Design for Biosecurity

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Lecture 49

World of Biohybrid Biosensors

Welcome back to the lecture series! In our previous class, we wrapped up our discussion on glucose biosensors, covering the entire spectrum of biosensing technologies. We explored how to process various samples, such as urine, blood, sweat, and other bodily fluids, to measure glucose levels. These methods can be categorized as either invasive or minimally invasive processes.

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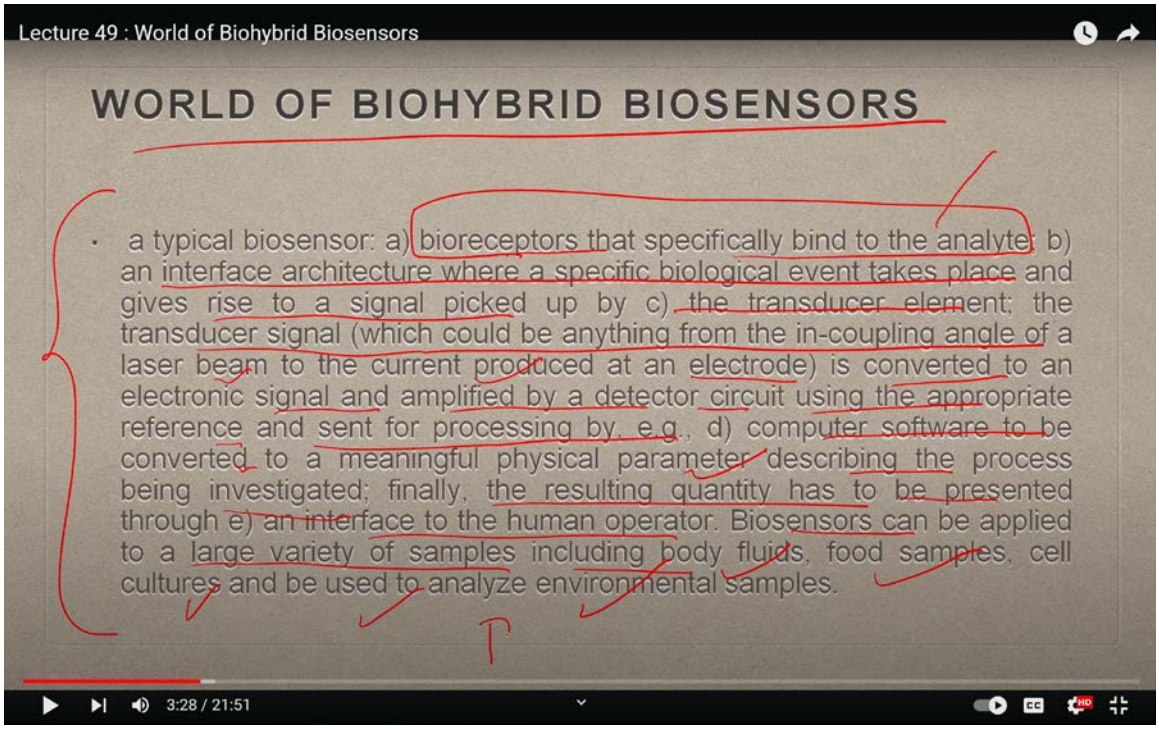

For instance, drawing blood is clearly an invasive procedure, while collecting urine is more non-invasive; however, it still relies heavily on the subject's excretion. The same principle applies to sweat analysis.

After that, we transitioned into non-invasive sensors and delved into an array of spectroscopic techniques, including Raman spectroscopy, near-infrared (NIR) spectroscopy, surface plasmon resonance (SPR), photoacoustic spectroscopy, thermal emission techniques, and tomography. We also discussed how these data are processed and the current acceptable limits for glucose sensing.

Today, we will take stock of the situation and return to the drawing board to summarize our findings, as well as explore the newer topics we will be discussing. This brings us to the fascinating world of bio-hybrid biosensors.

