Center for Biomolecular Integrated Circuits (CBIC)

Trevor Thornton

".....where biology meets silicon chips...."

CBIC philosophy:

Combine the high-speed/high-performance capabilities of advanced integrated circuit technology with the functionality of biological systems.

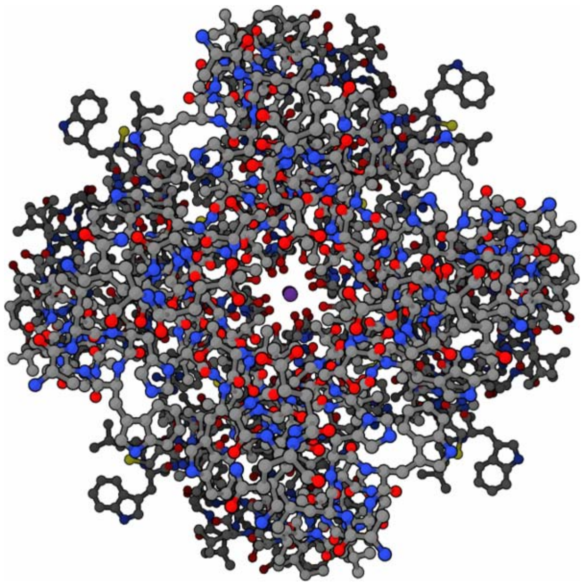
Modern computers can process terabytes of data in real-time, with great accuracy.

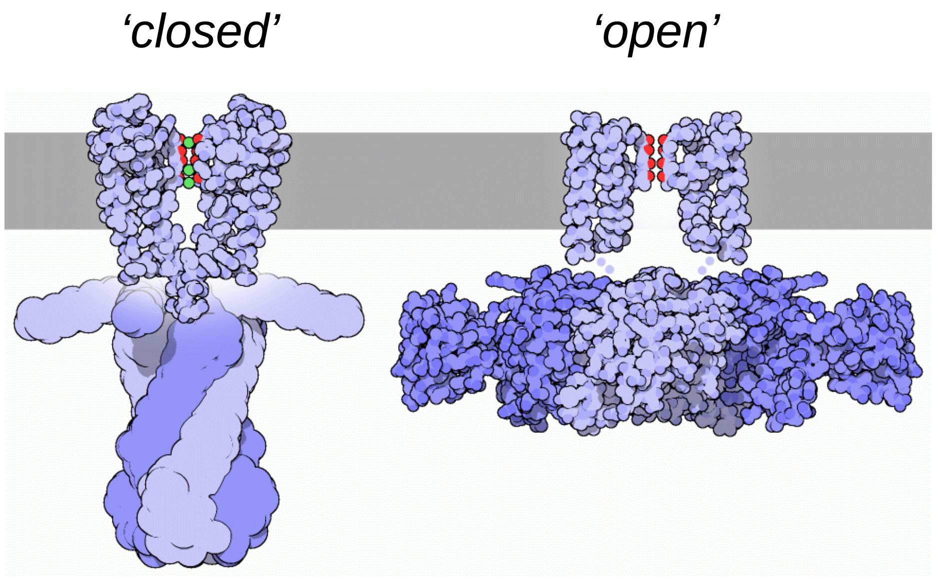
But they need to be controlled by software, are not good at sensing the environment, and cannot be easily adapted.

Billions of years of evolution has lead to molecular systems with very precisely controlled and highly sensitive functions.

But they are extremely sensitive to the environment and can be difficult to synthesize and/or modify.

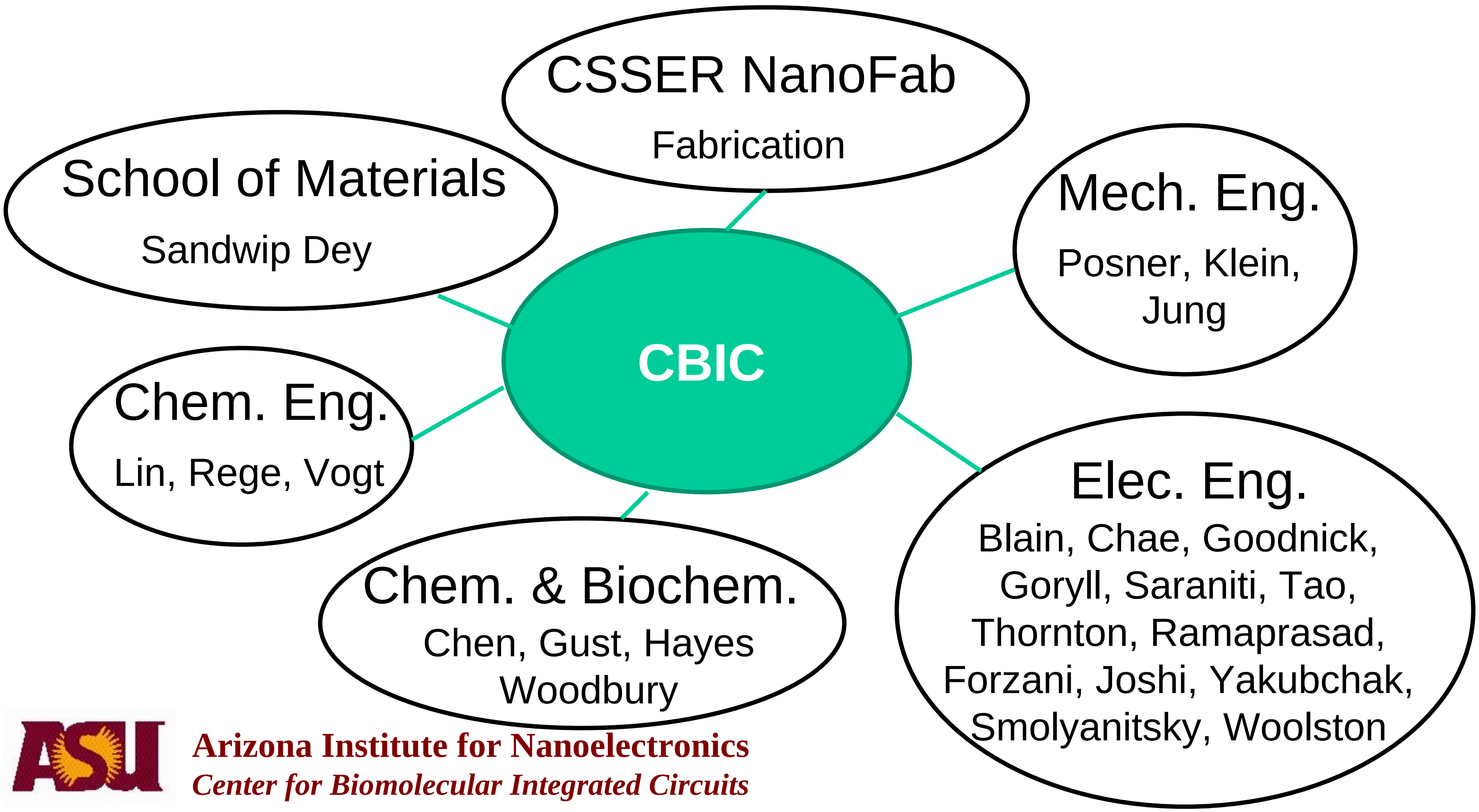
For example, different variations of potassium channels control the beating of the heart, secretion of hormones (e.g. insulin) and are involved in many important diseases.





This potassium channel responds to voltage differences across a cell membrane and can open or close to control the flow of potassium ions

- CBIC faculty are working on projects that combine ideas inspired by nature with modern electronic technologies.
- Approximately 2000 sq ft of laboratory space has been re-furbished for BioChip fabrication and testing of BioMEMS (micro-electro-mechanical systems) devices



1) <u>Stochastic Sensing of Bio-threats</u> (Thornton, Goodnick, Spanias, Goryll)

So-called 'false positives' are the greatest challenge facing sensing technology for critical life safety applications

The Chicken Defense
U.S. troops will be using poultry to detect chemical attacks in Iraq

BY SIMON ROBINSON
Friday, Feb. 21, 2003

A war against Iraq will see the debut of some of the most sophisticated weaponry ever used. But U.S. Marines will also rely on one of the most low-tech detection devices around: chickens. Worried that the pollution from blown oil installations will clog up complicated detection equipment and make it difficult to pick up deadly chemicals and nerve agents, U.S. marines will drive into battle across the dusty plains of Iraq with caged chickens atop their Hum-Vees.

