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A Review on Biosensors and Recent Development of Nanostructured Materials-Enabled Biosensors

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مراجعة حول المستشعرات الحيوية والتطورات الحديثة في المستشعرات الحيوية المعتمدة على المواد نانوية الهيكل

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Abstract:
A biosensor is an integrated receptor-transducer device that converts a biological response into an electrical signal. The design and development of biosensors have gained significant attention from researchers and scientists in recent decades due to their wide range of applications, including healthcare, disease diagnosis, environmental monitoring, water and food quality assessment, and drug delivery. Sensing technology utilizing nanomaterials, ranging from zero- to three-dimensional structures, offers advantages such as a high surface-to-volume ratio, excellent conductivity, shock-bearing capabilities, and color tenability. Nanomaterials (NMs) employed in the fabrication of Nano biosensors include nanoparticles (NPs), known for high stability and carrier capacity; nanowires (NWs) and Nano rods (NRs), capable of high detection sensitivity; carbon nanotubes (CNTs), offering large surface areas and high electrical and thermal conductivity; and quantum dots (QDs), providing color tenability. Furthermore, these nanomaterials can function as transduction elements. This review summarizes the evolution of biosensors, their classification based on receptors and transducers, and modern approaches utilizing nanomaterials such as noble metal and metal oxide NPs, NWs, NRs, CNTs, QDs, and dendrimers. Recent advancements in bio sensing technology facilitated by the expansion of nanotechnology are also discussed.

Keywords: Biosensors, Nanomaterials, Nano bio sensing, Gold Nanoparticles, Carbon Nanotubes, Quantum Dots.

الملخص
المستشعر الحيوي هو جهاز متكامل يجمع بين "المستقبل والمحول(receptor-transducer) "، يعمل على تحويل الاستجابة البيولوجية إلى إشارة كهربائية. وقد حظي تصميم وتطوير المستشعرات الحيوية باهتمام كبير من الباحثين والعلماء في العقود الأخيرة نظراً لنطاق تطبيقاتها الواسع، بما في ذلك الرعاية الصحية، وتشخيص الأمراض، والمراقبة البيئية، وتقييم جودة المياه والغذاء، وإيصال الأدوية. توفر تقنية الاستشعار التي تستخدم المواد النانوية (بدءاً من الهياكل صفرية الأبعاد وصولاً إلى ثلاثية الأبعاد) مزايا عديدة، مثل النسبة العالية للسطح إلى الحجم، والموصلية الممتازة، والقدرة على تحمل الصدمات، وقابلية ضبط الألوان. تشمل المواد النانوية (NMs) المستخدمة في تصنيع المستشعرات الحيوية النانوية كلاً من: الجسيمات النانوية (NPs) المعروفة باستقرارها العالي وقدرتها التحميلية الكبيرة، والأسلاك النانوية (NWs)والقضبان النانوية (NRs) القادرة على تحقيق حساسية كشف عالية، وأنابيب الكربون النانوية (CNTs) التي توفر مساحات سطحية شاسعة وموصلية كهربائية وحرارية عالية، والنقاط الكمومية (QDs) التي توفر خاصية ضبط الألوان. علاوة على ذلك، يمكن لهذه المواد النانوية أن تعمل كعناصر تحويل للإشارة. تلخص هذه المراجعة تطور المستشعرات الحيوية، وتصنيفها بناءً على المستقبلات والمحولات، والنهج الحديثة التي تستخدم المواد النانوية مثل الجسيمات النانوية للمعادن النبيلة وأكاسيد المعادن، والأسلاك والقضبان النانوية، وأنابيب الكربون، والنقاط الكمومية،

والتشعبات (dendrimers). كما تتم مناقشة التطورات الأخيرة في تكنولوجيا الاستشعار الحيوي التي يسرتها التوسعات في مجال تكنولوجيا النانو.

الكلمات المفتاحية: المستشعرات الحيوية، المواد النانوية، الاستشعار الحيوي النانوي، جسيمات الذهب النانوية، أنابيب الكربون النانوية، النقاط الكمومية.

1. Introduction

A sensor measures changes in a physical parameter in terms of another. Human senses exhibit varying degrees of sensitivity; for instance, sweetness can be detected at concentrations as low as 0.5% sugar in water, while saltiness typically requires concentrations between 0.1% and 0.2% sodium chloride [2]. The human visual field spans a horizontal range of approximately 180 to 200 degrees and a vertical range of roughly 130 degrees. A measure of 0.5 mm is considered a precise indicator of touch sensitivity (see Figure 1(a)).

Figure 1: (a) Tongue- Eyes- Hand, and (b) A biosensor is a sensor that detects biological molecules.

A biosensor is a sensor that detects biological molecules, converting the biological response into a measurable signal, as shown in Figure 1 (b).
Biological molecules, essential to living organisms and cells, are composed of carbon, hydrogen, oxygen, nitrogen, phosphorus, and sulfur (see Figures 2 and 3). The applications of biosensors are illustrated in Figure 4.

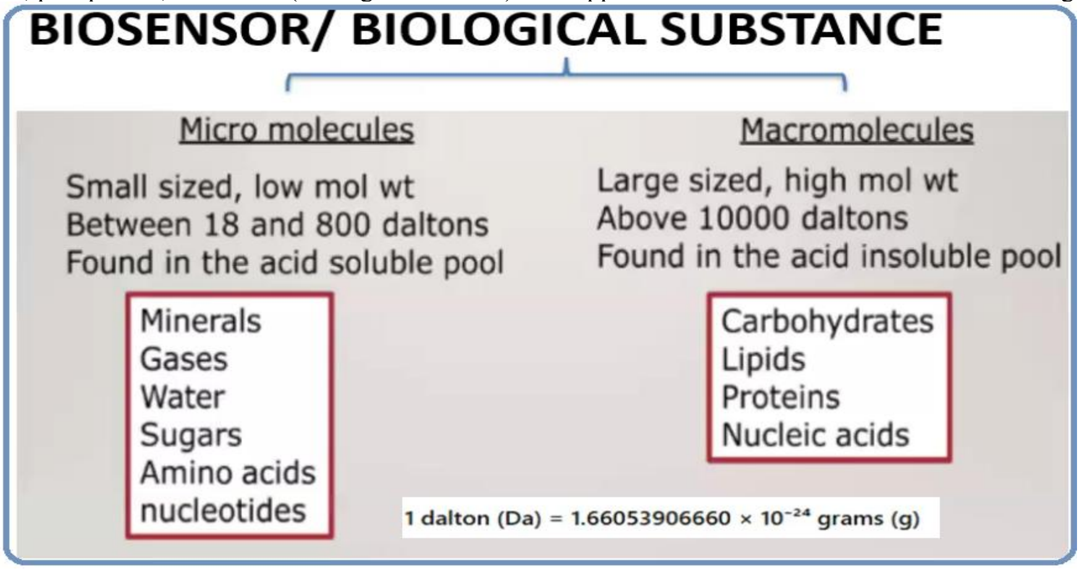

Figure 2: are organic molecules that are essential to the living organisms and cells and composed of carbon, hydrogen, oxygen, nitrogen, phosphorus and sulfur.

2. Classification of Sensors

Sensors are broadly classified into various categories depending on the physical quantity or analyte to be measured as illustrate in figure 4. These classifications include:
- **Energy Source**: Active and passive sensors.
- **Physical Contact**: Contact and non-contact sensors.
- **Comparability**: Absolute and relative sensors.
- **Signal Type**: Analog and digital sensors.
- **Signal Detection**: Physical, chemical, thermal, and biological [5,6].

