Mid-term Review

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BME 2111
Neural Signal Processing and Data Analysis
2023 Fall

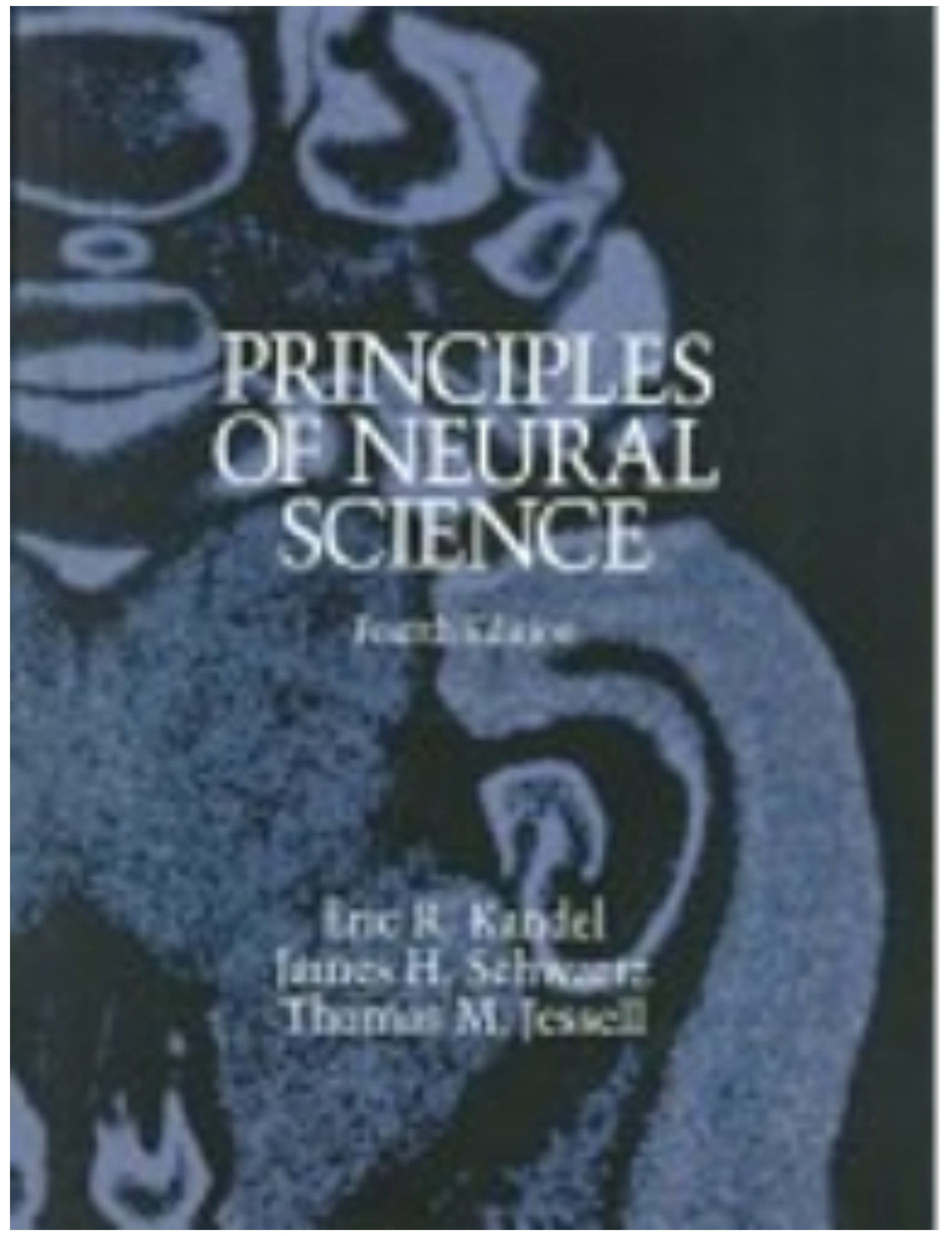
Mid-term exam

- December 5th, SIST 1D108
- 105 mins (13:00 - 14:45)
- 1 A4 cheat sheet allowed (2-sided)
- No electronic devices, books, notes allowed

Mid-term exam

- 30% of final score
- 100 pts in total (+ 10 pts bonus)
- 10 multiple choices (4 pts x 10) + bonus questions
- 12 short answers (5 pts x 12) + bonus questions
    - You can write however long you want, but the answers are not expected to exceed 100 words.
- 1 bonus problem (10 pts)

