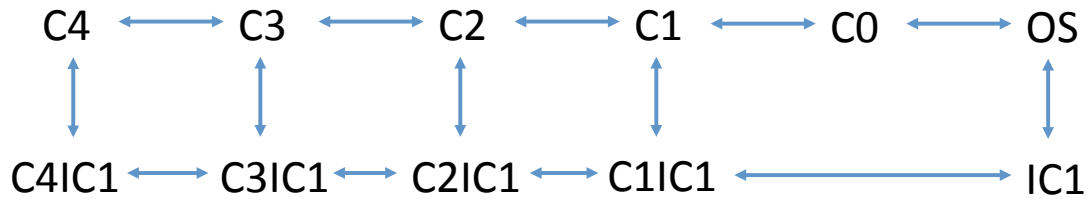


11 State Model



This is an 11 state model, representing a potassium channel with 4 independent voltage sensors and one inactivation mechanism. The number of voltage sensors in the closed state is indicated by $C4$, $C3$, $C2$, $C1$ and $C0$ respectively, and inactivation by $IC1$. Hence $C3IC1$ is the state in which 3 of the voltage sensors are in the closed conformation and the channel is inactivated. $C0$ is the pre-activated state, where all voltage sensors are in the open state but the channel is still closed and OS is the open state. The transitions rates are given by:

$$\begin{aligned}
 C4 \rightarrow C3 : & \quad 4k_c \exp\left(Z_c \frac{F(V-V_c)}{A}\right) \\
 C3 \rightarrow C4 : & \quad k_c \exp\left(-Z_c \frac{F(V-V_c)}{A}\right) \\
 C3 \rightarrow C2 : & \quad 3k_c \exp\left(Z_c \frac{F(V-V_c)}{A}\right) \\
 C2 \rightarrow C3 : & \quad 2k_c \exp\left(-Z_c \frac{F(V-V_c)}{A}\right) \\
 C2 \rightarrow C1 : & \quad 2k_c \exp\left(Z_c \frac{F(V-V_c)}{A}\right) \\
 C1 \rightarrow C2 : & \quad 3k_c \exp\left(-Z_c \frac{F(V-V_c)}{A}\right) \\
 C1 \rightarrow C0 : & \quad k_c \exp\left(Z_c \frac{F(V-V_c)}{A}\right) \\
 C0 \rightarrow C1 : & \quad 4k_c \exp\left(-Z_c \frac{F(V-V_c)}{A}\right)
 \end{aligned}$$

$$\begin{aligned}
 C4IC1 \rightarrow C3IC1 : & \quad 4v_c^{ic} k_c \exp\left(Z_c \frac{F(V-V_c)}{A}\right) \\
 C3IC1 \rightarrow C4IC1 : & \quad r_c^{ic} v_c^{ic} k_c \exp\left(-Z_c \frac{F(V-V_c)}{A}\right) \\
 C3IC1 \rightarrow C2IC1 : & \quad 3v_c^{ic} k_c \exp\left(Z_c \frac{F(V-V_c)}{A}\right) \\
 C2IC1 \rightarrow C3IC1 : & \quad 2r_c^{ic} v_c^{ic} k_c \exp\left(-Z_c \frac{F(V-V_c)}{A}\right) \\
 C2IC1 \rightarrow C1IC1 : & \quad 2v_c^{ic} k_c \exp\left(Z_c \frac{F(V-V_c)}{A}\right) \\
 C1IC1 \rightarrow C2IC1 : & \quad 3r_c^{ic} v_c^{ic} k_c \exp\left(-Z_c \frac{F(V-V_c)}{A}\right) \\
 C1IC1 \rightarrow IC1 : & \quad v_c^{ic} k_c \exp\left(Z_c \frac{F(V-V_c)}{A}\right) \\
 IC1 \rightarrow C1IC1 : & \quad 4r_c^{ic} v_c^{ic} k_c k_{cf}^{ic} \exp\left(-Z_c \frac{F(V-V_c)}{A}\right)
 \end{aligned}$$

$$\begin{aligned}
 C0 \rightarrow OS : & \quad k_o \\
 OS \rightarrow C0 : & \quad k_o r_o
 \end{aligned}$$

OS -> IC1 : k_i
 IC1 -> OS : $k_i r_i$

C1IC1 -> C1 : $k_i r_i (v_{ic}^c)^1$
 C1 -> C1IC1 : $k_i (r_{ic}^c v_{ic}^c)^1$
 C2IC1 -> C2 : $k_i r_i (v_{ic}^c)^2$
 C2 -> C2IC1 : $k_i (r_{ic}^c v_{ic}^c)^2$
 C3IC1 -> C3 : $k_i r_i (v_{ic}^c)^3$
 C3 -> C3IC1 : $k_i (r_{ic}^c v_{ic}^c)^3$
 C4IC1 -> C4 : $k_i r_i (v_{ic}^c)^4$
 C4 -> C4IC1 : $k_i (r_{ic}^c v_{ic}^c)^4$

With the conditions (stemming from microreversibility):

$$r_c^{ic} = r_{ic}^c$$

$$k_{cf}^{ic} = r_o$$

and $R = 8.134 \left[\frac{\text{J}}{\text{mol K}} \right]$ and $F = 96.485 \left[\frac{\text{J}}{\text{mV mol}} \right]$. V [mV] is the transmembrane voltage. Z_c is the equivalent charge for activation and V_c [mV] the voltage of half activation.

The model was fit directly to experimental current traces obtained with diverse voltage protocols and measured at 35C for a total of 65 traces. The fit was performed with the Data2Dynamics software (<https://github.com/Data2Dynamics/d2d>).