Mathematical Modelling of Surgical Site Infection

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Abstract

Surgical site infections are a common surgical complication and it is a serious socio-economic problem. Supplemental oxygen therapy is one of the therapies suggested that lead to enhanced wound healing. Oxygen is vital in all stages of wound healing and infection processes but the role of oxygen was not included explicitly in existing mathematical models of infection. In this project, several mathematical models incorporating wound healing, wound infection as well as the explicit role of oxygen are developed. In particular, a 5-species coupled nonlinear partial differential equation system with moving internal boundary, describing the spatio-temporal dependence of 5 cellular and chemical species: bacteria, chemoattractant, oxygen, neutrophils and vascular endothelial growth factor (VEGF), is developed and numerical solutions are obtained using finite difference methods. Moreover, methods such as fixed point iteration and boundary immobilisation are also employed to handle the complexity of the model. It is the first model that incorporates wound healing, infection processes and oxygen is also included explicitly. The model captures the biology well and it also predicts some unexpected and highly interesting phenomena which can be experimentally tested in the future.

Keywords Wound healing · Surgical site infection · Supplemental oxygen therapy · Mathematical modelling · Partial differential equations · Numerical solution

1 Introduction

Wound infections are a common surgical complication. They prolong a patient’s stay in hospital and also place a serious financial burden on healthcare providers worldwide; it is reported that wound infections cost the US health care system US$9.0 billion annually [7]. Since bacterial contamination of surgical wounds to some extent is unavoidable, effective therapies must be devised in order to control the bacteria before they are fully established. One such therapy suggested is supplemental oxygen therapy. It involves a patient breathing additional oxygen during and immediately after surgery. It is hypothesised that the additional oxygen leads to a more successful control of the bacterial growth as a result of neutrophils (white blood cell which consumes oxygen and destroys bacteria) exhibiting enhanced performance under additional oxygen [3]. To understand the complex role of oxygen in wound healing and infection processes to a greater extent, mathematical modelling and computer simulations can be used. The remaining of the report is organised as follows. Section 2 includes the relevant biology of the wound healing process. It is kept to a minimum and key species included in the mathematical models developed are emphasised. In Section 3, existing mathematical models are briefly discussed and several new mathematical models are presented, with one of them assuming a fixed wound edge and the other a moving wound edge. Nondimensionalisation and numerical results of the mathematical models are presented in Sections 4 and 5 respectively. Section 6 discusses the results and Section 7 concludes the report.

2 Biology

A normal healing wound is thought to progress through four stages: haemostasis, inflammation, cell proliferation and tissue remodelling [6], although these processes are interconnected and overlapping. During haemostasis, the blood flow is halted while during inflammation, the bacteria are
controlled and important chemical stimulants are released. The proliferation stage involves the production of collagen and formation of new blood vessels (angiogenesis) and the remodelling stage involves the increase in wound strength.

The role of oxygen in wound healing is extremely complex. It interacts with a number of cellular and chemical species. In this report, however, we are interested in the conditions under which bacteria are successfully controlled in a wound healing process instead of the details of the underlying angiogenesis, and hence we restrict ourselves to five most important interacting cellular and chemical species: bacteria, chemoattractant, oxygen, neutrophils and vascular endothelial growth factor (VEGF).

In a contaminated wound, bacteria release a chemoattractant, which attracts the neutrophils from surrounding blood vessels to come into the wound. At the same time, oxygen diffuses into the wound. When the concentration of oxygen in the wound reaches a certain level, the production of VEGF, which is a crucial species involved in wound healing, is initiated. However, as both bacteria and neutrophils consume oxygen, the level of oxygen might not be maintained, and hence production of VEGF and consequently wound healing might stop. Fortunately, neutrophils not only consume oxygen, their major role is to destroy bacteria. Once the bacteria are controlled, oxygen returns to a normal level and wound healing proceeds. The benefit of additional oxygen therapy is also apparent. When additional oxygen is introduced, neutrophils convert to reactive oxygen species and destroy bacteria more efficiently.

3 Mathematical Models

Biological processes can usually be mathematically modelled in one of the following three ways: a continuous reaction-diffusion model, a discrete model or a hybrid of the two. Continuous reaction-diffusion models describe the biological process as a continuum, modelling the concentrations of the cellular or chemical species in a continuum instead of tracking individual cells. As ordinary differential equations (ODEs) or partial differential equations (PDEs) are usually used, such models are easily amenable to mathematical analysis. One disadvantage is that these models can lead to non-physical results such as finite time blow up of cell densities [4]. On the other hand, discrete models describe the behaviour of individual cells and consequently provide more details than continuous models. They can be easily implemented but are, generally speaking, not suitable for mathematical analysis.

