

Analysis of a one dimensional biofilm model
by Lori Anne Pritchett

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Mathematical Sciences
Montana State University
© Copyright by Lori Anne Pritchett (2000)

Abstract:
Biofilm is a term used to describe the collection of organisms in an aqueous environment. A model which simulates a single species biofilm with one growth limiting substrate is derived. In this simple model, it is proved that the solution to the substrate equation is bounded. If diffusion is included in the biomass equations, then the biofilm volume fractions, thickness and velocity are also bounded. The model which does not include detachment suggests that a steady-state solution is possible if the inactivation rate is zero. It is also shown that a steady-state solution corresponding to the absence of active biomass is linearly unstable provided the bulk substrate satisfies an inequality involving the observed decay rate. Finally, this model is altered to include EPS. The production of EPS depends on the concentration level of a signaling chemical which is also included in the model. The numerical simulations of this new model indicate that a minimum production rate is needed for a significant amount of EPS to be produced.

ANALYSIS OF A

ONE DIMENSIONAL BIOFILM MODEL

by

Lori Anne Pritchett

A dissertation submitted in partial fulfillment
of the requirements for the degree

of

Doctor of Philosophy

in

Mathematical Sciences

MONTANA STATE UNIVERSITY
Bozeman, Montana

July 2000

D378
P9391

APPROVAL

of a dissertation submitted by

Lori Anne Pritchett

This dissertation has been read by each member of the dissertation committee and has been found to be satisfactory regarding content, English usage, format, citations, bibliographic style, and consistency, and is ready for submission to the College of Graduate Studies.

Dr. Jack D. Dockery Jack D. Dockery 7/12/2000
(Signature) Date

Approved for the Department of Mathematical Sciences

Dr. John R. Lund John Lund 7/14/00
(Signature) Date

Approved for the College of Graduate Studies

Dr. Bruce McLeod Bruce R. McLeod 7-18-00
(Signature) Date

STATEMENT OF PERMISSION TO USE

In presenting this dissertation in partial fulfillment of the requirements for a doctoral degree at Montana State University, I agree that the Library shall make it available to borrowers under rules of the Library. I further agree that copying of this dissertation is allowable only for scholarly purposes, consistent with "fair use" as prescribed in the U. S. Copyright Law. Requests for extensive copying or reproduction of this dissertation should be referred to Bell & Howell Information and Learning, 300 North Zeeb Road, Ann Arbor, Michigan 48106, to whom I have granted "the exclusive right to reproduce and distribute my dissertation in and from microform along with the non-exclusive right to reproduce and distribute my abstract in any format in whole or in part."

Signature Lani Pittsworth

Date July 14, 2000

I would like to dedicate this dissertation to my late grandparents, John Coleman and Ruby Pritchett, Glen and Edna Taylor and my late aunt, Colleen Baldy. I wish you could have lived to see the first doctor in the family.

ACKNOWLEDGEMENTS

I would like to thank my advisor, Dr. Jack D. Dockery, for his assistance. I would also like to thank Dr. Ken L. Bowers and Dr. Mark C. Pernarowski for reading and editing this manuscript. I am very grateful for all the support I have received from the faculty, staff and graduate students at Montana State University. In particular, I would like to thank Wendi Sonnenberg and Brian Beaudrie.

Finally, I would like thank my entire family for their encouragement, love and faith throughout this long process.

TABLE OF CONTENTS

LIST OF TABLES viii

LIST OF FIGURES ix

ABSTRACT xi

1. BIOFILM MODELS 1

2. DERIVATION OF THE MODEL 5

PHYSICAL SYSTEM 5
MODEL EQUATIONS INSIDE THE BIOFILM 7
Active Biomass 7
Inactive Biomass 8
Substrate 9
Velocity 10
Fluid-Biofilm Interface 11
BOUNDARY CONDITIONS 12
Biomass 12
Substrate 13
Velocity Potential 13
PRODUCTION TERMS 14
Active Biomass 14
Inactive Biomass 15
Substrate 15
ONE DIMENSIONAL MODEL 15
DIMENSIONLESS MODEL 20

3. SOLUTION PROPERTIES 23

A MAXIMUM PRINCIPLE FOR PARABOLIC EQUATIONS 23
SOLUTION BOUNDS 28
Bounds on S 31
Bounds on f 33
Bounds on v and L 37
BEHAVIOR AT THE INTERFACE 38

4. STEADY-STATE SOLUTIONS 42

EXISTENCE OF STEADY-STATE SOLUTIONS 43
Addition of Diffusion 55

Stability of the Steady-State Solutions 57
Constant Steady-State Solution 59
Non-Constant Steady-State 61

5. MODELING EPS PRODUCTION 71

Inclusion of EPS Production 71
Model Equations Inside the Biofilm 72
Substrate 73
Cell Density 74
Signaling Chemical 75
EPS 76
Velocity 78
Interface 79
One Dimensional Model with EPS Production 82
Dimensionless Model 84
Behavior at the Interface 86
Numerical Simulations of the Model 88
Numerical Implementation 92
Parameter Values 96
Solution Behavior 98

6. CONCLUDING REMARKS 104

REFERENCES CITED 108

APPENDICES 109

APPENDIX A – BIOFILM MODEL WITHOUT EPS 110
APPENDIX B – JACOBIAN MATRIX CODE 115
APPENDIX C – SUBSPACE ITERATION WITH A CAYLEY TRANSFORMATION 121
APPENDIX D – BIOFILM MODEL WITH EPS 125

LIST OF TABLES

Table		Page
1.	Model variables	17
2.	Model parameters and functions	17
3.	Typical values for the model parameters	22
4.	Dimensionless Parameters	22
5.	Eigenvalues for parameter set 1	65
6.	Eigenvalues for parameter set 2	66
7.	EPS model variables and functions	80
8.	EPS model parameters and functions	81
9.	EPS non-dimensional parameters	86
10.	Parameter values used in the numerical simulations	96

LIST OF FIGURES

Figure Page

1. Biofilm and Bulk Liquid 6
2. The sets E, Γ and $U_\epsilon(P)$ 24
3. The sets E, Ω_0, Ω_T, Γ_L and Γ_0 30
4. Region R and flow ψ 49
5. Eigenvector components for parameter set 1 67
6. Eigenvector components for parameter set 1 67
7. Eigenvector components for parameter set 2 68
8. Eigenvector components for parameter set 2 68
9. $S(z,t)$ where $\frac{1}{\varphi^2} = 3$, $\beta = 0.15$ and $S_b = 0.25$ 69
10. $f(z,t)$ where $\frac{1}{\varphi^2} = 3$, $\beta = 0.15$ and $S_b = 0.25$ 69
11. $L(t)$ where $\frac{1}{\varphi^2} = 3$, $\beta = 0.15$ and $S_b = 0.25$ 70
12. $S(z,t)$ when $k_p = 0$ 89
13. $C(z,t)$ when $k_p = 0$ 89
14. $f(z,t)$ when $k_p = 0$ 90
15. $e(z,t)$ when $k_p = 0$ 90
16. $L(t)$ when $k_p = 0$ 91
17. $S(z,t)$ when $k_p = 3$ 93

18. $C(z,t)$ when $k_p = 3$ 93

19. $f(z,t)$ when $k_p = 3$ 94

20. $e(z,t)$ when $k_p = 3$ 94

21. $L(t)$ when $k_p = 3$ 95

22. S, C, f, e and L for $k_p = 0$ 99

23. S, C, f, e and L for $k_p = 1$ 99

24. S, C, f, e and L for $k_p = 1.7$ 100

25. S, C, f, e and L for $k_p = 2$ 101

26. S, C, f, e and L for $k_p = 5$ 101

27. Final L value versus k_p 103

ABSTRACT

Biofilm is a term used to describe the collection of organisms in an aqueous environment. A model which simulates a single species biofilm with one growth limiting substrate is derived. In this simple model, it is proved that the solution to the substrate equation is bounded. If diffusion is included in the biomass equations, then the biofilm volume fractions, thickness and velocity are also bounded. The model which does not include detachment suggests that a steady-state solution is possible if the inactivation rate is zero. It is also shown that a steady-state solution corresponding to the absence of active biomass is linearly unstable provided the bulk substrate satisfies an inequality involving the observed decay rate. Finally, this model is altered to include EPS. The production of EPS depends on the concentration level of a signaling chemical which is also included in the model. The numerical simulations of this new model indicate that a minimum production rate is needed for a significant amount of EPS to be produced.

CHAPTER 1

BIOFILM MODELS

The term biofilm describes the collection of microorganisms that accumulate on surfaces in aqueous environments. Biofilms occur in a variety of places. Examples include: pipes in a waste-water treatment plant, medical implants and rocks in a stream bed. The presence of such build-up poses health risks and can effect a system's operation. Once a film forms on a surface, it is expensive to remove and it may return. Understanding the mechanisms that control the formation of biofilms could lead to better methods for prevention and removal.

Biofilms are complex systems. They contain both liquid and solid components. In each of these phases, several types of organisms and substrates are usually present. Studying the processes that take place inside a biofilm is difficult, since the thickness of most biofilms is on the order of 10 to 100 microns. With such a small scale, experiments are hard to design and perform. By using mathematical models, a particular process or environmental situation can be isolated and studied. The earliest models, developed in the late 1970's, were static models. The spatial distribution of the organisms and the thickness of the biofilm were fixed. The models described the substrate concentration inside a biofilm. The next generation of models allowed the thickness of the biofilm and the species distribution to evolve over time.

Wanner and Gujer [13] proposed one of the first dynamic models. The model is a set of partial differential equations derived from mass conservation principles. This model was one dimension in space and modeled variations in a direction perpendicular to the film's surface. Other transient models followed [6], and their development is similar to the approach taken by Wanner and Gujer. Although these models have been studied numerically, their solutions have not been studied mathematically. Furthermore, neither model includes the production of non-biomass substances. For example, most bacteria produce polymers that coat the cells in the biofilm. These polymers, called extracellular polymeric substances (EPS), allow the cells to attach to surfaces. It is believed that EPS contributes to other physical phenomenon inside a biofilm. Unfortunately the exact relationship between EPS and the observed physical changes is not well-understood. A mathematical model with EPS production would aid in the study of EPS formation in a biofilm. In this thesis, a general one dimensional biofilm model is derived and the solutions of this model are analyzed. This model is then adapted to include EPS production.

Chapter 2 contains the derivation of the model. The derivation is a slightly different approach than was used in [13] and [6]. Both [13] and [6] derived the model in only one spatial dimension. Although the final model in Chapter 2 is the same set of equations found in [13], these equations are the reduction of a three dimensional model to one dimension. This approach is used because a biofilm is a three dimensional

object. If a one dimensional model is used to study a biofilm it should be consistent with a three dimensional model.

Once this model is derived, Chapter 3 covers some of the qualitative properties. We will assume that a solution exists and is unique. With this assumption, we will show that the solution of the substrate equation is bounded. Under the assumption that biomass diffuses inside the biofilm, we prove that the solution related to the organism density is bounded. From this result, bounds on the biofilm thickness and velocity are proved. Another result found in this chapter is the behavior of the equation related to biomass density at the interface. It is proved that for all parameter values, the model tends to a steady-state value at the interface. This implies that the density of organisms at the film's surface approaches a fixed value.

With a small number of organisms present, a film quickly forms and then stabilizes at a thickness on the order of 100 microns. If the model duplicates this behavior, then the solutions would tend to a steady state solution. In Chapter 4, the existence and stability of steady state solutions is studied. The model without detachment included has two steady-state solutions. One is a trivial solution that corresponds to a biofilm with no active organisms present. This solution is linearly unstable if the organism growth rate at the interface is greater than the inactivation rate. The other solution exists if the inactivation rate is zero and if the organism growth rate at the interface is positive. The stability of this solution is analyzed numerically. The results are mixed, but most of the numerics indicate that the solution is stable.

Finally in Chapter 5, the model derived in Chapter 2 is altered to include EPS production. There is experimental evidence [3], [5], [8] that signaling chemicals control EPS production. Based on this information, the basic model is expanded to include EPS and chemical signaling. One description of a biofilm is a gel made up of EPS with cells embedded in the EPS. Using this description, the EPS is modeled like inactive biomass. However, the formation of EPS uses substrate when the signaling chemical reaches a threshold value. The numerical simulations of this new model indicate that there is a minimum rate at which the signaling chemical must be produced at before a significant amount of EPS is formed. Once this minimum has been exceeded the model predicts that most of the EPS occurs at the surface to which the film is attached and most of the organisms can be found near the interface. The model also appears to limit on steady-state solutions.

CHAPTER 2

DERIVATION OF THE MODEL

In this chapter, we will derive a one dimensional biofilm model. The derivation does not depend on specific transport, production or growth terms. A variety of functions for these quantities can be easily inserted into the model equations. Starting with a general three dimensional model, a one dimensional model is produced by assuming that only significant variations occur in a direction normal to the surface to which the film is attached. After establishing this one dimensional model, it is rescaled to a non-dimensional set of equations. It is this system that is studied in further detail in Chapter 3 and Chapter 4.

Physical System

We will assume that the biofilm is a single species biofilm with one growth limiting substrate present. The physical system is divided into two regions: the biofilm and the bulk liquid. The biofilm, attached to a surface called the substratum, consumes a substrate supplied in the bulk liquid. The fluid-biofilm interface, Γ, separates the two regions (See Figure 1).

To simplify the geometry of the problem, we will assume that the biofilm grows on a flat surface. Let $\mathbf{x} = (x, y, z)$. The yz plane corresponds to the substratum and x denotes the distance in the direction of the outward normal to this plane. We will

also assume that the model quantities are periodic in the yz plane. Therefore, the model will be derived inside a rectangular box with a square base with sides of length $2h$. The substratum is at the base of this box. The origin for the coordinate system is placed at the center of this square.

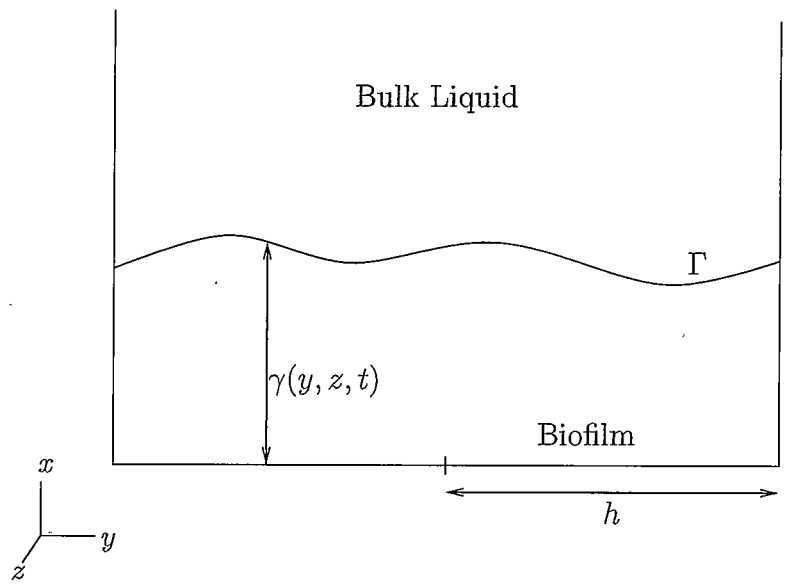


Figure 1. Biofilm and Bulk Liquid.

The composition of the biofilm is microorganisms and substrate. The organisms are called biomass. Although one species is present, it is divided into two subpopulations. Active biomass which consumes substrate and the inactive biomass which is inert material and does not consume substrate. The model consists of equations derived from mass balance principles that describe the substrate concentration, active and inactive biomass profiles inside the biofilm. This system of equations is coupled

with an equation that describes the evolution of the fluid-biofilm interface. We begin with the equations inside the biofilm.

Model Equations Inside the Biofilm

Active Biomass

Let $\rho(\mathbf{x}, t)$ be the active biomass density at $\mathbf{x}$ and time t. Consider an arbitrary control volume, Ω, found inside the biofilm compartment. The total mass of active cells in Ω is

$$\int_{\Omega} \rho(\mathbf{x}, t)\, d\sigma.$$

This quantity changes as new cells are created and as active biomass passes through the surface of Ω. Thus,

$$\frac{d}{dt}\int_{\Omega} \rho(\mathbf{x}, t)\, d\sigma = -\int_{\partial\Omega} \mathbf{J}_{\rho}(\mathbf{x}, t) \cdot \mathbf{n}\, d\tau + \int_{\Omega} F_{\rho}(\mathbf{x}, t)\, d\sigma$$

where $\partial\Omega$ is the boundary of Ω, $\mathbf{J}_{\rho}$ is the flux of active biomass, $\mathbf{n}$ is the outward direction normal to $\partial\Omega$ and F_{ρ} is the net production rate of active biomass.

Provided that the boundary of Ω is smooth and $\mathbf{J}_{\rho}$ is C^1, the divergence theorem states

$$\int_{\partial\Omega} \mathbf{J}_{\rho} \cdot \mathbf{n}\, d\tau = \int_{\Omega} \nabla \cdot \mathbf{J}_{\rho}\, d\sigma.$$

Therefore, the mass balance equation can be written as

$$\frac{d}{dt}\int_{\Omega} \rho\, d\sigma = \int_{\Omega} F_{\rho} - \nabla \cdot \mathbf{J}_{\rho}\, d\sigma.$$

If ρ is a C^1 function in $\mathbf{x}$ and t, then

$$\frac{d}{dt}\int_\Omega \rho(\mathbf{x},t)\,d\sigma = \int_\Omega \frac{\partial\rho}{\partial t}(\mathbf{x},t)\,d\sigma.$$

Since Ω is an arbitrary volume, this results in the partial differential equation

$$\frac{\partial\rho}{\partial t} + \nabla\cdot\mathbf{J}_\rho = F_\rho.$$

Cells inside a biofilm are not mobile. Their movement can only occur as the surrounding material expands. Thus, the flux of biomass is a convection process. If $\mathbf{v}(\mathbf{x},t)$ is the biomass velocity at $\mathbf{x}$, then

$$\mathbf{J}_\rho = \mathbf{v}\rho.$$

Hence, the active biomass equation in the biofilm is

$$\frac{\partial\rho}{\partial t} + \nabla\cdot(\mathbf{v}\rho) = F_\rho. \tag{2.1}$$

Inactive Biomass

Let $\bar{\rho}(\mathbf{x},t)$ be the inactive biomass density at $\mathbf{x}$ and time t. The total mass of inactive material found in a control volume Ω is

$$\int_\Omega \bar{\rho}(\mathbf{x},t)\,d\sigma.$$

Change in the total mass occurs from material transport and production of inactive biomass. Thus, the mass balance equation is

$$\frac{d}{dt}\int_\Omega \bar{\rho}(\mathbf{x},t)\,d\sigma = -\int_{\partial\Omega}\mathbf{J}_{\bar{\rho}}(\mathbf{x},t)\cdot\mathbf{n}\,d\tau + \int_\Omega F_{\bar{\rho}}(\mathbf{x},t)\,d\sigma$$

where the flux of inactive material is $\mathbf{J}_{\bar{\rho}}$ and the production rate of inactive material is $F_{\bar{\rho}}$. Following the same reasoning as above, this integral equation is equivalent to

$$\frac{\partial \bar{\rho}}{\partial t} + \nabla \cdot \mathbf{J}_{\bar{\rho}} = F_{\bar{\rho}}.$$

We assume that the transport of inactive biomass is the same as active biomass. Hence, the flux of inactive biomass is

$$\mathbf{J}_{\bar{\rho}} = \mathbf{v}\bar{\rho}.$$

With this equation, the inactive biomass equation inside the biofilm is

$$\frac{\partial \bar{\rho}}{\partial t} + \nabla \cdot (\mathbf{v}\bar{\rho}) = F_{\bar{\rho}}. \tag{2.2}$$

Substrate

If $S(\mathbf{x}, t)$ is the substrate concentration at $\mathbf{x}$ and time t, then the total amount of substrate found in Ω is

$$\int_{\Omega} S(\mathbf{x}, t)\, d\sigma.$$

Like the biomass, this quantity changes as substrate moves through Ω and as active biomass consumes substrate. This change in substrate can be expressed as

$$\frac{d}{dt}\int_{\Omega} S(\mathbf{x}, t)\, d\sigma = -\int_{\partial\Omega} \mathbf{n} \cdot \mathbf{J}_S(\mathbf{x}, t)\, d\tau - \int_{\Omega} F_S(\mathbf{x}, t)\, d\sigma$$

where $\mathbf{J}_S$ is the flux of substrate. The quantity F_S represents the rate of substrate usage inside the biofilm. F_S is assumed to be positive and the minus sign on the last

integral indicates that substrate is consumed and not produced inside the biofilm. Again, the divergence theorem and the assumption that Ω is an arbitrary volume leads to

$$\frac{\partial S}{\partial t} + \nabla \cdot \mathbf{J}_S = -F_S.$$

The transport of substrate is modeled by Fick's law; which states

$$\mathbf{J}_S = -D\nabla S$$

where the constant D is the diffusion coefficient for substrate. Thus, the equation for substrate is

$$\frac{\partial S}{\partial t} = D\nabla^2 S - F_S. \tag{2.3}$$

Velocity

In both biomass equations, the velocity field is not specified. To determine the velocity, we will make the following assumptions. Material inside a biofilm convects as new biomass is produced. Hence, the divergence of the velocity is proportional to the rate of biomass production. Thus,

$$\nabla \cdot \mathbf{v} = k\left(F_\rho + F_{\bar{\rho}}\right) \tag{2.4}$$

where k is the constant of proportionality. Since the velocity contains three components, this equation is not enough to determine $\mathbf{v}$. Therefore, we will also assume that the velocity field is irrotational. Under this assumption,

$$\mathbf{v}(\mathbf{x}, t) = \nabla\phi(\mathbf{x}, t) \tag{2.5}$$

where ϕ is a velocity potential. Combining equations (2.4) and (2.5) leads to

$$\nabla^2\phi = k\left(F_\rho + F_{\bar{\rho}}\right). \tag{2.6}$$

By using equation (2.6), equation (2.5) can be used to solve for $\mathbf{v}$. Using equation (2.5), the biomass equations can now be written as

$$\frac{\partial\rho}{\partial t} + \nabla\cdot(\rho\nabla\phi) = F_\rho \tag{2.7}$$

and

$$\frac{\partial\bar{\rho}}{\partial t} + \nabla\cdot(\bar{\rho}\nabla\phi) = F_{\bar{\rho}}. \tag{2.8}$$

Fluid-Biofilm Interface

If u is some physical quantity, then the material derivative of u is given by

$$\frac{Du}{Dt} = \frac{\partial u}{\partial t} + \mathbf{w}\cdot\nabla u$$

where $\mathbf{w}$ is the velocity. The material derivative is the change of u an observer would see while traveling along the vector field $\mathbf{w}$.

We will assume that the surface which separates the bulk liquid from the biofilm has no diffusional layer and that this surface can be described by the equation

$$u(x,y,z,t) \equiv x - \gamma(y,z,t) = 0. \tag{2.9}$$

We will also assume that biomass on this surface will remain on this surface as the biofilm grows. Thus, the material derivative of u is zero on the interface.

Let $\mathbf{v} = (v_1, v_2, v_3)$ be the limit of the velocity from inside the biofilm at the point $(\gamma(y,z,t), y, z)$. The material derivative of (2.9) evaluated on the interface is

$$\begin{aligned}\frac{D}{Dt}\left(x - \gamma(y,z,t)\right) &= -\frac{\partial \gamma}{\partial t} + \mathbf{v}\cdot\nabla\left(x-\gamma\right) \\ &= -\frac{\partial \gamma}{\partial t} + v_1\left(1 - \frac{\partial \gamma}{\partial x}\right) + v_2\left(-\frac{\partial \gamma}{\partial y}\right) + v_3\left(-\frac{\partial \gamma}{\partial z}\right).\end{aligned}$$

Since the material derivative is zero and $\mathbf{v} = \nabla\phi$, this can be written as

$$\frac{\partial \gamma}{\partial t} + \frac{\partial \phi}{\partial y}\frac{\partial \gamma}{\partial y} + \frac{\partial \phi}{\partial z}\frac{\partial \gamma}{\partial z} = \frac{\partial \phi}{\partial x}. \tag{2.10}$$

Boundary Conditions

Biomass

Since biomass does not interact or pass through the substratum a no-flux condition is placed along this surface. If $\mathbf{n}$ is the outward normal of the substratum surface, then for points on the substratum

$$\mathbf{n}\cdot(\mathbf{v}\rho) = 0, \quad \mathbf{n}\cdot(\mathbf{v}\bar{\rho}) = 0.$$

With the simple geometry placed on this problem, these boundary conditions are equivalent to

$$v_1(0,y,z,t)\rho(0,y,z,t) = 0, \quad v_1(0,y,z,t)\bar{\rho}(0,y,z,t) = 0$$

where v_1 is the x component of $\mathbf{v}$. Along the sides of the box, where $y = \pm h$ and $z = \pm h$, periodic boundary conditions are placed on ρ and $\bar{\rho}$. This choice is made to avoid mathematical complications that can arise with solid boundaries and is based on the assumption that ρ and $\bar{\rho}$ are periodic functions in the yz plane.

Substrate

Substrate does not interact or pass through the substratum. So a no-flux condition is appropriate. Using the geometry of the problem, the boundary condition is

$$\frac{\partial S}{\partial x}(0, y, z, t) = 0.$$

In the bulk liquid, substrate is fed in at a constant rate. If the fluid is well-stirred, the concentration is constant along Γ. If S_{bulk} is the concentration of the substrate in the bulk liquid, then

$$S(\gamma(y, z, t), y, z, t) = S_{bulk}.$$

Periodic boundary conditions are placed on S and $\mathbf{n} \cdot \nabla S$, where $\mathbf{n}$ is the outward normal direction along the sides of the box.

Velocity Potential

We will assume that the biofilm velocity at the substratum is zero. In terms of the velocity potential, this boundary condition is stated as

$$\mathbf{n} \cdot \nabla \phi(0, y, z) = 0$$

where $\mathbf{n}$ is the outward normal of the substratum. This simplifies to the condition

$$\frac{\partial \phi}{\partial x}(0, y, z, t) = 0.$$

Along the sides, periodic boundary conditions are placed on ϕ. At the interface, $\mathbf{v}$ is perpendicular to the surface; thus ϕ is constant on the interface. Since ϕ is a

potential, an arbitrary value for ϕ can be assigned on γ. Therefore, we set

$$\phi(\gamma(y,z,t),y,z,t) = 0.$$

Production Terms

In this section, we will specify the net biomass production and substrate usage functions. We will not assume specific kinetic terms. Instead the general form and mathematical properties of these functions is addressed.

Active Biomass

Active biomass is produced as it consumes substrate. It decreases as it converts to inactive biomass. We will assume that both the active biomass production and the conversion to inactive biomass occurs at rates proportional to the active biomass density. Under these assumptions,

$$F_\rho = R(S)\rho - K_i\rho \tag{2.11}$$

where K_i is the inactivation rate and R is the net production rate from substrate utilization. We assume that R has the following properties: $R \in C^1$ for $S \geq 0$, $R'(S) > 0$ and $R(0) < 0$. The last property allows a loss of biomass for low substrate concentrations. A Monod kinetic term is a common function used to model cellular reproduction in a biofilm [2]. A function with a Monod kinetic term which satisfies these properties is

$$R(S) = \frac{\hat{\mu}S}{K+S} - K_d \tag{2.12}$$

where $\hat{\mu}$ is a maximum growth rate and K is the Monod constant. The parameter K_d represents the organism decay rate.

