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Numerical methods for a nonlinear reaction–diffusion system modelling a batch culture of biofilm☆

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ABSTRACT

A biofilm is usually defined as a layer of bacterial cells anchored to a surface. These cells are embedded into a polymer matrix that keeps them attached to each other and to a solid surface. Among a large variety of biofilms, in this paper we consider *batch* cultures. The mathematical model is formulated in terms of a quasilinear system of diffusion–reaction equations for biomass and nutrients concentrations, which exhibits possible degeneracy and singularities in the nonlinear diffusion coefficient. In the present paper, we propose a set of efficient numerical methods that speeds up the solution of the model. Mainly, Crank–Nicolson finite differences techniques for discretisation are combined with a Newton algorithm for the nonlinearities. Moreover, some numerical examples show the expected behaviour of the biomass and nutrients concentrations and also clearly illustrate some theoretically proved qualitative properties related to exponential decays or convergence to a critical biomass concentration depending on the values of the model parameters.

1. Introduction

A biofilm is usually defined as a layer of bacterial cells anchored to a surface. These cells are embedded into a a biological matrix formed mainly by polymers called exopolysaccharides (EPS), that keeps them attached to each other and to a solid surface, thus protecting them and making difficult their removal [1,2]. In a simplified form, a biofilm can be understood as a group of microorganisms anchored to a surface. Actual studies estimate that less than 0.1% of all the aquatic microbial life are planktonic microorganisms [3]. Therefore, biofilms are the preferred microbial life form. This preference comes from the fact that the ability to stick to surfaces and form biofilms represents a competitive advantage with respect to a suspended bacteria alternative, because the latter can be easily washed out by water flow, while the former are protected against that phenomena and can grow in an environment with abundance of nutrients. The physical structure of biofilms allows the distinction of biological niches which guarantee the growth and survival of microorganisms that could not compete in a homogeneous system. Additionally, the microbial activity inside biofilms can modify the inner environment in order to make the biofilm more hospitable than the liquid region [4].

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The main points to be distinguished in a biofilm are the surface, the biofilm layer, the boundary layer the bulk liquid and the environmental conditions. The surface is where the bacteria are anchored, the biofilm itself is formed by cells of one or various species and the EPS, the boundary layer is optional (as it may exist or not), the bulk liquid is the region where the nutrients are located, and the environmental conditions characterise the biofilm development.

Sometimes biofilms can be beneficial, either for humans or for the natural ecosystem; however sometimes biofilms result to be harmful, thus causing health or economical problems. Sometimes, the former are industrially used on purpose, for example, in water treatment (drip irrigation filters, RBCs, biological reactors, etc.), or they naturally appear underground (contributing to soil or underground water decontamination), in rivers, lakes and coastal zones (where biofilms can be easily seen colonising rocks), or in plant life's roots. Clearly, the development of natural biofilms is essential for Earth's biosphere. Also bioremediation is currently becoming a highly growing area.

On the other hand, harmful biofilms appear in various situations. For instance, biofilms constitute an important problem in dental hygiene (dental plaque), infectious diseases (legionellosis) or diseases caused by different medical implants (pacemakers, artificial joints or catheters), as well as potable water contamination or the malfunction of heat transfers and heat exchangers. The harmful biofilms formation is an important problem in health industry, where they constitute a mayor source of food contamination (for example, in seafood, poultry or meat processing), with many consequences to consumers.

In general, prevention of harmful biofilm formation is quite hard, because they are capable of growing in very adverse conditions. Also, one must acknowledge the difficulty of biofilm elimination, because the bacteria forming the biofilm are more resilient to the immunological response of the host or to the possible antimicrobial agents.

Either motivated by the need to enhance their beneficial properties or in order to control their evolution, a lot of research has been developed to understand biofilm mechanisms and their modelling. This research tries to investigate the genetic, biochemical and physical mechanisms that contribute not only to the biofilm formation, but also to characterise its structure.

Many studies indicate that the biofilm structure determines the magnitude of the involved inner processes, such as the nutrients transference rate to the lower layers, the microbial agents diffusion rate or the ability to resist frictions. In this sense, various works highlight the microscopic techniques as the most promising for the observation of the developing process of biofilms and their structures. These works, that qualitatively characterise the most basic structures, have given way to others that achieve a quantitative characterisation. In that context, two main strategies can be distinguish: mathematical modelling and quantitative image analysis [5]. As we will show later, the present paper can be classified in the first approach.

Among a large variety of biofilms, this paper will focus on *Listeria monocytogenes* strains, a pathogen bacteria associated to food consumption and widely acknowledged by the food safety agencies (AESAN, EFSA), as a high risk bacteria, especially because of its high mortality rate (around 20%) on pregnant women and immunodeficient people (particular group at risk). The precise motivation comes from the experimental studies and characterisation of its biofilm structure, currently being developed at the Institute of Marine Research. For this purpose, *batch* cultures and cellular stain are used, thus allowing to visualise *in vivo* viable biofilm cells by means of a fluorescence microscope. This experimental study analyses the temporal evolution of the biofilm formation for different strains through the quantitative analysis of the resulting images.

In parallel to these experimental studies, the use of efficient mathematical models allows the prediction of the biofilm evolution for particular values of the involved parameters associated to different conditions. Moreover, it opens the possibility to control and optimise this evolution, in order to satisfy certain objectives. As indicated in Wanner et al. [1], the mathematical modelling of biofilms dates back to the 70s of the last century, with very simple initial models mainly focusing on the nutrients flux from the liquid region to the biofilm. Since these seminal models, biofilm modelling has largely evolved and modern models are grouped into cellular automata, discrete and continuous models [6–8]. The first two ones, specially cellular automata, are mainly based on local probability rules. Although their results highly agree with experiments, many physical issues remain actually unclear. For example, the results strongly depend on the discretisation, with significant qualitative and quantitative differences. Alternatively, continuum models usually consider the biofilm as a material, for example, as a viscous fluid. More precisely, a two-phase fluid can be considered, thus separating the fluid containing nutrients and the one containing biomass. In the continuous setting, the involved physical magnitudes usually are the solution of complex systems of nonlinear partial differential equations of convection–diffusion–reaction type. Due to their complexity, the analytical expression of these solutions are not available, so that efficient numerical methods to get enough accurate approximations are required.

Having in view the different characteristics of the particular biofilm, in the present paper we consider a continuum model. These main characteristics are: the number of cells in the batch culture is very high (greater than 10^5), so that the cellular growth is extremely slow, non motile cells are considered, and the cellular dispersion appears when a certain threshold of the cellular density is achieved. Taking into account the previous conditions, in order to describe biofilm formation of *L. monocytogenes* we consider the continuum model proposed in Eberl et al. [9]. This model is posed in terms of a system of nonlinear time dependent reaction–diffusion equations, with suitable boundary conditions depending on the particular regimes to be considered for the biofilm. Possible degeneracy and singularities in the biomass equation are the main difficulties from the theoretical and numerical point of views. In Eberl et al. [9], the numerical solution is mainly based on first order time discretisation schemes, combined with a central finite difference scheme in space. More precisely, the conditional stability of explicit scheme requires a smaller time step and is used for the biomass equation, while the nutrient transport is solved with the implicit scheme. More recently, in Duvnjak and Eberl [10] a transformation of unknown is applied to the biomass equation, so that the nonlinearity is shifted to the term of time derivative, while the diffusion part is

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