The process we are concerned with involves cellular and chemical species with high concentrations and reaction-diffusion models describing the continuum are therefore suitable here. Over the years, quite a large number of different models have been developed. They can be divided into two categories. Some of them model the underlying angiogenesis in great detail, but wound infection is not considered [2,6]. On the other hand, there also exist models that describe the infection process without considering angiogenesis or the role of oxygen [1].

In this project, new models incorporating both wound healing and infection processes are developed. As the number of cellular and chemical species involved in the actual processes is extremely large, it is extremely difficult, if not impossible, to develop a model that includes all species. The proposed
models include bacteria density ($b$), chemoattractant concentration ($c$), oxygen concentration ($w$), neutrophil density ($n$) and VEGF concentration ($v$), all of which are of great importance in the wound healing and infection processes.

For simplicity, a long, thin wound is considered, and hence essentially only one spatial dimension is needed. The spatio-temporal dependence of the species is modelled on $0 \leq x \leq L$, with $x = 0$ being the wound centre and $x = L$ the wound edge and $L$ potentially varies depending on $t$.

### 3.1 Fixed boundary model

For simplicity, a wound with fixed wound edge is considered first, that is, $0 \leq x \leq L$ with $L$ constant. As a result, the underlying angiogenesis or the closing of the wound is not considered and subsequently VEGF is not included in the model. A model involving four coupled nonlinear PDEs is developed.

#### 3.1.1 Partial differential equations (PDEs)

Initially, bacteria are only located at a small region close to the centre of the wound, with bacterial density of $b_i$. Bacteria are assumed to move by diffusion with diffusion coefficient $D_b$. Other terms are logistic growth with growth rate $\lambda_1$ and carrying capacity $b_0$, as well as the killing of bacteria, by a combination of neutrophils and oxygen, with killing rate $\lambda_2$.

$$\frac{\partial b}{\partial t} = D_b \frac{\partial^2 b}{\partial x^2} + \lambda_1 b (b_0 - b) - \lambda_2 wn b$$  \hspace{1cm} (1)

On the other hand, chemoattractant is released by bacteria. It changes due to a combination of diffusion with diffusion coefficient $D_c$, a growth term proportional to the amount of bacteria with growth rate $\lambda_3$, and a natural decay term with decay rate $\lambda_4$.

$$\frac{\partial c}{\partial t} = D_c \frac{\partial^2 c}{\partial x^2} + \lambda_3 b - \lambda_4 c$$  \hspace{1cm} (2)

Oxygen is also subject to diffusion with diffusion coefficient $D_w$, and is consumed by bacteria, neutrophils, as well as its natural decay, with decay rate $\lambda_5$ and scale factors $\lambda_6$ and $\lambda_7$ accounting for the difference in the rates of consumption by bacteria and neutrophils respectively.

$$\frac{\partial w}{\partial t} = D_w \frac{\partial^2 w}{\partial x^2} - \lambda_5 w(1 + \lambda_6 b + \lambda_7 n)$$  \hspace{1cm} (3)

Lastly, neutrophils are subject to diffusion with diffusion coefficient $D_n$, natural decay with decay rate $\lambda_8$, and are attracted by the chemoattractant and undergo chemotaxis up the chemoattractant gradient with chemotactic coefficient $\chi$. 
\[
\frac{\partial n}{\partial t} = D_n \frac{\partial^2 n}{\partial x^2} - \chi_n \frac{\partial c}{\partial x} - \lambda_8 n \quad (4)
\]

All four equations are satisfied in \((x, t) \in [0, L] \times [0, T]\), with \(T\) being the time frame of interest. Diffusion coefficients are placed outside the diffusion terms as they are assumed constant.

