7. Highlights

Science Highlights

- Living Mass Sensors for Characterization of Cell Growth
- Electrosprayed Nanoparticles for Gene Delivery
- Injectable Nanoscaffold to Improve Tissue Regeneration

Education Highlights

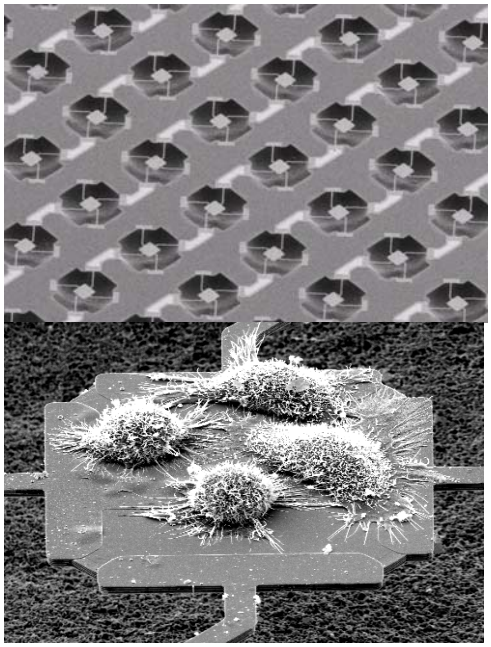
- Teaching the Teachers!

Shared Facilities Highlights

- Optical Trapping

NSF Highlights

Living Mass Sensors for Characterization of Cell Growth



(top) Array of silicon mass sensors on a chip, (bottom) cells grown on a mass sensor

Microsystems technology offers the possibility of handling, manipulating, and measuring miniscule samples, including single cell. By probing the physical properties of single cells through engineering-based approaches, we can precisely describe the physical properties of cell growth, division, and the cellular response to stimuli. The goal of our proposed work is to develop and implement a new class of MEMS devices that will permit the direct, long-term measurement of the mass of single cells during cell growth, mitosis, and apoptosis.

We have developed a novel array of MEMS mass sensors based on the combination of two advanced technologies that combine the areas of *micro-cantilever sensors* and *high throughput living cell arrays.* This engineered, hybrid sensory system will enable the positioning of single cells onto cantilever arrays followed by sensitive and precise measurements achieved through *laser Doppler vibrometry* and *electro-magnetic actuation*. By synergistically combining these powerful engineering processes, MEMS mass sensory arrays will provide a direct, biophysical measurement of cell mass. As a result, we have gained insight into the biological processes of cell growth through direct monitoring of changes in cell mass.

Primary Strategic Outcome Goal:

Determine mass of living cells versus time.

Secondary Strategic Outcome Goal:

Develop novel cellular characterization tools.

Does this highlight represent potentially transformative research? If so, please explain why. *For more information, see Report to Congress: Transformative Research at the National Science Foundation, April 16, 2008 and Important Notice 130: Transformative Research*

Yes

How well does the proposed activity broaden the participation of underrepresented groups (e.g., gender, ethnicity, disability, geographic, etc?)

N/A

What may be the benefits of the proposed activity to society?

This activity will help to understand the fundamental principles underlying cell division which could have impact on our understanding of diseases.

What is the intellectual merit of this activity?

Measurement of adherent cell mass versus cell growth has not been performed to date. The technology proposed here allows us to do this.

What are the broader impacts of this activity?

Integration of research in engineering and biology, and the development of new technology for characterization of living cells.

ENG/EEC 2010
Program Officer: Daniel De Kee

NSF Award Numbers:
0914790

Award Title: Center for Affordable Nanoengineering of Polymeric Biomedical Devices (CANPBD)

Start Date: 09/01/2009

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Awarded Amount to Date $15M

PI: L. James Lee, lee.31@osu.edu

Institution Name: The Ohio State University

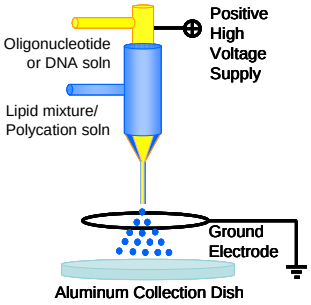
State Code: OH

Credit: Center for Affordable Nanoengineering of Polymeric Biomedical Devices (CANPBD), The Ohio State University

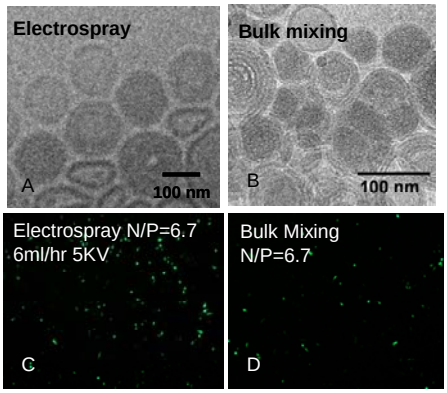
Submitted on 04/15/2010 by Rashid Bashir, rbashir@ad.uiuc.edu

NSF Highlights

Electrosprayed Nanoparticles for Gene Delivery



A coaxial electrospray device.