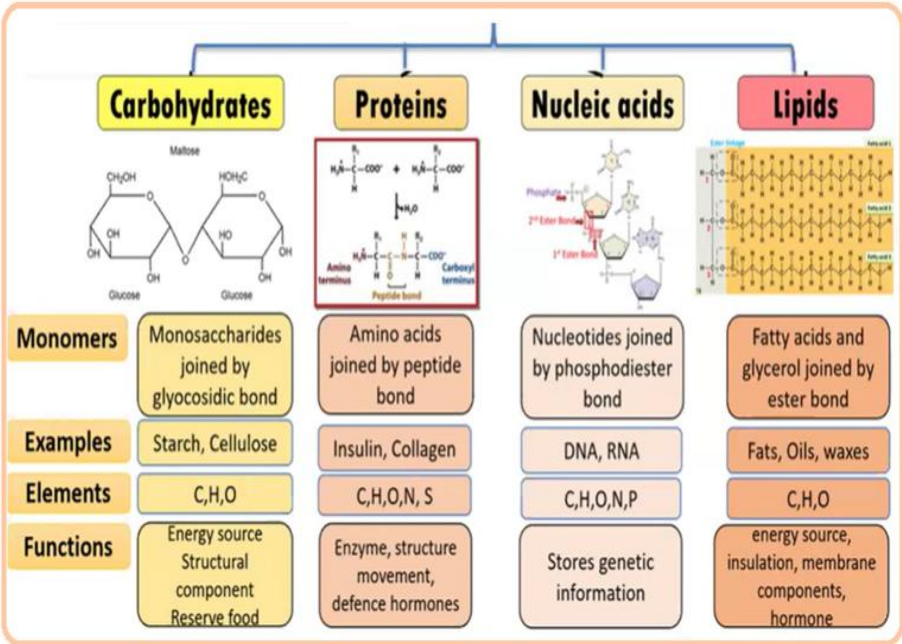

Figure 3: composed of carbon, hydrogen, oxygen, nitrogen, phosphorus and sulphur.

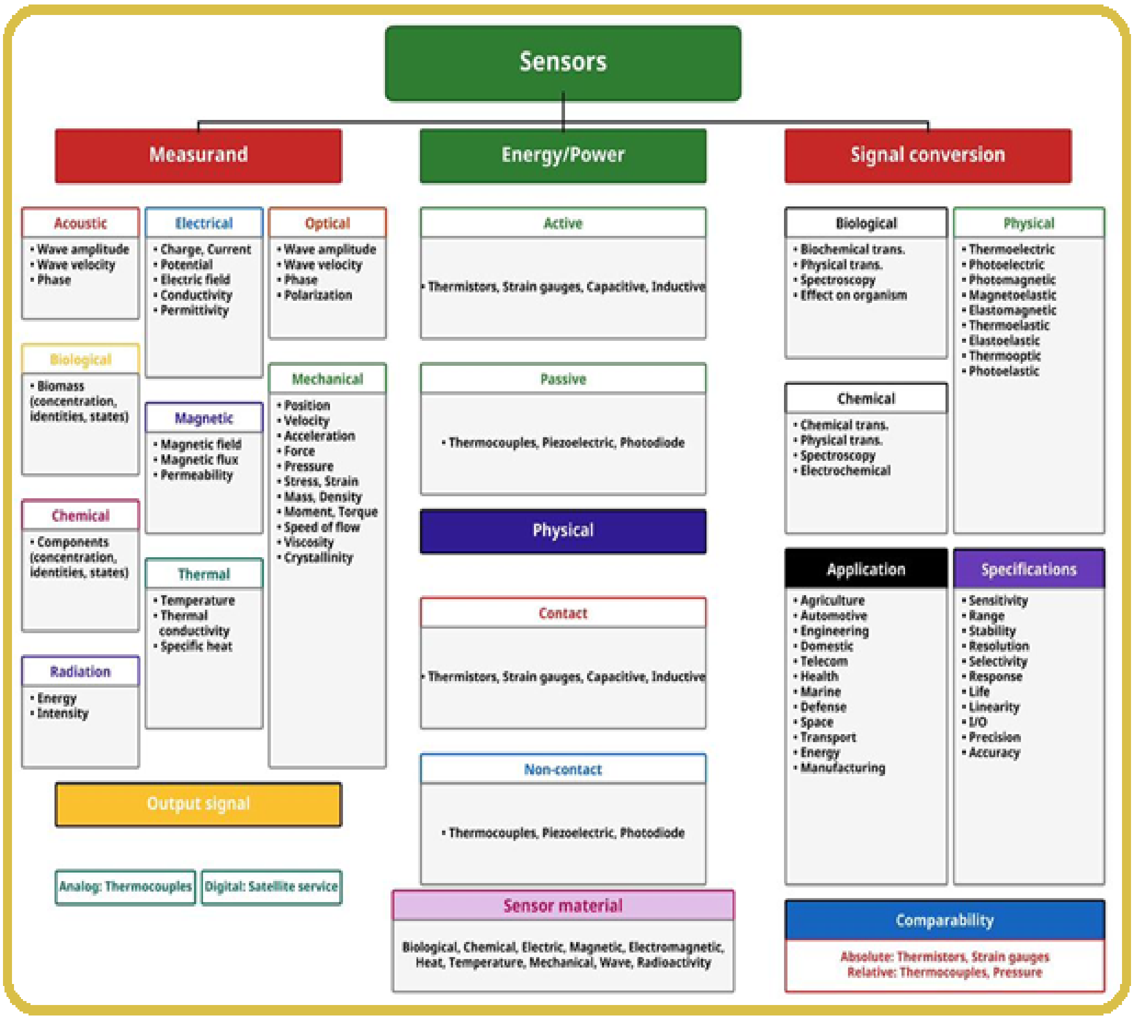

Figure 4: Classification of sensors based on measured, energy/power, physical contact, signal conversion, output signal, comparability, sensor material, specification, and applications. (reproduced from White Et al. Ref. [6]).

2.1 Biosensor, Design and Principle

A biosensor is a device or probe that integrates a biological element, such as an enzyme or antibody, with an electronic component to generate a measurable signal. The electronic component detects, records, and transmits information regarding physiological changes or the presence of chemical and biological materials. Biosensors vary in size and shape and are capable of detecting low concentrations of specific pathogens, toxic chemicals, or pH levels. A typical biosensor comprises an analyte, a bioreceptor, a transducer, electronics, and a display Figure 5. [7]

2.2 Biosensor System and Glucometer Application

The provided figure illustrates the fundamental components of a biosensor system and defines each part, culminating in an example application: the glucometer. A biosensor is an analytical device that combines a biological component with a physicochemical detector to enable the detection of a specific analyte.

2.3 Key Components of a Biosensor System

Target Analyte: This is the specific molecule that is detected by the biosensor.

Bioreceptor: This biological particle binds with the target analyte and undergoes a conformational change. This binding event is crucial for the biosensor's specificity.

Transducer: The transducer converts the bioreceptor's response from the analyte into an electric, measurable signal. This step is vital for translating biological recognition into an interpretable output.

Amplifier: The amplifier magnifies the signal manifold from the transducer, making it more noticeable and easier to analyze and interpret.

