Biophysics I (BPHS 3090)

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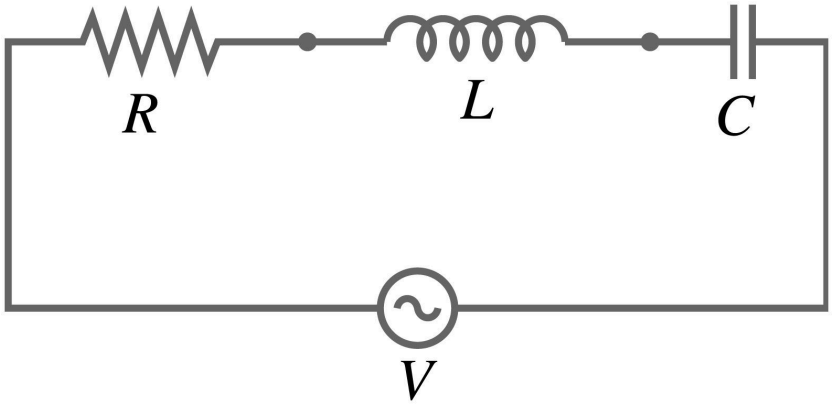
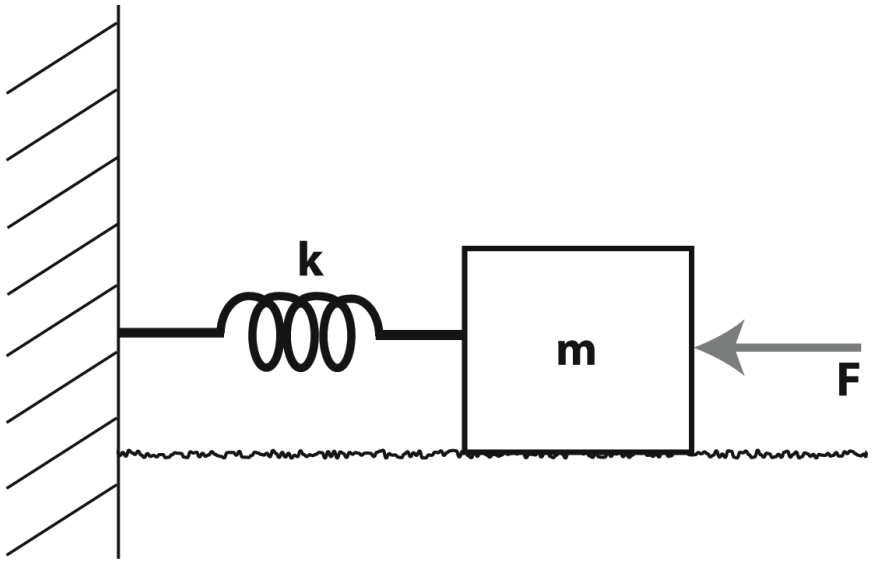
Website: http://www.yorku.ca/cberge/3090W2015.html

York University
Winter 2015
Lecture 12

Reference/Acknowledgement:
- TF Weiss (Cellular Biophysics)
- D Freeman

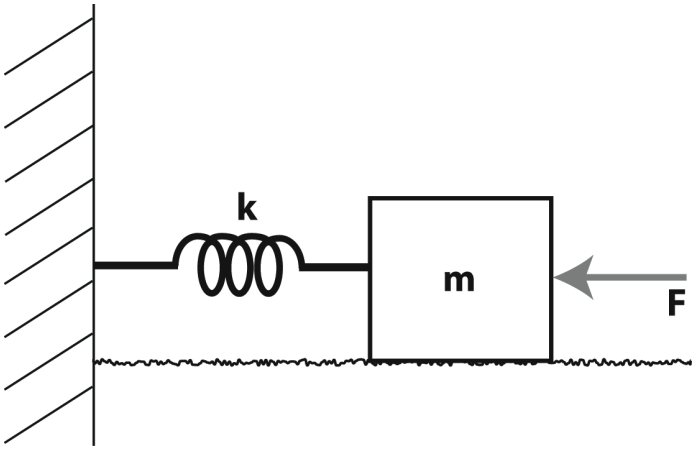
RLC circuit = Damped, Driven Harmonic Oscillator

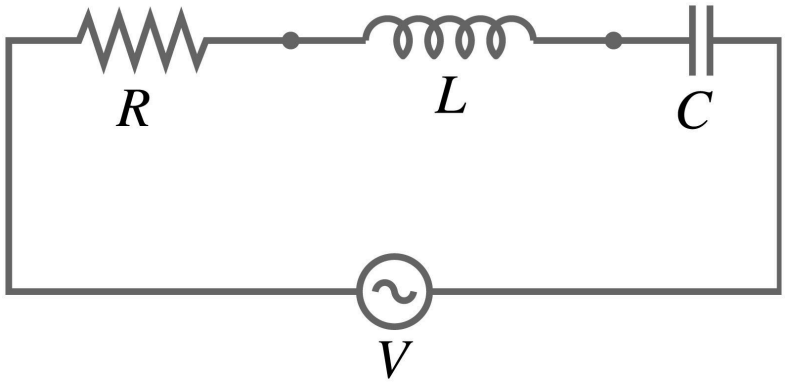




RLC circuit = Damped, Driven Harmonic Oscillator

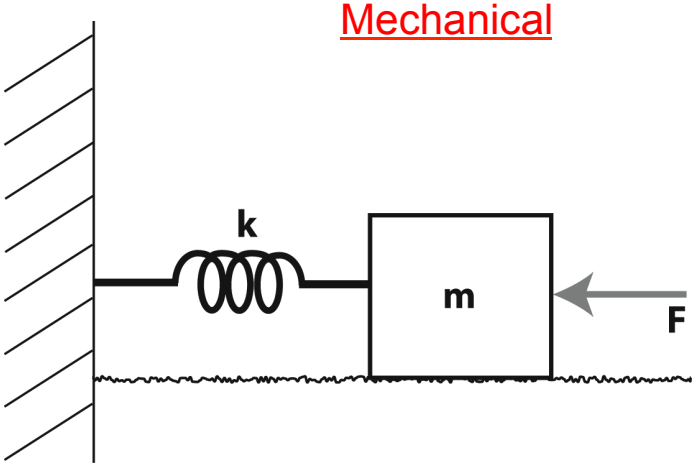
Mechanical		Electrical	
F (force)	←→	V (potential)	state variables
v (velocity)	←→	I (current)	
x (position)	←→	q (charge)	
m (mass)	←→	L (inductance)	
b (damping)	←→	R (resistance)	
k (spring)	←→	$1/C$ (capacitance)	



