A Numerical Model for Electroporation in Bacteria

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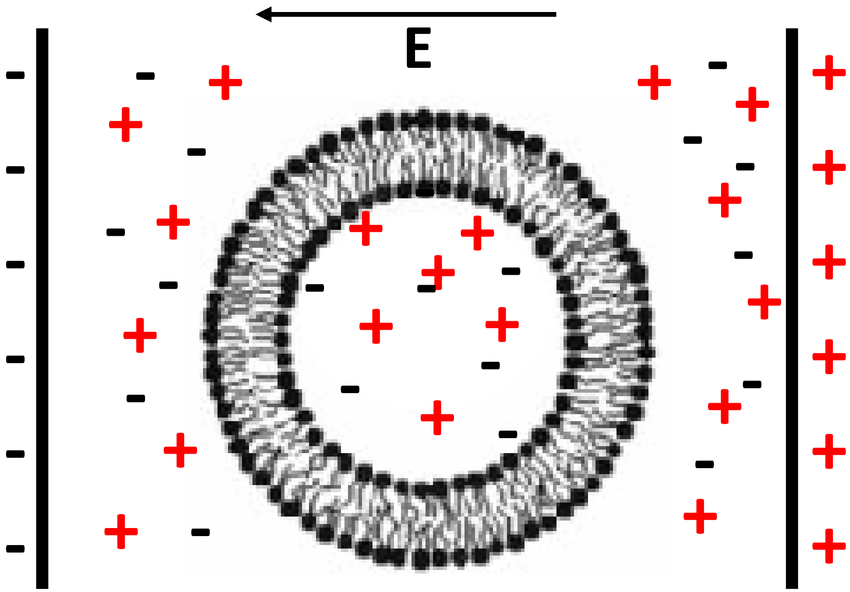
Electroporation

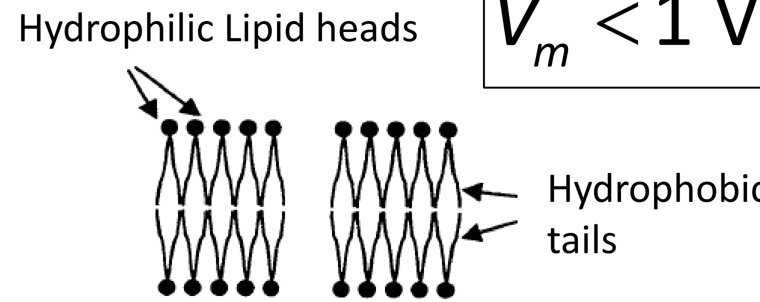


Electroporation is governed by the
Transmembrane Voltage (TMV)

$$V_m = 1.5ER\cos\theta$$

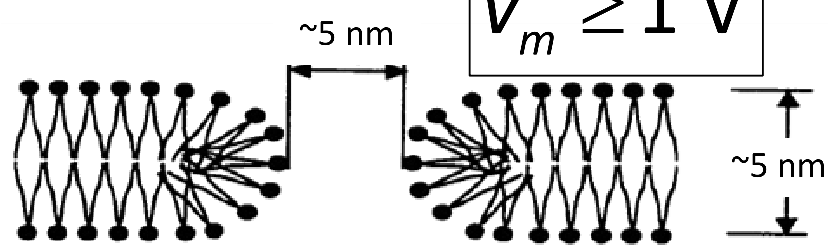
Schwan 1957, Tsong, *Biophysical Journal*, 1990.