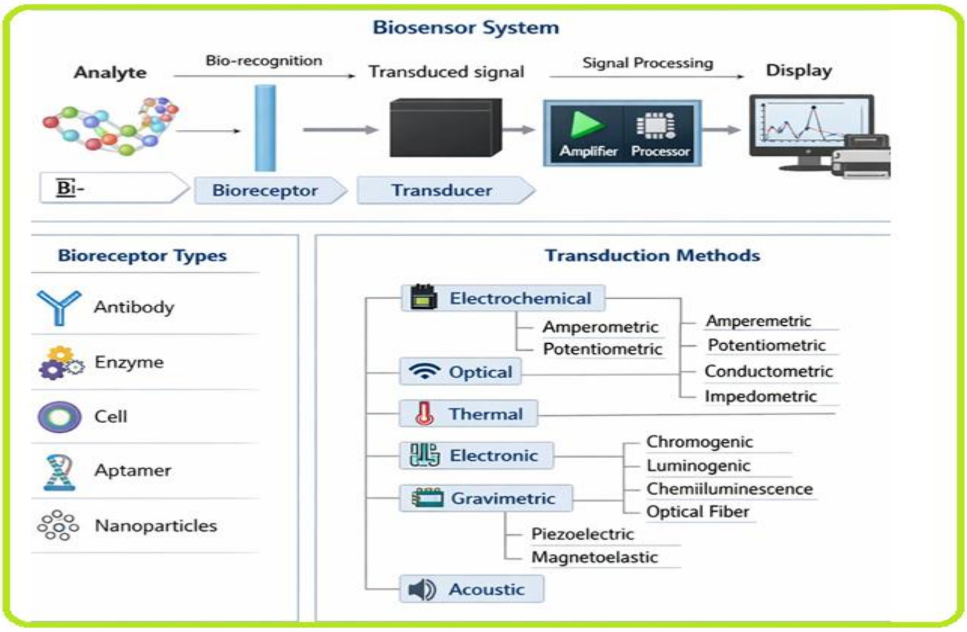

Figure 5: Schematic diagram of a typical biosensor [25].

Signal Processor: This unit filters the intensified signal and obtains the proper signal by cancelling noise, ensuring the accuracy and reliability of the measurement.

Recording and Display: This final stage visually represents the data to the users, allowing them to analyze the information and find solutions to problems.

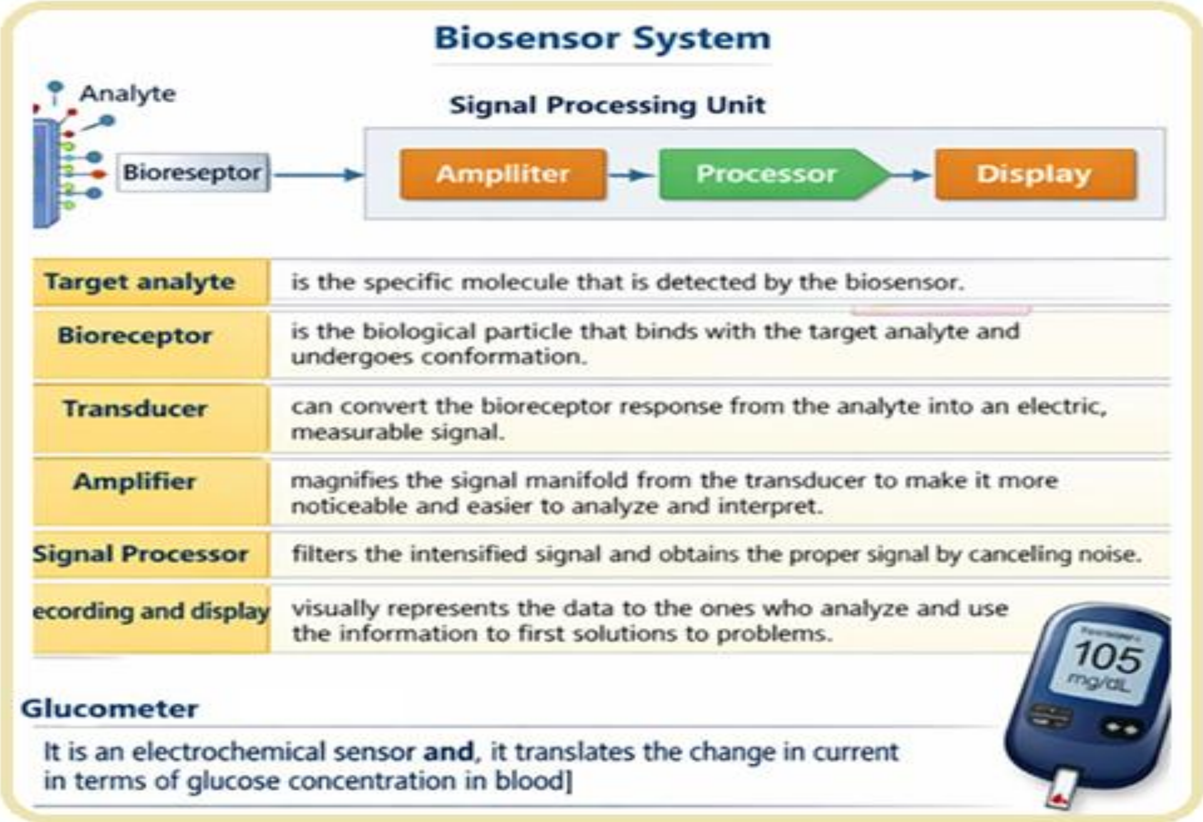

Figure 6: Biosensor system.

2.4 Application Example: Glucometer

Figure 6: Glucometer is an electrochemical sensor. It translates the change in current, resulting from the enzymatic reaction between glucose and the bioreceptor, into terms of glucose concentration in blood. This allows for rapid and accurate measurement of blood glucose levels, which is critical for diabetes management.

2.5 Detection Mechanisms

In an amperometric biosensor, a blood sample is collected on a test strip. An enzymatic reaction occurs where glucose oxidase reacts with glucose, converting it into gluconic acid and producing hydrogen peroxide. The hydrogen peroxide then reacts with a metal electrode, generating an electric current proportional to the glucose concentration. This signal is analyzed by the meter to display the blood glucose level.

- **Analyte:**

Chemical or biological or environmental elements that need to be sensed:

- **Analytes in Blood or Urine**:
  - Glucose, Cholesterol, lons, Bilirubin and Vitamins.
  - Ambient Conditions:
    - ✓ Humidity.
    - ✓ Changes in temperature and pressure Gases.

- **Natural Hazards**: Includes pesticides.
  - Environmental Pollutants: Such as carbon dioxide, methane, and various industrial, biochemical, and biological wastes.