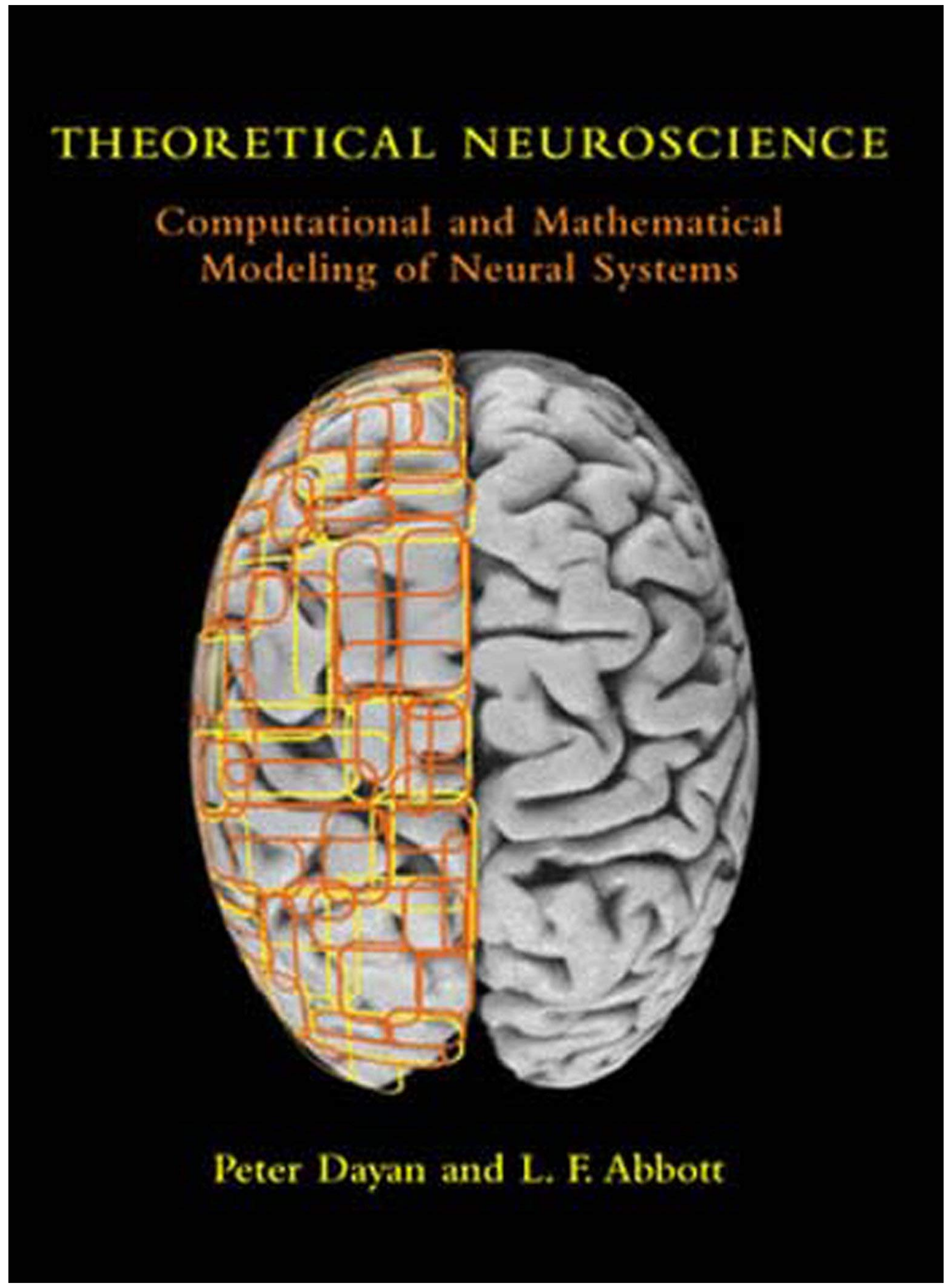
Roadmap



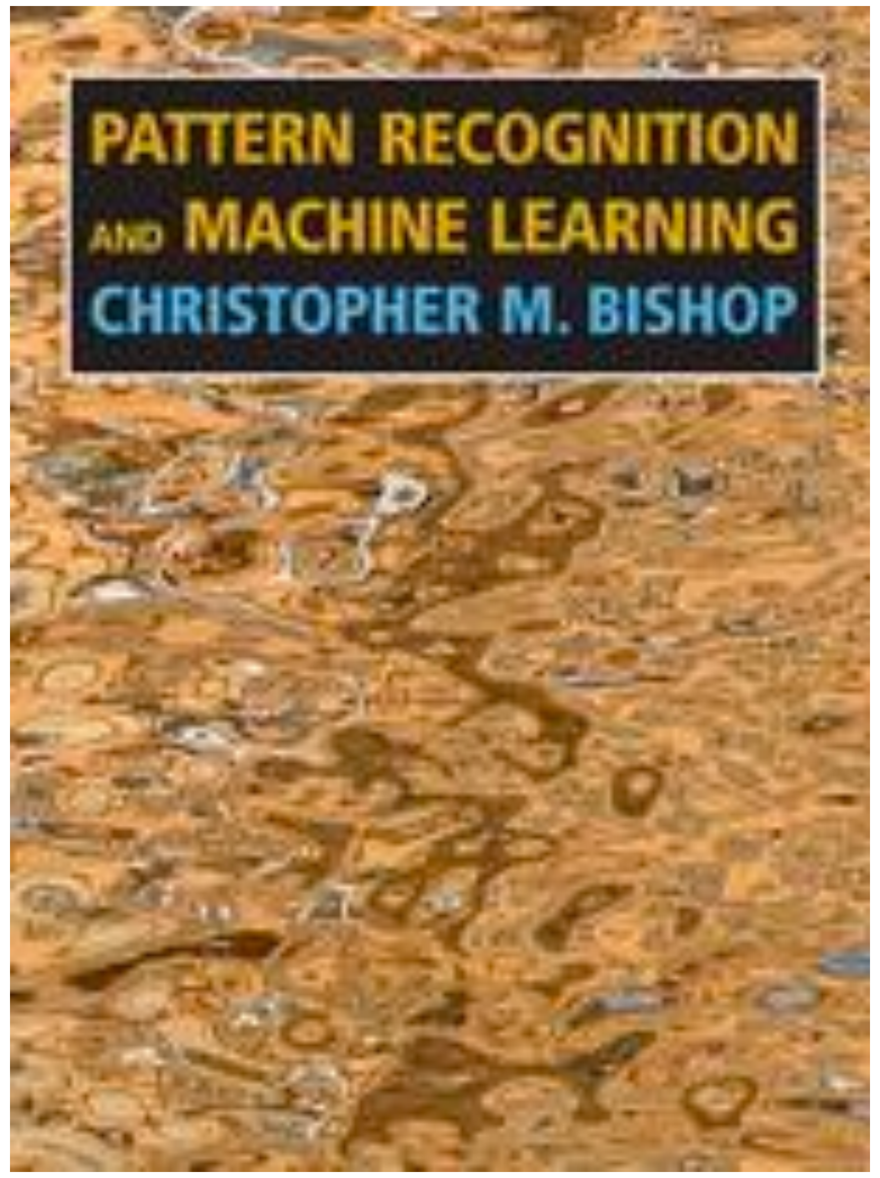
- Introduction to neuroscience
  - Chapter 1 – The brain and behavior
  - Chapter 2 – Nerve cells and behavior
- How are neural signals generated?
  - Chapter 7 – Membrane potential
  - Chapter 9 – Propagated signaling: the action potential
- How do neurons communicate with each other?
  - Chapter 10 – Overview of synaptic transmission
  - Chapter 12 – Synaptic integration

Roadmap

- Traditional neural signal processing methods
    - Theoretical Neuroscience, Chapter 1
    - Firing rate and spike train statistics



Topics we have covered in PRML so far



Chap. 4: Classification. Naive Bayes.

Neuroscience application: discrete neural decoding

Chap. 8: Graphical models.

Chap. 9: Mixture models. Expectation-maximization.

Neuroscience application: spike sorting

Chap. 12: Principal components analysis. Factor analysis.

Neuroscience applications: spike sorting, dimensionality reduction

Topics

- Brain and Behavior
  - History of neuroscience
    - Important scientists & contributions
      - e.g. What is the major contribution of Ramon y Cajal?
- Brain structure and functions:
  - CNS/PNS
  - Different brain structures and functions
    - e.g. What are the major functions of temporal lobe?
  - Key features of cerebral cortex

A Brief History

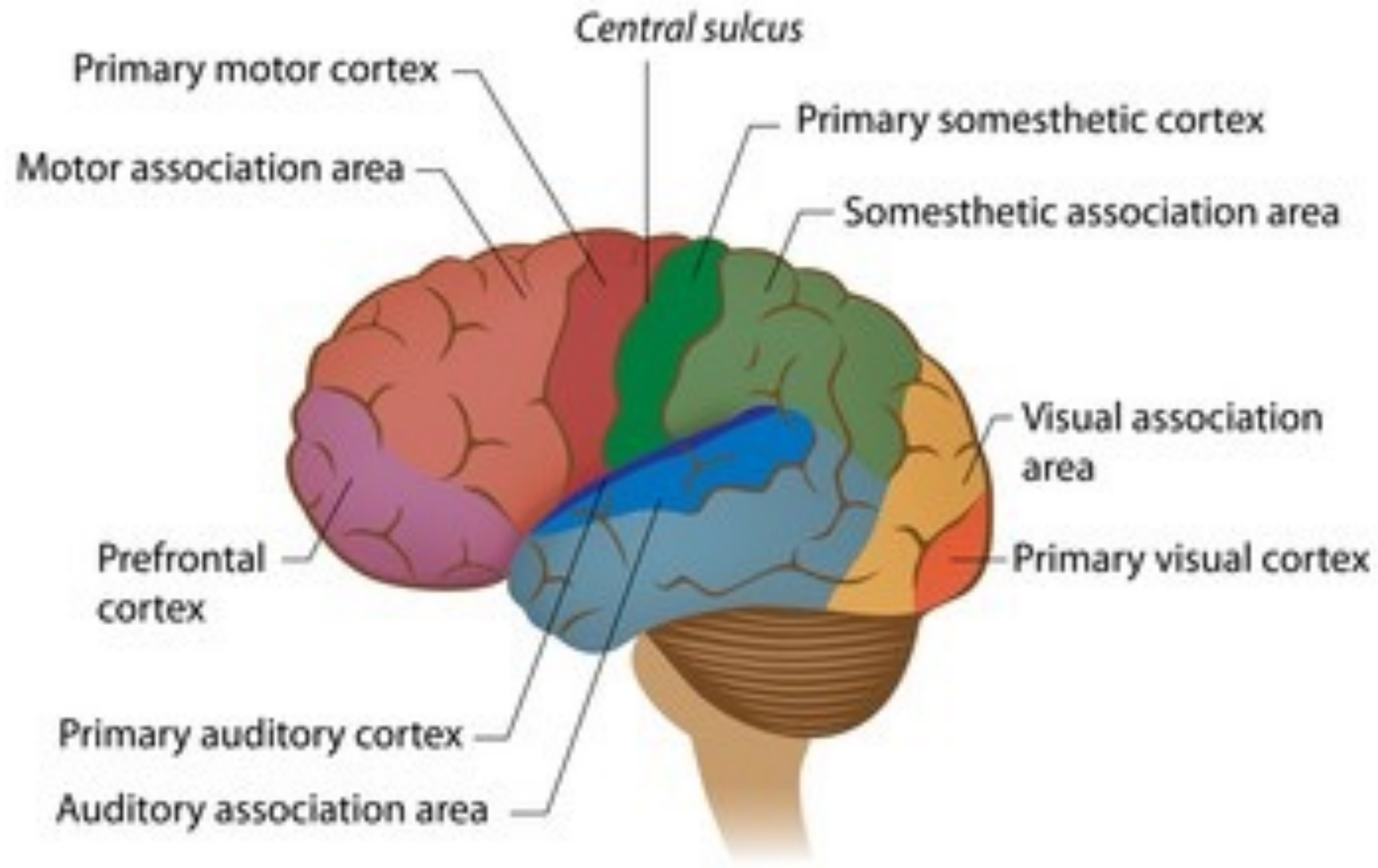
- Galen (100s) – mental activity occurs in the brain, not the heart! – nerves convey fluid secreted by the brain.
- Galvani (1700s) – muscle and nerve cells produce electricity.
- Golgi and Ramon y Cajal (1800s) – saw a network of discrete cells, not a continuous mass/web, with compound microscope.
- DuBois-Reymond, Muller & Helmholtz (1800s) – electrical activity of one nerve cell affects activity of adjacent cell in predictable ways.
- Ramon y Cajal's *neuron doctrine* (1800s) – individual neurons are the elementary signaling elements of the nervous system.
- Bernard, Erlich & Langley (1800s) – drugs bind specifically to receptors on the cell surface (membrane)→chemical basis of communication between nerve cells.
- Harrison (1920s) – two processes that grow out of cell body: dendrites and the axon.

Cellular Connectionism

- Wernicke, Sherrington & Ramon y Cajal (~1850) put forth a view of the brain termed *cellular connectionism:*
  - Individual neurons are the signaling units of the brain.
  - They are generally arranged in functional groups.
  - They connect to one another in a precise fashion.
- This is in opposition to a previous view termed *aggregate field*:
  - All brain regions participate in every mental operation.
  - Injury to a specific area of the brain affects all higher functions equally.

