The Conserved Phenylalanine in the K^+ Channel Voltage-Sensor Domain Creates a Barrier with Unidirectional Effects

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Kinetic simulations

For the kinetic calculations we assume that each voltage sensor S4 can be in one out of four different kinetic states (C3, C2, C1 or O) representing four different molecular configurations (Henrion et al., 2012):

$$C3 \underset{}{\overset{K}{<->}} C2 \overset{K}{<->} C1 \overset{K}{<->} O$$

For simplicity, we assume that the equilibrium constants between the states are equal and set to

$$K = \exp((V+50)/15),$$

where V is the absolute membrane voltage. The probability to find S4 in the O state is then

$$p_O = K^3 / (1 + K + K^2 + K^3)$$

Assuming that all four S4s must be in state O to allow the channel to be open, then the conductance versus voltage curve is described by

$$G(V) = p_O^4 = [K^3 / (1 + K + K^2 + K^3)]^4.$$

A closing kinetics 50 times faster in F290L compared to the wild-type *Shaker* K channel gives rise to the following voltage dependence:

$$G(V)_{x50} = p_O^4 = [K^3/50 / (1 + K + K^2 + K^3/50)]^4.$$

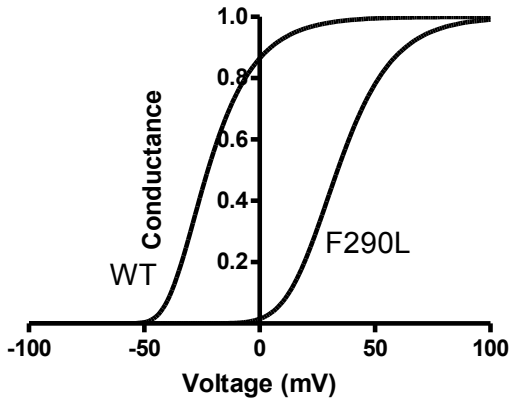

Fig. S1: Predicted conductance as a function of voltage in *Shaker* wild-type and F290L based on a model with four different kinetic states, using the simplified assumption of identical equilibrium constants between the states.

The wild-type curve is close to experimental data for the wild-type *Shaker* K channel and the F290L curve is close to experimental data for the F290L mutated *Shaker* K channel (see Fig 2 in the main paper). The mutation shifts the curve by 56 mV and makes the curve flatter (16% lower effective valence, despite no alteration in the voltage dependence of K above), both in harmony with experimental findings.