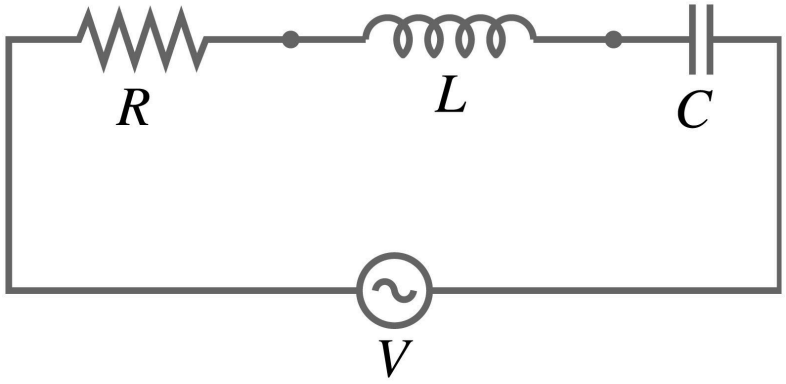


RLC circuit = Damped, Driven Harmonic Oscillator

Mechanical



Electrical



$$m\ddot{x} + b\dot{x} + kx = F_o e^{i\omega t}$$

$$L\ddot{q} + R\dot{q} + \frac{q}{C} = V_o e^{i\omega t}$$

RLC circuit = Damped, Driven Harmonic Oscillator

Mechanical Impedance

$$Z \equiv b + i\left[m\omega - \frac{k}{\omega}\right]$$

Electrical Impedance

$$Z \equiv R + i\left[\omega L - \frac{1}{\omega C}\right]$$

→ Admittance (Y) = (Impedance)$^{-1}$

→ Conductance (G) = (Resistance)$^{-1}$

Ohm's Law

'Simple' Version $V = IR$ $V, I \in \mathbb{R}$

'Complete' Version $\mathbf{V} = \mathbf{IZ}$ $\mathbf{V}, \mathbf{I} \in \mathbb{C}$

→ Note that DC (direct current) can be considered a special case of AC (alternating current). The 'complete' version of Ohm's Law thus allows for more dynamical behavior to be accounted for in an efficient fashion when using Fourier or Laplace transforms (and reduces to the 'simple' case for uni-directional currents).

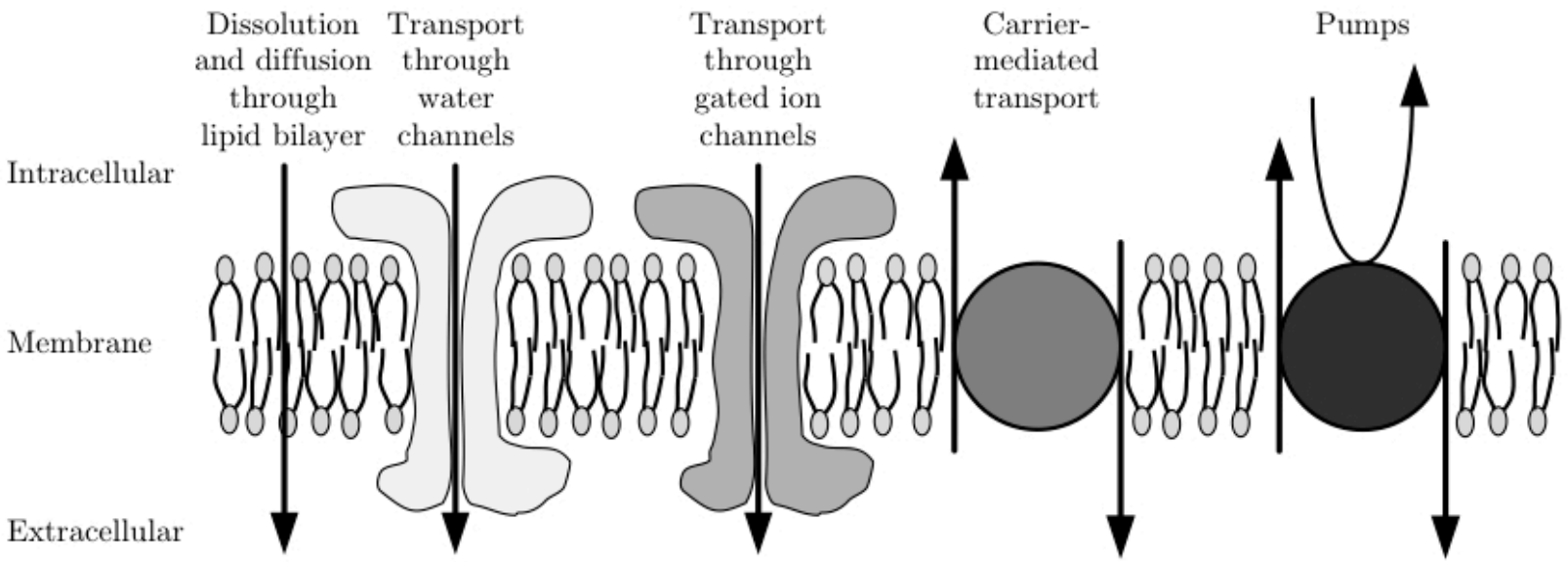

Dissolution and diffusion through lipid bilayer
Transport through water channels
Transport through gated ion channels
Carrier-mediated transport
Pumps
Intracellular
Membrane
Extracellular