$$V_m < 1\ \mathrm{V}$$



Hydrophobic pores

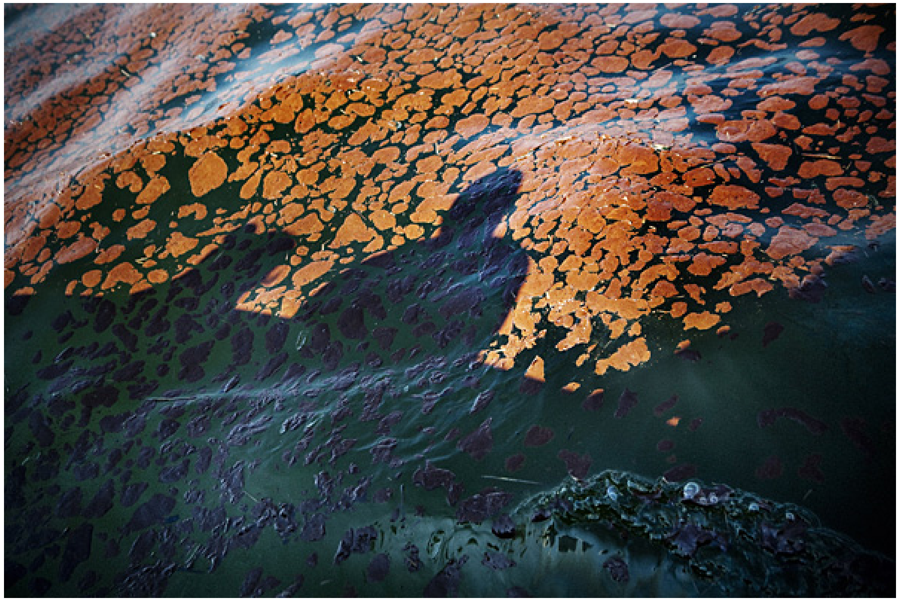
$$V_m \geq 1\ \mathrm{V}$$



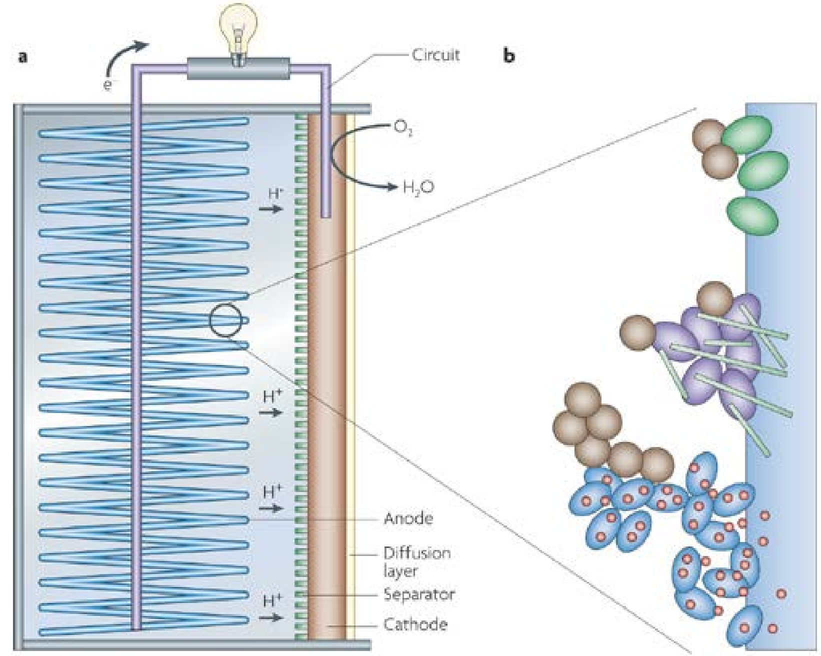
Hydrophilic pores

J.C. Neu, W. Krassowska, *Phys. Rev. E,* 1999.

Our Focus: Transformation of Bacteria



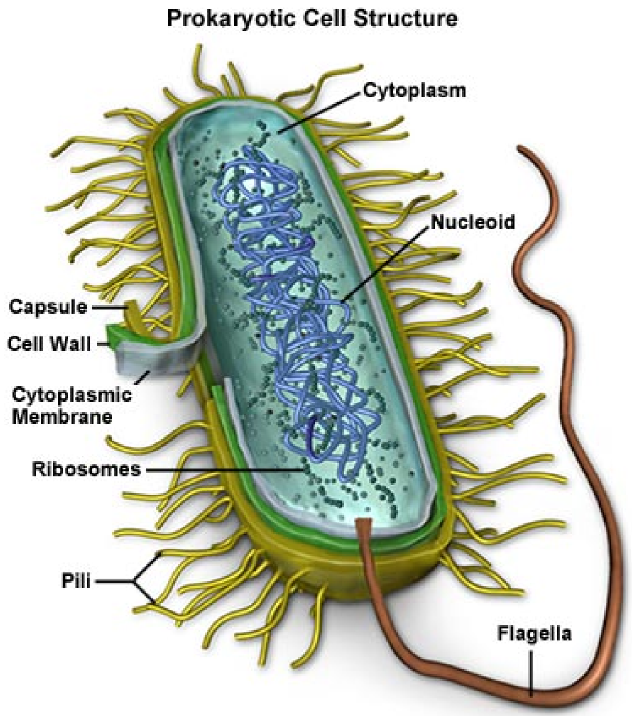
Deepwater Horizon Oil Spill
Credit: Getty Images



