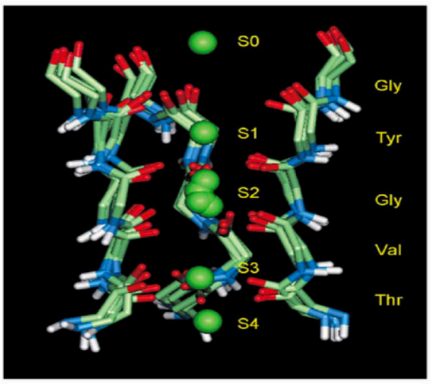
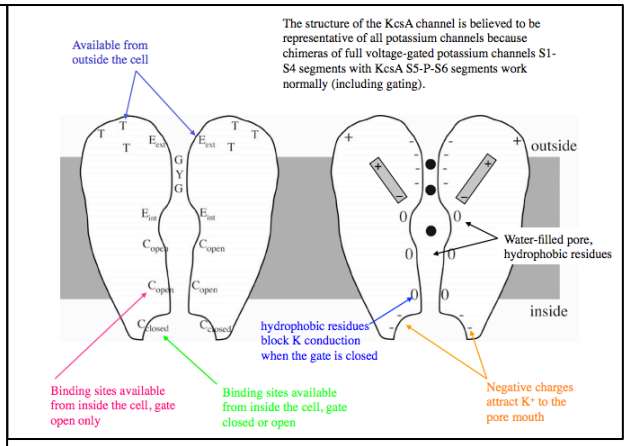


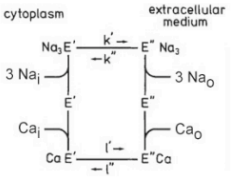
Fig. 5. Potassium ions in the selectivity filter as seen in the same simulation discussed in Fig. 4. Four snapshots from the simulation are superimposed, showing the filter regions of three of the four subunits, and the K^+ ions (green spheres) that occupy (at different times) sites S0 to S4.

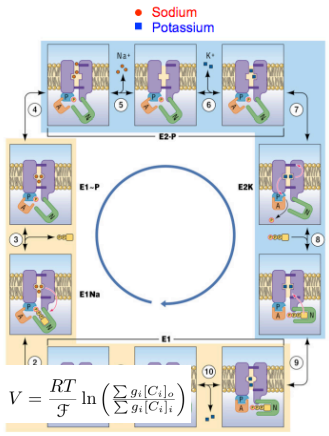


The sequence of steps in the Na-K ATPase is complex, involving separate transport of Na out, K in, and ATP cleavage.

Note the gates (black) that occlude the Na and K during the transport step.

Motivated by this model Läuger and others have analyzed a slightly simpler transporter, the Na-Ca cotransporter with a similar scheme.





$$V = \frac{RT}{\mathcal{F}} \ln\left(\frac{\sum_i g_i [C_i]_o}{\sum_i g_i [C_i]_i}\right)$$

The varieties of potassium channels (some of them):

1. *Voltage gated* – K_V like the delayed rectifier of the HH model. Some of these also have inactivation gates. These repolarize action potentials and limit the spiking rate during excitation.
2. *Calcium dependent - K(Ca)* There are two varieties of these:
   BK – gated by both *V* and *Ca*. Important for repolarization and for activity-dependent sensing.
   SK – gated by *Ca* only. Produce afterhyperpolarization (AHP) and help govern stability after bouts of activity (e.g. between bursts).
3. *H channels* – non-specific channels that are related to K channels. These have only an inactivation gate.
4. *Inward rectifier* – Non-V-gated channels whose conductance is often controlled by intracellular second messengers.
5. *Tandem pore domain* – contribute to the resting potential.

Varieties of calcium channels:

L-type – high threshold (>-30 mV), slow V inactivation, Ca^{++} inactivation.

P/Q, N, R – high threshold (>-20 mV), weak V inactivation, Ca^{++} inactivation.

T-type – low threshold (>-70 mV), strong V inactivation, no Ca^{++} inactivation.

These types were originally identified on voltage-clamp criteria, but have subsequently been associated with specific genes, with multiple genes for each type. They differ in pharmacology and in their localization.

2. Ion Flux

Nernst-Planck Equation

$$J = -uC\left[RT\frac{d\ln C}{dx} + z\mathcal{F}\frac{dV}{dx}\right]$$

$$I = -z\mathcal{F}uC\left[RT\frac{d\ln C}{dx} + z\mathcal{F}\frac{dV}{dx}\right]$$

GHK Equation

$$I_i = \frac{(z\mathcal{F})^2 u_i}{d}\Delta V\frac{C_i(d)e^{\frac{z_o\mathcal{F}\Delta V}{RT}} - C_i(0)}{e^{\frac{z_o\mathcal{F}\Delta V}{RT}} - 1}$$

$$\Delta V_{rest} = \frac{RT}{\mathcal{F}}\ln\left(\frac{u_K K_o + u_{Na} Na_o + u_{Cl} Cl_i}{u_K K_i + u_{Na} Na_i + u_{Cl} Cl_o}\right)$$

