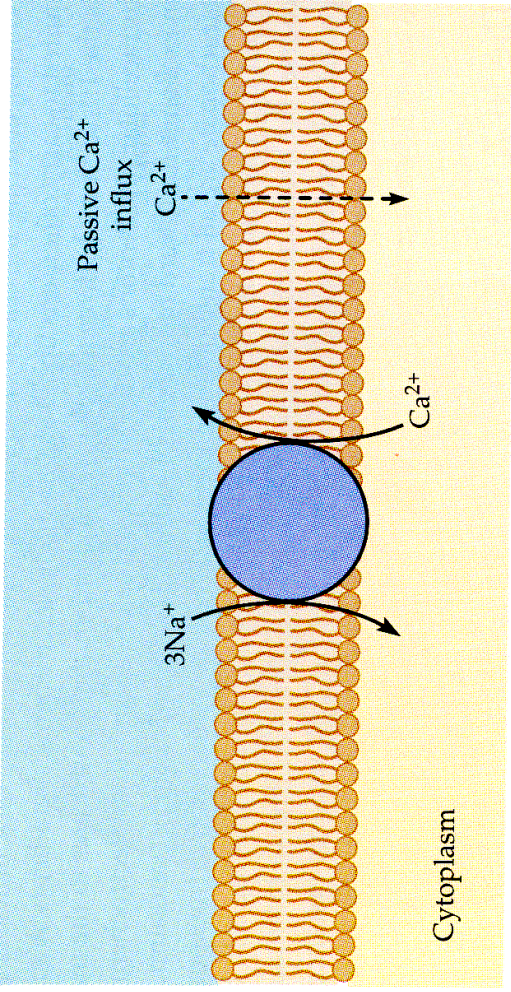


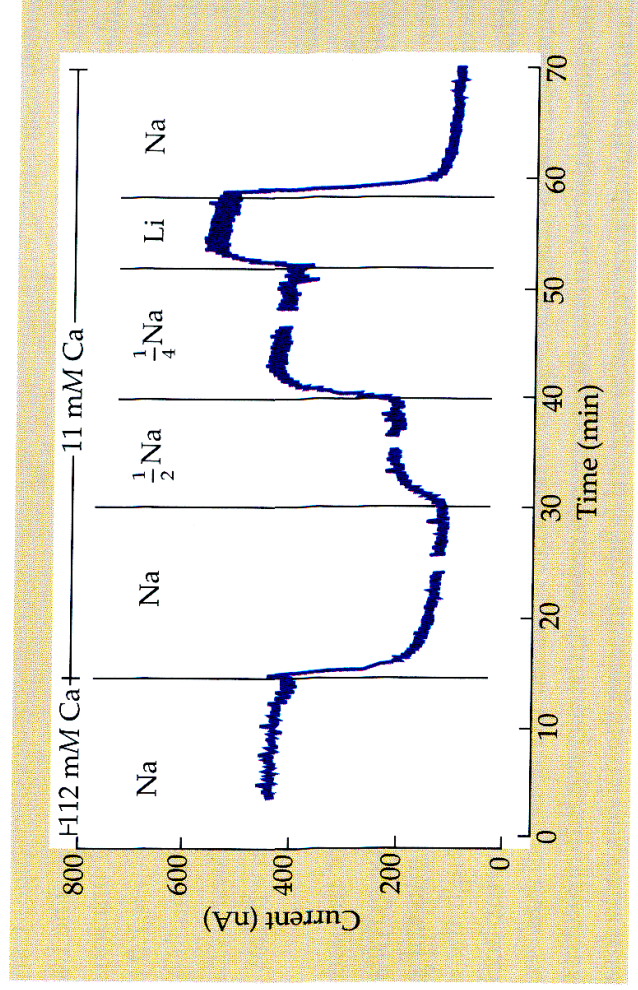
Sodium-Calcium Exchange

- NCX is acronym
- Stoichiometry
 - 3 (maybe 4) sodium exchanged for 1 calcium
- Charge transfer
 - Unequal => electrogenic
 - One proton flows in for each transport cycle
 - Small current produces small depolarization

(A)



(B)



Sodium-Calcium Exchange

- Does not hydrolyze ATP
- Driven by sodium concentration gradient
 - Inward sodium removed out by Na-K pump
 - Indirectly uses ATP
- Affinity $\sim 1.0 \mu\text{M}$
- Plasma membrane location only

