Introduction to Brain and Neuroscience (BM 1060)

Cellular, Synaptic and Molecular Neuroscience

Levels of abstraction in Neuroscience

Behaviour	Responses to stimuli, choices etc
Systems	e.g. Visual, Auditory, Motor
Areas	e.g. Frontal, Temporal lobes
Circuit	e.g. cortical column
Neurons	A Cell
Synapse	Connection between cells
Molecule	Molecules, ions entering/leaving the cell

Origins – Cajal & Golgi

Santiago Ramon y Cajal

- Father of modern Neuroscience
- Early sketches of various cell types
- Identified Neuron as the basic unit of NS

Camillo Golgi

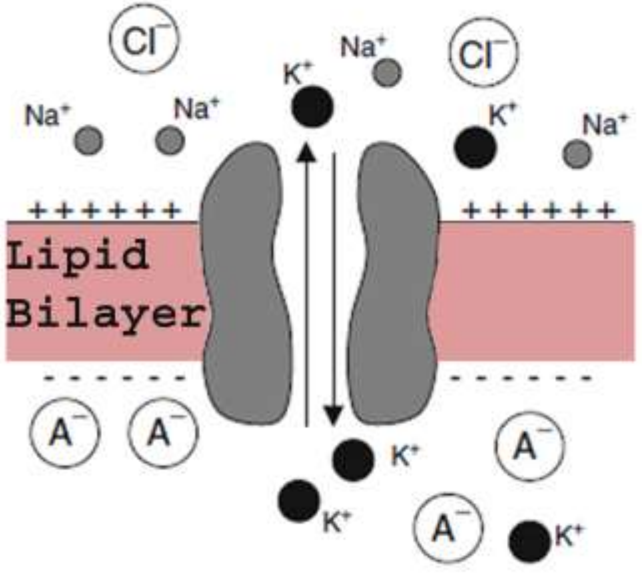
- Staining technique using Silver Nitrate to see cells under microscope

Cajal & Golgi

- Debates between Cajal and Golgi on Neuronal vs Reticular theory (entire brain is continuous) of NS
- Golgi and Ramón y Cajal were jointly awarded the Nobel Prize in Physiology or Medicine in 1906

Neurons

- A Cell : Basic unit of organization of the nervous system
- Can be thought of as
  - *Electrically excitable cells*
  - *bags of semi permeable membranes*
  - *Separates the Intra cellular from extra cellular space*
  - *Na^+, K^+, Ca^{2+}, Cl^- Ions flit in and out of the semi permeable membranes through ion channels*



(a)

Nernst Potential

- Equilibrium potential at zero ionic current
  (NOTE : when membrane is permeable to ONE ionic species only)
- Ionic current is caused by diffusion and electrostatic drift

$$V_{in} - V_{out} = -\frac{RT}{zF} ln \frac{[C_{in}]}{[C_{out}]}$$

  - R : Gas constant, T : Temperature, z : Valence of ion, F : Faraday's constant
  - [C] : concentration
  - At 25 C

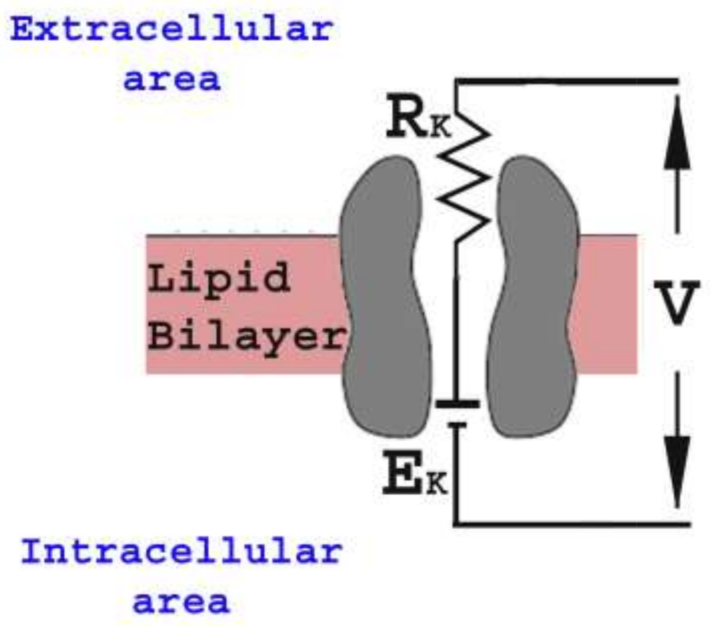
$$V_{in} - V_{out} = -\frac{25\ mV}{z} ln \frac{[C_{in}]}{[C_{out}]}$$

