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A simulation model of biofilms with autonomous cells: I. Analysis of a two-dimensional version

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Abstract

We introduce a single-cell based simulation model of biofilm growth. Each microbial cell is modelled as an autonomous agent whose behavior is controlled by thermodynamic parameters, mechanical properties, physiological rules and environmental conditions. In the two-dimensional version presented here, a cell is represented by a closed chain of self-avoiding beads linked together using the bond fluctuation algorithm. The cell is thus controlled both by the rigidity of its membrane and a pressure difference. The model is complemented by key features such as the explicit presence of nutrient diffusion and flow, the processes of cell-division and cell-death, and the attractive interactions between the cell and the surface on which the colony grows. Tuning the parameters of the model can lead to the growth and maturation of various types of biofilms. In this first article, we describe the main properties of a two-dimensional version of the model, and we discuss the extension to three dimensions.

Keywords: Biofilm; Bacteria; Monte Carlo simulation

1. Introduction

Biofilms are a common form of microbial community associated with surfaces in contact with liquids. For example, bacterial biofilms can be found growing in water pipes, on surgical instruments or on tooth surfaces. A distinguishing characteristic of biofilms is the presence of extracellular polymeric substances (EPS) in which the cells are embedded.

Mathematical models have been used for the last three decades in order to improve our understanding of the growth and behavior of microbial biofilms. Early models represented biofilms as spatially homogeneous steady-state films containing a single species [1]. Additional features, such as multiple types of nutrients, mixed microbial species and variable biofilm density were later included [2–4]. However, most of these models assumed a predetermined biofilm morphology. Consequently, they were unable to account for the experimentally observed 3D structural heterogeneity of the colonies. Furthermore, they made several assumptions about biofilm development. For instance, the direction of biomass displacement was taken to be

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perpendicular to the substratum, while cell detachment was determined by an arbitrary uniform removal rate or velocity. Such simple models are generally suitable for representing the aggregate activity of a biofilm on many square millimeters of surface area.

In recent years, several biofilm numerical models which deal with smaller scales have been proposed. They can be divided into two classes of models, namely the continuum models and the discrete models. The continuum models use a mean-field-type of approach [5–7]. Most of the discrete models utilize methods, such as cellular automata, to simulate the rules that govern the lives of microbial cells. These coarse-grained models use a set of local rules governing the growth of the biomass, the displacement of the growing biomass as well as its detachment. These methods produce realistic, structurally heterogeneous biofilms [8–15] but a major drawback is that they rely on speculative rules which control the global biomass development [16] instead of the cell themselves. Another sub-class of discrete models are the so-called individual-based (or particle-based) models [17–19]. The latter approaches have some similarity with our model in that they consider cells as individual agents.

Our aim is to design and implement a new Monte Carlo model based on the life of autonomous cells in order to investigate the resulting bacterial populations (biofilms) static and dynamic characteristics. One of the features of our model is that nutrient mass transfer is implemented explicitly, i.e., we do not need to calculate the nutrient concentration field. Note that such a feature is also present in some other biofilm models [15]. However, we are aware of the fact that a complete integration of subcellular processes in our model (e.g., bacteria biochemistry) will be not only difficult but also rather useless; moreover, these complex biochemical subcellular processes are species-dependent. As our aim is to integrate cellular processes into a generic population model, we have taken a simple (not to say simplistic) view of a cell by treating it as a black box with simple thermodynamic properties and physiological rules. Thus, phenomena like metabolism and maintenance have been integrated in a simple fashion.

Current computational resources allow scientists to model complex ecological societies interacting with one another. Our approach follows similar lines. By creating models of cells that include, at the algorithmic level, the most important factors that control and mimic cell interactions, division, growth, and death, we will explore the formation and development of colonies (or biofilms) and examine how the various parameters that define the nature of the cells and their environment affect the final result. In this article, we will first introduce an approach which is capable of producing useful simulations of cells and biofilms. In order to obtain a computer model that can be used to simulate large populations of interacting cells (possibly of different species), the model must obviously be simple. We thus use a lattice Monte Carlo (LMC) model with elements borrowed from computational polymer science. The model can easily be programmed and generalized to complex situations while retaining simple rules that can be parallelized to use multiprocessor computers. Finally, we present results from a preliminary study of a two-dimensional (2D) version of the model. The emphasis of this first study will be on the thermo-mechanical aspects of single cells near walls, and on the general properties of small biofilm colonies growing on a flat surface.

2. The model

In order to design a reliable and computationally reasonable model of biofilms, we must do two things: (a) first, we must choose the proper computational approach, i.e., the appropriate level of coarse-graining for the physics involved; (b) then, we must identify the essential processes that we must keep in the model. The description presented in this section focuses on a 2D version of the model for simplicity. Some properties of 3D models will be discussed in the last section.

2.1. The bond-fluctuation algorithm

We employ a LMC algorithm to model the various physical elements of the biofilms. This approach is directly inspired from polymer science. The whole problem will be reduced to a list of rules that control how "particles" jump from site to site on a lattice. The particles can be linked together in various ways, may interact with each other through various potentials, and their net motion can be biased by external fields. Finally, the lattice itself must possess some boundary conditions. The model is thus fully defined by these