Nanowire versus Photonic Biosensing

BE/ECE 247A - Biophotonics
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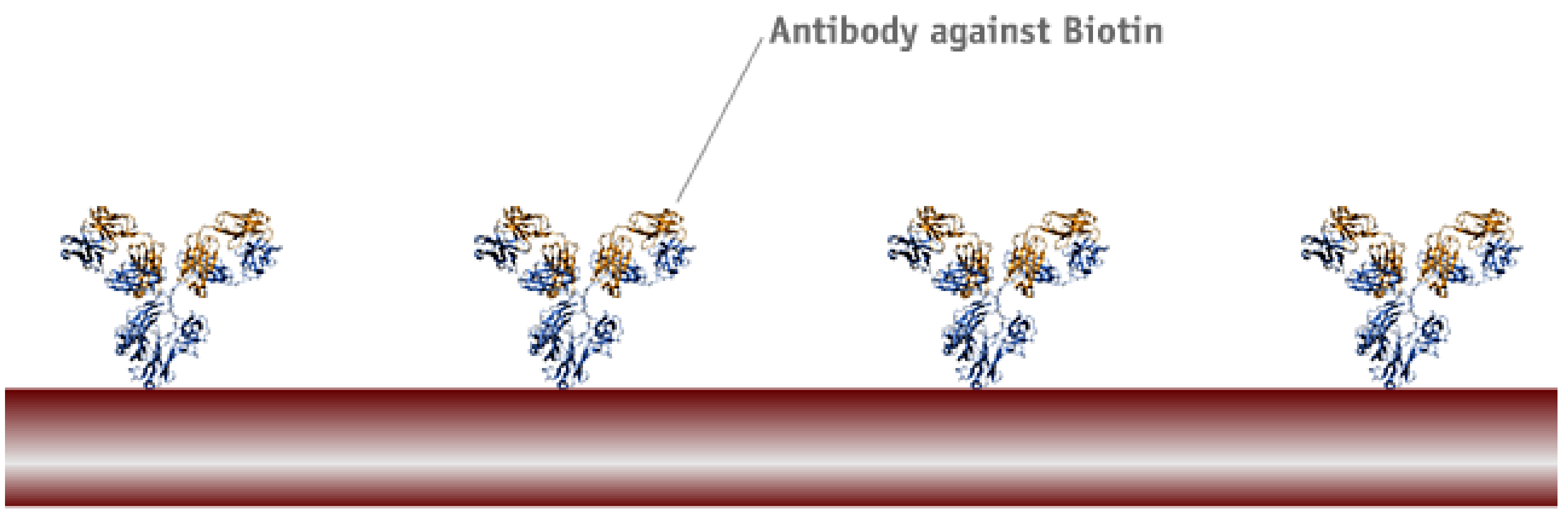
Outline

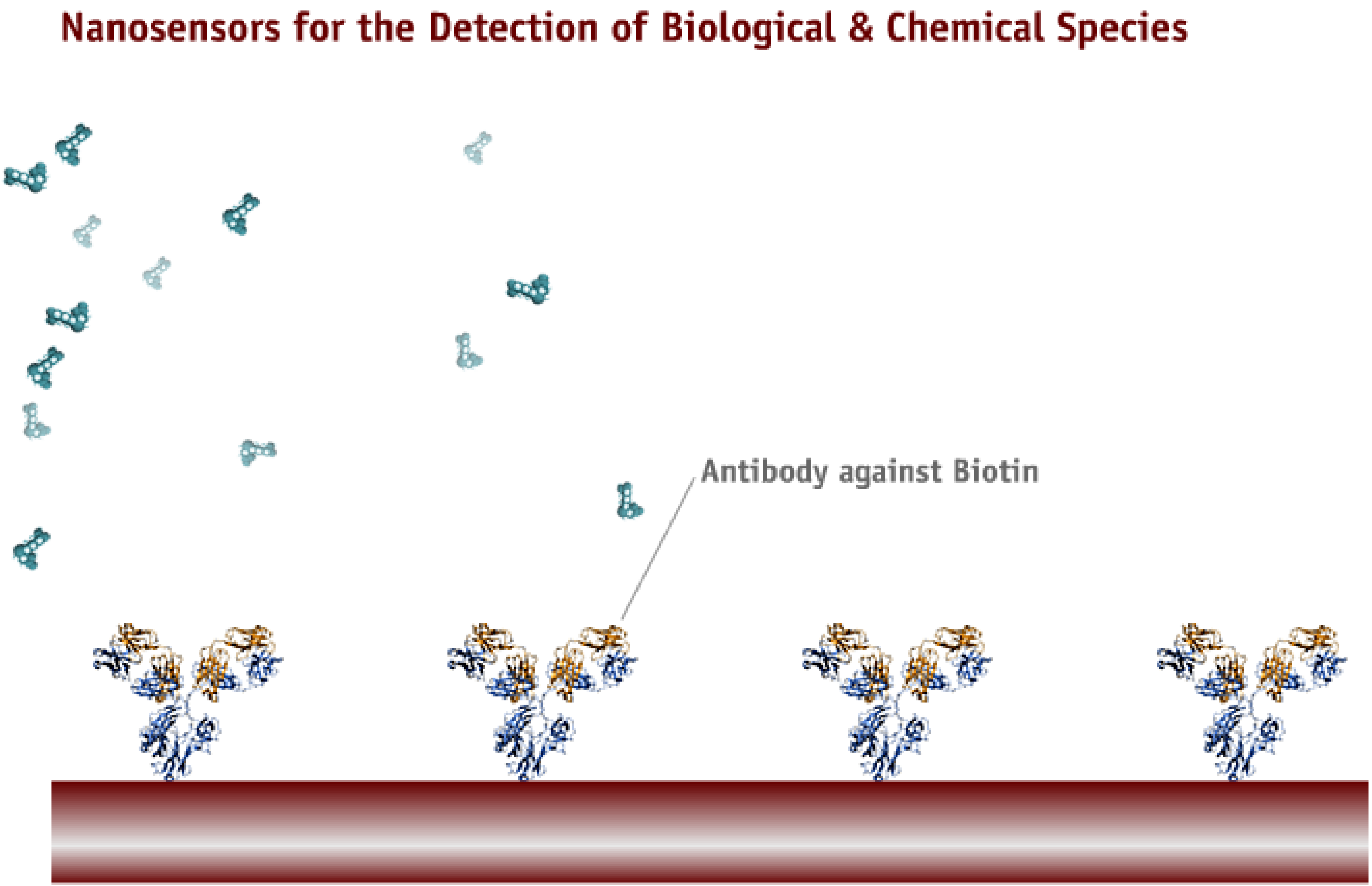
- Mechanics of nanowires
- Nanowire properties
- Examples of nanowire biosensing
- Biophotonics comparison - Nanogen technology
- Nanowire biosensing arrays
- Questions

