BENG 221 Mathematical Methods in Bioengineering

Fall 2012

Midterm

NAME: SOLUTIONS

- Open book, open notes.
- 3 hour limit, in one sitting.
- Return hardcopy before closing by 11am, Thursday November 1, 2012.
- No communication on the midterm anytime before closing other than with instructor and TAs.
- No computers or internet during the midterm, except for access to posted class materials and contact with instructor and TAs.

Problem 1 (30 points): The rise and fall of a single bacterial population $x(t)$ and a single nutrient $y(t)$ in a petri dish over time t are modeled by the following set of ordinary differential equations:

$$\begin{aligned} \frac{d}{dt}x(t) &= g\,x(t) + c\,y(t) \\ \frac{d}{dt}y(t) &= -d\,y(t) - e\,x(t) + q(t) \end{aligned}$$

where g is the intrinsic bacterial growth rate, c is the nutrition induced bacterial growth rate, d is the intrinsic nutrient decay rate, e is the nutrient consumption rate, and $q(t)$ is the spontaneous nutrient source generation over time. At time $t = 0$ the nutrient is fully depleted and the bacterial population is at an initial level x_0.

1. (5 points): Write the initial conditions. Are these sufficient to solve for a unique solution?

$$\begin{cases} x(0) = x_0 \\ y(0) = 0 \end{cases}$$

YES! (two conditions for two state variables)

2. (10 points): Find the Laplace transform $\tilde{x}(s)$ of the solution for the bacterial population $x(t)$ from the initial conditions. Under what condition on the parameters g, c, d, and e is the bacteria-nutrient system stable?

$$\begin{cases} s\,\tilde{x}(s) - x_0 = g\,\tilde{x}(s) + c\,\tilde{y}(s) \\ s\,\tilde{y}(s) - 0 = -d\,\tilde{y}(s) - e\,\tilde{x}(s) + \tilde{q}(s) \end{cases}$$

Eliminate $\tilde{y}$:

$$(s+d)\,\tilde{y} = -e\,\tilde{x} + \tilde{q}$$

$$(s-g)\,\tilde{x} = x_0 + c\,\tilde{y} = x_0 + c\,\frac{-e\tilde{x} + \tilde{q}}{s+d}$$

$$((s-g)(s+d) + ce)\,\tilde{x} = (s+d)\,x_0 + c\,\tilde{q}$$

$$\left(s^2 + (d-g)s + (ce - gd) \right) \tilde{x}(s) = (s+d)x_0 + c\tilde{q}$$

or
$$\tilde{x}(s) = \frac{(s+d)x_0 + c\tilde{q}(s)}{s^2 + as + b}$$

where
$$\begin{cases} a = d - g \\ b = ce - gd \end{cases}$$

The system is stable when $a > 0$ and $b > 0$ or

$$\begin{cases} d > g \\ ce > gd \end{cases}$$

(OK for the values given in Part 4.)

3. (5 points): Find the Fourier transfer function $H(j\omega)$ of the system with source input $q(t)$ and bacterial output $x(t)$.

The Fourier transform is the Laplace transform for $s = j\omega$, without I.C.

$$\Rightarrow X(j\omega) = \frac{c\,Q(j\omega)}{-\omega^2 + a j\omega + b} \quad \text{or} \quad H(j\omega) = \frac{X(j\omega)}{Q(j\omega)} = \frac{c}{-\omega^2 + a j\omega + b}$$

with

$a = d - g$

$b = ce - gd$

4. (10 points): Find the solution $x(t)$ from initial conditions and zero source $q(t) = 0$ for the following values of the constants: $g = 0$, $c = 1\ s^{-1}$, $d = 2\ s^{-1}$, and $e = 1\ s^{-1}$. Make sure to indicate the units.

$$a = d - g = 2 \quad (s^{-1})$$

$$b = ce - gd = 1 \quad (s^{-1})$$

$$\tilde{q} = 0$$

$$\Rightarrow \tilde{x}(s) = \frac{s+2}{s^2 + 2s + 1} x_0 = \left(\frac{1}{s+1} + \frac{1}{(s+1)^2} \right) x_0$$

Laplace tables: $x(t) = \left(e^{-t} + t e^{-t} \right) x_0$

$$= (1 + t)\, e^{-t}\, x_0$$

where t is in units seconds (s).

