Design for Biosecurity

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Lecture 48

Electromagnetic Sensing

Let us begin this class by delving into electromagnetic sensing, particularly focusing on the electromagnetic sensing of glucose. In our previous class, we explored photoacoustic spectroscopy, and before that, we discussed thermal emission spectroscopy. We covered the various challenges associated with these techniques, particularly the use of photoacoustics, which involves two different types of radiation or waves, and the application of quantum cascade lasers (QCLs). We also addressed how to manage parameters related to metabolic heat conformation. Prior to that, we examined time-of-flight and terahertz domain spectroscopy, and before that, we touched upon far-infrared spectroscopy. Of course, last week, we discussed Raman spectroscopy.

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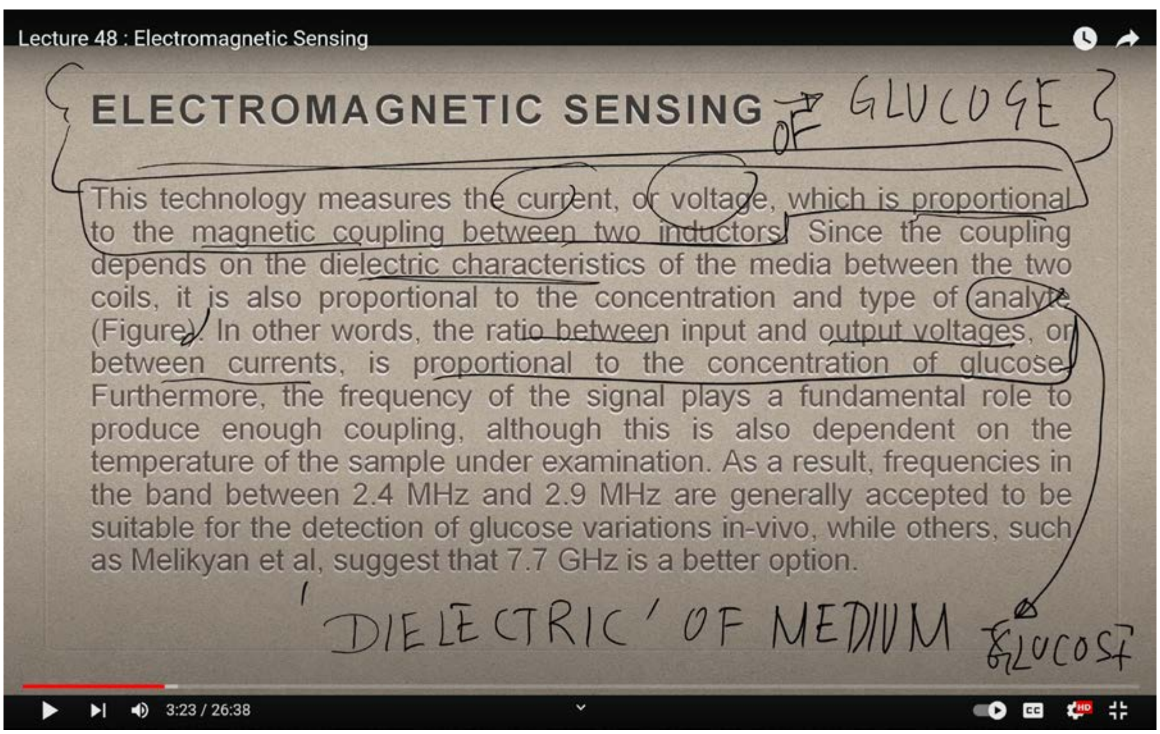

Today, we will continue along this same trajectory by highlighting another crucial aspect of non-invasive glucose sensing: electromagnetic sensing. As we have learned in our studies, particularly in standards 6 and 7, when a current flows through a conductor, it generates a magnetic field around it. This phenomenon marks the foundation of electromagnetism.

We've all witnessed this principle in action, such as in dynamos, where mechanical energy is converted into electrical energy. The relationship between magnetism and electricity is intrinsic, almost like a brother-sister connection. Thus, when we discuss electromagnetic sensing, it becomes fascinating to consider what exactly we are detecting.

