## Basic features of a cell electroporation model: Illustrative behavior for two very different pulses

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## Supplemental Information (SI)

## Idealized and actual pulse waveforms

To aid understanding we use idealized pulse waveforms. The pulses are trapezoidal, with linear ramps that define the rise and fall times, and a flat peak field strength. Again for simplicity, we label a pulse duration by the duration from start to end. The model can also be used with digitized experimental waveforms. Significant averaging occurs in computing cumulative solute transport, which supports our use of idealized waveforms for understanding basic behavior. There is underlying spatial averaging of  $U_{\rm m}(t)$  behavior that is are distributed over several hundred transmembrane node-pairs, and also integrating the solute transport rates with respect to time. Fig. SI-1 shows the two idealized pulse waveforms used here.

## Field amplification by a cell membrane

Fig. SI-2 shows the model's field amplification for both the passive (fixed membrane properties as in the Schwan model) and active properties (resting potential source and the dynamic EP model). For both cases the cell membrane effectively amplifies an applied field, such that the membrane response field,  $E_{\rm m}$ , is larger than the applied field  $E_{\rm e}$ . Field amplification diminishes for rapidly changing waveforms that create significant displacement currents, with dielectric properties then more important than conductive properties. Amplification is complicated once spatially distributed EP occurs, as the effective conductivity of the membrane then changes with location as well as with time.

Traditionally field amplification is defined as the ratio of changes, viz. membrane field change divided by applied field change. However, because of the importance of transmembrane field magnitude  $U_{\rm m}(t) = E_{\rm m}d_{\rm m}$  in governing pore creation, we use a slightly different definition: the ratio of membrane field,  $E_{\rm m}$  to the applied field. In our version the resting potential source makes a small contribution, which allows direct consideration of the strength, and sometimes polarity, of the local transmembrane voltage,  $U_{\rm m}$ .

In cases where we show the response at time where the field pulse changes slope, we use the slope just before that time. This means that the affect of rapid changes in the pulse do represent the times at which dielectric properties are important.



Fig. SI-1 An electric field pulse,  $E_e(t)$ , is applied via idealized planar electrodes spaced 100  $\mu$ m apart at the top and bottom of the system model. The results in the following figures are obtained for two different idealized trapezoidal pulses: (A) a 1.5 kV/cm, 100  $\mu$ s rise/fall times; and (B) a 40 kV/cm, 10 ns pulse with 1 ns rise/fall times.



Fig. SI-2 Amplification gain factor,  $E_m/Ee$ , is shown as a function of angle at different times. (A-B) show the response to a 1.5 kV/cm, 100  $\mu$ s pulse at the start and end of the pulse maximum. (C-D) show the response to a 40 kV/cm, 10 ns pulse at the start and end of the pulse maximum. In all figures, the dash-dotted curve represents the passive membrane amplification response, in which the dynamic electroporation model has been 'knocked out'. In C, the two curves are indistinguishable because the onset of electroporation has not yet occurred.