

Nanosensor Technologies and Applications Webinar

Friday, October 16, 2015
Webinar will begin at 12 PM EDT



Dr. Mayya Mayyappan
Chief Scientist for Exploration
Technology at NASA Ames
Research Center

This event will feature a Q&A segment with members of the public. Questions for the panel can be submitted to webinar@nnco.nano.gov from now until the end of the webinar at 1:30 pm. The moderator reserves the right to group similar questions and to omit questions that are either repetitive or not directly related to the topic.

Due to time constraints, it may not be possible to answer all questions.

>> **Lisa Friedersdorf:** Good afternoon. My name is Lisa Friedersdorf of the National Nanotechnology Coordination Office. It's my pleasure to welcome you to this webinar, "Nanosensor Technologies and Applications." This webinar is part of the series in support of the Nanotechnology for Sensors and Sensors for Nanotechnology Signature Initiative, one of the five signature initiatives of the National Nanotechnology Initiative. More information about the Signature Initiative and the Federal resources supporting the development of nanosensors can be found at nano.gov/sensorsnportal.



Sensor Technology



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Chang-Ki Baek and Jeong Soo Lee

For today's webinar I am pleased to introduce Dr. Meyya Meyyappan, Chief Scientist for Exploration Technology at NASA Ames. His [biographical information](#) is available on the [NASA website]. And with that, Meyya, I turn it over to you.



Webinar Outline



- Introduction, Sensor definitions
- Transduction Mechanisms
- Chemical Sensors
- Biosensors
- Radiation Sensor
- Challenges facing sensor development

>> **Dr. Meyya Meyyappan:** Thank you, Lisa. Good morning, everyone. Thank you for joining this webinar. I have designed this webinar as a fairly introductory discussion of sensor technology.

I will spend about 10 or 15 minutes talking about sensor definitions. I will spend a little bit of time talking about various transduction approaches. I will then dive into examples of nanochemical sensors, nanobiosensors, and a little bit on radiation sensors. Finally, I will close off with challenges facing nanosensor development. Hopefully, we should leave plenty of time at the end for your questions.

 **What is a Sensor?** 

- Sensor is a device that produces a measurable signal in response to a stimulus.
 - Exposure to certain species or change in environment may alter one or more properties of the sensor such as mass, conductivity or some other measurable physical property either directly or indirectly.
- Motivation is to monitor the environment around us to gain knowledge and use that knowledge later for different purposes.
- In the task of sensing, external effects must be accounted for
 - temperature
 - humidity
 - altitude
 - shock, vibration
 -
 -
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So what is a sensor? A sensor is a device that produces a measurable signal in response to an external stimulus. We may not always be able to measure exactly what we want in the first place. For example, you may not be able to measure concentration of a species in the ambient directly. On the other hand, because of potential changes in concentration, mass, conductivity or some other measurable property of a gas in the ambient, the physical properties of the sensing medium might change. So that way we can measure changes in the concentration (or other parameters) indirectly. When we deal with sensors, we have to keep in mind the impact of external effects; for example, temperature and humidity. Those two are very key external variables that will definitely impact whatever you are trying to measure. Then there are other possibilities, too, like altitude, shock, and vibration. Those could play a minor role.



Expectations



- Unlike instrumentation to achieve the same measurement, sensors must be small (size, mass.....)
- Inexpensive
- Reliable
- Accurate
- Stable
- Provide high resolution

Some definitions later.....

So what do we expect from a sensor? The gold standard[s], in many cases, are bulky instruments, but unlike these instruments, sensors are expected to be very small in terms of size and mass, and inexpensive. (Generally, we are not willing to pay the same price we would pay for a mass spectrometer or gas chromatograph.) Of course, it's got to be as reliable and accurate as a bulky instrument (which we use as the gold standard), as well as stable and capable of providing high resolution [measurements]. I will come back to these definitions a little bit later.



Where do we come across sensors?



- Physical, Chemical, Biological sensors in
 - Environmental monitoring
 - Medical diagnostics, Health care
 - Automotive
 - Civil aviation
 - Industrial manufacturing
 - Military
 - Security, threat monitoring
 -
 - Internet of things ?

We can come across physical, chemical, biological sensors in a variety of scenarios: monitoring the environment, clinical diagnostics, routine health checkups, automotive, civil aviation, industrial manufacturing, military, security, threat monitoring, and, of course, the Internet of Things (IoT) is right around the corner.



Some Common Examples of Sensors



- Household
 - Surge protectors
 - Automatic light switches
 - Smoke detectors
 - Fire detectors
 - Pilot light checking on stoves
- Automotive
 - Oil pressure
 - Oil temperature
 - Fuel level
- Aircraft
 - Wind speed
 - Altitude
 - Position

Here are some very basic day-to-day examples of sensors. In all of our houses, we have surge protectors, automatic light switches, smoke detectors, fire detectors, and even checking the pilot lights on stoves. In the automotive scenario, there are sensors to check and monitor the oil pressure and temperature and fuel gauge levels. And, of course, an aircraft is full of sensors. Here are another few examples: sensors to measure the wind speed, where you are in the sky, altitude, and position. So these are basic day-to-day examples of sensors that we can come across.



Some definitions



- **Accuracy** relates to how closely the sensor output matches the true value.
 - assessment is possible only if the sensor is calibrated against a standard or by comparing against another measurement system with a known accuracy
- **Error** is the difference between the sensor measurement and the actual value as established above
- **Resolution** is defined as the smallest incremental change in the measured environment that can produce a detectable increment in the output signal.
 - This is necessarily limited by the noise in the system

Source: Kalantar-Zadeh, Fry, Nanotechnology enabled sensors, Springer 2008

So now in the next five to ten minutes, I want to talk about the definitions that we come across in the sensor business. The first one is accuracy. By the way, when you take a look at the literature, especially in the nanosensor literature, accuracy is something that is rarely discussed. During the use of a sensor, we provide an external stimulus causing a change in the ambient. How do we know that the sensor output or what the sensor tells us is real? What is the true value? The only way you would know the true value is if you calibrate your sensor against a gold standard, an instrument that is commonly used. That's the way we can establish accuracy of a sensor. And then the difference between the standard and your sensor measurement, that is actually the error. So accuracy and error are things that one needs to assess before the sensors can become reliable. When you make a small change in the ambient, you may not necessarily see any changes in sensing. The smallest incremental change that you can measure from your sensor, as a result to a change in the ambient, is what we call the resolution. Obviously, resolution is going to be limited by the signal-to-noise ratio for the sensor system.



Definitions (continued)



- **Noise** refers to random fluctuation in the output signal even when the input (i.e. the environment being measured) is not changing.

Noise sources can be external or internal

External Sources

Mechanical vibration

Electromagnetic interference

Thermal changes in the environment

Internal Sources

Shot noise

1/f noise

Noise can come in many different forms. It can be external: the external noise source could be a simple mechanical vibration or you can have electromagnetic interference, or, of course, thermal changes in the environment. The internal sources of noise are shot noise and 1/f noise. Regardless of what the source of noise is, it is a random fluctuation of the output signal, even when your input is completely quiet and nothing changes in the ambient. This is why the resolution is going to depend on what the noise in your system is.



Internal Noises



- *Electronic Noise*, which results from random variations in current or voltage. Origin: from thermal energy, which causes charge carriers to move about in random motions. It is unavoidable and present in all electronic circuits.
- *Shot Noise*, which manifests as the random fluctuations in a measured signal, caused by the signal carriers' (electrons, holes, photons, etc.) random arrival time.
- *Generation-Recombination Noise*, or *g-r noise*, that arises from the generation and recombination of electrons and holes in semiconductors.
- *Pink Noise*, also known as *1/f noise*, is associated with a frequency spectrum of a signal, and has equal power per octave. The noise components of the frequency spectrum are inversely proportional to the frequency. Pink noise is associated with self-organizing, bottom-up systems that occur in many physical (e.g. meteorological: thunderstorms, earthquakes), biological (statistical distributions of DNA sequences, heart beat rhythms) and economical systems (stock markets).

[Additional definitions for noise can be found in slide 10.]



More Definitions



- **Drift** is the gradual change in the sensor response over time even when the input environment is constant and stable
- **Minimum detectable signal**
The minimum signal that can be extracted when noise is taken into account. If the noise is high with respect to the input, it is hard to extract a clear, meaningful signal from the noise.
- **Detection limit**
It is the smallest value of the variable that can be measured by the sensor

Most of the sensors have their response drifting over a period of time, even when the ambient that you are measuring is completely stable. It is important to know what this drift is. It is not something you necessarily have to worry about, because the sensor drift is gradual, and, over time that slope can be very small. On the other hand, when a real event happens—let's say, again, we are measuring concentration of a species and the ambient—and there is a sudden change in the concentration of that species, that slope is going to be much, much larger than the gradual drift that you come across in all sensors. But if you don't even know that your sensor drifts, then there is just no way you can distinguish between the real event and whether something is happening because of the drift. Your signal processing algorithm or pattern recognition algorithm can be trained to distinguish between this gradual slope because of drift and then the sudden changes in slope that arise because of an actual event.

The minimum detectable signal is obviously taking noise into account, as pointed out earlier on. If the noise is too high with respect to the input, then whatever you measure is totally meaningless.

The detection limit is the smallest value of the variable that you can measure using your sensor.



Definitions (continued)



- **Stability** refers to the sensor's ability to produce the same output value when the input conditions are constant over a period of time.
- **Repeatability**
This refers to the sensor's ability to produce the same response in successive measurements for the same input, when all operating and environmental conditions are constant.
- **Reproducibility**
This refers to the ability to reproduce an identical response for a given input after some condition has been changed. For example, shutting down and restarting the sensor system should be able to give the same response for the same input concentration, just as it was prior to shutdown.

Stability is the ability of the sensor to produce the same output value when the input conditions remain the same. That's how you know the sensor is stable because the input conditions don't change at all. However, if the output conditions are varying, this would mean the sensor is totally unstable.

Repeatability refers to the sensor's ability to keep producing the same response over and over again, even if you keep making measurements one after the other for the same input while keeping all the operating conditions the same.

Reproducibility is slightly different. Let's say you have a sensor and you make a measurement, and now you shut the sensor down, then you restart the sensor system, but you go back to the same ambient condition or input condition. Obviously, you would have to get the same output.



More Definitions



- **Sensor range or span** represents the range of input conditions that will yield measurable output signals
 - Operation outside the range
 - may be meaningless
 - may suffer from large inaccuracies
 - may even damage the system
- **Sensor response time** is the time needed by the sensor to arrive at a stable value in response to a stimulus.
 - If a step change is introduced in the input, response time is the time required for the sensor to reach 95% of the final value.

The sensor range or span represents the range of input conditions for which you can get meaningful output signals. If you try to operate outside of the range, the results you would observe may be totally meaningless, or you may get data that could be completely inaccurate. In some cases, you might wind up damaging the system.

As for the response time: let's assume there is a sudden step change in the external stimulus. Then the response time is the time needed for the sensor to arrive at a stable value in response to the change in stimulus. Usually, the percent of the final value is taken as a benchmark. Generally, in the literature, that last 5% is ignored. If you introduce a step change, response time is the time required for the sensor to reach 95% of the final value.



More Definitions



- **Sensor recovery time** is the time required for the sensor to reach 95% of its final value when the source of the stimulus is removed.
- **Sensitivity** is the ratio of the incremental change in the sensor output signal to an incremental change in the ambient under measurement.
- **Selectivity** refers to the ability of the sensor to discriminate the one component under pursuit in the presence of several others

Recovery time is the reverse of response time. When you take away the stimulus, the step change is whatever time it takes to approach 95% of the final value.

The last two definitions are sensitivity and selectivity. Sensitivity is a ratio: the delta [change] in the sensor output signal over the delta [change] in the ambient stimulus. Selectivity is defined by absolute discrimination: if you're looking for one analyte, what is the possibility of identifying that analyte alone and absolutely nothing else without any confusion (even if there are many other things present in the ambient).

