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:

\[
\begin{align*}
\frac{dx(t)}{dt} &= g \cdot x(t) + c \cdot y(t) \\
\frac{dy(t)}{dt} &= -d \cdot y(t) - e \cdot x(t) + q(t)
\end{align*}
\]

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?

\[
\begin{align*}
x(0) &= x_0 \\
y(0) &= 0
\end{align*}
\]

\text{YES! (two conditions for two state variables)}

2. (10 points): Find the Laplace transform \( \bar{x}(s) \) 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?

\[
\begin{align*}
\{ & \\
S \bar{x}(s) - x_0 &= g \bar{x}(s) + c \bar{y}(s) \\
S \bar{y}(s) - 0 &= -d \bar{y}(s) - e \bar{x}(s) + q(s)
\end{align*}
\]

Eliminate \( \bar{y} \):

\[
\begin{align*}
(S + d) \bar{y} &= -e \bar{x} + \bar{q} \\
(S - g) \bar{x} &= x_0 + c \bar{y} = x_0 + c \bar{y} = x_0 + c \frac{-e \bar{x} + \bar{q}}{s + d}
\end{align*}
\]

\[
((S - g)(S + d) + ce) \bar{x} = (S + d) x_0 + c \bar{q}
\]
\[(s^2 + (d-g)s + (ce-gd)) \tilde{x}(s) = (s+d)x_0 + c\tilde{q}(s)\]

\[\alpha \tilde{x}(s) = \frac{(s+d)x_0 + c\tilde{q}(s)}{s^2 + \alpha s + \beta}\]

where

\[\alpha = d-g\]
\[\beta = ce-gd\]

The system is stable when \(\alpha > 0\) and \(\beta > 0\) or

\[\begin{align*}
&\alpha > g \\
&ce > gd
\end{align*}\]

(OK for the values given in Part 4.)
3. (5 points): Find the Fourier transfer function $H(jw)$ of the system with source input $q(t)$ and bacterial output $x(t)$.

The Fourier transform is the Laplace transform for $s = jw$, without I.C.

$$X(jw) = \frac{C \, \Omega(jw)}{\omega^2 + ajw + b} \quad \text{or} \quad H(jw) = \frac{X(jw)}{\Omega(jw)} = \frac{C}{\omega^2 + ajw + b} \quad \text{with} \quad a = d - g \quad \text{and} \quad \Omega = ce^{-gd}$$

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.

$$a = d - g = 2 \, (s^{-1})$$
$$b = ce^{-gd} = 1 \, (s^{-1})$$
$$\hat{q} = 0$$

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

Laplace table: \[ X(s) = (e^{-t} + t e^{-t}) x_0 \]

\[ = (1 + t) e^{-t} x_0 \]

where $t$ is in units seconds ($s$).
Problem 2 (30 points): Consider the following homogeneous partial differential equation with homogeneous boundary conditions:

\[ \frac{\partial}{\partial t} u(x, t) = D \frac{\partial^2}{\partial x^2} u(x, t) \quad \text{with} \quad \begin{cases} u(x, 0) = g(x) \\ u(0, t) = 0 \\ \frac{\partial}{\partial x} u(L, t) = 0 \end{cases} \]  \hspace{1cm} (1)

This partial differential equation is approximated using finite differences as:

\[ u(x, t + \Delta t) = u(x, t) + \eta \left( u(x + \Delta x, t) - 2u(x, t) + u(x - \Delta x, t) \right) \]  \hspace{1cm} (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 \( n \):

\[ u_{i}[n+1] = u_{i}[n] + \eta \left( u_{i+1}[n] - 2u_{i}[n] + u_{i-1}[n] \right), \quad i = 1, \ldots N - 1; n = 0, \ldots \infty. \]  \hspace{1cm} (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 \( \Delta x \) and \( \Delta t \) such that your finite difference approximation resolves at least 100 points (\( i = 0, \ldots N = 100 \)) over the \([0, L]\) interval.

\[ L = N \Delta x \quad \Rightarrow \quad \Delta x = \frac{L}{N} = \frac{1 \text{ m}}{100} = 0.01 \text{ m} = 1 \text{ cm} \]

\[ \eta = D \frac{\Delta t}{\Delta x^2} \quad \Rightarrow \quad \Delta t = \eta \frac{\Delta x^2}{D} = \frac{\eta L^2}{N^2 D} = \frac{0.1 \text{ m}^2}{10,000 \cdot 0.01 \text{ m}^2/s} = 0.01 \text{ s} \approx 1 \text{ ms} \]

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

\[ u_i[0] = g_i, \quad i = 1, 2, \ldots, N-1 (, N) \]
3. (5 points): Write the finite difference approximation to the boundary condition at $x = 0$, in terms of $u_0[n]$.