### 3.1.2 Initial conditions (ICs) and boundary conditions (BCs)

For the ICs, within the wound, only bacteria is non-zero over a small region close to the centre of the wound initially, all other species are assumed to be zero over the entire wounded domain. And for BCs, at the centre of the wound, zero-flux boundary conditions for all four species are imposed due to symmetry. At the boundary which is adjacent to a major blood vessel (which is not modelled explicitly here), bacteria and chemoattractant are assumed to be zero at all times, whereas oxygen and neutrophils are assumed to have the same level as in the major blood vessel. The ICs and BCs are summarised as follows:

\[
b(x, 0) = b_i H(L_b - x)
\]

where \(H(x)\) is the Heaviside step function. Also,

\[
c(x, 0) = 0 \quad w(x, 0) = 0 \quad n(x, 0) = 0
\]

for all \(x \in [0, L]\) and

\[
\left. \frac{\partial b}{\partial x} \right|_{x=0} = 0 \quad \left. \frac{\partial c}{\partial x} \right|_{x=0} = 0 \quad \left. \frac{\partial w}{\partial x} \right|_{x=0} = 0 \quad \left. \frac{\partial n}{\partial x} \right|_{x=0} = 0
\]

\[
b(L, t) = 0 \quad c(L, t) = 0 \quad w(L, t) = w_0 \quad n(L, t) = n_0
\]

for all \(t \in [0, \infty)\).

### 3.2 Moving boundary model

Since it is unrealistic for a wound to have a fixed wound edge over the course of a healing process, we then move to a model where we allow the wound edge to move. To represent this, we assume that the wound is closing at a rate proportional to the advection of vascular endothelial growth factor (VEGF), a main species in wound healing.

As the wound closes, two separate regions appear: the wounded tissue and the healed tissue and the five species behave slightly differently in the two regions. The two regions can be described by \([0, L(t))\) and \([L(t), L_2]\) with \(L(t)\) being the internal moving boundary and \(L_2\) the boundary of the domain (outer boundary) under consideration.

VEGF is assumed to be subject to diffusion with diffusion coefficient \(D_v\) and natural decay with decay rate \(\lambda_{10}\). Also, the production of VEGF is initiated when oxygen concentration is within
$w_L \leq w \leq w_H$, with production rate $\lambda_9$. That is, VEGF is produced if the oxygen concentration in the wound is not too low, but when the oxygen concentration exceeds a certain level, the body would shut down the production of VEGF as a high concentration of oxygen signals the healthy state of the tissue and no further VEGF is needed.

The governing equation is

$$\frac{\partial v}{\partial t} = D_v \frac{\partial^2 v}{\partial x^2} + \lambda_9 H(w - w_L)H(w_H - w) - \lambda_{10} v$$

(5)

VEGF is assumed to be zero everywhere in the wound initially, zero at the outer boundary at all times, and has zero-flux at the centre of the wound. That is:

$$v(x, 0) = 0$$

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

$$\left. \frac{\partial v}{\partial x} \right|_{x=0} = 0 \quad \text{and} \quad v(x, L(t)) = 0$$

for all $t \in [0, \infty)$.

The rate of change of the wound edge is proportional to advection of VEGF at the (moving) boundary, with rate constant $\mu$. $L(t)$ satisfies

$$\frac{dL}{dt} = -\mu \left. \frac{\partial v}{\partial x} \right|_{x=L(t)}$$

with $L(0) = L_0$.

An mentioned above, the species behave slightly differently in the two regions. As new capillaries are formed in the healed tissue, the diffusion of the species are dominated by the blood flow in that region. As a result, bacteria, chemoattractant, oxygen, neutrophils and VEGF in the newly healed tissue diffuse at a much high rate. That is, the diffusion coefficients now depend on $x$. For simplicity, the diffusion coefficients are assumed to have the following forms:

$$D_b(x) = \begin{cases} D_{b1} & \text{on } 0 \leq x < L(t) \\ D_{b2} & \text{on } L(t) \leq x \leq L_2 \end{cases}$$

$$D_c(x) = \begin{cases} D_{c1} & \text{on } 0 \leq x < L(t) \\ D_{c2} & \text{on } L(t) \leq x \leq L_2 \end{cases}$$

$$D_w(x) = \begin{cases} D_{w1} & \text{on } 0 \leq x < L(t) \\ D_{w2} & \text{on } L(t) \leq x \leq L_2 \end{cases}$$

$$D_n(x) = \begin{cases} D_{n1} & \text{on } 0 \leq x < L(t) \\ D_{n2} & \text{on } L(t) \leq x \leq L_2 \end{cases}$$

$$D_v(x) = \begin{cases} D_{v1} & \text{on } 0 \leq x < L(t) \\ D_{v2} & \text{on } L(t) \leq x \leq L_2 \end{cases}$$
with $D_{c2}$ being a larger real constant than $D_{c1}$. In the healed tissue, there are new capillaries that have grown in from the major blood vessel (at $x = L_2$). When bacteria, chemoattractant, neutrophils, oxygen and VEGF enter these capillaries they will undergo random motion. But as the blood travels around randomly in the new vessels and at a relatively high rate, the diffusion of the species will be dominated by the random motion of the blood and it is reasonable to assume that

