Synthesis of quaternary ammonium coated surfaces

Roest, Steven

Chapter 1

General introduction and aim of this thesis

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Life expectancy, especially in Western societies, is increasing and with an aging population the need for biomaterial implants and devices to maintain quality of life at an acceptable level is growing as well. Various biomaterials are used as implants or devices including ceramics, metals and polymers. As an example, nowadays estimates of surgeons performance include one million total hip replacements and a quarter of a million knee replacements every year.[1] The number one cause of failure of biomaterial implants and devices is biomaterial-associated infection (BAI). Failure rates depend strongly on the implant site, but are generally in the range of 0.5 – 5%.[2] Besides from being costly[3] BAIs have severe clinical consequences. For orthopedic and plastic surgery, BAI may result in disabilities or psychological trauma.[4] In the case cardiovascular implants, BAI even has a high mortality risk.[5]

BAI starts off with the initial bacterial adhesion to the biomaterial implant surface, after which adhering bacteria grow into a biofilm (Figure 1.1). A biofilm is a slimy layer that holds bacteria together in a complex mixture of macromolecules including exopolysaccharides, proteins and DNA.[6-7] Importantly, with respect to the medical treatment, these encaged bacteria are able to withstand host immune responses and are much less susceptible to antibiotics than their planktonic counterparts.[8] Once a biofilm is formed, treatments often fail and the sole solution is usually to remove the implant, cure the patient and replace the implant after the patient is recovered.

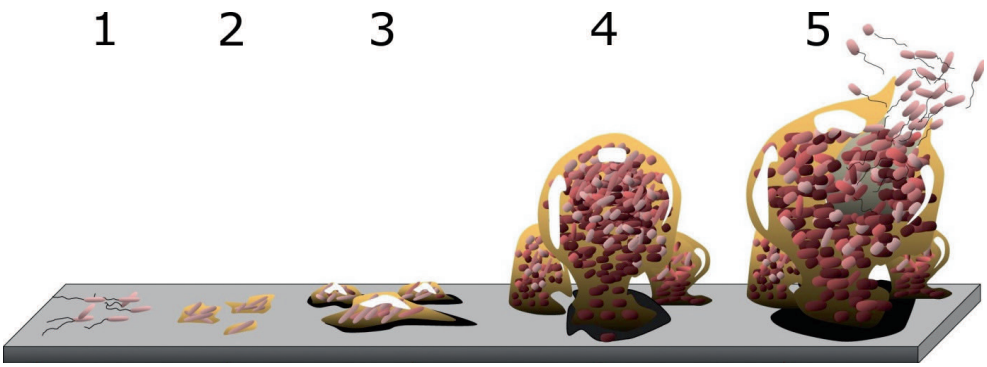

Figure 1.1 Development of a biofilm. Stage 1: Initial adhesion. Stage 2: Irreversible attachment and colonization. Stage 3: Accumulation. Stage 4: Maturation. Stage 5: Dispersal. Figure adapted from Monroe[9] and reproduced with permission.

Considering the recalcitrance of BAI to treatment, including antibiotic treatments, a frequently taken approach is to chemically make infection-resistant materials or coatings to prevent the development of BAI. Therefore, the aim of this thesis is to explore the preparation of a coating that kills bacteria upon contact and to evaluate *in vitro* the resistance of such coatings against bacterial adhesion and biofilm formation. Evaluations will not only involve the ability of the coatings to inhibit biofilm formation, but also encompass a study on phagocytosis of contact-killed bacteria, as the development of a layer of dead bacteria may interfere with the contact-killing abilities of such coatings. Bacterial contact-killing coatings will be prepared by tethering quaternary-ammonium-compounds (quats) to a substrate covered by a hyperbranched polymer.

Quats are potent cationic antimicrobials used in everyday consumer products, like deodorants, contact lens solutions and mouth- and hair-rinse products, as well as in numerous industrial processes.[10] Antimicrobial action of quats starts when they approach bacterial cell surfaces close enough to interact through hydrophobic and electrostatic attractions[11-13] between positively charged quat-molecules and negatively charged moieties of bacterial cell surfaces.[14] Upon their adsorption, quat-molecules replace Ca^{2+} and Mg^{2+} ions from the cytoplasmic membrane to maintain charge neutrality in the membrane. This ion exchange destabilizes the intracellular matrix of a bacterium,[15] as the hydrophobic tail interdigitates into the hydrophobic bacterial membrane over the entire surface area of a bacterium,[16-18] causing disruption of the proton motive force and leakage of intracellular fluid containing essential molecules. Both processes result in bacterial cell death.[19] Also when immobilized on a surface, quats possess the potential to kill adhering bacteria, but this mechanism is largely unexplained.

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