Rate Constants

$$k_i = (const)e^{\frac{-(G+\lambda z\mathcal{F}\Delta V)}{RT}}$$

Flux Across Barrier

$$J_{AB} = k_i A,\ J_{BA} = k_{-i}B,$$

$$J = J_{AB} - J_{BA}$$

$$J = (const)e^{\frac{-(G+\lambda z\mathcal{F}\Delta V)}{RT}}\left(A - Be^{\frac{z\mathcal{F}\Delta V}{RT}}\right)$$

$$\frac{RT}{\mathcal{F}} = 26mV$$

1. Equilibrium

Free energy (equal at equil

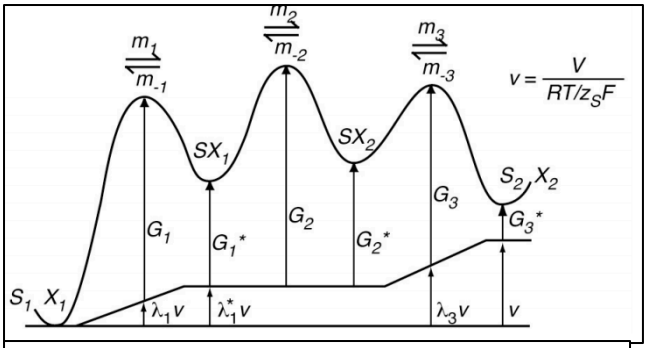
$$\mu_i = \mu_i^o + RT\ln C_i + z_i\mathcal{F}V$$

Equilibrium is defined as

$$\Delta G = 0 \text{ or } \mu_s^1 = \mu_s^2$$

Nernst Equation

$$E = \frac{RT}{z\mathcal{F}}\ln\frac{C_1}{C_2}$$



$$k_1 = \alpha e^{-G_1/RT} \quad m_1 = k_1 e^{-\lambda_1 v} \quad k_{-1} = \alpha e^{-(G_1 - G_1^*)/RT} \quad m_{-1} = k_{-1} e^{-(\lambda_1 - \lambda_1^*)v}$$

$$k_2 = \alpha e^{-(G_2 - G_1^*)/RT} \quad m_2 = k_2 \quad k_{-2} = \alpha e^{-(G_2 - G_2^*)/RT} \quad m_{-2} = k_{-2}$$

$$k_3 = \alpha e^{-(G_3 - G_2^*)/RT} \quad m_3 = k_3 e^{-(\lambda_3 - \lambda_1^*)v} \quad k_{-3} = \alpha e^{-(G_3 - G_3^*)/RT} \quad m_{-3} = k_{-3} e^{-(\lambda_3 - 1)v}$$

2. Ion Flux

Nernst-Planck Equation

$$J = -uC\left[RT\frac{d\ln}{dx} + z\mathcal{F}\frac{dV}{dx}\right]$$

$$I = -z\mathcal{F}uC\left[RT\frac{d\ln}{dx} + z\mathcal{F}\frac{dV}{dx}\right]$$

GHK Equation

$$I_i = \frac{(z\mathcal{F})^2 u_i}{d}\Delta V\frac{C_i(d)e^{\frac{z_o\mathcal{F}\Delta V}{RT}} - C_i(0)}{e^{\frac{z_o\mathcal{F}\Delta V}{RT}} - 1}$$

$$\Delta V_{rest} = \frac{RT}{\mathcal{F}}\ln\left(\frac{u_K K_o + u_{Na} Na_o + u_{Cl} Cl_i}{u_K K_i + u_{Na} Na_i + u_{Cl} Cl_o}\right)$$

Rate Constants

$$k_i = (const)e^{\frac{-(G+\lambda z\mathcal{F}\Delta V)}{RT}}$$

Flux Across Barrier

$$J_{AB} = k_i A,\ J_{BA} = k_{-i}B,$$

$$J = J_{AB} - J_{BA}$$

$$J = (const)e^{\frac{-(G+\lambda z\mathcal{F}\Delta V)}{RT}}\left(A - Be^{\frac{z\mathcal{F}\Delta V}{RT}}\right)$$

$$\frac{RT}{\mathcal{F}} = 26mV$$

State Vector

$$\dot{\vec{X}} = \begin{bmatrix}\dot{V}\\ \dot{\omega}\end{bmatrix} = \begin{bmatrix}F_1(\vec{x})\\ F_2(\vec{x})\end{bmatrix} = \vec{F}(\vec{X})$$

Nullclines for MLE case

$$\dot{V} = 0 \to \omega = \frac{I_{ext} - \vec{G_{Ca}} m_\infty (V - E_{Ca}) - \vec{G_L}(V - E_L)}{\vec{G_K}(V - E_K)}$$

$$\dot{\omega} = 0 \to \omega = \omega_\infty(V)$$

Jacobian

$$J = \left[\begin{array}{cc}\partial F_x/\partial x & \partial F_x/\partial y\\ \partial F_y/\partial x & \partial F_y/\partial y\end{array}\right]\Bigg|_{eq\_pt}$$

$$\vec{x}(t) = \sum_{i=1}^{N} a_i \vec{e_i} e^{\lambda_i t}$$