The Abdus Salam
International Centre
for Theoretical Physics
50th Anniversary 1964-2014

2584-17

Spring College on the Physics of Complex Systems

26 May - 20 June, 2014

Theoretical Neuroscience
Lectures 1-5

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Northwestern University
USA

Theoretical Neuroscience

ICTP, Trieste, June 2014

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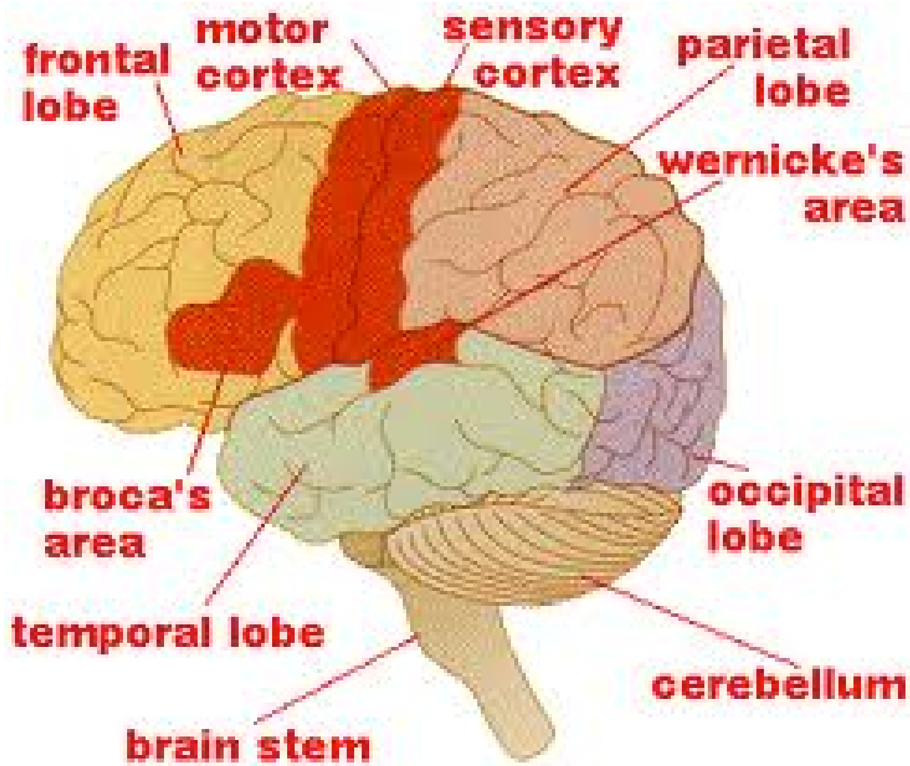
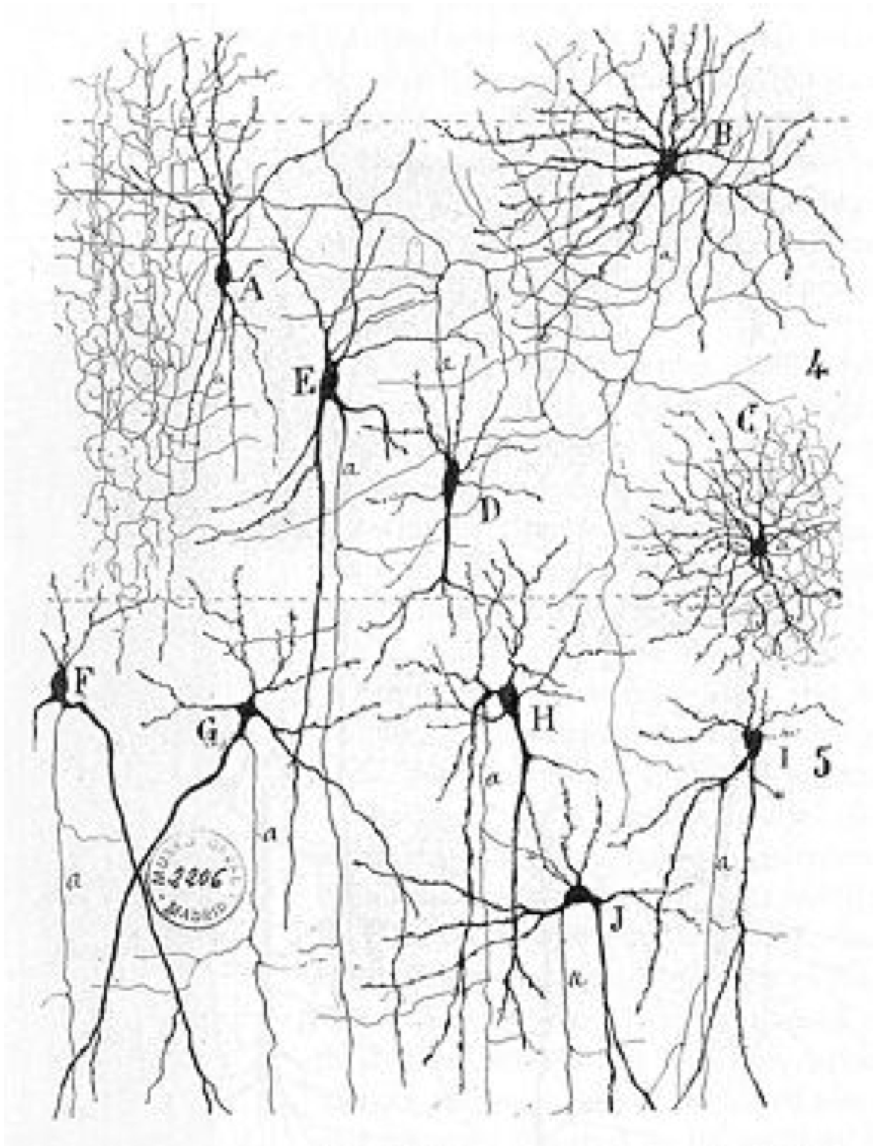
The human brain

The human brain

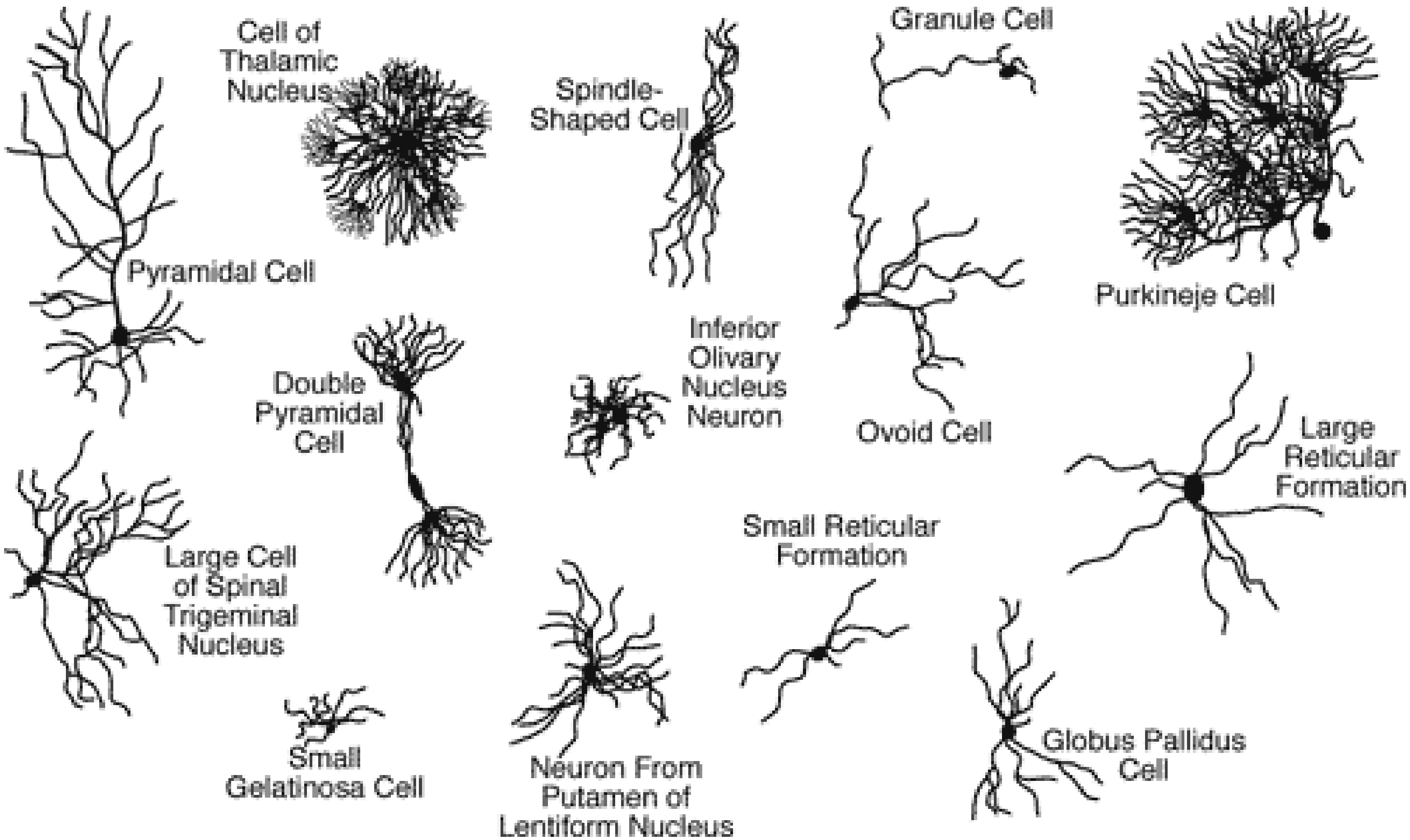


Neurons

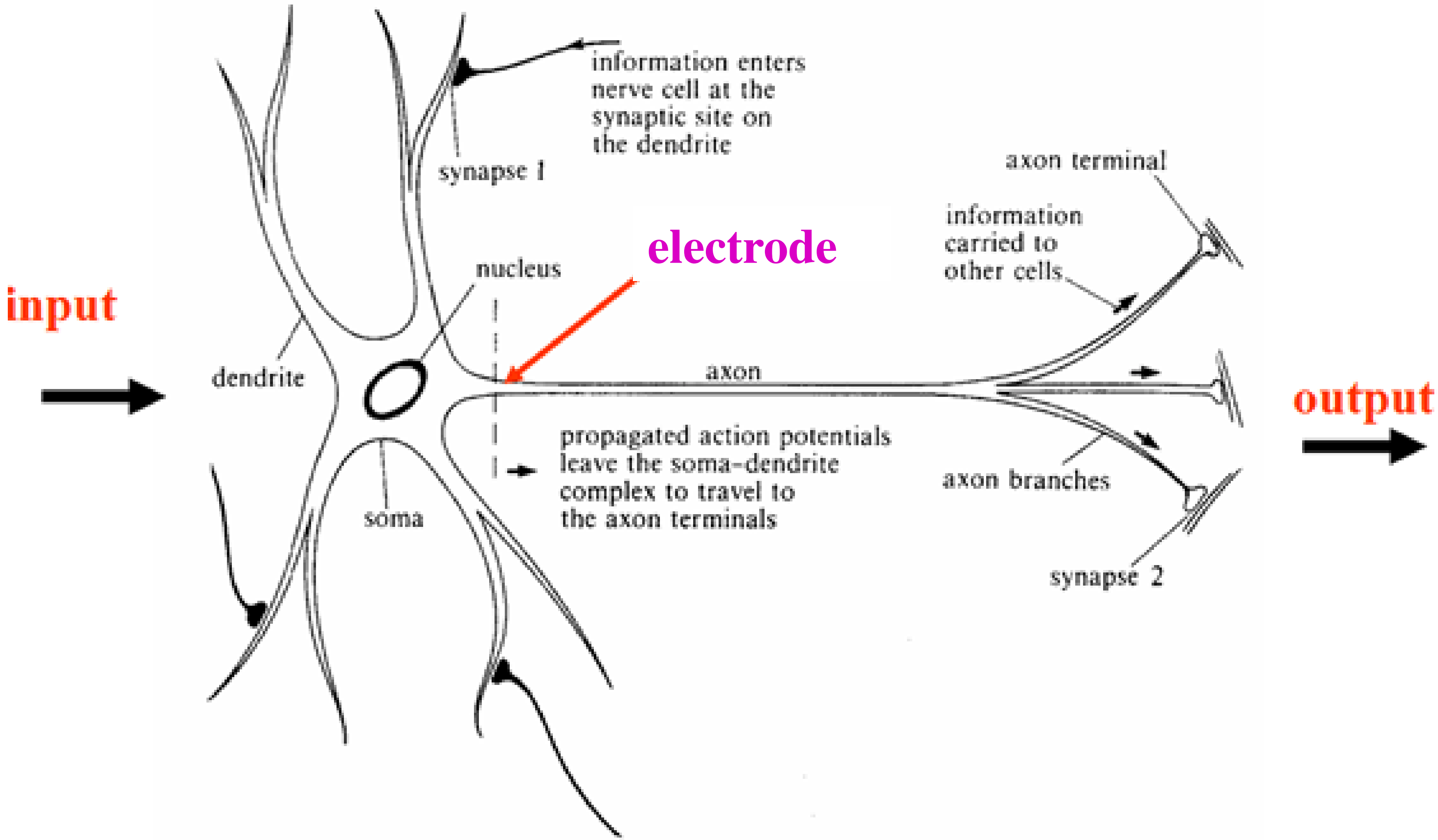
About 85 billion neurons, of which about 15 billion are in the cortex.



