Sex, Drugs, & Sleep:
Revisiting Rhythms, Exponentials, & Sigmoidal Functions

IMPLEMENTING BEST PRACTICES
IN COURSES BELOW CALCULUS

FOUNTAIN VALLEY, CA
6 September 2008

Mike Martin
Johnson County Community College
staff.jccc.edu/mmartin

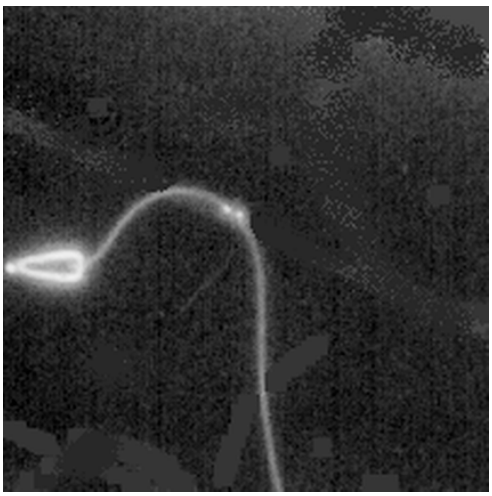
JCCC Johnson County Community College 12345 College Blvd Overland Park KS 66210 913-469-8500

McGill

KU KU

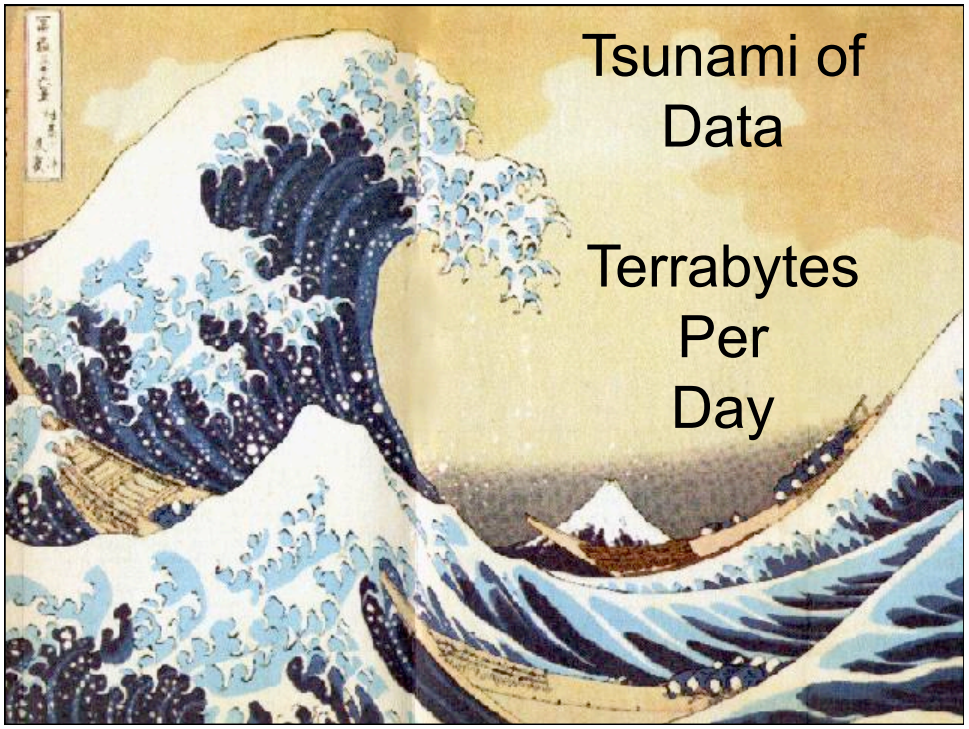
Motility & Reproduction

- Rhythms are ubiquitous in nature
- Sexual reproduction produces generations of offspring
- Observations, more generally, are discrete in nature
- Can we revisit, reframe sequences in courses ?
  - Difference Equations
  - Modeling



http://www.cco.caltech.edu/~brokawc/Demo1/BeadExpt.html
courtesy of Charles Brokaw, Cal Tech

1


Tsunami of Data
Terrabytes Per Day

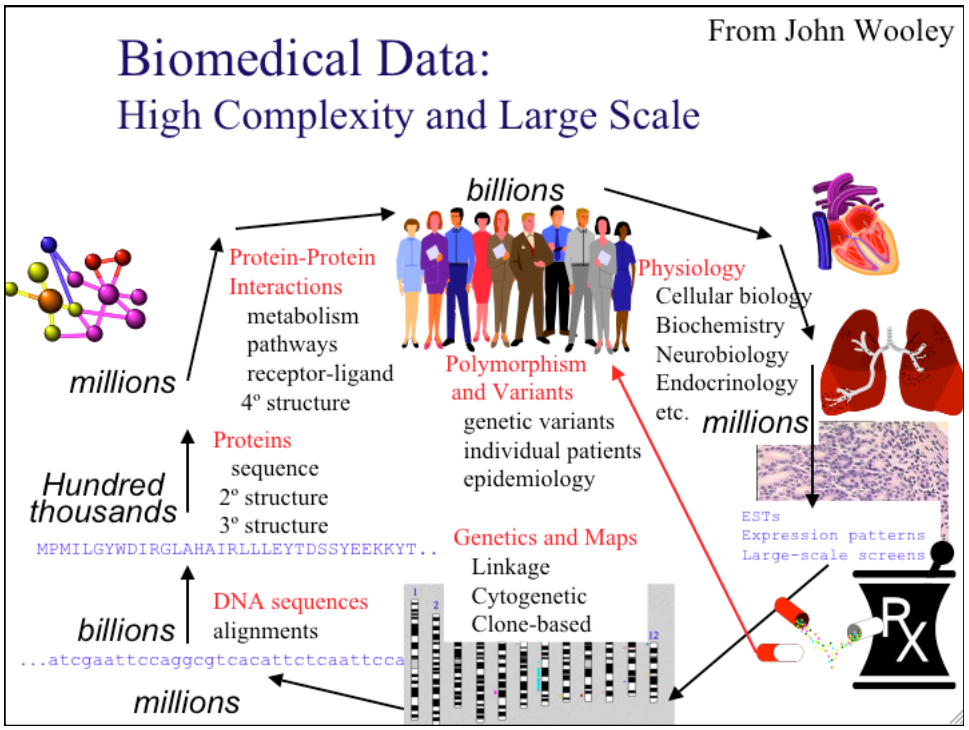
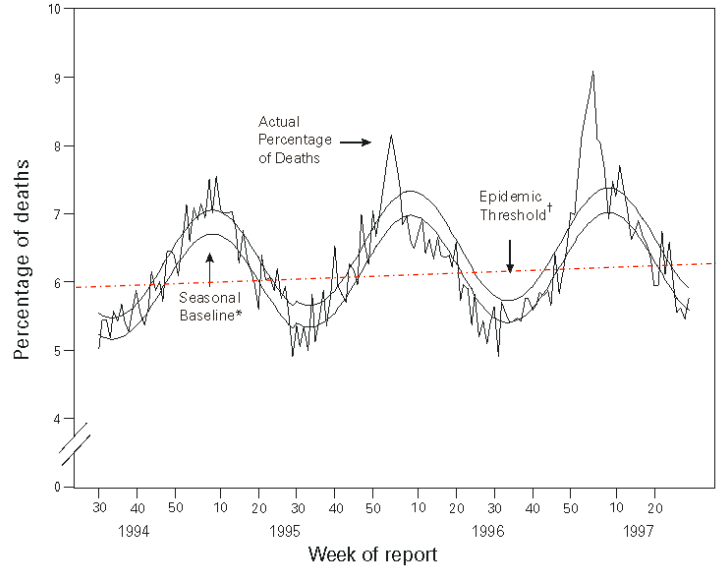

From John Wooley
Biomedical Data:
High Complexity and Large Scale
billions
millions
Protein-Protein Interactions
metabolism
pathways
receptor-ligand
4° structure
Physiology
Cellular biology
Biochemistry
Neurobiology
Endocrinology
etc.
millions
Polymorphism and Variants
genetic variants
individual patients
epidemiology
Hundred thousands
Proteins
sequence
2° structure
3° structure
MPMILGYWDIRGLAHAIRLLLEYTDSSYEEKKYT..
ESTs
Expression patterns
Large-scale screens
Genetics and Maps
Linkage
Cytogenetic
Clone-based
billions
DNA sequences
alignments
...atcgaattccaggcgtcacattctcaattcca
millions
Rx