The chickens, which were otherwise destined for Kuwaiti dinner tables, will work in the same way as canaries in coal mines used to. Small traces of poisonous gases or chemical agent will kill the birds — or Poultry Chemical Confirmation Devices, as the Marines call them — and warn troops to put on their gas masks. "A sky full of oil can mask some chemicals," says Warrant Officer Jeff French, a nuclear, biological and chemical officer for a marine battalion in Kuwait. "Using chickens may sound basic but it's still one of the best ways we have of detecting chemical agent."

Dubbed Operation Kuwaiti Field Chicken (KFC), the use of chickens is sure to enrage animal activists. But chickens were used to detect for chemicals during the first Gulf War and, says French, consider that the alternative may be dozens of dead troops. Consider too that marines and soldiers will face nerve-racking moments with or without chickens. U.S. troops in Kuwait have been training to fight and live in their protective suits but at some point after a chemical attack they will have to take them off.

After testing for chemicals, one or two men — usually of different sizes and races — will remove their masks in a "selective unmasking." Those who keep their masks on will study the skin and pupils of the unmasked for symptoms of lingering airborne chemicals. "Using chemicals is a really unfair way of fighting," says French. "The best way to describe it is if I blindfolded you and came and kicked you in the groin as hard as I can. It's just not fair. But whatever Saddam throws at us, we'll be ready."

The idea to use chickens was Marine Chief Warrant Officer Stacy Jeambert's. Jeambert served in the Marines in the Gulf War and remembers buying five chickens to use as detectors. This time around he has ordered 250 from a local Kuwaiti supplier. "We've built a chicken coop and we're going to fatten them up so they're real healthy." A lot of people ask Jeambert "why chickens and not sheep, pigs or goats? The truth is they eat too much." What about pigeons or the classic canary? "You and I both know those birds are not that hardy and will try to fly away." Chickens, on the other hand, are more docile creatures. "I think it gives everyone a little more sense of comfort," says Jeambert. "The men are already joking that we'll have to give them medals for valor."

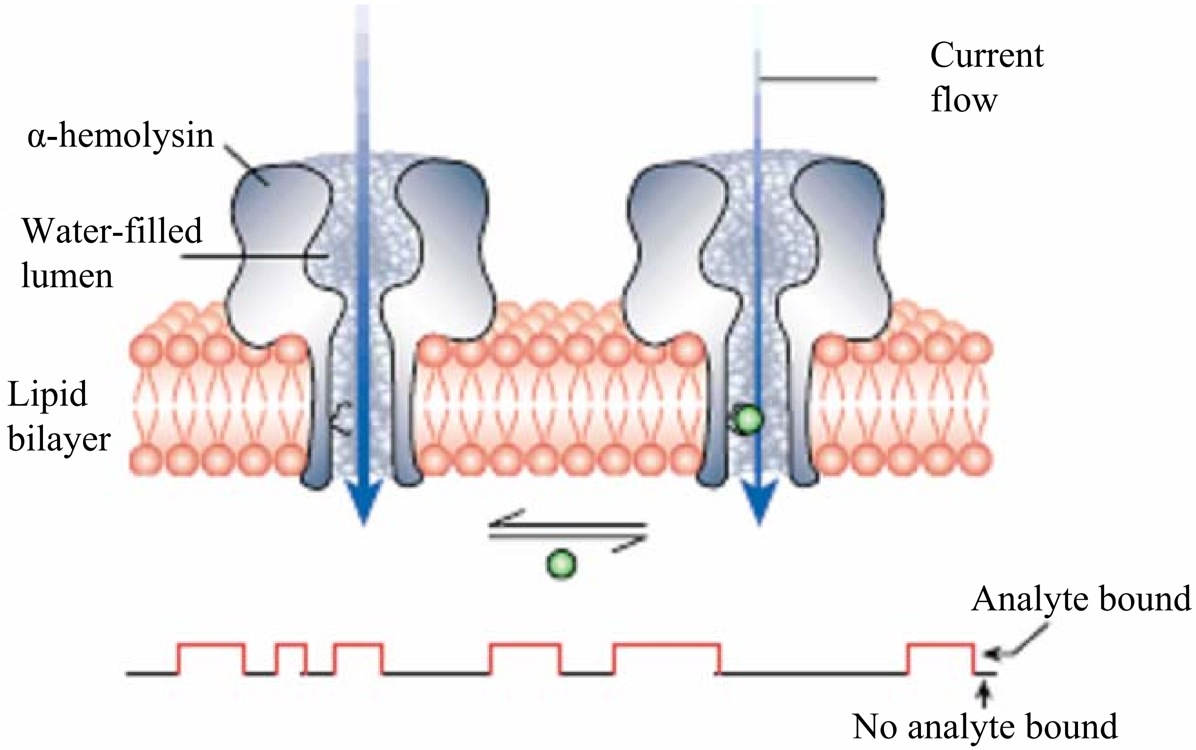
TIMEeurope.com
http://www.time.com/time/europe/me/daily/0,13716,423690,00.html

SCOTT NELSON/GETTY IMAGES

DESERT MISSION: U.S. troops will be installing new safety features to their Hum-Vees ... live chickens.

1) Stochastic Sensing of Bio-threats (cont)

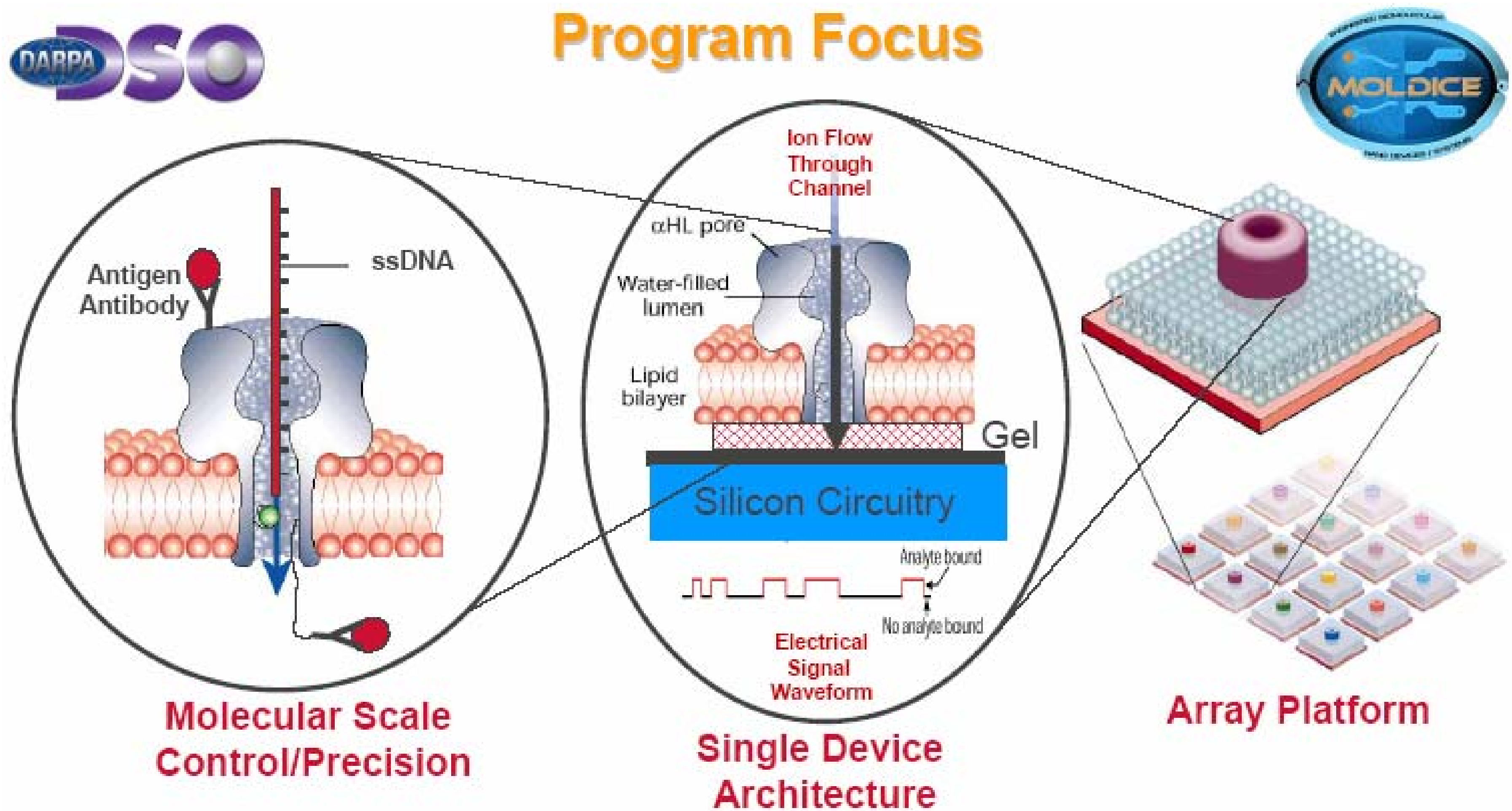
One way to reduce the rate of false positives is to use stochastic sensing