Neurons

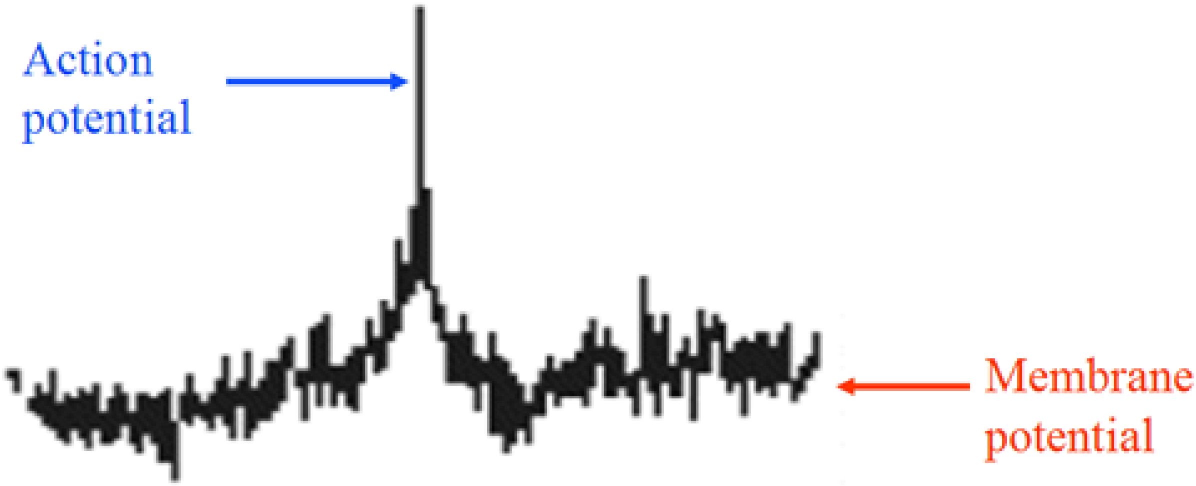

Cell of Thalamic Nucleus
Spindle-Shaped Cell
Granule Cell
Pyramidal Cell
Purkineje Cell
Inferior Olivary Nucleus Neuron
Double Pyramidal Cell
Ovoid Cell
Large Reticular Formation
Small Reticular Formation
Large Cell of Spinal Trigeminal Nucleus
Small Gelatinosa Cell
Neuron From Putamen of Lentiform Nucleus
Globus Pallidus Cell

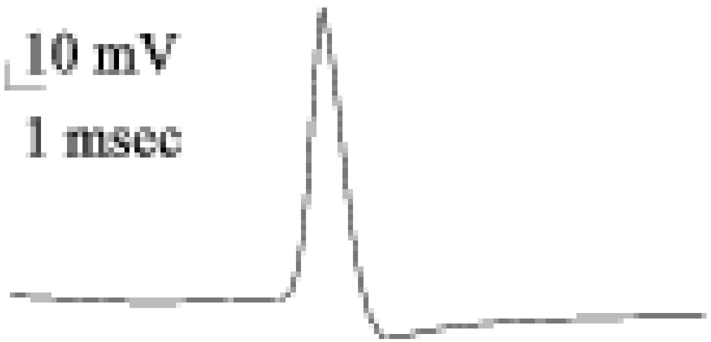
Neurons

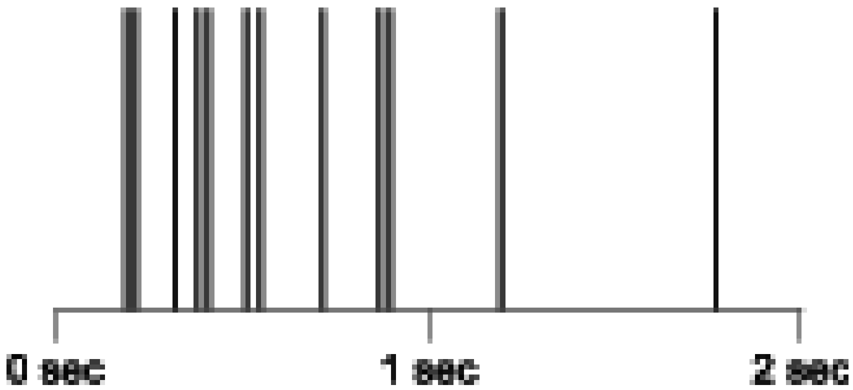


input
output
electrode
information enters nerve cell at the synaptic site on the dendrite
synapse 1
nucleus
dendrite
soma
axon
axon terminal
information carried to other cells
propagated action potentials leave the soma-dendrite complex to travel to the axon terminals
axon branches
synapse 2

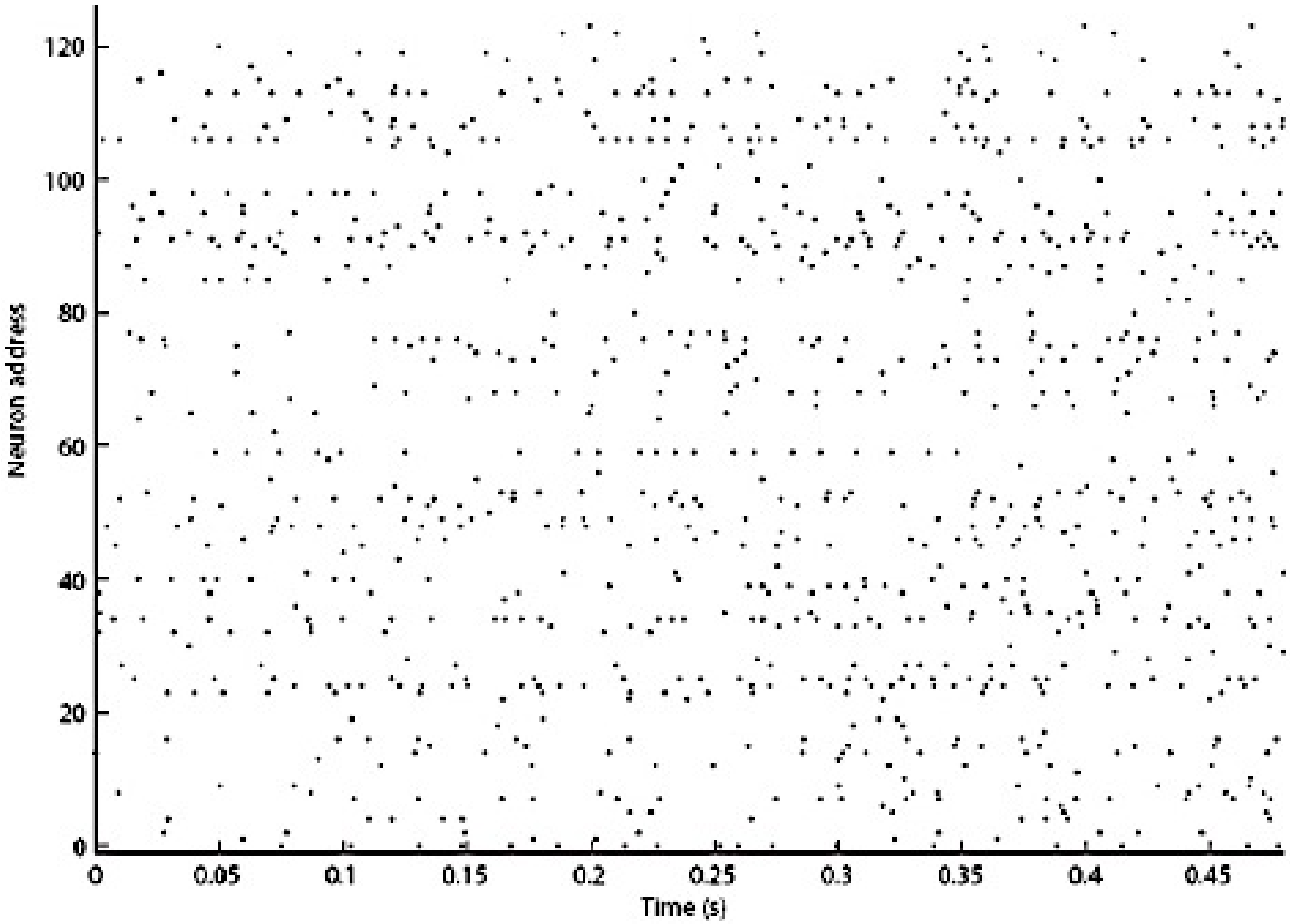
Spikes: action potentials



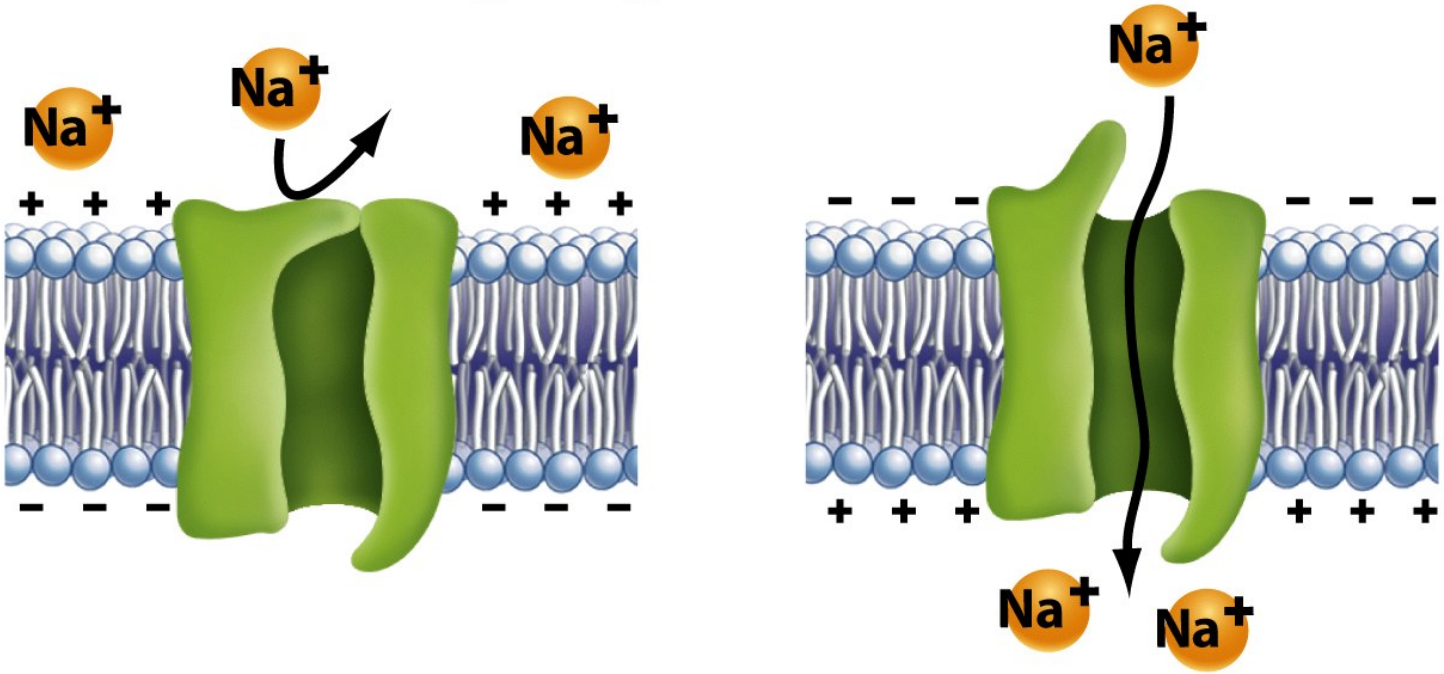




From single neurons to multiple neurons



Voltage gated ion channels

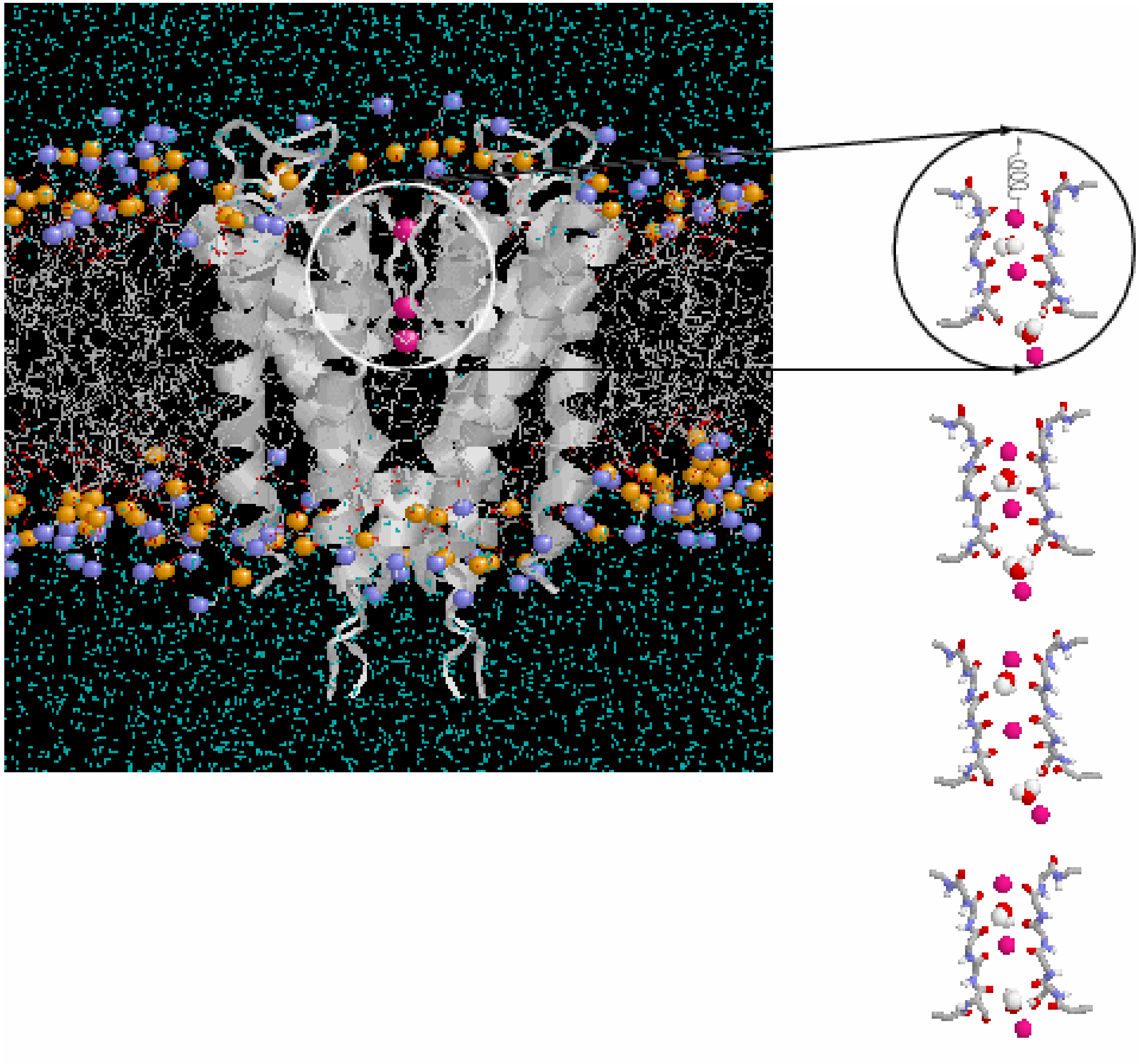


At the resting potential, voltage-gated Na^+ channels are closed.

