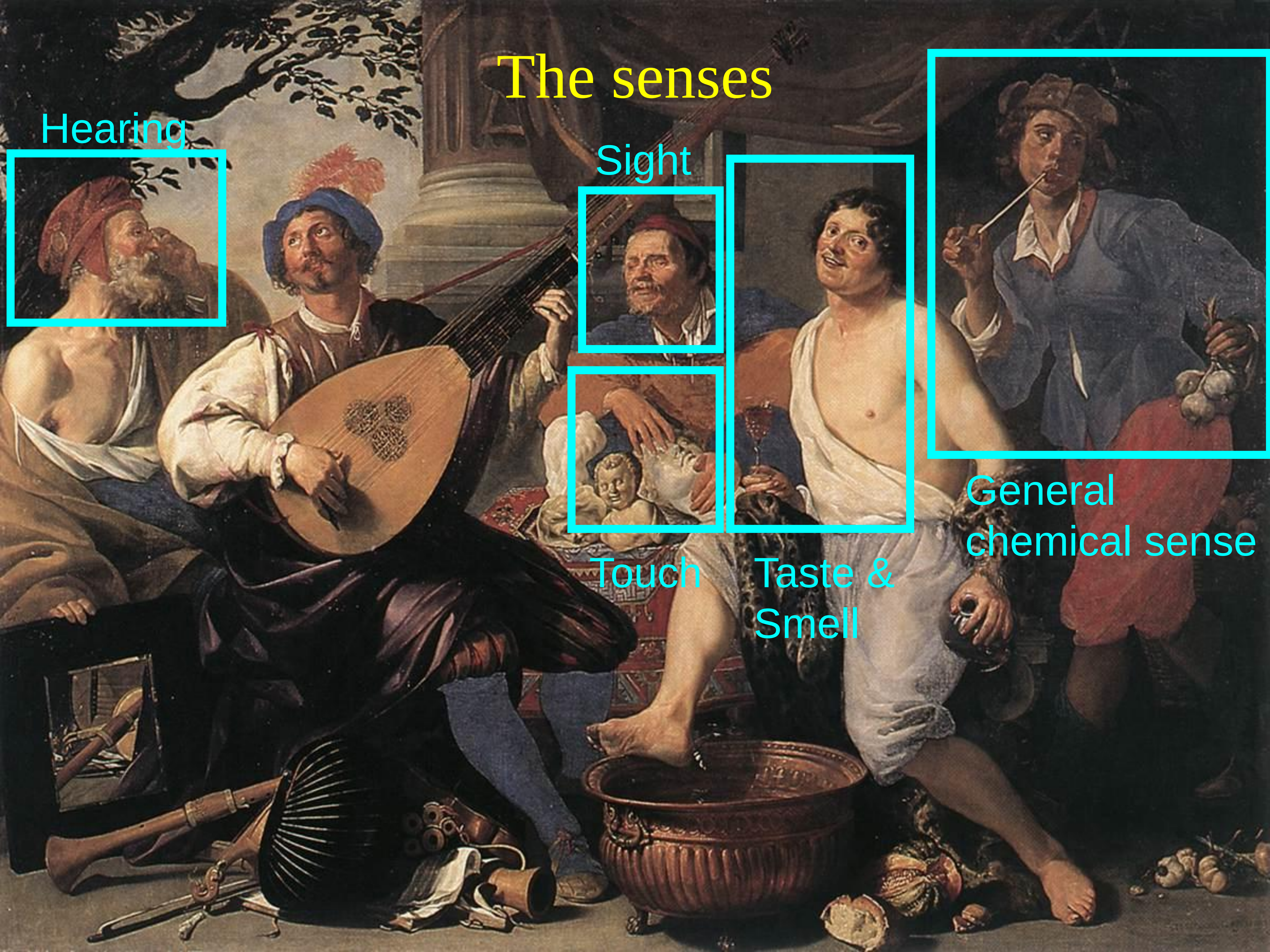
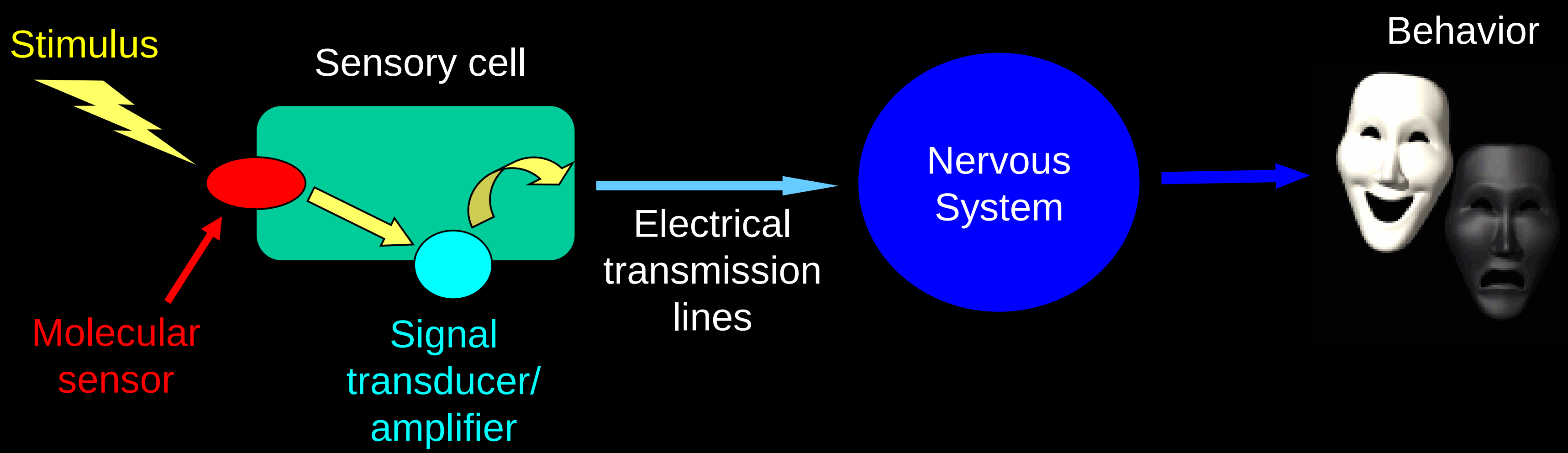
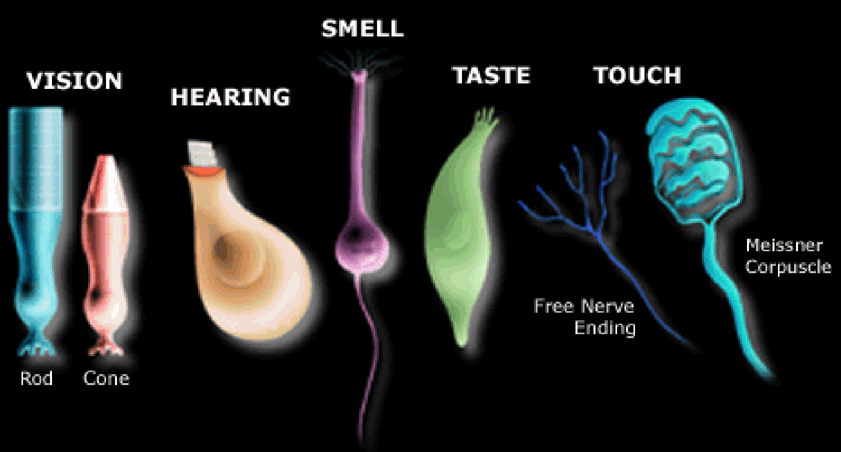
Information capacity in the nervous system I


The senses
Hearing
Sight
Touch
Taste &
Smell
General
chemical sense

General Scheme of the Sensory System



Quality detection: Specialized sensory cells



Spread of electric signals: passive vs. active propagation

Passive propagation:

- “Basic” electrical properties of cells
- Conductance is voltage-independent
- Decays with space and time
- Important biological function!

Active propagation:

- “Special” electrical properties of cells
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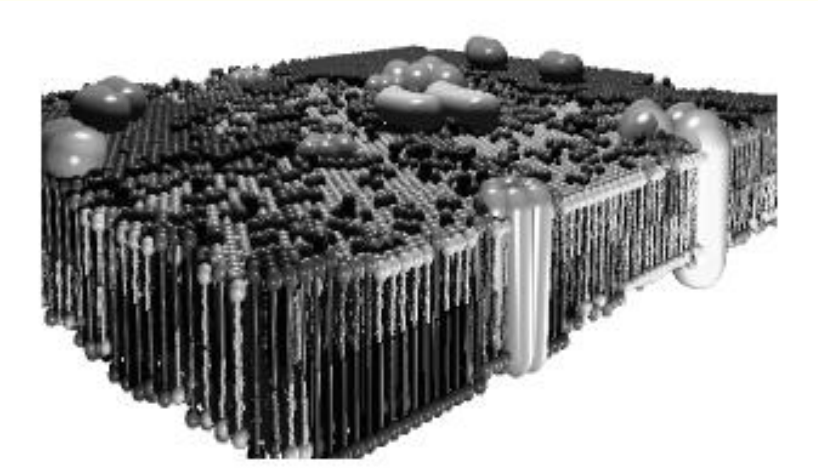
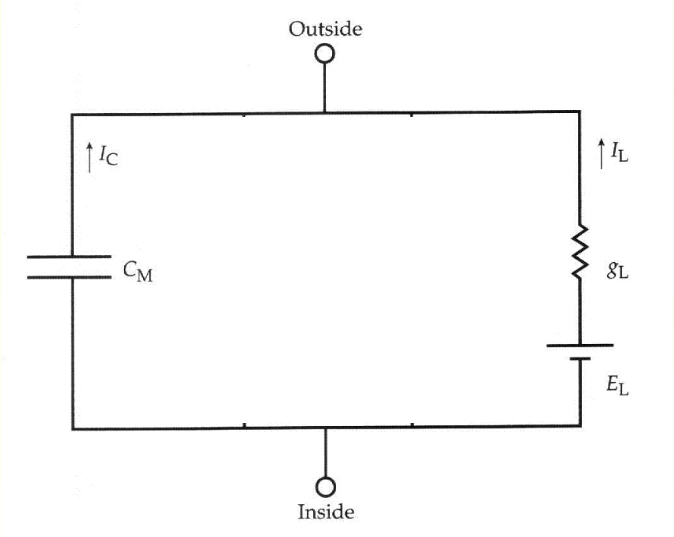


Membrane model:



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$$I_{STIMULUS} = C\frac{dV}{dt} + \frac{(V - V_{REST})}{R}$$

$$R(V,t) = R$$

$$V(t) = V_{REST} + I_{STIMULUS} R\left(1 - \mathrm{e}^{-t/RC}\right)$$

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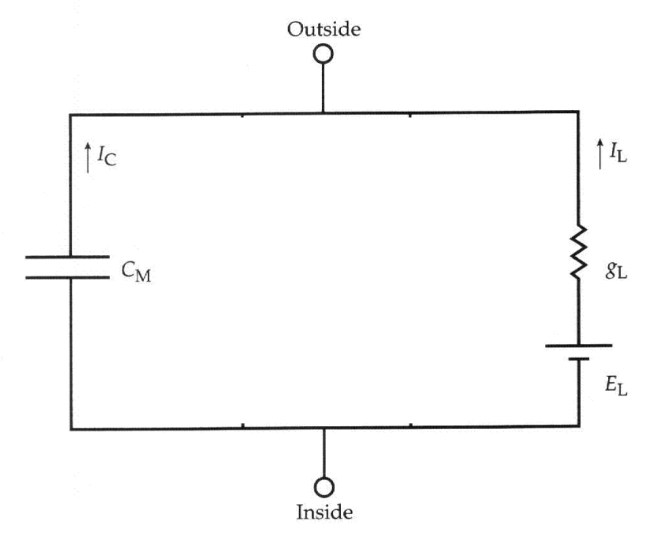

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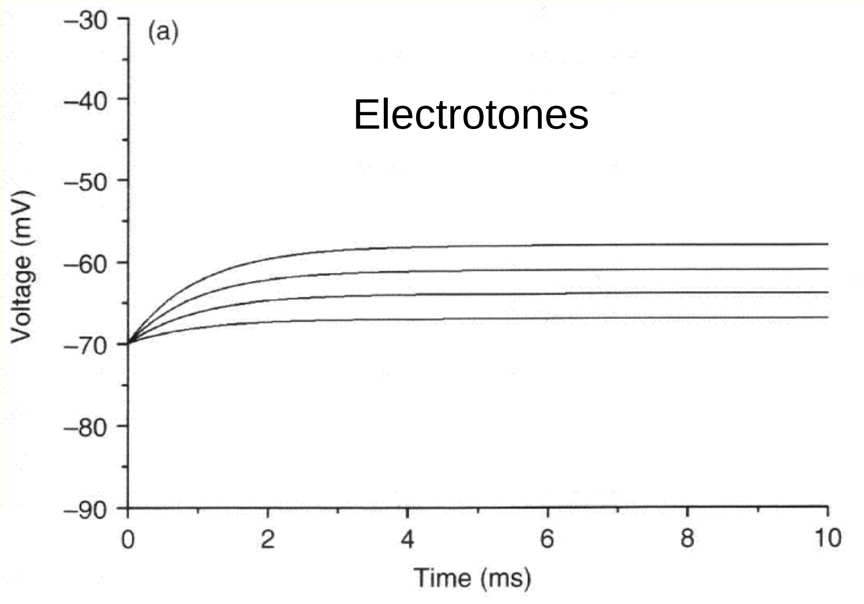

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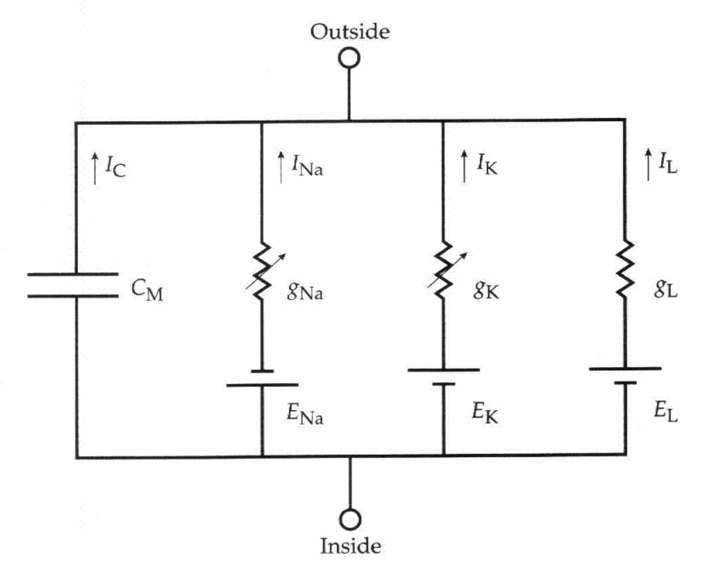
$$I_{STIMULUS} = C\frac{dV}{dt} + \frac{(V - V_{REST})}{R(V,t)}$$

Active properties

Membrane model:



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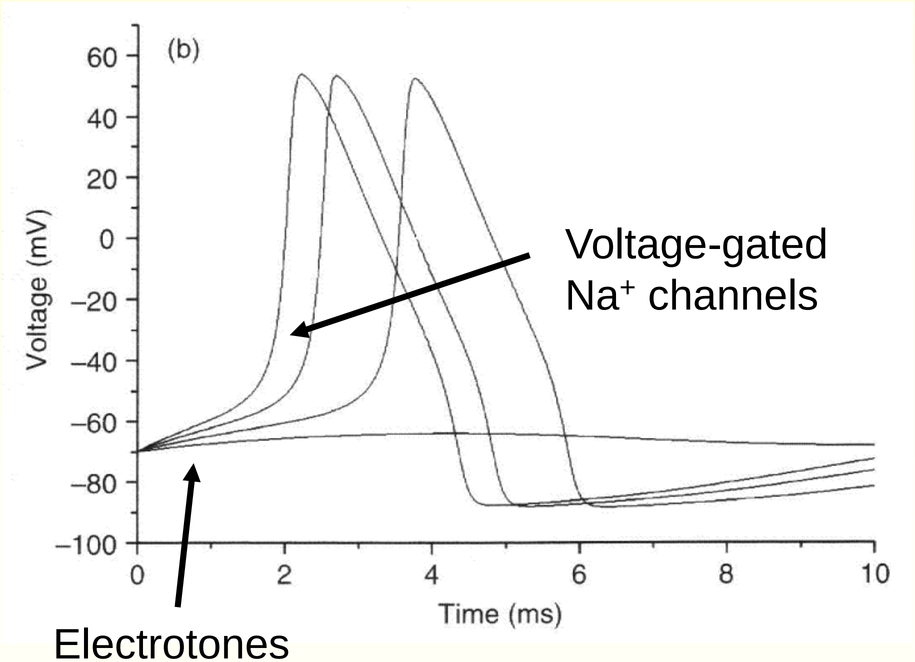
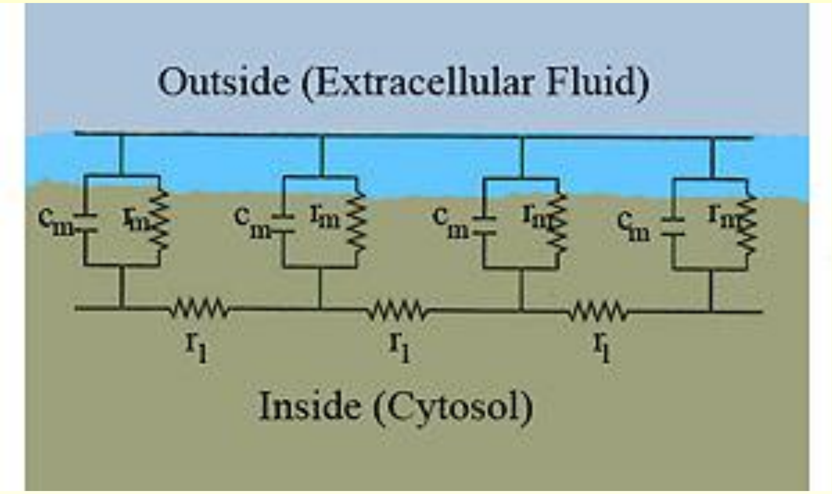
Active properties



Conduction along the axons: Cable theory

The Cable equation:

Axon equivalent circuit:



$$I_i = -\frac{\partial V}{\partial x}\frac{1}{r_i} \qquad I_m = -\frac{\partial I_i}{\partial x}$$

$$I_m = \frac{1}{r_i}\frac{\partial^2 V}{\partial x^2} = I_C + I_I$$

$$I_m = \frac{1}{r_i}\frac{\partial^2 V}{\partial x^2} = c_m \frac{\partial V}{\partial t} + \frac{V}{r_m}$$

$$V = \frac{r_m}{r_i}\frac{\partial^2 V}{\partial x^2} - r_m c_m \frac{\partial V}{\partial t}$$

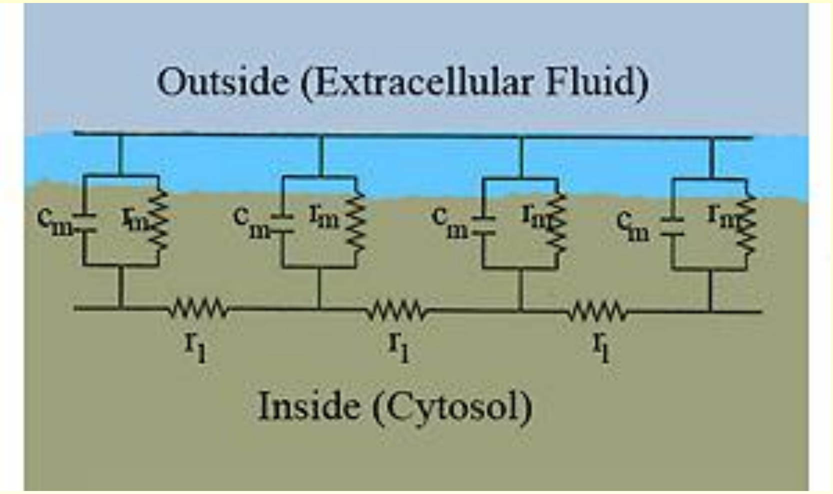
Cable equation (Hodgkin and Rushton, 1946)

Conduction along the axons: Cable theory

The Cable equation: Steady-state

$$V(x,t) = \frac{r_m}{r_i}\frac{\partial^2 V}{\partial x^2} - r_m c_m \cancel{\frac{\partial V}{\partial t}}^{\,0}$$

Axon equivalent circuit:



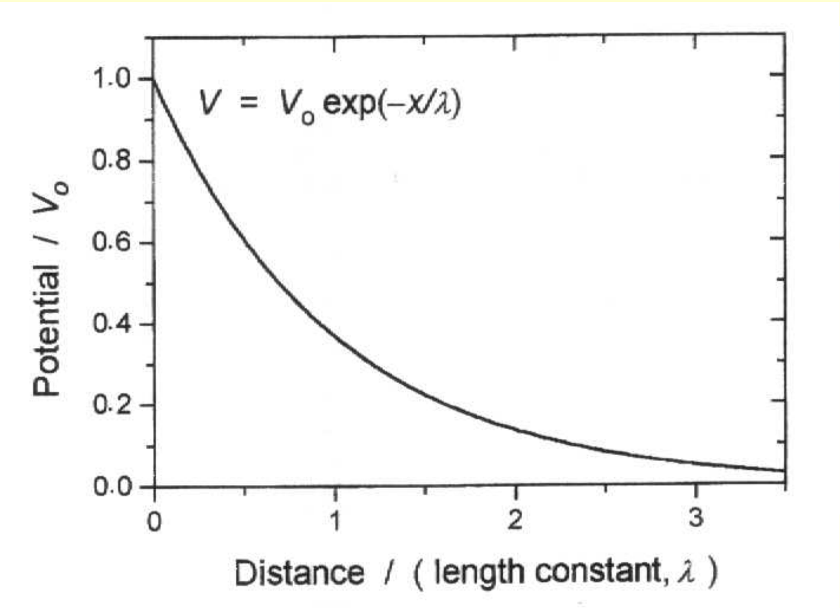
$$\left.\begin{aligned} V(x) &= \frac{r_m}{r_i}\frac{\partial^2 V}{\partial x^2} \\ V(x=0) &= V_0 \\ V(x=\infty) &= 0 \end{aligned}\right\}$$

$$V(x) = V_0 e^{-x/\lambda}$$

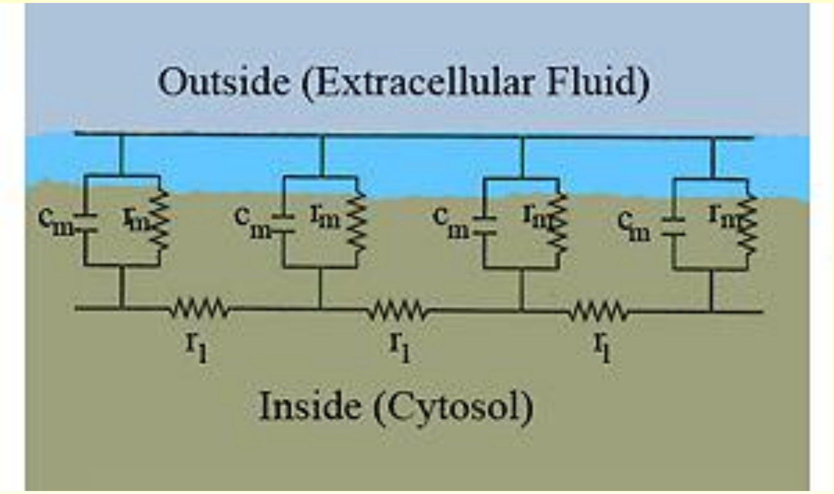
$$\lambda = \sqrt{r_m / r_i}$$ → Space constant $\lambda = \sqrt{\dfrac{a\rho_m}{2\rho_i}}$

Conduction along the axons: Cable theory

The Cable equation: Steady-state



Axon equivalent circuit:



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$$\lambda = \sqrt{r_m / r_i}$$ ⟶ Space constant $\lambda = \sqrt{\dfrac{a\rho_m}{2\rho_i}}$

Conduction along the axons: Cable theory

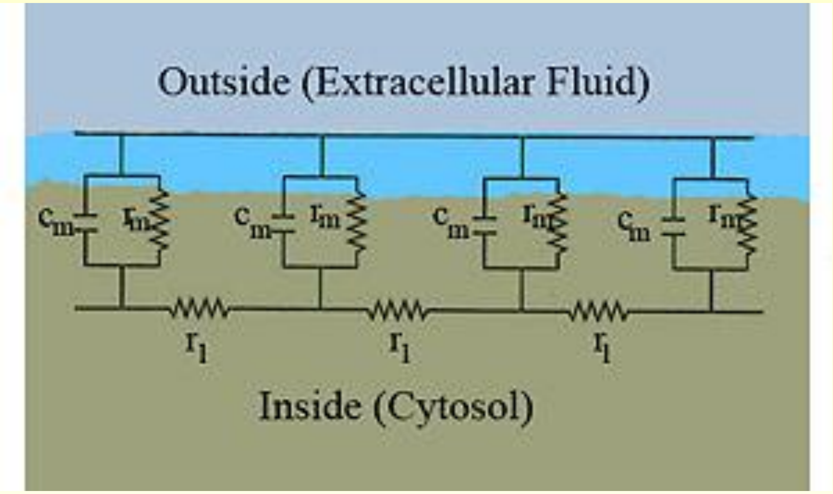
The Cable equation: Time dependency

$$V(x,t) = \frac{r_m}{r_i}\frac{\partial^2 V}{\partial x^2} - r_m c_m \frac{\partial V}{\partial t}$$

$$V(x,t) = \lambda^2 \frac{\partial^2 V}{\partial x^2} - \tau_m \frac{\partial V}{\partial t}$$

$$X = \frac{x}{\lambda} \qquad T = \frac{t}{\tau_m} = \frac{t}{r_m c_m}$$

Axon equivalent circuit:



Initial condition:

$$V(x; t=0) = 0$$

Boundary conditions:

$$V(x=0; t) = V_0$$

$$V(x=\infty; t) = 0$$

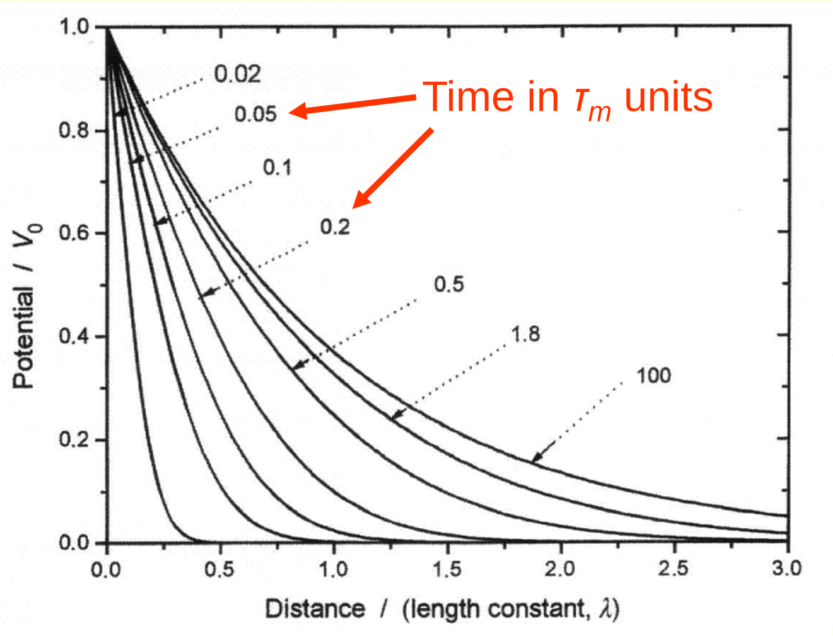
$$V(x,t) = \frac{1}{2}V_0\left\{e^{-X} Erfc\left(\frac{X}{2\sqrt{T}} - \sqrt{T}\right) + e^{X} Erfc\left(\frac{X}{2\sqrt{T}} + \sqrt{T}\right)\right\}$$

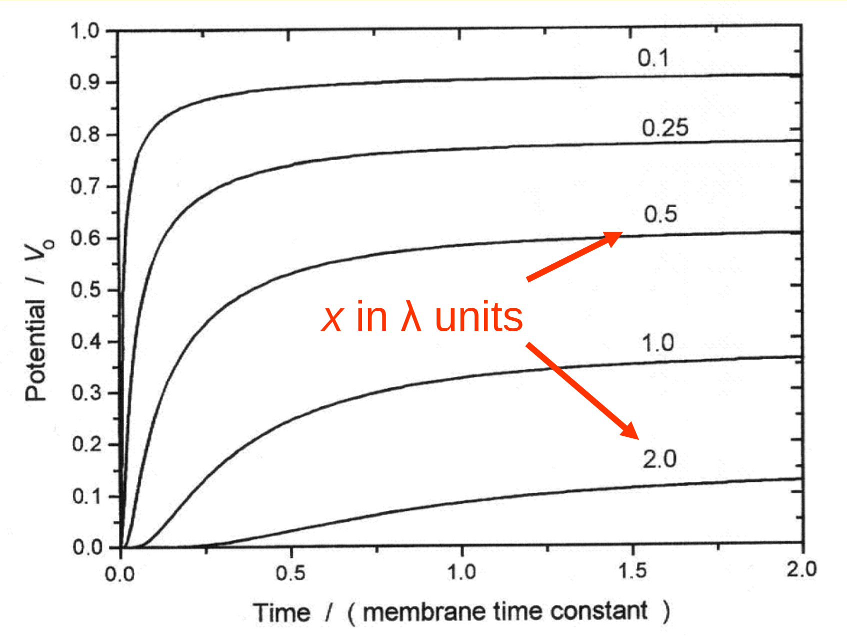
$$Erfc(x) = \frac{2}{\sqrt{\pi}}\int_0^x e^{-u^2}du$$