H. Bayley and P. S. Cremer, Nature, 413: 226-230 (2001)

- Engineered pore for sensing of analytes (single molecule detection)
- Measure the conductivity through a single protein pore with an engineered binding site
- Frequency of occurrence of events–concentration of analyte
- Signature– *τ, Δg, etc.* –identity of analyte

1) Stochastic Sensing of Bio-threats (cont)



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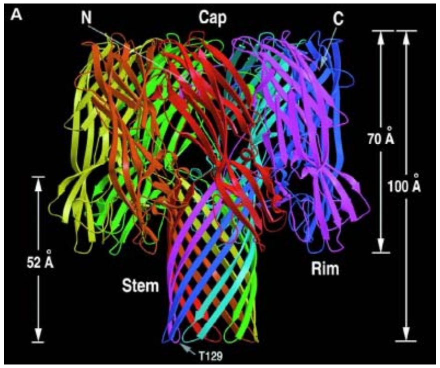
2) <u>Nanoparticle Toxicity</u> (Posner, Thornton, Westerhof)

Nanoparticles such as 'nanosilver' are being used in a growing number of commercial products

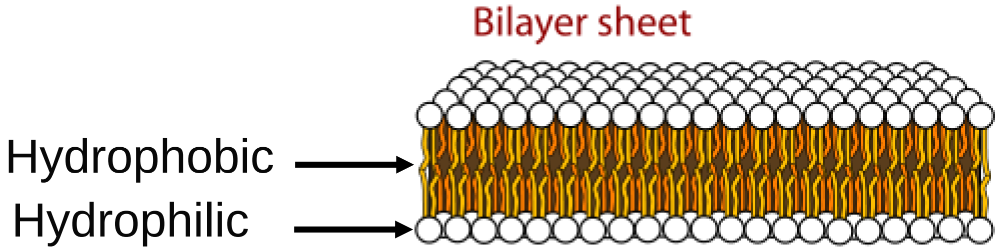
..but we don't know their long term effect on the body or in the environment

Some naturally occurring toxins work by puncturing holes in cells e.g. alpha-hemolysin



2) Nanoparticle Toxicity (cont)

We are using a lipid bilayer (think soap bubble) as a model for a cell wall.



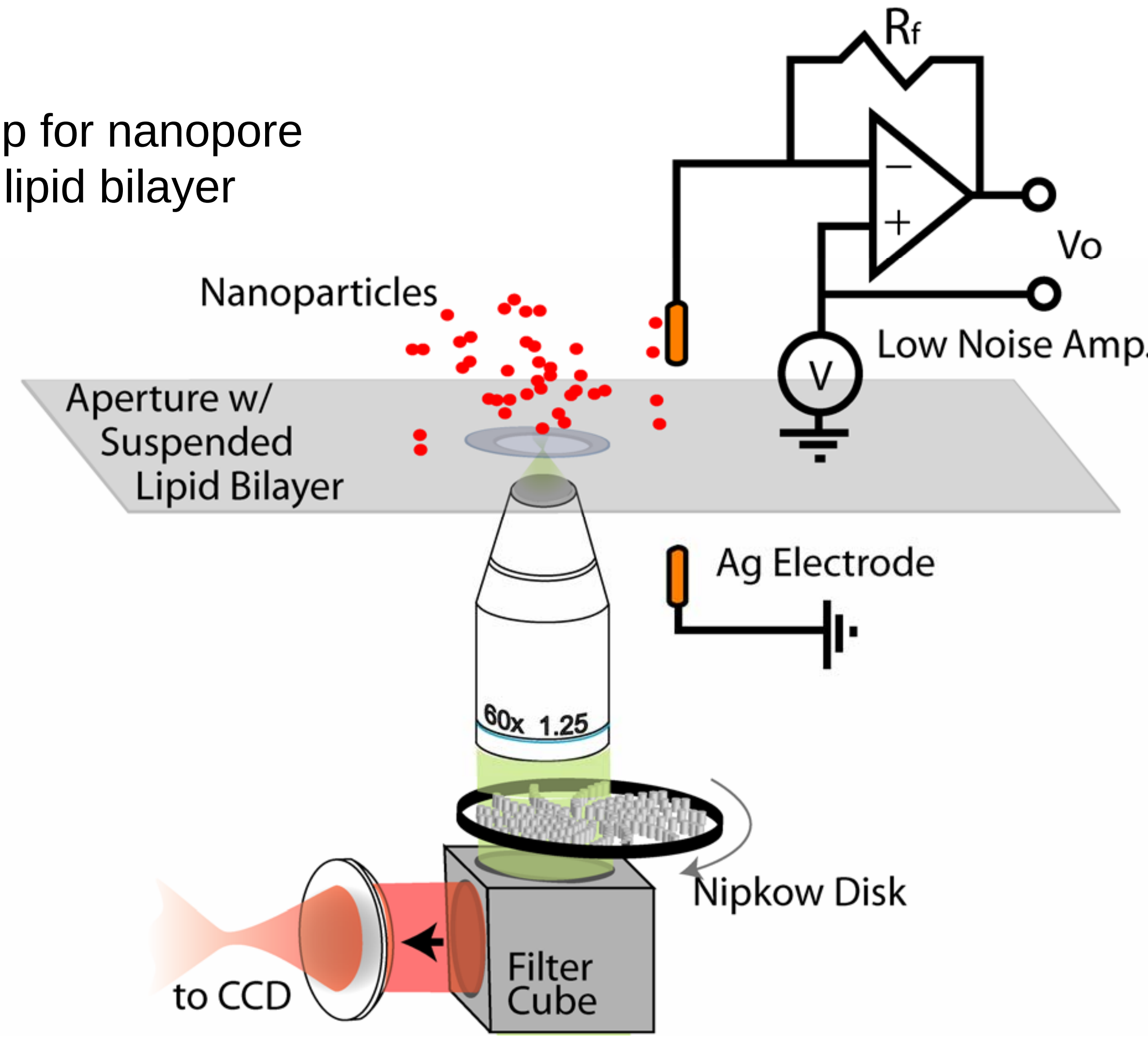
The lipid bilayer has an enormous resistance – very little current will flow across it.

In the presence of nanoparticles we see large current spikes suggesting that the membrane is being disrupted.

Experimental Setup

2) Nanoparticle Toxicity (cont)

Dual measurement setup for nanopore formation in suspended lipid bilayer membranes.