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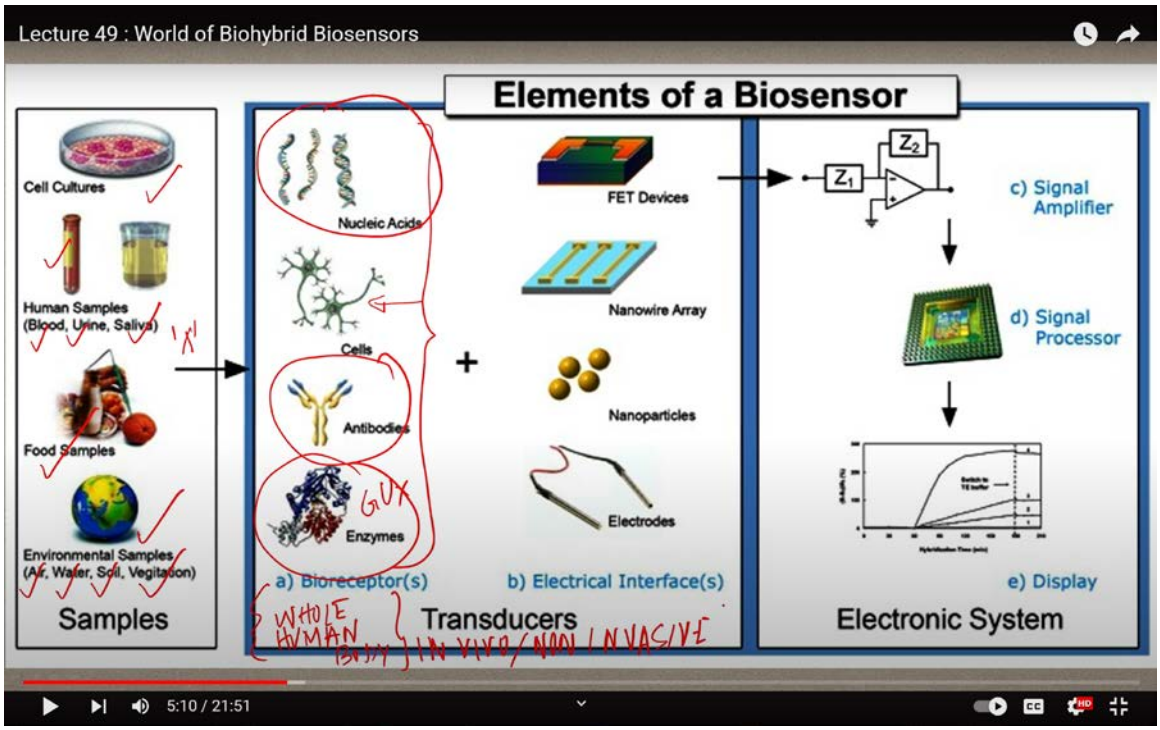

A typical biosensor consists of three essential components. First, there is the bioreceptor, which is specifically designed to bind to the analyte of your choice, this could be anything you are interested in measuring. Second, we have the interface architecture, where a specific biological event occurs, resulting in a measurable signal.

The third component is the transducer element. This transducer converts the signal from the biological event into an electronic signal. This could involve anything from the angle

of an incoming laser beam to the current generated at an electrode. The electronic signal is then amplified by a detector circuit, which uses appropriate references before being sent for processing.

Finally, specialized computer software translates this data into meaningful physical parameters that describe the process being investigated. The resulting information is then presented to the human operator through a user-friendly interface.

Biosensors have a broad range of applications, from analyzing body fluids and food samples to assessing environmental samples and cell cultures. The versatility of biosensors makes them invaluable tools in various fields.

When we discuss the definition of a biosensor, we are essentially looking at its fundamental building blocks. To help visualize this concept, I encourage you to refer to the pictorial representation in the next slide, which illustrates the various elements involved in biosensing.

