
Chemical Sensor Arrays

Participant Guide

Description and Estimated Time to Complete

Chemical Sensor Arrays (CSAs) are MEMS devices that gather, detect, measure, and identify a substance or several substances in a minute sample. That sample could be a few drops of blood, an unknown gas or smell, or an unknown liquid. Many of these arrays are cantilever-based, using micro and nano-sized cantilevers. This unit provides information about MEMS Chemical Sensor Arrays, primarily the cantilever-based arrays. It covers how they work and where they are used.

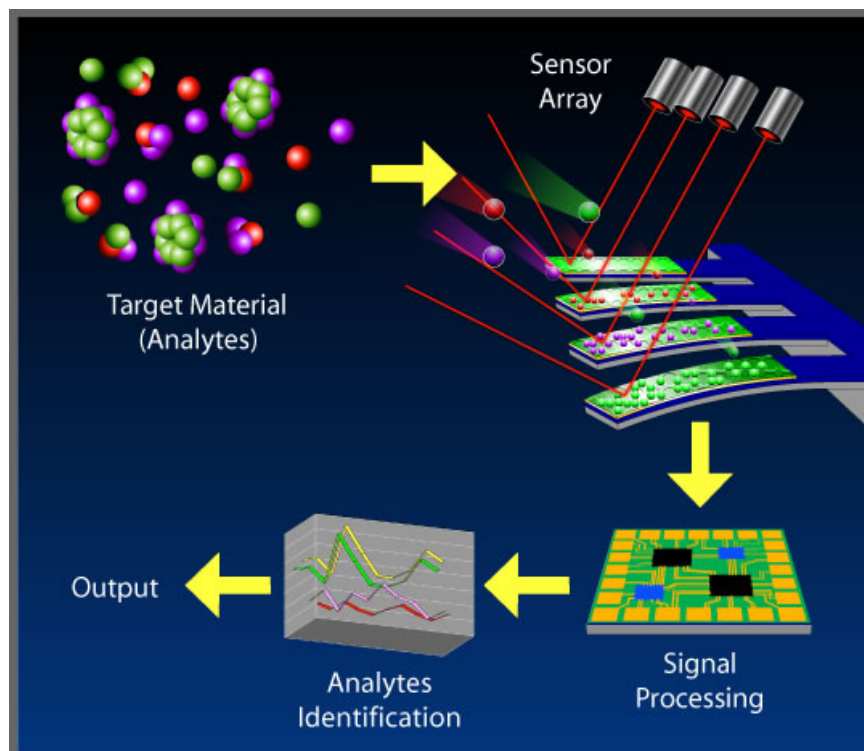
It would be to your benefit to have reviewed SCME's "How Does a Cantilever Work?" prior to completing this unit.

Estimated Time to Complete

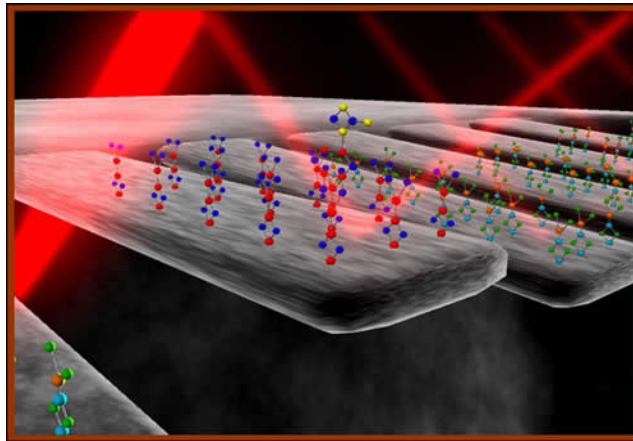
Allow approximately 20 minutes

Introduction

A Chemical Sensor Array (CSA) is an array of microtransducers and supporting integrated circuits (*see process flow diagram below*). A CSA is designed to detect and measure the amount or concentration of one or more substances contained in a sample environment. The substances, referred to as target materials or analytes, could be specific gas molecules or atoms, antibodies or proteins, mercury vapor or volatile organic compounds. One or more analytes in a sample are detected and the quantity measured using microtransducers. The system electronics analyze and identify the type and/or quantity of analytes.



The microtransducers of CSAs could be optical devices, electronic diodes, microcantilevers, biological cells and molecules (biological, physical or chemical). The application and, more specifically, the target material being analyzed, determine the type of transducer used. The most common transducer used in CSAs is the microcantilever.



Chemical Sensor Array with Analytes

In a cantilever-based CSA, the target material is detected when it comes in contact with a chemically sensitive material on a cantilever's surface (*see figure above*). The amount of target material is measured by monitoring a change in one or more of the cantilever's mechanical or electrical properties, such as displacement, resistance, or resonant frequency.

This unit will focus on the applications of chemical sensor arrays and the operation of cantilever-based CSA operation. Many of the following applications are not cantilever-based, but rather an array of electrodes, diodes, or biomolecules use to detect specific molecules.

Objectives

- State at least five applications of a MEMS CSA.
- Compare and contrast the operations of a static and dynamic cantilever-based CSA.
- Describe at least two operating characteristics of a CSA.