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

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.

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

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

\[
\frac{\partial}{\partial t} u(x, t) = D \frac{\partial^2}{\partial x^2} u(x, t) + q(x, t) \quad \text{with} \quad \begin{cases} 
    u(x, 0) = g(x) \\
    u(0, t) = h(t) \\
    \frac{\partial u}{\partial x}(L, t) = f(t)
\end{cases}
\]

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

- **PDE:** \( u_i[n+1] = u_i[n] + \eta (u_{i+1}[n] - 2u_i[n] + u_{i-1}[n]) + \Delta t q_i[n] \), \( i = 1, 2, \ldots, N-1 \)
  \( m = 0, 1, \ldots, \infty \)

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

- **B.C. @ x=0 (VALUE):** \( u_0[n] = h_0[n] \), \( i = 0 \)
  \( n = 0, 1, \ldots, \infty \)

- **B.C. @ x=L (FLUX):** \( u_N[n+1] = u_N[n] + \eta (u_{N-1}[n] - u_N[n]) + \Delta x f_0[n] + \Delta t q_i[n] \), \( i = N-1 \)
  \( n = 0, 1, \ldots, \infty \)
Problem 3  (40 points): Oxygen diffuses in a slice preparation of brain tissue of thickness $L = 1 \text{ mm}$ with diffusivity $D = 1 \text{mm}^2 / \text{s}$. The slice is perfused with oxygenated solution generating constant and equal (opposing) influx of oxygen $\Phi_{ox} = 0.1 \text{ \mu mol / mm}^2 \text{s}$ on both sides, into the tissue. Oxygen is consumed by the tissue at a constant rate $R = 0.2 \text{ \mu mol / mm}^3 \text{s}$. At initial time $t = t_0$, the oxygen concentration is $u_0 = 1 \text{ \mu mol / mm}^3$ 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.

\[
\text{PDE} : \quad \frac{\partial}{\partial t} u(x,t) = D \frac{\partial^2}{\partial x^2} u(x,t) - R
\]

\[
\frac{1}{S} \quad \frac{\text{\mu mol}}{\text{mm}^3} = \frac{1}{S} \quad \frac{\text{\mu mol}}{\text{mm}^2} = \frac{\text{\mu mol}}{\text{mm}^3 \text{S}} \quad \text{OK!}
\]

\[
\text{I.C. @ t_0} : \quad u(x, t_0) = u_0
\]

\[
\frac{\text{\mu mol}}{\text{mm}^3} = \frac{\text{\mu mol}}{\text{mm}^3} \quad \text{(OK)}
\]

\[
\text{FLUX B.C. @ 0} : \quad -D \frac{\partial}{\partial x} u(0, t) = \Phi_{ox}
\]

\[
\frac{1}{S} \quad \frac{1}{\text{mm}} \quad \frac{\text{\mu mol}}{\text{mm}^3} = \frac{\text{\mu mol}}{\text{mm}^2 \text{S}} \quad \text{OK!}
\]

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

\[
\text{(SAME UNITS)}
\]
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?

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

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 basic functions $\cos \left( \frac{\pi n}{L} x \right)$:

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

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

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 \( L, D, \Phi_{ox} \), and \( R \) for such solution to exist. Is the solution unique? Why is finding this solution useful in solving the original problem?

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

Integrating twice:

\[
M_p(x) = \frac{R}{2D} x^2 + ax + b \quad \text{where} \ a \ \text{and} \ b \ \text{are integration constants}.
\]

B.C. on flux:

\[
\begin{align*}
\text{at} \ x = 0: & \quad -Da = \Phi_{ox} \quad \Rightarrow \quad a = -\frac{\Phi_{ox}}{D} \\
\text{at} \ x = L: & \quad -RL - Da = -\Phi_{ox} \quad \Rightarrow \quad RL = 2\Phi_{ox} \quad \Rightarrow
\end{align*}
\]

A solution can only exist if \( \Phi_{ox} = \frac{1}{2} RL \).