Conduction along the axons: Cable theory

The Cable equation: Time dependency

Axon equivalent circuit:





$$V(x,t) = \frac{1}{2} V_0 \left\{ e^{-X} Erfc\left(\frac{X}{2\sqrt{T}} - \sqrt{T} \right) + e^{X} Erfc\left(\frac{X}{2\sqrt{T}} + \sqrt{T} \right) \right\}$$

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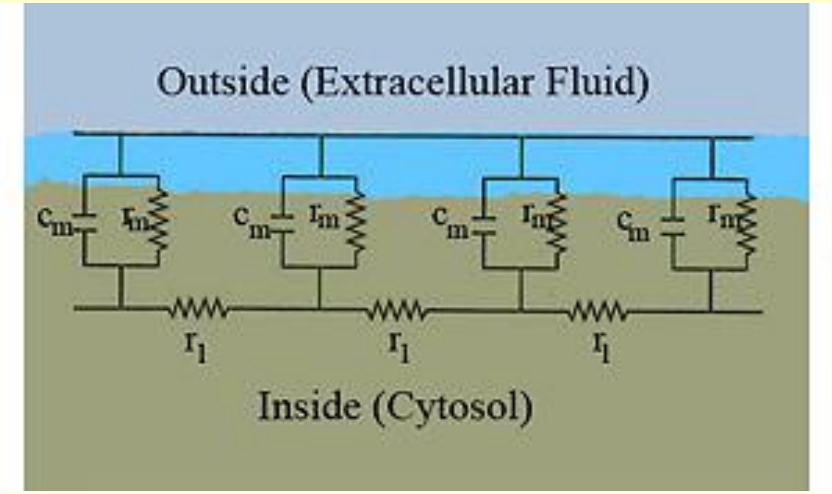
Conduction along the axons: Cable theory

So far for a pasive cable...
What about a “real” axon?

$$\frac{1}{r_i}\frac{\partial^2 V}{\partial x^2} = c_m \frac{\partial V}{\partial t} + \frac{V}{r_m}$$

$$\frac{1}{r_i}\frac{\partial^2 V}{\partial x^2} = c_m \frac{\partial V}{\partial t} + i_{Na} + i_K + i_L$$

Axon equivalent circuit:



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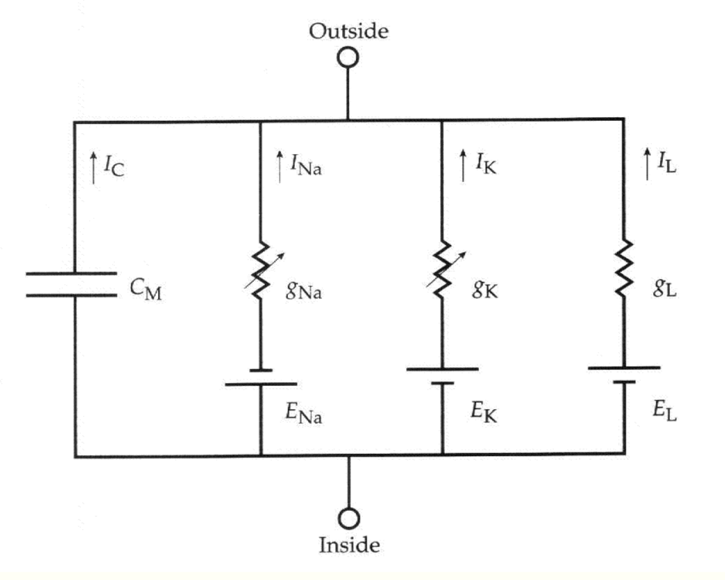
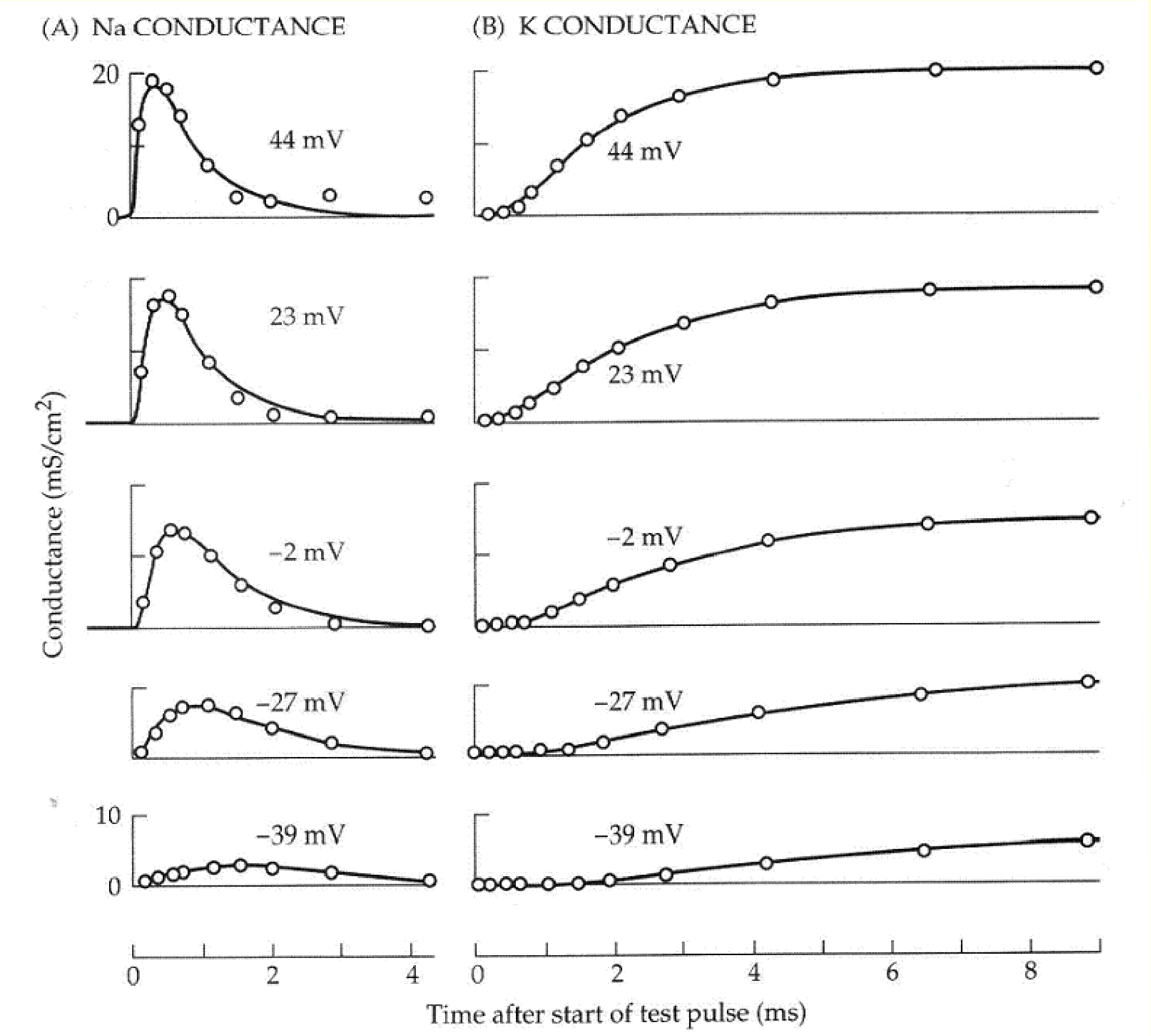


Voltage-gated channels

Classical biophysics of the squid giant axon



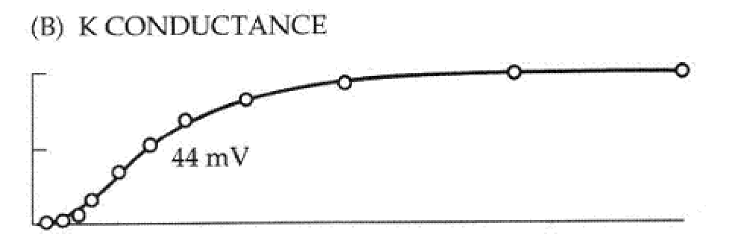
Voltage-gated channels

Classical biophysics of the squid giant axon

The Hodgkin-Huxley model of nerve excitability: the **HH model**

Nerve potassium channel:

$$I_K = n^4 \bar{g}_K \left(V - V_K\right) \qquad 1 - n \underset{\beta_n}{\overset{\alpha_n}{\rightleftarrows}} n$$



$$\frac{dn}{dt} = \alpha_n \left(1 - n\right) - \beta_n n \qquad \begin{cases} \tau_n = \dfrac{1}{\alpha_n + \beta_n} \\ \\ n_\infty = \dfrac{\alpha_n}{\alpha_n + \beta_n} \end{cases} \qquad n(t) = n_\infty - \left(n_\infty - n_0\right)\exp\left(-\frac{t}{\tau_n}\right)$$

Voltage-gated channels

Classical biophysics of the squid giant axon

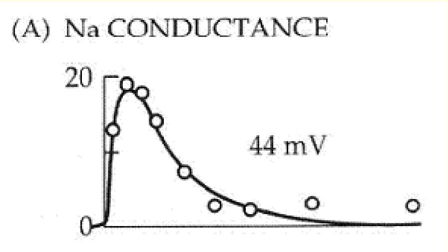
The Hodgkin-Huxley model of nerve excitability: the **HH model**

Nerve sodium channel:

$$I_{Na} = m^3 h \bar{g}_{Na}\left(V - V_{Na}\right)$$

$$1-m \underset{\beta_m}{\overset{\alpha_m}{\rightleftarrows}} m$$

$$1-h \underset{\beta_h}{\overset{\alpha_h}{\rightleftarrows}} h$$



$$\frac{dm}{dt} = \alpha_m\left(1-m\right) - \beta_m m$$

$$\frac{dh}{dt} = \alpha_h\left(1-h\right) - \beta_h h$$

$$\begin{cases} \tau_m = \dfrac{1}{\alpha_m + \beta_m} & \tau_h = \dfrac{1}{\alpha_h + \beta_h} \\[2ex] m_\infty = \dfrac{\alpha_m}{\alpha_m + \beta_m} & h_\infty = \dfrac{\alpha_h}{\alpha_h + \beta_h} \end{cases}$$

$$m^3\left(t\right)h\left(t\right) = \left[m_\infty - \left(m_\infty - m_0\right)\exp\left(-\frac{t}{\tau_m}\right)\right]^3 \cdot \left[h_\infty - \left(h_\infty - h_0\right)\exp\left(-\frac{t}{\tau_h}\right)\right]$$

Voltage-gated channels

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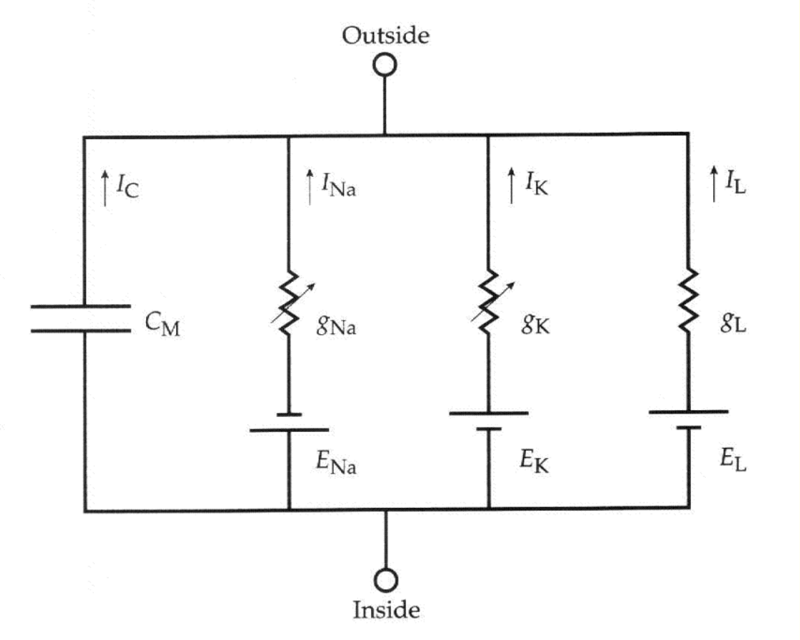
The Hodgkin-Huxley model of nerve excitability: the **HH model**

Nerve membrane conductances:

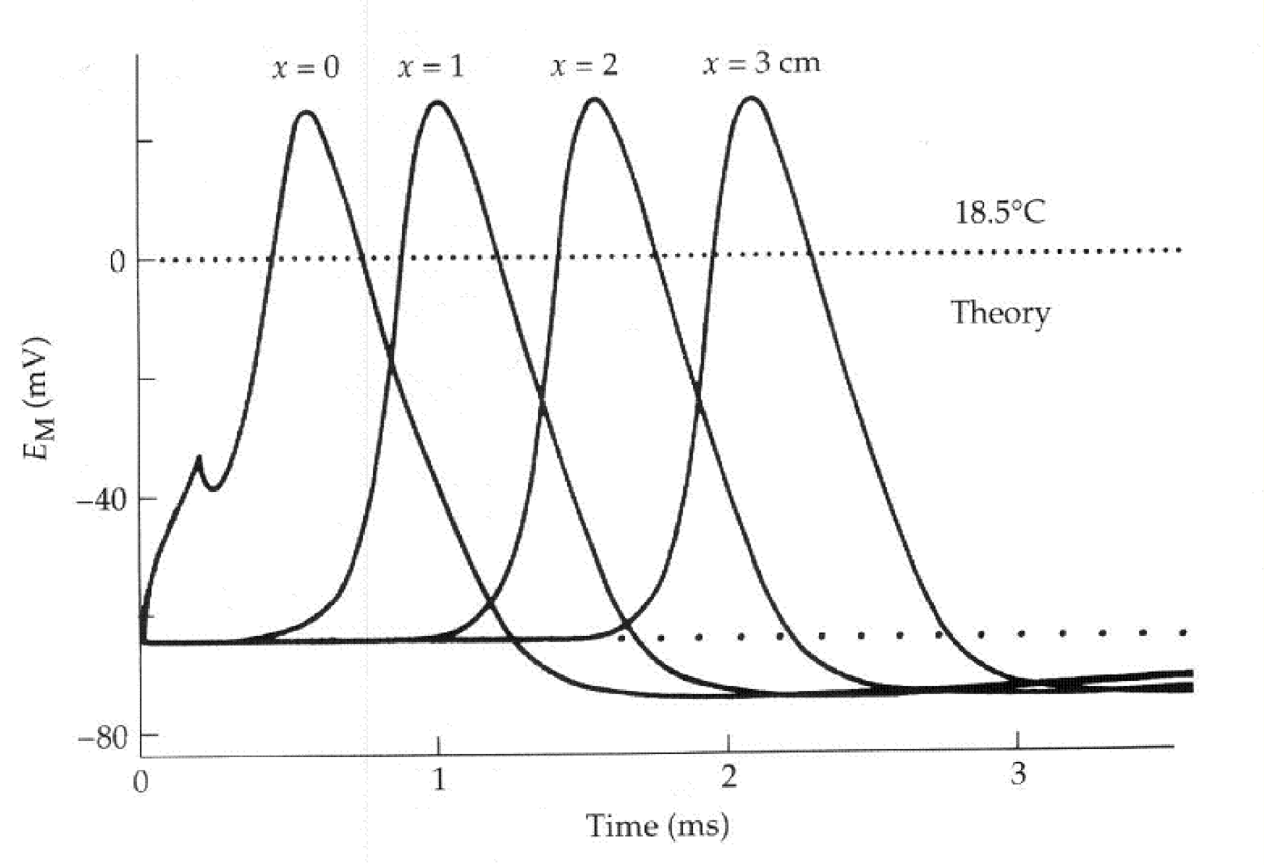


$$I_T = m^3 h \bar{g}_{Na}\left(V - V_{Na}\right) + n^4 \bar{g}_K\left(V - V_K\right) + \bar{g}_{Leak}\left(V - V_{Leak}\right)$$