Brain has Distinct Functional Regions

- CNS is bilateral and symmetrical.
- Modern imaging techniques confirm that <u>different regions are specialized for different functions.</u>



Brain has Distinct Functional Regions

- CNS is bilateral and symmetrical.
- Modern imaging techniques confirm that <u>different regions are specialized for different functions.</u>
- However, <u>*parallel distributed processing*</u> (functions served by more than one neural pathway) in operation.
- CNS has 7 major parts:
  1) skin, joints, muscles of limbs / trunk
  2) breathing, heart rate
  3) movement: 4←→7
  4) learning motor skills
  5) eye movements
  6) info gate keeper 7←→rest
  7) higher brain funtions: sensory, motor, memory, emotion

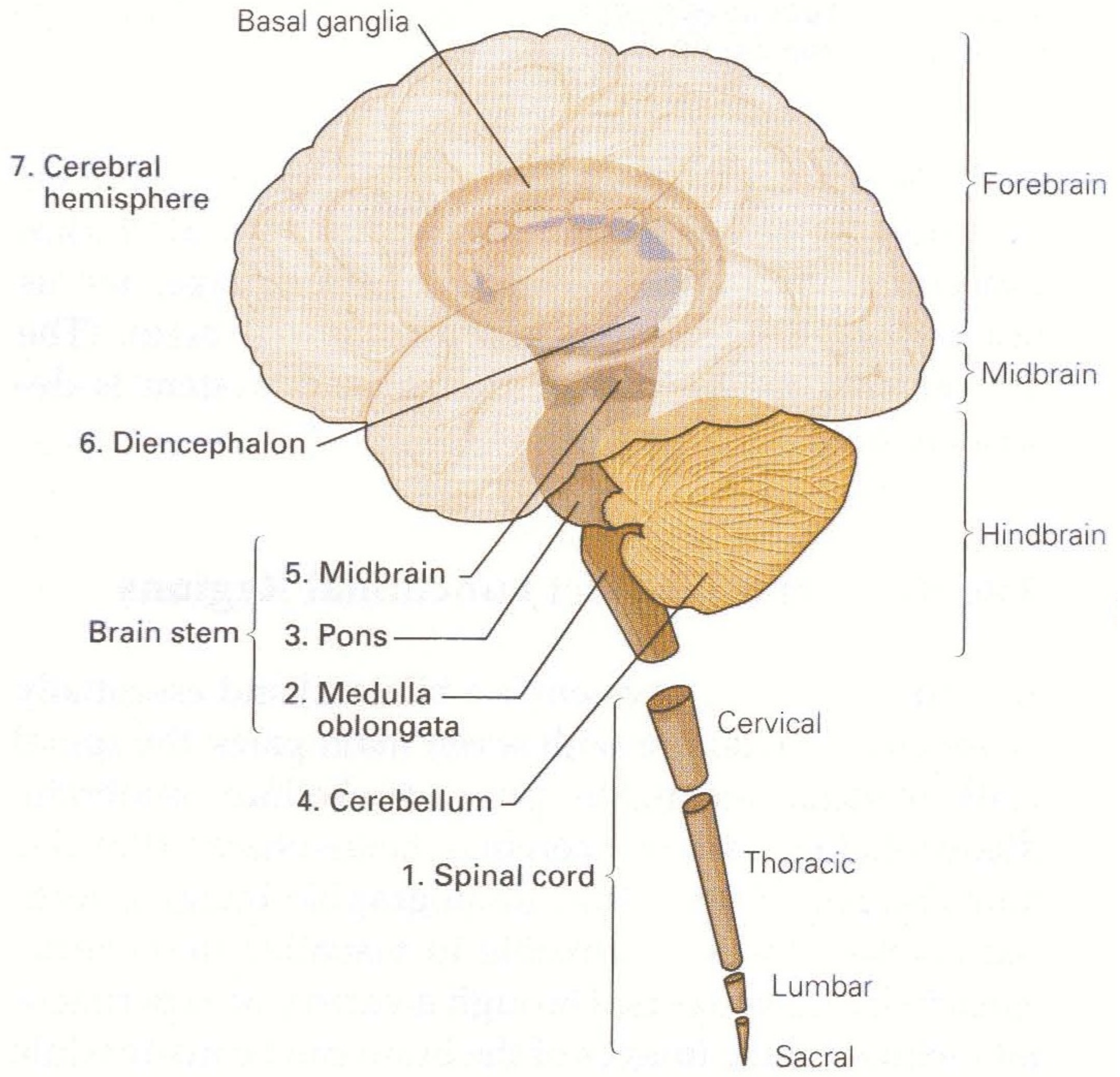


Figure 1-2A The central nervous system can be divided into seven main parts.

Cerebral Cortex

- Brain operations responsible for our cognitive abilities occur in the cerebral cortex.
- Cerebral cortex – “furrowed gray matter” covering the two cerebral hemispheres.
- Folds increase surface area: gyri (crests) and sulci (grooves)
- Four anatomically distinct lobes:
  • Frontal – planning future action and the control of movement
  • Parietal – somatic sensation, relationship between body and space
  • Temporal – hearing, learning, memory and emotion
  • Occipital – vision

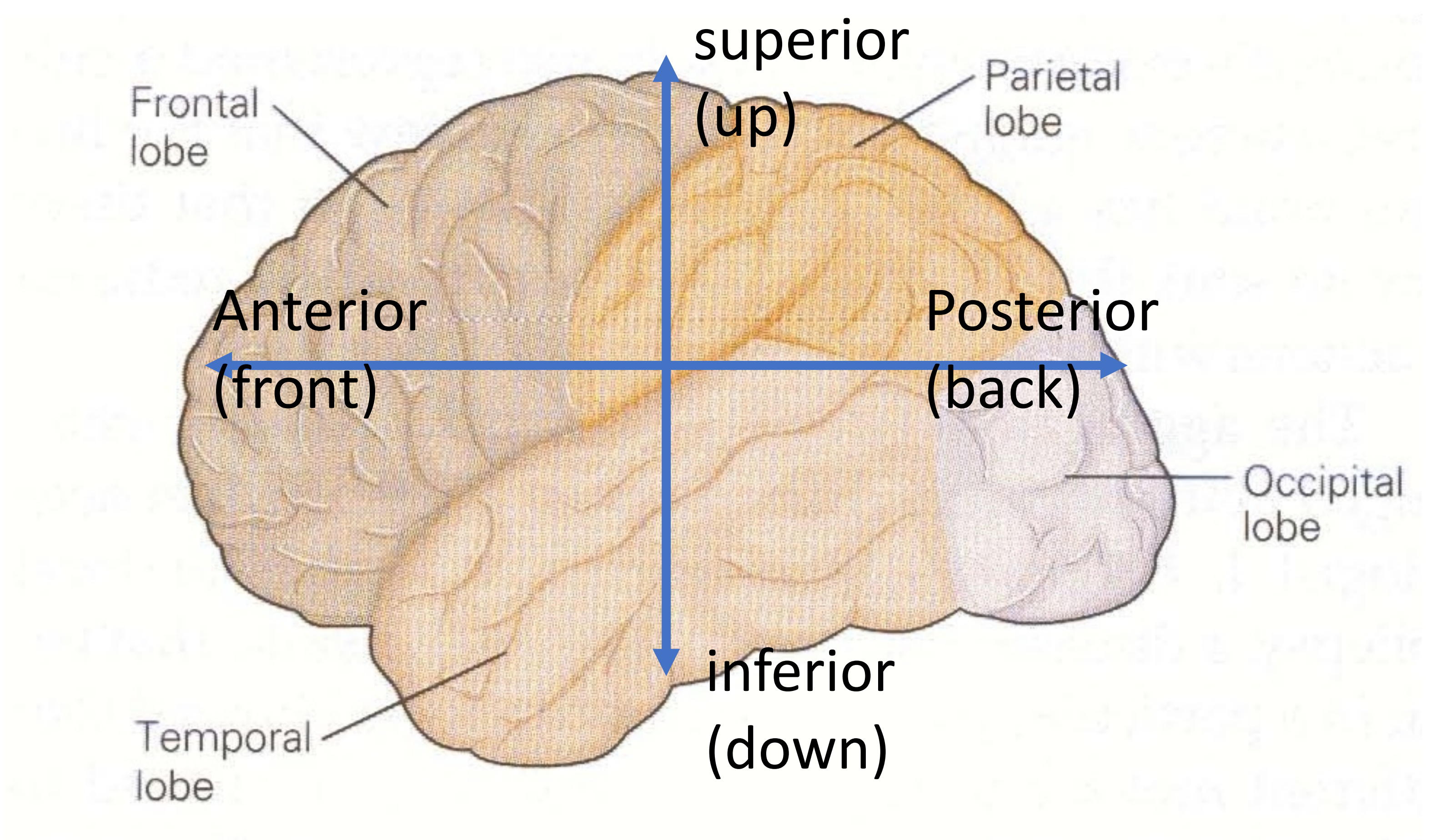
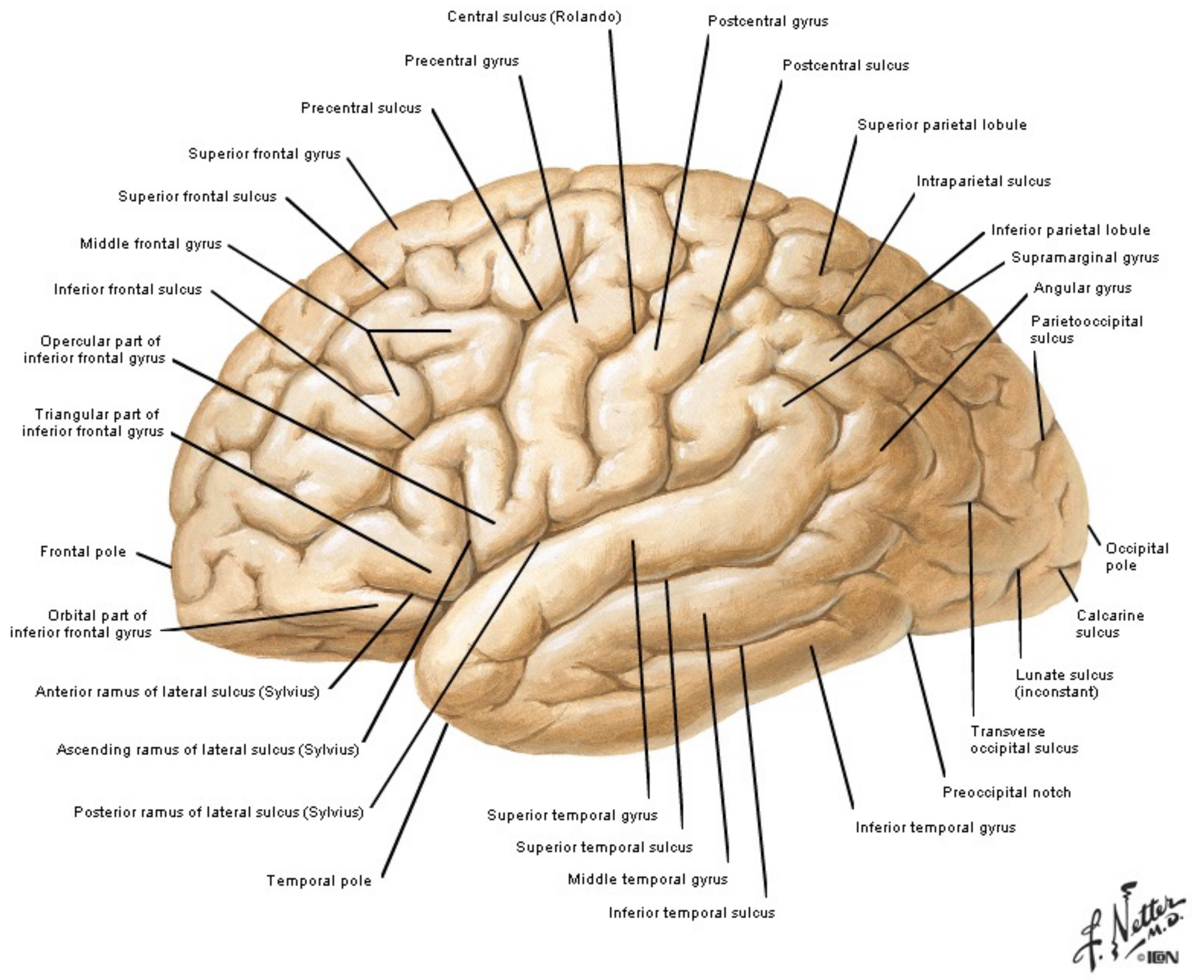