Inactive Biomass

Inactive biomass does not consume substrate. Once biomass has become inert it can not become active. We also assume that inactive biomass does not decay. Therefore, the net production of inactive biomass is

$$F_{\bar{\rho}} = K_i \rho. \tag{2.13}$$

Substrate

Substrate consumption is proportional to the active biomass density. Thus,

$$F_S = \frac{1}{Y} G(S) \rho \tag{2.14}$$

where Y is a yield coefficient and G is a function with the following properties: $G \in C^1$ for $S \geq 0$, $G'(S) > 0$ and $G(0) = 0$. Again, a Monod equation is the typical choice to model substrate usage [2]. Notice, that

$$G(S) = \frac{\hat{\mu} S}{K + S} \tag{2.15}$$

satisfies the properties given above. As before, $\hat{\mu}$ represents a maximum growth rate and K is the Monod constant.

In summary, the model equations are

$$\frac{\partial S}{\partial t} = D\nabla^2 S - \frac{1}{Y}G(S)\rho, \tag{2.16a}$$

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \nabla \phi) = R(S)\rho - K_i \rho, \tag{2.16b}$$

$$\frac{\partial \bar{\rho}}{\partial t} + \nabla \cdot (\bar{\rho} \nabla \phi) = K_i \rho, \tag{2.16c}$$

$$\nabla^2 \phi = kR(S)\rho, \tag{2.16d}$$

$$\mathbf{v} = \nabla \phi \tag{2.16e}$$

inside the biofilm with the equation

$$\frac{\partial \gamma}{\partial t} + \frac{\partial \phi}{\partial y}\frac{\partial \gamma}{\partial y} + \frac{\partial \phi}{\partial z}\frac{\partial \gamma}{\partial z} = \frac{\partial \phi}{\partial x} \tag{2.17}$$

for the interface and boundary conditions

$$\frac{\partial S}{\partial x}(0, y, z, t) = 0, \tag{2.18a}$$

$$v_1(0, y, z, t)\rho(0, y, z, t) = 0, \quad v_1(0, y, z, t)\bar{\rho}(0, y, z, t) = 0, \tag{2.18b}$$

$$\frac{\partial \phi}{\partial x}(0, y, z, t) = 0, \tag{2.18c}$$

$$S(\gamma(y, z, t), y, z, t) = S_{bulk}, \tag{2.18d}$$

$$\phi(\gamma(y, z, t), y, z, t) = 0. \tag{2.18e}$$

Table 1 and 2 list the variables and parameters in the model. The last column in each table displays the units. The symbol m_s is substrate mass units, m_ρ and $m_{\bar{\rho}}$ are mass units of active and inactive biomass, l and t are units of length and time.

Symbol	Description	Units
S	Substrate concentration	$m_s\, l^{-3}$
ρ	Active biomass density	$m_\rho\, l^{-3}$
$\bar{\rho}$	Inactive biomass density	$m_{\bar{\rho}}\, l^{-3}$
$\mathbf{v}$	Velocity	$l\, t^{-1}$
ϕ	Velocity potential	t^{-1}
γ	Interface height	l

Table 1. Model variables.

Symbol	Description	Units
S_{bulk}	Bulk liquid substrate concentration	$m_s\, l^{-3}$
D	Diffusion constant	$l^2\, t^{-1}$
Y	Yield coefficient	$m_\rho\, m_s^{-1}$
K_i	Inactivation rate	t^{-1}
k	Constant of proportionality	$m_\rho^{-1}\, l^3$
R	Active biomass growth rate (substrate related)	t^{-1}
G	Substrate utilization rate	t^{-1}
$\hat{\mu}$	Maximum growth rate	t^{-1}
K	Monod constant	$m_s\, l^{-3}$
K_d	Decay rate	t^{-1}

Table 2. Model parameters and functions.

Provided that the change of the model quantities in the yz plane is small, this model can be reduced to one spatial variable. Under this assumption, the equations inside the biofilm reduce to

$$\frac{\partial S}{\partial t} = D\frac{\partial^2 S}{\partial x^2} - \frac{1}{Y}G(S)\rho, \tag{2.19a}$$

$$\frac{\partial \rho}{\partial t} + \frac{\partial}{\partial x}\left(\rho\frac{\partial \phi}{\partial x}\right) = R(S)\rho - K_i\rho, \tag{2.19b}$$

$$\frac{\partial \bar{\rho}}{\partial t} + \frac{\partial}{\partial x}\left(\bar{\rho}\frac{\partial \phi}{\partial x}\right) = K_i\rho, \tag{2.19c}$$

$$\frac{\partial^2 \phi}{\partial x^2} = kR(S)\rho, \tag{2.19d}$$

$$v = \frac{\partial \phi}{\partial x} \tag{2.19e}$$

and the interface equation is

$$\frac{d\gamma}{dt} = \frac{\partial \phi}{\partial x}\left(\gamma(t), t\right). \tag{2.20}$$

With one spatial variable, we can solve for the velocity. By integrating equation (2.19d) and using the boundary condition (2.18c), the velocity is given by

$$v(x,t) = k\int_0^x R(S(\xi,t))\rho(\xi,t)\,d\xi. \tag{2.21}$$

To determine the constant k, we will assume that the biomass density is constant. Under this assumption, the densities ρ and $\bar{\rho}$ can be written as

$$\rho(x,t) = \rho_0 f(x,t),$$

$$\bar{\rho}(x,t) = \rho_0 \bar{f}(x,t)$$

where f is the volume fraction of active biomass, $\bar{f}$ is the volume fraction of inactive biomass and ρ_0 is the intrinsic density of the cells. Substituting these equations into

equations (2.19b) and (2.19c) yields

$$\frac{\partial f}{\partial t} + \frac{\partial}{\partial x}(vf) = R(S)f - K_i f, \tag{2.22a}$$

$$\frac{\partial \bar{f}}{\partial t} + \frac{\partial}{\partial x}(v\bar{f}) = K_i f. \tag{2.22b}$$

We will assume that f and $\bar{f}$ satisfy

$$f + \bar{f} = 1 - \epsilon_l$$

where ϵ_l is the liquid volume fraction. If ϵ_l is constant, this equation allows us to solve for the constant k. By adding equations (2.22a) and (2.22b), we have

$$(1 - \epsilon_l)\frac{\partial v}{\partial x} = R(S)f.$$

Comparing this to equation (2.21) leads to

$$kR(S)\rho_0 f(x,t) = \frac{1}{1-\epsilon_l} R(S)f(x,t).$$

Therefore, k satisfies the equation

$$k = \frac{1}{\rho_0(1-\epsilon_l)}$$

and the velocity equation is

$$v(x,t) = \frac{1}{1-\epsilon_l}\int_0^x R(S(\xi,t))f(\xi,t)\,d\xi. \tag{2.23}$$

In one dimension, γ represents the thickness of the biofilm. To simplify the notation, let $L = \gamma$. Since $v = \dfrac{\partial \phi}{\partial x}$, equation (2.20) leads to the differential equation

$$\frac{dL}{dt} = \frac{1}{1-\epsilon_l}\int_0^{L(t)} R(S(\xi,t))f(\xi,t)\,d\xi \tag{2.24}$$

which describes how the thickness of the biofilm changes.

Dimensionless Model

Let $\hat{x} = \frac{x}{\hat{l}}$ where $\hat{l}$ denotes the characteristic length scale of a biofilm which is typically on the order of 100 microns [2]. The time variable is re-scaled as

$$\hat{t} = t\hat{\mu}$$

and the model variables are re-scaled to

$$\hat{S} = \frac{S}{K}, \quad \hat{f} = \frac{f}{1-\epsilon_l}, \quad \hat{v} = \frac{v}{\hat{l}\hat{\mu}}, \quad \hat{L} = \frac{L}{\hat{l}}.$$

With this choice, we define the dimensionless parameters

$$\epsilon = \frac{\hat{l}^2 K}{D}, \quad \alpha = \frac{K_i}{\hat{\mu}}.$$

The functions G and R are also re-scaled to

$$\hat{G}(\hat{S}) = \frac{1}{\hat{\mu}} G(K\hat{S}) \tag{2.25a}$$

and

$$\hat{R}(\hat{S}) = \frac{1}{\hat{\mu}} R(K\hat{S}). \tag{2.25b}$$

If G and R are defined by equations (2.15) and (2.12), then

$$\hat{G}(\hat{S}) = \frac{\hat{S}}{1+\hat{S}}$$

and

$$\hat{R}(\hat{S}) = \frac{\hat{S}}{1+\hat{S}} - \frac{K_d}{\hat{\mu}}.$$

This motivates the definition of the following parameters

$$\frac{1}{\varphi^2} = (1-\epsilon_l)\frac{\hat{\mu}\hat{l}^2\rho_0}{YKD}, \quad \beta = \frac{K_d}{\hat{\mu}}.$$

The bulk substrate concentration is re-scaled as

$$S_b = \frac{S_{bulk}}{K}.$$

Dropping the hats, the dimensionless model becomes

$$\epsilon\frac{\partial S}{\partial t} = \frac{\partial^2 S}{\partial x^2} - \frac{1}{\varphi^2}\frac{S}{1+S}f, \tag{2.26a}$$

$$\frac{\partial f}{\partial t} + \frac{\partial}{\partial x}(vf) = \frac{S}{1+S}f - \beta f - \alpha f, \tag{2.26b}$$

$$\frac{dL}{dt} = v\left(L(t),t\right), \tag{2.26c}$$

$$v(x,t) = \int_0^x \left(\frac{S(\xi,t)}{1+S(\xi,t)} - \beta\right) f(\xi,t)\, d\xi \tag{2.26d}$$

with the boundary conditions

$$\frac{\partial S}{\partial x}(0,t) = 0, \tag{2.27a}$$

$$S(L(t),t) = S_b, \tag{2.27b}$$

$$v(0,t)f(0,t) = 0. \tag{2.27c}$$

Values for the model parameters are found in a variety of sources [13], [6],[12]. Typical values are found in Table 3 and how this translates to the size of the parameters in the dimensionless model are found in Table 4.

Symbol	Description	Order of Magnitude	Units
S_{bulk}	Bulk liquid substrate concentration	Varies	g cm^{-3}
D	Diffusion constant	10^{-5}	cm^2 s^{-1}
Y	Yield coefficient	10^{-1}	g of biomass/g of substrate
K_i	Inactivation rate	10^{-6}	s^{-1}
ρ_0	Intrinsic biomass density	10^{-3}	g cm^{-3}
$\hat{\mu}$	Maximum growth rate	10^{-5}	s^{-1}
K	Monod constant	$10^{-8} - 10^{-6}$	g cm^{-3}
K_d	Decay rate	10^{-6}	s^{-1}
ϵ_l	Liquid volume fraction	10^{-1}	-

Table 3. Typical values for the model parameters.

Symbol	Definition	Order of Magnitude
ϵ	$\frac{\hat{l}^2\hat{\mu}}{D}$	10^{-4}
α	$\frac{K_i}{\hat{\mu}}$	10^{-1}
$\frac{1}{\varphi^2}$	$(1-\epsilon_l)\frac{\hat{l}^2\hat{\mu}\rho_0}{YKD}$	$10^{-1} - 10^{1}$
β	$\frac{K_d}{\hat{\mu}}$	10^{-1}
S_b	$\frac{S_{bulk}}{K}$	$10^{-1} - 10$

Table 4. Dimensionless Parameters.

CHAPTER 3

SOLUTION PROPERTIES

Basic questions about the solution to the model equations include existence and uniqueness, bounds on solutions and limiting behavior. The vector function $\mathbf{u}(x,t) = [S(x,t), f(x,t), v(x,t), L(t)]^T$ is a solution to the system provided each component satisfies the appropriate equation and satisfies the given initial conditions. Furthermore, each function is C^1 in the t variable, C^2 in the x component for S and C^1 in the x component for f and v. Due to the mixed nature of the equations in the model, the existence and uniqueness of solutions is difficult to establish. Therefore, we will assume that solutions exist and are unique for $0 \leq t \leq T_1$ for some time T_1. In this chapter, two results are presented. Under the assumption that solutions exist and are unique, bounds for S, f, v and L are proved. The last section describes the limiting behavior of the f solution at the boundary $x = L(t)$.

A Maximum Principle for Parabolic Equations

What follows are several well-known results for parabolic equations. Their proofs are omitted, but can be found in [10]. These theorems lead to a maximum principle and a comparison theorem for certain types of non-linear parabolic equations.

Consider a bounded domain, E, in the xt plane where E is bounded below by $t = 0$ and above by $t = T_1$. Let the closure of E be denoted by $\bar{E}$ and the boundary

of E is denoted by ∂E. For each point $P = (x^*, t^*)$ in $\bar{E}$, let

$$U_\epsilon(P) = \{(x,t) : 0 < t^* - t < \epsilon \text{ and } |x - x^*| < \epsilon\}.$$

The parabolic interior of $\bar{E}$, denoted by $\widetilde{E}$, is the set of points where

$$U_\epsilon(P) \subset E$$

for some $\epsilon > 0$. The parabolic boundary, Γ, is the set $\bar{E} \setminus \tilde{E}$ (See Figure 2).

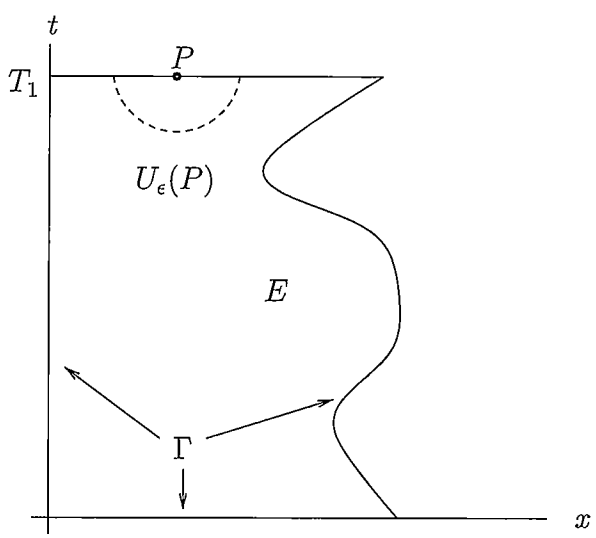


Figure 2. The sets E, Γ and $U_\epsilon(P)$.

Let $Z(E)$ be the set of continuous functions, u, on $\bar{E}$ where $\dfrac{\partial u}{\partial x}$, $\dfrac{\partial u}{\partial t}$ and $\dfrac{\partial^2 u}{\partial x^2}$ are also continuous on E. A function is admissible if it is a member of this set. For this class of functions, we define the linear operator L acting on u as

$$L[u] = a(x,t)\frac{\partial^2 u}{\partial x^2} + b(x,t)\frac{\partial u}{\partial x} - \frac{\partial u}{\partial t} \tag{3.1}$$

where a, b are bounded functions on $\bar{E}$ with $a(x,t) \geq 0$. L is called a parabolic operator. If there exists a $\mu > 0$ such that $a(x,t) \geq \mu > 0$ for all (x,t) in E, then L is said to be uniformly parabolic. Also consider the operator B acting on u in $\Gamma \setminus \{(x,t) : t = 0\}$ as

$$B[u] = c(x,t)u + d(x,t)\frac{\partial u}{\partial n} \tag{3.2}$$

where c and d are non-negative functions on Γ, n is an outward normal direction and $c^2 + d^2 > 0$ for all points in Γ. B is the boundary operator.

Suppose L is a uniformly parabolic operator and consider a function h on E such that $h \leq 0$. Suppose u is an admissible function which satisfies the differential inequality

$$(L + h)[u] = a(x,t)\frac{\partial^2 u}{\partial x^2} + b(x,t)\frac{\partial u}{\partial x} + h(x,t)u - \frac{\partial u}{\partial t} \geq 0. \tag{3.3}$$

Theorem 1. *Let P be a point on ∂E where the normal derivative at P is not parallel to the t axis. Let $U(P)$ be a closed ball where $U(P)$ is tangent to ∂E at P and the interior of $U(P)$ is contained in E. If $M = \max_{\bar{E}} u$ is attained at P and $u < M$ in $U(P)$ except at P, then for any outward direction of E denoted by ν*

$$\frac{\partial u}{\partial \nu}(P) > 0.$$

Theorem 2. *If $M = \max_{\bar{E}} u$ is attained at some point P in the parabolic interior of E and $M \geq 0$, then $u \equiv M$ on all line segments where t equals a constant which lie directly below this point.*

The next theorem provides a maximum principle for solutions of (3.3) when h is bounded above. The theorem, as stated below, is found in [1].

Theorem 3. ***(Maximum Principle)*** *Suppose u is an admissible function which satisfies (3.3) where $h(x,t) \leq K < +\infty$ and u also satisfies the inequality $B[u] \leq 0$. If $u(x,0) \leq 0$, then $u(x,t) \leq 0$ in $\bar{E}$.*

Furthermore, either

$$u(x,t) < 0 \tag{3.4a}$$

in E or there exists some $t^* \leq T_1$ such that

$$u(x,t) \equiv 0 \tag{3.4b}$$

for all $t \leq t^*$.

Proof. Consider the function $v = u(x,t)e^{-\lambda t}$ where $\lambda > K$. Notice that,

$$\begin{aligned}(L+h-\lambda)[v] &= a(x,t)\frac{\partial^2 v}{\partial x^2} + b(x,t)\frac{\partial v}{\partial x} + h(x,t)v - \lambda v - \frac{\partial v}{\partial t} \\ &= a(x,t)e^{-\lambda t}\frac{\partial^2 u}{\partial x^2} + b(x,t)e^{-\lambda t}\frac{\partial u}{\partial x} + h(x,t)ue^{-\lambda t} + \\ &\qquad - \lambda u e^{-\lambda t} - \frac{\partial u}{\partial t}e^{-\lambda t} + \lambda u e^{-\lambda t} \\ &= (L+h)[u]e^{-\lambda t} \geq 0\end{aligned}$$

Since $h - \lambda < 0$, the conclusions of Theorem 1 and 2 hold. Let $\bar{M} = \max_{\bar{E}} v$.

Assume, to reach a contradiction, that $\bar{M} > 0$. Since v is continuous, it must attain its maximum on $\bar{E}$. Let P be the point where $v(P) = \bar{M}$.

Suppose P lies in the parabolic interior of E. From Theorem 2, $v \equiv \bar{M}$ for all horizontal line segments where t equals a constant below P including $t = 0$. However, this implies $u(x, 0) > 0$ for some x. If P does not occur in the parabolic interior of E, it must lie on Γ.

Since $u(x, 0) \leq 0$, P can not occur on Γ where $t = 0$. Now suppose that P is on Γ where $t \neq 0$. By Theorem 1, the outward normal derivative of v is

$$\frac{\partial v}{\partial n}(P) > 0.$$

At this same point, the function u and its outward normal derivative are positive. Since either $c(P) > 0$ or $d(P) > 0$, the boundary operator at this point is

$$B[u](P) = cu(P) + d\frac{\partial u}{\partial n}(P) > 0$$

which contradicts the assumption that $B[u] \leq 0$. Therefore, v cannot attain its maximum on $\bar{E}$; which is a contradiction. Thus $\bar{M} \leq 0$ and it follows that $u \leq 0$ on $\bar{E}$.

To establish the last conclusion of the theorem, suppose $u(P) = 0$ for some P in E. At this point, $v(P) = 0$. Since $v \leq 0$ on $\bar{E}$, v attains its maximum at an interior point. From Theorem 2, we conclude that $v \equiv 0$ for all $t \leq t^*$ which implies $u = 0$ for all $t \leq t^*$. □

Theorem 3 leads to a comparison theorem for a special class of non-linear parabolic equations. We will use this theorem to prove that the solutions are bounded.

Theorem 4. ***(Comparison Theorem)*** *Consider the differential operator P. Define P acting on an admissible function u as*

$$P[u] = a(x,t)\frac{\partial^2 u}{\partial x^2} + b(x,t)\frac{\partial u}{\partial x} + h(x,t,u) - \frac{\partial u}{\partial t}$$

where $a(x,t) \geq \mu > 0$ and continuous; $b(x,t)$ is a bounded continuous function and h is a continuous function that is locally Lipschitz in u.

Suppose u_1 and u_2 are admissible functions where

$$P[u_2] \leq P[u_1] \text{ on } E$$

and

$$B[u_1] \leq B[u_2] \text{ on } \Gamma \setminus \{(x,t) : t = 0\}.$$

If $u_1(x,0) \leq u_2(x,0)$, then $u_1(x,t) \leq u_2(x,t)$ for all $0 \leq t \leq T$. Furthermore, either $u_1(x,t) < u_2(x,t)$ on E or there exists a $t^* \leq T$ such that $u_1(x,t) \equiv u_2(x,t)$ for all $0 \leq t \leq t^* \leq T$.

Proof. Let $v = u_1 - u_2$ and consider the linear operator $L + \bar{h}$ where

$$\bar{h}(x,t) = \begin{cases} \dfrac{h(x,t,u_1(x,t)) - h(x,t,u_2(x,t))}{u_1(x,t) - u_2(x,t)} & u_1 \neq u_2 \\ 0 & u_1 = u_2 \end{cases}.$$

Since h is locally Lipschitz in u, $\bar{h}$ is bounded above. The conclusions follow by applying Theorem 3 to v. □

Solution Bounds

In this section, we will provide bounds on S, f, v and L. Although G and R are usually defined as

$$G(S) = \frac{S}{1+S}$$

and

$$R(S) = \frac{S}{1+S} - \beta,$$

the results of this section do not depend on these specific functions. Recall from Chapter 2, both functions are C^1, $G'(S)$, $R'(S) \geq 0$ for $S \geq 0$ and $G(0) = 0$.

To use the the theorems from the previous section, we must identify the sets E and Γ (See Figure 3). Recall, we assume that solutions exist and are unique.

The solution curve of (2.26c) will define one of the boundaries of E. However, E must be a bounded set in the xt plane and we will only consider sets where $x \geq 0$. If $L(t)$ is the solution to (2.26c), then $L(t)$ is a C^1 function. L corresponds to the thickness of a biofilm where we assume that $L(0) \neq 0$. Let $T_2 = \sup\{0 < t < T_1 | L(t) > 0\}$. By continuity, $T_2 \neq 0$. For any finite time, T, where $0 < T < T_2$, let

$$\Omega_t = (0, L(t)) \times \{t\} \tag{3.5}$$

and define the set E as

$$E = \bigcup_{0<t<T} \Omega_t. \tag{3.6}$$

The sets $\overline{\Omega}_0$, $\{0\} \times [0,T]$, $\overline{\Omega}_T$ and $\{(L(t),t)|0 \leq t \leq T\}$ are the boundary of E where $\overline{\Omega}_0$ and $\overline{\Omega}_T$ represent the closure of Ω_0 and Ω_T. The parabolic interior of E is

$$\widetilde{E} = \bigcup_{0<t\leq T} \Omega_t. \tag{3.7}$$

The parabolic boundary, Γ, is the union of the sets $\overline{\Omega}_0$, Γ_0 and Γ_L where

$$\Gamma_0 = \{0\} \times [0,T),$$

and

$$\Gamma_L = \{(L(t),t)|0 \leq t < T\}.$$

Notice that Γ_0 is a straight line and Γ_L is a C^1 curve in the xt plane. Thus every point in these sets satisfy the hypotheses of Theorem 1.

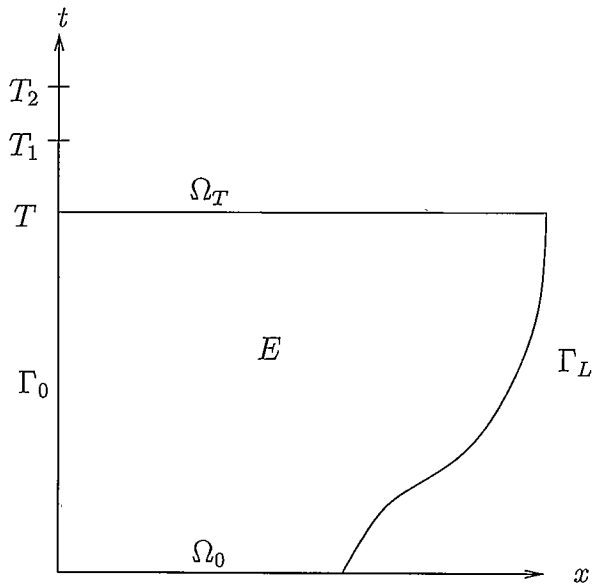


Figure 3. The sets E, Ω_0, Ω_T, Γ_L and Γ_0.

Bounds on S

On the sets E and Γ define the operator P acting on an admissible function u as

$$P[u] \equiv \frac{1}{\epsilon}\frac{\partial^2 u}{\partial x^2} + \frac{1}{\epsilon}g(x,t,u) - \frac{\partial u}{\partial t} \tag{3.8}$$

where the function g is

$$g(x,t,u) = \begin{cases} -\dfrac{1}{\varphi^2}G(u)f(x,t) & u \geq 0 \\ 0 & \text{otherwise} \end{cases}. \tag{3.9}$$

Since $G(0) = 0$, g is a continuous function. The following lemma shows that g is in fact locally Lipschitz in u.

Lemma 1. *The function $g(x,t,u)$ defined by (3.9) is locally Lipschitz in u.*

Proof. Let $u_1 < u_2$. g is differentiable in the u argument except at $u = 0$. If 0 is not in the interval $[u_1, u_2]$, let

$$K = \frac{|f(x,t)|}{\varphi^2} \begin{cases} \max\limits_{[u_1,u_2]} G'(u) & u_1 > 0 \\ 0 & u_2 < 0 \end{cases}.$$

Notice that $K = \max\limits_{[u_1,u_2]} |g_u(x,t,u)|$. By the Mean Value Theorem, there exists $\tilde{u}$ in the interval $[u_1, u_2]$ such that

$$\begin{aligned} \frac{|g(x,t,u_2) - g(x,t,u_1)|}{|u_2 - u_1|} &= \left| \frac{g(x,t,u_2) - g(x,t,u_1)}{u_2 - u_1} \right| \\ &= \left| \frac{\partial g}{\partial u}(x,t,\tilde{u}) \right| \\ &\leq K. \end{aligned}$$

If 0 is in the interval of $[u_1, u_2]$, let $K = \frac{|f(x,t)|}{\varphi^2} \max_{[0,u_2]} G'(u)$. Since $u_1 \leq 0 \leq u_2$, the Mean Value Theorem can be used again to show

$$\begin{aligned}
\frac{|g(x,t,u_2) - g(x,t,u_1)|}{|u_2 - u_1|} &= \frac{|g(x,t,u_2)|}{u_2 - u_1} \\
&= \frac{|f(x,t)|}{\varphi^2} \frac{G(u_2)}{u_2 - u_1} \\
&< \frac{|f(x,t)|}{\varphi^2} \left(\frac{G(u_2) - G(0)}{u_2 - 0} \right) \\
&= \frac{|f(x,t)|}{\varphi^2} G'(\tilde{u})
\end{aligned}$$

for some $0 \leq \tilde{u} \leq u_2$. □

Now define the boundary operator B acting on u defined on $\Gamma \setminus \Omega_0$ as

$$B[u] \equiv c(x,t)u(x,t) + d(x,t)\frac{\partial u}{\partial n}(x,t) \tag{3.10}$$

where n is the outward normal direction and the functions c and d are

$$c(x,t) = \begin{cases} 1 & (x,t) \in \Gamma_L, \\ 0 & \text{otherwise,} \end{cases}$$

$$d(x,t) = \begin{cases} 1 & (x,t) \in \Gamma_0, \\ 0 & \text{otherwise.} \end{cases}$$

The operators P and B satisfy the hypotheses of Theorems 4. Using these two operators, the following proposition provides conditions for bounds on the S solution.

