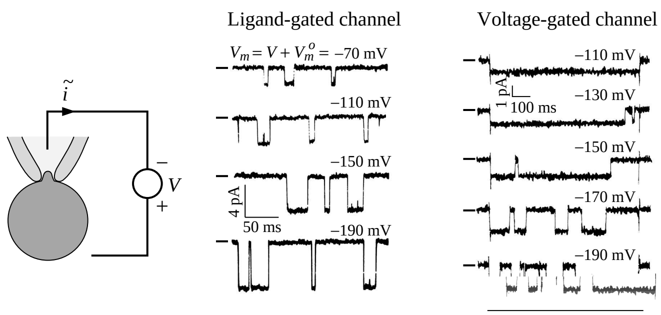
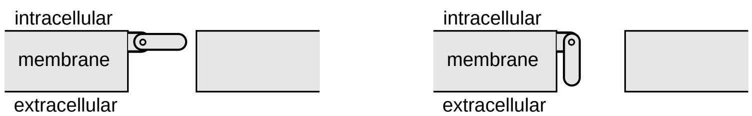
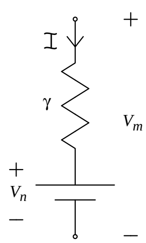


Model of ion channel has two parts

1. Two-state gate model of kinetics

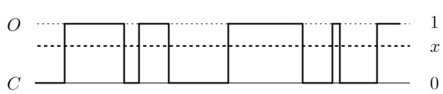


2. Passive electrodiffusive model of permeation



State occupancy

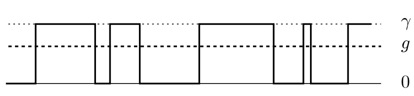
$\tilde{s} = \begin{cases} 0 \text{ if closed} \\ 1 \text{ if open} \end{cases}$



probability of open $= x$
$x =$ average state occupancy
(many statistically independent channels)

Single-channel conductance

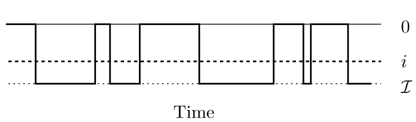
$\tilde{g} = \begin{cases} 0 \text{ if closed} \\ \gamma \text{ if open} \end{cases}$



$g =$ average channel conductance
$= \mathrm{E}[\ \tilde{g}\ ] = 0 \times \Pr[\text{closed}] + \gamma \times \Pr[\text{open}]$
$= 0(1-x) + \gamma x = \gamma x$

Single-channel current

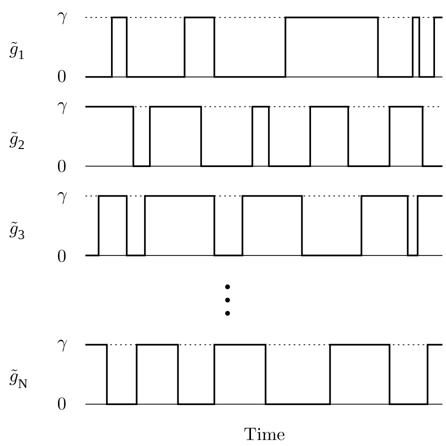
$\tilde{i} = \begin{cases} 0 \text{ if closed} \\ \mathcal{I} \text{ if open} \end{cases}$



$i =$ average channel current
$= \mathrm{E}[\ \tilde{i}\ ] = 0 \times \Pr[\text{closed}] + \mathcal{I} \times \Pr[\text{open}]$
$= 0(1-x) + \mathcal{I}x = \mathcal{I}x$
$= \gamma(V_m - V_n)x = g(V_m - V_n)$
deterministic

random variables (˜)

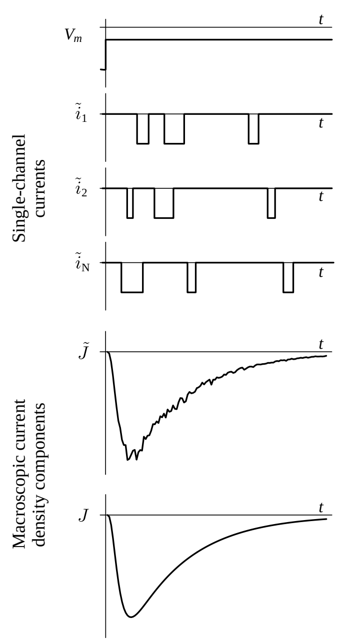
Relation between microscopic and macroscopic variables is statistical.
Assume cell has N identical channels that are statistically independent.