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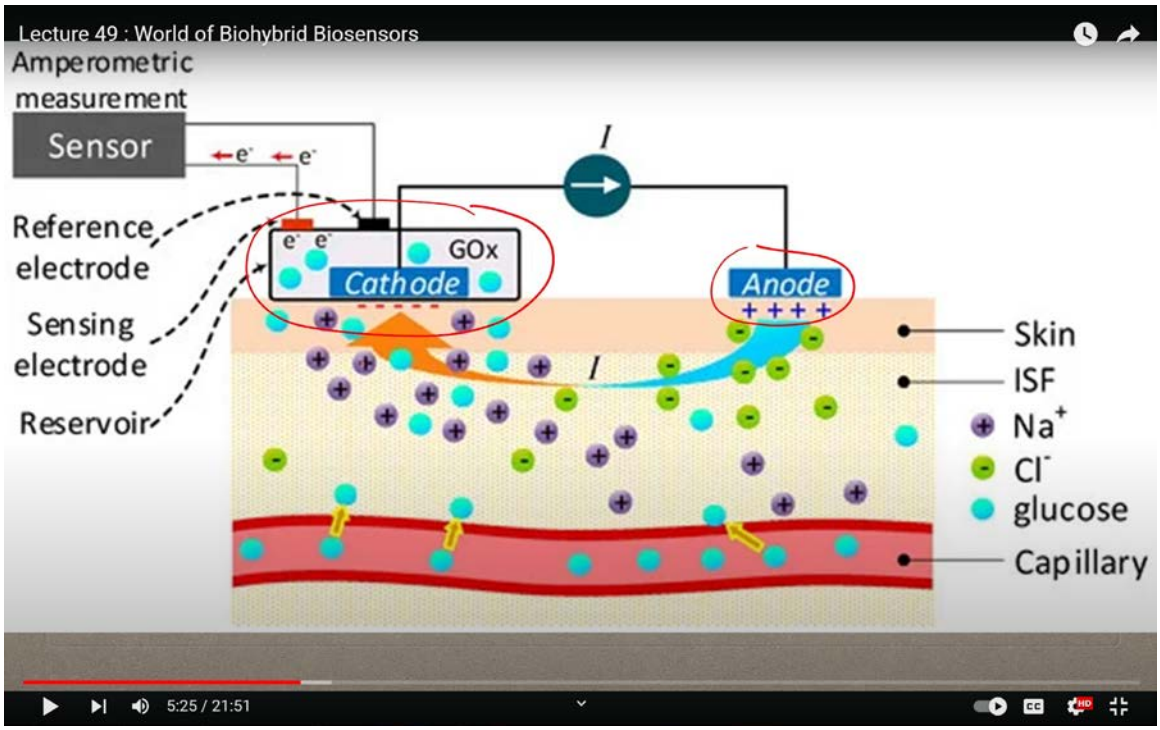

These samples can originate from a multitude of sources: they might be derived from cell cultures, human samples such as blood, urine, or saliva, or even food samples. Additionally, they can include environmental samples encompassing air, water, soil, and vegetation, essentially, anything and everything we encounter in our surroundings.

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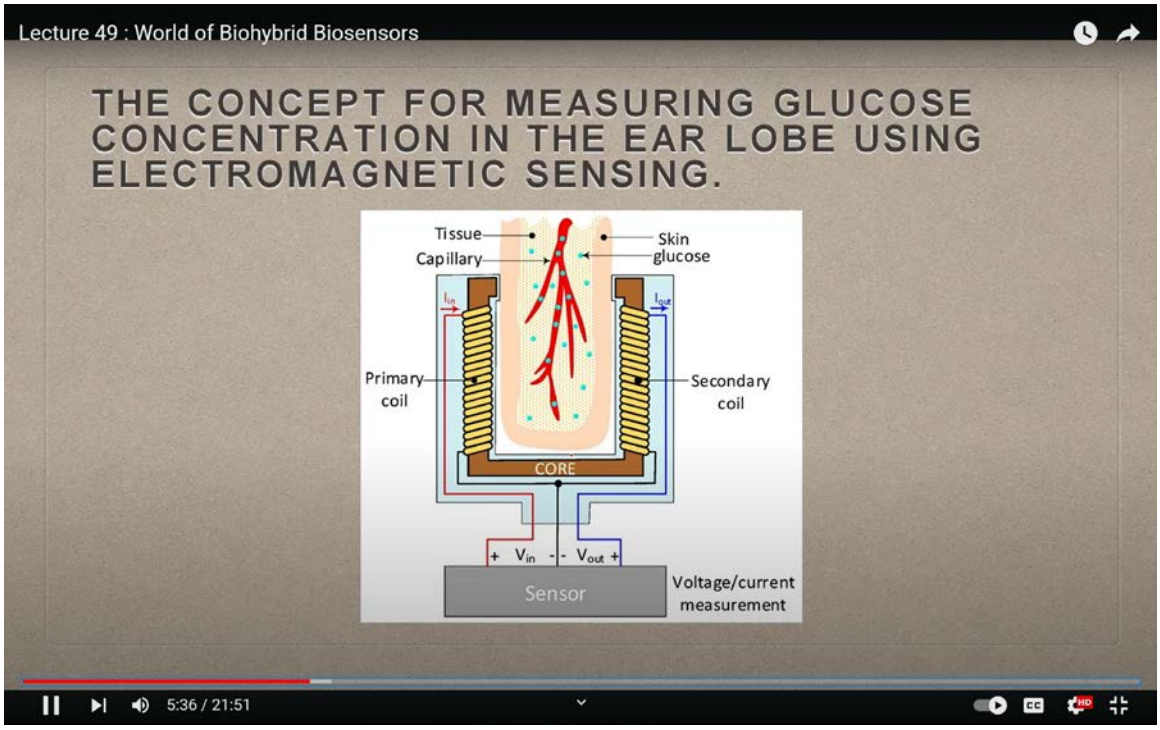

As we examine these samples, it's crucial to identify the specific compound of interest, which we will refer to as compound X. To detect this compound, we employ a biological element, which could be a nucleic acid, a cell, an antibody, or an enzyme. These categories are broad and encompass various options. For example, we previously discussed glucose oxidase as an enzyme and explored the roles of antibodies and nanobodies in biosensing. While we touched on nucleic acid hybridization, we haven't yet delved into the cell-based aspects. However, we've certainly covered the human body as a whole, particularly in the context of in vivo or non-invasive sensing using diverse spectroscopic tools.

