Design for Biosecurity

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Lecture 50

Whole Cell Biosensor

Welcome back to the next class! In our previous session, we wrapped up by exploring how the human nose can distinguish between various volatile compounds emitted from different sources. You might be surprised to learn that when you compare the human nose to that of a dog or an insect, you'll discover that both dogs and insects possess highly evolved olfactory systems. In fact, they rank second in the evolutionary hierarchy, while we rank third. This evolutionary advantage is indeed beneficial; after all, we have the ability to walk and see the world around us. However, this has led to a compromise in our nasal sensing capabilities compared to those of dogs and insects.

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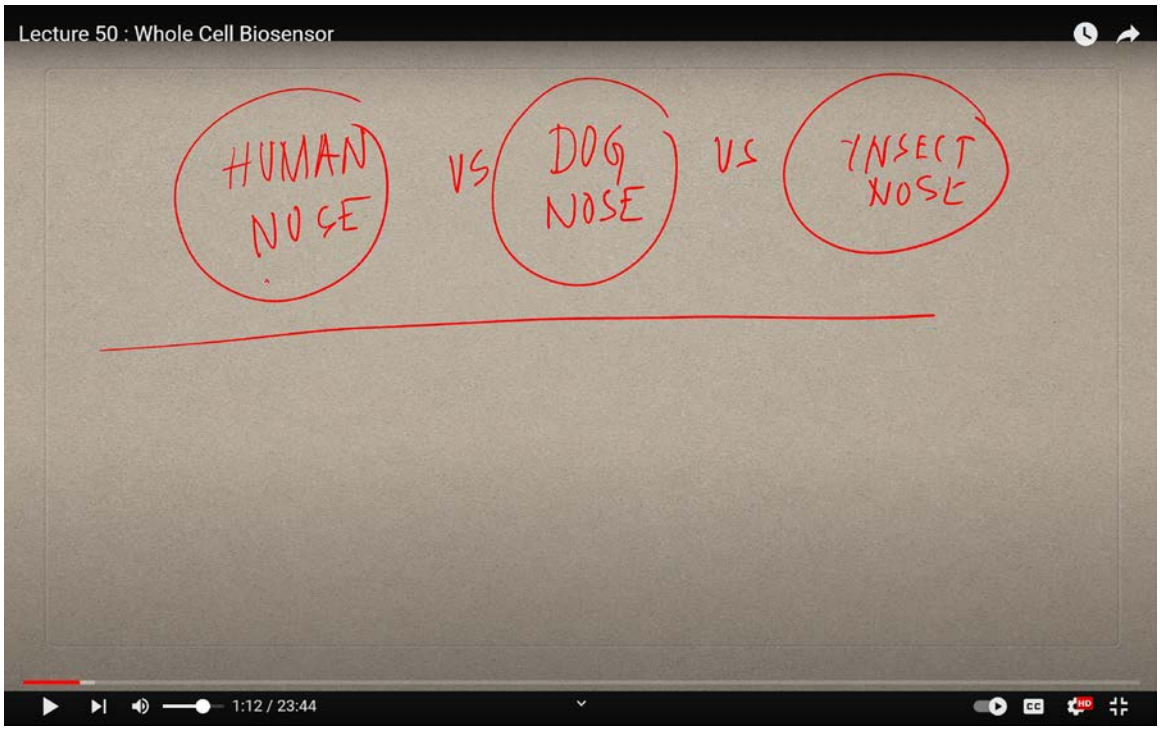

Now, let's circle back to our discussion on different cell types within the body. While we touched on various cell types, our focus has been on excitable cells. Excitable cells are those that generate biological or electrical impulses, and these impulses can vary depending on the type of stimulus they receive. Each type of stimulus results in a distinct electrical impulse. So first, let’s delve into the different types of excitable cells found in our bodies.

