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BIOSENSORS ON IMPLANTS

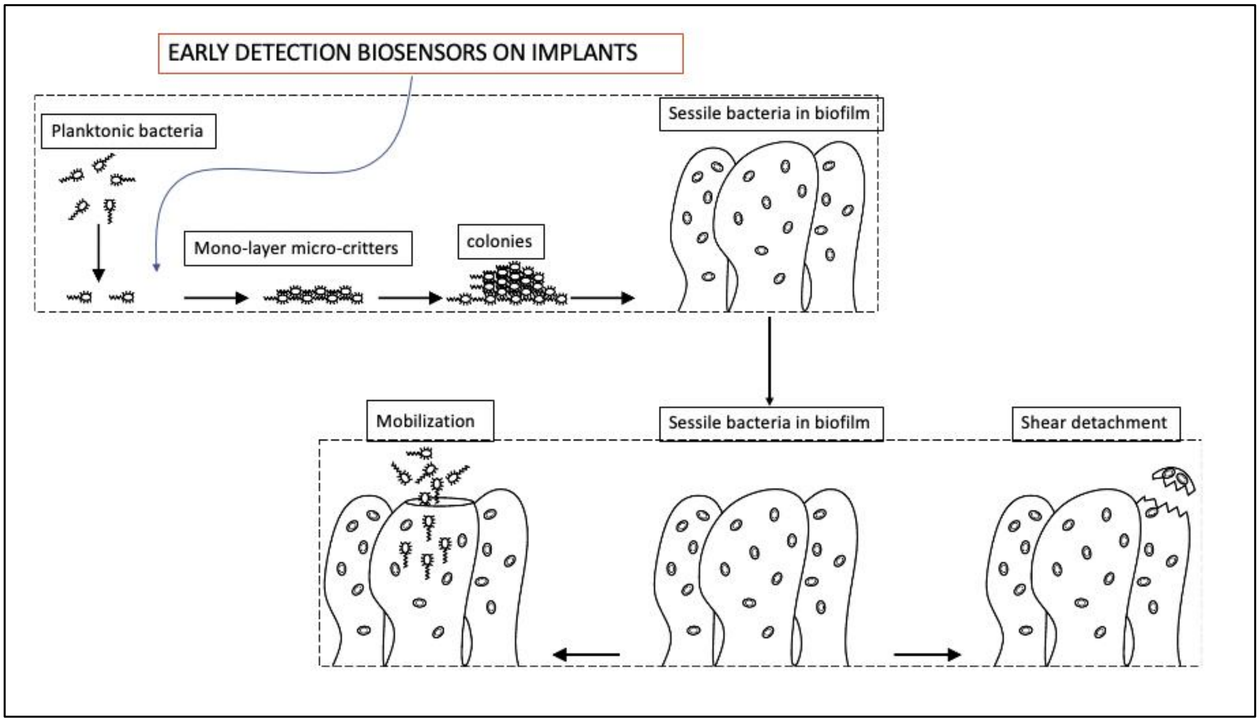
PRE-INFECTION DETECTION

Orthopedic infections result from bacteria that differentiate, aggregate, and attach to implants with a hydrated polymeric matrix that forms the biofilm. The biofilm can be considered as a structured organized community of bacterial cells with functional heterogeneity. Different gene expression produces varieties of specialized bacterial cells that provide different functions within the community. At various stages of infection, different types of planktonic cells can perform different functions such as float, attach to surfaces, form single monolayer micro-critters, and twitch to form microcolonies. After attachment, synthesis of extracellular polysaccharide matrix is initiated to form sessile bacteria within the biofilm. Biofilm communities then show a programmed pattern of detachment and release of planktonic cells that spread and multiply, expanding the infection. Additionally, sessile bacteria housed within the biofilm exhibit different phenotypes that are resistant to antibiotics since they can exist in a starved state.

Therefore, medical device infections occur in a slow, progressive, and staged fashion, where a few hundred planktonic bacterial cells, that may initially present as “scouts”, eventually develop into hundreds of billions of bacterial cells. This happens through a very sophisticated hormonal communication system and differentiation of various specialized cells. In this manner a few hundred undetected *scouts* turn into and invading *army of bacterial cells* that eventually colonize the implant and bone.

Current art only allows detection of orthopedic infections at a late stage when colonization has already occurred.