Calculate equilibrium potentials

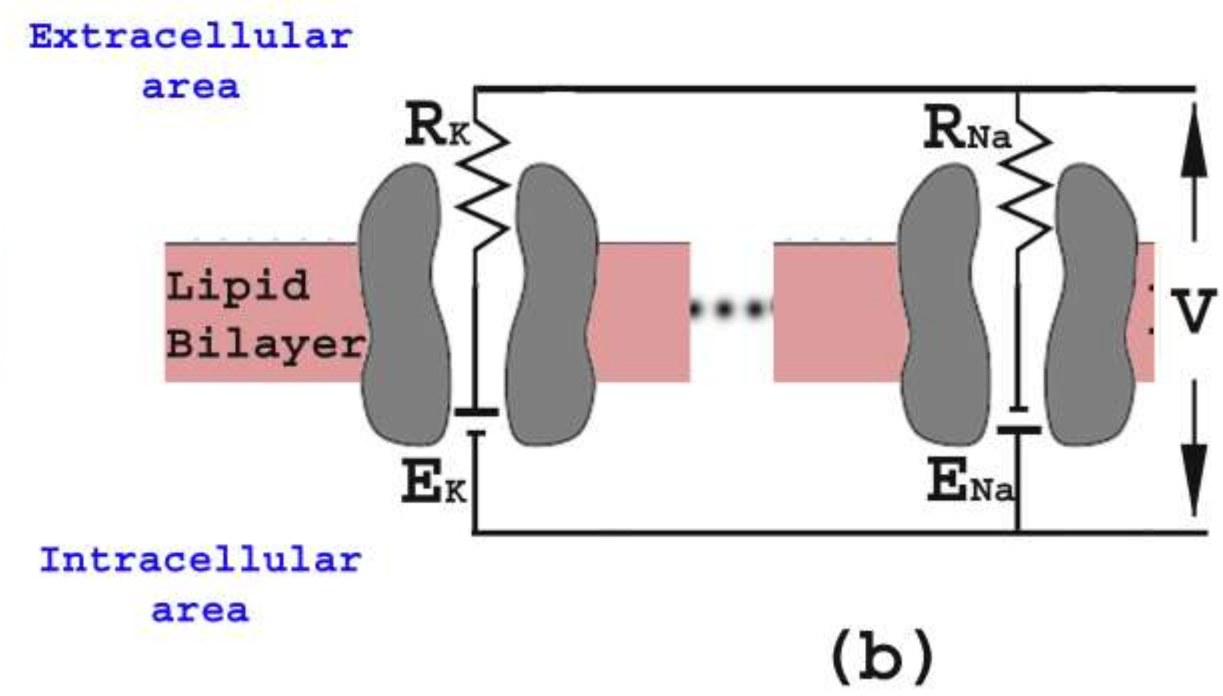
	Inside (mM)	Outside (mM)
Frog muscle (Conway 1957)		
K^+	124	2.25
Na^+	10.4	109
Cl^-	1.5	77.5
Ca^{2+}	4.9†	2.1
Squid axon (Hodgkin 1964)		
K^+	400	20
Na^+	50	440
Cl^-	40–150	560
Ca^{2+}	0.4†	10