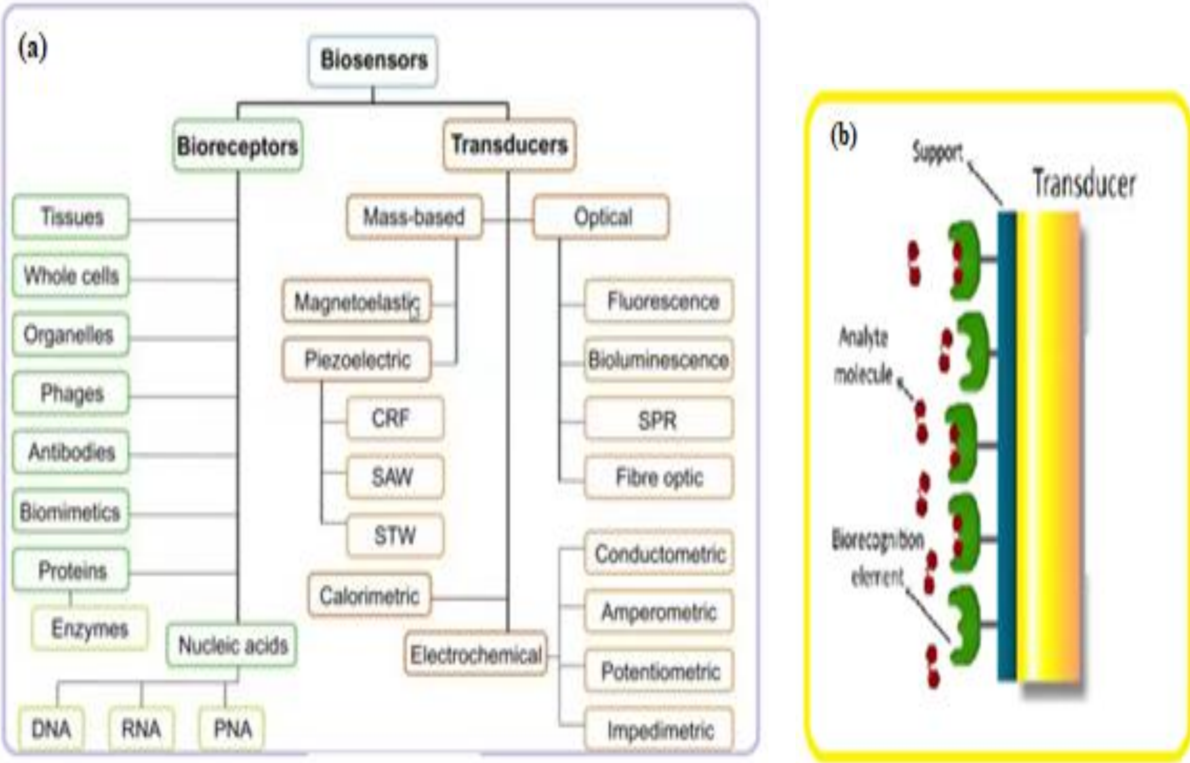

Figure 7: (a) Detection Mechanisms and (b) Bioreceptor Transducers Convert[4].

2.6 BIORECEPTOR/BRE: something which needs to be fixed on the surface of the sensor so that the analyte comes and interacts with it see figure 7(a).

2.7 Transducers Convert analyte-BRE interaction into a measurable output.

2.8 Antifouling Agent: antifouling agents are crucial for enhancing the performance and longevity of biosensors by preventing the accumulation of unwanted biological materials that can interfere with signal detection. These agents, which include polymeric coatings, biochemical agents, and natural extracts see in figure 7(b).

2.9 Obtaining a Blood Sample: collect a drop of blood, which is placed on a test strip.
2.10 Chemical Reaction: The enzyme glucose oxidase on the strip reacts with glucose, converting it into gluconic acid and producing hydrogen peroxide see in figure8.

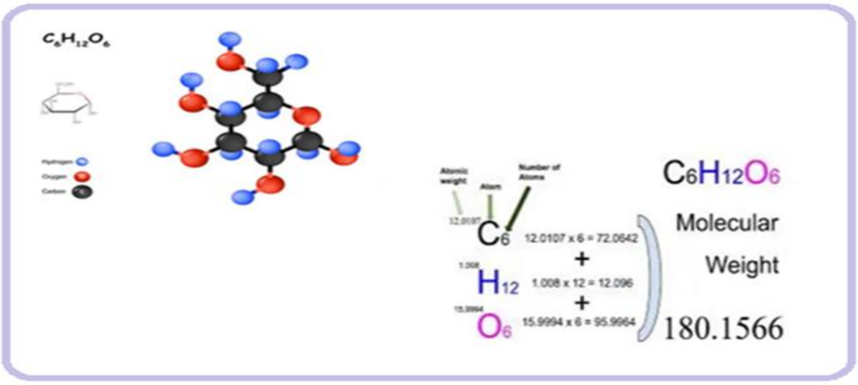

Figure 8: Moleule/Amperometric Biosensor [5]

2.11 Generating an Electrical Signal: Hydrogen peroxide reacts with the metal electrode, generating an electric current proportional to the glucose concentration.

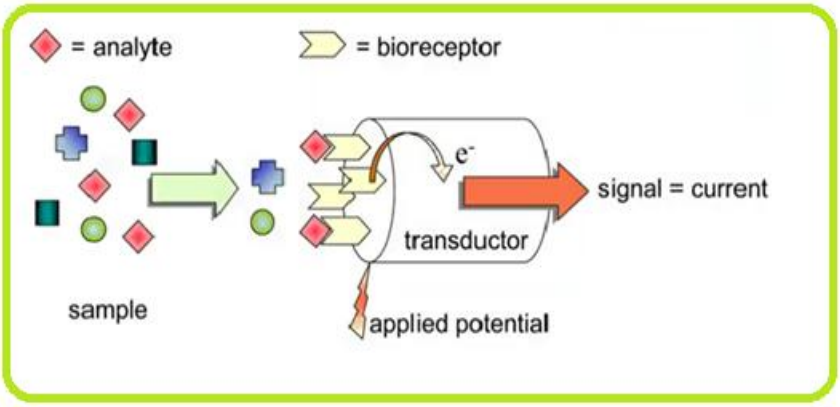

Figure 9: Bioreceptor Transducers Convert.

2.12Analysing the Signal: The glucose meter measures the current and calculates the blood glucose level, displaying it on the screen see figure 9.

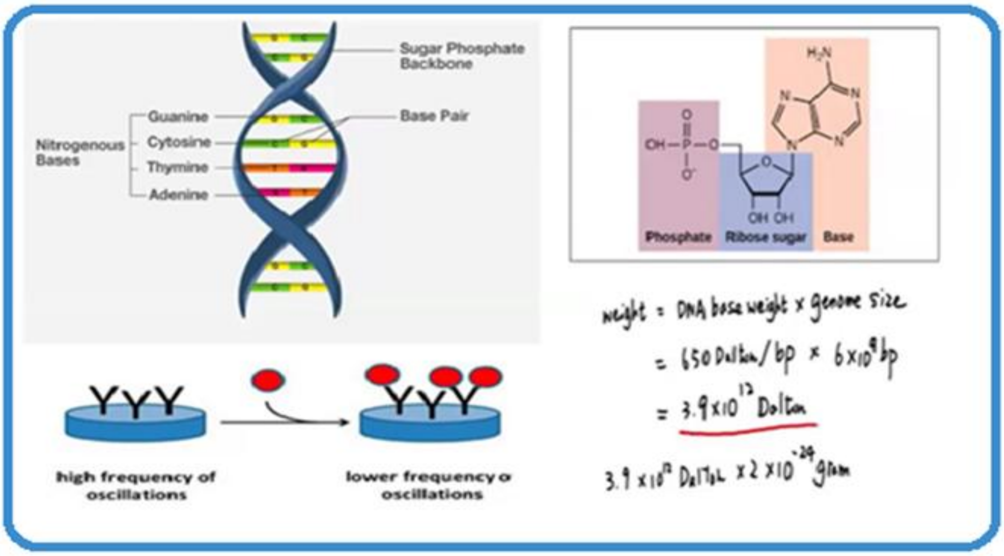

Figure 10: DNA MOLEULE/CANTILEVER BIOSENROR[4].

In figure10 Blue disc represents a piezoelectric crystal, Red ball is DNA, Y is Bioreceptor. The piezoelectric crystal vibrates at a specific frequency (its natural frequency). The change in frequency is measured by the system.

