Position Paper: BioMEMS - At the Interface of In Vivo Intervention and In Vivo Diagnostics

Abraham P. Lee.
Microsystems Technology Office, Defense Advanced Research Project Agency
Arlington, Virginia 22203-1714

Designing a Paradigm Shift: BioMEMS Over the last 12 years, Microelectromechanical Systems (MEMS) has produced commercial products such as accelerometers, chip-scale digital mirror displays, and inkjet printer heads. Most recently, the biotech and biomedical community has accelerated their investments in MEMS for biological applications. Sales in a subset of MEMS, namely Biochips and Microfluidics, has reached over 21% of the MEMS market in 1996. The estimate is that by 2003, microfluidics applications will account for 41% of the total MEMS market. Researchers are confident of "BioMEMS " potential since the market potential is larger than MEMS alone. The BioMEMS industry is less conservative, and it's a little bit dangerous because we know less what works and what doesn't. Because BioMEMS have the potential for being disposable, there is a constant re-supply market. On the other hand, a MEMS pressure sensor or an accelerometer may last for up to 10 years. Although BioMEMS products are just beginning to reach the marketplace, the global MEMS market topped out at $1 billion in 1998 and is projected to reach more than $10 billion by 2003.

BioMEMS applies microdevices to biological and medical problems. In their simplest form, technologies in the BioMEMS arena leverage advances in microfabrication and micromachining to create faster, cheaper, hands-off micro- and nano-scale laboratories. In more sophisticated forms, BioMEMS devices offer an avenue to artificial organs, personalized drug therapies, and new ways to view cell communication. BioMEMS can be characterized into two categories: 1. Biomedical MEMS that deals in vivo with the body and the host anatomy and, 2. biotechnological MEMS that deals in vitro with the biological samples from the host. Examples of biomedical MEMS include minimally-invasive therapy precision surgery, biotelemetry, drug delivery, biosensors, and other physical sensors. Examples of biotech MEMS include gene sequencing, functional genomics, drug discover, pharmacogenomics, diagnostics, and pathogen detection/ID.

As advances in genomics and proteomics provide us with more and more information regarding the origin of diseases, more and more of the human body's complex signatures are available to be read by BioMEMS "barcode readers". Chip-scale, MEMS -based transdermal devices are enabling continuous access to body fluids and the continuous monitoring of molecular, cellular and physiological biomarkers. On the other hand, this transdermal conduit can enable continuous transdermal delivery of drugs and other appropriate antidotes, perhaps in a real-time feedback configuration.

The goal of DARPA's Bio-Fluidic Chips (BioFlips) Program is to demonstrate IC-like microfluidic processors that are reconfigurable and can be self-calibrated for the handling of complex biofluids. The program will integrate these new BioMEMS devices for the presymptomatic detection of infected personnel through "skin patch" chip detectors that detect invading pathogens and/or the resulting host defense biomarkers. These bio-fluidic chips will integrate diagnostics, rapid detection and potentially treatment in one single chip. Another area that will feel the impact of BioMEMS is patient monitoring. By implanting miniature endocrine devices, for instance, patient medication or the need for additional testing can be added more rapidly than today's techniques allow. BioFlips will provide the technology foundation for wearable, wristwatch-sized chips that directly assess the vitality of personnel (such as their fatigue level or whether they have been exposed to biological or chemical warfare agents) through continuous body fluids monitoring.

There are numerous military application for these BioMEMS technologies. The commander will one day have real-time access to the readiness-for-war status of his troops with parameters ranging from drug use to biological agent infection. The chips can also be used for triage in combat casualty care situations. MEMS biofluidic chips can also be used in a testing scenario, where the commander can correlate the warfighter's performance with his/her health status using the most sensitive biomarkers expressed in the circulating body fluids. Performance enhancement drugs can be administered real-time during urgent missions (e.g. air force pilot or missile launcher personnel). Future testing would incorporate the "whole" system, from "flesh to hardware" so that the testing can reflect the true "war scenario".

Civilian medical applications include the presymptomatic detection of host defense biomarkers and the continuous monitoring of high-risk (e.g post-surgery) or chronically-ill patients. Through BioMEMS and microfluidics, the on-chip integration of in vitro diagnostics and in vivo therapy (sample acquisition and drug delivery) will be made possible. Currently, technologies and procedures for diagnostics and therapeutics/treatment are separate and seldom overlap.

There are three sectors that are interested in BIOMEMS but motivated by different factors. The government, motivated by national healthcare, biowarfare defense and combat casualty care. The biotech industry, represented by small companies developing microarray biochips and motivated by drug discovery and genomics based diagnostics. The biomedical industry represented by traditional medical device/instrumentation companies and motivated by microsurgery, drug delivery, implants and point-of-care diagnostics. The recent surge of bioengineering centers/departments across the nation is also highly motivated by the potential of BIOMEMS to improve healthcare quality while simultaneously reducing healthcare costs.

The promise of BioMEMS technology rests on the ability to deliver mass-producible, microdevices that are cheap and reliable. Basic device designs in the field draw directly on designs for MEMS for the auto industry and telecommunications, but refining those designs and finding just the right materials for biological and medical applications are consuming researchers current attention. The favored material for traditional MEMS platforms is silicon, but this material is not transparent and is expensive to micromachine. Silicon is a workhorse at a functional level, but is not necessarily bio-compatible. When devices are implanted or interact with the human body, other substrates that work in concert with the body or mimic it are required. Research efforts are shifting to plastics, polymers, and elastomers.

Satisfying substrate requirements, integrating disparate components, and overcoming device aspects the size of a human hair requires an interdisciplinary research and engineering effort.

Although electrical and mechanical engineers have dominated the MEMS field, teams of engineers, biochemists, molecular biologists, physicists, and clinicians are needed to push BioMEMS efforts forward. Otherwise, BioMEMS will remain just a research field.