Mechanics of Nanowires

Nanosensors for the Detection of Biological & Chemical Species



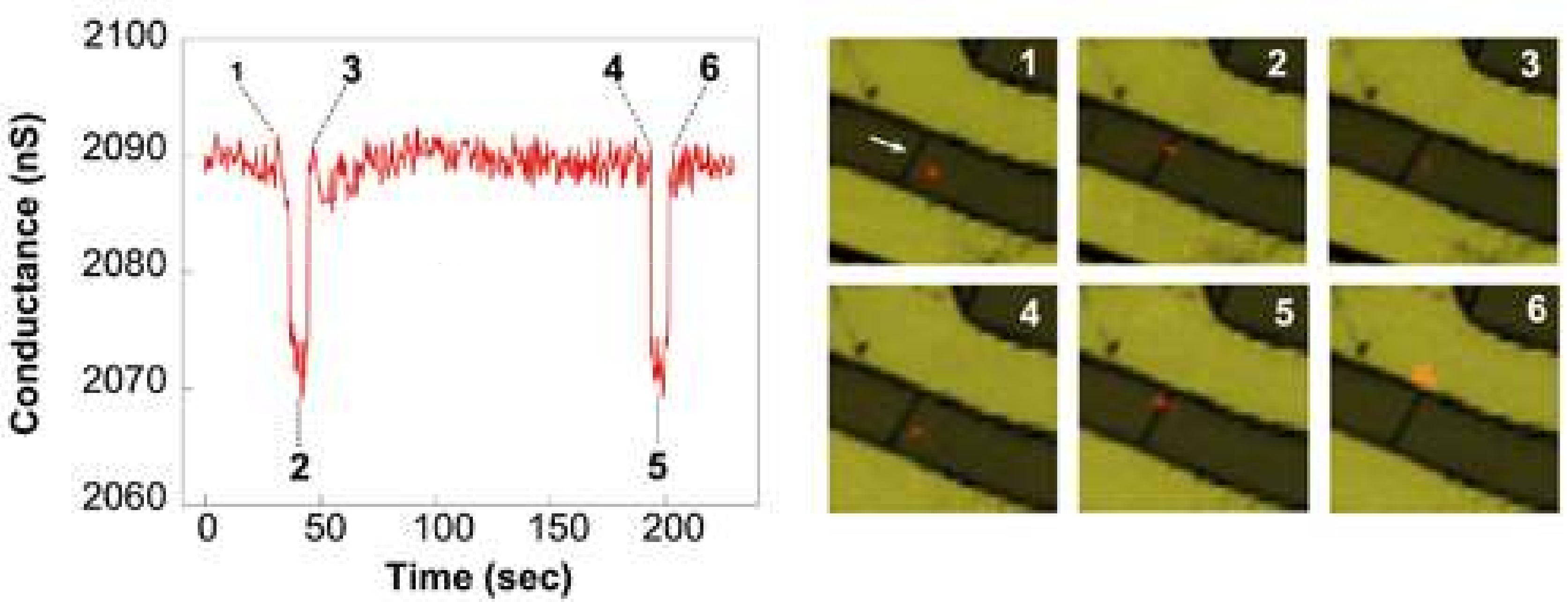
Mechanics



Nanosensors for the Detection of Biological & Chemical Species
Antibody against Biotin

Mechanics

Nanosensors for the Detection of Biological & Chemical Species



Sensing a single virus. Conductance decreases are caused by the binding of a single virus (red) to the nanowire (black).

Zhuang Research Lab, Harvard, 2006

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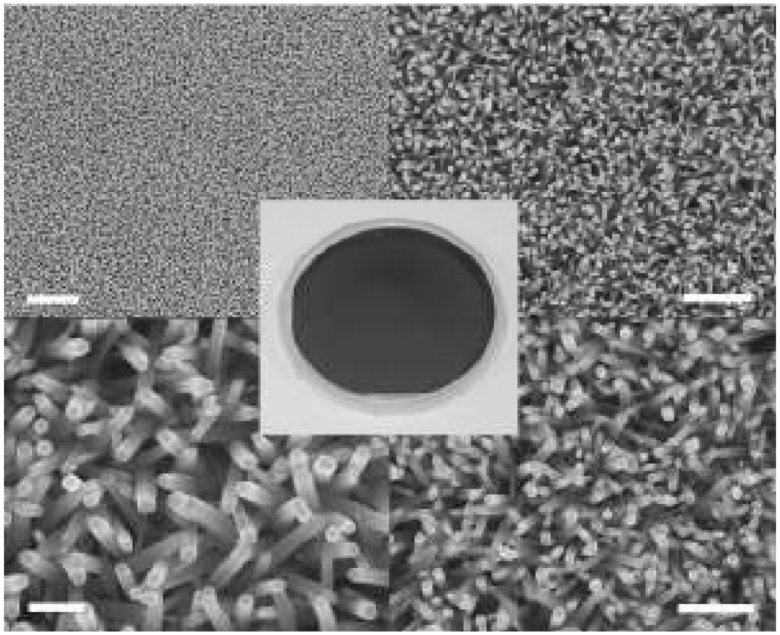
Nanowire Overview

- Dimensions on the order of 10^{-9} m.
  - Lateral size constrained to <= tens of nm (side to side).
  - Longitudinal size unconstrained (top to bottom).
  - High surface to volume ratios.
- Types:
  - Metallic: Ni, Pt, Au.
  - Semiconducting: InP, Si, GaN.
  - Insulating: SiO_2, TiO_2.
  - Molecular repeating units: DNA.
- Refer to as one dimensional material:
  - Because typical aspect ratio between length and width is >= 1000.
  - Electrons are quantum confined laterally.



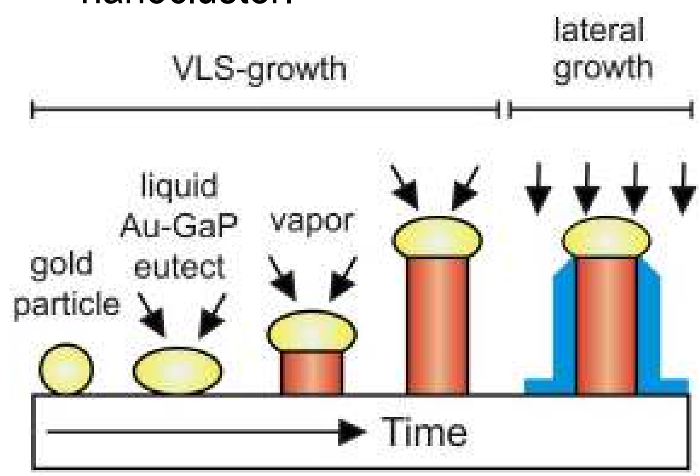
ZnO nanowire array on a 4” Si wafer. The coated wafer is in the center, surrounded by SEM images of the array at different magnifications and locations in the aqueous solution.

Greene LE et al. Angew. Chem. Int. Ed. 2003 copyright Wiley-VCH 2003.

Nanowire Formation

- Grown by promoting the crystallization of solid-state structures along one direction.
- Drawback: must be done in a lab.
- Suspended nanowire
  - Wire in a vacuum chamber held at the extremities.
  - Chemically etch or bombard a larger wire with high energy particles.
- Deposited nanowire:
  - Wire deposited on a different natured surface.
- Synthesized from elements:
  - Vapor-Phase
  - Vapor-Solid
  - Vapor-Liquid-Solid (VLS) Synthesis