3. **Optical sensors**

devices that tedect light and convert it into measurable signals see in figure 11.

$$\mathbf{E(x,t) = Eo\ cos(kx - wt+\phi)\ \check{z}}$$

Where:

E(x,t) is the electric field at position x and time t.
Eo is the amplitude of the electric field (the maximum strength of the electric field).
k is the wave number, defined as $k = 2\pi/\lambda$ (where λ is the wavelength).
ω is the angular frequency, defined as $\omega = 2\pi f$ (where f is the frequency).
ϕ is the phase constant, indicating the initial phase of the wave.

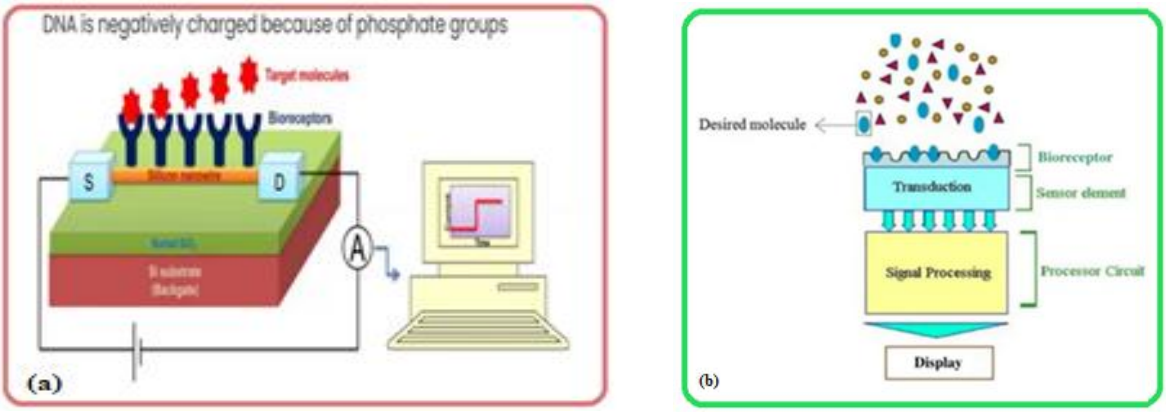

Figure 11: (a) Optical sensor and (b) measurable signals [3].

3.1 Immobilization

Immobilization refers to the process of attaching or confining biological molecules—such as enzymes, antibodies, or cells—to a solid support or substrate. This restricts their movement while maintaining their functionality. Advantages include increased stability, enhanced reusability, easier separation, controlled environment, and increased local concentration see in Figure 12.

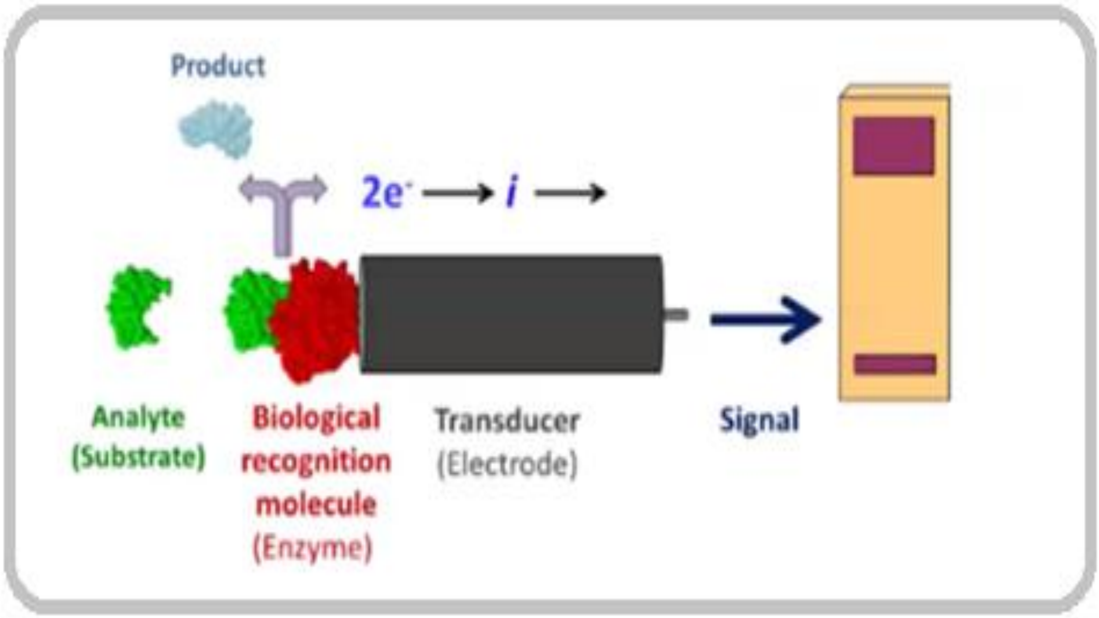

Figure 12. biosensor fabrication.

3.2 Sensor Characterization

- **Sensitivity**: Measures the change in output relative to a change in the input.
- **Selectivity**: The ability to distinguish the target analyte from other interfering substances.
- **Accuracy**: The degree of closeness between a measured value and the true standard value.
- **Limit of Detection (LOD)**: The lowest concentration of an analyte that can be reliably detected.
- **Dynamic Range**: The range between the LOD and the maximum detectable concentration.
- **Response Time**: The time required for a sensor to reach 95% of its final response.
- **Resolution**: The ability to distinguish between two closely spaced signals.
- **Repeatability**: Consistency under identical conditions.
- **Reproducibility**: Consistency under different conditions.
- **Linearity**: Direct proportional relationship between input and output.
- **Noise**: Unwanted signal fluctuations.

- **Reusability**: Ability to maintain performance over multiple uses.
- **Shelf Life**: Stability over an extended period.
- **Figure of Merit**: Ratio of sensitivity to the width of the spectral curve.
- **Increased Stability**: Stabilizes enzymes and catalysts, making them less susceptible to denaturation and degradation.
- **Enhanced Reusability**: Allows for multiple uses of the same enzyme or catalyst without significant loss of activity.
- **Easier Separation**: Facilitates the separation of the enzyme or catalyst from the reaction mixture, simplifying purification and downstream processing.
- **Controlled Reaction Environment**: Enables better control over reaction conditions (e.g., pH, temperature) due to the fixed position of the catalyst.
- **Increased Local Concentration**: Higher local concentration of active sites can enhance reaction rates under certain conditions.

4. Sensor

Sensor characterisation involves evaluating and describing the performance, sensitivity, and reliability of a sensor.

.4.1 **Sensitivity**:

- Measures how much the sensor's output changes in response to a change in the input (analyte concentration).
- A higher sensitivity means the sensor can detect smaller changes in analyte levels.

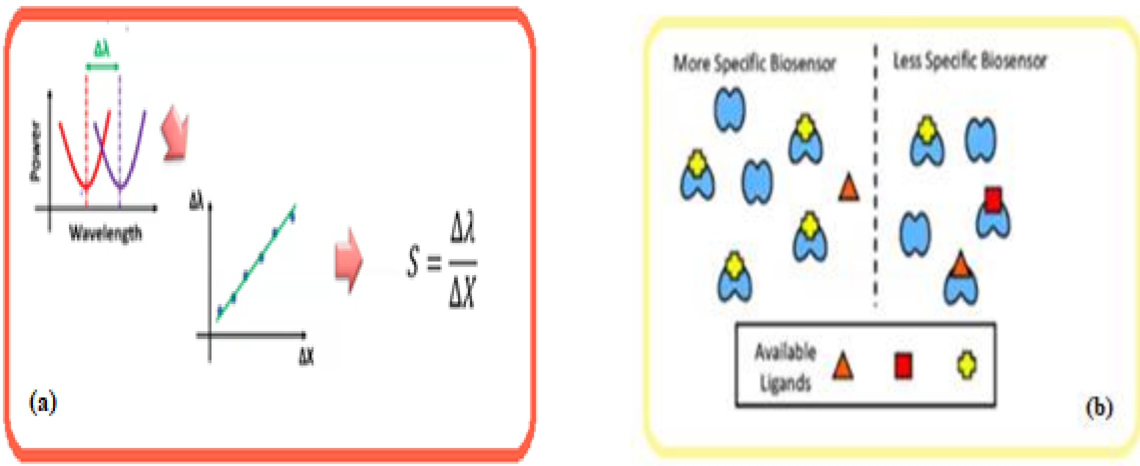

Figure 13. (a) Analyte concentration and (b) Selectivity [1] [20].