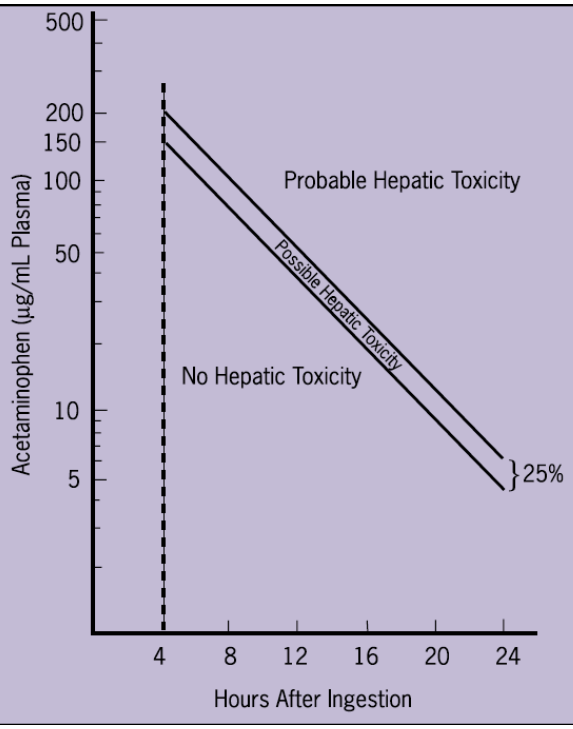
FIGURE 6. Percentage of deaths attributed to pneumonia or influenza as reported from the 121 cities mortality reporting system during the 1994–95, 1995–96, and 1996–97 seasons — United States



*The seasonal baseline is the expected percentage of deaths attributed to pneumonia and influenza during each week.

†The epidemic threshold is 1.645 standard deviations above the seasonal baseline of deaths attributed to pneumonia and influenza.

4

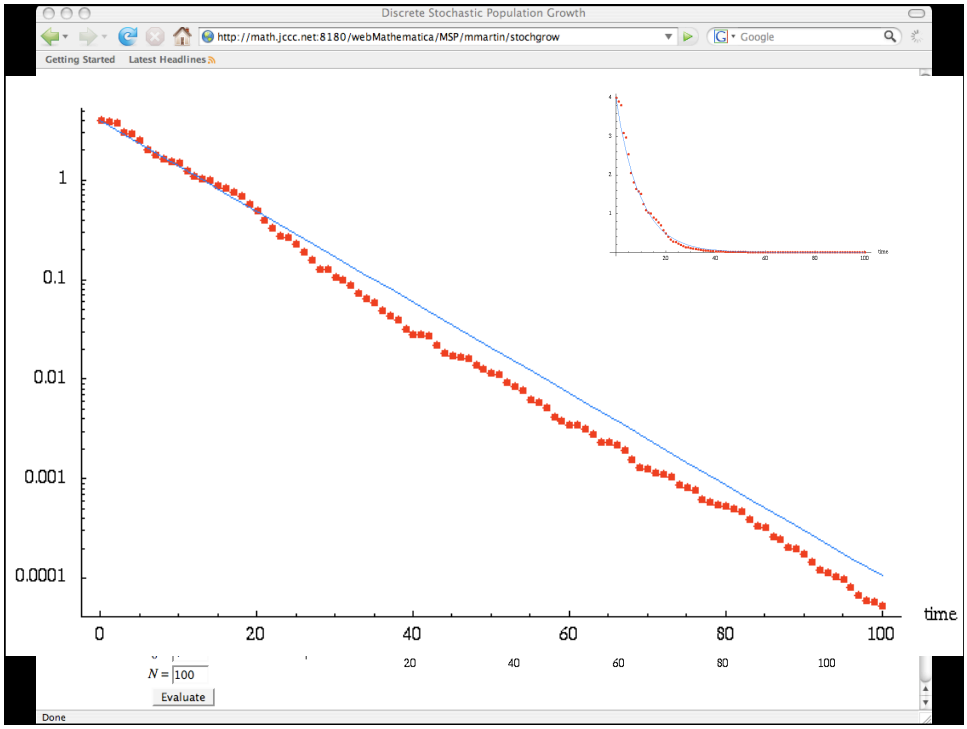


Treatment

- Goals
  - Symptoms
  - Disease
- Delivery
  - Continuous
  - Discrete

SOURCE: Pharma Literature Accompanying Product

5

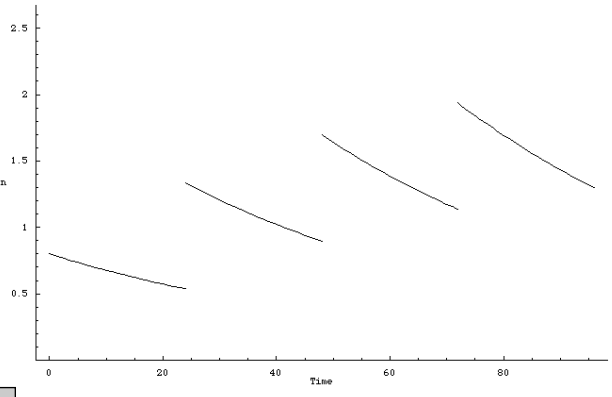


Drug Delivery:
Uniform Dosing with Exponential Decay

$$\frac{dc}{dt} = -\frac{c}{\tau}$$

with a dosing of c_o
on each interval of length T
for a total of N intervals

$$c(t) = c_o e^{-t/\tau}$$



How can you interpret τ?
What does the value of τ mean relative to that of T?
Overcoming thresholds

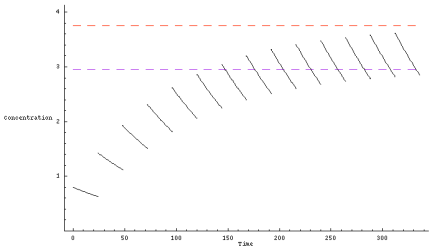
Exploration

7

Limiting Behavior

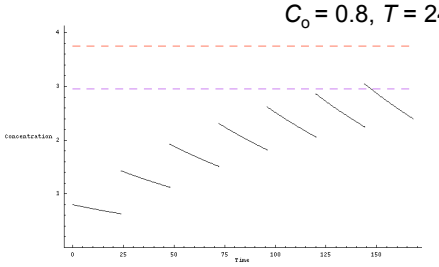
Both upper and lower concentration amounts for a given dosing period reach a limit over time:

Geometric Sequences & Series
Stable Equilibria

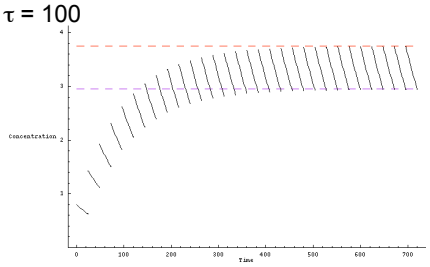


$N = 14$

$C_o = 0.8,\ T = 24,\ \tau = 100$



$N = 7$



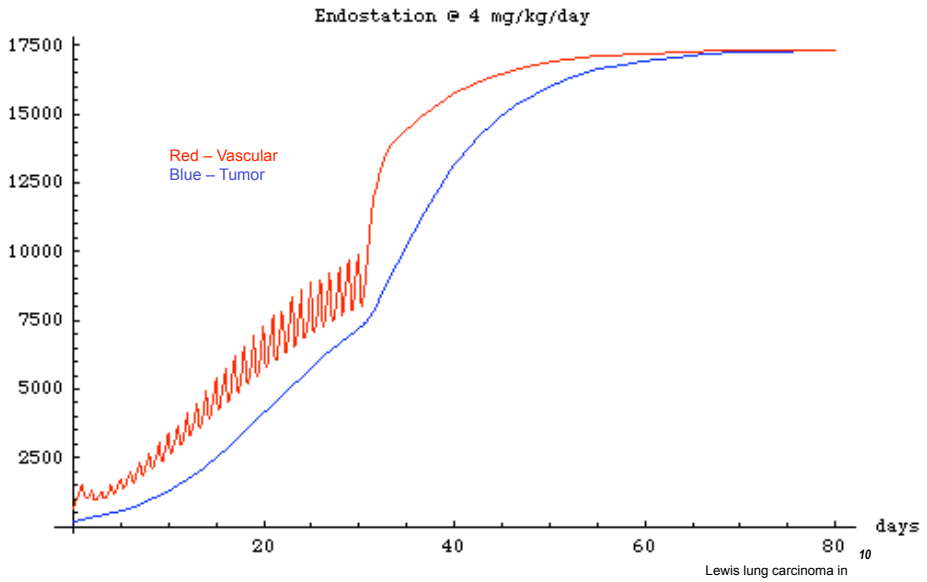
$N = 30$

Observations

- Hybrid Model: Continuous & Discrete
- Limiting Behavior: Anticipated & Verified by Geometric Series
- Complex Network of Interconnected Systems
  - Absorbed in Gut
  - Mixes in the Blood Stream
  - Tissues & Organs via Beating Heart