$$\tilde{\mathcal{G}} = \sum_{n=1}^{N} \tilde{g}_n$$

$$\approx \mathcal{G} = N\mathrm{E}[\ \tilde{g}\ ] = Ng$$

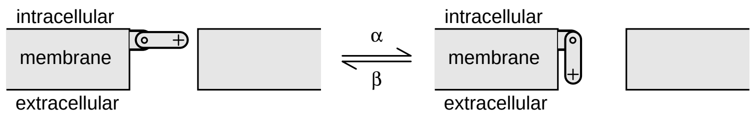
$$G = \frac{\mathcal{G}}{A} = \frac{N}{A} g$$



$$\tilde{J} = \frac{1}{A} \sum_{n=1}^{N} \tilde{i}_n$$

$$J = \frac{N}{A} \mathrm{E}[\ \tilde{i}\ ] = \frac{N}{A} g(V_m - V_n)$$

First-order reversible reaction



Assume $\mathcal{N}$ channels per unit area, of which $n(t)$ are open.

$$\frac{dn(t)}{dt} = \alpha(\mathcal{N} - n(t)) - \beta n(t)$$

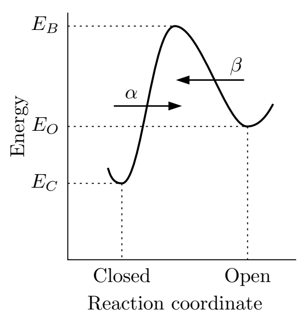
$$n(t) = n_\infty + (n(0) - n_\infty)\, e^{-t/\tau_x} \; ; \qquad n_\infty = \frac{\alpha}{\alpha+\beta}\; \mathcal{N} \; , \quad \tau_x = \frac{1}{\alpha+\beta}$$

Assume $\mathcal{N}$ is large.

$$x(t) = \text{probability gate is open} \approx \frac{n(t)}{\mathcal{N}}$$

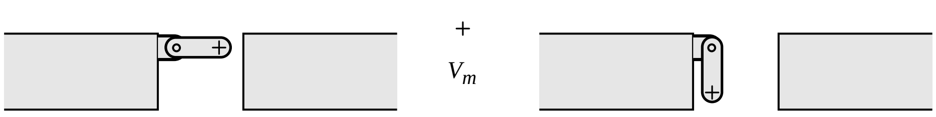
$$x(t) = x_\infty + (x(0) - x_\infty)\, e^{-t/\tau_x} \; ; \qquad x_\infty = \frac{\alpha}{\alpha+\beta} \; , \quad \tau_x = \frac{1}{\alpha+\beta}$$

Theory of absolute reaction rates (volume 1, chapter 6)

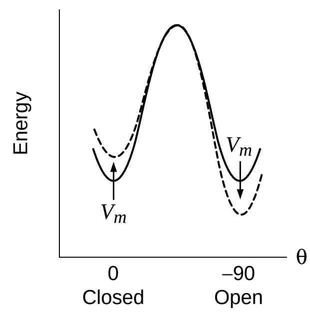


$$\alpha = Ae^{(E_C - E_B)/kT}$$
$$\beta = Ae^{(E_O - E_B)/kT}$$

Potential energy of an ion channel



The potential energy of an ion channel includes mechanical, chemical, and electrical contributions, each of which can be different in different conformations. Electrical potential energy depends on both the distribution of charge in the gate and on transmembrane potential. Therefore, E_B, E_O, and E_C depend on V_m.