Johnston & Wu, Foundations of Cellular Neurophysiology

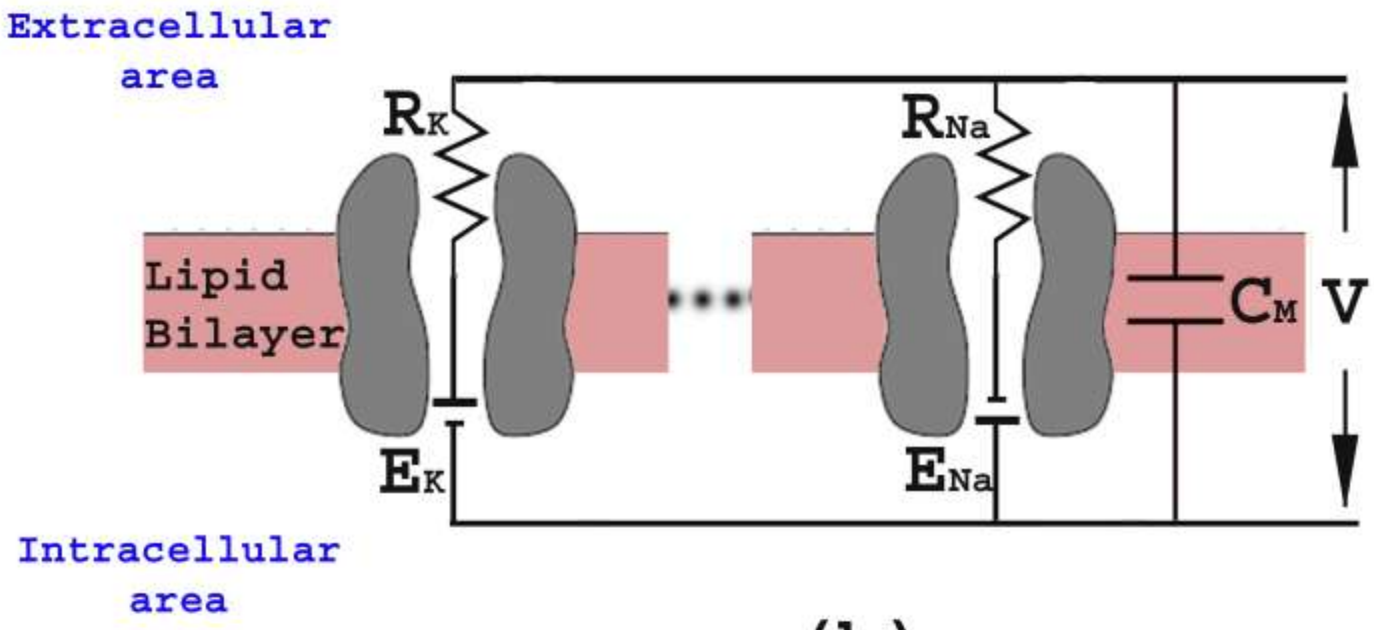
Modeling an ion channel : a potassium channel



