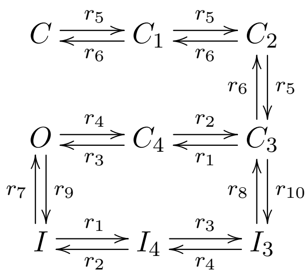
$r_4 = 11\,S^{-1}$
$r_5 = 34\,S^{-1}$
$r_6 = 190\,S^{-1}\text{mM}^{-1}$

3. **Multistate models:**

Example: Na^+ channel by Vandenberg & Bezanilla (1991)



(3.45)

3.3.3 Solving Markov equations

First order kinetics

$$C \underset{r_2}{\overset{r_{1j}}{\rightleftharpoons}} O \tag{3.46}$$

$$\Rightarrow \frac{dC}{dt} = r_2 \cdot O - r_1 \cdot C \tag{3.47}$$

$$\frac{dO}{dt} = r_1 \cdot C - r_2 \cdot O \tag{3.48}$$

$$\text{With} \quad C = 1 - O \quad \text{follows}$$

$$\frac{dO}{dt} = r_1(1-O) - r_2 \cdot O \, (= r_1 - (r_1 + r_2)O) \tag{3.49}$$

$$\text{Let} \quad O = O^* \quad \text{be the initial condition at } t_0 = 0$$

$$\Rightarrow O(t) = O^\infty + K_1 \exp(-t/\tau_1)$$

$$K_1 = O^* - O^\infty \tag{3.50}$$

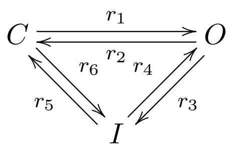
$$O^\infty = \frac{r_1}{r_1 + r_2} \tag{3.51}$$

$$\tau_1 = \frac{1}{r_1 + r_2} \tag{3.52}$$

Check:

$$
\begin{aligned}
\frac{dO}{dt} &= K_1 \left(-\frac{1}{\tau_1}\right) \exp(-t/\tau_1) - \frac{1}{\tau_1} O^\infty + \frac{1}{\tau_1} O^\infty \\
&= \left(-\frac{1}{\tau_1}\right) O(t) + \frac{1}{\tau_1} O^\infty \\
&= (r_1 + r_2) \cdot O^\infty - (r_1 + r_2)\, O(t) \\
&= r_1 - (r_1 + r_2)\, O(t)
\end{aligned}
$$

Second order kinetics



(3.53)

$$
\begin{aligned}
\Rightarrow \frac{dO}{dt} &= r_1 C - (r_2 + r_3) \cdot O + r_4 I \\
&= r_1(1 - O - I) - (r_2 + r_3)\, O + r_4 I \qquad (3.54) \\
\frac{dI}{dt} &= r_6(1 - O - I) - (r_4 - r_5)\, I + r_3 O \qquad (3.55)
\end{aligned}
$$

General solution:

Initial conditions $O = O^*$, $I = I^*$

$$
\begin{aligned}
O(t - t_0) &= O^\infty + K_1 \exp(-(t - t_0)/\tau_1) + K_2 \exp(-(t - t_0)/\tau_2) \qquad (3.56) \\
I(t - t_0) &= I^\infty + K_3 \exp(-(t - t_0)/\tau_1) + K_4 \exp(-(t - t_0)/\tau_2 \qquad (3.57)
\end{aligned}
$$

with

$$
\begin{aligned}
K_1 &= \frac{(O^* - O^\infty)(a + 1/\tau_2) + b(I^* - I^\infty)}{\frac{1}{\tau_2} - \frac{1}{\tau_1}} \qquad (3.58) \\
K_2 &= (O^* - O^\infty) - K_1 \qquad (3.59) \\
K_3 &= K_1 \frac{-a - 1/\tau_1}{b} \qquad (3.60) \\
K_4 &= K_2 \frac{-a - 1/\tau_1}{b} \qquad (3.61) \\
O^\infty &= \frac{br_6 - dr_1}{ad - bc} \qquad (3.62) \\
I^\infty &= \frac{cr_1 - ar_6}{ad - bc} \qquad (3.63) \\
a &= -(r_1 + r_2 + r_3)\,, \quad b = -r_1 + r_4, \\
c &= r_3 - r_6\,, \quad d = -(r_4 + r_5 + r_6) \qquad (3.64) \\
\tau_{1/2} &= -\frac{a + d}{2} \pm \frac{1}{2}\sqrt{(a - b)^2 + 4bc} \qquad (3.65)
\end{aligned}
$$

Higher order kinetics are typically solved numerically.