Figure 1-2B The four lobes of the cerebral cortex.



Topics

- Nerve cells
  - Glia and neurons
    - e.g. What are the major functions of glia cells?
- Divergence and convergence of neuronal connections
  - Key organizational features of the brain
    - How to build complex neural circuits?

Divergence (fan-out) & Convergence (fan-in)

- The previous circuit was greatly (overly) simplified.
- Sensory neurons often diverge – allows a single sensory neuron to exert wide and diverse influence.
- Motor neurons often receive converging inputs – allows a single motor neuron to integrate diverse information from many sources.

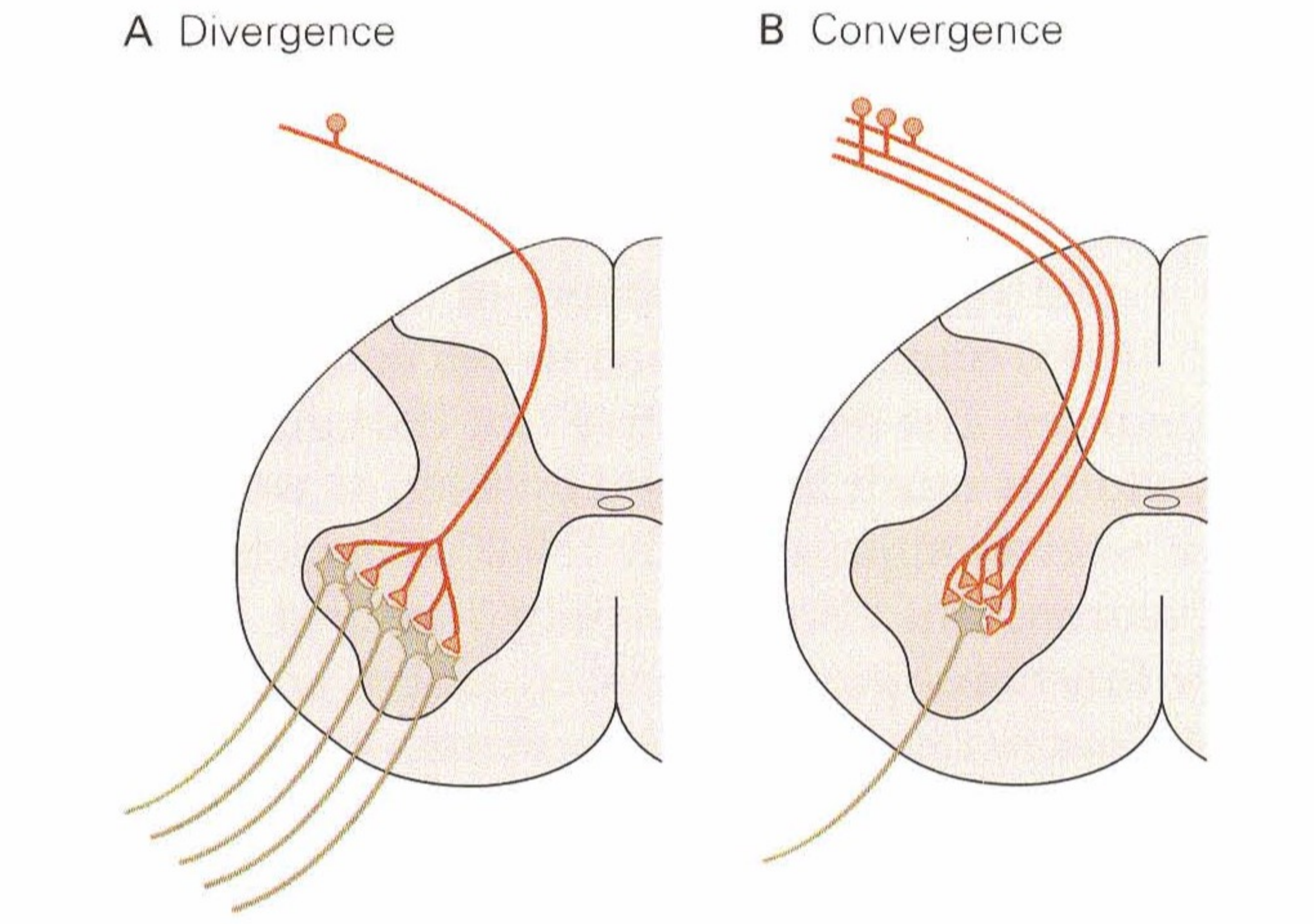


Figure 2-6 Diverging and converging neuronal connections are a key organizational feature of the brain.

A. In the sensory systems receptor neurons at the input stage usually branch out and make multiple, divergent connections with neurons that represent the second stage of processing. Subsequent connections diverge even more.

B. By contrast, motor neurons are the targets of progressively converging connections. With convergence, the target cell re-

Feed-forward & Feedback Inhibition

- The previous two circuits were still greatly (overly) simplified.
- Reciprocal feed-forward inhibition assures that extensor and flexor muscles are not simultaneously strongly activated.
- Negative feedback inhibition helps regulate drive signal.
- The BIG PICTURE here is that neural circuits can be quite complex and sophisticated.
- Intriguing to consider how they were “designed” and “built” – beyond the scope of this course.

