Piezoelectric Biosensors

By: Bojan Gavrilovic & Jaskaran Dhillon

Outline

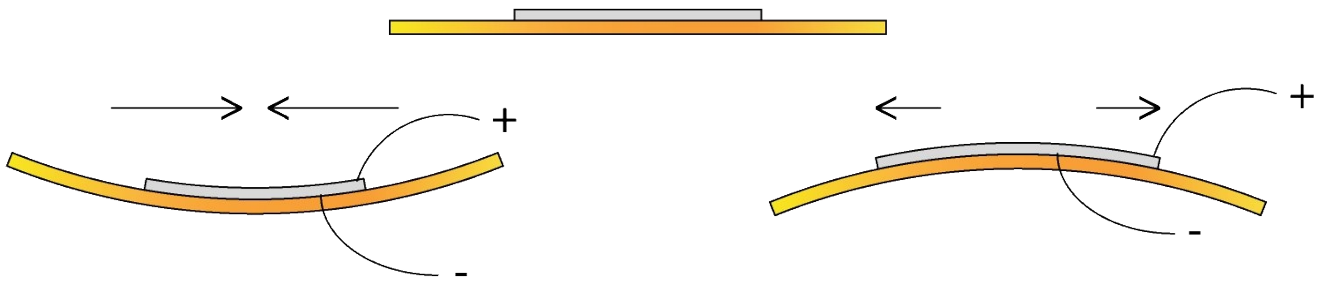
- Introduction:
  - What are piezoelectrics?
- History of piezoelectrics
  - Who discovered piezoelectrics?
  - Applications of piezoelectrics throughout history
- Biosensors:
  - Piezoelectrics as biosensors

Introduction

- What is Piezoelectricity?
  - Piezoelectricity is the potential difference created across certain materials due to an applied mechanical stress.
- *Piezo* - To squeeze or press

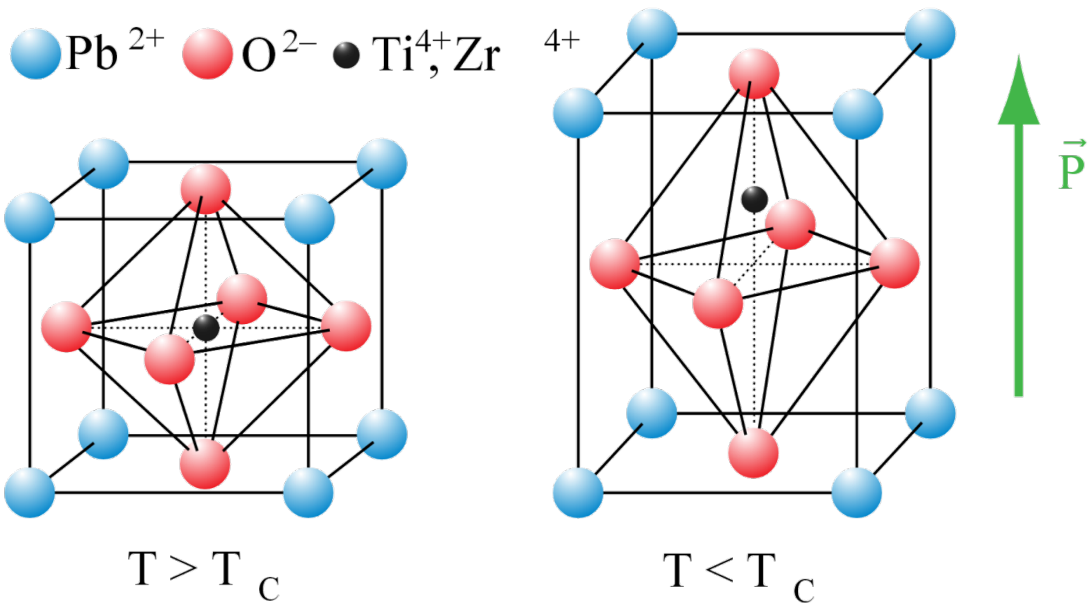
Piezoelectric Materials

- When a mechanical stress is applied to a piezoelectric material, the deformation in the material can decrease the separation between cations and anions which produces an internal potential difference.