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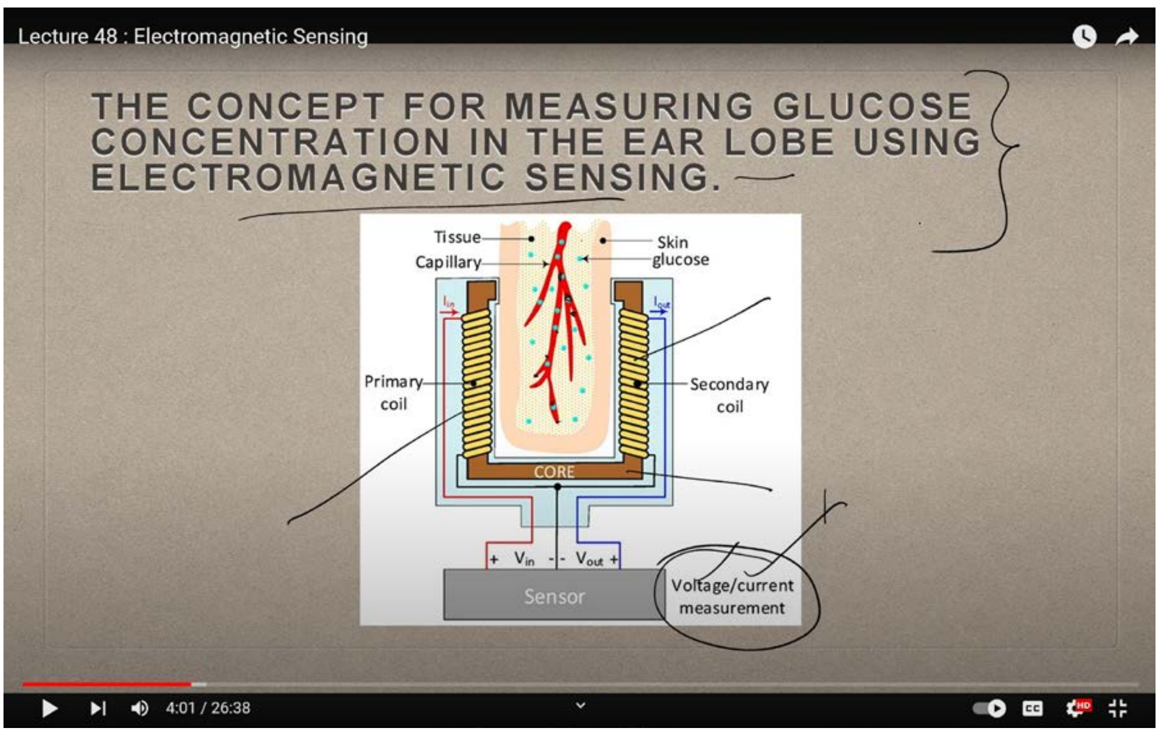

This technology measures the current or voltage that is proportional to the magnetic coupling between two inductors. Since this coupling is influenced by the dielectric properties of the medium, something you may want to revisit, the medium in our case is blood. The interaction between the two coils also varies based on the concentration and type of analyte present. Here, the analyte of interest is glucose. In simpler terms, the ratio of the input to the output voltage, or the current, correlates with the concentration of glucose.

To clarify this concept, let’s take a look at the illustration. In the diagram, you can see the tissue, the blood capillary, the skin, and the glucose. Here, we have the inductor coils: the primary coil and the secondary coil. This setup includes a core and a magnet.

In this arrangement, the sensor measures either the voltage or the current, depending on the quantity of glucose molecules present in the capillaries. The specific application for measuring glucose concentration typically takes place in the earlobe, as this area contains a high density of capillaries, providing ample access. While this method is effective in the earlobe, it is important to note that it can also be implemented in other areas, provided the magnet and device are securely affixed. Thus, a clip is often used to stabilize the setup.

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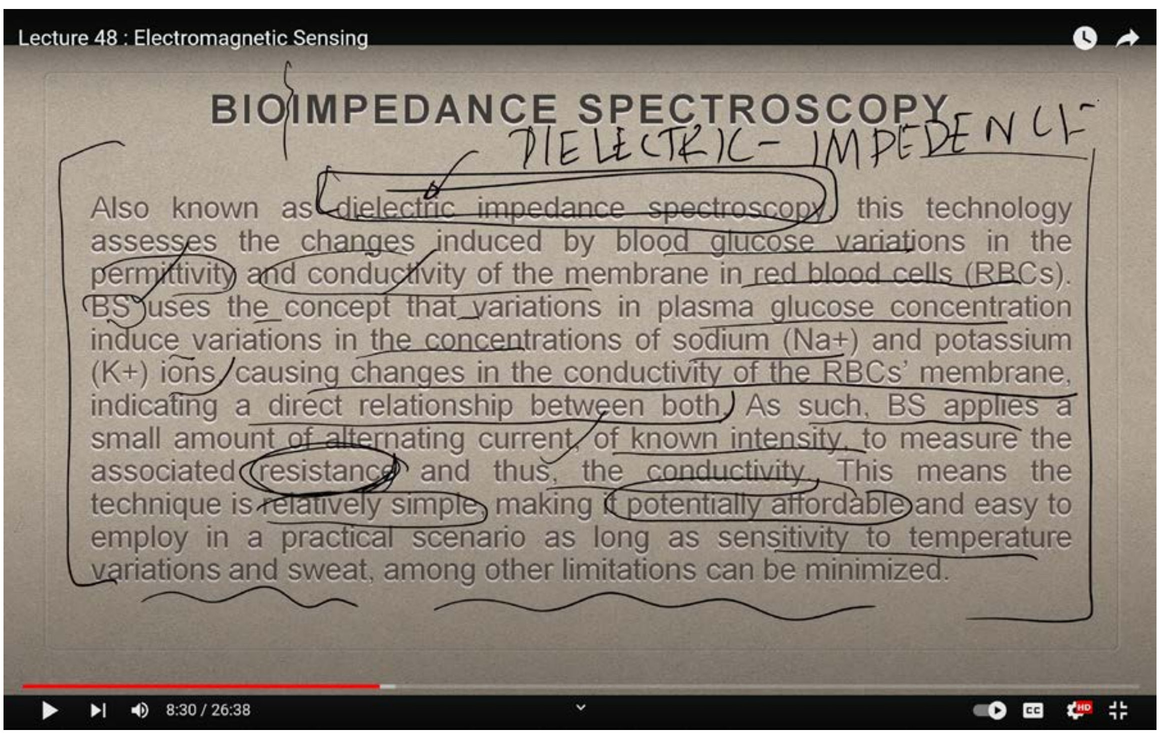

