Louisiana EPSCoR
Volume 3
Number 9
Sep. 2006
Experimental Program to Stimulate Competitive Research

Thinking Small is Big Research

Think small…smaller…smaller… Only if you reach 100 to 1,000 times smaller than the thickness of a human hair, will you be in the neighborhood in which a multi-institutional, interdisciplinary team of Louisiana researchers is developing microscale to nanoscale medical devices.

The focus of the Center for BioModular Multi-Scale Systems (CBM^2) team is on solving scientific challenges in the design and development of BioMicroElectroMechanical Systems (BioMEMS), smart, miniature, low-cost biomedical devices that promise to revolutionize biomedical discovery and clinical practice.

"Because they offer faster analysis time and better sensitivity when compared to traditional benchtop systems, BioMEMS have gained wide acceptance for use as analytical tools," says Dr. Steve Soper, CBM^2 Director and LSU William L. & Patricia Senn Jr. Professor of Chemistry. "We are also developing devices that detect biopathogens for homeland defense and portable devices that read DNA signatures for forensics and paternity testing."

CBM^2's core facilities are situated on the pastoral setting of the South Campus of Louisiana State University and A&M College (LSU). Located some three-and-a-half miles from the main LSU campus, the facility is a 35,000 square foot building that contains 22 laboratory suites, four conference rooms and 30 offices.

The CBM^2 team includes investigators with expertise in microsystems, engineering, materials, chemistry, and biological sciences from the participating institutions and LSU's Center for Advanced Microstructures and Devices (CAMD). (See *CBM^2 Participating Institutions* on page 2.) The 27 research-active faculty are mentoring 150 graduate students and have had over 100 publications in peer-reviewed journals per year since its founding just over two years ago.

"The Center also provides laboratory space for researchers and students from the various institutions involved as well as lab space for visiting scientists to conduct work and evaluate the technologies," says Dr. Soper. "Additionally, plans are evolving to build core facilities and instrumentation to support the fabrication of nanometer to micrometer scale structures and materials research.

"Being off-campus, it provides better access to outside users of major research instrumentation, which is especially critical for researchers in Southeast Louisiana who had their research infrastructure devastated by the 2005 hurricanes. We are, for example, currently sharing our facility with the LSU Dental School, which has been temporarily displaced."

Among the challenges of current CBM^2 projects are improved DNA sequencing, "personal genome" projects, and faster, more efficient procedures to identify a predilection or presence of a disease. The following are examples of just some of those research projects.

Researchers in the **Microfabrication and Chip Assembly Lab** are working on the development of new Lab-on-a-Chip devices that integrate multiple laboratory functions on a single chip of only millimeters to a few square centimeters in size. These miniaturized

Professor Steve Soper, left, Dr. Suzanne Lassiter and Dr. Musundi Wabuyele in the CBM^2 DNA Sequencing Laboratory.

systems can perform the same functions as large benchtop instruments commonly used in research and clinical labs, but at a much faster rate and with fewer reagents, which will significantly reduce assay costs.

"All of the operations are processed inside channels narrower than the width of a human hair," explains CBM^2 Research Associate Dr. Mateusz L. Hupert. "One extremely powerful technique that takes 45-90 minutes in a benchtop machine can be completed in less than five minutes in the microchip."

Another Center focus is the discovery of new biomarkers and the assays around those biomarkers. These assays can be used for a variety of applications, such as disease diagnostics, forensics and/or homeland defense applications. The Center personnel are moving many of these assays to microchip systems for point-of-care operation.

A **Dry Etching and Molding Lab** is developing a microfluidic platform configured in a 96-well format that can collect DNA from clinical samples and make it ready for molecular profiling.

"Plastic biochemical analysis devices, manufactured by a mass production molding process developed by CBM^2, are bio-compatible and will enable the realization of highly parallelized biochemical analysis at a low cost in fabrication and operation," says Research Associate Dr. Daniel Park. "These highly parallel systems will be used for discovering new drug candidates for therapeutic targets in conjunction with Tulane Professor Prescott Deininger."

An objective of the **Nanosystems Lab** is to develop technology to create nanostructures that are 100 to 1,000 times smaller than the thickness of hair in a cost effective way. The key technology being used is nanoimprint lithography (NIL), a molding technique that Dr. Sunggook Park, LSU Assistant Professor of Mechanical Engineering, compares to making waffles.