(A,B) Cryo-TEM pictures of lipid-ODN nanoparticles show distinctly different structures depending on the production method**.**
(C,D) The green dots correspond to cells transfected with DNA/polycationic nanoparticles produced by electrospray and bulk mixing.

Credit: CANPBD

Bundling genes into nanoparticles made of lipids or polymers is a way to improve the delivery of these materials to targeted cells in the body that does not involve viruses. Common techniques for making nanoparticles included bulk mixing and solvent depletion. Limitations associated with these techniques include poor control over the particle size and/or the length of time required to remove the solvent.

We have shown that a coaxial electrospray device (upper figure), is a powerful tool to rapidly produce structured nanoparticles for gene delivery. In this device a solution containing oligonucleotides (ODN) or DNA flows through the center needle, and a lipid mixture or a polycation solution flows through the outer needle. An aerosol is produced by applying a positive high voltage. For lipid based systems, the large surface area of the aerosol ensures rapid removal of the solvent.

The structure and the delivery efficiency of nanoparticles produced by coaxial electrospray differ from those produced by bulk mixing. For example, the lipid-ODN nanoparticles[1] produced by coaxial electrospray (middle figure) have unilamellar structure rather than the multilamellar structure of the lipid-ODN nanoparticles produced by bulk mixing. Furthermore, DNA-polycationic nanoparticles[2] produced by coaxial electrospray have higher gene delivery efficiency than those produced by bulk mixing (lower figure). Finally, because the particles are produced as an aerosol, this technique may provide useful in pulmonary gene or drug delivery.

1. Wu et al., Molecular Pharmaceutics, **6**, 1371–1379 (2009)
2. Wu et al., Biotech. Bioeng., **105**, 834 -841, (2010)

Primary Strategic Outcome Goal:

Structured nanoparticles for gene delivery.

Secondary Strategic Outcome Goals:

Improving the efficiency of gene delivery.

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No

How well does the proposed activity broaden the participation of underrepresented groups (e.g., gender, ethnicity, disability, geographic, etc?)

Our Center involves several institutions across the US including Oakwood University, an HBCU, and also involves faculty and students are from groups normally underrepresented in the STEM fields.

What may be the benefits of the proposed activity to society?

This activity explores alternative methods for gene delivery that do not require viral vectors.

What is the intellectual merit of this activity?

This activity provides an alternative way to rapidly produce nanoparticles for gene delivery, and that may be highly suitable for pulmonary delivery of genes or drugs.

What are the broader impacts of this activity?
Merit Review Broader Impacts Criterion: Representative Activities, July 2007

The results of this research have been presented at national conferences and published in the open literature. Pulmonary delivery of genes is hampered by the difficulty of aerosolizing delicate biomolecules. Unlike shear-based aerosolization techniques, electrospray does not damage these materials and, thus, may provide an alternative gene delivery route.

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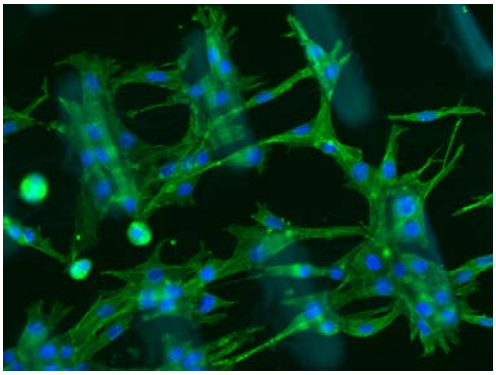
NSF Highlights

Injectable Nanoscaffold to Improve Tissue Regeneration



Rod-like scaffolds alter cellular organization, function and ultimately enhance tissue regeneration.

In May of 2008, the World Health Organization (WHO) announced that cardiovascular disease in now the number one killer on the planet over taking infectious diseases for the first time. In the United States heart disease is currently the leading cause of death with 2.6 Million Americans being affected by heart muscle injury annually. Although these patients have some treatments available to them, none reverse the physical damage to the heart muscle. The inadequate mass of functional muscle cells is the main underlying cause of heart failure and is being addressed by tissue engineering and more recently stem cell approaches.

Researchers at the University of California, San Francisco and the University of Illinois at Chicago have developed an implantable, biodegradable technology that enhances regeneration of heart muscle tissue. A therapeutic nanostructure has been developed to aid the endogenous repair processes for the recovery of damaged and failing cardiac muscle tissue. This technology combines a physical scaffold with controlled size and shape, which allows for proper tissue growth, in conjunction with a potent growth factor peptide which enhances the native stem cell population within the heart.