With this understanding, as you view the accompanying images, the concepts will become clearer. For instance, picture a minimally invasive anode and cathode implanted in your

body, measuring glucose levels. Similarly, consider a scenario where measurements are taken from the earlobe using a device that employs non-invasive techniques, yet still effectively measures glucose.

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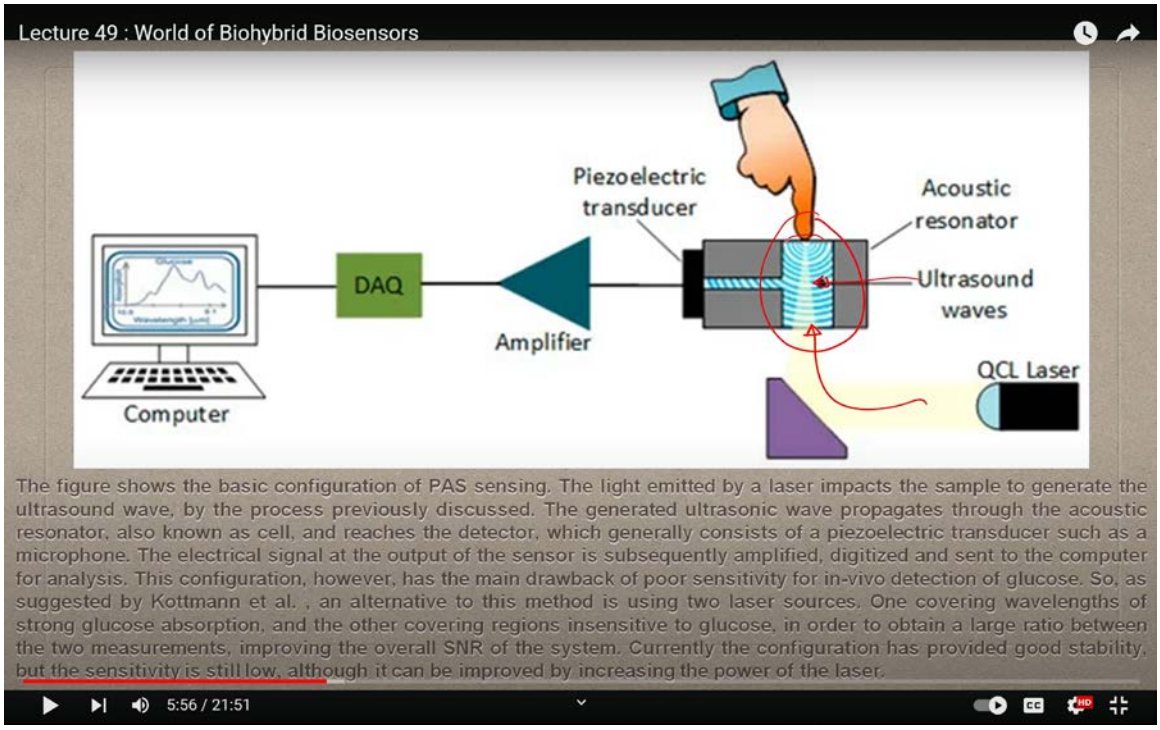

In the realm of photoacoustic spectroscopy, imagine a laser beam interacting with ultrasound waves, with the changes being monitored by a piezoelectric transducer. When you observe these various methodologies in light of the visual representation, it becomes evident how these elements are seamlessly integrated.

Moving on, let’s discuss the second key component: the electrical interface. This interface may consist of electrodes, nanoparticles, nanowires, or field-effect transistor (FET) devices. FETs, in particular, are a type of transistor that can amplify signals detected by nanowire devices. These signals are then processed by amplifiers before being displayed for interpretation.

Our journey now takes us into the world of hybrid biosensors featuring electrical interfaces, with a focus on whole-cell biosensing or whole-cell biosensors. This section will

predominantly concentrate on the group of elements associated with whole cells.

