7. Highlights

University Name: The Ohio State University (OSU)
Cooperative Agreement Number: NSEC-CANPBD Grant #0914790

Science Highlights: http://www.nsec.ohio-state.edu/research_III.html

- Highlight Title: Nanochip Electroporation (NEP): Giving Cells a Shot
  Author Name: L. James Lee

- Highlight Title: Nanotechnology 'Racetracks' for Brain Tumor Treatments
  Author Name: John J. Lannutti

Education Highlight: http://www.nsec.ohio-state.edu/education_III.html

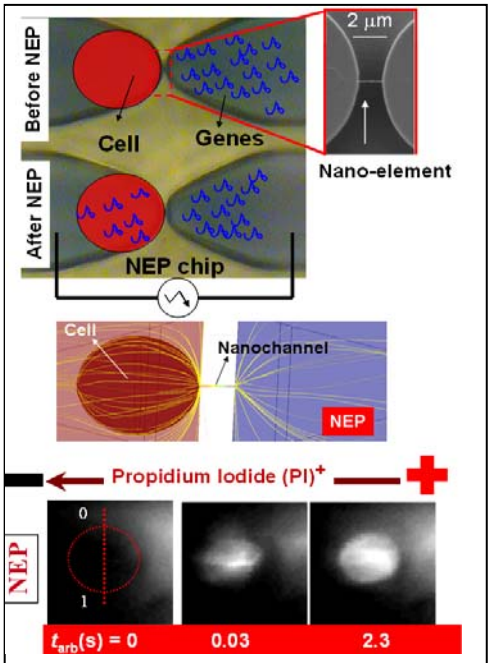
- Highlight Title: Practice Makes Perfect!
  Author Name: Prem Rose Kumar

Shared Facilities Highlight: http://www.nsec.ohio-state.edu/research_III.html

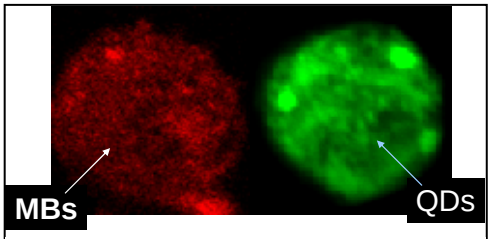
- Highlight Title: Mobile Magnetic Tweezers
  Author Name: R. Sooryakumar

NSF Highlights

Nanochip electroporation (NEP): giving cells a shot



Apparatus and operation of NEP (**Top**). Rapid convective transfection of cancer cell during NEP (**Bottom**).



Transfection of cancer cells by MBs (**Left**) and QDs (**Right**).

The ability to deliver precise amounts of biomolecules and nanofabricated probes into living cells offers tremendous opportunities for biological studies and therapeutic applications. It may also play a key role in the non-viral generation of engineered stem cells and induce pluripotent stem cells with high efficiency and non-carcinogenic properties. Within the past year, our group developed a new technology, nanochannel electroporation (NEP), allowing transfection of many small sized and delicate cells with precise control over dose and timing. Cell mortality from NEP is virtually zero.

The basic element of NEP consists of two microchannels connected by a nanoscale channel. The cell to be transfected is positioned in one microchannel against the nanochannel and the other microchannel is filled with the biomolecules to be delivered. A voltage pulse(s) lasting milliseconds (ms) is then delivered between the two micro-channels causing transfection. We achieve dose control by adjusting the duration and number of pulses. Alternatively, the voltage level and/or the agent concentration can be changed.

Injecting nano-probes into a cell with uniform spatial distribution that can detect, localize, quantify and monitor the specific genes in individual cells are required for advancement in disease therapy, drug discovery and medical diagnostics, but not achievable by conventional delivery methods. However, our novel NEP technique is capable of delivering detecting/imaging agents, including molecular beacons (MBs), quantum-dots (QDs), aptamers and their combinations into isolated individual cells with controlled dose and location. NEP is a powerful tool that can deliver small/large nucleic acids as well as nano-particles provide sensitive detection and mapping of RNAs/protein inside cells with real-time monitoring.