Proposition 1. *Let $\bar{S}$ be a solution to*

$$\epsilon\frac{\partial \bar{S}}{\partial t} = \frac{\partial^2 \bar{S}}{\partial x^2} + g(x,t,\bar{S}) \qquad \text{for all } (x,t) \in E$$

$$\frac{\partial \bar{S}}{\partial x}(0,t) = 0, \quad \bar{S}(L(t),t) = S_b \qquad \text{for } 0 < t < T$$

$$\bar{S}(x,0) = S_b \qquad 0 < x < L_0$$

If $S_b > 0$, then $0 < \bar{S}(x,t) \leq S_b$ for all $(x,t) \in E$.

Proof. If $\bar{S}$ is a solution to the system above, then $P[\bar{S}] = 0$ and $B[\bar{S}] = 0$. Notice that for the functions $u_1 = 0$ and $u_2 = S_b$

$$P[0] = 0,$$

$$P[S_b] = -\frac{1}{\epsilon\varphi^2}G(S_b)f(x,t),$$

$$B[0] = 0,$$

$$B[S_b] = \begin{cases} 0 & \text{on } \Gamma_0, \\ S_b & \text{on } \Gamma_L, \end{cases}$$

hence $P[S_b] \leq P[\bar{S}] \leq P[0]$ and $B[0] \leq B[\bar{S}] \leq B[S_b]$. By Theorem 4, it follows that $0 \leq \bar{S} \leq S_b$. Since $S_b \neq 0$, the second condition of Theorem 4 cannot hold. Therefore, $\bar{S}$ is strictly greater than zero. □

From this proposition, it follows that $0 < S \leq S_b$. Since $\bar{S} > 0$, $g(x,t,\bar{S}) = -\frac{1}{\varphi^2}G(\bar{S})f(x,t)$ which implies $\bar{S} = S$.

Bounds on f

Unfortunately Theorem 4 can not be applied to the f equation. If, however, we assume that biomass diffuses in the biofilm, the f equation is parabolic and Theorem 4 can be applied.

Assuming that biomass diffuses inside the biofilm, a new flux $\mathbf{J}_i$ for biomass is

$$\mathbf{J}_i = v\rho_i - D_i\frac{\partial \rho_i}{\partial x}.$$

Here ρ_i is either the active or inactive cell density and D_i is the diffusion coefficient. If it is assumed that the inactive biomass diffuses at the same rate as the active biomass, the dimensionless equations found in (2.26) become

$$\epsilon\frac{\partial S}{\partial t} = \frac{\partial^2 S}{\partial x^2} - \frac{1}{\varphi^2}G(S)f, \tag{3.12a}$$

$$\frac{\partial f}{\partial t} = d\frac{\partial^2 f}{\partial x^2} + \left(R(S)(1-f) - \alpha\right)f - v\frac{\partial f}{\partial x}, \tag{3.12b}$$

$$\frac{dL}{dt} = v\left(L(t), t\right) \tag{3.12c}$$

where

$$v(x,t) = \int_0^x R(S(\xi,t))f(\xi,t)\,d\xi. \tag{3.12d}$$

If D_f is the diffusion constant of f then the parameter d is defined as

$$d = \frac{D_f}{D}. \tag{3.13}$$

The definition of the variables and other parameters remains unchanged. We will assume that the parameter $d \ll 1$ and is small compared to the other parameters in

the model. If biomass does not interact or pass through the substratum, the no-flux boundary condition at $x = 0$ is

$$v(0,t)f(0,t) - d\frac{\partial f}{\partial x}(0,t) = 0.$$

Since $v(0,t) = 0$, this reduces to

$$\frac{\partial f}{\partial x}(0,t) = 0.$$

With the addition of the diffusion, a boundary condition at $x = L$ must be placed on f. For example, if we assume that the cell density at the interface is a prescribed function of t, then the boundary condition for f at $x = L$ is

$$f(L,t) = a(t) \tag{3.14}$$

where $a(t)$ is a non-negative function and $a(t) \leq 1$ for all t. Other types of boundary conditions, like no-flux or a Robin type condition could also be applied. For these linear boundary conditions, the results of the proposition below still hold.

Proposition 2. *Suppose f solves*

$$\frac{\partial f}{\partial t} = d\frac{\partial^2 f}{\partial x^2} - v(x,t)\frac{\partial f}{\partial x} + (R(S)(1-f) - \alpha)\, f \qquad \text{for all } (x,t) \in E$$

$$\frac{\partial f}{\partial x}(0,t) = 0 \quad f(L(t),t) = a(t) \qquad \text{for } 0 < t < T.$$

If $0 \leq f(x,0) \leq 1$ for all $x \in \Omega_0$, then for all $(x,t) \in E$, $0 \leq f(x,t) \leq 1$.

Proof. Consider the operator P acting on an admissible function u as

$$P[u] \equiv d\frac{\partial^2 u}{\partial x^2} - v(x,t)\frac{\partial u}{\partial x} + (R(S)(1-u) - \alpha)\, u.$$

Since $0 < S \leq S_b$, R is continuous and bounded. Notice that the non-linear term is quadratic in u and hence continuously differentiable in the u argument. Therefore, the operator P satisfies the hypotheses of Theorem 4. Now define on $\Gamma \setminus \Omega_0$ the boundary operator as

$$B[u] = c(x,t)u(x,t) + d(x,t)\frac{\partial u}{\partial n}$$

where the functions c and d are

$$c(x,t) = \begin{cases} 1 & (x,t) \in \Gamma_L, \\ 0 & \text{otherwise}, \end{cases}$$
$$d(x,t) = \begin{cases} 1 & (x,t) \in \Gamma_0, \\ 0 & \text{otherwise}. \end{cases}$$

B also satisfies the hypothesis of Theorem 4.

Notice for $u_1 = 0$ and $u_1 = 1$,

$$P[0] = 0,$$

$$P[1] = -\alpha,$$

$$B[0] = 0,$$
$$B[1] = \begin{cases} 1 & (x,t) \in \Gamma_L, \\ 0 & (x,t) \in \Gamma_0. \end{cases}$$

Thus, $P[1] \leq P[f] \leq P[0]$ and $B[0] \leq B[f] \leq B[1]$. Therefore by Theorem 4, $0 \leq f(x,t) \leq 1$ for all $(x,t) \in E$. □

Typically $f(x,0)$ is a non-zero constant function. Using arguments that are similar to those used for the S equation, it follows that $f(x,t) > 0$.

Bounds on v and L

The S solution is bounded and with the addition of diffusion to the f equation, the f solution is also bounded. Since the v and L equations are integrals involving functions of S and f, bounds can be derived for v and L provided diffusion is included in the f equation.

Proposition 3. *Suppose diffusion of f is included in the model equations. If $L(t)$ solves the differential equation*

$$\frac{dL}{dt} = v(L(t), t)$$

$$L(0) = L_0$$

where

$$v(x,t) = \int_0^x R(S(\xi,t)) f(\xi,t)\, d\xi,$$

then for all $(x,t) \in E$

$$|v(x,t)| \leq |R(S_b)|\, x$$

and

$$L(t) \leq L_0 \exp |R(S_b)|\, t.$$

Proof. By Propositions 1 and 2, S and f are bounded below by zero and above by S_b and 1 respectively. Since $R'(S) > 0$, for all $(x,t) \in E$

$$|v(x,t)| = \left| \int_0^x R(S(\xi,t)) f(\xi,t)\, d\xi \right|$$

$$\leq x\, |R(S_b)|\,.$$

Thus for all $0 < t < T$

$$\frac{dL}{dt} = v(L(t), t) \leq L(t)\,|R(S_b)|$$

and solving this differential inequality leads to the bound for $0 \leq t \leq T$

$$L(t) \leq L_0 \exp\left(|R(S_b)|\,t\right).$$

□

Behavior at the Interface

Consider the solution curve for the differential equation

$$\frac{dx}{dt} = v(x(t), t)$$

$$x(0) = x_0 \in \Omega_0$$

where

$$v(x,t) = \int_0^x R(S(\xi,t))f(\xi,t)\,d\xi.$$

Let $\dot{F}$ denote the derivative of F along the solution curve. On this curve,

$$\dot{f} = \frac{\partial f}{\partial t} + \frac{dx}{dt}\frac{\partial f}{\partial x} = \frac{\partial f}{\partial t} + v(x,t)\frac{\partial f}{\partial x}$$

and using (2.26b) this leads to the differential equation

$$\dot{f} = (R(S)(1-f) - \alpha)\,f. \tag{3.15}$$

Along the curve that corresponds to the interface, S is equal to a constant, S_b. So at the interface, a simple first order differential equation

$$\dot{f} = (R(S_b)(1-f) - \alpha)\, f \tag{3.16}$$

holds. The equilibria solutions of this ODE are summarized in the lemma below.

Lemma 2. *Consider the first order initial value problem*

$$\dot{x} = (a_1(1-x) - a_2)x, \tag{3.17a}$$

$$x(0) = x_0 \tag{3.17b}$$

where the parameter a_2 is non-negative. Solutions exist and are unique for all parameter values. If $a_1 = a_2$ or $a_1 = 0$ a bifurcation occurs and (3.17a) *has one equilibrium solution, $x = 0$. Solutions of* (3.17) *decay to zero if $x_0 > 0$ and approach $-\infty$ if $x_0 < 0$. Otherwise,* (3.17a) *has two equilibrium solutions, $x = 0$ and $x = 1 - \frac{a_2}{a_1}$. For parameter values where $a_1 > a_2$, $x = 0$ is unstable and $x = 1 - \frac{a_2}{a_1}$ is stable. If $a_1 < a_2$, then $x = 0$ is stable and $x = 1 - \frac{a_2}{a_1}$ is unstable.*

Proof. Notice that the right-hand side of (3.17a) is quadratic in x, hence it's locally Lipschitz in x. Therefore, a unique solution of (3.17) exists.

If $a_1 = 0$ equation (3.17a) reduces to

$$\dot{x} = -a_2 x \tag{3.18}$$

and if $a_1 = a_2$ then (3.17a) reduces to

$$\dot{x} = -a_2 x^2. \tag{3.19}$$

In both cases, there is only one equilibrium solution. Also, $\dot{x} < 0$ for all non-zero x values in both equations. If $x_0 > 0$, the solutions of (3.18) or (3.19) are decreasing functions and bounded below zero. Thus, the solutions must limit on zero. If $x_0 < 0$, the solutions are strictly decreasing and are not bounded below. These solutions will approach $-\infty$.

For all other values of a_1 and a_2, the two equilibrium solutions can easily be found by setting the right-hand side of (3.17) to zero and solving for x. Notice that the derivative of the right-hand side is

$$F'(x) = a_1(1-x) - a_2 - a_1 x.$$

An equilibrium solution is stable provided $F'(x) < 0$. If $F'(x) < 0$ the equilibrium solution is unstable. Evaluating this at the equilibrium solutions gives

$$F'(0) = a_1 - a_2$$

and

$$F'\left(1 - \frac{a_2}{a_1}\right) = a_2 - a_1.$$

The stability conditions follow directly from these equations. □

Notice that in the region where $x = 1 - \frac{a_2}{a_1}$ is stable, it also holds that

$$0 < 1 - \frac{a_2}{a_1} \leq 1.$$

In the set of parameter values where $x = 1 - \frac{a_2}{a_1}$ is unstable, it follows $1 - \frac{a_2}{a_1} > 1$ if $a_1 < 0$ and $1 - \frac{a_2}{a_1} < 0$ if $a_1 > 0$.

Applying this to equation (3.16), it follows that the value of f at $x = L(t)$ approaches $1 - \dfrac{\alpha}{R(S_b)}$ if $R(S_b) > \alpha$ and approaches zero if $R(S_b) < \alpha$. This result indicates that the cell net growth rate must exceed the inactivation rate for a viable cell population to exist at the interface. It follows that f is bounded at $x = L(t)$ between 0 and 1 for all parameter values.

CHAPTER 4

STEADY-STATE SOLUTIONS

The initial formation of a biofilm is not well understood. It is known by experimentation that with a small of amount biomass present, the biofilm quickly increases in size and stabilizes at a thickness that ranges from 20 to 500 microns [2]. Active organisms are always present in these biofilms. In the model, this behavior corresponds to a stable steady-state solution with $f \geq 0$. The existence of steady-state solutions and the stability of those solutions are studied in this chapter.

In this chapter, we will assume that the functions R and G are

$$G(S) = \frac{S}{1+S},$$
$$R(S) = \frac{S}{1+S} - \beta.$$

Only solutions with $f \geq 0$ are considered. Since biofilms typically have active organisms present, a steady-state solution with $f \equiv 0$ is considered a trivial steady-state solution.

In [13], numerical simulations showed that the active volume fraction and substrate profiles were non-negative. However, the model also predicted unbounded growth unless a detachment function was included in the biomass equations or a sloughing term was added to the biofilm thickness equation. We will prove that if the inactivation rate is non-zero then only a trivial steady-state solution will exist. We

will also show that if the inactivation rate is zero, then under certain conditions a non-trivial steady solution exists. Finally, we will prove that the trivial steady-state solution is linearly unstable for certain parameter values.

Existence of Steady-State Solutions

The steady-state equations are given by (see equations (2.26))

$$\frac{d^2S}{dx^2} = \frac{1}{\varphi^2}\frac{S}{1+S}f, \tag{4.1a}$$

$$v\frac{df}{dx} = \left(\left(\frac{S}{1+S} - \beta\right)(1-f) - \alpha\right)f, \tag{4.1b}$$

$$\int_0^L \left(\frac{S(\xi)}{1+S(\xi)} - \beta\right) f(\xi)\, d\xi = 0 \tag{4.1c}$$

where

$$v(x) = \int_0^x \left(\frac{S(\xi)}{1+S(\xi)} - \beta\right) f(\xi)\, d\xi. \tag{4.1d}$$

The corresponding boundary conditions for this problem are

$$\frac{dS}{dx}(0) = 0, \;\; S(L) = S_b, \;\; v(0)f(0) = 0. \tag{4.2}$$

The parameter α controls which steady-state solutions are possible. The first proposition shows that if α is positive, then only a trivial steady-state solution exits.

Proposition 4. *For $\alpha > 0$, the solution $S(x) \equiv S_b$, $f(x) \equiv 0$ and any real number L is the only solution of (4.1) where $f(x) \geq 0$.*

Proof. Notice that if equation (4.1b) is integrated from 0 to L and integration by parts is applied, we obtain

$$\begin{aligned}\int_0^L v\frac{df}{dx}\,d\xi &= vf\Big|_0^L - \int_0^L f\frac{dv}{dx}\,d\xi \\ &= -\int_0^L f\frac{dv}{dx}\,d\xi.\end{aligned}$$

Now using equation (4.1b) and equation (4.1d) the expression above leads to

$$\int_0^L \left(\left(\frac{S(\xi)}{1+S(\xi)} - \beta\right)(1-f(\xi)) - \alpha\right) f(\xi)\,d\xi = -\int_0^L \left(\frac{S(\xi)}{1+S(\xi)} - \beta\right) f^2(\xi)\,d\xi.$$

Simplifying this expression results in the integral equation

$$\int_0^L \left(\left(\frac{S(\xi)}{1+S(\xi)} - \beta\right) f(\xi) - \alpha f(\xi)\right)\,d\xi = 0,$$

which by using equation (4.1c) implies

$$\alpha\int_0^L f(\xi)\,d\xi = 0.$$

If $f \geq 0$, the calculation above shows that $f \equiv 0$. Thus the integral condition in (4.1c) will be satisfied for any S or L. Furthermore, if $f \equiv 0$ is substituted into equation (4.1a), the boundary conditions on S imply that S must be the constant function $S(x) = S_b$. So $S(x) = S_b$, $f(x) = 0$ and any real valued L satisfies that steady state equations. □

It should be pointed out that a similar argument could be applied to a higher dimensional model with more than one species present. Recall from Chapter 2, if ρ_i is the density of some organism in the biofilm then the mass balance principles state

$$\frac{\partial}{\partial t}\int_\Omega \rho_i\,d\sigma + \int_\Omega \rho_i \mathbf{v}\cdot\mathbf{n}\,d\sigma = \int_\Omega F_i\,d\sigma$$

where Ω is an arbitrary volume and $\mathbf{n}$ is the outward normal direction of Ω. If Ω is the entire biofilm, then this equation at steady-state is

$$\int_{\partial\Omega} \rho_i \mathbf{v}\, d\tau = \int_{\Omega} F_i\, d\sigma.$$

However, at steady-state the velocity is zero on the substratum and interface. The periodic boundary conditions will cancel out the remaining integrals on $\partial\Omega$. Therefore, the integral on the right-hand side is zero. If F_i is non-negative, then F_i must be identically zero. Furthermore, if F_i is proportional to ρ_i or some other biomass density, we conclude that this density is identically zero. This argument is not valid if a detachment term or some other function that models removal of biomass is included in F_i; in this situation, F_i may change sign.

We now consider the case $\alpha = 0$. For any β, there is a constant steady-state solution, namely $S(x) = S_b$,$f(x) = 0$ and L any real number. Other solutions exist for certain β values. The conditions for the existence of these steady-state are summarized in the next theorem.

Theorem 5. ***(Existence of Steady-State Solutions)*** *The existence of solutions to* (4.1) *fall into two categories.*

If $\beta < \dfrac{S_b}{1+S_b}$, *then two steady-state solutions exist; the constant steady-state solution:* $S(x) \equiv S_b$, $f(x) \equiv 0$ *and* L *any real number and the solution* $f(x) \equiv 1$, $\tilde{L} < \infty$ *and* $\tilde{S}$ *where* $\tilde{S}$ *and* $\tilde{L}$ *solve the differential equation*

$$\frac{d^2\tilde{S}}{dx^2} = \frac{1}{\varphi^2}\frac{\tilde{S}}{1+\tilde{S}} f \tag{4.3a}$$

with boundary conditions

$$\frac{d\tilde{S}}{dx}(0) = 0, \quad \tilde{S}(\tilde{L}) = S_b. \tag{4.3b}$$

If $\beta > \dfrac{S_b}{1+S_b}$, *then only one steady-state solution, the constant steady-state will exist.*

To prove this theorem, it will be demonstrated that for $\beta \neq \dfrac{S_b}{1+S_b}$ the only solutions for (4.1b) are the constant solutions $f(x) = 0$ and $f(x) = 1$. Once this has been established, then (4.1) can be reduced to a differential equation for S and an integral equation involving L. The existence of a unique solution to this reduced problem is proved.

Lemma 3. *If* $\beta \neq \dfrac{S_b}{1+S_b}$ *and* $\alpha = 0$, *then the only possible solutions to* (4.1b) *are* $f(x) \equiv 1$ *and* $f(x) \equiv 0$

Proof. Notice that equation (4.1b) can be written as

$$\begin{aligned} v\frac{df}{dx} &= -\left(\frac{S}{1+S} - \beta\right) f^2 + \left(\frac{S}{1+S} - \beta\right) f \\ &= -\frac{dv}{dx} f + \frac{dv}{dx} \end{aligned}$$

which leads to

$$\frac{d(vf)}{dx} = \frac{dv}{dx},$$

which can be re-written as

$$\frac{d}{dx}(v(f-1)) = 0.$$

Since $v(0) = 0$,

$$v(x)\,(f(x) - 1) = 0$$

for all $x \in [0, L]$.

Two possibilities can occur: either $f(x) \equiv 1$ or $v(x) \equiv 0$. If $v(x) \equiv 0$ then it must also be true that

$$v'(x) = \left(\frac{S(x)}{1 + S(x)} - \beta\right) f(x) = 0$$

for all $x \in [0, L]$. If $\dfrac{S(x)}{1 + S(x)} - \beta = 0$, then at $x = L$

$$\frac{S_b}{1 + S_b} - \beta = 0$$

which is a contradiction. Thus if $v(x) \equiv 0$, it follows that $f(x) \equiv 0$. □

Lemma 4. *If $f(x) \equiv 0$ and $\alpha = 0$, then the solution to* (4.1a) *is $S = S_b$ and* (4.1c) *is satisfied for any L.*

Proof. If $f(x) \equiv 0$ then equation (4.1c) is satisfied for any L and the boundary conditions on S can only be satisfied by the constant solution $S(x) \equiv S_b$. □

The next two propositions consider the case of $f(x) \equiv 1$. When $f(x) \equiv 1$, (4.1) reduces to a differential equation and integral equation that must be satisfied simultaneously. The first proposition proves the existence and uniqueness of solutions to the differential equation. The second proves that a unique solution, with the addition of the integral equation will exist provided $\beta < \dfrac{S_b}{1 + S_b}$.

Proposition 5. *For any $l > 0$, there exists a unique solution to the differential equation*

$$\frac{d^2S}{dx^2} = \frac{1}{\varphi^2}\frac{S}{1+S} \tag{4.4a}$$

with boundary conditions

$$\frac{dS}{dx}(0) = 0, \qquad S(l) = S_b. \tag{4.4b}$$

Proof. Let $u = S$ and $w = \frac{dS}{dx}$. The two dimensional system equivalent to (4.4) is

$$u' = w \tag{4.5a}$$

$$w' = \frac{1}{\varphi^2}\frac{u}{1+u}. \tag{4.5b}$$

This system has one equilibrium solution $(0,0)$ and the linearization about this equilibrium solution is

$$J = \begin{bmatrix} 0 & 1 \\ \frac{1}{\varphi^2} & 0 \end{bmatrix} \tag{4.6}$$

which has eigenvalues $\lambda_{\pm} = \pm\frac{1}{\varphi}$, hence $(0,0)$ is a saddle point. Consider the phase portrait of (4.5) in the region $u \geq 0$. In this region let,

$$H(u,w) = \frac{w^2}{2} - \frac{1}{\varphi^2}\left(u - \ln\left(1+u\right)\right). \tag{4.7}$$

One can easily check that the level sets of (4.7) are invariant for the flow generated by (4.5).

The unstable manifold lying in the first quadrant is given by

$$w = \frac{\sqrt{2}}{\varphi}\sqrt{u - \ln(1+u)}. \tag{4.8}$$

Let R be defined as the following region in the phase portrait (see Figure 4)

$$R = \left\{ (u, w) : 0 < w < \frac{\sqrt{2}}{\varphi}\sqrt{u - \ln(1+u)} \text{ and } 0 \leq u \leq S_b \right\}. \tag{4.9}$$

Along $w = 0$, the vector field points to the interior of R. So a trajectory starting at

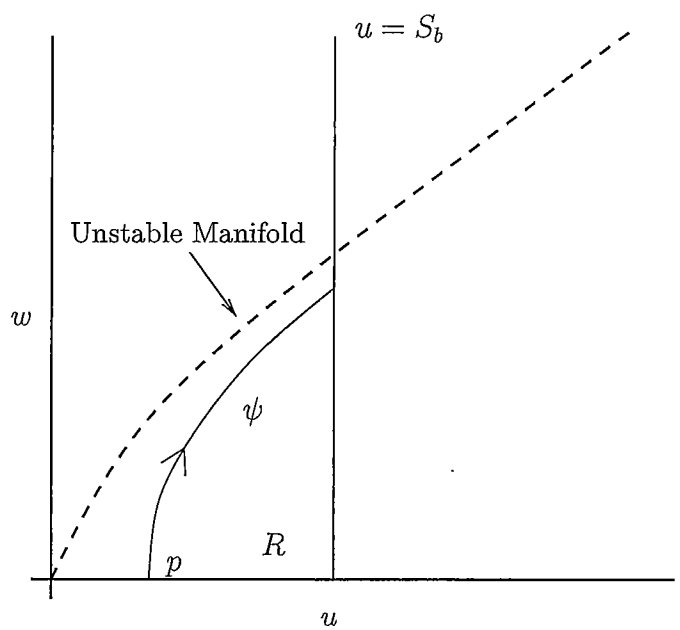


Figure 4. Region R and flow ψ.

$w = 0$ will immediately enter R. Let p be the point where the trajectory, ψ, enters R. This trajectory can not cross $w = 0$ at a later time since $u > 0$ in R. Furthermore, ψ must exit R in a finite amount of time. Since ψ cannot cross the unstable manifold, it must exit across $u = S_b$. This trajectory corresponds to a solution of (4.4) where $\dot{L}$ is the length of time ψ is in R and $S(0) = p$. The length of time ψ spends in R will depend on p. By integrating along ψ, the relationship between p and L can be

derived from H:

$$L(p) = \frac{\varphi}{\sqrt{2}} \int_p^{S_b} \frac{du}{\sqrt{F(u) - F(p)}} \quad \text{where } F(u) = u - \ln(1+u). \tag{4.10}$$

As $p \to 0$, the trajectory ψ approaches the unstable manifold, thus

$$\lim_{p \to 0} L(p) = +\infty.$$

To calculate the limit as $p \to S_b^-$, let $r^2 = S_b - p$ and

$$I(p) = \int_p^{S_b} \frac{du}{\sqrt{F(u) - F(p)}}. \tag{4.11}$$

$I(p)$ can not be explicitly calculated; furthermore the integral has an integrable singularity. To work around this difficulty, a Taylor expansion for $I(S_b - r^2)$ about $r = 0$ will be calculated. Consider

$$g(u;p) = \sqrt{\frac{A(u-p)}{F(u) - F(p)}} \quad \text{where } A = \frac{p}{1+p}. \tag{4.12}$$

The expansion of (4.12) about $u = p$ is

$$g(u;p) = 1 - \frac{1}{4(1+p)p}(u-p) + O\left((u-p)^2\right). \tag{4.13}$$

It follows that

$$\begin{aligned} \frac{1}{\sqrt{F(u) - F(p)}} &= \frac{1}{\sqrt{A(u-p)}} \cdot g(u;p) \\ &= \frac{1}{\sqrt{A(u-p)}} - \frac{1}{4\sqrt{A}(1+p)p}\sqrt{u-p} + O\left((u-p)^{\frac{3}{2}}\right). \end{aligned}$$

By evaluating this expression at $p = S_b - r^2$ and integrating this equation, the expansion for $I(S_b - r^2)$ is

$$I(S_b - r^2) = 2\sqrt{\frac{1+S_b}{S_b}}r - \left(\frac{1}{S_b\sqrt{S_b(1+S_b)}} - \frac{1}{6S_b(1+S_b)}\right) r^3 + O\left(r^5\right) \tag{4.14}$$

and therefore

$$\lim_{p \to S_b^-} L(p) = 0.$$

Since $L(p)$ is continuous on $(0, S_b)$, for any $l > 0$ there exists a p such that $L(p) = l$. It follows that a solution to

$$\frac{d^2S}{dx^2} = \frac{1}{\varphi^2} \frac{S}{1+S},$$
$$\frac{dS}{dx}(0) = 0, \quad S(l) = S_b$$

exists for each $l > 0$. We will now show that the function $L(p)$ is a monotone decreasing function of p by proving $L' < 0$.

