Spatio-temporal dynamics of the cystic fibrosis airway microbiome

**Abstract**

**Introduction**

**Methodology**

**Model equations**

Our model consists of three coupled partial differential equations with state variables corresponding to aerobic bacteria , anaerobic bacteria and oxygen concentration . Each variable is a function of time and location, where we will consider locations in both one- and two-spatial domains. Local dynamics for the bacterial communities are governed by logistic growth with oxygen-dependent growth rates, background death at per capita rates and , and death due to oxygen toxicity at rate for the anaerobic community (1-4). We incorporate spatial dynamics into the model by adding diffusion terms for each variable with corresponding diffusion coefficients , where we assume that .

We use Michaelis-Menten kinetics to model the oxygen-dependent growth rates of the two communities, wherein each community’s growth is determined by a maximum growth rate and half-saturation concentration , and slope factor (5, 6). We assume that the aerobic community grows faster as the oxygen concentration increases and take as the aerobic growth function. The anaerobic community should grow slower as oxygen increases, hence we take the anaerobic growth function as ).

We assume that there is no production or intrinsic decay of oxygen in the interior of the spatial domain so that oxygen dynamics are determined by consumption by aerobic bacteria at rate and diffusion. Then the full model can be written as

This system can be nondimensionalized by introducing the scaled quantities , , , , and and scaled parameters , , , , , and (7, 8). Dropping the \*’s, the scaled system is

where and represent derivates and Laplacian with respect to the scaled time and space variables, respectively. When working in two spatial dimensions we will most often be solving the model on a circular domain, and it will be convenient to use polar coordinates. In that case, we will have , , and where and have their usual meanings for polar coordinates. We solve the model numerically using the pdepe function in MATLAB and the FEniCS package for Python (9-11).

**Boundary and initial conditions**

The domain of our model can be considered as the interior of a mucus plug lodged in an airway with boundaries at the air-mucus interface (12). In one spatial dimension, we can take the domain as the interval and in two dimensions a circle of radius . We assume oxygen is at a steady-state outside of the boundary and diffuses into the domain from the air-mucus interface while bacteria can diffuse throughout the domain but not cross the boundary. We model this using constant Dirichlet boundary conditions (BCs) for oxygen, i.e., in one dimension and in two dimensions. The no-flux BCs on and can be expressed in one dimension as the homogenous Neumann conditions , where is an outward unit normal vector at the boundary. In two dimensions these conditions are . Initial conditions for oxygen are based on predicted oxygen profiles in mucus plugs, with oxygen concentrated near the boundaries and declining toward the interior (12). Initial conditions for the bacterial communities will typically be Gaussian functions.

**Results**

**Simulations of anerobic and anaerobic communities**

**Critical domain**

Our model can be used to predict the minimum diameter a mucus plug must be to allow for anaerobic bacteria to survive in its interior. The critical domain size problem asks how large a habitat must be to support a population, or the size a refuge must be for an animal to survive (13-15). Here, we consider how large a mucus plug must be to have a hypoxic region in which anaerobic bacteria can survive.

Assume oxygen is fixed in space and is distributed according to with corresponding to the air-mucus boundary. Consider the anaerobic population governed by

on the domain . The critical domain size is the minimum length of the domain such that *f* will go extinct if and *f* will have a non-trivial steady state if At steady state, , so the distribution of *f* is the solution of the ODE

where Since we can write , and letting the steady state distribution is the solution of the system

The Jacobian of this system is

and constant solutions at and . At both of these solutions we have

with eigenvalues .

**Analytical**

**1D**

**2D**

**Traveling wave solution**

A traveling wave solution is a function that satisfies a PDE while maintaining its shape in time (16-18).

**Analytical**

**1D**

**Discussion**

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