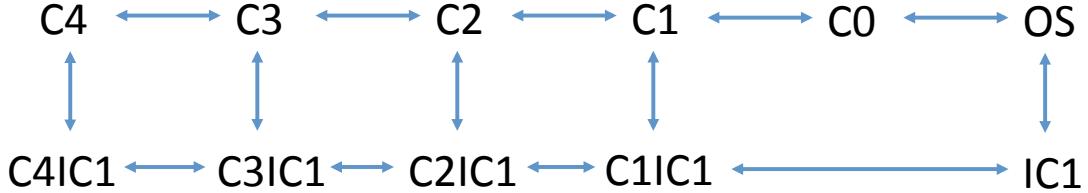


11 State Model



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 C_4, C_3, C_2, C_1 and C_0 respectively, and inactivation by IC_1 . Hence C_3IC_1 is the state in which 3 of the voltage sensors are in the closed conformation and the channel is inactivated. C_0 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:

$$C_4 \rightarrow C_3 : 4k_c \exp(H_{kc}\Delta T) \exp\left(Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_3 \rightarrow C_4 : k_c \exp(H_{kc}\Delta T) \exp\left(-Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_3 \rightarrow C_2 : 3k_c \exp(H_{kc}\Delta T) \exp\left(Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_2 \rightarrow C_3 : 2k_c \exp(H_{kc}\Delta T) \exp\left(-Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_2 \rightarrow C_1 : 2k_c \exp(H_{kc}\Delta T) \exp\left(Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_1 \rightarrow C_2 : 3k_c \exp(H_{kc}\Delta T) \exp\left(-Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_1 \rightarrow C_0 : k_c \exp(H_{kc}\Delta T) \exp\left(Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_0 \rightarrow C_1 : 4k_c \exp(H_{kc}\Delta T) \exp\left(-Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_4IC_1 \rightarrow C_3IC_1 : 4v_c^{ic}k_c \exp(H_{kc}\Delta T) \exp\left(Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_3IC_1 \rightarrow C_4IC_1 : r_c^{ic}v_c^{ic}k_c \exp(H_{kc}\Delta T) \exp\left(-Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_3IC_1 \rightarrow C_2IC_1 : 3v_c^{ic}k_c \exp(H_{kc}\Delta T) \exp\left(Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_2IC_1 \rightarrow C_3IC_1 : 2r_c^{ic}v_c^{ic}k_c \exp(H_{kc}\Delta T) \exp\left(-Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_2IC_1 \rightarrow C_1IC_1 : 2v_c^{ic}k_c \exp(H_{kc}\Delta T) \exp\left(Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_1IC_1 \rightarrow C_2IC_1 : 3r_c^{ic}v_c^{ic}k_c \exp(H_{kc}\Delta T) \exp\left(-Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_1IC_1 \rightarrow IC_1 : v_c^{ic}k_c \exp(H_{kc}\Delta T) \exp\left(Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$IC_1 \rightarrow C_1IC_1 : 4r_c^{ic}v_c^{ic}k_c k_{cf}^{ic} \exp(H_{kc}\Delta T) \exp\left(-Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{A}\right)$$

$$C_0 \rightarrow OS : k_o$$

$$OS \rightarrow C_0 : k_o r_o$$

$$\text{OS} \rightarrow \text{IC1} : k_i \exp(H_{ki}\Delta T)$$

$$\text{IC1} \rightarrow \text{OS} : k_i r_i \exp(H_{ki}\Delta T) \exp(H_{ri}\Delta T)$$

$$\text{C1IC1} \rightarrow \text{C1} : k_i r_i (v_{ic}^c)^1 \exp(H_{ki}\Delta T) \exp(H_{ri}\Delta T) \exp(H_{vic}^c\Delta T)$$

$$\text{C1} \rightarrow \text{C1IC1} : k_i (r_{ic}^c v_{ic}^c)^1 \exp(H_{ki}\Delta T) \exp(H_{ric}^c\Delta T) \exp(H_{vic}^c\Delta T)$$

$$\text{C2IC1} \rightarrow \text{C2} : k_i r_i (v_{ic}^c)^2 \exp(H_{ki}\Delta T) \exp(H_{ri}\Delta T) \exp(H_{vic}^c\Delta T)$$

$$\text{C2} \rightarrow \text{C2IC1} : k_i (r_{ic}^c v_{ic}^c)^2 \exp(H_{ki}\Delta T) \exp(H_{ric}^c\Delta T) \exp(H_{vic}^c\Delta T)$$

$$\text{C3IC1} \rightarrow \text{C3} : k_i r_i (v_{ic}^c)^3 \exp(H_{ki}\Delta T) \exp(H_{ri}\Delta T) \exp(H_{vic}^c\Delta T)$$

$$\text{C3} \rightarrow \text{C3IC1} : k_i (r_{ic}^c v_{ic}^c)^3 \exp(H_{ki}\Delta T) \exp(H_{ric}^c\Delta T) \exp(H_{vic}^c\Delta T)$$

$$\text{C4IC1} \rightarrow \text{C4} : k_i r_i (v_{ic}^c)^4 \exp(H_{ki}\Delta T) \exp(H_{ri}\Delta T) \exp(H_{vic}^c\Delta T)$$

$$\text{C4} \rightarrow \text{C4IC1} : k_i (r_{ic}^c v_{ic}^c)^4 \exp(H_{ki}\Delta T) \exp(H_{ric}^c\Delta T) \exp(H_{vic}^c\Delta T)$$

With the conditions (stemming from microreversibility):

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

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

$$H_{ric}^c = 0$$

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 and $\Delta T = T - 298.15$ [K] is the difference with room temperature. Z_c is the equivalent charge for activation and V_c [mV] the voltage of half activation at 25C.

The model was fit directly to experimental current traces obtained with diverse voltage protocols and measured at 3 different temperatures (15C, 25C and 35C) for a total of 195 traces. The fit was performed with the Data2Dynamics software (<https://github.com/Data2Dynamics/d2d>).