Add another channel for Sodium



Add a model Lipid Bilayer



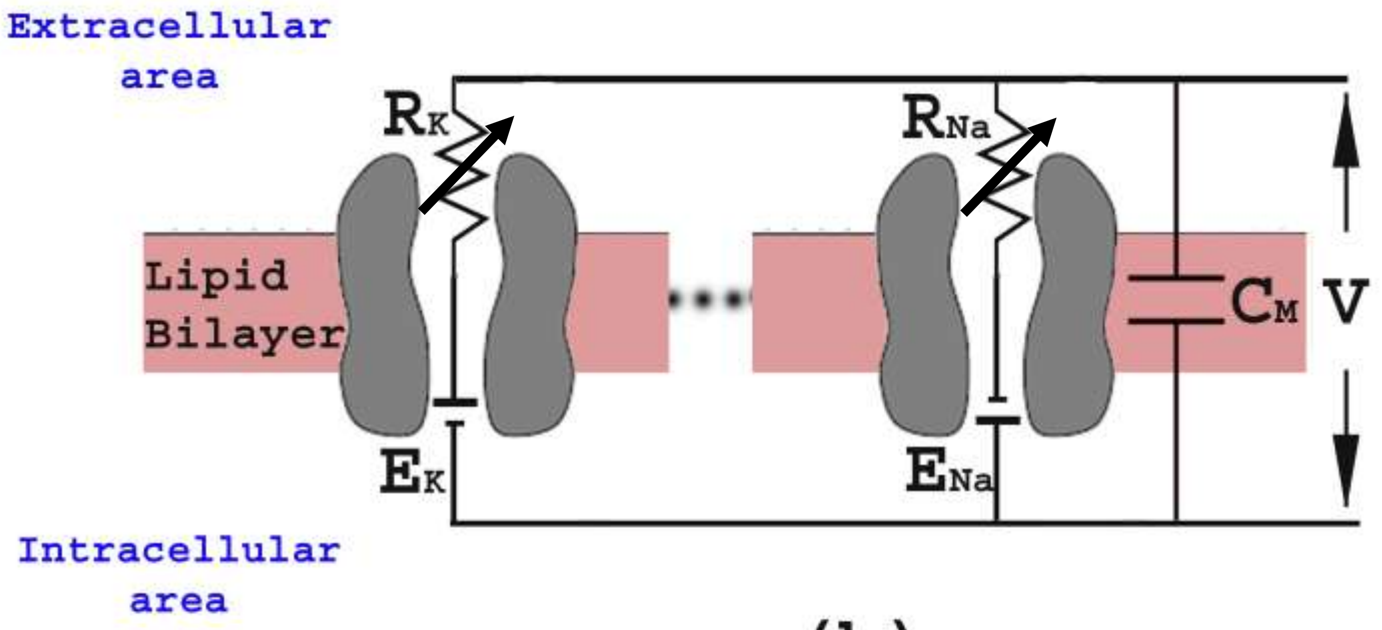
(b)

Applying Kirchoff….

$$I_{inj} = i_c + i_{Na} + i_K$$

$$I_{inj} = C_m \frac{dV}{dt} + (V - E_K)g_K + (V - E_{Na})g_{Na}$$

Conductance varies with time, voltage and temperature



(b)

Emergence of the AP (Qualitative)

- At Rest
- *K^+ channel moderate conductance, Na^+ channel very low conductance, at around resting membrane potentials*
- *So what will be the resting membrane potential be like? (Take a guess)*

- Depolarisation
- *Deposit some charge inside*
- *What happens if K^+ channel is the only active conductance?*
- *What happens if Na^+ channel is also active albeit with low conductance?*

- At highly depolarized states ?