Problem 2 (30 points): Consider the following homogeneous partial differential equation with homogeneous boundary conditions:

$$\frac{\partial}{\partial t}u(x,t) = D\,\frac{\partial^2}{\partial x^2}u(x,t) \qquad \text{with} \qquad \begin{cases} u(x,0) &= g(x) \\ u(0,t) &= 0 \\ \frac{\partial}{\partial x}u(L,t) &= 0 \end{cases} \tag{1}$$

This partial differential equation is approximated using finite differences as:

$$u(x,t+\Delta t) = u(x,t) + \eta\,(u(x+\Delta x,t) - 2u(x,t) + u(x-\Delta x,t)) \tag{2}$$

or, equivalently, evaluated on the grid as sequences $u_i[n] = u(i\Delta x, n\Delta t)$ for integer values of i and n:

$$u_i[n+1] = u_i[n] + \eta\,(u_{i+1}[n] - 2u_i[n] + u_{i-1}[n]), \qquad i = 1,\ldots N-1; n = 0,\ldots\infty. \tag{3}$$

1. (10 points): For length $L = 1\ m$, diffusivity $D = 0.01\ m^2/s$ and update constant $\eta = 0.1$, find the grid constants Δx and Δt such that your finite difference approximation resolves at least 100 points ($i = 0,\ldots N = 100$) over the $[0, L]$ interval.

$$L = N\Delta x \Rightarrow \Delta x = \frac{L}{N} = \frac{1\ m}{100} = 0.01\ m = 1\ cm$$

$$\eta = D\frac{\Delta t}{\Delta x^2} \Rightarrow \Delta t = \eta\frac{\Delta x^2}{D} = \frac{\eta L^2}{N^2 D} = \frac{0.1 \cdot 1 m^2}{10{,}000 \cdot 0.01 \frac{m^2}{s}} = 0.001\ s$$

$$= 1\ ms$$

2. (5 points): Write the finite difference approximation to the initial conditions at $t = 0$, in terms of $u_i[0]$, for given $g_i = g(i\Delta x)$.

$$u_i[0] = g_i, \qquad i = 1, 2, \ldots, N-1\ (, N)$$

3. (5 points): Write the finite difference approximation to the boundary condition at $x = 0$, in terms of $u_0[n]$.

$$u_0[n] = 0, \qquad n = 0, 1, \ldots \infty$$

4. (10 points): Write the finite difference approximation to the boundary condition at $x = L$, in terms of $u_N[n]$ and its neighbors on the grid.

$$u(L, t+\Delta t) = u(L,t) + \frac{\Delta t}{\Delta x}\left(-D \frac{u(L,t) - u(L-\Delta x, t)}{\Delta x} + D \frac{\partial}{\partial x} u(L,t) \right)$$

INFLUX from the left

OUTFLUX to the right $= 0$ because of B.C.

$$\Rightarrow u_N[n+1] = u_N[n] + \eta \left(u_{N-1}[n] - u_N[n] \right),$$

$$n = 0, 1, \ldots \infty$$

5. **BONUS** (10 extra points, no partial credit–*only pursue this if you have time left after completing everything else*): Write the finite difference approximations to the non-homogeneous partial differential equation with non-homogeneous boundary conditions:

$$\frac{\partial}{\partial t}u(x,t) = D\,\frac{\partial^2}{\partial x^2}u(x,t) + q(x,t) \qquad \text{with} \qquad \begin{cases} u(x,0) &= g(x) \\ u(0,t) &= h(t) \\ \frac{\partial}{\partial x}u(L,t) &= f(t) \end{cases} \tag{4}$$