Primary strategic Outcome Goal:

Develop new material and structures that can be used for tissue engineering.

Secondary strategic Outcome Goals:

Understand how biophysical signals can regulate cell behavior in vitro and in vivo

Does this highlight represent potentially transformative research? If so, please explain why. *For more information, see Report to Congress: Transformative Research at the National Science Foundation, April 16, 2008 and Important Notice 130: Transformative Research*

Yes, it may alter the way in which treatment is administered after a heart attack. It represents a new approach to restore tissue function.

How well does the proposed activity broaden the participation of underrepresented groups (e.g., gender, ethnicity, disability, geographic, etc?)

Every Engineering Research Center involves the participation of several institutions across the U.S., as well as a diverse faculty and student body.

What may be the benefits of the proposed activity to society?

This would be a non-invasive approach to regeneration function cardiac tissue. The microrods are biocompatible and injectable so that they can be administered locally to the patient.

What is the intellectual merit of this activity?

This research has lead to new knowledge in how cells respond to physical cues and how those structures can be used to modulate tissue repair.

What are the broader impacts of this activity?
Merit Review Broader Impacts Criterion: Representative Activities, July 2007

Results of the research have been presented at major professional meetings and have led to several peer reviewed publications.

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NSF Highlights
Teaching the Teachers!

Whetstone High School teacher Lori Jackson demonstrates vascular tissue modeling.

Prof. Susan Olesik demonstrates phase change using liquid Nitrogen ice cream.

Credit: Nanoscale Science and Engineering Center for Affordable Nanoengineering of Polymeric Biomedical Devices (CANPBD), The Ohio State University, Columbus, Ohio.

As part of our outreach efforts to introduce nanotechnology into high school classrooms, the NSEC Center for Affordable Nanoengineering of Polymeric Biomedical Devices (CANPBD) conducts a one-day workshop for area high school science teachers each year. Up to 40 teachers from high schools in and around central Ohio participate in this workshop, learn about nanotechnology, observe and perform experiments, and receive kits that contain materials for hands-on classroom activities. Experiments range in complexity from measuring a nanometer to modeling tissue engineering using nanotechnology. The teachers also tour the Nanoscale Science and Engineering Center cleanroom facility at Nanotech West on Kinnear Road, and observe researchers at work on cutting edge nanotechnology projects. Afternoon activities include a fun and hugely popular cryogenics and phase change demonstration involving the preparation of liquid Nitrogen ice cream.

The following Nanotechnology experiments are demonstrated:

- Modeling tissue engineering using nanotechnology
- Electrospun nanofibers
- Superhydrophobicity and Superhydrophilicity (Nanograss); nanofibers on your clothes
- Measuring Magnetic Field Strengths using Ferrofluids
- Rheology and Nanoscale Suspension Behavior
- Nanofibers: Measuring the Visible to Understand the Invisible
- Introduction to Sun Protection
- Measuring the Large and the Small (Laser Pointer)
- Wavelength and Resolution: Demonstration of why SEM improves resolution of images over visual light microscopy using pegboards of decreasing size
- Nanofabric: Demonstration of commercially available stain-resistant fabric developed using nanotechnology (superhydrophobicity)
- Electrospinning: Demonstration of a portable electrospinning apparatus designed by CANPBD for educational use

A detailed workshop write-up with links to the methodology for each experiment is available at http://www.nsec.ohio-state.edu/teacher_workshop.html.

Primary Strategic Outcome Goal:

To train science teachers to introduce Nanotechnology to their high school students.

Secondary Strategic Outcome Goals:

To demonstrate that selected topics can be incorporated into high school curricula within the parameters of school district requirements.

Does this highlight represent potentially transformative research? If so, please explain why. *For more information, see Report to Congress: Transformative Research at the National Science Foundation, April 16, 2008 and Important Notice 130: Transformative Research*

No

How well does the proposed activity broaden the participation of underrepresented groups (e.g., gender, ethnicity, disability, geographic, etc?)

By providing easy to understand activities to high school science teachers, our Center strives to improve interest in Nanotechnology and enhance future enrollment in STEM disciplines at the high school and college levels. Through partnership with area schools that have high numbers of underrepresented students, we encourage active participation by diverse groups.

What may be the benefits of the proposed activity to society?

This workshop provides research opportunities for a diverse population from area school districts who may not otherwise be able to participate in cutting edge scientific research.

What is the intellectual merit of this activity?

Stimulating interest in science and cultivating intellectual curiosity.

What are the broader impacts of this activity?
Merit Review Broader Impacts Criterion: Representative Activities, July 2007

Increased enrollment in STEM disciplines.