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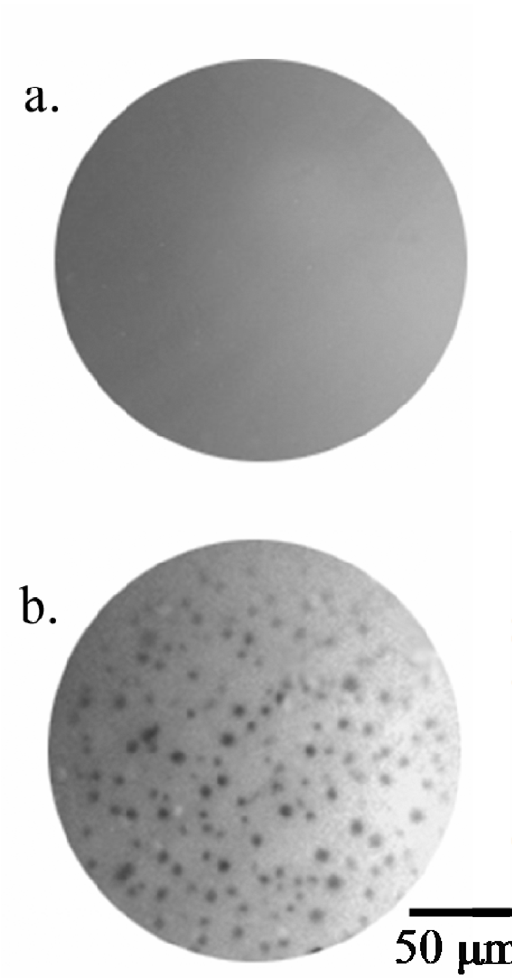
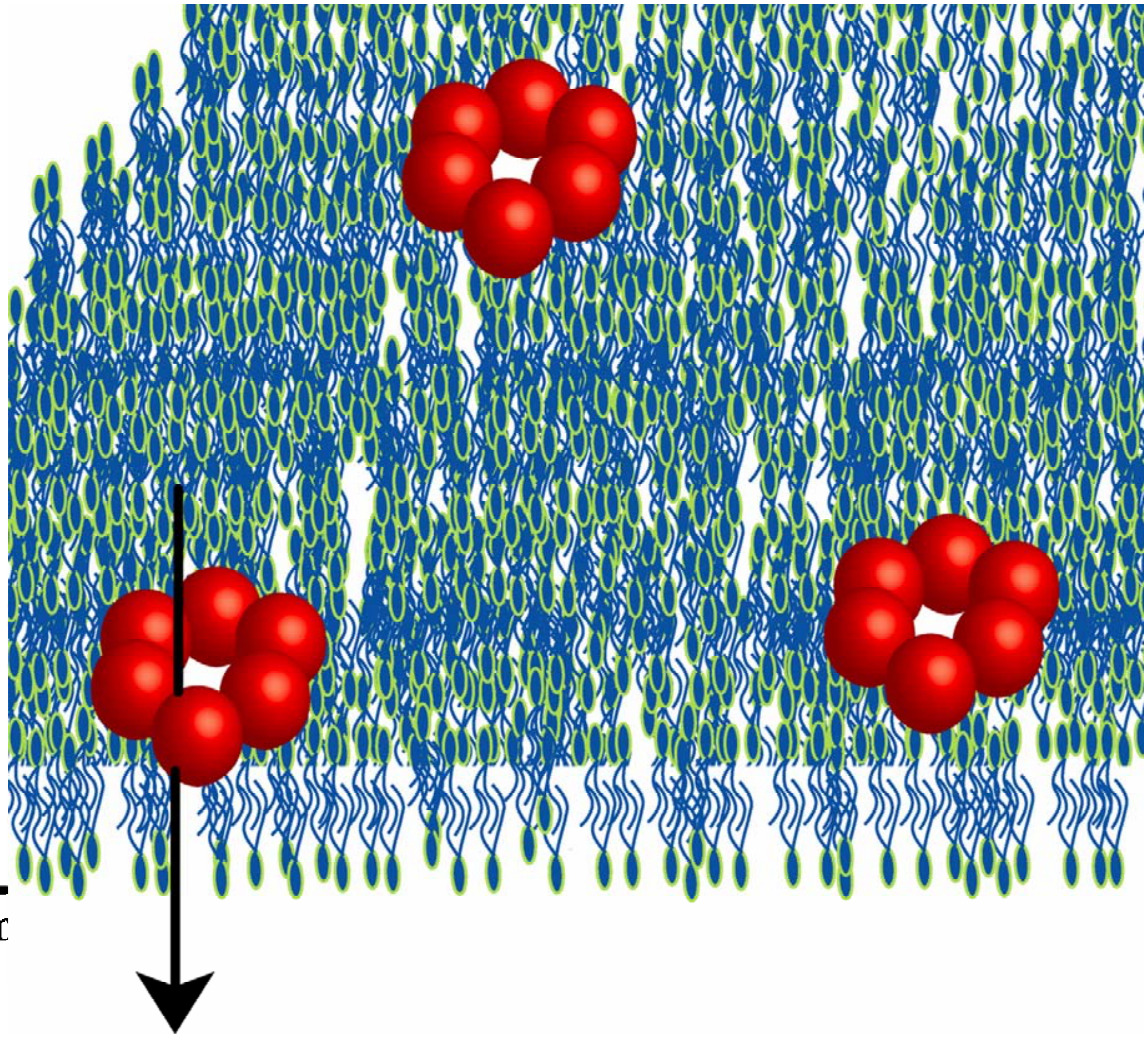
2) <u>Nanoparticle Toxicity</u> (cont)



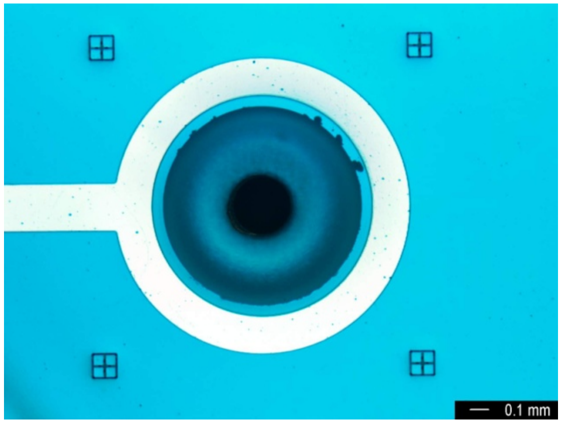


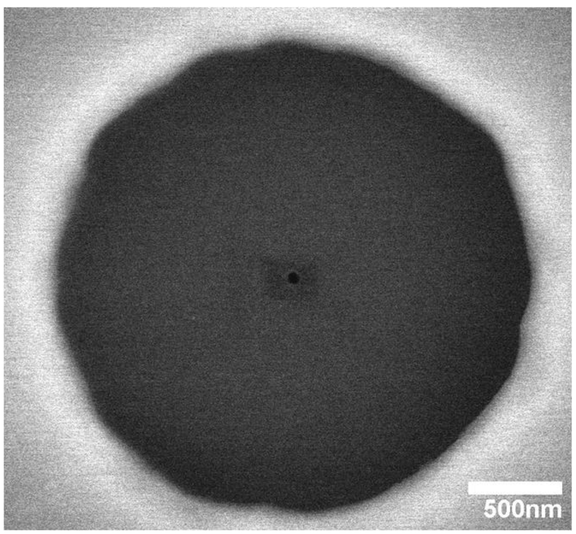
3) Nanopore Biosensors

Coulter counting is a method of detecting particles in solution originally developed in the 1950s to count red blood cells.

