

PREVENTING BACTERIAL SURFACE CONTAMINATION AND INFECTION VIA MATHEMATICAL MODELLING

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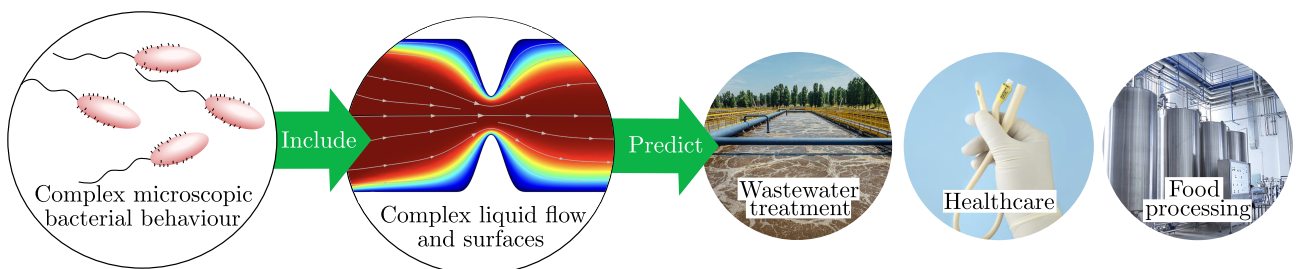
Motivation: Dense surface-associated colonies of bacteria known as biofilms cause the fouling of products in food processing, damage the efficacy of wastewater treatment and are the cause of nearly half of all healthcare-associated infections. Biofilms have been shown to promote antibiotic resistance; therefore infections in implanted medical devices such as catheters and intravenous lines are extremely difficult to treat clinically, costing the NHS an estimated £1bn/yr. Biofilm prevention costs are similarly high in other industries; UK businesses spend £1bn/yr on wastewater management and decontamination processes during food processing cost an estimated \$10.2bn/yr globally. The prevention of biofilm formation requires understanding how bacteria can adhere to surfaces and proliferate.

Problem: A key challenge for predicting biofilm formation is to determine how changes to bacteria behaviours and dynamics alter their ability to adhere to surfaces. Such microscopic changes could be caused by altered motility owing to a mutation, or by an altered environment owing to the addition of decontamination products. In this work, we address the problem of controlling bacterial attachment by building a mathematical model, capable of exploring biofilm formation and prevention methods virtually. Existing continuum models, which track bacteria density, often approximate bacteria as passive particles. However, bacteria exhibit complex behaviour close to walls including acceleration or reorientation and can even migrate upstream along walls, all of which quantitatively alter their adhesion. Neglecting this complexity means these models incorrectly predict biofilm location and formation rates. Models which do account for the complexity of bacteria, known as active fluid models, are extremely computationally costly to use, as they require the tracking of not only bacterial density but also further metrics such as bacterial orientation and any variation in the transporting flow.

Method: We have developed a novel mathematical model that describes the flow of dilute bacterial suspensions in large-scale fluid systems, systematically linking microscopic bacterial surface interactions to adhesion rate and location. We first use perturbation theory to analyse how bacteria are transported in large-scale industrial systems, which are characterised by large, relatively fast, flows in pipes and tanks. We then use tools from classical mathematical boundary layer theory to combine these flow mechanics with relevant microscopic bacteria behaviours to create a reduced model for bacterial adhesion to walls. This reduced model can be used at a fraction of the computational cost of existing active fluid models, while also incorporating more realistic bacteria dynamics. We apply our novel reduced model to the case of bacterial adhesion to a flat plate to calculate how two key aspects of bacterial behaviour - motility and hydrodynamic interaction with boundaries - alter their adhesion.

Achievements: We have demonstrated that bacterial motility leads to enhanced adhesion of bacteria to surfaces, with the most enhancement occurring for spherical bacteria compared to rod-shaped or ellipsoidal bacteria. We have further demonstrated that bacterial motility leads to a hydrodynamic attraction to surfaces and the adhesion of bacteria at an even higher rate. We have derived fundamental scalings for how these adhesion rates depend on the distance from the source of bacteria, validating these scalings against numerical simulations of individual bacteria.

Impact: Our work provides both a new advance in mathematical modelling, as well as quantitative predictions which can be easily interpreted and implemented by manufacturers to guide the design of antimicrobial medical devices, reduce fouling during food processing and increase the efficacy of wastewater treatment, with potential impacts on millions of people in the UK and worldwide.



Schematic of the approach of our mathematical model and the sectors of UK industry which it impacts.