Figure 2.19

Example → Auditory hair cells as RLC Systems

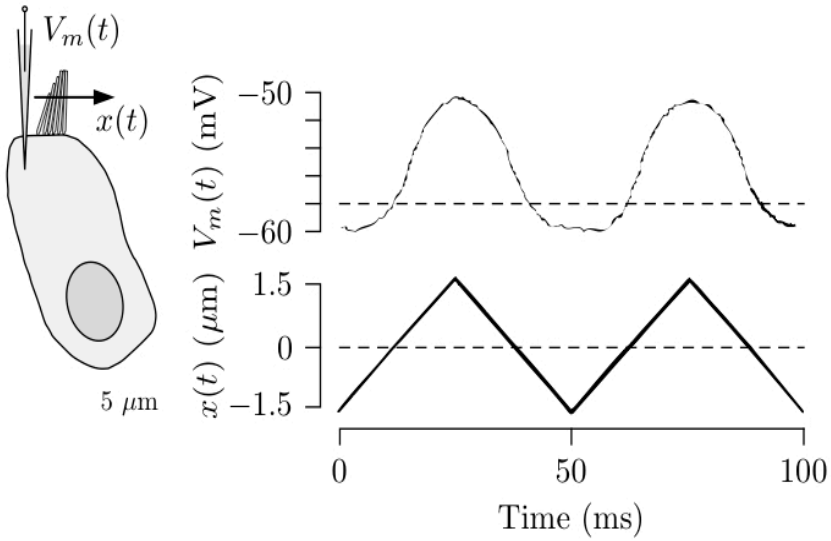
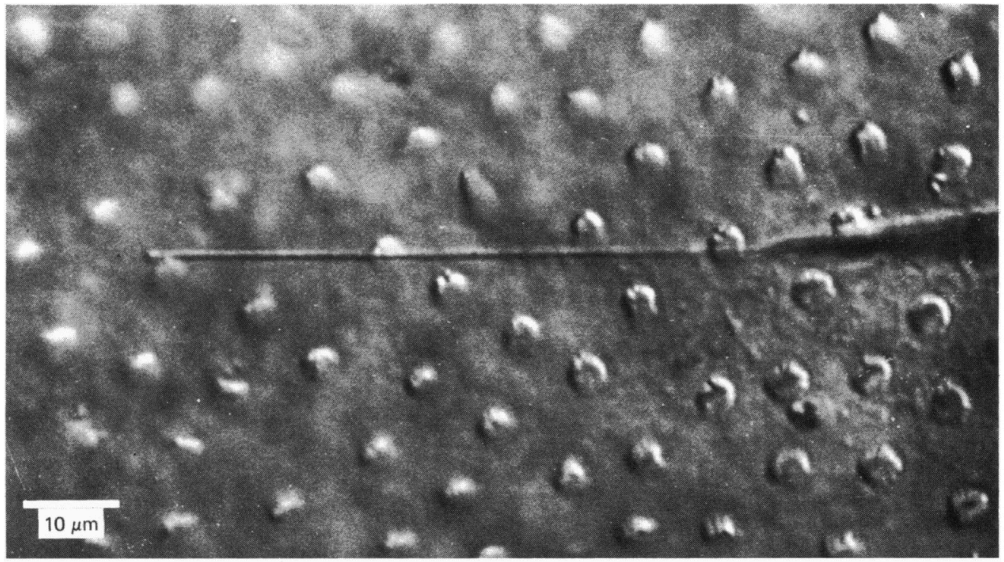
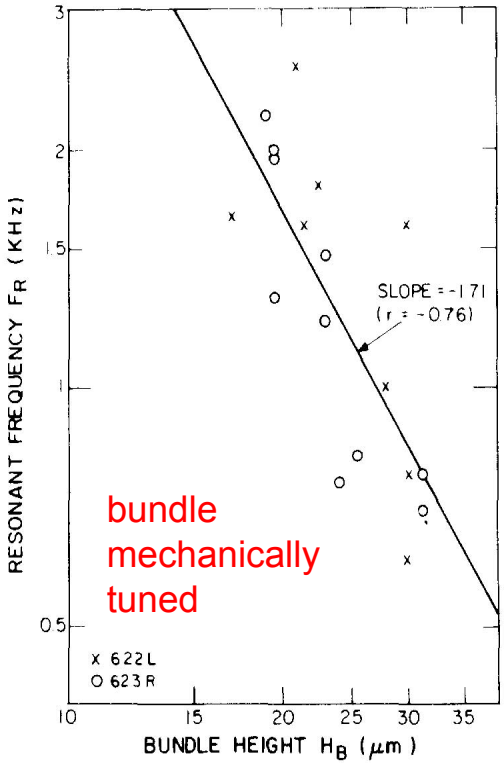


Figure 1.5



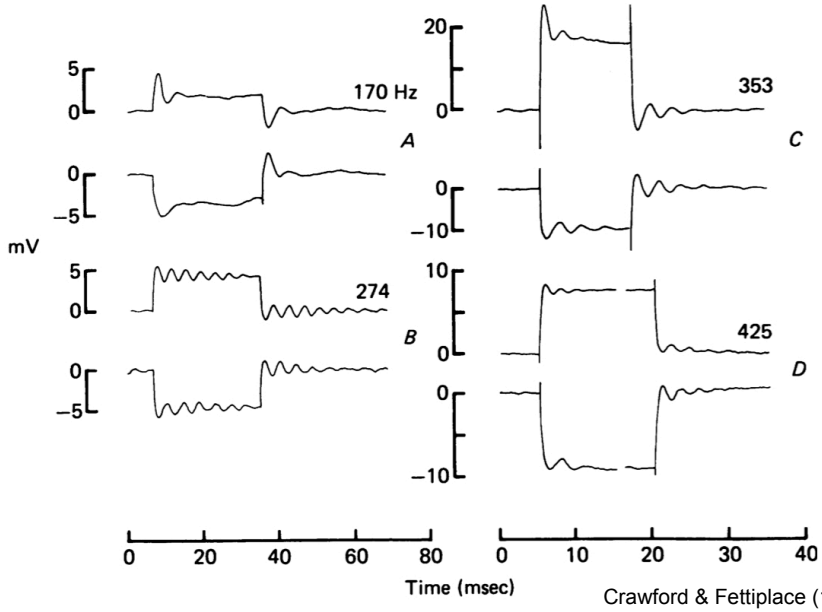
Crawford & Fettiplace (1985)

Ex. Auditory hair cells



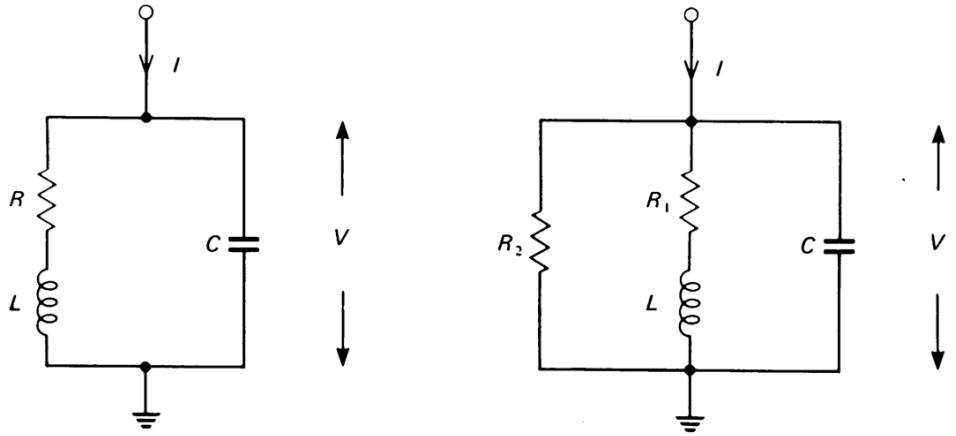
bundle mechanically tuned

Frishkopf & DeRosier (1983)



membrane electrically tuned

Crawford & Fettiplace (1981)



