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Immersed Boundary Approach to Biofilm Spread on Surfaces

Ana Carpio[1,*] and Rafael González-Albaladejo[1]

[1] *Departamento de Matemática Aplicada, Universidad Complutense, 28040 Madrid, Spain.*

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Abstract. We propose a computational model to study the growth and spread of bacterial biofilms on interfaces, as well as the action of antibiotics on them. Bacterial membranes are represented by boundaries immersed in a fluid matrix and subject to interaction forces. Growth, division and death of bacterial cells follow dynamic energy budget rules, in response to variations in environmental concentrations of nutrients, toxicants and substances released by the cells. In this way, we create, destroy and enlarge boundaries, either spherical or rod-like. Appropriate forces represent details of the interaction between cells, and the interaction with the environment. We can investigate geometrical arrangements and the formation of porous structures. Numerical simulations illustrate the evolution of top views and diametral slices of small biofilm seeds, as well as the action of antibiotics. We show that cocktails of antibiotics targeting active and dormant cells can entirely eradicate a biofilm.

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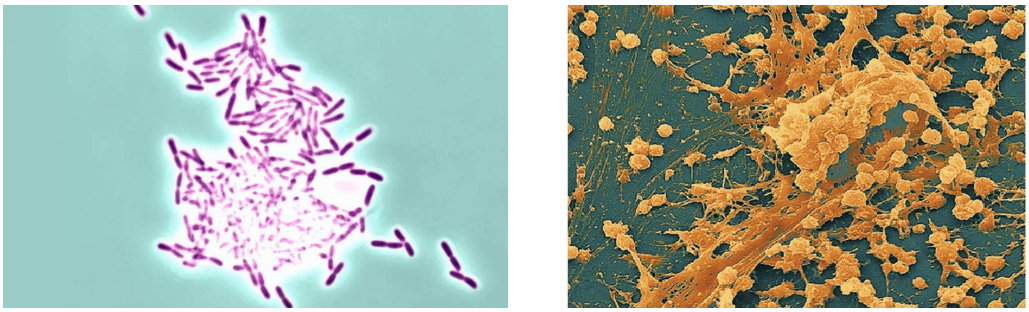
Key words: Hybrid multiscale models, immersed boundary methods, dynamic energy budget models, bacterial biofilm, antibiotic resistance.

1 Introduction

Biofilms are formed by bacteria glued together by a self-produced polymeric matrix and attached to a moist surface [1]. The polymeric envelop makes biofilms extremely resistant to antibiotics, disinfectants and chemical or mechanical aggressions [2]. Experiments reveal that their structure varies according to environmental conditions. When they grow in flows [3,4,6,7], we see scattered bacteria immersed in large chunks of polymer. When

*Corresponding author. *Email addresses:* ana_carpio@mat.ucm.es (A. Carpio), rafael09@ucm.es (R. González-Albaladejo)



(a) (b)

Figure 1: Experimental views of incipient biofilms on surfaces. Bacteria plus polymeric slime for (a) rod-like bacteria (Courtesy of Professor Vernita Gordon, University of Texas at Austin [11]) and (b) spherical bacteria (reprinted from [12]).

they form on interfaces with air or tissue, volume fractions of polymer are very small [8–10] and biofilms resemble aggregates of spherical or rod-like particles, see Fig. 1 for a view of very early stages. As they mature, three dimensional sheets are formed, see Fig. 2.

Modeling bacterial growth in the biofilm habitat is a complex task due to the need to couple cellular, mechanical and chemical processes acting on different times scales. Many approaches have been proposed, ranging from purely continuous models [8] to agent based descriptions [4–7, 9, 10] and hybrid models combining both [13, 14]. Complexity increases when we aim to take bacterial geometry into account, issue that we intend to address here borrowing ideas from immersed boundary (IB) methods [22]. These methods have already been adapted to simulate different aspects of biofilms in flows, such as finger deformation [7], attachment of floating bacteria [15], and viscoelastic behavior [16]. Cell growth and division were addressed by removing the incompressibility constraint on the surrounding flow and including 'ad hoc' inner sources [17]. Recent extensions to multicellular growth consider closely packed deformable cells attached to each other [18, 19]. Biofilms growing on interfaces differ from multicellular tissues in several respects. First, bacterial shapes are more rigid, usually spheres or rods. Second, bacteria remain at a short, but variable, distance of each other. To describe their evolution we need to take into account at least:

- Bacterial activities, such as growth, division and death in response to the environmental conditions.
- Chemical processes, such as diffusion of oxygen, nutrients, and toxicants (waste products, antibiotics) and production of autoinducers.
- Mechanical processes, such as the interaction of the fluid with the immersed structures and the interaction between the structures themselves.