One of the primary excitable cell types is the neuron, which constitutes our nervous system. Another critical type is the cardiac myocyte, which forms the bulk of the heart tissue and includes the specialized cardiac pacemaker cells. Additionally, there are hybrid cells known as neuroendocrine cells, which play a vital role in secretion processes by utilizing electrical impulses. In the entire animal kingdom, these represent the only set of electrically active cells. All of these cells generate measurable electrical potential.

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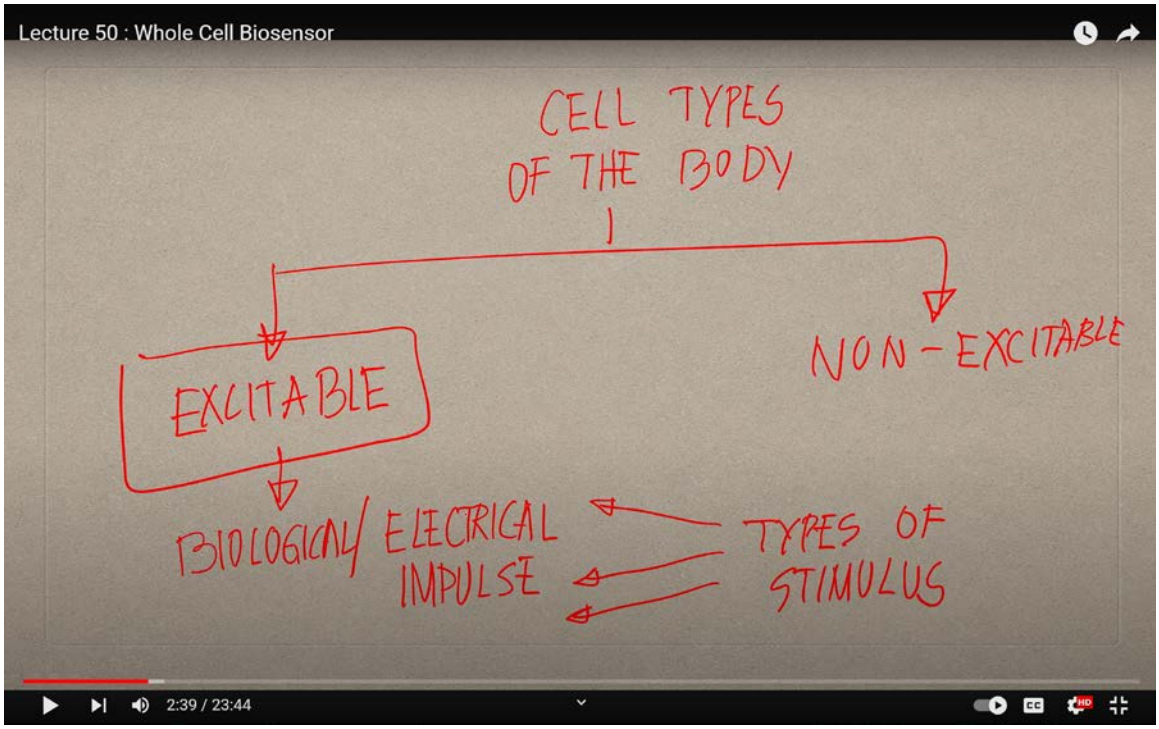

So, when we refer to cells as being electrically active, what does that entail? Do they continuously generate current, and if so, what type of current is it? To understand the term "electrically active," we need to clarify what it means, how it functions, and where and

when it applies. Before we can fully grasp the concept of electrically active cells, we must address these essential questions.

What is the nature of the electrical activity within a cell that can be leveraged for the development of electrochemical biosensors? How can this electrical activity be utilized in biosensing applications? For instance, both neurons and cardiomyocytes display similar characteristics. If you were to place an electrode outside these cells and another electrode inside, you could measure the voltage difference between them. This measurement is fundamental in understanding the electrical activity that can be capitalized on for biosensing technologies.

