PIEZOELECTRIC BIOSENSORS

Greek *piezo* means to squeeze or press.

A material that generates an electric charge when mechanically deformed. Conversely, when an external electric field is applied to piezoelectric materials they mechanically deform.

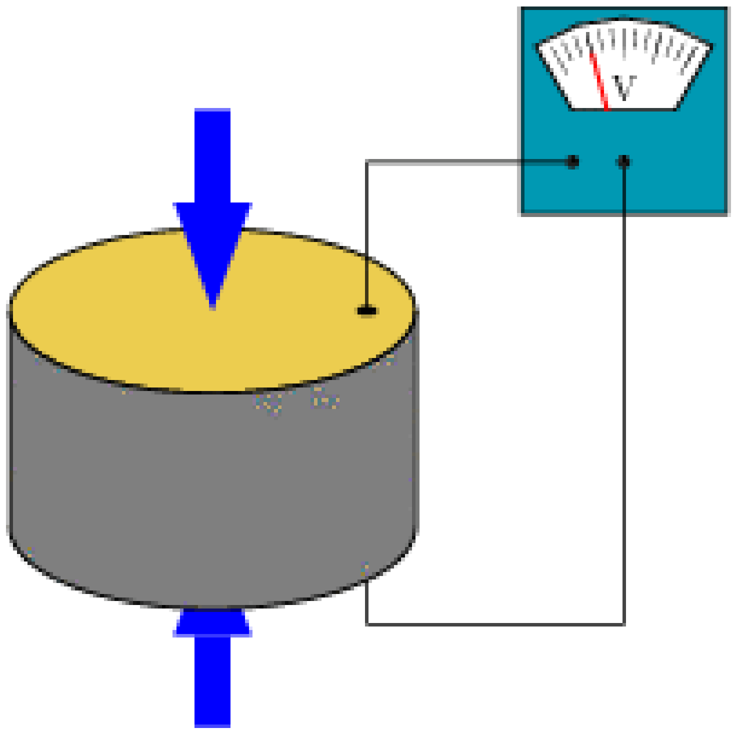


Fig. A piezoelectric disk generates a voltage when deformed

The piezoelectric effect is used to measure changes in pressure, acceleration, temperature, strain, or force by converting them to an electrical charge.

Many materials, both natural and man-made, exhibit piezoelectricity

Example:

Naturally-occurring crystals: berlinite ($AlPO_4$, structurally identical to quartz), cane sugar, quartz, Rochelle salt, topaz, Dry bone, Tendon, Silk , Wood, Enamel etc.

Man-made crystals: gallium orthophosphate ($GaPO_4$), Langasite ($La_3Ga_5SiO_{14}$), Man-made ceramics, Polyvinylidene fluoride

Mechanism:

The piezoelectric effect is closely related to the occurrence of electric dipole moments (P) in solids.

The P may either be induced for ions on crystal lattice sites with **asymmetric charge** surroundings or may directly be carried by molecular groups (as in cane sugar).

Dipole moment can be defined as the product of magnitude of charge and the distance of separation between the charges (C.m).
In the simple case of two point charges, one with charge +*q* and one with charge −*q*, the ***electric dipole moment*** **p** is:

$$P = qd$$

Where **d** is the *displacement vector* pointing from the negative charge to the positive charge.

The dipole moment of an array of charges, $$\mathbf{p} = \sum_{i=1}^{N} q_i \mathbf{d_i} \ ,$$

Piezoelectricity is caused by dipole density [Cm/m^3]) (Cm is coulomb-meter) in the bulk.

Piezoelectric materials also show the opposite effect, called **converse piezoelectric effect**, where the application of an electrical field creates mechanical deformation in the crystal.

Thus an anisotropic crystals (crystals without a center of symmetry) can generate an electric dipole when mechanically squeezed.
The effect can also work in an opposite way in that an anisotropic crystal deformed (oscillate) when voltage is applied on it.

Analyte can be determined from the electricity produced on the crystal surface through interaction with either crystal alone or electrode.