4.2 Selectivity: Measures the sensor's ability to distinguish between the target analyte and other substances (interferents) present in the sample shown figure 13(a). High selectivity is essential to avoid false readings caused by similar compounds.

4.3 Accuracy: refers to the degree of closeness of a measured value to a true or accepted standard value see figure 13(b).

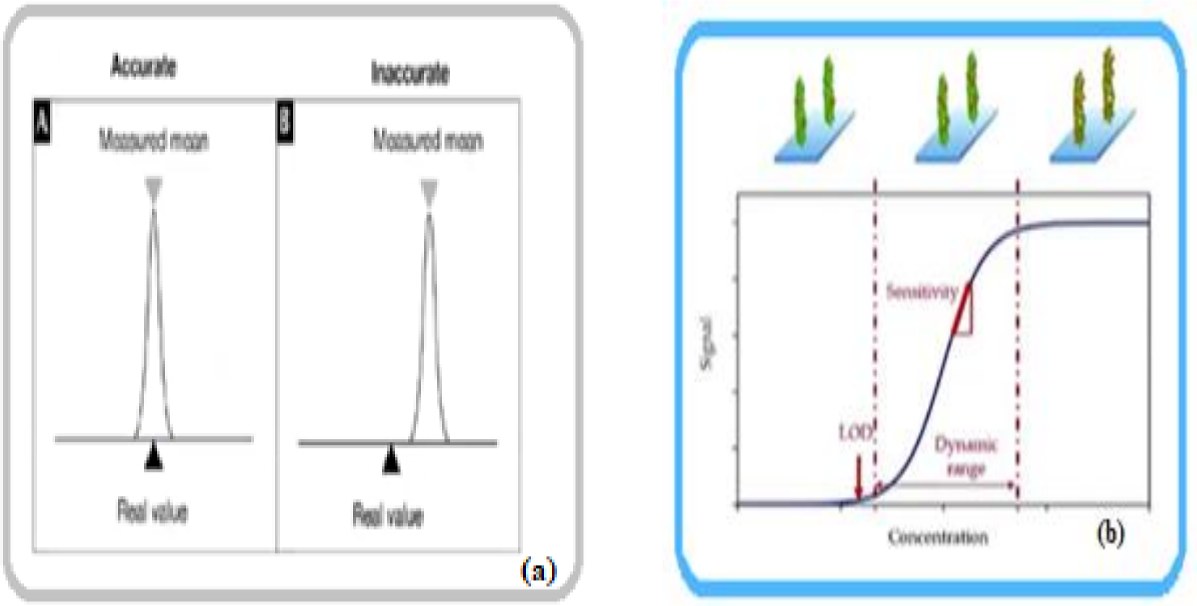

Figure 14: (a) Accuracy [and (b) Dynamic Range [4].

4.4 The Limit of Detection (LOD): is the lowest concentration of an analyte that can be reliably detected, see Figure 14 (a).
4.5 Dynamic Range: The range of input values over which the sensor can accurately measure. It is the difference between the minimum [LOD] and maximum detectable see figure 14(b) inputs.
4.6 Response Time: The time taken for the sensor to have 95% of response to a change in input, see figure 15 (a).

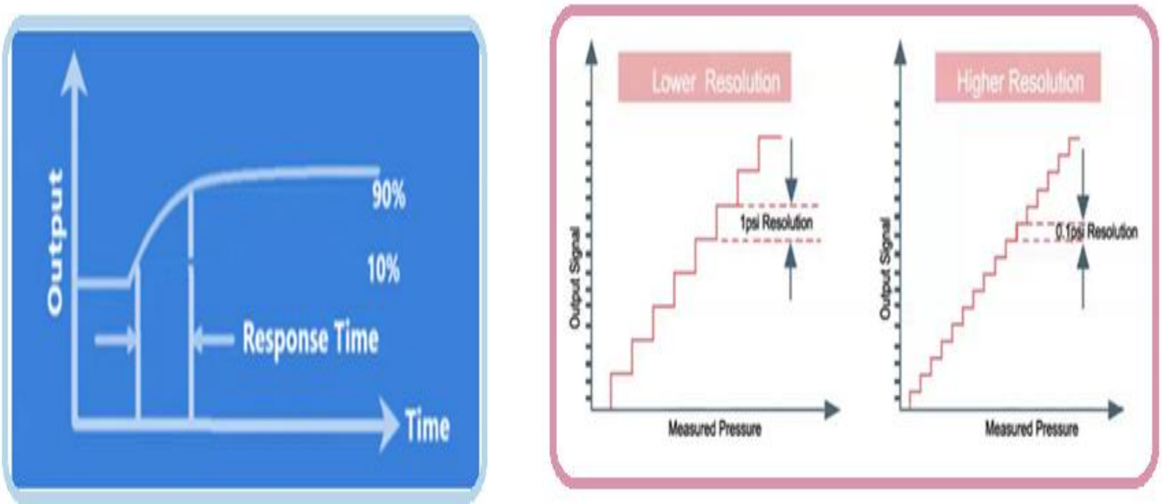

Figure 15: (a) Response Time and (b). Resolution [8].

Resolution refers to the ability of a sensor, instrument, to distinguish between two closely spaced objects or signals and to provide clear and detailed measurements see in figure 15(b).
Repeatability refers to the ability of a measurement system or instrument to produce the same results when the same measurement is repeated under identical conditions see in figure16.
4.7 **Reproducibility** refers to the ability of an experiment or measurement to yield consistent results when it is conducted under different conditions, as by different operators, using different equipment, or in different locations.