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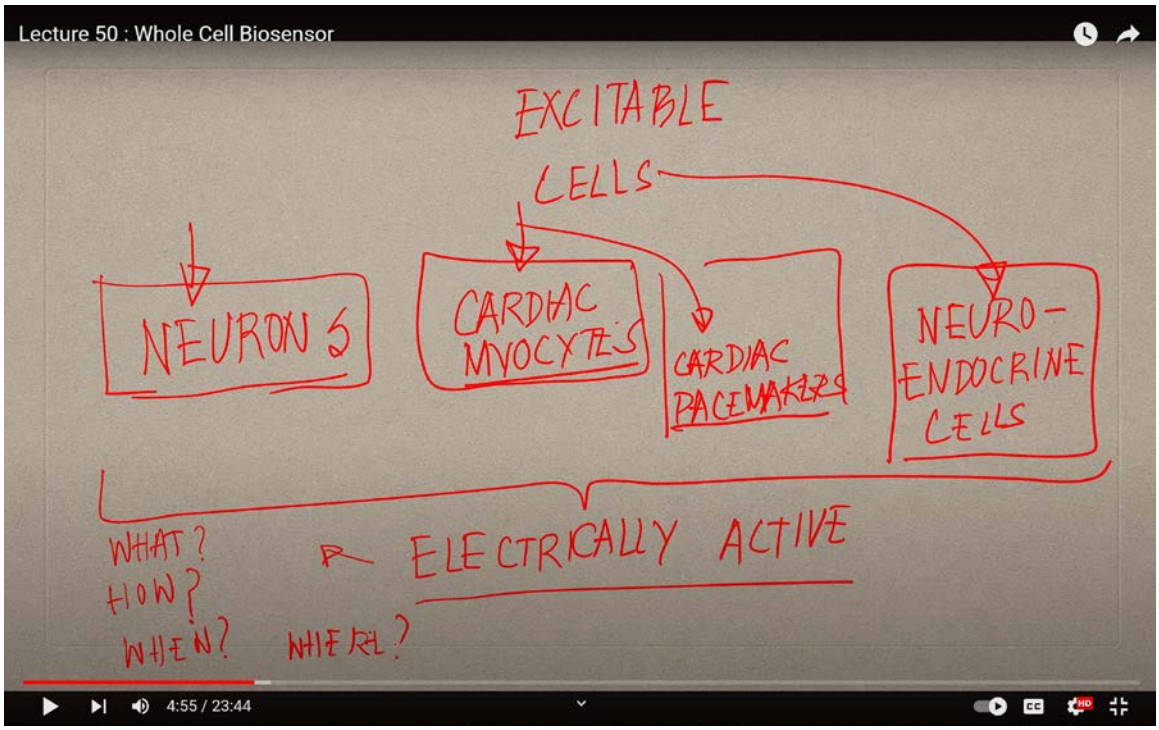

So, here we have the electrode positioned outside, which we'll refer to as E_O, and the electrode situated inside, denoted as E_I. When you measure the difference between these two electrodes, E_O - E_I, it illustrates the voltage across them.

For instance, picture the electrode outside, let's call it E_O, and the one inside, E_I. When you attempt to measure the voltage across these electrodes, you'll find that the majority of these

electrically active cells reside at a resting potential of approximately -70 millivolts. In some cases, this value can drop to as low as -80 millivolts, while certain specialized cells might rest at around -40 millivolts. These specialized cells, operating at -40 to -35 millivolts, are what we refer to as spontaneously active. I will explain the concept of spontaneous activity shortly.