→ electrical measurements indicate both mechanical and electrical resonances

Sensory cells of the inner ear can behave like RLC circuits

- Voltage-gated channels (e.g., calcium-activated "BK" potassium channels) have intrinsic dynamics that can give rise to electric tuning

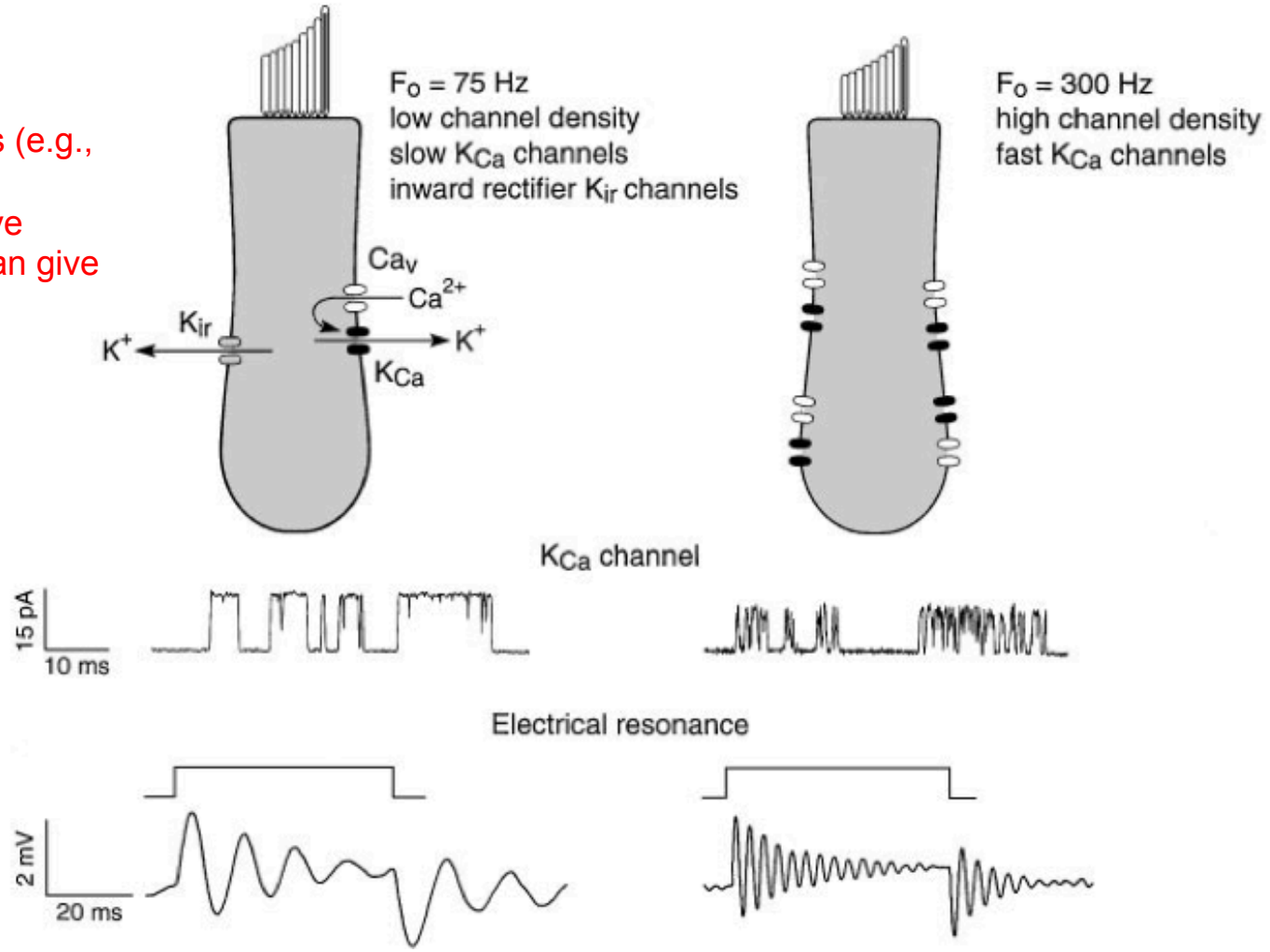


Figure 1 Schematic drawing of two hair cells from the turtle basilar papilla, with resonant frequencies (F_o) of 75 and 300 Hz. The low-frequency cell has a longer hair bundle, and a low density of Ca^{2+} and Ca^{2+}-activated K^+ (K_{Ca}) channel complexes. The number of channel complexes increases with (F_o). Beneath each cell are shown representative K_{Ca} (BK) single-channel records and ringing voltage responses to extrinsic current steps for cells tuned approximately to these two frequencies. The timing of the extrinsic current is shown above the voltage records. The single-channel records and the voltage ringing were from different sets of experiments (22, 23).

Fettiplace & Fuchs (1999)

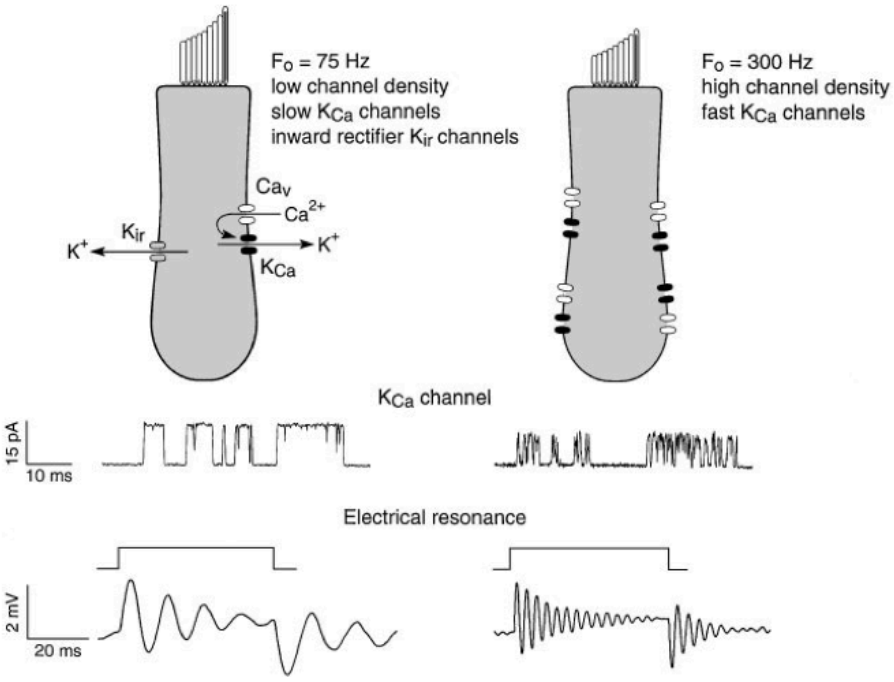
Sensory cells of the inner ear can behave like RLC circuits