Key Terms (Definitions can be found in the Glossary at this end of this unit)

Analytes
Cantilever
Chemical Sensor Array
MEMS
Piezoresistive
Resonant frequency
Selectivity

Chemical Sensor Array Applications

The MEMS Chemical Sensor Array (CSA) is an analytical tool used in a variety of applications and microenvironments. It is currently used to monitor glucose levels in diabetics, detect fuel leaks in a space shuttle, identify toxic gases in an environment, identify various types of cells in a blood sample, and analyze DNA hybridization. Common applications of MEMS CSAs are found in the following fields:

- Medical
- Forensics
- Environmental control
- Aerospace
- Fragrance design
- Food production
- Security and defense

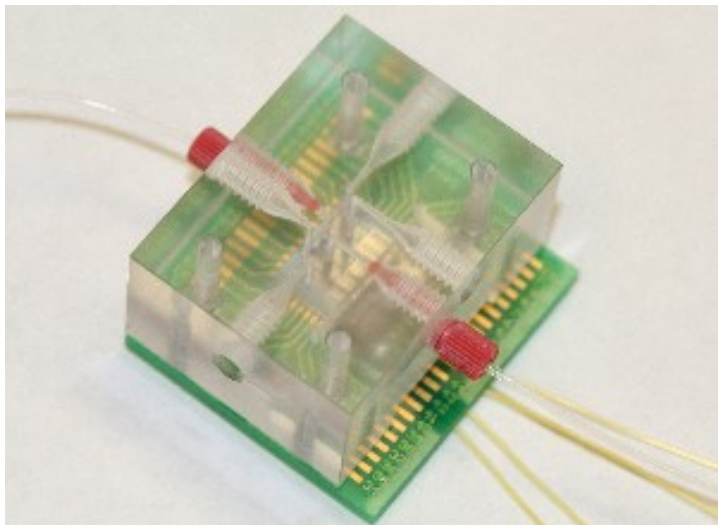
Within these fields, CSAs are used for the following applications (to name just a few):

- Detection of chemical vapors
- Detection of biological agents (medical as well as biowarfare agents)
- Vibration monitors
- Medical diagnostics and therapeutics
- Olfactory applications
- Sample analysis (gas or liquids)

Following are brief descriptions of some chemical arrays that are already on the market or currently being tested for the market.

Lab-on-a-Chip (LOC) Array

A lab-on-a-chip (LOC) is a MEMS that incorporates several laboratory functions on a single chip. An LOC can consist of a chemical sensor array designed to sense one or more analytes, a micropump to handle the flow of the sample to and from the array, and the electronics to control the device and analyze the output of the CSA.



This Lab-on-a-chip (LOC) is a miniaturized, portable version of a blood-count machine that is being tested by astronauts. One portion of the LOC uses a CSA to analyze blood samples in real-time to diagnose infection, allergies, anemia or deficiencies in the immune system.¹

*Lab-on-a-chip – Blood Analysis Chemical Sensor Array
[Photo courtesy of Y. Tai, California Institute of Technology]*

The Artificial Nose (or ENose)

For fragrance design, food production, and gas detection, the CSA is used as an artificial olfactory system (an artificial nose). It analyzes a fragrance by separating the component particles that when combined, provide an overall scent. In food production, MEMS CSAs are used to detect specific compounds in a food's odor, such as the odor of a fish or meat. By analyzing the amount of the compounds present, a CSA can determine the freshness of the meat or the presence of contaminants.²

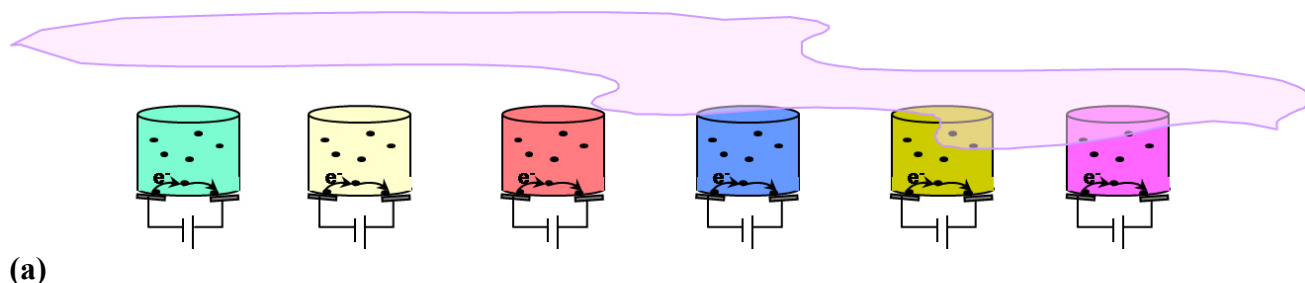


The picture is the ENose developed by NASA and tested on the International Space Station in late 2008. The ENose Sensor Unit (the darker-looking metal object) is housed in its Interface Unit (white). The ruler, shown for size comparison, is 12 inches (about 30.5 cm) long.³

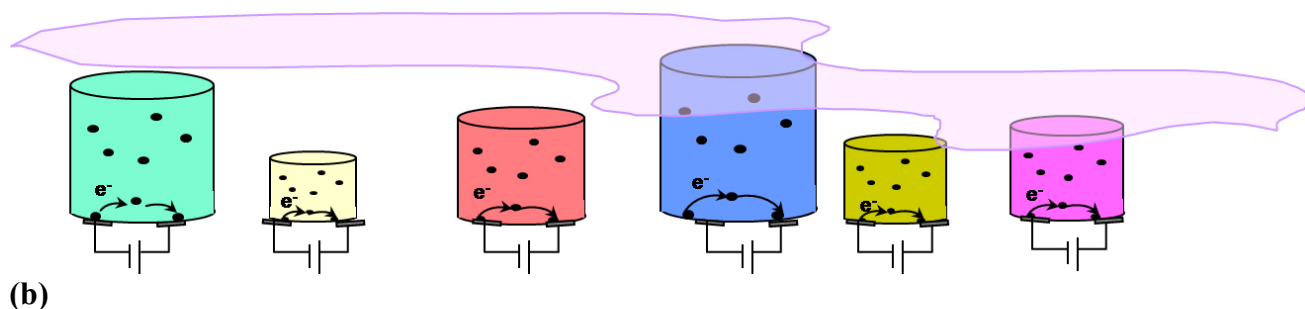
*The ENose developed by NASA's Advanced Environmental Monitoring and Control division
[Graphic source: NASA]*

For gas detection, the artificial nose can detect a specific gas or the composition of a gas. The artificial nose is currently used in the space station to detect ammonia.³ In counterterrorism CSAs are being designed to detect toxic and hazardous gases in the field. Such devices could be incorporated into the helmets or clothing of military personnel.

