

## SESSION 7

# MICROFABRICATED BIOSENSING DEVICES: MEMS, MICROFLUIDICS, AND MASS SENSORS

**Antonio J. Ricco**

The capability to microfabricate sensors, actuators, and the components of microsystems has become commonplace in the past decade. Microelectromechanical systems, or MEMS, commonly describes devices and integrated microsystems in the micrometer to millimeter size range, fabricated using technologies akin to the lithographic patterning and physical/chemical feature definition processes developed for electronic semiconductor chips. As the acronym implies, MEMS devices differ from traditional electronic components in the inclusion of mechanical features: actual moving parts, or simply structures for which physical parameters such as pressure, stress, or acceleration perturb the device mechanically to produce a signal, or where mechanical effects are used to implement device function, e.g. in an actuator. In the past ten years, MEMS devices have found increasing commercial success in applications ranging from intravenous blood pressure transducers to automobile airbag accelerometers to digital light projectors,

MEMS is expanding from its roots in electromechanical devices in multiple directions at once. Explosive growth in optical telecommunications applications (followed unfortunately in the commercial world by a smaller but nearly as impressive implosion) stretched the capabilities of, and demands upon, this technology. The emergence and integration of nanotechnology—manifested in both nanostructured materials and in sub-micron fabrication approaches—only recently pushed device feature size into the nanometer range.

The context of “mechanical” in MEMS expanded in the early 1990s from the solid phase to include the liquid: microfluidic systems use similar fabrication approaches to traditional MEMS, but manipulate and interrogate liquid streams and droplets rather than solid structures. MEMS has cautiously pushed the range of materials of construction beyond those of the semiconductor industry, with increasing use of polymers offering the promise of less expensive devices for some applications, and integration of diverse materials enhancing functionality for others. Discrete devices are now giving way to integrated subsystems that include input/output capabilities, data processing, closed-loop sensing and actuation, and multiparameter measurements from a single microsystem.

While it is an area with enormous promise, biosensing is arguably the most challenging area into which MEMS and allied technologies are presently expanding. The interface between wet, salty biological samples and materials/devices adapted from the microelectronics industry is not an easy one: electrical connections must be well encapsulated while leaving biochemical or biomechanical interfaces exposed to the sample. Added to the handful of physical parameters measured or controlled by traditional MEMS devices are many thousands of biochemical measurands, often requiring a unique, tailored interfacial sensing material for each and every analyte: a different antibody for each protein, a different strand of nucleic acid for each gene. The range of materials that must be used in device manufacture is much vaster than for physical or even chemical sensors, and many pose unique challenges for deposition, characterization, and maintenance of long-term viability: these offer opportunities for high-impact technological advances.

In biosensing the manipulation of materials properties is critical, for the interface between the physical device and the biological measurand requires simultaneously satisfying conditions for selective, predictable biological interactions and providing reproducible perturbation of sufficient magnitude for reliable detection. Further complicating the design of the biochemical interface are the ultralow limits of detection demanded by some applications, which thus require exceptional stability and high sensitivity: a single molecule, a single surface receptor, or a single copy of a gene from one cell may be the ultimate analytical target for the early detection of cancer or the analysis of a virulent pathogen.

Because direct measurement of scarce targets in a dilute and complex biological milieu is so challenging, the drive to miniaturize, integrate, and automate the techniques of the biochemical laboratory in a “MEMS-like” fashion has spawned major activity in microfluidics. Foremost among the goals is the so-called “sample-to-answer” device that accepts a raw biological sample, performs a complex series of biochemical manipulations—everything from filtration to “amplification” (replication) to purification—and then detects multiple target analytes with high sensitivity, high selectivity, and wide dynamic range.

The advantages touted for microfluidics, a number of them being inherent advantages of integrated MEMS in general, include: miniaturization to conserve costly reagents and limited samples; parallelization to handle many samples in parallel; multiplexing to analyze multiple targets for each sample; automation and integration to save time, labor, and manual sample transfers, decreasing the chance of human error and thereby improving reliability and accuracy. These benefits can be realized using a toolbox of microcomponents including channels, reservoirs, fluid interconnects, valves, pumps, electrodes, electrical interconnects, sensors, and detectors which are used to implement such functions as dispensing, distributing, mixing, filtering, preconcentrating, diluting, binding, releasing, washing, heating, separating and detecting. Combining several diverse building blocks to accomplish multiple preparative tasks is far from routine or commonplace, but will have significant impact when it is.

The greatest academic activity and much commercial attention have focused recently on systems that use electrokinetic means to motivate and separate species in fluidic channels, attractive features being the lack of moving parts—only the application of high voltage to on-chip electrodes is necessary—as well as the ability to both pump liquids and to effect high-resolution separations according to molecular size and charge. Nonetheless, the clever utilization of capillary-flow and pressure-driven fluid movement have shown significant promise and versatility as well, with pressure being supplied by external pumps or pressurized gas, chip-mounted micromachined pumps, on-chip electrolysis of water, or by spinning the chip to achieve centrifugal pumping. As with other MEMS approaches to biosensing, materials compatibility, manufacturability, and longevity are critical parameters for fluidic systems. In contrast to most MEMS, microfluidic devices have been developed most often on glass (silica) or polymer substrates, owing to bio/chemical materials compatibility, use of very high electric fields, and/or the use of high sensitivity optical detection at relatively short wavelengths.

A final biosensing approach in which MEMS technologies have played a key role is mass sensing. This approach is attractive because it is a “label-free” method, i.e. the inertial mass of the analyte molecules leads to a detector response. This is to be contrasted with many popular optical or electrochemical methods in which a fluorophore or electroactive “tag” molecule is attached specifically to the species to be detected. Mass detection does not, however, remove the need for specific interfacial biochemical recognition: analyte molecules must be selectively recognized and anchored in preference to all other species. Herein lies a key limitation (and a key area for improvement) of label-free detection: nonspecific adsorption. Suitable reference devices and clever surface chemistries have the potential to prevent false positive signals from arising due to simple physical adsorption of a component of the sample matrix.

Nanotechnology should eventually play a particularly important role for mass sensors, because increasing the number of receptor sites on the probe surface typically enhances sensitivity in direct proportion. “Meso-scale” thin-film materials (many of which have been rechristened nanomaterials) retain many advantageous characteristics—such as well-defined binding sites—of molecular monolayers, but are tens to thousands of molecular diameters in thickness and may incorporate controlled porosity to provide selective access to internal binding sites as well.

The MEMS devices utilized for mass detection include (1) those utilizing the piezoelectric effect to generate in a small “slab” of material traveling or standing acoustic waves, the propagation characteristics of which are perturbed by changes in the mass or mechanical properties of a thin film upon the oscillating device surface, and (2) those taking the form of micro- or nano-fabricated cantilevers, the resonant frequency of which is a sensitive function of the inertial mass of the cantilever and whatever sticks to it. A principal limitation of both types of oscillating mechanical device when used in biosensing is the potential for intolerable levels of damping of the acoustic wave by the liquid. In the case of piezoelectric devices, those acoustic modes that lack a surface-normal component of motion, or those whose propagation velocities are slower than the speed of sound in water, are only weakly damped. For micro/nano cantilevers, oscillation in liquids is (barely) possible, but an effective alternative is to design a biochemical interaction that alters the stress in a thin film on one side of the devices surface, thereby changing its static bend, which can be read out optically, capacitively, or using built-in silicon piezoresistors. Making such transduction a general-purpose approach to biosensing remains to be demonstrated and, generally, providing specific biochemical coatings on micron-sized cantilever tips is a challenge.