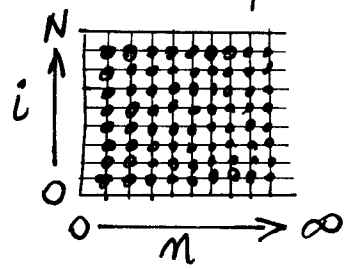
in terms of $u_i[n]$ for given g_i as defined above, and given $q_i[n] = q(i\Delta x, n\Delta t)$, $h_0[n] = h(n\Delta t)$, and $f_0[n] = f(n\Delta t)$. Indicate the range of valid indices i and n for each equation including initial/boundary conditions.

or: $n+1$

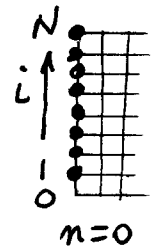
- PDE: $u_i[n+1] = u_i[n] + \eta\left(u_{i+1}[n] - 2u_i[n] + u_{i-1}[n]\right) + \Delta t\, q_i[n]$,

  $i = 1, 2, \ldots N-1$

  $n = 0, 1, \ldots \infty$

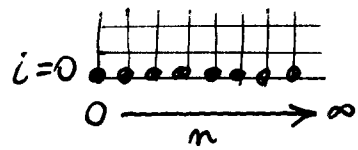


- I.C. @ $t=0$: $u_i[0] = g_i$, $i = 1, 2, \ldots, N$



- B.C. @ $x=0$ (VALUE): $u_0[n] = h_0[n]$,

  $n = 0, 1, \ldots \infty$

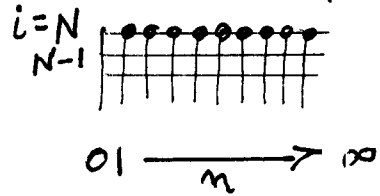


or: $n+1$

- B.C @ $x = L$ (FLUX):

  $u_N[n+1] = u_N[n] + \eta\left(u_{N-1}[n] - u_N[n] + \Delta x\, f_0[n]\right) + \Delta t\, q_N[n]$,

  $n = 0, 1, \ldots \infty$



Problem 3 (40 points): Oxygen diffuses in a slice preparation of brain tissue of thickness $L = 1\ mm$ with diffusivity $D = 1mm^2\,/\,s$. The slice is perfused with oxygenated solution generating constant and equal (opposing) influx of oxygen $\Phi_{ox} = 0.1\ \mu mol\,/\,mm^2 s$ on both sides, into the tissue. Oxygen is consumed by the tissue at a constant rate $R = 0.2\ \mu mol\,/\,mm^3 s$. At initial time $t = t_0$, the oxygen concentration is $u_0 = 1\ \mu mol\,/\,mm^3$ uniform inside the tissue.

1. (10 points): Write down the partial differential equation with initial and boundary conditions for oxygen concentration $u(x,t)$ in the tissue. Verify consistency in the units.

PDE :
$$\frac{\partial}{\partial t} u(x,t) = D \frac{\partial^2}{\partial x^2} u(x,t) - R$$
$$\frac{1}{s} \quad \frac{\mu mol}{mm^3} = \frac{mm^2}{s} \frac{1}{mm^2} \frac{\mu mol}{mm^3} = \frac{\mu mol}{mm^3\, s} \qquad \text{OK!}$$

I.C. @ t_0 :
$$u(x,t_0) = u_0$$
$$\frac{\mu mol}{mm^3} = \frac{\mu mol}{mm^3} \qquad (\text{OK})$$

FLUX B.C. @ 0 :
$$-D \frac{\partial}{\partial x} u(0,t) = \Phi_{ox}$$
$$\frac{mm^2}{s} \frac{1}{mm} \frac{\mu mol}{mm^3} = \frac{\mu mol}{mm^2\, s} \qquad \text{OK!}$$

FLUX B.C. @ L :
$$-D \frac{\partial}{\partial x} u(L,t) = -\Phi_{ox}$$

(SAME UNITS)

2. (10 points): Solve a modified version of this problem, for the homogeneous partial differential equation with homogeneous boundary conditions and initial conditions $u(x, t_0) = \delta(x - x_0)$. What does this solution represent, and why is finding this solution useful in solving the original problem?