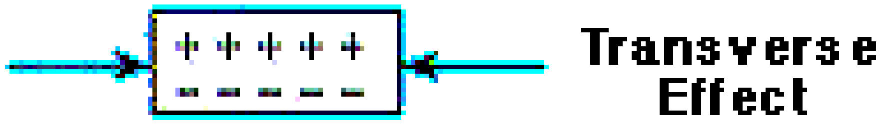
Principle of operation

The way a piezoelectric material is cut produces three main operational modes:

(a)Transverse effect: A force applied along a neutral axis (y) displaces charges along the (x) direction, perpendicular to the line of force. The amount of charge (C_x) depends on the geometrical dimensions of the respective piezoelectric element. When dimensions a , b , c apply,

$$C_x = d_{xy} F_y b / a$$

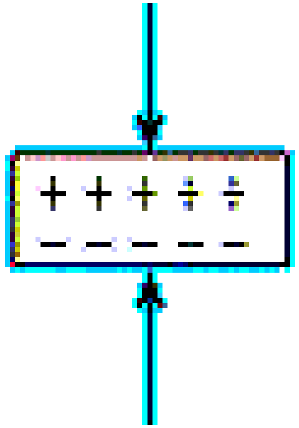
where a is the dimension in line with the neutral axis, b is in line with the charge generating axis and d is the corresponding piezoelectric coefficient.



(b) Longitudinal effect: The amount of charge displaced is strictly proportional to the applied force and independent of the piezoelectric element size and shape. Putting several elements mechanically in series and electrically in parallel is the only way to increase the charge output. The resulting charge is

$$C_x = d_{xx} F_x n$$

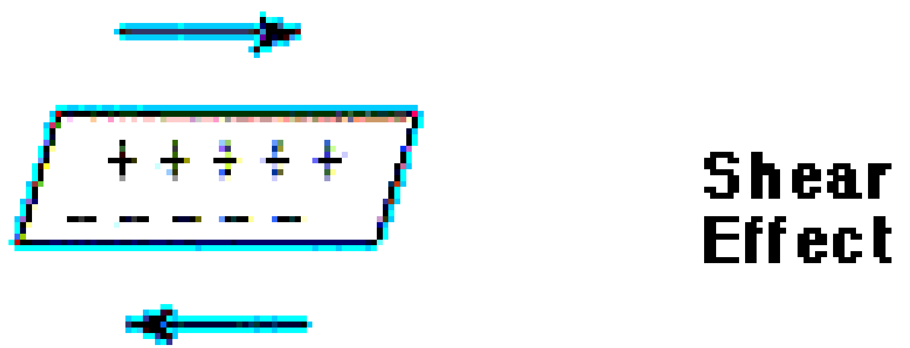
where d_{xx} is the piezoelectric coefficient for a charge in x-direction released by forces applied along x-direction. F_x is the applied Force in x-direction and n corresponds to the number of stacked elements



Longitudinal Effect

(c) Shear effect: The charges produced are strictly proportional to the applied forces and independent of the element size and shape. For n elements mechanically in series and electrically in parallel the charge is

$$C_x = 2\, d_{xx}\, F_x\, n$$



In contrast to the longitudinal and shear effects, the transverse effect makes it possible to fine-tune sensitivity on the applied force and element dimension.

The bound mass on the crystal surface causes slowing of oscillation.
For the common quartz crystals, the frequency shift (Δf) is directly proportional to the change of mass (Δm) on the crystal, as described by **Sauerbrey:**

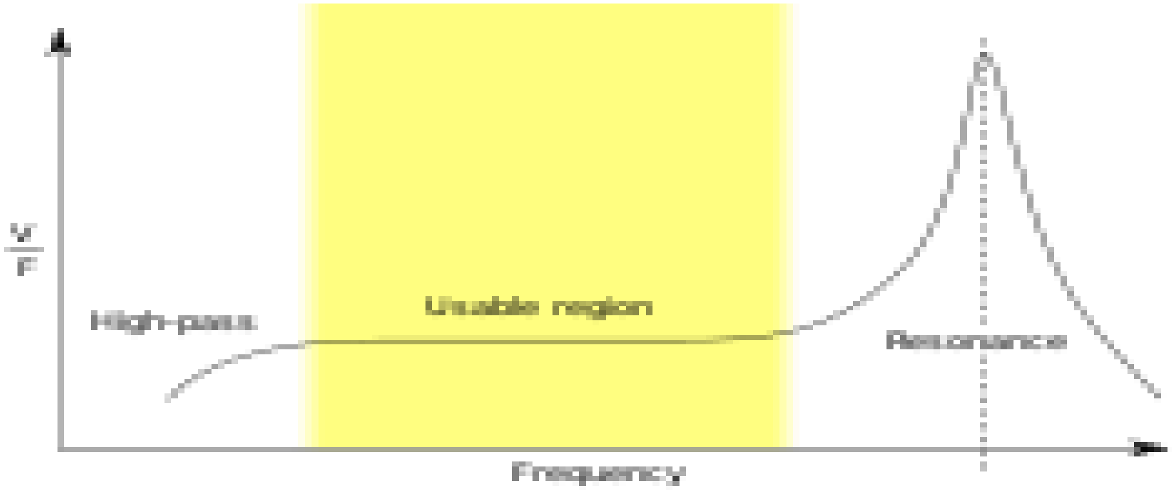
$$\Delta f = \frac{-2 f_0^2 \Delta m}{A \sqrt{(\rho_q \mu_q)}} = -2.3 \times 10^6 \ f_0^2 \frac{\Delta m}{A}$$

f_0 is the fundamental mode of the crystal oscillation (in hertz),
A is the piezoelectrically active area (in centimeters),
ρ_q means density (2.648 g/cm^3), and
μ_q means shear modulus (2.947 × 1011 g/cm·s^2) of quartz.