The presentations in this session focused on the challenges of selectively, sensitively, and robustly coupling biochemical analytes to MEMS in general, and to micro/nanodevices that respond to mass or mechanical perturbations in particular. The complexity of biological samples was addressed by the implementation of a range of laboratory processes in integrated chip format to both reduce the complexity of the sample and make it more readily detectable. The role of interfacial chemistry is central to biosensing with such systems, and there is a key enabling role and opportunity for structured as well as molecularly defined materials.

The sorts of biosensing applications where an effective combination of MEMS and interfacial materials can have major impact include diagnostic devices that rapidly measure cellular, genetic, and proteomic signatures and patterns (*not* single analytes;) new approaches for the massively *parallel*, high information-content drug discovery process; and the high-sensitivity, low-false-positive *multiplexed* detection of biological and biochemical pathogens.

## ULTRASONIC BIOSENSORS

Amit Lal

### DRIVERS AND ROADBLOCKS

Ultrasonic sensors utilize the change in mass of a sensor and the corresponding effect on frequency or time-of-travel to measure bound biomolecules, either by specific or unselective binding. The commercially available devices generally have used resonant quartz crystals (QCM-Quartz Crystal Microbalance), or surface acoustic wave (SAW) devices to measure the change in surface acoustic wave. One of the key advantages offered by ultrasonic mass measurement sensors is electronic readout, and the measurement of frequency, which can be measured with high degree of precision using conventional electronics. This electronic compatibility makes these sensors comparatively more accessible. The application of these sensors in thin-film deposition equipment has led to widespread commercial availability of QCM and SAW mass sensors.

Last ten years have seen a tremendous increase in new device architectures for ultrasonic mass sensing, predominantly driven by the broad development of micromachining techniques. Recent activities in ultrasonic mass-based sensors have been largely driven by micromachining technology, and the corresponding devices designed at the microscale. The first case of using micromachining for biosensors came from Richard M. White's (University of California-Berkeley) group. He used the ability to fabricate silicon-nitride suspended membranes and piezoelectric thin films to launch flexural plate waves on the silicon-nitride thin films. One of the main advantages of FPW device is that the wave speed in the membrane can be smaller than in water. This leads to energy trapping near the membrane allowing sensor operation in water continuously as biomolecules attach or detach. This is a major improvement over QCM or SAW devices where biosensing involved the drying of the sensor after placing in solution containing the analyte molecules, and comparing the frequency or wave speed before and after the attachment. The FPW sensor also works at lower frequencies enabling inexpensive electronics to be used. Various investigators in Europe and Japan have followed the FPW work. Further challenge in FPW development has been the sensitivity to many variables like temperature and pressure, being addressed by reference and active sensors. A major possible development in this device is a large array of sensors with integrated electronics for massive parallel analyte detection enabling applications in mass markets such as contaminant monitoring in the food industry.

Stanford group led by Pierre Khuri-Yakub have developed an all-surface micromachining process to electrostatically excite flexural plate waves and other modes. Electrostatic excitation has the advantage of not requiring piezoelectric thin film technology. The group has also tried to develop integrated electronics, which could lead to arrays. The use of electrostatics, however, entails the use of a DC bias, which can make portable devices harder to implement.

Another approach to FPW excitation is being developed in the SonicMEMS group at Cornell in which bulk-piezoelectric PZT ceramics (PZT-Lead Zirconate Titanate Oxide ceramics) are being used to excite an array of silicon nitride membranes. The higher power excitation onto any micromachined membrane surface allows for frequency addressable sensor activation, and still have sensor operate at 5 volts or lower. The problem of nonlinearity and high voltage bias in electrostatics is eliminated, and using commercially available piezoelectric materials eliminates the problem of using special piezoelectric film. They have demonstrated very low voltage (<1 Vpp) excitation of FPW. Using piezoresistive sensors for feedback, FPW sensors can be implemented with electronic feedback.

Another advantage micromachined thin structures is easy excitation of high-amplitude ultrasound that leads to second order nonlinear effects in fluids. Acoustic streaming and radiation forces have been utilized by many research groups (Berkeley, Cornell, Stanford, and USC-E.S.Kim). Acoustic streaming can be used for functions such as pumping and separation, which are independent of sample electrical conductivity or dielectric properties, and without requiring electrodes inside the sample, as acoustic waves can be projected from the outside. This can enable microfluidic operation, in addition to sampling, in a very general microfluidic framework. Recently, acoustic chromatography (SonicMEMS laboratory) was developed in which two degrees of acoustic fields were used to focus antibody-coated beads at specific locations and to separate bioentities by size (or mass), using a device operating from 1Volt power supply. Acoustically actuated surface micromachines have been used to trap particles in streaming-induced vortices. This leads to sample concentration or localization of the analyte near the sensor. Such operations in more integrated systems are the key to integrating various functions using the same set of actuators.

### **CRITICAL PARAMETERS IN THE PROCESS OF BIOSENSOR DEVELOPMENT**

Sonic biosensor development has progressed largely by scientists investigating biological applicability of sensors made for measuring physical quantities. Furthermore, the sensors have been developed without regard to total system integration. The use of microfluidics and micromachining has led to sensors that have been developed specifically for biosensing, and system integration has been the focus. The current development process is focusing on developing technologies that will make field portable systems in a low-cost framework. This process needs to continue to make biosensing more feasible for mass applications. Arrays of mass-based biosensors should be easily developed, but has not been done yet. Hence, a critical parameter in mass-biosensing process development is the further focus of programs on system integration to develop a sensor capable of measuring a vast number of analytes. Mass-based biosensor biochips with additional detection modalities such as dielectric measurements could provide multidimensional information about samples for which specific binding sites cannot be developed or do not exist.

The biosensor development also needs a critical focus on the modeling of the interaction between biomolecules and sensor surfaces. This process might lead to a better understanding of how sensor sensitivities could be improved at the interface rather than the mass-to-electronics transduction level. Nonspecific binding needs to be understood to investigate how different energy sources can optimize desired binding. Better surface design, perhaps using nanopatterning, could lead to higher sensor sensitivities. Inclusion of the attached biomolecules and the related effect on the sonic field could lead to novel sensing in which both mass and elasticity changes are modeled leading to better understanding of the subject and/or multi-analyte measurement techniques. The nanoscale effects in binding need to be understood, especially in the presence of large proteins or DNA molecules. This understanding could lead to a better model for calibrating sonic biosensors. Hence, a critical parameter in process will be to include modeling and experimental investigators to study the interface between the sensor and the target molecule.