As you can see, there are a whole lot of definitions. If you take a look at the literature, especially in the nanosensor literature, people generally talk about sensitivity and occasionally detection limit by extrapolating the IUPAC [International Union of Pure and Applied Chemistry] definition of “three times the signal-to-noise ratio.” The other two things that are commonly covered are recovery time and response time. These are generally applied to gas sensors. And a lot of other concepts are not discussed at all; that is something we have to keep in mind.



Acceptable sensor parameters in some common fields



	Domestic	Industrial	Medical	Automotive	Environmental
Acceptable cost (£)	1	500	Disposable 10, non-disposable 250	5	Disposable 10, non-disposable 250
Acceptable error (%)	10.0	0.1 – 5.0	0.1 – 2.0	1.0 – 5.0	1.0 – 10.0
Mean time between failures (hours)	10 ³ during 10 years of intermittent use.	10 ³ during 10 years of continuous use.	Disposable 150 during 1 week of continuous use, non-disposable 5 × 10 ³ during 5 years of intermittent use.	1.5 × 10 ⁴ during 10 years of intermittent use.	Disposable 150 during 1 week of continuous use, non-disposable 10 ⁴ during 10 years of intermittent use.
Temperature range (°C)	-20 to 400	-200 to 1500	Disposable 10 to 50, non-disposable 0 to 250	-30 to 400	-30 to 100
Response time (secs)	1	0.1 – 10	1	10 ⁻³ – 1	100

Source: R. G. Jackson, Novel Sensors and Sensing, IOP (2004)

[Slide 15 has a brief summary of acceptable sensor parameters in some common fields.]

 **Physical Effects employed in Signal Transduction** 

- Photoelectric effect
- Photodielectric effect
- Photoluminescence effect
- Electroluminescence effect
- Chemiluminescence effect
- Doppler effect
- Barkhausen effect
- Hall effect
- Nernst effect
- Thermoelectric (Seebeck/Peltier/Thomson) effect
- Thermoresistive effect
- Piezoresistive effect
- Piezoelectric effect
- Pyroelectric effect
- Magneto-mechanical effect
- Magnetoresistive effect
- Faraday rotation effect
- Magneto-optic Kerr effect
- Kerr and Pockels effect

Source: Kalantar-Zadeh and Fry, Springer (2008)

For the next five or ten minutes, I'm going to talk about transduction approaches. As I mentioned in the beginning of my presentation, you may not be able to measure the variable of interest directly; for example, a species concentration. We end up measuring it indirectly by a change in mass, conductivity, or some other physical property of the sensing medium. What you want in these measurable things is basically a connection to physical effects. I have a list here of the physical effects: photoelectric, photodielectric, etc. I am not going to go through all of these; I will pick and choose about four or five transduction mechanisms that are very common.



Transduction Platforms

 **Transduction Platforms** 

- Conductometric, Capacitive
- Optical
- Electrochemical
- Solid State
- Acoustic wave based

Transducer is a device that converts energy from one form to another.

While a sensing layer or active medium directly responds to the external change, the transducer converts that response into an externally measurable quantity.

In any type of sensor, there is a sensing layer or medium, which directly responds to an external stimulus. The transducer is the one that converts the response into a measurable quantity. In that sense, a transducer is a simple device that converts energy from one form to another. The common platforms or common transduction approaches are conductometric, capacitive, optical (which is very common), electrochemical, solid state devices, and acoustic, wave-based approaches.

Ames Research Center **Conductometric and Capacitive Transducers**

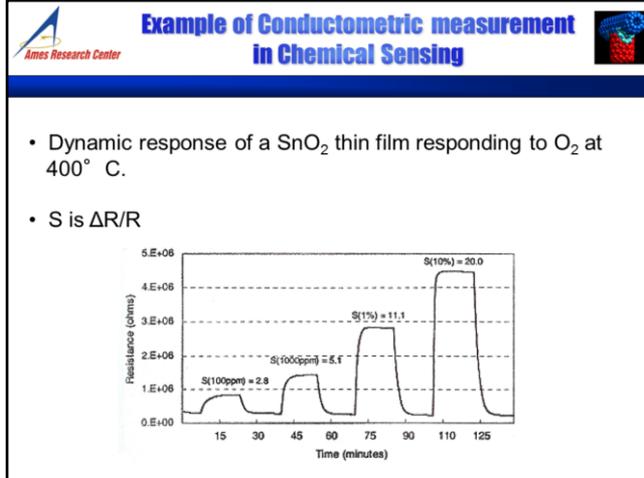
- The sensing material is applied over a pair of electrodes on a substrate. Electrical conductivity or capacitance can be measured in response to an applied voltage.

$V = R I$ Ohm's Law

$Q = C V$ Q is charge & C is Capacitance = $\epsilon A/d$
 ϵ is dielectric constant, A is electrode area
d is distance between electrodes

- Both Conductance and Capacitance measurements can be under DC or AC conditions.
- Interdigitated electrodes are very common

The simplest transducers are based on measuring conductivity, resistance, and capacitance. As you can see in this image, you have a simple electrode system: two electrodes covering a conducting layer that is connected to a circuit. You can measure the conductivity or capacitance in response to an applied voltage. If it is based on conductivity measurement, it is governed by Ohm's law. If it's a capacitance, then it is a proportional correlation of charge to voltage. You can measure the capacitance and the resistance both under AC and DC conditions, depending on what's convenient. Instead of using a simple two-electrode system covering the conductive layer on a substrate, it is very common to use interdigitated fingers. These interdigitated fingers provide a good area of coverage. When you review the sensor literature, even in the case of acoustic waves, the use of interdigitated fingers can be very common.



This is an example of what the output would look like when you measure resistance in response to a gas or vapor. The thin film here is composed of tin dioxide. The analyte is oxygen at 400 degrees centigrade. What is plotted is the resistance as a function of time. At every bump, you can see an increase in resistance that is correlated with oxygen levels (in parts per million or ppm). The first bump is about 100 ppm and the next bump is 1,000 ppm, then it is 1% and then 10%. Obviously the resistance increases when the concentration of oxygen increases. Normally, instead of just plotting resistance, it's common to calculate the change in resistance: the instantaneous resistance upon exposure to the analyte minus the baseline resistance. Then that is generally normalized by the baseline resistance. That's the one that is commonly plotted; you will see it in the examples I'm going to talk about later as well as in the literature.



Solid State Transducers



- Consist of metal-semiconductor, semiconductor-semiconductor junctions and work by measuring the change in the electric field distribution in response to a change in environment.
- Direct measurements of: Current, Voltage, Capacitance, Impedance
- Different forms
 - p-n diodes
 - Bipolar junction transistors
 - Schottky diodes
 - MOS capacitors
 - Field effect transistors

The solid state transducers are either metal-semiconductor junction or semiconductor-semiconductor junction. You can measure the current voltage behavior of these junctions in response to a change in the environment. The different forms could be simple p-n diodes all the way up to bipolar junction transistors, Schottky diodes, MOS (metal oxide semiconductor) capacitors, and the most common form, which is the field effect transistor. We will see field effect transistor examples as we go along.

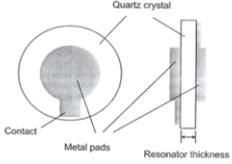
 **Acoustic Wave Transducers** 

- Employ piezoelectric materials
- Two types of acoustic waves
 - Bulk acoustic waves (BAW): waves propagate in the bulk of a solid
 - Surface acoustic waves (SAW): wave propagation confined to a region near the surface of the solid
- When used for sensing, perturbations in the acoustic wave's fields are measured.
 - when the AW propagates through the bulk or surface, any changes in the propagation path affect the velocity and amplitude of the wave; these changes can be monitored by measuring the frequency or phase characteristics
 - The results can be correlated to physical or chemical properties of the environment

Acoustic wave transducers use piezoelectric materials. There are two types of acoustic waves commonly used by the sensor community: one is bulk acoustic wave, the way it propagates in the bulk of the solid; the other one is the surface acoustic wave, where the wave propagation is completely confined to a region very close to the surface. When we use it for a sensor, we are looking for changes in the acoustic wave field. The acoustic wave propagates through the bulk or surface. When the ambient changes, what happens is the propagation path of the acoustic wave changes and that will affect the velocity and amplitude of the wave. Those are the things that we would measure and then we would correlate back to the nature of the ambient. It could be physical changes in the ambient, like pressure or temperature, or it could be chemical changes to the ambient by a change in concentration of something like ammonia, nitric oxide, or whatever is present in the ambient. Both physical and chemical properties can change the propagation path of the acoustic wave, thus providing an opportunity to measure changes in the ambient.

 **Quartz Crystal Microbalance** 

- QCM is a BAW resonator
 - Quartz substrate machined into thin disks
 - metal pads deposited on both sides for application of electric signals.
- The quartz crystal transforms the applied electric signal into acoustic waves
 - The trapped AWs bounce back and forth within the crystal resulting in resonance
 - Any addition of mass on the quartz crystal (for example, gas adsorption) increases its thickness, thus changing wave characteristics.
- Additional sensing layer can be added to the quartz, that is specific to a given species. Helps with selectivity
- Environmental monitoring, gas sensors, biosensors



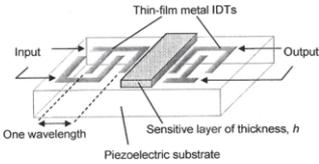
Here is an example of a bulk acoustic wave resonator: it is a simple quartz crystal microbalance. The quartz substrate is micro-machined into a thin disk and then you deposit metal pads on both sides for applying the electric signal. One pad is used for applying the signal and the other is used to measure the output. The acoustic waves are trapped between these two pads and bounce back and forth within the crystal resulting in resonance. When something changes in the ambient (for example, the mass of the quartz crystal changes because something from the ambient gets absorbed, like a gas), then the thickness of the quartz crystal increases and that will change the wave character completely. That's the information that is used to back calculate what is in the ambient. Instead of using plain quartz, it's also possible to add sensitive layers to the quartz in order to get some kind of selectivity. Commonly, the quartz crystal microbalance has been used for monitoring the environment, for gas sensors, and even for biosensors.



SAW Transducers



- Interdigitated Transducers (IDTs) are patterned on the surface of a piezoelectric crystal. A sensitive layer may be used that is responsive to the species of interest.
- An alternating voltage is applied to input IDT which launches the acoustic wave. The wave travels along the surface to the output IDT where it is converted back to electrical signal.
- Can be used in sensing
 - Temperature
 - Acceleration
 - Force, pressure
 - Electric field, magnetic field
 - Gas flow
 - Ionic, vapor concentrations
 - Biosensing



Surface acoustic wave or SAW transducers are a bit more complicated. They commonly use the interdigitated finger approach that I mentioned earlier on. These interdigitated transducers are patterned on the surface of the same type of piezoelectric crystal. Here you can use a sensitive layer in order to provide some selectivity. You then apply an AC voltage to the input side of the interdigitated finger in order to launch the acoustic wave. The wave will travel along the surface to the output side of the interdigitated finger. There, it is converted back into an electrical signal. SAW transducers have been extensively used to measure temperature, acceleration, force and pressure, electric field, magnetic field, even gas flows, ionic and vapor concentrations, and for biosensing.



- Can be used to monitor changes in conductivity of a sensing layer
 - metal oxides, conducting polymers are examples
 - Their conductivity change in response to various oxidizing or reducing gases/vapors.
 - Depositing these layers in the active area makes this into a chemical sensor.
- Shift in the operational frequency f , after adding the conducting layer:

$$f = f_0 \frac{k^2}{2} \frac{1}{1 + (\sigma_{SH} / \sigma_{OR})^2}$$

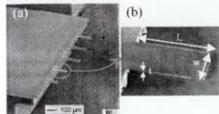
- k^2 : electromechanical coupling coefficient
 f_0 : operational frequency
 σ_{SH} : sheet conductivity of the sensitive layer
 σ_{OR} : Product of SAW mode velocity and substrate permittivity.

[Dr. Meyyappan did not speak to this slide, but it is included in the interest of completeness.]