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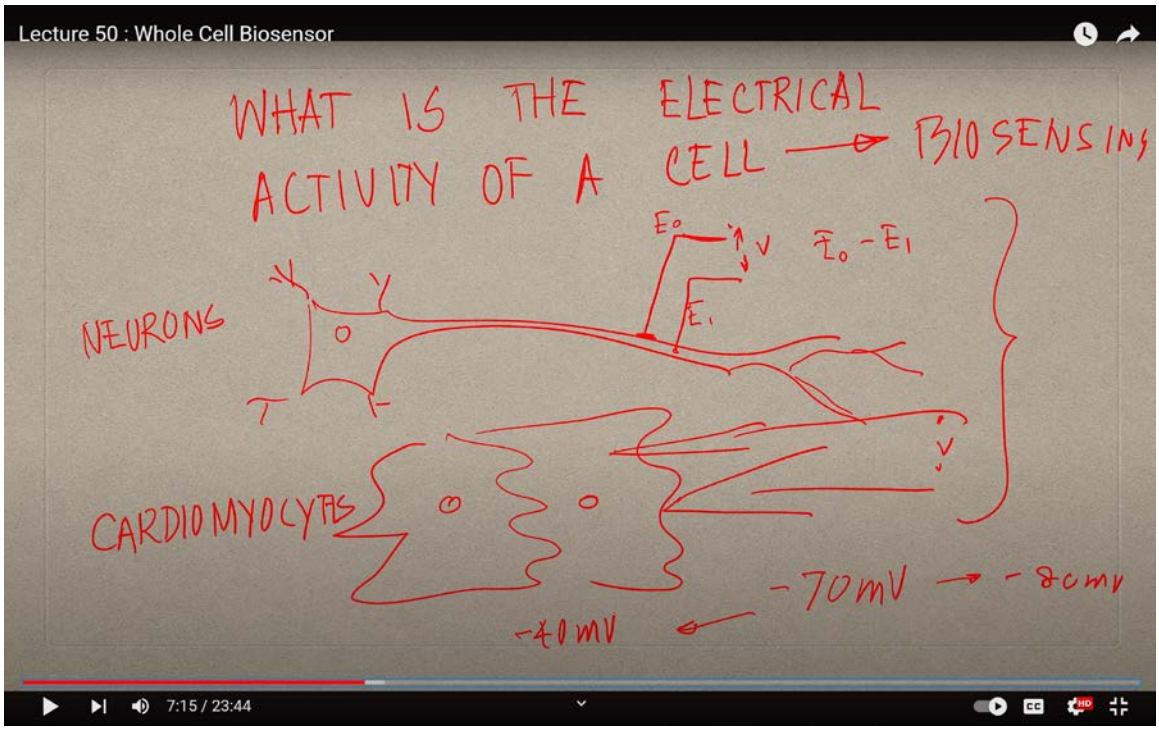

Typically, both cardiomyocytes and neurons maintain a potential between -70 and -80 millivolts, and endocrine cells follow suit. Now, let's visualize what this means using a graph. Imagine graph paper, where the y-axis represents voltage and the x-axis denotes time in milliseconds. On the y-axis, you could mark values like 10, 20, 30, 40, 50, 60, 70, and 80 millivolts, and descending down to -10, -20, -30, -40, -50, -60, -70, and -80 millivolts.

As you plot these values, you'll observe that the cells, neurons, cardiomyocytes, and neuroendocrine cells, will exhibit voltmeter readings that oscillate over time, resembling a waveform. On the other hand, pacemaker cells operate at around -40 millivolts.