$$D_{b2} = D_{c2} = D_{w2} = D_{n2} = D_{v2}.$$ 

As well as the usual initial conditions and boundary conditions imposed at the centre and the outer boundary of the domain ($x = L_2$), interface conditions at the internal moving boundary are also imposed to provide sufficient conditions for the numerical solutions of the PDEs. We demand that the level of each species are equal at the two side of the moving internal boundary as well as their flux terms:

$$\lim_{x \to L^-(t)} b = \lim_{x \to L^+(t)} b \quad \lim_{x \to L^-(t)} -D_b \frac{\partial b}{\partial x} = \lim_{x \to L^+(t)} -D_{b2} \frac{\partial b}{\partial x}$$

$$\lim_{x \to L^-(t)} c = \lim_{x \to L^+(t)} c \quad \lim_{x \to L^-(t)} -D_c \frac{\partial c}{\partial x} = \lim_{x \to L^+(t)} -D_{c2} \frac{\partial c}{\partial x}$$

$$\lim_{x \to L^-(t)} w = \lim_{x \to L^+(t)} w \quad \lim_{x \to L^-(t)} -D_w \frac{\partial w}{\partial x} = \lim_{x \to L^+(t)} -D_{w2} \frac{\partial w}{\partial x}$$

$$\lim_{x \to L^-(t)} n = \lim_{x \to L^+(t)} n \quad \lim_{x \to L^-(t)} -D_n \frac{\partial n}{\partial x} = \lim_{x \to L^+(t)} -D_{n2} \frac{\partial n}{\partial x}$$

$$\lim_{x \to L^-(t)} v = \lim_{x \to L^+(t)} v \quad \lim_{x \to L^-(t)} -D_v \frac{\partial v}{\partial x} = \lim_{x \to L^+(t)} -D_{v2} \frac{\partial v}{\partial x}$$

### 4 Nondimensionalisation

All the independent and dependent variables can be made dimensionless for ease of numerical solutions and analysis. We demonstrate this using the moving boundary model from Section 3.2.
Finally the dimensionless interface conditions are:

\[ b^* = \frac{b}{b_0}, \quad c^* = \frac{c}{D_w}, \quad w^* = \frac{w}{w}, \quad n^* = \frac{n}{n}, \quad v^* = \frac{D_wv}{\lambda_9 L_2} \]

Using the following set of scale factors,

\[ x^* = \frac{x}{L_2}, \quad t^* = \frac{D_w t}{L_2^2} \]

\[ \delta_b = \frac{D_n}{D_w}, \quad \delta_c = \frac{D_c}{D_w}, \quad \delta_n = \frac{D_n}{D_w} \]

\[ k_1 = \frac{\lambda_1 b_0 L_2^2}{D_w}, \quad k_2 = \frac{\lambda_3 \tilde{w} n L_2^2}{D_w}, \quad k_3 = \frac{\lambda_5 b_0 L_2^2}{D_w}, \quad k_4 = \frac{\lambda_4 L_2^2}{D_w} \]

\[ k_5 = \frac{\lambda_5 L_2^2}{D_w}, \quad k_6 = \lambda_0 b_0, \quad k_7 = \lambda_7 \tilde{n}, \quad k_8 = \frac{\lambda_8 L_2^2}{D_w} \]

\[ b_i^* = \frac{b_i}{b_0}, \quad L_i^* = \frac{L_i}{L_2} \]

The dimensionless PDEs are:

\[
\begin{align*}
\frac{\partial b^*}{\partial t^*} &= \delta_b \frac{\partial^2 b^*}{\partial x^*^2} + k_1 b^*(1 - b^*) - k_2 w^* n^* b^* \\
\frac{\partial c^*}{\partial t^*} &= \delta_c \frac{\partial^2 c^*}{\partial x^*^2} + k_3 b^* - k_4 c^* \\
\frac{\partial w^*}{\partial t^*} &= \frac{\partial^2 w^*}{\partial x^*^2} - k_5 w^*(1 + k_6 b^* + k_7 n^*) \\
\frac{\partial n^*}{\partial t^*} &= \delta_n \frac{\partial^2 n^*}{\partial x^*^2} - \frac{\partial}{\partial x^*} \left( \lambda n^* \frac{\partial c^*}{\partial x^*} \right) - k_8 n^* \\
\frac{\partial v^*}{\partial t^*} &= \delta_v \frac{\partial^2 v^*}{\partial x^*^2} + H(w^* - w_i^*) H(w^* - w^*) - k_{10} v^*
\end{align*}
\]