Let $u = p + (S_b - p)\phi$, then (4.10) becomes

$$L(p) = \frac{\varphi}{\sqrt{2}}(S_b - p) \int_0^1 \frac{d\phi}{\sqrt{F\left(p + (S_b - p)\phi\right) - F(p)}}.$$

Set $G(\phi, p) = F\left(p + (S_b - p)\phi\right) - F(p)$ and let

$$I(p) = (S_b - p) \int_0^1 [G(\phi, p)]^{-\frac{1}{2}} \, d\phi.$$

It follows that

$$I'(p) = -\int_0^1 [G(\phi, p)]^{-\frac{1}{2}} \, d\phi - (S_b - p) \int_0^1 \frac{1}{2} [G(\phi, p)]^{-\frac{3}{2}} \, G_p \, d\phi$$

where

$$G_p = F'\left(p + (S_b - p)\phi\right) \cdot (1 - \phi) - F'(p).$$

Since

$$F''(u) = \frac{1}{(1+u)^2} > 0,$$

F' is a monotone increasing function, so we have

$$\begin{aligned} G_p &= F'\left(p + (S_b - p)\phi\right) \cdot (1-\phi) - F'(p) \\ &\geq F'\left(p + (S_b - p)\phi\right) - F'(p) \\ &\geq 0. \end{aligned}$$

$G(\phi, p)$ is positive for any $0 < p < S_b$ and for all $0 < \phi < 1$, thus $I'(p) < 0$ for any $0 < p < S_b$. It follows that $L(p)$ is monotone decreasing and hence the solution to (4.4) is unique for each $l > 0$ □

Proposition 6. *If* $\beta < \dfrac{S_b}{1+S_b}$ *then there exists a unique* L *such that*

$$\frac{d^2 S}{dx^2} = \frac{1}{\varphi^2}\frac{S}{1+S}, \tag{4.16a}$$

$$\frac{dS}{dx}(0) = 0, \quad S(L) = S_b, \tag{4.16b}$$

$$\int_0^L \left(\frac{S(\xi)}{1+S(\xi)} - \beta\right) d\xi = 0. \tag{4.16c}$$

Proof. From (4.7), if a trajectory enters at point p and exits the region R at time L then

$$\frac{dS}{dx}(L) = \frac{\sqrt{2}}{\varphi}\sqrt{F(S_b) - F(p)}. \tag{4.17}$$

If equation (4.16a) is substituted into equation (4.16c), then (4.16c) is equivalent to an additional boundary condition

$$\frac{dS}{dx}(L) = \frac{1}{\varphi^2}\beta L. \tag{4.18}$$

Combining this equation with (4.17), we find that

$$\beta = \frac{\sqrt{2}\varphi\sqrt{F(S_b) - F(p)}}{L}. \tag{4.19}$$

Since p depends on L, (4.16) will have a solution provided there exists an L which solves (4.19).

It was shown in the previous proposition that $L(p)$ is a monotone decreasing function of p. Hence $L(p)$ is invertible. So the problem can be formulated in the following manner: Equation (4.16a) with boundary conditions found in (4.16b) has a unique solution for any $L > 0$. This problem coupled with the integral condition in (4.16c) has a unique solution provided there exists a unique $0 < p < S_b$ which solves (4.19). This equation can be written in terms of p as

$$\frac{\beta}{2} = \frac{\sqrt{F(S_b) - F(p)}}{I(p)} \equiv H(p) \tag{4.20}$$

$$\text{where } I(p) = \int_p^{S_b} \frac{du}{\sqrt{F(u) - F(p)}}.$$

As $p \to 0^+$, $H(p) \to 0$ since

$$\lim_{p \to 0^+} \sqrt{F(S_b) - F(p)} = \sqrt{F(S_b)} < +\infty$$

and

$$\lim_{p \to 0^+} I(p) = +\infty.$$

For the right endpoint, as $p \to S_b$, both the numerator and denominator approach zero. To calculate this limit, define $r^2 = S_b - p$. For the numerator, the Taylor

expansion about $r = 0$ is

$$\sqrt{F(S_b) - F(S_b - r^2)} = \sqrt{\frac{S_b}{1+S_b}}r - \frac{1}{4}\sqrt{\frac{1+S_b}{S_b}}\frac{1}{(1+S_b)^2}r^3 + O\left(r^5\right). \tag{4.21}$$

In Theorem 5, an expansion about $r = 0$ was derived for the denominator. So as $p \to S_b^-$

$$\frac{\beta}{2} = \frac{\sqrt{F(S_b) - F(p)}}{I(p)} = \frac{\sqrt{\frac{S_b}{1+S_b}}r + O\left(r^3\right)}{2\sqrt{\frac{1+S_b}{S_b}}r + O\left(r^3\right)} \to \frac{S_b}{2(1+S_b)}. \tag{4.22}$$

Therefore as $p \to S_b^-$, $\beta \to \frac{S_b}{1+S_b}$. Since $H(p)$ is continuous, it follows that there exists a p which solves (4.20). To show that this solution is unique, we will show $H(p)$ is a monotone function of p.

Note,

$$H'(p) = \frac{I(p)\left(\frac{1}{2}\left(F(S_b) - F(p)\right)^{-\frac{1}{2}}\right)\left(-\frac{p}{1+p}\right) - I'(p)\left(F(S_b) - F(p)\right)^{\frac{1}{2}}}{I(p)^2} \tag{4.23}$$

and thus the numerator will determine the sign of H'. The numerator of (4.23) can be written as

$$\frac{1}{2}\left(\frac{I(p)\cdot\left(-\frac{p}{1+p}\right) - 2I'(p)\left(F(S_b) - F(p)\right)}{\sqrt{F(u) - F(p)}}\right) \tag{4.24}$$

and the sign of this expression is determined by the sign of

$$I(p)\cdot\left(-\frac{p}{1+p}\right) - 2I'(p)\left(F(S_b) - F(p)\right). \tag{4.25}$$

From from the proof of Proposition 5,

$$I'(p) = -\frac{1}{(S_b - p)}I(p) - h(p) \quad \text{where } h(p) = \frac{(S_b - p)}{2}\int_0^1 \left(G(\phi, p)\right)^{-\frac{3}{2}}\cdot G_p d\phi.$$

Thus (4.25) becomes

$$-I(p)\left(\frac{p}{1+p}-\frac{2\left(F(S_b)-F(p)\right)}{S_b-p}\right)+2h(p)\left(F(S_b)-F(p)\right). \tag{4.26}$$

It is clear that $I(p)$ and the second term in the sum above are positive. For the remaining term, notice

$$\frac{p}{1+p}-2\frac{F(S_b)-F(p)}{S_b-p}<2\left(\frac{p}{1+p}-\frac{F(S_b)-F(p)}{S_b-p}\right). \tag{4.27}$$

By the Mean Value Theorem, there exists a $p\leq\tilde{p}\leq S_b$ such that

$$\frac{F(S_b)-F(p)}{S_b-p}=F'(\tilde{p})=\frac{\tilde{p}}{1+\tilde{p}}$$

Since $F''(p)=\frac{1}{(1+p)^2}>0$, F' is an increasing function and hence

$$\frac{p}{1+p}-\frac{F(S_b)-F(p)}{S_b-p}=\frac{p}{1+p}-\frac{\tilde{p}}{1+\tilde{p}}<0.$$

Therefore $H'(p)>0$ and if $\beta<\dfrac{S_b}{1+S_b}$, there exists a unique solution of (4.20) given by $H^{-1}(\beta)=p$. It follows that there is a unique L which solves (4.16) □

Addition of Diffusion

Since only constant valued solutions of f are possible, a natural modification to the model would be the addition of diffusion of biomass in the biofilm. Recall from Chapter 3, if diffusion of biomass within the biofilm is allowed then the dimensionless

equations (2.26) become

$$\epsilon\frac{\partial S}{\partial t} = \frac{\partial^2 S}{\partial x^2} - \frac{1}{\varphi^2}\frac{S}{1+S}f, \tag{4.28a}$$

$$\frac{\partial f}{\partial t} = d\frac{\partial^2 f}{\partial x^2} + \left(\left(\frac{S}{1+S} - \beta\right)(1-f) - \alpha\right) f - v\frac{\partial f}{\partial x}, \tag{4.28b}$$

$$\frac{dL}{dt} = v\left(L(t), t\right) \tag{4.28c}$$

where

$$v(x,t) = \int_0^x \left(\frac{S(\xi,t)}{1+S(\xi,t)} - \beta\right) f(\xi,t)\, d\xi. \tag{4.28d}$$

Since a second order spatial derivative occurs in the equation, another boundary condition at $x = L$ must be placed on f. We consider a mixed boundary condition of the form

$$a(t)f(L,t) + b(t)\frac{\partial f}{\partial x}(L,t) = 0 \tag{4.29}$$

where $a^2 + b^2 > 0$ for all t. If $a(t)$ and $b(t)$ are non-negative functions, only a trivial steady-state solution with $f(x) \geq 0$ exists.

Proposition 7. *If* $a(t)f(L,t) + b(t)\frac{\partial f}{\partial x}(L,t) = 0$, $a(t) \geq 0$ *and* $b(t) \geq 0$ *then* $f \equiv 0$ *is the only non-negative steady-state solution to* (4.28b).

Proof. The steady-state equation for f is

$$d\frac{d^2 f}{dx^2} - \frac{d\,(vf)}{dx} + \left(\frac{S}{1+S} - \alpha - \beta\right) f = 0. \tag{4.30}$$

By integrating (4.30) from 0 to L and using the conditions

$$\int_0^L \left(\frac{S(\xi)}{1+S(\xi)} - \beta\right) f(\xi)\, d\xi = 0, \tag{4.31}$$

$v(L) = 0$ and $f'(0) = 0$, it follows that

$$f'(L) = \frac{\alpha}{d} \int_0^L f(\xi)\, d\xi. \tag{4.32}$$

If f is non-negative and is not identically equal to zero, the above calculation implies that $f'(L) > 0$. Hence, if f is non-negative and $f(L) = 0$, then we have $f'(L) \leq 0$ which leads to a contradiction. Thus this calculation also implies that $f(L) > 0$. Therefore,

$$af(L) + bf'(L) > 0$$

which contradicts the boundary condition. Thus $f \equiv 0$ is the only non-negative steady-state solution. □

Notice that this proposition covers no-flux and homogeneous boundary conditions. If a no-flux boundary condition is placed at $x = L$, then

$$v(L,t)f(L,t) - d\frac{\partial f}{\partial x}(L,t) = 0.$$

At steady-state, $v(L,t) = 0$ and therefore this boundary condition becomes

$$f'(L) = 0$$

which is covered in the case $a = 0$ and $b = 1$. For homogeneous boundary conditions, $f(L,t) = 0$ and this corresponds to $a = 1$ and $b = 0$.

Stability of the Steady-State Solutions

For the analysis in this section, it is convenient to transform the equations to a fixed spatial domain. Let $z = \dfrac{x}{L(t)}$ define the transformation to the fixed domain of $[0, 1]$. Under this change of variables, the model equations become

$$\epsilon \frac{\partial S}{\partial t} = \frac{1}{L^2}\frac{\partial^2 S}{\partial z^2} + \epsilon \frac{z}{L}\frac{dL}{dt}\frac{\partial S}{\partial z} - \frac{1}{\phi^2}\frac{S}{1+S} f, \tag{4.33a}$$

$$\frac{\partial f}{\partial t} = \left(\left(\frac{S}{1+S} - \beta\right)(1-f) - \alpha\right) f - (v - v(1,t)z)\frac{\partial f}{\partial z}, \tag{4.33b}$$

$$\frac{dL}{dt} = L v(1,t), \tag{4.33c}$$

where

$$v(x,t) = \int_0^x \left(\frac{S(\zeta,t)}{1+S(\zeta,t)} - \beta\right) f(\zeta,t)\, d\zeta. \tag{4.33d}$$

The boundary conditions are

$$\frac{\partial S}{\partial z}(0,t) = 0,\ S(1,t) = S_b \tag{4.34a}$$

and

$$v(0,t) f(0,t) = 0. \tag{4.34b}$$

If diffusion of biomass is included, equation (4.33b) becomes

$$\frac{\partial f}{\partial t} = \frac{1}{L^2}\frac{\partial^2 f}{\partial z^2} - (v - v(1,t)z)\frac{\partial f}{\partial z} + \left(\left(\frac{S}{1+S} - \beta\right)(1-f) - \alpha\right) f \tag{4.35}$$

and the boundary condition at $z = 1$ for f is added, for example

$$f(1,t) = 0. \tag{4.36}$$

Constant Steady-State Solution

The trivial solutions, $\tilde{S} \equiv S_b$, $f \equiv 0$ and any real number $\tilde{L}$, are present for all parameter values. Although this solution does not match a realistic biofilm, its mathematical stability can still provide insight to biofilm growth. Such a solution represents a biofilm with no active organisms. The conditions for the instability of this solution will indicate when active organisms are present in a biofilm. For this analysis, diffusion of f will be included.

The linearization of (4.33) about a constant solution is

$$\epsilon \frac{\partial S}{\partial t} = \frac{1}{\tilde{L}^2} \frac{\partial^2 S}{\partial z^2} - af, \tag{4.37a}$$

$$\frac{\partial f}{\partial t} = \frac{d}{\tilde{L}^2} \frac{\partial^2 f}{\partial z^2} + bf, \tag{4.37b}$$

$$\frac{\partial v}{\partial z} = cf, \tag{4.37c}$$

$$\frac{dL}{dt} = c \int_0^{\tilde{L}} f(\zeta)\, d\zeta. \tag{4.37d}$$

The parameters a, b and c are defined to be

$$a = \frac{1}{\varphi^2} \frac{S_b}{1+S_b}, \quad b = \frac{S_b}{1+S_b} - \alpha - \beta, \quad c = \frac{S_b}{1+S_b} - \beta.$$

A linear system like (4.37) has solutions of the form

$$\sum_{k=-\infty}^{+\infty} \mathbf{u}_k \exp(\lambda_k t + ikz) \text{ where } \mathbf{u}_k \in \mathbb{R}^4.$$

The steady-state solution is unstable if there exists a non-trivial solution to (4.37) with $Re(\lambda_k) > 0$ for some k. The corresponding wave number, k, indicates which

node, e^{ikz}, dominates the instability under small perturbations. We consider solutions to (4.37) of the form

$$S = \hat{S}e^{\lambda t+ikz}, \tag{4.38a}$$

$$f = \hat{f}e^{\lambda t+ikz}, \tag{4.38b}$$

$$v = \hat{v}e^{\lambda t+ikz}, \tag{4.38c}$$

$$L = \hat{L}e^{\lambda t}. \tag{4.38d}$$

When (4.38) is substituted into (4.37), the linear equations for $\hat{S}, \hat{f}, \hat{v}$ and $\hat{L}$ are

$$\left(\lambda + \frac{k^2}{\hat{L}^2}\right)\hat{S} + a\hat{f} = 0, \tag{4.39a}$$

$$\left(\lambda + d\frac{k^2}{\hat{L}^2} - b\right)\hat{f} = 0, \tag{4.39b}$$

$$-c\hat{f} + ik\hat{v} = 0, \tag{4.39c}$$

$$-c(e^{-ikL_0} + i)\hat{f} + \lambda\hat{L} = 0. \tag{4.39d}$$

By requiring non-trivial solutions, λ can be determined from the characteristic polynomial of the coefficient matrix of (4.39). From this the dispersion relations are

$$\lambda(k^2) = -\frac{1}{\tilde{L}^2}k^2, \tag{4.40a}$$

$$\lambda(k^2) = b - \frac{d}{\tilde{L}^2}k^2, \tag{4.40b}$$

$$\lambda(k^2) = 0. \tag{4.40c}$$

Thus $\lambda(k^2) > 0$ when $b > 0$. Furthermore the largest eigenvalue is b and is attained when $k^2 = 0$ for all parameter values. This corresponds to the constant

mode dominating. Notice that the condition of instability is independent of d. When $d = 0$, the range of k^2 values where $\lambda(k^2) > 0$ is infinite and the maximum eigenvalue is achieved at all k values.

The zero eigenvalue, which is present in both cases, corresponds to the eigenvector $[0, 0, 0, 1]^T$. This is a reflection of the degeneracy of the L solution.

In terms of the original parameters of the model, the condition $b > 0$ is equivalent to

$$\alpha + \beta < \frac{S_b}{1 + S_b} \tag{4.41}$$

provides a relationship between the bulk substrate, maximum growth and observed decay rate for which the trivial steady-state is linearly unstable. Recall that this solution corresponds to a biofilm with no active biomass. If condition (4.41) is satisfied, the model will not limit on a solution where $S \equiv S_b$ and $f \equiv 0$. Thus if (4.41) is satisfied, the model predicts that the active organisms density will not approach zero.

Non-Constant Steady-State

Without an analytical solution for $\tilde{S}$ or $\tilde{v}$, it is impossible to explicitly calculate the dispersion relations for the non-constant steady-state. So a numerical approach to approximate the eigenvalues was used. The eigenvalues were computed from the Jacobian of the linearization of (4.33) about the non-constant steady-state solution.

For the non-constant steady-state, $f \equiv 1$, $\tilde{S}$, $\tilde{L}$ and $\tilde{v}$ solve equation (4.4), the linearization of (4.33) about this solution is

$$\frac{\partial S}{\partial t} = \frac{1}{\tilde{L}^2}\frac{\partial^2 S}{\partial z^2} - \frac{1}{\varphi^2}\frac{1}{(1+\tilde{S})^2}S - \frac{1}{\varphi^2}\frac{\tilde{S}}{(1+\tilde{S})^2}f + \epsilon z\tilde{S}'v(1) - \frac{2\tilde{S}''}{\tilde{L}^3}L, \tag{4.42a}$$

$$\frac{\partial f}{\partial t} = -\tilde{v}\frac{\partial f}{\partial z} - \left(\frac{\tilde{S}}{1+\tilde{S}} - \beta\right)f, \tag{4.42b}$$

$$\frac{\partial v}{\partial z} = \frac{1}{(1+\tilde{S})^2}S + \left(\frac{\tilde{S}}{1+\tilde{S}} - \beta\right)f, \tag{4.42c}$$

$$\frac{dL}{dt} = \tilde{L}v(1). \tag{4.42d}$$

Discretizing (4.33) in space using N mesh points results in a system of $2N+2$ ODEs. If the Jacobian of this system is evaluated at the steady-state, the eigenvalues of that matrix should approach the eigenvalues of the continuous system as $N \to +\infty$. The MATLAB code that generates this matrix is listed in Appendix B.

With a reaction-diffusion equation for S, the discrete system will have large negative eigenvalues. For example, a uniform grid with $N = 32$ points has negative eigenvalues where $|\lambda| = O(10^8)$. Due to the presence of these eigenvalues, a standard iteration technique is not efficient for computing eigenvalues with positive real part near zero. So a method using a Cayley transformation combined with a subspace iteration was applied.

Before the subspace iteration, the Jacobian is preconditioned by a Cayley transformation. A Cayley transformation of matrix A is

$$T(A) = (A - \alpha_1 I)^{-1}(A - \alpha_2 I) \tag{4.43}$$

where $\alpha_1 > \alpha_2$ are real valued parameters. The eigenvalues of $T(A)$ are given by $\theta_i = T(\lambda_i) = \dfrac{\lambda_i - \alpha_2}{\lambda_i - \alpha_1}$ where λ_i is an eigenvalue of A. Under this transformation, the eigenspace of A is preserved. This transformation has a very useful property. Eigenvalues to the right of the line $Re(\mu) = \dfrac{1}{2}(\alpha_1 + \alpha_2)$ are mapped outside the unit circle and eigenvalues to the left are mapped inside the unit circle. Unwanted negative eigenvalues with a large modulus are moved to a region where they cannot be detected by subspace iteration.

Let A be an $N \times N$ matrix and suppose the eigenvalues of A are ordered by decreasing modulus. Subspace iteration approximates an orthogonal basis for the subspace of eigenvectors corresponding to $|\lambda_1| \geq |\lambda_2| \geq \cdots \geq |\lambda_m|$ where $1 \leq m \leq N$. The algorithm for the method is:

1. Compute a random $N \times m$ matrix.

2. Orthogonalize this matrix and set it equal to Q_0.

3. for $k = 1$ to K do

   Set $V = AQ_{k-1}$.

   Find Q_k such that $Q_k R = V$ and $Q_k^H Q = I$.

   end loop

4. Solve $Q_K^H A Q_K z_i = \mu_i z_i$ for μ_i and z_i for $i = 1, \ldots, m$.

5. Set $\hat{\lambda}_i = Q_K z_i$ as the approximate eigenvalues.

The convergence of the method is summarized by the theorem below. Further details on subspace iteration with a Cayley transformation can be found in [9].

Theorem 6. ***(Subspace Convergence Theorem)*** *Let A be an $N \times N$ matrix. Suppose the N eigenvalues of A are simple and ordered by decreasing modulus as follows: $|\lambda_1| \geq |\lambda_2| \geq |\lambda_3| \geq \ldots \geq |\lambda_N|$. Under mild assumptions on the initial subspace Q_0 and if K is large enough, then there exists $\hat{\lambda}_i$ for $i = 1, \ldots, m$ such that*

$$\left|\hat{\lambda}_i - \lambda_i\right| = O\left(\left|\frac{\lambda_i}{\lambda_{m+1}}\right|^{-K}\right) \tag{4.44}$$

Notice that one can improve the convergence rate by increasing the number of eigenvalues sought. Also observe that the method will not converge to eigenvalues where $|\lambda| < 1$.

Numerical approximations of the $\tilde{S}, f \equiv 1, \tilde{v}$ and $\tilde{L}$ steady-state were computed on a uniform spatial grid with four different parameter sets. Starting with $N = 8$, the simulations ran until the 1-norm of the right-hand side was $O\left(10^{-7}\right)$. The grid size was doubled until $N = 64$. For each N, the Jacobian was constructed and its eigenvalues calculated using $\alpha_1 = 1$ and $\alpha_2 = -3$ in the Cayley transformation. With this choice of parameters, eigenvalues to the right of the line $Re(\mu) = -1$ are mapped outside the unit circle. The transformed matrix was used in the subspace iteration algorithm to compute 6 eigenvalues. The MATLAB code for the eigenvalue calculation can be found in Appendix C. The subspace method concluded when $\left\|Jz_i - \hat{\lambda}_i z_i\right\|_1 = O\left(10^{-4}\right)$ for $i = 1, \ldots, 5$. Results for parameter sets 1 and 2 are listed in Tables 5 and 6. The

other parameter sets had similar results. A positive eigenvalue was detected for all parameter values and grid sizes. Furthermore, the positive eigenvalue did not decrease significantly in magnitude in any of the simulations as N was increased.

Parameters	N	Eigenvalues	Residuals
$\beta = 0.15$	8	2.50429×10^{-2}	1.7639×10^{-11}
		-5.84660×10^{-4}	1.8877×10^{-10}
		-2.64304×10^{-2}	6.5049×10^{-11}
$S_b = 0.25$	16	2.50429×10^{-2}	2.4688×10^{-10}
		-1.45757×10^{-4}	1.3379×10^{-9}
		-2.53345×10^{-2}	1.3082×10^{-9}
$\epsilon = 1.65 \times 10^{-4}$	32	2.49889×10^{-2}	1.5269×10^{-9}
		-3.64140×10^{-4}	1.5353×10^{-9}
		-2.50618×10^{-2}	2.3523×10^{-9}
$\frac{1}{\phi^2} = 1.5$	64	2.49755×10^{-2}	4.1949×10^{-9}
		-9.10191×10^{-6}	1.1905×10^{-8}
		-2.49937×10^{-2}	1.0602×10^{-8}

Table 5. Eigenvalues for parameter set 1.

Each component of the eigenvector associated with this positive eigenvalue is plotted for two parameter sets for $N = 8$ through $N = 64$. Components associated with the S equation are plotted separately from the components of the f equation. The L component for each N is listed above the plots of the f components (see Figures 5 through 8). The components corresponding to the S and L equations seem to be decreasing in magnitude as N increases. The eigenvector components for the f equation are virtually identical for all grid sizes and parameter values. The component corresponding to the f equation at $x = 0$ is nearly -1 while the remaining

Parameters	N	Eigenvalues	Residuals
		4.64483×10^{-2}	4.4079×10^{-11}
$\beta = 0.1$	8	-9.59495×10^{-4}	1.0093×10^{-10}
		-4.84119×10^{-2}	7.4396×10^{-11}
		4.60486×10^{-2}	7.6566×10^{-11}
$S_b = 0.25$	16	-2.39180×10^{-4}	1.4696×10^{-10}
		-4.65297×10^{-2}	2.8499×10^{-10}
		4.59491×10^{-2}	4.2974×10^{-10}
$\epsilon = 1.65 \times 10^{-4}$	32	-5.97521×10^{-5}	1.3387×10^{-9}
		-4.60688×10^{-2}	1.9500×10^{-9}
		4.59243×10^{-2}	1.7691×10^{-9}
$\frac{1}{\phi^2} = 1.5$	64	-1.49353×10^{-5}	5.8687×10^{-9}
		-4.59542×10^{-2}	8.9652×10^{-9}

Table 6. Eigenvalues for parameter set 2.

values are almost zero. This is a perturbation where biomass is removed from the substratum. However, the L component is positive in all cases. This implies growth at the interface. If biomass is removed, the thickness should decrease. If this eigenvalue and eigenvector are converging to a positive eigenvalue and non-trivial solution to the linear system, the solution is not continuous and the perturbation does not fit the physical constraints of the model. This eigenvector appears to be limiting on a spurious solution to the linearized equations.

The other detected eigenvalues are negative or have a negative real part. It should also be noted that the numerical simulation limits on the steady-state solution with initial conditions $S(z,0) = S_b$, $f(z,0) = 1$ and $L(0) = 0.05$. The output of one of these simulations is plotted in Figures 9, 10 and 11. This numerical evidence indicates that the solution is stable.

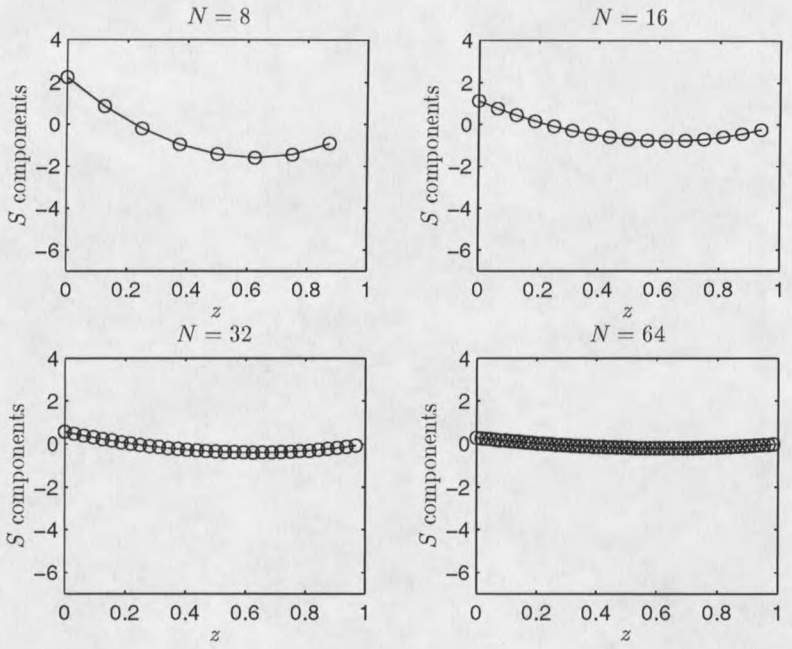


Figure 5. Eigenvector components for parameter set 1.

