A NUMERICAL MODEL FOR ELECTROPORATION IN BACTERIA

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Electroporation

Electroporation is governed by the Transmembrane Voltage (TMV)

\[ V_m = 1.5ER \cos \theta \]


Our Focus: Transformation of Bacteria

• 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

• 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** ($\sigma = \text{conductivity}$)
  \[ \nabla \cdot \left( \sigma + \varepsilon_0 \varepsilon_r \frac{\partial}{\partial t} \right) \nabla \phi = 0 \]

- **Transmembrane voltage (TMV)**
  \[ V_m \equiv (\phi_{\text{inside}} - \phi_{\text{soft}})_{\text{membrane}} \]

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

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

- **Membrane current density**
  \[ J(t) = \frac{V_m \sigma_{m,0}}{h} + \frac{V_m N(t) \sigma_p \pi r_p^2 A}{h} + C_m \frac{\partial V_m}{\partial t} \]

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

Electrical Conductivity [S/m]

Radial Distance from Cell Membrane [nm]

Soft Layer

Electroporation Buffer

$2\lambda_{D,0.1x}$

$2\lambda_{D,0.5x}$

$2\lambda_{D,1.0x}$
Induced Transmembrane Voltage

No Soft Layer

100-nm Soft Layer

Insets show TMV vs. time at positive-facing pole

\[ \rho_E(\phi) \equiv -V_m \]

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

Insets show TMV vs. time at positive-facing pole
Pore Density vs. Position

A. No Soft Layer

B. 100-nm Soft Layer

All data shown at $t = 1 \text{ ms}$ (pulse truncated)

Insets show mesh used for each case
Pore Radius vs. Position

No Soft Layer

100-nm Soft Layer

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 $t = 1 \text{ ms}$ (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