The dimensionless ICs and BCs are:

\[
\begin{align*}
\left. \frac{\partial b^*}{\partial x^*} \right|_{x^* = 0} &= 0 & \left. \frac{\partial c^*}{\partial x^*} \right|_{x^* = 0} &= 0 & \left. \frac{\partial w^*}{\partial x^*} \right|_{x^* = 0} &= 0 & \left. \frac{\partial n^*}{\partial x^*} \right|_{x^* = 0} &= 0 & \left. \frac{\partial v^*}{\partial x^*} \right|_{x^* = 0} &= 0 \\
b^*(1, t^*) &= 0 & c^*(1, t^*) &= 0 & w^*(1, t^*) &= 1 & n^*(1, t^*) &= 1 & v^*(1, t^*) &= 0 \\
b^*(x^*, 0) &= b_i^* H(L_i^* - x^*) & c^*(x^*, 0) &= 0 & w^*(x^*, 0) &= 0 & n^*(x^*, 0) &= 0 & v^*(x^*, 0) &= 0
\end{align*}
\]

Finally the dimensionless interface conditions are:

\[
\begin{align*}
\lim_{x^* \to 1^-} b^* &= \lim_{x^* \to 1^+} b^*, & \lim_{x^* \to 1^-} -D_b \frac{\partial b^*}{\partial x^*} &= \lim_{x^* \to 1^+} -D_{b2} \frac{\partial b^*}{\partial x^*} \\
\lim_{x^* \to 1^-} c^* &= \lim_{x^* \to 1^+} c^*, & \lim_{x^* \to 1^-} -D_c \frac{\partial c^*}{\partial x^*} &= \lim_{x^* \to 1^+} -D_{c2} \frac{\partial c^*}{\partial x^*} \\
\lim_{x^* \to 1^-} w^* &= \lim_{x^* \to 1^+} w^*, & \lim_{x^* \to 1^-} -D_w \frac{\partial w^*}{\partial x^*} &= \lim_{x^* \to 1^+} -D_{w2} \frac{\partial w^*}{\partial x^*}
\end{align*}
\]
\[
\lim_{x^* \to 1^-} n^* = \lim_{x^* \to 1^+} n^* \\
\lim_{x^* \to 1^-} v^* = \lim_{x^* \to 1^+} v^*
\]

5 Numerical results

A finite difference method is employed to solve the PDE systems and the details of the numerical method are included in Section 9.1.

Briefly, independent and dependent variables are discretised, spatial and temporal derivatives are also discretised using the finite difference method based on Taylor series expansion. In particular, temporal derivatives are discretised using the backward difference method, and the spatial derivatives are discretised using a second order centred difference method. Also, a first order upwind scheme is employed for the advection terms. As a consequence of the nonlinearity in the original PDEs, the corresponding algebraic equations obtained are also nonlinear. The traditional way of solving a linear PDE is to express the algebraic equations in a tridiagonal matrix system. Here, to linearise the algebraic equations, fixed point iteration method is used.

Boundary immobilisation method (BIM) is employed to solve the moving boundary problem. Details of this techniques are illustrated through a test problem, which is included in Section 9.2.

Use the scaling

\[
\bar{x} = \begin{cases} 
\frac{x}{L(t)} & \text{on } 0 \leq x < L(t) \\
1 + \frac{x - L(t)}{L_2 - L(t)} & \text{on } L(t) \leq x \leq L_2
\end{cases}
\]

the domain for the scaled spatial variable is then \(0 \leq \bar{x} < 1\) and \(1 \leq \bar{x} \leq 2\) for wounded tissue and healed tissue respectively, i.e. the moving internal boundary problem is transformed to a fixed boundary problem. As above, we can use the finite difference method to solve the PDEs, and due to the nonlinear nature of the PDEs, fixed point iteration is used.

As tridiagonal matrix systems are formed and solved, and due to the high dimensions of the matrix systems, the numerical scheme is quite sensitive. It only produces reasonable numerical solutions when a certain range of parameters are used. As the real parameters coming from biology literature range over a large spectrum of magnitudes, the numerical scheme breaks down quite easily. In particular, matrix inversion is involved in the solution of tridiagonal systems but undesirable singular matrices often result. To overcome this, although not ideal, instead of using parameters from the biology literature, suitable parameters are chosen in such a way that reasonable qualitative behaviours of the biological species are obtained. Figure 1 is the numerical solution of the moving
6 Discussion

As shown in the simulation in Figure 1, initially, there is a small density of bacteria located at the centre of the wound. As time elapses, the bacteria (red) proliferate and diffuse outwards, releasing a chemoattractant (yellow). At the same time, oxygen (green) diffuses into wound and neutrophils come in as well mainly due to chemotaxis. The wound edge (black dashed line) moves slowly as a consequence of the production of VEGF (pink) near the wound edge. When the neutrophils encounter the bacteria, they destroy the bacteria and the infection is controlled. The model captures the underlying biology quite well, although without using real parameters from biology literature.