Ames Research Center **Cantilever based Transducer**

- A microcantilever that resonates because of the environment change or adsorption of species on its surface.
 - Resonant frequency changes due to the above
 - Useful to monitor mass, heat, temperature, stress, radiation
- Typical frequencies: 100 MHz to 5 GHz depending on cantilever material and dimensions.
- Shift in frequency due to added mass:

$$\Delta m = K/4\pi^2 \left[\frac{1}{f_1^2} - \frac{1}{f_0^2} \right]; k \text{ is spring constant.}$$
- Monitoring biological interactions: antigen-antibody interaction; hybridization of DNA strands.
- Minimum detectable mass of a cantilever $\sim 10^{-15}$ g.



Another type of sensor that is popular is a cantilever-based transducer. You can make a microcantilever similar to what you would see in the atomic force microscope (AFM). The microcantilever would resonate when there is any change in the environment or some gas or vapor gets adsorbed on the surface (so you are actually monitoring the resonance frequency change). This will be used to monitor mass, heat, temperature, stress, radiation, and number of other things. Typical operating frequencies are 100 megahertz to 5 gigahertz. That depends on the cantilever material: either silicon, silicon nitride, or carbon nanotubes. The material properties ultimately dictate the operating frequency. People have used cantilever-based transducers extensively for monitoring biological interactions, antigen-antibody interactions, or hybridization of DNA strands. The minimum detectable mass of a cantilever is about 10 to the minus 15 grams. Researchers have also engineered new approaches to exploit multiple cantilevers. Each one of those cantilevers can interact with a set of molecules to achieve multiplexing. All sorts of things have been done with cantilever-based transducers, especially by people working on biosensors.

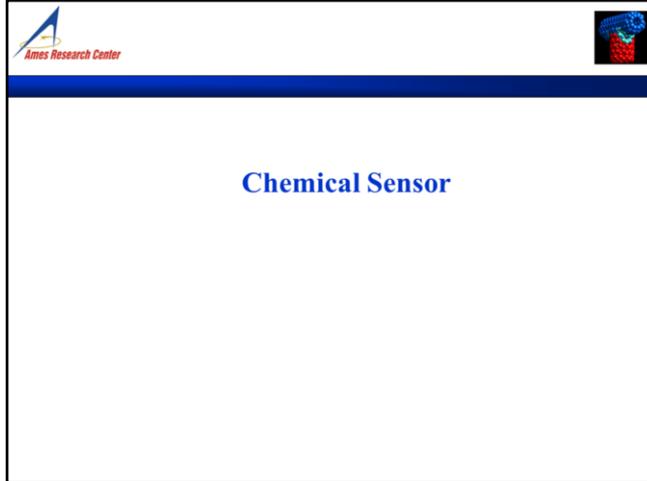


Electrochemical Transducers



- They generate signals which result from the presence and interaction of chemical species
 - They make use of chemical effects to monitor species concentration
 - Two main effects: voltammetry, amperometry.
- **Voltammetry:** Two dissimilar materials are brought into contact which results in the development of a contact potential.
- **Amperometry or Galvanic Effect:** When two different conducting materials are placed in an electrolyte solution, a potential difference develops.

Electrochemical transducers are also very common. You can measure electrochemical signals from the presence as well as the interaction of chemical species. There are two main approaches: one is voltammetry and the other one is amperometry. In voltammetry, you bring two dissimilar materials into contact, which results in the development of a contact potential. Amperometry is a galvanic effect: two different conducting materials are placed into an electrolyte solution, which triggers a potential difference. These two approaches are very common.



Now I'm going to move on to sensor applications. I will first start with chemical sensors.

 **What is a chemical sensor?** 

- Chemical sensors analyze our environment, that is they detect what all are present and in what quantities
- Peter Grundler, Chemical Sensors, Springer 2001
- A chemical sensor is a device that transforms chemical information ranging from concentration of a specific sample component to total composition analysis, into an analytically useful signal.
- IUPAC, 1991
- Chemical sensors are small-sized devices comprising a recognition element, a transduction element, and a signal processor capable of continuously and reversibly reporting a chemical concentration.
- J. Anal. Chem., 1990

There are several definitions of a chemical sensor. The one from IUPAC refers to a chemical sensor as “a device that transforms chemical information ranging from concentration of a specific sample component to total composition analysis into an analytical useful signal.” There are some minor variations, one published a year earlier in the *Journal of Analytical Chemistry*, and then by others. Essentially, a chemical sensor allows us to analyze the environment (similarly to the bulky instruments mentioned earlier, but it's much smaller in size).

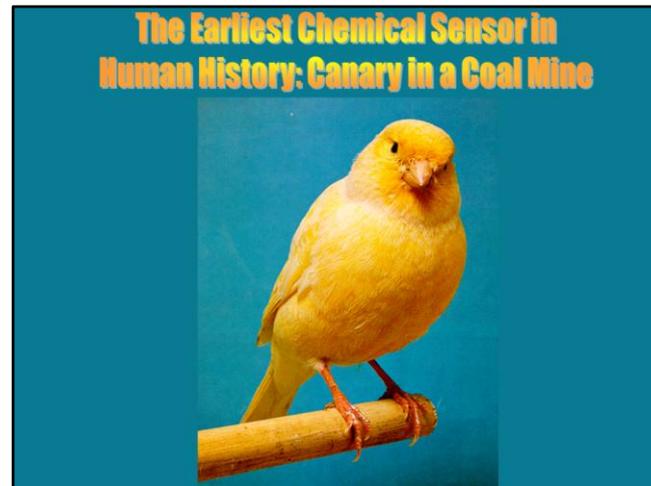


**Analytical Instruments for
Chemical Detection**

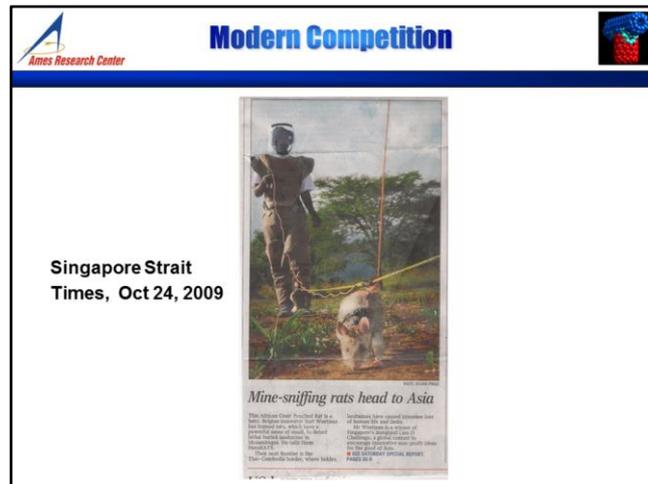


- Mass spectrometer
- Glow discharge mass spectrometer
- Residual gas analyzer
- Gas chromatography
- UV or IR Spectroscopy
 - FTIR
 - Raman Spectroscopy
- Nuclear Magnetic Resonance (NMR)

As a benchmark for chemical sensors, there are analytical instruments today that are being used in the laboratory for chemical detection: mass spectrometers, glow discharge mass spectrometers, residual gas analyzers, gas chromatographers, UV or IR spectroscopy, and NMR. These are typical, bulky instruments that can be expensive and are currently used for chemical detection and analysis.



The earliest chemical sensor in human history is the canary bird in a coal mine. At the start of a mining expedition, miners would send the bird down a mining area. If the bird came back in a couple of minutes, it would signal that it was safe to start their mining work.



Another interesting example is the use of mine sniffing rats—I saw this actually a few years ago in a Singaporean newspaper. In addition to chocolate being the major export from Belgium, mine sniffing rats were another big export from Belgium. Apparently the rats were used because they were five times cheaper than dogs to train and maintain. The interesting thing here is that we are now in 2015 and we are talking about dogs, cats, rats, and birds for chemical sensing. In many cases, those may probably be cheaper than any of the sensors that we can buy today in the market. They are also probably more reliable. And that's the sad state of sensor development at this point. We want to be able to do as well as some of those species, but at a cost that actually is cheaper or comparable.

 **Chemical Sensor Classification by
Signal Transduction Approach** 

- Optical sensors, following absorbance, reflectance, luminescence, fluorescence, refractive index, optothermal effect and light scattering
- Electrochemical sensors, among them voltammetric and potentiometric devices, chemically sensitized field effect transistor (CHEMFET) and potentiometric solid electrolyte gas sensors
- Electrical sensors including those with metal oxide and organic semiconductors as well as electrolytic conductivity sensors
- Mass sensitive sensors, i.e. piezoelectric devices and those based on surface acoustic waves
- Magnetic sensors (mainly for oxygen) based on paramagnetic gas properties
- Thermometric sensors based on the measurement of the heat effect of a specific chemical reaction of adsorption which involves the analyte
- Other sensors, mainly based on emission or absorption of radiation

Peter Grundler, Springer (2007)

[Dr. Meyyappan did not speak to this slide, but it is included in the interest of completeness.]

Ames Research Center **Applications for Chemical Sensors**

Gas/Vapor	Application
H ₂	Combustion gas detection in aircraft/spacecraft, fuel cells
NH ₃	Industrial, medical
NO ₂	Air quality monitoring
Ethanol	Breath analyzer, food quality, wine quality
Oxygen	Combustion
NO	Pollution monitoring
N ₂ O	Greenhouse gas, anesthetic use
CO	Pollution, home safety
CH ₄	Coal mining
HCl, Cl ₂	Chemical industry
SO ₂	Chemical industry
H ₂ S	Chemical industry
Benzene, toluene, octane	Volatile organic compound monitoring, industrial emission
Formaldehyde	Indoor air quality, industrial emission
Nitroarsene	Bomb detection
Nerve gas	Security, threat detection





Applications for chemical sensors are ubiquitous. Chemical sensors can be applied to pollution monitoring, environmental monitoring, coal mining, the chemical industry, and [for sensing] volatile/organic compounds. There are a whole variety of things that you can measure.



Other Applications for Chemical Sensors



- Monitoring of fish spoilage
- Coffee bean roasting
- Classifying bananas according to ripeness
- Sorting teas according to quality
- Establishing roasting times for almonds
- Wine identification
- Beer quality monitoring
- Air quality monitoring in agricultural storage
- Identification of appropriate time for artificial insemination of cows by monitoring estrus
- Fluid leaks in cooling systems

Source: Albert et al, Chem. Rev., 100, 2595 (2000)

I highly recommend this review paper from a research group at CalTech in *Chem Review*. It discusses the construction of an electronic “nose.” It also provides historical context about its development. Quality monitoring, wine identification, establishing roasting times for almonds, and how much time you should be roasting your coffee beans, and classifying bananas according to ripeness. Actually, the examples with the references are given in that review paper. So these are all some interesting applications for gas and vapor sensing.



What Do We Expect from a Well-Designed Chemical Sensor System?



- First, a single device has no value. We need a system consisting of:
 - Sensor array (Electronic Nose, Pattern recognition...)
 - Pre-concentrator?
 - Sample delivery, Microfan? Jet?
 - Signal processing chip
 - Readout unit (data acquisition, storage)
 - Interface control I/O
 - Integration of the above
- Criteria for Selection/Performance
 - Sensitivity (ppm to ppb as needed)
 - Absolute discrimination
 - Small package (size, mass)
 - Low power consumption
 - Rugged, reliable
 - Preferably, a technology that is adaptable to different platforms
 - Amenable for sensor network or sensor web when needed

What do we expect from a well-designed chemical sensor system? You will see a single device generally has no value. We would need a system that consists of: a sensor array (e.g., electronic “nose”), a pre-concentrator (although it would be nice if you don't need it), a sample delivery unit (which could rely on diffusion to bring the sample gas or vapor to your sensor or you need some kind of microfan or jet depending on the application), a signal processing chip, an interface control (for input/output), etc. Integration of all of the above is where the hierarchical nanoscale to micro to macroscale integration occurs. Nanoscale, in most of these cases, may be a nanomaterial. The platform itself could be micro-fabricated as you will see. And then, of course, when you put everything together, it's macroscale. There is a systematic and hierarchical integration of the nano-to-micro-to-macroscales.