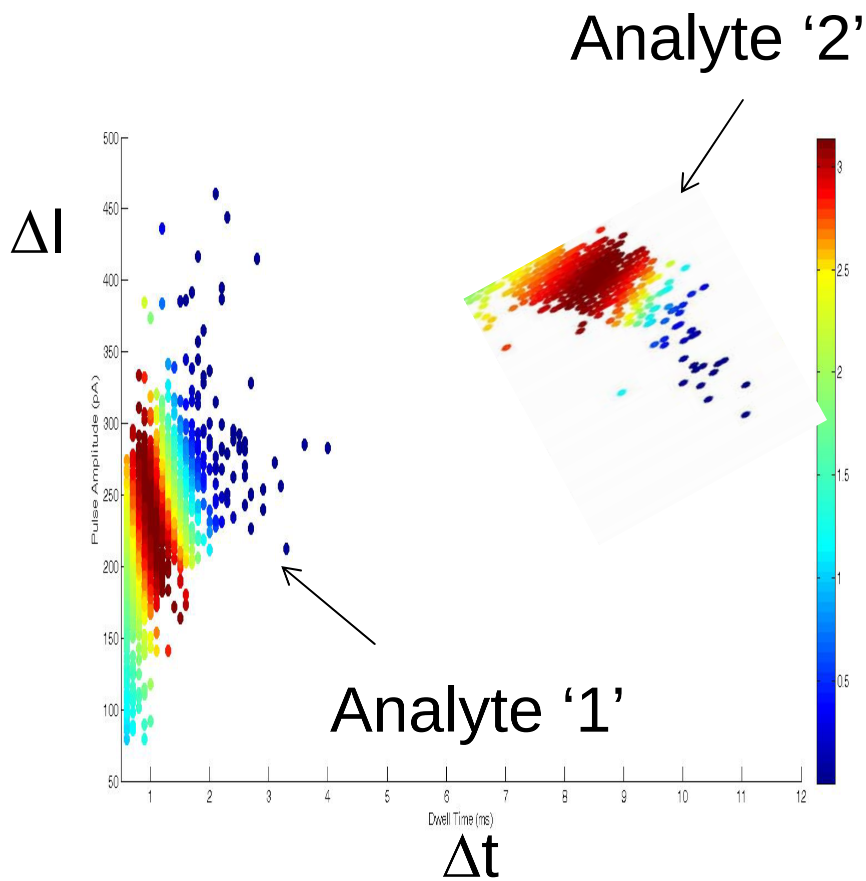
By reducing the pore diameter to < 100 nm we can detect particles of biological significance e.g. proteins, DNA etc.

3) Nanopore Biosensors (cont)





Use statistical signal processing to distinguish between different analytes



Conclusions

The interface between the hard world of inorganic materials and the soft world of biology holds many promises but there are many issues to overcome….

Any questions…?

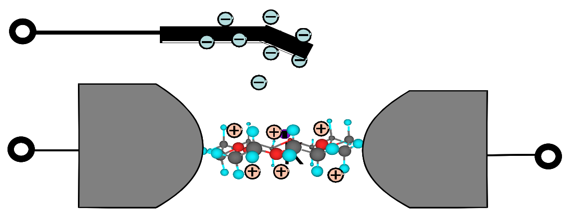
Molecular Electronics & Molecular Sensors

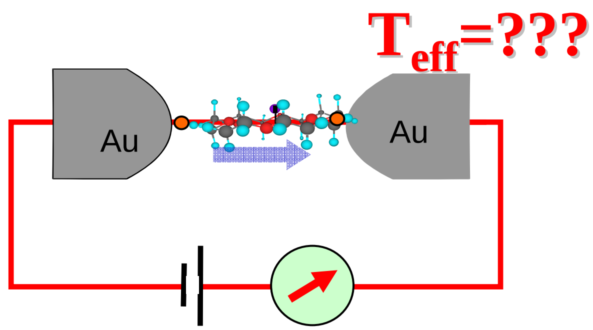
N.J. Tao
Arizona State University

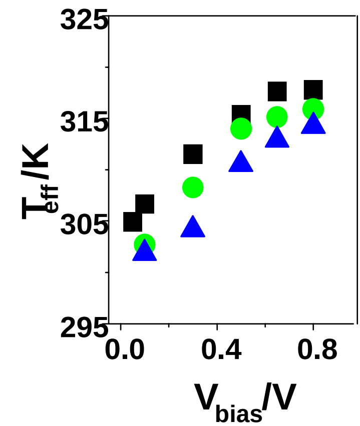
a Institute for Nanoelectronics
or Biomolecular Integrated Circuits

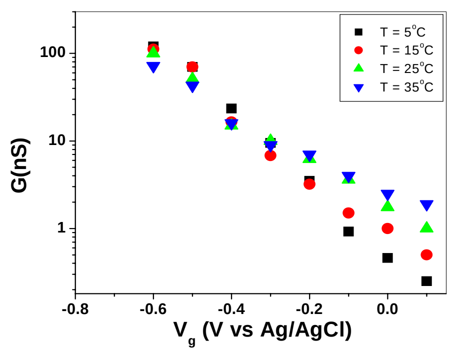
4/4/08, AINE kickoff

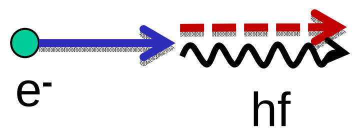
Molecular Electronics

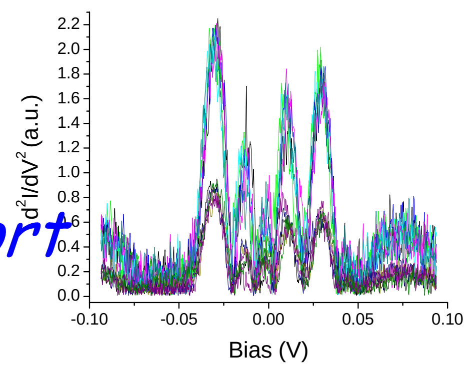


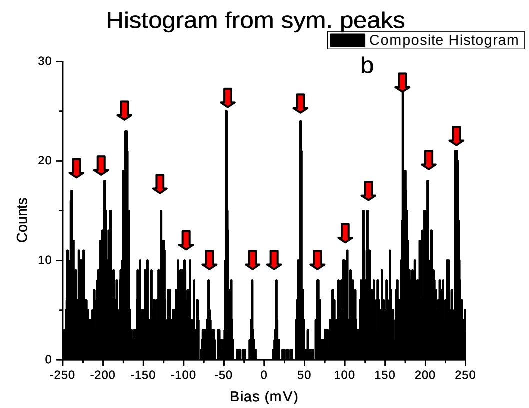












Gate Controlled Transport

Electron-Phonon Interactions

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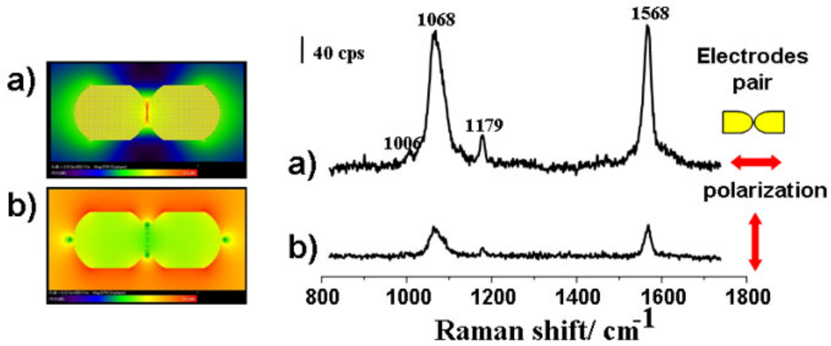
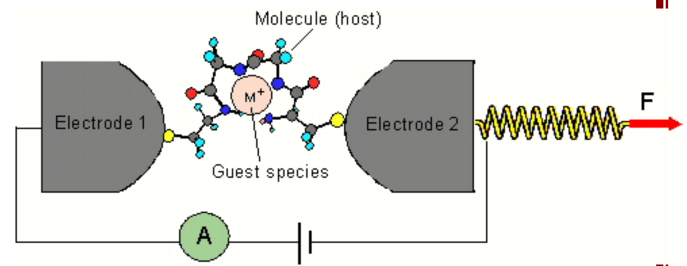
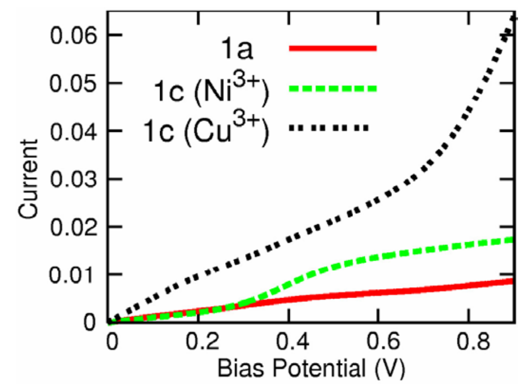