Any area of skin where you can apply a clip and where a thin layer of skin overlays a blood vessel is suitable for this technique. The earlobe, for example, works perfectly. The clip mechanism is essential because it securely holds the two inductors in place, along with the magnet positioned nearby.

Moreover, the signal frequency is crucial for generating sufficient coupling, and it also depends on the temperature of the sample being examined. Frequencies within the range of 2.4 megahertz to 2.9 megahertz are generally recognized as suitable for glucose detection. Therefore, the key takeaway for you is that 2.4 to 2.9 megahertz is the optimal range for detecting variations in glucose levels in vivo. However, it’s worth noting that researchers like Malayakan have suggested that 7.7 megahertz might be a more effective frequency.

There is extensive research being conducted in the realm of electromagnetic sensing due to its accessibility; this area of the body has abundant blood flow, making it easier to detect glucose levels. The fundamental principle here is that the signal exchanged between the inductor coils changes based on the number of glucose molecules present in the blood vessels. This forms the backbone of this technology.

Next in line is bioimpedance spectroscopy. When we mention impedance, we refer to a form of obstruction or resistance, also known as dielectric impedance spectroscopy. This technology evaluates the changes caused by fluctuations in blood glucose levels on the permittivity and conductivity of the membranes of red blood cells. In discussing dielectric properties, terms like permittivity and conductivity are key. As I previously mentioned, understanding the basic principle behind measuring the dielectric constant will introduce you to these terminologies.

Bioimpedance spectroscopy is founded on the concept that variations in plasma glucose concentration lead to changes in the concentrations of sodium and potassium ions, which in turn affect the conductivity of the red blood cell membranes, indicating a direct relationship between the two. This method involves applying a small amount of alternating current of known intensity to measure the associated resistance, known as impedance resistance, and thus, conductivity.

This technique is relatively straightforward, which could make it a cost-effective and practical option, provided that sensitivity to temperature variations and sweat, among other limitations, can be minimized. However, this raises an important point regarding field conditions, where you lack control over temperature or humidity. How can you obtain accurate data in such environments? These parameters can significantly alter the dielectric properties of the sample or the blood, depending on factors such as temperature, moisture levels, and the concentrations of sodium and potassium ions.

Thus, while bioimpedance spectroscopy is indeed a simple and effective technique, it is more scientifically accurately referred to as dielectric impedance spectroscopy. This term emphasizes the resistance measured within the medium, which, in this case, is the blood.

The changes in the dielectric properties of blood or red blood cells (RBCs) are closely tied to the concentration of glucose present. RBCs act as carriers of glucose because they contain hemoglobin, to which glucose binds. Imagine these RBCs filled with hemoglobin; each hemoglobin molecule can be either saturated with oxygen, known as oxyhemoglobin, or desaturated, referred to as carboxyhemoglobin.