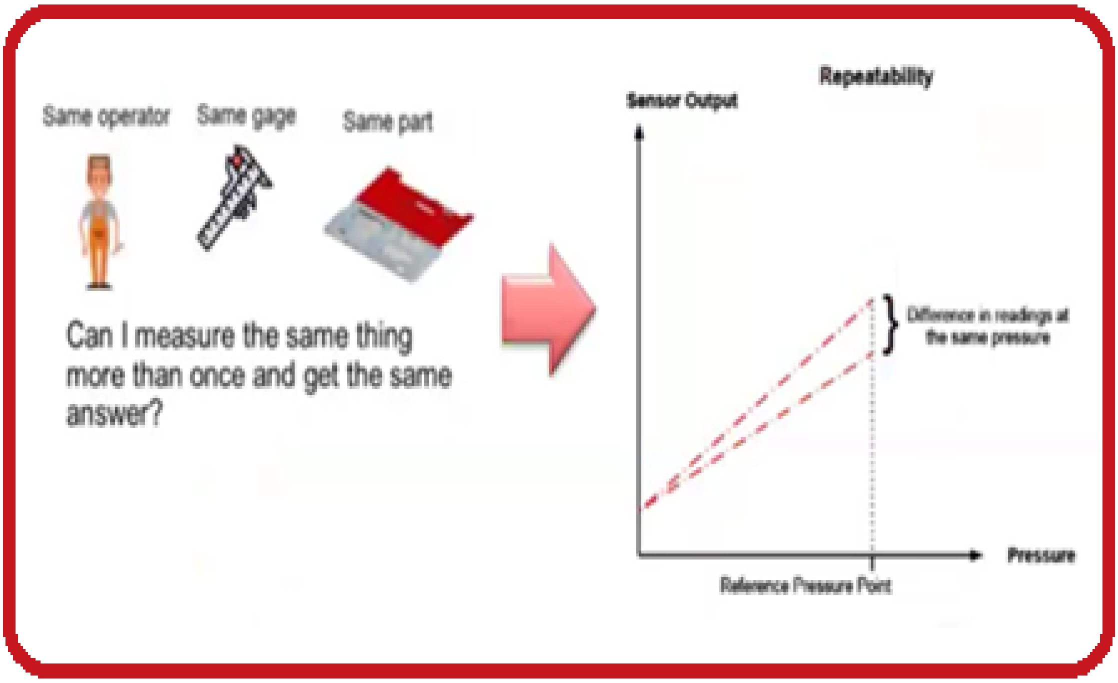

Figure 16: Repeatability [19].

4.8 **Linearity**: A linear sensor will have a direct proportional relationship between input and output see in figure17.

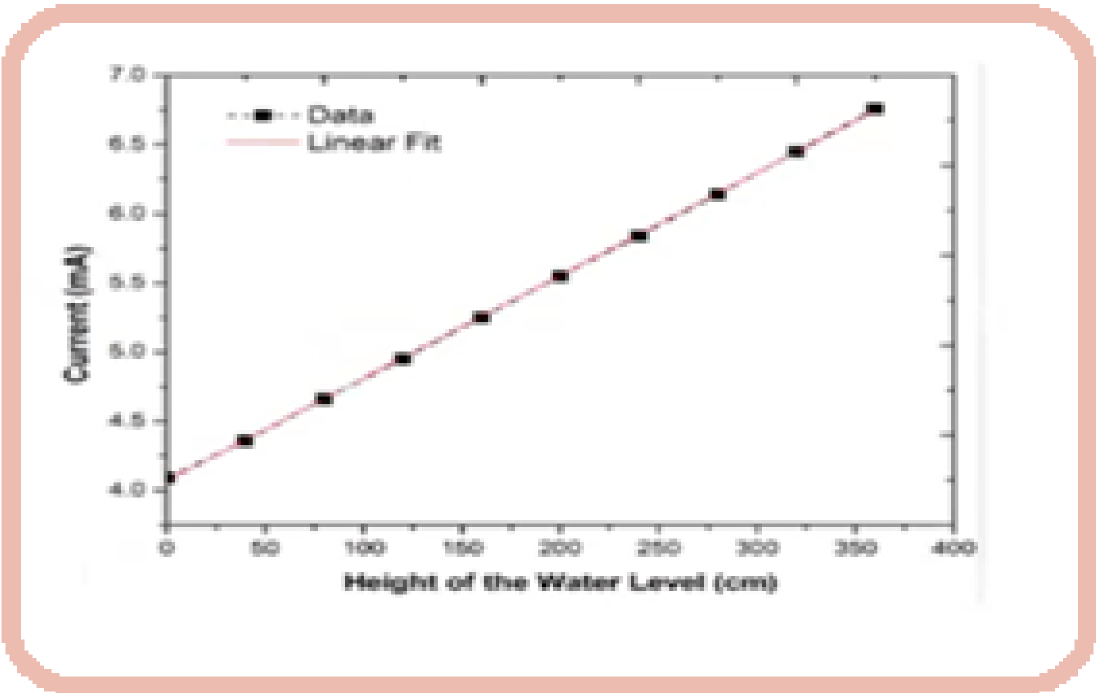

Figure 17: Linearity [11].

4.9 **Noise**: in sensor characterization refers to unwanted signals or fluctuations that can obscure or distort the true measurement of the sensor's output see in figure 18.

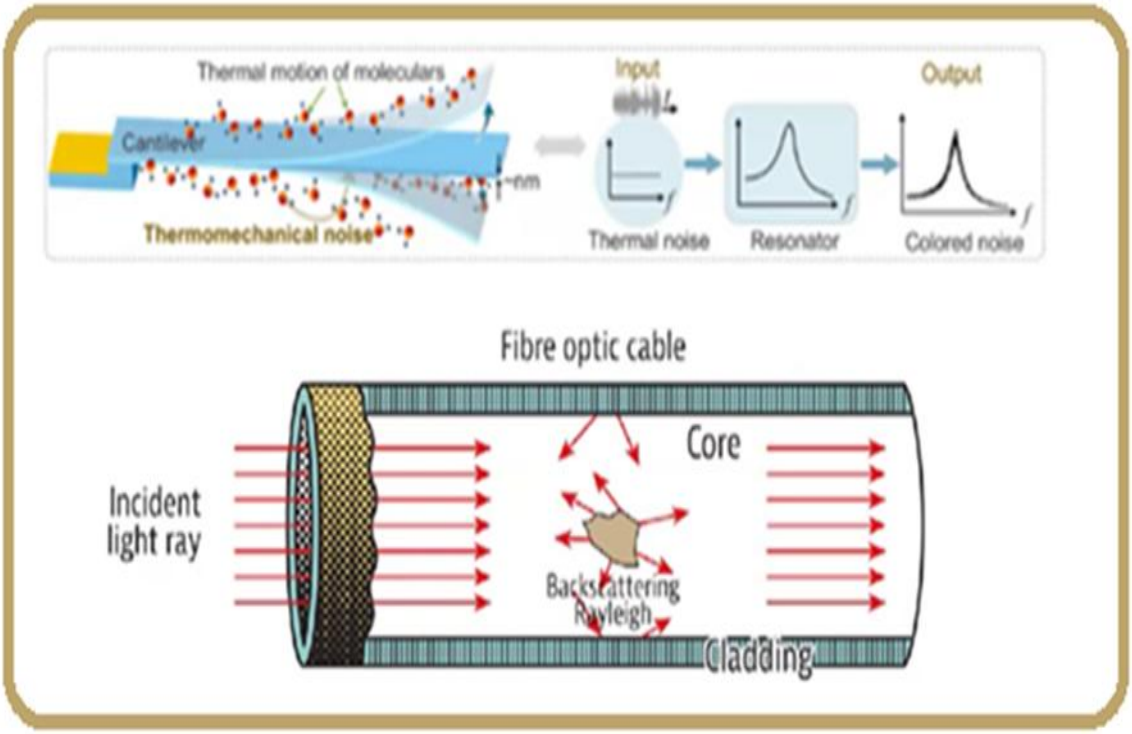

Figure 18: Noise.

4.10 Reusability: refers to the ability of a sensor or measurement system to maintain its performance and accuracy over multiple uses or measurements without significant degradation shown in figure19.