Our NEP chip is also integrated with other technologies including antibody microarrays, optical and magnetic tweezers to create an Automated Cell to Biomolecule Analysis (ACBA) platform. Future efforts by the group are focused on loading large numbers of cells using microfluidics and optical techniques, either through the use of centrifugal forces or automated optical tweezers.

Primary Strategic Outcome Goal:
Establish quantitative calibration of the NEP conditions used vs. the number of molecules being injected by single cell PCR (Polymer Chain Reaction) for fully quantitative measurements.

Secondary Strategic Outcome Goals:
Develop new technologies to transfect large number of cells by NEP.

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 cancer therapy, disease treatment and stem cell research.

What is the intellectual merit of this activity?
NEP allows precise and fast delivery of small and large nucleic acids as well as nanoparticles with no cell damage, increasing our understanding of disease therapy, drug discovery and medical diagnostics.

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 submitted for publications in highly reputed journals. NEP is capable to deliver precise amount of biomolecules and nanofabricated probes into living cells with real-time imaging facilitating the research of other CANPBD projects.

NSF Award Number:
0914790

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

Start Date: 10/01/2009

Expires: 09/30/2014

Awarded Amount to Date $: 12.5 M

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 03/15/2011 by L. James Lee, lee.31@osu.edu, Professor of Chemical and Biomolecular Engineering

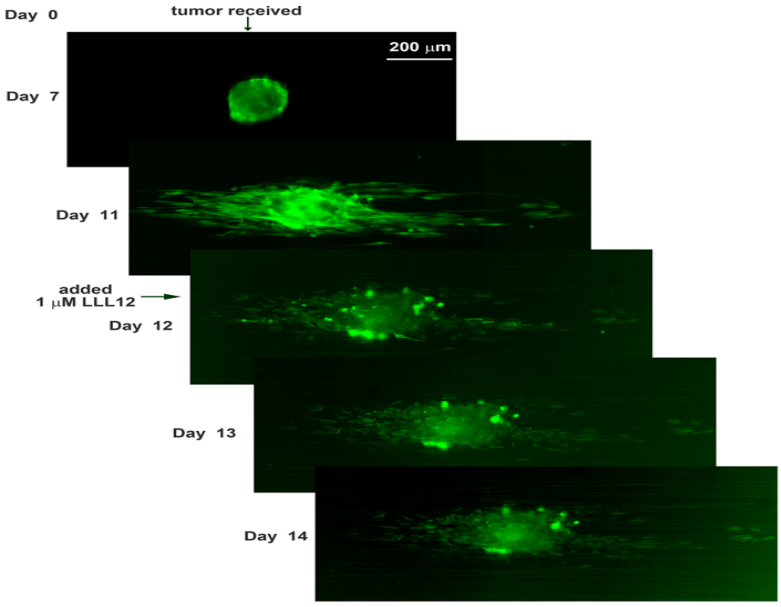
NSF Highlights

Nanotechnology 'Racetracks' for Brain Tumor Treatments

Glioblastoma Multiforme (GBM) is the most common tumor originating within the central nervous system (CNS) and accounts for over 15,000 deaths annually in the US. US Senator Ted Kennedy and columnist Robert Novak were both recent victims of this deadly disease. Infiltration and dispersion of tumor cells into the surrounding normal brain tissue is a hallmark of GBM, and death is nearly always a result of this localized recurrence. However, despite widespread recognition of the importance of dispersion, current laboratory research utilizes two- and three-dimensional cell culture products that do not resemble brain tissue either chemically or down at the nanoscale. In addition, existing three-dimensional products make it difficult to see the cells. Not surprisingly, chemotherapeutic drugs emerging from such cell culture products do not improve clinical responses to treatment.

Nanofiber Coated Plates (NCP), a recent innovation emerging from the Center for Affordable Nanoscale Polymeric Biomedical Devices (CANPBD), consists of a nanofiber-based cell culture device capable of assessing the dispersal of these brain tumor cells. GBM cells cultured on highly aligned nanofiber scaffolds accurately reproduced the elongated morphology that has been described for these cells migrating through neural tissue. In addition, migration of these cells reproduced molecular properties of three-dimensional migration. These analyses revealed that efficient cell migration on aligned nanofibers correlated with the activation of specific signaling pathways. NCP is now a physical product commercially available from Nanofiber Solutions LLC, a spin-off of the CANPBD. NCP has been patented by the Ohio State University as a result of 5 years of research funded by the National Science Foundation. Results show that this product allows assessment of tumor cell motility as well as demonstrating that motile GBM cells are more resistant than non-motile cells to chemotherapeutic drugs.