Piezoelectric Materials

- The piezoelectric effect is observed below the Curie temperature
- Unit cells of the material become non-centrosymmetric below the Curie temperature



Converse Piezoelectric Effect

- The reverse of the piezoelectric effect is also observed in piezoelectric materials
- When a potential difference is applied across these materials, they will mechanically deform

History and Applications

- 1880
  - The Curie brothers, two French physicists discover the piezoelectric effect

The Curie Brothers and their Parents

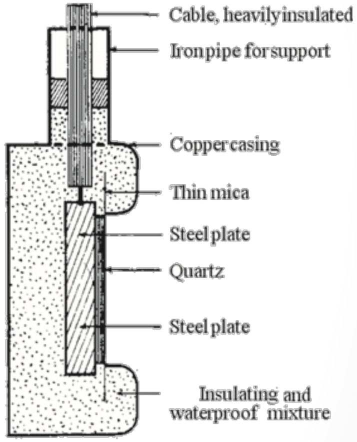
Pierre and Marie Curie

History and Applications

- 1881
  - Gabriel Lippmann discovers the converse piezoelectric effect
- World War I (1917)
  - Piezoelectrics used in a practical application for the first time:
    - Paul Langevin, a French physicist worked closely with Robert William Boyle, a Canadian physicist , to develop an ultrasonic submarine detector which uses quartz to emit a high frequency chirp

Paul Langevin
(1872–1946)

Robert W. Boyle
(1883–1955)



History and Applications

- Post World War I
  - Piezoelectrics become more widely used as a reliable transducer.
  - Used in:
    - Record players
    - Measuring viscosity and elasticity in materials research
    - Finding flaws in materials such as cast metal
- World War II
  - Fredrick R. Lack of Bell Telephone Laboratories developed the "AT-cut" crystal
    - These "AT-cut" crystals are able to operate using the piezoelectric effect through a much wider range of temperatures.
    - These crystals were used in aviation radio.

Modern Day Applications

Application	Function
Electric Cigarette Lighter	Spring loaded hammer strikes piezoelectric creating a spark
Loudspeakers	Voltage is applied to vibrate a piezoelectric polymer film in order to create sound
Fire Alarms	Vibrating piezoelectric produces high pitched sound
Energy Harvesting	Piezoelectrics embedded in surfaces deform in response to displacement in the surface producing a voltage
Microbalances	Piezoelectrics can measure very sensitive changes in mass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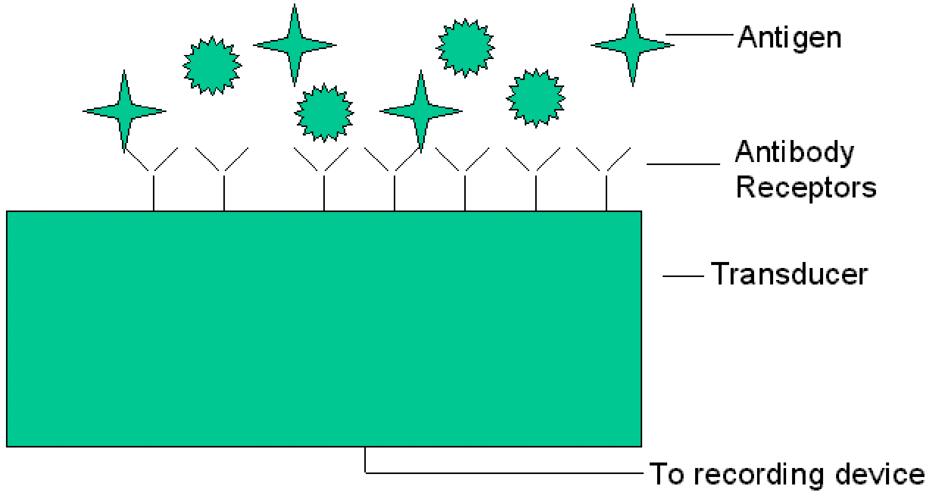
Piezo Electricity

