors using a variety of techniques such as electrodeposition or chemical vapor deposition. Biomedical applications for these structures include biosensing, imaging, drug and gene delivery, and vaccine applications.

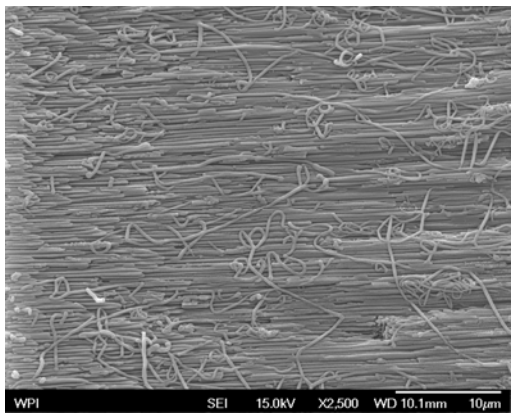
We propose a template assisted wetting approach to fabricate segmented polymer nanorods using biodegradable polymers for controlled drug delivery. This project first studies the in vitro polymer degradation and drug release kinetics of homogeneous nanorods fabricated from individual polymers to understand the influence of the size and aspect ratio of 1D polymer nanorods. Based on this understanding, we design and fabricate heterogeneous segmented nanorods from two different alternating polymers for controlled drug release. Since the template-assisted fabrication approach provides us unprecedented control over the size, spacing, and length of the heterogeneous polymer nanorods, the effects of segment spacing, size of the nanorods, and aspect ratio on the drug release kinetics can be investigated.

As a proof of concept, polystyrene and



Above and below: TEM images showing PS (dark) and PMMA (light) segmented nanorods with core shell morphology





Above: SEM image showing the cross section of an AAO template filled with polycaprolactone

poly(methyl methacrylate) were used as model polymers to fabricate segmented structures. Anodized aluminum oxide membranes with an average pore size of 200 nm were wetted at 150C by multilayered thin films of PS and PMMA. We were able to fabricate segmented nanorods and unique core-shell morphology. Based on these results we have optimized conditions for segmented nanorods, and have selected polycaprolactone and poly(DL-lactide) for the fabrication of biodegradable segmented nanorods. The length and morphology of the nanorods is characterized using SEM and TEM. The degradation kinetics of these heterogeneous nanostructures is determined using GPC and the drug release from the polymer segments is monitored using UV-vis spectroscopy. Results obtained for the heterogenous segmented nanorods are compared with the homogenous, single polymer nanorods.

Protein nanocapsules for drug and gene delivery

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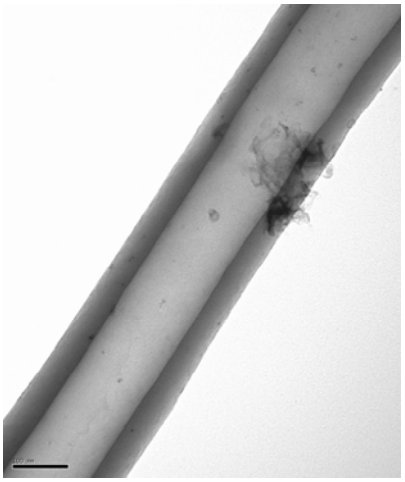
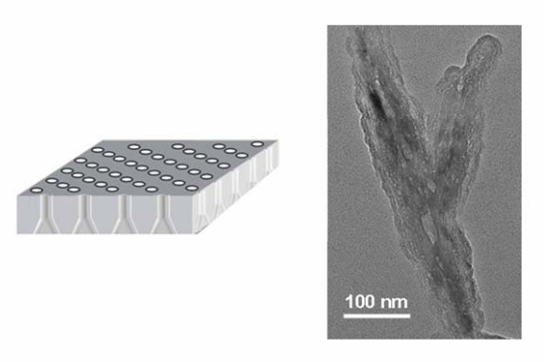
Bionanomaterials have recently begun to spark a great amount of interest and could potentially revolutionize biomedical research. Nanoparticles, nanocapsules, and nanotubular structures are becoming attractive options in drug and gene delivery. The size of the delivery vehicles greatly impacts cellular uptake and makes it highly desirable to precisely control the diameter and length of nanocarriers to make uniform nanoparticles at low cost. Carbon nanotubes have shown great potential within the field of drug and gene delivery.



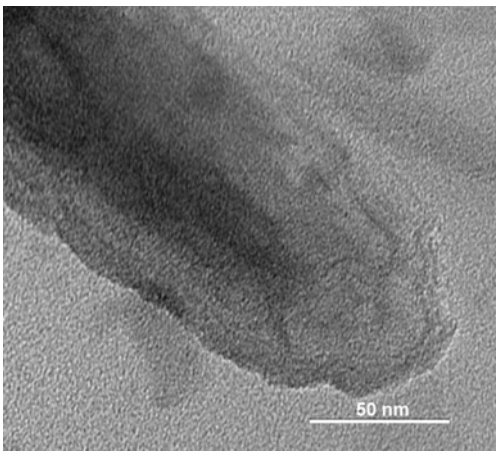
Above: TEM image showing avidin and glucose oxidase nanotube walls

However, their insolubility and cytotoxicity could severely delay FDA approval. A desirable alternative would be to fabricate nanostructures from biomaterials such as proteins, peptides or liposomes, which are already FDA approved.

In this paper we demonstrate the preparation of protein nanocapsules with both ends sealed using a template-assisted alternate immersion method combined with controlled cleaving. Glucose oxidase nanocapsules with controllable diameter, wall thickness, and length were fabricated and characterized with SEM and TEM. The biochemical activity of glucose oxidase in the form of nanocapsules after processing was confirmed using UV spectrometry. Our future work will explore proteins suitable for drug encapsulation and cellular uptake and will focus on optimizing the cleaving process to gain precise control over the length of the nanocapsules.



Above: Schematic illustrating a Y-junction AAO template and a TEM image of a Y-junction glucose oxidase nanocapsule



Above: TEM image showing the closed end of a glucose oxidase nanocapsule