$$\frac{\partial u}{\partial t} = D \frac{\partial^2 u}{\partial x^2} \quad \text{with} \quad \begin{cases} u(x, t_0) = \delta(x - x_0) \\ \frac{\partial u}{\partial x}(0, t) = 0 \\ \frac{\partial u}{\partial x}(L, t) = 0 \end{cases}$$

Solution is the GREEN'S FUNCTION $G(x, t; x_0, t_0)$

Separation of variables:

$$u(x,t) = \sum_{n=0}^{\infty} A_n \cos\left(\frac{\pi n}{L} x\right) e^{-\left(\frac{\pi n}{L}\right)^2 D t}$$

I.C @ t_0:

$$u(x, t_0) = \delta(x - x_0) = \sum_{n=0}^{\infty} A_n \cos\left(\frac{\pi n}{L} x\right) e^{-\left(\frac{\pi n}{L}\right)^2 D t_0}$$

Orthogonality in the basis functions $\cos\left(\frac{\pi n}{L} x\right)$:

$$\begin{cases} A_0 = \frac{1}{L} \\ A_n = \frac{2}{L} \cos\left(\frac{\pi n}{L} x_0\right) e^{+\left(\frac{\pi n}{L}\right)^2 D t_0}, \quad n = 1, 2, \ldots \infty \end{cases}$$

$$\Rightarrow G(x, t; x_0, t_0) = \frac{1}{L} + \frac{2}{L} \sum_{n=1}^{\infty} \cos\left(\frac{\pi n}{L} x_0\right) \cos\left(\frac{\pi n}{L} x\right) e^{-D\left(\frac{\pi n}{L}\right)^2 (t - t_0)}$$

Why? See 4. (OK to use the Green's table)

3. (10 points): Find a particular (steady-state) solution $u_p(x)$ to the original problem (but disregarding the initial conditions) that does not depend on time. Find the conditions on the parameters L, D, Φ_{ox}, and R for such solution to exist. Is the solution unique? Why is finding this solution useful in solving the original problem?

$$D \frac{d^2}{dx^2} u_p(x) - R = 0 \quad \text{with} \quad \begin{cases} -D \frac{d}{dx} u_p(0) = \Phi_{ox} \\ -D \frac{d}{dx} u_p(L) = -\Phi_{ox} \end{cases}$$

Integrating twice:

$$u_p(x) = \frac{R}{2D} x^2 + ax + b$$ where a and b are integration constants.

B.C. on flux $-D \frac{d}{dx} u_p = -Rx - Da$:

@ $x = 0$: $-Da = \Phi_{ox} \Rightarrow a = -\frac{\Phi_{ox}}{D}$

@ $x = L$: $-RL - Da = -\Phi_{ox} \Rightarrow RL = 2\Phi_{ox} \Rightarrow$

A solution can only exist if $\Phi_{ox} = \frac{1}{2} R.L$

ok for the values given: $0.1 \frac{\mu mol}{mm^2 s} = \frac{1}{2} \, 0.2 \frac{\mu mol}{mm^3 s} \cdot 1 \, mm$

The solution is NOT unique because b is left undetermined.

$$u_p(x) = \frac{R}{2D} x^2 - \frac{\Phi_{ox}}{D} x + b, \quad \text{for arbitrary } b$$

$$= \frac{R}{2D} x^2 - \frac{RL}{2D} x + b$$

$$= -\frac{R}{2D} x(L-x) + b$$

Why? See 4.

4. (10 points): Now find the full solution $u(x,t)$ to the original problem from the initial conditions.