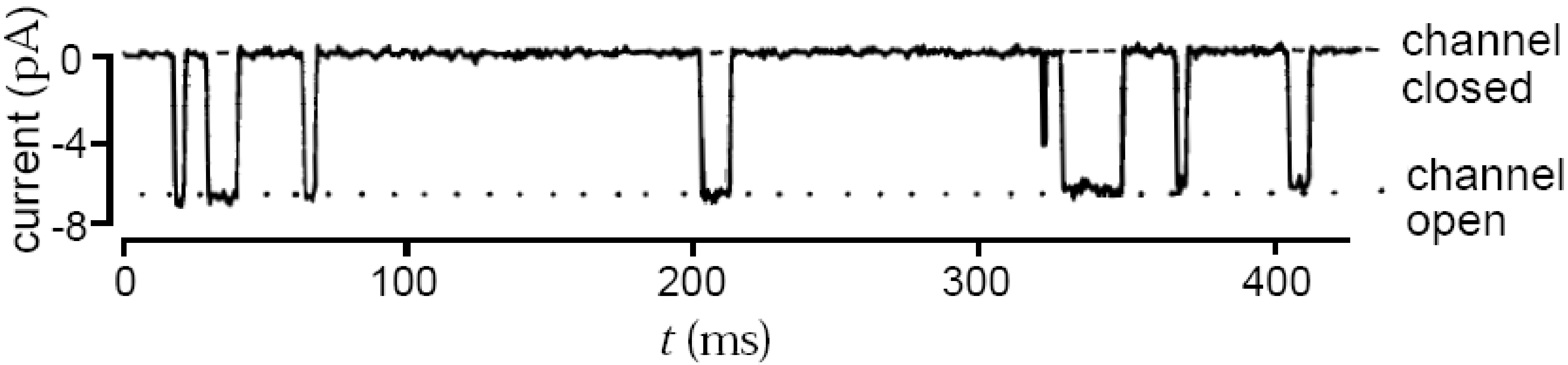
When the membrane is depolarized, conformational changes open the voltage-gated channel.

Figure 45-8c Biological Science, 2/e

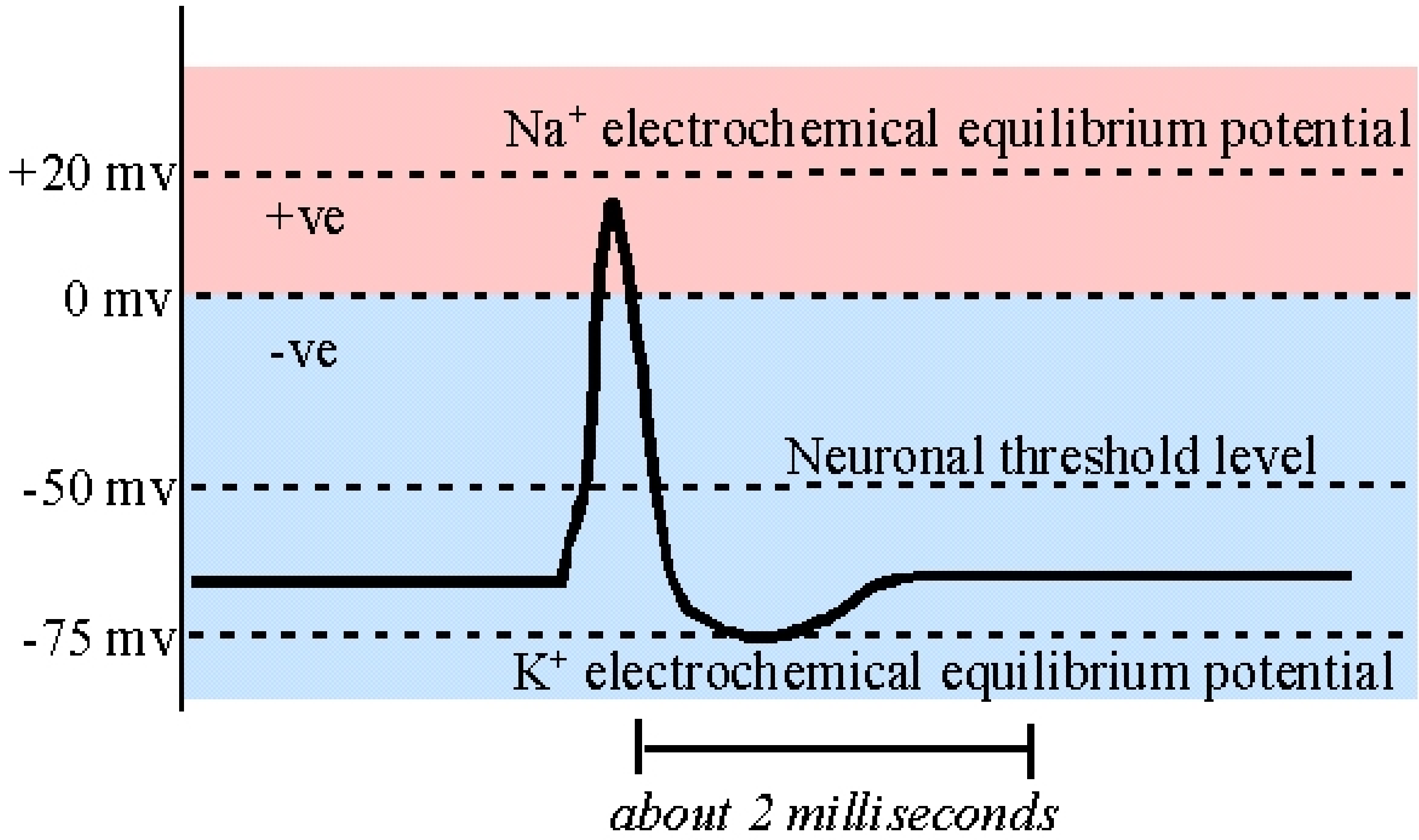
Morphology of ion channels



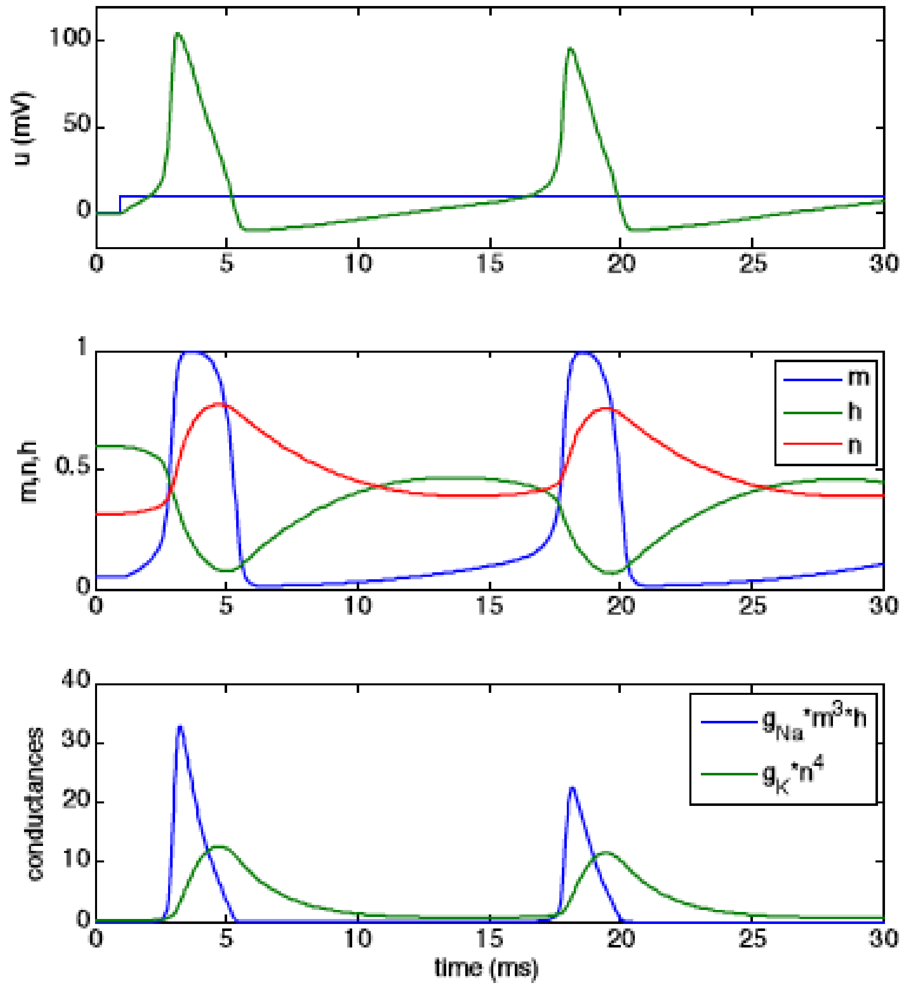
Ion channels



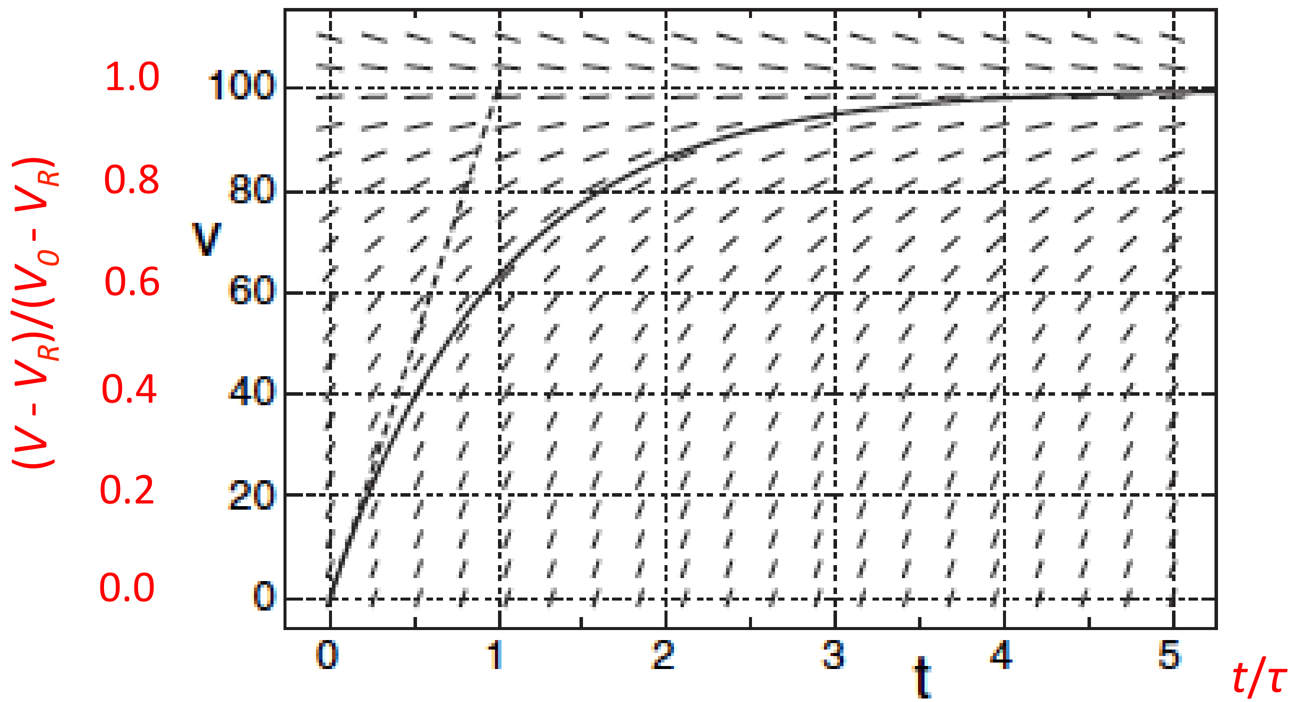
Generation of action potential



Hodgkin-Huxley model of action potential



Integrate-and-Fire Neuron (IFN): constant I_e



$$V_R = 0 \quad V_0 = 100\,\text{mv} \quad \tau = 1\,\text{ms}$$

labels in red: dimensionless quantities

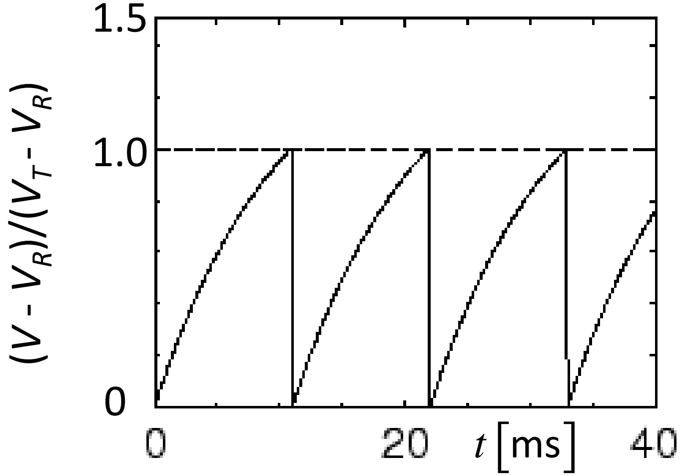
Courtesy of Bill Kath, Northwestern U.

