PhD Defense by Opeyemi Ajayi

Title: Impact of cell substratum adhesion pattern and cluster spatial distribution on the development of Staphylococcus aureus biofilm under physiologically-relevant shear rates.

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Abstract:
Bacterial cells, in nature, prefer to exist as a surface-attached coalescent community of slime-encased cells known as biofilms. This biofilm-forming existence offers several advantages to the cells, including evasion of host immune response, resistance to antimicrobials and antibiotics, communal expression of metabolites, and overall increased survivability in unfavorable environmental conditions. Biofilm formation has been observed for several species of bacteria across multiple scientific disciplines and affecting a wide variety of industries including the food industry, waste treatment, and healthcare. In healthcare settings, S. aureus is a major etiological agent of biofilm-based infections in humans. Furthermore, the hydrodynamic environment of the cardiovascular system complicates the eradication of biofilm-based infection due to metastasis of eroded cells to multiple infection sites. Therefore, remediation efforts of staphylococcal infections are aimed at the prevention and disruption of biofilm development. Regardless of infection site, pathogenesis is initiated by adhesion of planktonic cells to host tissue or implanted biomaterials, culminating in the formation of mature biofilm that can subsequently seed planktonic cells. In S. aureus the transition of adhered bacterial cells into biofilm depends on cellular production and detection of a signal peptide molecule called auto-inducer peptide (AIP). Biofilm development and virulence are regulated by the sensing mechanism of the cells to their local AIP concentration. With this in mind, I hypothesized that biofilm development may be inhibited by specifying initial parameters within the biofilm environment that influence local AIP concentrations; these parameters include fluid shear stress as well as the geometric features of initial cell-substrate adhesion, including distance between adhesion sites and the area of the adhesion sites on the substrate. The broad objectives of this study were to characterize and quantify the morphology of S. aureus biofilms under fluid flow that were initiated on substrates with micro patterned cell-adhesion sites of controlled spacing, size, and total area. First, the underlying mechanism of biofilm-dependent growth was predicted via in silico simulation of AIP concentration. Then laboratory experiments demonstrated that: 1) increased spacing between micro colonies correlated with diminished S. aureus biofilm development; and 2) inhibition of biofilm development was greater when exposed to increased fluid shear stress. These findings unveil new strategies to potentially slow down or prevent biofilm-based infections in the human cardiovascular system.