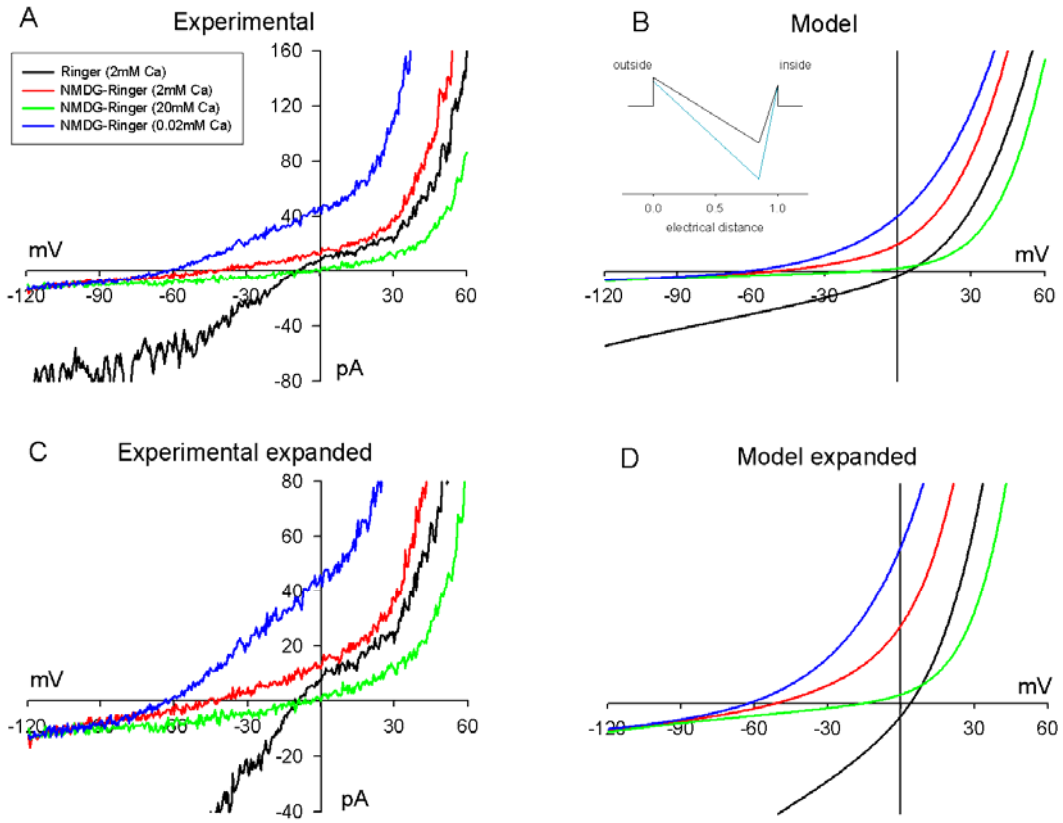
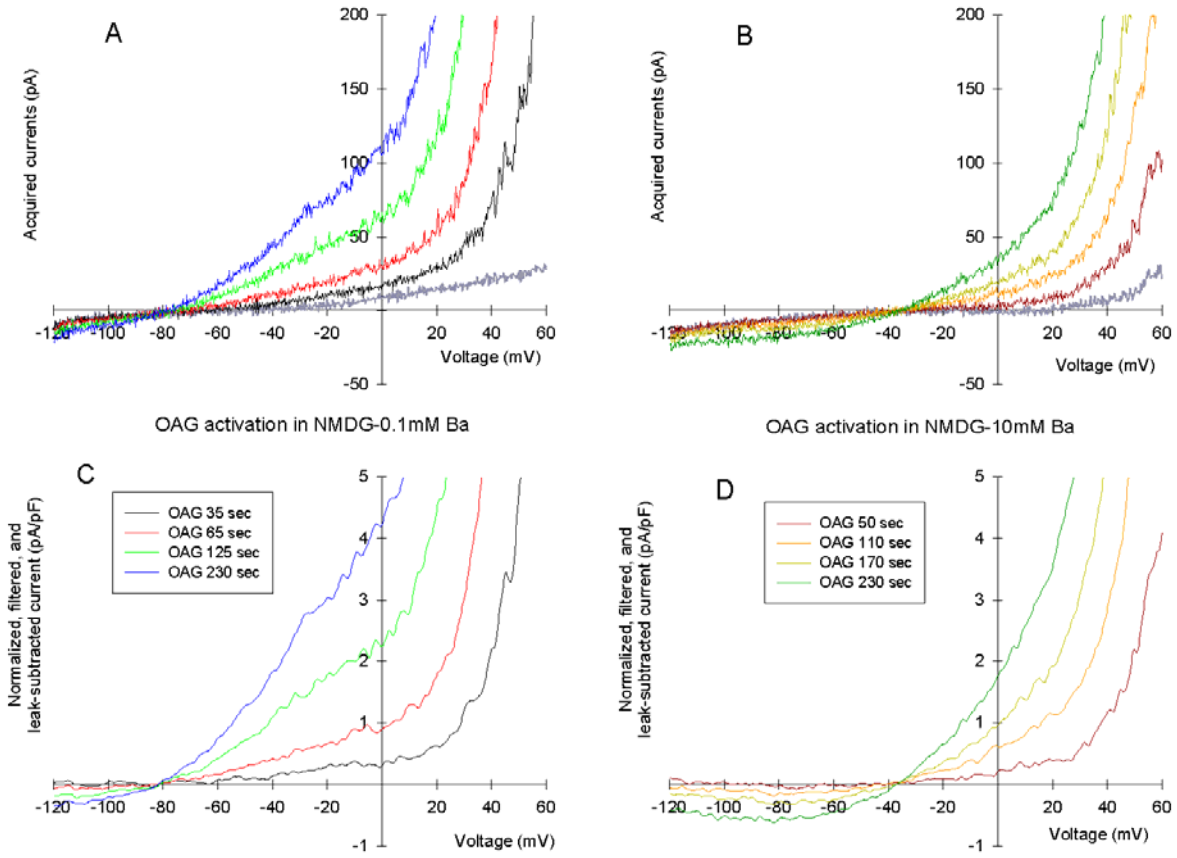
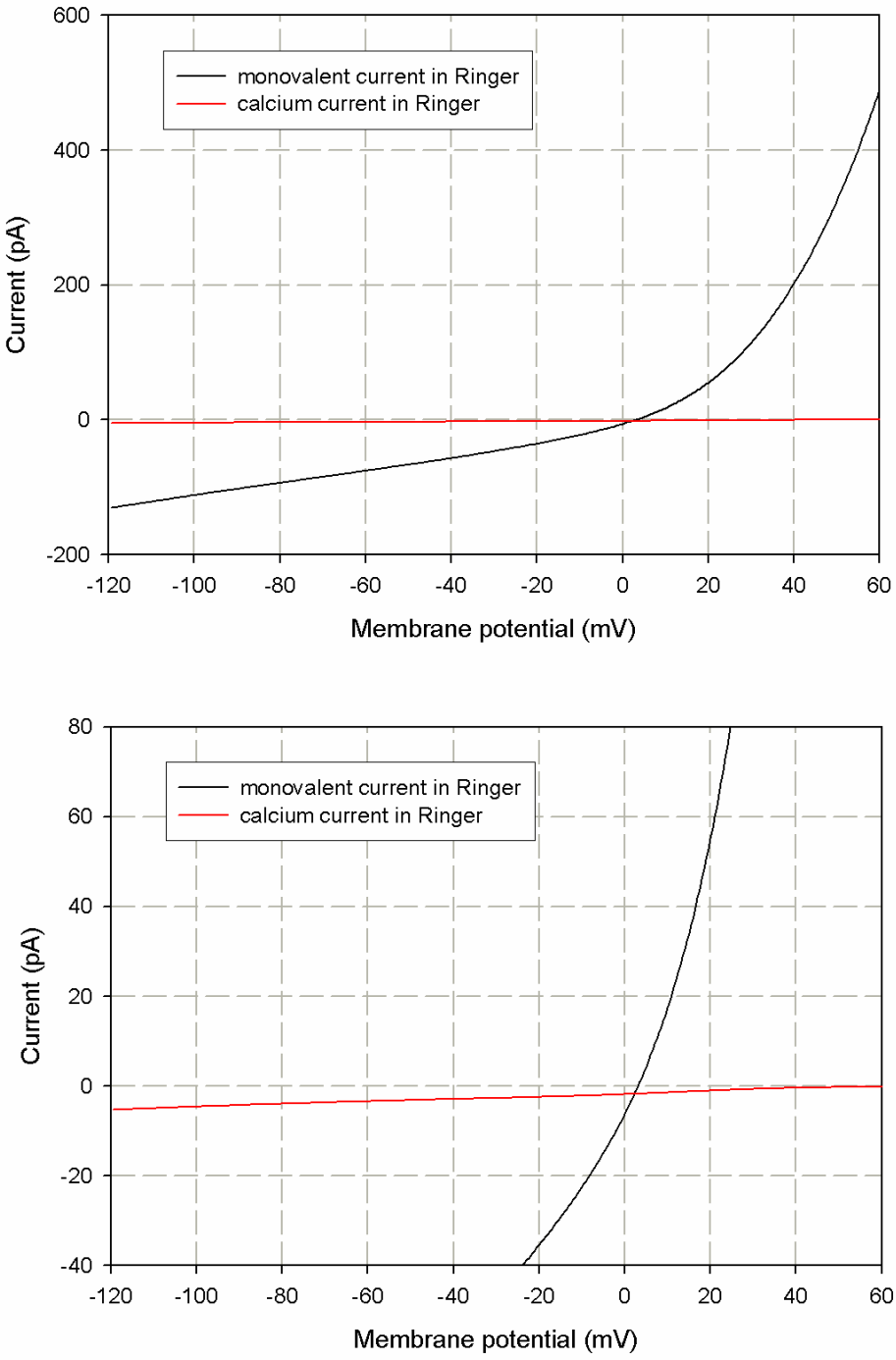


Supplementary Fig 1. **Effect of extracellular Ca^{2+} on whole-cell currents in TRPC6-expressing HEK cells: NMDG buffer with 4 K^+.** *Panel A.* Currents were recorded as described in the legend to Fig 1 in HEK cells stably expressing TRPC6. TRPC6 was activated by superfusion with normal Na^+-containing Ringer's solution containing 100 µM OAG. A representative I-V plot under this condition is shown (black trace). The extracellular solution was changed to NMDG-4K^+ with 0.02 (blue trace), 2 (red trace), or 20 mM Ca^{2+} (green trace). *Panel B.