9

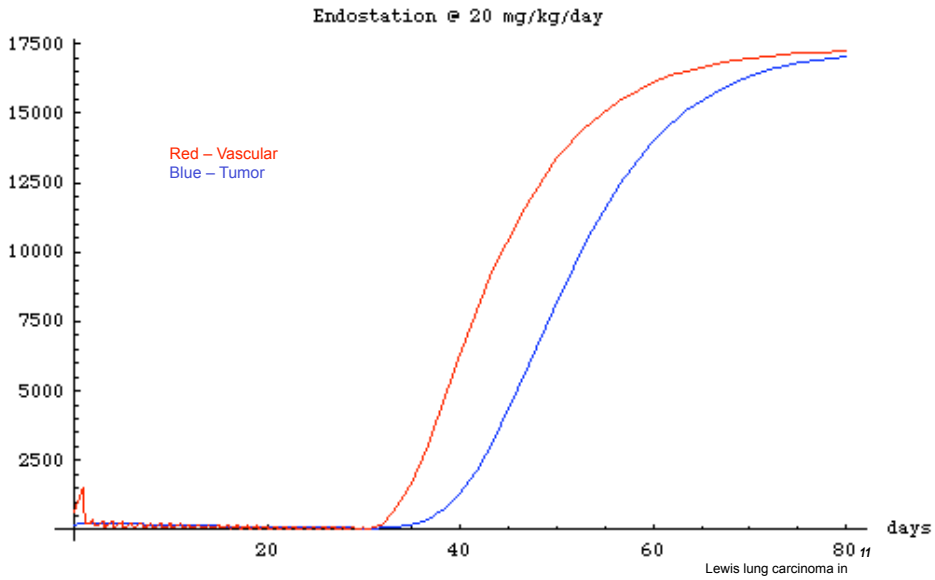
Antiangiogenics: Endostatin



Lewis lung carcinoma in Mice [Hahnfeldt et al, 1999]:

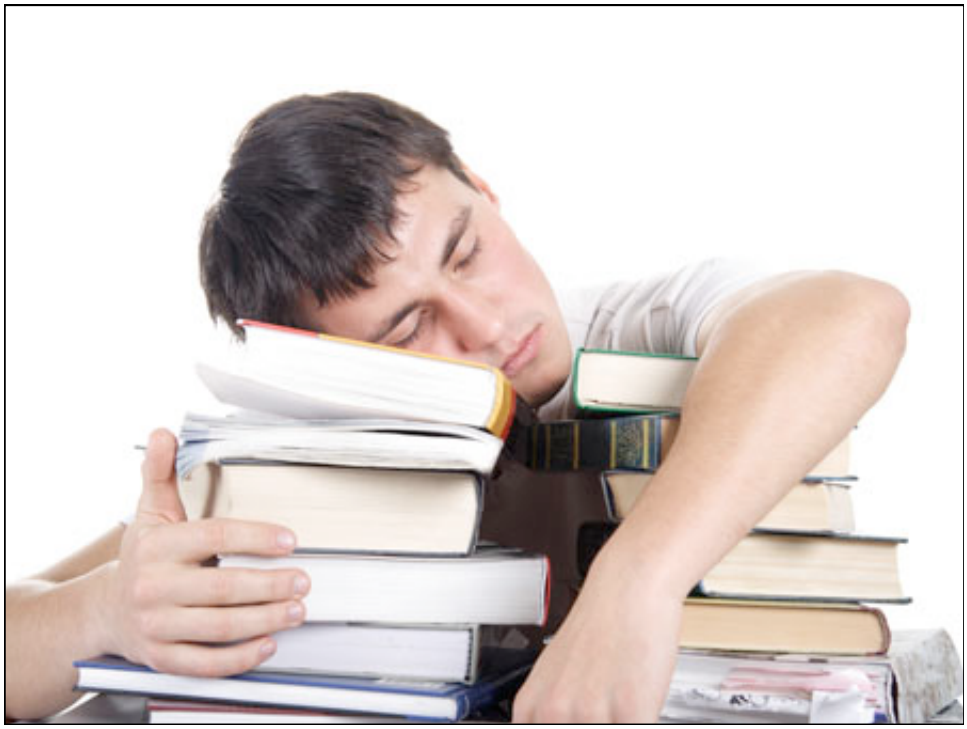
10

Antiangiogenics: Endostatin



Lewis lung carcinoma in Mice [Hahnfeldt et al, 1999]:

11

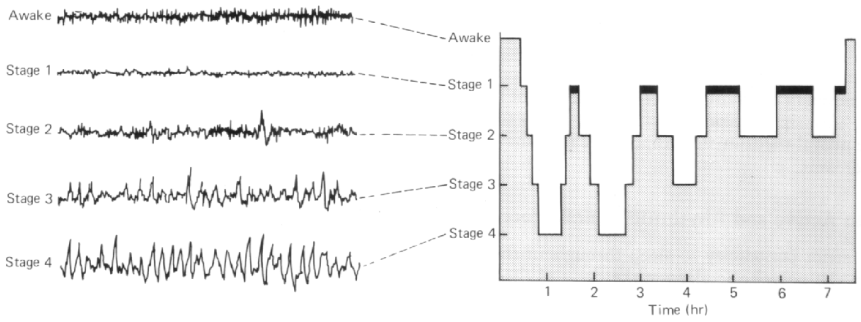


Sleep – The Final Frontier

Oscillatory processes
with many time-scales:

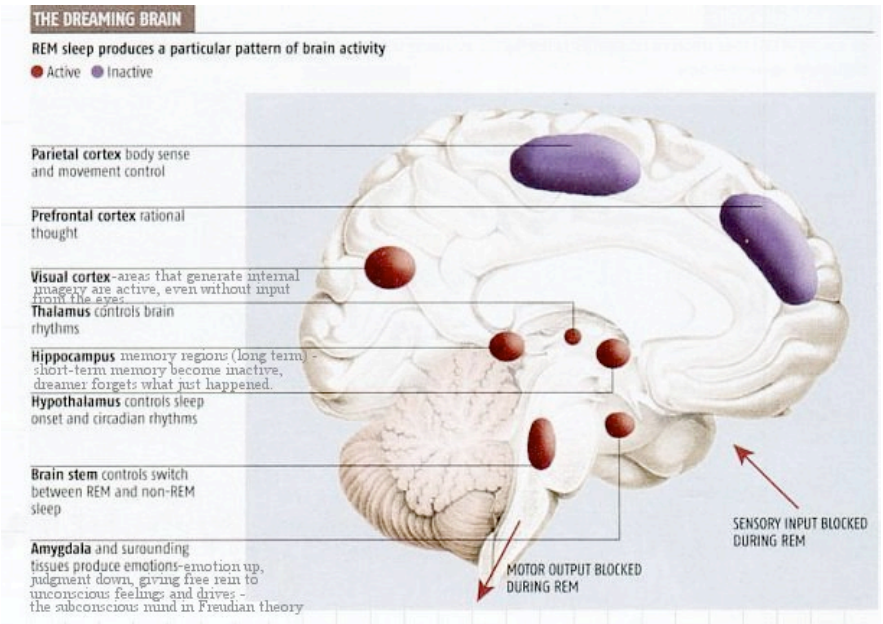
- Circadian
  24 hours
- Internal Sleep Structures
  minutes-hours
- Neuronal Activity
  milliseconds