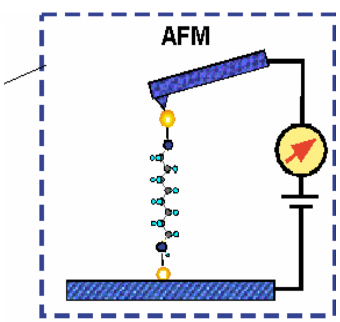
(A) (B)

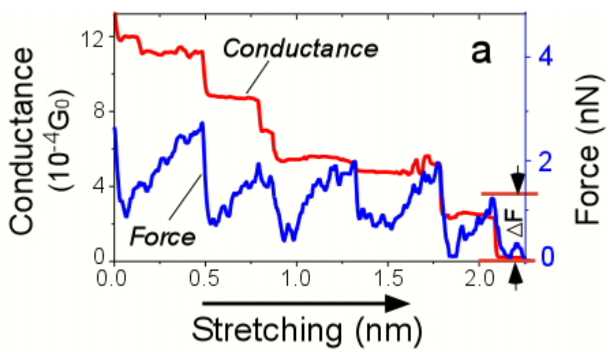
Raman Spectroscopy





Molecular Recognition



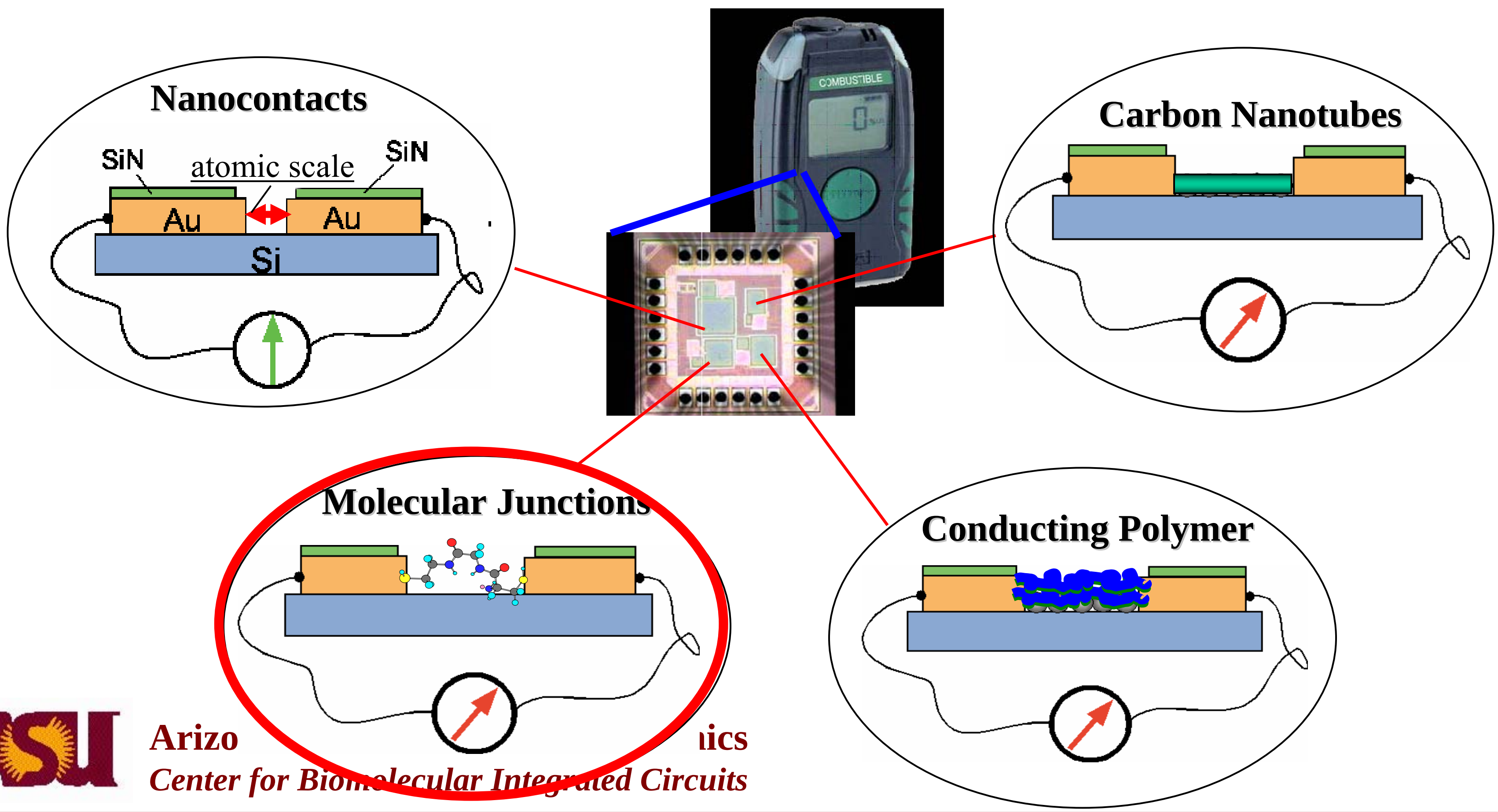


Electromechanics

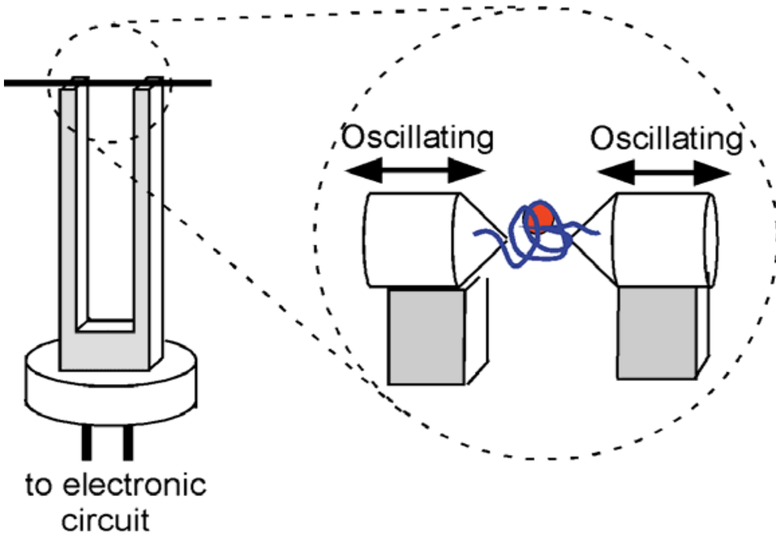
Nano- Sensors

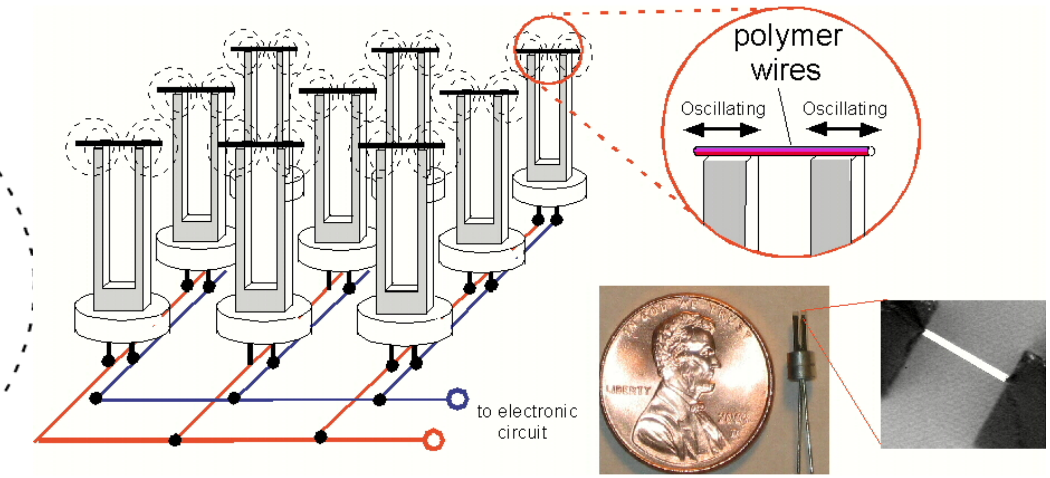
(With Motorola)

