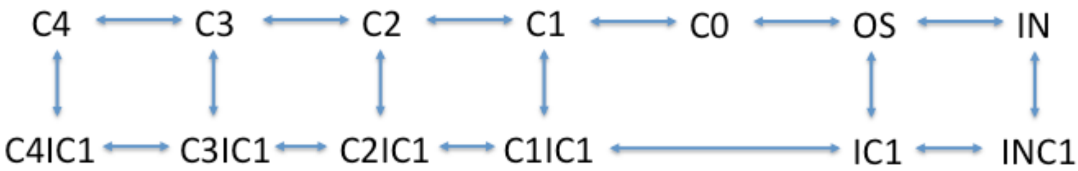
13 State Model



This is a 13 state model, representing a potassium channel with 4 independent voltage sensors and two inactivation mechanism. The number of voltage sensors in the closed state is indicated by *C4*, *C3*, *C2*, *C1* and *C0* respectively, C-type inactivation by *IC1* and N-type inactivation by *IN*. Hence *C3IC1* is the state in which 3 of the voltage sensors are in the closed conformation and the channel is C-type inactivated and *INC1* has all 4 sensors in the open conformation but is both C-type and N-type 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:

C4 -> C3 : $4\mathrm{k}_c \exp\left(\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C3 -> C4 : $\mathrm{k}_c \exp\left(-\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C3 -> C2 : $3\mathrm{k}_c \exp\left(\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C2 -> C3 : $2\mathrm{k}_c \exp\left(-\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C2 -> C1 : $2\mathrm{k}_c \exp\left(\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C1 -> C2 : $3\mathrm{k}_c \exp\left(-\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C1 -> C0 : $\mathrm{k}_c \exp\left(\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C0 -> C1 : $4\mathrm{k}_c \exp\left(-\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C4IC1 -> C3IC1 : $4\mathrm{v}_c^{ic}\mathrm{k}_c \exp\left(\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C3IC1 -> C4IC1 : $\mathrm{r}_c^{ic}\mathrm{v}_c^{ic}\mathrm{k}_c \exp\left(-\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C3IC1 -> C2IC1 : $3\mathrm{v}_c^{ic}\mathrm{k}_c \exp\left(\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C2IC1 -> C3IC1 : $2\mathrm{r}_c^{ic}\mathrm{v}_c^{ic}\mathrm{k}_c \exp\left(-\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C2IC1 -> C1IC1 : $2\mathrm{v}_c^{ic}\mathrm{k}_c \exp\left(\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C1IC1 -> C2IC1 : $3\mathrm{r}_c^{ic}\mathrm{v}_c^{ic}\mathrm{k}_c \exp\left(-\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C1IC1 -> IC1 : $\mathrm{v}_c^{ic}\mathrm{k}_c \exp\left(\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

IC1 -> C1IC1 : $4\mathrm{r}_c^{ic}\mathrm{v}_c^{ic}\mathrm{k}_c\mathrm{k}_{cf}^{ic} \exp\left(-\mathrm{Z}_c \frac{\mathrm{F(V-V}_c)}{\mathrm{A}}\right)$

C0 -> OS : k_o

OS -> C0 : $\mathrm{k}_o r_o$

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 : $k_i (r_{ic}^c v_{ic}^c)^4$

OS -> IN : k_n
IN -> OS : $k_n r_n$
IC1 -> INC1 : $k_n r_n^{ic} v_n^{ic}$
INC1 -> IC1 : $k_n r_n v_n^{ic}$

IN -> INC1 : $k_i r_{ic}^n v_{ic}^n$
INC1 -> IN : $k_i r_i v_{ic}^n$

With the conditions (stemming from microreversibility):

$$r_c^{ic} = r_{ic}^c$$
$$r_n^{ic} = r_{ic}^n$$
$$k_{cf}^{ic} = r_o$$

and $R = 8.134 \left[\frac{J}{mol\ K}\right]$ and $F = 96.485 \left[\frac{J}{mV\ mol}\right]$. 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).