Stages of sleep

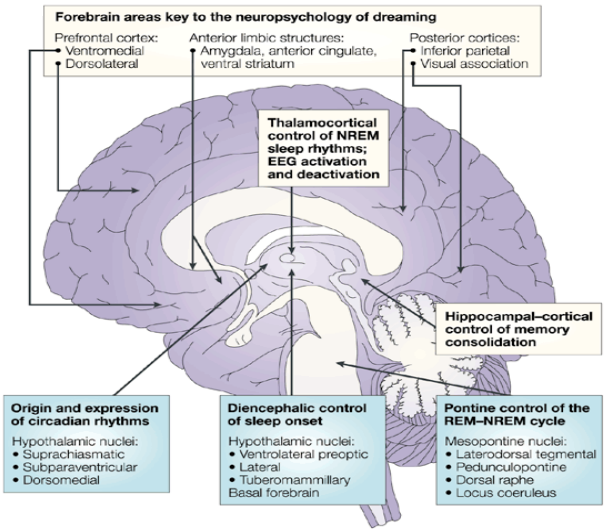


-- Spindles: 7 - 15 Hz
-- Delta: 1 - 4 Hz
-- Slow Osc. .5 - 1 Hz

These sleep rhythms arise from interactions between cortical neurons and two groups of cells within the thalamus: RE and TC cell.

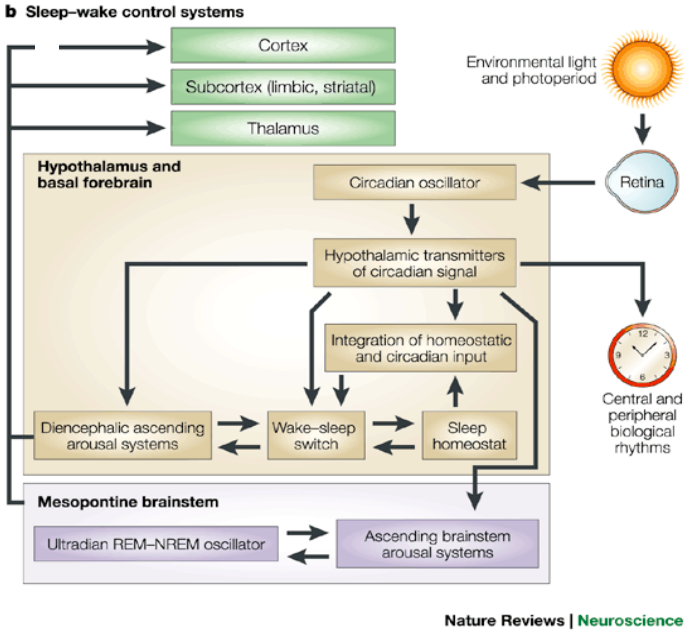


Sleep involves many parts of the brain



Hobson, Nature Reviews Neuroscience 2002

There are Many Interactions to Generate the Sleep-Wake Cycle



Sleep Models

Timing of sleep & wake
2-Process Model (Borbely)
Kronauer (circadian rhythm)

Thalamocortical sleep rhythms
Biophysical models for thalamic and cortical cells
Generation of EEG sleep-rhythms

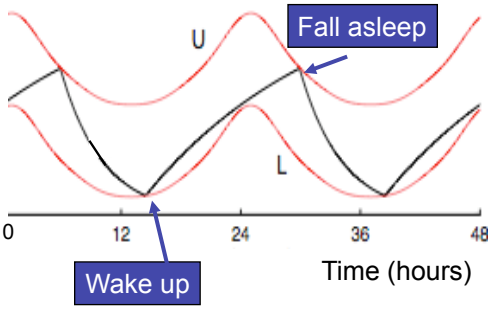
Hypothalamic sleep/wake switch
Interactions of sleep-promoting and wake promoting
cell groups in hypothalamus & brainstem

Two-Process Model (Borberly)

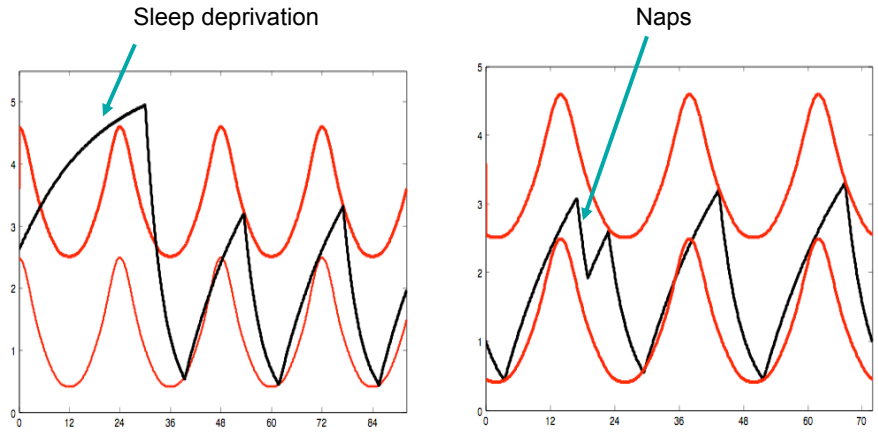
Timing of sleep & wake determined by 2 processes:

- Circadian Pacemaker
- Sleep Homeostat

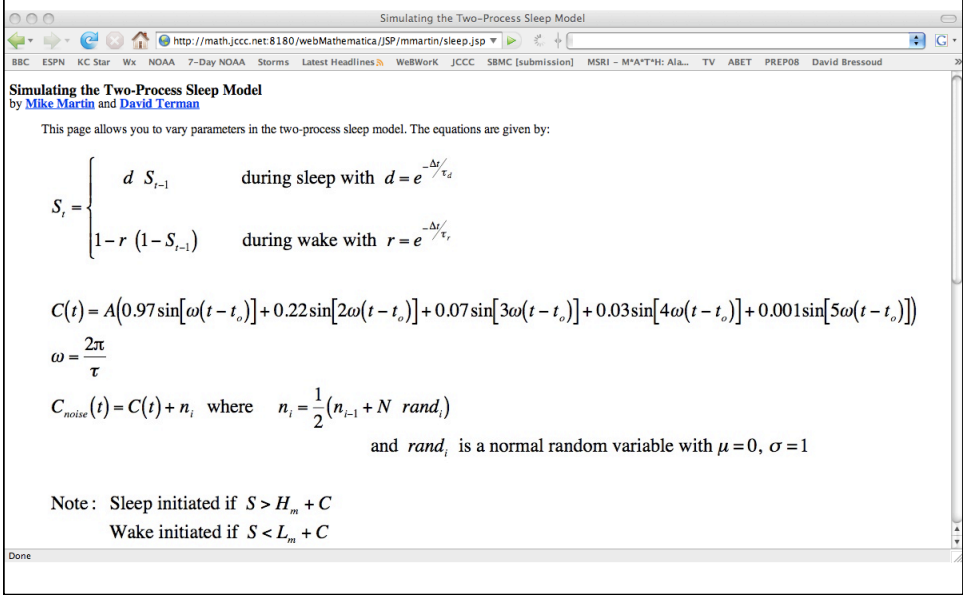
Vertical axis represents the build-up process of slow wave activity (SWA) in the EEG during wake, & the decay of SWA during sleep



