

## Nanoengineered Shells for Encapsulation and Controlled Release

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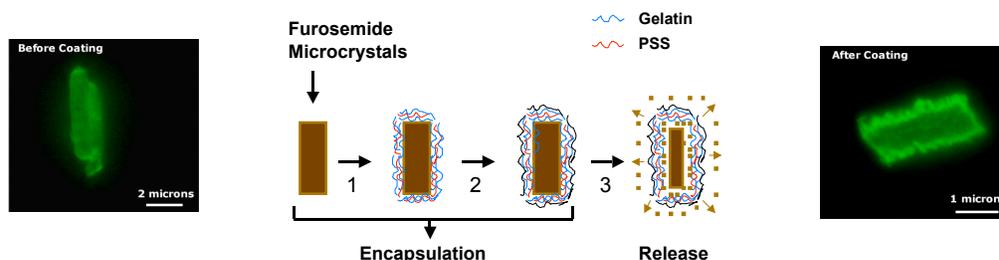
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The project NANOSHELLS is developing new technologies based on nano-encapsulation to solve industrial problems related to controlled release of drugs and other chemicals. The overall objective of NANOSHELLS is to make the breakthrough necessary to enable the production and application of nano-capsules with targeted controlled release properties of chemicals. In the related study, we are developing bionanoreactors based on encasing of enzymes in polymeric micro- and nanoshells. The fundamental aspect of this research is developing of bio/catalytic chemistry in nano-confined volume (i.e., inside the polyelectrolyte micro- and nanoshells). A production of such shells is based on nanoassembly via layer-by-layer adsorption of oppositely charged components: linear polyelectrolytes, proteins, and nanoparticles.

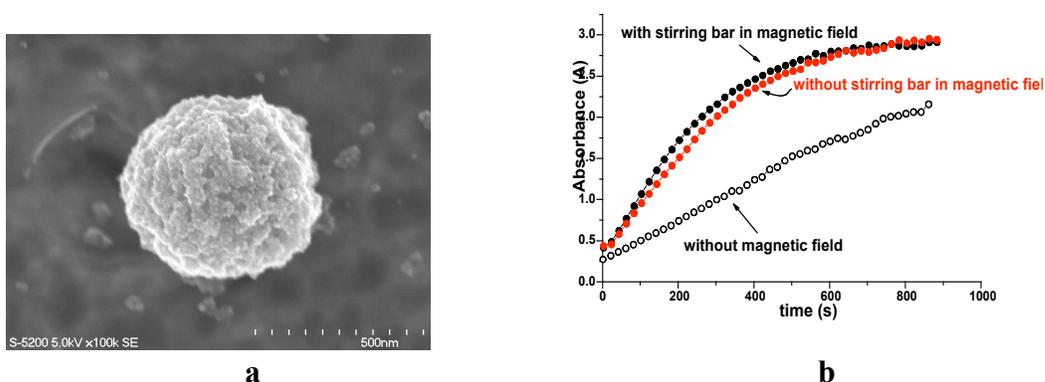
For this, first, we are developing new types of nanoparticles used as core/vectors for active molecules. The second phase involves nano-engineered ultrathin layer assembly to build a capsule shell of pre-determined composition, designed for special release properties, around the active materials [1-4].

**Drug Nanoencapsulation:** We synthesized 500-nm diameter particles of important drugs: furosemide, dexamethasone, nifedipine, niclosamide, theophylline and paclitaxol, then assembled very thin walls around these drug cores, using only a few molecular layers of biocompatible polymers. We are introducing antibodies into the wall of these shells, which will target and anchor the capsules to the sick cells. An example of results for these experiments is given in the figure below. Furosemide crystals were encapsulated with polyions and gelatin to control the release of the drug in aqueous solutions. Charged linear polyions and gelatin were alternatively deposited on drug nanocrystals through layer-by-layer nanoassembly. Sequential layers of six gelatin / poly(styrenesulfonate) (PSS) bilayers were adsorbed, with a corresponding total capsule wall thickness of 110 nm. The release of furosemide from the coated microparticles was measured in aqueous solutions of pH 1.4 (acidic gastric environment) and 7.4 (blood pH). At both pH values, the release rate of furosemide from the encapsulated particles was reduced by 300 times compared to uncoated furosemide, which shows that nanoencapsulation is a method of achieving prolonged drug release through self-assembly of polymeric shells on drug microcrystals. By varying the wall composition, we can change the rate of drug release.



