BME 565 / BME 665

Introduction to Computational Neurophysiology

Instructors: Patrick Roberts, Tamara Hayes

Administrivia

- Course website: http://www.bme.ogi.edu/BME665
- Course mailing list: bme665@bme.ogi.edu
  - Send all questions to the list, rather than to the instructors directly. Others may have similar questions
- Office hours by appointment. Please use email to communicate, rather than leave voice mail.
  - robertspa@ohsu.edu
  - hayest@bme.ogi.edu
- Text:
  - *Theoretical Neuroscience* (2001, 2005) Peter Dayan & L. F. Abbott
  - Also to be used (available in the library):
    - *Biophysics of Computation: Information Processing in Single Neurons* (1998) Christof Koch
    - *Spiking Neuron Models* (2002) Wulfram Gerstner & Werner M. Kistler
    - *Spikes: Exploring the neural code* (1999) Fred Rieke et. al.

Course outline (20 classes, 10 weeks)

Approach will be “bottom-up” starting with biophysical models of neurons and moving to information coding

- Part A: Biophysical models of single neurons
  - Using the simulation package NEURON as well as Matlab, we will explore the effects of membrane currents and neuron morphology on the responses of neurons to stimuli
- Part B: Information coding: simplifying the model
  - We will explore the effects of synaptic connections in small networks using Matlab
- Part C: Higher-level models of neuronal processing
  - A brief exploration of learning in neuronal systems

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Desired outcomes:

1. To help students understand how computational models can be used to analyze, explain and predict the physiological behavior of neurons and assemblies of neurons.
2. To help students to develop an intuition for the dynamics of neural processes in single neurons and in networks.
3. To provide students with hands-on experience using current research tools to investigate the concepts underlying these computational models.

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Evaluation

1. Weekly homework: exercises using modeling concepts with simulations (pass/fail)
2. Take-home exams (2), one after each of the first 2 sections (graded on 0-4 scale)
3. Final project (work in groups of 2). Graded on a 0-4 scale.

Late assignments accepted only with instructor approval prior to the due date.

Grading:

A+	Superior performance in all aspects of the course
A	Superior performance in most aspects; high quality in remainder
A-	High quality performance in all or most aspects of the course
B+	Satisfactory performance in most aspects; high quality in some
B	Satisfactory performance in the course
B-	Satisfactory performance in most aspects; some sub-standard work

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Text and reading materials

Recommended text:

Theoretical Neuroscience (2001, 2005) Peter Dayan & L. F. Abbott

Also useful:

Biophysics of Computation: Information Processing in Single Neurons (1998) Christof Koch

Spiking Neuron Models (2002) Wulfram Gerstner & Werner M. Kistler

Spikes: Exploring the Neural Code (1997) Fred Rieke et. al.

The Nature of Mathematical Modeling (1999) Neil Gershenfeld

Primary literature readings will be assigned relating to topics discussed in class.

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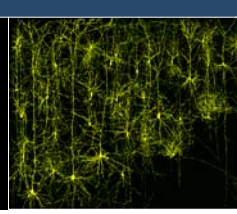
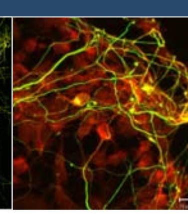
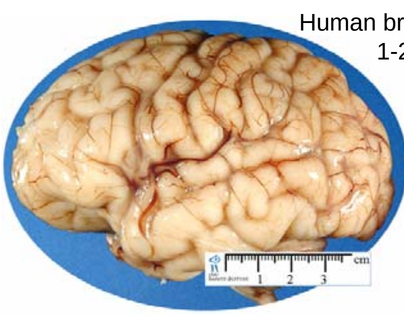
Why computational neurophysiology?