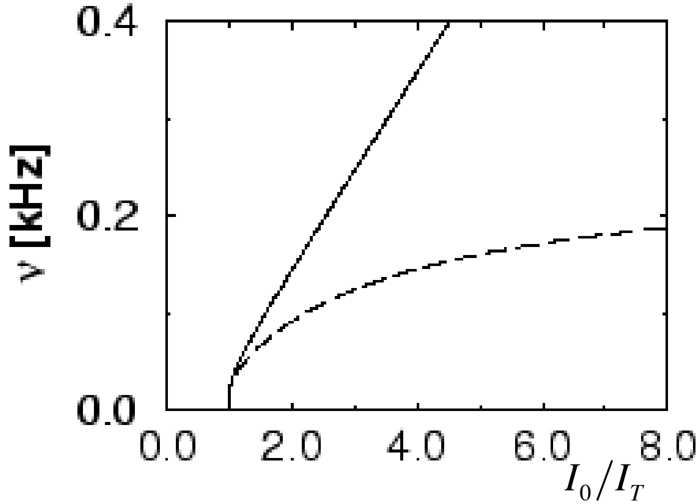
Integrate-and-Fire Neuron (IFN): constant I_e

$$V - V_R = \left(V_0 - V_R\right)\left(1 - e^{-\left(\frac{t}{\tau}\right)}\right)$$

$$V_0 = R\,I_e + V_R > V_T$$

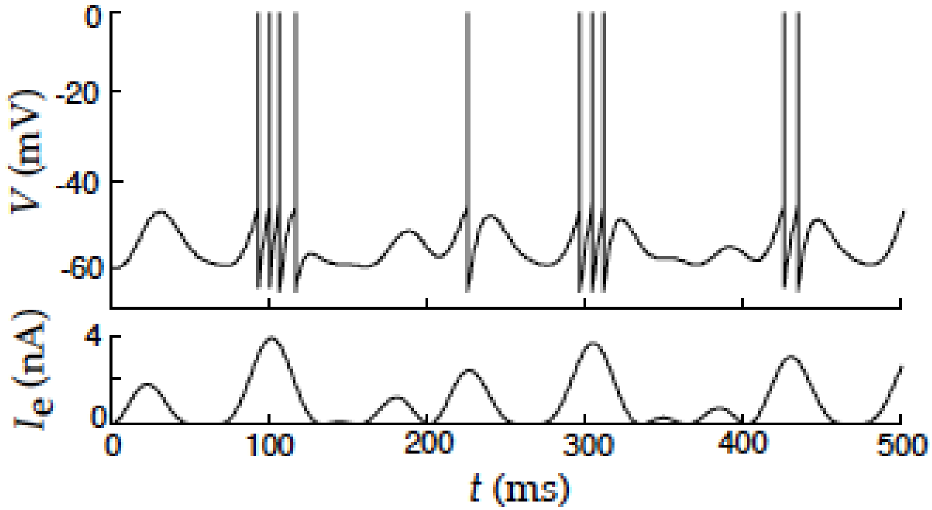
$$\left(V - V_R\right)/\left(V_0 - V_R\right) = 1 - e^{-\left(\frac{t}{\tau}\right)}$$





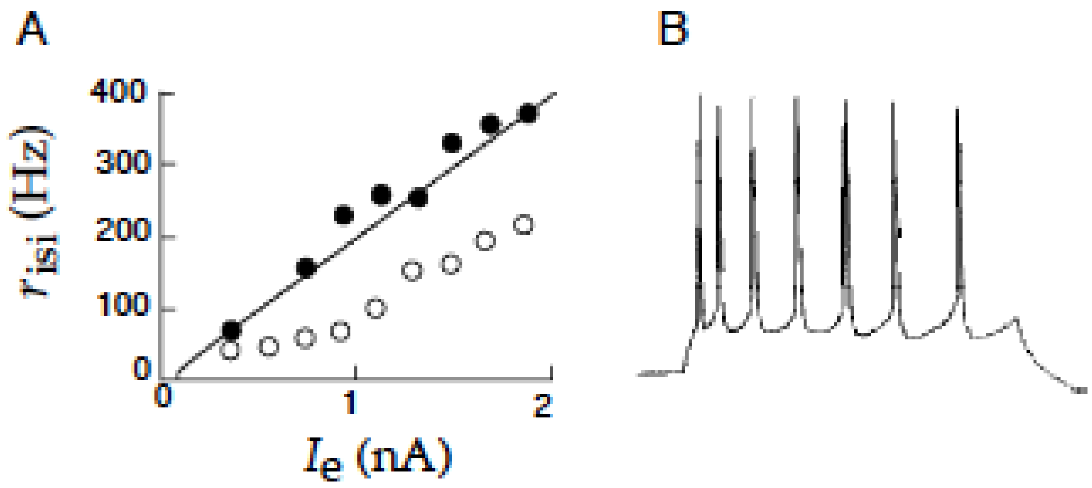
$$\left(V_0 - V_R\right) = 1.5\left(V_T - V_R\right) \qquad \tau = 10\,\mathrm{ms}$$

Integrate-and-Fire Neuron (IFN): $I_e(t)$



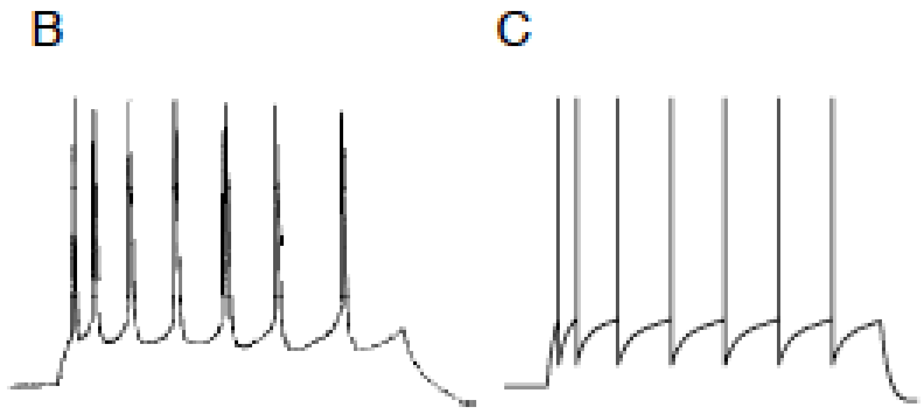
$$V_R = E_L = -65mV \quad E_T = -50mV \quad \tau_m = 10ms \quad R_m = 10M\Omega$$

Spike adaptation



$$V_R = E_L = -65mV \quad E_T = -50mV \quad \tau_m = 30ms \quad R_m = 90M\Omega$$

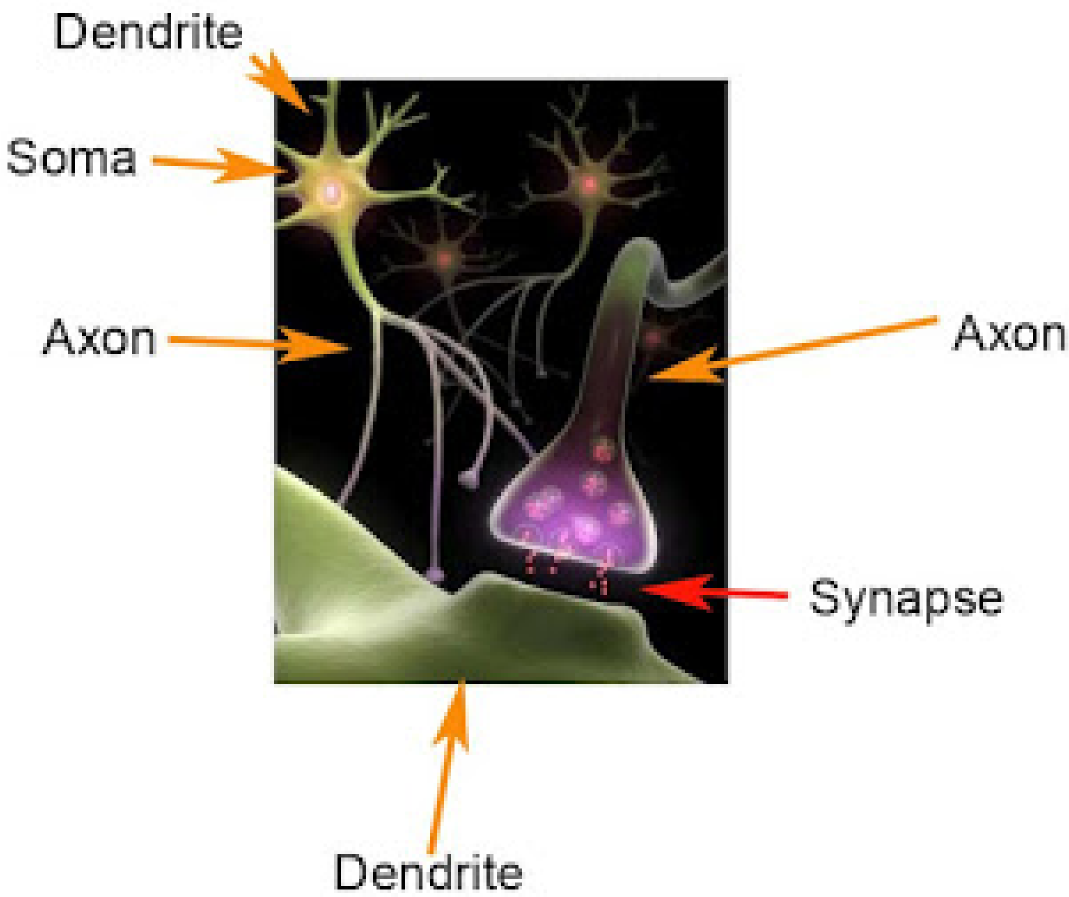
Spike adaptation



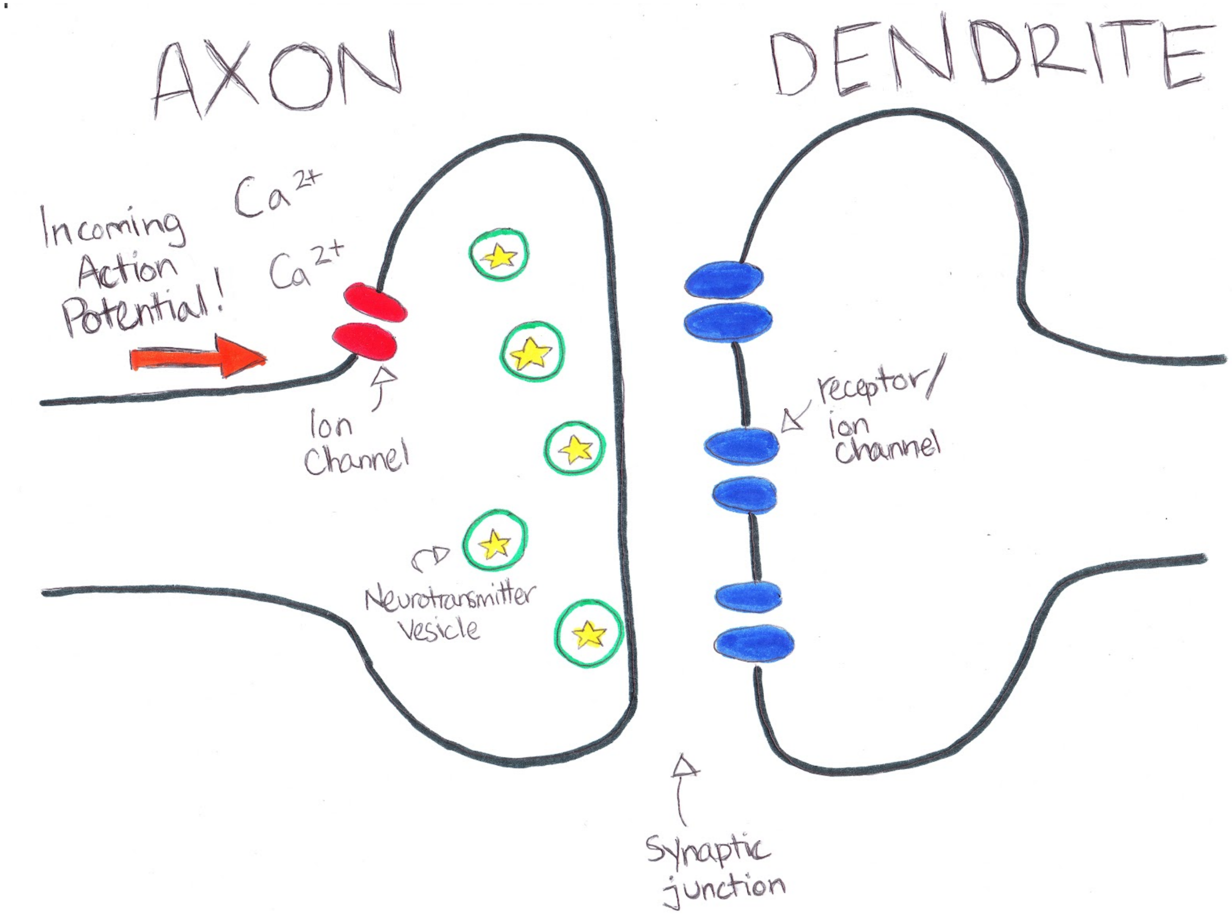
$$V_R = E_L = -65mV \quad E_T = -50mV \quad \tau_m = 30ms \quad R_m = 90M\Omega$$