If you are in charge of selecting a sensor for a certain application, what would be the criteria you would use for selecting a sensor from so many competitive sources? The first thing everybody thinks about is sensitivity; that depends on the application. Sometimes it is parts per million, sometimes parts per billion. If it is something serious like security, it could be even parts per trillion for something like sarin gas. Another important thing is absolute

discrimination (the selective identification of the very particular analyte you are looking for). Obviously, a small package would be beneficial, as well as low power consumption. In that sense, the lifetime will depend on the power consumption of the sensor itself. Also, the sensor technology should be adaptable to different platforms. For example, one platform could be to monitor ambient conditions inside buildings. On the other hand, if you're a security officer walking around with a handheld device, perhaps the sensor could be adaptable in a small portable unit like a flashlight. The sensors hopefully could be networked into a sensor web or sensor network. Technology that is adaptable to different platforms is also preferable. These are some of the things we expect from a sensor system.

 **Mammalian Olfactory System** 

- Contains approximately 1000 different olfactory receptor genes; upon odor simulation, responses from many receptors are sent to the olfactory bulb & then to the olfactory cortex for processing
- Olfactory receptors are NOT highly selective to any specific analytes. One receptor may respond to many analytes. Many receptors may respond to a given analyte.
- Pattern recognition methods are thought to be the approach used by mammalian olfactory system.



I just want to go over a little bit about how the mammalian olfactory system works. In mammalian noses, we have thousands of different olfactory receptor genes. It's not like we have a cell dedicated to smell coffee and a cell completely dedicated for chocolate. What I'm saying is we don't have cells that come with a priority for selective identification of particular analytes. Any given odor can elicit signals from a bunch of cells, and likewise one particular cell can give a response to a bunch of different odors. The pattern recognition methods, right from our childhood—from the first time as a baby we come across a banana and our mom tells us that it is a banana, and that smell and that name gets registered in our brains—we constantly learn as we go along in our life registering more and more information correlating between that smell and the name. That type of pattern recognition method is what we need when we develop an electronic nose as well.



Electronic Nose



- Pioneering work by K.C. Persaud and G. Todd, Nature (1982), put together a sensor array for odor recognition.
- Each of the sensor in the array responds to a broad range of gases with much duplication.
- Multiple sensors will respond to the same analyte but not in the same way, also not to all the same gases.
- Signal processing involves analysis of the array responses with pattern recognition algorithms.

The idea of electronic nose was introduced by two scientists from Warwick in England in 1982. They put together a sensor array for recognizing odors. Each of the sensors in the array responded to a broad range of gases with quite a bit of duplication. The researchers used signal processing to do the array response and came up with selectivity by using a pattern recognition algorithm.



Most Odors are Complex



- Cheese, beer, wine, fruits, fish....
- These odors are complex in that they are chemical mixtures, but they are distinctive odors.
- Once our olfactory system senses the odor, the brain processes the response patterns and matches to stored response patterns.
- Similarly, in e-nose, NO NEED to breakdown the complex mixture into individual chemicals, prior to or during the analysis. All that is needed is composite odor identification; we are not looking for precise chemical composition of the mixture in a wine or fish....

Most odors in life are complex (whether it's cheese, beer, or wine) because they're chemical mixtures and have distinct odors. In our olfactory system, once we sense the odor, based on our memory, we recognize what it is. Similarly, with the electronic nose, we really don't need to break down the complex mixture or odor into individual chemicals to do any type of analysis.

 **The Different Classes of Chemical Compound Found in Coffee Aroma and the Numbers of Different Molecules Within Each Class** 

Class	Number in class	Class	Number in class
Hydrocarbons	31	Phenols	44
Alcohols	19	Furans	108
Aldehydes	28	Thiophenes	26
Ketones	70	Pyrroles	74
Acids	20	Oxazoles	28
Esters	30	Thiazoles	27
Lactones	8	Pyridines	13
Amines	21	Pyrazines	79
Thiols, sulfides	13	Others	31
		TOTAL 670	

For example, the coffee aroma has 670 classes of compounds in there; a variety of hydrocarbons, alcohols, ketones, acids, pyridine, and pyrosine, all of those things. It makes no sense trying to get a breakdown of any of those compounds. In the electronic nose construction, we simply just go for the composite odor.



- Attention for applications in noninvasive detection of various metabolic and disease states
- History
 - Hippocrates (Greek) recognized exhaled breath as a noninvasive tool
 - 1784: Lavoiser detected CO in the exhaled breath of guinea pigs
 - Chinese village doctors recognized diabetic symptoms from sweet-smelling breath (acetone)
- Gas chromatography has been used recently to analyze VOCs human in human breath varying in concentrations from millimolar (10^{-3} M) down to picomolar (10^{-12} M)
 - nearly 400 compounds
 - Another study says ~ 3500 compounds

A similar approach is used for breath analysis. There is anecdotal evidence that 100 years ago Chinese village doctors recognized diabetes symptoms from the sweet smelling breath of people. But modern biochemists figured out the sweet smell comes from acetone. Gas chromatography analysis has shown there are approximately 400 compounds in the human breath.



Breath Analysis – Biomarkers

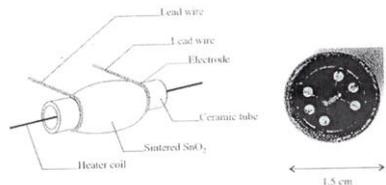


- Numerous compounds have been identified as potential indicators of one or more diseases. Some key biomarkers:
 - NO for oxidative stress, asthma
 - CO for cardiovascular diseases, diabetes, nephritis,
 - NH₃ may differentiate between viral and bacterial infections in the lung, to justify the use of antibiotics
 - NH₃ for indirect measurement of urea level when monitoring renal diseases.
 - Acetone: increased levels associated with diabetics
 - Ethanol -¹⁴C for impaired liver function
 - aminopyridine for impaired liver function
 - aldehydes in lung cancer patients

Interestingly, the medical community in the last couple of decades kept coming up with key biomarkers in human breath for a variety of diseases. In the case of nitrous oxide, it can be an indication of oxidative stress or asthma; for carbon monoxide, it can be an indicator for cardiovascular diseases and diabetes; individuals who are undergoing kidney dialysis seem to show excess ammonia in their breath compared to the normal population. The increased level of acetone is associated with diabetes. Some types of aldehydes are in excess concentration in patients with lung cancer. This list of biomarkers has been on the increase in the last decade or so.

 **Metal Oxide Gas Sensor – Taguchi Sensor** 

- Consists of a ceramic support tube containing a platinum heater coil.
 - Sintered tin oxide is coated outside the tube (may contain catalysts)
 - Gas sensing based on change in electrical resistance
 - Typical catalysts: Pt, Pd



The diagram illustrates the internal structure of a Taguchi sensor. It shows a cross-section of a ceramic tube containing a heater coil. The tube is coated with sintered tin oxide (SnO₂) on the outside. Two electrodes are attached to the tube, and lead wires are connected to them. A top-down view of the sensor shows the sintered SnO₂ coating and a 1.5 cm scale bar.

One of the earliest examples of metal oxide-based gas sensors is named after a Japanese scientist from the 1960s. It is called the Taguchi sensor. It consists of a ceramic support coated with sintered tin oxide, and contains a platinum heater coil. The sintered tin oxide is the sensing layer. Occasionally, it contains a catalyst; typically, platinum or palladium. The gas sensing is based on the change in electrical resistance.



Oxide Sensors: Sensing Mechanism



Under ambient conditions, oxygen molecules get readily adsorbed onto the oxide nanowire surface and form surface O_2^- and O^- species:

$$O_2(g) + e \rightarrow O_2^-(ads) \quad (1)$$

$$O_2(ads) + e \rightarrow 2O^-(ads) \quad (2)$$

This depletes the electrons near the surface of an n-type nanowire leading to a higher resistance state. Now when this surface layer is exposed to a reducing gas environment as in the following cases, electrons are released from the respective surface reactions which transfer back into the conduction band and increase the conductivity of the nanowires.

$$2 H_2 + O_2^-(ads) \rightarrow 2 H_2O + e \quad (3)$$

$$2 C_2H_5OH + O_2^- \rightarrow 2 CH_3CHO + 2 H_2O + e \quad (4)$$

$$2 NH_3 + 3 O^-(ads) \rightarrow N_2 + 3 H_2O + 3e \quad (5)$$

$$CO + O^-(ads) \rightarrow CO_2 + e \quad (6)$$

When the sensor is exposed to an oxidizing species such as NO_2 , the resistance increases since NO_2 adsorbs and forms negatively charged surface species, NO_2^- .

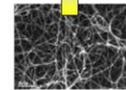
Here is how the oxide sensor works: under normal ambient conditions, oxygen molecules are readily absorbed onto an oxide nanowire surface, where they form surface oxygen and negative ions. The electrons located near the surface get depleted, which leads to a higher resistance state. When you expose this surface to a reducing gas environment like hydrogen or ammonia or carbon monoxide, you end up releasing the electrons back from surface reactions, which increases the conductivity of the nanowires. The tin oxide-based thin film sensor is currently the most commonly used. A number of companies have used these oxide-based sensors and sell them in the form of chemical field effect transistors.



Why nanomaterials/nanosensors for chemical sensing?



- Compared to existing systems, potential exists to improve sensitivity limits, and certainly size and power needs
- Why? Nanomaterials have a large surface area. Example: SWCNTs have a surface area $\sim 1600 \text{ m}^2/\text{gm}$ which translates to the size of a football field for only 4 gm.
- Large surface area \rightarrow large adsorption rates for gases and vapors \rightarrow changes some measurable properties of the nanomaterial \rightarrow basis for sensing
 - Dielectric constant
 - Capacitance
 - Conductance
 -
 -
 -



4 grams

One issue with the oxide-based sensors is that they work only at elevated temperatures: 200, 300 degrees centigrade, or above. The other type of sensor commercially available is based on conducting polymers. When a gas or vapor gets absorbed onto the conducting polymer, the polymer swells. And that disturbs the conducting network. So the resulting conductivity changes, which forms the basis for sensing. The issue with that type of sensor is that generally the sensitivity is not that great. But both types of sensors, the oxide sensors and the conducting polymer sensors, have been used to put together electronic noses. The Cal Tech review article I referred to earlier gives an extensive set of examples of electronic noses using these two commercially available sensors. Compared to these two sensors, there are opportunities for using nanomaterials to improve sensitivity limit, and certainly to reduce the size and power requirements.

An important advantage of nanomaterials in oxide-based sensors is that they can operate at room temperature. That alone helps to reduce the power consumption relative to tin oxide-based sensors. The reason for the sensitivity is the nanomaterials, like graphene, all have a very large surface area. For example, as far back as 10 years ago we got several samples from Rick Smalley at Rice University of HiPco single-walled carbon nanotube

(SWCNT) samples, and measured the surface area of those SWCNTs to be as high as 1600 square meters per gram. Sometimes when you throw around numbers like that, people don't get a feel for what those numbers mean. Here is a helpful illustration: it only takes about four grams of these SWCNTs to cover an entire football field; that's a very large surface area! This ultimately results in large adsorption rates for gases and vapors. After adsorption, if some measurable property of the nanomaterial changes (it could be the resistance; it could be capacitance, dielectric constant), you can measure or monitor one of those variables, which forms the basis for sensing.



Dependence of Sensitivity on Nanowire Radius



The conductance G of a NW exposed to a gas is given by

$$G = \frac{\pi r^2}{\ell} n_e e \mu_e$$

Here r and ℓ are radius and length of the nanowire, and μ_e is the electron mobility. * n_e depends on the surface density of the chemisorbed species, N_s and charge transfer

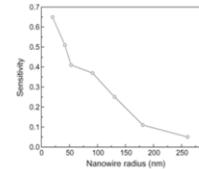
coefficient α :

$$n_e = n_0 - \frac{2\alpha N_s}{r}$$

where n_0 is the electron density prior to gas exposure. This yields

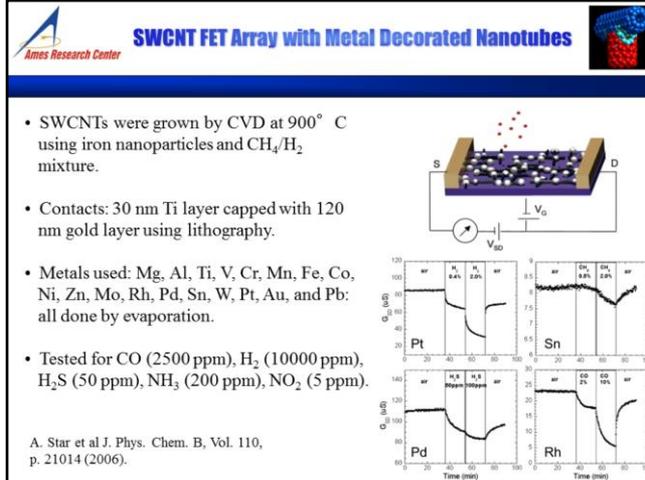
$$\frac{\Delta G}{G_0} = \frac{1}{r} \frac{2\alpha N_s}{n_0}$$

showing clearly the inverse dependence of sensitivity on the nanowire radius.