### **CRITICAL ISSUES FOR MANUFACTURABILITY**

Current QCM and SAW sensors are commercially available and are manufactured in large numbers. This industry has been setup because of the QCM markets in thin-film deposition systems, and the SAW markets in the communication markets. So the use of these sensors for biosensing has been ongoing and the literature is full of studies of DNA and protein detection using QCM and SAWs. Unfortunately, the modifying the packaging for biosensing of sensors developed for other applications leads to added cost and incompatibilities from sensor to sensor. Each sensor in general needs to be calibrated separately. The requirement of drying the sensors after binding leads the inclusion of human element that also effectively increases cost of operation. The markets are apparently not big enough where economies-of-scale have led to decreased cost of production. However, if the development of system integration where sensors can operate in liquids and can operate in parallel does occur, the market for such sensors might increase with a corresponding decrease in cost. Hence, a critical issue for manufacturability is the development of bigger market via an easy to use sensor that senses more than one result.

The manufacturability of these new sensor platforms requires further development of these devices in microfabrication companies. So far mass-biosensors have not been needed in the same quantities as integrated circuits are needed. Lower volumes means that the high cost of setting up and maintaining a fabrication facility has to be leveraged by many kinds of devices, each produced in relatively few numbers. There are some MEMS commercial setups to handle such lower volumes per batch. These companies, although increasing in number, are struggling with cost of development of such processes to make many sensors and packaging. Hence, the high cost of manufacturing process development is a critical parameter in manufacturability. This can be partially solved by further R&D on sensors that can work for a large class of molecules without the need for manufacturing methodology change. Another solution is the hybrid manufacturing where different sensor components are made in high volume factories and assembled to be biosensors.

Another critical issue of manufacturability is the lack of expertise in all areas (microfabrication, chemistry, biology, fluidics, electronics) in the smaller companies developing these sensors. A critical issue therefore is to bring together large (big-companies, many-investigator grants at universities) and small entities (e.g. small companies), and provide enough financial incentive for the development of a biosensor development that integrates manufacturability and addresses mass-usage from the start. Inclusion of biosensing expertise in relevant bio-analytes could be included in projects from the beginning. Hence, a critical need in manufacturability is the use of teams of different expertise to perform holistic system design.

## OVERSEAS ACTIVITIES

There are numerous medical groups working on using QCM and SAW sensors. They are too numerous to mention here. The groups developing new directions in Europe and Asia are listed below. The list is of course not comprehensive.

England: Enzyme technology and sonic sensors, Christopher Bucke, University of Westminster, Department of BioSciences

Germany: TU-Wien, E. Benes, W. Burger, M. Gröschl, A. Schaffner, F. Trampler, W. Bolek, T. Gaida, O. Doblhoff, F. Hager, "Trapping of suspended biological particles by use of ultrasonic resonance fields". In: Ultrasonics International '93, Conference Proceedings, Butterworth-Heinemann, Oxford, UK [1993], pp. 515-518 (ISBN 0 750618 779).

Germany: University of Magdeburg, IMOS, Auge, J.; Hauptmann, P.; Hartmann, J.; Rösler, S.; Lucklum, R.: Versatile microcontrolled gas sensor array system using the quartz microbalance principle and pattern recognition methods. *Sensors and Actuators B*, 26-27, (1995), 181 - 188.

Germany: University of Tübingen: W. Gopel: Parallel Frequency Readout of an Array of Mass-Sensitive Transducers for Sensor Applications, *Microelec. Eng.*, 53 (2000) 229-232

Germany: Fraunhofer, Munich: Hengerer, A.; Decker, J.; Prohaska, E.; Hauck, S.; Kößlinger, C.; Wolf, H.: Quartz crystal microbalance (QCM) as a device for the screening of phage libraries. In: *Biosensors and bioelectronics* 14 (1999) 2, pp. 139-144

Japan: Shizuoka University, Shiokawa, Surface Acoustic Wave Sensor for Liquid-phase Application (S. Shiokawa, J. Kondoh), *IEEE '99 Ultrasonic Symposium* (1999. 10).

Japan: QCM arrays: Morizumi and Nakamoto, Tokyo Institute of technology, Characterization of Phospholipid Sensing Films for QCM Gas/Odor Sensors - K. Nakamura, T. Nakamoto, and T. Moriizumi (Tokyo Institute of Technology)

Japan, Quartz micromachining, University of Tokyo, Fujita and Ikeda.

Japan, University Tohoku University, Ultrasonics and Quartz micromachining

Singapore: Institute of Materials Research and Engineering, Sean O'Shea, QCM biosensors

Switzerland: University of NeuChatel: Phillipe Luginbuhl and N. F. de Rooij, Ph. Luginbuhl, S.D. Collins, G.-A. Racine, M.-A. Grétilat, N.F. de Rooij, K.G. Brooks, N. Setter, Flexural-Plate-Wave Actuators Based on PZT Thin Film, *Proceedings of IEEE 10th Annual Internat. Workshop on Micro Electro Mechanical Systems, MEMS '97, Nagoya, Japan*, pp. 327-332, 1997

## MICRO- AND NANOFABRICATED FLUIDIC DEVICES FOR BIOSENSING

J. Michael Ramsey

### Lab-on-a-Chip

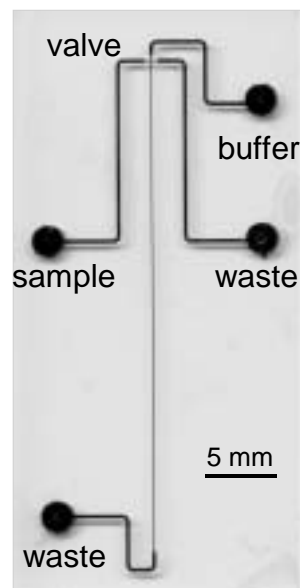
#### Objectives

- Integrate multiple steps of a measurement protocol into a microfabricated fluidic device
- Utilize existing laboratory principles taking advantage of scaling where possible
- Design devices that can be mass produced

ornl

### Microfluidic Devices

- Materials
  - silica
  - plastics
- Dimensions
  - 20-100  $\mu\text{m}$  wide
  - 0.05-30  $\mu\text{m}$  deep
  - 1-20  $\text{cm}^2$  substrates
- Volumes
  - 1-1000 pL injections
  - 1-100  $\mu\text{L}$  reservoirs
- Fluid transport
  - electrokinetic
  - pressure or vacuum
  - capillary forces



ornl

## Functional Elements

I/O

pipette  
inkjet  
electrospray

separations

electrophoretic  
chromatographic  
sizing  
heterogeneous

filters

physical  
polymeric  
SPE

cytometry

immunoassay  
staining  
cell sorting

reactions

stopped flow  
continuous flow  
thermal cycling

detection

fluorescence  
absorbance  
refractive index  
scattering  
electrochemical  
MS

ornl

## Lab-on-a-Chip Benefits

- Automation
- Reagent consumption reduced  $10^4 - 10^6$
- Speed -  $10^2$
- High quality data
- Highly parallel assays at low cost
- Inexpensive / disposable devices (chips)
- Standardized platforms
- Calibration - QA/QC
- CAD/A - Rapid prototyping