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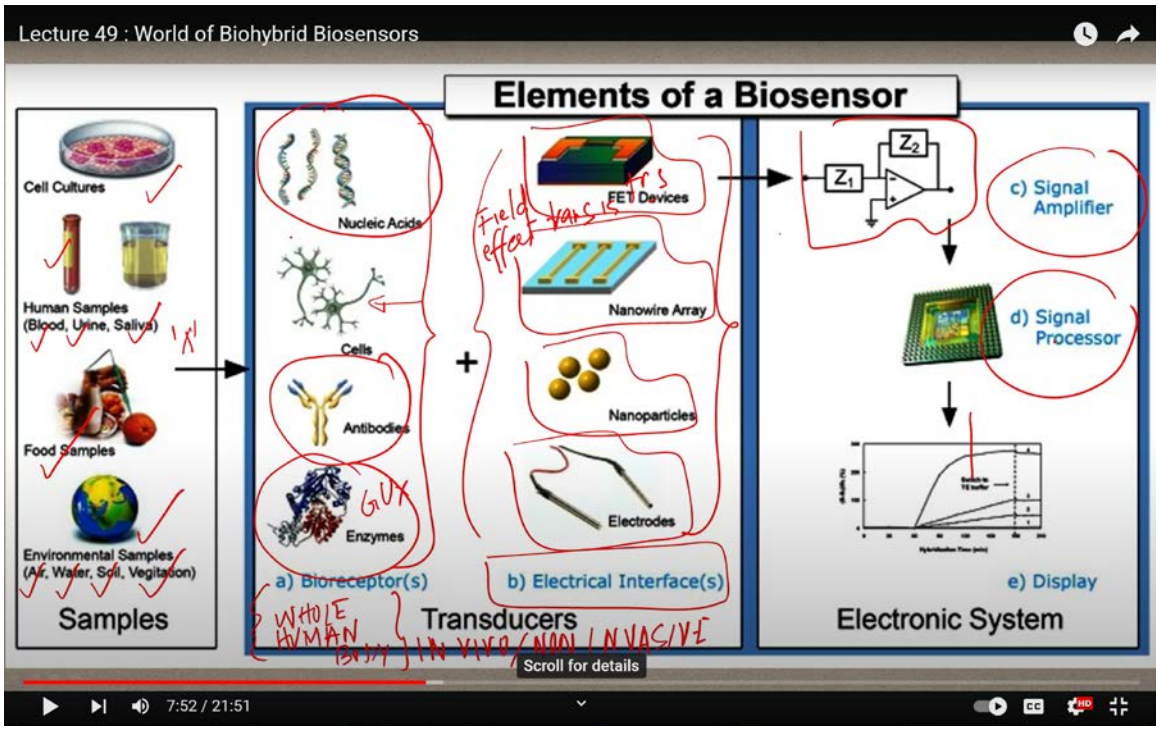

Before we transition into this topic, it's essential to outline several key conditions that must be fulfilled to successfully construct a biosensor for the non-specialist market. What are these conditions? We will briefly analyze them before diving deeper into whole-cell biosensing. For a biosensor to be effective, the biocatalyst must exhibit a high degree of specificity for the analyte, remain stable under normal storage conditions, demonstrate minimal variation between assays, and maintain low variability throughout the assays. This point regarding consistency between assays is absolutely critical.

The fluctuation of results indicates an unhealthy sign that compromises the fidelity of the biosensor. Moving on to the second aspect, it is crucial that the reactions occurring within the biosensor are as independent and manageable as possible, particularly concerning physical parameters like stirring, pH, and temperature. This independence allows for the analysis of a sample with minimal pretreatment. If the reaction involves a cofactor or coenzyme, these should be immobilized alongside the enzyme to ensure optimal

performance.

Essentially, when collecting a signal, the interface should facilitate minimal interference, enabling the detection of the signal without significant difficulty.

Furthermore, the response of the biosensor should be accurate, precise, reproducible, and linear across the concentration range of interest, without requiring dilution or concentration. It must also be free from electrical noise or any disturbances induced by the transducer. It's important to recognize that most devices come with their own inherent noise levels. If the noise produced by these devices is greater than the biological signals being measured, it will interfere with the readings. Thus, prioritizing noise cancellation or selecting devices with minimal noise is essential for the success of biosensors.