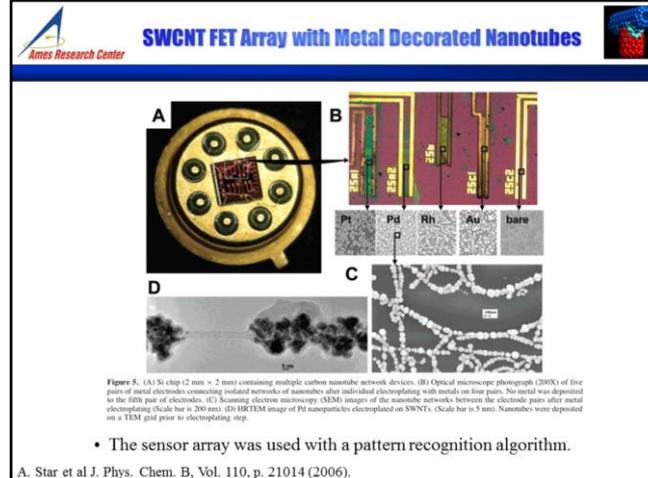


Z. Fan and J.G. Lu, IEEE Trans. Nanotech. 5, 393 (2006)

Please refer to the reference in slide 46. An important point here is that there is an inverse dependence between the nanowire or nanotube radius and the sensitivity. $\Delta G / G_0$ is the normalized change in conductivity, and there is a one-over-radius dependence. So the smaller the radius, the larger the sensitivity.



In the literature, papers on carbon nanotubes, graphene, a variety of inorganic nanowires, and even emerging 2D nanomaterials (e.g., molybdenum disulfide-based sensors) have focused on the type of material being used and the resulting change upon exposure to a gas or vapor. However, there's very little information about selectivity and many other things that I defined earlier on. I would say there are only about, out of over 1,000 papers, maybe a handful—five or six—that talk about selectivity at all.



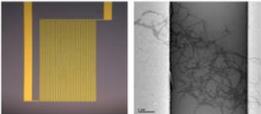
A first good example I want to discuss is from Professor Alexander Star at the University of Pittsburgh. Here, he uses an array of gas sensors (eight sensors). There's got to be a variation since it doesn't make sense for all eight sensors to be identical. So the way he made them different is, from the baseline SWCNT material, he introduced variations in the metals sputtered on the carbon nanotubes. The group tried a wide variety of materials like magnesium, aluminum, titanium, rhodium, and palladium. The sensor was tested for carbon monoxide, hydrogen, hydrogen sulfide, ammonia, and nitric oxide. The key thing was that the signal processing was done using intelligent pattern recognition, which is called principal component analysis. The researchers were able to show that they can selectively identify carbon monoxide and hydrogen sulfide and other gases. That's one example that you will find in the literature, which talks about selective discrimination using an electronic nose-type approach, with carbon nanotubes as a baseline nanomaterial in a sensor configuration.



SWCNT Chemiresistor



- Easy production by simple microfabrication, compared to FETs
- 2 Terminal I-V measurement
- Low energy barrier - Room temperature sensing
- Low power consumption: 50-100 μ W/sensor




Processing Steps

1. Interdigitated microscale electrode device fabrication
2. Disperse purified nanotubes in DMF (dimethyl formamide)
3. Solution casting of CNTs across the electrodes

Jing Li et al., Nano Lett., 3, 929 (2003)

The next one is from our group. Professor Star's work used SWCNTs in the form of a field effect transistor. That means you have the source, drain, and then there is a back gate, and then the SWCNTs are deposited to connect between the source and the drain.

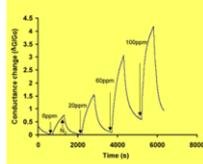
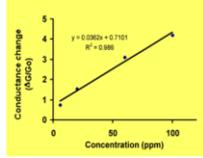
What we have here is a simple two-terminal device. You see a pair of bus bar gold electrodes fabricated on a silicon substrate, and then in between the bus-bar electrodes, you see interdigitated fingers, which are about 2-5 micrometers wide and the gap is two to five micrometers. We have also made them recently using a printed circuit board (PCB). But when you use PCBs, generally it's hard to do 2-5 micrometer finger widths. In this case, the finger width and gap both go up to about 50 micrometers up to 100 micrometers. What is shown here is the carbon nanotubes bridging two adjacent fingers. The energy barrier for room temperature sensing is also pretty low for consumption; typically 50 microwatts per sensor.



Ames Research Center

SWCNT Sensor Testing and Training



Detection limit for NO₂ is 4 ppb.

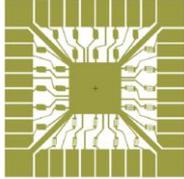
- Test condition:
Flow rate: 400 ml/min
Temperature: 23 °C
Purge gas (N₂); Carrier gas: Air
- Measure response to various concentrations, plot conductance change vs. concentration
- Sensor recovery can be speeded up by exposing to UV light, heating or AC bias. Also, sensor refreshing.
- Sensitivity in the ppb-ppm range

The sensor needs to be trained in the laboratory before you construct the electronic “nose” [as shown in slide 50].

Nanosensing Approach: Selectivity

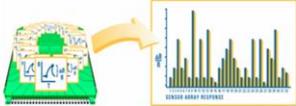
Ames Research Center

- Use a sensor array
- Variations among sensors - critical
 - physical differences
 - coating
 - doping
 - oxide nanowires, nanoparticles
 - graphene, its variations



Operation:

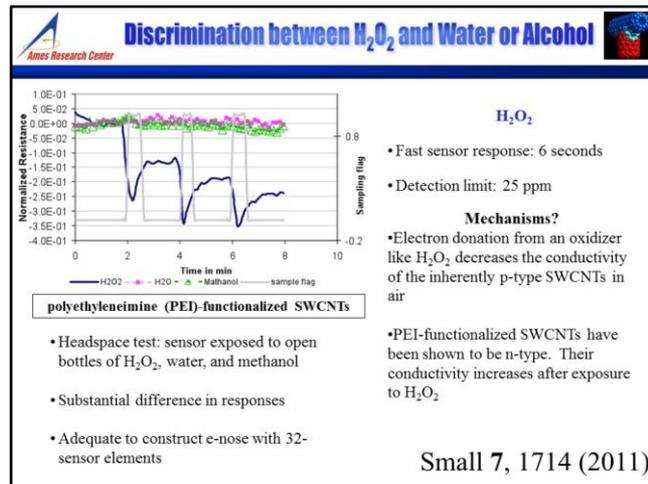
1. The relative change of current or resistance is correlated to the concentration of analyte.
2. Array device "learns" the response pattern in the *training* mode.
3. Unknowns are then classified in the *identification* mode.



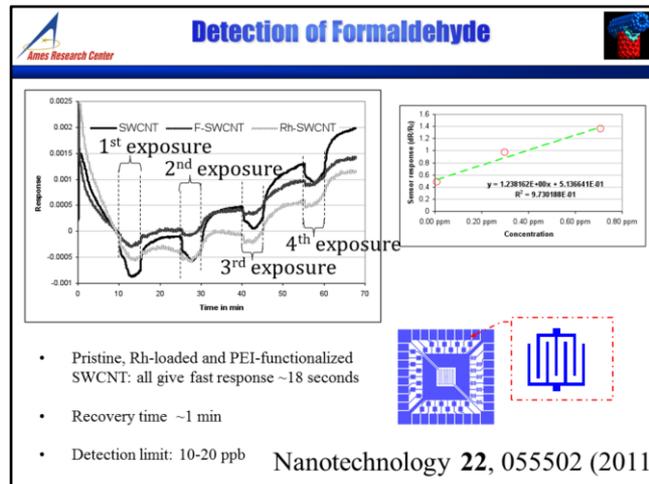
Using pattern matching algorithms, the data is converted into a unique response pattern

Take for example a sensor chip with 32 sensors (eight in each of the four quadrants). These 32 sensors are not identical – there are some critical differences. The sensors in the chip can be composed of pristine SWCNTs and, in some cases, coatings are added to the SWCNTs (e.g., platinum or palladium). Carbon nanotubes are not necessarily the material of choice; in a couple of sensors, you can add graphene or zinc oxide nanoparticles. The most important thing is to have variation across your sensor elements. The chip will be “trained” in the laboratory to “learn” the response patterns. Let's say you expose the 32-sensor chips to five parts per million nitrogen dioxide (NO₂) and then you measure the change in resistance of each of those sensors. They all would be different because the sensor medium is different. Some are pristine nanotubes, some have doping, and some have coatings. The 32 different sensors could give 32 different responses (or normalized resistance as mentioned earlier). It is important to note that you don't need all 32 sensors to give a response to NO₂: it's ok if three or four are giving strong responses, and in fact, it's preferable to have six or seven of them not respond at all, because potentially the other six or seven could respond to something else. We are looking to establish a fingerprint here. You repeat this training exercise for various analyte concentrations (say again NO₂), and start out with 5, 10, 20, 50 ppm. That's what is illustrated in the previous slide. You also need to prepare a calibration curve. In addition, you have to repeat

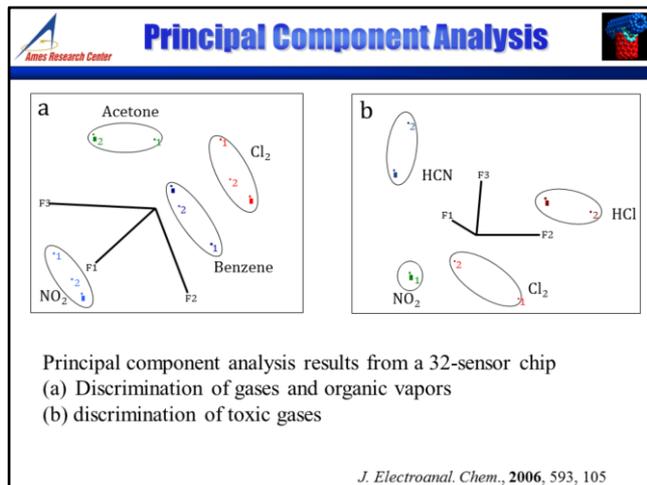
this procedure for various humidity levels because the humidity may have an impact on the sensor response (so you start with dry conditions). In many cases, the impact of the humidity may be reasonably linear, unless there are some strong chemical interactions going on. In that sense, you may have to repeat this for five or six humidity levels and then you can interpolate. Obviously, when you put a sensor system together, you need to simultaneously measure the temperature and the humidity so that way you can do interpolation for the prevailing conditions.



[Dr. Meyyappan did not speak to this slide, but it is included in the interest of completeness.]



[Dr. Meyyappan did not speak to this slide, but it is included in the interest of completeness.]



All of this information that you generate during the “training” portion of chemsensor development is what you store in the processing chip. Later on, you use principal component analysis or whatever your favorite pattern recognition method is. Under actual conditions, you are trying to figure out if an analyte is present and if it is present, what is the actual concentration. Here is the result of a principal component analysis. This shows that we can discriminate on the left figure acetone, benzene, versus nitrogen dioxide and then some toxic gases on the right side like HCN (hydrogen cyanide), HCl (hydrochloric acid), chlorine, nitric oxide.