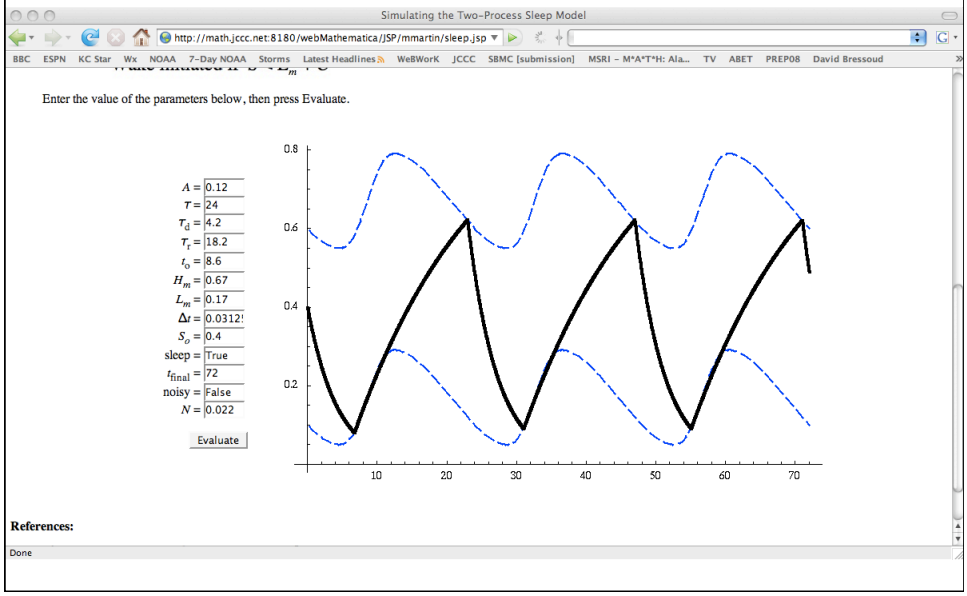
2-process model predicts effects of:

