average of two to three days, increase hospital expenditure by approximately $1 billion in the US (Behlau and Gilmore 2008), cause approximately 100,000 deaths per annum in US hospitals and an annual 40,000 deaths in European hospitals and, furthermore, have unquantifiable effects on patient morbidity (Francolini and Donelli 2010).

Biomaterial-associated infections are characterized by their recalcitrance to conventional treatments due to the nature of bacterial growth within highly regulated sessile microbial communities encased in self-produced amorphous matrix substances, known as biofilms (Donlan and Costerton 2002) (Fig. 1). Implant removal and revision surgeries are often required, causing additional expense for the healthcare provider, and increased patient morbidity and potential mortality (McCann et al. 2008).

The device surface itself often lends to an increased susceptibility to microbial colonization as a consequence of factors such as surface energy, hydrophilicity, roughness and chemistry. Modification of these properties to render surfaces less attractive for bacterial adherence therefore constitutes a rational method to prevent infection, and can be achieved through coating with hydrogels such as polyethylene oxide or polyethylene glycol (Kaper et al. 2003; Kingshott et al. 2003). The antimicrobial efficacy of these 'passive' coatings is, however, limited and dependent on the bacterial challenge. Alternatively, drug-eluting device coatings, developed to combat infection through the localized release of bioactive agents and the subsequent generation of high concentrations of drug directly at the biomaterial-tissue interface, thus mitigating concerns over systemic toxicity (Campoccia et al. 2006), have become one of the most widely researched strategies to prevent device-associated infection (Zilberman and Elsner 2008). Antibiotic use is associated with issues such as the possible emergence of super-infections, promotion of bacterial resistance, and changes in the local microbiological flora (Goodman et al. 2013), therefore the employment of non-antibiotic agents is preferred. Release kinetics must be carefully controlled to achieve therapeutically-active concentrations of drug when required and prevent premature exhaustion of the active agent (Goodman et al. 2013).

Up to 25% of bloodstream infections reported in intensive care units are a consequence of bacterial adherence to central venous catheters, thus highlighting the

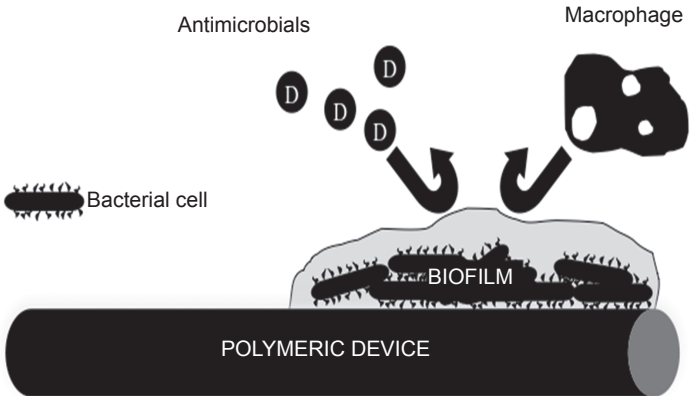

Fig. 1. Biofilm-associated bacterial resistance to the innate immune system and administered antimicrobials.