Gases/Vapors Tested



Analyte	Sensitivity/Detection Limit
CH ₄	1 ppm in air
Hydrazine	10 ppb tested by KSC
NO ₂	4.6 ppb in air
NH ₃	0.5 ppm in air
SO ₂	25 ppm in air
HCl	5 ppm in air
Formaldehyde	10 ppb in air tested by JPL
Acetone	10 ppm in air
Benzene	20 ppm in air
Cl ₂	0.5 ppm in air
HCN	10 ppm in N ₂
Malathion	Open bottle in air
Diazinon	Open bottle in air
Toluene	1 ppm in air
Nitrotoluene	256 ppb in N ₂
H ₂ O ₂	3.7 ppm in air
DMMP	100 ppb in air

[Dr. Meyyappan did not speak to this slide, but it is included in the interest of completeness.]

First Nano Product in Space

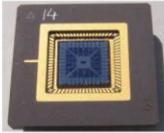





NASA Ames chemical sensor module was on a secondary payload of a Navy satellite (Midstar-1) launched via Atlas V on March 9, 2007. Sensor data downloaded for 60 days.



The nanosensor module (5" x 5" x 1.5") contained a chip of 32 sensors, a data acquisition board, sampling system, and a tank with 20ppm NO₂ in N₂.



A 32-channel sensor chip (1cm x 1cm) with different nanostructured materials for chemical sensing

This sensor chip was integrated in the JPL E-nose aboard the International Space Station in January 2009 to monitor air quality in the crew cabin, especially formaldehyde.

This chemsensor is the only nano product I am aware of that has been tested in space. We sent this in January 2009 in the JPL electronic nose to monitor air quality and look for formaldehyde.



We've also integrated this chip-based sensor into a smartphone.



Biosensor



What is the need for biosensing?



Applications:

- Clinical diagnostics
- Health care, Routine health check up
- Early warning bio threat detection
- Water quality monitoring
- Food quality monitoring
- Environmental monitoring

Goal: To perform an entire set of analytical operations associated with sensing on a chip level rapidly (~minutes)

[Dr. Meyyappan did not speak to this slide, but it is included in the interest of completeness.]



What is expected from a well-designed biosensing system?

- Small size, mass
- Low power consumption
- Minimal (chemical) resources and human processing
- Reasonably rapid analysis
- Negligible false alarms
- Multiplexing capability for detecting multiple targets
- Reliability and robustness
- Technology amenable to large scale production reduce costs.

Now moving along to biosensors. What is expected from a well-designed biosensing system? Again, similar thing: small size, mass, and low power consumption. Also, one thing unique to biosensors is minimizing chemical resources and human processing because generally biosensors will require a lot of pre-processing. In addition, it will be great to include reasonably rapid analysis with negligible false alarm. Multiplexing for multiple biomarkers, reliability, and robustness are also some of the things we expect from a well-designed biosensing system.



Simple model for Biosensing



- Balance equation for probe or receptor molecule density N

$$\frac{dN}{dt} = k_f (N_0 - N) \rho_s - k_r N$$

- N_0 : initial density of probes on the nanowire surface
- k_f and k_r : rate constants for attachment and detachment
- ρ_s : density of the targets

- The first term on the right hand side represents the target-probe conjugation and the second term stands for detachment events.

- The target density is given by:

$$\frac{d\rho}{dt} + \nabla \cdot \nabla \rho = D \nabla^2 \rho$$

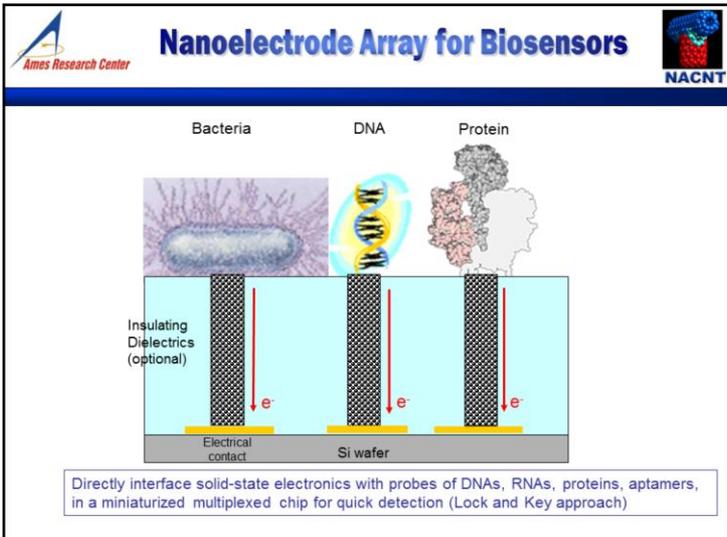
Nair and Alam, APL 2006

The model in this slide was developed by Professor Alam at Purdue University. The group developed a simple equation to balance for probe or receptor molecules. The time-dependent equation has two terms: one is how many of those probes and targets interact or conjugate; the second term stands for spontaneous detachment of the probe. The target biomarker density is given by the simple diffusion equation.

 **Insight from Modeling** 

- A one dimensional NW/NT based sensor can give one to four orders of magnitude higher detection limit than a planar thin film sensor
- Going further down to 0-d (spherical) geometry offers no further advantage
- Trade-off between the response time and detection limit

Combining these two equations and solving them, the group came up with a few insights. A one-dimensional nanowire-based sensor can give one to four orders of magnitude higher detection limit than a planar thin film sensor. Second, going further down to zero-dimension (e.g., a spherical particle) does not provide any advantages. Third, there is always a tradeoff between the response time and the detection limit. If you're looking for a single molecule deduction, the time it's going to take is long. So those are the three key points from the modeling work that was done at Purdue.



Now, I want to give some examples. The first example is a nanoelectrode array for biosensors. With nanoelectrodes, you can directly interface with DNA, RNA, aptamers, proteins as probe molecules. When the probe and the target are hybridized or conjugated, you are looking to get an electrochemical signal, which you can measure using cyclic voltammetry or impedance spectroscopy as mentioned earlier on.

Ames Research Center

Nanoelectrode for Sensors

Nanoscale electrodes create a dramatic improvement in signal detection over traditional electrodes

Traditional Macro- or Micro- Electrode

Nanoelectrode Array

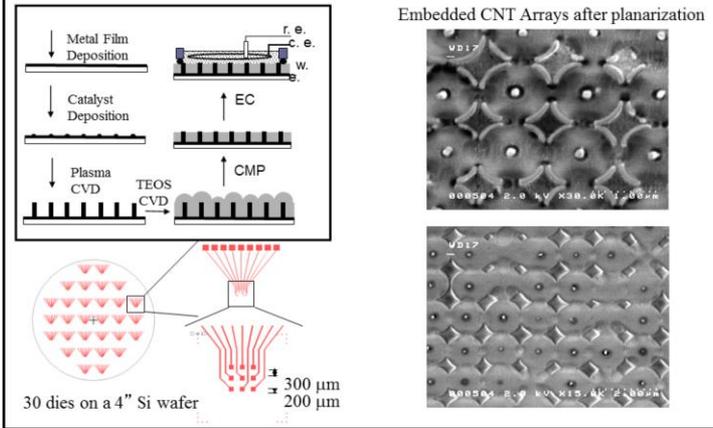
- **Scale difference** between macro-/micro- electrodes and molecules is tremendous
- **Background noise** on electrode surface is therefore significant
- **Significant amount** of target molecules required

- CNT tips are at the **scale close to molecules**
- **Dramatically reduced background noise**
- Multiple electrodes result in **magnified signal and desired redundancy** for statistical reliability.

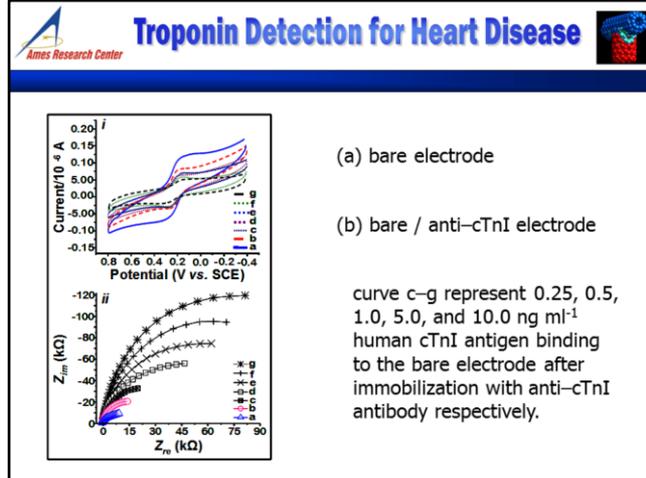
Candidates: ~~SW~~CNTs, ~~MW~~NNTs, Vertical CNFs or Vertical SiNWs

Source: Jun Li

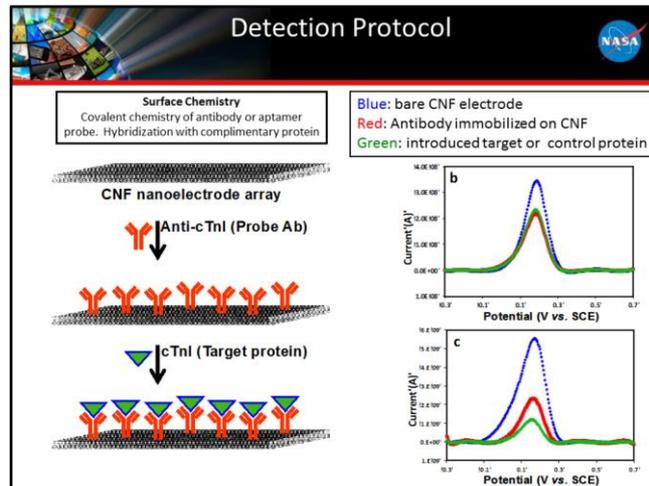
Why would you want to have a nanoelectrode? The traditional micro or macro-electrodes are substantially bigger than the size of the biomolecule that you're looking for. Electrical engineers will tell you that the background noise is proportional to the surface area. Also, you would need a significant amount of target molecules. If you take the same microelectrode and you divide it into mini-nanoelectrodes, the size difference between the electrode and the biomolecule that you are looking for is dramatically reduced and you can also dramatically reduce the background noise. Researchers have used single-walled carbon nanotubes, multi-walled carbon nanotubes, graphene, carbon nanofibers, silicon nanowires, and zinc oxide nanowires to construct nanoelectrodes.



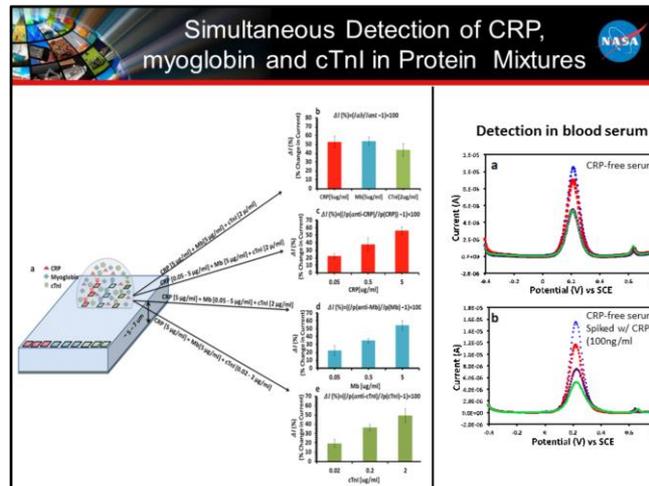
Here, I am showing how we have used carbon nanofibers to engineer nanoelectrode arrays. You start out with a silicon wafer where you pattern a catalyst. Plasma chemical vapor deposition (CVD) is then used to grow carbon nanofibers. Each one is an individual freestanding carbon nanofiber, approximately 50 nm in diameter. After you finish the growth process, you can fill the space between individual carbon nanofibers with silicon dioxide using tetraethylorthosilicate chemical vapor deposition (TEOS CVD). You can then finish off with chemical-mechanical polishing to provide a smooth silicon dioxide surface at the top with carbon nanofiber edges “poking” above the silicon dioxide surface by a couple of nanometers, allowing for interaction with probe molecules; whether it is DNA, RNA, aptamer, or protein. The image shown here is the top silicon dioxide surface with white dots indicating the location of carbon nanofiber edges coming out of the surface. You can use whatever protocol is appropriate for attaching your probe molecules.