Microbial Fuel Cell Schematic
Credit: Logan, B. *Nature Rev. Microbio.* 2009

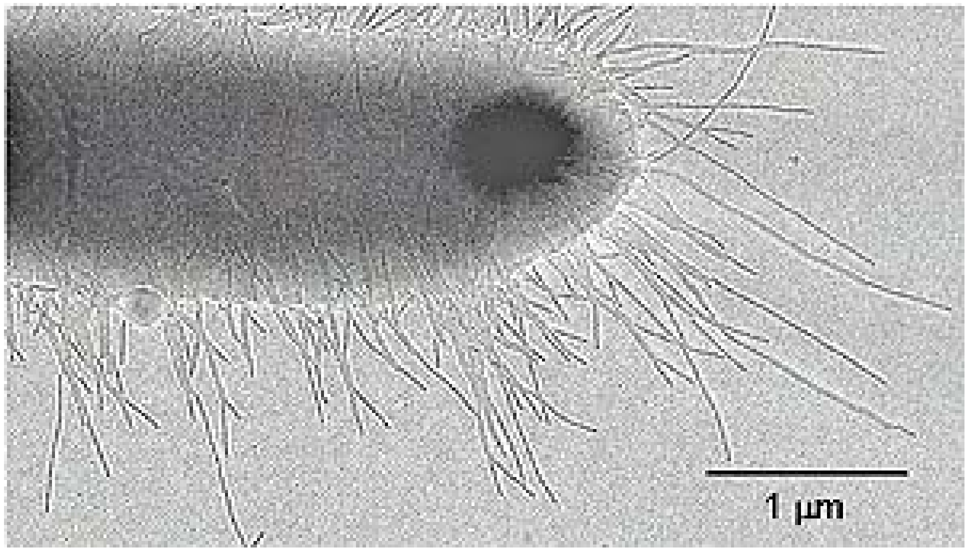
- Electroporation protocols exist for a tiny fraction of bacteria on earth
- Goal: understand the principles governing successful DNA transfer into bacteria
- Here: COMSOL model to understand effect of bacterial physiology on electroporation

Bacterial Physiology



micro.magnet.fsu.edu/cells/procaryotes/images/procaryote.jpg

Pili on the surface of an *Escherichia coli* bacterium



www.daviddarling.info/encyclopedia/P/pilus.html

- Outside the (inner) plasma membrane, most bacteria exhibit a “soft layer” consisting of (e.g.) fimbriae, sex pili, capsules, flagella, etc.
- The soft layer generally carries a net charge
- Charge distribution in the soft layer affects polarizability (Dingari & Buie, 2014)

Governing Equations

- Electric potential inside/outside cell (σ = conductivity)

$$\nabla \cdot \left(\sigma + \varepsilon_0 \varepsilon_r \frac{\partial}{\partial t} \right) \nabla \phi = 0$$

- Transmembrane voltage (TMV)

$$V_m \equiv \left(\phi_{inside} - \phi_{soft} \right)_{membrane}$$

- Pore creation/destruction rate

$$\frac{dN}{dt} = \alpha \exp\left(V_m / V_{ep} \right)^2 \left[1 - \frac{N}{N_{eq}\left(V_m \right)} \right]$$

Pore density [#/cm²]

Characteristic voltage for electroporation

- Pore radius evolution

$$\frac{dr}{dt} = \frac{D}{kT} \left\{ \frac{V_m^2 F_{\max}}{1 + r_h / \left(r + r_t \right)} + 4\beta \left(\frac{r_*}{r} \right)^4 \frac{1}{r} - 2\pi\gamma + 2\pi\sigma_{eff} r \right\}$$

Electrical energy

Steric repulsion of lipid heads

Line tension

Effective membrane/liquid interfacial tension

- Membrane current density

$$J\left(t \right) = \frac{V_m \sigma_{m,0}}{h} + \frac{V_m N\left(t \right) \sigma_p \pi r_p^2 A}{h} + C_m \frac{\partial V_m}{\partial t}$$

Protein channels

Current through electropores

Capacitive charging

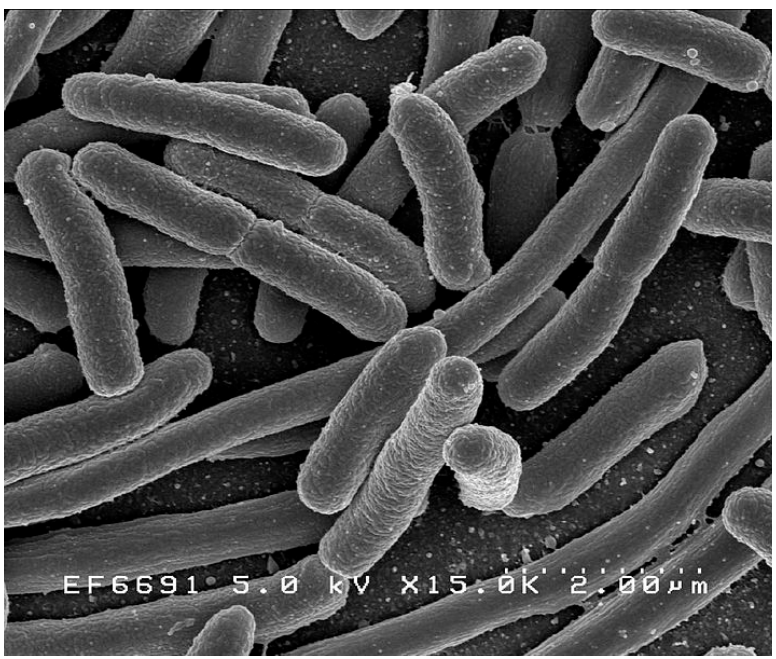
DeBruin & Krassowska, *Biophys. J.* 1999 (Part I)