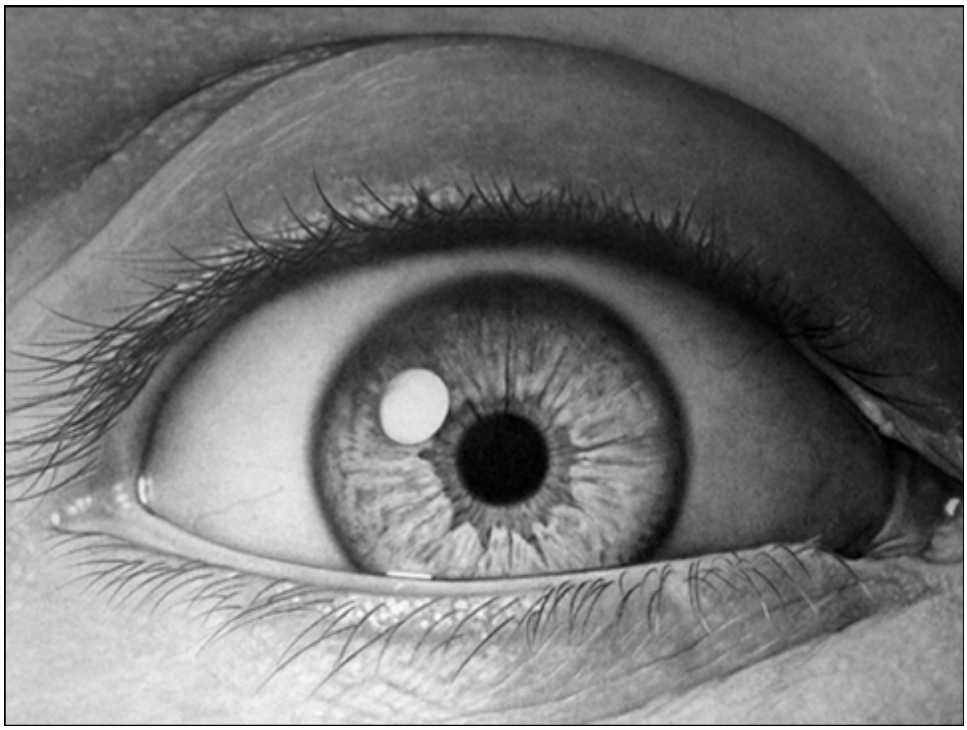


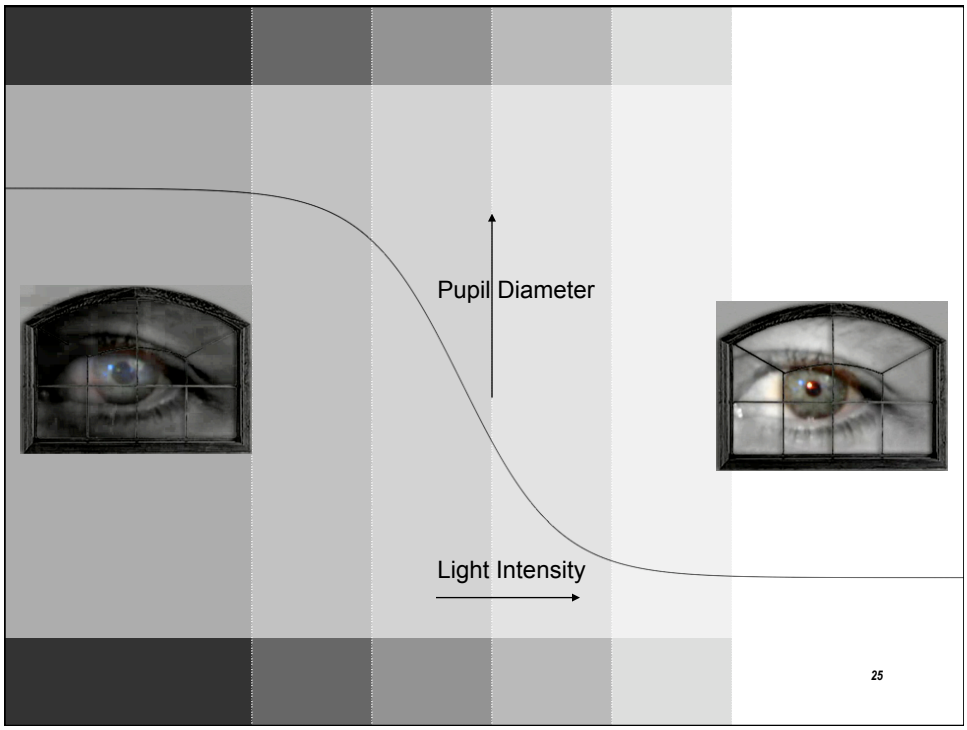
Sleep Simulations on the Web

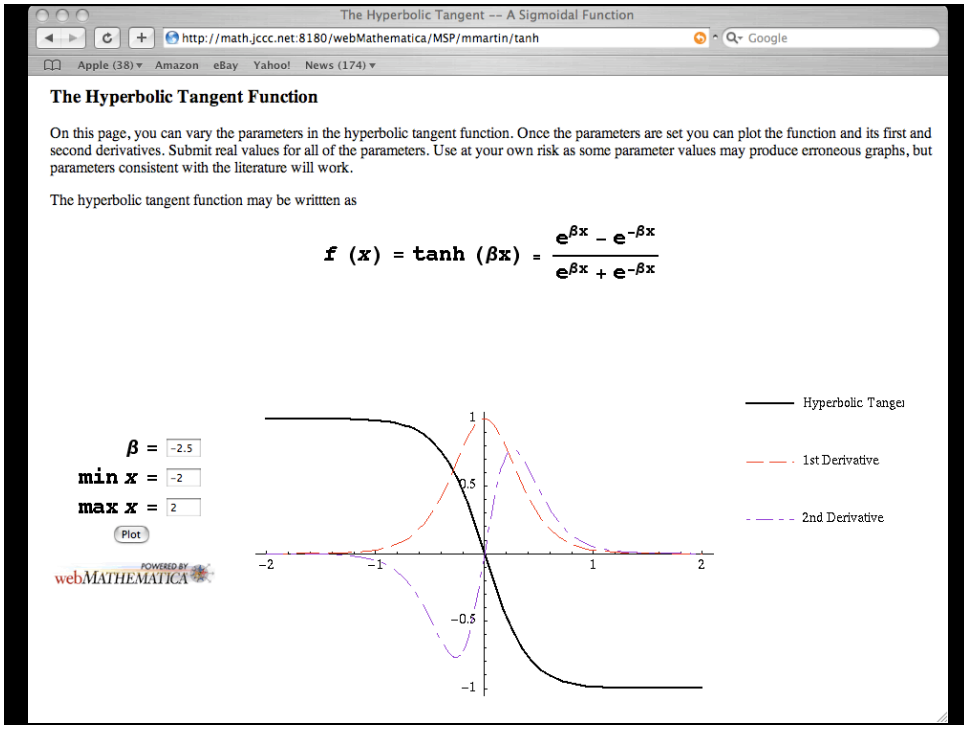


Experiential Parameter Investigations & Computations

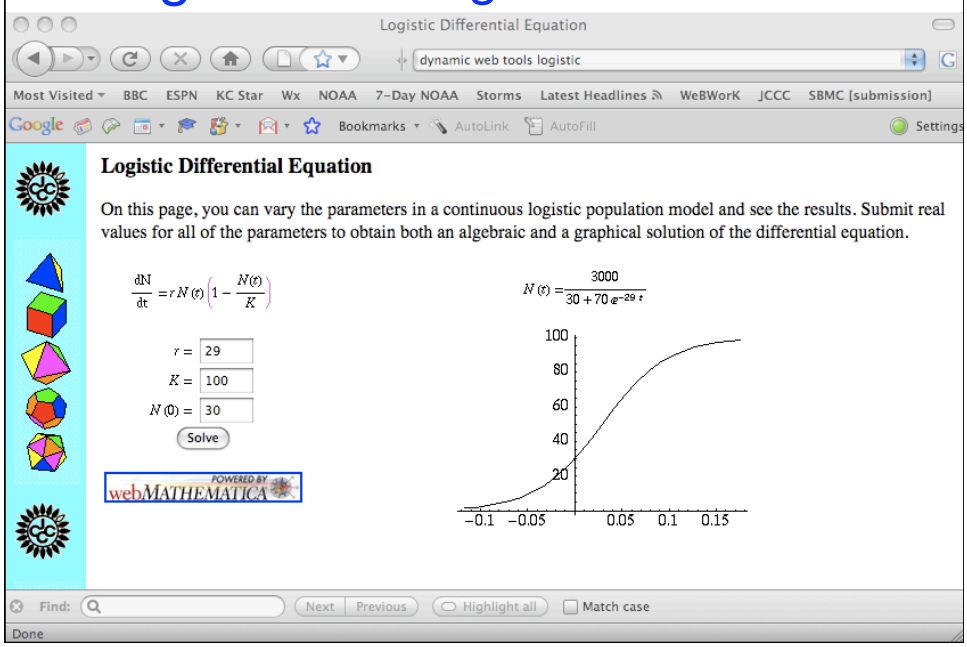




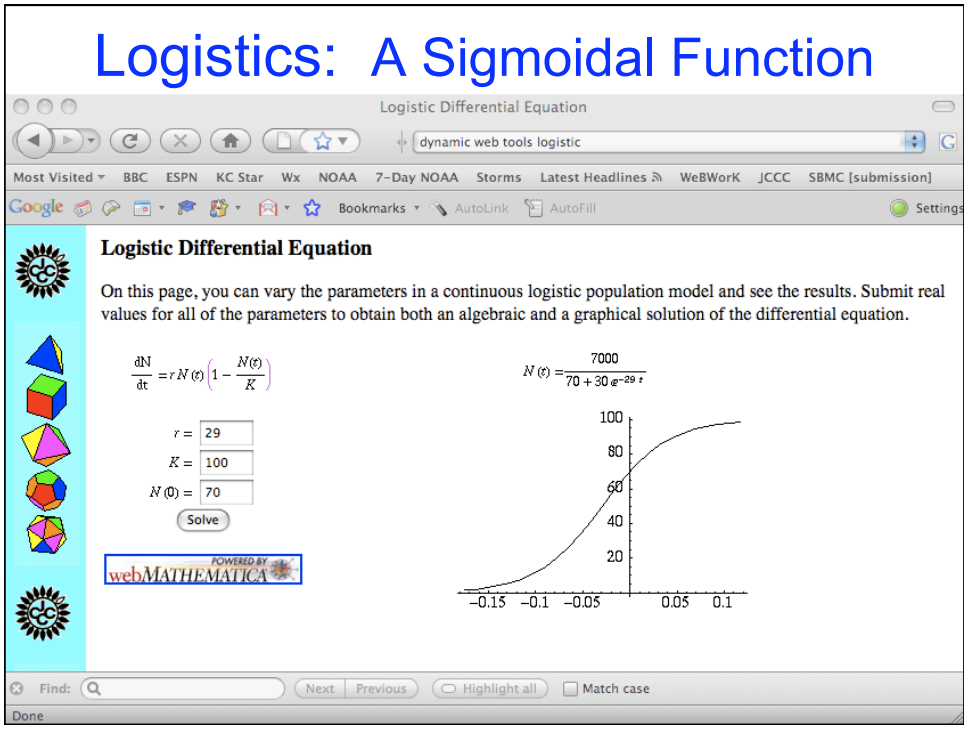

Pupil Diameter
Light Intensity
25

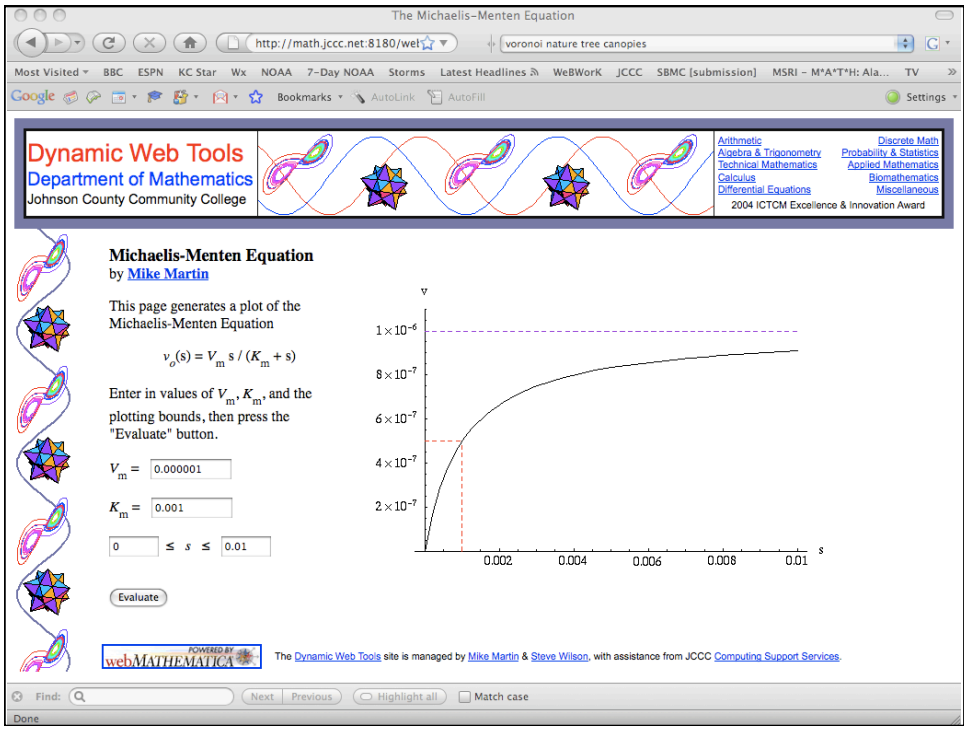


Logistics: A Sigmoidal Function



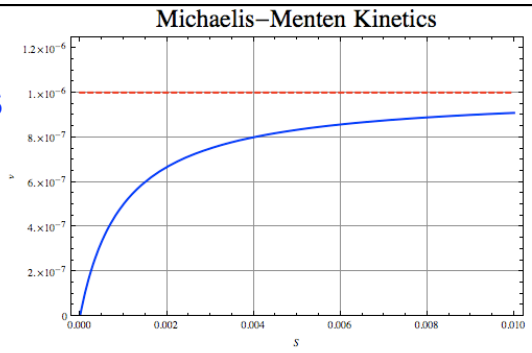
Logistics: A Sigmoidal Function

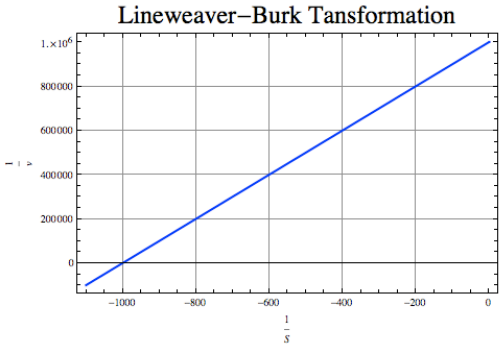


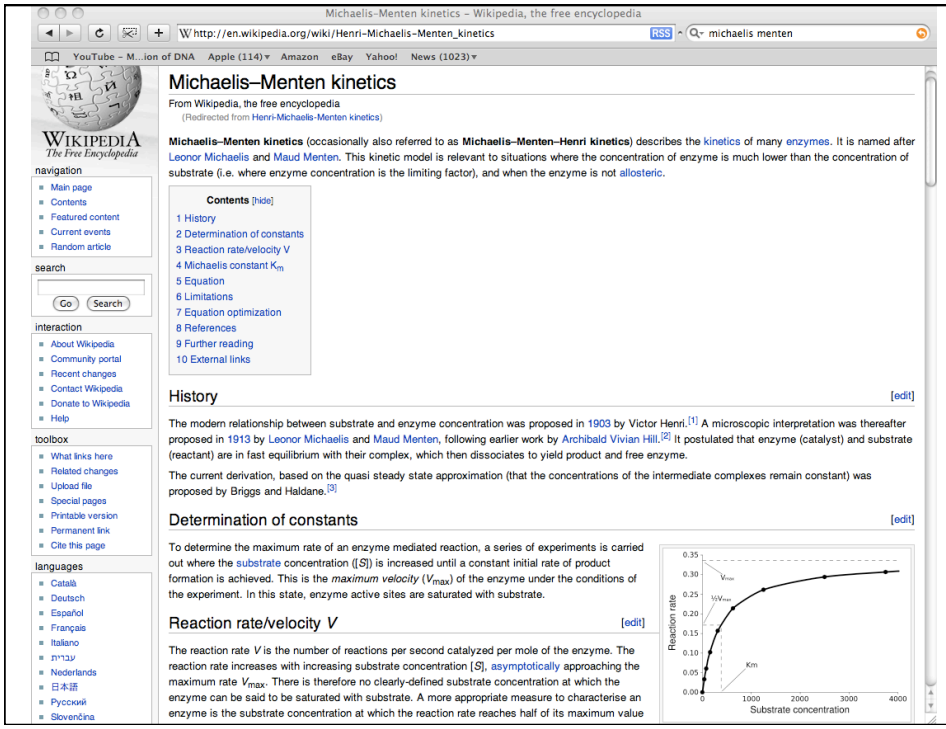


Enzyme Kinetics

Leonor Michaelis and Maude Lenora Menten







Models of Growth

Models for Growth with Saturation

http://math.jccc.net:8180/\

BBC ESPN KC Star Wx NOAA 7-Day NOAA Storms Latest Headlines WeBWorK JCCC SBMC [submission] MSRI – M*A*T*H: Ala... TV ABET

Comparing Models of Growth
by Mike Martin and Helen Byrne

This page allows you to analyze solutions to three different models. Each of the models start with a given differential equation and initial condition. The differential equations themselves have built-in assumptions and an analysis of their solutions relative to the observed phenomena will help to validate (or not) the model themselves. Here are the three differential equations and initial condition and their respective solutions:

$$\frac{dN}{dt} = k\ N \quad \text{with} \quad N(0) = N_o \quad \Rightarrow \quad N(t) = N_o e^{kt}$$

$$\frac{dN}{dt} = k\ N\left(1 - \frac{N}{\theta}\right) \quad \text{with} \quad N(0) = N_o \quad \Rightarrow \quad N(t) = \frac{\theta N_o}{N_o + (\theta - N_o)e^{-kt}}$$

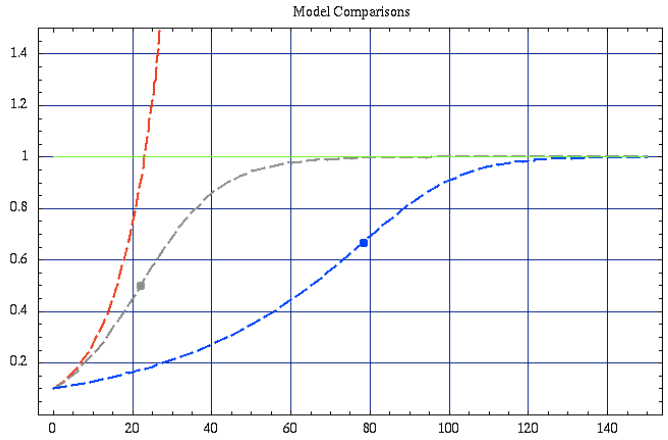
$$\frac{dN}{dt} = \frac{k}{\alpha}\ N\left[1 - \left(\frac{N}{\theta}\right)^{\alpha}\right] \quad \text{with} \quad N(0) = N_o \quad \Rightarrow \quad N(t) = \theta\left(\frac{N_o^{\alpha}}{N_o^{\alpha} + (\theta^{\alpha} - N_o^{\alpha})e^{-kt}}\right)^{1/\alpha}$$

Done

Exponentials, Sigmoids, & Points of Inflection

k = 0.1
α = 4
θ = 1.0
N_o = 0.1
$t_{initial}$ = 0
t_{final} = 150

Evaluate



References:

Byrne, H., *Cancer Modeling and Simulation*, Chapman & Hall/CRC, Boca Raton, FL, 2003.

Excitable Media

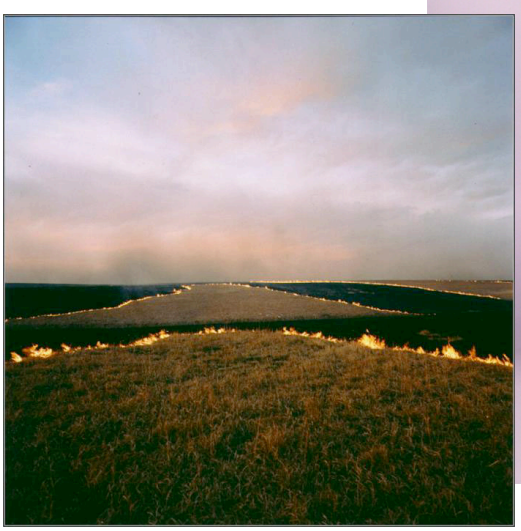
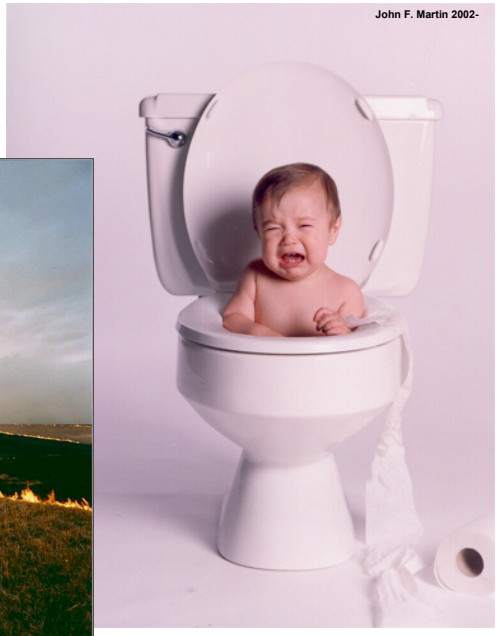


Photo: Larry Schwarm



John F. Martin 2002-

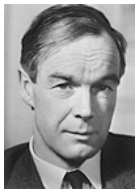
Photo: Cruel Mother

34

Excitability

Action Potentials

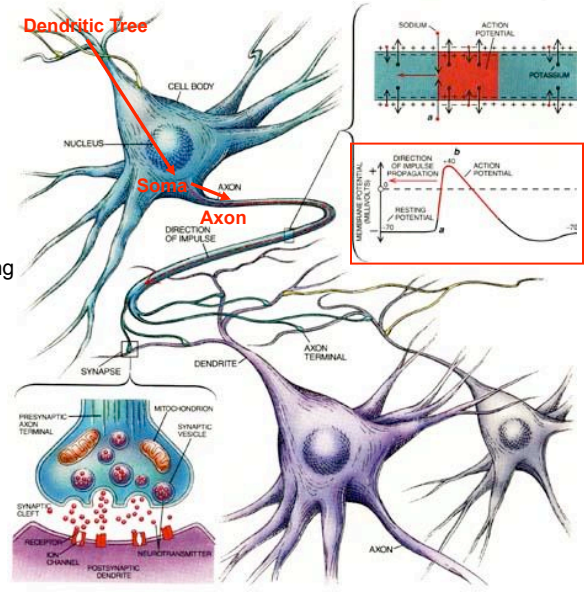
- Neurons
  - Networks
  - Variability
  - Ion Channel Gating
- Other Cells