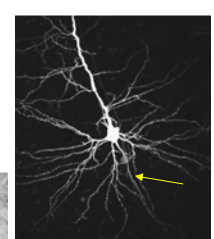




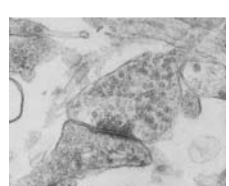
10^5 neurons in a fruit fly
10^6 in mouse
10^{11} in human

Human brain
1-2kg



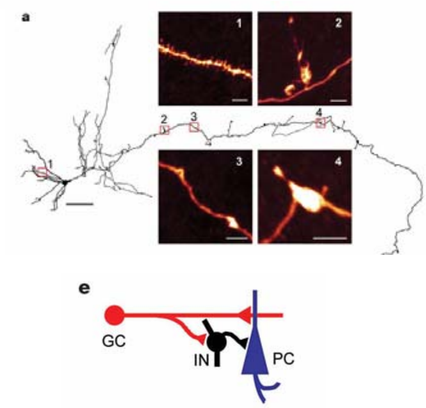
Pyramidal cell: R ~20µm
- axon R ~ 1µm, L~1cm





Synapses: ~ 10^{14} in human cortex
~ 10^3 per neuron

An important tool for neuroscience research



- Enhances our understanding of cellular neurophysiology
- Generates new hypotheses about interactions between neurons
- Allows us to test hypotheses before undertaking costly experiments
- Allows us to develop models of neuronal learning

From: Mori et. al. *A frequency-dependent switch from inhibition to excitation in a hippocampal unitary circuit*. Nature **431**, 453-456 (23 September 2004)

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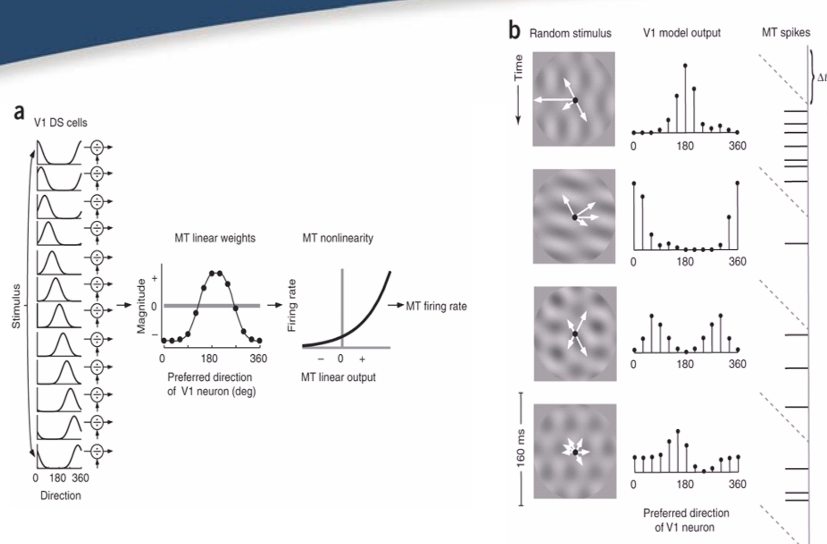
A tool for understanding higher-order brain function



From: Rust et. al. *How MT cells analyze the motion of visual patterns*. **Nature Neuroscience** 9, 1421 – 1431, 2006

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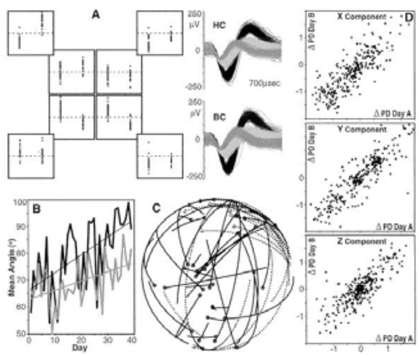
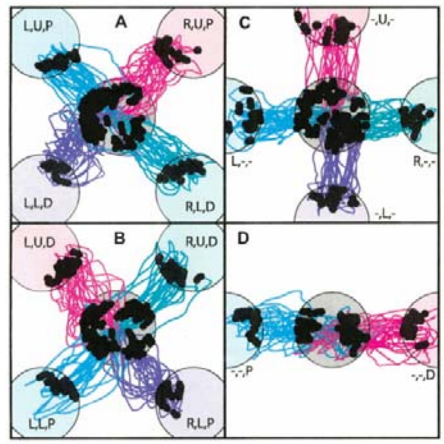
A tool for neuroprosthetic device research