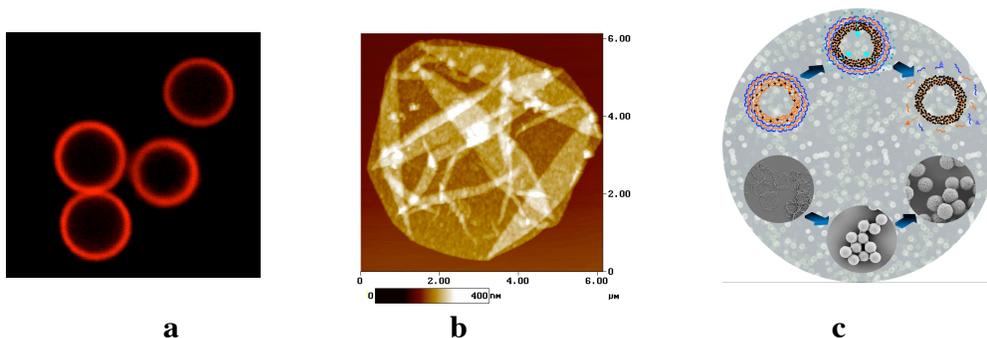
**Fig. 1** Illustration of furosemide microcrystal encapsulation with (PSS/Gelatin)<sub>6</sub> shell showing the drug crystal fluorescence before and after coating. PSS = poly(styrenesulfonate).

**Bionanoreactors and Chemistry in Nano/confined Volume:** Organized multilayers of nanoparticles (9-nm diameter silica or 12-nm magnetite) and glucose oxidase (GOx) were assembled in alternation with oppositely charged polyelectrolytes on 420-nm latex particles. Stepwise growth of the multilayer films on latex was confirmed by microelectrophoresis and transmission electron microscopy (Fig. 2a). The inclusion of silica layers on latex yields a higher surface area, resulting in greater GOx adsorption and thereby increasing the catalytic activity of the bioreactor. The bioactivity was proportional to the core surface area and also to the number of GOx layers in the shells. Also the presence of magnetic nanoparticles allows self-stirring of the nanoreactors with rotating magnetic field and enhances its productivity (Fig. 2b).



**Fig. 2.** (a) SEM image of 420-nm latex covered with two monolayers of magnetite particles; less dense glucose oxidase (GOx) layers are not visible. (b) Time trace of the product absorbance at 500 nm for the enzymatic activity assay of {(PEI/PSS) + (PEI/12-nm magnetite)<sub>2</sub> + (PEI/GOx)<sub>2</sub>} biocolloids in two different conditions: without magnetic field (circle) and within magnetic field. PEI- poly(ethyleneimine).

In another approach, after the polycation / polyanion shell was formed, we dissolved the melano formaldehyde latex cores at pH 1 and obtained hollow polymer capsules with wall thickness of 40 nm (Fig. 3a). These capsules were loaded with enzymes (glucose oxidase, peroxidase, hemoglobin, myoglobin, or urease). Enhanced biocatalytic activity of such encapsulated enzymes was demonstrated. Proteins in such biocolloids are protected against high molecular weight denaturing agents and inhibitors while small substrate molecules can readily reach the enzyme.



**Fig. 3 Confocal cross-sectional image of 4-micron diameter shell with 20 nm thick wall of (PSS/PAH)<sub>4</sub> composition (a), and AFM-image of the collapsed shell (b). Concept of loading such capsules with enzymes and monomers for synthesis of nano/confined polymer particles. PAH - poly(allylamine).**

Polyion microshells loaded with peroxidase we used for micro/confined synthesis of phenol polymers inside the capsules. An encapsulated enzyme was used both as a biocatalyst and as a template for monomer polymerization. Synthesis of inorganic materials in nano/confined capsule volume (such as CaCO<sub>3</sub> and YF<sub>3</sub>) is currently under development [5].

**Nano-Biosensors:** Layer-by-layer self-assembly was utilized to design a new type of micro/nanosensors consisting of nanoorganized shells of enzymes for biospecific recognition and fluorescent indicator loaded inside the 100-5000 nm shells. Using a variety of templates, polymer/enzyme composite shells are deposited within an ultrathin film containing indicator and reference dyes. Templates include large planar surfaces such as microscope slides, optical fibers for specific sensor probes, and micro/nanoparticles. An alternative approach involves encapsulation of active sensor molecules within the micro/nanoshell using pre- and post-encapsulation processes. Currently, K<sup>+</sup>, Na<sup>+</sup>, and O<sub>2</sub> sensors have been demonstrated, but the versatility of the approach for extension to many other analytes will be discussed [6-8].

“Overview” documents posted on the website: <http://www.latech.edu/tech/engr/ifm>

## References

For further information about this project email [ylvov@coes.latech.edu](mailto:ylvov@coes.latech.edu)

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