On the other hand, during the investigation, several interesting phenomena are observed. One particular interesting phenomenon is revealed in Figure 2. As shown, as neutrophils approach the wound centre in response to the build up of chemoattractant, bacteria at the wound centre escape from the neutrophils by diffusing away from the wound centre. Interestingly, neutrophils then move in the same direction as the bacteria as if they are chasing the bacteria. Eventually, neutrophils arrive at where the bacteria are and destroy them successfully. The implication is significant. The spatio-temporal dependence of the species are governed by a set of 5 PDEs which are derived based on simple assumptions. Interesting phenomena like this reconfirm the power of mathematical modelling of biological processes. It predicts biological insights which might or might not be accurate, but certainly provides interesting biological hypotheses which can be tested.

7 Future Work

First of all, a large number of biological parameters are involved in the mathematical models. A literature review of the parameters has been attempted, but due to time constraints of the project, artificial parameters that give reasonable qualitative biological behaviour are used. A more extensive literature review should be conducted to search for real parameters to allow the development of models that capture the quantitative behaviour as well as the qualitative one. On the other hand, symmetry of the surgical wound is assumed throughout. As a result, one spatial dimension is used. The models can be extended to higher dimensions to handle wounds with irregular geometry. Also, in the model developed, a generic bacterial species is considered. In practice, bacteria behave significantly differently and surgical wound infections are not caused by a single species of bacteria. In particular, bacteria can be largely divided into aerobes and anaerobes, both of which are sources of surgical wound infections. Aerobes consume oxygen and thrive in the presence of oxygen, whereas anaerobes cannot use oxygen for growth. The different behaviours bacteria exhibit in response to oxygen can provide useful and important information revealing the optimal strategies to treat surgical site infections with supplemental oxygen.
Fig. 1. Numerical solution of the moving boundary model from Section 3.2. Parameters are chosen to give biologically reasonable qualitative behaviours. Bacteria is shown in red, chemoattractant in yellow, oxygen in green, neutrophils in blue and VEGF in pink. The six panels show time solution at times 0, 3, ..., 15.
Fig. 2. Numerical solution of the moving boundary model from Section 3.2. Parameters are chosen to give biologically reasonable qualitative behaviours. Interesting testable biological insight from the model: when neutrophils reach the bacteria, bacteria escape outwards and neutrophils chase and destroy them.


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9 Appendix

9.1 Numerical method
Instead of using built-in differential equation solvers in numerical packages such as MATLAB, the coupled nonlinear partial differential equations are solved by using our own finite difference method. We demonstrate the method here using mainly the bacteria PDE from the mixed boundary model in Section 3.1.

9.1.1 Discretisation
The PDEs are solved numerically with \((x,t) \in [0,L] \times [0,T]\). We first choose \(n_x\) and \(n_t\), and let \(\Delta x = \frac{L}{n_x}\), \(\Delta t = \frac{T}{n_t}\) such that
\[
x_i = i \Delta x \quad \text{for} \quad i = 0, \ldots, n_x \quad \text{and} \quad t_k = k \Delta t \quad \text{for} \quad k = 0, \ldots, n_t.
\]
\(\Delta x\) and \(\Delta t\) are then the space and time step size respectively. For each \((x_i, t_k)\), let
\[
b^k_i \approx b(x_i, t_k)
\]
and we solve for \(b^k_i\) for each node. Due to the parabolic nature of the equations, backward in time and centred in space standard finite difference approximations for the derivatives based on Taylor series expansions of the function are chosen.

\[
\frac{b^{k+1}_i - b^k_i}{\Delta t} \approx D_b \frac{b^{k+1}_{i+1} - 2b^{k+1}_i + b^{k+1}_{i-1}}{\Delta x^2} + \lambda_1 b^{k+1}_i (b_0^k - b^{k+1}_i) - \lambda_2 w_i^{k+1} n_i^{k+1} b^{k+1}_i
\]

for all \(i = 1, \ldots, n_x - 1, \quad k = 0, \ldots, n_t - 1\).