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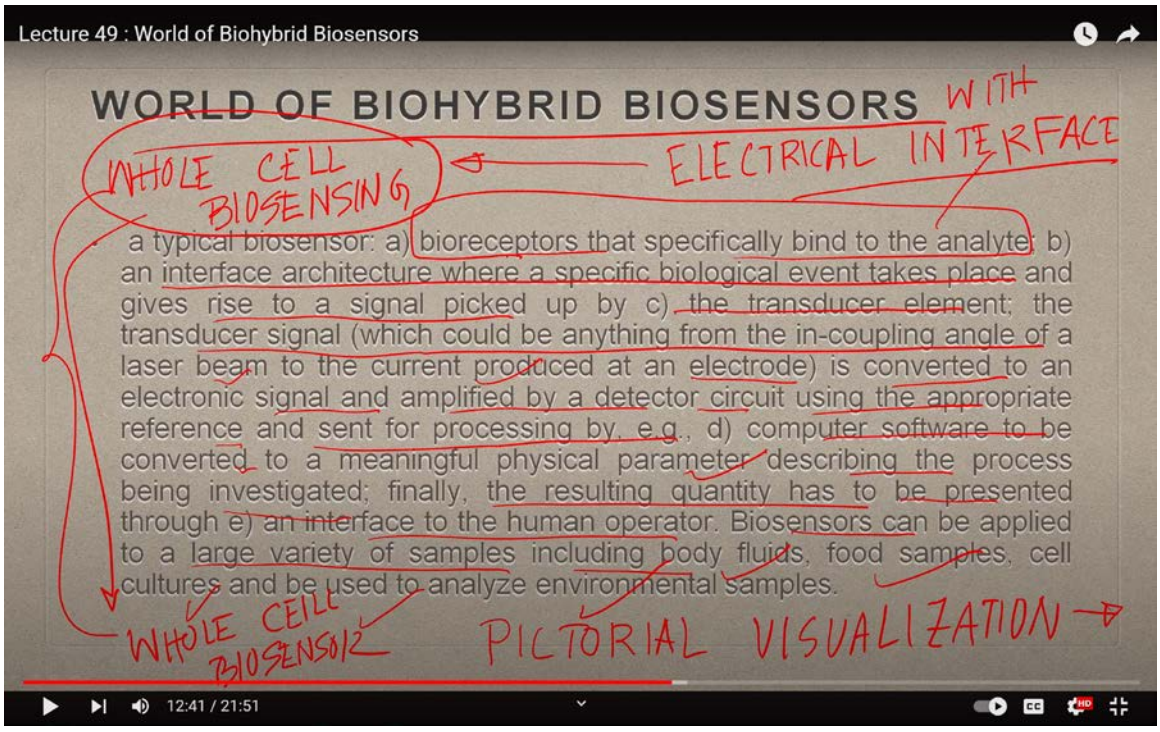

For biosensors intended for invasive monitoring in clinical settings, the probe must be small and biocompatible, ensuring that it has no toxic or antigenic effects. Additionally, the biosensor should resist inactivation or proteolysis, meaning the materials used should not lead to any form of inactivation or breakdown.

To enable rapid measurement of analytes from human samples, it is desirable for the biosensors to provide real-time analysis. Finally, the biosensor should be cost-effective, small, portable, and user-friendly, suitable for operation by semi-skilled personnel.

These are the fundamental considerations we need to keep in mind. In this class, we will focus specifically on electrical interfaces, particularly in relation to cell-based or whole-cell biosensors, which offer a real-time perspective. When we discuss whole-cell biosensors, we are referring to devices that are primarily utilized for research and diagnostic purposes, and they have significant implications for drug detection, pathogen identification, and even the detection of potential terror agents.