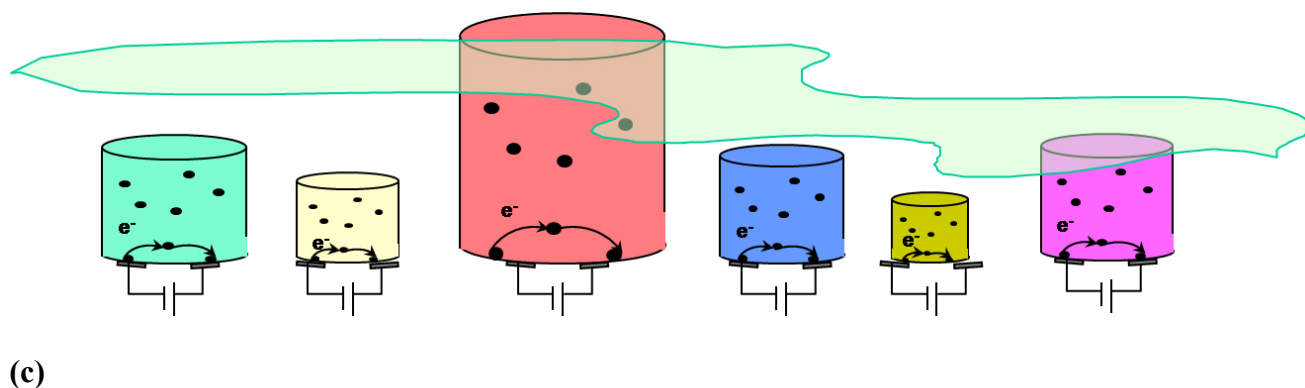
How Does the ENose Work?⁴



The ENose uses a collection of 16 different polymer films on a set of electrodes. The graphic (a) illustrates six films/electrodes. These films are specially designed to conduct electricity based on their resistance. A baseline resistance reading is established (a) with no odors (ambient air). When a substance -- such as the stray molecules from an ammonia leak -- is absorbed into these films, the films expand slightly (b), changing their resistivity. The amount of expansion of each film determines the amount of its electrode current.



Because each film is made of a different polymer, each one reacts to a chemical compound in a slightly different way. While the changes in resistivity in a single polymer film would not be enough to identify a compound, the varied changes in 16 films produce a distinctive, identifiable pattern for a specific compound. Graphic (c) shows a different compound being sensed.



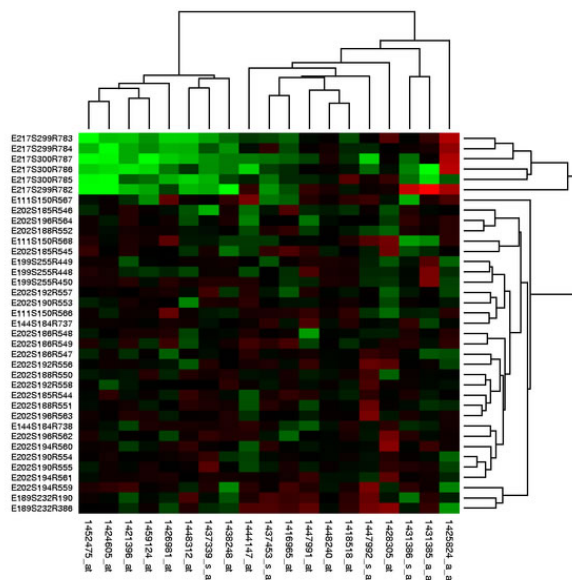
[Graphics Courtesy of NASA's Advanced Environmental Monitoring and Control division]

Bio-Sensors

In medical diagnostics, CSAs are used as bio-sensors to analyze samples for substances such as antibodies, proteins, antigens, and DNA. They are used for glucose monitors, pH sensors, protein binding, DNA detection, and gene expression profiling.

DNA or gene microarrays are biosensors used to analyze and measure the activity of genes. These arrays enables scientists and doctors to analyze complex biological problems:

- Identify the genetic variations that could play a role in diseases such as Alzheimer's and Parkinson's.
- Analyze and test for viruses that cause diseases such as SARS (Severe Acute Respiratory Syndrome), HIV, tuberculosis, and other infectious diseases.
- Analyze a patient's blood to determine the best drug and dosage for that patient's particular disease.



Researchers can use microarrays and other methods to measure changes in gene expression (activity) and thereby learn how cells respond to a disease or to some other challenge.⁵ Gene expression microarrays (*image right*) measure tens of thousands of genes on a single GeneChip™ and provide scientists the data to understand regulatory processes at the cellular level.

CSAs in Destructive Environments

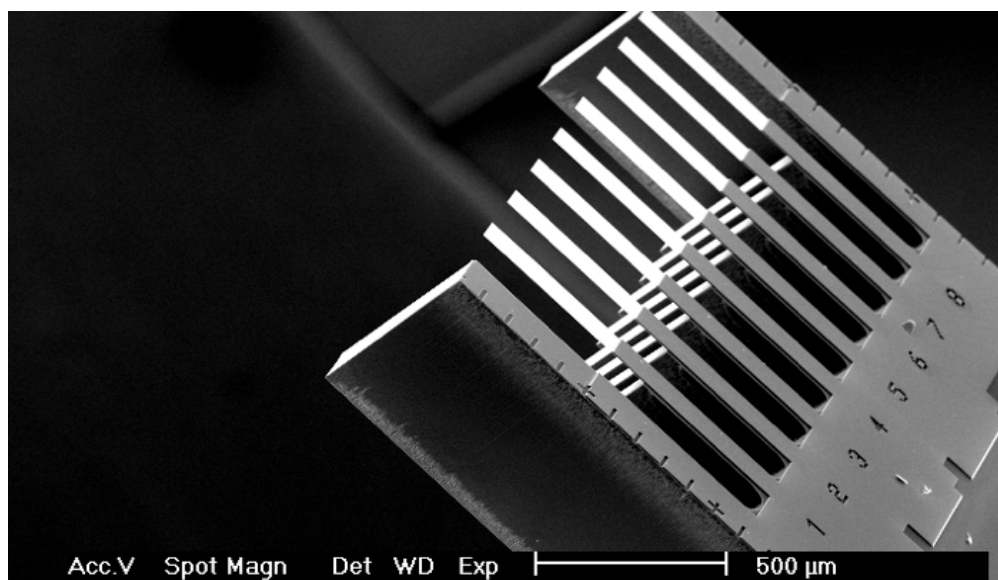
Due to their small size, design and packaging, MEMS CSAs are used in environments that are destructive to comparable macrosensors and where other types of sensors are ineffective. Such environments include

- electric and magnetic fields,
- hazardous chemical vapors,
- nuclear radiation,
- radio frequency (RF) radiation, and
- contaminated and hazardous liquids.