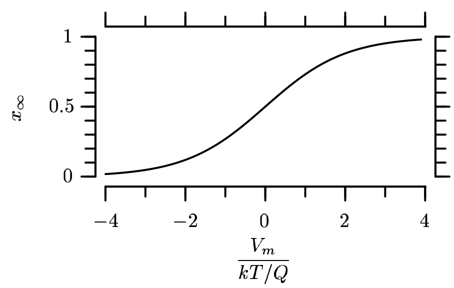


Example

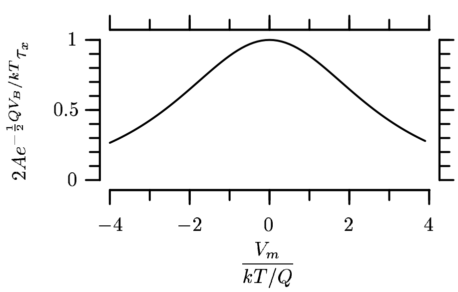
$$E_B = \frac{1}{2}QV_B\ ; \quad E_C = \frac{1}{2}QV_m\ ; \quad E_O = -\frac{1}{2}QV_m$$

$$\alpha = A\ e^{\frac{1}{2}Q(V_m - V_B)/kT}\ ; \quad \beta = A\ e^{-\frac{1}{2}Q(V_m + V_B)/kT}$$

$$x_\infty = \frac{\alpha}{\alpha + \beta} = \frac{1}{1 + \beta/\alpha} = \frac{1}{1 + e^{-QV_m/kT}}$$



$$\tau_x = \frac{1}{\alpha + \beta} = \frac{1}{A\left(e^{\frac{1}{2}Q(V_m - V_B)/kT} + e^{-\frac{1}{2}Q(V_m + V_B)/kT}\right)}$$
$$= \frac{1}{Ae^{-\frac{1}{2}QV_B/kT}\left(e^{\frac{1}{2}QV_m/kT} + e^{-\frac{1}{2}QV_m/kT}\right)}$$