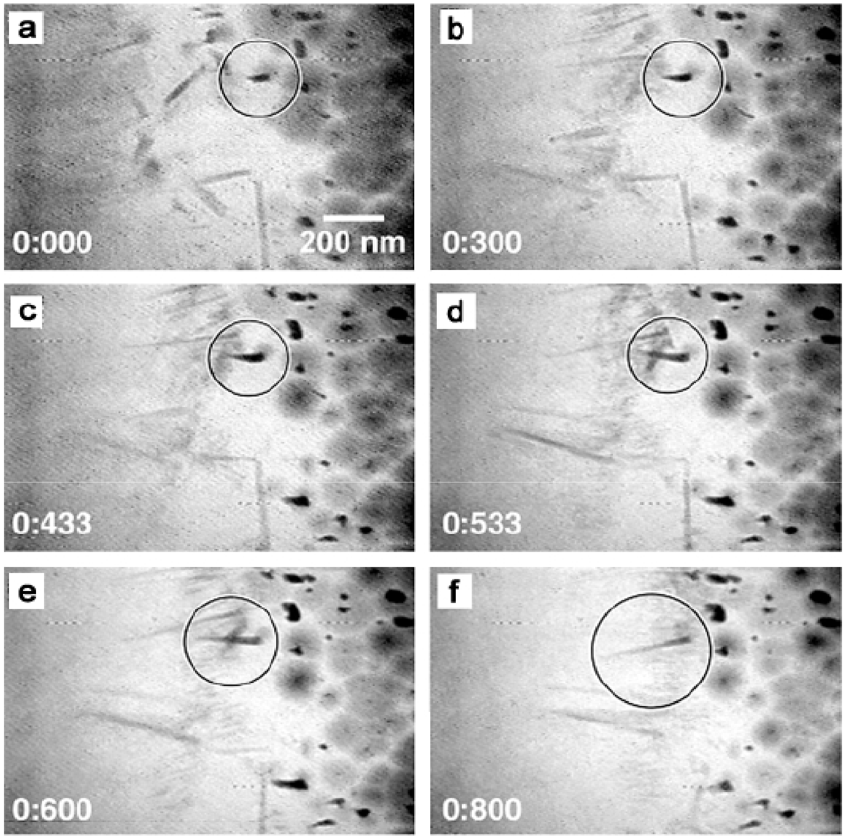
- VLS Mechanism:
  - Source material (laser ablated particles or feed gas e.g. Silane) is exposed to a catalyst (liquid metal e.g. gold nanoclusters).
  - Source enters nanoclusters.
  - When supersaturation is reached source will solidify and grow out of the nanocluster.



http://www.nanowirephotonics.com/images/nanowire_growth_schem.jpg

Nanowire Formation cont.

- Benefits of VLS:
  - Catalyst size controls thickness.
  - Growth time controls length.
  - Great uniformity in diameter (10 nm over scale of > 1 μm).
- Drawbacks of VLS:
  - Difficult to apply to metals.
  - Must use metals as a catalyst, but this may contaminate the semiconductor NW and thereby change its properties.
  - Need to analyze equilibrium phase diagrams to choose the appropriate catalyst so that the solvent can form a liquid alloy with the target material.



Video frames showing the real-time GaN nanowire growth process at ~ 1050 °C. Frame time is in (second:millisecond).

Stach EA et al. Nano Lett. 2003 copyright AM. Chem. Soc., 2003.

Nanowire Conductance

- Conductivity of NW << bulk material.
  - Due to scattering from boundaries.
- Strongly influenced by edge effects:
  - Atoms that are not fully bound to the surface may cause the NW to conduct electricity poorly.
  - Big concern as NW shrink in size and ratio of partially to fully bound atoms increases.
- Energy is quantized:
  - Integer multiples of the Landauer const, G.

$$G = \frac{2e^2}{h} \cong 12.9k / \Omega$$

  - Described by the sum of transports by separate channels of different quantized energy levels.
  - Smaller diameter NWs have fewer channels.

- Quantized conductivity is more pronounced in semiconductors (Si, GaAs) than in metals, because electron density and m* are lower.
- Lack crystalline order, because NW is only periodic along its axis. All other directions will assume any energetically favorable orientation.
- ZnO shows quantum confinement effects on the size range order < 8nm.
- Conductivity in NW is enhanced by exposing NW to photons of energy greater than their bandgap.
- Utilizing the sensitive dependence of NW conductivity on adsorbate molecules, Yang et al. demonstrated NO_2 detection on a SnO_2 nanoribbon bathed in UV light.

Nanowire Future Considerations

- Some types of nanoparticles are proving to be toxic. Would not be able to use these in a biotechnology setting without certain safety measures.
- How can we address individual elements in a high-density array?
- Desire to merge synthesis and assembly into a single step.
- **Demonstrate high selectivity.**
- **PCR (Polymerase Chain Reaction) step.**
- Standardizing and getting components to work together.
- Array alignment.
- Non-specific binding.
- Real world samples.

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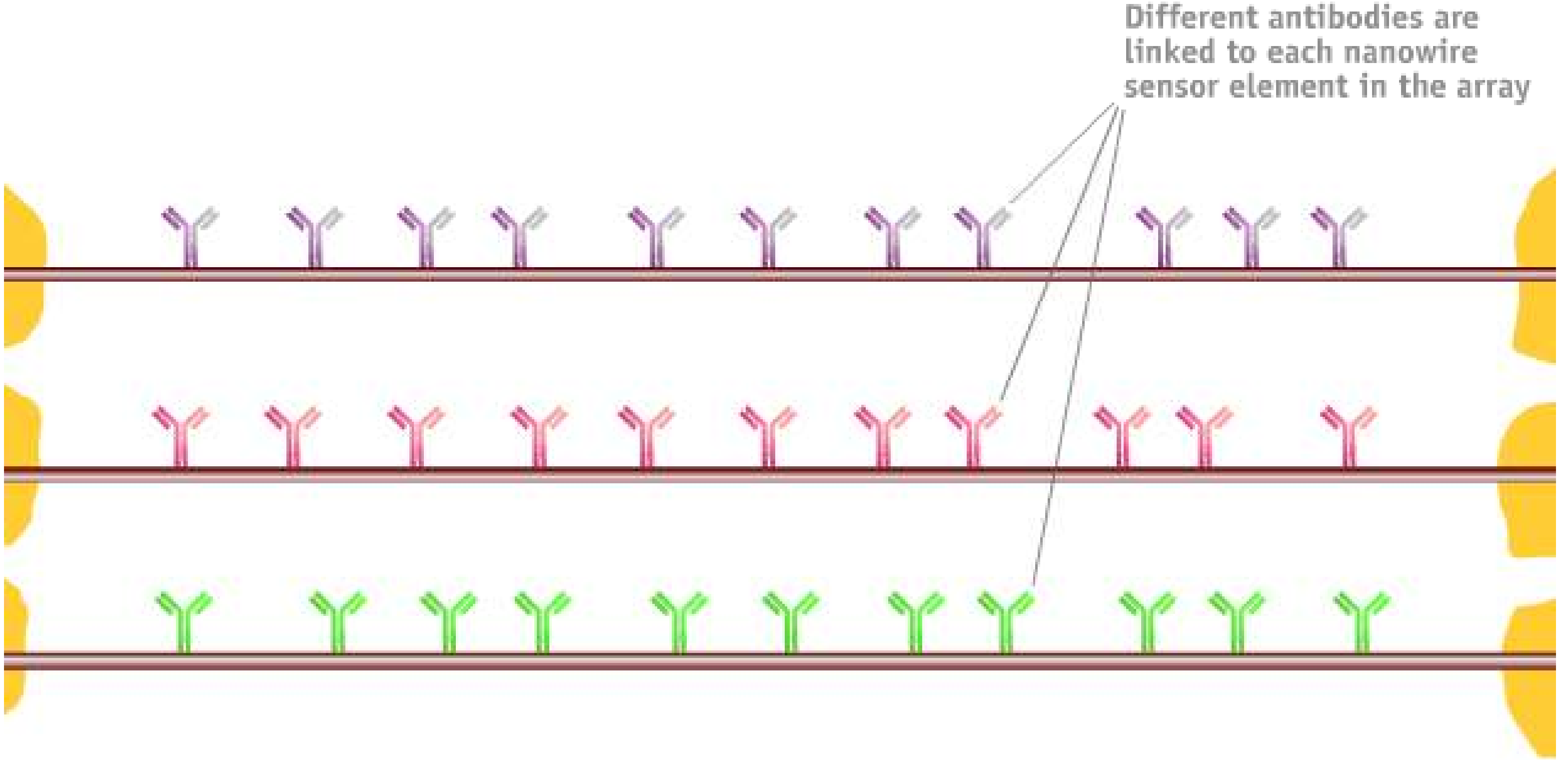
Sensing