Poison's tooth method with $\underset{(3.)}{u_p(x)}$ and $\underset{(2.)}{G(x,t;x_0,t_0)}$:

$$u(x,t) = u_p(x) + u_H(x,t) \quad \text{where:}$$

$$\frac{\partial}{\partial t} u_H(x,t) = D \frac{\partial^2}{\partial x^2} u_H(x,t) \quad \text{and} \quad \begin{cases} u_H(x,t_0) = u_0 - u_p(x) \\ \frac{\partial u_H}{\partial x}(0,t) = 0 \\ \frac{\partial u_H}{\partial x}(L,t) = 0 \end{cases}$$

$$\text{or} \quad u_H(x,t) = \int_0^L \underbrace{G(x,t;x_0,t_0)}_{\text{GREEN'S @ } t_0} \underbrace{(u_0 - u_p(x_0))}_{u_H \text{ I.C. @ } t_0} dx_0$$

$$\text{where} \quad u_0 - u_p(x_0) = u_0 - b + \frac{R}{2D} x_0 (L - x_0)$$

$$\text{Equivalently:} \quad u_H(x,t) = \sum_{n=0}^{\infty} A_n \cos\left(\frac{\pi n}{L} x\right) e^{-\left(\frac{\pi n}{L}\right)^2 D (t-t_0)}$$

$$\text{where} \quad A_0 = \frac{1}{L} \int_0^L \left(u_0 - b + \frac{R}{2D} x_0 (L - x_0)\right) dx_0$$

$$A_n = \frac{2}{L} \int_0^L \left(u_0 - b + \frac{R}{2D} x_0 (L - x_0)\right) \cos\left(\frac{\pi n}{L} x_0\right) dx_0,$$

$$n = 1, 2, \ldots \infty$$

$$A_0 = \frac{1}{L}\int_0^L \left(u_0 - b + \frac{R}{2D}\, x_0(L-x_0)\right) dx_0$$

$$= u_0 - b + \frac{R}{2DL}\underbrace{\int_0^L x_0(L-x_0)\,dx_0}_{\left[\frac{x_0^2 L}{2} - \frac{x_0^3}{3}\right]_0^L = \left(\frac{1}{2}-\frac{1}{3}\right)L^3 = \frac{1}{6}L^3}$$

$$= u_0 - b + \frac{RL^2}{12D} \qquad \left(\frac{\frac{\mu mol}{mm^3 \cancel{s}} \cdot \cancel{mm^2}}{\frac{\cancel{mm^2}}{\cancel{s}}} = \frac{\mu mol}{mm^3} \text{ ok!} \right)$$

$$A_n = \frac{2}{L}\int_0^L \left(u_0 - b + \frac{R}{2D}\, x_0(L-x_0)\right)\cos\left(\frac{\pi n}{L}x_0\right) dx_0$$

$$= \frac{2}{L}\,\frac{L}{\pi n}\left(\underbrace{\left[\left(u_0 - b + \frac{R}{2D}\, x_0(L-x_0)\right)\sin\left(\frac{\pi n}{L}x_0\right)\right]_0^L}_{=0} - \int_0^L \frac{R}{2D}(L-2x_0)\sin\left(\frac{\pi n}{L}x_0\right)dx_0\right)$$

$$= \frac{R}{DL}\left(\frac{L}{\pi n}\right)^2\left(\left[(L-2x_0)\cos\left(\frac{\pi n}{L}x_0\right)\right]_0^L - \underbrace{\int_0^L (-2)\cos\left(\frac{\pi n}{L}x_0\right)dx_0}_{=0}\right)$$

$$= \frac{RL}{D\pi^2 n^2}\left(L + L(-1)^n\right) = \begin{cases} \frac{2RL^2}{\pi^2 D}\frac{1}{n^2} & \text{for } n = \text{even} \\ 0 & \text{for } n = \text{odd} \end{cases}$$

$$\Rightarrow u(x,t) = u_p(x) + u_H(x,t) =$$

$$-\frac{R}{2D}x_0(L-x_0) + \cancel{b} + u_0 - \cancel{b} + \frac{RL^2}{12D}$$

$$+ \sum_{\substack{n=2,4,6,\ldots \\ (n \text{ even})}}^{\infty} \frac{2RL^2}{\pi^2 D}\cdot\frac{1}{n^2}\cos\left(\frac{\pi n}{L}x\right)\cdot e^{-\left(\frac{\pi n}{L}\right)^2 D(t-t_0)}$$