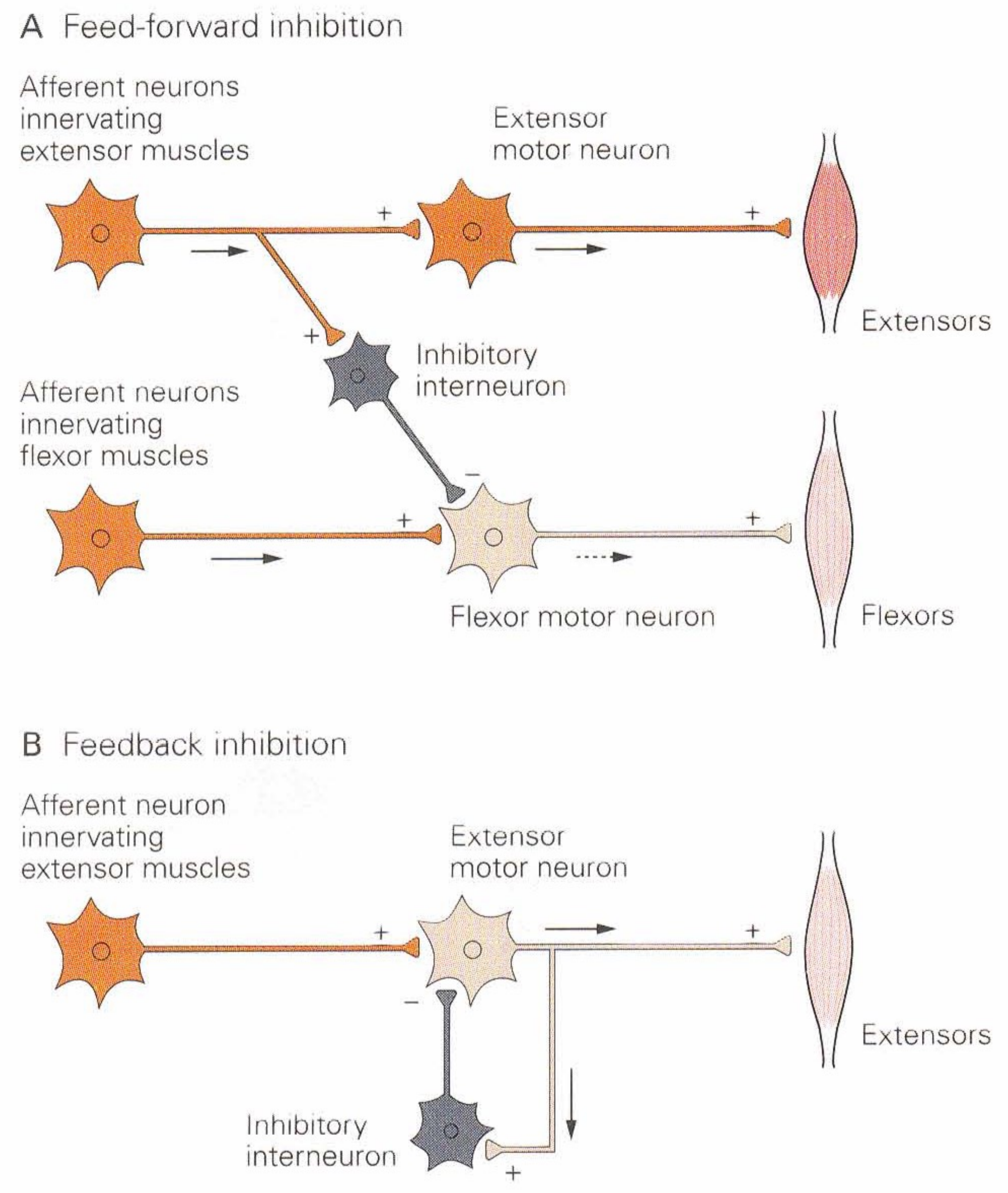


Figure 2-7 Inhibitory interneurons can produce either feed-forward or feedback inhibition.

Topics

- Membrane potential
  - Resting membrane potential: what are the contributing factors?
  - Nernst equation
    - e.g. Compute the resting state membrane potential using Nernst equation.
  - Na+ channels and K+ channels
    - e.g. which one mainly contributes to resting state potential?
  - Na-K pump
    - e.g. why does maintaining resting state potential consume energy?

Topics

- Action potentials
  - Properties of Na and K channels
    - e.g. Which one determines the rising edge of AP?
  - Short-term and long-term depolarization
    - e.g. what causes short-term depolarization?
  - Key features of action potentials
    - Refractory period
  - Ionic dynamics underlying action potentials

Hodgkin-Huxley Measurements & Model Explain APs

1) Depolarization event.
2) Na+ channels open fast (g_{Na} UP).
3) Inward Na^+ current.
4) Further depolarization.
5) Further Na^+ channels open.
6) Positive feedback continues...
7) $V_m \rightarrow E_{Na}$.
8) Na^+ channels inactivate (g_{Na} *DOWN*).
9) K^+ channels start opening (g_K *UP*).
10) Outward current decreases V_m.
11) $V_m \rightarrow E_K$. Hyperpolarizes beyond resting potential (*after potential*).
12) Absolute refractory period (due to Na^+ inactivation).
13) Relative refractory period (due to increased opening of K^+).

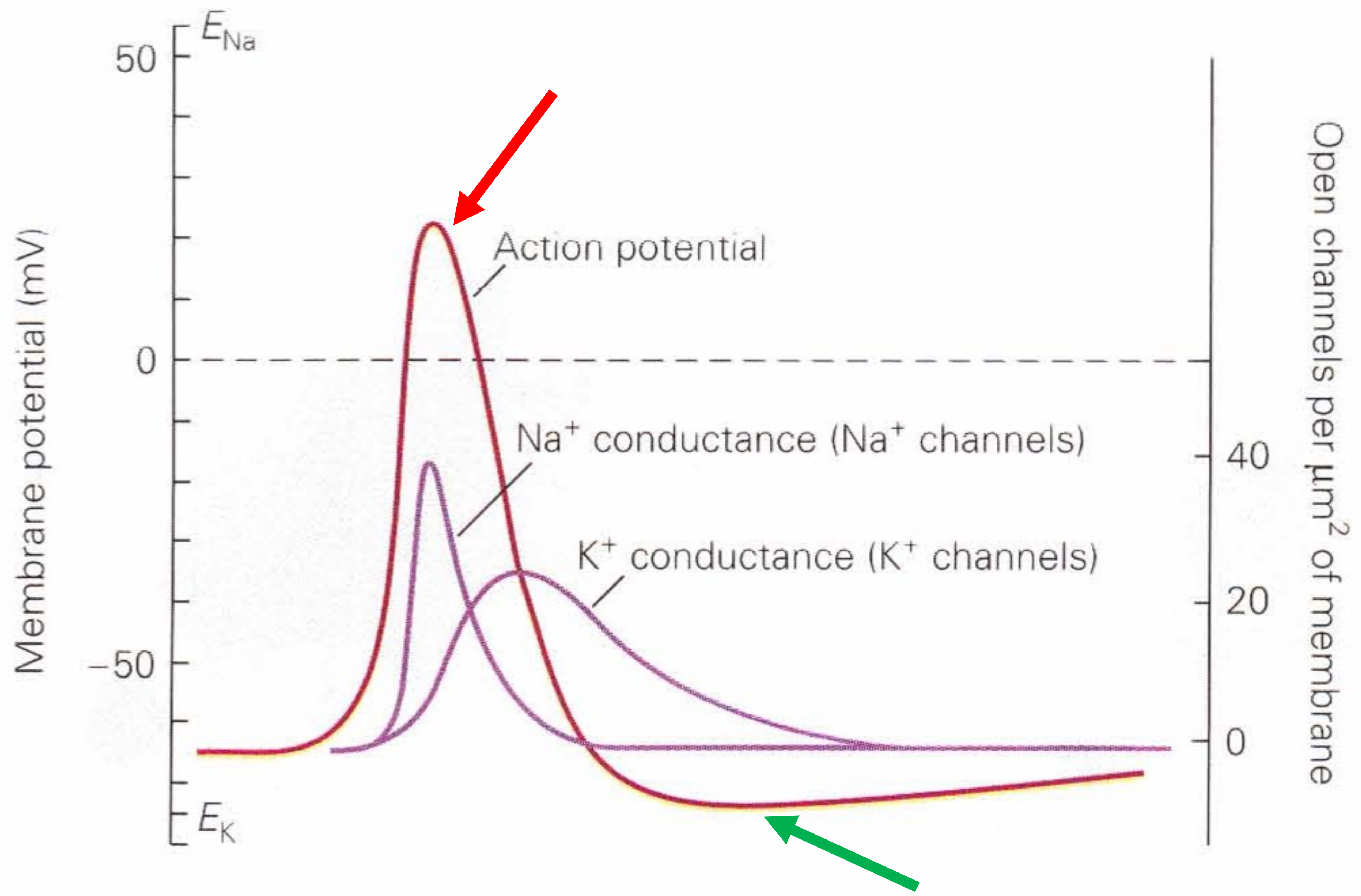
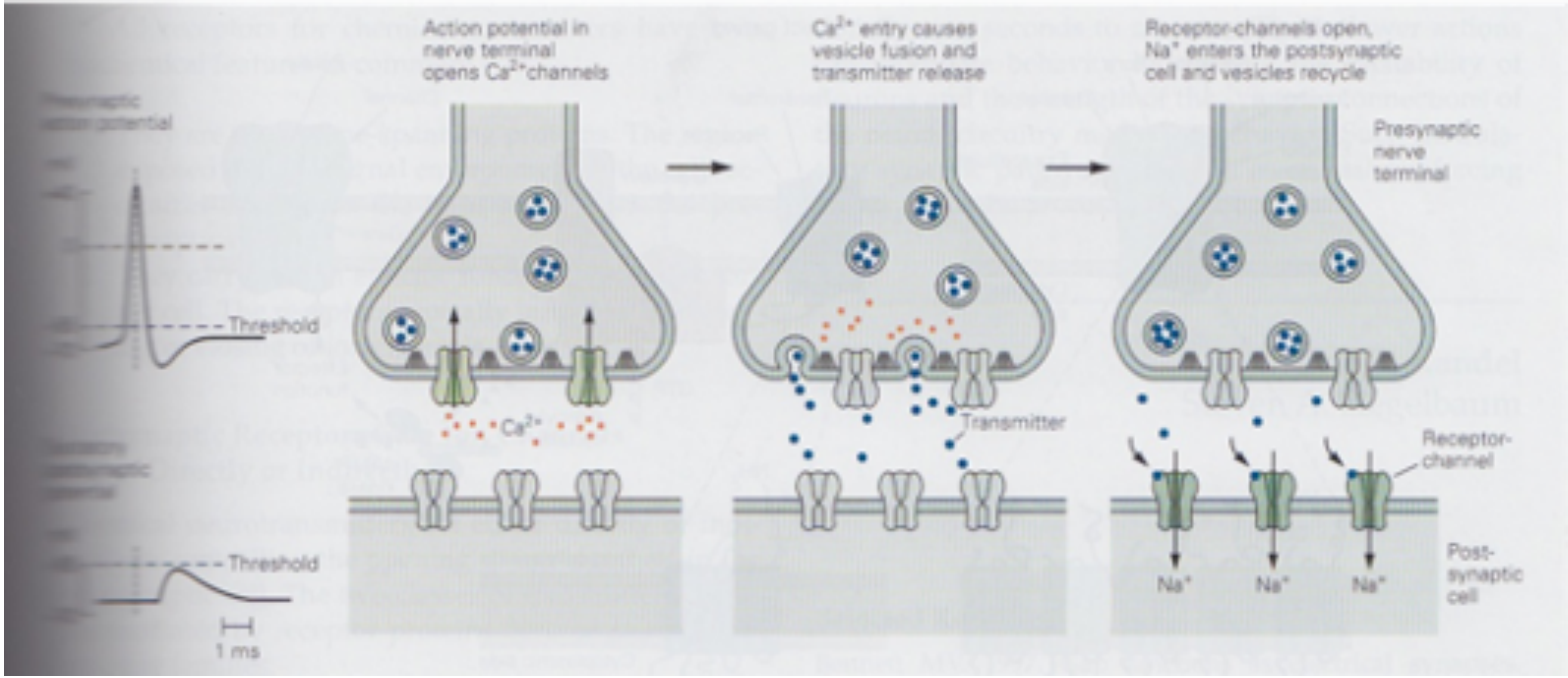