At the boundaries, we have:
\[
\frac{b^k_1 - b^k_0}{\Delta x} = 0 \quad \text{and} \quad b^k_{n_x} = 0
\]
for all \(k = 1, \ldots, n_t\).
9.1.2 Fixed point iteration

Due to the nonlinear nature of the PDE, the approximate discretised equations are also nonlinear and may be solved using fixed point iteration. Let $b_i^{k(m)}$ be the value of $b_i^k$ at its $m$-th fixed point iteration. We first start with an initial guess $b_i^{k(0)}$ at each node, and $b_i^{k(1)}$ etc are found iteratively. For instance, at the $(m+1)$-th iteration, $b_i^{k(m)}$ has already been found from the last iteration, and the discretised equation can be linearised in the following manner:

$$\frac{b_i^{k+1(m+1)} - b_i^k}{\Delta t} = D_b \frac{b_i^{k+1(m+1)} - 2b_i^{k+1(m+1)} + b_i^{k+1(m+1)}}{\Delta x^2} + \lambda_1 b_i^{k+1(m+1)}(b_0 - b_i^{k+1(m+1)}) - \lambda_2 w_i^{k+1(m)} n_i^{k+1(m)} b_i^{k+1(m+1)}.$$ 

Now the nonlinearity presented in the last two terms are resolved (as $b_i^{k(m)}$ are known) and the resulting linear system can be solved quite easily.

9.2 Moving internal boundary test problem

Although the numerical method is largely the same for both models, the moving internal boundary model is solved by using a boundary immobilisation method. To demonstrate the method, and for simplicity, consider the following test problem instead:

$$0 = D \frac{\partial^2 c}{\partial x^2} - (\lambda_1 + \lambda_2) c \quad \text{on} \quad 0 \leq x \leq L(t)$$

with $\frac{\partial c}{\partial x} \bigg|_{x=0} = 0$ and

$$0 = D \frac{\partial^2 c}{\partial x^2} - \lambda_1 c \quad \text{on} \quad L(t) < x \leq L_2$$

with $c(L_2, t) = c_b$ and interface conditions

$$\lim_{x \to L(t)^-} c = \lim_{x \to L(t)^+} c$$

and

$$\lim_{x \to L(t)^-} \frac{\partial c}{\partial x} = \lim_{x \to L(t)^+} \frac{\partial c}{\partial x}$$

The moving internal boundary $L(t)$ satisfies

$$\frac{dL}{dt} = -k$$

with $L(0) = L_2$. To solve the PDEs numerically, we use a boundary immobilisation method. The principles of boundary immobilisation is to use a time-dependent scaling to immobilise the (internal) boundary. Introduce the new spatial variable $\bar{x}$ with the definition

$$\bar{x} = \begin{cases} 
\frac{x}{L(t)} & \text{on} \quad 0 \leq x \leq L(t) \\
1 + \frac{x - L(t)}{L_2 - L(t)} & \text{on} \quad L(t) \leq x \leq L_2
\end{cases}$$
With this transformation, in terms of this new spatial variable, the PDE system is transformed into one with a fixed boundary and may be solved in the usual way. The transformed PDE system becomes:

\[
0 = D \frac{1}{L^2(t)} \frac{\partial^2 c}{\partial \bar{x}^2} - (\lambda_1 + \lambda_2)c \quad \text{on} \quad 0 \leq \bar{x} < 1
\]

with \( \frac{\partial c}{\partial \bar{x}}|_{\bar{x}=0} = 0 \) and

\[
0 = D \frac{1}{(L_2 - L(t))^2} \frac{\partial^2 c}{\partial \bar{x}^2} - \lambda_1 c \quad \text{on} \quad 1 \leq \bar{x} \leq 2
\]

with \( c(2, t) = c_b \) and interface conditions

\[
\lim_{\bar{x} \to 1^-} c = \lim_{\bar{x} \to 1^+} c
\]

and

\[
\lim_{\bar{x} \to 1^-} \frac{1}{L(t)} \frac{\partial c}{\partial \bar{x}} = \lim_{\bar{x} \to 1^+} \frac{1}{L_2 - L(t)} \frac{\partial c}{\partial \bar{x}}
\]

To solve the PDEs numerically, we introduce the following notations:

\[
c_w(\bar{x}, t) = c(\bar{x}, t) \quad \text{on} \quad 0 \leq \bar{x} < 1
\]

and

\[
c_h(\bar{x}, t) = c(\bar{x}, t) \quad \text{on} \quad 1 \leq \bar{x} \leq 2
\]