Facilities, Continued on pg 2

Facilities, *continued from pg 1*

"It starts with a batter-like substance that is stamped with a patterned surface similar to a waffle iron. Heat and pressure are applied and within a short period of time the original 'batter' leaves the machine with a highly patterned surface. Patterns smaller than 10 nanometers have been created," he says.

Currently, the Nanosystems Lab has two primary foci: understanding the fundamental chemical and mechanical interactions occurring during the NIL process, e.g. what happens to the batter and waffle iron as the waffle iron grooves become increasingly small? The intent is to develop NIL into a more reliable, versatile technology that can fabricate nanostructures for various applications.

The investigators are also working to integrate nanostructures into micro- and macroscopic systems. "The target application is bio-related systems to allow researchers to analyze, manipulate and study the many bio-entities with nanosize dimensions, such as proteins and enzymes," says Dr. S. Park, who recently received a National Science Foundation CAREER award to support his work.

He adds that the high-throughput, low-cost NIL technology being developed in the Nanosystems Lab could be adopted at the industrial level and has the potential to promote economic development by attracting external research funding and investment and creating new Louisiana jobs.

A **DNA Sequencing Lab** is developing a modular-based microsystems approach for analyzing the primary structure of the human genome. The initial goal of the Human Genome Project was to unravel the sequence of our genome at a cost of $2.7 billion. Using today's state-of-the-art technologies, it still costs over $10 million, the use of many machines and highly trained people as well as over one month of intense work to sequence an individual's genome," says CBM² Research Associate Dr. Hong Wang.

"The new challenge, a 'personal genome project' or ultra low cost sequencing, has sequencing goals of delivering sequence information from an entire genome at $100,000 in 2009, and $1,000 by 2014. Once the latter is approached, every individual can have his genome sequenced for his doctor's reference."

According to Dr. Wang, a microfluidic sequencing system that greatly reduces the reagent consumption and labor cost is the most promising approach toward the near-term goal of $100,000. "A several hundred square foot sequencing lab could be adapted on a several square inch microfluidic chip or Lab-on-a-chip," he adds.

CBM² Participating Institutions

The Center for BioModular Multi-Scale Systems is the centerpiece of a 2004 $9 million National Science Foundation EPSCoR grant matched by $3 million from the Board of Regents Support Fund and $1.5 million from the participating institutions.

A multi-institutional, interdisciplinary collaboration, CBM² includes researchers with expertise in microsystems, engineering, materials, chemistry and biological systems at LSU, LSU's Center for Advanced Microstructures and Devices (CAMD), the LSU Health Sciences Center in New Orleans, Tulane Health Sciences Center, and Xavier University in New Orleans.

"The information obtained from the human genome project has already been used for diagnosing and predicting a person's predisposition for certain genetic diseases, including breast cancer, colon cancer and Alzheimer's disease," he says. "A low cost, ultra fast sequencing technology, including the modular microfluidic DNA sequencing system developed in our lab, is critical to expanding the number of diseases on this list. In collaboration with LSU Professor Mark Batzer, this high throughput instrument will be used for understanding the structure of repeats found in the human genome, which can be used for DNA forensics."

A **DNA Imaging Lab** project will significantly speed up the ability to view molecular signatures of certain diseases using BioMEMS. "Because a patient's sample is extremely sensitive to environmental contaminants, the rapid processing of clinical specimens is essential," explains Research Associate Dr. Feng (Frank) Xu.

"We integrate the fabrication of waveguides in a microfluidic chip. The excitation light is delivered to fluorescent probes contained in a fluidic channel, making possible the sensitive detection of biomolecules. If there is no fluorescent signal, we know immediately that the sample is normal."

"Our ultimate goal is to build a national 'Center of Excellence' in micro-/nano fabrication for biology and medical purposes," says Dr. Soper.

Referring to a CBM² project funded by one of Korea's largest nanotechnology research programs, Director of Louisiana EPSCoR Dr. Michael Khonsari adds:

"CBM²'s pioneering research and development on the design and fabrication of functional, high-performance biological tools and devices is putting Louisiana on the map as a major player at the international level."

Louisiana EPSCoR
P.O. Box 3677
Baton Rouge, LA 70821-3677