Voltage-gated channels

Classical biophysics of the squid giant axon

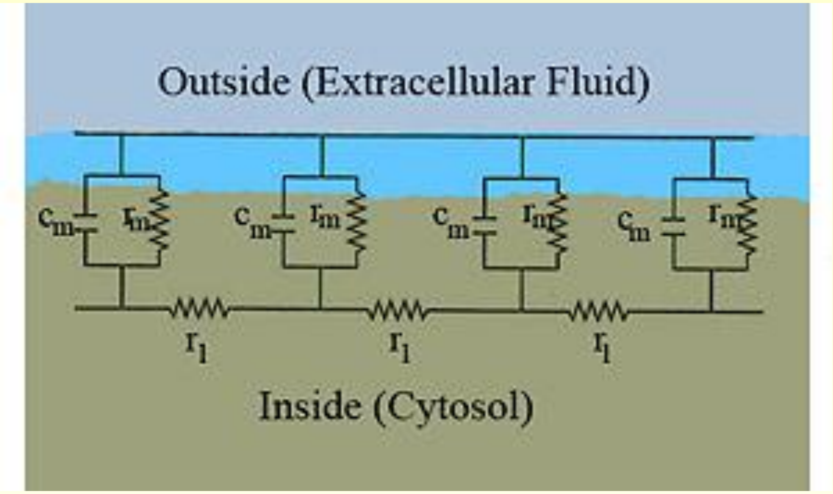
The Hodgkin-Huxley model of nerve excitability: the **HH model**



Conduction along the axons: Cable theory

So far for a pasive cable...
What about a “real” axon?

Axon equivalent circuit:



$$\frac{1}{r_i}\frac{\partial^2 V}{\partial x^2} = c_m \frac{\partial V}{\partial t} + \frac{V}{r_m}$$

$$\frac{1}{r_i}\frac{\partial^2 V}{\partial x^2} = c_m \frac{\partial V}{\partial t} + i_{Na} + i_K + i_L$$

$$\frac{a}{2\rho_i}\frac{\partial^2 V}{\partial x^2} = C_m \frac{\partial V}{\partial t} + \underbrace{I_{Na} + I_K + I_L}_{} \quad \text{(per unit area)}$$

$$I_T = m^3 h \bar{g}_{Na}\left(V - V_{Na}\right) + n^4 \bar{g}_K \left(V - V_K\right) + \bar{g}_{Leak}\left(V - V_{Leak}\right)$$

Hodgkin-Huxley Cable equation

Conduction along the axons: Cable theory

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$$\frac{a}{2\rho_i}\frac{\partial^2 V}{\partial x^2} = C_m \frac{\partial V}{\partial t} + m^3 h \overline{g}_{Na}\left(V - V_{Na}\right) + n^4 \overline{g}_K \left(V - V_K\right) + \overline{g}_{Leak}\left(V - V_{Leak}\right)$$

Now let’s take into account that the excitation propagates as a wave:

$V\left(x,t\right) = V\left(x - \theta t\right)$ θ: velocity of the wave

Then: $$\frac{\partial^2 V}{\partial x^2} = \frac{1}{\theta^2}\frac{\partial^2 V}{\partial t^2}$$

$$\frac{a}{2\rho_i \theta^2}\frac{\partial^2 V}{\partial t^2} = C_m \frac{\partial V}{\partial t} + m^3 h \overline{g}_{Na}\left(V - V_{Na}\right) + n^4 \overline{g}_K \left(V - V_K\right) + \overline{g}_{Leak}\left(V - V_{Leak}\right)$$

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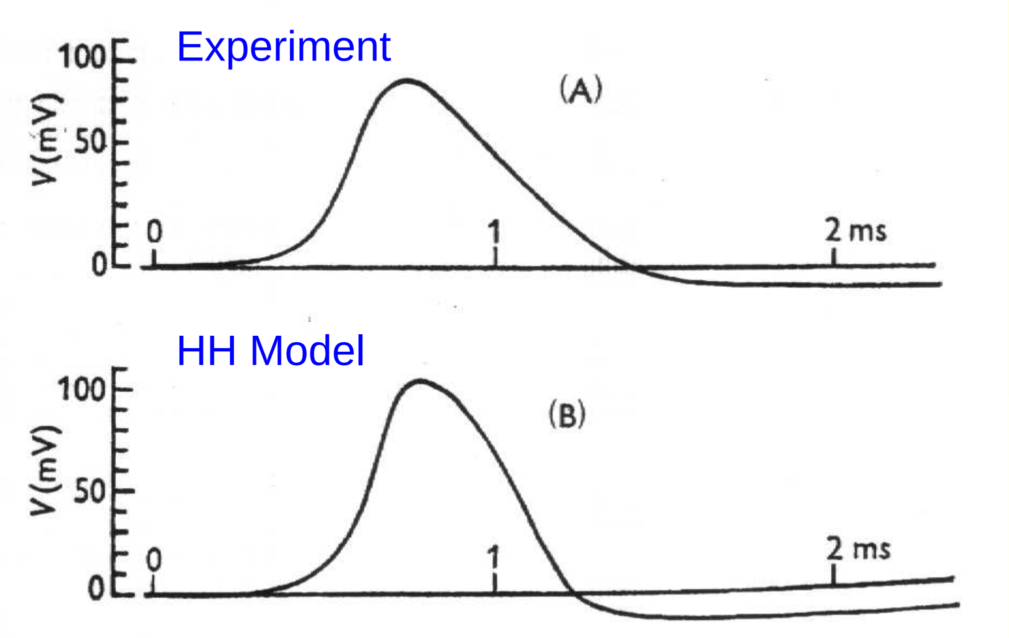


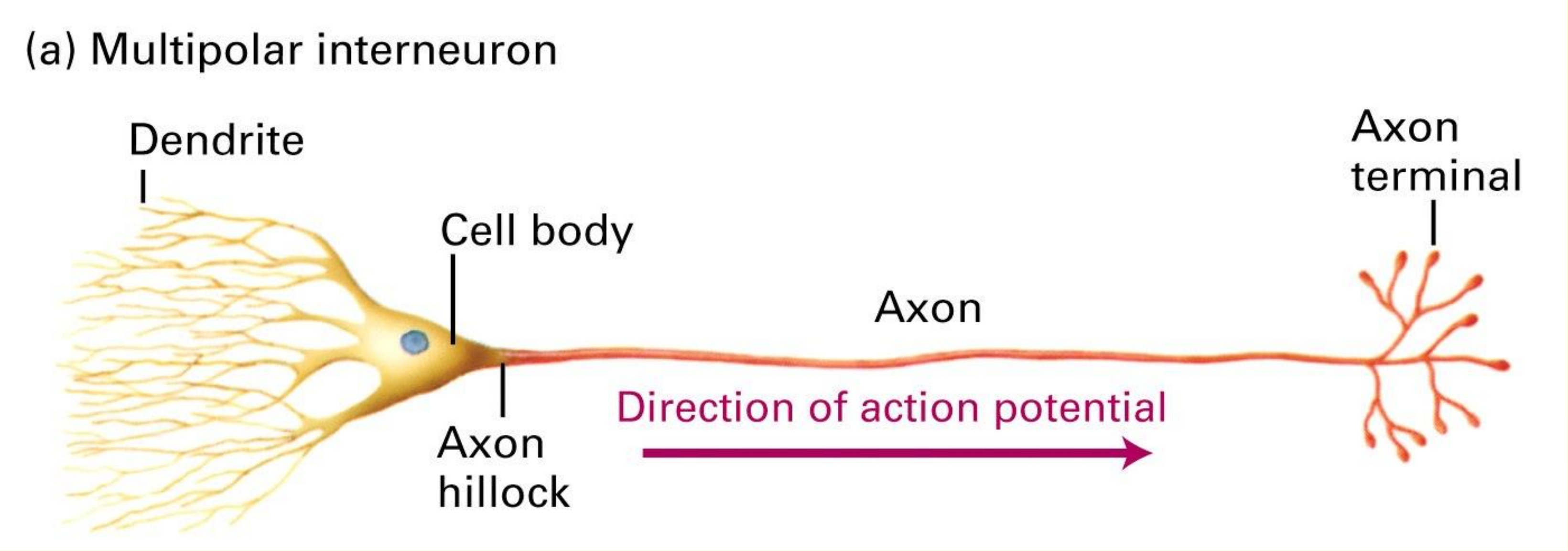
$$a = 0.24 \text{ mm}$$

$$\rho_i = 3.45\ \Omega \cdot \text{cm}$$

$$\theta_{Experimental} = 21.2 \text{ m} \cdot \text{s}^{-1}$$

$$\theta_{Model} = 18.8 \text{ m} \cdot \text{s}^{-1}$$

Conduction along the axons: Cable theory



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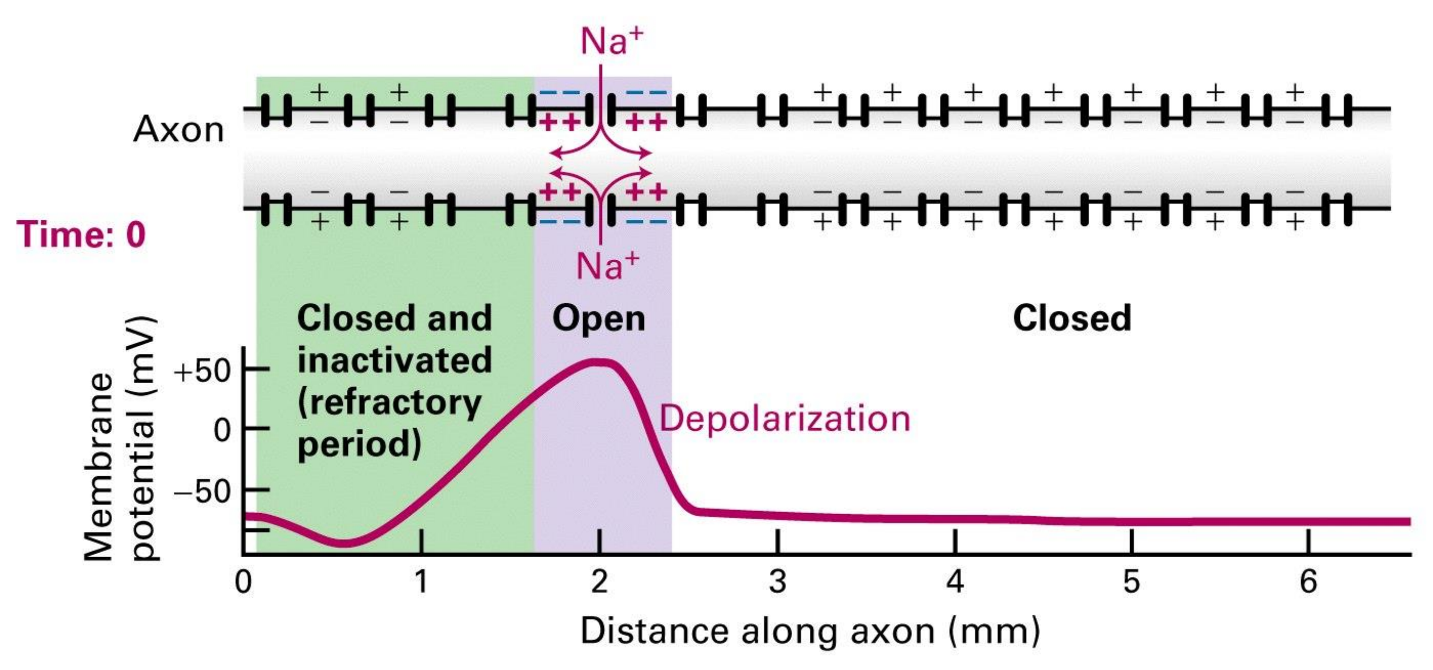