- An integrated sensor that can detect different species
- Sensing elements: Array of electrically wired **nanojunctions**

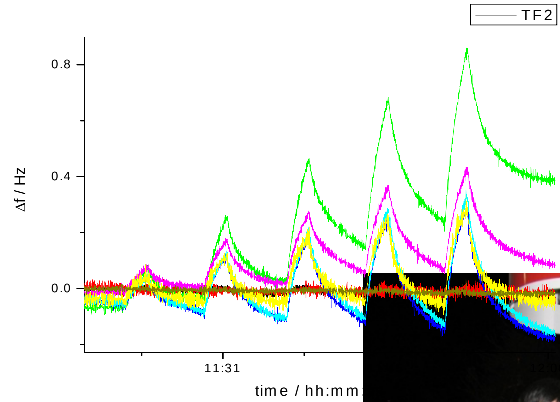


MEMS Sensors



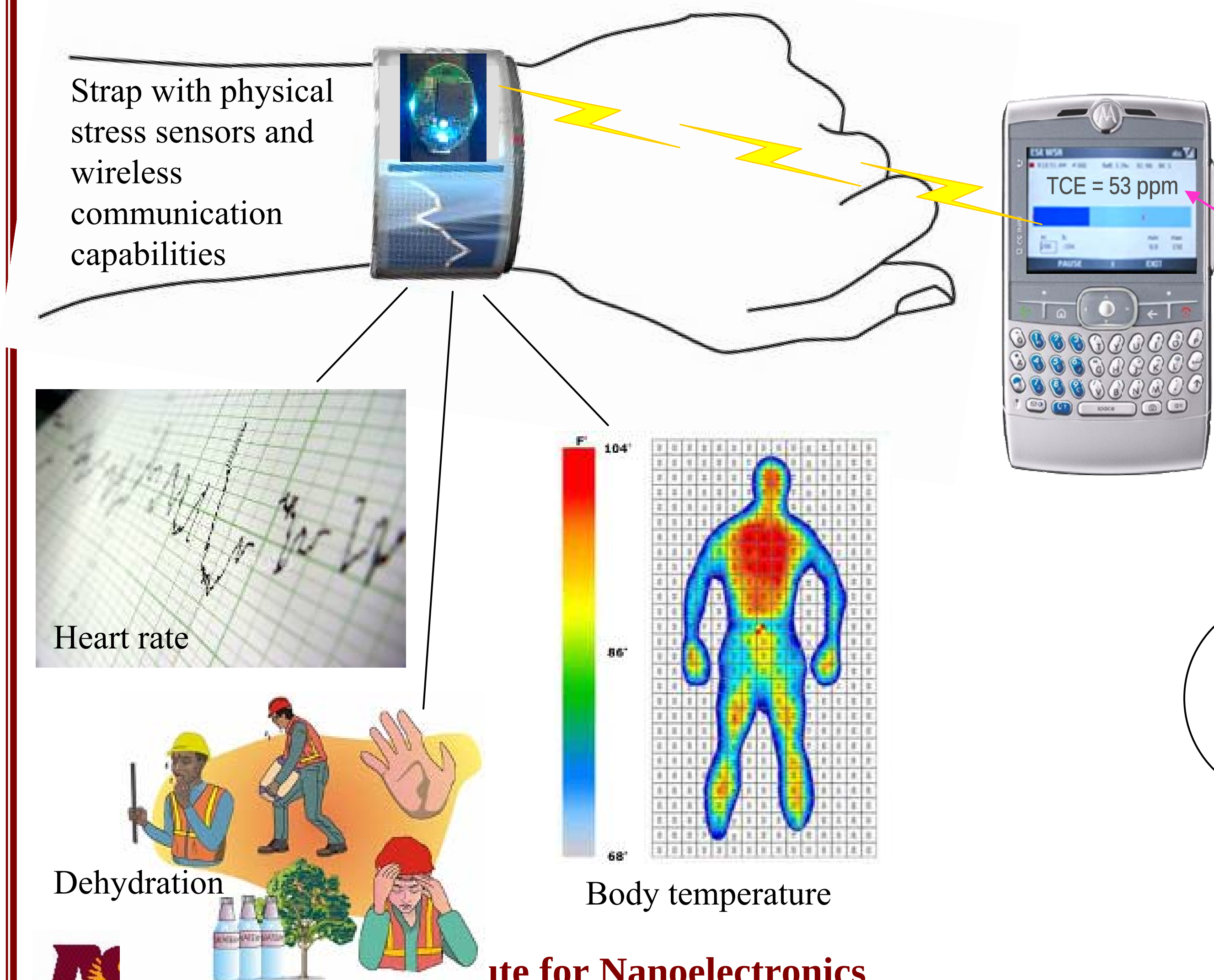


$$f = \frac{1}{2\pi}\sqrt{\frac{k}{m}}$$

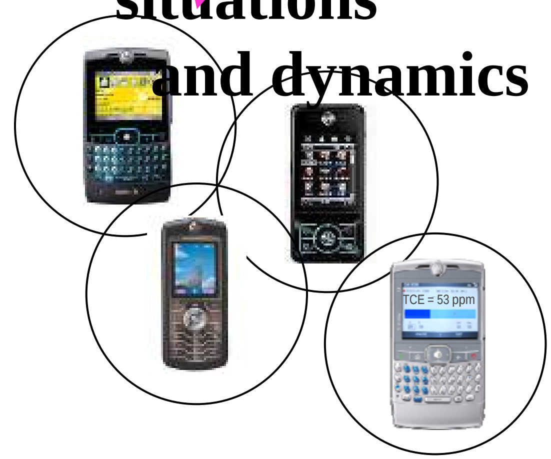


- **Conventional**: detects changes in m
- **Our approach**: detects changes in k (or Force).

Wireless Sensors



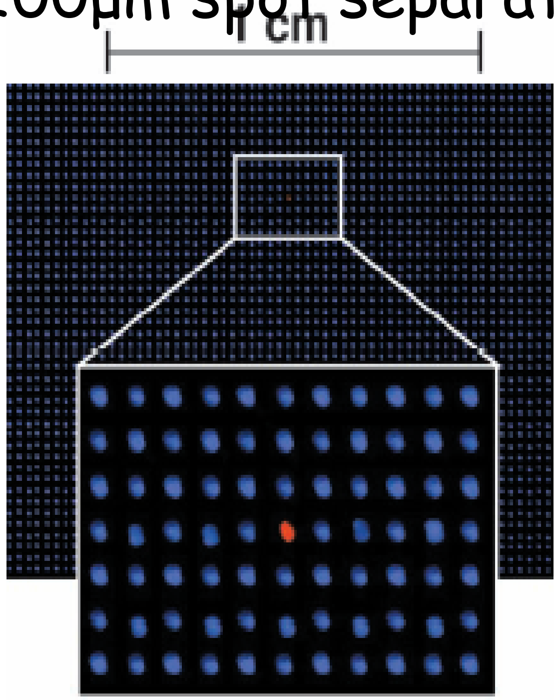
Correlate stress to:
- **Environmental conditions**
- **Group situations and dynamics**