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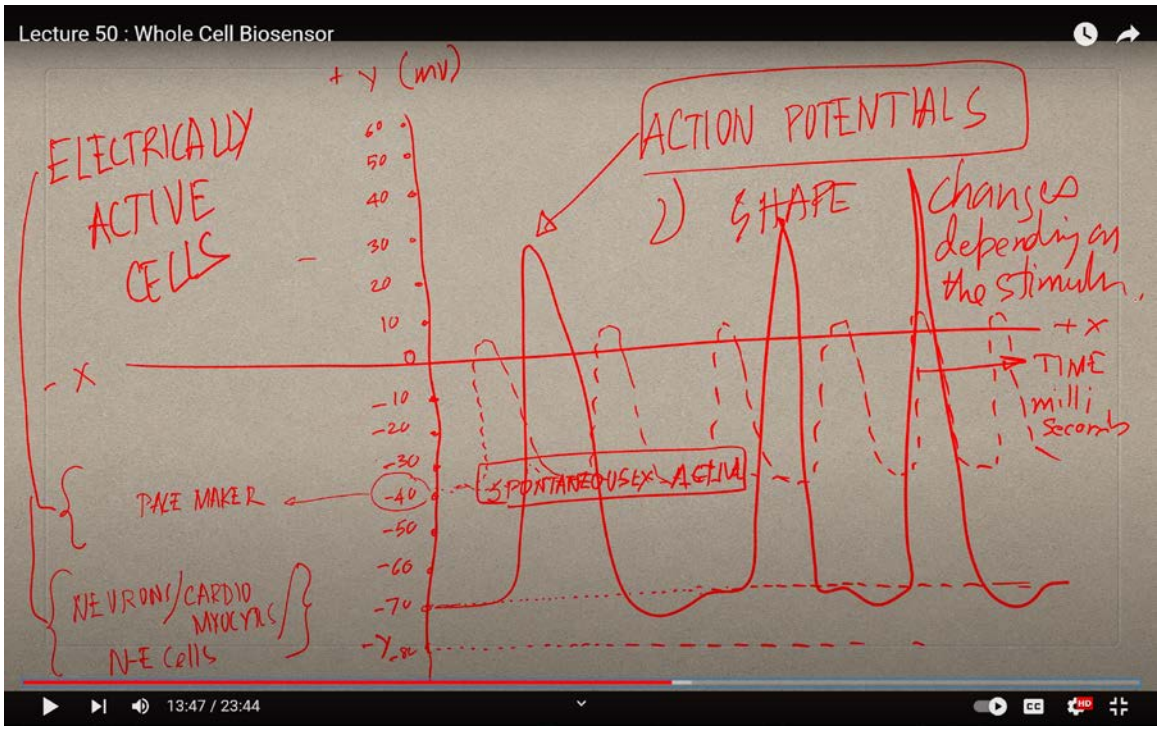

Now, here's something fascinating about pacemaker cells. When I draw their voltage line, it won’t be a straight line; rather, it will display interesting fluctuations. When I describe them as spontaneously active, that’s precisely what I mean! What causes this spontaneous activity and the resulting voltage shift is a topic for future discussions, but for now, let’s focus on the events taking place.

In contrast, the other category of electrically active cells, which respond to specific stimuli, displays a different voltage pattern. These cells exhibit changes, but their response is not spontaneous. When capturing these voltage changes, you'll see fluctuations across their membranes. At times, the voltage overshoots zero, suggesting that the cell is undergoing a significant shift, almost as if it’s in a state of shock, or that the membrane potential has dramatically altered.

As I mentioned earlier, the inside of the cell is typically more negative. So, during these events, the polarity shifts from about -70 millivolts, perhaps rising to +10 millivolts, before returning to its original state. This unique electrical event characterizes the activity within

these cells and underscores their fascinating behavior.