* I-V relationships predicted by the single site pore permeation model with the parameter set given in the legend to Fig 5. The simulated I-V plots are shown for the experimental ionic conditions shown in panel A. *Panels C and D.* Same as panels A and B with an expanded current scale to better visualize the reversal potentials under each condition.



Supplementary Fig 2. **Activation of TRPC6 in low or high Ba^{2+} buffer.** *Panels A and B.* Currents were recorded as described in the legend to Fig 1 in HEK cells stably expressing TRPC6. TRPC6 was activated by superfusion with NMDG-$0K^{+}$-Ringer's solution containing 0.1 mM Ba^{2+} (*Panel A*) or 10 mM Ba^{2+} (*Panel B*) plus 100 µM OAG. I-V plots are shown before OAG and as a function of time after addition of OAG (see *inset, panels C and D*). *Panels C and D*. Currents from Panels A and B were leak-subtracted, normalized to capacitance, and filtered at 200 Hz.



Supplementary Fig 3. **Model predications for Ca^{2+} and monovalent current via TRPC6.** *Upper Panel.* The figure shows I-V plots for TRPC6 for monovalent current (*black trace*) and Ca^{2+} currents (*red trace*) in normal Na^{+}-containing Ringer's solution as predicted by the single site pore model. *Lower Panel*. Same as in the upper panel with an expanded current scale.