Sodium-Calcium Exchange

- Theoretical capacity $\sim 50x$ greater than PMCA
- Actual capacity depends on membrane potential
 - Depolarization may reverse pump direction
 - Ion concentration change may reverse direction
 - Increase in intracellular sodium
 - Decrease in extracellular sodium
 - Decrease in intracellular calcium
 - Increase in extracellular calcium

Sodium-Calcium Exchange

- Energy dissipated by sodium entry = charge * driving force = $3 (E_{Na} - V_R)$
- Energy dissipated by calcium extrusion = $2 (E_{Ca} - V_R)$
- Reversal potential of pump

$$V_r = 3E_{Na} - 2 E_{Ca}$$

$$E_{NaCa} = \frac{RT}{F} \left(4 \ln \frac{[Na_o]}{[Na_i]} - \ln \frac{[Ca_o]}{[Ca_i]} \right)$$

Sodium-Calcium Exchange

- Equation for ion flux through pump:

$$flux_p = \frac{V_{NCX}}{F} \cdot area \cdot \left(\frac{[Ca_i]^m}{K_{NCX} + [Ca_i]^m} \right) \cdot (V_M - E_{NaCa})$$

V_{ncx} is maximal pump capacity (per unit area)

Area is area of membrane

F is Faraday's constant, converts to current

Middle term indicates internal calcium binding as MM pump

Squid Axon

Ion	Conc in	Conc out	Equilibrium Potential
Na ⁺	50	440	55
K ⁺	400	20	-76
Cl ⁻	40	560	-66
Ca ⁺⁺	0.4	10	145

Concentration in millimoles,
potential in millivolts.

Mammalian Neuron

Ion	Conc in	Conc out	Equilibrium Potential
Na ⁺	18	145	56
K ⁺	135	3	-102
Cl ⁻	7	20	-76
Ca ⁺⁺	0.0001	1.2	125

Concentration in millimoles,
potential in millivolts.

Calcium in cell is much higher, but is heavily buffered.
Thus this value represents *free* calcium.

Reversal Potential

- Equilibrium potential also called reversal potential, E_R
 - If membrane potential (V_M) is greater than E_R , then potassium ions flow out
 - Diffusional tendency greater than electrostatic force
 - If V_M is lower than E_R , then potassium ions flow in.
 - Diffusional tendency less than electrostatic force
 - If $V_M = E_R$, then forces balance, no net flow

Goldman-Hodgkin-Katz Equation

- Resting potential depends on concentration of all ions to which membrane is permeable.
- Relative contribution of each ion depends on
 - Concentration gradient
 - Permeability (relative to potassium)

$$E_R = \frac{RT}{zF} \ln \left(\frac{p_K K_o^+ p_{Na} Na_o^+ P_{Cl} Cl_i}{p_K K_i p_{Na} Na_i P_{Cl} Cl_o} \right)$$

Passive Ionic Currents

- Relation between voltage difference, concentration gradient, conductance
 - Larger conductance = larger current
 - Larger difference between V_M and E_R = larger current
 - Larger conductance = larger current

$$I = G_M (V_M - E_R)$$

Calcium Pumps

- Calcium is highly regulated because it influences many other processes
- Thus, there are many calcium regulatory mechanisms
 - Buffers
 - Several pumps and exchangers
 - Calcium is stored within mitochondria and ER

Calcium Pumps

- Calcium-magnesium ATPase pumps
 - Plasma membrane (PMCA)
 - Extrudes calcium to extracellular space
 - Binds one calcium ion each cycle
 - Affinity $\sim 300 - 600$ nM
 - Smooth Endoplasmic Reticulum (SERCA)
 - Sequesters calcium in SER
 - Binds two calcium ions each cycle
 - Affinity ~ 100 nM

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 - Decrease in intracellular calcium
 - Increase in extracellular Calcium

Sodium Calcium Exchange

- Structure
 - 11 transmembrane segments
 - Large intracellular loop between segments 5 and 6
 - Contains regulatory domain
 - 120 kDa
 - Single subunit: 970 amino acids

Sodium Calcium Exchange

- Potassium is co-factor in some neurons
 - Retinal rods
- NCKX is acronym
- Stoichiometry
 - 4 sodium : 1 potassium : 1 calcium
 - Additional energy from potassium gradient
- Unlikely to reverse