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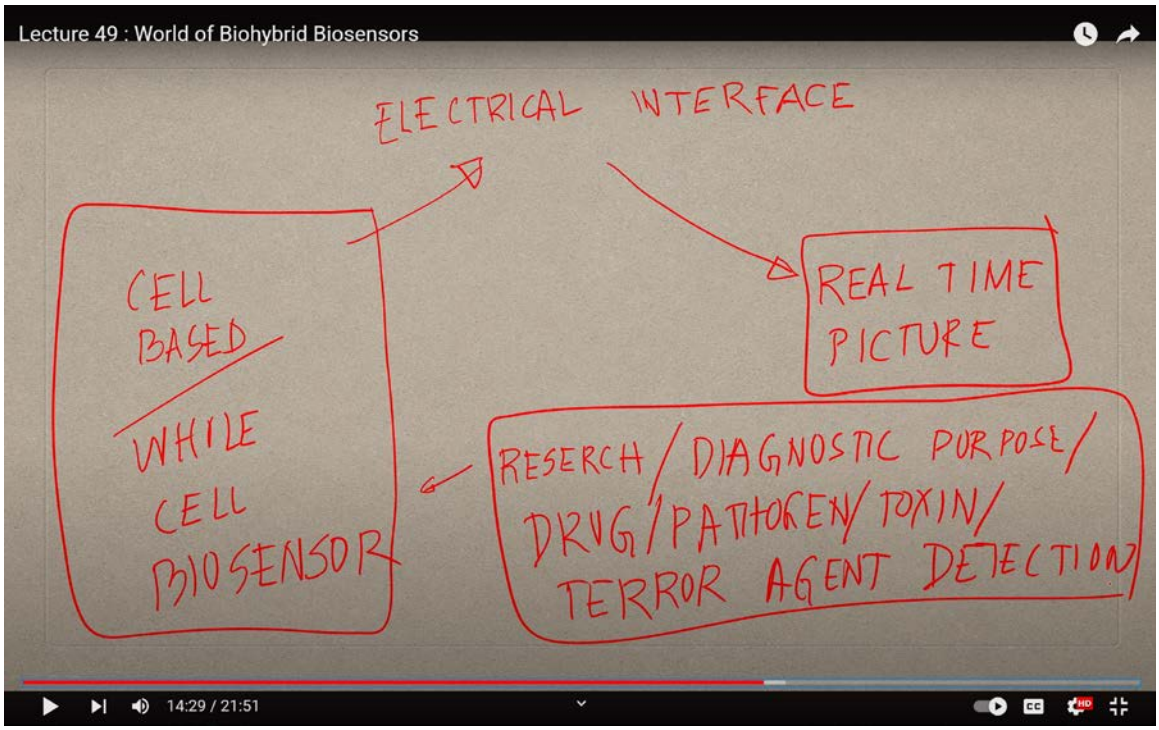

This is a step beyond the routine diagnostics we have previously discussed, such as analyzing serum for elevated glucose levels or diagnosing diseases. In this context, we aim to interface cells within an in vitro setup. This means we will be working in scenarios outside the body. For instance, we might take specific cells from a subject, integrate them into an electrical interface, and monitor their activity when exposed to drugs, chemicals,

and other agents.

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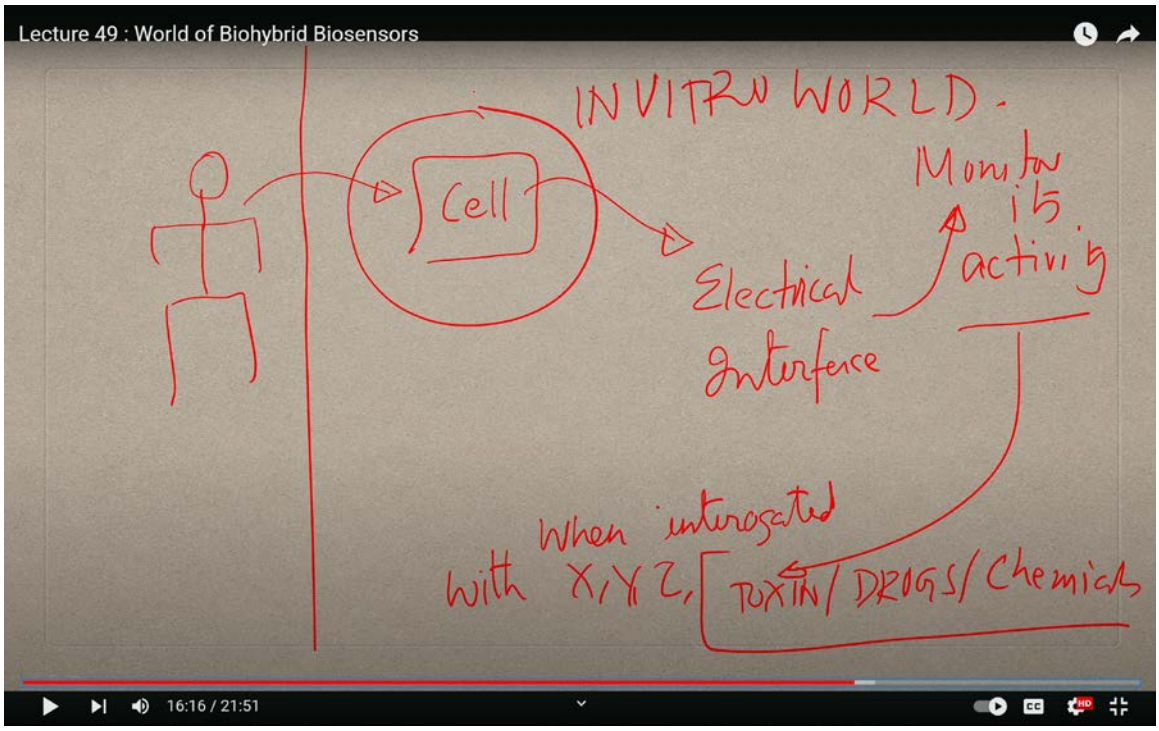

So, in essence, when we extract cells, we enter the expansive realm of in vitro studies. Now, what types of cells are we discussing here? What are the preferred cell types for this sensing process? When we look at the human body, we can see that it operates as an electrically active system, or a bioelectrically active system, depending on how you prefer to frame it. To classify the cells from the perspective of biosensing, we can divide them into two categories: electrically active and electrically inactive cells.