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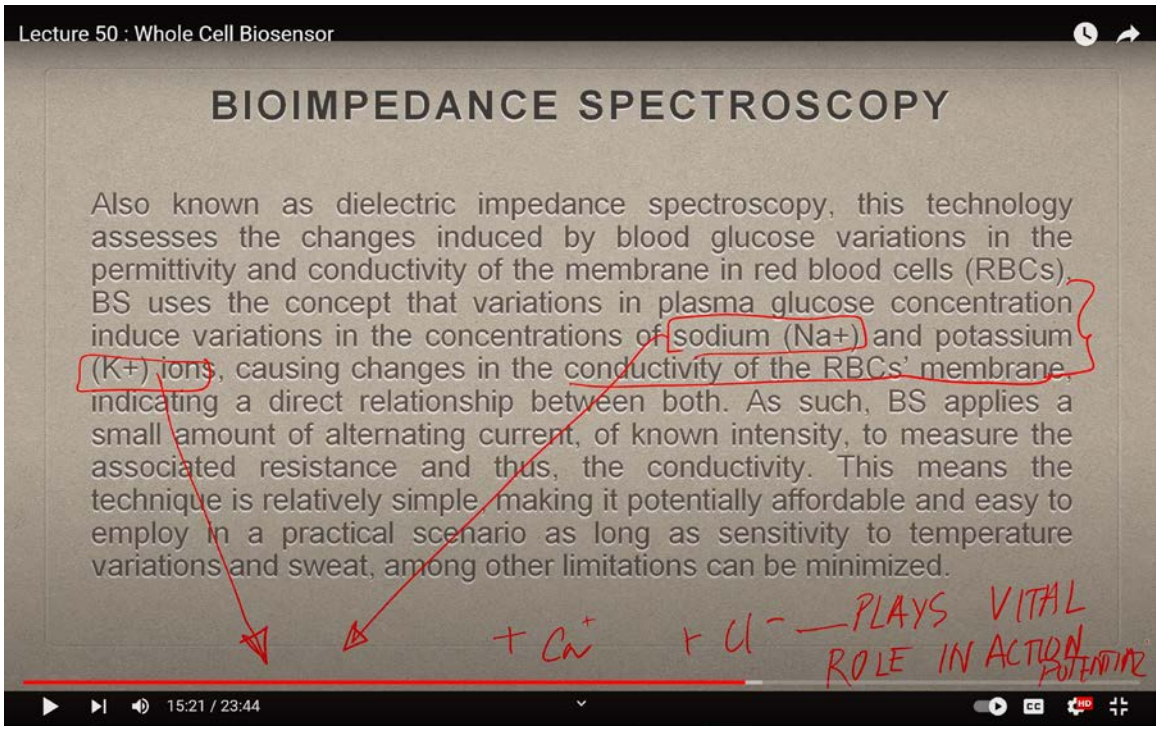

The electrical events and traces you see are famously referred to as "action potentials" in biological literature. These action potentials exhibit distinct frequencies and shapes, and intriguingly, both their frequency and shape vary depending on the type of stimulus applied. But why are these action potentials generated? What are the unique factors that contribute to their characteristics?

To provide you with some context, let's revisit one of the minimally invasive sensors I mentioned earlier. I hinted that we would return to this topic from a different perspective. In the previous class, I showed you a diagram where the anode and cathode were depicted. In that illustration, you can see various molecules, specifically ions, such as sodium ions and chloride ions, without delving into glucose at this moment, as it's not pertinent to our current discussion. Nevertheless, these ions, along with potassium ions, are crucial to our understanding.

Reflecting on our earlier discussions, we explored impedance spectroscopy, where we

examined the role of sodium and potassium ions in altering the conductivity of the red blood cell (RBC) membrane. Together with calcium and chloride, these four ions are vital in generating action potentials, as we discussed in the context of bi-impedance spectroscopy. Later, we also covered their significance in the reverse electrodialysis (RI) technique. Now, we're back to the foundational principles of how these ions function.

So, how do sodium, potassium, chloride, and calcium ions collectively play such a critical role? Let's consider a familiar concept: seawater or ocean water. You're all likely aware that seawater has a very high concentration of sodium chloride (NaCl). It is widely believed that life originally evolved from this saline environment. In conditions of extremely high salinity, only a few life forms can survive, while most terrestrial life forms must adapt to survive. To thrive in such an environment, they developed mechanisms to prevent desiccation caused by the high osmotic pressure from the surrounding water.