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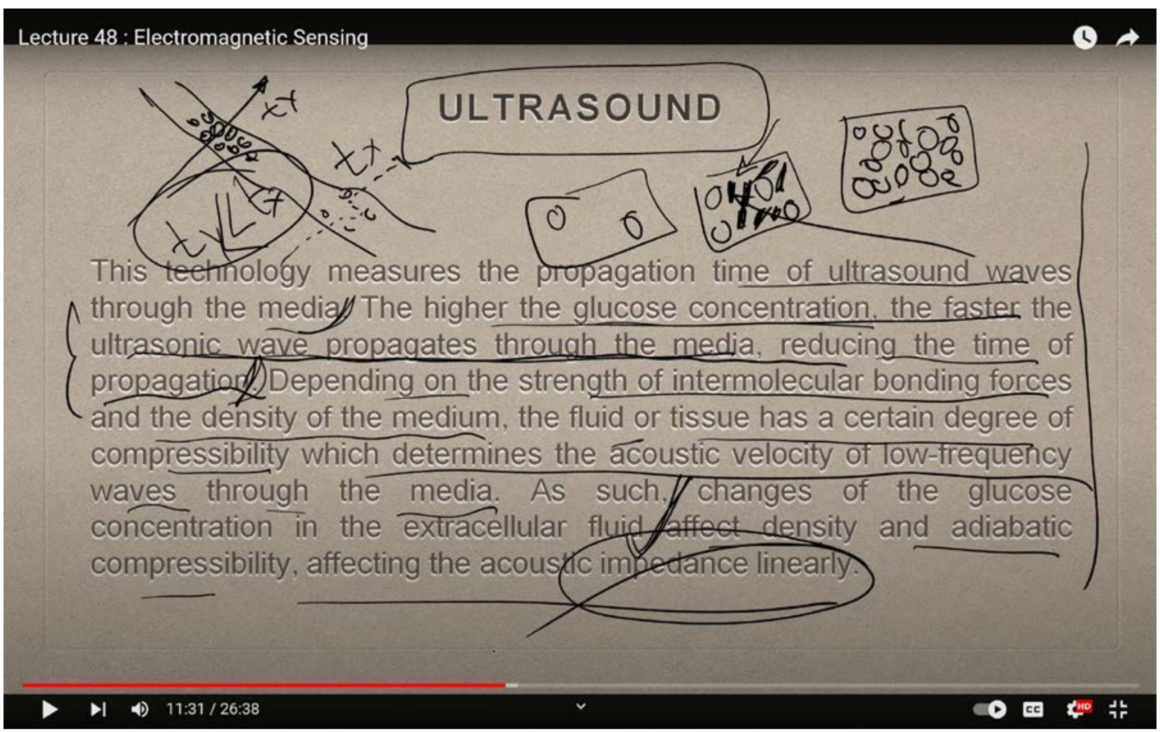

Now, let’s discuss the application of ultrasound in this context. This technology measures the propagation time of ultrasound waves as they travel through a medium. The fascinating part is that the higher the glucose concentration, the faster the ultrasonic wave propagates through the medium, leading to a reduced propagation time.

To illustrate this concept, consider different substrates: in a solid substrate, sound travels very quickly; in a liquid substrate, the speed is slower; and in a gaseous substrate, it travels even more slowly. For example, if you have a liquid and you increase the glucose concentration, what happens? The sound waves will travel faster. Picture this: if you place your ear on a railway line, you can hear a train approaching because sound travels rapidly in solid mediums. This basic principle, which you've likely encountered in your earlier studies, is precisely what's at play here.

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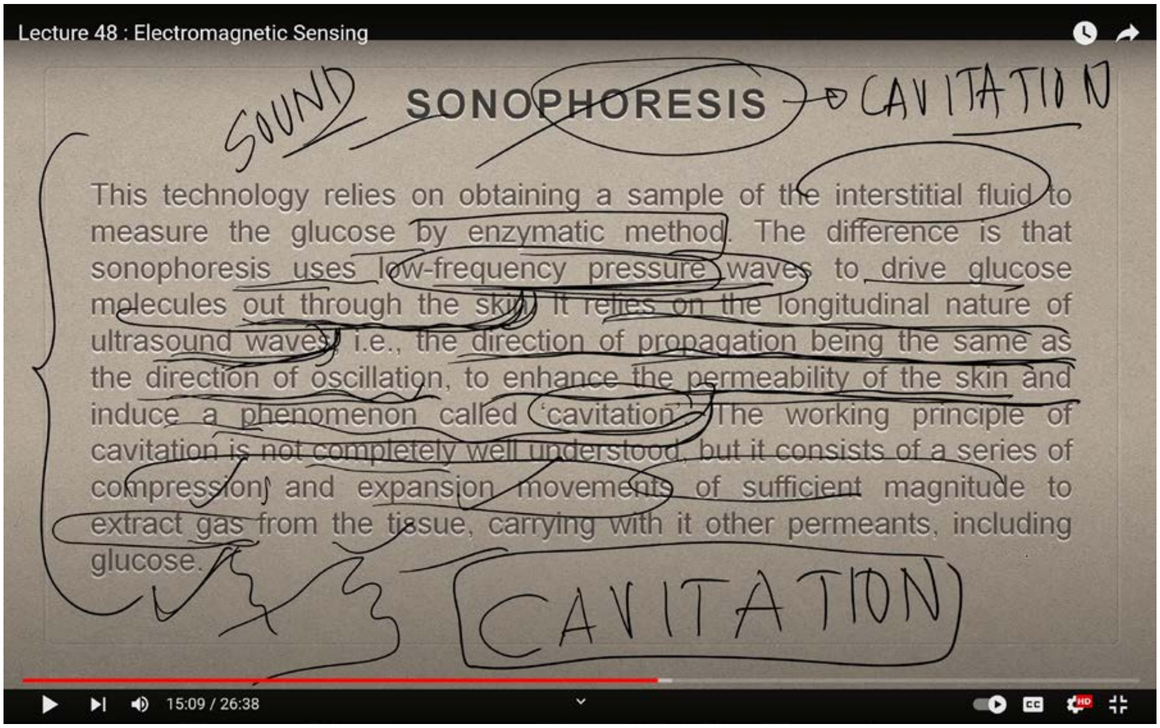

As the glucose concentration increases, the ultrasonic wave propagates more swiftly through the medium, thereby reducing the propagation time. If your capillary has a higher glucose concentration, the ultrasound will travel faster compared to a capillary with a lower concentration. Thus, if we denote the propagation times as T_x and T_y, where T_y represents the faster time associated with higher glucose levels, we can see that T_y will be significantly less than T_x. This time difference is exactly what you are measuring in terms of wave propagation.

