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Mathematical analysis of a model describing the invasion of bacteria in burn wounds

D. Hilhorst[a], J.R. King[b], M. Röger[c,*]

[a] *Laboratoire de Mathématiques, Université de Paris-Sud, 91405 Orsay Cedex, France*
[b] *Centre for Mathematical Medicine, Theoretical Mechanics Section, School of Mathematical Sciences, University of Nottingham, Nottingham NG7 2RD, UK*
[c] *Department of Mathematics and Computing Science, Eindhoven University of Technology, 5600 MB Eindhoven, The Netherlands*

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Abstract

We investigate a reaction–diffusion system for a parabolic equation coupled with an ordinary differential equation on an unbounded space domain. This system arises as a model for host tissue degradation by bacteria and involves a parameter describing the degradation rate that is typically very large. We prove the existence and uniqueness of solutions to this system and the convergence to a Stefan-like free boundary problem as the degradation rate tends to infinity.

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1. Introduction and main results

The development of alternative treatments for bacterial infections has become a major issue in recent years. The formulation and analysis of suitable mathematical models can serve as a valuable tool in understanding the basic mechanisms underlying such infections and in providing insight into possible means of fighting the spread of bacteria in host tissue. We take our cue here from [12], where a mathematical model of host tissue degradation by extracellular bacteria was

* Corresponding author. Tel.: +31 40 247 20 82; fax: +31 40 244 24 89.
E-mail addresses: Danielle.Hilhorst@math.u-psud.fr (D. Hilhorst), John.King@nottingham.ac.uk (J.R. King), mroeger@win.tue.nl (M. Röger).

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introduced and analysed by formal asymptotic expansion methods. In this paper we continue and complement this investigation by a rigorous mathematical analysis.

The ability of certain extracellular bacterial pathogens, such as *Pseudomonas aeruginosa*, to degrade the tissue of an infected patient (thereby releasing nutrient to the bacteria) can result in the infection becoming lethal. The release by *Pseudomonas aeruginosa* of the virulence determinants that lead to tissue degradation is under the control of a 'quorum-sensing' system that allows the bacterial population to grow to a level at which the host immune defences can be overcome before the virulence factors are expressed (see [12,16,1] for further background and references). The rapid development of antibiotic resistance among bacteria has added urgency to the task of enhancing the understanding of such behaviour, with quorum-sensing systems providing possible alternatives targets for treatment. The model with which we are concerned here assumes that the cell signalling between bacteria which underpins quorum sensing has been effective in upregulating (almost) the entire population, leading to the release of virulence determinants wherever the bacteria are present. This obviates the need to keep explicit account of the (growing) bacterial population, the model instead involving just two variables, namely the concentration of virulence determinants and the volume fraction of healthy tissue.

Under such assumptions, the non-dimensionalised model equations take the form (see [12])

$$\partial_t u = \Delta u - u + w - \gamma k u(1 - w), \tag{1.1}$$

$$\partial_t w = k u(1 - w), \tag{1.2}$$

where u, w are time and space dependent functions and $\gamma, k > 0$ are fixed parameters. The variable u describes the concentration of degradative enzymes produced by the bacteria, and $(1 - w)$ corresponds to the volume fraction of healthy tissue, the population density of bacteria being taken to be proportional to w. The key parameter $k > 0$ is typically very large in practise and governs the degradation ratio of the tissue. As spatial domain the upper half-space is chosen and initial and boundary data are prescribed. By a formal asymptotic expansion analysis in [12], a free boundary problem was obtained in the limit $k \to \infty$. There, for unknowns u, w, the upper half-space splits into a region where $u = 0$ and a second region where $u > 0$ and $w = 1$. The common boundary of these two regions moves according to a Stefan-like condition.

We include in our analysis the possibility of a diffusion term in Eq. (1.2). This might be of interest in other applications and is convenient for mathematical purposes. To give a precise formulation of the problem denote the upper half-space of $\mathbb{R}^n$ by $\mathbb{R}^n_+ := \{x = (x_1, \ldots, x_n) \in \mathbb{R}^n : x_n > 0\}$ and by $\vec{e}_n = (0, \ldots, 0, 1)^T$ the n-th standard unit vector. Moreover let a time interval $(0, T)$ be given and set

$$Q_T := (0, T) \times \mathbb{R}^n_+,$$

$$S_T := (0, T) \times (\mathbb{R}^{n-1} \times \{0\}).$$

We consider initial data $\bar{u}_0, \bar{w}_0$ with

$$\bar{u}_0 \in L^1(\mathbb{R}^n_+), \quad 0 \le \bar{u}_0 \le 1, \tag{1.3}$$

$$\bar{w}_0 \in L^1(\mathbb{R}^n_+), \quad 0 \le \bar{w}_0 \le 1. \tag{1.4}$$

In the applications a typical choice for w_0 is a characteristic function of a set which motivates our assumptions on the regularity of the initial data.

Finally we define for an open interval $I \subset \mathbb{R}$ and an open set $\Omega \subset \mathbb{R}^n$ the spaces

$$W^{1,2}_{\mathrm{p}}(I \times \Omega) := H^{1,p}(I; L^p(\Omega)) \cap L^p(I; H^{1,p}(\Omega)),$$