ornl

## Applications

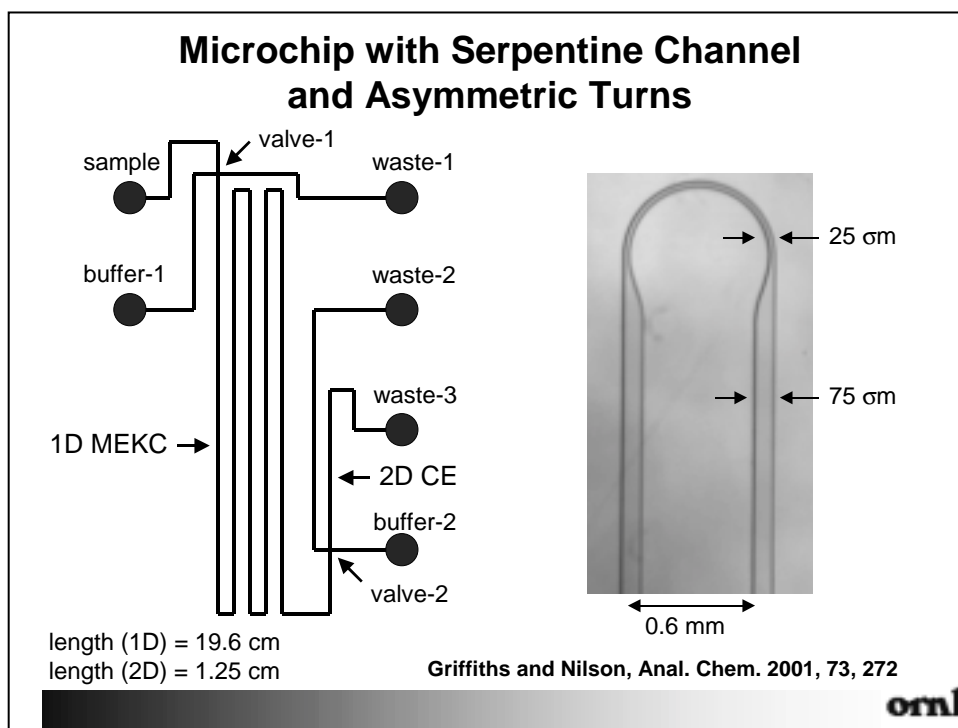
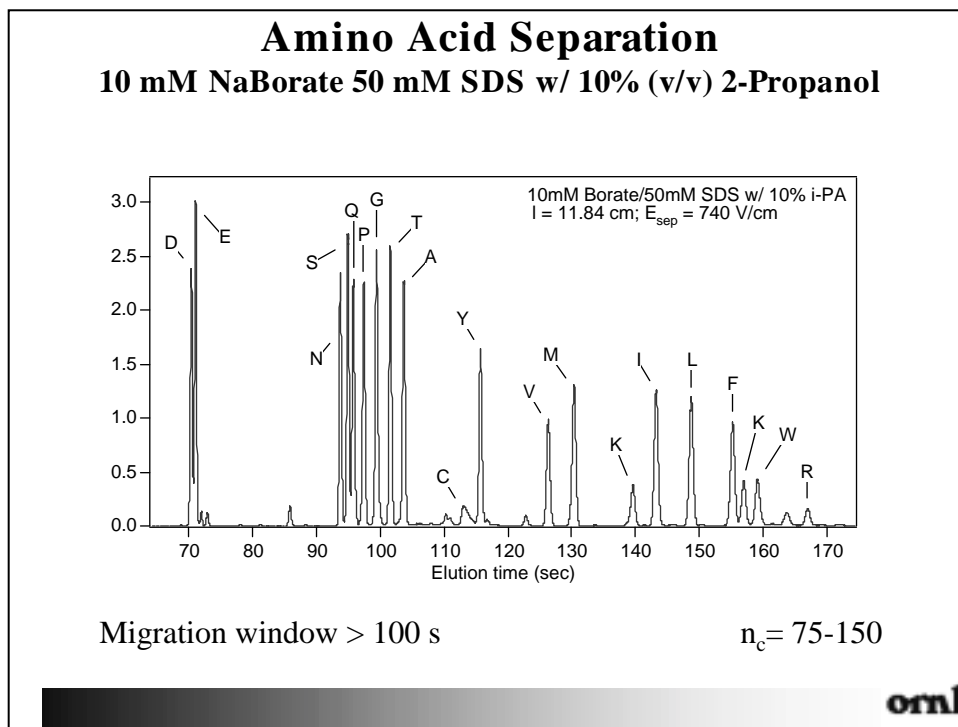
- In-situ Measurements
  - Process Control
  - Environmental Monitoring
- Field Analysis
  - Environmental Monitoring
  - Forensics
- Medical Diagnostics
  - Point-of-Care
  - Emergency Care
  - Closed-Loop Monitoring/Dosing
- High-throughput Laboratory Analysis
  - Combinatorial Discovery
  - DNA Sequencing
  - Proteomics
  - DMPK
  - Forensics

