|  |  |  |  |
| --- | --- | --- | --- |
| *Rate* | *WT* | *S225L* | *F351A* |
| *kS4 (s-1)* | 1.0 | 1.0 | 1.0 |
| *zOn S4 (e0)* | 0.29 | 0.29 | 0.29 |
| *zOff S4 (e0)* | −0.66 | −0.66 | −0.66 |
| *V50 S4 (mV)*  *c* | −52.5  0.5 | −2.5  0.5 | −52.5  0.5 |
| *e (s-1)*  *d (s-1)* | 0.5  12 | 0.5  12 | 0.5  12 |
| *zOn gate (e0)* | 0.063 | 0.063 | 0.063 |
| *zOff gate (e0)* | −0.087 | −0.087 | −0.087 |
| *V50 gate (mV)* | −58.5 | −58.5 | 81.5 |
| L | 2.89 | 2.89 | 2.89 |

**Supplementary File 4a. Parameters for KV7.1 model in Figure 3 – figure supplement 1.** The rates and gating charges z associated with each transition for wild-type KV7.1+KCNE1 were determined from a gobal fit of data in a previous study (Osteen *et al.*, 201025 and 201226). Rates modified for each mutation are indicated in gray.

(*V*) *= kS4\*exp(zOn S4F(V- V50 S4)/RT),*

(*V*) *= kS4\*exp(zOff S4F(V- V50 S4)/RT),*

en(*V*) *= e\*(exp(zOn gateF(V- V50 gate)/RT))n,*

dn(*V*) *= d\*(exp(zOff gateF(V- V50 gate)/RT))n,* where n is the number of activated S4s.

'(*V*) *= c\**(*V*)*\*exp(zOff S4F(V- V50 S4)/RT)* and '(*V*) *= c\**(*V*)*\*(exp(zOff gateF(V- V50 gate)/RT))*, to ensure detailed balance. *R*, *T*, and *F* have their usual thermodynamic meaning.

25. Osteen, J.D., Gonzalez, C., Sampson, K.J., Iyer, V., Rebolledo, S., Larsson, H.P. & Kass, R.S. KCNE1 alters the voltage sensor movements necessary to open the KCNQ1 channel gate. *Proc Natl Acad Sci U S A* **107,** 22710-22715 (2010).

26. Osteen, J.D., Barro-Soria, R., Robey, S., Sampson, K.J., Kass, R.S. & Larsson, H.P. Allosteric gating mechanism underlies the flexible gating of KCNQ1 potassium channels. *Proc Natl Acad Sci U S A* **109,** 7103-7108 (2012).

|  |  |  |  |
| --- | --- | --- | --- |
| *Rate* | *WT* | *S225L* | *F351A* |
| *kS4 (s-1)* | 0.464 | 0.464 | 0.464 |
| *zOn S4 (e0)* | 0.44 | 0.44 | 0.44 |
| *zOff S4 (e0)* | −0.35 | −0.35 | −0.35 |
| *V50 S4 (mV)* | −116.4 | −66.4 | −116.4 |
| *kgate (s-1)* | 0.203 | 0.203 | 0.203 |
| *zOn gate (e0)* | 0.44 | 0.44 | 0.44 |
| *zOff gate (e0)* | −0.77 | −0.77 | −0.77 |
| *V50 gate (mV)* | −7.6 | −7.6 | +132.4 |

**Supplementary File 4b. Parameters for KV7.1+KCNE1 model in Figure 3 – figure supplement 1.** The rates and gating charges z associated with each transition for wild-type KV7.1+KCNE1 were determined in a previous study (Barro-Soria *et al.*, 201424). Rates modified for each mutation are indicated in gray. *R*, *T*, and *F* have their usual thermodynamic meaning.

(*V*) *= kS4\*exp(zOn S4F(V- V50 S4)/RT),*

(*V*) *= kS4\*exp(zOff S4F(V- V50 S4)/RT),*

(*V*) *= kgate\*exp(zOn gateF(V- V50 gate)/RT),*

(*V*) *= kgate\*exp(zOff gateF(V- V50 gate)/RT).*

24. Barro-Soria, R., Rebolledo, S., Liin, S.I., Perez, M.E., Sampson, K.J., Kass, R.S. & Larsson, H.P. KCNE1 divides the voltage sensor movement in KCNQ1/KCNE1 channels into two steps. *Nat Commun* **5,** 3750 (2014).