Pucihar, Miklavcic & Kotnik, *IEEE Trans. Biomed. Eng.* 2009

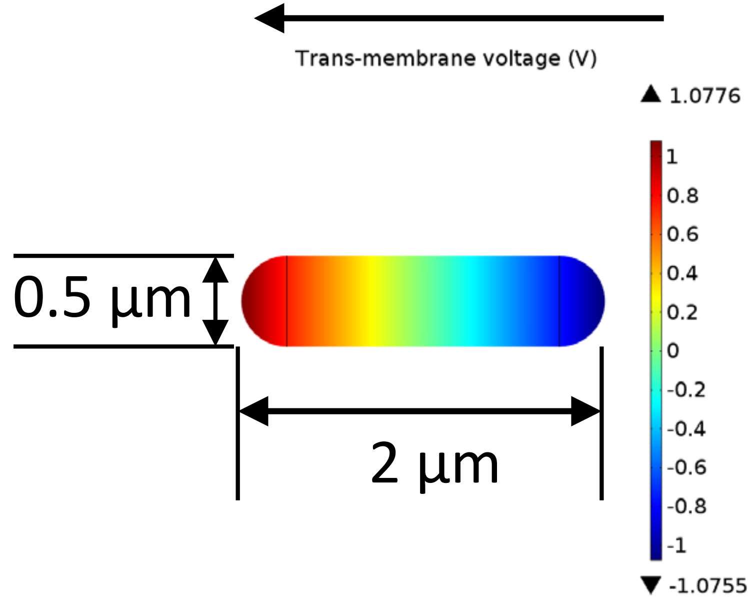
Numerical Implementation

- COMSOL Multiphysics
- 2D axisymmetric geometry
- 36,353 mesh elements
- Time-dependent solve (through pulse duration)