From: Taylor et. al. *Direct Cortical Control of 3D Neuroprosthetic Devices* . **Science** 7 June 2002: Vol. 296. no. 5574, pp. 1829 - 1832

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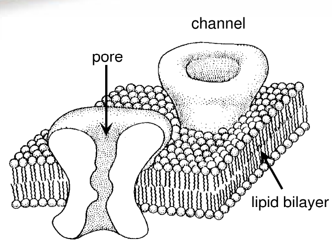
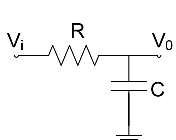
Electrical properties of neurons

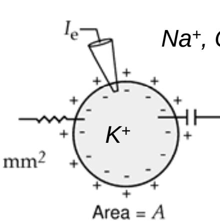


Membrane resistance
Membrane potential
Membrane capacitance
Ion channels
Resting potential (~ -70 mV)
Equilibrium potential

E_K -70mV
E_{Na} +50mV
E_{Ca} +150mV



$\Delta V = I_e R_m$
$R_m = r_m / A$
$r_m \approx 1\ \mathrm{M\Omega\ mm^2}$



$Q = C_m V$
$C_m = c_m A$
$c_m \approx 10\ \mathrm{nF/mm^2}$

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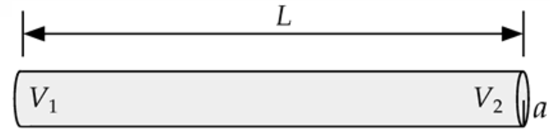
Cable properties of neurons



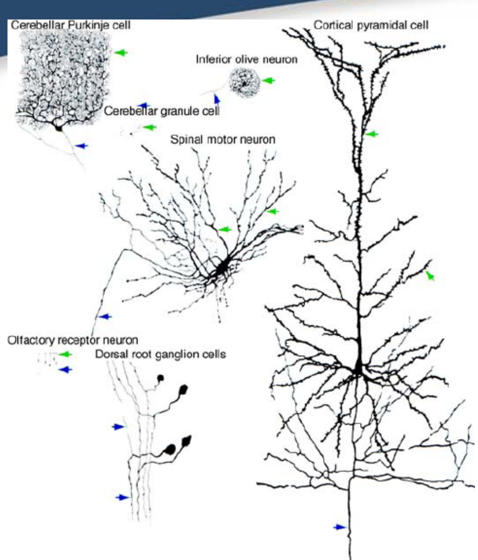
$$I_L = (V_2 - V_1)/R_L$$

$$R_L = r_L L/\pi a^2 \quad r_L \approx 1\ \mathrm{k\Omega\ mm}$$

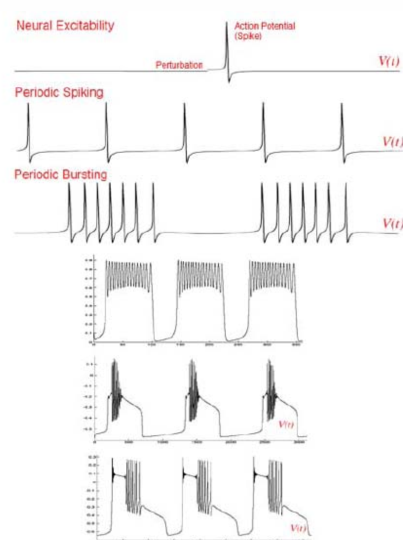
Intracellular resistance
Current in the cable

Learn what typical values are for membrane and channel resistances, capacitances, and equilibrium potentials. This will give you intuition about what should or shouldn't happen when channels open and close.