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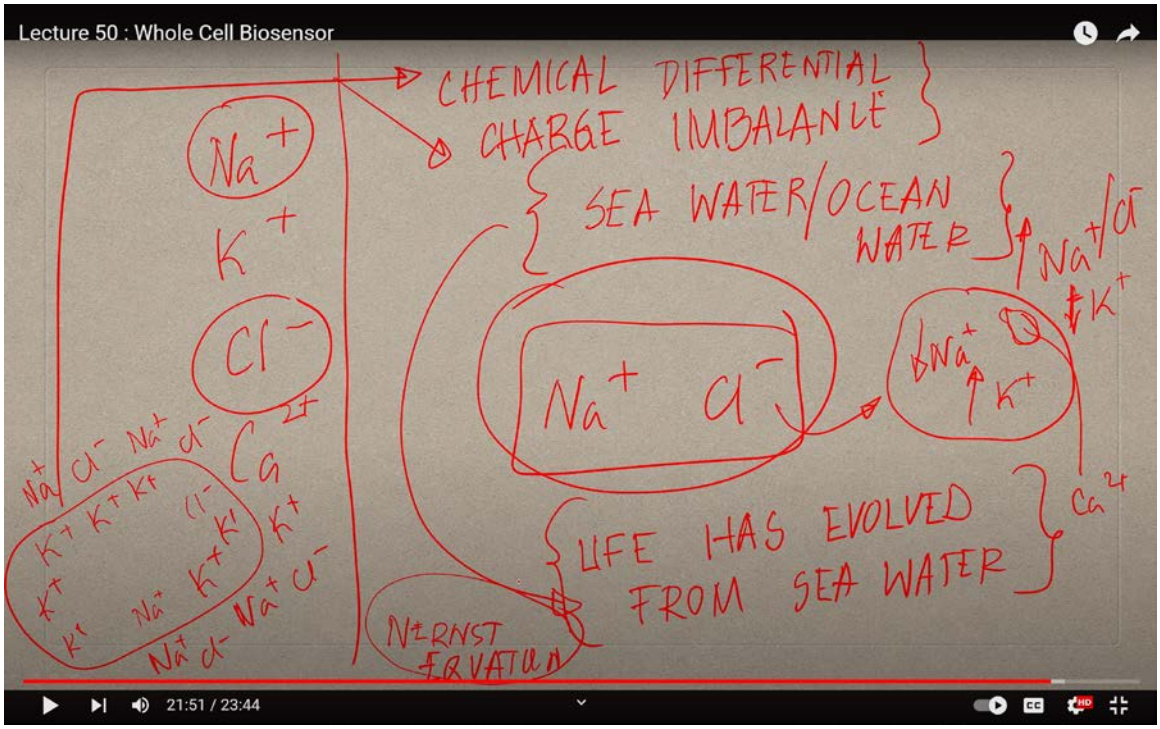

While the exact timeline of when the first cell evolved remains uncertain, whether it was four billion years ago or two billion years ago, or whether it was a microbial cell, we do

know that the first evolved cell created a compartment that allowed for a lower sodium concentration inside compared to the higher concentration outside. In addition, it maintained a higher concentration of potassium inside. Conversely, outside the cell, there is a higher concentration of potassium, while a unique pocket inside the cell prevents calcium from freely moving. This intricate balance of ion concentrations is fundamental to the functioning of action potentials and, by extension, to the very essence of life itself.

Outside the cell, there is a higher concentration of chloride and sodium ions, while the interior of the cell has a lower concentration of both sodium and chloride. When we examine the cell membrane in this context, we see a significant contrast. The extracellular environment is rich in positively charged ions, particularly sodium, whereas the intracellular environment has a lesser amount of sodium and chloride but a greater concentration of potassium ions. Interestingly, the opposite is true outside the cell, where there is less potassium.