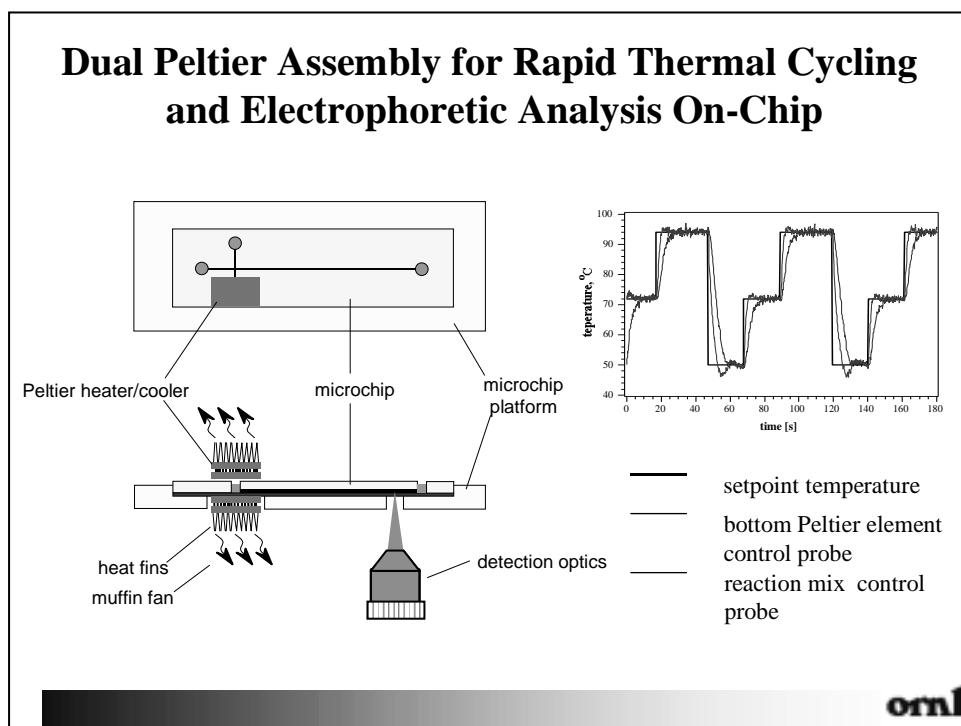
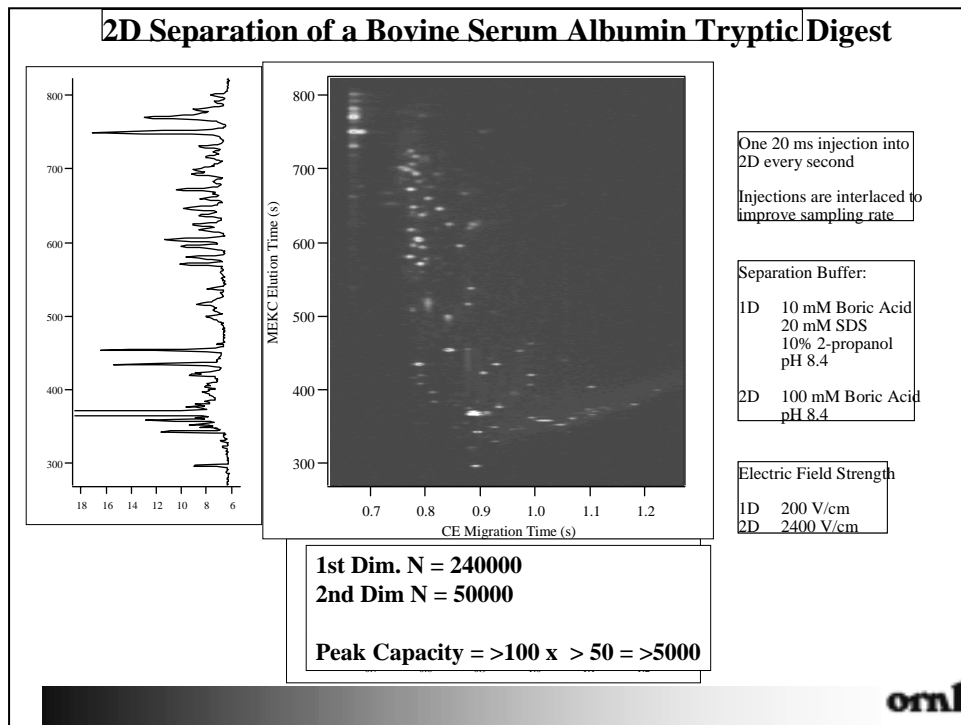
The logo for the organization, consisting of the lowercase letters 'oml' in a bold, sans-serif font.

## Pathogen Identification

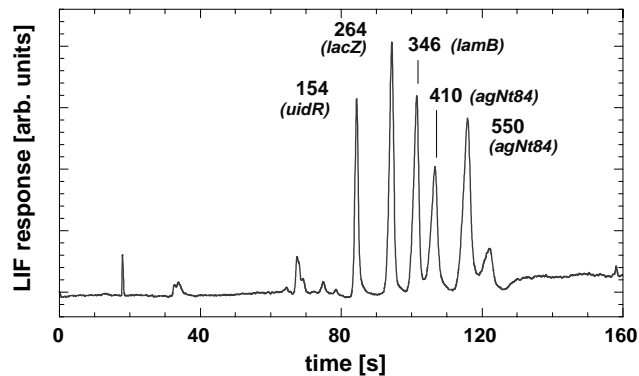
- Assay
  - genetic diagnostics
  - immunoassay
  - other?
- Preprocessing

The logo for the organization, consisting of the lowercase letters 'oml' in a bold, sans-serif font.





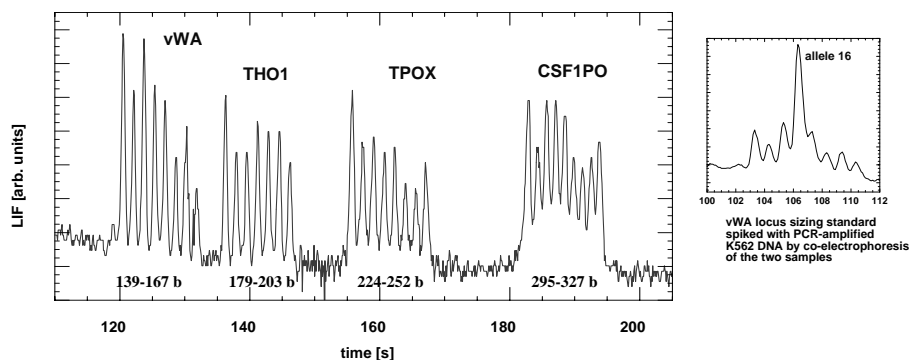
## Integrated Cell Lysis, Multiplex PCR & Electrophoretic Separation



target: *E. coli* with plasmid  
 primers: 5 sets  
 PCR cycles: 25  
 sieving medium: 3% DMPA  
 intercalating dye: TO PRO  
 separation field strength: 100 V/cm