1. Mechanical motion deflects bundle, causing a transduction current to depolarize the cell

2. "Depolarization opens voltage-gated Ca^{2+} channels, promoting a rise in internal Ca^{2+} that activates BK channels"

3. "The large outward K^+ current hyperpolarizes the membrane, closing the Ca^{2+} channels, which leads to the first cycle of the oscillation"

4. "As the cell hyperpolarizes and intracellular Ca^{2+} transients dissipate, the BK channels partially close, but due to the continued extrinsic current, the membrane swings positive to initiate another cycle of Ca^{2+} influx."



"Since the BK channels are already partly activated, a smaller fraction of K^+ current is recruited on the second cycle, which will have a smaller amplitude than the first. Because the K^+ equilibrium potential (−80 mV) is negative to the resting potential (−50 mV), the BK channels behave as part of a negative feedback loop, but the time course of their activation delays the feedback and hence generates damped oscillatory responses. Such negative feedback also produces sharp tuning for sinusoidal stimuli, and the frequency at which the cell is maximally sensitive, the resonant frequency, should be influenced by the size and speed of the feedback."

Fettiplace & Fuchs (1999)

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Modeling Hair Cell Tuning by Expression Gradients of Potassium Channel β Subunits

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ABSTRACT The receptor potential of sensory hair cells arises from the gating of mechanosensitive cation channels, but its amplitude and time course also depend on the number and kinetics of voltage-gated ion channels in each cell. Prominent among these are "BK" potassium channels encoded by the *slo* gene that support electrical tuning in some hair cells. Hair cells tuned to low frequencies have slowly gating BK channels, whereas those of higher-frequency hair cells gate more rapidly. Alternative splicing of the *slo* gene mRNA that encodes the pore-forming α subunit can alter BK channel kinetics, and gating is dramatically slowed by coexpression with modulatory β subunits. The effect of the β subunit is consistent with low-frequency tuning, and β mRNA is expressed at highest levels in the low frequency apex of the bird's auditory epithelium. How might an expression gradient of β subunits contribute to hair cell tuning? The present work uses a computational model of hair cell-tuning based on the functional properties of BK channels expressed from hair cell α and β *slo* cDNA. The model reveals that a limited tonotopic gradient could be achieved simply by altering the fraction of BK channels in each hair cell that are combined with β subunits. However, complete coverage of the tuning spectrum requires kinetic variants in addition to those modeled here.

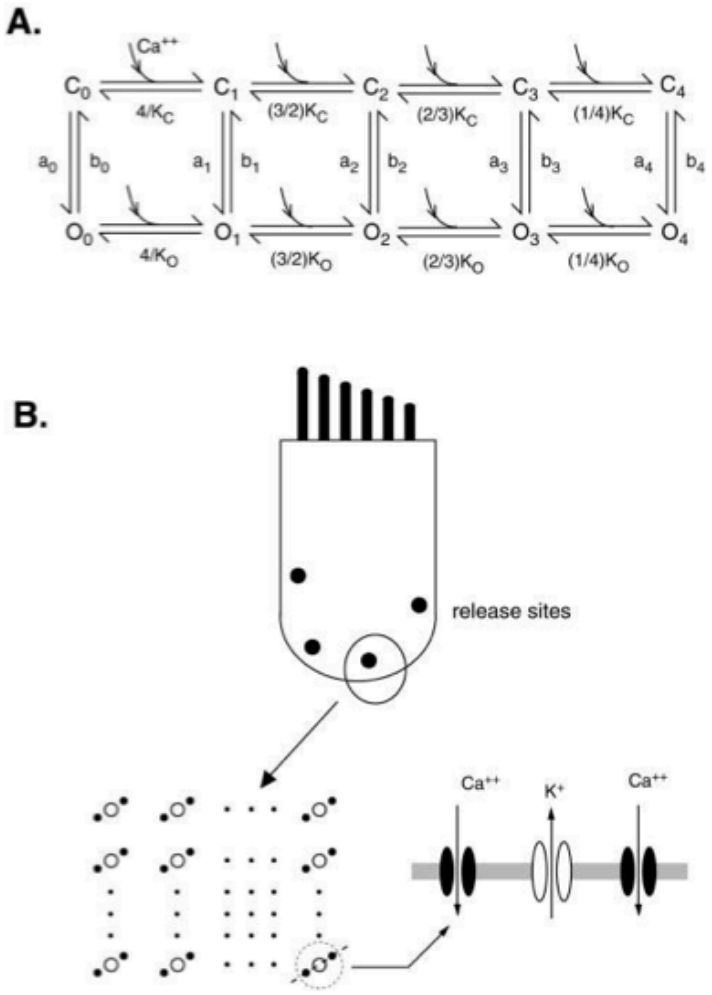


FIGURE 1 BK channel and hair cell models. (*A*) The allosteric (voltage-dependent MWC) scheme for BK channels has horizontal transitions that are calcium dependent and vertical transitions that are voltage dependent. The voltage-dependent MWC version assumes that each calcium-binding step has the same affinity. However, binding of calcium to the closed states may differ from the binding to the open states. The subscripts to the closed and open states indicate the number of calcium ions bound. Voltage-dependent gate movements between closed and open states are thought to occur allosterically with a single rate constant. a_x and b_x are the vertical transition rates that are dependent upon voltage. K_{CX} and K_{OX} are the dissociation constants for the binding of x^{th} calcium ion to the closed and open states respectively. (*B*) The hair cell model incorporates BK channels into functional units with two adjacent voltage-gated calcium channels. These are shown as clusters, as might occur at transmitter release active zones, but each BK channel is gated independently by its associated calcium channels. The number and kinetic properties of BK channels varies between model cells, but the ratio of two calcium channels to one BK channel remains constant, as do the gating properties of the voltage-gated calcium channels.

