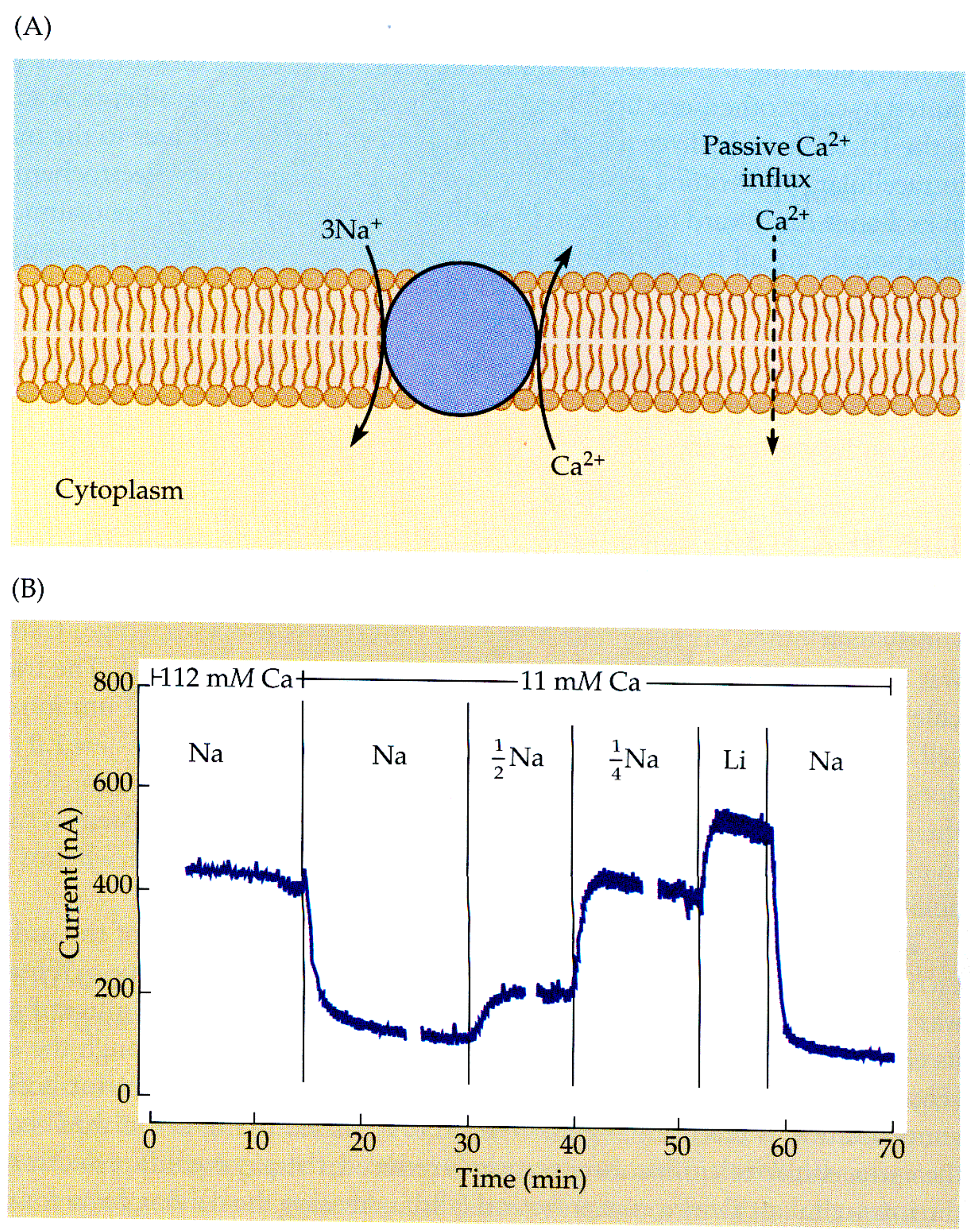
Sodium-Calcium Exchange

- 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)
3Na+
Passive Ca2+
influx
Ca2+
Ca2+
Cytoplasm
(B)
112 mM Ca
11 mM Ca
Na
Na
1/2 Na
1/4 Na
Li
Na
Current (nA)
800
600
400
200
0
0
10
20
30
40
50
60
70
Time (min)

Sodium-Calcium Exchange

- Does not hydrolyze ATP
- Driven by sodium concentration gradient
  - Inward sodium removed out by Na-K pump
  - Indirectly uses ATP
- Affinity ~ 1.0 μM
- Plasma membrane location only

Sodium-Calcium Exchange

- Theoretical capacity ~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

  $Vr = 3E_{Na} - 2\,E_{Ca}$

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

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 ~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 extracellular sodium
    - 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