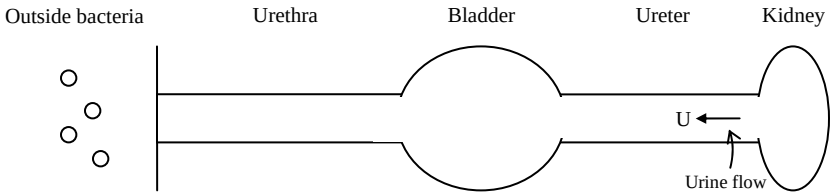
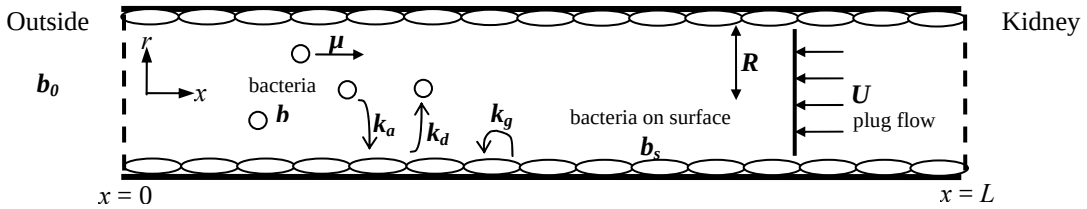
Final Review Session Example Problem

Bacterial Migration during Urinary Tract Infection

12/03/2004



Urinary tract infection (UTI) is a family of inflammatory infections of the urethra, bladder, ureter, or the kidney, caused by exogenous bacteria that migrate through the urinary tract (see above). One of the most severe types of UTI is pyelonephritis – inflammatory infection of the kidney – whose infection process we would like to understand with our modeling efforts. In our approach, we assume that the only defense mechanism is through the flow of urine, which delays the bacterial migration towards the kidney. Further, we will ignore infections of the urethra, bladder, and ureter and regard the urinary tract as a long, cylindrical tube:



Let b be the bacteria in solution/fluid in units of [moles/volume] and b_s be the bacteria on the tract wall in units of [moles/area]. Bacteria in fluid b migrate with migration coefficient μ. They also tend to attach to the wall and dissociate from the wall with reaction rates k_a and k_d, which take into account the impediment of wall attachment and facilitation of detachment through the flow of urine:

$$k_a = \frac{k_{a,0}}{U_0 + U} \qquad k_d = k_{d,0}\left(U_0 + U\right)$$

where U_0 is some basal fluid flow rate, $k_{a,0}$ and $k_{d,0}$ are reaction constants in absence of fluid flow. Once attached to the tract wall, bacteria can grow with a growth rate of k_g. Let's assume that the bacterial migration on the wall is negligible compared to the migration in the fluid at all times. For simplicity, the urine flow is modeled as plug flow.

Our overall goal is to find the bacterial flux into the kidney. Let's start. The following outlines a general strategy to solving this type of problem.

Assumptions

Before starting a model, one should always consider the assumptions given in the problem and assumptions that you can make to simplify your model. Let's face it: we only have a few days to solve this problem and we don't want to spend most of the time doing the math. If you spend too much time to solve an equation, you probably didn't simplify your model enough.

The mathematics of a problem is usually defined by the geometry and the processes that govern the system. The way we drew the model, we currently have a 2-dimensional cylindrical model with convection and diffusion, and a heterogeneous reaction at the boundaries. We can't really do anything about the processes in this model, since they are all key characteristics of the model. But we don't have to keep the cylindrical geometry if we can do it otherwise.

The first and most important assumption is to recognize that $\boldsymbol{R} << \boldsymbol{L}$. This is a reasonable assumption since the urinary tract (including the bladder) is very long and very thin. Then, we can eliminate the radial coordinate axis and make this problem a 1-dimensional linear problem in x. Does this simplification make the model trivial? Not really! Instead of the heterogeneous reaction, we can assume homogeneous bacterial attachment throughout the channel; the urine flow is already independent of r. This approach may make no physical sense; but the resulting insight will be sufficient for the goal of this model (the total flux at $x = L$). So no problems here!