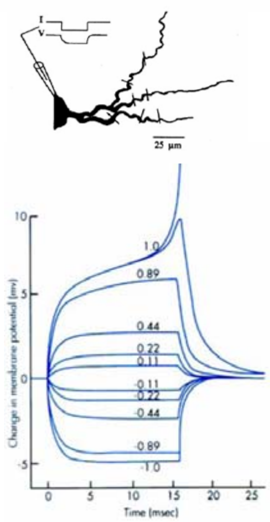
Part A: Biophysical models of single neurons

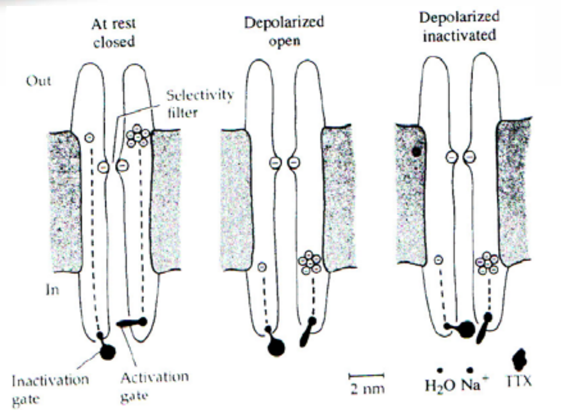


The Human Brain: An Introduction to Its Functional Anatomy (1999) John Nolte



E.M. Izhikevich, Neural Excitability, Spiking, and Bursting
Int. J. Bifurcation and Chaos (2000), 10:1171--1266.





$$C\frac{dV}{dt} = \overset{\text{injected current}}{I} - \overset{\text{sodium current}}{\bar{g}_{Na} m^3 h (V - V_{Na})} - \overset{\text{potassium current}}{\bar{g}_K n^4 (V - V_K)} - \overset{\text{leak current}}{g_L (V - V_L)}$$

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Linear Differential Equations

- Simplest differential equation $\frac{dy}{dt} = f(t) \Rightarrow y(t_1) - y(t_0) = \int_{t_0}^{t_1} f(t)dt$
- If linear in *y*, the equation can be written in terms of a linear operator

$$L_N(y) = \frac{d^N y}{dt^N} + A_1(t)\frac{d^{N-1}y}{dt^{N-1}} + \ldots + A_{N-1}(t)\frac{dy}{dt} + A_N(t)y$$

- If $L_N(y) = 0$ then the equation is homogenous and it will have *N* linearly independent solutions $u_1(t), u_2(t), \ldots, u_N(t)$
- Any arbitrary linear combination of those solutions is also a solution, called the general solution:

$$y_g(t) = \sum_{n=1}^{N} C_n u_n(t)$$

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Linear differential equations (cont.)

- One approach to solving a differential is to guess the functional form of the solution
- Often try $y = e^{rt}$ as the solution for the homogeneous part of the equation
- Substitution of this guess gives the characteristic equation:

$$r^N + A_1 r^{N-1} + \ldots + A_{N-1} r + A_N = 0$$

- The real part of the roots represent exponentially growing or decaying solutions, the complex part represents oscillatory behavior
- If the roots are distinct, the general solution is:

$$y_g = \sum_{n=1}^{N} C_n e^{r_n t}$$

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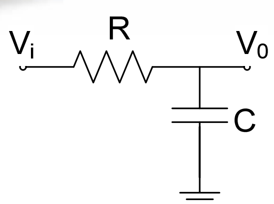
Linear differential equations: example



$$RC\frac{dV_0}{dt} = V_i - V_0 \qquad \Rightarrow RC\frac{dV_0}{dt} + V_0 = V_i$$

If we assume a solution of the form $y = e^{rt}$ the characteristic equation gives:

$$RC \cdot r + 1 = 0 \qquad \Rightarrow V_0 = Ae^{-t/RC}$$

Hence, the undriven response simply discharges the capacitor.