The Cantilever-based CSA

The most common CSA transducer is the microcantilever. Its versatility and low construction costs make it an ideal transducer for a variety of analytes. CSA microcantilevers are typically 10 – 500 μm long, up to 100 μm wide, and up to 2 μm thick. The top or bottom surface or both surfaces are coated with a chemically reactive material designed specifically for the analyte targeted.² For static CSA's in optical fiber array applications, the standard pitch of the microcantilevers is 250 μm , with a typical spring constant of 0.02 N/m and resonance frequency of 4 kHz.²

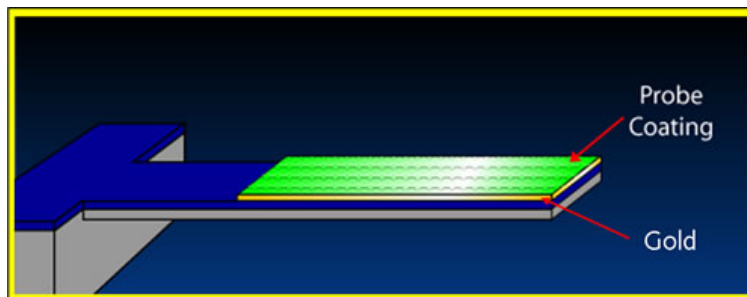
The scanning electron image below is of a microcantilever CSA developed by the Cantilever Array Sensor Group at the Swiss Nanoscience Institute. Such cantilevers are being developed for “applications in chemistry, physics, biochemistry and medicine”. They are ideal for such applications because they “are miniaturized, ultrasensitive and fast-responding sensors.”¹³



Microcantilever Chemical Sensor Array
[Image courtesy of Dr. Christoph Gerber, Institute of Physics, University of Basel]

How does a Cantilever-Based CSA work?

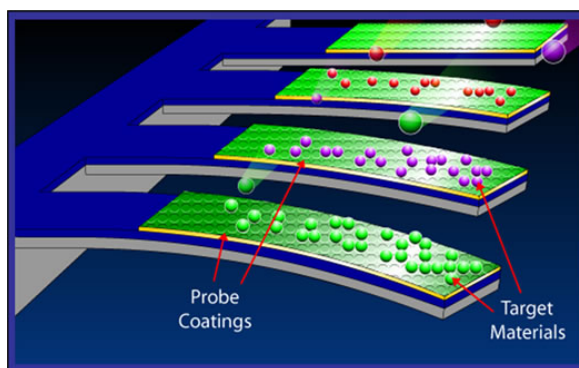
Cantilever Construction



Chemically Reactive Probe Coating

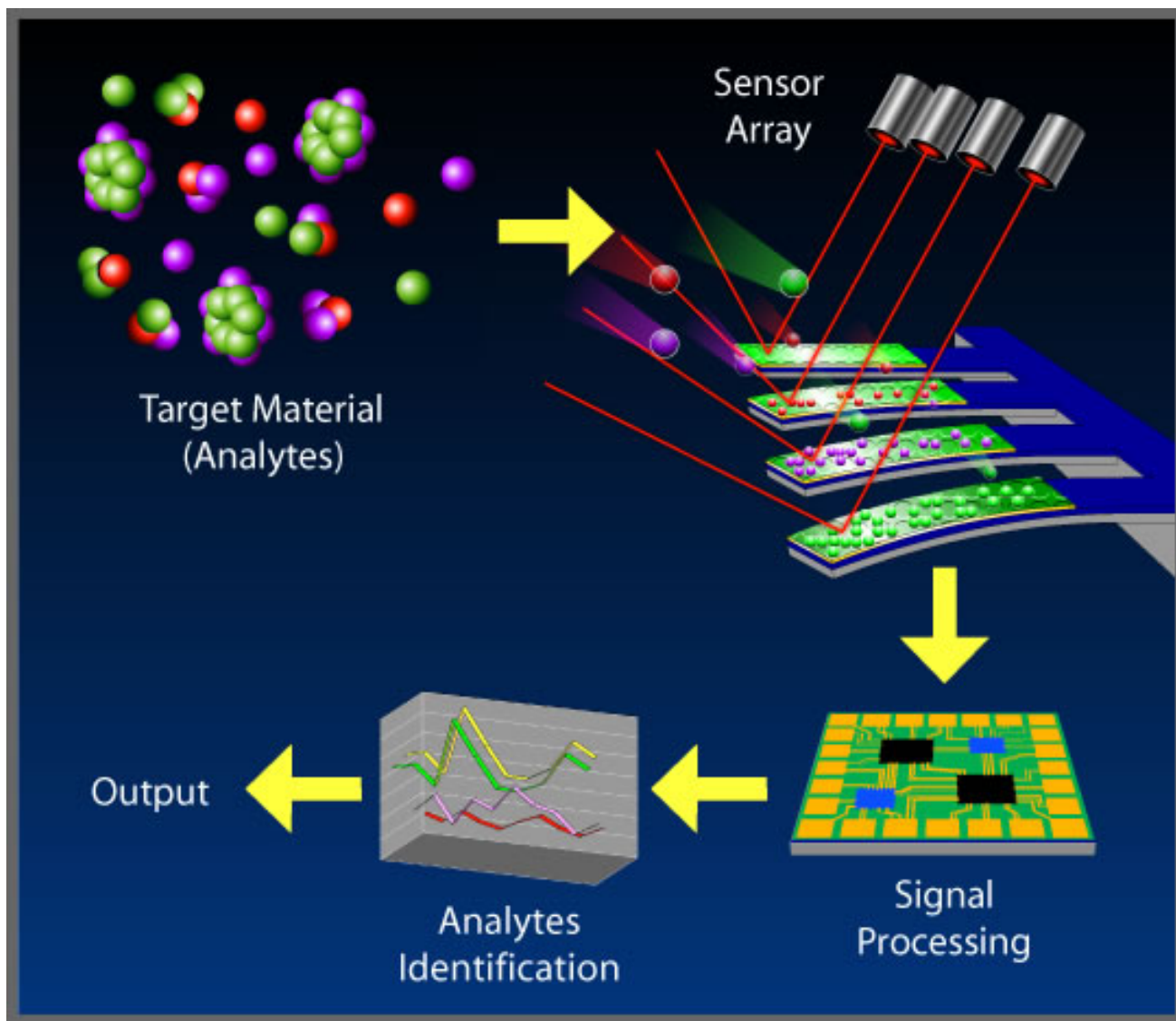
The primary components of a CSA are the microcantilever transducers. The suspended end of each microcantilever is coated with a probe material that has an attraction to specific molecules in the test environment. For cantilever-based CSAs, the cantilevers can be constructed with different surface materials on the top and the bottom. In some CSAs, the top surface is coated with a chemically reactive coating (probe coating) which may exist at the suspended end of the cantilever or may cover the entire top surface. In the fabrication process, the deposition of this selective coating is referred to as "functionalizing the surface." By functionalizing the surface, the cantilever can be designed to have the target material "stick to" or adsorbed to a specific portion of the cantilever's surface (e.g. the tip, the middle, the full length of the cantilever or both the top and bottom surfaces). The fabrication process can be designed to selectively coat only the desired portion of the cantilever's surface with the chemically reactive coating.