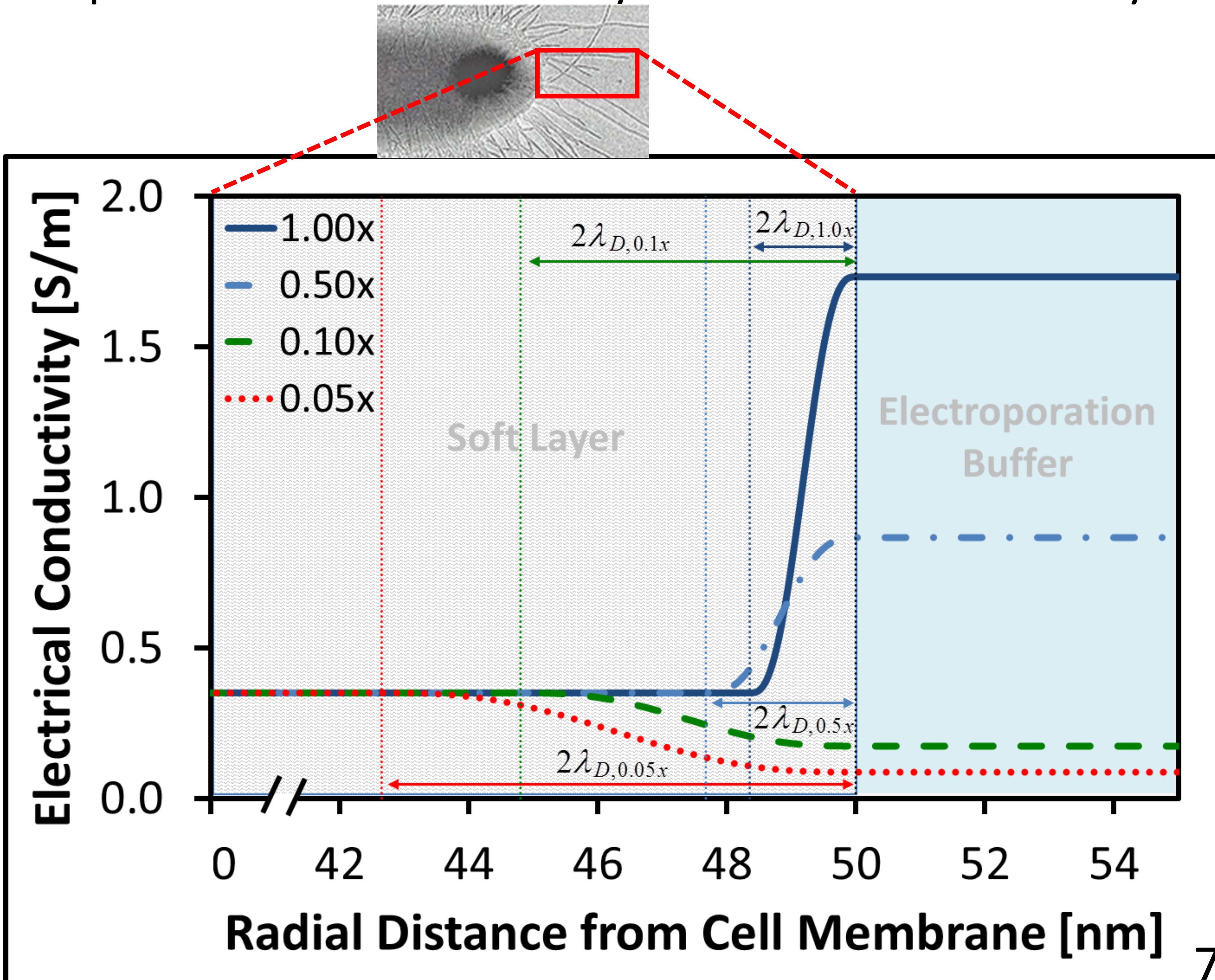
$$E = 12.5 \text{ kV/cm}$$



SEM of *E. coli* (Wikimedia commons)



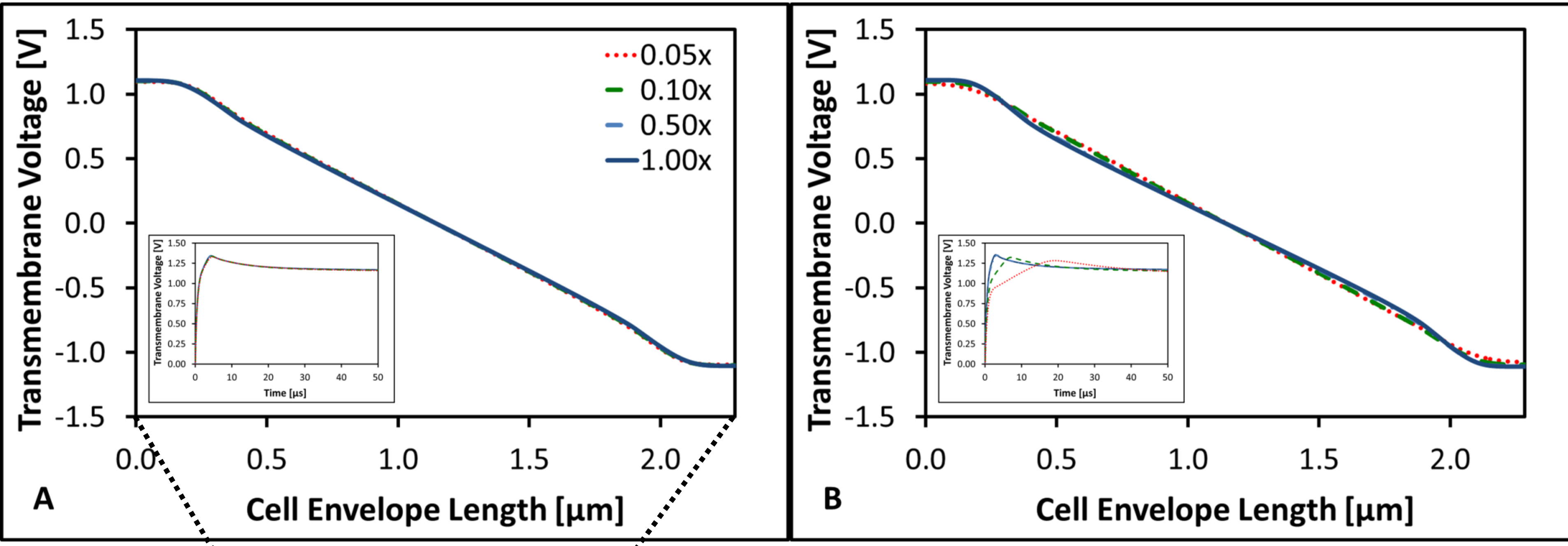
Imposed Conductivity Profile in Soft Layer

