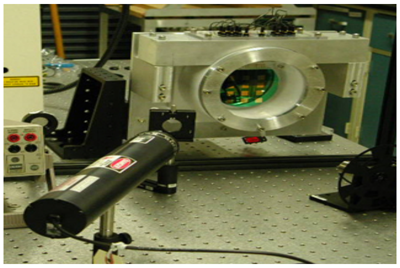
# Biological Micro-Electrical Mechanical Systems (bioMEMS)



**Micro-electrical mechanical systems (MEMS) created new capabilities for semiconductor chips, but their applications for biotechnology are only beginning to be explored. bioMEMS combine the potential of cell-sized systems with the advantages of a billion years of biological evolution. They enable dramatic new possibilities for detecting, analyzing, and manipulating biomaterials, from proteins to bacteria to blood. Researchers at the University of Maryland engage in cutting edge research in bioMEMS to revolutionize mechanized drug discovery processes, non-invasive therapies, point of care medical diagnostics, and biochemical detection devices.**

Reza Ghodssi and Don DeVoe integrate organic and microfluidic substances with MEMs devices to create novel systems that enable extremely precise detection of bacterial pathogens and biochemical molecules. Their research, which fosters innovations such as handheld contamination detectors, has important applications for homeland security, food safety, and any other environment that demands hyper-sensitive sensing.

Pamela Abshire and Elisabeth Smela build nano-scale biochips that combine integrated circuits with living biological cells. These "labs on a chip" can be housed in the body, or, like the devices Ghodssi develops, carried in public spaces and used wherever on-the-spot detection of chemical substances may be important.

Gary Rubloff and Ben Shapiro develop microfluidics technologies that extend bioMEMS' ability to respond to their environments. Their work with electronic deposition of biomolecules and microfluidic steering promises breakthroughs in tissue analysis, drug discovery, and targeted drug delivery.
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## *Handheld Biohazard Detection*

Reza Ghodssi merges bio- and nano-technology to create portable devices that detect individual molecules with unprecedented sensitivity. He fabricates nanoscale sensors consisting of vibrating cantilevers coated with chitosan, a glue-like extract from crab shell waste. These devices can detect even a single bacterium trapped by the sticky chitosan.

Systems Ghodssi develops will drive a range of innovations in medical diagnostics, environmental monitoring, and ultra-rapid biohazard detection. A sensor installed in a large HVAC system could detect and isolate airborne pathogens before they spread. Soldiers could carry palm-sized bio-weapon detectors into war zones. Consumers could test a fast-food burger for contamination before their fries got cold.

**Reza Ghodssi** ghodssi@umd.edu http://www.isr.umd.edu/faculty/gateways/ghodssi.htm

## *Rapid, Precise Identification of Target Molecules*

Don DeVoe develops polymer microfluidic biochips that can rapidly detect diseases, bio-hazards, and other bio-markers from tiny clinical samples, all with extremely precise specificity. These chips are networks of nano-scale chambers and tunnels that control a flow of liquid, which in turn transmits biochemical information from cells in the chambers.

By identifying how individual molecules are differentially regulated by their surroundings, DeVoe "programs" chips for a range medical diagnostic purposes, including rapidly distinguishing between healthy and cancerous tissue, accurately identifying stages of cancer, and determining the best treatment regimens for patients. He is currently expanding the technology to examine more complex cellular arrangements, including human tissue.

DeVoe also develops nanofilament silicon chips and nanopore sensors for handheld pathogen detection systems, and microfluidic methods for detecting the molecular signatures of explosives.

**Don DeVoe** ddev@umd.edu http://www.nanocenter.umd.edu/faculty/faculty_detail.php?user_id=75

## *Cell Clinics – Nano-Laboratories for Automated Pathogen Detection and Response*

Elisabeth Smela, Pamela Abshire, and Benjamin Shapiro (see below) recently won the University of Maryland's Invention of the Year Award for their "cell clinic" pathogen detection system. The key nanotechnology – integrated sensor actuation control – "captures" and characterizes individual cells rather than group averages. As a result, these biological-machine hybrids are much more specific and sensitive than existing chemical sensors. They should thus eliminate false alarms, and even differentiate between strains of the same toxin.

Abshire and Smela plan to use this technology to reduce an entire biological laboratory to the size of a computer chip. Such "labs on a chip" could lead to fundamental new biology (such as understanding immune system activation or cancer cell growth), and markedly improved in vivo diagnostics and drug/toxicity screening.

## *Adaptive Circuits – Mechanized Troubleshooters for Integrated Circuitry*

Abshire and Smela also improve nanotechnologies that optimize the performance and minimize resource usage of integrated circuits. For example, Abshire uses histogram equalization to develop adaptive circuits, which use information captured from the environment to automatically troubleshoot imperfections in integrated circuits and systems. Adaptive circuits can even add new features, such as self-adjusting analog-to-digital converters. The technology has enormous potential for adaptive sensory-signal processing. For example, if an enemy jamming device was blocking frequencies used by military hardware, the adaptive circuits could rapidly re-engineer the system to use other frequencies.

**Pamela Abshire** pabshire@umd.edu http://www.ece.umd.edu/meet/faculty/abshire.php3
**Elisabeth Smela** smela@umd.edu http://www.nanocenter.umd.edu/faculty/faculty_detail.php?user_id=76

## *bioMEMS Drug Discovery "On Demand"*

Gary Rubloff's bioMEMS automatically fabricate microfluidic devices that insert biological elements into targets only on demand. Incorporating integrated sensors, Rubloff electrically programs the deposition of bioactive chitosan surfaces. Proteins, enzymes, DNA, and viruses all retain their critical biological activity when attached to these surfaces. In research unique to the University of Maryland, Rubloff has begun reconstructing the enzyme catalytic pathway responsible for "quorum sensing," whereby bacteria become aggressive and develop into pathogens. His artificial pathway provides a test bed for identifying new anti-microbial drugs that simply shut down the growth of bacteria before the formation of antibiotic resistance.

Rubloff develops technology to capture individual cells and "interrogate" their responses to various stimulants. This ability to understand and control reactions at the nano-scale level is the fundamental element underlying all nanotechnology innovations.

**Gary Rubloff** rubloff@umd.edu http://www.isr.umd.edu/faculty/gateways/rubloff.htm

## *Fluid Vehicles for Steering Nanoparticles to Targets*

Combining bioMEMS with control theory, Benjamin Shapiro steers nanoparticles to targets such as pathogenic cells. Shapiro provides bioMEMS with the basic elements of feedback control – dynamic responses to errors and uncertainty. Sensors he develops can detect the position of nanoparticles (such as cells carrying drugs or diagnostic markers) in relation to their target. He then guides the particles as needed by moving a microfluidic buffer that surrounds them. Rather than steering directly, which could change cell properties, Shapiro uses magnetic fields to steer this surrounding buffer. He can direct nanoparticles to a target the size of one micron.

The simple, inexpensive equipment Shapiro uses (such as micro-tweezers) suggests that his research will enable cost-effective targeted drug delivery and point of care diagnostics. One of his current efforts is steering chemotherapy-coated nanoparticles to deep tissue tumors.

**Benjamin Shapiro** – benshap@umd.edu http://www.controlofmems.umd.edu/index.html