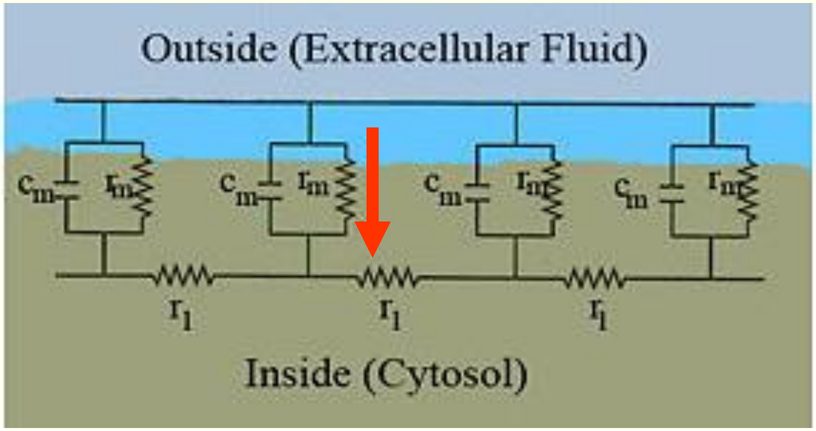

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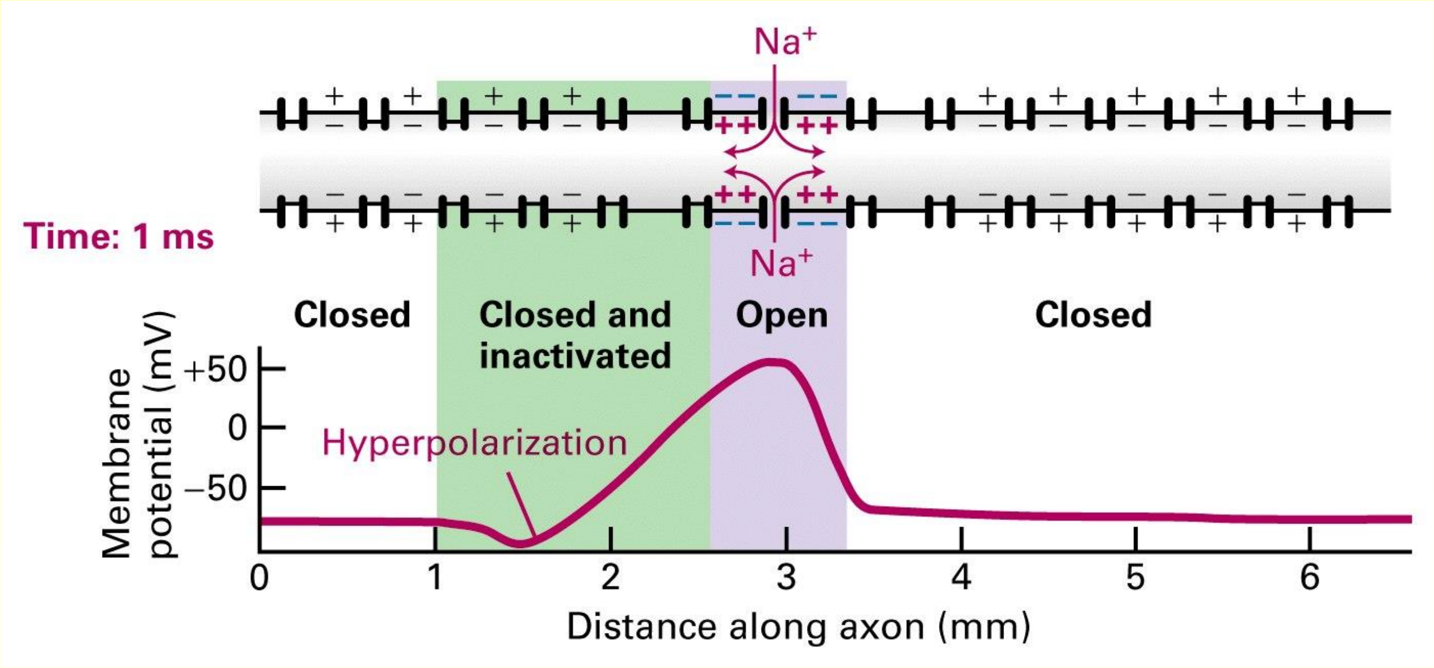
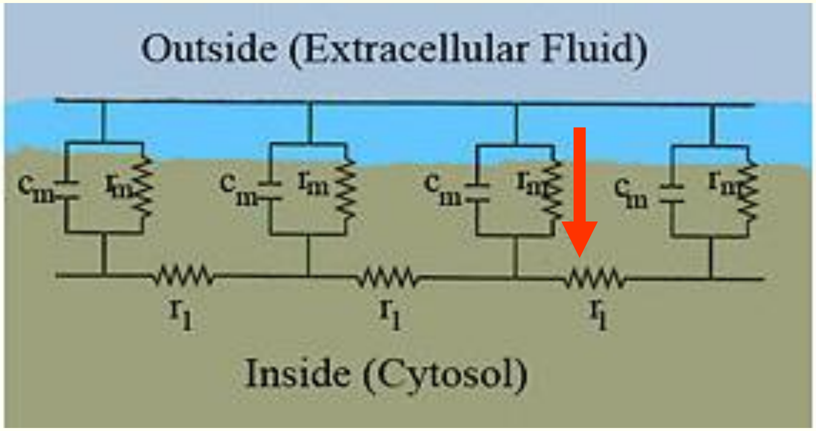
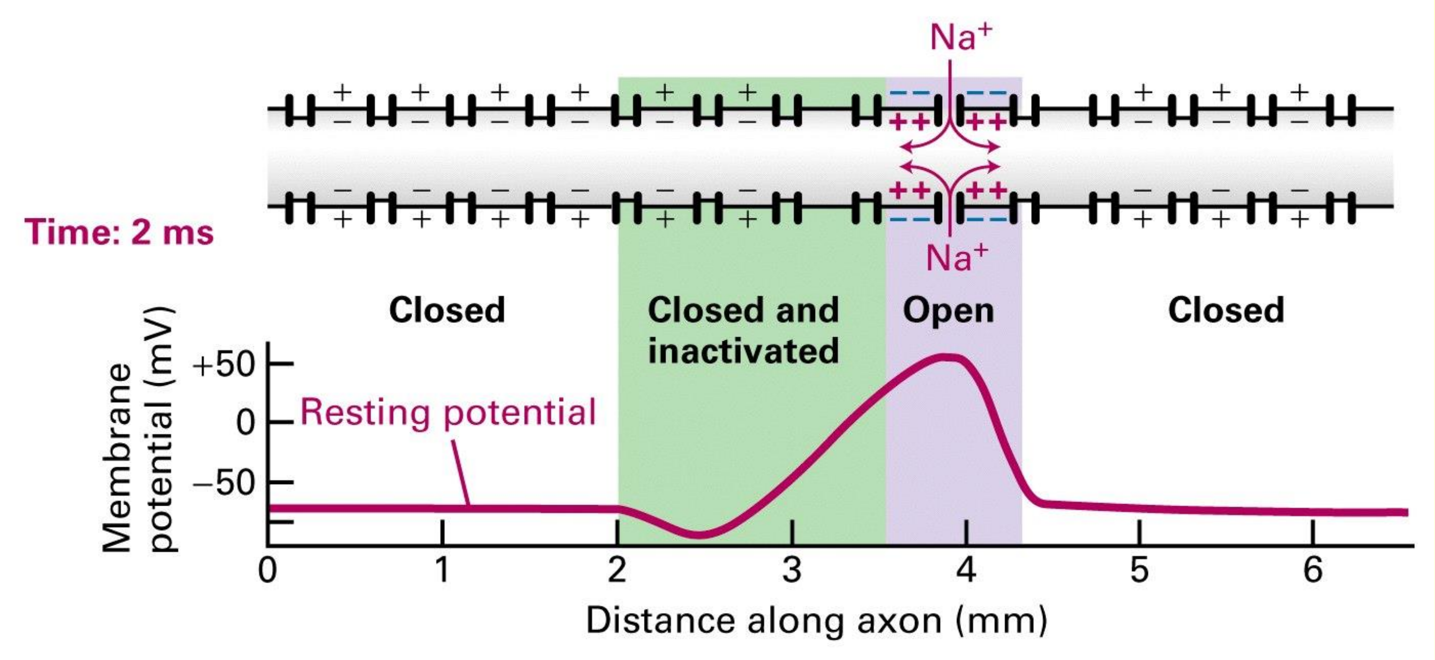
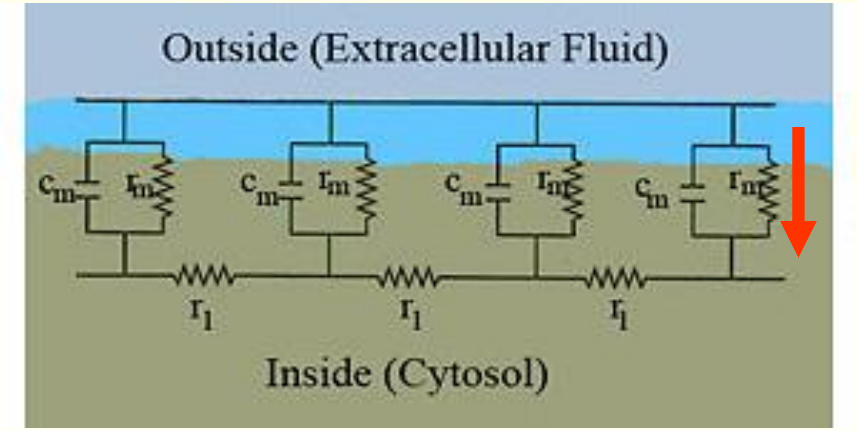




Conduction along the axons: Cable theory





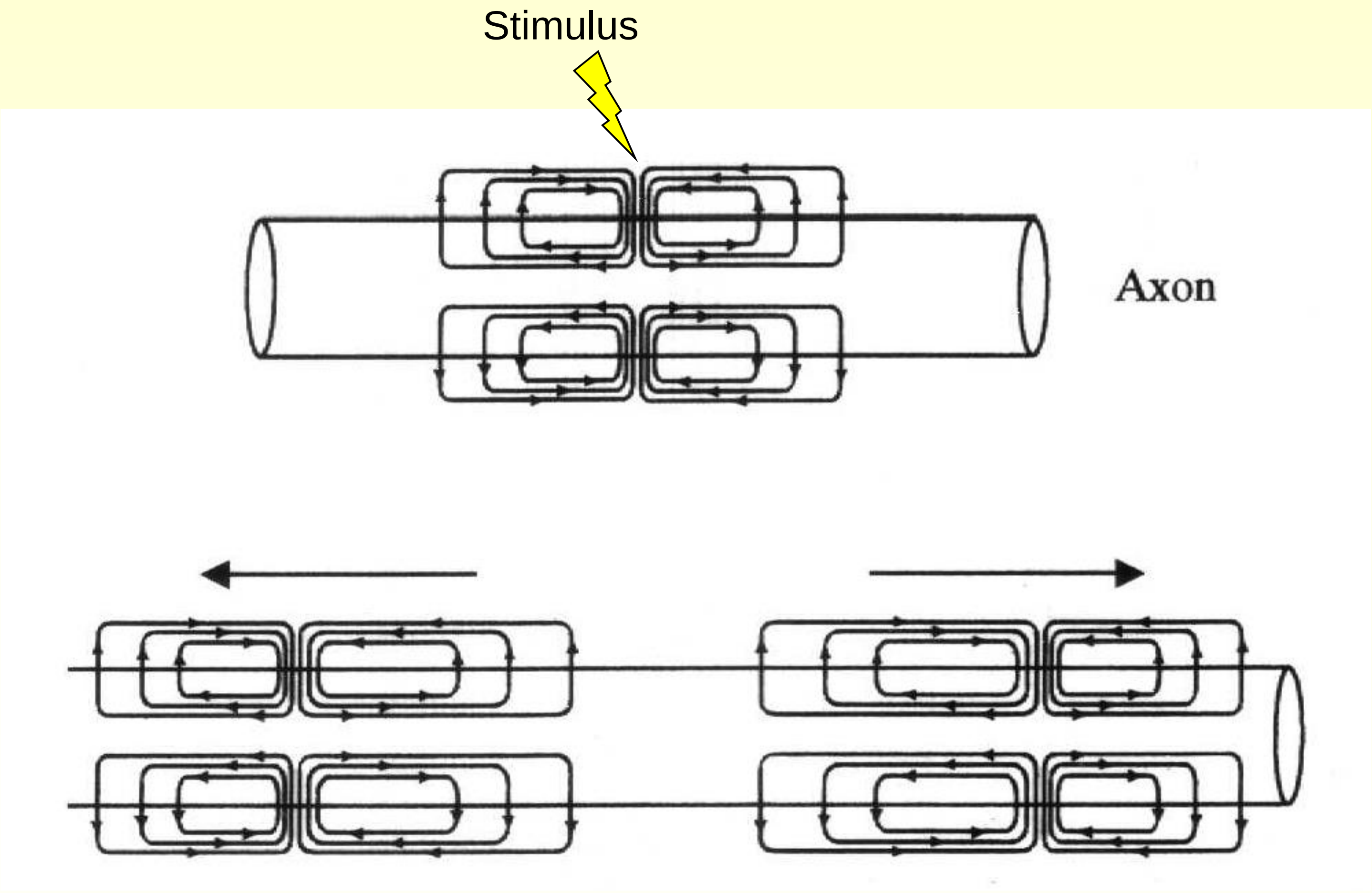
Sodium channel gating

$$C \leftrightarrow O \leftrightarrow I$$

Refactory period

Conduction along the axons: Cable theory

The conduction of the excitation relies on *local current loops (Hermann loops)*



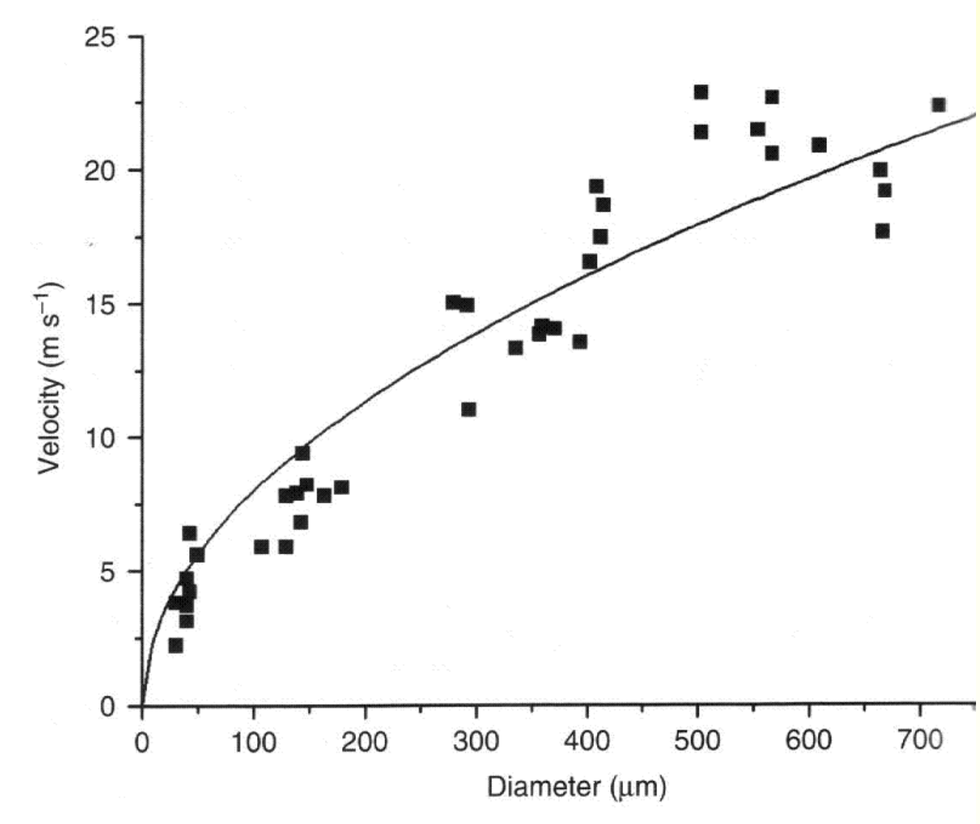
Conduction along the axons: Cable theory

What are the determinants of the conduction velocity?

$$\frac{a}{2\rho_i C_m \theta^2}\frac{\partial^2 V}{\partial t^2} = \frac{\partial V}{\partial t} + m^3 h \frac{\bar{g}_{Na}}{C_m}(V - V_{Na}) + n^4 \frac{\bar{g}_K}{C_m}(V - V_K) + \frac{\bar{g}_{Leak}}{C_m}(V - V_{Leak})$$

$$\frac{a}{2\rho_i C_m \theta^2} = \frac{1}{k} = \text{constant}$$

$$\theta = \sqrt{\frac{ka}{2\rho_i C_m}}$$



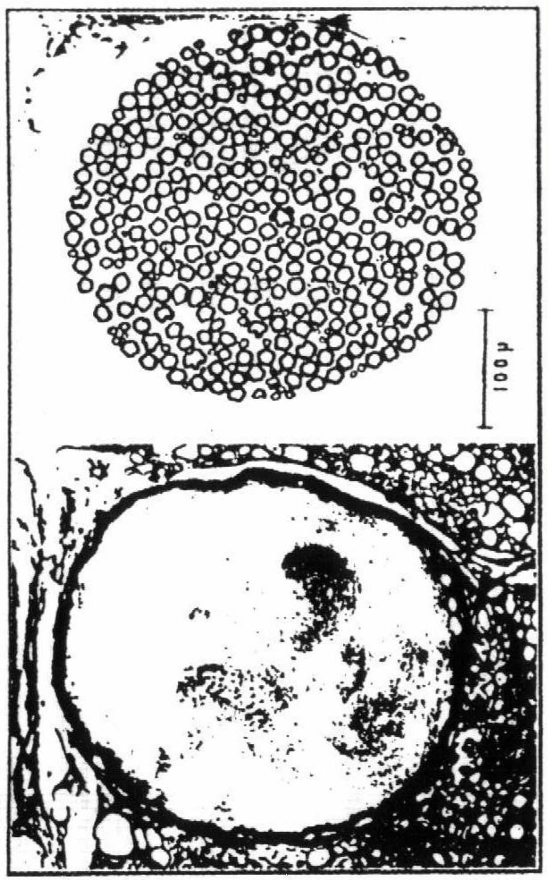
Conduction along the axons: Cable theory

What are the determinants of the conduction velocity?

