Design for Biosecurity

Prof. Mainak Das

Department of Design

Indian Institute of Technology, Kanpur

Lecture 12

Components for Designing Biosensors

Welcome back to the twelfth lecture in this series. We've now entered the third week, and as I mentioned in our previous classes, we will be exploring both pathogens and sensors concurrently. While we will dive into the intricate details of sensor design later, at this point, our focus will be on establishing a solid understanding of the fundamentals.

In our last session, we covered the basics of the causative agent of anthrax, how it spreads and how it enters the human body through cutaneous or surface contact, inhalation, or ingestion of contaminated substances. We also discussed how individuals who use certain drugs might be exposed to anthrax, a phenomenon primarily observed in Europe but not yet in the United States.

Additionally, we touched upon an emerging anthrax situation affecting workers in the welding, steel, and iron industries. We also reviewed the 2001 anthrax attack in the United States, discussing how it was orchestrated and how the investigation concluded in 2010.

Today, we'll shift our focus to the basic sensor modules used for detecting anthrax. To start, let's consider what anthrax looks like. Anthrax exists in two forms: vegetative cells and spores. The biggest challenge lies in detecting the spores, as vegetative cells, being in a growth phase, secrete numerous metabolites and present various active surface molecules. These structural and functional features make vegetative cells easier to detect.

Spores, on the other hand, are in a dormant state, exhibiting minimal surface expression. They essentially remain inert, silently sitting there without revealing much of their presence. This dormancy makes them difficult to detect, as you need to identify signals that are extremely unique to these spores. Another challenge is that while trying to detect

spores, you must avoid crushing them, as doing so could increase the risk of spreading contamination.

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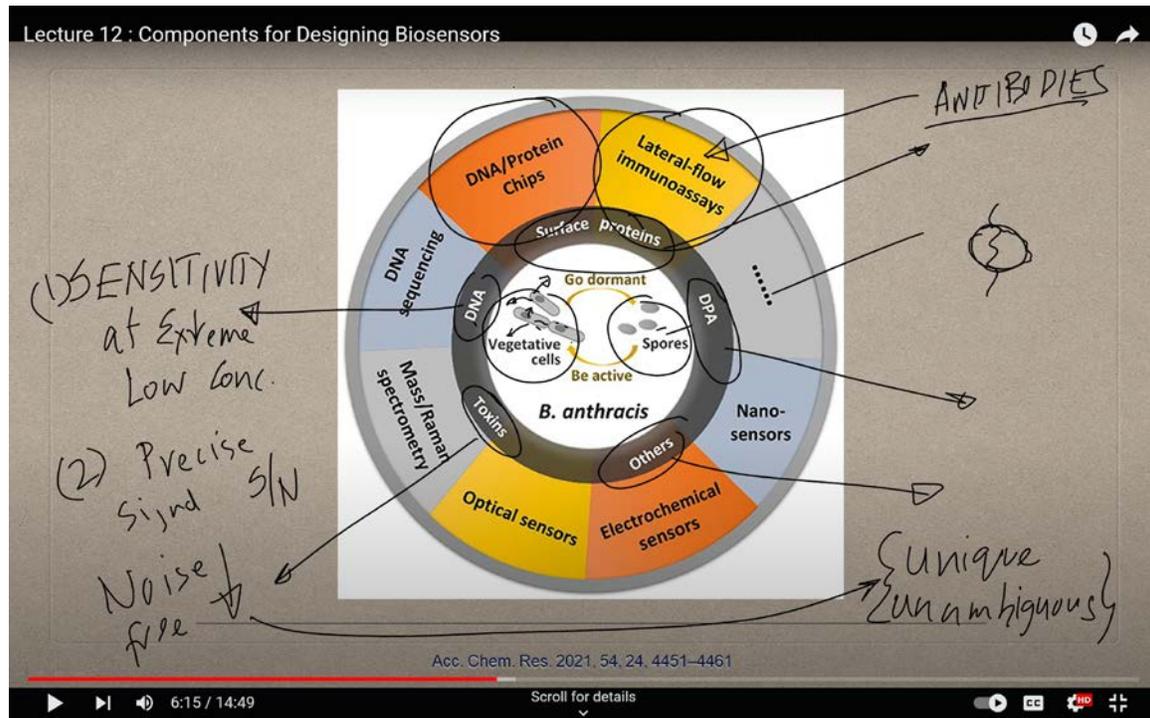
So, what are the target elements we're focusing on? One key target is the surface proteins, looking for signature proteins on the spore's surface, as well as other markers like dipicolinic acid (DPA), DNA, toxins, or any other minor features that have yet to be fully understood. These elements may be present in very low concentrations, making detection even more challenging.