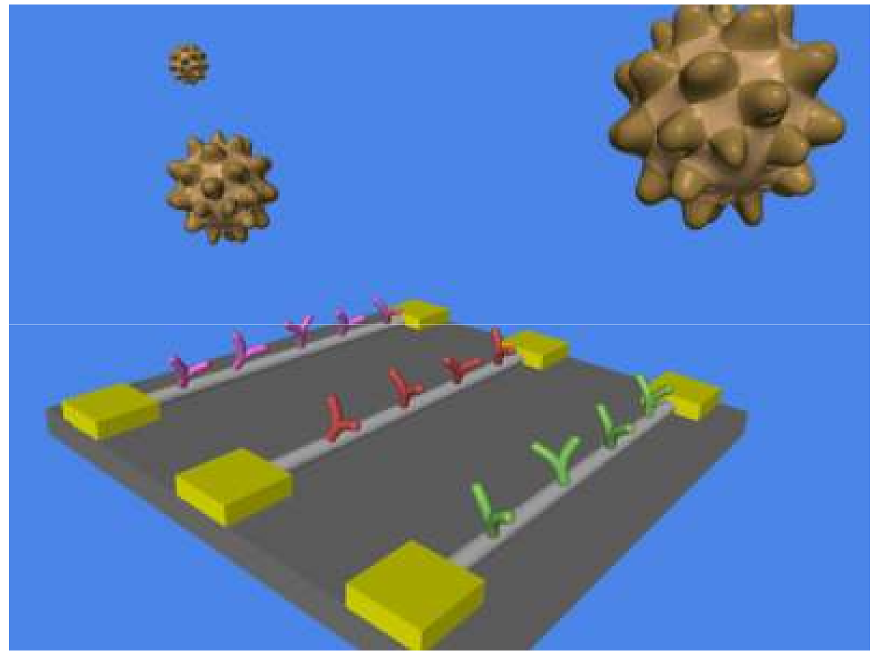
Nanosensors for the Detection of Biological & Chemical Species

Nanowire sensors modified with different antibody receptors can selectively recognize many different species in parallel and thereby enable high throughput screening for diagnostics and drug discovery.



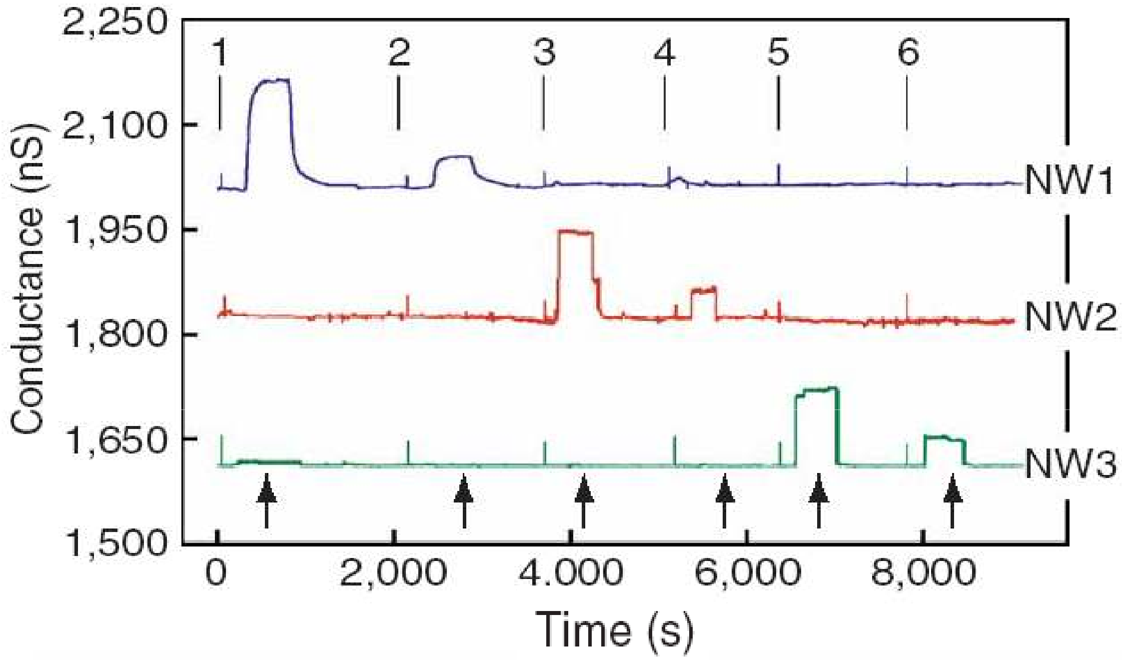
Applications

- Antibody binding to nanowire
  - Couple aldehyde propyltrimethoxysilane to cleaned Si nanowire surface
  - Link free aldehyde group to specific antibody
  - Block unreacted aldehyde group with ethanolamine
- Antigen-Antibody Complex
  - P-Type
    - Negative charge – increase in conductance
    - Positive charge –decrease in conductance
  - N-Type
    - Vice versa



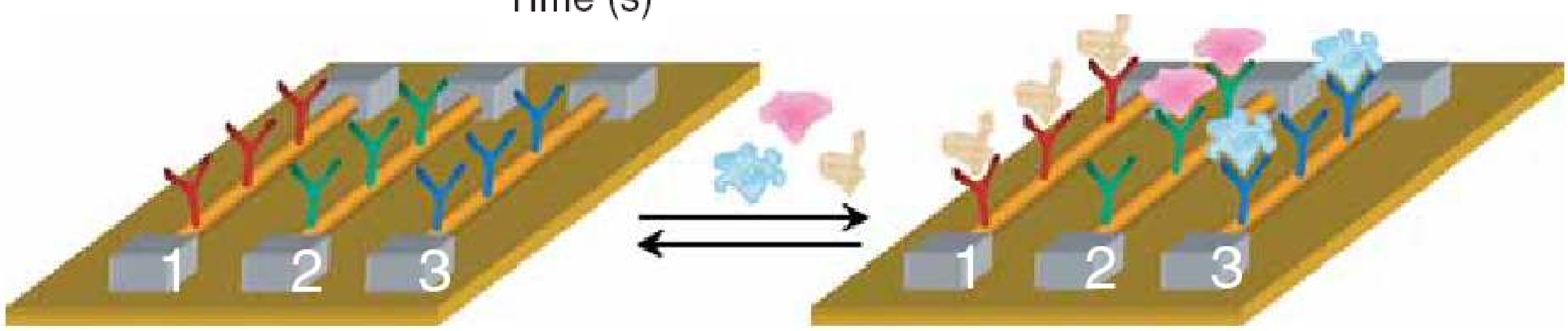
Single virus binding to sensor array

Sensor Network Example – Cancer Markers

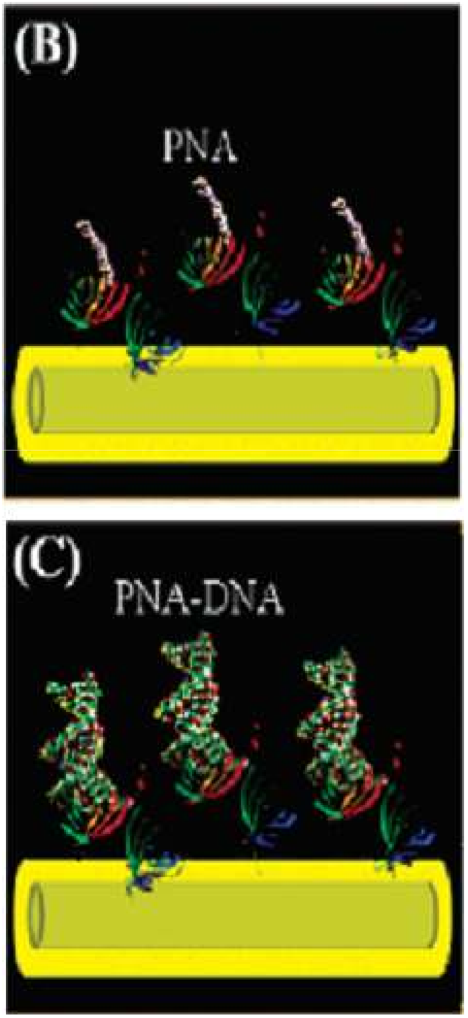


Multiplexed detection of cancer marker proteins.