To look for a particular solution we must know the input V_i and then choose an ansatz V_0 :

Assume periodic forcing $V_i = e^{i\omega t}$ and a solution of the form: $V_0 = Ae^{i\omega t}$

Substitution yields: $RCAi\omega + A = 1 \qquad \Rightarrow A = \frac{1}{1 + i\omega RC}$

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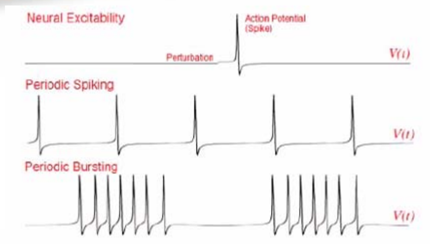
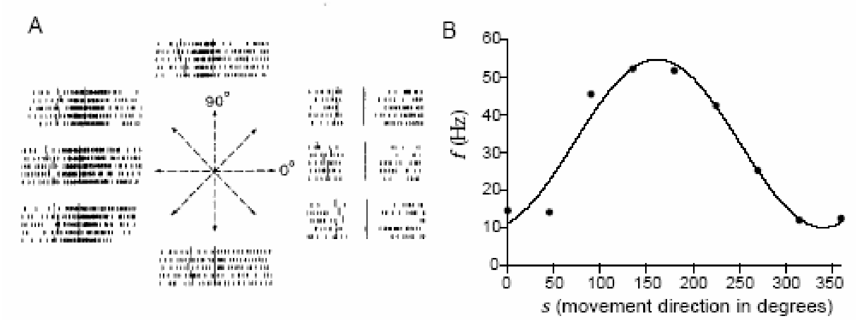
Part B: Information coding





Spike-count rates

- Treat action potentials as a series of n spikes occurring at times ti
- Then the spike sequence can be considered a series of Dirac functions:

$$\rho(t) = \sum_{i=1}^{n} \delta(t - t_i) \qquad \text{note:} \qquad \int d\tau \rho(\tau) = n$$

So, the spike-count rate r for an interval T is given by:

$$r = \frac{n}{T} = \frac{1}{T}\int_0^T d\tau \rho(\tau)$$

Note: this is not time-dependent

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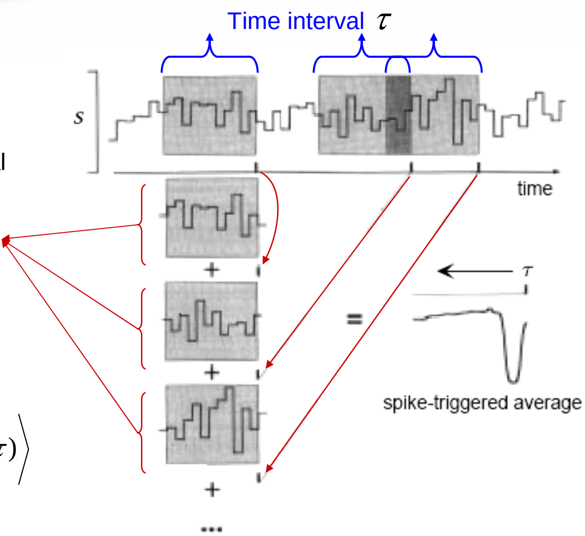
Representing the Stimulus: Spike-triggered average

Average over all
n spikes in a trial

$$\frac{1}{n}\sum_{i=1}^{n} s(t_i - \tau)$$



Then, average
over trials:

$$C(\tau) = \left\langle \frac{1}{n}\sum_{i=1}^{n} s(t_i - \tau) \right\rangle$$

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The neuron's view

$$P[s \mid r]$$

How do we find an
optimal *s*?

Conditional firing rate
probability density

$$P[s \mid r] = \frac{P[r \mid s]P[s]}{P[r]}$$

Probability of
stimulus (the *prior*)

Probability of
response *r*

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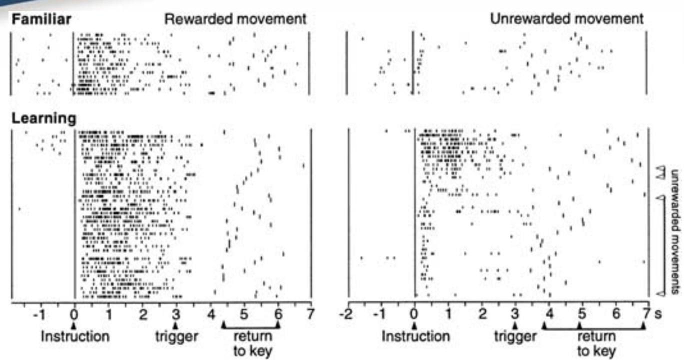
Part C: Higher-level models of neuronal processing