To effectively detect these spores, we need an extremely sensitive sensor capable of identifying nanoscopic levels of toxins, DNA, surface proteins, DPA, and other markers. Most biosensors are built on fundamental principles that emphasize high sensitivity at extremely low concentrations. Additionally, precision in the signal is crucial, the signal-to-noise ratio must be very low, ideally creating a near noise-free system. The signal detected should be both unique and unambiguous, ensuring that we accurately identify the presence of anthrax spores.

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In summary, designing biosensors for anthrax detection involves overcoming significant challenges, particularly in detecting the dormant spore form. The sensors must be incredibly sensitive and precise, able to detect minute quantities of specific markers without risking contamination spread. As we continue, we'll explore the specific types of sensors developed for this purpose and how they function in real-world scenarios.

Let's explore the various sensors in use or under development. One prominent type is the lateral flow immunoassay, which primarily involves antibodies. These antibodies are specifically developed to target Bacillus anthracis. In any immunoassay, the goal is to identify antibody molecules that react to the pathogen. Additionally, we have DNA or protein chips, which are integral to the detection process.

To better understand this, let's revisit an earlier concept where we discussed the DNA and RNA structures, along with plasmids and various proteins like the lethal factor and extracellular polyglutamate (PGA). These are key target molecules. Returning to our current slide, we see that these elements are pivotal in sensor design.

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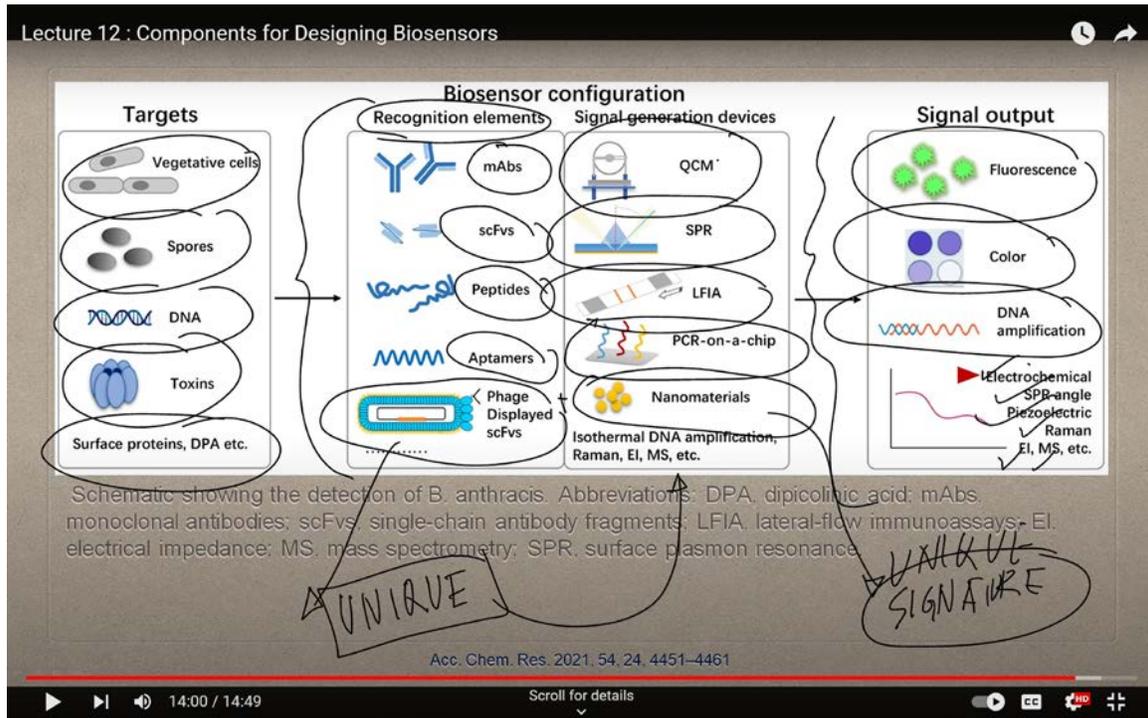
In the context of DNA or protein chips, DNA sequencing plays a crucial role. It involves matching DNA sequences to identify specific patterns, aiding in the detection process. Beyond this, we employ mass spectrometry, Raman spectrometry, and other spectroscopy techniques, primarily to detect toxins and other molecules. Optical sensors also play a significant role by utilizing fluorescent probes or other light-dependent mechanisms to produce unique signals.