There is a need for early detection of infections. We believe incorporation of biosensors on implants allows detection of a clinical infection <u>before it ever occurs</u>. This can be regarded as “pre-infection” detection. This is similar in concept to the “Pre-cogs” of the movie Minority Report, who could foresee “premediated murders” before they ever occurred. In a similar fashion, biosensors on implants can detect clinical infections before they ever occur.

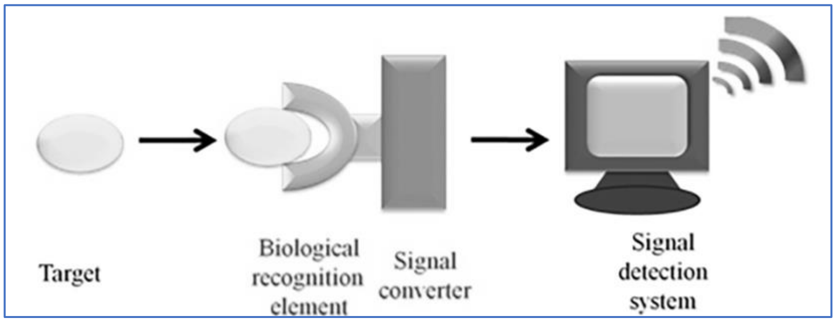


Estimated cost of treating a *pre-infection* may simply be the cost of one week of oral antibiotics. Estimated cost of treating cost of treating an infection after colonization maybe as high as $200,000.

Biosensors on implants provide a *Prosthetic Infection-Point of Care* (PI- POC) diagnostic system, which allows continuous monitoring of biologically and physically relevant parameters, directly at the actual site of contamination.

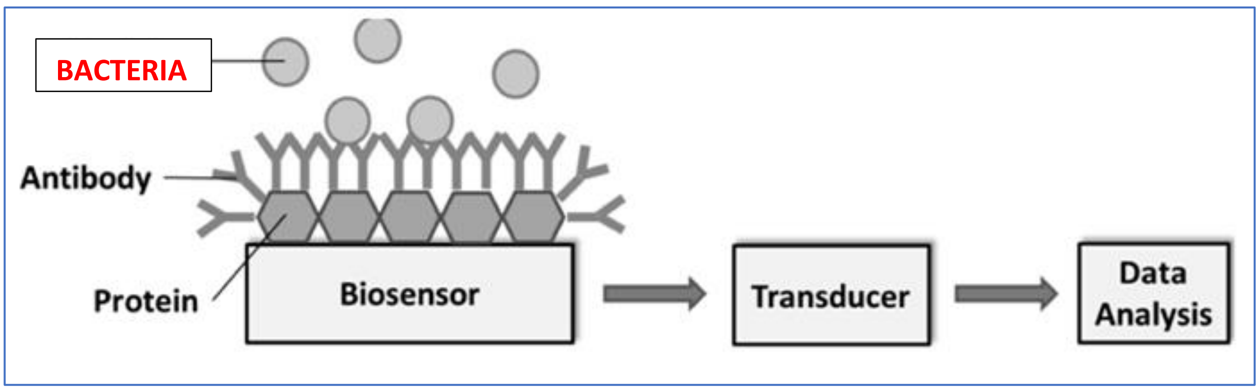
A biosensor includes two components: a bioreceptor and a transducer. In its most basic form, the bioreceptor is a biomolecule that recognizes a target analyte, and a transducer converts the recognition event into a measurable signal. A uniqueness of the biosensor includes that these two components are integrated into a single sensor (unit), which measures the target analyte without use of a reagent. A simplicity and a speed of measurement requiring no specialized laboratory skills are some advantages of a biosensor.

Biosensor research has experienced explosive growth over the last two decades. A modern biosensor is an analytical device that converts a biological response into a quantifiable processable signal. Biosensors are employed in disease monitoring, drug discovery, detection of pollutants and disease-causing microorganisms.



Bioreceptors are analyte specific, passive, continuous and direct systems. They are small, self-sustained, self-contained, nonstop in situ monitoring units that automatically send SOS signals when a relevant analyte is detected.

The analytes of interest may be the bacteria itself such as MRSA, Bacterial metabolites such as leukocyte esterase, alpha defensing, nitrates, and WBCs. They could also include metal debris such as cobalt, chromium, and titanium.



Traditional sensors used on implants, on the other hand, are bulky, require a battery, printed circuit boards, antennas, communications links, and data collection units. These characteristics make the traditional sensors less efficient and more difficult to incorporate within implants.