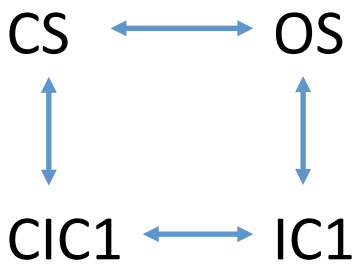
# 4 State Model




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

OS -> CS : $k_c \ \exp(H_{kc}\Delta T) \exp\left(-Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{RT}\right)$

OS -> IC1 : $k_i \ \exp(H_{ki}\Delta T)$

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

IC1 -> CIC1 : $r_c^{ic} v_c^{ic} k_c \exp(H_{kc}\Delta T) \ \exp\left(-Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{RT}\right)$

CIC1 -> IC1 : $v_c^{ic} k_c \exp(H_{kc}\Delta T) \ \exp\left(Z_c \frac{F(V-V_c-H_{vc}\Delta T)}{RT}\right)$

CIC1 -> CS : $k_i r_i v_{ic}^c \exp(H_{ki}\Delta T) \exp(H_{ri}\Delta T) \exp(H_{vic}^c \Delta T)$

CS -> CIC1 : $k_i r_{ic}^c v_{ic}^c \exp(H_{ki}\Delta T) \exp(H_{ric}^c \Delta T) \exp(H_{vic}^c \Delta T)$

With the conditions (stemming from microreversibility):

$$r_c^{ic} = r_{ic}^c$$
$$H_{ric}^c = 0$$

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 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).