On the bottom of the cantilever, the coating may be to be neutral so that it will not react with any of the substances in the sample environment. However, some applications have the probe coating on both the top and bottom surfaces of the cantilever.



Probe Coating and Analytes (Target Material)

The probe material is a chemically sensitive substance that experiences a chemical change when it adsorbs a specific target material (analyte). By designing a CSA with a different probe coating on each cantilever, a CSA can be used to detect several different substances within the same sample. The figure (*Probe Coating and Analytes*) illustrates an array that can detect three different analytes (green, purple and red). The fourth microcantilever is the reference cantilever.



How a CSA Works

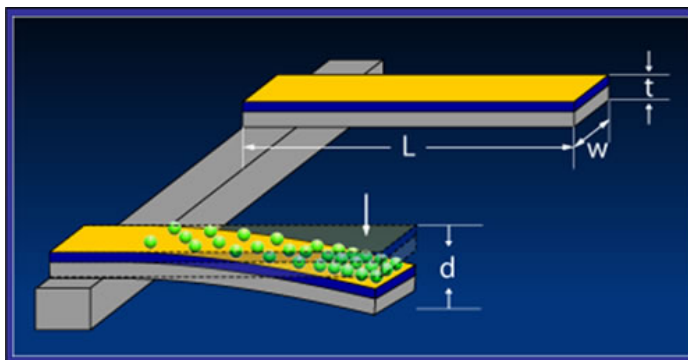
(Refer to figure: "How a CSA works") When a target material in the sample adsorbs to the probe coating on a cantilever's surface, it causes a minute, but measurable change in the cantilever's mechanical or electrical properties. As more target material adsorb to the cantilever's surface, the resulting change is measured. This change is processed by the integrated circuitry (Signal Processing) of the MEMS into relative data. This data is analyzed and compared to reference data for determining the type and amount of material (Analytes Identification).

One or more of the cantilever's properties are monitored. The properties monitored depend on the design of the system. Some systems monitor a static property such as displacement or resistance. Others monitor a dynamic property such as resonant frequency. (Note about resonant frequency: Mechanical systems *like* to vibrate at a natural frequency which is a property of their geometric design. The natural frequency is at or near the system's resonant frequency.)

An Interesting Fact

It is interesting to note, that prior to the onset of micron and nano-technology, these minute changes in the mechanical properties of such small devices were considered negligible. However, current technology provides innovative methods for measuring these negligible changes allowing microscale components to be monitored and measured like their macroscopic equivalents.

Mass-Sensitive Transducer

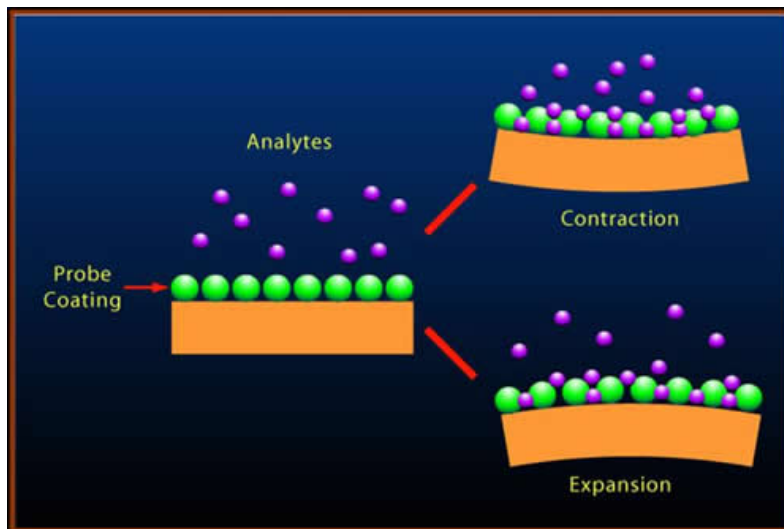


Microtransducer affected by change in mass

Since cantilever transducers are very small (from a few nanometers to hundreds of microns in size), their sensitivity is high compared to similar macrotransducers. The overall mass of a microcantilever is measurably affected by the chemisorption or adsorption of a very small quantity or mass of material (even a few molecules or atoms can be detected). A small change in mass causes a measurable change in one or more of these cantilever's properties. For example, more mass causes a greater displacement or a lower resonant frequency. This type of cantilever transducer is referred to as a mass-sensitive transducer.