More recently, we demonstrated that tumor tissue obtained from a high-grade glioma obtained directly from a human patient during neurosurgery could be directly cultured onto NCP and tested for inhibitors of cell migration.



Primary Strategic Outcome Goal:

Assessment of tumor cell motility.

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?)

Every Nanoscale Science and Engineering 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?

The development of effective chemotherapeutic treatments for brain cancer patients. Personalized nanomedicine allowing predictive testing of chemotherapy prior to administration to the patients themselves.

What is the intellectual merit of this activity?

This research has led to the development of a new cell culture product, thus enabling new drug development and the increased potential for more practical uses in a clinic setting.

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 development of a new company creating jobs in the biomedical sector while manufacturing cell culture products that are now available commercially. Reduced trial-and-error testing of chemotherapies and and the resultant greater targeting of mobile tumor cells will be highly beneficial to patients.

Facilitating the research of other CANPBD projects through easy manipulation of micrometer sized objects
ENG/EEC 2010

NSF Award Number:
0914790

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

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

Institution Name: The Ohio State University

State Code: OH

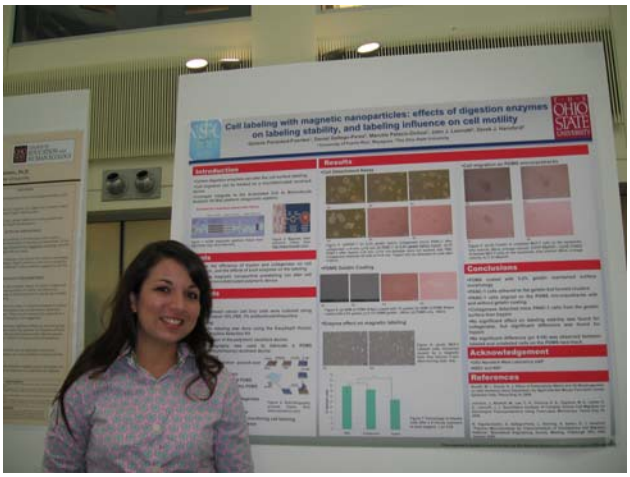
Credit: Center for Affordable Nanoengineering of Polymeric Biomedical Devices (CANPBD), The Ohio State University

Submitted on 03/30/2011 by John J. Lannutti, Professor, Department of Materials Science and Engineering

NSF Highlights

Practice Makes Perfect!

2010 CANPBD REU Interns (pictured above and below) Present their Nanotechnology Research Projects at a Poster Session for Undergraduates



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

Interested in being a researcher in nanotechnology but not sure what it entails? The Research Experience for Undergraduates (REU) Program at the Center for Affordable Nanoengineering of Polymeric Biomedical Devices (CANPBD) at The Ohio State University provides opportunities for potential doctoral students to experience engaging research in nanobiotechnology. The REU Program is a summer internship funded by the National Science Foundation. Students from all over the country participate in this program to work in our research laboratories mentored by a team of faculty, postdoctoral researchers, and doctoral students. Interns in the CANPBD REU Program perform cutting edge research in nanotechnology, learn how to write a technical paper, present their research in a poster session, and interact with other students with similar interests. Previous REU participants have reported that participating in the CANPBD REU Program helped open doors to reputable graduate schools, professional schools, or longer internships in industry.