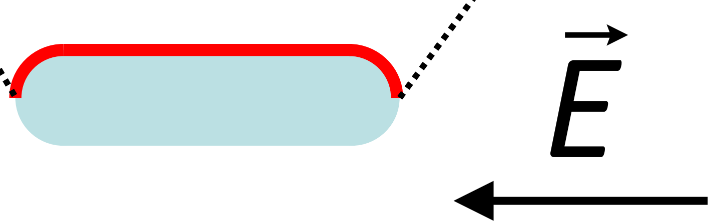


Induced Transmembrane Voltage

No Soft Layer

100-nm Soft Layer



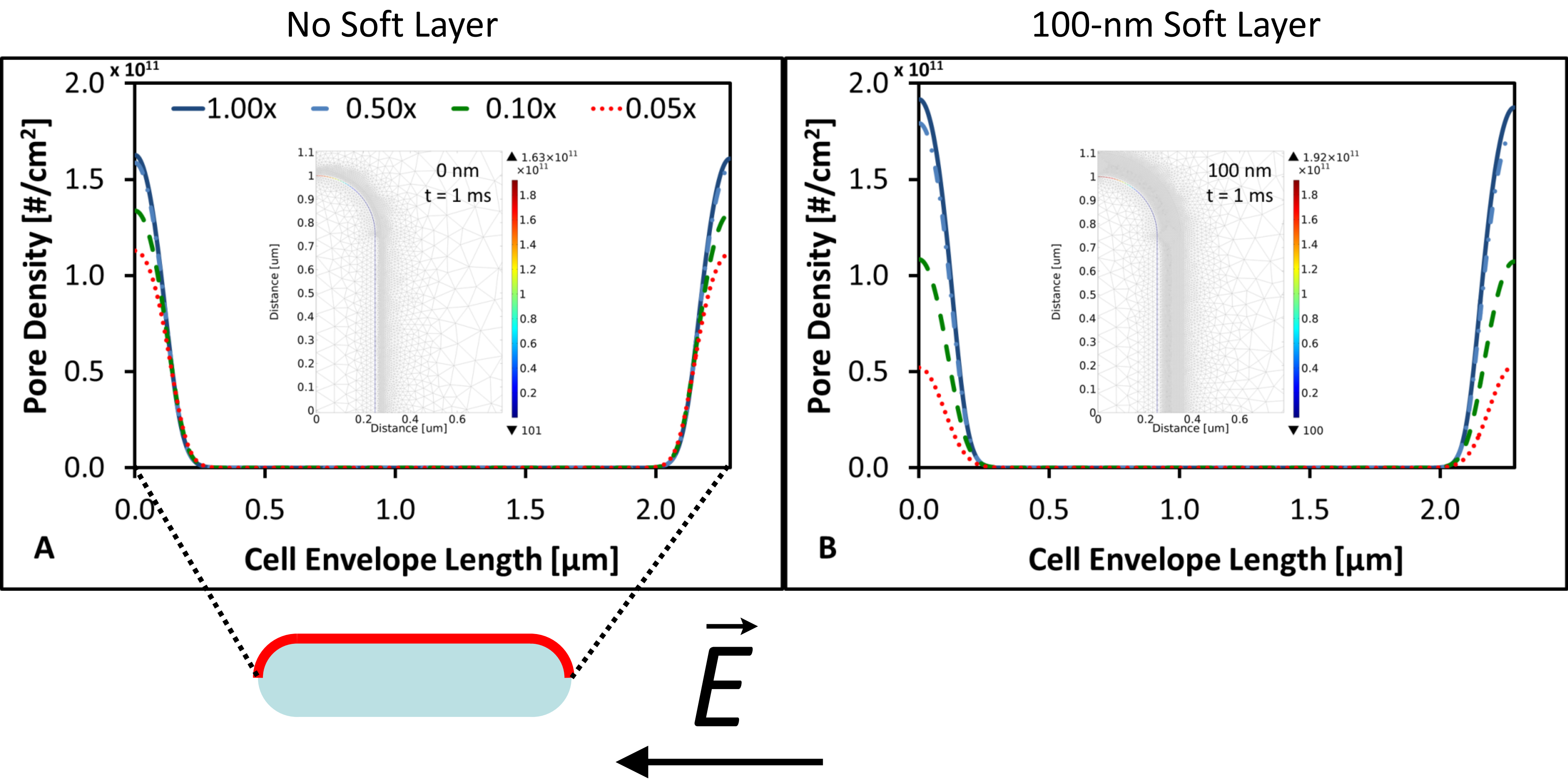


$$V_m \equiv \left(\phi_{inside} - \phi_{soft}\right)_{membrane}$$

All data shown at *t* = 1 ms (pulse truncated)