Important properties of the channel

- Non-linearity
- Rectification

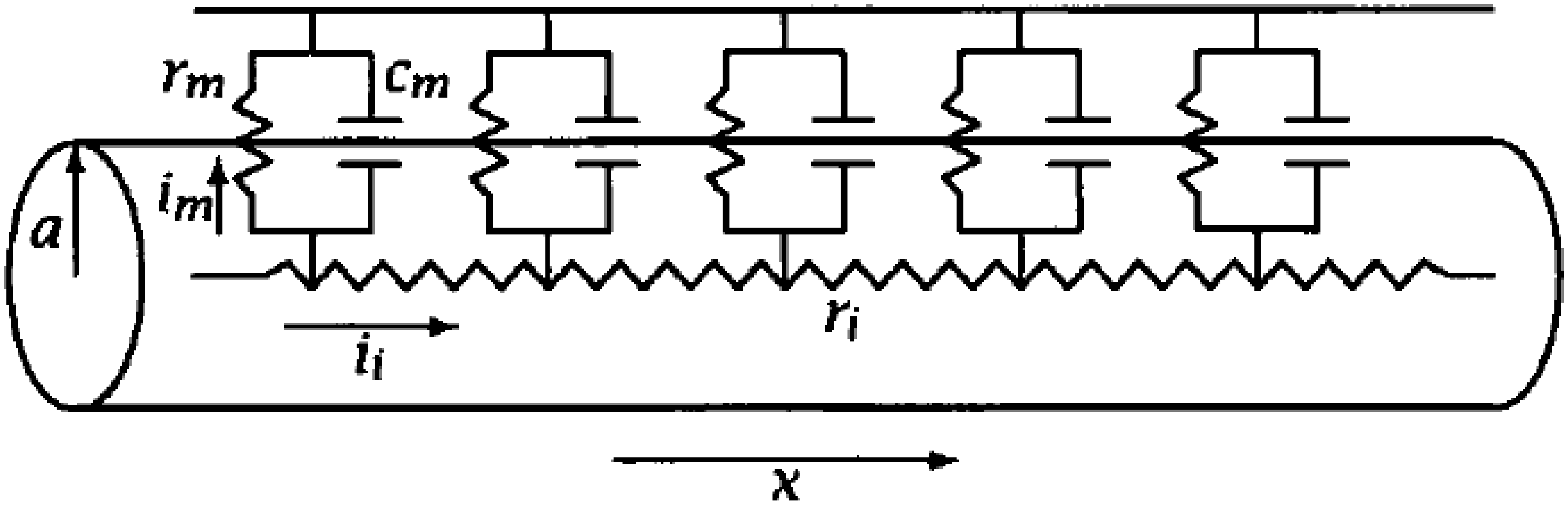
Quantitative analysis : Hodgkin-Huxley

- Hodgkin, Huxley 1952, series of papers
- Nobel prize (1963) in physiology or medicine