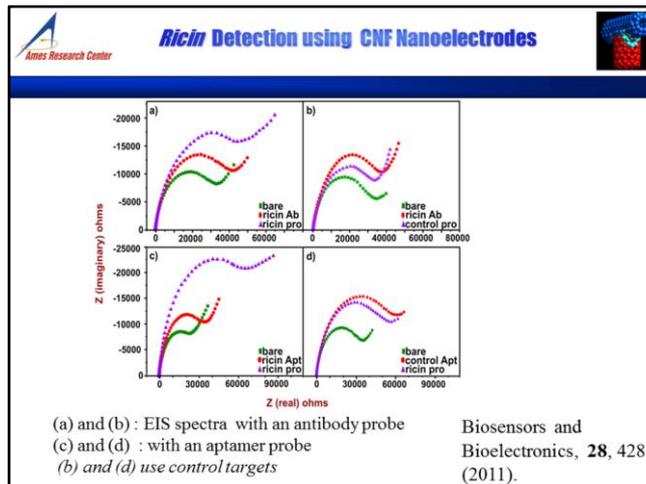
Here is an example of a biosensor. Troponin is a common biomarker for heart disease. In this figure, the top chart summarizes results from cyclic voltammetry and the bottom chart from impedance spectroscopy. Focusing on the impedance spectroscopy results, the blue curve shows results from the bare electrode; the purple one is right after you attach the antibody for the troponin; and the red curve is after the addition of the target biomarker in human serum. Obviously, as the concentration increases, the signal is bigger. Using this sensor, you can get a signal from a concentration as small as 2 nanograms per milliliter of troponin binding to the electrode. That number is actually smaller than what the medical community is looking for.



[Dr. Meyyappan did not speak to this slide, but it is included in the interest of completeness.]



We have been able to detect three key biomarkers using this platform. One is the cardiac troponin I mentioned. The other one is the cardiac reactive protein and the third one is myoglobin. We were able to do all three of them on the same chip. So this is an example of multiplexing.

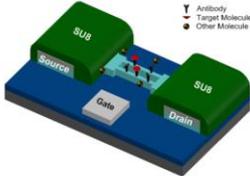
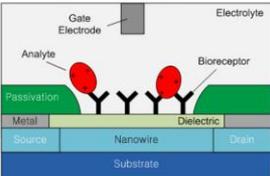


We have used the same chip to detect ricin, a bio threat. The top curves are using ricin antibodies. The bottom curves are using the ricin aptamer. The right curves are control samples. In each chart, the green curve is the bare electrode, the red one is after attaching the antibody or the aptamer, and the purple curve is the signal after the conjugation. In the left curves, whether you use the antibody or the ricin aptamer, you get substantial signal after the binding event. What distinguishes between the antibody and the aptamer: the aptamer is harder to work with but much more robust than the antibody, particularly when it comes to lifetime issues of the probe.

Ames Research Center **Biological FET - BioFET**

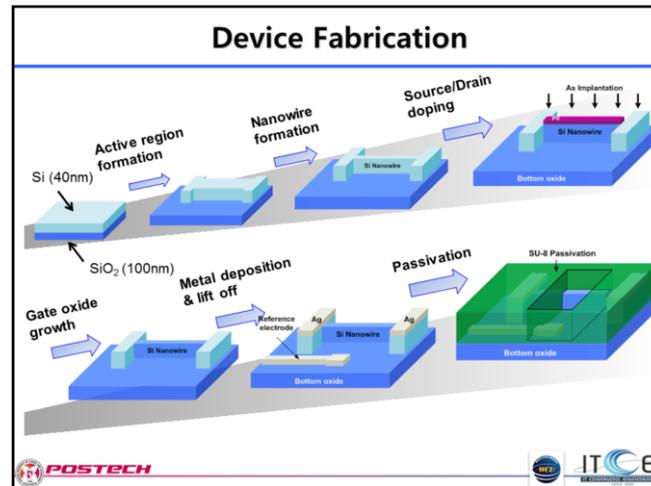
- Electrode-electrolyte-insulator-semiconductor-electrode system
- Bio probes fixed to insulator
- Hybridization of targets causes change in underlying silicon
- Major question:
 “How much does BioFET current change upon probe-target hybridization?”

- ❑ Uses mainstream CMOS technology
 - ↳ Affordable
 - ↳ Direct electrical conversion
 - ↳ Integrated - signal proc. & telemetry circuits
- ❑ No fluorescent labeling
- ❑ No expensive μ array readers

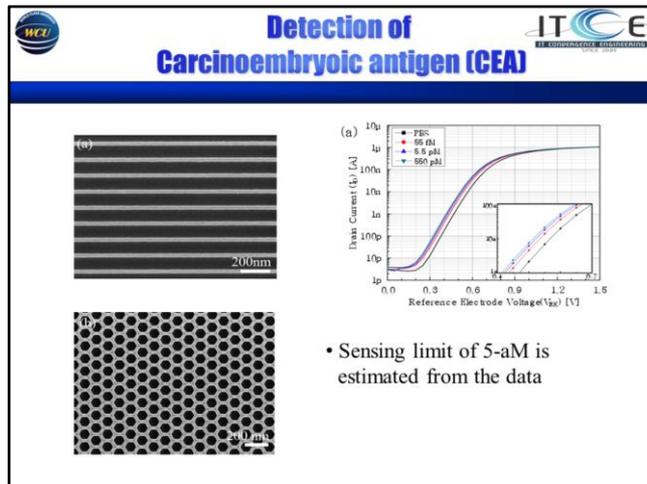



Legend:
 Y Antibody
 ● Target Molecule
 ● Other Molecule

Bio-FETs are also very common alternatives to nanoelectrodes. The change in the current voltage characteristics of the FET, when the probe and the target bind, provides a very sensitive means to do biosensing.

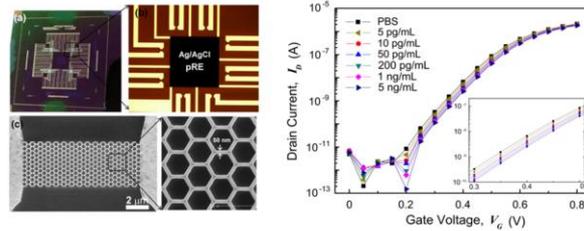


[Dr. Meyyappan did not speak to this slide, but it is included in the interest of completeness.]



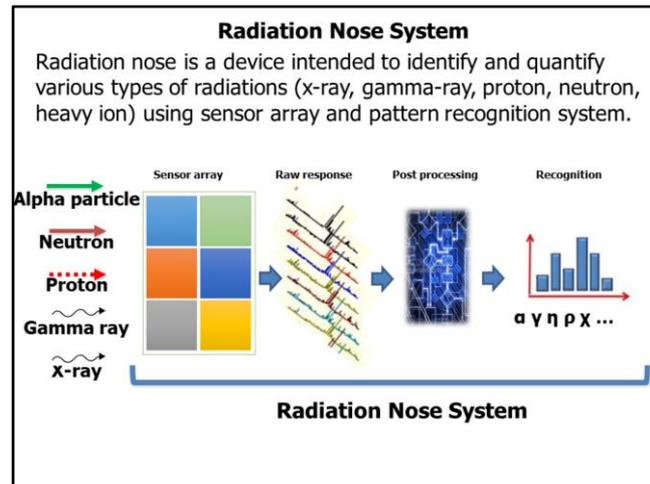
[Dr. Meyyappan did not speak to this slide, but it is included in the interest of completeness.]

Detection of Cardiac Troponin I



Detection limit ~ 5 pg/ml

[Dr. Meyyappan did not speak to this slide, but it is included in the interest of completeness.]



I want to spend a couple of minutes talking about radiation sensors. When you take a look at the literature, you will see many examples of using nanomaterials for chemical and biosensors because of the ubiquitous need for these sensors. But the need for radiation sensors is relatively lower, reserved only for Homeland Security, the military, and NASA (e.g., for monitoring radiation levels in the crew cabin during a trip to Mars). It's possible to construct the radiation nose just like an electronic nose. But you need to have multiple devices that respond to different types of radiation.

Innovation: Breaking Stereotype

Since 1960 ~

**SiO₂(solid)
high-k(solid)**

Gate

S **D**

- Solid-state Gate Dielectric
- Insulating gate to drain

**Fluid
Gas/Liquid**

Gate

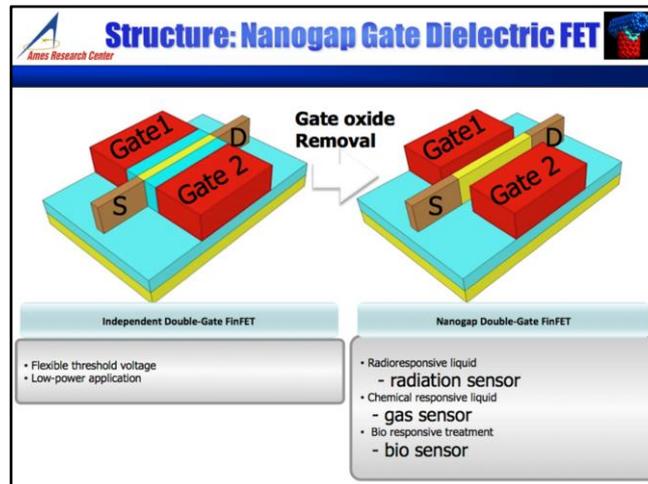
S **D**

<Fluid Gate Dielectric>

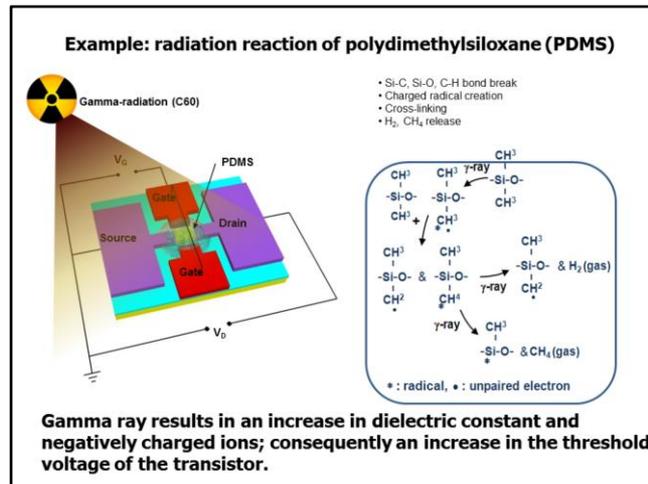
- Stimuli responsive fluid
- Exchangeable
- Drop-on-demand

"The guys like us who work with the stuff every day consider *silicon dioxide the greatest gift from God*",
John S. Suehle, NIST

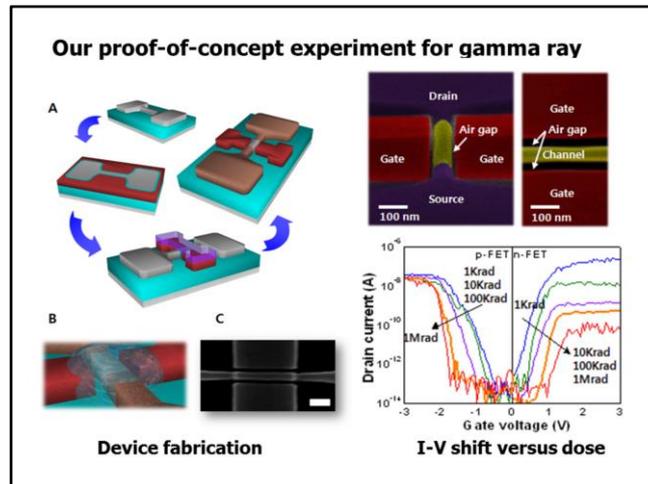
One of the common radiation sensors is based on metal-oxide-semiconductor field-effect transistors (MOSFETs). Based on past experience, incident radiation has been shown to affect current voltage curves of MOSFETs or complementary metal oxide semiconductor (CMOS) devices. So the reverse engineering has allowed people to use MOSFETs in a solid state radiation conductor. It's very hard to construct the radiation nose based on just silicon dioxide as a dielectric.