Lieber Research Group, Harvard, 2005



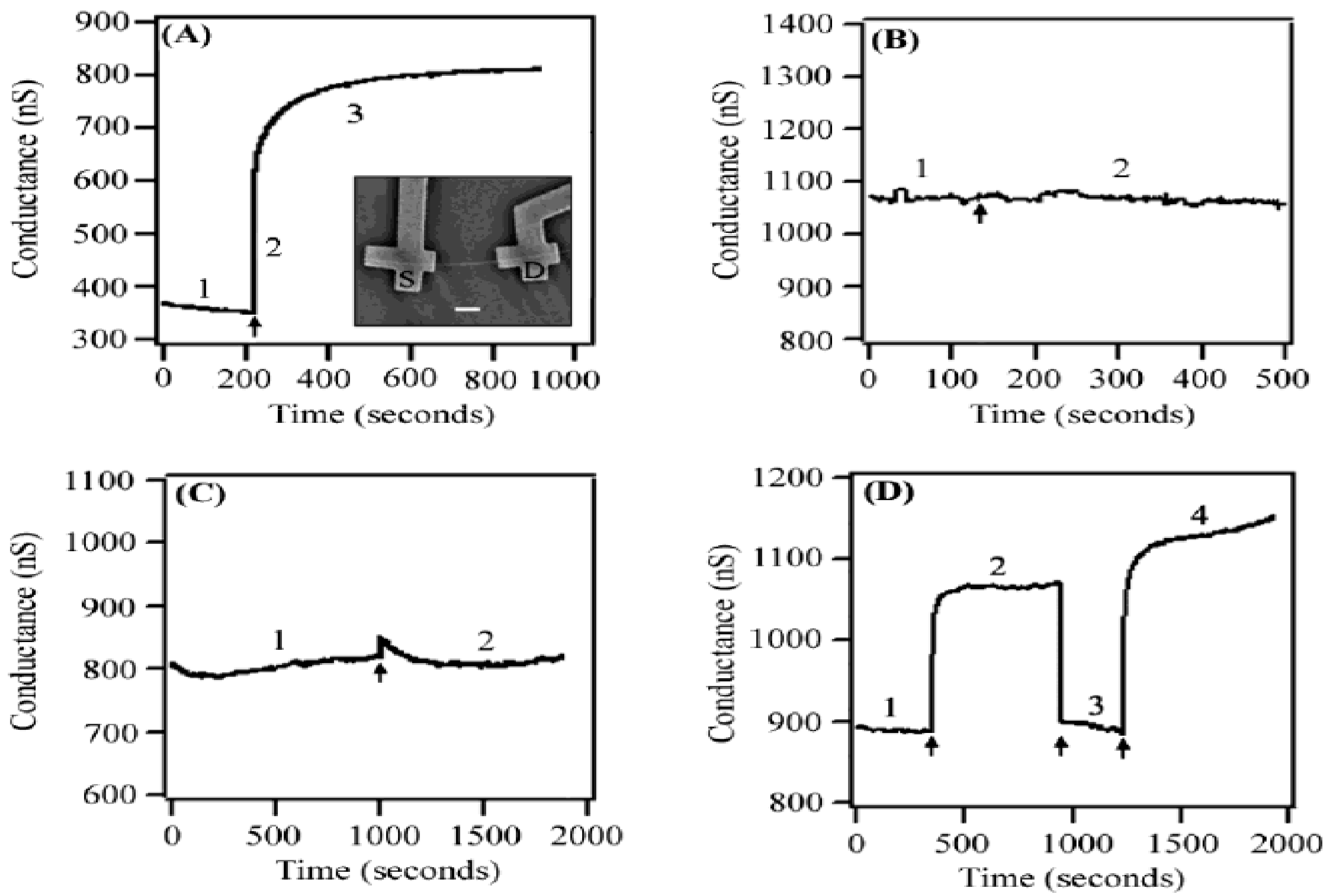
Cystic Fibrosis Transmembrane Receptor (CFTR)



Hahm et al. 2004 Nano Lett.

- Complementary to Wild Type
- Mutated gene- 75% cause of Cystic Fibrosis
- Charged oligonucleotides
  - Increase in negative surface charge density
- Increase in Conductance
  - Mutated vs. Wild Type
- Mutated Gene has some nonspecific binding
- Label free detection of CFTR gene

Change In Conductance



Hahm et al. 2004 Nano Lett.

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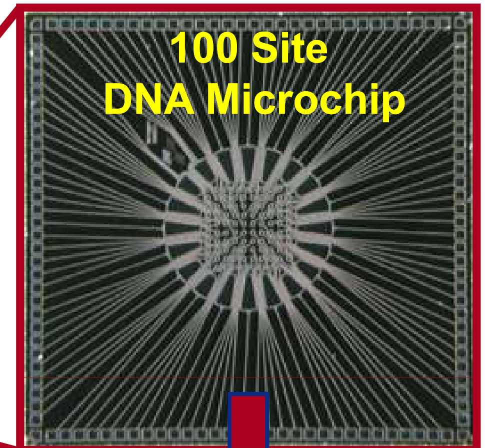
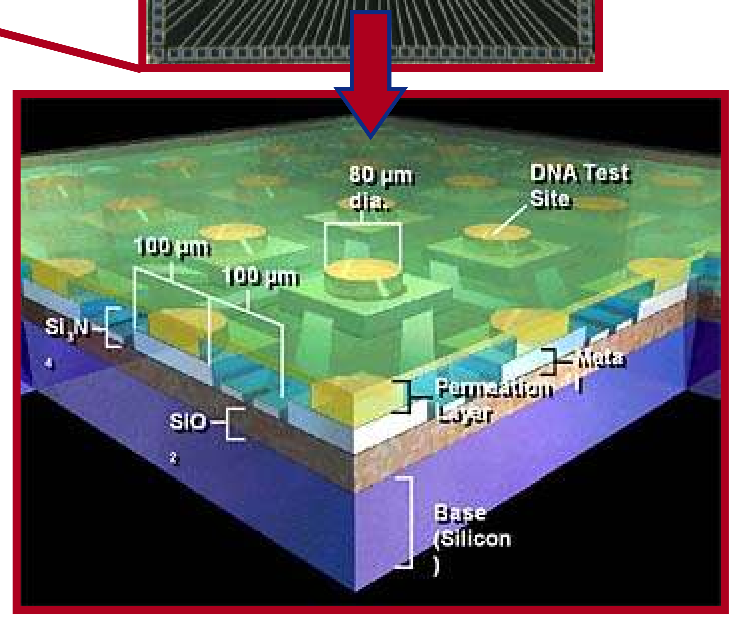
Current Biophotonics Technology: Nanogen