If you decide to stick with the 2-dimensional model, assumptions such as ignoring the radial convection compared to the radial diffusion, quantified as

$$Pe_R = \frac{v_R R}{\mu} << 1,$$

can simplify your understanding of the processes involved in the problem and the governing equations tremendously.

Governing equations

Governing equations tell you what processes depend on which parameters, as well as how many boundary conditions you need. The general governing equations with convection, diffusion and reaction in 1-dimensional, linear coordinates are as follows:

Flux: $$\vec{N}_i = -D_i \frac{\partial c_i}{\partial x} + \vec{v} c_i$$

Conservation of species: $$\frac{\partial c_i}{\partial t} = -\frac{\partial N_i}{\partial x} + R_v$$

Ultimately, we will be interested in the transport of bacteria in fluid, b (since b_s is assumed stationary):

$$\frac{\partial b}{\partial t} = \mu \frac{\partial^2 b}{\partial x^2} + U \frac{\partial b}{\partial x} + R_v$$

Note that U is against the direction of the coordinate axis, so $v = -U$.

Reactions

The homogeneous (or volumetric) reaction term R_v is unknown, so let's figure it out (refer to the sketch). Note that the reaction rate has the units of concentration or density per time.

For species b: $$R_b = \frac{\partial b}{\partial t} = k_d b_s - k_a b$$

For species b_s: $$R_{b_s} = \frac{\partial b_s}{\partial t} = -k_d b_s + k_a b + k_g b_s$$

Then, the governing equation for b becomes

$$\frac{\partial b}{\partial t} = \mu \frac{\partial^2 b}{\partial x^2} + U \frac{\partial b}{\partial x} + k_d b_s - k_a b$$

Uh, oh. The equation is both dependent on b and b_s! What do we do now? Another assumption must be made. Here, a time scale comparison might be useful.

We are interested in the bacterial flux into the kidney…our time scale of interest is the bacterial migration process in the fluid, which occurs much slower than the bacterial attachment process. So, we can assume the bacterial density on the wall to be essentially constant, leading to the quasi-steady-state approximation of b_s.

$$\frac{\partial b_s}{\partial t} = -k_d b_s + k_a b + k_g b_s \approx 0 \Rightarrow b_s = \frac{k_a}{k_d - k_g} b$$

Then, our governing equation for b becomes

$$\frac{\partial b}{\partial t} = \mu \frac{\partial^2 b}{\partial x^2} + U \frac{\partial b}{\partial x} + \left(\frac{k_g k_a}{k_d - k_g} \right) b$$

Initial/Boundary conditions

This is the one of the most difficult part of the problem, since there is really no right answer! We don't know yet if we should assume steady-state, so we will write down the initial condition. We set our initial condition to be right before the bacterial invasion into the urinary tract.

I.C. $$b(x, t = 0) = 0$$

For simplicity, outside of the tract, we shall assume a constant bacterial concentration b_0 at all times (This ensures that there is also constant influx of bacteria into the tract at all times).

B.C. #1 $$b(x = 0, t) = b_0$$

The right boundary condition is much more obscure. Here are three possibilities:

1. $\left.\frac{\partial b}{\partial x}\right|_{x=L} = c$ (the flux at $x = L$ is constant)

2. $\left.\frac{\partial b}{\partial x}\right|_{x=L} = 0$ (there is no change in bacterial density at $x = L$)

3. $b(x = L, t) = 0$ (no bacteria at $x = L$)

All three choices make physical sense. Which one is the *best* one? The first possibility introduces another variable c. We have enough variables, we don't need one more. Also, remember what our goal of this problem is…to find the flux at $x = L$. If it is set equal to a constant, it defeats the purpose. For that reason, second possibility is also eliminated.
The third possibility is the best one by elimination; when the bacteria reach the boundary, they are immediately absorbed by the kidney. Note that the B.C. does not constrain the flux at $x = L$.