Figure 9-10 **The sequential opening of voltage-gated Na^+ and K^+ channels generates the action potential.** One of Hodgkin and Huxley's great achievements was to separate the total conductance change during an action potential, first detected by Cole and Curtis (see Figure 9-1) into separate components attributable to the opening of Na^+ and K^+ channels. The shape of the action potential and the underlying conductance changes can be calculated from the properties of the voltage-gated Na^+ and K^+ channels.

Topics

- Synaptic transmission and integration
  - Electrical and chemical synapses
    - <u>e.g. what’s the difference between the two?</u>
  - Synaptic transmission at chemical synapses
    - How does signal propagate from one neuron to another through synapse?
    - Temporal and spatial summations
  - Diversity of information transmission
    - Different neural transmitters
    - Different ion channel receptors, excitatory & inhibitory

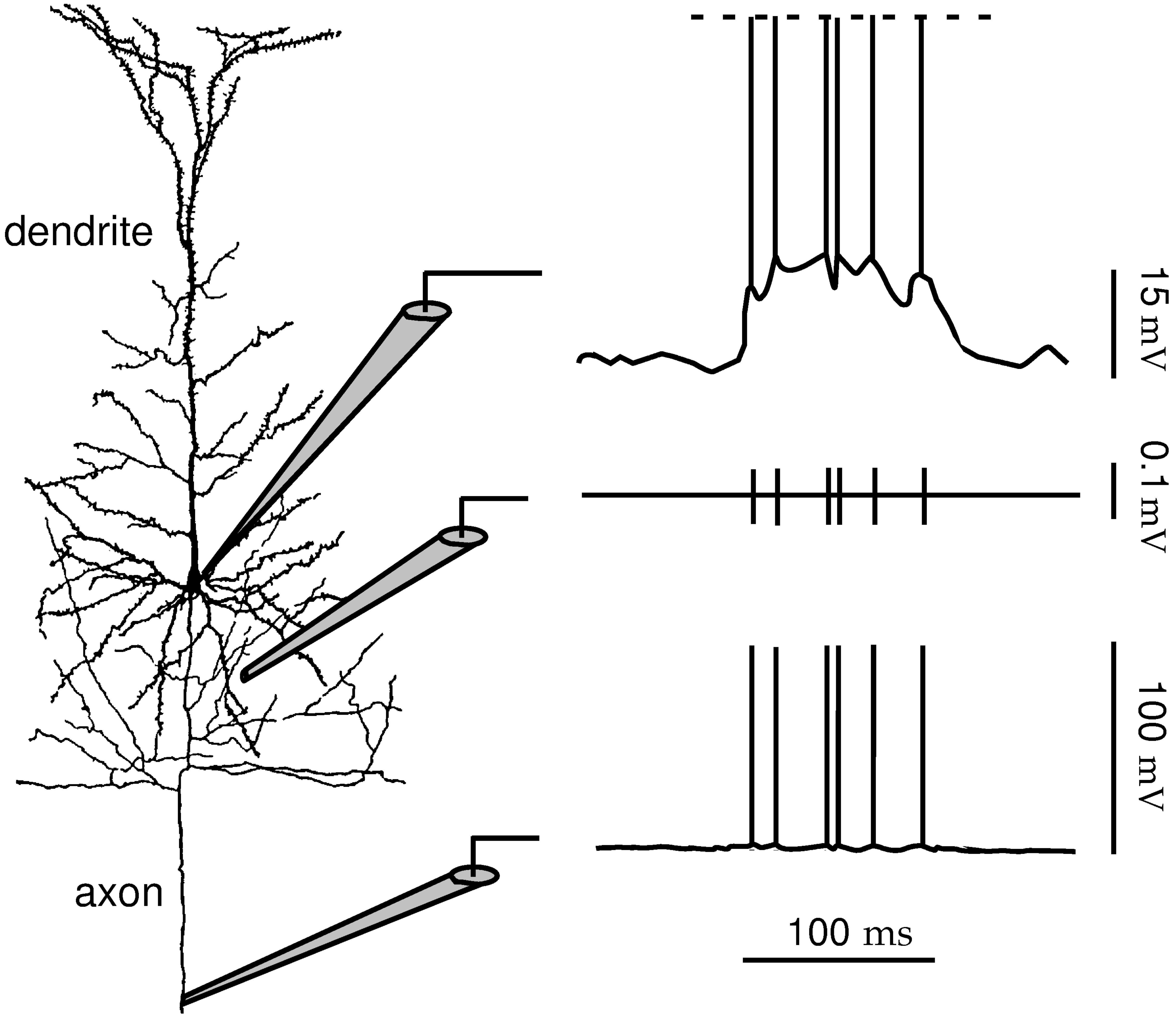


Action potential in nerve terminal opens Ca²⁺channels
Ca²⁺ entry causes vesicle fusion and transmitter release
Receptor-channels open, Na⁺ enters the postsynaptic cell and vesicles recycle
Presynaptic action potential
Threshold
Ca²⁺
Transmitter
Presynaptic nerve terminal
Receptor-channel
Na⁺
Na⁺
Na⁺
Post-synaptic cell
Threshold
1 ms