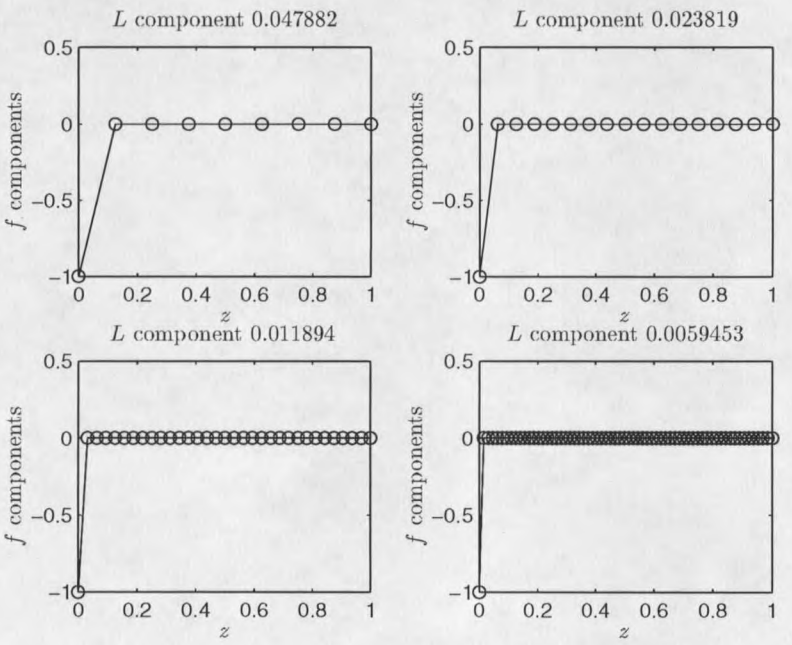


Figure 6. Eigenvector components for parameter set 1 .

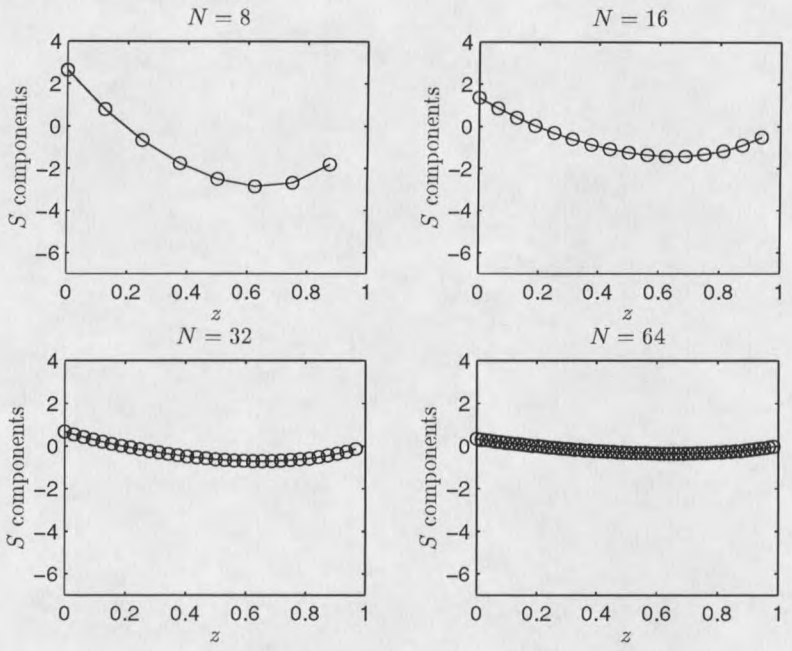


Figure 7. Eigenvector components for parameter set 2.

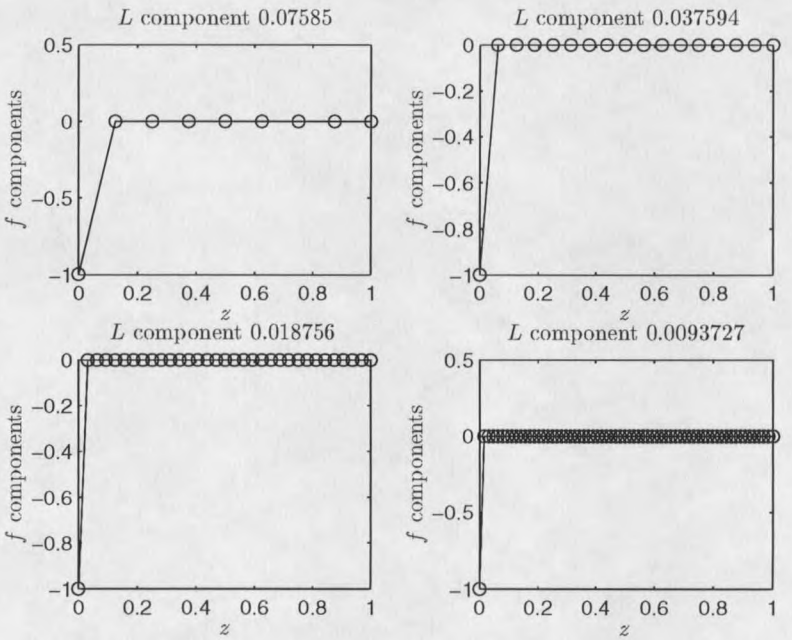


Figure 8. Eigenvector components for parameter set 2.

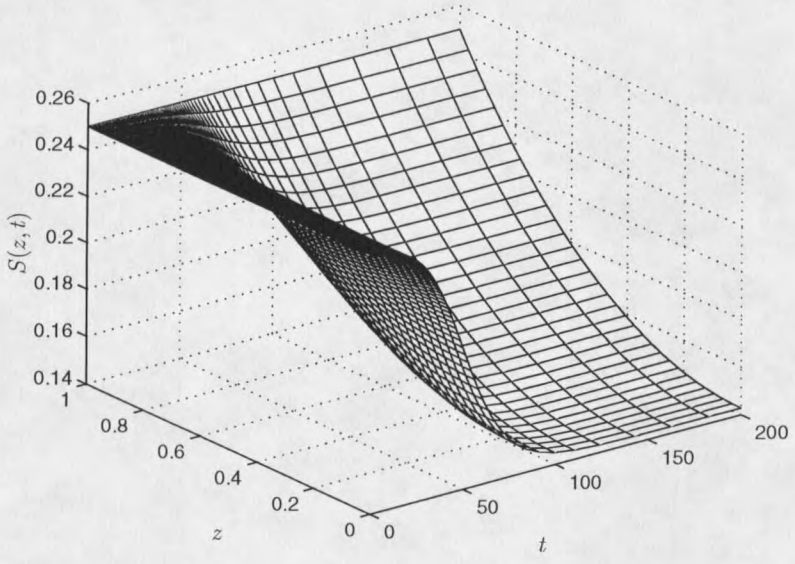


Figure 9. $S(z,t)$ where $\dfrac{1}{\varphi^2} = 3$, $\beta = 0.15$ and $S_b = 0.25$.

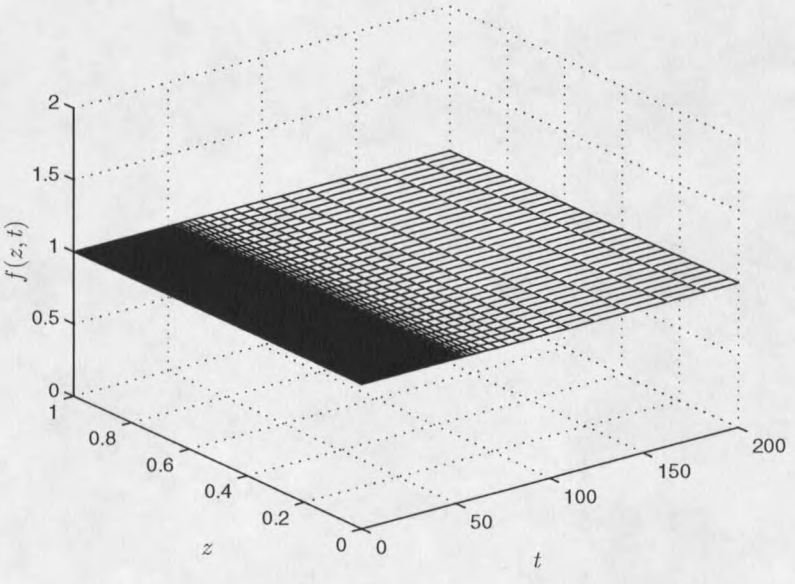


Figure 10. $f(z,t)$ where $\dfrac{1}{\varphi^2} = 3$, $\beta = 0.15$ and $S_b = 0.25$.

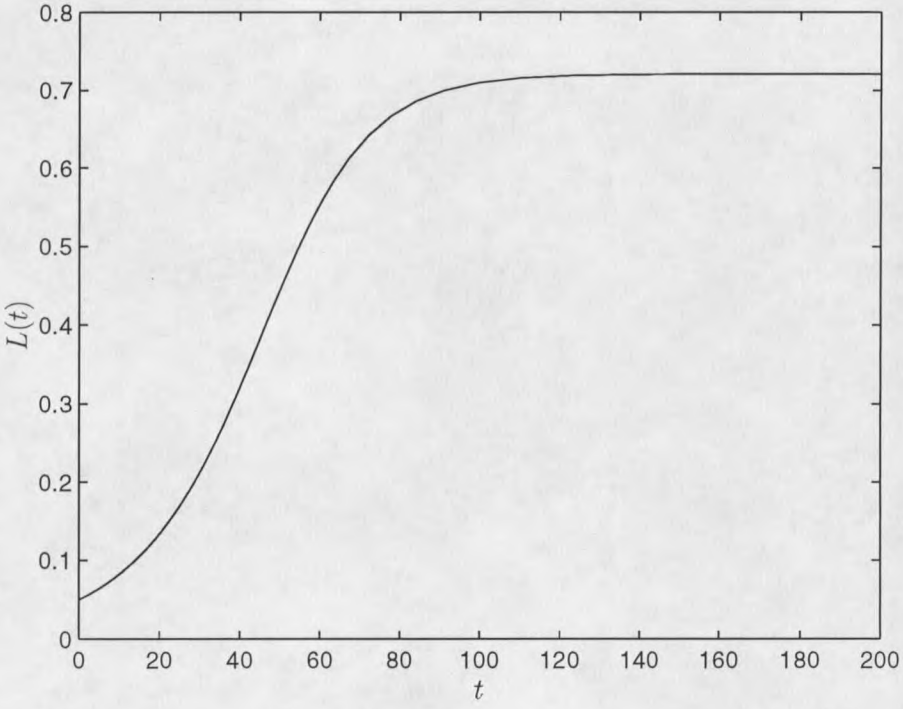


Figure 11. $L(t)$ where $\frac{1}{\varphi^2} = 3$, $\beta = 0.15$ and $S_b = 0.25$.

CHAPTER 5

MODELING EPS PRODUCTION

Inclusion of EPS Production

The composition of a biofilm is a complex mixture of fluid, organisms and extracellular polymers. Extracellular polymers, or EPS, are polymer chains formed inside the cells. As these chains pass through the cell wall they attach to the cell. Once outside, these substances form a gelatinous matrix in the biofilm with the cells embedded in this matrix. EPS contributes to the integrity of the biofilm structure and allows the biofilm to attach to the substratum [2]. The presence of EPS also seems to govern other processes. For example, it has been observed that the presence of EPS affects the cell distribution in a biofilm [3], [5], [8] . It is clear that EPS is an important substance that should be accounted for in any biofilm model.

The mechanisms which control and produce EPS are not fully understood, nor is the relationship between EPS and other processes [2]. It was discovered recently that bacteria produce chemicals which allow a cell to communicate with other cells in the biofilm. This cell-to-cell communication is called quorum sensing. The tendency of some bacteria to form into clusters at sufficient densities may be attributed to quorum sensing. Experimental evidence indicates that the signaling chemicals that facilitate this phenomenon also effect EPS processes.

This connection was studied by comparing a wild biofilm to a mutant biofilm. In a mutant biofilm, the cells were genetically altered to not produce signaling chemicals. The resulting biofilm had a uniform cell distribution and little EPS present. In a wild biofilm where the organisms did produce these chemicals, a significant amount of EPS was present. The cells also grouped into clusters and the wild biofilm was as much as four times thicker than the mutant biofilm. When the signaling chemicals were added to the mutant biofilm, the cells produced more EPS and formed cell clusters like the wild biofilm. It has been proposed [4] that the cells continually produce these chemicals that diffuse out into the biofilm. As the cell density increases, the chemicals approach a threshold concentration and once this threshold is reached the chemicals are part of a system that alters the cell's DNA sequence. After this has occurred, the cells use substrate for growth and EPS formation.

Motivated by these results a one dimensional biofilm model that incorporates this chemical production and EPS will be developed and studied in this chapter. The focus of this study is the inclusion of new products, not the exact replication of experimental results. The derivation follows the model development outlined in Chapter 2.

Model Equations Inside the Biofilm

The same physical system that was used in Chapter 2 will be used here. Recall that the biofilm grows in a box with a square base with sides of length $2h$. The origin

is at the center of the base and the direction normal to the base of the box is denoted by x. The substratum corresponds to the set of points where $x = 0$. The set of points where $y = \pm h$ and $z = \pm h$ are on the sides of the box. As before, we will assume that the model variables are periodic in the yz plane.

We will assume that only one signaling chemical is present and that the cells produce one type of EPS. The amount of inactive biomass and rate at which cells become inactive is negligible and will not be included in the model. Equations for the substrate concentration, the signaling chemical concentration, cell density and EPS density are derived from mass balance principles coupled with an equation for the interface. Substrate concentration, cell density, velocity and the height of the interface are denoted by S, ρ, v and γ, respectively.

Substrate

Recall equation (2.3) from Chapter 2 that the substrate concentration is given by

$$\frac{\partial S}{\partial t} = D_S \frac{\partial^2 S}{\partial x^2} - F_S \tag{5.1}$$

where D_S now denotes the diffusion constant and F_S is the rate of substrate usage. F_S is proportional to the cell density. It is believed that the cells partition substrate utilization into growth and EPS production [11]. Using substrate for EPS production is called growth related EPS formation. We will assume that growth related formation only occurs when the signaling chemical reaches a threshold value. If C^* is this

threshold concentration, the substrate usage rate is

$$F_S = \frac{1}{Y_\rho} G(S)\rho - \frac{1}{Y_e} K_g^e G(S)\rho H(C - C^*)$$

where H is the heaviside function. Y_ρ and Y_e are yield coefficients for cell reproduction and EPS formation. K_g^e is the growth related formation constant. G represents the substrate utilization rate. Recall, from Chapter 2 that G is C^1, $G'(S) > 0$ for $S \geq 0$ and $G(0) = 0$. For this model, G is again taken to be

$$G(S) = \frac{\hat{\mu} S}{K_S + S} \tag{5.2}$$

where $\hat{\mu}$ is the maximum growth rate and K_S is the Monod constant. The boundary conditions for S are the same as the boundary conditions used in the previous model; no-flux at the substratum and periodic conditions for S and $\mathbf{n} \cdot \nabla S$ along the sides of the box.

Cell Density

When we refer to a cell in the biofilm it is assumed that it is an active organism i.e., inactive material is not included in the present model. The cell density is modeled exactly like the active biomass density in equation (2.1) from Chapter 2 with the rate of inactivation equal to zero. Thus, the equation for cell density is

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \mathbf{v}) = R_\rho(S)\rho$$

where R_ρ is the net organism production rate. R_ρ is a function of substrate concentration and has the same properties as R from Chapter 2: R_ρ is C^1, $R'_\rho(S) > 0$ for

$S \geq 0$ and $R_\rho(0) < 0$. We will use the same function from the previous model, that is

$$R_\rho(S) = G(S) - K_d^\rho \tag{5.3}$$

where G is the substrate utilization rate and K_d^ρ is the cellular decay rate. The boundary conditions for ρ are identical to the boundary conditions found in Chapter 2, a no-flux condition at the substratum and periodic conditions along the sides of the box.

Signaling Chemical

Let $C(\mathbf{x}, t)$ denote the signaling chemical concentration at $\mathbf{x}$ and time t. Consider an arbitrary volume Ω inside the biofilm. The change in the amount of this chemical in Ω is expressed as

$$\frac{\partial}{\partial t}\int_\Omega C(\mathbf{x}, t)\, d\sigma = -\int_{\partial\Omega} \mathbf{J}_C \cdot \mathbf{n}\, d\tau + \int_\Omega F_C\, d\sigma$$

where $\mathbf{n}$ is the outward normal direction of Ω, $\mathbf{J}_C$ is the flux of C and F_C is the net production of C. Recall from Chapter 2 that this integral equation is equivalent to the partial differential equation

$$\frac{\partial C}{\partial t} + \nabla \cdot \mathbf{J}_C = F_C.$$

The transport of C is modeled by Fick's law; thus the flux of C is

$$\mathbf{J}_C = -D_C \nabla C$$

where the constant D_C is the diffusion coefficient of C. We will assume that the cells produce this chemical at a rate proportional to the cell density and that the chemical does not decay. Therefore, the net production term is

$$F_C = K_p \rho(\mathbf{x}, t)$$

where K_p is a constant.

The signaling chemical does not interact with or pass through the substratum and we will assume that this chemical is removed by the bulk fluid at the interface. Based on these assumptions, appropriate boundary conditions at the substratum and interface are

$$\frac{\partial C}{\partial x}(0, y, z) = 0,$$

$$C(\gamma(y, z, t), y, z) = 0.$$

Along the sides of the box, we will assume that C and $\mathbf{n} \cdot \nabla C$ are periodic.

EPS

If $\rho_e(\mathbf{x}, t)$ is the density of EPS, then the change in total mass of EPS in Ω is

$$\frac{\partial}{\partial t} \int_\Omega \rho_e(\mathbf{x}, t)\, d\sigma = -\int_{\partial\Omega} \mathbf{J}_e \cdot \mathbf{n}\, d\tau + \int_\Omega F_e\, d\sigma$$

where $\mathbf{J}_e$ is the flux of EPS and F_e is the net production of EPS. This is equivalent to

$$\frac{\partial \rho_e}{\partial t} + \nabla \cdot \mathbf{J}_e = F_e.$$

If we model the biofilm as a gel with cells embedded in this gel, then EPS convects in the biofilm as the surrounding material expands or contracts. Therefore, the flux of EPS is modeled as

$$\mathbf{J}_e = \mathbf{v}\rho_e$$

where $\mathbf{v}(\mathbf{x}, t)$ is the velocity of the biofilm material at $\mathbf{x}$. The production of EPS depends on the cell density, substrate concentrations and signaling chemical concentrations. We will assume that the rate of EPS formation is proportional to cell density. The proportionality coefficient will depend on the substrate and signaling chemical. Recall from Chapter 4, that if the removal of material is not included in the model equations, the model will not have a meaningful steady-state solution. Thus, we will also assume that EPS decays at some rate proportional to the EPS density. With these assumptions, the EPS net formation rate is

$$F_e = R_e(S, C)\rho - K_d^e\rho_e$$

where K_d^e is the decay rate and R_e is the EPS formation rate.

Once the signaling chemical reaches a threshold value, the cells will use substrate to reproduce and form EPS. However, the cells produce EPS even if the signaling chemical is below the threshold. At these concentration levels, the substrate for EPS formation comes from cell maintenance. This loss is accounted for in the K_d^ρ term in R_ρ.

Therefore, the EPS formation rate is given by

$$R_e(S, C) = K_n^e + K_g^e G(S) H(C - C^*). \tag{5.4}$$

K_g^e is the growth related formation constant and K_n^e is the non-growth related EPS formation rate.

EPS does not pass through the substratum, thus ρ_e satisfies a no-flux condition at the substratum. With the simple geometry of this model, this reduces to

$$v_1(0, y, z, t)\rho_e(0, y, z, t) = 0$$

where v_1 is the x component of the velocity field. Periodic boundary conditions are placed on ρ_e for $y = \pm h$ and $z = \pm h$.

Velocity

The cell and EPS equations contain a velocity term which needs to be specified. We will assume that the divergence of the velocity field is proportional to the rate of material production in the biofilm. Therefore,

$$\nabla \cdot \mathbf{v} = k_1 R_\rho(S)\rho + k_2 \left(R_e(S, C)\rho - K_d^e \rho_e\right)$$

where k_1 and k_2 are constants. This equation is not enough to determine the three components of the velocity vector, so we will also assume that the velocity field is irrotational. This assumption leads to the equation

$$\nabla^2 \phi = k_1 R_\rho(S)\rho + k_2 \left(R_e(S, C)\rho - K_d^e \rho_e\right)$$

where ϕ is a velocity potential. The same boundary conditions for ϕ from the previous model are used here.

Interface

Recall, that the interface is described by the equation

$$x - \gamma(y, z, t) = 0.$$

Following the same derivation found in Chapter 2, the fluid-biofilm interface is given by

$$\frac{\partial \gamma}{\partial t} + \frac{\partial \phi}{\partial y}\frac{\partial \gamma}{\partial y} + \frac{\partial \phi}{\partial z}\frac{\partial \gamma}{\partial z} = \frac{\partial \phi}{\partial x}$$

with the same boundary conditions that were used in Chapter 2.

In summary, the model equations inside the biofilm are

$$\frac{\partial S}{\partial t} = D_S \nabla^2 S - \frac{1}{Y_\rho} G(S)\rho - \frac{1}{Y_e} K_g^e G(S)\rho H(C - C^*), \tag{5.5a}$$

$$\frac{\partial C}{\partial t} = D_C \nabla^2 C + K_p \rho, \tag{5.5b}$$

$$\frac{\partial \rho}{\partial t} + \nabla\left(\rho \nabla \phi\right) = R_\rho(S)\rho, \tag{5.5c}$$

$$\frac{\partial \rho_e}{\partial t} + \nabla\left(\rho_e \nabla \phi\right) = R_e(S, C)\rho - K_d^e \rho_e, \tag{5.5d}$$

$$\nabla^2 \phi = k_1 R_\rho(S)\rho + k_2\left(R_e(S, C)\rho - K_d^e \rho_e\right), \tag{5.5e}$$

$$v = \nabla \phi \tag{5.5f}$$

with the interface equation

$$\frac{\partial \gamma}{\partial t} + \frac{\partial \phi}{\partial y}\frac{\partial \gamma}{\partial y} + \frac{\partial \phi}{\partial z}\frac{\partial \gamma}{\partial z} = \frac{\partial \phi}{\partial x}. \tag{5.5g}$$

The boundary conditions are

$$\frac{\partial S}{\partial x}(0,y,z,t) = 0,\ S(\gamma(y,z,t),y,z,t) = S_{bulk}, \tag{5.6a}$$

$$\frac{\partial C}{\partial x}(0,y,z,t) = 0,\ C(\gamma(y,z,t),y,z,t) = 0, \tag{5.6b}$$

$$v_1(0,y,z,t)\rho(0,y,z,t) = 0,\ v_1(0,y,z,t)\rho_e(0,y,z,t) = 0, \tag{5.6c}$$

$$\frac{\partial \phi}{\partial x}(0,y,z,t) = 0. \tag{5.6d}$$

Periodic boundary conditions are placed on ρ, ρ_e, S, $\mathbf{n}\cdot\nabla S$, C, $\mathbf{n}\cdot\nabla C$, ϕ and $\mathbf{n}\cdot\nabla\phi$ for $y = \pm h$ and $z = \pm h$. The model variables, parameters and functions are listed in Tables 7 and 8. The symbols m_s, m_c, m_ρ and m_e are mass units of substrate, signaling chemical, cells and EPS and l and t represent units of length and time.

Symbol	Description	Units
S	Substrate concentration	$m_s\ l^{-3}$
C	Signaling chemical concentration	$m_c\ l^{-3}$
ρ	Cell density	$m_\rho\ l^{-3}$
ρ_e	EPS density	$m_e\ l^{-3}$
γ	Interface height	l
$\mathbf{v}$	Velocity	$l\ t^{-1}$
ϕ	Velocity potential	t^{-1}
G	Substrate usage rate	$m_s\ m_\rho^{-1}\ t^{-1}$
H	Heaviside function	-
R_ρ	Cellular growth rate	t^{-1}
R_e	EPS formation rate	$m_e\ m_\rho^{-1}\ t^{-1}$

Table 7. EPS model variables and functions.

Symbol	Description	Units
S_{bulk}	Bulk substrate concentration	$m_s\ l^{-3}$
D_S	Substrate diffusion coefficient	$l^2\ t^{-1}$
D_C	Chemical diffusion coefficient	$l^2\ t^{-1}$
Y_ρ	Cellular yield coefficient	$m_s\ m_\rho^{-1}$
Y_e	EPS yield coefficient	$m_s\ m_e^{-1}$
K_S	Monod constant	$m_s\ l^{-3}$
$\hat{\mu}$	Maximum growth rate	t^{-1}
C^*	Signaling chemical threshold concentration	$m_c\ l^{-3}$
K_p	Chemical production rate	$m_c\ m_\rho^{-1}\ t^{-1}$
K_d^ρ	Cellular decay rate	t^{-1}
K_n^e	Non-growth related EPS formation rate	$m_e\ m_\rho^{-1}\ t^{-1}$
K_g^e	Growth related EPS formation constant	$m_e\ m_\rho^{-1}$
K_d^e	EPS Decay rate	t^{-1}
k_1	Velocity proportionality constant	$m_\rho^{-1}\ l^3$
k_2	Velocity proportionality constant	$m_e^{-1}\ l^3$

Table 8. EPS model parameters and functions.