$$r_m \Delta_{sa} = 0.06 \quad \tau_{sa} = 100ms \quad E_K = -70m$$

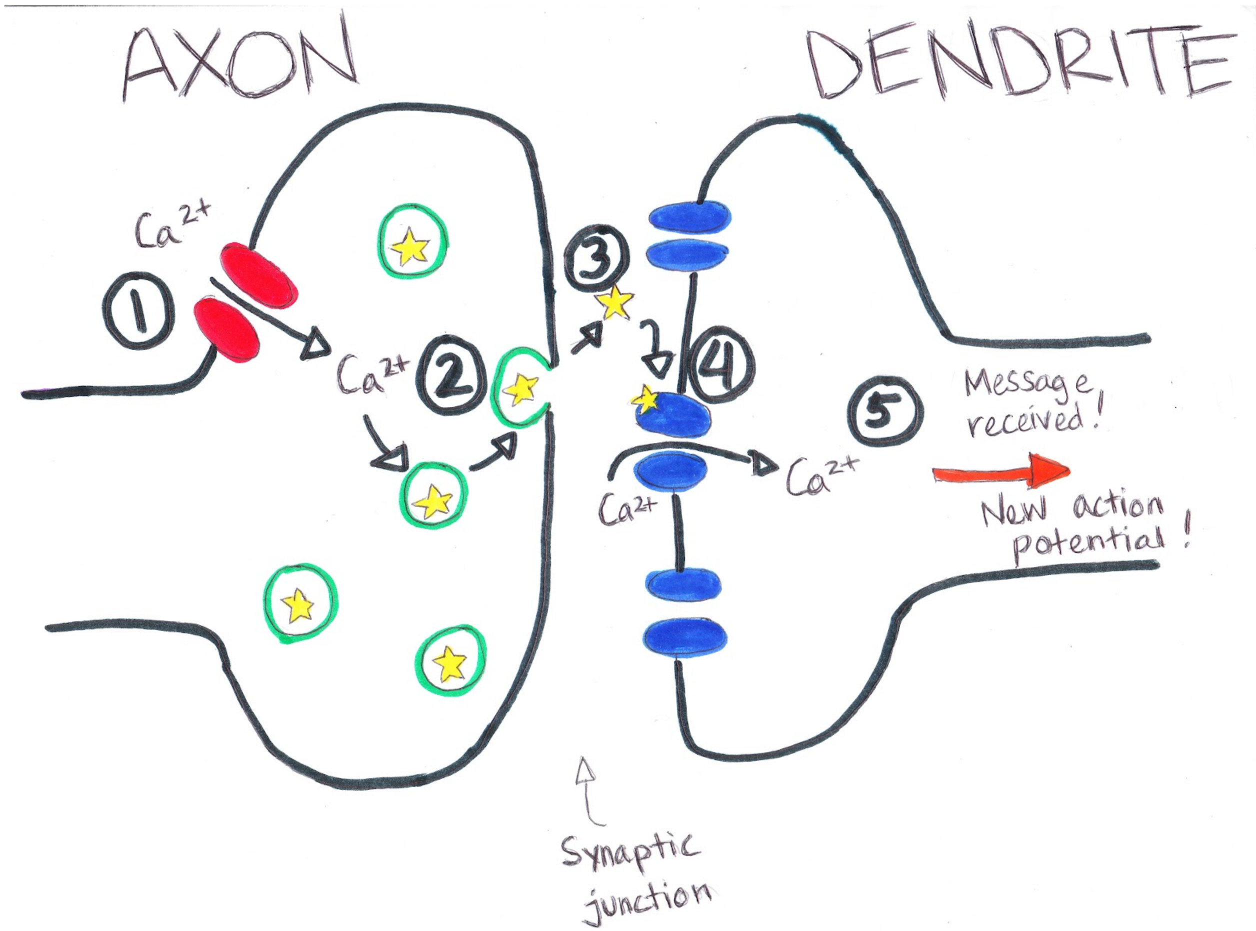
Synapses



Synapses

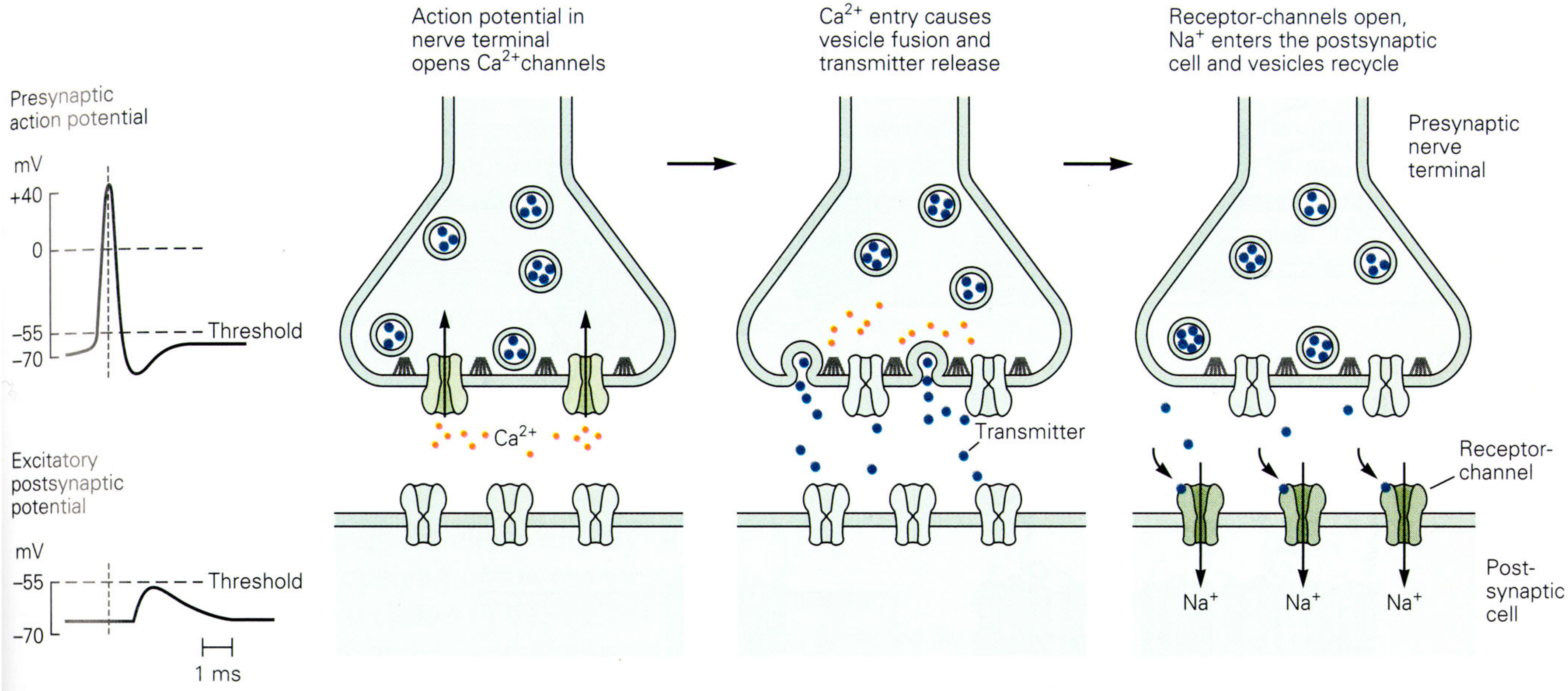

AXON
DENDRITE
Incoming Action Potential!
Ca^{2+}
Ca^{2+}
Ion Channel
Neurotransmitter Vesicle
receptor/ ion channel
Synaptic junction

Synapses



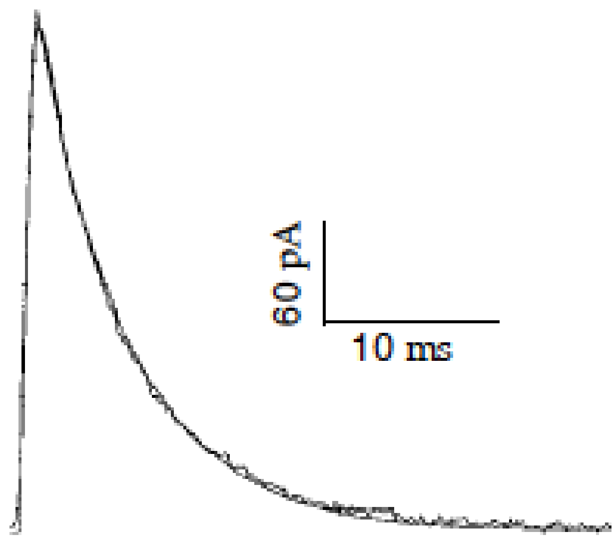
AXON
DENDRITE
Ca^{2+}
1
Ca^{2+}
2
3
4
5
Message received!
Ca^{2+}
Ca^{2+}
New action potential!
Synaptic junction

Synaptic transmission



The presynaptic action potential causes Ca^{++} channels to open. Calcium influx causes vesicles to fuse with the membrane and release neurotransmitter. The neurotransmitter causes receptor channels to open in the postsynaptic site, triggering a depolarization: an excitatory post-synaptic potential (EPSP).

Postsynaptic conductance



$$\alpha_s = 0.93ms^{-1} \quad \beta_s = 0.19ms^{-1} \quad T = 1ms$$

Postsynaptic conductance

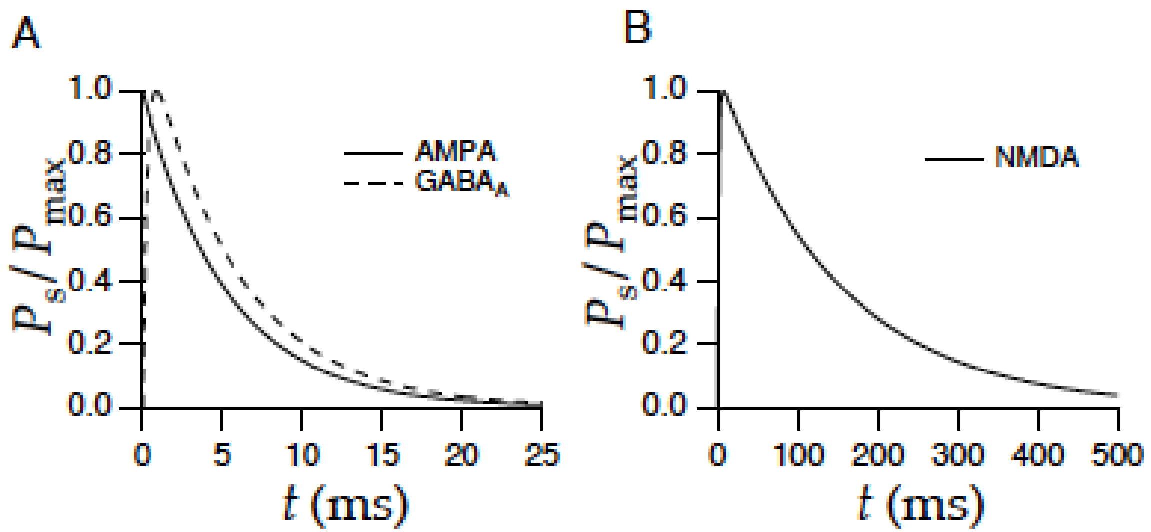
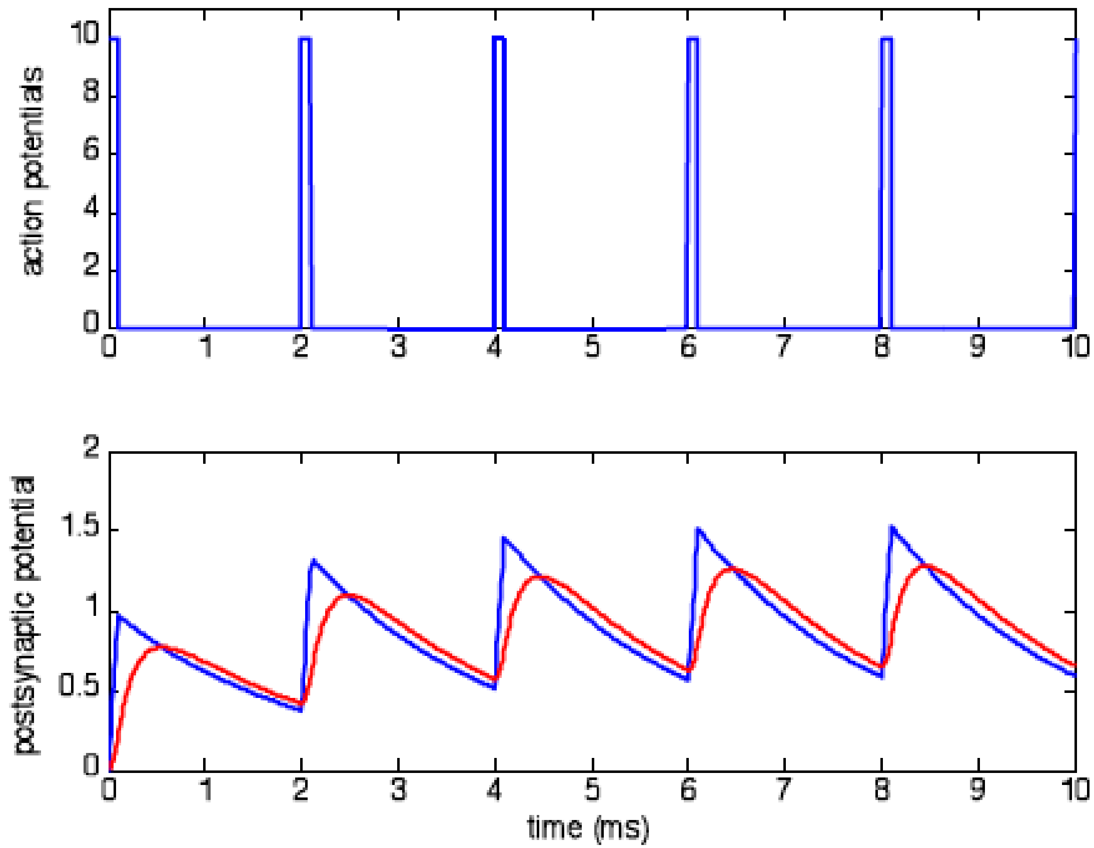
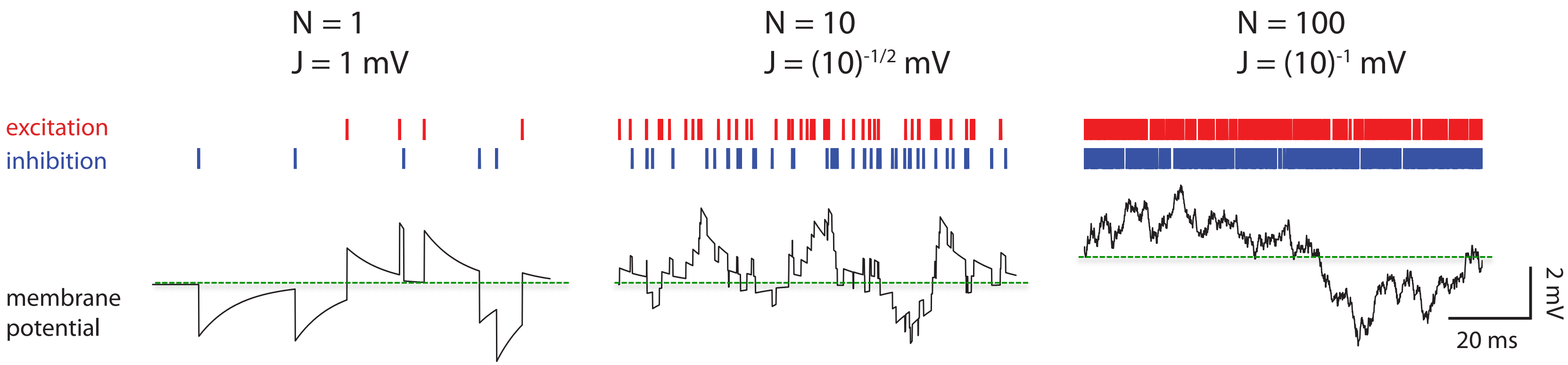


Figure 5.15 Time-dependent open probabilities fitted to match AMPA, $GABA_A$, and NMDA synaptic conductances. (A) The AMPA curve is a single exponential described by equation 5.31 with $\tau_s = 5.26$ ms. The $GABA_A$ curve is a difference of exponentials with $\tau_1 = 5.6$ ms and $\tau_{rise} = 0.3$ ms. (B) The NMDA curve is the differences of two exponentials with $\tau_1 = 152$ ms and $\tau_{rise} = 1.5$ ms. (Parameters are from Destexhe et al., 1994.)