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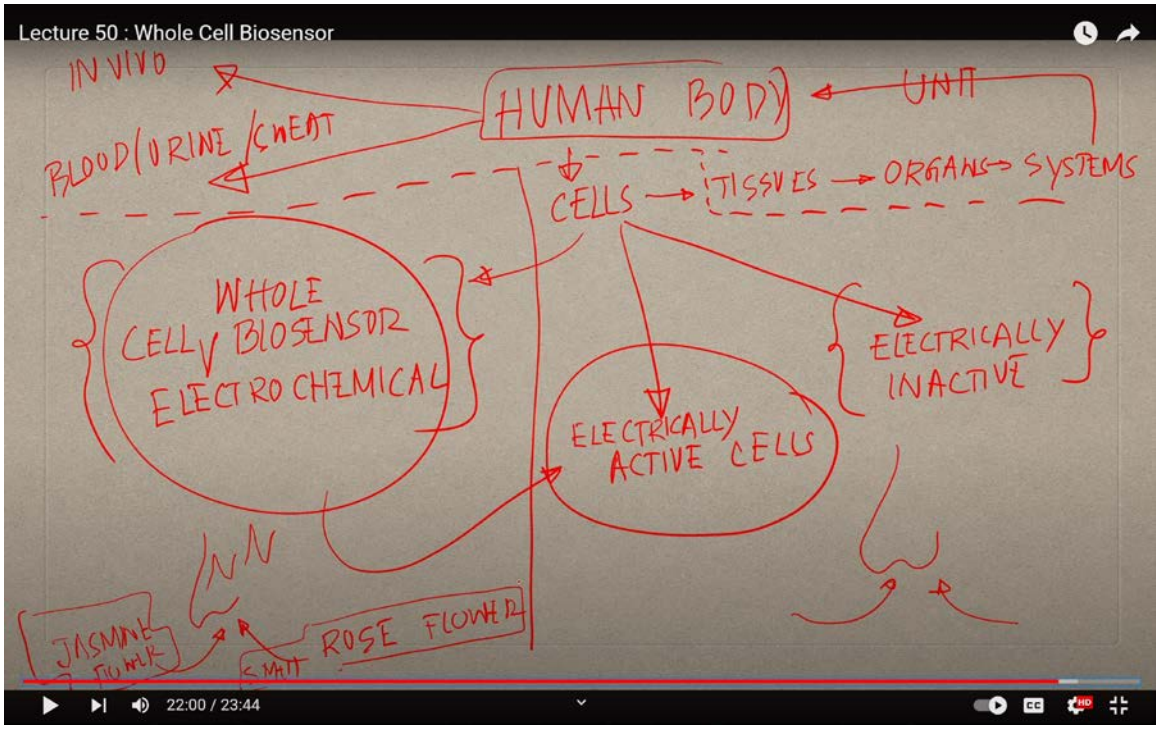

This disparity between sodium and potassium concentrations generates two distinct types

of forces. Firstly, there is a chemical differential: with higher sodium concentration outside and lower sodium concentration inside, one might wonder what happens if these two environments are connected. Naturally, the two levels would strive to reach equilibrium. This situation creates both a chemical imbalance and a charge imbalance. You might ask, "Why is there a charge imbalance?" Essentially, inside the cell, there is less sodium and more potassium, while outside, there is more sodium and less potassium.

When we place an electrode inside the cell compared to one outside, we observe that in every cell of the body, there exists a resting potential of approximately minus 80 millivolts. This indicates a significant potential difference. But the question arises: what determines this electrical potential of -0.1 volts, and why does the cell maintain this specific electrode potential? This inquiry leads us to explore fundamental principles embodied in the Nernst equation. In our next class, we will delve deeply into the Nernst equation, examining the mechanisms behind action potentials and how they can be harnessed for our primary objective: whole-cell biosensors.

This brings us back to our original topic, whole-cell biosensors and electrochemical biosensing. As we conclude this session, I want to emphasize that in our next class, we will explore how action potentials are generated, the significance of the Nernst equation, the roles of ion channels, and the distinctions between voltage-gated and ligand-gated ion channels. We will also discuss various types of gating mechanisms, including voltage gating, ligand gating, light-sensitive channels, and vibration-sensitive channels, which are collectively known as mechanosensitive channels. All of these components are integral to the electrically active elements of our bodies and hold tremendous potential for advancing the next generation of biosensor technologies.

So, with that, I will close today’s class. In our upcoming session, we will continue our exploration into whole-cell biosensing and how these innovations are paving the way for groundbreaking human-on-a-chip systems, representing the next frontier in biomedical technology. Thank you!