Moreover, the fluid or tissue's degree of compressibility influences the acoustic velocity and the frequency of the waves traveling through the medium. This is determined by the strength of intermolecular bonding forces and the medium's density. Consequently, fluctuations in glucose concentration in the extracellular fluid will impact both density and adiabatic compressibility, thereby affecting the acoustic impedance in a linear fashion. This represents yet another intriguing method of utilizing ultrasound to assess glucose concentration.

Next, we encounter a technology known as sonophoresis. This innovative technique focuses on obtaining samples of interstitial fluid to measure glucose levels through enzymatic methods. What sets sonophoresis apart is its use of low-frequency pressure waves to drive glucose molecules out through the skin. It capitalizes on the longitudinal nature of ultrasound waves, where the direction of propagation aligns with the direction of oscillation, thereby enhancing the skin's permeability and inducing a phenomenon known as cavitation.

Although the working principle of cavitation is not entirely understood, it involves a series of compression and expansion movements that are sufficiently powerful to extract gases from tissues, along with other permeants, including glucose. So, in summary, sonophoresis relies on cavitation to facilitate the extraction of glucose by employing low-frequency waves to push glucose molecules out through the skin, thereby increasing skin permeability and making it easier to obtain interstitial fluid samples for measurement.

In the process of sonophoresis, you significantly alter the size of the skin's pore cavities. Essentially, you are modifying the diffusion potential of the skin, which facilitates the release of glucose molecules. This is precisely what sonophoresis aims to achieve.

Now, to clarify the term "sonophoresis": it involves using sound waves to create microscopic fractures in the skin, effectively increasing its permeability. By doing this, you create tiny pores, allowing substances to escape through these openings. The technology primarily focuses on obtaining samples of interstitial fluid to measure glucose levels through enzymatic methods.

Sonophoresis employs low-frequency pressure waves to drive glucose molecules out through the skin. By enhancing the skin's permeability, it leverages the longitudinal nature of ultrasound waves, where the direction of propagation aligns with the oscillation direction, thereby inducing a phenomenon known as cavitation.

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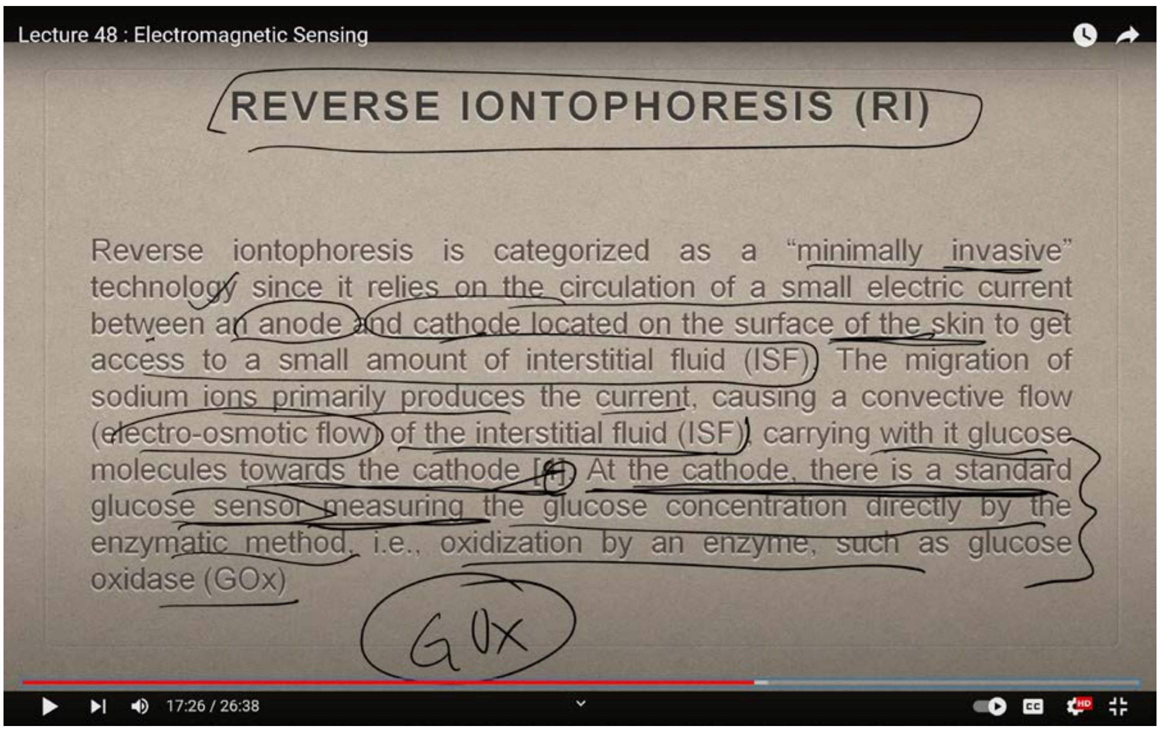

While the exact working principle of cavitation is not entirely understood, it involves a series of compression and expansion movements powerful enough to extract gases from the tissue. This process also carries other permeants, such as glucose. Cavitation is fascinating in that it requires the material to return to its original shape, which takes time.