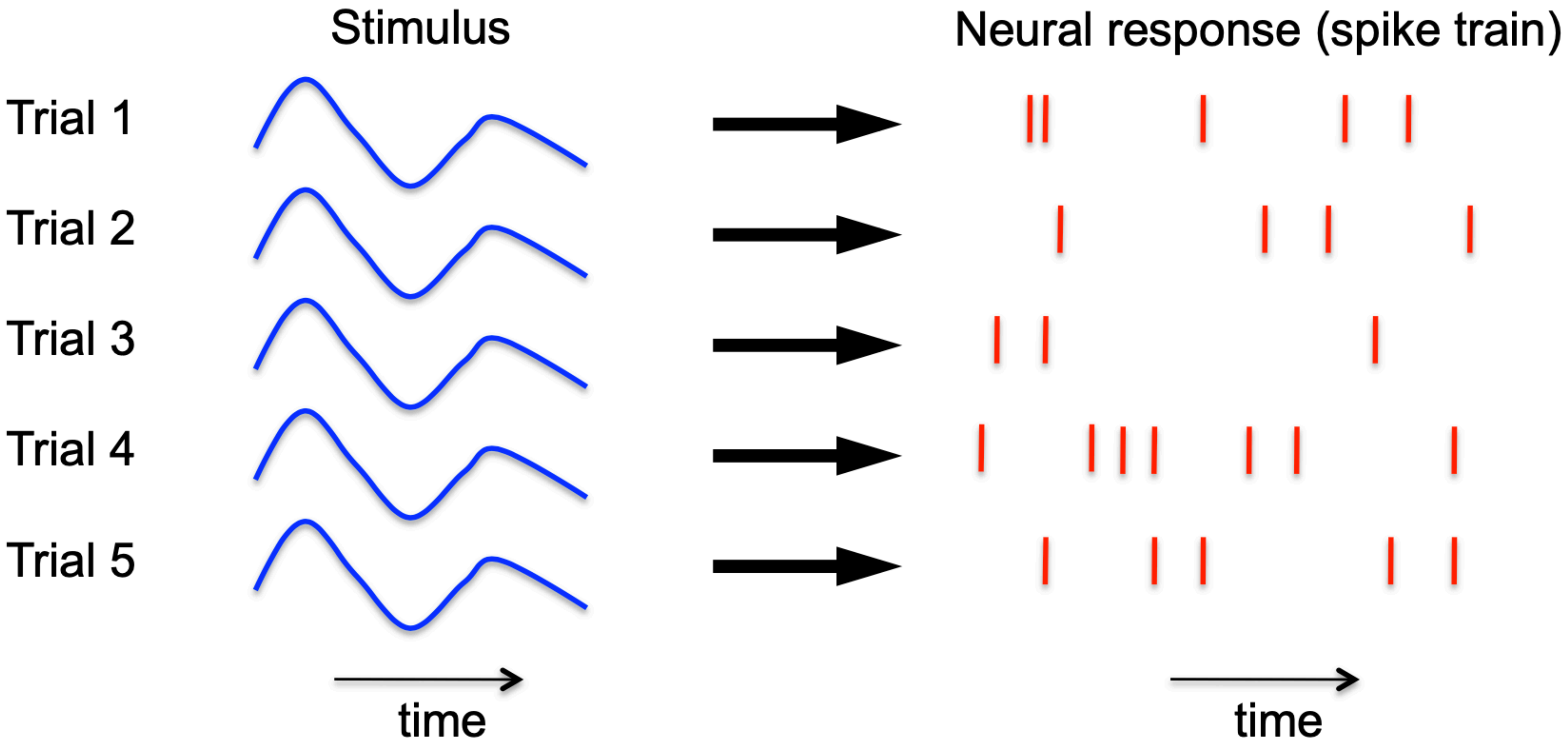
Topics

- Firing rates and spike statistics
  - Neuronal firing is probabilistic. How and Why?
  - What are spike trains?
  - What is firing rate?
  - Estimation of time-varying firing rates
  - Tuning curves
  - Spike-triggered average

Intra- & Extra-Cellular Recordings

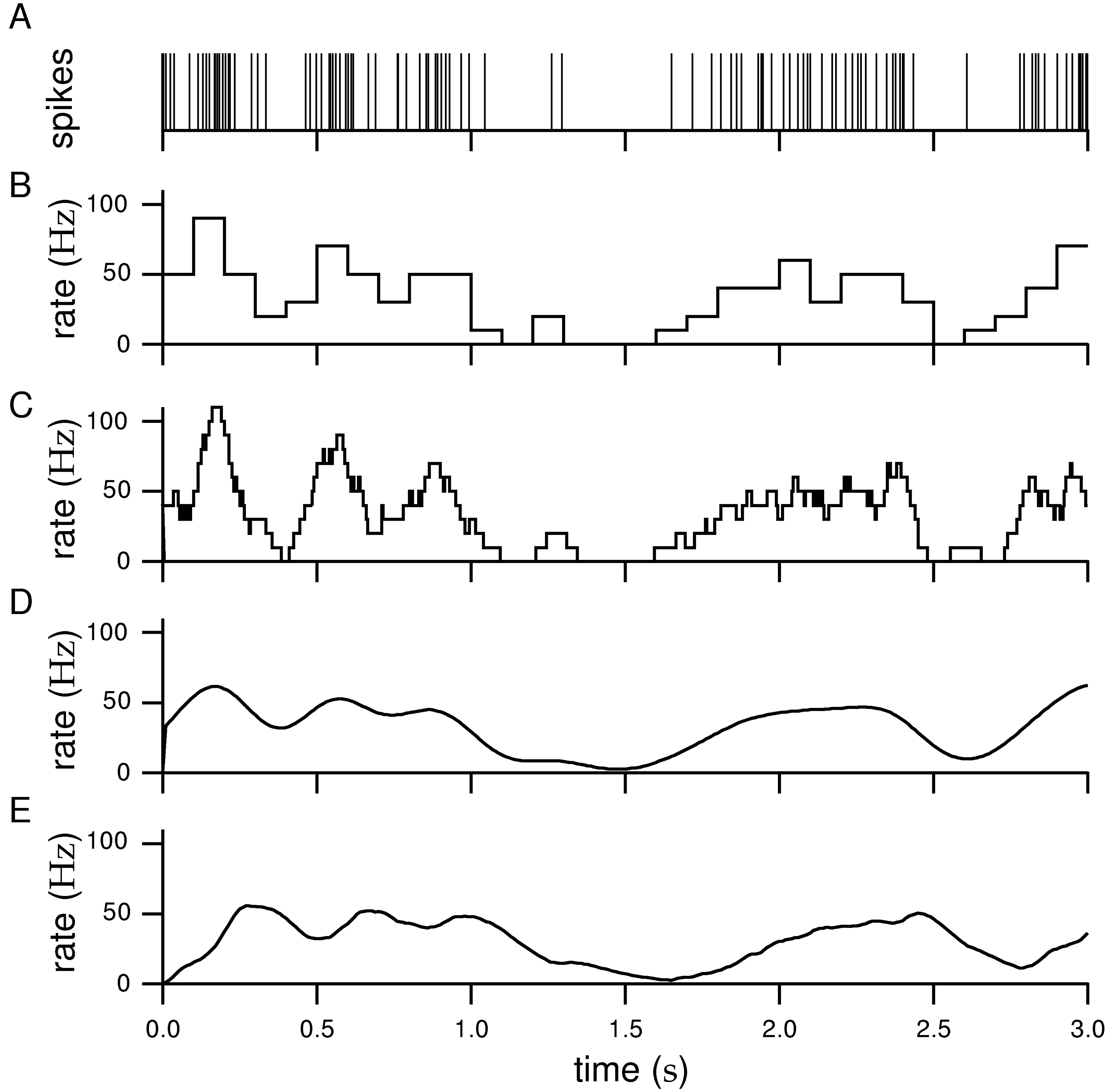


- Intra-cellular recording at soma (APs and subthreshold potentials).
- Extra-cellular recording near soma (APs, no subthreshold potentials).
- Intra-cellular recording in axon (APs, no subthreshold potentials).


Stimulus
Neural response (spike train)
Trial 1
Trial 2
Trial 3
Trial 4
Trial 5
time
time

Estimating Time-Varying Firing Rates

- There are many ways to approximate a time-varying firing rate from a spike train:



Raw spike train

Counts in 100 ms windows (non-overlapping)