Pictured at left are five of our nine Summer 2010 REU interns. Some of the exciting research projects they worked on are:

- Synthesis and Biophysical Properties of Polymerized Human Serum
- Nanocharacterization of Microvesicles Secreted from Isolated Cells
- Microfluidic Mixers for Rapid Cell Labeling
- Cell Transport Between Parallel Plates
- Synthesis of Multifunctional Nanoparticles for Cancer Imaging, Therapeutics, and Diagnostics
- Cell labeling with Magnetic Nanoparticles: Effects of Digestion Enzymes on Labeling Stability, and Labeling Influence on Cell Motility
- Detecting and Manipulating DNA with Electrical Impedance Spectroscopy Motivation Results
- Developing a Model for White Matter for Investigating Glioma Cell Migration
- Manipulation of Liposome Nanoparticle Fabrication for Gene Delivery to Optimize Chemotherapy

For additional information on this valuable research training program, and a picture gallery linked to posters of research projects, please visit the CANPBD REU web page at http://www.nsec.ohio-state.edu/education_II.html.

Primary Strategic Outcome Goal:

Encouraging interest in nanotechnology research.

Secondary Strategic Outcome Goals:

Preparing capable undergraduates for doctoral studies.

Does this highlight represent potentially transformative research? *If so, please explain why.*

No

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

The CANPBD REU Program provides a valuable pipeline for the recruitment of underrepresented minority groups into doctoral programs in science and engineering at The Ohio State University. During the past three years, the minority population in our REU Program has been at 80% or higher.

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

The training that REU interns receive at CANPBD, prepares them for doctoral studies and future careers in STEM disciplines.

What is the intellectual merit of this activity?

Stimulating interest in science and engineering, and cultivating intellectual curiosity.

What are the broader impacts of this activity?

Increased enrollment in STEM disciplines.

ENG/EEC 2010
Program Officer: Daniel De Kee

NSF Award Number:
0914790

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

Start Date: 10/01/2009

Expires: 09/30/2014

Awarded Amount to Date: $12.5M

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

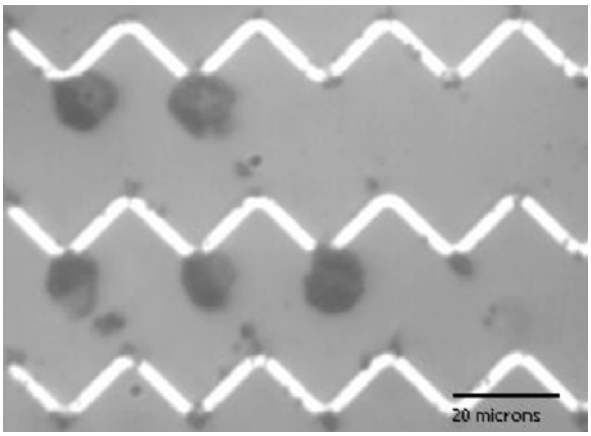
Institution Name: The Ohio State University

State Code: OH

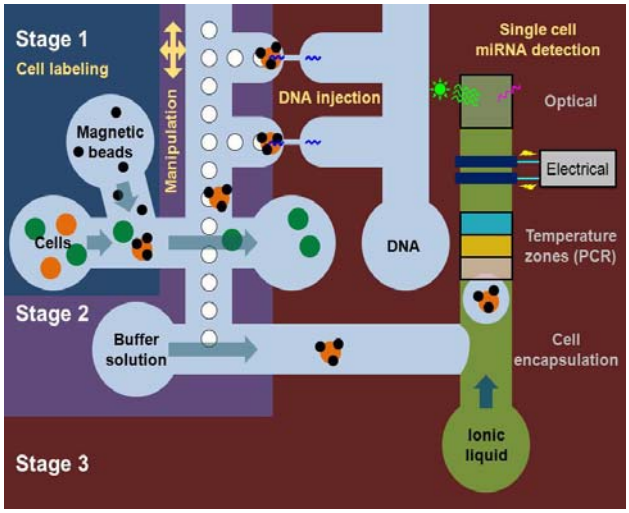
Credit: Center for Affordable Nanoengineering of Polymeric Biomedical Devices (CANPBD), The Ohio State University

Submitted on 03/15/2011 by Prem Rose Kumar, Education Director, CANPBD, The Ohio State University

NSF Highlights
Mobile Magnetic Tweezers



Trapping of several T-lymphocyte cells at vertices of a magnetic zigzag wire patterned on a silicon wafer. The cells are then transported along the wires by weak (~100 Oe) external fields.