For instance, when the skin expands, it subsequently takes time for it to revert to its original form. During this period of retraction, some molecules are exuded from the skin, depending on their concentration. Imagine this as a surface being exposed to sound waves: at a microscopic level, the skin expands and then contracts, allowing certain molecules to escape during that brief moment of expansion. It’s a remarkable concept to consider!

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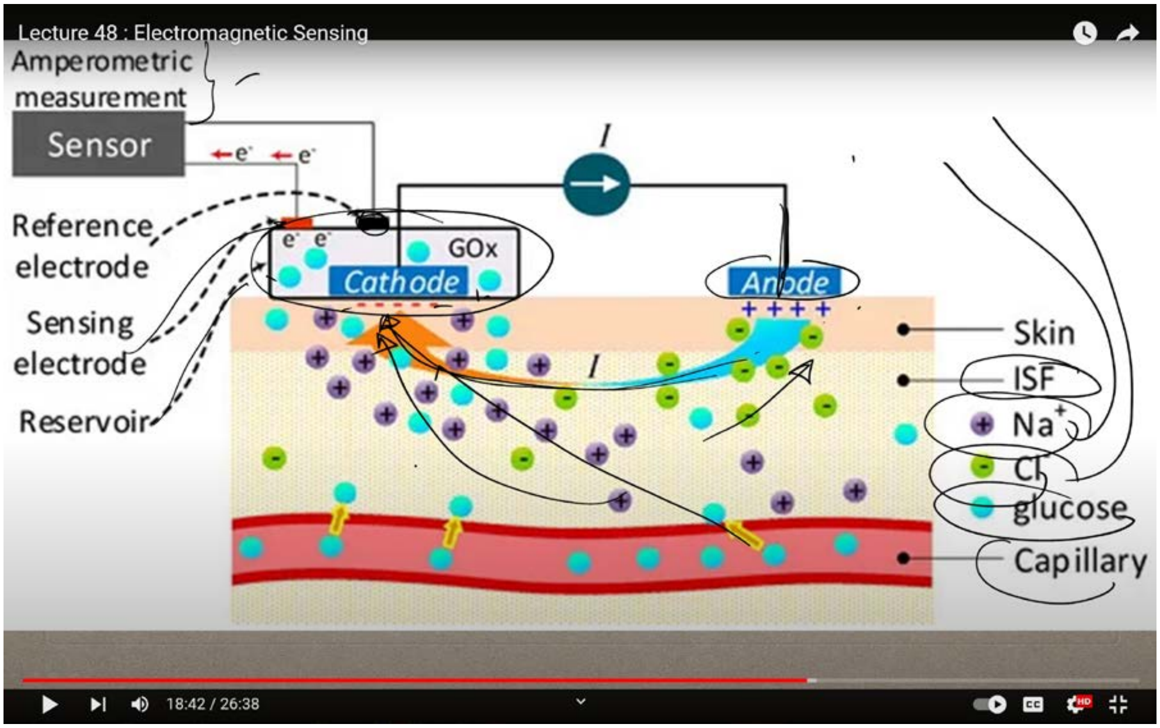

Now, let's discuss another innovative technology: reverse iontophoresis, commonly referred to as RI. This method is categorized as a minimally invasive technology because it involves circulating a small electric current between an anode and a cathode placed on the skin's surface to access a small amount of interstitial fluid. Picture this setup with the anode and cathode embedded in the skin; it's all part of the minimally invasive technical textiles designed for such purposes.

In this process, the migration of sodium ions primarily generates the current, which in turn causes a convective or electroosmotic flow of the interstitial fluid, effectively transporting glucose molecules toward the cathode. At the cathode, a standard glucose sensor directly measures glucose concentration through enzymatic methods. This is where the glucose oxidase assay comes into play, specifically at the cathode. The term "reverse iontophoresis" reflects the fact that you are actively drawing glucose out using embedded electrodes in your body.

Let's delve into the workings of reverse iontophoresis, which involves the integration of both a cathode and an anode for measurement purposes. At the cathode, we perform the crucial measurement. Essentially, the migration of sodium ions generates the current, leading to a convective or electroosmotic flow within the interstitial fluid, which carries glucose molecules toward the cathode. At this point, we utilize a standard glucose sensor for measurement.