Hodgkin-Huxley equations

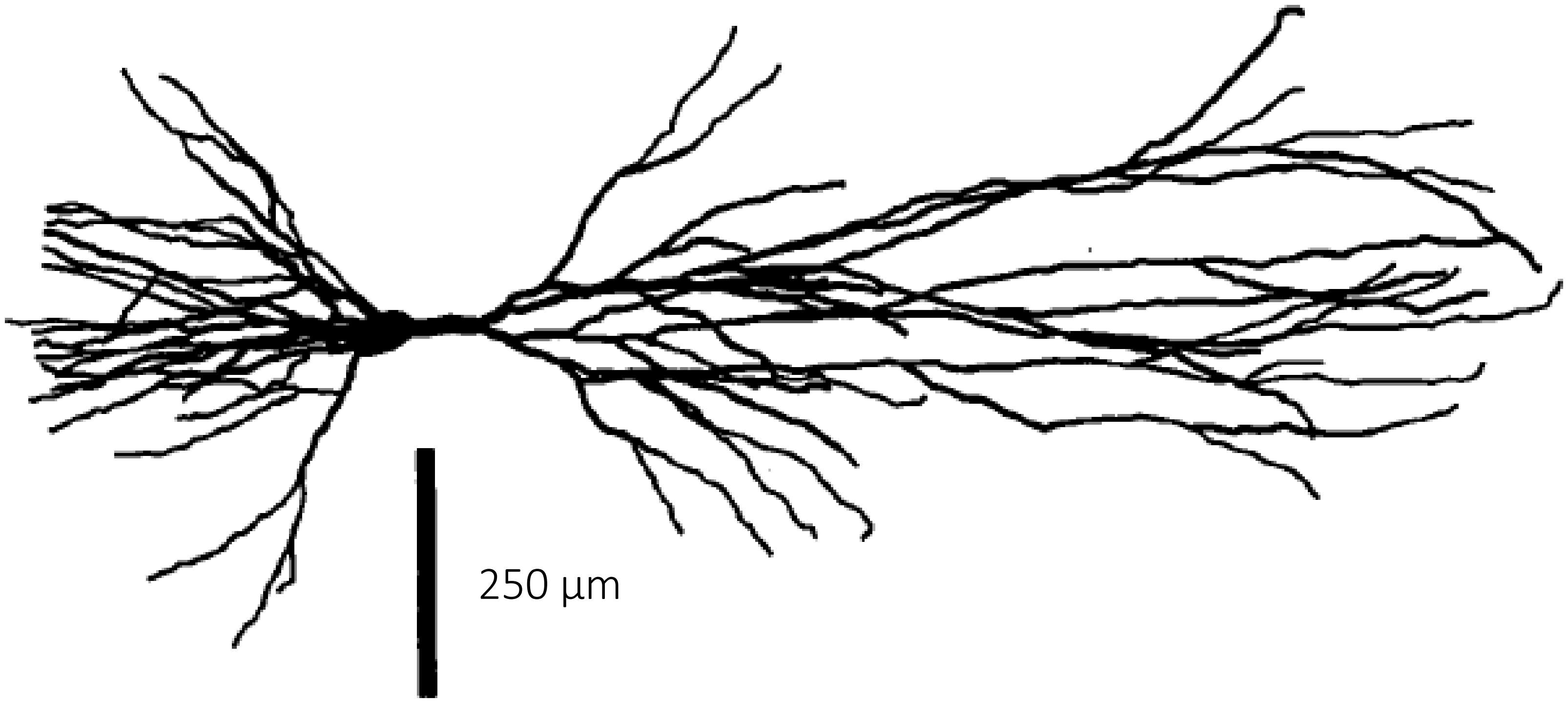
$$
\begin{aligned}
I_{inj} &= C_m.\frac{dV}{dt} + I_{ion}(V,t) \\
I_{ion}(V,t) &= g_{Na}(V,t).(V - E_{Na}) + g_K(V,t).(V - E_K) + g_L.(V - E_L) \\
g_{Na}(V,t) &= m^3(V,t).h(V,t).\overline{g}_{Na}(V - E_{Na}) \\
g_K(V,t) &= n^4.(V,t).\overline{g}_K(V - E_K) \\
\frac{dm}{dt} &= \frac{m_\infty(V) - m}{\tau_m(V)} \\
\frac{dn}{dt} &= \frac{n_\infty(V) - n}{\tau_n(V)} \\
\frac{dh}{dt} &= \frac{h_\infty(V) - h}{\tau_h(V)}
\end{aligned}
$$

Neurons are not point objects !