Predicted reward

Stimulus (0 or 1)

Learning rate

Prediction error

Actual reward

$$v = wu$$

$$\Delta w = \varepsilon \delta u$$

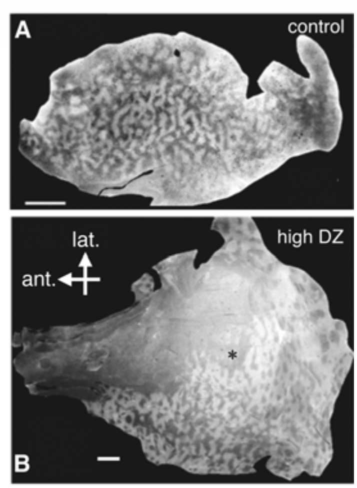
$$\text{where } \delta = r - v$$

Result of suppressed inhibition

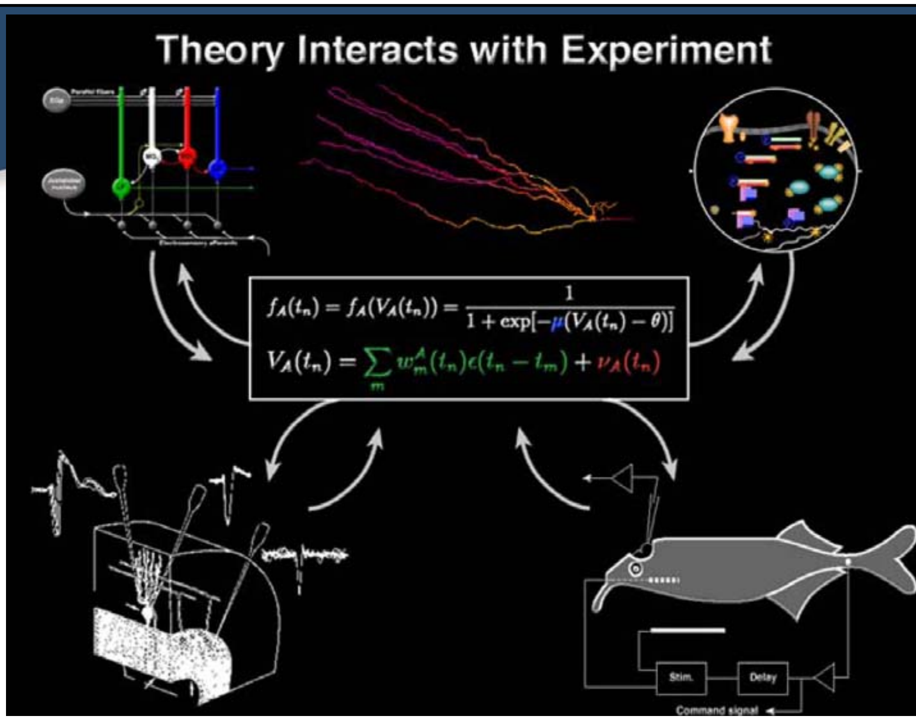
- High dose (35 mM, 0.2 µl/hour) diazepam treatment. Diazepam potentiates chloride flux through the GABAA receptor
- A: control hemisphere
- B: high dose yields an area of column desegregation

$$\tau_w \frac{d\vec{w}}{dt} = \langle v\vec{u} \rangle = \vec{Q} \cdot \vec{w}$$

$$\sum_i w_i^2 = \text{constant}$$



Fagiolini et al., *Science*, Vol 303, Issue 5664, 1681-1683, 2004



Useful background material

- More facts about neurons.
  http://www.dna.caltech.edu/courses/cns187/references/brain.pdf
- More depth about solving linear differential equations.
  http://www.physics.ohio-state.edu/~physedu/mapletutorial/tutorials/diff_eqs/homo_lnr.htm
- A Linear Algebra review.
  http://www.dna.caltech.edu/courses/cns187/references/matrices.pdf

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