omni

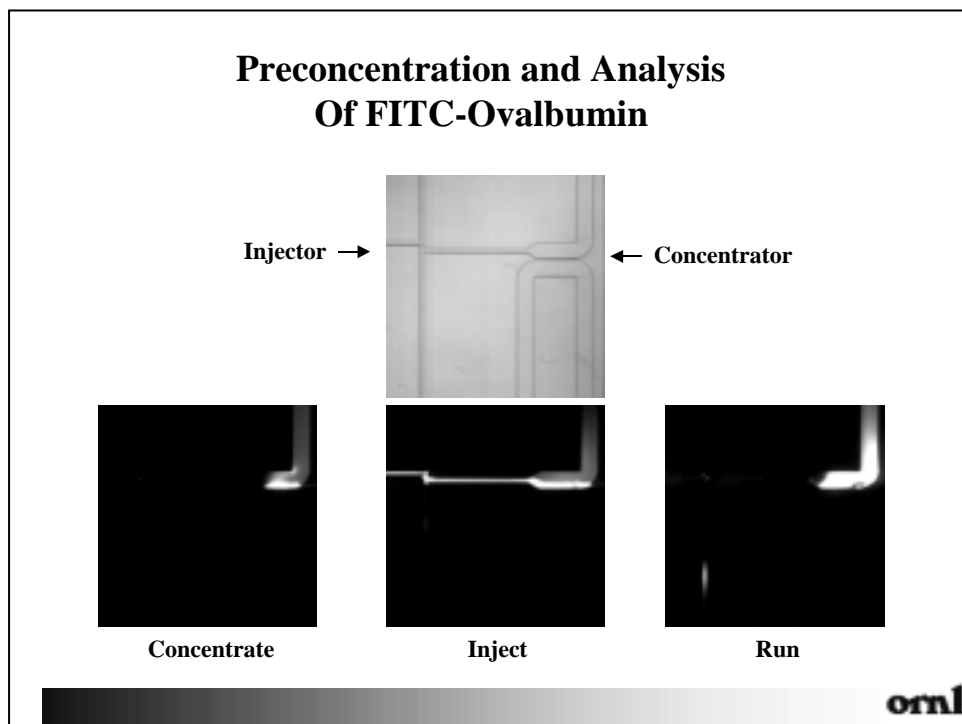
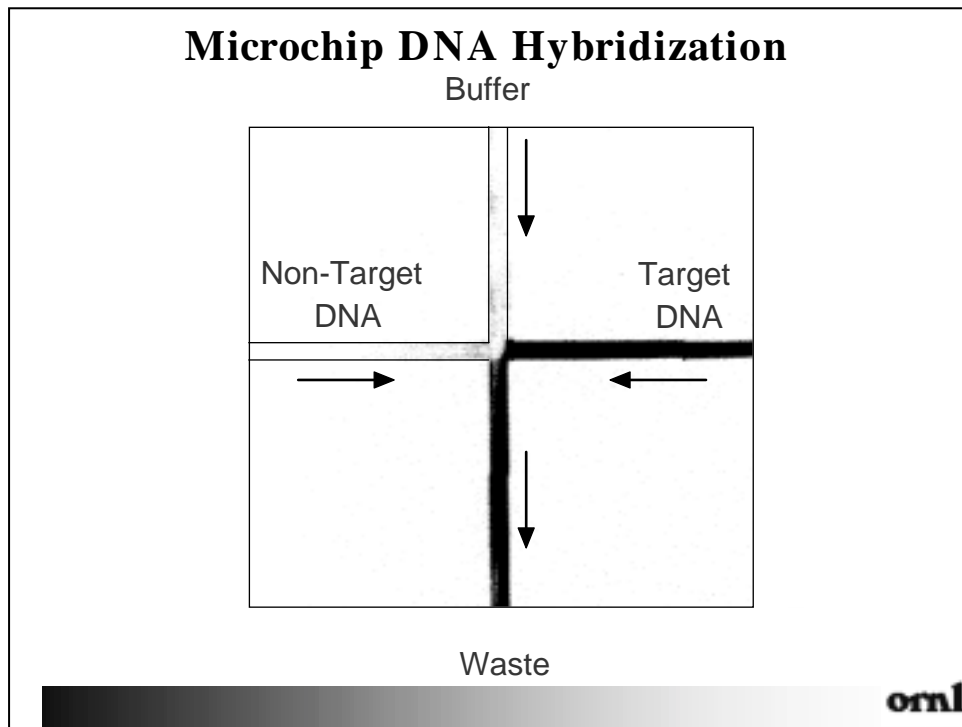
## DNA Typing at Human STR Loci



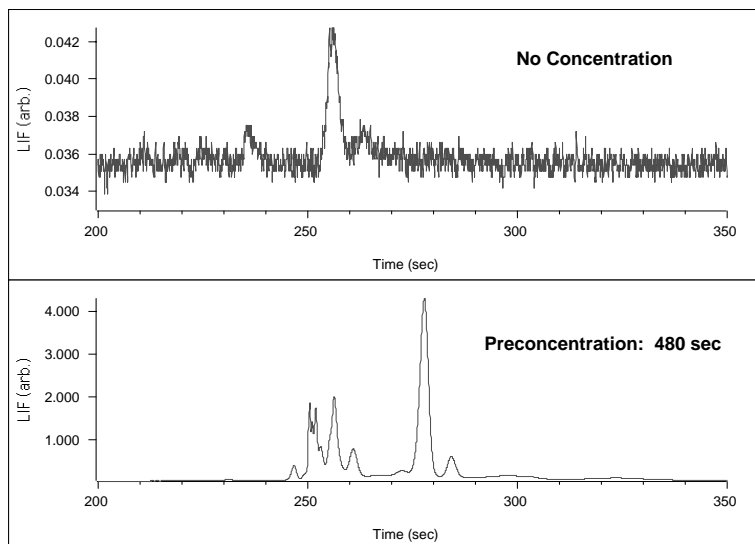
vWA locus sizing standard  
 spiked with PCR-amplified  
 K562 DNA by co-electrophoresis  
 of the two samples

CTTv Allelic Ladder  
 Sieving matrix: 4% LPA, 7 M urea, 0.5x TBE  
 Separation distance: 3 cm  
 Field strength: 225 V/cm

omni



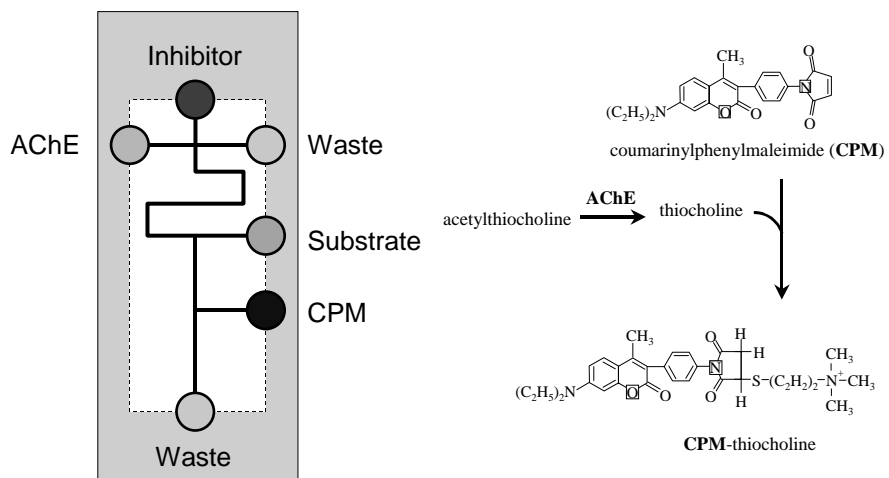
## Preconcentration and Analysis of Protein Mixture



Sample: FITC-labeled proteins (Sigma High Mol.Wt. Standard).  
 Buffer: CE Protein Buffers (Bio-Rad). Separation: 7 cm; 300 V/cm.