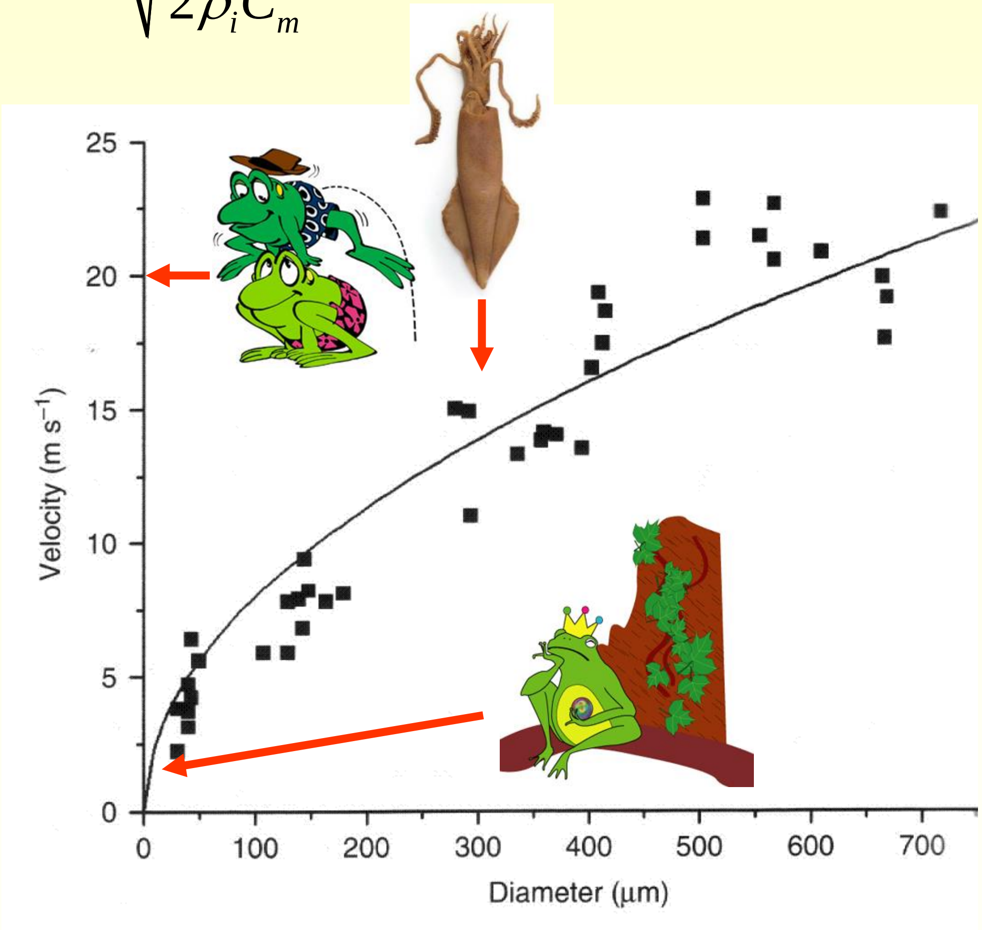
How can vertebrates achive high velocity with thin nerves?