Biosensors

- What is a biosensor?
  - Tool that converts biochemical signal into a electrical signal
  - Has two components
    - Receptor: a biomolecule that recognizes a target molecule (the analyte)
    - Transducer: a device for converting the recognition event into a measurable signal

Biosensors

- Two classes of bio-recognition:
  - Bio-affinity
    - receptor-ligand
    - antibody-antigen binding.
  - Bio-metabolic
- Very difficult to measure receptor-ligand and antibody-antigen binding electronically



Piezoelectric Biosensors

- Piezoelectric immunosensor:
  - Can detect antigens in the picogram range
  - Can detect antigens in the gas phase as well as the liquid phase

- Piezoelectric Biosensors work by measuring the change in frequency which occurs when the antigen binds to the antibody receptor

- The change in frequency is related to the change in mass by the Sauerbrey equation

Piezoelectric Biosensors

- Sauerbrey Equation

$$\Delta f = -\frac{2{f_0}^2}{A\sqrt{p_q \mu_q}} \Delta m$$

  - f_0 : Resonant Frequency
  - Δf : Frequency Change
  - Δm : Mass Change
  - A : Piezoelectrically active crystal area
  - p_q : Density of quartz
  - μ_q : Shear modulus of quartz for AT- cut crystal

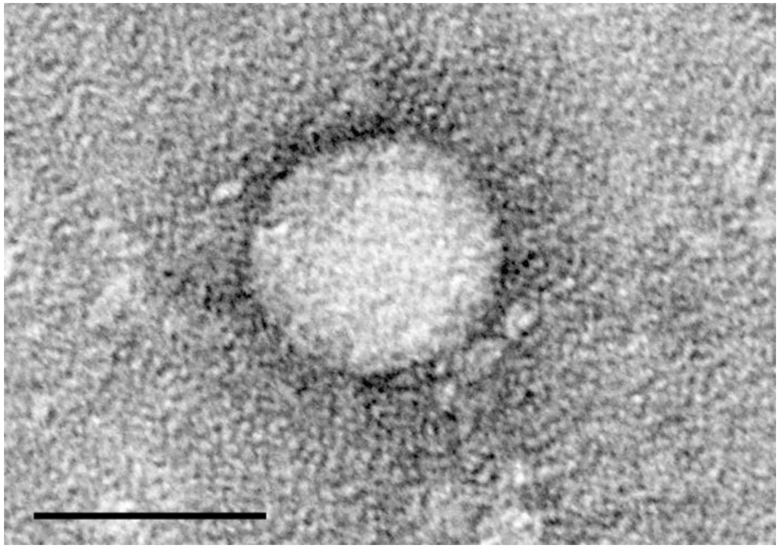
Current Uses as Biosensors

- Piezoelectric materials are used in a wide variety of detection based applications as biological transducers.

- For example:
  - Detection of cancer
    - Detecting specific cancer biomarkers
  - Determining drug effectiveness
  - DNA hybridization detection
    - Comparing DNA strands
  - Detection of the hepatitis C virus

Hepatitis C Virus

- Hepatitis C is an infectious disease which affects mainly the liver and is caused by the Hepatitis C Virus
- HCV is a virus that is usually spread through blood to blood contact
- HCV is a small, enveloped, single-stranded, positive-sense RNA virus.



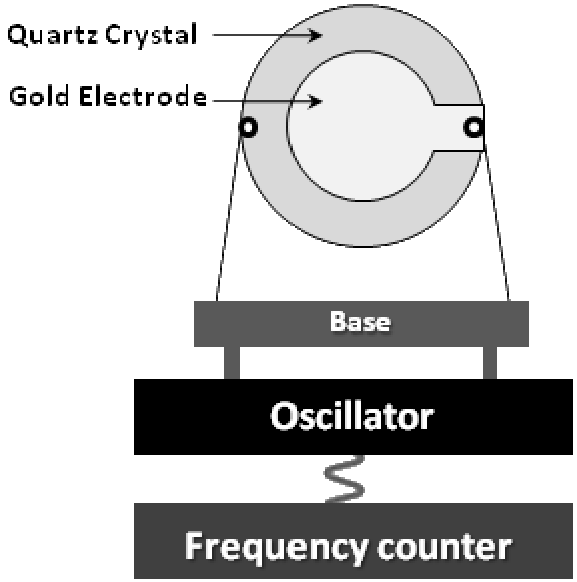
Detection of the Hepatitis C Virus

- Preparation and Immobilization:

  - Gold electrodes are first coated in a monolayer of cystamine
  - AT-cut quartz crystals are then cleaned with acetone and incubated with cystamine
  - Oligonucletide probes which act as the receptor for the hepatitis C virus are activated using a glutaraldehyde solution
  - Oligonucleotide probes are finally immobilized and attached to the gold electrodes using either avidin or streptavidin
  - The gold electrodes are then attached to the AT-cut quartz crystal plate

Detection of the Hepatitis C Virus

- The piezoelectric crystal is connected to an oscillator which applies a voltage across it and a frequency counter which monitors the frequency.



Detection of the Hepatitis C Virus

- Detection:

  - The modified piezoelectric crystal is placed in the flow through cell
  - Serum from patients with HCV was then put through the flow through cell
  - Strands of the HCV attached to the oligonucletide probes
  - This binding results in a change of the mass of the crystal
  - Finally this can be observed as a negative change in frequency of the crystal, corresponding to the Sauerbrey equation

Detection of the Hepatitis C Virus

- Flow through Cell

Detection of the Hepatitis C Virus

- Results from a previously used method of detection (Amplicor assay) showed that samples 1-9 were HCV positive and samples 21-25 were HCV negative

- The following table shows that the piezoelectric biosensor was able to detect the HCV virus in samples 1-9 and even some of samples 21-25 by detecting a negative change in frequency of at least 10Hz

Table 3
Specific response (change of frequency Δf_2 in Hz) of PCR products (25× diluted) obtained using piezosensors (smooth and rough surfaces) modified with different oligonucleotide probes

Sample no.	Probe immobilized/on surface					
	HCV 1 avidin/smooth	HCV 2A/C avidin/smooth	HCV 2B avidin/smooth	HCV 2B streptavidin/smooth	HCV 3 avidin/smooth	HCV 3 avidin/rough
1	0	**−179**	**−31**	nd	**−97**	nd
2	**−70**	**−45**	−8.2	16	**−31**	12
3	0	11	15	**−17**	13	**−48**
4	15	7	**−39**	3	37	**−22**
5	0	25	**−228**	−2.3	12	**−16**
6	**−17**	**−12**	37	**−39**	**−14**	6.3
7	22	3	19	**−36**	**−58**	9.2
8	**−17**	22	111	**−42**	**−12**	**−48**
9	**−27**	63	33	8.3	**−27**	**−22**
21	56	5	102	nd	27	**−13**
22	31	126	**−53**	**−49**	**−48**	**−24**
23	0	81	**−80**	**−72**	0	9.5
24	0	5	0	−8.4	38	16
25	0	43	0	16	**−27**	6

nd: not determined. Values indicating positive response (signal below −10 Hz) are in boldface. The response was calculated as a difference between frequencies obtained before and after interaction of the sensing surface with individual samples.

HCV 1	Biotin-COC TCA ATG CCT GGA GAT
HCV2A/C	Biotin-CAC TCT ATG CCC GGC CAT
HCV2B	Biotin-CAC TCT ATG TCC GGT CAT
HCV3	Biotin-CGC TCA ATA CCC AGA AAT

Piezoelectric Biosensors

- These results show that piezoelectric biosensors are very sensitive to mass changes and due to this are more reliable in comparison to alternative biosensors such as the Amplicor assay.
- Piezoelectric biosensors are extremely sensitive, much faster then alternatives such as the Amplicor assay and can be as specific as the coating applied to them.

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