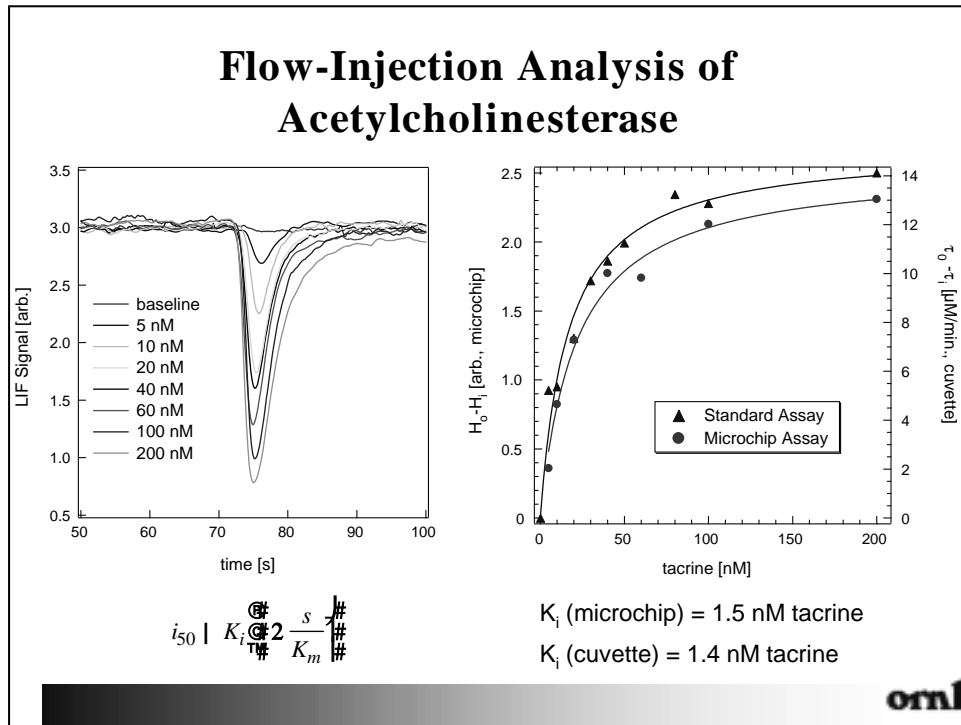
omni

## Acetylcholinesterase (AChE) Assay



Anal. Chem., 71, 5206 (1999)

omni



### Microchip Flow Cytometry

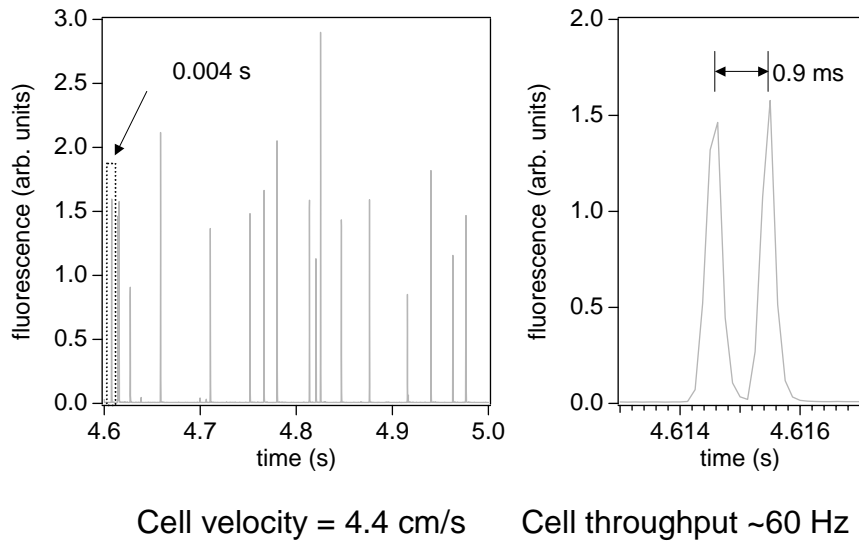
#### Hydrodynamic Focusing of Eukaryotic Cells

- Electroosmotic focusing - latex spheres
- Electrophoretic focusing - E. coli
- Jurkat Cells - acute T cell leukemia (8-10  $\mu\text{m}$  dia.)
- Sub-ambient pressure applied to waste reservoir using a syringe pump
- Cell velocities up to 5 cm/s implemented (500nL/s)

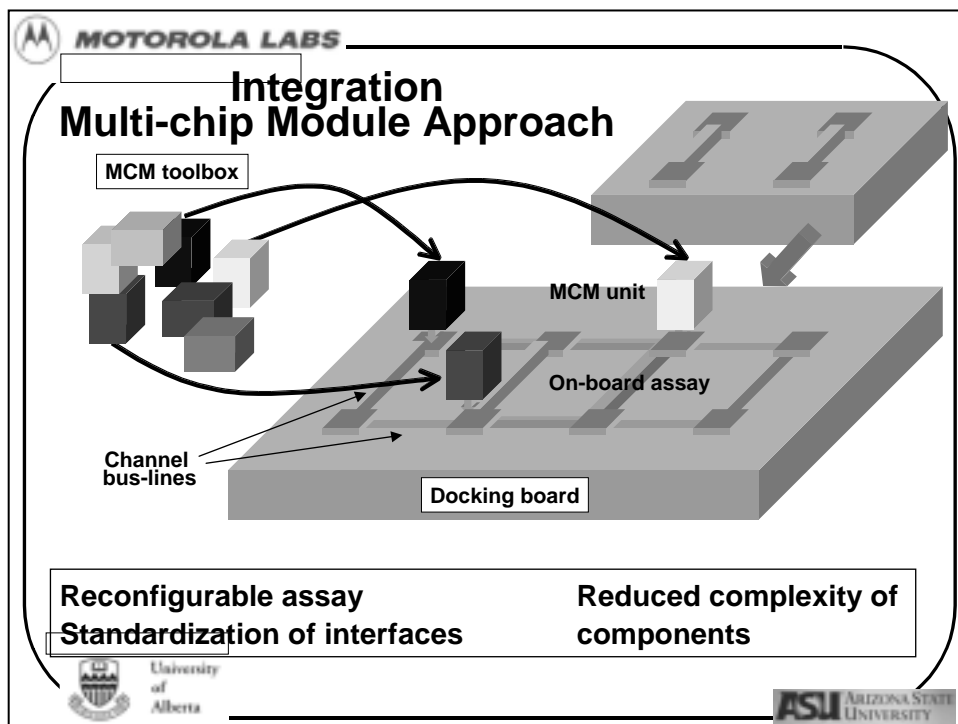
A 5 s integrated CCD image of Jurkat cells labeled with Calcein

