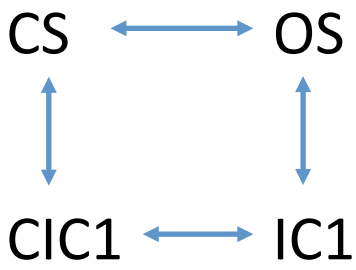
4 State Model



This is a 4 state model, with a closed state *CS*, an open state *OS*, an inactivated state *IC1* and a closed-inactivated state *CIC1*. The transitions rates are given by:

CS -> OS : $k_c \exp\left(Z_c \frac{F(V-V_c)}{A}\right)$
OS -> CS : $k_c \exp\left(-Z_c \frac{F(V-V_c)}{A}\right)$
OS -> IC1 : k_i
IC1 -> OS : $k_i r_i$
IC1 -> CIC1 : $r_c^{ic} v_c^{ic} k_c \exp\left(-Z_c \frac{F(V-V_c)}{A}\right)$
CIC1 -> IC1 : $v_c^{ic} k_c \exp\left(Z_c \frac{F(V-V_c)}{A}\right)$
CIC1 -> CS : $k_i r_i v_{ic}^c$
CS -> CIC1 : $k_i r_{ic}^c v_{ic}^c$

With the condition (stemming from microreversibility):

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

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).