To clarify, reverse iontophoresis operates with embedded anodes and cathodes. At the cathode, we perform glucose oxidase amperometric measurements. Here, we measure the current using the reference electrode of the sensing electrode in the reservoirs where glucose oxidase is immobilized. By applying a small current, we alter the flow of the interstitial fluid, allowing glucose molecules to migrate towards the cathode.

As this process unfolds, sodium ions are moving toward the cathode, while chloride ions travel toward the anode, creating a potential across the system. This movement is facilitated in the capillaries, causing a disturbance that justifies the name "reverse iontophoresis." This technique cleverly employs sodium and chloride ions, ultimately measuring glucose concentrations as well.

It’s fascinating to note that all these techniques, in one way or another, involve the agitation of the skin. For instance, using sound waves or anodes can stimulate the capillaries, while lasers can induce agitation in the system. The aim is to maximize the chances of obtaining accurate data sets. However, despite the availability of numerous sensors, a significant challenge remains: the sheer volume of data that needs to be analyzed. This necessitates advanced algorithms and powerful computers to effectively process the diverse data generated by these technologies.

There are a multitude of glucose-sensing technologies to explore, including those developed at esteemed institutions like Caltech and the University of Waterloo. Additionally, various other research centers and universities, such as the University of Maryland, KTH (Korean Institute of Technology), and Tohoku University, have made significant contributions to biosensing technologies for various applications.

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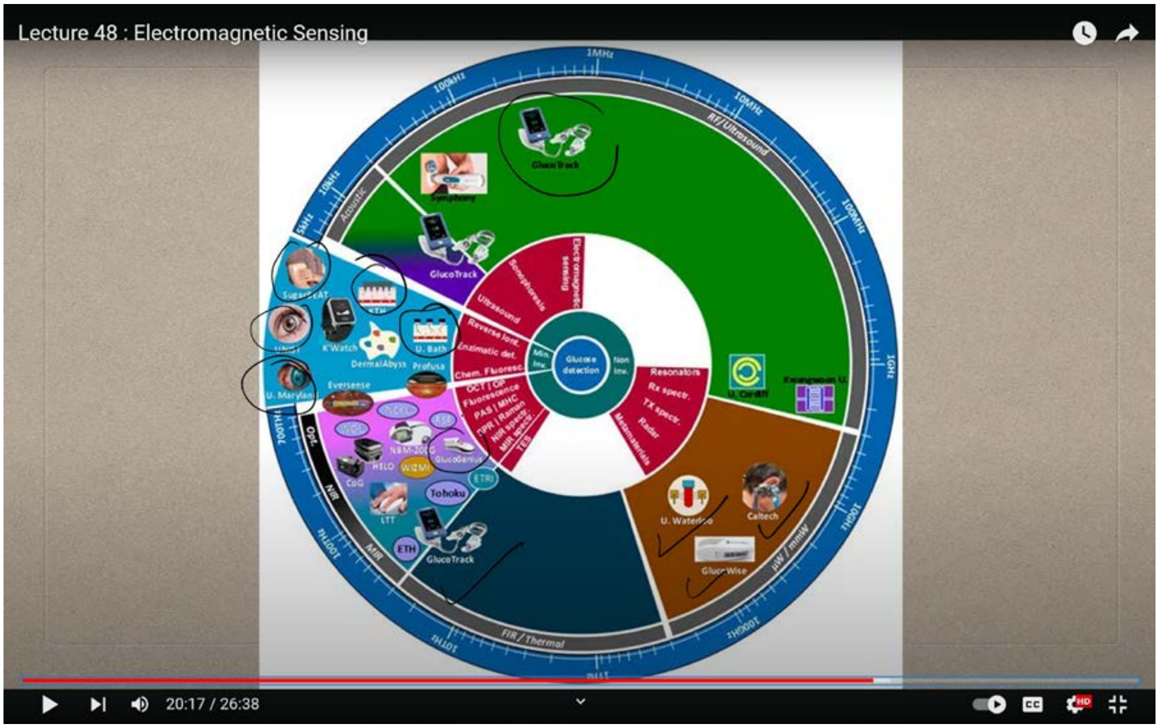

While many of these advancements focus on glucose sensing, it is essential to recognize their broader implications. As mentioned in the previous class, glucose sensing serves as a foundation for a range of biosensors applicable to different areas, including biodefense and bioterrorism. The versatility of these sensors allows for changes in the analyte being measured; if we can measure glucose effectively, we can also adapt the technology to quantify other substances with relative ease.

And therein lies a significant challenge, translating these advancements into practical applications. This issue largely stems from the multitude of technologies that have been tested for a simple molecule like glucose. The real difficulty lies in how we can effectively translate these findings into usable solutions.

To recap, let's revisit the concept of reverse iontophoresis. In this technique, we utilize embedded anodes and cathodes, with most measurements taking place at the cathode. By injecting a current, we facilitate the mobility of sodium ions, chloride ions, and, of course, the glucose present in the interstitial fluid.