One Dimensional Model with EPS Production

To reduce the model to one dimension, we will assume that the variation of all model quantities in the y and z directions is negligible. Under this assumption, the model equations reduce to

$$\frac{\partial S}{\partial t} = D_S \frac{\partial^2 S}{\partial x^2} - \frac{1}{Y_\rho} G(S)\rho - \frac{1}{Y_e} K_g^e G(S)\rho H(C - C^*), \tag{5.7a}$$

$$\frac{\partial C}{\partial t} = D_C \frac{\partial^2 C}{\partial x^2} + K_p \rho, \tag{5.7b}$$

$$\frac{\partial \rho}{\partial t} + \frac{\partial}{\partial x}\left(\rho \frac{\partial \phi}{\partial x}\right) = R_\rho(S)\rho, \tag{5.7c}$$

$$\frac{\partial \rho_e}{\partial t} + \frac{\partial}{\partial x}\left(\rho_e \frac{\partial \phi}{\partial x}\right) = R_e(S, C)\rho - K_d^e \rho_e, \tag{5.7d}$$

$$\frac{\partial^2 \phi}{\partial x^2} = k_1 R_\rho(S)\rho + k_2 \left(R_e(S, C)\rho - K_d^e \rho_e\right), \tag{5.7e}$$

$$v = \frac{\partial \phi}{\partial x}, \tag{5.7f}$$

and the interface equation is

$$\frac{d\gamma}{dt} = \frac{\partial \phi}{\partial x}(\gamma(t), t). \tag{5.7g}$$

By integrating equation (5.7e) and using the boundary condition $\frac{\partial \phi}{\partial x}(0, t) = 0$, the velocity is given by the integral equation

$$\begin{aligned} v(x, t) = \int_0^x & k_1 R_\rho(S(\xi, t))\rho(\xi, t) \\ & + k_2 R_e(S(\xi, t), C(\xi, t))\rho(\xi, t) - k_2 K_d^e \rho_e(\xi, t)\, d\xi. \end{aligned} \tag{5.8}$$

The constants k_1 and k_2 are unknown. To find k_1 and k_2, we will assume that the cell and EPS densities can be written as

$$\rho(x,t) = \rho_0 f(x,t)$$

$$\rho_e(x,t) = \rho_1 e(x,t)$$

where ρ_0 and ρ_1 are intrinsic densities with f and e volume fractions of cells and EPS. With this assumption, equations (5.7c) and (5.7d) become

$$\frac{\partial f}{\partial t} + \frac{\partial}{\partial x}(vf) = R_\rho(S)f, \tag{5.9a}$$

$$\frac{\partial e}{\partial t} + \frac{\partial}{\partial x}(ve) = \frac{\rho_0}{\rho_1}R_e(S,C)f - K_d^e e. \tag{5.9b}$$

Furthermore, we will also assume that the volume fractions f and e satisfy

$$f + e = 1 - \epsilon_l$$

where ϵ_l is the liquid volume fraction which is constant. If equations (5.9a) and (5.9b) are added together, this assumption leads to

$$\frac{\partial v}{\partial x} = \frac{1}{(1-\epsilon_l)}\left(\left(R_\rho(S) + \frac{\rho_0}{\rho_1}R_e(S,C)\right)f - K_d^e e\right). \tag{5.10}$$

By comparing this equation to equation (5.7e), one solution for the parameters k_1 and k_2 is

$$k_1 = \frac{1}{\rho_0(1-\epsilon_l)},\ k_2 = \frac{1}{\rho_1(1-\epsilon_l)}. \tag{5.11}$$

Therefore, the velocity is given by

$$\begin{aligned} v(x,t) = \frac{1}{1-\epsilon_l}\int_0^x & R_\rho(S(\xi,t))f(\xi,t) \\ & + \left(\frac{\rho_0}{\rho_1}R_e(S(\xi,t),C(\xi,t))\right)f(\xi,t) - K_d^e e(\xi,t)\,d\xi. \end{aligned} \tag{5.12}$$

With an equation for v, equations (5.7c) and (5.7d) can be written as

$$\frac{\partial f}{\partial t} + v\frac{\partial f}{\partial x} = \left(R_\rho(S)\left(1 - \frac{f}{1-\epsilon_l}\right) - \frac{\rho_0}{\rho_1(1-\epsilon_l)} R_e(S,C) f + \frac{K_d^e}{1-\epsilon_l} e \right) f, \tag{5.13}$$

$$\frac{\partial e}{\partial t} + v\frac{\partial e}{\partial x} = \left(\frac{\rho_0}{\rho_1} R_e(S,C)\left(1 - \frac{e}{1-\epsilon_l}\right) - \frac{1}{1-\epsilon_l} R_\rho(S) e - \frac{K_d^e}{1-\epsilon_l} e \right) f. \tag{5.14}$$

In one dimension, γ represents the distance from the substratum. To simplify the notation, we let $L = \gamma$. The differential equation

$$\begin{aligned} \frac{dL}{dt} = \frac{1}{1-\epsilon_l} \int_0^{L(t)} & R_\rho(S(\xi,t)) f(\xi,t) \\ & + \left(\frac{\rho_0}{\rho_1} R_e(S(\xi,t), C(\xi,t)) \right) f(\xi,t) - K_d^e e(\xi,t)\, d\xi \end{aligned} \tag{5.15}$$

describes how the interface moves.

Dimensionless Model

Let $\hat{x} = \dfrac{x}{\hat{l}}$ where $\hat{l}$ is the characteristic length scale on the order of 100 microns. Let $\hat{t} = t\hat{\mu}$ where $\hat{\mu}$ is the maximum growth rate. For a dimensionless model, consider the rescaled variables defined as

$$\hat{S} = \frac{S}{S_{bulk}},\ \hat{C} = \frac{C}{C^*},\ \hat{f} = \frac{f}{(1-\epsilon_l)},\ \hat{e} = \frac{e}{1-\epsilon_l},$$
$$\hat{L} = \frac{L}{\hat{l}},\ \hat{v} = \frac{v}{\hat{\mu}\hat{l}}.$$

The functions G, R_ρ and R_e are rescaled to

$$\hat{G}(\hat{S}) = \frac{1}{\hat{\mu}} G(S_{bulk}\hat{S}) = \frac{\hat{S}}{k_s + \hat{S}},$$
$$\hat{R}_\rho(\hat{S}) = \frac{1}{\hat{\mu}} R_\rho(S_{bulk}\hat{S}) = \frac{\hat{S}}{k_s + \hat{S}} - \beta,$$
$$\hat{R}_e(\hat{S},\hat{C}) = \frac{1}{\hat{\mu}} R_\rho(S_{bulk}\hat{S}, C^*\hat{C}) = k_n + k_g \frac{\hat{S}}{k_s + \hat{S}} H(\hat{C} - 1)$$

where the dimensionless parameters are

$$k_s = \frac{K_S}{S_{bulk}},\ \beta = \frac{K_d^\rho}{\hat{\mu}},\ k_n = \frac{K_n^e \rho_0}{\hat{\mu}\rho_1},\ k_g = \frac{K_g^e \rho_0}{\rho_1}.$$

Dropping the hat notation, the model equations in (5.7) become

$$\epsilon_1 \frac{\partial S}{\partial t} = \frac{\partial^2 S}{\partial x^2} - \sigma_1 G(S) f - \sigma_2 G(S) f H(C-1), \tag{5.16a}$$

$$\epsilon_2 \frac{\partial C}{\partial t} = \frac{\partial^2 C}{\partial x^2} + k_p f, \tag{5.16b}$$

$$\frac{\partial f}{\partial t} = -v\frac{\partial f}{\partial x} + \left(R_\rho(S)(1-f) - R_e(S,C)f + k_e e\right) f, \tag{5.16c}$$

$$\frac{\partial e}{\partial t} = -v\frac{\partial e}{\partial x} + \left(R_e(S,C)(1-e) - R_\rho(S)e - k_e e\right) f, \tag{5.16d}$$

$$\frac{dL}{dt} = v(L(t),t), \tag{5.16e}$$

where

$$v(x,t) = \int_0^x \left(R_e(S(\xi,t),C(\xi,t)) + R_\rho(S(\xi,t))\right) f(\xi,t) - k_e e(\xi,t)\, d\xi. \tag{5.16f}$$

The boundary conditions are

$$\frac{\partial S}{\partial x}(0,t) = 0,\ S(L(t),t) = 1, \tag{5.17}$$

$$\frac{\partial C}{\partial x}(0,t) = 0,\ C(L(t),t) = 0, \tag{5.18}$$

$$v(0,t)f(0,t) = 0,\ v(0,t)e(0,t) = 0. \tag{5.19}$$

The non-dimensional parameters in (5.16) are listed in Table 9. Unfortunately, many of the parameters introduced in this model are difficult to determine, thus the relative sizes of the dimensionless parameters can not be calculated. The parameter values used in the simulations are identified in Numerical Simulation of the Model.

Symbol	Definition	Symbol	Definition
ϵ_1	$\frac{\hat{l}^2\hat{\mu}}{D_S}$	ϵ_2	$\frac{\hat{l}^2\hat{\mu}}{D_C}$
σ_1	$(1-\epsilon_l)\frac{\rho_0\hat{\mu}\hat{l}^2}{Y_\rho D_S S_{bulk}}$	σ_2	$(1-\epsilon_l)\frac{\rho_0 K_g^e\hat{\mu}\hat{l}^2}{Y_e D_S S_{bulk}}$
k_s	$\frac{K_S}{S_{bulk}}$	k_p	$(1-\epsilon_l)\frac{K_p\rho_0\hat{l}^2}{D_C C^*}$
β	$\frac{K_d^\rho}{\hat{\mu}}$	k_e	$\frac{K_d^e}{\hat{\mu}}$
k_n	$\frac{K_n^e\rho_0}{\hat{\mu}\rho_1}$	k_g	$\frac{K_g^e\rho_0}{\rho_1}$

Table 9. EPS non-dimensional parameters.

Behavior at the Interface

Since the f and e equations are hyperbolic and the values of S and C are fixed at $x = L(t)$, we have a system of non-linear differential equations for f and e at the interface. Recall, that if $\dot{F}$ represents the derivative of F along the solution curves of

$$\frac{dx}{dt} = v(x(t), t),$$

$$x(0) = x_0,$$

then

$$\dot{F} = \frac{\partial F}{\partial t} + v(x(t), t)\frac{\partial F}{\partial x}.$$

On the solution curve that corresponds to the interface, f and e satisfy the equations

$$\dot{f} = (r(1-f) - k_n f + k_e e)f, \tag{5.20a}$$

$$\dot{e} = (k_n(1-e) - re - k_e e)f \tag{5.20b}$$

where the parameter r is

$$r = \frac{1}{k_s + 1} - \beta. \tag{5.21}$$

The non-zero equilibrium of (5.20) is stable if r, k_n and $k_g > 0$.

Lemma 5. *The system in* (5.20) *has a non-zero equilibrium. This solution is stable if* r, k_n *and* $k_e > 0$.

Proof. One can easily show that the only non-zero equilibrium is

$$\tilde{f} = \frac{k_e + r}{r + k_n + k_e}, \tag{5.22a}$$

$$\tilde{e} = \frac{k_n}{r + k_n + k_e}. \tag{5.22b}$$

The Jacobian of (5.20) evaluated at (5.22) is

$$J = \begin{bmatrix} -\dfrac{k_n k_e + r(r + k_n + k_e)}{r + k_n + k_e} & \dfrac{k_e(r + k_e)}{r + k_n + k_e} \\ 0 & -(r + k_e) \end{bmatrix}. \tag{5.23}$$

Clearly, the eigenvalues of J are negative if r, k_n and $k_e > 0$. Thus the equilibrium solution is stable. □

We assume that $k_e, k_n \geq 0$, so the solution is stable if $r > 0$. The parameter r is related to the cellular production rate at the interface. If $r > 0$, then the cellular production rate at the interface is positive. This leads to the conclusion that the cellular production rate must be positive for a non-zero population to exist at the interface. Also notice that $\tilde{f}$ and $\tilde{e}$ are bounded between 1 and 0.

Numerical Simulations of the Model

In this section, we will examine how EPS forms in a biofilm by solving the model numerically. Simulating a thin film which initially has no EPS, we will analyze where EPS forms in the biofilm and how the presence of EPS effects the cell distribution in the biofilm as the biofilm grows.

When deriving the model, the initial formation of the biofilm is not considered. The equations are derived under the assumption that a film has already formed. Thus we take the model variables to be $S = 1$, $C = 0$, $f = 1$, $e = 0$ and $L = 0.05$ at $t = 0$. These values represent a very thin film (5 microns) with no EPS or chemical present. With these initial conditions, numerical simulations indicate that the model tends to a steady-state solution.

After some experimentation, it was found that the parameter k_p had the greatest influence on what type of steady-state solutions the model converged to. For some values of k_p, the final f solution was nearly constant (see Figures 12 through 16).

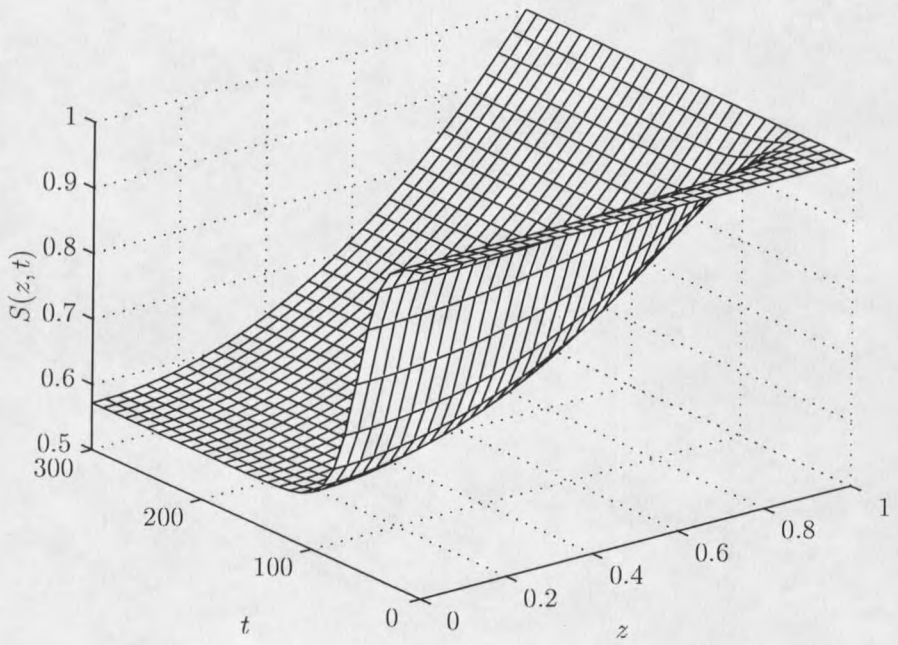


Figure 12. $S(z,t)$ when $k_p = 0$.

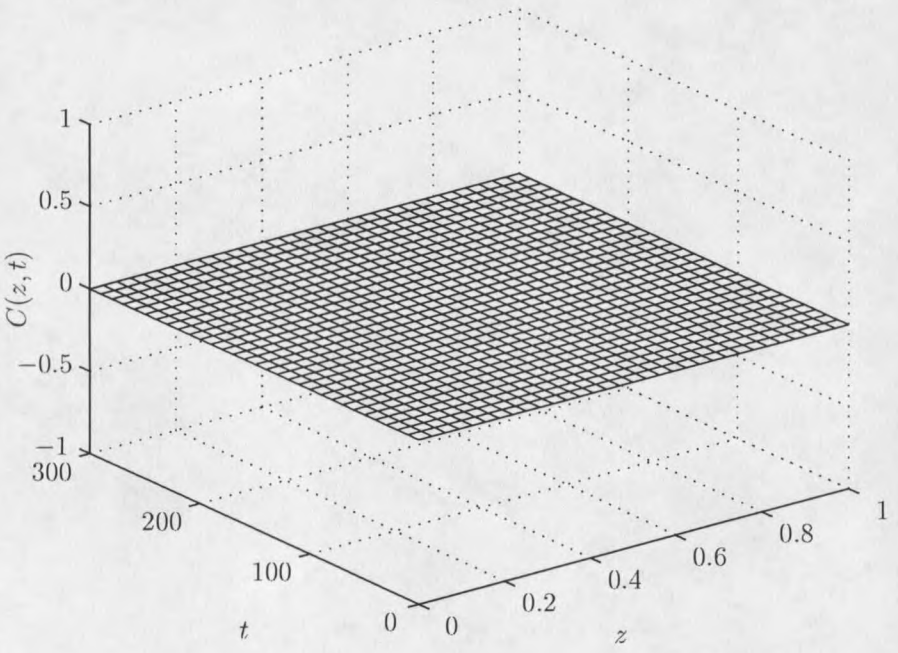


Figure 13. $C(z,t)$ when $k_p = 0$.

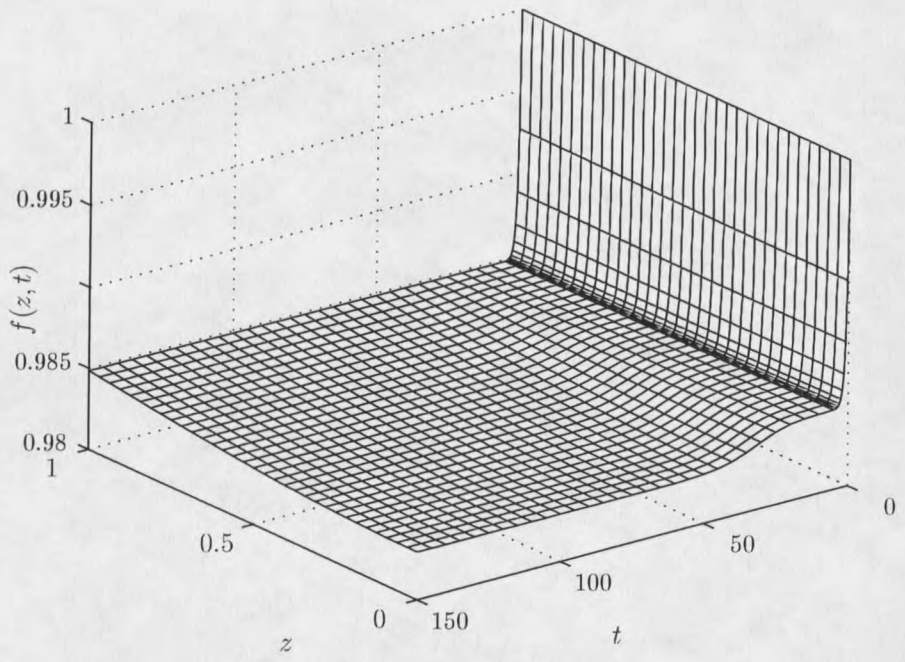


Figure 14. $f(z,t)$ when $k_p = 0$.

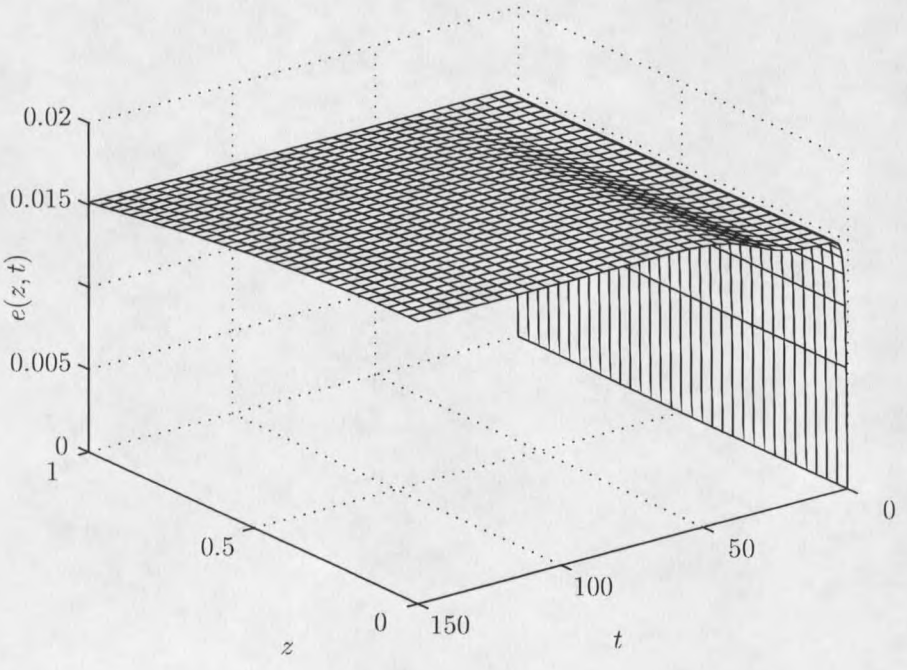


Figure 15. $e(z,t)$ when $k_p = 0$.

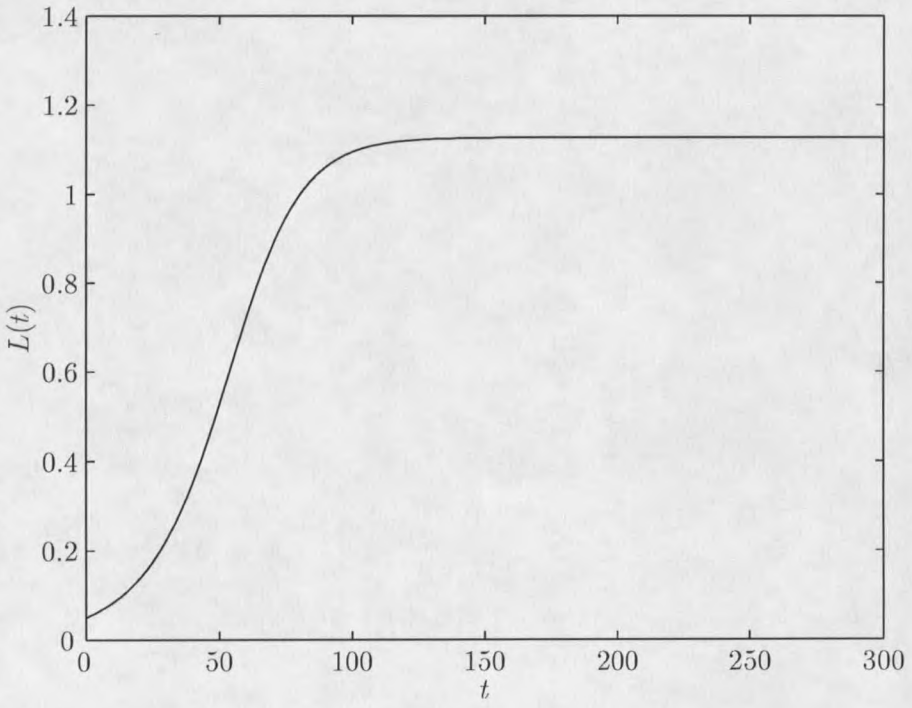


Figure 16. $L(t)$ when $k_p = 0$.

For larger values of k_p, the f solution was approximately 0.5 at the substratum and 0.985 at the interface (see Figures 17 through 21).

What follows is one numerical experiment where the model was simulated for different values of k_p. All other parameter values were fixed in these simulations, but similar results were observed in other parameter sets.

Numerical Implementation

Before solving the model numerically, the equations were transformed to a fixed spatial domain. Let $z = \frac{x}{L(t)}$. Under this transformation, the model equations become

$$\epsilon_1 \frac{\partial S}{\partial t} = \frac{1}{L^2}\frac{\partial^2 S}{\partial z^2} + \epsilon_1 \frac{z}{L}\frac{dL}{dt}\frac{\partial S}{\partial z} - \sigma_1 G(S) f - \sigma_2 G(S) f H(C-1), \tag{5.24a}$$

$$\epsilon_2 \frac{\partial C}{\partial t} = \frac{1}{L^2}\frac{\partial^2 C}{\partial z^2} + \epsilon_2 \frac{z}{L}\frac{dL}{dt}\frac{\partial C}{\partial z} + k_p f, \tag{5.24b}$$

$$\frac{\partial f}{\partial t} = -(u(z,t) - z u(1,t))\frac{\partial f}{\partial z} + (R_\rho(S)(1-f) - R_e(S,C) f + k_e e)\, f, \tag{5.24c}$$

$$\frac{\partial e}{\partial t} = -(u(z,t) - z u(1,t))\frac{\partial e}{\partial z} + (R_e(S,C)(1-e) - R_\rho(S) e - k_e e)\, f, \tag{5.24d}$$

$$\frac{dL}{dt} = u(L(t),t) \tag{5.24e}$$

where

$$u(z,t) = \int_0^z \left[\left(R_e(S(\zeta,t), C(\zeta,t)) + R_\rho(S(\zeta,t)) \right) f(\zeta,t) - k_e e(\zeta,t) \right] d\zeta. \tag{5.24f}$$

By dividing the interval $[0,1]$ into N subintervals and approximating (5.24) at each mesh point, this system of partial differential equations is reduced to a system of $4N+3$ ordinary differential equations. The spatial derivatives in (5.24a) and (5.24b)

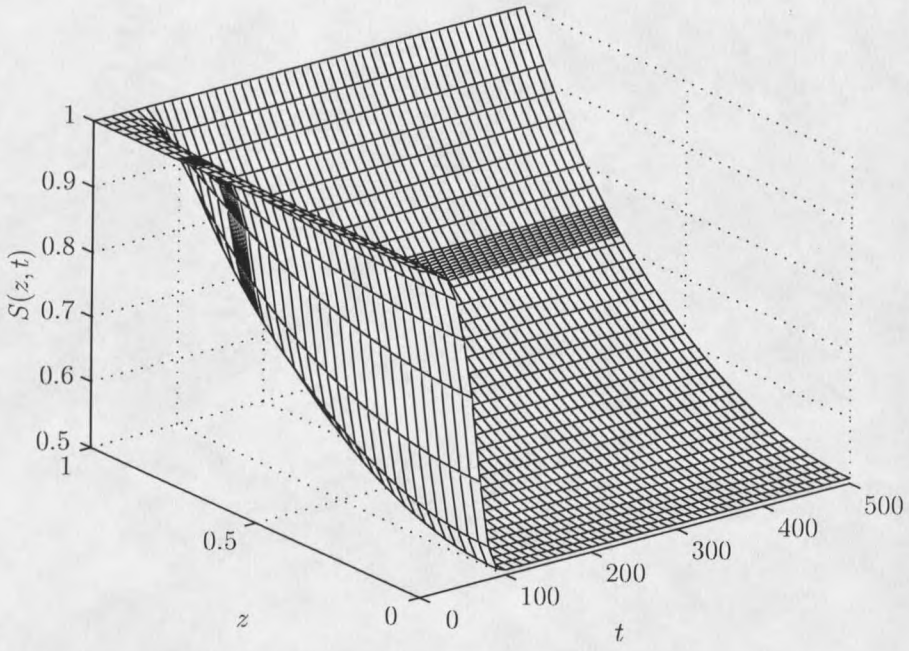


Figure 17. $S(z,t)$ when $k_p = 3$.

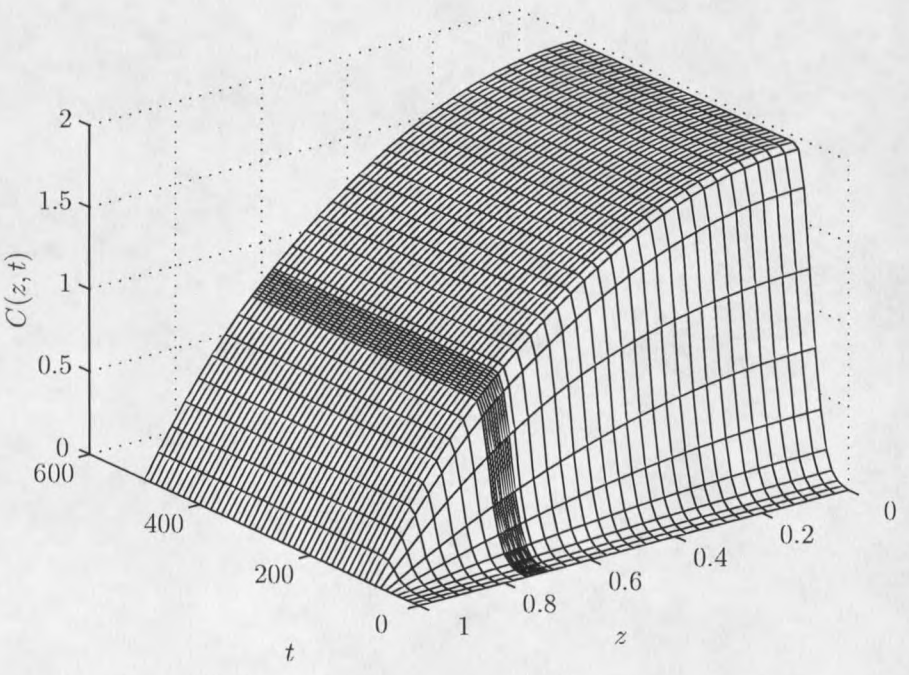


Figure 18. $C(z,t)$ when $k_p = 3$.