Alan Lloyd Hodgkin
1914-1998

Andrew Fielding Huxley
1917-

Nobel Prize 1963

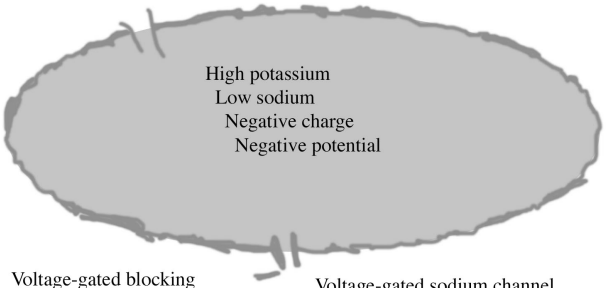


35

Basic Elements of Neural Dynamics

Voltage-gated potassium channel that opens slowly when potential exceeds resting potential

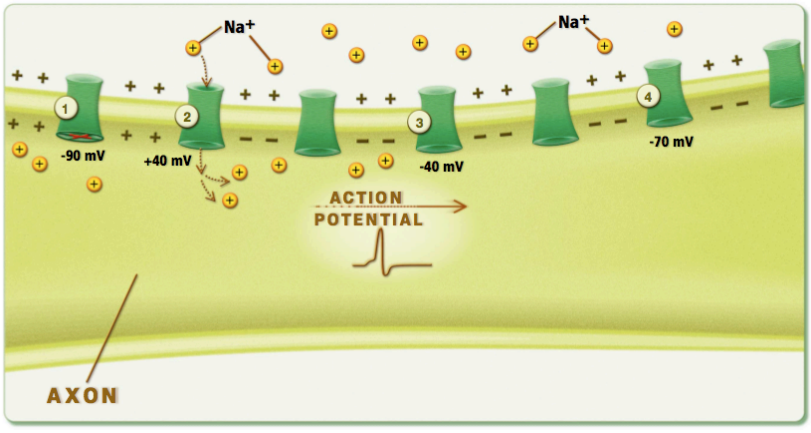
Low potassium
High sodium



Voltage-gated blocking mechanism blocks channel slowly when potential exceeds resting potential

Voltage-gated sodium channel opens quickly when potential exceeds threshold

36



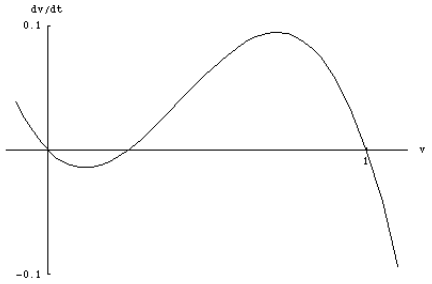
37

Fitzhugh-Nagumo – A Simple Construction

- Cell potential can be scaled to more convenient values
- Let *v* represent this potential & abide by the following:

$v = 0$ **resting potential**
$v = \alpha$ **threshold potential**
$v = 1$ **potential with Na^+ channels open**

- Small deviations above the resting potential are not amplified and the potential returns to rest
- If cell potential raised above threshold a cell moves to higher potential found when Na^+ channels open



$$\frac{dv}{dt} = -v(v-\alpha)(v-1) \qquad 0 < \alpha < 1$$

38

Effects of Constant Applied Current

- So far we have considered a resting cell receiving a single pulse of positively charged ions; now consider giving the cell a constant input of ions
- The current describes the rate at which ions enter the cell and is therefore proportional to the derivative of the potential
- If the current applied is I_{app}, we add I_{app} to the rate of change of potential and obtain a more general form of the Fitzhugh-Nagumo equations

$$\frac{dv}{dt} = -v(v-\alpha)(v-1) - w + I_{app}$$
$$\frac{dw}{dt} = \varepsilon(v - \gamma w)$$

- The *v*-nullcline is shifted up by I_{app} units
- The *w*-nullcline is unchanged

39

Math Tools on the Web

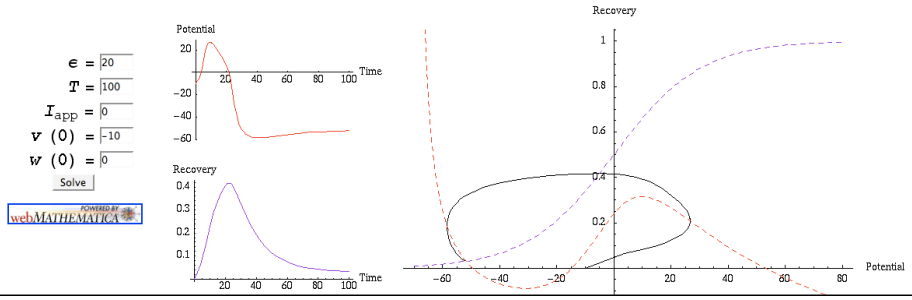
Morris-Lecar System of Differential Equations

On this page, you can vary the parameters in the Morris-Lecar system of diffferential equations. Submit real values for all of the parameters to obtain graphical solutions of the system as functions of time and in the phase plane. Nullclines (or isoclines) are plotted in the phase plane. A numeric solution on the interval $[0, T]$ is produced using *Mathematica*'s numerical ODE solver, NDSolve. Initial values for both the potential, v, and recovery, w, must be input.

The Morris-Lecar equations may be written:

$$\epsilon \frac{dV}{dt} = -2.2\left(1 + \tanh\left(\frac{V+1}{15}\right)\right)(V-100) - 8W(V+70) - 2(V+50) + I_{app}$$

$$\frac{dW}{dt} = 0.020\cosh\left(\frac{V}{60}\right)\left(1 + \tanh\left(\frac{V}{30}\right) - 2W\right)$$



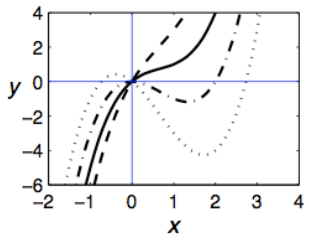


Figure 1.1.5: The function $y = x^3 - 2x^2 + bx$, with $b = -2$ (dotted), $b = 0$ (dash-dot), $b = 2$ (solid) and $b = 4$ (dashed)

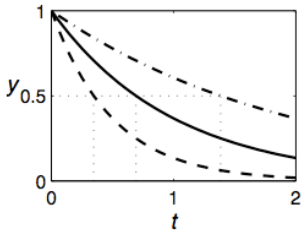


Figure 1.1.3: The function $y = e^{-kt}$, with $k = 0.5$ (dash-dot), $k = 1$ (solid) and $k = 2$ (dashed), showing the points $(T, 0.5)$

Institute for Advanced Study / Park City Mathematics Institute

PREP
Professional Enhancement Programs of the MAA

mbi
Mathematical Biosciences Institute
The Ohio State University

Acknowledgements

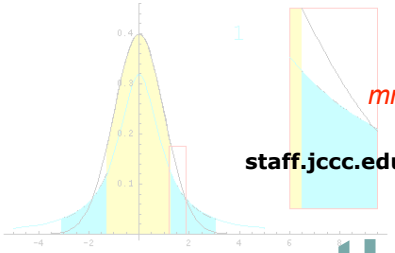
- Tim Comar
  Benedictine University
- Glenn Ledder
  University of Nebraska – Lincoln
- Steve Wilson
  Johnson County Community College
- John Jungck
  Beloit College
- David Terman
  Ohio State University
- Helen Byrne
  University of Nottingham

NSF

Contact

Mike Martin
JCCC

Photo: Larry Schwarm



mmartin@jccc.edu

staff.jccc.edu/mmartin/webmath.html

math.jccc.edu

webMATHEMATICA POWERED BY