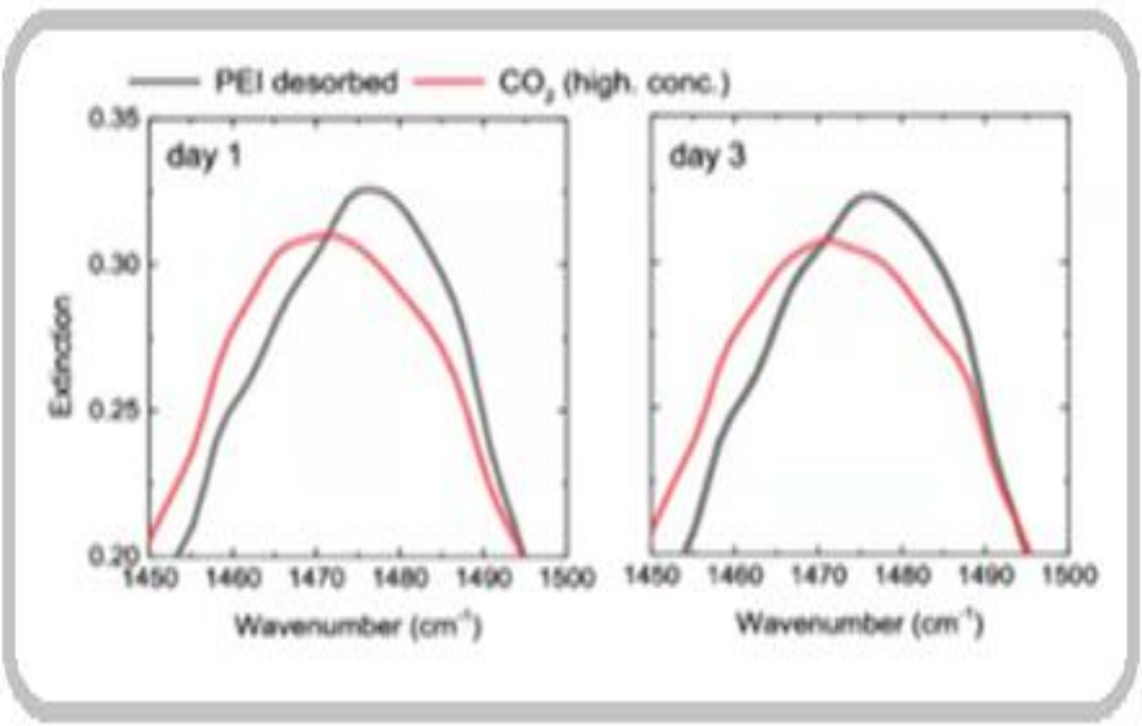

Figure 19: Reusability [11].

4.11 Shelf Life: what happens to the performance when kept for long time see in figure 20.

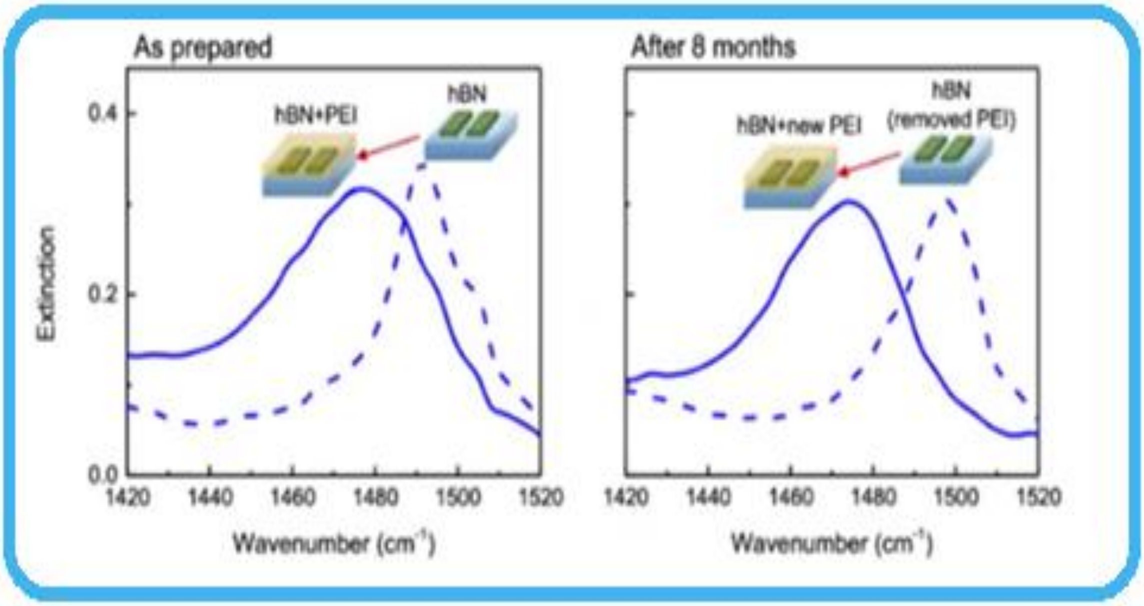

Figure 20: Shelf Life [13].

Figure 21 of Merit: this is the ratio of the sensitivity of the sensor to the width of the spectral curve. The figure of merit - it means that a sensor is good, when the full width half maximum is small and the sensitivity is large.

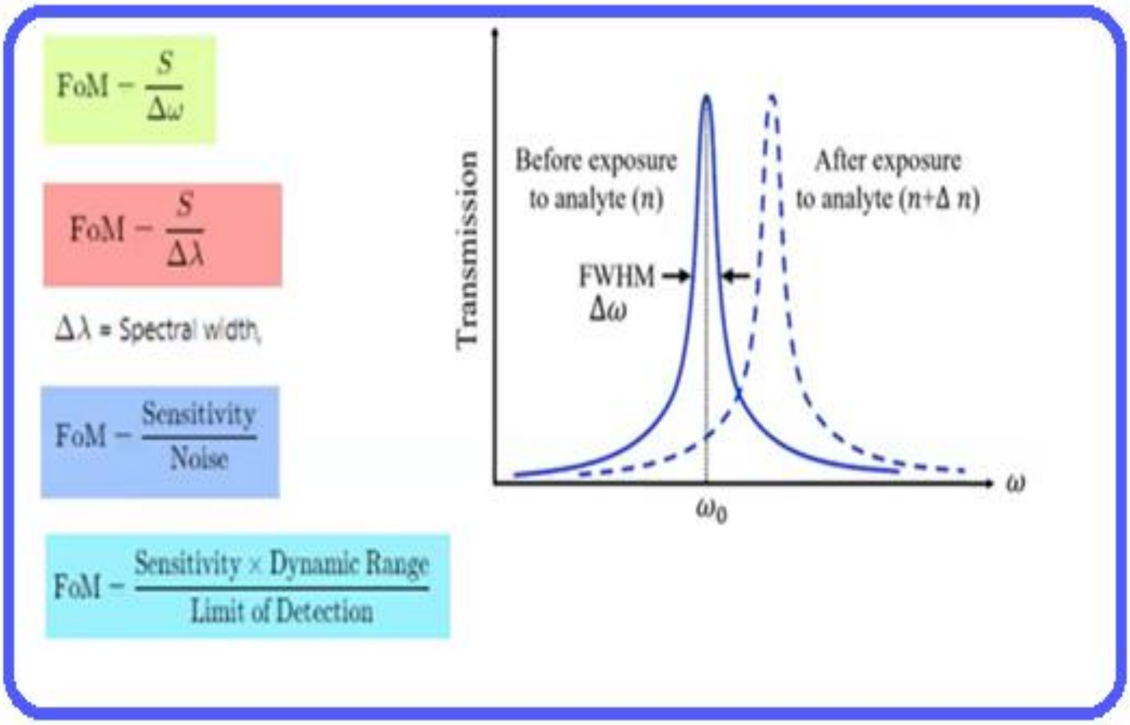

Figure 21: Merit [27].

5. Conclusion

In this review, the types and mechanisms of biosensors have been discussed, with a focus on various receptors, transducers, and nanomaterials. Biosensors offer versatile applications across engineering, medicine, toxicology, food safety, and drug delivery. The integration of nanotechnology continues to drive advancements in biosensing precision and efficiency.

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