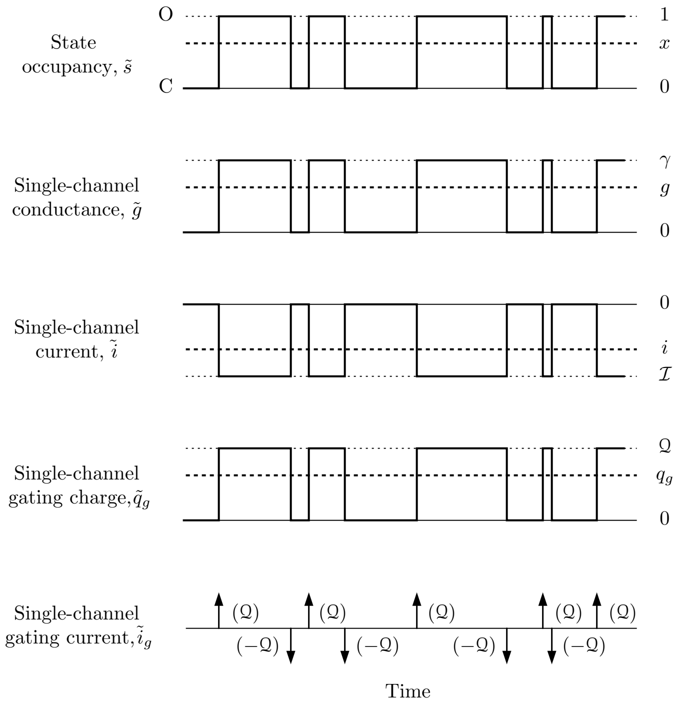


Figure 6.33

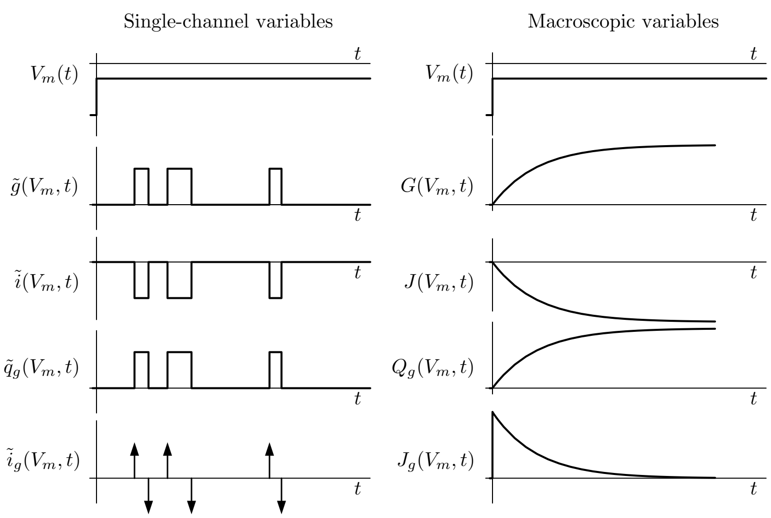


Figure 6.52

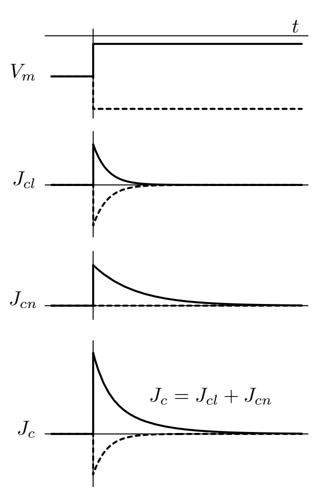


Figure 6.20

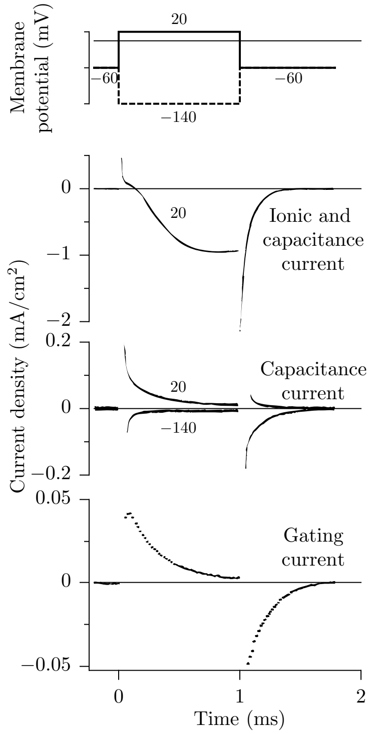


Figure 6.21

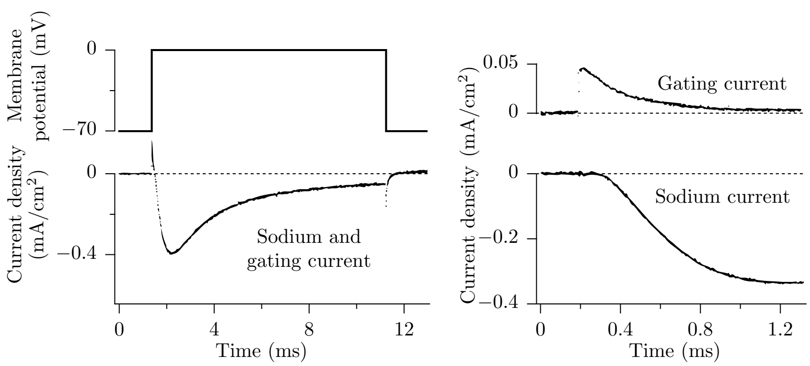


Figure 6.22

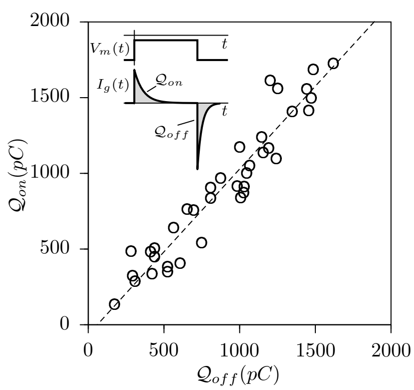


Figure 6.24

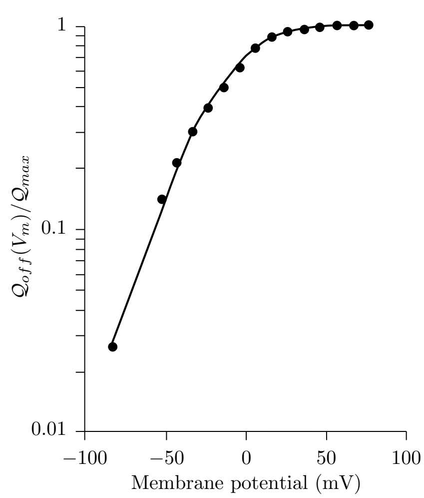


Figure 6.25