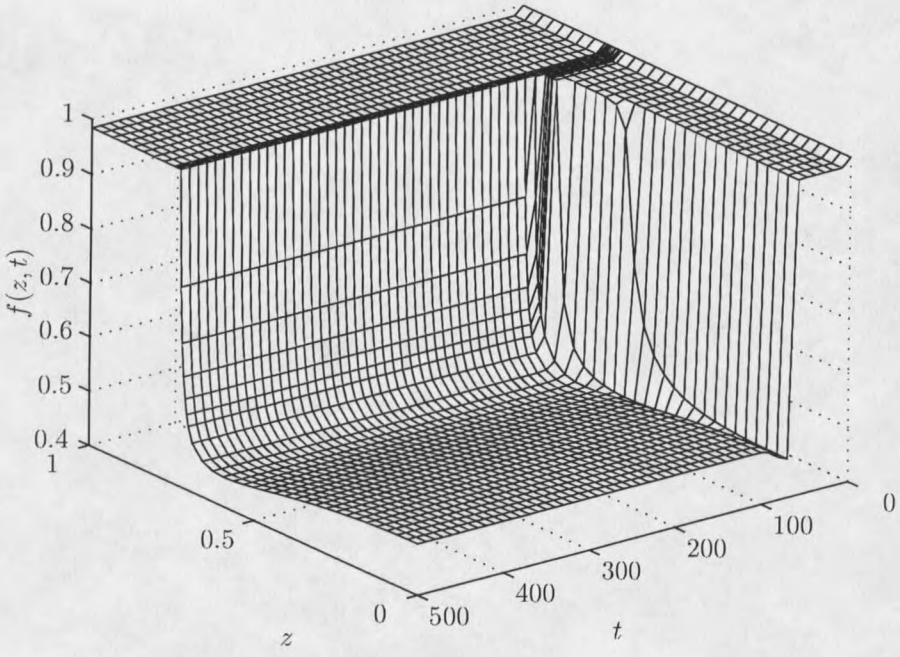


Figure 19. $f(z,t)$ when $k_p = 3$.

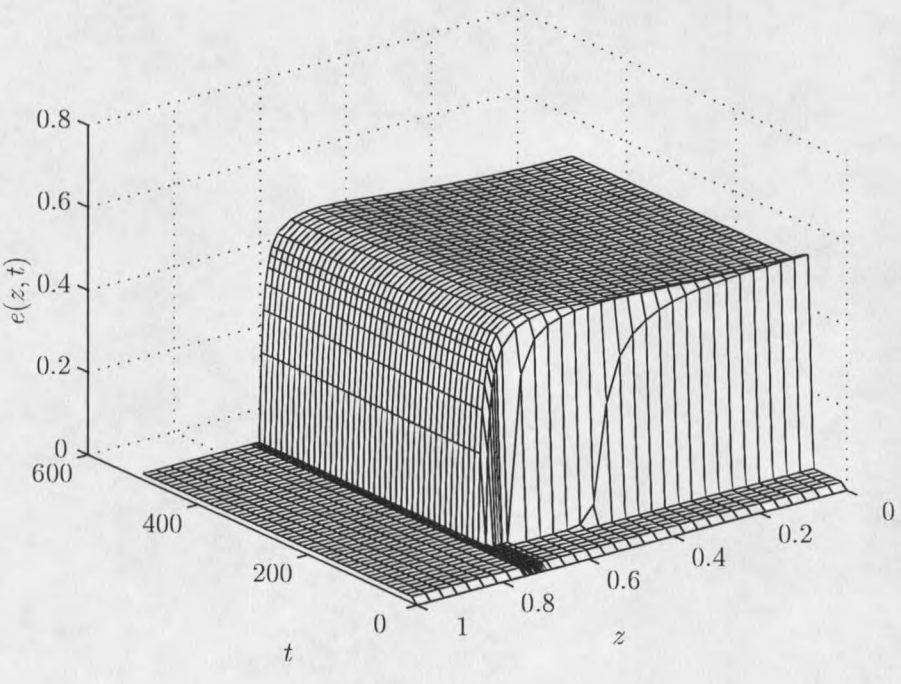


Figure 20. $e(z,t)$ when $k_p = 3$.

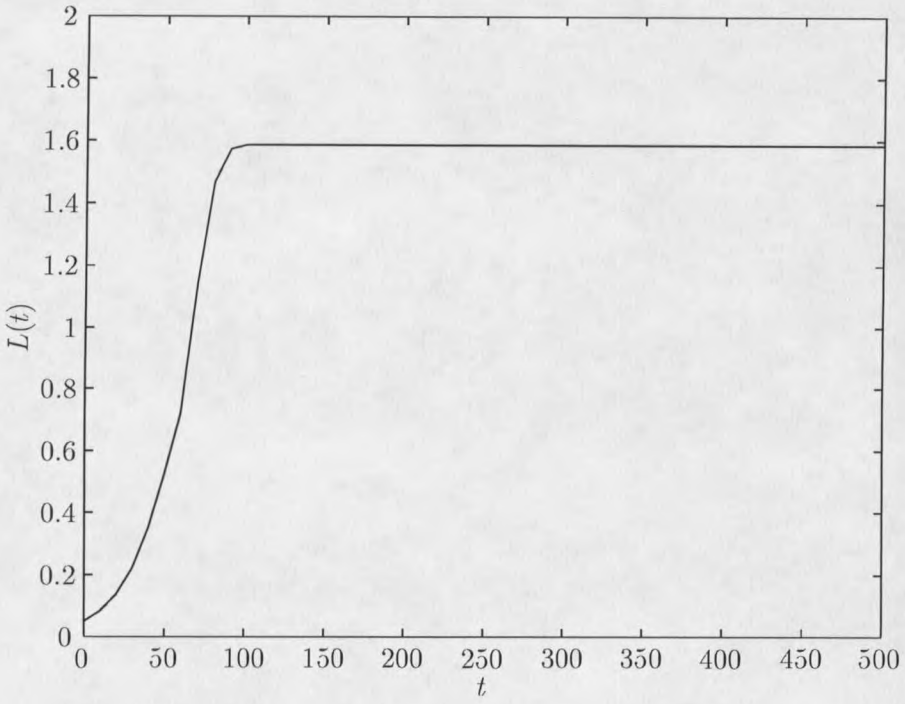


Figure 21. $L(t)$ when $k_p = 3$.

were approximated with a centered difference scheme. The spatial derivatives in (5.24c) and (5.24d) were approximated with an up-winding scheme. The trapezoid method was used to calculate the integral in (5.24f).

The convergence of this scheme depends on the differentiability of the terms in (5.24). Since the heaviside function is not continuous, it was approximated with the function

$$h(x) = \frac{1}{2}\left(\tanh\left(\frac{x}{\varepsilon}\right) + 1\right) \tag{5.25}$$

where ε is a small parameter.

As ε approaches zero, h approaches the heaviside function. In the simulations, ε was set equal to $\varepsilon = 10^{-6}$. The MATLAB code that generates the system of ordinary differential equations is listed in Appendix D.

For each simulation, a uniform mesh with $N = 32$ was used. At the end of the run, if the solutions had steep gradients the mesh was refined to include more points where the rapid change occurred. The system was then solved on this new mesh. The system was solved with the ode23s package in MATLAB. The ode23s package is designed to solve stiff differential equations. The package uses a Runge-Kutta scheme with an adaptive time step algorithm. Each run concluded when the 1-norm of the right-hand side was $O\left(10^{-6}\right)$.

Parameter Values

The order of magnitude for some of the parameters like D_C and K_p is not known. To simulate the model, the values for the dimensionless parameters were based on experimental observations reported in the literature and numerical experimentation. These parameter values are tabulated in Table 10

Symbol	Value	Symbol	Value
ϵ_1	10^{-4}	ϵ_2	10^{-4}
σ_1	5	σ_2	1
k_S	4	k_p	$0-5$
β	0.15	k_e	0.6
k_n	5×10^{-2}	k_g	5

Table 10. Parameter values used in the numerical simulations.

The diffusion of substrate occurs on a much smaller time scale than the reproduction of cells [12]. We will assume that it also occurs on a smaller time scale than EPS formation. We will assume that the diffusion of the signaling chemical occurs on a similar time scale. Thus, the parameters ϵ_1 and ϵ_2 are very small when compared to other parameters in the model and $\epsilon_1 = \epsilon_2$. From the previous model, $\epsilon = O(10^{-4})$. We will use the same value for ϵ_1 and ϵ_2 in this model. In [3], a mutant biofilm that did not produce signaling chemicals had a small amount of EPS present. Thus we take the parameter k_n to be small when compared to other parameters in the model. However, it should also be at least an order of magnitude greater than ϵ_1. Thus, a value of $k_n = 5 \times 10^{-2}$ was used.

In [11], a model with similar EPS formation rates was used to calculate Y_e, Y_ρ and K_g^e. Values for Y_e and Y_ρ were reported such that $\frac{Y_e}{Y_\rho} \approx 2$. In the same paper, a value of 0.4 was reported for K_g^n. In terms of the dimensionless parameters, these values give an approximation to the ratio of σ_1 and σ_2 as

$$\frac{\sigma_1}{\sigma_2} = \frac{Y_e}{Y_\rho} K_g^e \approx 5. \tag{5.26}$$

Using values from [12], σ_1 was set at $\sigma_1 = 5$ and (5.26) defined $\sigma_2 = 1$. From the same paper, the parameters k_s and β were set equal to $k_s = 4$ and $\beta = 0.15$. An EPS degradation rate that was about four times greater than the cellular degradation rate was reported in [7]. Thus, k_e was defined as $k_e = 0.6$.

The parameter k_g had the greatest effect on the f and e profiles near the substratum. It is believed that EPS enables the cells to attach to the substratum. So

a reasonable solution should have a significant amount of EPS at the substratum. After some experimentation, the value $k_g = 5$ resulted in profiles where f and e were each about 0.5 at the substratum.

Solution Behavior

During the simulation, the S and C solutions quickly approached monotone functions. The final f, e and L values depended on the parameter k_p.

When the parameter $k_p = 0$, the model corresponds to a biofilm where the organisms do not produce a signaling chemical. The numerical simulation produced e and f steady-state solutions that were almost constant. The final substrate profile was a monotone increasing function where the substrate at the substratum was about 0.55. The C solution was zero for all time t. The L solution approached 1.12 (see Figure22). As k_p was increased, the final S, f and e profiles were identical to the steady state solutions in the $k_p = 0$ case. The C profile limited on a monotone decreasing function where the maximum was less than 1 (see Figure 23). The signaling chemical did not reach the threshold at any point inside the biofilm.

Once k_p was increased past 1.6, the steady-state profiles changed. With $k_p > 1.6$, the steady-state solution for C was still a monotone decreasing function, but the value of C at the interface was greater than 1. In the region where $C > 1$, the final f profile is about 0.5. To satisfy the boundary condition at $x = 1$, C drops below 1 at some point in $[0, 1]$. Once C drops below 1, the f profile pulls up to a solution that is close to the $k_p = 0$ steady-state solution. Where $C > 1$, e is high and then

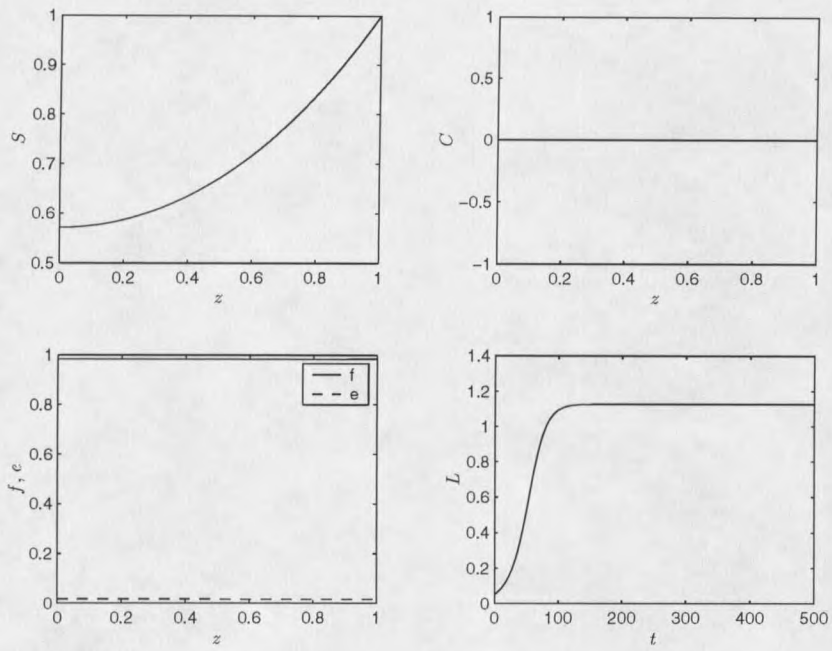


Figure 22. S, C, f, e and L for $k_p = 0$.

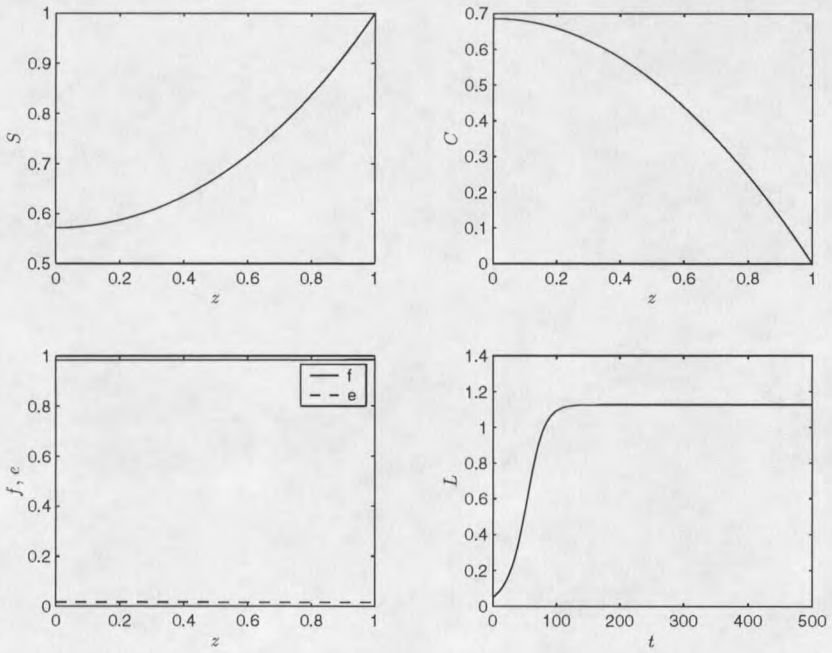


Figure 23. S, C, f, e and L for $k_p = 1$.

drops quickly once C falls below 1 (see Figures 24 and 25). The substrate profile is

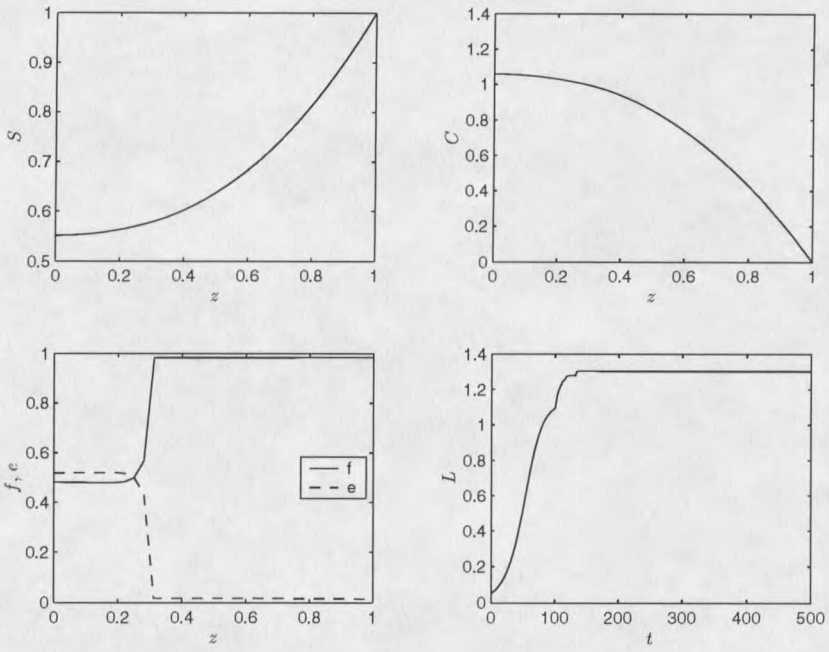


Figure 24. S, C, f, e and L for $k_p = 1.7$.

an increasing function, but the value at the interface is now slightly below 0.5. Since $C > 1$, the growth related EPS formation terms are non-zero and more substrate is used. As k_p increased, the C solution remains a monotone decreasing function, but the value of C at $z = 0$ increases. This increases the length of the interval where $C > 1$. Thus, the steep gradient seen in the f and e solutions drifts towards $z = 1$ (see Figures 25 and 26). The dramatic changes in the f and e solutions can be seen in the L versus t plots. Notice the discontinuity in $\dfrac{dL}{dt}$ when $k_p > 1.6$ (see Figures 24, 25 and 26). This occurs as C approaches 1. Once the chemical reaches threshold, the growth related EPS terms are activated and EPS is rapidly created. With more EPS

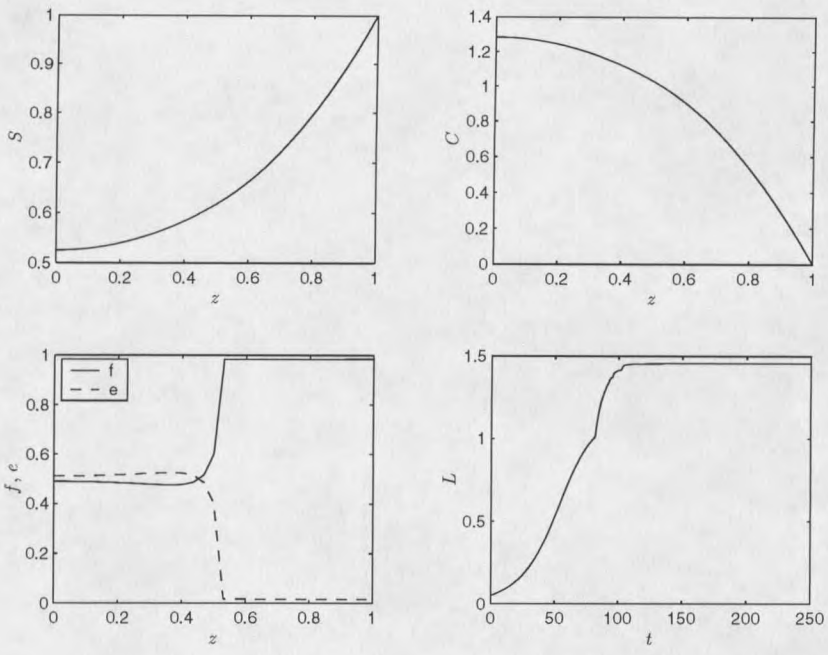


Figure 25. S, C, f, e and L for $k_p = 2$.

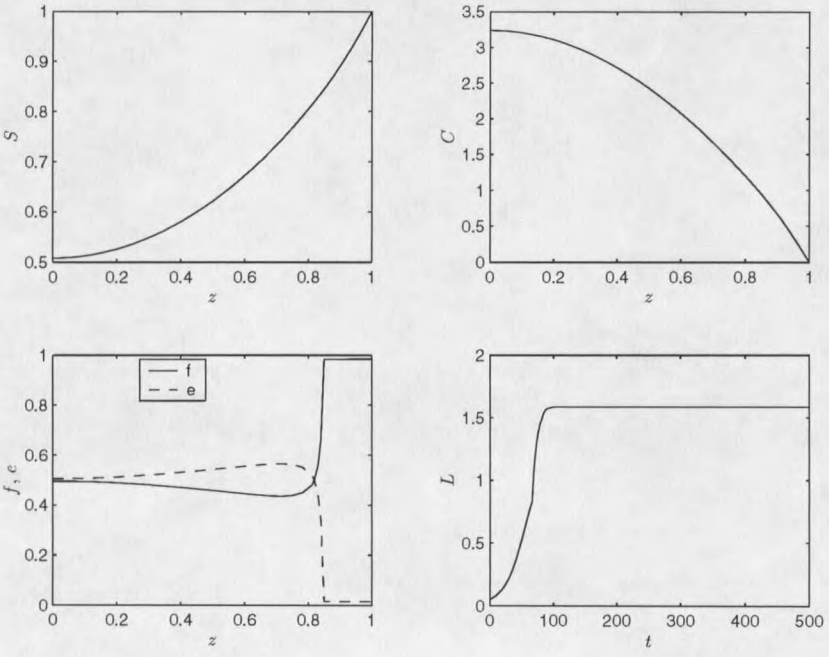


Figure 26. S, C, f, e and L for $k_p = 5$.

being produced, the steady-state value for L increases. When $k_p > 1.6$, the limiting thickness quickly increased and continued to increase as the value of k_p was raised (see Figure 27).

This behavior of the solutions and the parameter k_p is a result of the signaling chemical production. Recall, that the production of C was proportional to the cell density. For any set of parameters, there is a maximum number of organisms that can survive in the biofilm. For $k_p < 1.6$, the cell density reaches this maximum before the chemical reaches the threshold concentration. Thus, little EPS is produced and the steady state profile is a uniform cell distribution. Once $k_p > 1.6$, the signaling chemical reaches the threshold before the organisms reach their maximum. With the chemical above threshold, the growth related production terms are non-zero and a significant amount of EPS is produced.

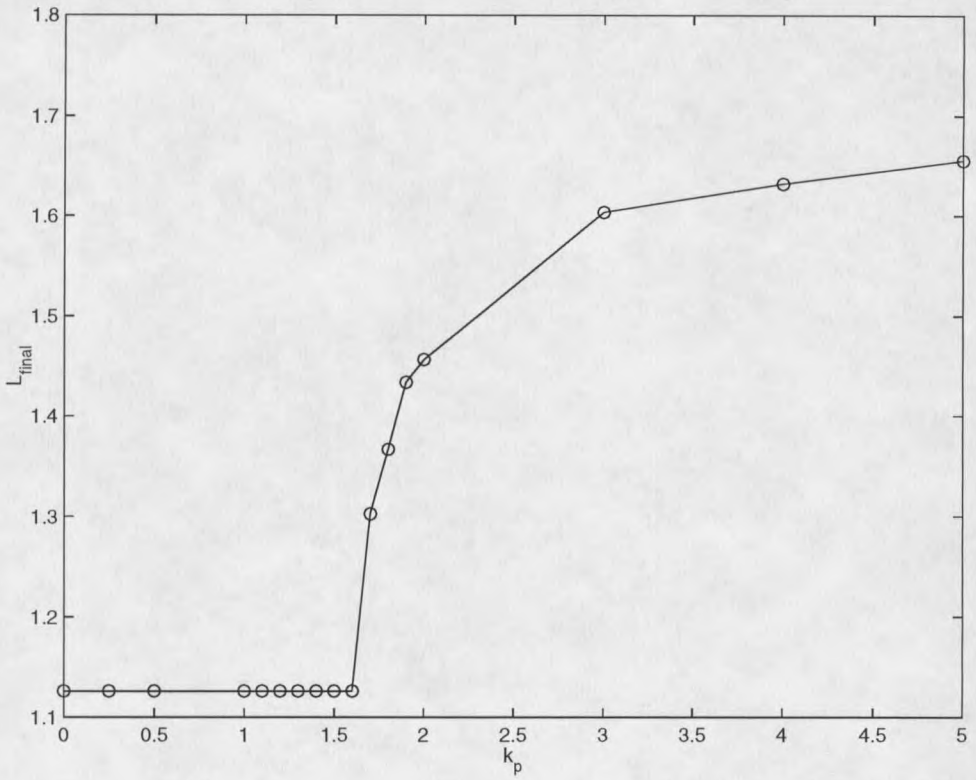


Figure 27. Final L value versus k_p.

CHAPTER 6

CONCLUDING REMARKS

The model presented here does not represent a realistic biofilm. It does not take into account multiply species, detachment or liquid phase components. However, several features arise in the model that correspond to observed physical characteristics in biofilms.

Under the assumption that solutions exist and are unique, the solution to the substrate equation is bounded. These bounds imply that the substrate level can not exceed the concentration of substrate found in the bulk fluid. The strict lower bound implies that the substrate concentration must stay above zero if the initial concentration is positive. If we further assume that biomass diffuses, bounds on the active biomass, velocity and thickness can be established.

$f(x,t)$ approaches a steady state value at the interface for all parameter values. This value is non-zero if the organism growth rate at the interface is greater than the inactivation rate. Thus, the model predicts that the density of organisms at the film's surface reaches a steady state value. Numerically, this behavior has the f profile fixed at $x = L$ while L continues to increase; similar to traveling wave behavior.

One aspect of this model, that is not observed in a biofilm, is the absence of steady state solutions where f is not a constant function. Although the f solution approaches a steady state value at the interface, the system does not have a steady state solution

where f is non-negative and not identically equal to zero if the inactivation rate is greater than zero. This is a direct result of inactive biomass accumulating in the biofilm without including some type of removal. In general for any type of biomass, the net production term must change sign in the biofilm; otherwise only a trivial steady state solution is possible. The steady state solution that corresponds to a biofilm with no inactive biomass present is not physically possible, since this solution only exists if the inactivation rate is zero. But the S and L solutions for this steady state do have favorable properties. The substrate profile is a monotone increasing function and the L solution is roughly 100 microns when the model parameters fall into an appropriate range of values.

The stability analysis for the steady state where $f = 0$ indicates that a minimum value for the bulk substrate is needed to support a biofilm. This trivial steady state, which corresponds to a biofilm with no active organisms, is linearly unstable if

$$\frac{S_b}{1+S_b} - \beta - \alpha > 0.$$

Solving for S_b in this inequality leads to

$$\frac{\alpha+\beta}{1-(\alpha+\beta)} < S_b,$$

which is a lower bound for S_b. If the bulk substrate satisfies this inequality, a solution with a small amount of active organisms present can not approach a solution where the active organisms disappear. Thus, if the bulk substrate concentration is above this minimum, active organism are always present in the biofilm. The stability of the

$f = 1$ solution is not clear. Estimates of the eigenvalues indicated that a positive eigenvalue was present. However, the model with initial conditions $S = S_b$, $f = 1$ and $L = 0.05$ will limit on this steady state.

Most biofilm models do not include diffusion of biomass. But this assumption leads to a system with bounded solutions and a system that is much easier to solve numerically. One difficulty with adding diffusion to the biomass equation is a linear homogenous boundary condition of the form

$$a(t)f(L(t),t) + b(t)\frac{\partial f}{\partial x}(L(t),t) = 0$$

will only allow steady state solutions where $f = 0$ to exist. One possible fix for this problem is the inclusion of a detachment term or a mixed boundary condition that is not equal to zero. If either of these are applied to the model the argument presented in Chapter 4 is no longer valid.

When EPS production is included, the model tends to a steady state where the final organism and EPS profiles depend on the parameter k_p. If $k_p = 0$, the solutions for f and e tend to functions that are nearly constant. This behavior is also observed for parameter values where $k_p \leq 1.6$. Once k_p is greater than 1.6 a bifurcation occurs. The solutions for f and e now limit on functions where a sharp change in the profiles occurs when C drops below 1. The contrast in solutions where $k_p = 0$ and $k_p > 1.6$ mimics the differences seen in wild and mutant biofilms. The change in solution behavior at $k_p = 1.6$ implies there is a minimum rate at which the signaling chemical must be produced at for growth related EPS formation to occur.

Like the original biofilm model, the model with EPS does not include all of the known mechanisms for EPS production. There are least two signaling chemicals that contribute to growth related EPS formation. Both of these chemicals decay on a time scale that should not be ignored in the model [4]. The addition of another signaling chemical would not be difficult. But allowing the signaling chemical to decay could drastically change the f and e solutions. From the steady state equation for C, the C solution is a decreasing function provided $f \geq 0$. Since the f and c solutions depend on where C is greater than 1, the result is lower cell densities near the substratum. If a decay term like kC is added, then C may not be a decreasing function. In this case, the f solution could have a local minimum inside the biofilm.

REFERENCES CITED

[1] N.F. Britton. *Reaction-Diffusion Equations and Their Applications to Biology.* Academic Press, 1986.