Non-dimensionalizing the equation

Normalizing the equation gives you a lot of advantages. Not only do clean up your equation, you will be able to identify key parameters, such as the Damköhler or Peclet numbers, which will tell you what terms can be neglected simplifying the problem tremendously. Also, if you are asked for certain time constants (such as diffusion time scales, convection time scales), you can deduce them by normalizing the equations.

Let

$$c = \frac{b}{b_0} \qquad \xi = \frac{x}{L} \qquad \tau = \frac{U}{L^2}t$$

(you can set $\tau = t/t^*$ and find t^* after substituting in…it works out to be $t^* = L^2/U$)

Then,

$$\frac{\partial c}{\partial \tau} = \frac{\partial^2 c}{\partial \xi^2} + Pe\frac{\partial c}{\partial \xi} + \alpha c$$

$$\text{where } Pe = \frac{UL}{\mu} \text{ and } \alpha = \frac{L^2}{\mu}\left(\frac{k_g k_a}{k_d - k_g}\right)$$

$$\text{with } c(\xi, 0) = 0,\ c(0, \tau) = 1,\ c(1, \tau) = 0$$

Note that the ratio Pe/α will determine which term is dominating your problem. If Pe is large, clearly, convection is dominating your problem; if α is large, reaction is dominating your problem.

Steady-state solution

Our parameter of interest is *U*, the variable we can vary over a wide range (I shall not comment further). Since we are interested in the flux of bacteria into the kidney in terms of *U*, we may not even need the transient solution. Always justify for yourself if we can assume steady-state since the problem might not always tell you. (Btw, it is not difficult to solve the transient problem)

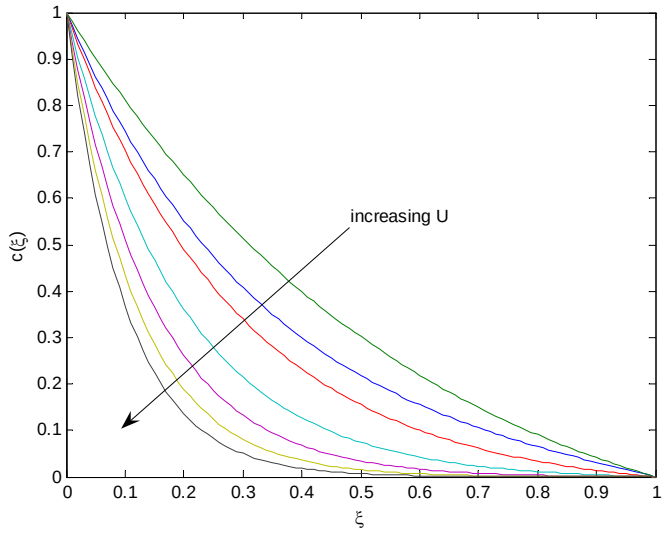
At steady-state:

$$c(\zeta) = \frac{e^{\lambda_1} e^{\lambda_2 \xi} - e^{\lambda_2} e^{\lambda_1 \xi}}{e^{\lambda_1} - e^{\lambda_2}} \text{ with } \lambda_{1,2} = -\frac{Pe}{2} \pm \sqrt{\left(\frac{Pe}{2}\right)^2 - \alpha}$$

and the bacterial flux to the kidney can be determined by

$$N_b = -\frac{\mu b_0}{L} \left.\frac{\partial c}{\partial \xi}\right|_{\xi=1} - U b_0 c(\xi = 1)$$

The graph of c is given below.



It is up to you now to interpret the data.

Manipulations of the model

Let's say cranberry juice causes $k_a \rightarrow 0$. Then we would be left with the following equation.

$$0 = \frac{\partial^2 c}{\partial \xi^2} + Pe \frac{\partial c}{\partial \xi}$$

The result is a decrease in the bacterial flux to the kidney and a lower probability of UTI.