So what we did is use the following structure: it is a common MOSFET with a source, drain, and a gate. Where the silicon dioxide used to be, we left it as a nano gap, and filled it with liquid gel. (You can find liquid gels with dielectric constant comparable to silicon dioxide.)

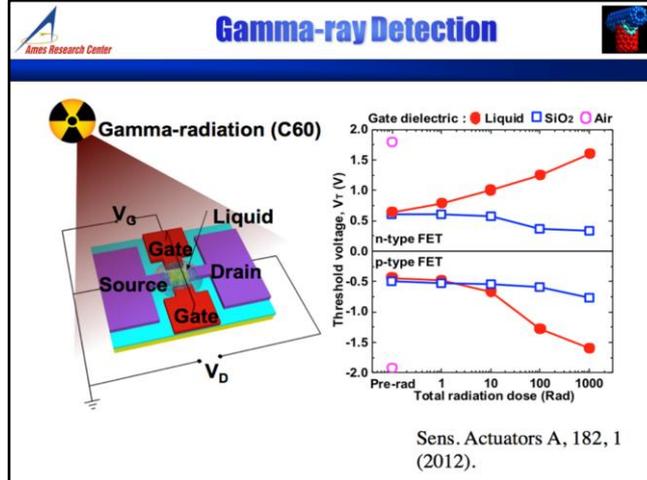


The interesting thing is that these liquid gels respond to radiation, and it's possible to find different gels that can respond to different types of radiation. For example, a common gel like polydimethylsiloxane (PDMS) responds to gamma radiation. Exposure to gamma radiation changes the dielectric constant of the PDMS, which results in the change in the current voltage curve.

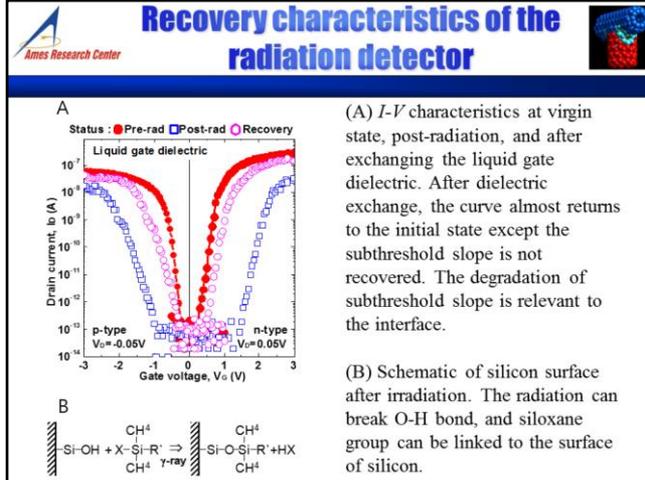


Here is an actual device, colored for enhancement: you can see the gate and the air gap. The air gap is filled with PDMS. We constructed both p-type devices and n-type devices, which have completely different current voltage characteristics depending on what the radiation dosage of the gamma rays is. You can also look for another gel that could respond to x-rays, a gel that responds to alpha particles, and another that will respond to uranium. Then you can put together a radiation nose; this concept is similar to the electric nose for chemical sensors.

So with that, I want to wrap up with sensor challenges. Then we can open up for questions.



[Dr. Meyyappan did not speak to this slide, but it is included in the interest of completeness.]



(A) I - V characteristics at virgin state, post-radiation, and after exchanging the liquid gate dielectric. After dielectric exchange, the curve almost returns to the initial state except the subthreshold slope is not recovered. The degradation of subthreshold slope is relevant to the interface.

(B) Schematic of silicon surface after irradiation. The radiation can break O-H bond, and siloxane group can be linked to the surface of silicon.

[Dr. Meyyappan did not speak to this slide, but it is included in the interest of completeness.]



Challenges for Nano Chemsensors



- Most studies in the literature just focus on material response to exposure of a given gas; rarely information on selectivity, effects of interferants (humidity for example) is given.
- Long term stability? Reliability? Life time? Sensor-to-sensor variation?
- Impact of nanomaterial quality (serious problem with CNT sensors).
- Sensor refreshing?
- Construction of sensor arrays as e-nose.
- Breathe sensors => all humidity, domination!
- Large scale fabrication
 - 'Pick and play' approaches, aligning NTs/NWs won't work
 - *In situ* CVD? Unlikely
- IoT is coming!

For the nanochem sensors, as I mentioned earlier on, most papers in the literature focus on material response, exposure of a given gas. And there's absolutely no information on selectivity. What we need is more work talking about construction of electronic noses using these nanomaterials. We also need to talk about interference; for example, humidity is a simple interference, and also sometimes close neighboring molecules could give you confusing signals. So if you're interested in benzene, you have to be wary of toluene; if you're interested in methane, you have to be wary of ethane, etc. Long-term stability, reliability, and lifetime sensor-to-sensor variation are also important challenges. The impact of nanomaterial quality is a serious problem with carbon nanotube sensors. Regardless of who your supplier is for carbon nanotubes, there will be variation in the material quality from batch to batch when you buy from the same vendor. That includes variation in impurity levels or defect levels. The construction of electronic noses using sensor arrays is another challenge. Once you train a selective number of test sensors in the lab, the training data will be dumped into millions of other sensors during manufacturing. In the electronic nose business, you are not going to be training every single sensor, especially if you are making a million sensors. But if your material quality from your source of supplier is going to be different every other week, you are not going to be in the electronic nose business for long. The breath sensor faces a

different challenge and it is mostly humidity. Maybe more than 90% is related to humidity. We need to limit the effect of humidity with the use of filters or other similar devices. Finally, the Internet of Things will drive the demand for sensor reliability and quality. However, we shouldn't connect our entire world using an IoT based on sensors that are totally unreliable and unstable.



Challenges for Nano Biosensors



- Benchmark against gold standards in terms of sensitivity, selectivity
- Large scale fabrication
 - Especially an issue with NT/NW devices
 - Device to device variation
 - Bottom up vs. top down
- Integration with microfluidics
 - Not serious with paper-based devices
- Probe life time? antibody vs. aptamer?
- Minimize pre-processing needs, total time
- Sensor reliability? Robustness?
- Multiplexing capability
 - complexity vs. economics

The same issues apply to nanobiosensors, but there are a couple of other unique issues too. Large-scale fabrication is one of them: we need to look at device-to-device variation. In all of these cases, the important thing is benchmarking against the gold standard. The biosensor has a unique need. We need to integrate with microfluidics. But on the other hand, if you're going for a paper-based substrate, then there is no need to fabricate separate microfluidics because of the wicking action of the paper, and the microfluidics part is self-integrated. As for the probe lifetime, it refers to my previous discussion on antibody versus aptamer. We have also to minimize preprocessing needs. Sensor reliability and robustness are both important challenges. The multiplexing capability, that's generally the complexity versus economics. You can come up with a biosensor platform that is going to do 10 biomarkers. It's very complex to make but it also could be very expensive. So the complexity versus economics would dictate the multiplexing goals of developers.

So with that, I'm going to stop right here. We have a good 10 to 12 minutes for questions before we close it up.

Thank you.

Transition to Q&A

***Can you please provide examples of
nanosensors that are currently
available in the market?***

[At the time of the webinar, Dr. Meyyappan was unaware of commercially available nanosensors. The following examples have been identified during the review process as part of the preparation of this transcript:

- Veridex's CellSearch® uses a ferrofluid reagent that consists of nanoparticles with a magnetic core surrounded by a polymeric layer and coated with target antibodies.
- The Verigene™ system by Nanosphere is an automated platform based on disposable test cartridges. Samples loaded onto the cartridge are treated for nucleic acid extraction, purification, and hybridization, which is carried out using oligonucleotide-conjugated gold nanoparticles.
- Corgenix ReEBOV Ebola rapid diagnostic test (RDT) utilizes gold nanoparticles.]

***Can you explain why going down to zero-D would not offer further advantages for biosensing?
What about for 2D geometry?***

That model is from Purdue; it's a simple model taking into account the probe number balance and the target concentration data, which is essentially diffusion-based. Convection could also play a role. So based on that, the researchers did not see any advantage with using spherical geometry (a nanoparticle). Based on that model, you could conclude when you have a single layer of graphene and when the same layer is identically rolled into a carbon nanotube, the carbon nanotube-based biosensing is much more sensitive than the graphene. That's based on limited assumptions of that model. But there may be something unique for graphene for that biomarker.

***Did you come across any electron
tunneling or spectroscopy-based
sensing mechanisms?***

Not that I can think of off the top of my head. It's likely but I haven't kept up with it so unfortunately the answer to the question is I don't know.

How does integration of nanosensors into a network or a sensor web impact the requirements for sensitivity?

In principle, that should not actually impact the requirement for sensitivity. Think of a scenario: in your state, the state government decides to monitor air quality, say 50,000 square miles and then you are distributing 100 sensors across your state. The sensitivity of all the sensors should be the same but the networking capability or the networking requirement should not alter that expectation from individual sensor. The network cannot dictate the requirement for sensor sensitivity. We have to be able to have identical sensors in the network.

What is the typical density of carbon nanotubes in the sensors illustrated in your presentation?

I used single-walled carbon nanotubes on the chemical sensor that I talked about, which is a chemresistive sensor that uses interdigitated fingers. Essentially, you are depositing single-walled carbon nanotubes as a thin film bridging the entire bus bar electrode. I don't remember the density itself. It could be about 10^9 per centimeter squared. For the biosensor, when you use a carbon nanofiber or nanowire or zinc oxide nanowire as a nanoelectrode, the density is determined quite a bit more robustly. For example, if you want your electrode to behave like a nanoelectrode, then the radial diffusion layer surrounding the carbon nanofiber or silicone nanowire should not overlap with the radial diffusion layer of the neighboring wire. In that sense if your carbon nanofiber diameter is 50 nanometers, so typically the neighbor nanofiber or the nanoelectrode should be about 1.2 to 1.5 micrometers away. So essentially think of placing individual nanotubes or nanowires approximately 1.5 micrometers away from each other. That will give you an idea of what the density is going to be.

When do you see nanosensors [becoming available] as part of a smart watch?

In comparison to the first question (whether there are any nanosensors in the market), smart watches are already in the market. Nanosensors have to be available for other platforms to begin with. Potentially gas sensors that monitor pollution like sulfur dioxide or nitric oxide, if they are reliable, could be integrated into smart watches. For example, the phone sensor that I referred to briefly, that's a technology that we have licensed to several companies. They are currently working on integrating them with the Bluetooth version of a smartphone. I think some of those companies probably could have something in the market in the next two or three years. So in principle, somebody could make it even smaller and put it in the smart watch. So if I'm optimistic, it could be five years.

What, in your opinion, is the most important molecular target for biosensing?

That depends on what your application is. If you're into water quality, an important target could be bacteria. But on the other hand, in healthcare applications there are a lot of targets. Some of the most common targets you would see in the recent literature, particularly in the last two, three years, are cardiac biomarkers. You also would see in many of the sensor journals an enormous number of publications with glucose or cholesterol as targets.

***Can you describe methods for
sensor refreshing?***

In the chemical sensor that I talked about, let's say the sensor works for quite a few days. Typically these molecules are absorbed physically; there is rarely any kind of chemical binding. Generally, these molecules would spontaneously desorb. But regardless, when you begin to see declining sensor performance, this could mean that other molecules could be bound to your sensor. The easiest way to refresh is by using heating. You can normally heat graphene or carbon nanotubes to 70, 80 degrees centigrade and that will drive off those molecules. A little more involved way is to attach UV/LED light sources. One advantage of UV is that it can break bonds stronger than physisorption but it's a little more complicated to integrate in the sensor.

>>Lisa Friedersdorf: So Meyya, I want to thank you very much for an informative webinar. I'd like to thank all of the participants today and point out that our next Sensors NSI webinar in this series is scheduled for Tuesday, November 3, at noon. The title is "A Regulatory Case Study for the Development of Nanosensors." More information on this webinar, including registration information, will be available soon on nano.gov. Information about this webinar series, webinars for the Nanotechnology Knowledge Infrastructure Signature Initiative, and also

webinars for our small and medium-sized businesses, is available on nano.gov/publicwebinars. With that, I thank you all very much and wish you a good afternoon.