Electrochemical sensors are another critical tool. These sensors detect surface proteins, DNA, toxins, and other target molecules by capturing their electrochemical signatures. But what exactly is an electrochemical signature? It refers to the transfer of electrons, either the donation of electrons by a molecule to a receiver or the acceptance of electrons from a receiver. By quantifying this electron transfer, we extract an electrical signature from the chemical reaction. This process can also work in reverse: an electrical impulse can alter the chemical nature of a molecule, and that change can be recorded as a chemical signature.

For instance, if a toxin donates an electron, the sensor captures that event; conversely, if the toxin accepts an electron and is reduced, that signature is also captured. The key is that these signatures must be unique, occurring at specific potentials or voltages.

We also have nanosensors, which aren't as exotic as they may sound. They are essentially various types of sensors that incorporate nanoengineering tools or nanomaterials during their manufacturing process.

Thus, the sensors we have discussed include lateral flow immunoassays, DNA protein chips, DNA sequencing methods, mass spectrometry, Raman spectroscopy, optical sensors, electrochemical sensors, and nanosensors.

Now, let's delve deeper into the targets these sensors are designed to detect: vegetative cells, spores, DNA, toxins, surface proteins, DPA, and more. The recognition elements for these targets include monoclonal antibodies (or antibody fragments), peptides, aptamers, and phage display techniques. We will explore each of these elements in detail, so rest assured, we will cover everything comprehensively.

Let me outline the basic configuration of a biosensor and how it is designed to identify specific elements. The goal here is to recognize these elements because they produce unique signatures. It's crucial to identify which elements will give you these distinct signatures, as these are the molecules that will set off a unique signal.

To study and detect these unique signatures, we rely on specific methodologies. One of the first techniques we'll discuss is QCM, or quartz crystal microbalance. Following that, we'll explore SPR, or surface plasmon resonance, and LFIA, which stands for lateral flow immunoassays. Another important technique is PCR on a chip, which involves polymerase chain reaction technology miniaturized for chip-based applications. Additionally, various nanomaterials are used to conjugate with recognition elements, further enhancing the detection and identification process by providing unique signatures specific to different situations.

As for the signal output, we have various possibilities. The recognition element interacts with a signal generation device, and the output might manifest as a fluorescent signal, a

color change, DNA amplification, or an electrochemical response. Other potential outputs include changes in SPR angle, piezoelectric effects, Raman shifts, and mass spectrometry signals (EIMS), among others. These outputs serve as the signature responses that indicate the presence of the target molecules.

When designing biosensors for biosecurity, it's imperative to have a deep understanding of biology, particularly the molecular events that lead to the generation of different recognition elements. A thorough knowledge of biochemistry and microbiology is essential. But that's just the beginning, understanding the basic physics behind the devices used is equally important. Techniques like quartz crystal microbalance, surface plasmon resonance, and even the lateral flow PCR processes are all fundamentally physical in nature. Therefore, one must grasp the physical principles underlying these devices.

In addition to understanding the devices themselves, it's crucial to know how to process the signals they produce. Signals will be generated, but discerning between noise and the actual signal is key. You must be adept at filtering out background noise to isolate the relevant signal for your specific case study. Without this ability, you may have all the tools at your disposal, but you won't be able to make meaningful use of them. It's not just about having the equipment; it's about interpreting the data correctly and extracting valuable information from these tools.

Next, we'll discuss the practical applications, starting with a detailed look at quartz crystal microbalance.