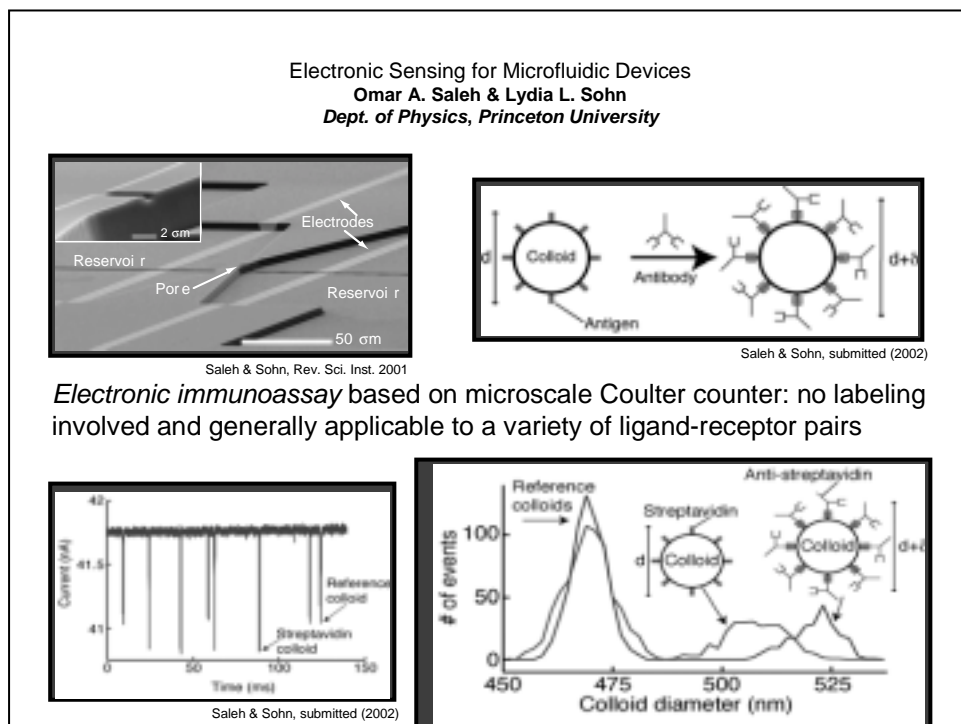
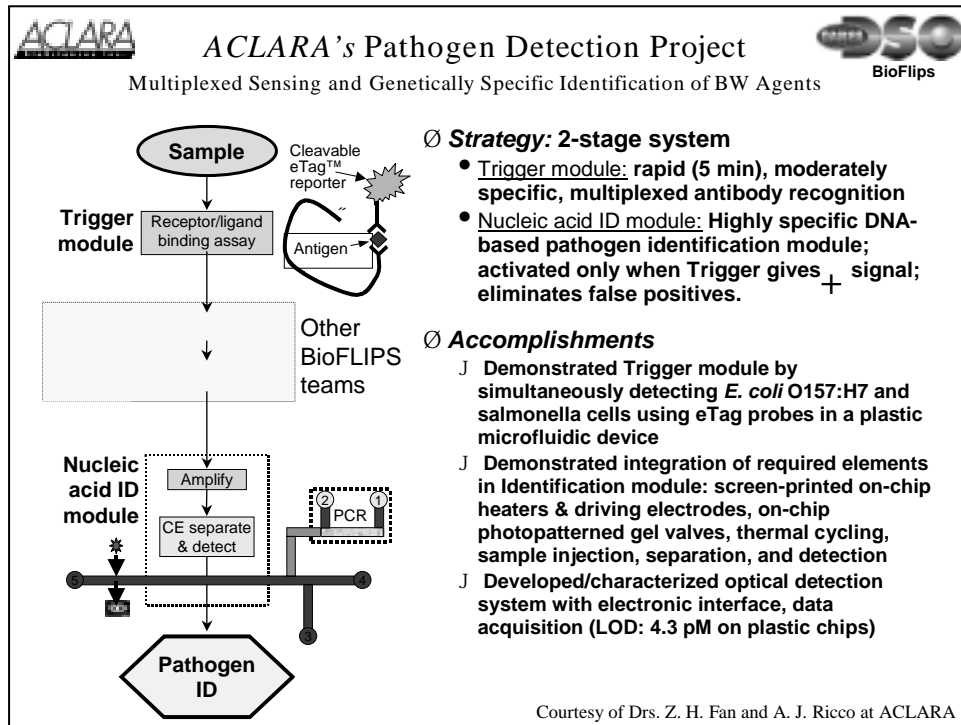
**oml**

### Flow Cytometry of Calcein Labeled Jurkat Cells



ornl





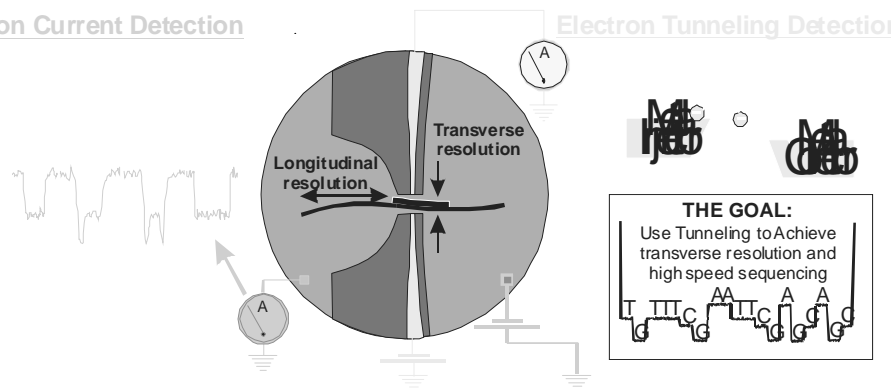
# SINGLE BIO-MOLECULE SOLID STATE NANOPORE SENSORS

Jene Golovchenko and Daniel Branton

Harvard University

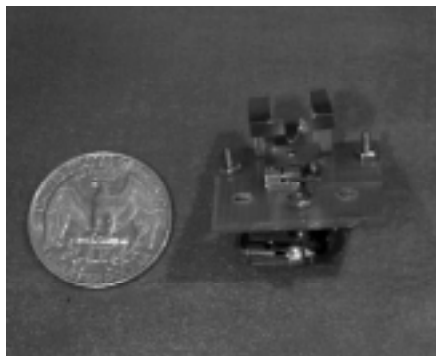
Ion Current Detection

Electron Tunneling Detection

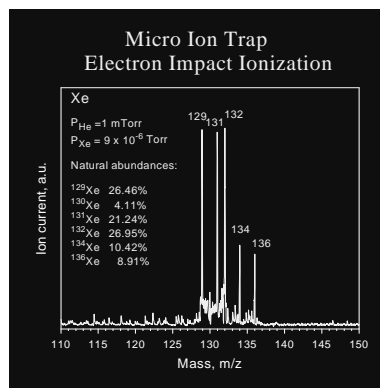


## Micro Ion Trap Mass Spectrometry

### 1 mm Ion Trap MS



- 0.2 - 0.25 Dalton Resolution
- Compact MS for in-situ and field apps.
- Arrays to address high throughput



W.B. Whitten, P.T.A. Reilly, J.M. Ramsey

oml

## Personal Laboratory Workstation



## LabChip™ Applications



**DNA Sizing**  
**RNA quantification**  
**Protein Sizing**  
**Cell Assays**



## Caliper HT SNP Screening System



**100,000 loci  
per day per chip**

**1 nL samples**



## Surface Tension Driven Fluidics

**Biosite Inc.**

**Sandwich Immunoassay Panels**



Pathogens (2)  
Parasites (3)  
Heart attack  
DOA (8)

## Issues

- Depends on Application Scenario
  - in situ monitoring
  - field measurement
  - laboratory



oml

## Issues

- Analysis volume
  - Could impact sensitivity
  - Preprocessing required for low abundance species
- Shelf life
  - Reagents preloaded?
- Continuous use
  - Reagent stability
  - Contamination
  - Clogging



oml

## Suggestions

- Near-term (< 5 yrs)
  - HT lab assays
  - Field assays
- Transition from research to  $\beta$ -unit
  - Funding?
- Leverage from commercial investments
  - Focused on biotech applications
- Research investments in new technologies
  - Someone must invest in next generation strategies

The logo for ORNL (Oak Ridge National Laboratory) is located in the bottom right corner of the slide. It consists of the lowercase letters "ornl" in a bold, sans-serif font.

## Disclosure

The author has potential financial interest in the following companies

- Caliper Technologies
- Aclara

The logo for ORNL (Oak Ridge National Laboratory) is located in the bottom right corner of the slide. It consists of the lowercase letters "ornl" in a bold, sans-serif font.