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Supporting Material

A Modeling Study of T-type Ca²⁺ Channel Gating and Modulation by L-Cysteine in Rat Nociceptors

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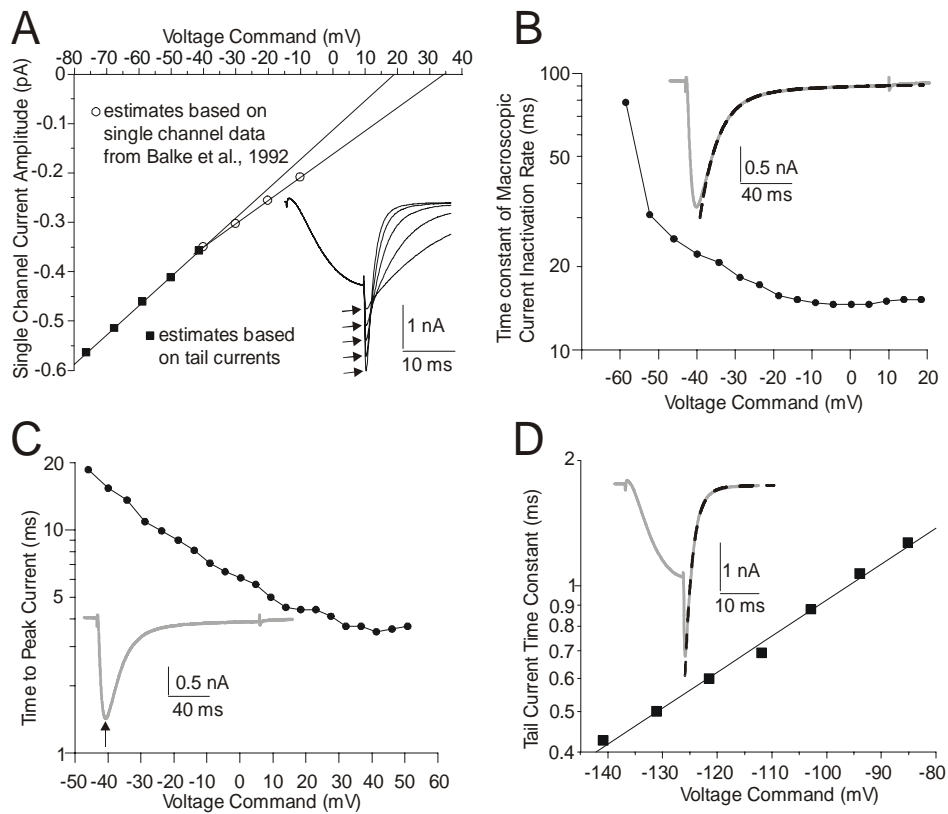


Figure 1: Data supporting various parameters and constraints used in the different models. A, plot of estimated single channel current amplitude versus voltage. The filled boxes represent estimations of single channel current amplitude versus voltage derived from T-channel-mediated tail currents, as described in Materials and Methods. (inset) tail currents (elicited by voltage commands to -90 mV through -50 mV) used in the estimation of single channel amplitude versus voltage. The line through the data points is the best fit as determined by linear regression. The open circles represent values of single channel current amplitude extrapolated from Figure 5B of Balke et al., 1992. B, plot of the time constant of macroscopic inactivation versus voltage. The family of current records fitted is the average of 6 sets of control activation records. The time constant of inactivation was derived by fitting the first $\frac{1}{2}$ of the relaxing phase of the current records with a single exponential function (inset). C, plot of time to peak current versus voltage for the same family of current records shown in (B). The time to peak current was measured from the beginning of the voltage command to the peak of the current (inset). D, plot of tail current decay rate versus voltage. The tail currents (elicited by voltage commands to -160 mV through -100 mV) were fitted with a single exponential function (inset) as described in the methods. In (A) and (D) the tail current records were the average of 7 sets of deactivation records. In (A-D) the x-axis (voltage command) has been adjusted for $3.5 \text{ M}\Omega$ of R_c .

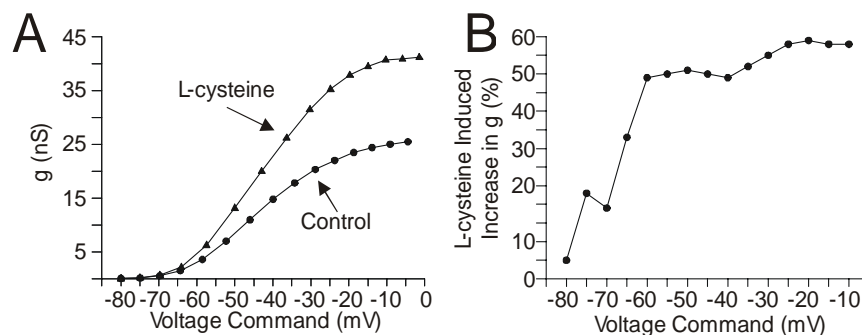


Figure 2, Effects of L-cysteine treatment on T-channel-mediated conductance. A, conductance versus voltage under control conditions (circles), and following treatment with L-cysteine (triangles). Conductance was calculated from the 6 sets of activation data obtained from the Nelson et al. study (15) using the formula: $g = I/(V-V_r)$, where V = voltage command corrected for $3.5 \text{ M}\Omega$ R_S , and V_r = reversal potential. The data was normalized and fitted with the Boltzmann function: $g = g_{max}/(1 + \exp((V_r - V_{1/2})/k))$, where $V_{1/2}$ = the membrane potential where the current was $\frac{1}{2}$ activated, and k = slope. $V_{1/2} = -42.5$ mV for control conditions and -41.9 mV for L-cysteine conditions. B, percent increase in conductance induced by L-cysteine over control level versus membrane voltage. The data points were extrapolated manually from the plot depicted in (A).