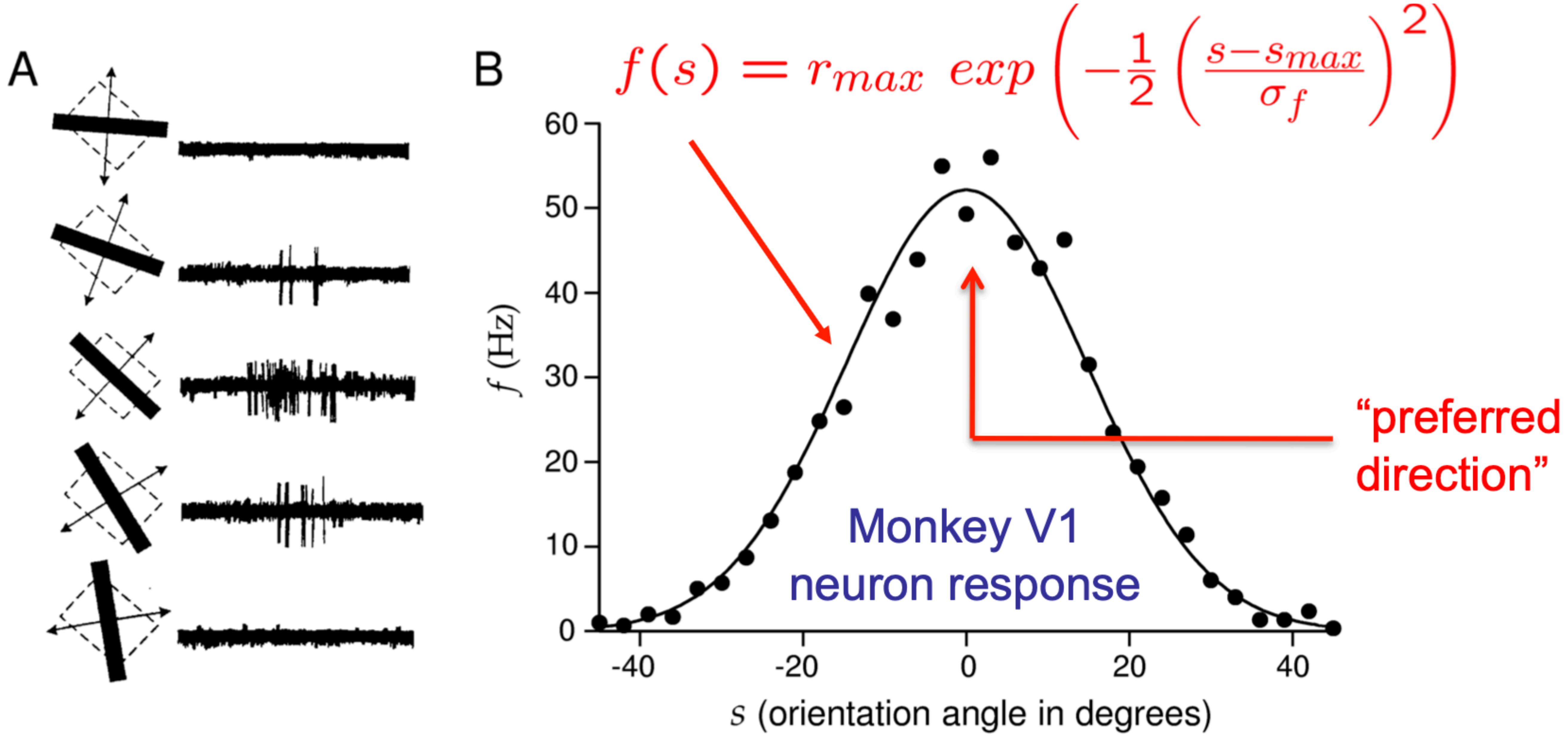
Counts in 100 ms windows (sliding)

Convolution with Gaussian

Convolution with one-sided exponential

Tuning Curves

- Neural responses typically depend on many different stimulus properties.
- Here we consider the dependence on just one stimulus attribute.
- Simple approach:
  - Count the number of spikes fired during the presentation of a stimulus.
  - Repeat stimulus presentation many times to better estimate the mean count.
  - Vary the stimulus attribute of interest, *s*.
  - Plot result and (optionally) fit parameterized function to data.



Topics

- Classification
  - What is classification?
  - Classifying using probabilistic generative model
    - Model: what's the formulation? What are the parameters?
    - Training and test phases: how to solve the MLE?
  - Hyperplanes and linear classifiers
    - Classifiers with linear decision boundaries
      - e.g. what is LDA? What's the objective function?
      - e.g. What is SVM? What's the objective function?

Topics

- Graphical models
  - What is a probabilistic graphical model?
  - What is conditional independence in PGM?
    - Examples shown in the lecture slides.
  - What is the PGM for generative models?
    - Classifier, GMM
  - Exponential family
    - What is the canonical form?
    - Examples: Bernoulli, multinomial, Gaussian, Poisson, gamma
  - Generalized linear models
    - Logistic regression
    - Linear regression
    - What are the link functions & distributions?

Generalized linear model: exponential family

- For a numeric random variable x:

$$p(x|\eta) = h(x)\exp\left\{\eta^T T(x) - A(\eta)\right\} = \frac{1}{Z(\eta)} h(x)\exp\left\{\eta^T T(x)\right\}$$

  Is an exponential family distribution with natural (canonical) parameter η

- Function $T(x)$ is a sufficient statistic
- Function $A(\eta) = \log Z(\eta)$ is the log normalizer
- Examples: Bernoulli, multinomial, Gaussian, Poisson, gamma

Generalized linear model: exponential family

- Example: multivariate Gaussian

$$p(x \mid \mu, \Sigma) = \frac{1}{(2\pi)^{k/2} |\Sigma|^{1/2}} \exp\left\{ -\frac{1}{2}(x-\mu)^T \Sigma^{-1} (x-\mu) \right\}$$

$$= \frac{1}{(2\pi)^{k/2}} \exp\left\{ -\frac{1}{2}\mathrm{Tr}(\Sigma^{-1} x x^T) + \mu^T \Sigma^{-1} x - \frac{1}{2}\mu^T \Sigma^{-1} \mu - \log |\Sigma| \right\}$$

- Exponential family representation:

$$\eta = \left[\Sigma^{-1}\mu; -\frac{1}{2}\mathrm{vec}(\Sigma)^{-1} \right] = [\eta_1, \mathrm{vec}(\eta_2)], \quad \eta_1 = \Sigma^{-1}\mu, \eta_2 = -\frac{1}{2}\Sigma^{-1}$$

$$T(x) = [x; \mathrm{vec}(xx^T)]$$

$$A(\eta) = \frac{1}{2}\mu^T \Sigma^{-1} \mu + \log |\Sigma| = -\frac{1}{2}\mathrm{Tr}(\eta_2 \eta_1 \eta_1^T) - \frac{1}{2}\log(-2\eta_2)$$

$$h(x) = (2\pi)^{-k/2}$$

Generalized linear model: exponential family

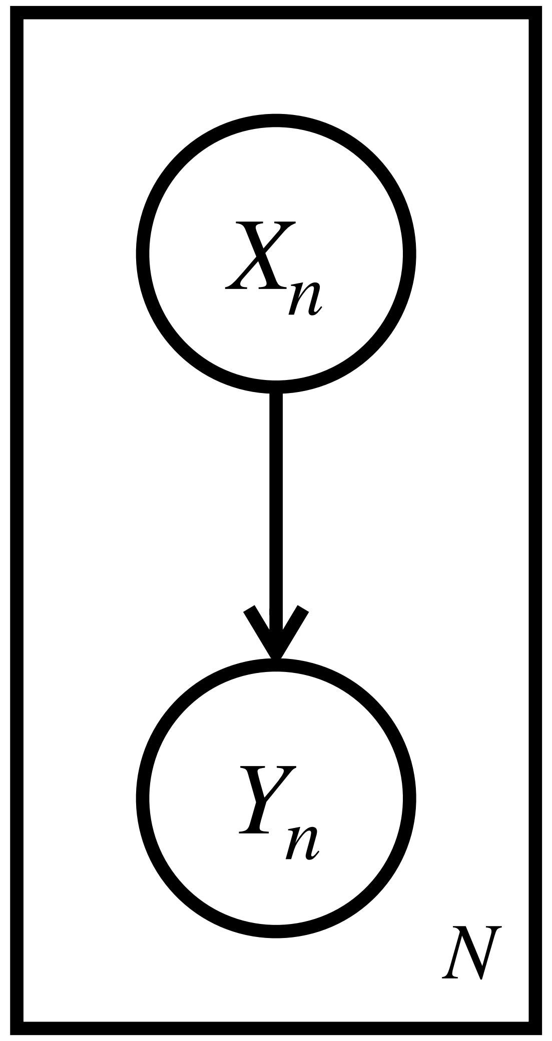
- Example: Poisson distribution

$$P(x|\lambda) = \frac{\lambda^x}{x!}\exp\{-\lambda\}$$
$$= \frac{1}{x!}\exp\{x\log\lambda - \lambda\}$$

- Exponential family representation:

$$\eta = \log\lambda$$
$$T(x) = x$$
$$A(\eta) = \lambda = e^{\eta}$$
$$h(x) = \frac{1}{x!}$$

Generalized Linear Models (GLMs)



- The graphical model
  - Linear regression: what is the graphical model?
  - Discriminative linear classification (logistic regression): what is the graphical model?
  - Commonality:
    - model $\mathbb{E}_p(Y) = \mu = f(\theta^T X)$
    - What is $p()$? The conditional distribution of Y
    - What is $f()$? The response function
- GLM
  - The observed input x is assumed to enter into the model via a linear combination of its elements $\xi = \theta^T x$
  - The conditional mean μ is represented as a function $f(\xi)$ of ξ, where f is known as the response function
  - The observed output y is assumed to be characterized by an exponential family distribution with conditional mean μ

Topics

- Spike sorting
  - What is spike sorting?
  - Why do we need spike sorting?
  - Spike sorting algorithms
- Clustering
  - Definition
  - Goal
  - What’s the difference between clustering and classification?
  - K-means Algorithm
    - How does it work?
    - How to choose K?
  - Gaussian mixtures
    - How does it work?
    - Relationship between K-means and GMM

Topics

- EM algorithm
  - What is the likelihood decomposition? Graphic demonstration.
  - What are the two steps?
    - What is the E-step?
    - What is the M-step?

Topics

- Principal component analysis
- What is the mathematical formulation?
- How to find the solution?
- What are the principal components representing?