$$\theta = \sqrt{\frac{ka}{2\rho_i C_m}}$$

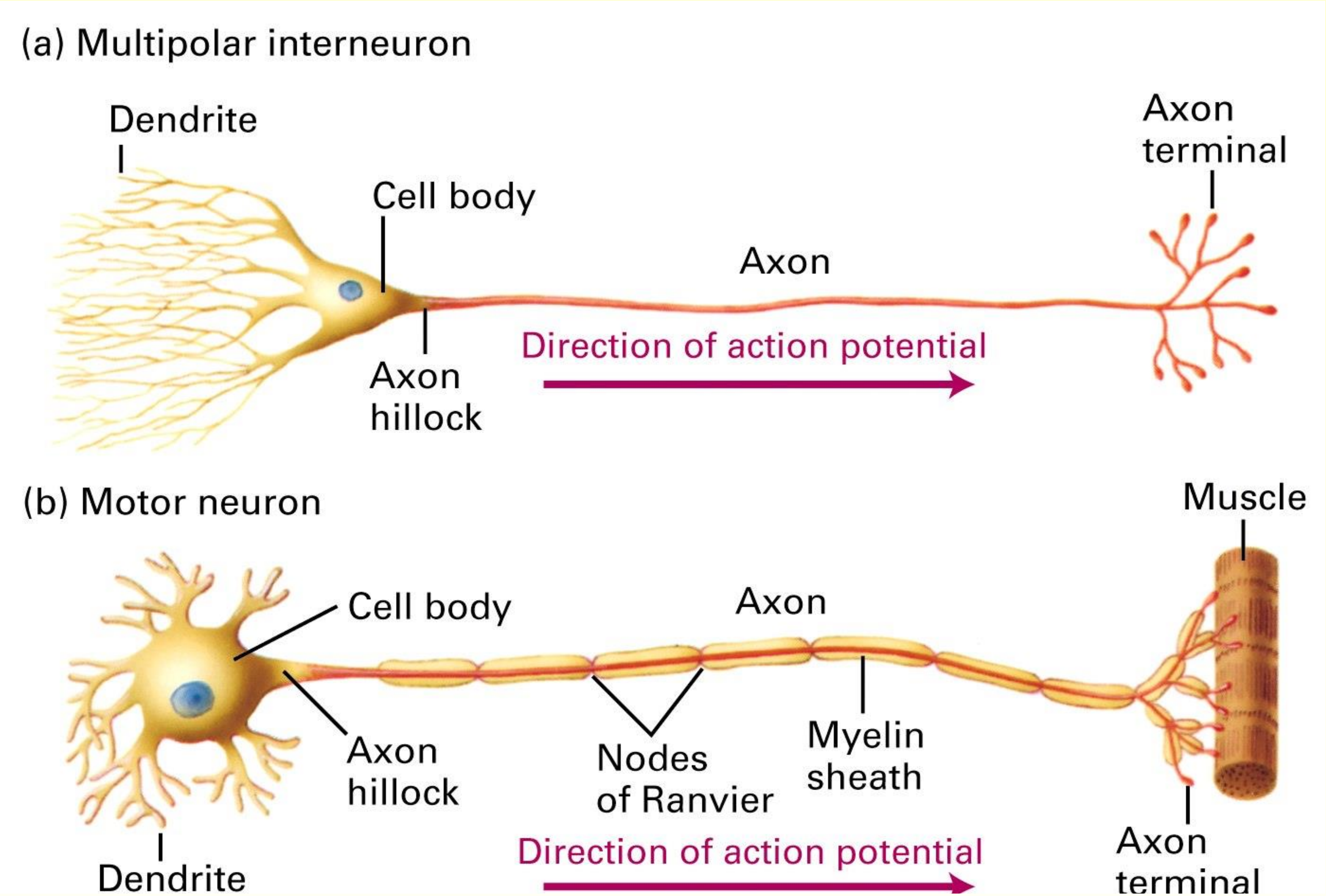
Frog sciatic nerve



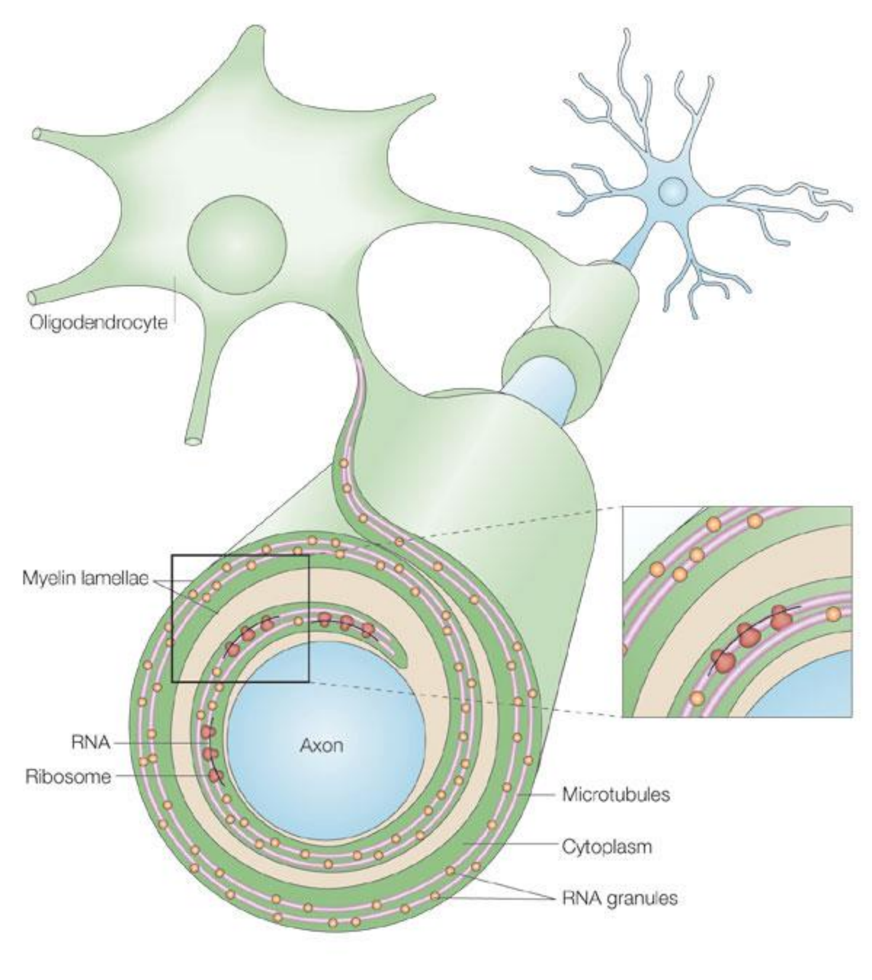
Squid giant axon



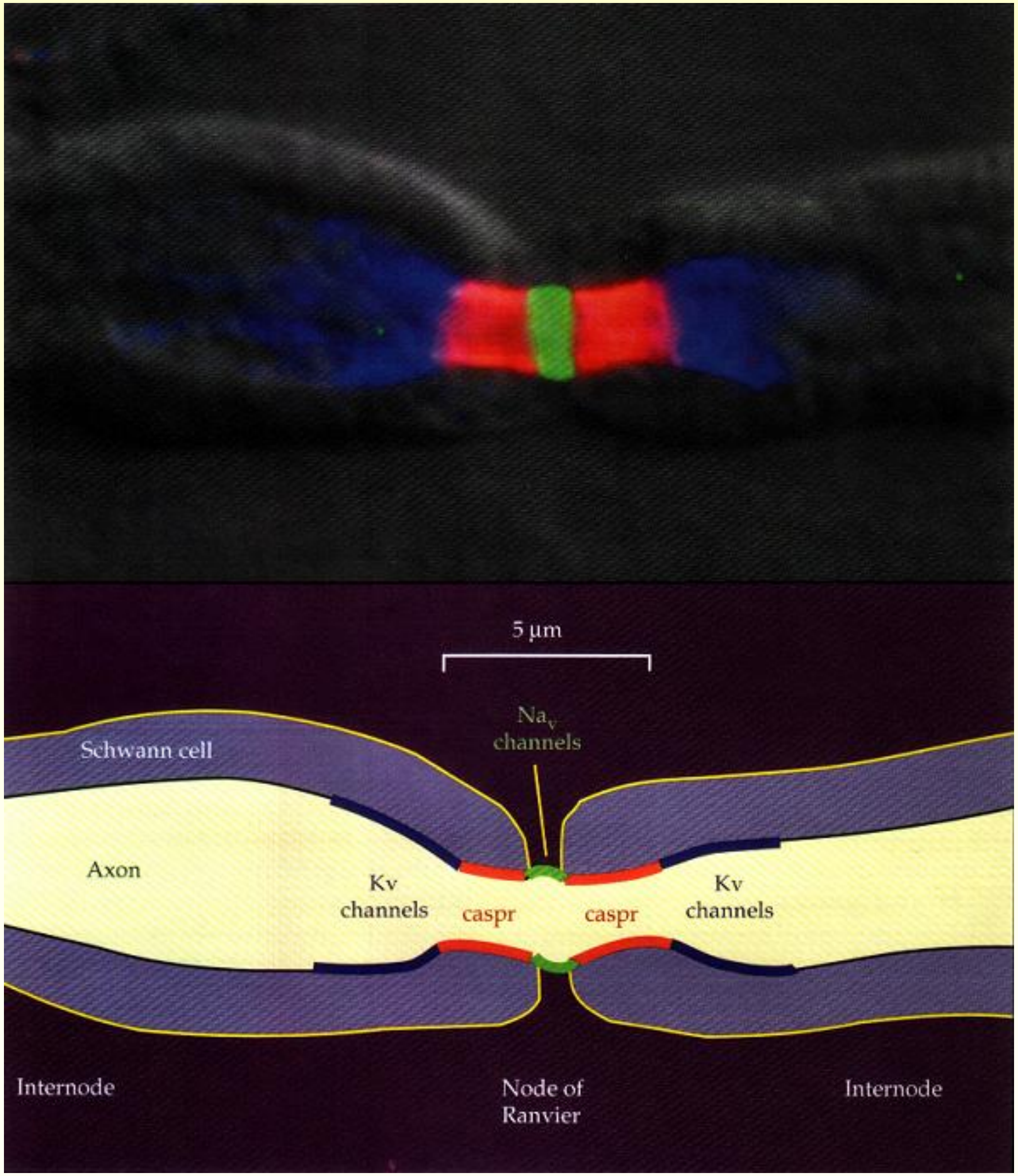
Conduction along myelinated axons



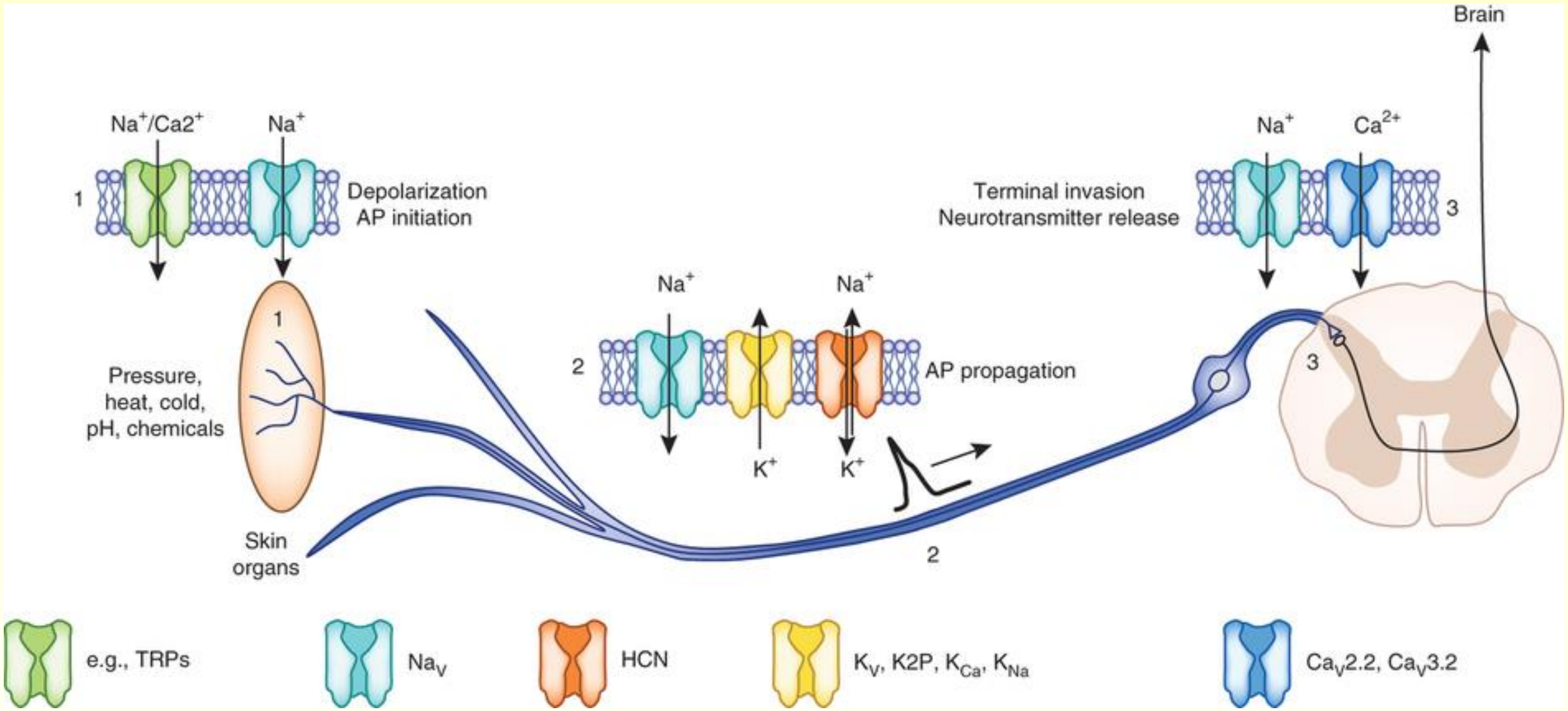
Conduction along myelinated axons



Conduction along myelinated axons

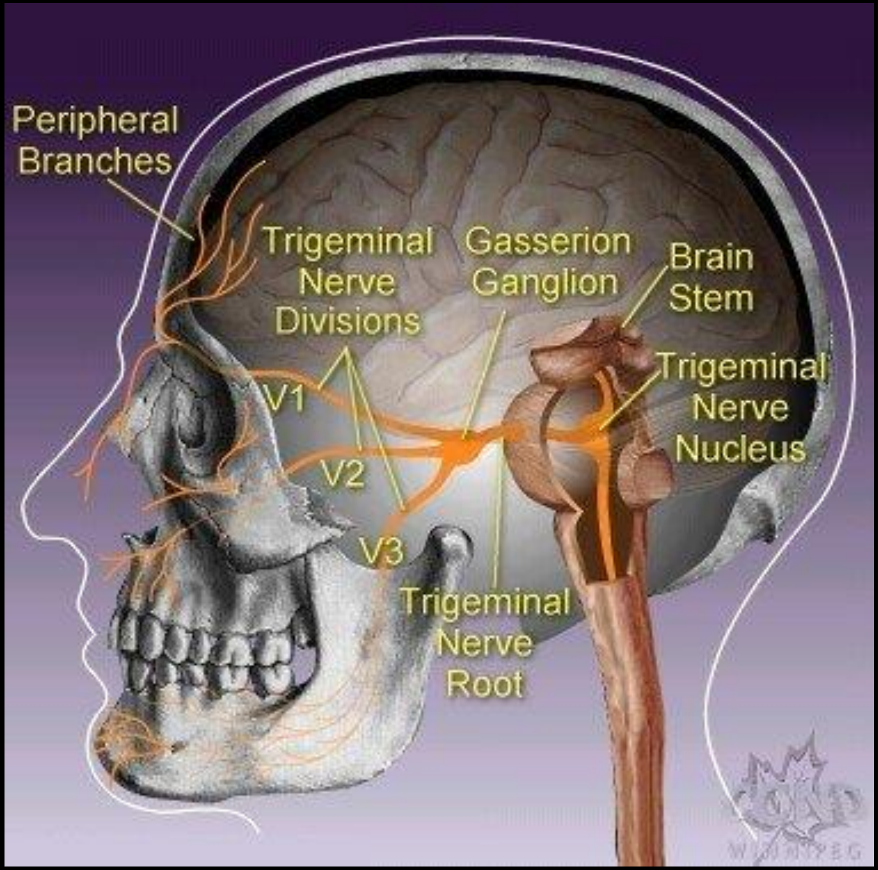


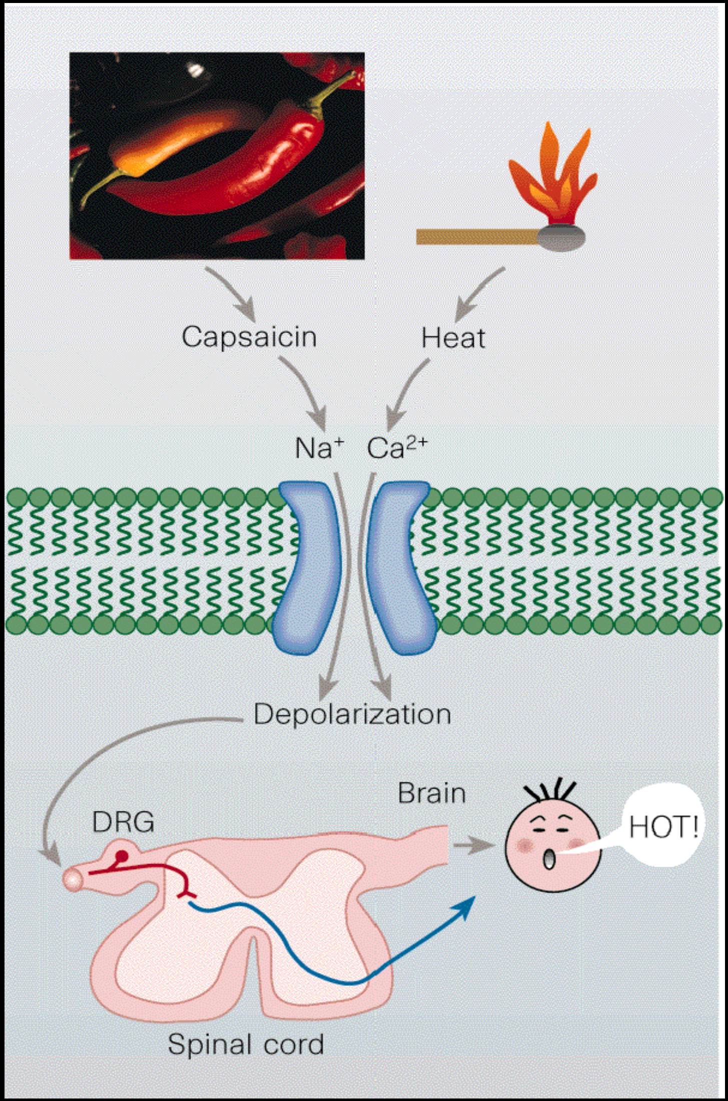
Generation of action potentials in sensory nerve endings



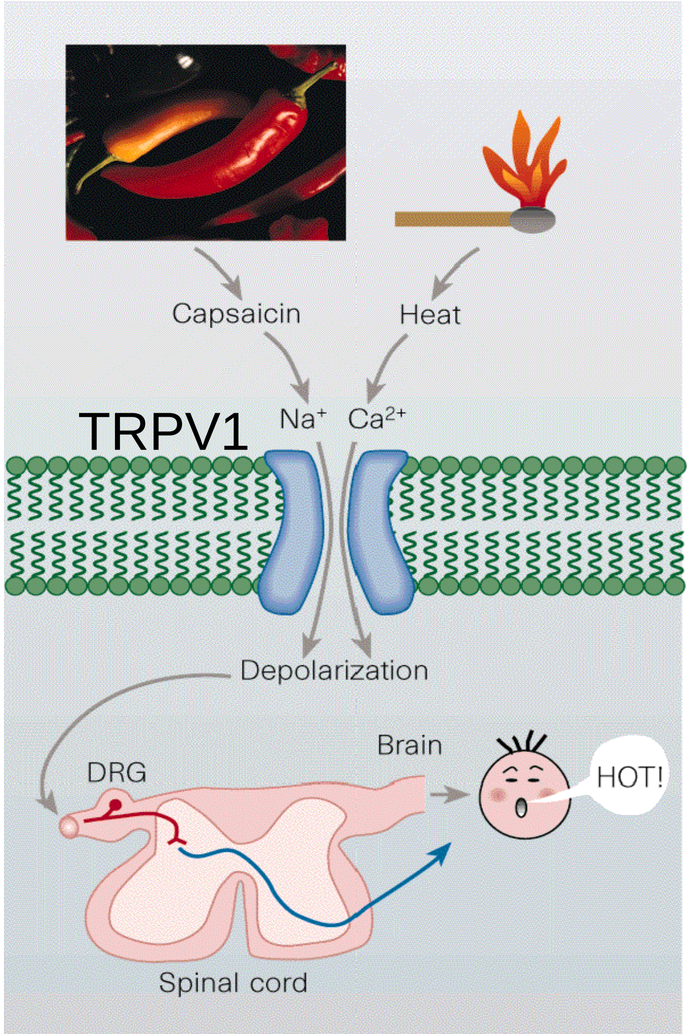
TRPV1: an excitatory channel in the pain pathway

