**Supplemental Tab. S1. Parameters for the concentration- and Ca2+-dependent electrophysiological effects of the N-lobe, C-lobe, and N-lobe plus C-lobe.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | N-lobe | | C-lobe | | N+C-lobe | |
|  | 80 (nM) | 2 (μM) | 80 (nM) | 2 (μM) | 80 (nM) | 2 (μM) |
| Ymax (%) | 234.89 | 137.27 | 94.75 | 116.04 | 245.00 | 35.41 |
| Kdf (nM) | 65.14 | 20.75 | 9.65 | 6.04 | 3.53 | 0.67 |
| nf | 1.2 | 2 | 1 | 1.3 | 2.04 | 2.04 |
| Kdi (nM) |  |  |  |  | 5.22 | 3.69 |
| ni |  |  |  |  | 3.76 | 3.76 |
| R2 | 0.99 | 0.99 | 0.99 | 0.99 | 0.98 | 0.97 |

We assumed a model for the effects of CaM on the Ca2+ channels that involved two CaM-induced effects, one for facilitation (***F***) and the other for inhibition (***I***). Then, the channel activity (***A***) as the overall effect of CaM is ***A* =** Amax***⋅ F⋅ I***, where Amax is the maximum effect of CaM. The theoretical curve for the CaM-*NPo* relationship is given by *NPo* (%) = Amax***⋅*** ([CaM] / Kdf) ^ nf / (1 + ([CaM] / Kdf) ^ nf)) / (1+ ([CaM] / Kdi) ^ ni). Kdf and Kdi are the [Ca2+] for the 50% facilitatory and inhibitory effects, and nf and ni are the respective apparent Hill’s coefficients.