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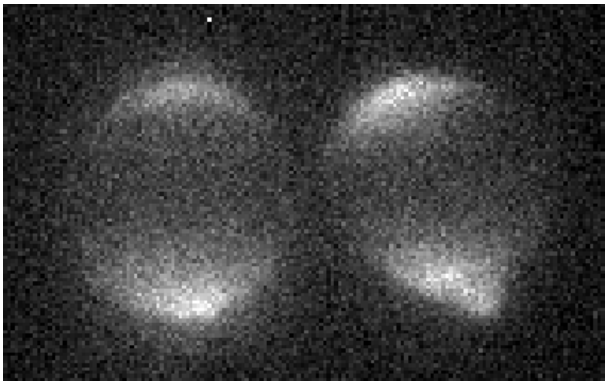
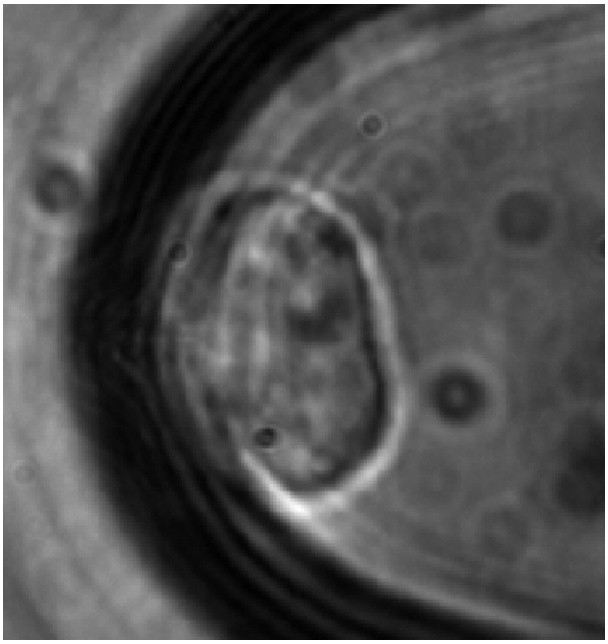
NSF Highlights
Optical Trapping



Two cells held in optical traps. The cells have been electroporated, allowing PI dye to stain the contents near the poles.



A mouse embryonic stem cell held against a nano-channel in an optical trap.

Optical trapping allows the manipulation of micrometer sized particles through the use of focused laser beams. Optical trapping is particularly useful as a nondestructive, noninvasive method of manipulating cells.

Within the past year the optical trapping group has collaborated with Dr. Lee's group to examine the properties of bulk electroporation. Electroporation is a commonly used method of delivering drugs and genes to cells in a laboratory setting by creating small pores in the cell membrane through the use of electric fields. By using optical trapping technology it was possible to easily observe single cell electroporation of a cell in suspension. Similar previous experiments had focused on cells attached to a surface; a situation which is not the case in conventional bulk electroporation. Additional experiments utilized optical trappings ability to manipulate multiple objects to examine cell shielding effects. By manipulating two cells positions relative to each other the effects of orienting the cells close to each other and far from each other, as well as parallel and perpendicular to the electric field were examined. It was found that electroporation occurred at lower values for the critical field when the cells were positioned perpendicular to the field, and at higher field values when they were positioned parallel to the field. Additionally, a small shift in the location of the pores was predicted by theory for the perpendicular case, and this was observed experimentally.

Dr. Lee's group has also developed technology to produce arrays of nano-channels for the purpose of gene/drug delivery to large numbers of cells with high transfection rates and high viability by electroporation. Optical trapping techniques facilitate easy probing of the properties of this nano-channel electroporation by allowing cells to be placed directly up against the nanochannels. Current experiments are focused on determining the effects of the field on the delivered “dosage.” Future experiments hope to use optical trapping to transfect at least several hundred cells for the purposes of cell culturing.

Future efforts by the group are focused on manipulating large numbers of cells using optical techniques, either through the use of optical waveguide trapping or by so called opto-electronic trapping.

Primary Strategic Outcome Goal:

Exploring the physical properties of cells and biological molecules using laser trapping.

Secondary Strategic Outcome Goals:

Manipulating large groups of objects using optical trapping.

Does this highlight represent potentially transformative research? If so, please explain why. *For more information, see Report to Congress: Transformative Research at the National Science Foundation, April 16, 2008 and Important Notice 130: Transformative Research*

No

How well does the proposed activity broaden the participation of underrepresented groups (e.g., gender, ethnicity, disability, geographic, etc?)

This project does not directly address underrepresented groups.

What may be the benefits of the proposed activity to society?

This activity could improve the efficiency of gene or drug delivery in a laboratory setting with potential applications in stem cell research.

What is the intellectual merit of this activity?

Optical trapping allows a wide variety of single cell and even single molecule experiments, increasing human understanding of biological systems

What are the broader impacts of this activity?
Merit Review Broader Impacts Criterion: Representative Activities, July 2007

Facilitating the research of other CANPBD projects through easy manipulation of micrometer sized objects

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