It is important to note that due to the micron size of the cantilever and the nano size of the analyte, the cantilever's *bend or displacement* is due to a small amount of mass, not weight. Weight is mass affected by the force of gravity. A diving board is a cantilever that *bends* due to the weight of a person standing on its suspended end. The microcantilever has too little mass to be affected by the force of gravity.

Stress-Induced Curvature



Stress-induced curvature

Mass-sensitive transducers are not as effective as the transducer and analytes get smaller. For applications such as biomedical diagnostics and gas detection, the analytes can be nano-sized particles (1 to 100 nm). For such applications, cantilever displacement is dependent upon a surface stress caused by the chemisorption of the analytes on or within the probe coating. When the analytes adsorb into the probe coating an expansion or contraction occurs (*see figure*). This causes the cantilever to bend or flex. This is called "stress-induced curvature."

Static and Dynamic CSAs

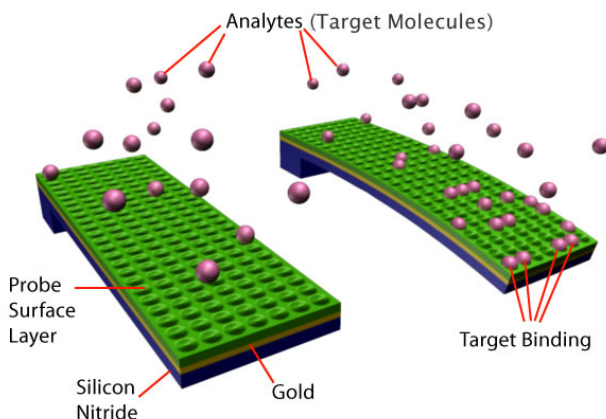
There are two operational modes used to detect changes in the cantilever's mechanical or electrical properties: **Static and Dynamic**.

The **static mode** measures the bending or flexing of the cantilever due to stress or a change in mass. When the probe coating captures the target analytes, the cantilever bends due to an increase in mass or stress of the probe coating. This bending is a measurable static response.

The **dynamic mode** measures a shift in the cantilever's resonant frequency due to an increase in mass. When the probe coating captures the target analytes, the cantilever's resonant frequency shifts to a lower frequency. This shift is due to an increase in mass which is seen as an increase in the cantilever's overall mass.

Static Mode

In the static mode of operation, as the chemically reactive surface selectively adsorbs the target material, the cantilever bends due to an increase in mass or surface stress caused by an increase of analytes bonding to the probe coating's molecules (*see figure*). The bending causes a measurable cantilever displacement. This displacement can be measured by sensing a change in angular deflection (Δ angular deflection) or change in resistance (ΔR).



Cantilever displacement due to surface stress

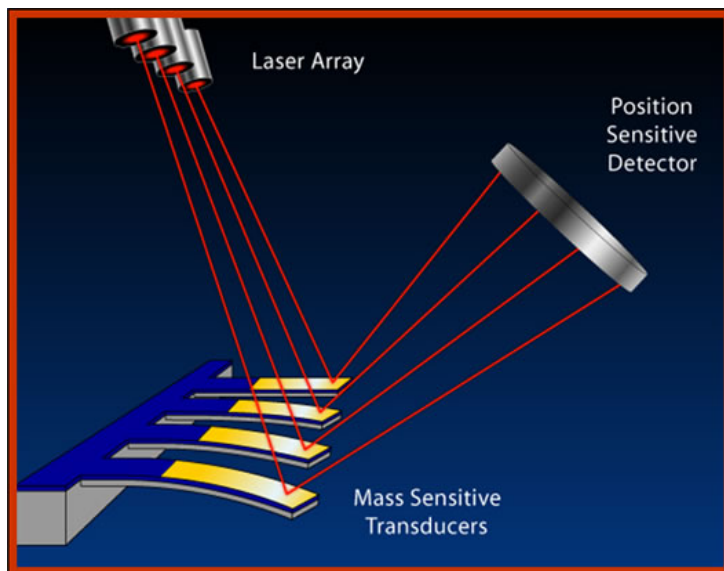
Static - ΔR

To measure a change in resistance, the microcantilevers are constructed with a piezoresistive layer. This layer is usually a doped silicon layer fabricated into the cantilever during construction. As the target material is adsorbed by the chemically reactive layer the cantilever bends. This creates a measurable change in the resistance of the cantilever's piezoresistive layer.

Static – Δ angular deflection

To measure a change in angular deflection, a reflective layer consisting of a material such as gold is coated onto the surface of the cantilever prior to the chemically reactive layer. A laser beam is directed to and reflected from the cantilever's surface creating a reference angle. As the cantilever bends, the change in the angular deflection is detected by measuring the change in position of the reflected beam.

With both measurements, the amount of change in resistance or change in angular deflection is related to the amount of target material adsorbed in the probe coating.



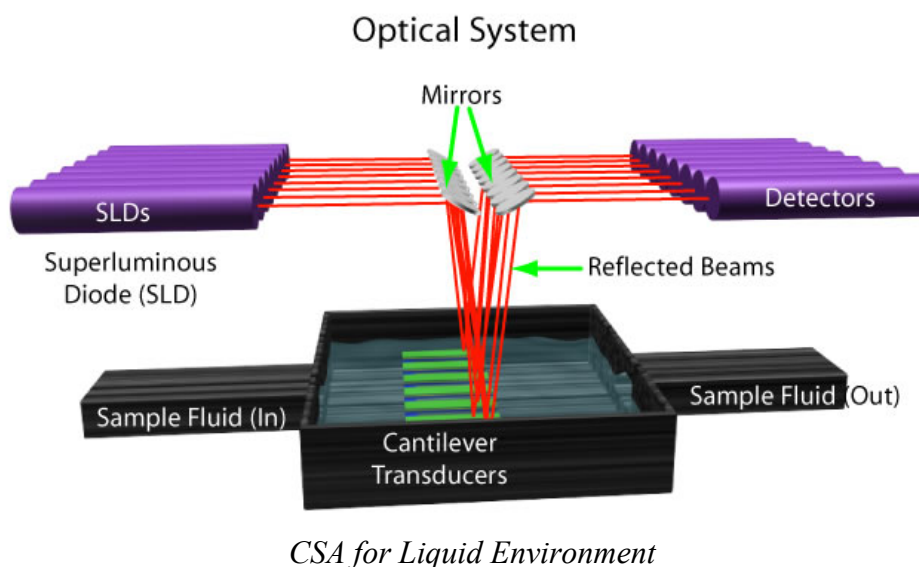
Measuring Displacement with a change in Angular Deflection