- **Capsaicin receptor**
- **Activated by noxious heat and acidosis**

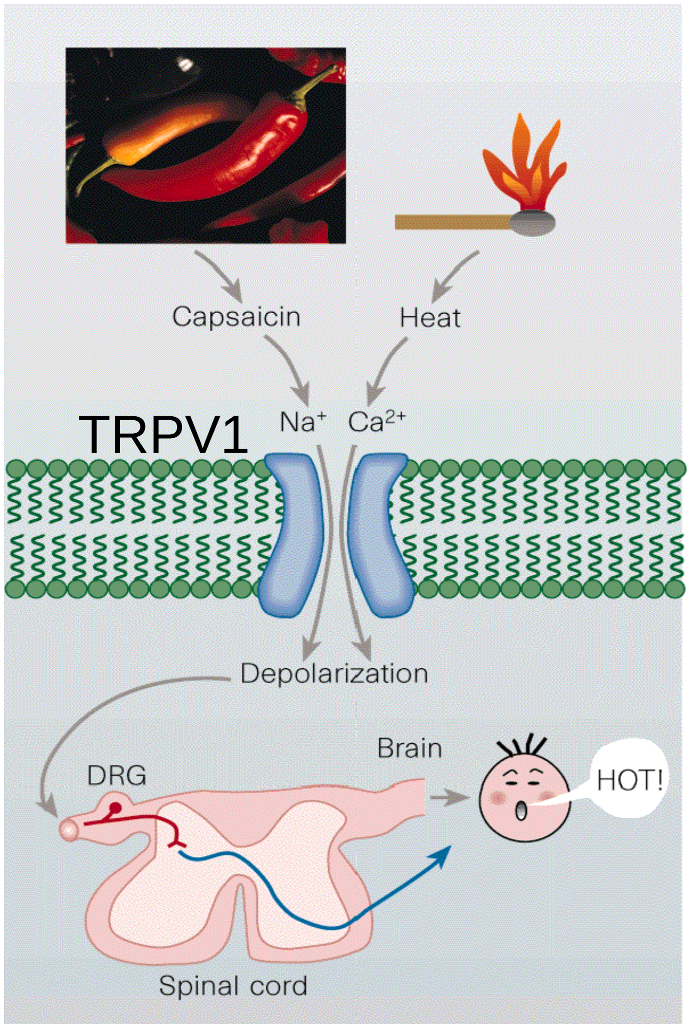


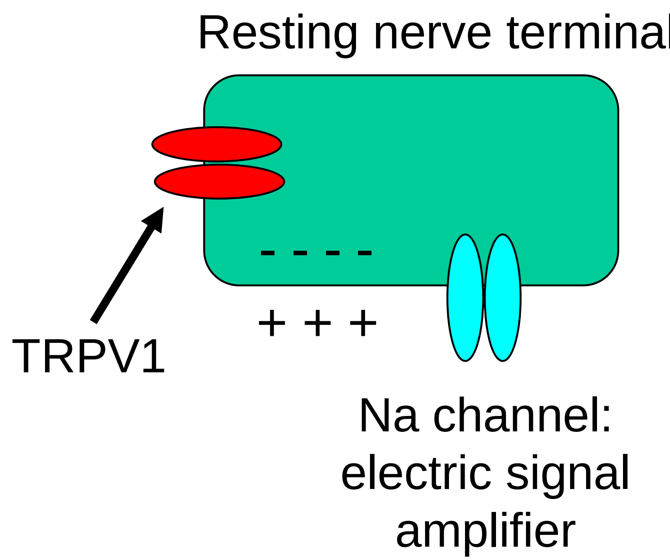


Ion channels as key molecular sensors

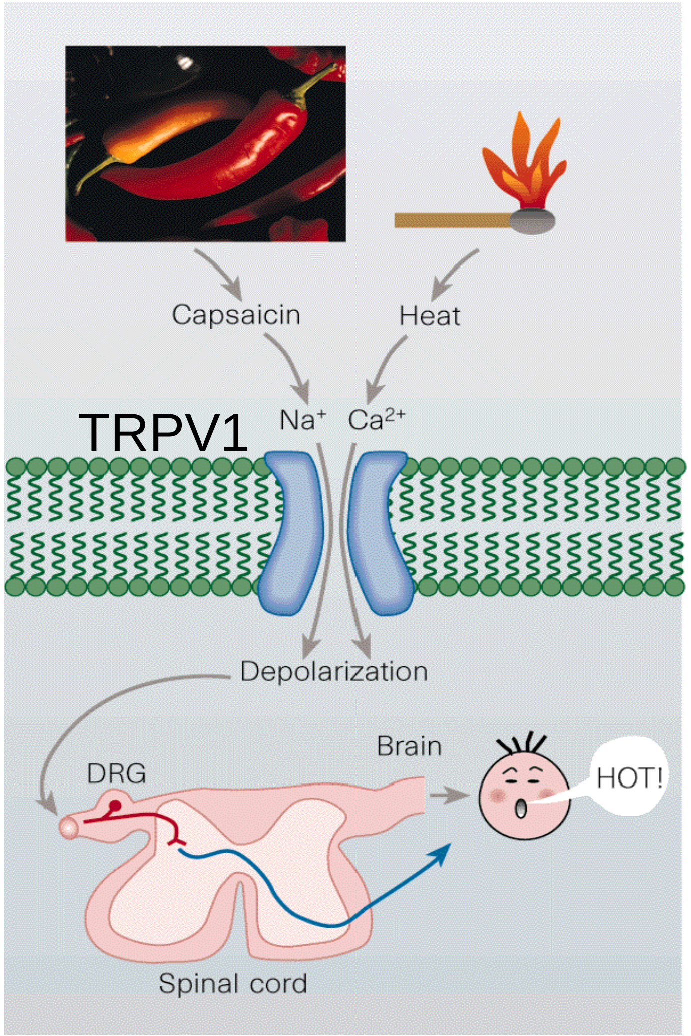


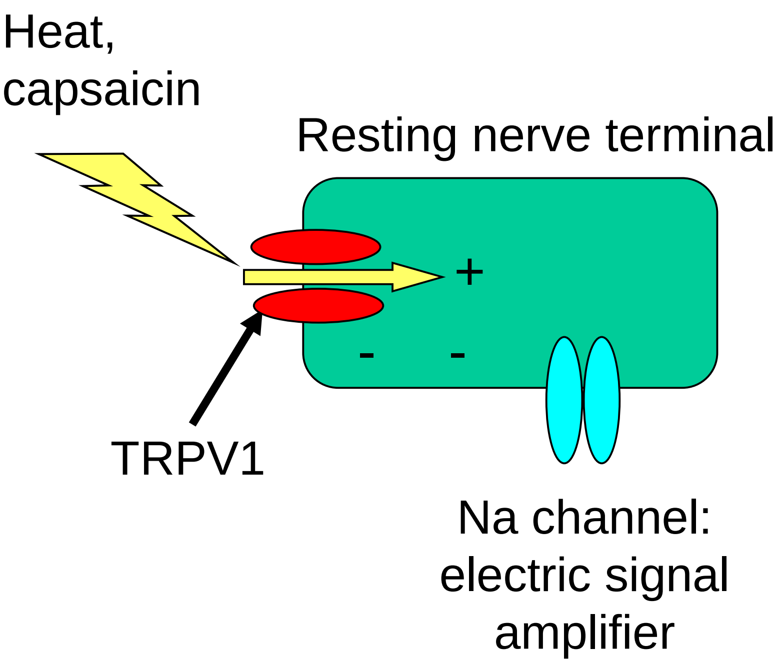
Ion channels as key molecular sensors



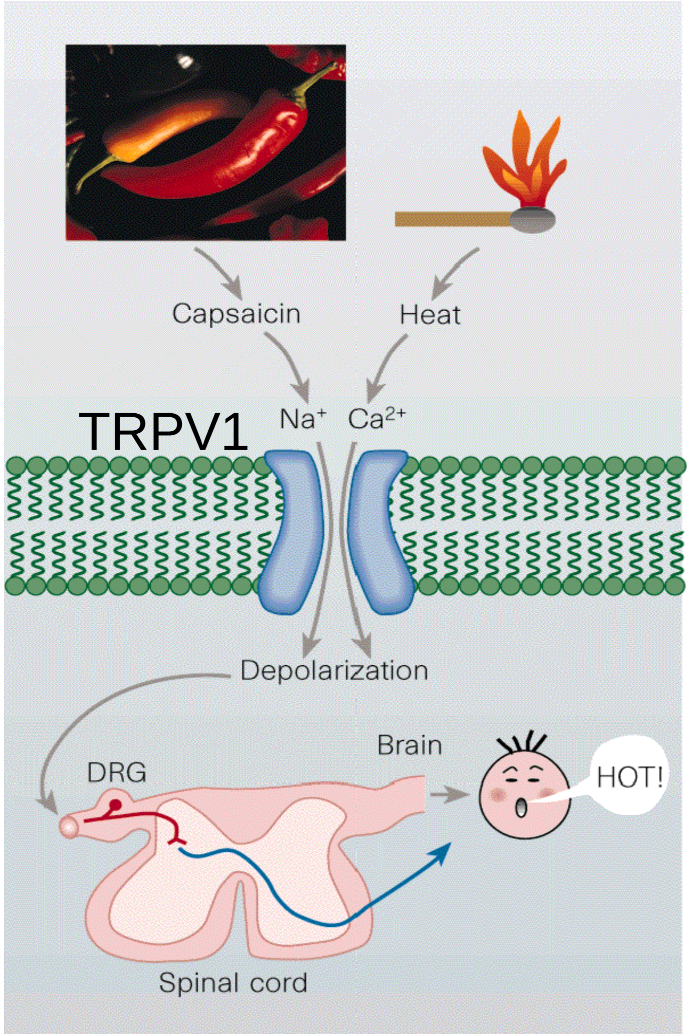


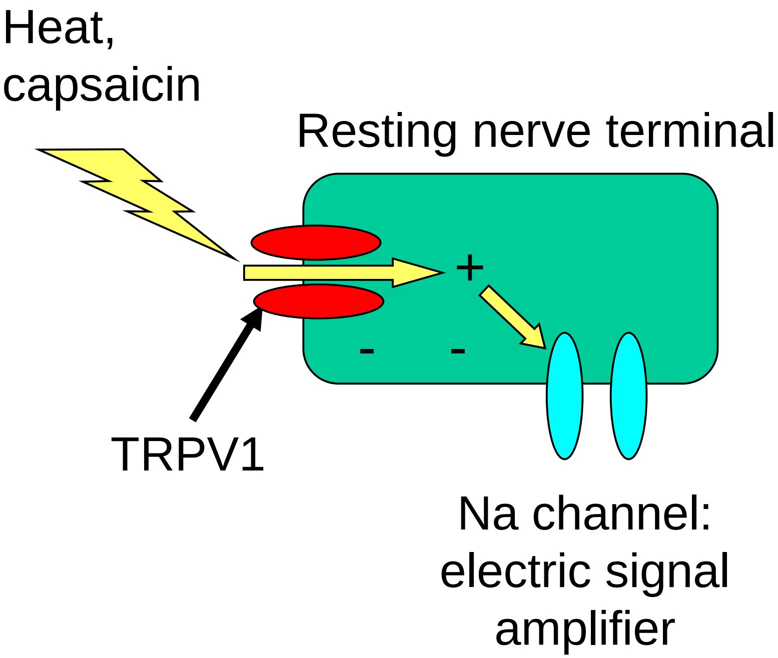
Ion channels as key molecular sensors



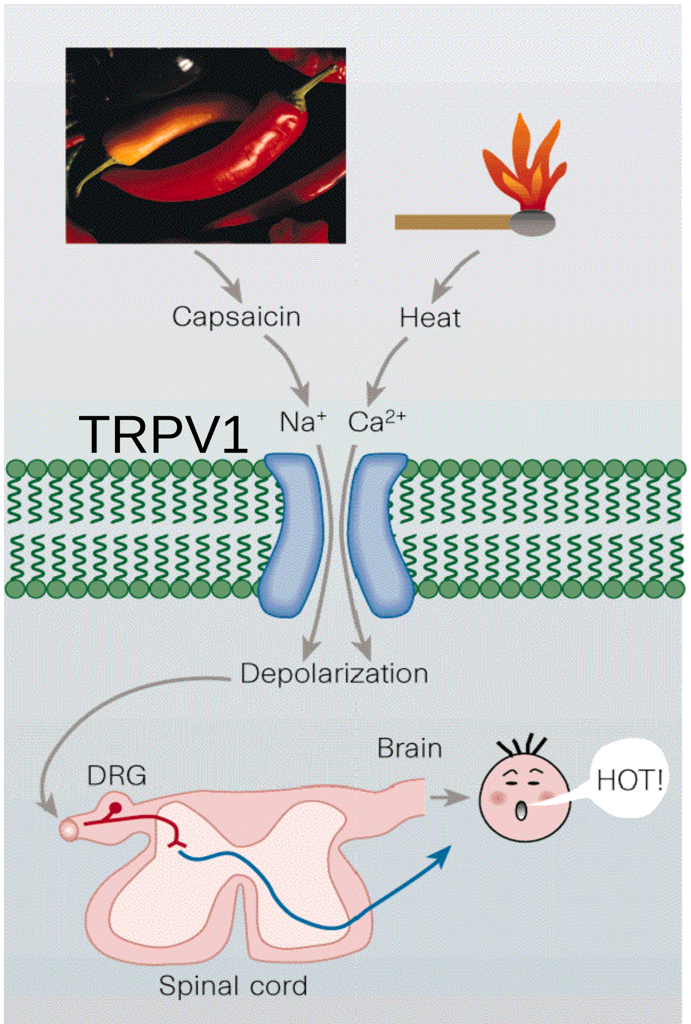


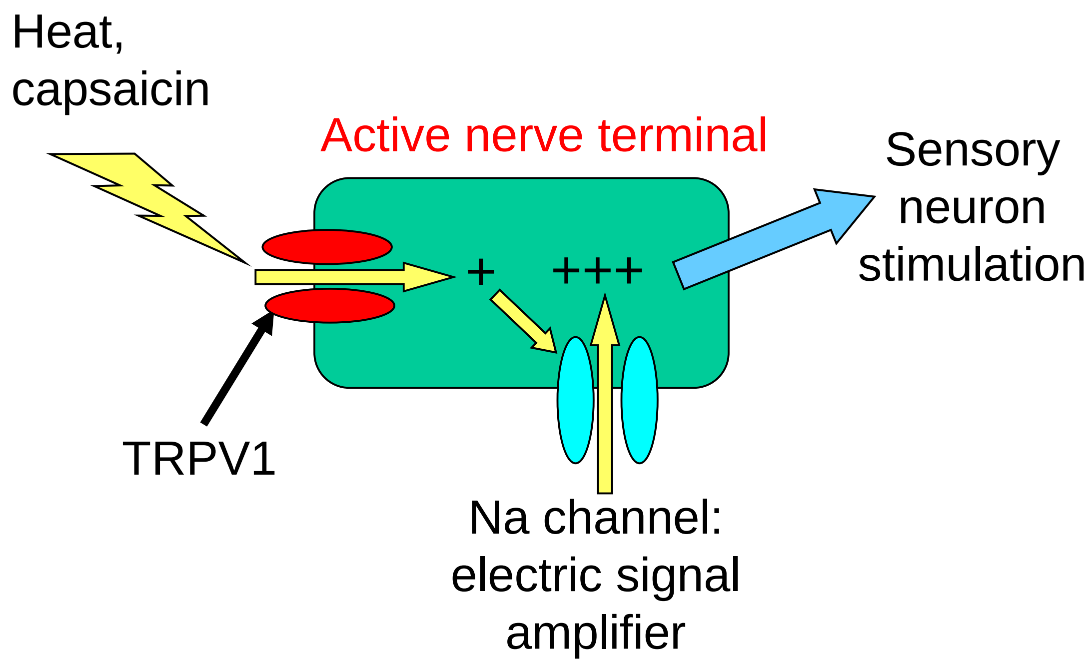
Ion channels as key molecular sensors





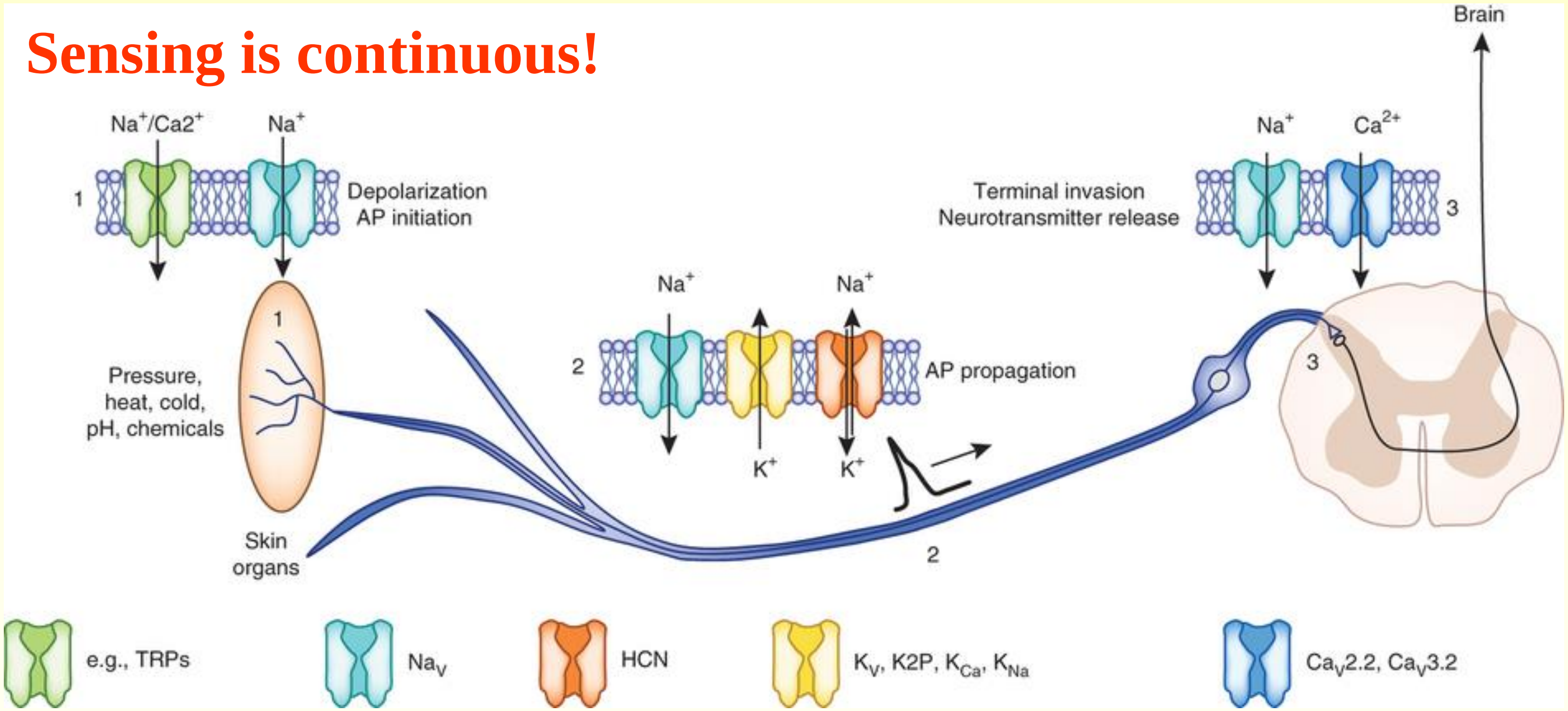
Ion channels as key molecular sensors





Sensing versus Conduction

Sensing is continuous!



Conduction is discrete!