Discretising the PDEs in the usual way and letting \( L_k \approx L(t_k) \) and \( c_i^k \approx c(x_i, t_k) \) gives

\[
0 = D \left( \frac{(c_w)_i^{k+1} - 2(c_w)_i^{k} + (c_w)_{i-1}^{k}}{\Delta \bar{x}^2} \right) - (\lambda_1 + \lambda_2)(c_w)_i^{k}, \quad i = 0, \ldots, n_x
\]

with \( (c_w)_0^k = (c_w)_1^k \) and

\[
0 = \frac{D}{(L_2 - L_k)^2} \left( \frac{(c_h)_{i+1}^{k+1} - 2(c_h)_i^{k} + (c_h)_{i-1}^{k}}{\Delta \bar{x}^2} \right) - \lambda_1 (c_h)_i^{k}, \quad i = n_x, \ldots, 2n_x
\]

with \( (c_h)_{2n_x}^k = c_b \).

To implement the interface conditions, we first discretise them:

\[
(c_w)_{n_x}^k = (c_h)_{n_x}^k
\]

\[
\frac{1}{L_k} \frac{(c_w)_{n_x}^k - (c_w)_{n_x-1}^k}{\Delta \bar{x}} = \frac{1}{L_2 - L_k} \frac{(c_h)_{n_x+1}^k - (c_h)_{n_x}^k}{\Delta \bar{x}}
\]

The associated tridiagonal matrix is:
\[
\begin{bmatrix}
1 & -1 & 0 & \cdots & \cdots & \cdots & \cdots & \cdots & 0 \\
\alpha_w & \beta_w & \gamma_w & 0 & 0 & \cdots & \cdots & \cdots & 0 \\
0 & 0 & 0 & \cdots & \cdots & \cdots & \cdots & \cdots & \vdots \\
0 & 0 & \alpha_w & \beta_w & \gamma_w & 0 & \cdots & \cdots & \cdots \\
0 & \cdots & \cdots & 0 & 1 & -1 & 0 & \cdots & \cdots & 0 \\
0 & \cdots & 0 & -\frac{1}{L_k \Delta x} & \frac{1}{L_k \Delta x} & -\frac{(L_2 - L_k) \Delta x}{L_k \Delta x} & \frac{(L_2 - L_k) \Delta x}{(L_2 - L_k) \Delta x} & 0 & \cdots & 0 \\
\vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\
0 & \cdots & \cdots & 0 & \alpha_h & \beta_h & \gamma_h & 0 & \cdots & \cdots \\
0 & \cdots & 0 & \alpha_h & \beta_h & \gamma_h & 0 & \cdots & \cdots & 0 \\
0 & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \vdots & \vdots \\
0 & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & 0 & 1 
\end{bmatrix}
\]

with \(\alpha_w, \beta_w\) and \(\gamma_w\) being the coefficients of \((c_w)_i^{k-1}\), \((c_w)_i^k\) and \((c_w)_i^{k+1}\) respectively, for each internal node. Similarly, \(\alpha_h, \beta_h\) and \(\gamma_h\) are the coefficients of \((c_h)_i^{k-1}\), \((c_h)_i^k\) and \((c_h)_i^{k+1}\) respectively. Due to its linear nature, the system can be solved without using fixed-point or other iterative methods. This test problem is a quasi-steady state problem and hence the simple form of the transformed PDEs. The PDEs in the moving boundary model developed contains time derivative of the quantities, and as a result, advection-like terms appear in the governing equations.

To demonstrate, the time differential operator has the form:

\[
\frac{\partial}{\partial t} = \frac{\partial}{\partial \bar{x}} + \frac{\partial}{\partial \bar{x}} \frac{\partial L(t)}{\partial \bar{x}} = \begin{cases} 
\frac{\partial}{\partial t} - \frac{\bar{x}}{L(t)} \frac{dL}{d\bar{x}} \frac{\partial}{\partial \bar{x}} & \text{on } 0 \leq \bar{x} < 1 \\
\frac{\partial}{\partial t} - \frac{2 - \bar{x}}{L_2 - L(t)} \frac{dL}{d\bar{x}} \frac{\partial}{\partial \bar{x}} & \text{on } 1 \leq \bar{x} \leq 2 
\end{cases}
\]

Advection-like terms appear as a consequence of the new spatial variable being time-dependent. This does not cause too much trouble as the PDE system are solved numerically, with advection terms discretised using first order upwinding.

**References**