Dynamic Mode

In the dynamic CSA, the cantilevers are initially excited by a piezoelectric, magnetic, electrostatic or thermal actuation. Target molecules in the sample environment attach to each of the cantilevers' surfaces. As with the static mode, the selective probe material on the cantilevers' surfaces determines which molecules adsorb to which surface. This adsorption changes the cantilever's mass resulting in a change in resonant frequency. The amount of change in resonant frequency is a function of the amount of mass loading. The change in mass is dependent upon the concentration of the target material within the sample environment and the amount of time the cantilever is exposed to the sample.

Watch this YouTube video to see a dynamic mode biosensor in action: **Microcantilevers as Biosensors** [<https://youtu.be/rPJJa0QMxcbs>]

Static or Dynamic?



The type of CSA (static or dynamic) used for a specific application is determined by the sample environment. In liquid environments the damping effect of the liquid on the cantilever's movement can make frequency measurements very difficult resulting in false readings. Therefore, static CSA's are primarily used in liquid environments (*see figure above*). In gaseous environments, both static and dynamic CSA's are used. In order to gather more information from the sample and ensure its accuracy, some CSAs use a combination of static and dynamic modes.

Operating Characteristics of CSAs

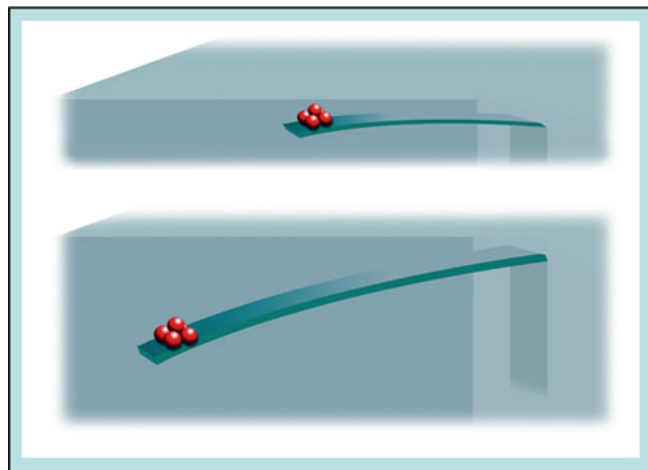
A few of the operating characteristics considered in the design of CSA microcantilevers include

- sensitivity,
- selectivity,
- response time,
- size, and
- power consumption.

Cantilever-based CSAs have proven to be highly sensitive, highly selective, and to have fast response times. Because each cantilever in an array can be coated with a different probe material, a single cantilever array can be designed to detect a large number of different analytes. It can also be designed to have redundancy (nominally identical sensors) in order to reduce false positives (greater accuracy) and yield a better response. Such an array can analyze a broad spectrum of materials within a single complex mixture. For example, rather than have to take several vials of bloods to test for different analytes using various test processes, technicians could place a drop of blood on a CSA and it could test for all of the different analytes simultaneously.

Mass Sensitivity

Cantilever transducers have an inherently high mass sensitivity due to the small mass of the cantilever itself. The physical properties of the cantilever (width, thickness, length and material) are used to further enhance its sensitivity to minute changes in mass. For example, the physical geometry of the cantilever affects its resonant frequency. A long cantilever will have a lower resonant frequency than a shorter cantilever of the same material, thickness and width. A thicker cantilever is inherently stiffer, yielding a higher frequency. Therefore, the CSA designer must know what detection electronics are best suited for the operational frequencies and match the cantilever design to the electronics.



Cantilever length - short vs. long

Response Time

The response time for a microcantilever is the time it takes for the cantilever to respond to the target material on its surface and produce a change in the output. The response time is affected by several parameters, three of which are

- the concentration of the target material in the environment,
- the probe material itself, and
- the method used to interpret the change in a mechanical property.

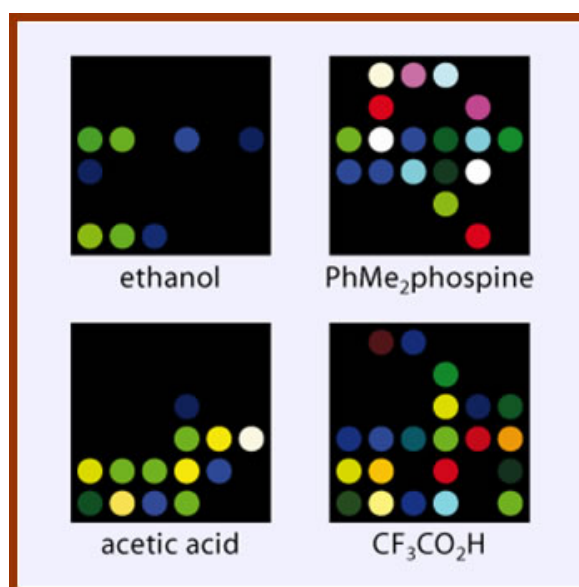
For the best response time, the chemical reaction between the target material and the probe material

must be as fast as possible. The more time it takes for the adsorption to occur, the slower the response time. Once the chemical reaction occurs, the change it creates in the frequency, resistance or deflection must be sensed quickly in order to generate an immediate output. In a CSA this change is measured by integrated circuits directly interfaced with the monitored characteristic of the cantilever (i.e. the piezoresistance, resonant frequency, or angular deflection). This direct measurement coupled with the time required for the chemical reaction to occur on the cantilever's surface determine the sensor's response time.