Synaptic transmission



Integrate-and-Fire Neuron (IFN): subthreshold fluctuations of membrane potential



Synaptic inputs: N excitatory and N inhibitory neurons firing at 50 Hz

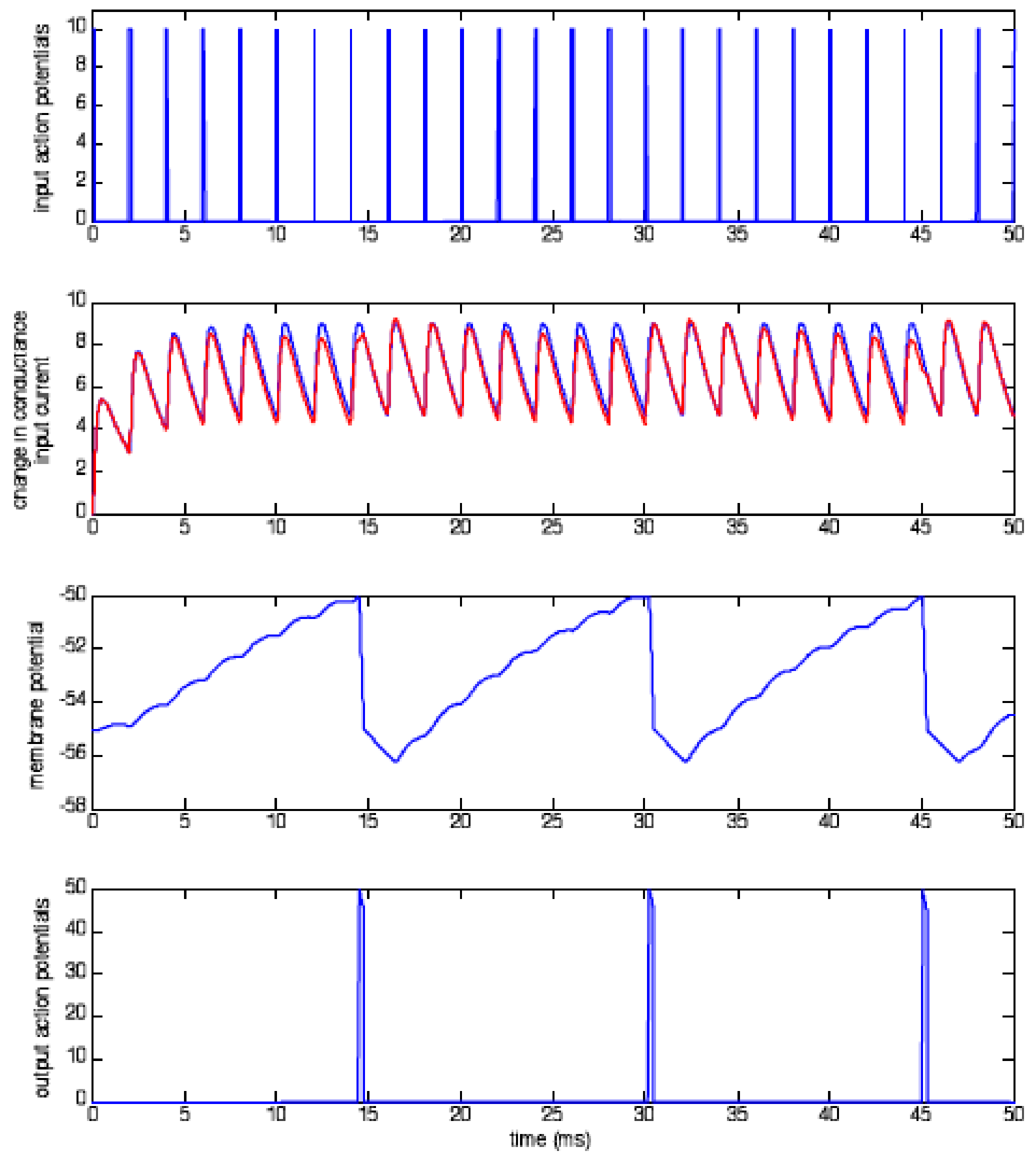
EPSP (excitatory postsynaptic potential) = $J = \dfrac{J_0}{\sqrt{N}}$

IPSP (inhibitory postsynaptic potential) = $J = -\dfrac{J_0}{\sqrt{N}}$

$J_0 = 1\,\text{mv}$

Simulation: courtesy of Brent Doiron, U. Pittsburgh

Synaptic transmission



Train of input spikes

Change in conductance s (blue)
Change in input current (red)

Membrane potential

Output spikes

A small network, N=2

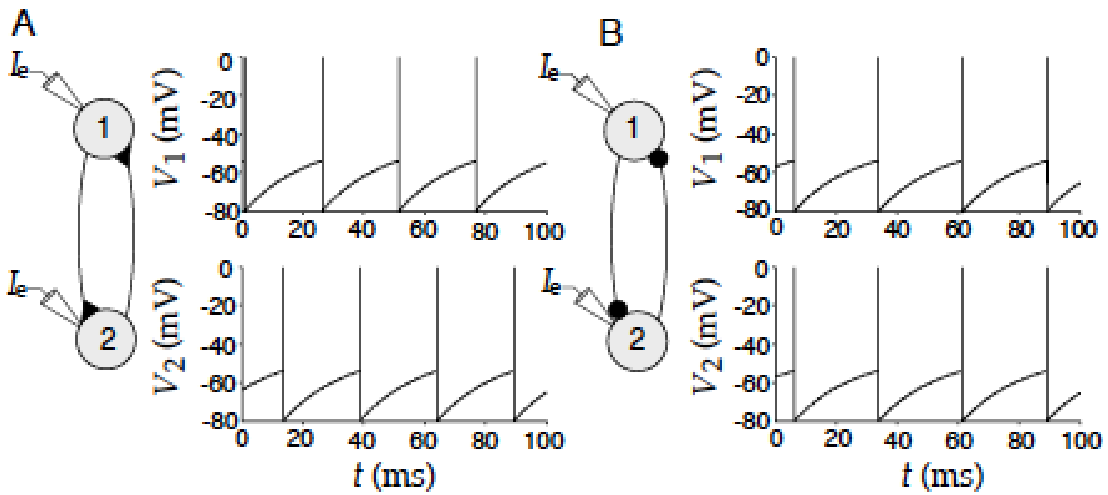
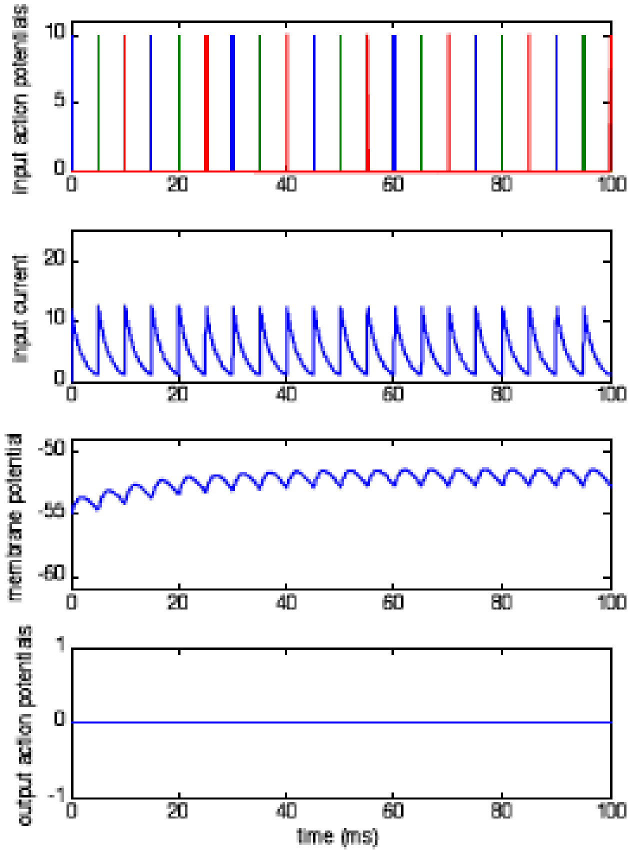


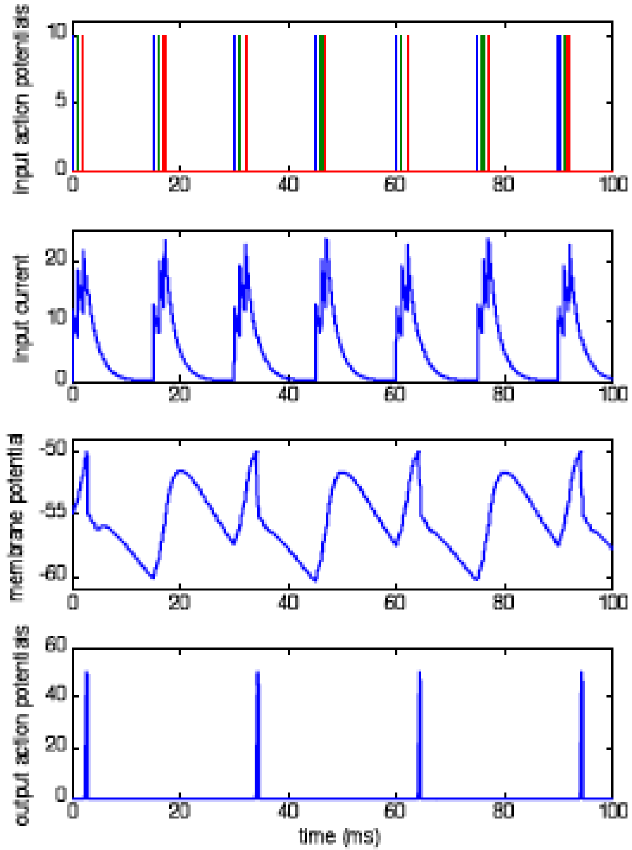
Figure 5.20 Two synaptically coupled integrate-and-fire neurons. (A) Excitatory synapses ($E_s = 0$ mV) produce an alternating, out-of-phase pattern of firing. (B) Inhibitory synapses ($E_s = -80$ mV) produce synchronous firing. Both model neurons have $E_L = -70$ mV, $V_{th} = -54$ mV, $V_{reset} = -80$ mV, $\tau_m = 20$ ms, $r_m \overline{g}_s = 0.05$, $P_{max} = 1$, $R_m I_e = 25$ mV, and $\tau_s = 10$ ms.

Timing of synaptic inputs

Input: three neurons

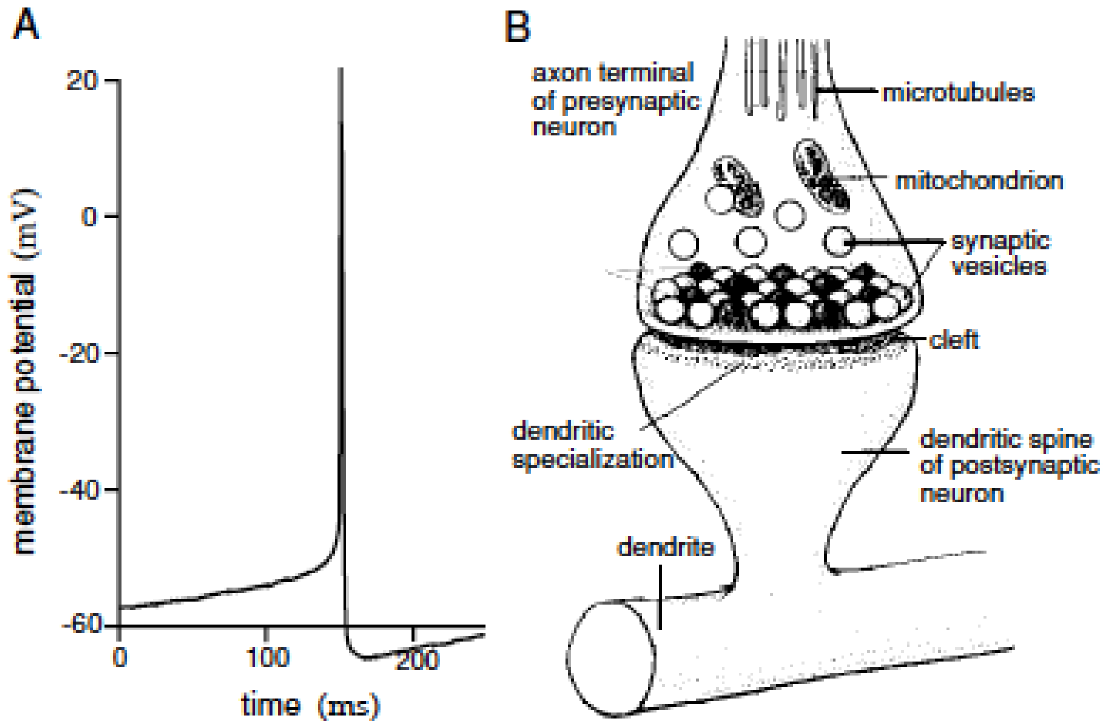


unsynchronized spikes



synchronized spikes

Communicating through spikes



Hodgkin and Huxley

Hodgkin and Huxley felt that they could not be sure that they understood the ionic basis of the action potential until they could reproduce its shape with these equations. Kacy Cole told me that Alan and/or Andrew had expressed to him their reservations about whether or not they would achieve this goal. After having chosen the form of the equations to be used, they consolidated all of their data to find the appropriate voltage sensitive rate constants. Then, because the Cambridge Univ. computer was "off the air for 6 months or so, while it underwent major modifications", in the spring of 1951, Huxley began the slow work of using a Brunsviga 20 manually cranked calculator with numbers entered by a set of adjusting levers (projecting from the wheels that were rotated by the hand crank). The output was a line of digits on the wheels to be read and transcribed to paper. First, he found that the time and voltage-sensitivities of the ionic conductances could be reproduced. Then the long process of numerical integration of the action potential began. Tabular records of the rate and state variables were entered into the the levers and transcribed from the dials for small increments of time. Huxley used a tedious iterative, error-correcting, numerical integration method to estimate and correct for numerical integration errors. The fact that the whole process for calculation of a 5mS interval, showing the initiation of and recovery following an action potential, could be accomplished in 8 hours is astonishing. The calculated action potentials were - with the exception of a small "gratuitous bump" late in the falling phase - excellent reproductions of the experimental observations under a variety of conditions.