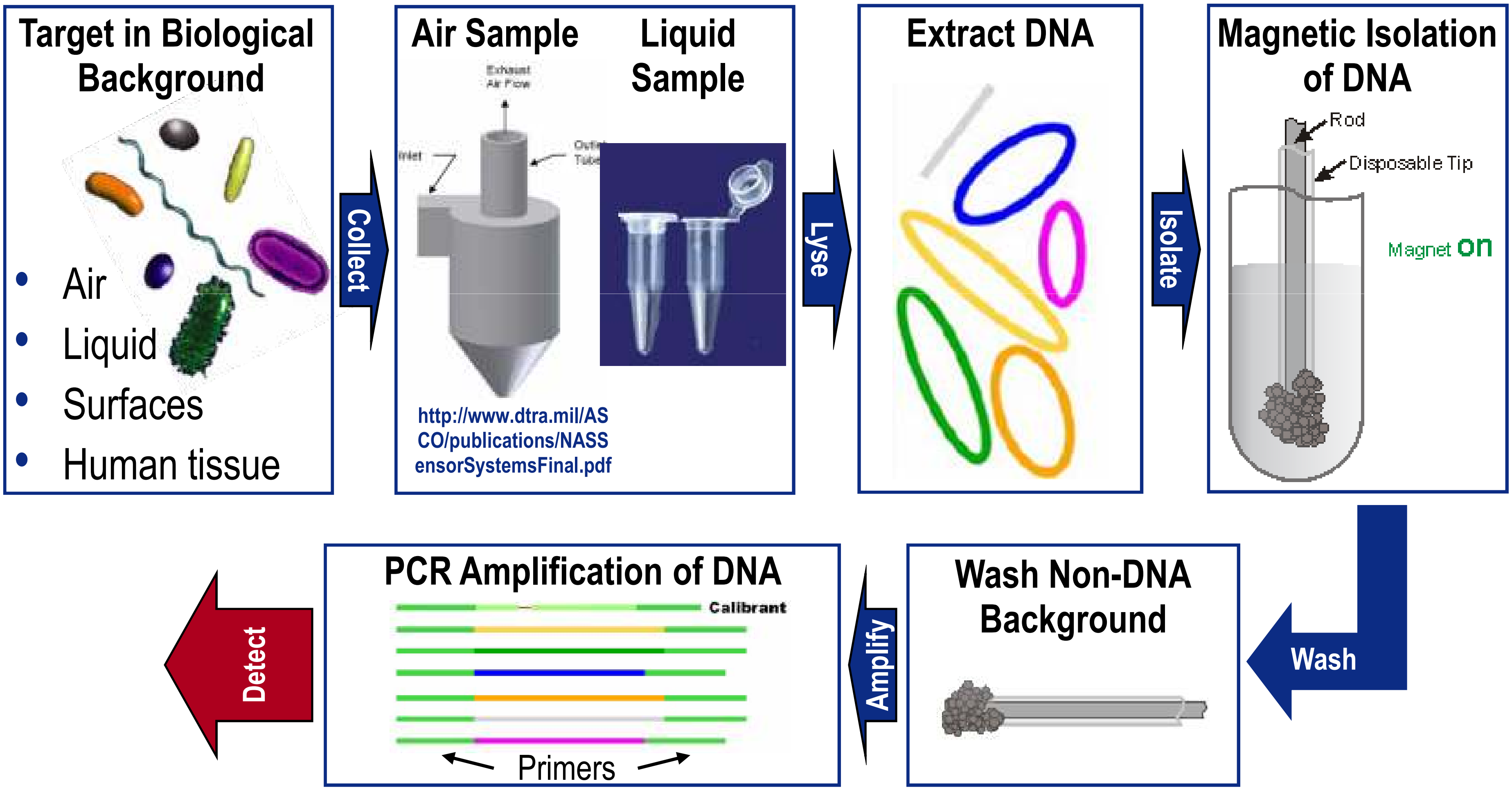
- Nanogen instrumentation overview (first generation)
  - Microfluidics
  - Electronics
  - Optics





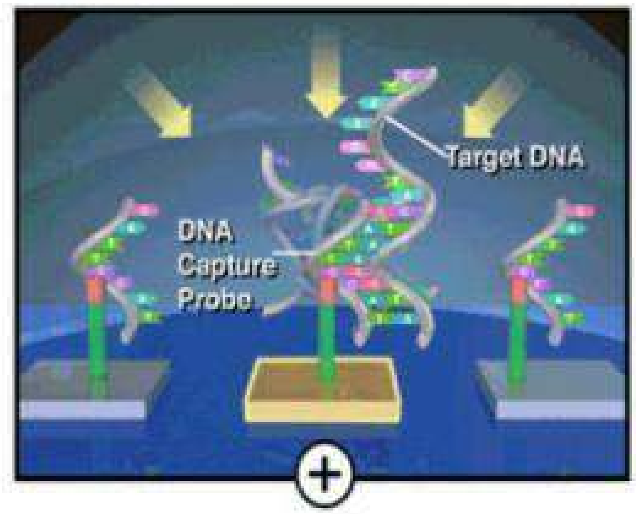
Current Biophotonics Technology: Nanogen

- Sample preparation



Current Biophotonics Technology: Nanogen

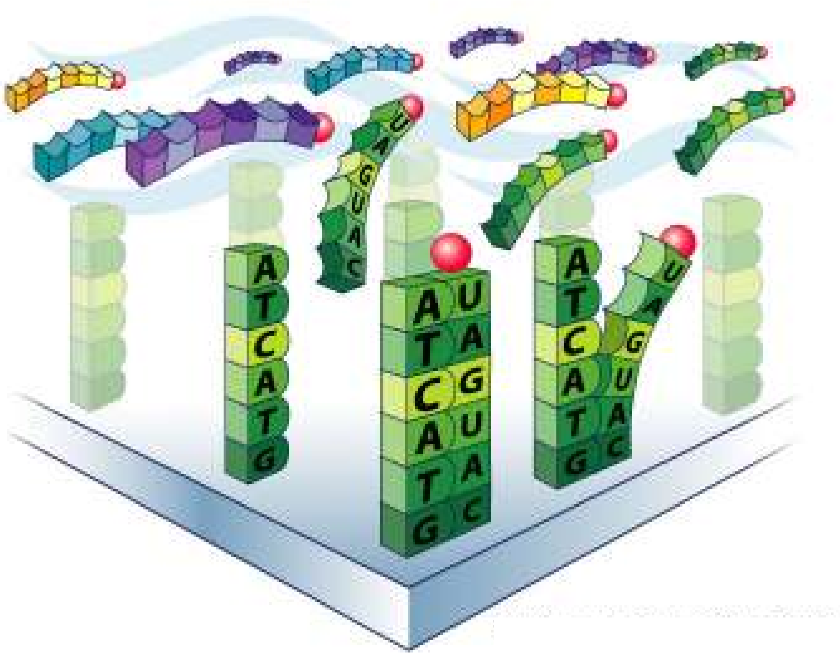
- Electronic addressing and binding technology
  - Uniquely address each site on the array
  - Apply positive voltage to test site to attract negatively charged DNA
  - Bind DNA capture probe via biotin-streptavidin bond
  - Design array for multiplexed reactions