The Sauerbrey equation is reliable for calculating frequency shift when the ambient environment is not unaltered.
Upon a change in the surrounding environment, since viscosity has an impact on frequency shift, the equation described by **Kanazawa** and coworkers for quartz crystal should be consulted.

$$\Delta f = f_0^{3/2} \sqrt{\frac{\Delta(\rho_l \eta_l)}{\pi \rho_q \eta_q}}$$

The equation states that frequency shift is proportional to an increase of ambient viscosity η *(*the symbols with index *l* relate to the ambient liquid and *q* to quartz crystal).



Frequency response of a piezoelectric sensor;
output voltage vs applied force

Piezoelectric biosensors can be of two different types:

- Bulk acoustic wave (BAW) and Surface acoustic wave (SAW) piezoelectric sensors.
- In BAW the wave propagates through the interior of the substrate.
- In SAW the wave propagates on the surface of the substrate.

These sensors apply an electric field that creates mechanical stress (wave), which moves through/on the substrate, and in the last step, is converted back to an electric field before we can measure it.

As the wave propagates through/on the surface of the substrate, its velocity continually changes (as kown by measuring the change in the frequency). This can be related to the physical mass being measured.

A **quartz crystal microbalance (QCM)** is one of the simplest BAW devices.

- This piezoelectric technique is known for its excellent sensitivity, and hence it has wide applications in the medical, aeronautical, and telecommunications, fields.
- These are suitable for label-free and real-time biosensing.
- **They can attained detection limits to the pico level and hence are suitable to measure various gases such as ammonia, hydrogen, methane, and carbon monoxide.**
- These sensors have good compatibility with integrated circuits (IC) technology and can be easily manufactured by photolithography, which renders them inexpensive.

Example: A rapid method for the diagnosis of tuberculosis and other infections caused by mycobacteria

Almost all current methods of diagnosing TB have drawbacks:

- They TB [skin test (TST) and TB blood test] stend to be either nonspecific or too time-consuming.
- In most cases of pulmonary and extrapulmonary TB, diagnosis depends upon culturing the mycobacterial organism, a process requiring 4-8 weeks.
- some of them do not have the high specificity or sensitivity required for proper diagnosis

Materials and fabrication:

•Construction of antibody-based piezoelectric crystals capable of detecting mycobacterial (*M. tuberculosis*) antigens.