µArrays for Protein Detection

Robotic Spotting/Printing Technique

- ~50-200µm spot size with ~200µm spot separation
- 6-16 spots/ mm^2

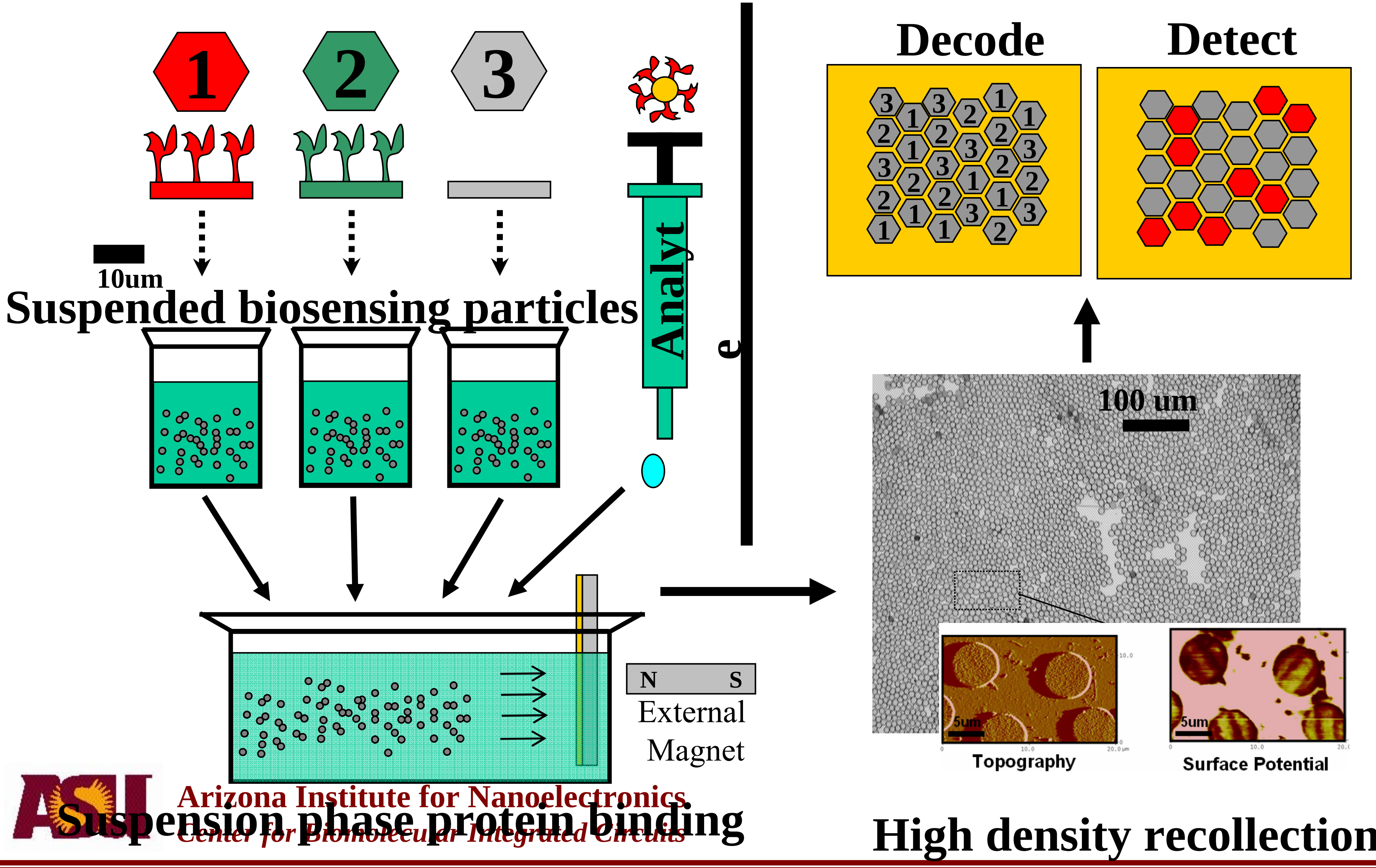


Macbeath et al.

Drawbacks:

- Cross contamination
- Droplet adhesion
- Protein dehydration
- Fluorescence quenching
- Limited coding scheme

Random Protein Arrays



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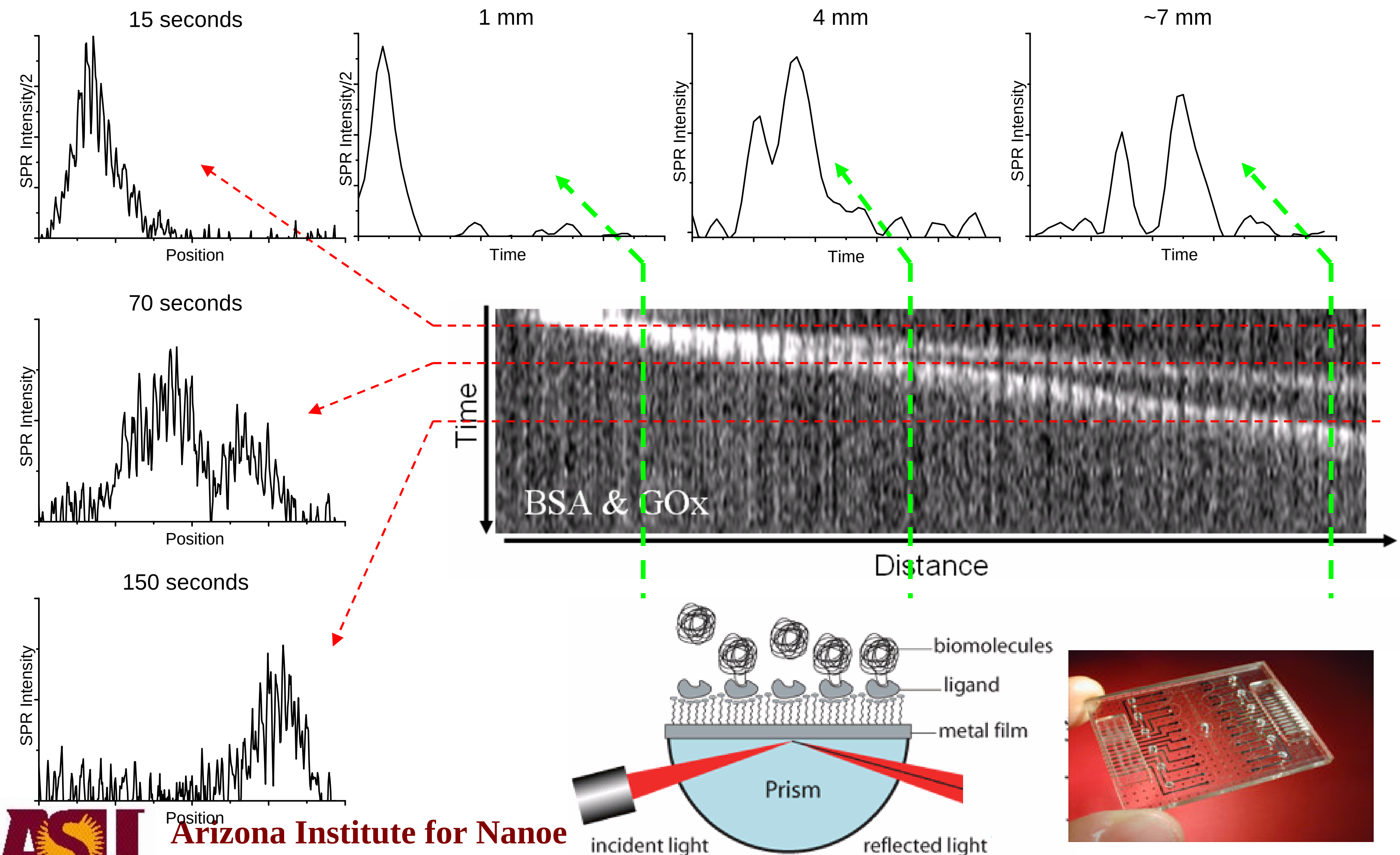
Label-Free: Protein Separation



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