Non-Cantilever Based CSAs

The type of CSA discussed in this unit is a cantilever-based CSA that uses mass or stress sensitive transducers. There are variations of CSAs that use other types of transducers that may be better suited for a specific application and its requirements. Following is a short description of other types of non-cantilever based CSAs.

Optical Sensor Array



Partial output from a Colorimetric Optical Array.

In optical sensor arrays the chemical reaction between the probe coating and the target analytes affects an optical property of the transducer. This results in a change in the optical signal such as color (wavelength) or light intensity.

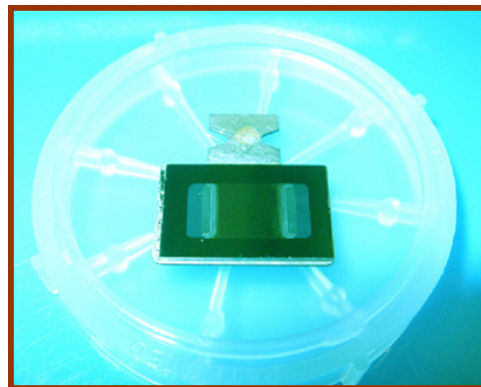
The graphic shows a partial output from a colorimetric optical array. A colorimetric sensor arrays act as an "optoelectronic nose" by using an array of multiple dyes whose color changes are based on the full range of intermolecular interactions. The four volatile organic compounds in the graphic have four different patterns as identified by the sensor array. This particular array can sense up to 15 analytes simultaneously in the same sample.

Schottky Diode Array

In a Schottky Diode Sensor Array the target material absorbs (diffuses) through the probe coating to a metal layer. The metal layer serves as a gate for a diode. Any change at the gate causes a change in the diode's electrical characteristics.

Schottky Diode Sensor Array

*[Image source: University of California, Santa Barbara,
Department of Chemical Engineering.]*



Cell-based Sensor Array

The Cell-based Sensor Array uses biological cells as the transducers to detect the presence of specific molecules (analytes) within the cells' environment. There are several types of molecular transducers being developed and tested.

One type of molecular transducer uses cell amplification. When a cell interacts with the analytes a chemical change occurs within the cell causing the production of many "so-called second messenger" molecules. This is essentially a biological gain or cell signal amplification. A chemical change within the cell or an electrical activity can be monitored to measure the amount of amplification. The amount of amplification indicates the amount of analytes in the sample.⁶

CSAs Working Together

With the variety of sensor arrays available, a system can be developed to mimic the human senses. Cantilever-based arrays distinguish between different smells and tastes, optical arrays react to different wavelengths and intensities (sight), and acoustic arrays detect a change in acoustic properties as a result of interacting with the environment (hearing).

A CSA can be used in combination with other sensors or as a stand-alone device. Its versatility, reliability, selectivity and design flexibility make it an ideal sensor system for a variety of applications, many of which are still being realized.

Summary

A Chemical Sensor Array is an array of microtransducers and supporting integrated circuits. A CSA is designed to detect and measure the amount or concentration of one or more substances contained in a sample environment.

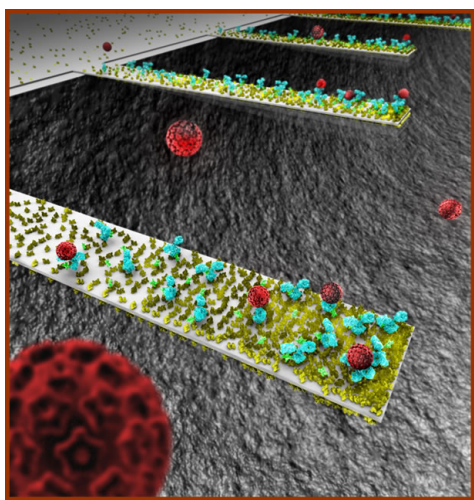
The cantilever-based CSA uses an array of microcantilevers to detect and measure specific materials within a sample environment. The micron size of the cantilevers results in higher selectivity, improved sensitivity, faster response time and low construction costs. These characteristics make the cantilever CSA a very popular sensor for a wide range of applications.

Food For Thought

What are some additional applications where CSA's could be used to detect a combination of gases, scents or particles?

In the dynamic mode, which microcantilever would be more sensitive to mass loading – one 100 microns in length or 60 microns in length? (Assume the thickness, width and materials are the same for both cantilevers).

In many applications, dynamic mode or static mode CSAs could be used. Below is a CSA used to detect a specific virus in the bloodstream. Based on your knowledge of the microcantilever modes of operation, which mode – dynamic or static – do you think would be best for this application and why?



Nanocantilevers coated with antibodies (blue-green) that capture viruses (red spheres). As the cantilevers identify and capture more virus molecules, one or more of the mechanical or electrical characteristics of the cantilevers can change and be detected by an electronic interface.*

The size of the particle being detected and captured is one of the factors affecting the size of the cantilever. [Image generated and printed with permission by Seyet, LLC]

**Antibodies are proteins produced in the blood in response to the presence of an antigen (e.g., virus, bacteria, toxin).*

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Glossary

Analytes: A substance or chemical constituent that is undergoing analysis or being measured.

Cantilever: A beam supported at one end and with the other end suspended freely outwards.

Chemical Sensor Array: An array of sensors that chemical reacts with a target material resulting in a measurable change (i.e. resonant frequency or mass) with the sensor.

Chemisorption: The molecular bonding of gas to a solid.

Piezoresistive: The piezoresistive effect describes the changing electrical resistance of a material due to applied mechanical stress.

Resonant frequency: The frequency at which a moving member or a circuit has a maximum output for a given input.

Selectivity: The pumping speeds for specific gases. Pumps that are selective do not pump all gases at the same rate.

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