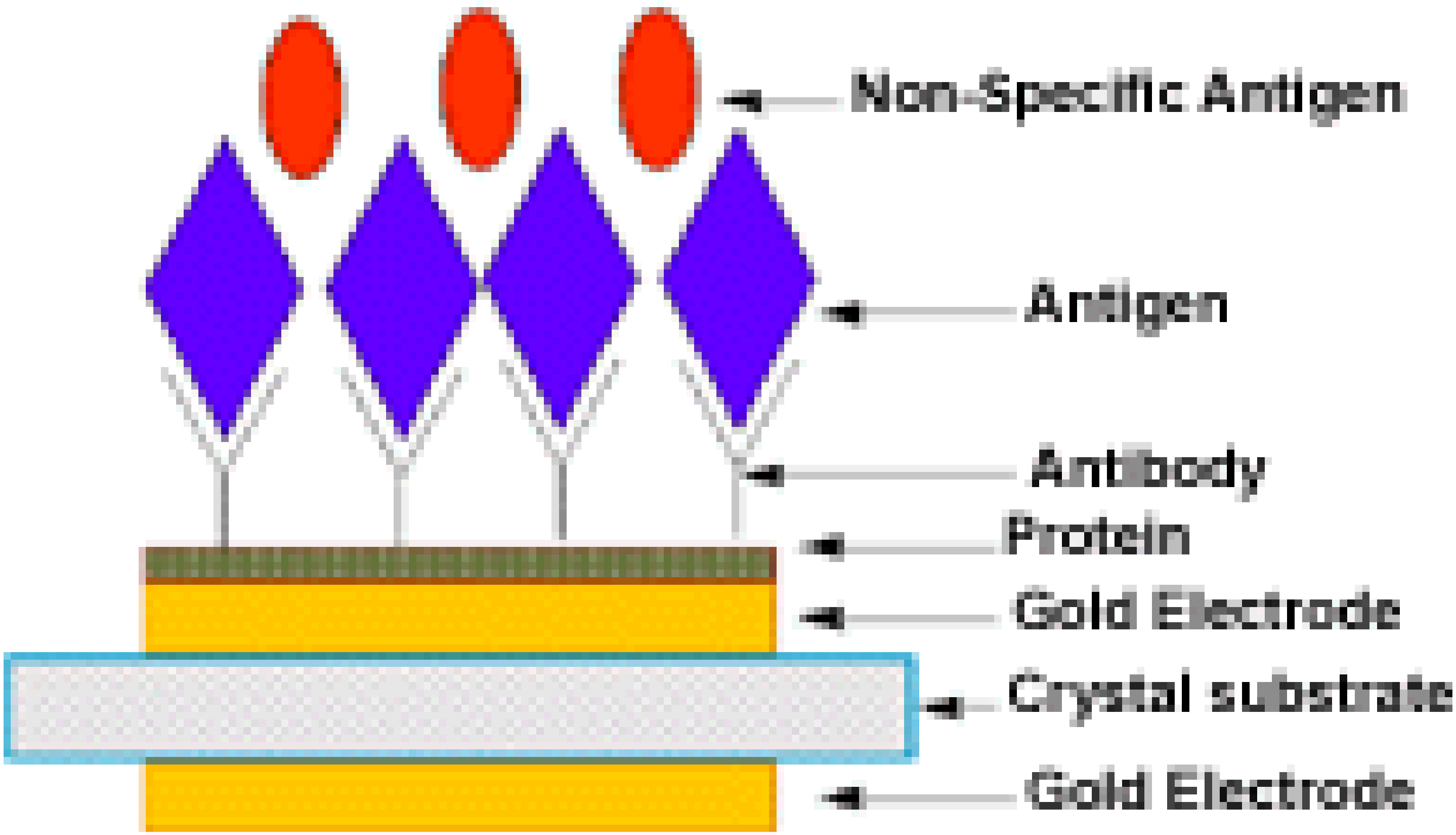
•The antigen here is a secretory protein and potent T cell antigen.

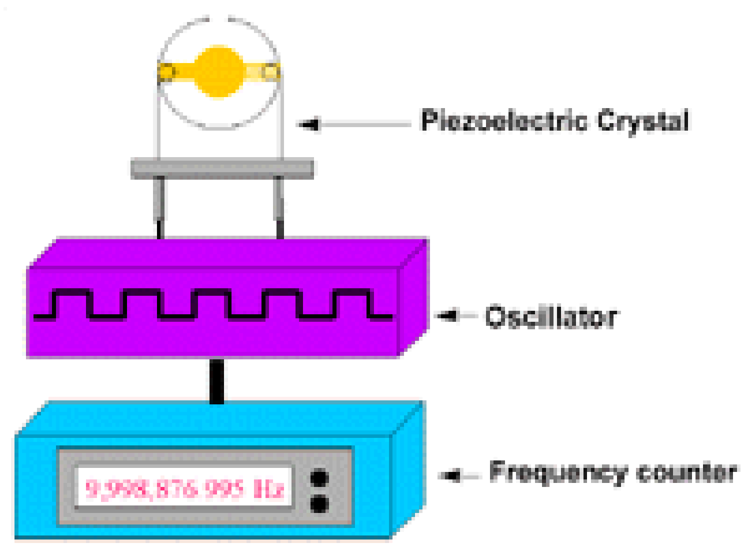
•Detector crystal is alpha quartz crystals.
•These crystals are insoluble in water and resistant to high temperatures up to 579°C with no loss of piezoelectric properties.
•The crystals were 10 MHz AT-cut quartz crystals with an electrode coating deposited on each side using sputtering method.

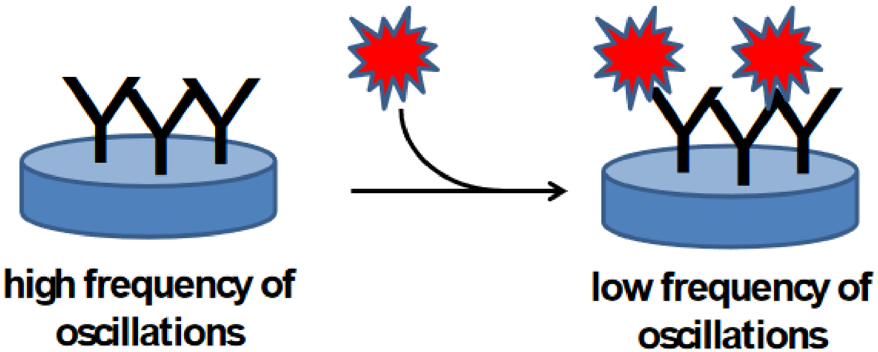
•The optimum thickness of the gold electrode layer was estimated at 1,000 Angstroms.
•The crystal was mounted on a holder with stainless steel with leads.