Hodgkin and Huxley

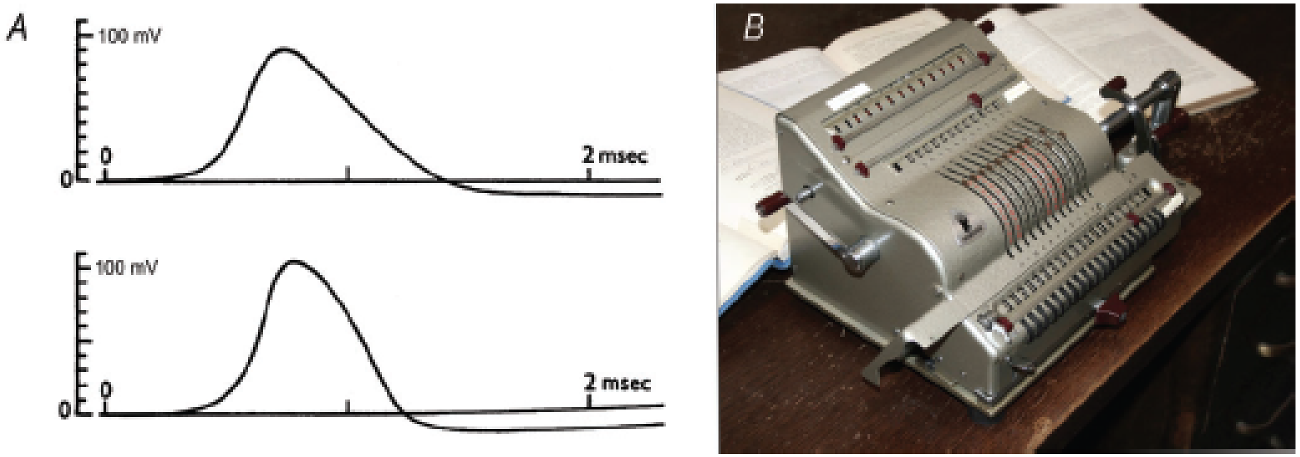
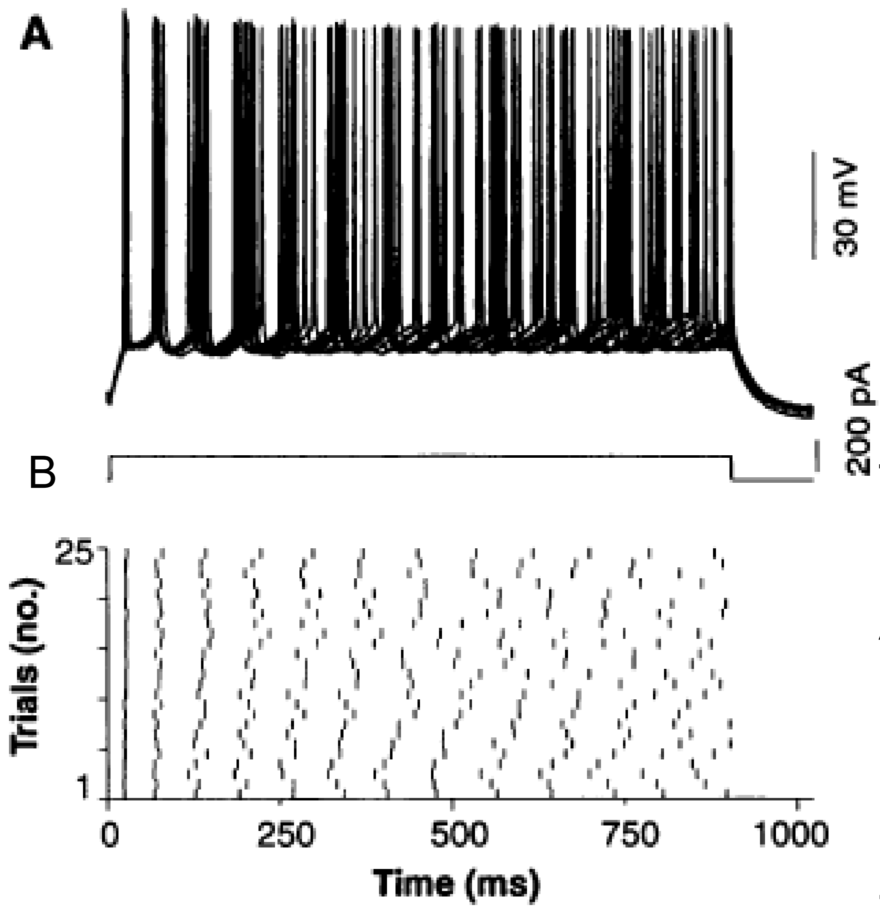


Figure 6. Modelling the action potential
A, calculated (upper) and measured (lower) action potentials in squid giant axons. Using their qualitative descriptions of *n*, *m* and *h* based upon the infinity proportions and rate constants, Hodgkin and Huxley iteratively calculated the current carried by Na^+ and K^+ flowing across the membrane. By assuming that these currents flowed for a short period of time, they derived a new voltage. Since every iteration produced a new voltage, a new set of *n*, *m* and *h* variables had to be calculated for the next time step. To produce such a trace required many hundreds of iterations. Figure taken from Hodgkin & Huxley (1952*e*). *B*, the Brunsviga 20 (produced in Braunschweig by Brunsviga Maschinenwerke, Grimme, Natalis & Co.), one of the most popular mechanical calculators. It was produced up to the early 1970s and marketed with the slogan 'Brains of Steel'. This particular one was photographed in what was Alan Hodgkin's space in the basement of the Physiological Laboratory in Cambridge and, whilst its original owner is unknown, it has belonged to Richard Adrian, then Trevor Lamb and now Hugh Robinson. Photograph taken by Christof Schwiening.

Variability of neural responses



VARIABILITY!!

Rat neocortical slices
Regular firing neuron, layer 5

Suprathreshold stimulation:
dc current pulse, 150 pA, 900 ms

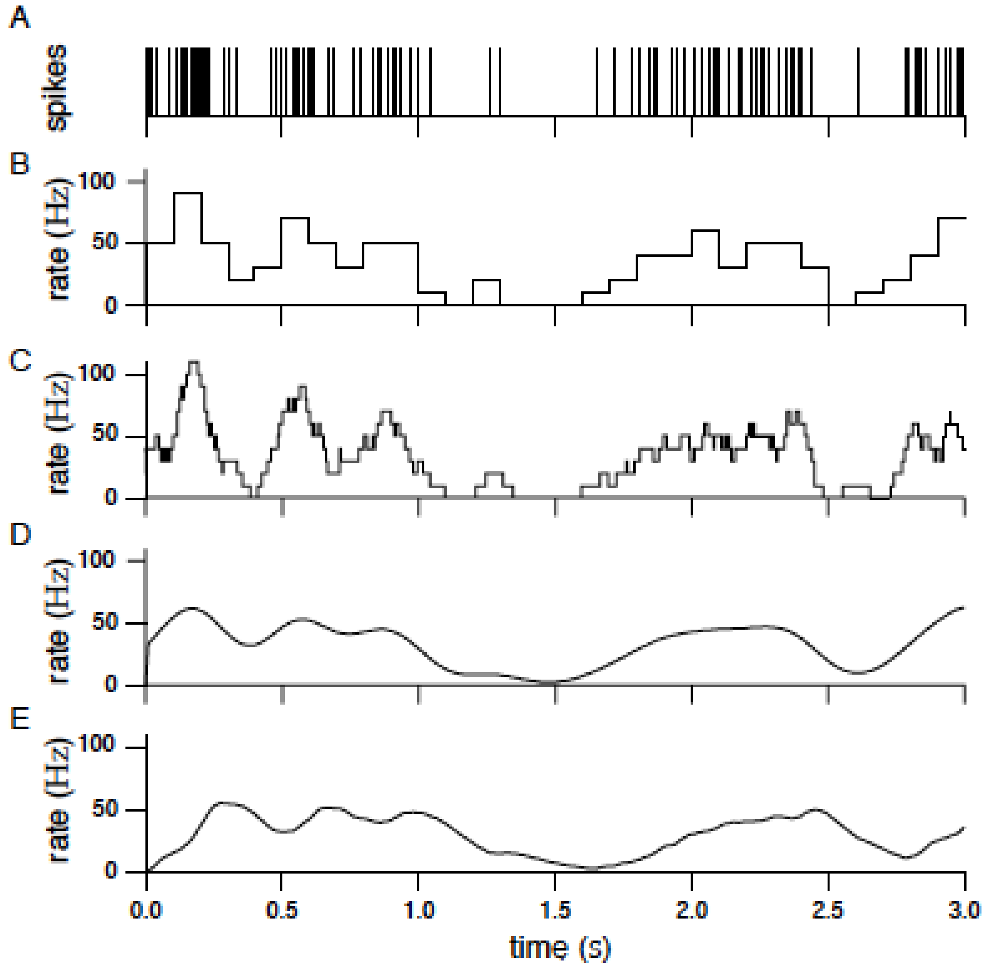
Response: spike trains, mean firing rate about 14 Hz.

A: The first 10 spike trains are shown superimposed

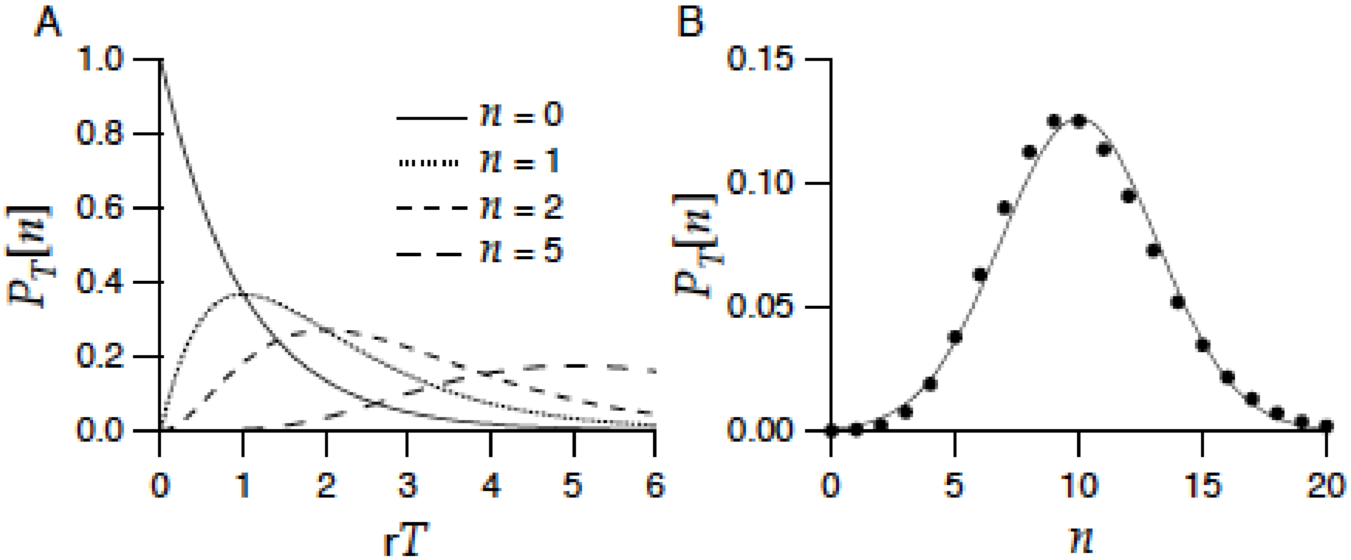
B: The first 25 consecutive spike trains are shown as raster plots

Mainen, Sejnowski, *Science* (1995)