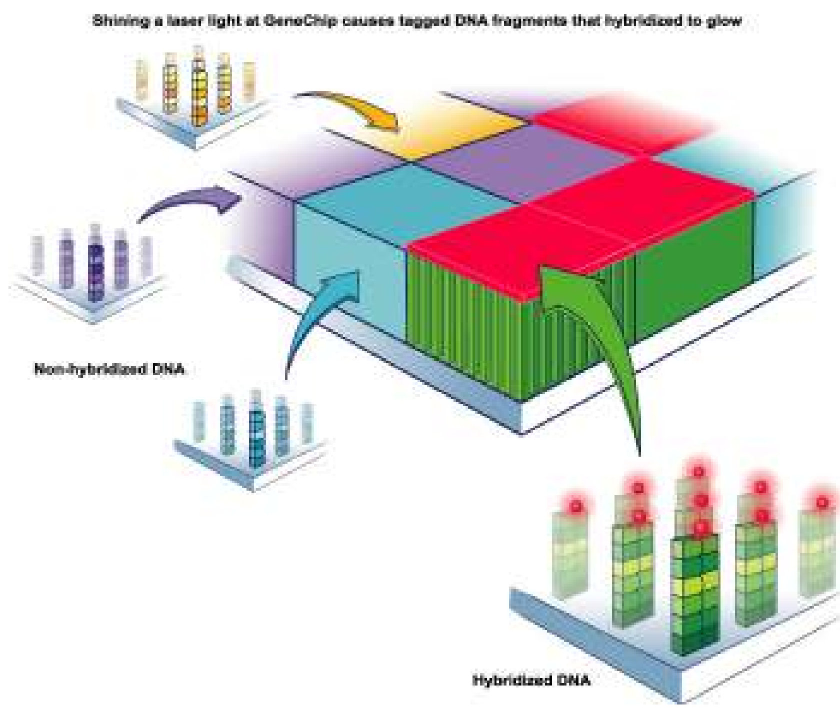
Current Biophotonics Technology: Nanogen

- Fluorescence detection of reporter probes*

Reporter probes specifically hybridize to target DNA. Wash to remove non-hybridized reporter probes



Hybridized reporter probes fluoresce when scanned with a laser



*Images from Affymetrix

Current Biophotonics Technology: Nanogen

- Future direction: miniaturization for point-of-care or fieldable diagnostics
  - Requires significant effort to engineer electronics, microfluidics and optics to fit in small footprint
  - Size of device and speed of detection limited by sample preparation and PCR

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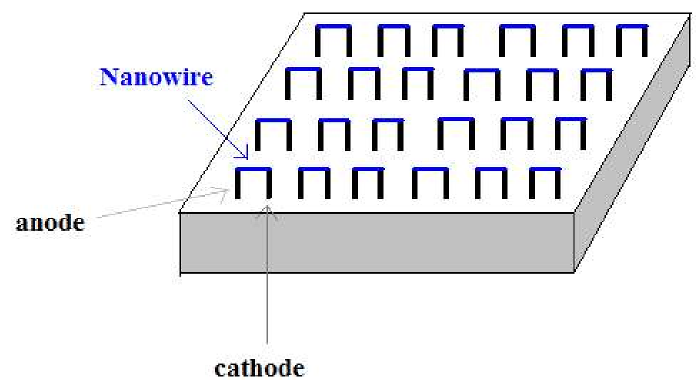
Nanowire Biosensing Arrays

- Combine Nanogen's electronic addressing technology with nanowire sensing to form a nanowire array.

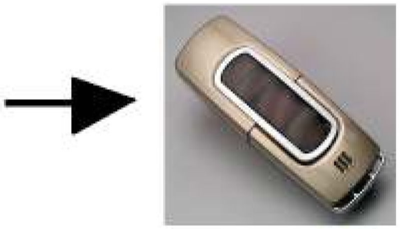
- Contributions from Nanogen:
  - Electric field assistance for molecule accumulation.
  - Fluidics technology research.
  - Circuit design (contacts layout).
  - Individual electrode addressing.

- Contribution from nanowires:
  - Potential elimination of PCR due to 10^3 higher sensitivity in NWs than conventional techniques.
  - Increase in signal to noise ratio by removing fluorescence.
  - Eliminate optics→Reduce size.
  - High selectivity reduces error.



Future Challenges

- Limitations of current flowing through nanowires?
- Growing nanowires in a uniform array.
  - Application of E-field?
  - Charged gold particle?
- Reduction of NW array spacing to increase multiplexing.
- How to integrate a current transducer into Nanogen's circuit layout.
  - Hall Effect Transducer?
- Detection site number cut in half due to anode and cathode.
- Real world sample detection.
- How many test runs will nanowires withstand?
- Cost?
- Proving this is a better technology than the current options.
  - Research and development time.



References

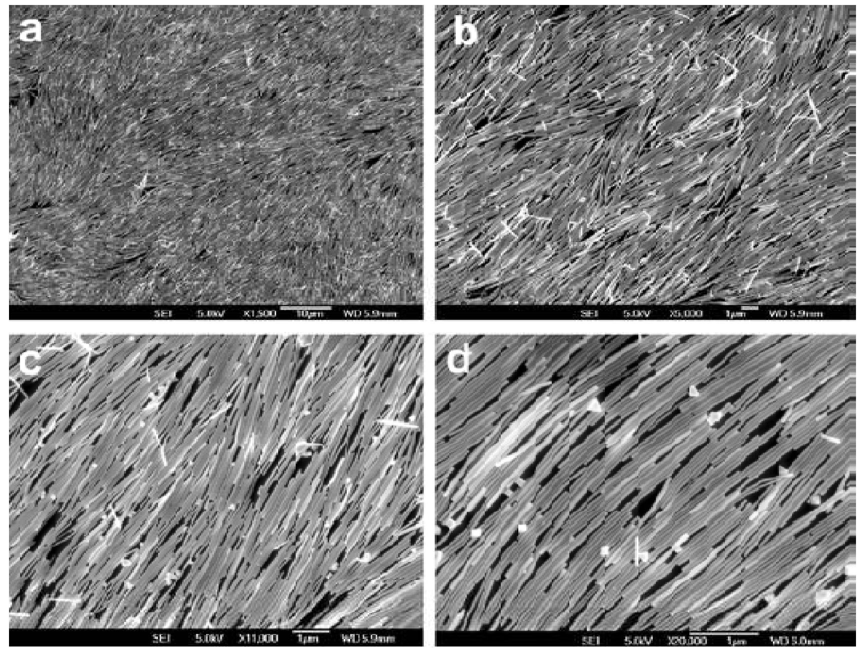
- Dr. Dalibor Hodko. Director of Advanced Technology, Nanogen, San Diego, CA.
- Matt Law, Joshua Goldberger, and Peidong Yang. 2004. Semiconductor Nanowires and Nanotubes. *Annu. Rev. Mater. Res. 34:83-122.*
- Gengfeng Zheng, Fernando Patolsky, Yi Cui, Wayne U Wang and Charles M Lieber. 2005. Multiplexed electrical detection of cancer markers with nanowire sensor arrays. *Nature Biotechnology Vol. 23 10:1294-1301.*
- Jim Kling. 2006. Moving diagnostics from the bench to the bedside. *Nature Biotechnology Vol. 24 8:891-3.*
- http://en.wikipedia.org/wiki/Nanowire.
- Bernstein, Michael. "Tiny nanowire could be next big diagnostic tool for doctors" *Medical News Today*, Dec 17, 2003.
- F. Patolsky, G. Zheng and C.M. Lieber, "Fabrication of silicon nanowire devices for ultrasensitive, label-free, real-time detection of biological and chemical species," Nat. Protocols. Accepted for publication.
- F. Patolsky, G. Zheng and C.M. Lieber, "Nanowire-Based Biosensors," Anal. Chem. 78, 4260-4269 (2006).
- F. Patolsky, G. Zheng, O. Hayden, M. Lakadamyali, X. Zhuang, C. M. Lieber, " Electrical detection of single viruses ", ***Proc. Natl. Acad. Sci. USA*** **101 ,** 14017-14022 (2004).
- J. Hahm and C.M. Lieber, "Direct Ultrasensitive Electrical Detection of DNA and DNA Sequence Variations Using Nanowire Nanosensors," Nano Lett. 4, 51-54 (2004).
- www.nanogen.com.
- www.integratednano.com

Questions?