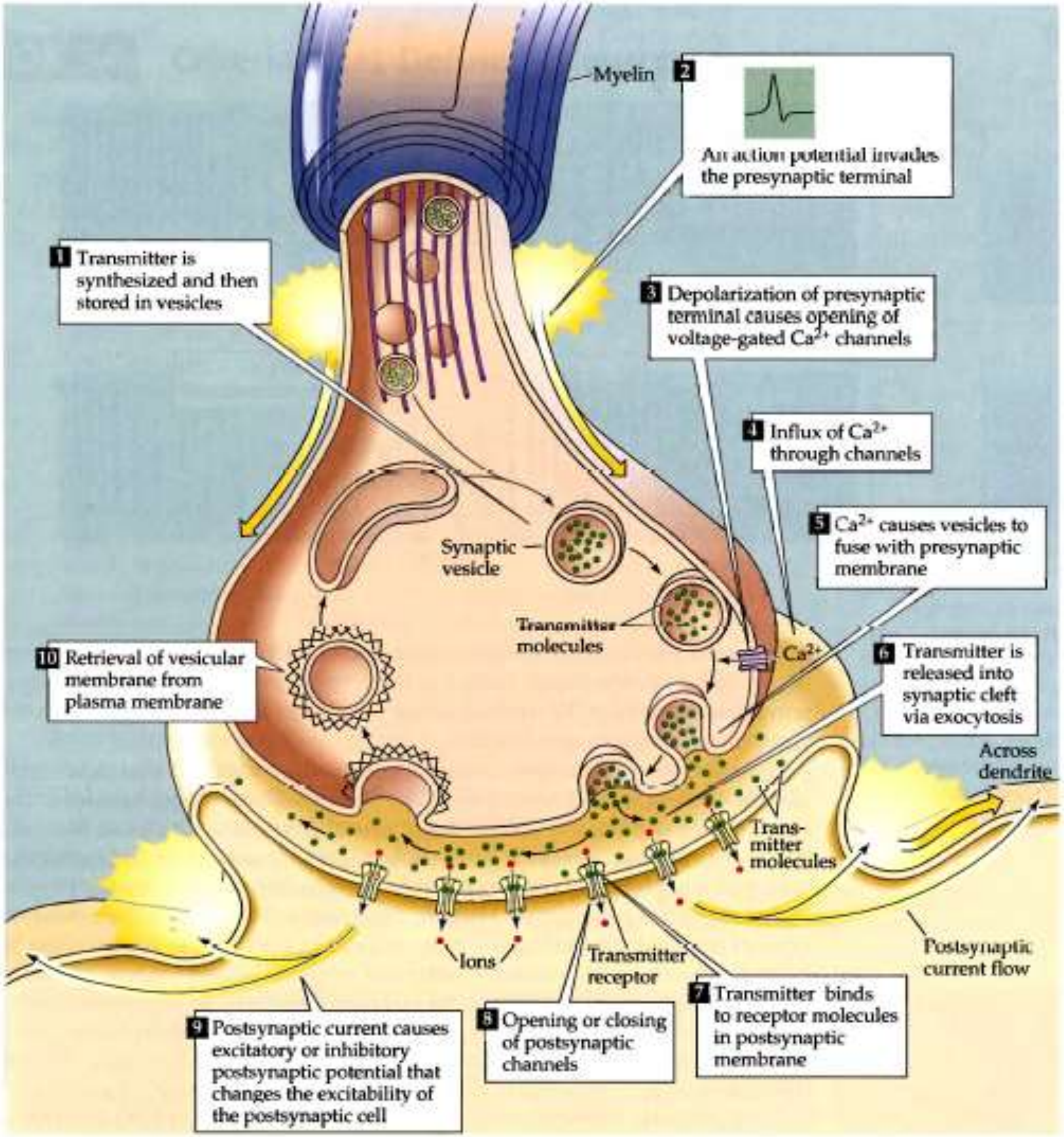
Johnston & Wu, Foundations of Cellular Neurophysiology

A rat hippocampal CA3 cell



Johnston & Wu, Foundations of Cellular Neurophysiology

Synapses



Myelin
2 An action potential invades the presynaptic terminal
1 Transmitter is synthesized and then stored in vesicles
3 Depolarization of presynaptic terminal causes opening of voltage-gated Ca^{2+} channels
4 Influx of Ca^{2+} through channels
5 Ca^{2+} causes vesicles to fuse with presynaptic membrane
Synaptic vesicle
Transmitter molecules
Ca^{2+}
6 Transmitter is released into synaptic cleft via exocytosis
10 Retrieval of vesicular membrane from plasma membrane
Across dendrite
Trans-mitter molecules
Ions
Transmitter receptor
Postsynaptic current flow
7 Transmitter binds to receptor molecules in postsynaptic membrane
8 Opening or closing of postsynaptic channels
9 Postsynaptic current causes excitatory or inhibitory postsynaptic potential that changes the excitability of the postsynaptic cell

Synapse model

- Ligand gated ion channel
- mathematical treatment similar to voltage gated ion channels
- add $((V - E_{AMPA})g_{syn})$ term
- Excitatory or Inhibitory synapses
- *Excitatory : e.g. AMPA*
- *Inhibitory : e.g. GABA*

Molecular modeling

Modeling the movement of ions within cells or synapses

E.g. https://www.youtube.com/watch?v=Hjt-7V_K2Gc