As you know, the human body is composed of billions of cells, organized hierarchically: cells form tissues, tissues form organs, organs constitute systems, and these systems integrate to create the body as a cohesive unit. In our previous lectures, we have explored how we measure various parameters of the human body through in vivo methods, utilizing samples like blood, urine, and sweat. Now, we are shifting our focus to the extraction of cells from the human body, particularly in the context of whole-cell biosensors, or, more specifically, whole-cell electrochemical biosensors.

To grasp the concept fully, it's essential to categorize the body's cells into these two distinct groups. Our primary interest lies in electrically active cells because they are capable of generating electrical impulses, which vary based on the stimuli they receive. For instance, consider your nose; it can distinguish between the scent of a rose and that of a jasmine flower. When we talk about these scents, we're referring to volatile compounds that are present in the environment.

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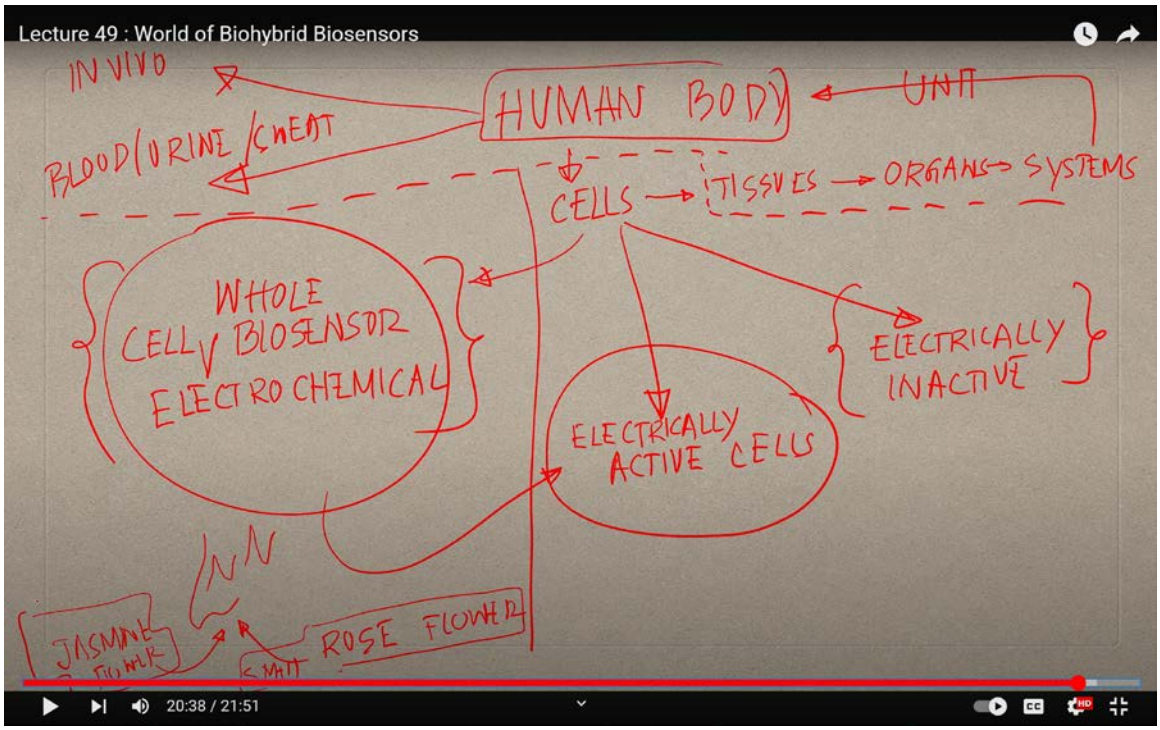

These volatile compounds elicit different biological signals in the form of electrical activity within your body. This is precisely what we aim to exploit and utilize. In our next class, we will delve into how these unique characteristics can be harnessed to construct whole-cell biosensors, powerful tools in the domains of basic research, diagnostics, and drug discovery, including toxin detection, pathogen identification, and the detection of potential terror agents. So, let's wrap up today's class here. In our next session, we will start by examining how to differentiate between these smells and the corresponding signals they produce, as well as the tools we need to interpret them effectively. Thank you!