•A silver composite was used to connect the electrode to wire.
•The crystals were 14 mm in diameter, and the electrodes on both sides of the crystal were 8 mm in diameter.

Experimental apparatus for the piezoelectric sensor







Sensitivity : 10^5 CFU ml^{-1}

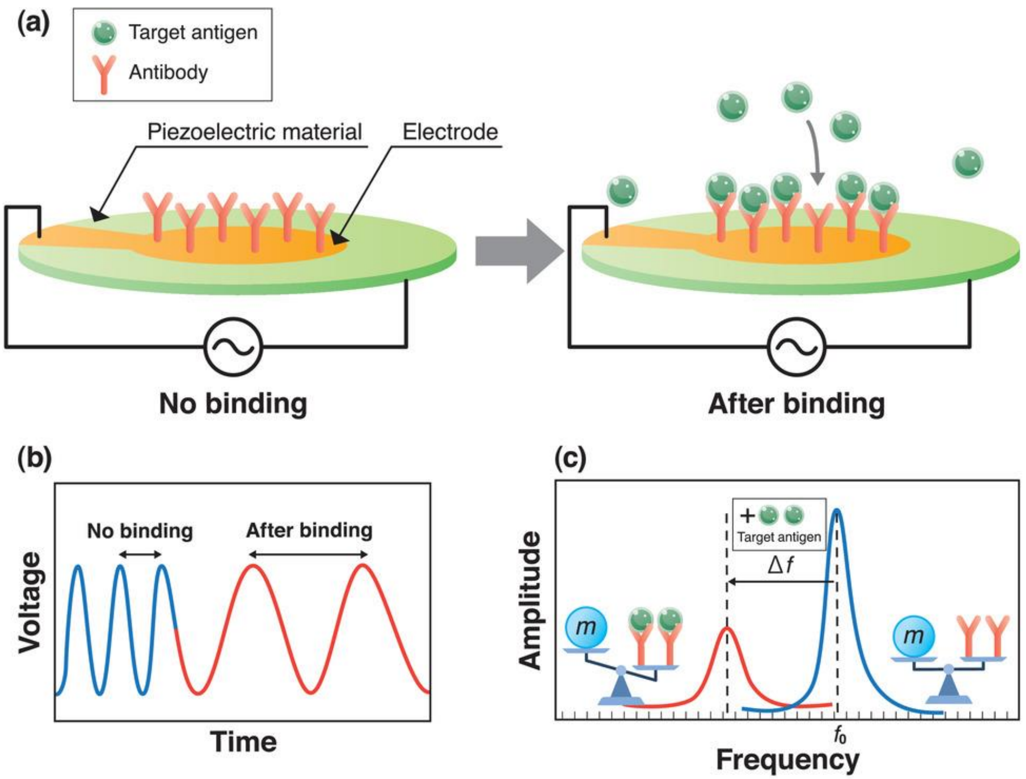
Advantages: fast, reusable, label-free, requires minimal sample preparation and is easily operated.

Disadvantage: density, temperature, viscosity and electrical conductivity of the sample may affect the results and require calibration correction

Srivastava et al. RSC Adv., 2016,6, 17759-17771

- The crystal is driven by a low-frequency transistor oscillator (1-30 V power supply) and set at 9 V.
- The frequency of the vibrating crystal was monitored by a frequency counter.
- The crystal electrodes were first modified with a coating of **protein A for better adhesion of the antibodies** to the surface of the transducer.
- Protein A is a polypeptide isolated from *Staphylococcus aureus* that binds specifically to the IgG antibodies, without interacting at the antigen site.
- This property permits the formation of tertiary complexes consisting of protein A, antibody, and antigen.
- After each step in the coating process-first with the metal depositions and then with the biomolecular analytes-the frequency reading was recorded.
- The crystals were methodically dried and following each step the frequency of the crystal was recorded.
- The difference in frequency change between the control and experimental crystals were compared.

Example: Piezoelectric biosensors for COVID-19 and Other Viruses



Basic concept of virus detection using piezoelectric material. a) Operation principle of a piezoelectric biosensor; b,c) schematics of voltage to time (b) and amplitude to frequency (c) during detection.

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THANKS