NeuBeh 532/PBIO 532: Quantitative methods in neuroscience

Organization (or …)

• 1st week
  - Tues lecture on math
  - Thurs nitty-gritty (make sure you look at tutorial prior to Thurs!)
• 2nd week
  - Tues/Thurs journal clubs run by you (sign up for topics)

Topics

• weeks 1/2: Differential equations
• weeks 3/4: Linear systems and Fourier analysis
• weeks 5/6: Stochastic processes and spike generation
• weeks 7/8: Linear algebra and color space
• weeks 9/10: Principle components analysis and dimensional reduction

Course website
http://rieke-server.physiol.washington.edu/~lab/People/Fred/Classes/545/545.html
NeuBeh 532/PBIO 532: Quantitative methods in neuroscience

Computers and Matlab
- PBIO computer room (next door)
- PBIO laptops (check out)
- Personal machines (how many?)
- Matlab tutorial (web site)

*formulate a plan on this*

Grades
- Project (due last week of class, 50%)
- Paper presentation during journal club (30%)
- Participation in class discussions (10%)
- Tutorial problem sets (10%)
Objectives this week:

• relate box-and-arrow models to DEQs
• basic properties of simple DEQs and intuition for their behavior
• techniques for solving DEQs: analytical and numerical

Next week:

• applications of DEQs in neuroscience
Biophysical models of phototransduction

\[ \frac{dG}{dt} = S - PG \]
Hodgkin-Huxley model and neural coding

\[ I = C_m \frac{dV}{dt} + g_K n^4 (V - V_K) + g_{Na} m^3 h (V - V_{Na}) + g_{leak} (V - V_{leak}) \]

\[ \frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m \]
Physical models for neural computation

\[ m \frac{d^2 x(t)}{dt^2} = F(t) - kx(t) \]
Example 1: Integrator

\[ \frac{dx(t)}{dt} = \alpha y(t) \]

- vestibuloocular system: \( y(t) \) angular velocity readout from vestibular system, \( x(t) \) control signal for eye muscles
- catalysis: \( y(t) \) catalyst, \( x(t) \) substrate (e.g. G-protein cascades/phototransduction)
\[ y(t < 0) = 0 \quad \rightarrow \quad \frac{dx(t)}{dt} = 0 \quad \rightarrow \quad x(t < 0) = A \]

\[ y(0 < t < T) = 1 \quad \rightarrow \quad \frac{dx(t)}{dt} = \alpha \quad \rightarrow \quad x(0 < t < T) = A + \alpha t \]

\[ y(t > T) = 0 \quad \rightarrow \quad \frac{dx(t)}{dt} = 0 \quad \rightarrow \quad x(t > T) = A + \alpha T \]
Example 2: Leaky (more realistic) integrator

\[
\frac{dx(t)}{dt} = \alpha y(t) - \beta x(t)
\]

- steady-state behavior: \( x_{ss} = y_{ss} \)
- dynamics: controlled by \( \beta \)
assume initial condition $x(0) = 0$

\[
y(t < T) = 0 \quad \rightarrow \quad \frac{dx(t)}{dt} = 0 \quad \rightarrow \quad x(t < 0) = 0
\]

\[
y(0 < t < T) = 1 \quad \rightarrow \quad \frac{dx(t)}{dt} = \alpha - \beta x(t) \quad \rightarrow \quad x(0 < t < T) = \frac{\alpha}{\beta} (1 - e^{-\beta t})
\]

\[
y(t > T) = 0 \quad \rightarrow \quad \frac{dx(t)}{dt} = -\beta x(t) \quad \rightarrow \quad x(t > T) = \frac{\alpha}{\beta} (e^{-\beta T} - 1)e^{-\beta t}
\]
Two DEQs worth remembering the solutions to

Exponential (e.g. first-order decay):

\[ \frac{dx(t)}{dt} = -\beta x(t) \rightarrow x(t) = Ae^{-\beta t} \]

Sinusoid (e.g. mass on spring):

\[ \frac{d^2x(t)}{dt^2} = -\alpha x(t) \rightarrow x(t) = A \sin(t\sqrt{\alpha} + \phi) \]
Example 2: Feedback

\[
\frac{d x(t)}{d t} = \frac{\alpha y(t)}{(1 + \gamma x(t))^n} - \beta x(t)
\]

- Recurrent connections and fine tuning, e.g. stability in vestibuloocular system
- Speed kinetics, e.g. phototransduction
- Amplification, e.g. auditory system and outer hair cells

In general cannot solve DEQs for feedback analytically - hence numerical methods.
TAYLOR SERIES APPROXIMATION

\[
f(x_1) = f(x_0) + (x_1-x_0) \frac{df}{dx} \bigg|_{x_0} + (x_1-x_0)^2 \frac{d^2f}{dx^2} \bigg|_{x_0} + \ldots
\]

KEY:

\[f(x_0) \gg (x_1-x_0) \frac{df}{dx} \bigg|_{x_0}\]

i.e. expand about small parameter
\[ \frac{dx(t)}{dt} = \frac{\alpha y(t)}{(1 + \gamma x(t))^n} - \beta x(t) \]
Example 3: Rate-limiting step and its importance in coupled systems

Why important?
- Identify of step that controls kinetics
- Likely site of adaptation when adaptation alters kinetics

\[
\begin{align*}
\frac{dr(t)}{dt} &= -\sigma r(t) \\
\frac{dp(t)}{dt} &= \gamma r(t) - \phi p(t)
\end{align*}
\]
\[
\frac{dr(t)}{dt} = -\sigma r(t)
\]
\[
\frac{dp(t)}{dt} = \gamma r(t) - \phi p(t)
\]

Output identical when $\square$ and $\square$ swapped
\[
\frac{dr(t)}{dt} = -\sigma r(t)
\]
\[
\frac{dp(t)}{dt} = \gamma r(t) - \phi p(t)
\]

- Alteration of non-rate limiting step changes amplitude, not kinetics.
- Alteration of rate limiting step changes both.
Feedback in a multiple step model

\[
\begin{align*}
\frac{dr(t)}{dt} & = -\sigma[p(t)] r(t) \\
\frac{dp(t)}{dt} & = \gamma r(t) - \phi p(t) \\
\sigma[p(t)] & = \sigma_0 p^h(t)
\end{align*}
\]

Introduction of feedback can give rise to ‘emergent’ time scale
\[
\begin{align*}
\frac{dr(t)}{dt} &= -\sigma[p(t)]r(t) \\
\frac{dp(t)}{dt} &= \gamma r(t) - \phi p(t) \\
\sigma[p(t)] &= \sigma_0 p^h(t)
\end{align*}
\]
What I hope you have learned:

- characterization of steady-state behavior and identification of important time constants can give intuition to how system behaves

- analytical/numerical approaches to solving DEQs

- some simple examples and their behavior