Insets show TMV vs. time at positive-facing pole

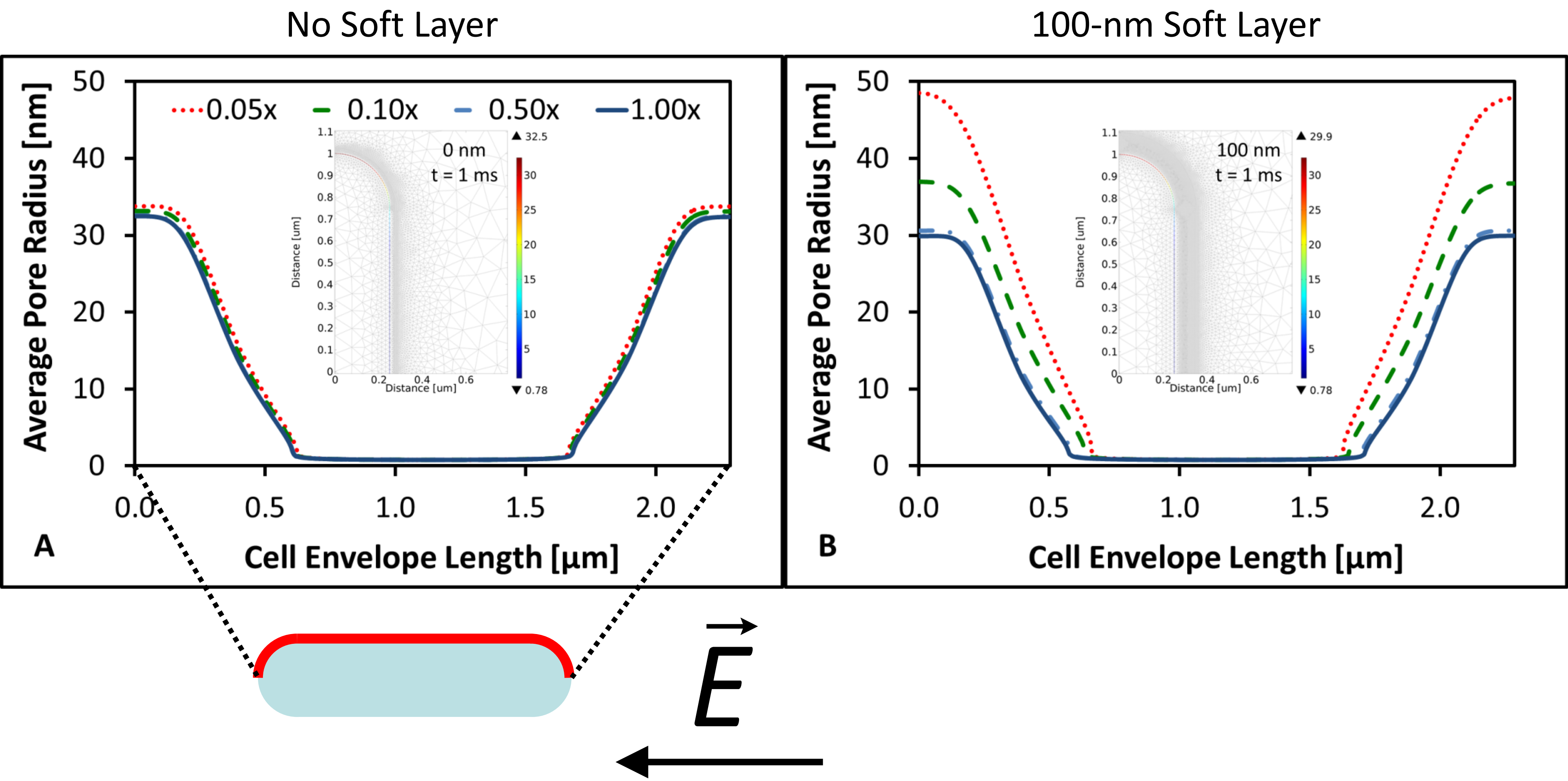
Pore Density vs. Position



All data shown at *t* = 1 ms (pulse truncated)