.
Platform to: (Stage 1) magnetically label select group of rare cells from mixed population of cells; (Stage 2) manipulate targeted cells to individual ionic droplet or towards gene therapy, (Stage 3) move droplet-encapsulated cell across detection platform for electrical and/or optical analysis. Transport is achieved through patterned magnetic disks and weak external magnetic fields.

Magnetic tweezers allows for programmable manipulation of large numbers of micrometer-sized magnetic particles through the use of traps patterned (wires or disks) onto a surface and controlled via external magnetic fields. Since, when conjugated with appropriate antibodies, magnetic particles will bind to biological cells, the tweezers will enable controlled manipulation of cells within native fluid environments. The advantages of this technology include the wide tunable force range, convenience of remote access, selectiveness to objects with designed magnetic signatures. In addition to low cost and biocompatibility, the platform geometry allows easy observation with a standard microscope as well as for trapping and detecting large numbers of cells concurrently within lab-on-chip devices.

One important potential application of the magnetic tweezers is its functionality as a platform to select a group of rare cells from within a large heterogeneous population of cells – as for example circulating tumor cells in a blood sample. Towards this end the magnetic tweezers group along with collaborators has built poly(dimethylsiloxane) PDMS-silicon microfluidic devices which input a mixed sample of labeled and unlabeled cells and output separated samples. Currently, these devices are being tested for efficiency of cell labeling with magnetic particles; quantifying the efficiency of cell separation; and optimizing design parameters. The device is being integrated with other novel detection technologies being developed within the NSEC to analyze the targeted cells for their biological properties within a single microfluidic device.

In order to transport the cells to the detection stage, individual cells are encapsulated within single ionic droplets that function as microscopic containers that are conveyed through combined fluid- and magnetic-forces. This on-command encapsulation and detection is being developed in collaboration with Dr. Bashir's group at the University of Illinois, Urbana Champaign.

Future efforts by the group are focused on labeling, separating and detecting a few (~10) rare targeted cells from a population of tens of thousands of cells through use of the mobile magnetic tweezers. By detecting rare circulating tumor cells and isolating them, it provides a platform for clinical research, and development of therapeutic pathways for diagnosis and treatment of such tumors, that is not available today. The project integrates the expertise of a broad range of scientists that are central to the development of a single microscopic device that would accomplish this critical need.

Primary Strategic Outcome Goal:

Isolate and explore properties of cells using magnetic tweezers and novel detection schemes for diagnosis and evaluation of the impact of experimental therapy on cells.

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*

This research provides a revolutionary approach to select, transport and interrogate rare biological cells from a heterogeneous cell population. Integrating this magnetic tweezers-based technology within nano- and micro-scale devices for transporting biological and inert entities offers potential applications across diverse fields ranging from electronics to medicine.

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

The joystick and voice activated protocols as well as the low cost technology will enable teachers and students (middle and high school) from a variety of ethnicities and backgrounds to learn about important aspects in engineering and how they are applied to biology and medicine.

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

The ability to remotely control and manipulate individual or multiple cells and tiny magnetic particles will not only contribute to medicine and biology but also permit new types of nanotechnology-based devices such as miniature pumps and engines to be created.

What is the intellectual merit of this activity?

The application of directed forces to a single or large ensemble of individual ultra small objects in near-native environments is a major challenge in current engineering or biological research. The use of nano-scale magnetism to organize the energy landscape in materials at the nano-to micron-scale will underlie the development of novel on-chip structures with embedded biological and engineering functionalities.

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

The mobile magnetic tweezers offer the control needed for rapid progress at the frontiers of several branches of science and engineering. The tiny (pico-Newton) forces are ideally suited for manipulating biological cells and molecules from the sub-cellular to multi-cell scale. Nanoscale engineering will benefit from options for organizing, manipulating and analyzing individual tiny objects and integrating them into functional devices. The research trains graduate and undergraduate students in emerging interdisciplinary fields as nanotechnology and biotechnology that need a skilled work force.

Facilitating the research of other CANPBD projects through easy manipulation of micrometer sized objects
ENG/EEC 2010
NSF Award Number:
0914790
Award Title: Center for Affordable Nanoengineering of Polymeric Biomedical Devices (CANPBD)
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 03/15/2011 by R. Sooryakumar, sooryakumar.1@osu.edu