Before this, we discussed sonophoresis, which operates based on the intriguing and somewhat enigmatic phenomenon known as cavitation. We also explored ultrasound technology, where we established that a higher concentration of glucose in the blood results in faster sound wave propagation. Remember, this is a mechanical wave, a sound wave at its core.

Then we delved into bioimpedance spectroscopy, which takes into account the dielectric properties of blood and red blood cells (RBCs). Following that, we examined the concept of measuring glucose concentration through electromagnetic sensing, which involves two inductor coils and a magnet. This method investigates how changes occur due to the glucose levels present, focusing on the medium's dielectric properties, such as permittivity.

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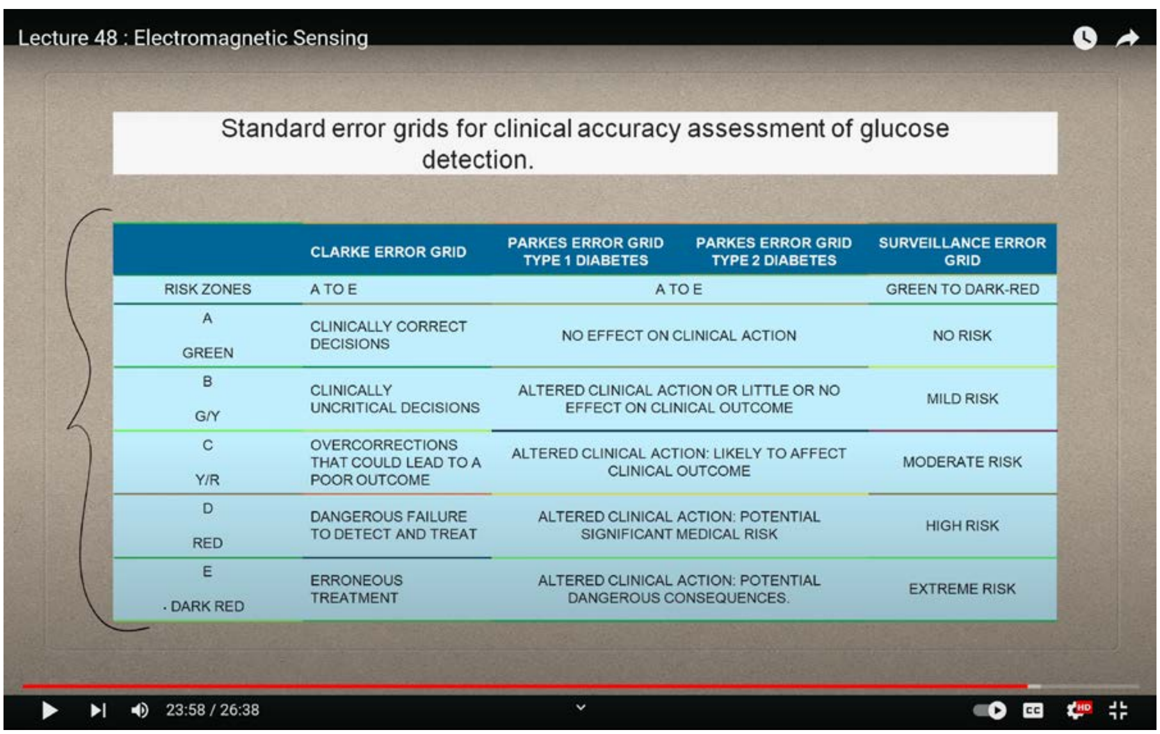

Moving further back, we touched on photoacoustic spectroscopy and metabolic heat conformation. Before that, we discussed thermal emission spectroscopy, time-of-flight techniques, terahertz time-domain spectroscopy, far-infrared, Raman spectroscopy, midinfrared spectroscopy, and near-infrared spectroscopy. We also examined optical coherence tomography (OCT) technology and optical polarimetry, alongside techniques like fluorescence resonance energy transfer (FRET) for glucose monitoring.

Overall, as we reflect on these discussions, we can appreciate the different levels of detection techniques we've explored. We have examined both in vitro and non-invasive in vitro methods.

With this overview of glucose sensing technologies, I hope you all feel more familiar with the advancements available worldwide. The sky truly is the limit when it comes to the technologies you can explore and the wonderful work you can accomplish in this field. We are only at the beginning of what is possible, especially concerning flexible electronics and the integration of biosensors into technical textiles. These applications span a wide range, from civilian uses to strategic applications in the Army, Navy, and Air Force, with a keen focus on bioterrorism.

Moreover, there is immense potential for individuals skilled in data mining, data analysis, and optimization algorithms, particularly for centralized data sensing platforms. This will be especially critical in warfare zones, where real-time data mining can significantly impact the future well-being of soldiers.

As I conclude, I leave you with a vision of a future where our clothing and fabrics are embedded with countless sensors, creating a world that is radically different from our own. In this new reality, we may have the capability to predict diseases or identify pathogens, potentially foreseeing situations that could lead to heart attacks.

Thank you for your attention, and I look forward to our next class, where we will delve deeper into the fascinating world of sensors and their transformative role in human advancement. Thank you!