Ok for the values given: \( 0.1 \ \mu\text{mol} / \text{mm}^2 \text{s} = \frac{1}{2} \ 0.2 \ \mu\text{mol} / \text{mm}^3 \text{s} \cdot 1 \ \text{mm} \)

The solution is NOT unique because \( b \) is left undetermined.

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

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

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

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

Poisson's tenth method with \( M_p(x) \) and \( G(x,t) \): \( (3.0) \)

\[
m(x,t) = M_p(x) + M_H(x,t)
\]

where:

\[
\frac{\partial}{\partial t} M_H(x,t) = \frac{D}{\alpha^2} \frac{\partial^2}{\partial x^2} M_H(x,t) \quad \text{and} \quad \begin{cases} M_H(x,0) = M_0 - M_p(x) \\ \frac{\partial M_H}{\partial x}(0,t) = 0 \\ \frac{\partial M_H}{\partial x}(L,t) = 0 \end{cases}
\]

or \( M_H(x,t) = \int_{0}^{L} G(x,t; x_0, t) (M_0 - M_p(x_0)) \, dx_0 \)

\( \text{Green's @ t} \quad \text{m_H I.C. @ t} \)

where \( M_0 - M_p(x_0) = M_0 - b_0 + \frac{R}{2D} x_0 (L-x_0) \)

Equivalently:

\[
M_H(x,t) = \sum_{n=0}^{\infty} A_n \cos\left(\frac{n\pi}{L} x\right) e^{-\left(\frac{n\pi}{L}\right)^2 D(t-t_0)}
\]

where \( A_0 = \frac{1}{L} \int_{0}^{L} (M_0 - b_0 + \frac{R}{2D} x_0 (L-x_0)) \, dx_0 \)

\[
A_n = \frac{2}{L} \int_{0}^{L} (M_0 - b_0 + \frac{R}{2D} x_0 (L-x_0)) \cos\left(\frac{n\pi}{L} x_0\right) \, dx_0,
\]

\( n = 1, 2, \ldots, \infty \)
\[ A_0 = \frac{1}{L} \int_0^L \left( \mu_0 - b + \frac{R}{2D} \ x_0 (L-x_0) \right) \, dx_0 \]

\[ = \mu_0 - b + \frac{R}{2DL} \int_0^L x_0 (L-x_0) \, dx_0 \]

\[ \left[ \frac{x_0^2 L}{2} - \frac{x_0^3}{3} \right]_0^L = \left( \frac{1}{2} - \frac{1}{3} \right) L^3 = \frac{1}{6} L^3 \]

\[ = \mu_0 - b + \frac{RL^2}{12D} \left( \frac{\mu_0}{mm^3/s^2} \cdot \frac{m^2}{mm^2} = \frac{\mu_0}{mm^3} \right) \]

\[ A_n = \frac{2}{L} \int_0^L \left( \mu_0 - b + \frac{R}{2D} \ x_0 (L-x_0) \right) \cos \left( \frac{\pi m x_0}{L} \right) \, dx_0 \]

\[ = \frac{2}{L} \frac{L}{\pi m} \left[ \left( \mu_0 - b + \frac{R}{2D} \ x_0 (L-x_0) \right) \sin \left( \frac{\pi m}{L} x_0 \right) \right]_0^L \]

\[ - \int_0^L \frac{R}{2D} \ (L - 2x_0) \sin \left( \frac{\pi m x_0}{L} \right) \, dx_0 \]

\[ = \frac{R}{DL} \left( \frac{L}{\pi m} \right)^2 \left[ \left( L - 2x_0 \right) \cos \left( \frac{\pi m x_0}{L} \right) \right]_0^L - \int_0^L \left( -2 \right) \cos \left( \frac{\pi m x_0}{L} \right) \, dx_0 \]

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

\[ \Rightarrow \mu(x,t) = \mu_p(x) + \mu_H(x,t) = \]

\[ - \frac{R}{2D} \ x_0 (L-x_0) + b + \mu_0 - b + \frac{RL^2}{12D} \]

\[ + \sum_{n=2,4,6,\ldots}^{\infty} \frac{2RL^2}{\pi^2 D m^2} \cos \left( \frac{\pi m}{L} x \right) e^{-\left( \frac{\pi m}{L} \right)^2 D (t-t_0)} \]