4 Modeling neurons II: Spatio-temporal models

4.1 The cable equation

The cable theory describes the movement of charges in highly anisotropic domains (e.g. long cables). Since neuronal dendrites can be approximated as thin cables, we can make use of this theory to derive an initial spatio-temporal model for V_m.
Assume that charges can only move in axial direction of the cable (tangential to the membrane). We will denote this direction by x. Thus V_m is now a quantity that depends on x and t. Assuming that current flows from x to $x + \Delta x$, Ohm's law states

$$\Delta V = -R_L I_L$$

With

$$R_L = r_L \cdot \frac{\Delta x}{\pi a^2}$$

where r_L is the intracellular resistivity follows

$$\Delta V = -r_L \frac{\Delta x}{\pi a^2} \cdot I_L \tag{4.1}$$

$$\Leftrightarrow I_L = -\pi a^2 \cdot \frac{\Delta V}{r_L \Delta x} \tag{4.2}$$

With $\Delta x \to 0$ follows

$$I_L = -\frac{\pi a^2}{r_L} \cdot \frac{\partial V}{\partial x}$$

Balance of fluxes:

$$0 = -\frac{\pi a^2}{r_L} \frac{\partial V}{\partial x}\Big|_L + \frac{\pi a^2}{r_L} \frac{\partial V}{\partial x}\Big|_R - 2\pi a \Delta x (i_m - i_e) - 2\pi a \Delta x C_m \frac{\partial V}{\partial t} \tag{4.3}$$

$$\Rightarrow C_m \frac{\partial V}{\partial t} = \frac{1}{2\pi a \Delta x} \cdot \left(\frac{\pi a^2}{r_L} \frac{\partial V}{\partial x}\Big|_R - \frac{\pi a^2}{r_L} \frac{\partial V}{\partial x}\Big|_L \right) - (i_m - i_e) \tag{4.4}$$

For $\Delta x \to 0$:

$$= \frac{1}{2\pi a}\frac{\partial}{\partial x}\left(\frac{\pi a^2}{r_L}\frac{\partial V}{\partial x}\right) - (i_m - i_e) \qquad (4.5)$$

$$= \frac{1}{2a \cdot r_L}\frac{\partial}{\partial x}\left(a^2\frac{\partial V}{\partial x}\right) - (i_m - i_e) \qquad (4.6)$$

$\Rightarrow$ **Cable equation**

$$\boxed{C_m \frac{\partial V}{\partial t} = \frac{1}{2ar_L}\ \frac{\partial}{\partial x}\left(a^2\frac{\partial V}{\partial x}\right) - i_m + i_e} \qquad (4.7)$$

$\uparrow \qquad \uparrow \qquad \uparrow$

time- and space-dependent PDE

4.1.1 Boundary and branching conditions

A unique solution of the cable equation requires initial and boundary conditions, as well as branching point conditions.

Boundary conditions:

$$\frac{\pi a^2}{r_L}\frac{\partial V}{\partial x}\Big|_{end} = 0 \qquad (4.8)$$

i.e. no charge flux at the end of dendrites and axons.

Initial conditions: e.g. resting potential

Branching points:

1. Matching of the membrane potential at neighboring compartments $1 \dots n$ of branching points x_* leads to

$$V_1(x_*) = V_2(x_*) = \cdots = V_n(x_*) \qquad (4.9)$$

2. The sum over all currents in x_* equals zero (flux conservation):

$$\sum_{i=1}^{n} I_i(x_*) = \sum_{i=1}^{n}\left(\frac{\pi a^2}{r_L}\frac{\partial V}{\partial x}\right)\Big|_{x_*} = 0 \qquad (4.10)$$

4.1.2 Stationary solution of the cable equation

Assumptions:

1. We will only consider dendrites, i.e. no nonlinear effects, such as Hodgkin-Huxley currents
2. Electrode stimulation (point injection)
3. constant radius, i.e. a independent of x

Linearizing i_m leads to:

$$i_m = \frac{V - V_{rest}}{r_m}. \tag{4.11}$$

$$\text{Let} \quad v := V - V_{rest}$$

$$\Rightarrow \quad i_m = \frac{v}{r_m} \tag{4.12}$$

$$\Rightarrow \quad c_m \frac{\partial v}{\partial t} = \underbrace{\frac{a}{2r_L} \frac{\partial^2 v}{\partial x^2}}_{\text{see (3)}} - \underbrace{\frac{v}{r_m} + i_e}_{\text{see (1) + (2)}} \qquad \text{(linearized cable equation)}$$

$$\text{Let} \quad \tau_m := r_m c_m \quad \text{and} \quad \lambda := \sqrt{\frac{a r_m}{2 r_L}} \quad \text{electrotonic length}$$

$$\Rightarrow \quad \tau_m \frac{\partial v}{\partial t} = \lambda^2 \frac{\partial^2 v}{\partial x^2} - v + r_m i_e \tag{4.13}$$

Infinite cable

We can derive an analytic solution for the stationary case in an infinitely long cable:

1. $V = 0$ for $|x| \to \infty$
2. constant electrode current, i.e. $\frac{\partial V}{\partial t} = 0$

$$\Rightarrow \lambda^2 \frac{d^2 V}{dx^2} = V - r_m i_e \tag{4.14}$$

3. $\left.\begin{array}{lll} i_e & \neq 0 & \text{for} - \varepsilon \leq x \leq \varepsilon \\ i_e & = 0 & \text{else} \end{array}\right\}$ point injection

   For $i_e = 0$ we get:

   $$\lambda^2 \frac{d^2 v}{dx^2} = v$$

   The general solution then reads: $v(x) = B_1 \exp(-x/\lambda) + B_2 \exp(x/\lambda)$
   B_1, B_2 are determined by the boundary conditions (see below).