

Supplemental Fig. 1. The simple model can also account for the effects of EGTA-AM on activity-dependent recovery. In Figure 8, the importance of activity-dependent recovery is evaluated by eliminating it entirely. This does not equate with the conditions of Fig. 7, in which EGTA-AM is applied to reduce residual calcium. EGTA-AM does not eliminate residual calcium, but rather speeds its decay. The model does not explicitly track residual calcium, so to model the effects of EGTA-AM, we adjusted the rate of decay ( $\tau_D$ ) of the calcium-bound sensor that regulates the fast recovery process (*CaD*). Experimental data are shown using filled circles for control, and open circles for EGTA-AM. All data are in the presence of CTZ. Red lines show results of the model using the parameters in Table 1 (F set for 3 Cae, with no desensitization component), and blue lines show results of the model with  $\tau_D$  at 45% of control. A, The conditioning train. Reducing  $\tau_{\rm D}$  to 45% of control does not greatly change the results of the model during the conditioning train. This matches the effects of EGTA. *B*, Test pulses. Reducing  $\tau_D$  slows recovery from depletion. These model results suggest that even brief transients of residual calcium are sufficient to drive the calcium-dependent process during trains, but not at longer intervals. This could account for the significantly slower recovery for the test pulses after EGTA-AM application, despite small changes in the conditioning train (Fig. 7).