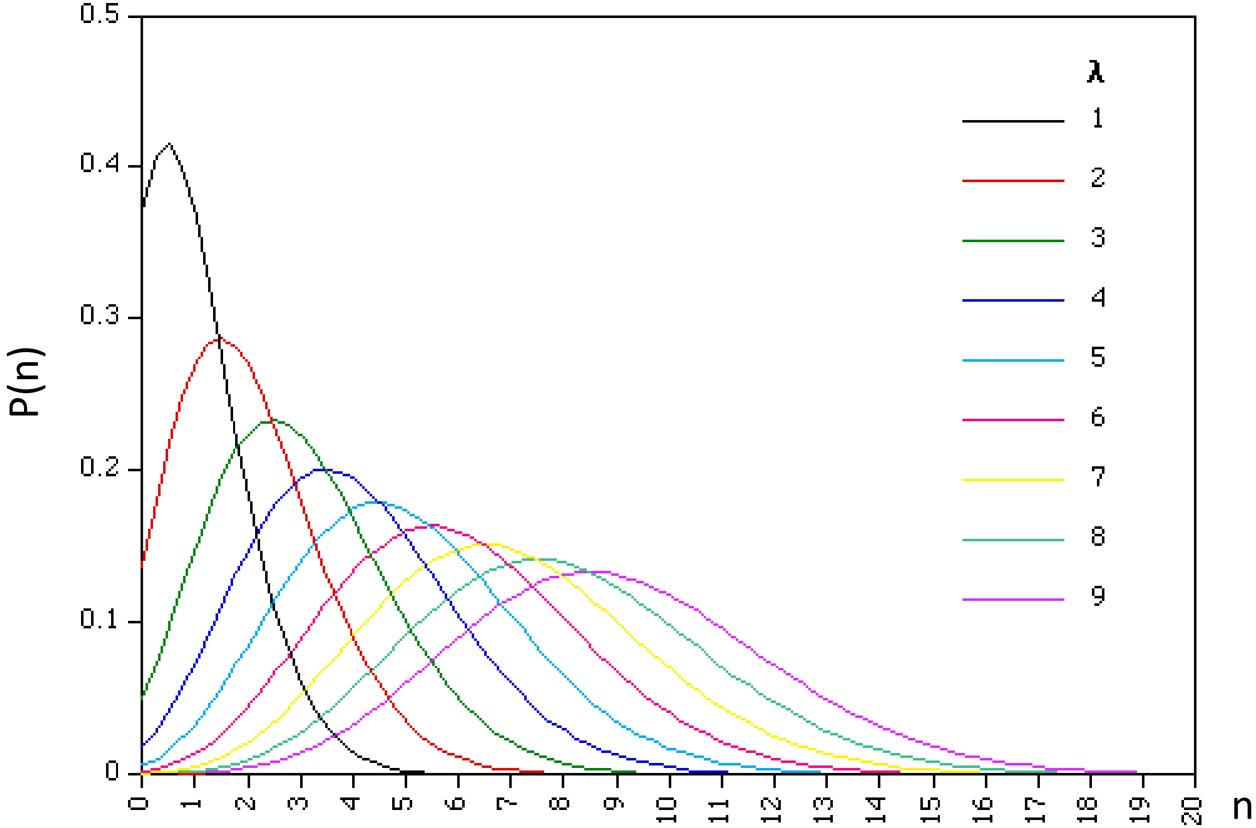
Estimation of firing rates



Poisson statistics

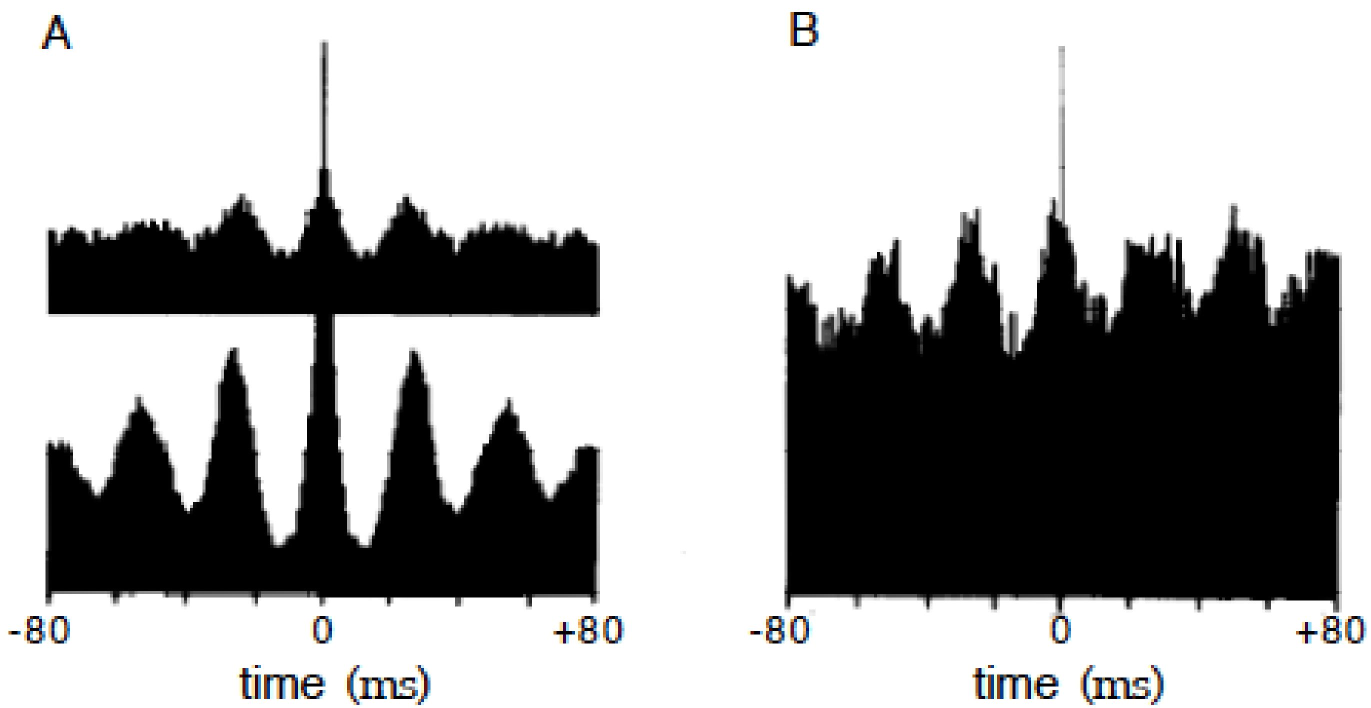


Poisson statistics

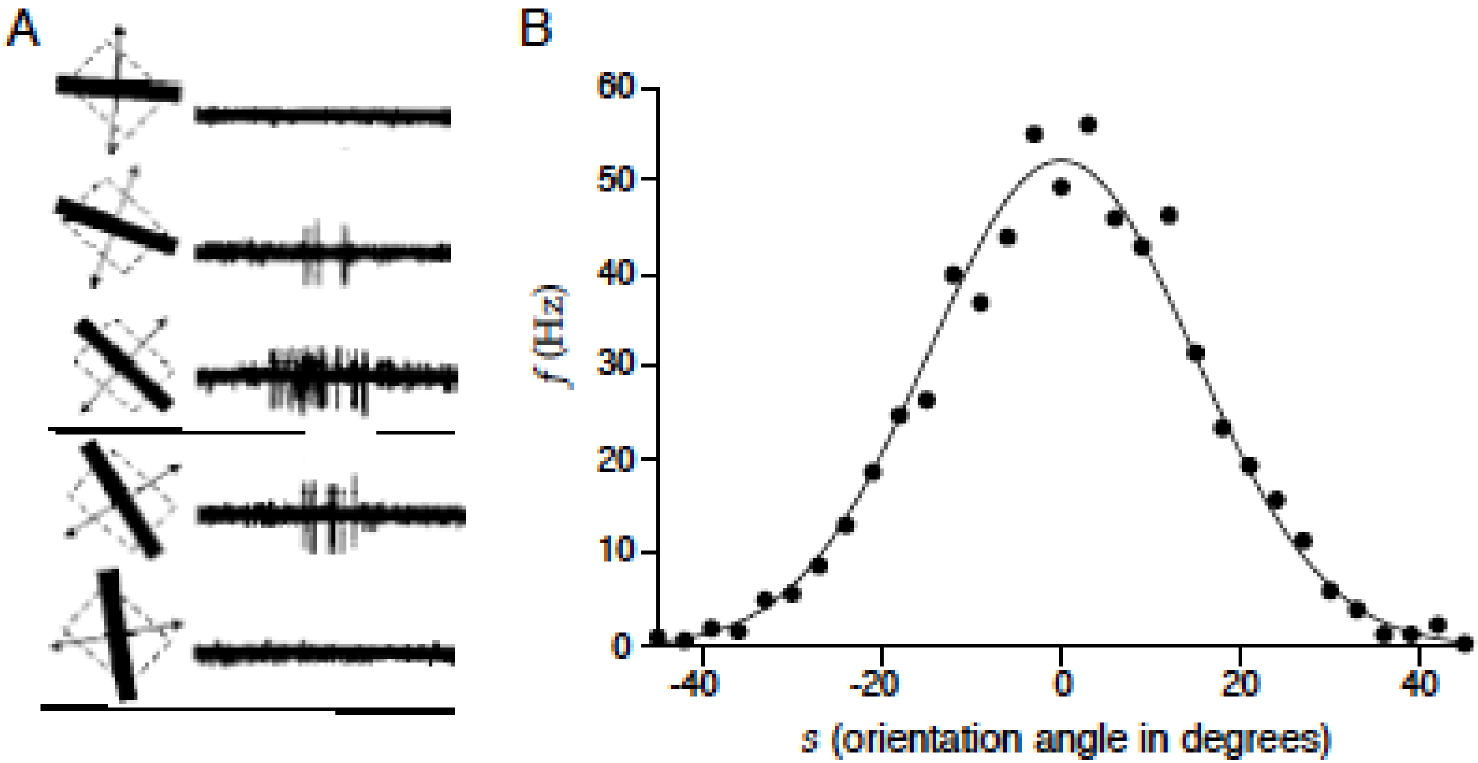


$$P(n) = \frac{\lambda^n}{n!} e^{-\lambda}$$

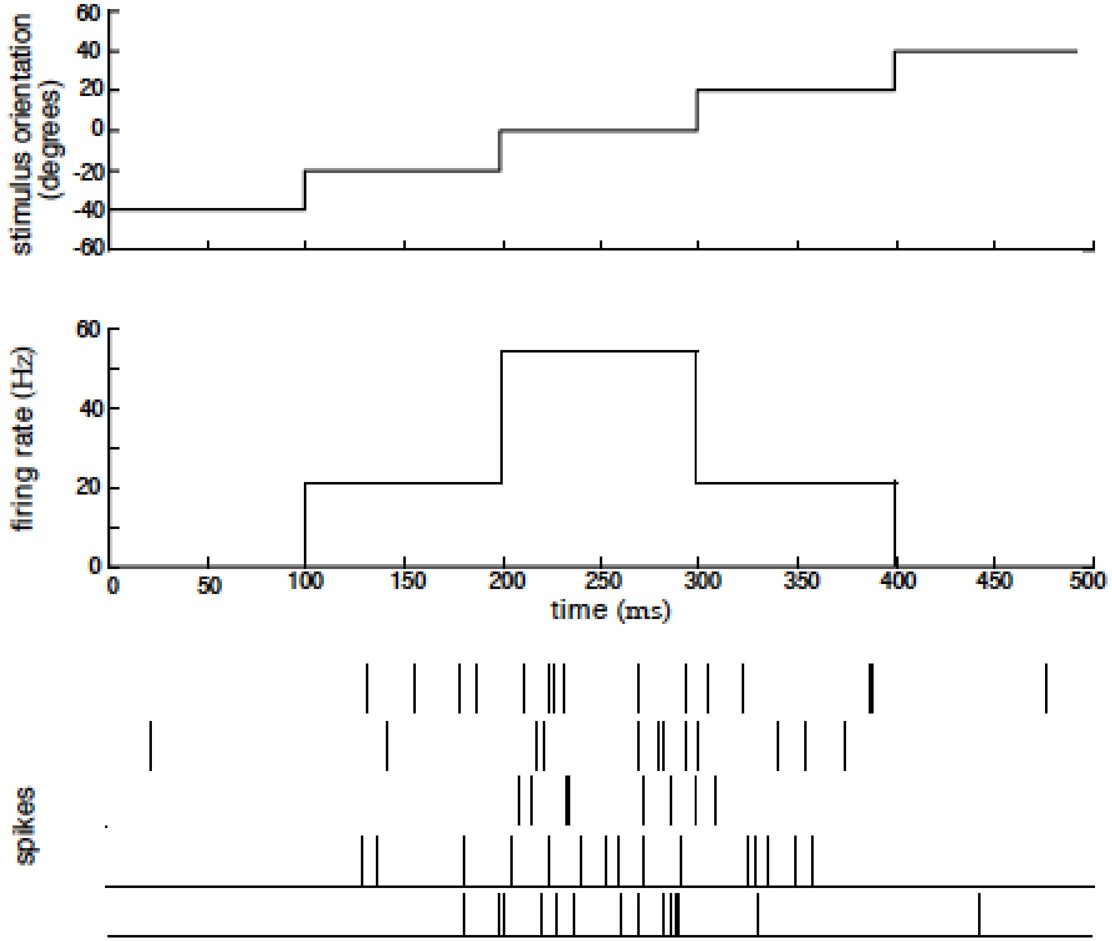
Correlation functions



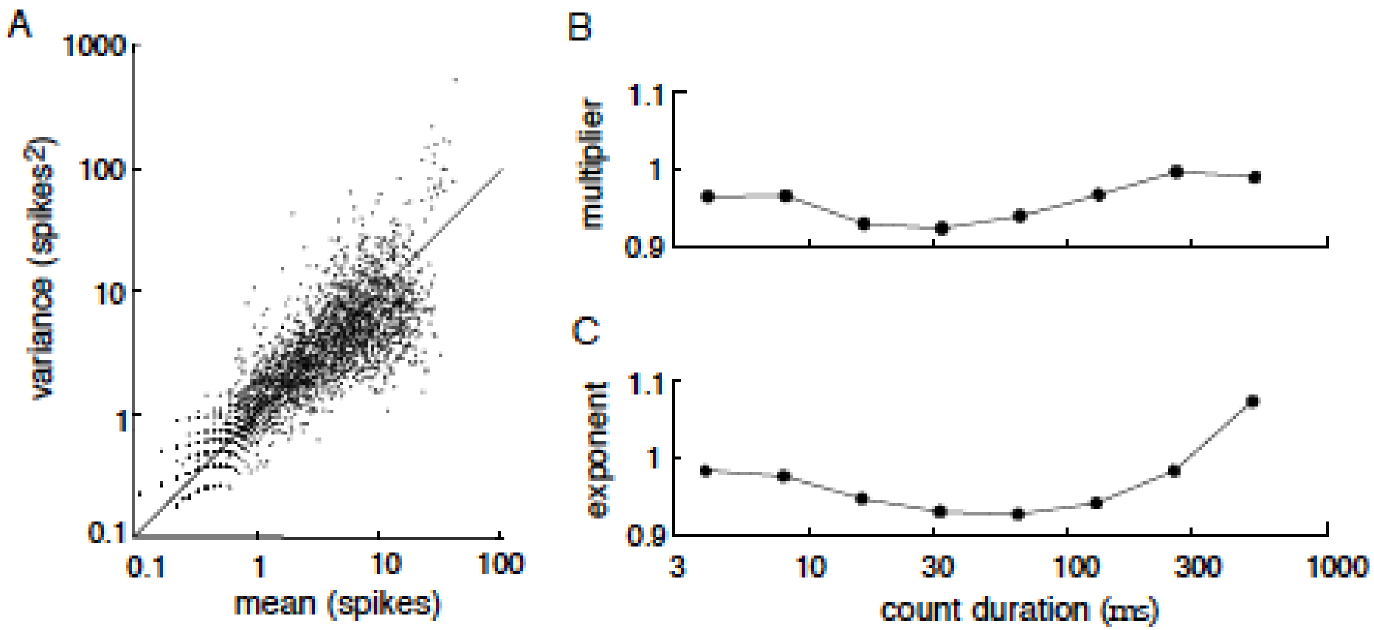
Orientation selectivity in V1: tuning curve



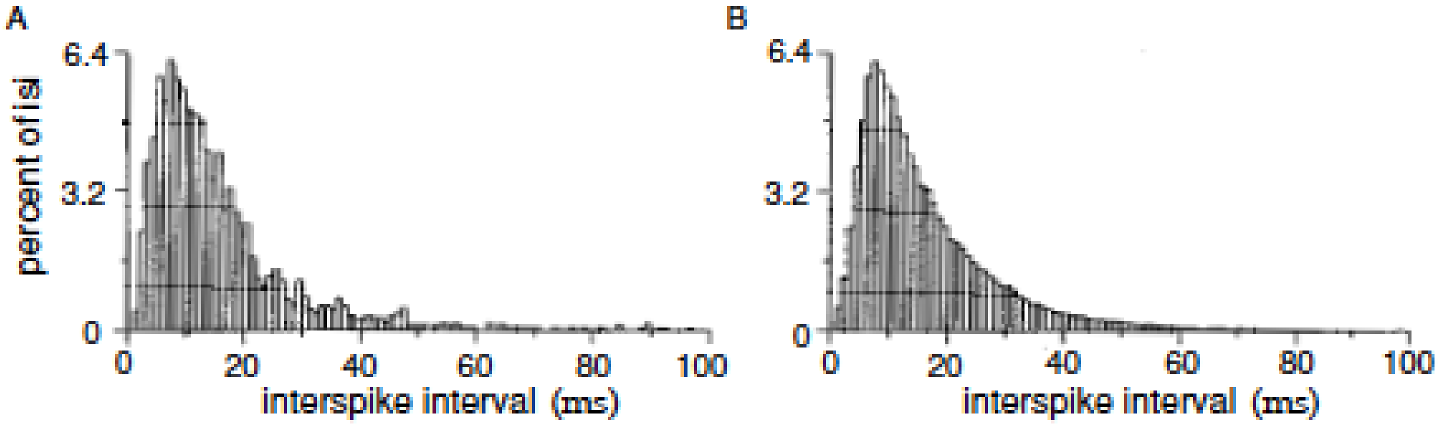
Orientation selectivity in V1: spiking neuron



Comparison with data: Fano factor



Comparison with data: interspike intervals



$$p(\tau) = \tau e^{-r\tau}$$

Poisson statistics

$$p(\tau) = \frac{\tau (r\tau)^j e^{-r\tau}}{j!}$$

Poisson statistics with refractory period

Comparison with data: coefficient of variation