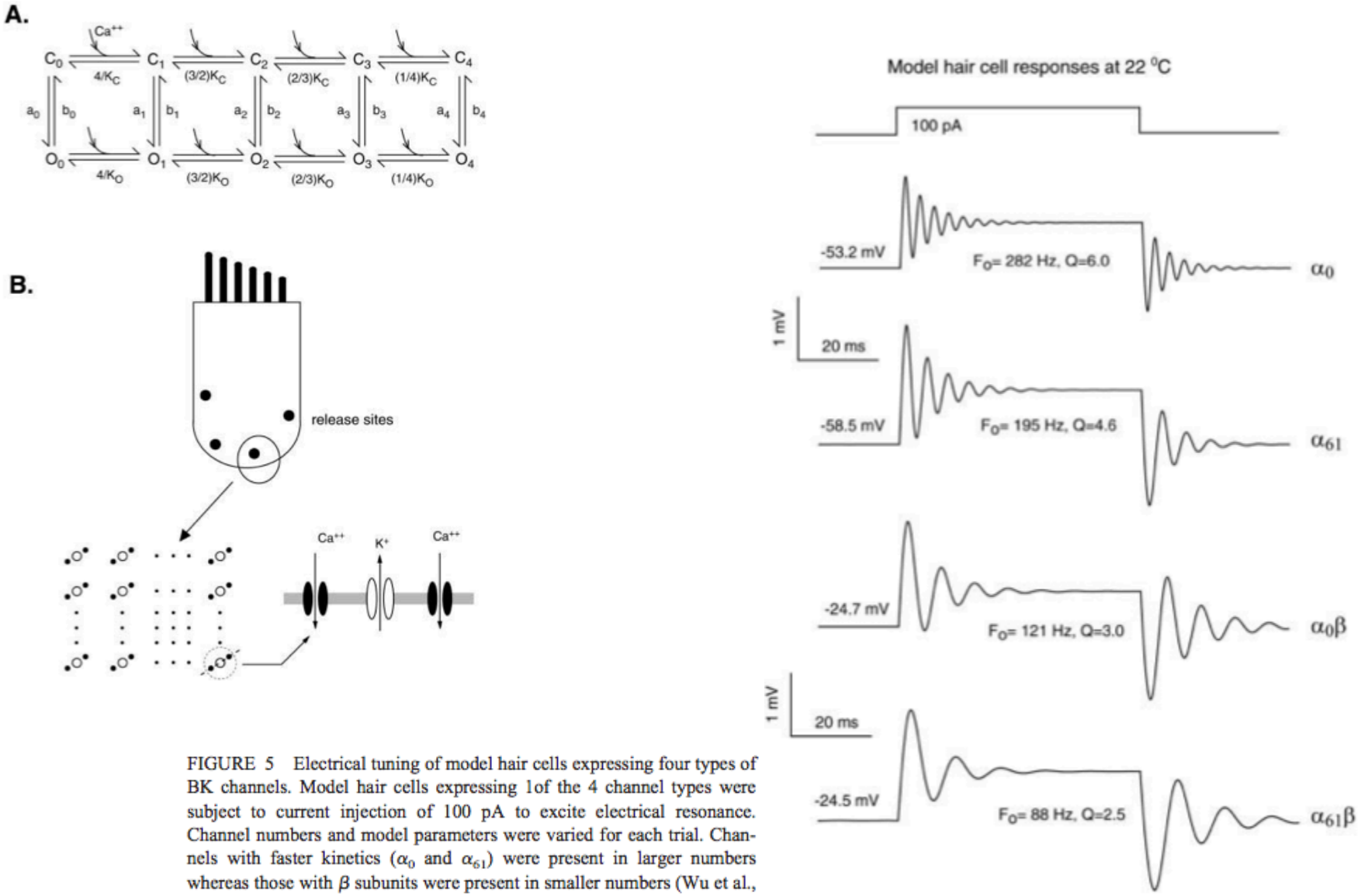
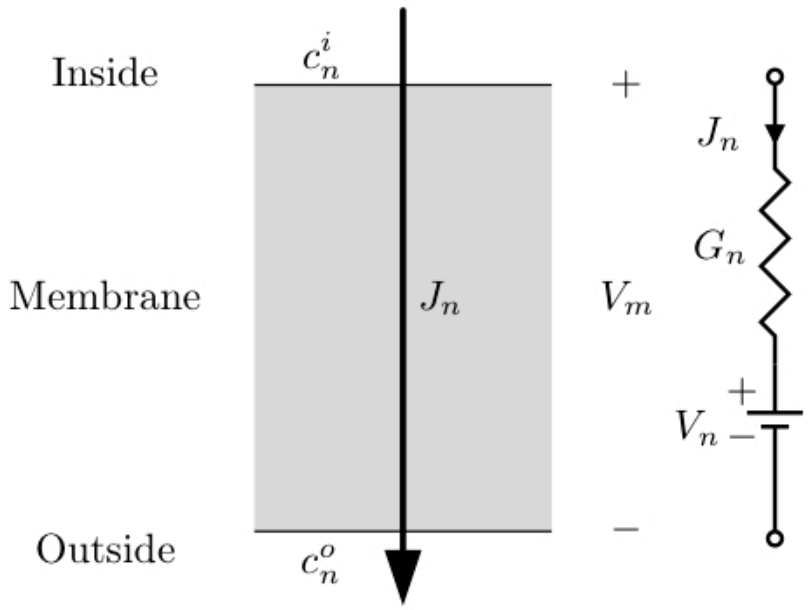


FIGURE 5 Electrical tuning of model hair cells expressing four types of BK channels. Model hair cells expressing 1of the 4 channel types were subject to current injection of 100 pA to excite electrical resonance. Channel numbers and model parameters were varied for each trial. Channels with faster kinetics (α_0 and α_{61}) were present in larger numbers whereas those with β subunits were present in smaller numbers (Wu et al., 1995). The four channels span a electrical tuning frequency range from 88 Hz to 282 Hz. The resonant frequency and the quality of tuning for positive current injection are shown below each trace. α_0 and α_{61} produced electrical resonance at resting hair cell voltages of ~ -55 mV. Hair cells containing $\alpha_0\beta$ or $\alpha_{61}\beta$ resonated at resting potentials that were more depolarized (~ -25 mV).

Ramanathan & Fuchs (2002)

Looking ahead from this point.....