Further Information

Nanowire Sensing

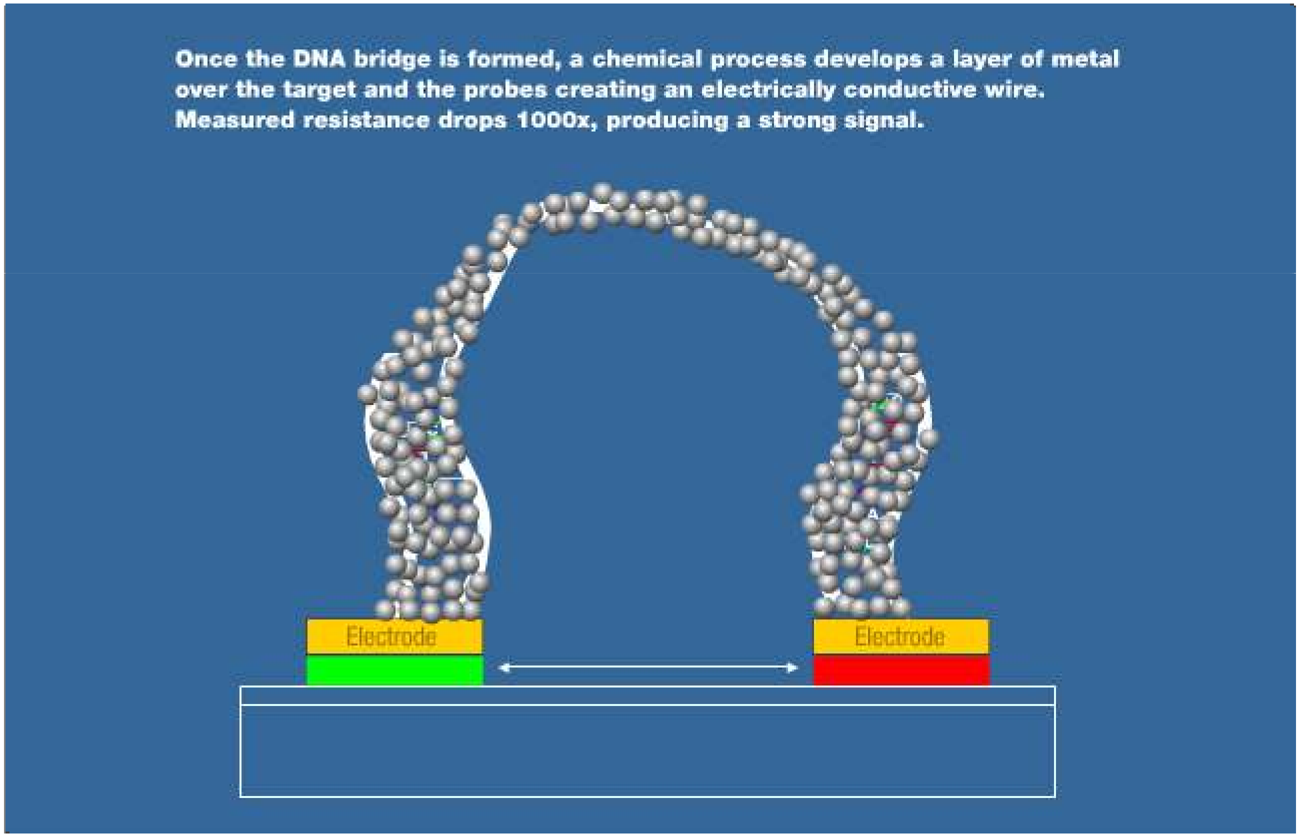
- Langmuir-Blodgett (LB) assembly:
  - Uniaxial compression of a NW-surface monolayer floating on an aqueous subphase will cause the NW to align over a large area (> 20 cm^2).
- Yang et al. used LB assembly to create a molecule-specific chemical sensor.
  - Using silver wires with well-faceted pentagonal cross sections and sharp pyramidal tips causes the closely packed NW film to act as a great substrate for surface-enhanced Raman Spectroscopy (SERS).
  - Achieved slightly better sensitivities than other types of SERS substrates.



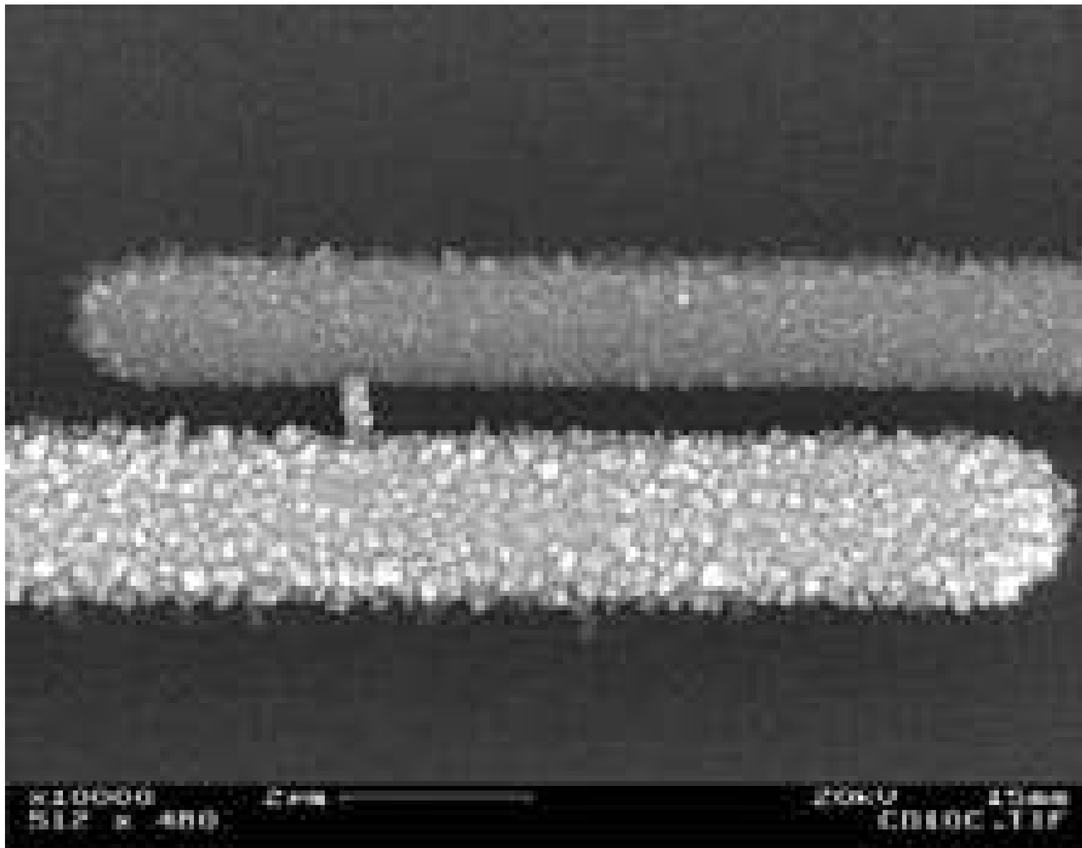
Different magnification images taken using scanning electron microscopy of the LB silver nanowire monolayer deposited onto a Si wafer.

Tao A et al. Nano Lett. 2003 copyright AM. Chem. Soc., 2003.

DNA Bridge Wires – If spacing between the anode and cathode can be reduced to 5 microns.



DNA Bridge



SEM of a metalized DNA bridge
Integrated Nano-Technologies, LLC, 2005