Insets show mesh used for each case

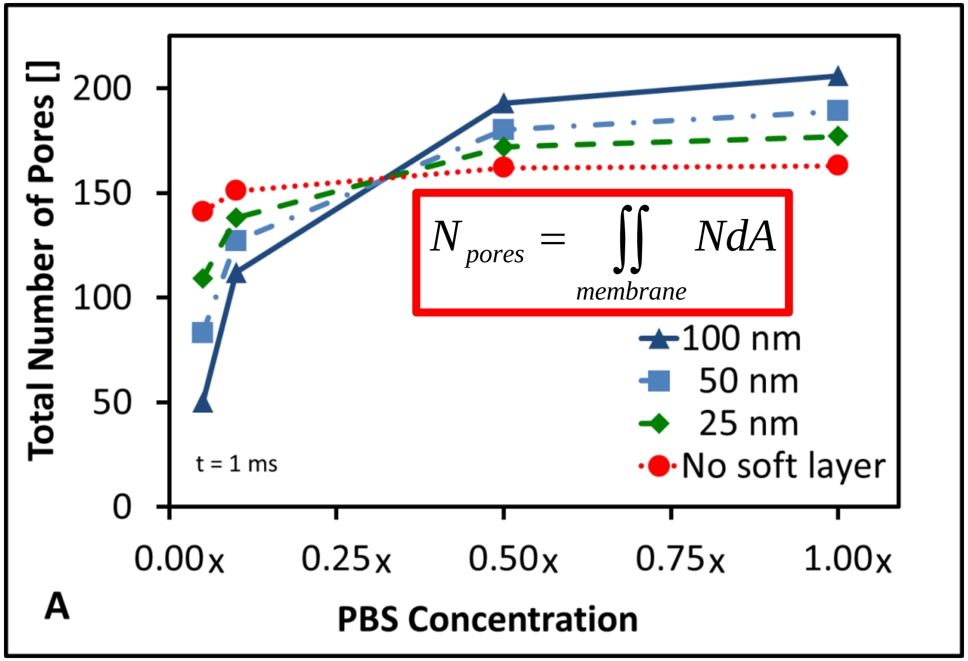
Pore Radius vs. Position

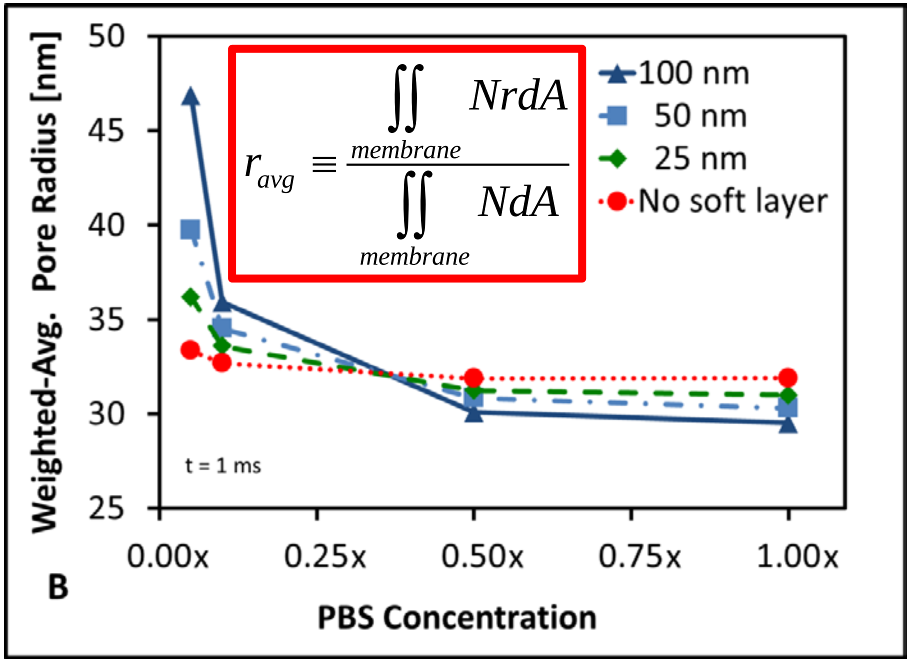


All data shown at t = 1 ms (pulse truncated)

Insets show mesh used for each case

Total Pores, Average Radius





Both the number and the size of pores created depend more strongly on buffer concentration when the soft layer is present

All data shown at *t* = 1 ms (pulse truncated)

Conclusions

- The presence of a soft layer tends to **amplify** the effect of varying background conditions (e.g. conductivity) on the pore size and number
- This work elucidates the effect of buffer concentration on bacterial electroporation

Ongoing Work

- Enhance model of soft-layer transport to include
  - Dissociation of pH-dependent ionogenic groups
  - Donnan potential
- Explore correlation between electroporation amenability and cell envelope properties (e.g. polarizability)

Thank you

Simulation Details

- Customized Mesh