Model of Steady-State Electrodiffusion through Membranes



Consider Different Charged Solutes in Parallel

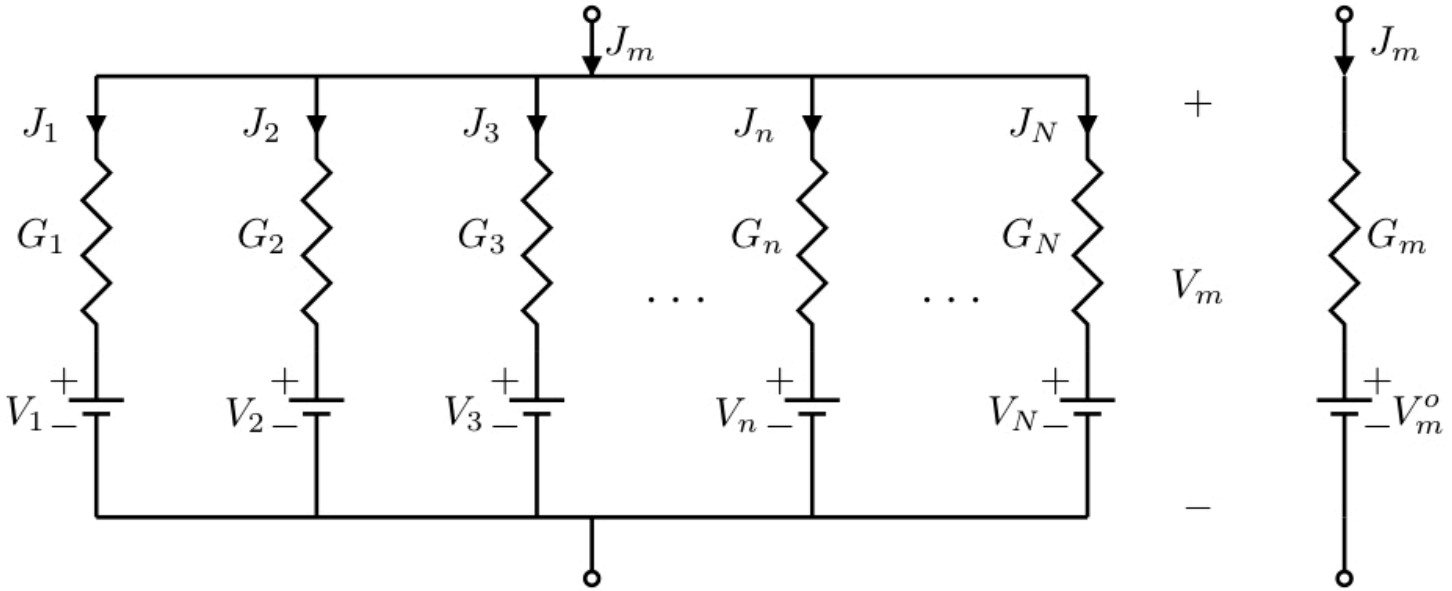
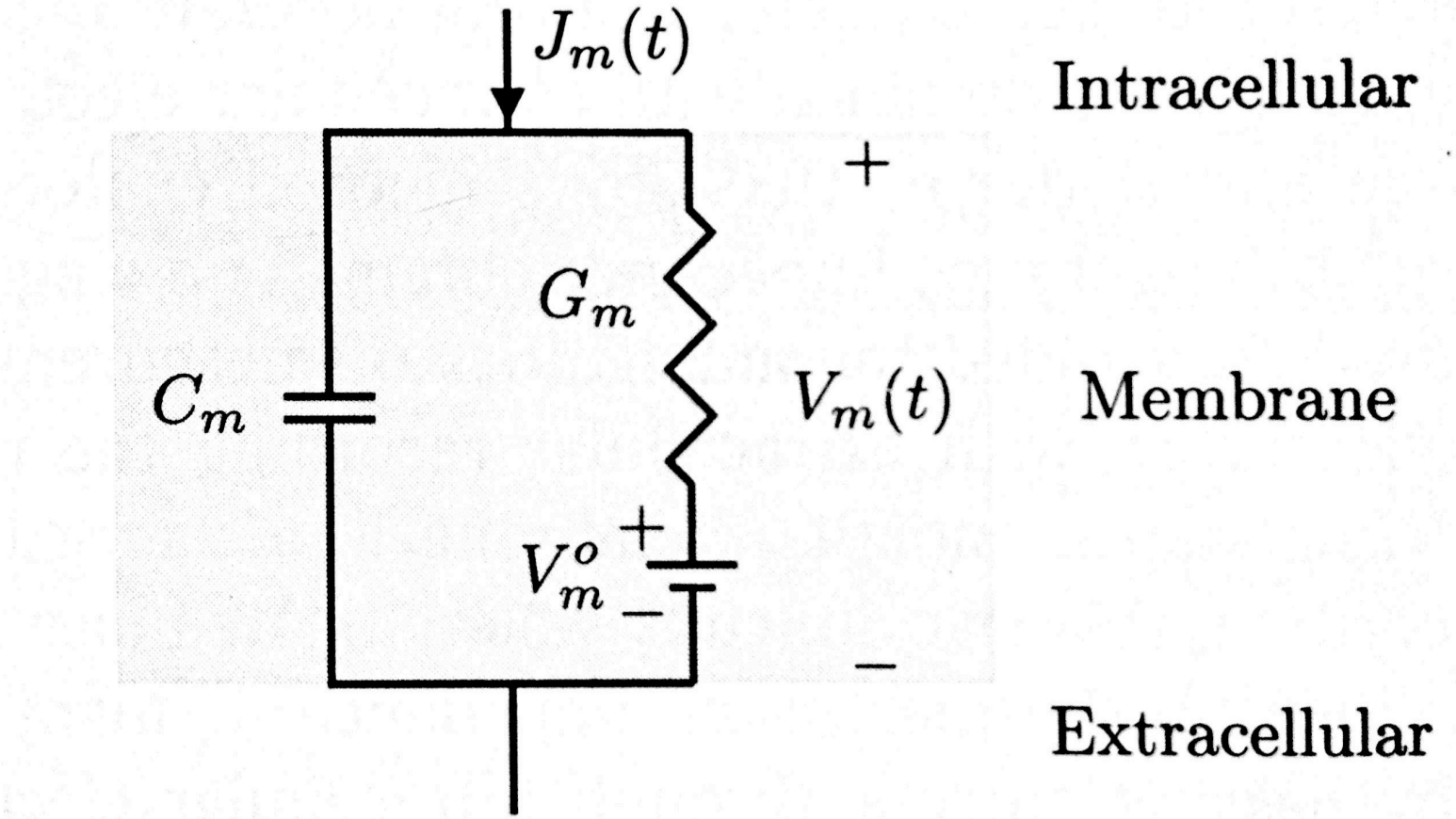