[2] W. G. Characklis and K. C. Marshall, editors. *Biofilms.* Wiley series in ecological and applied microbiology. John Wiley & Sons, Inc., 1st edition, 1990.

[3] D.G. Davies, M.R. Parsek, J.P. Pearson, B.H. Iglewski, J.W. Costerton, and E.P. Greenberg. The involvement of cell-to-cell signaling in the development of a bacterial biofilm. *Science*, 280:295–298, April 10, 1998.

[4] J.D. Dockery and J.P. Keener. A mathematical model for quorum sensing in pseudomonas aeruginosa. *Bulletin of Mathematical Biology*, (in press).

[5] M. Dworkin. *Microbial cell-cell interactions.* American Society for Microbiology, 1991.

[6] V. Gadani, P. Villon, J. Manem, and B. Rittmann. A new method to solve a non-steady-state multispecies biofilm model. *Bulletin of Mathematical Biology*, 55(6):1039–1061, 1993.

[7] K.M. Hsieh, G.A. Murgel, L.W. Lion, and M.L. Shuler. Interactions of microbial biofilms with toxic trace metals:1.observation and modeling of cell growth, attachment, and production of extracellular polymer. *Biotechnology and Bioengineering*, 44:219–231, 1994.

[8] R. Losick and D. Kaiser. Why and how bacteria communicate. *Scientific American*, 276(2), 1997.

[9] K. Meerbergen, A. Spence, and D. Roose. Shift-invert and cayley transforms for the detection of eigenvalues with largest real part of nonsymmetric matrices. *BIT Numerical Mathematics*, 1994.

[10] M.H. Protter and H.F. Weinberger. *Maximum Principles in Differential Equations.* Prentice-Hall, Inc., 1967.

[11] J.A. Robinson, M.G. Trulear, and W.G. Characklis. Cellular reproduction and extracellular polymer formation by pseudomonas aeruginosa in continuous culture. *Biotechnology and Bioengineering*, XXVI:1409–1417, 1984.

[12] C. T. Skowlund. Effect of biofilm growth on steady-state biofilm models. *Biotechnology and Bioengineering*, 35:502–510, 1990.

[13] O. Wanner and W. Gujer. A multispecies biofilm model. *Biotechnology and Bioengineering*, 28:314–328, 1986.

APPENDICES

APPENDIX A

BIOFILM MODEL WITHOUT EPS

```
function F=F(t,Y)
%This function evaluates the model
% equations on the mesh x_0=0,x_1,x_2,...,x_N=1
% The model parameters are stored in the MAT
% file ModelParms. The numerical parameters
% are stored in NumParms.

load ModelParms Epsilon Alpha Beta gam Sb
load NumParms x

N=length(x)-1;
Trap_Rule=trap_rulematrix(x);
[D2,Dcenter,Dpos,Dneg]=set_diffmatrices(x);

S=Y(1:N,1);    %<---Note: The S=Ssoln-Sb
f=Y(N+1:2*N+1,1);
L=Y(2*N+2,1);


%%%%Compute Velocity term
G=SubstrateUsage([S+Sb;0+Sb]);

u=Trap_Rule*((G-Beta).*f);
a=u-u(N+1,1).*x;

%Separate convective term into positive and negative parts
  apos=max(a(2:N,1),0);
  aneg=-max(-a(2:N,1),0);
  Lambdapos=spdiags(apos,0,N-1,N-1); Lambdaneg=spdiags(aneg,0,N-1,N-1);

%%%%Compute the Cell source term
b=((G-Beta).*(1-f)-Alpha).*f;


%%%%Define the f eqn at the x=0 boundary
  dfdt(1,1)=b(1,1);

%%%%Define S eqns at the points x_0,x_1,...,x_{N-1}
  dSdt(:,1)=(1/L/L)*(D2*S)+...
                          +Epsilon*(x(1:N,1).*(u(N+1,1)*Dcenter*S))+...
                          -gam*G(1:N,1).*f(1:N,1);

%%%%Define f eqns at the points x_1,x_2,...,x_{N-1}
  dfdt(2:N,1)=-(Lambdapos*Dpos + Lambdaneg*Dneg)*f+b(2:N,1);

%%%%Define the f eqn at the x=1 boundary
  dfdt(N+1,1)=b(N+1,1);

%%%%Define the L eqn
  dLdt=L*u(N+1,1);

  d=[1/Epsilon*ones(N,1);ones(N+1+1,1)];
```

```
  M=spdiags(d,0,2*(N+1),2*(N+1));

  F=M*[dSdt;dfdt;dLdt];

%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
%FUNCTIONS
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function y=SubstrateUsage(S)
%Calculates the substrate usage term


y=S./(S+1);
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function A=trap_rulematrix(x);
%This file creates the matrix that evaluates the volterra
% integral \int_a^x F(x') dx' at the mesh points defined
% by the vector x
% x=mesh points
%

N=length(x);
x=reshape(x,N,1);
dx=x(2:N,1)-x(1:N-1,1);

A=sparse(N,N);

for i=2:N
  A(i,1)=dx(1,1);
  A(i,i)=dx(i-1,1);
  for j=2:i-1
  A(i,j)=dx(j-1,1)+dx(j,1);
  end
end;

A=0.5*A;
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function [D2,Dcenter,Dpos,Dneg]=set_diffmatrices(x)
%Given the mesh x, this function adjusts the difference
% matrices to fit the boundary conditions
%

N=length(x)-1;
dx=x(2:N+1,1)-x(1:N,1);

[D2,Dcenter,Dpos,Dneg]=diff_ops(x);      %<---Define the 1st and 2nd Order
                                         %     Difference operators
Trap_Rule=trap_rulematrix(x);            %<---Define Trap rule matrix
```

```
%Adjust D2 to fit the Boundary conditions.
D2=[(1/dx(1,1)/dx(1,1))*[-2,2],sparse(1,N-2);D2(:,1:N)];
   %at x=0 No-flux and homogenous at x=1

Dcenter= [sparse(1,N);Dcenter(:,1:N)];
   %at x=0 No-flux
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function [A,B,C,D]=diff_ops(x)
%[A,B,C,D]=DIFF_OPS returns the 2nd order difference operator (A)
% the centered 1st order diffrence operator (B), the upwind
% 1st order difference operators (C) and (D)
% x is the mesh points for these difference operators.
% The difference operators approximate the first and second
% derivatives of the interior points points found in x
%
% For example, if f is a column vector where
% f=[F(x_0),F(x_1),...F(x_i),...,F(x_N)] for i=1,..,N-1
% Then A*f approximates the second derivative of F at the points
% x_i for i=1,...,N-1

N=length(x)-1;
x=reshape(x,N+1,1);

if sort(x)~=x
  fprintf(1,'The mesh vector must have the points in accending order! \n');
  A=[]; B=[]; C=[]; D=[];
  return
  end;

dx=x(2:N+1,1)-x(1:N,1);

if min(dx)<1e-9
  fprintf(1,'WARNING!!!! Delta-x less than machine tolerences \n');
  A=[]; B=[]; C=[]; D=[];
  return
  end;

%%%2nd Order Difference Operator
a1=2./dx(1:N-1,1)./(dx(1:N-1,1)+dx(2:N,1));
a2=2./dx(1:N-1,1)./dx(2:N,1);
a3=2./dx(2:N,1)./(dx(1:N-1,1)+dx(2:N,1));
A=spdiags([a1, -a2, a3],[0:2],N-1,N+1);

%%%1st Order Centered Difference Operator
b1=-1./(dx(1:N-1,1)+dx(2:N,1));
b2=-b1;
B=spdiags([b1 b2],[0 2],N-1,N+1);

%%%1st Order a>0 Difference Operator
c1=-1./dx(1:N-1,1);
c2=-c1;
```

```
C=spdiags([c1 c2],[0 1],N-1,N+1);

%%%1st Order a<0 Difference Operator
d1=-1./dx(2:N,1);
d2=-d1;
D=spdiags([d1 d2],[1 2],N-1,N+1);
%-------------------------------------------------------------------------
%-------------------------------------------------------------------------
```

APPENDIX B

JACOBIAN MATRIX CODE

```
function J=Jacobian(x,Y0,fname)
% Computes the Jacobian of F.m at the steady state solution Y0
% Note the vector Y0 is
% S0=Y0(1:N,1);
% f0=Y0(N+1:2*N+1,1);  steady state approx on x
% L0=Y0(2*(N+1),1);
%
%
% fname.mat stores the parameter values. x is the mesh
% used to calculate Y0.
%

%%%%Load the ModelParmeters
%%%%

load(fname,'Sb','Beta','gam','Epsilon')


%%%%Set N+1=# of mesh points and define the
%%%% mesh dependent quanities
N=length(x)-1;
Trap_Rule=trap_rulematrix(x);
[D2,Dcenter,Dpos,Dneg]=set_diffmatrices(x);


S0=Y0(1:N,1);
f0=Y0(N+1:2*N+1,1);
L0=Y0(2*(N+1),1);

%%%%Check to see if the sizes match
  if length(x)~=length(f0)
    sprintf('WARNING!!!! The length of x does not match the steady state')
    J=[]
    return
    end;

%%%%Set J as a sparse matrix
J=sparse(2*(N+1),2*(N+1));

%Evaluate the function G and the
% derivatives of S and f at the
% steady-state solutions.

G=SubstrateUsage([S0;0]+Sb);
dGdS=DSubstrateUsage([S0;0]+Sb);

%Evaluate the Cell source term and
% its derivatives at steady state
b=((G-Beta).*(1-f0)-Alpha).*f0;
dbdS=dGdS.*(1-f0).*f0;
dbdf=(G-Beta).*(1-2*f0);
```

```
%Compute the steady-state Solution for u
u0=Trap_Rule*((G-Beta).*f0);

%Compute dS0dx and df0dx
% Formulas based on the assumption that
% S0 and f0 solve the steady
% state equations
% df0dx is  evaluated on the
% interior points x_1,x_2,...,x_{N-1}
% dS0dx is evaluated on
% the mesh points x_0,x_1,...,x_{N-1}
dS0dx=(L0^2)*Trap_Rule(1:N,:)*(gam*G.*f0);
df0dx=(1./u0(2:N,1)).*((G(2:N,1)-Beta).*(1-f0(2:N))-Alpha).*f0(2:N,1);


%INT is a matrix when multiplied by Y gives
% a column vector where the entries correspond
% to the linearized integrand used to compute u.
% u=Trap_Rule*INT*Y, u(1)=Trap_Rule(N+1,:)*INT*Y

IS=spdiags(dGdS.*f0,0,N+1,N);
Iff=spdiags((G-Beta),0,N+1,N+1);
Aught=sparse(N+1,1);

INT=[IS Iff Aught];

Aught=sparse(N-1,1); %<---Sparse column vector

%%%%%%%%%
%%%%
%%%% BEGIN Building J
%%%%
%%%%%%%%%

%%%%S equations at x_0=0,x_1,x_2,...,x_{N-1}
dFSdS=-gam*spdiags(dGdS(1:N,1).*f0(1:N,1),0,N,N);
dFSdf=-gam*[spdiags(G(1:N,1),0,N,N),sparse(N,1)];
dFSdL=-2*gam*G(1:N,1).*f0(1:N,1)/L0;


xdS0dx=x(1:N,1).*dS0dx;
EpsxdSdxU1=Epsilon*xdS0dx*Trap_Rule(N+1,:)*INT; %<--x*Sprime*u(1)

J(1:N,:)=[(1/L0/L0)*D2+dFSdS, dFSdf, dFSdL]+EpsxdSdxU1;

%%%%f equation at x_0=0,x_1,x_2,x_3,...,x_{N-1},x_N=1

%Seperate the velocity term into negative and positive componets
u0pos=max(u0(2:N,1),0);
u0neg=-max(-u0(2:N,1),0);
Lambdapos=spdiags(u0pos,0,N-1,N-1); Lambdaneg=spdiags(u0neg,0,N-1,N-1);
```

```
Diff=[sparse(1,N+1);Lambdapos*Dpos+Lambdaneg*Dneg;sparse(1,N+1)];

dFfdS=spdiags(dbdS,0,N+1,N);
dFfdf=spdiags(dbdf,0,N+1,N+1);
dFfdL=sparse(N+1,1);


xf0prime=x(2:N,1).*df0dx;
U=-(spdiags(df0dx,0,N-1,N-1)*Trap_Rule(2:N,:)*INT+...
           -xf0prime*Trap_Rule(N+1,:)*INT);     %<--Terms involving u and u(1)

J(N+1:2*N+1,:)=[dFfdS,dFfdf-Diff,dFfdL]+...
                    +[sparse(1,2*(N+1));U;sparse(1,2*(N+1))];


%%%%L equation
J(2*(N+1),:)=L0*Trap_Rule(N+1,:)*INT;

%%%%%Multiply S equation by 1/Epsilon
d=[(1/Epsilon)*ones(N,1); ones(N+1+1,1)];

M=spdiags(d,0,2*(N+1),2*(N+1));

J=M*J;

%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
%FUNCTIONS
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function [dydS]=DSubstrateUsage(S)
%Calculates the derivatives of the
% Substrate Usage function

dydS=1./(S+1).^2;
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function y=SubstrateUsage(S)
%Calculates the substrate usage term

y=S./(S+1);
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function A=trap_rulematrix(x);
%This file creates the matrix that evaluates the volterra
% integral \int_a^x F(x') dx' at the mesh points defined
% by the vector x
% x=mesh points
%

N=length(x);
x=reshape(x,N,1);
```

```
dx=x(2:N,1)-x(1:N-1,1);

A=sparse(N,N);

for i=2:N
  A(i,1)=dx(1,1);
  A(i,i)=dx(i-1,1);
  for j=2:i-1
  A(i,j)=dx(j-1,1)+dx(j,1);
  end
end;

A=0.5*A;
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function [D2,Dcenter,Dpos,Dneg]=set_diffmatrices(x)
%Given the mesh x, this function adjusts the difference
% matrices to fit the boundary conditions
%

N=length(x)-1;
dx=x(2:N+1,1)-x(1:N,1);

[D2,Dcenter,Dpos,Dneg]=diff_ops(x);      %<---Define the 1st and 2nd Order
                                         %     Difference operators
Trap_Rule=trap_rulematrix(x);            %<---Define Trap rule matrix

%Adjust D2 to fit the Boundary conditions
D2=[(1/dx(1,1)/dx(1,1))*[-2,2],sparse(1,N-2);D2(:,1:N)];
   %at x=0 No-flux and homogenous at x=1

Dcenter= [sparse(1,N);Dcenter(:,1:N)];
   %at x=0 No-flux
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function [A,B,C,D]=diff_ops(x)
%[A,B,C,D]=DIFF_OPS returns the 2nd order difference operator (A)
% the centered 1st order diffrence operator (B), the upwind
% 1st order difference operators (C) and (D)
% x is the mesh points for these difference operators.
% The difference operators approximate the first and second
% derivatives of the interior points points found in x
%
% For example, if f is a column vector where
% f=[F(x_0),F(x_1),...F(x_i),...,F(x_N)] for i=0,..,N
% Then A*f approximates the second derivative of F at the points
% x_i for i=1,...,N-1

N=length(x)-1;
x=reshape(x,N+1,1);

if sort(x)~=x
```

```
  fprintf(1,'The mesh vector must have the points in accending order! \n');
  A=[]; B=[]; C=[]; D=[];
  return
  end;

dx=x(2:N+1,1)-x(1:N,1);

if min(dx)<1e-9
  fprintf(1,'WARNING!!!! Delta-x less than machine tolerences \n');
  A=[]; B=[]; C=[]; D=[];
  return
  end;

%%%2nd Order Difference Operator
a1=2./dx(1:N-1,1)./(dx(1:N-1,1)+dx(2:N,1));
a2=2./dx(1:N-1,1)./dx(2:N,1);
a3=2./dx(2:N,1)./(dx(1:N-1,1)+dx(2:N,1));
A=spdiags([a1, -a2, a3],[0:2],N-1,N+1);

%%%1st Order Centered Difference Operator
b1=-1./(dx(1:N-1,1)+dx(2:N,1));
b2=-b1;
B=spdiags([b1 b2],[0 2],N-1,N+1);

%%%1st Order a>0 Difference Operator
c1=-1./dx(1:N-1,1);
c2=-c1;
C=spdiags([c1 c2],[0 1],N-1,N+1);

%%%1st Order a<0 Difference Operator
d1=-1./dx(2:N,1);
d2=-d1;
D=spdiags([d1 d2],[1 2],N-1,N+1);
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
```

APPENDIX C

SUBSPACE ITERATION WITH A CAYLEY TRANSFORMATION

```
function [V,D,RES]=eigenvalue(alpha,A,OPTIONS)
%[V,D,RES]=EIGENVALUE(alpha,A,OPTIONS)
%
% computes the eigenvalues of A where
% real(lambda)>-alpha
% A must be an n-by-n matrix.
% OPTIONS(1,1)= the number of eigenvalues returned
% OPTIONS(1,2)= number of iterations
% If OPTIONS is empty then the default values of
% m=min(5,floor(n/2)) and itermax=10 are used
%
% The eigenvalues of A are returned along in
% diagonal matrix D. RES=norm(A*V-V*D,1)
%
%
%
[r,c]=size(A);
m=OPTIONS(1);
rho=OPTIONS(2);
K=10;
TOLflag=0;

if r~=c
  fprintf(1,'WARNING!!!!! A must be a square matrix \n');
  V=[];  D=[]; RES=[];
  return
  end;

if m>r
  fprintf(1,'WARNING!!!!! m Can not exceed the size of the matrix')
  V=[]; D=[]; Res=[];
  return
  end

a1=1;
a2=2*alpha-a1;

I=speye(r,c);
T=I+(a1-a2)*inv(A-a1*I); %<---Generalized Cayley Transform

Q=orth(rand(r,m+1));
[u,ev]=mysubspace(T,K,Q);
RES=norm(T*u(:,1:m)-u(:,1:m)*diag(ev(1:m)),1);

while RES>rho & K<=2^10
  K=2*K;
  Q=orth(rand(r,m+1));
  [u,ev]=mysubspace(T,K,Q);

  RES=norm(T*u(:,1:m)-u(:,1:m)*diag(ev(1:m,1)),1);
  end;
```

```
if K>1000
  TOLflag=1;
  end;

%Sort the eigenvalues with decending real part
evalues=(a2-a1*ev(1:m))./(1-ev(1:m));
[evalues,Index]=complex_sort(evalues);
D=diag(evalues,0);

for j=1:m
  V(:,j)=u(:,Index(j));
  RES(j,1)=norm(A*V(:,j)-V(:,j)*D(j,j),1);
end;

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%FUNCTIONS
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
function [U,ev]=mysubspace(A,k,Q)
% A n-by-n matrix to compute eigenvalues of by iteration
% k index on loop
% Q n-by-m matrix whose columns are initial set of
%   orthogonal vectors
%
% The columns of U are the approximate eigenvectors
% ev is a m-by-1 vector of the eigenvalues
for l=1:k
   V=A*Q;
   Q=orth(V);
   end

 A=full(A);
 [Z,D]=eig((Q')*A*Q);
 [ev,U]=sort_eigenvalues(diag(D),Q*Z);
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
function [lambda,x]=sort_eigenvalues(oldlambda,oldx)
%Sorts eigenvalues by increasing magnitude

[AbsX,Index]=sort(abs(oldlambda));

m=length(oldlambda);
k=0;
for j=m:-1:1
  k=k+1;
  lambda(k,1)=oldlambda(Index(j),1);
  x(:,k)=oldx(:,Index(j));
  end
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
function [Y,I]=complex_sort(y)
%y is a column or row vector. COMPLEX_SORT
% returns the vector y sorted by increasing real
% part. I is the index matrix
```

```
M=length(y);
y=reshape(y,M,1);
Yreal=real(y); Yim=imag(y);
[d1,I]=sort(Yreal);

for m=1:M
  d2(m,1)=Yim(I(m),1);
  end

  Y=d1+i*d2;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

APPENDIX D

BIOFILM MODEL WITH EPS

```
function F=F_eps(t,Y)
%Equations for the biofilm model with EPS
% production. The model parameters are stored in
% a MAT file. The difference matrices and the trapezoid rule
% matrix are stored in a seperate MAT file. The difference
% matrices Dcenter and D2 have been altered in set_numparms.m
% to match the no-flux b.c and homogenous b.c.
% The S soln has been shifted to Shat=S+1; so that
% the S eqn. has a homogenous b.c. at x=1.

load ModelParms Epsilon ke kp
load NumParms x N
load NumParms D2 Dcenter Dpos Dneg
load NumParms Trap_Rule

S=Y(1:N,1);
C=Y(N+1:2*N,1);
f=Y(2*N+1:3*N+1,1);
e=Y(3*N+2:4*N+2,1);
L=Y(4*N+3,1);

Shat=[S+1;1]; Chat=[C;0]; %<---Include the values at x=1
%%%%Compute Velocity term
Rf=CellProdRate(Shat);
Re=epsProdRate(Shat,Chat);

u=Trap_Rule*((Rf+Re).*f-ke*e);
a=u-u(N+1,1).*x;

%%Separate convective term into positive and negative parts
  apos=max(a(2:N,1),0);
  aneg=-max(-a(2:N,1),0);
  LambdaPos=spdiags(apos,0,N-1,N-1); LambdaNeg=spdiags(aneg,0,N-1,N-1);

%%%%Compute the Substrate Usage term
G=SubstrateUsage(Shat,Chat);

%%%%Compute the Cell and and EPS source terms
b1=(Rf.*(1-f)-Re.*f+ke*e).*f;
b2=(Re.*(1-e)-Rf.*e-ke*e).*f;
%b2=(Re.*(1-e)-Rf.*e).*f-ke*(1-e).*e;

%%%%Compute the Substrate (S) and Chemical (C) Eqns.
%%%% On the mesh points x_0,x_1,x_2,...,x_{N-1}
X=spdiags(x(1:N),0,N,N);

dSdt=(1/L/L)*(D2*S)+...
              Epsilon*u(N+1,1)*X*Dcenter*S+...
                -G(1:N,1).*f(1:N,1);

dCdt=(1/L/L)*(D2*C)+...
              Epsilon*u(N+1,1)*X*Dcenter*C+...
```

```
                +kp*f(1:N,1);

%%%%Compute the Cell (f) and EPS (e) Eqns.

    %%Define the eqns at the x=0 boundary
    dfdt(1,1)=b1(1,1);
    dedt(1,1)=b2(1,1);

    %%Define eqns in the interior x_1,x_2,x_3,...,x_{N-1}
    dfdt(2:N,1)=-(LambdaPos*Dpos+LambdaNeg*Dneg)*f+b1(2:N,1);
    dedt(2:N,1)=-(LambdaPos*Dpos+LambdaNeg*Dneg)*e+b2(2:N,1);

    %%Define the eqns at the x=1 boundary
    dfdt(N+1,1)=b1(N+1,1);
    dedt(N+1,1)=b2(N+1,1);

%%%%Compute the L eqn.
  dLdt=L*u(N+1,1);


d=[1/Epsilon*ones(2*N,1);ones(2*N+3,1)];
M=spdiags(d,0,4*N+3,4*N+3);

F=M*[dSdt;dCdt;dfdt;dedt;dLdt];

%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
%FUNCTIONS
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function y=SubstrateUsage(S,C)
%Calculates the substrate usage term

load ModelParms gam1 gam2 ks

R=S./(S+ks);
H=heaviside(C-1);

y=(gam1+gam2*H).*R;

%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function y=CellProdRate(S)

%Calculates the Cell Production Rate

load ModelParms ks Beta

n=length(S);
S=reshape(S,n,1);
```

```
y=(S./(ks+S))-Beta;
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function y=epsProdRate(S,C)

%Calculates the EPS Production Rate

load ModelParms ks kn kg

H=heaviside(C-1);  %<---Heaviside function

y=kn+kg*H.*(S./(ks+S));
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function y=heaviside(x)

%Approximates Heaviside function

h=1e+6;

y=0.5*(tanh(h*x)+1);
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function A=trap_rulematrix(x);
%This file creates the matrix that evaluates the volterra
% integral \int_a^x F(x') dx' at the mesh points defined
% by the vector x
% x=mesh points
%

N=length(x);
x=reshape(x,N,1);
dx=x(2:N,1)-x(1:N-1,1);

A=sparse(N,N);

for i=2:N
  A(i,1)=dx(1,1);
  A(i,i)=dx(i-1,1);
  for j=2:i-1
  A(i,j)=dx(j-1,1)+dx(j,1);
  end
end;

A=0.5*A;
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function [D2,Dcenter,Dpos,Dneg]=set_diffmatrices(x)
%Given the mesh x, this function adjusts the difference
% matrices to fit the boundary conditions
%
```

```
N=length(x)-1;
dx=x(2:N+1,1)-x(1:N,1);

[D2,Dcenter,Dpos,Dneg]=diff_ops(x);      %<---Define the 1st and 2nd Order
                                         %     Difference operators
Trap_Rule=trap_rulematrix(x);            %<---Define Trap rule matrix

%Adjust D2 to fit the Boundary conditions
D2=[(1/dx(1,1)/dx(1,1))*[-2,2],sparse(1,N-2);D2(:,1:N)];
   %at x=0 No-flux and homogenous at x=1

Dcenter= [sparse(1,N);Dcenter(:,1:N)];
   %at x=0 No-flux
%-----------------------------------------------------------------------
%-----------------------------------------------------------------------
function [A,B,C,D]=diff_ops(x)
%[A,B,C,D]=DIFF_OPS returns the 2nd order difference operator (A)
% the centered 1st order diffrence operator (B), the upwind
% 1st order difference operators (C) and (D)
% x is the mesh points for these difference operators.
% The difference operators approximate the first and second
% derivatives of the interior points points found in x
%
% For example, if f is a column vector where
% f=[F(x_0),F(x_1),...F(x_i),...,F(x_N)] for i=1,..,N-1
% Then A*f approximates the second derivative of F at the points
% x_i for i=1,...,N-1

N=length(x)-1;
x=reshape(x,N+1,1);

if sort(x)~=x
  fprintf(1,'The mesh vector must have the points in accending order! \n');
  A=[]; B=[]; C=[]; D=[];
  return
  end;

dx=x(2:N+1,1)-x(1:N,1);

if min(dx)<1e-9
  fprintf(1,'WARNING!!!! Delta-x less than machine tolerences \n');
  A=[]; B=[]; C=[]; D=[];
  return
  end;

%%%2nd Order Difference Operator
a1=2./dx(1:N-1,1)./(dx(1:N-1,1)+dx(2:N,1));
a2=2./dx(1:N-1,1)./dx(2:N,1);
a3=2./dx(2:N,1)./(dx(1:N-1,1)+dx(2:N,1));
A=spdiags([a1, -a2, a3],[0:2],N-1,N+1);

%%%1st Order Centered Difference Operator
```

```
b1=-1./(dx(1:N-1,1)+dx(2:N,1));
b2=-b1;
B=spdiags([b1 b2],[0 2],N-1,N+1);

%%%1st Order a>0 Difference Operator
c1=-1./dx(1:N-1,1);
c2=-c1;
C=spdiags([c1 c2],[0 1],N-1,N+1);

%%%1st Order a<0 Difference Operator
d1=-1./dx(2:N,1);
d2=-d1;
D=spdiags([d1 d2],[1 2],N-1,N+1);
%-------------------------------------------------------------------
%-------------------------------------------------------------------
```

MONTANA STATE UNIVERSITY - BOZEMAN
3 1762 10337345 0