Figure 7.24

Equivalent

Lipid Bilayer Acts as a Capacitor



Circuit Model for Membrane

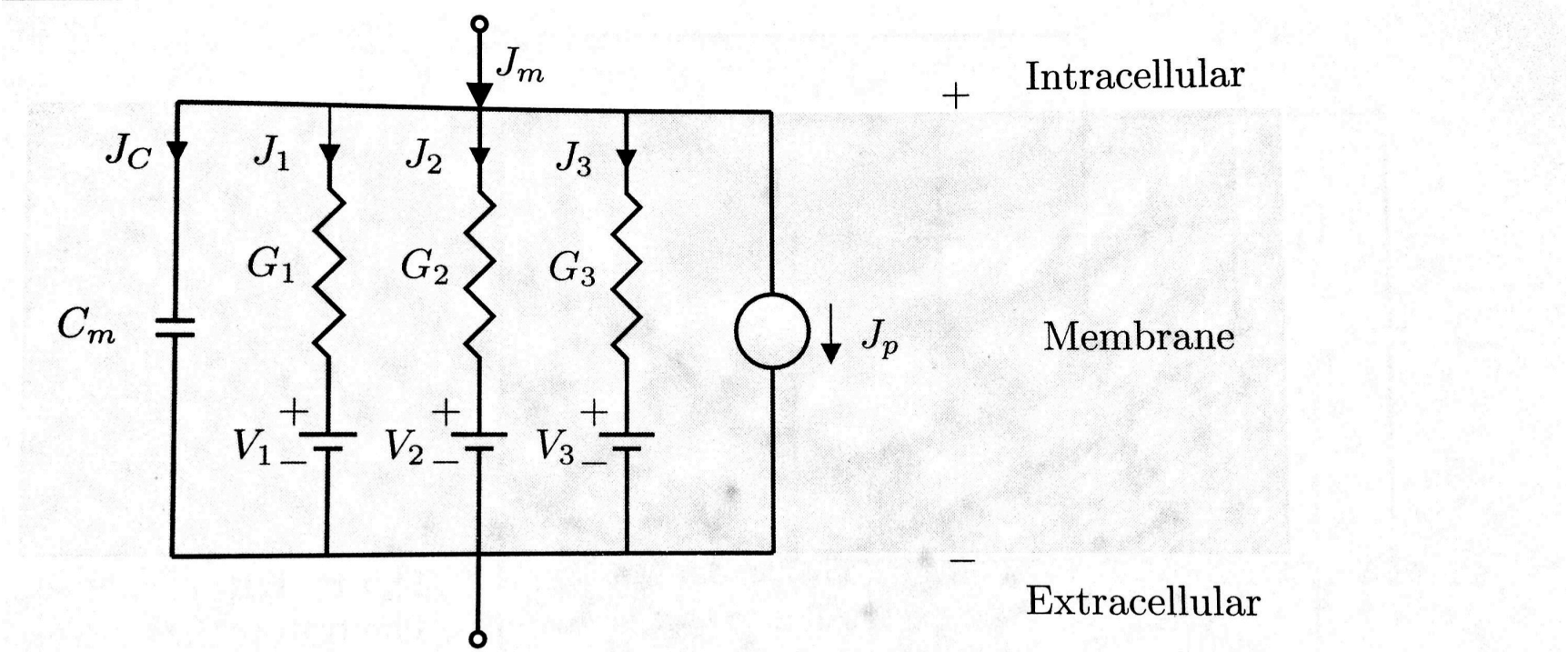
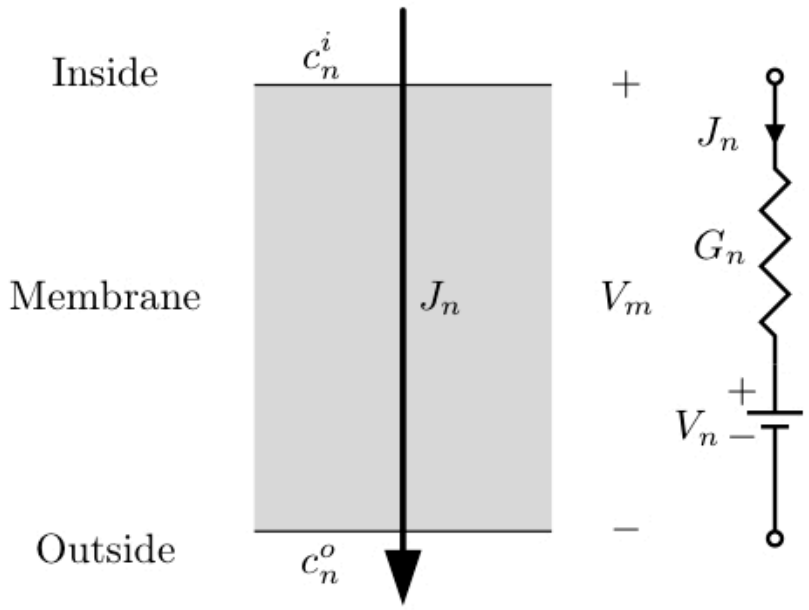


Figure 1.18 Macroscopic model of a unit area of membrane. C_m represents the capacitance of a unit area of membrane and represents the insulating properties of the lipid bilayer. G_n represents the conductance of a unit area of membrane for the n^{th} ion. V_n is the Nernst equilibrium potential of the n^{th} ion. The series combination of G_n and V_n represents conduction through a population of ion channels permeable to ion n. J_p represents the net current density due to other mechanisms, primarily the current carried by active transport mechanisms.

Model of Steady-State Electrodiffusion through Membranes



Eqns. of Electrodiffusion

Nernst-Plank Equation

$$J_n(x,t) = -z_n F D_n \frac{\partial c_n(x,t)}{\partial x} - u_n z_n^2 F^2 c_n(x,t) \frac{\partial \psi(x,t)}{\partial x}$$

Continuity

$$\frac{\partial J_n(x,t)}{\partial x} = -z_n F \frac{\partial c_n(x,t)}{\partial t}$$

Poisson's Equation

$$\frac{\partial^2 \psi(x,t)}{\partial x^2} = -\frac{1}{\epsilon} \sum_n z_n F c_n(x,t)$$

Nernst-Plank Equation → Electrodiffusion

current density

$$J_n(x,t) = -z_n F D_n \frac{\partial c_n(x,t)}{\partial x} - u_n z_n^2 F^2 c_n(x,t) \frac{\partial \psi(x,t)}{\partial x}$$

diffusion

electric drift