Nanoelectropulse-Driven Membrane Perturbation and Permeabilization

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Molecular biophysics

Electromanipulation

of Biological Cells

Internal Membrane Effects

Electric Field (MV/m)

External Membrane Effects

Electroporation

Drug delivery

Membrane

Nanoporation

Gene therapy

Gene regulation

Molecular biosensing

Molecular biology

Membrane targeting

Cell fusion, Cell biology

Computation

Facilities

5.0 ns

1.0 ns

10.0 ns

Advances in Nanoelectrofluidic Processing

Phospholipid Disruption

Membrane Permeabilization

Additional Pulsed Power Technology

Capacitive Discharge Technology

Analysis of Biological Membranes

Studying Membrane Dynamics

Membrane Dynamics

Molecular Dynamics

Light scattering

Physical properties

Frictional properties

Surface tension

Fluorescence

Fluorescence

Potentiometry

Pulse Number

30 pS

50 pS

100 pS

1.5 ns leading edge

4.8 nm

Water: Simple Point Charge model

Coulomb cutoff: 1 nm with Particle-Mesh-Ewald

Simulation time step: 2 fs

Electric field (MV/m; mV/nm): 200 to 1000

Fluorescence Intensity Change

Nanoporation of DOPC-DOPS in Water with PS Translocation

(dioleoylphosphatidylcholine-dioleoylphosphatidylserine)

USC NanoPulser for Intracellular Electroperturbation

Multichannel NIPX Microchamber

Grid electrodes on Pyrex sheets, for Standard Membrane Slides

Membrane Dipoles

Dye movements

Phase contrast

Molecular dynamics

Nanosecond, megavolt-per-meter pulsed electric fields are

intracellular events – high power, low total energy – which cause:

1. Apoptosis (programmed cell death) – capase activation, PAR

2. Membrane phospholipid translocation – immune system semaphore

3. Calcium bursts – widespread signal?

Molecular Dynamics — DOPC-DOPS in Water

(dioleoylphosphatidylcholine-dioleoylphosphatidylserine)

Transmembrane potential: 

\[ \Delta \psi \approx \begin{cases} \psi_E & \text{for } \psi_E \approx \Delta \psi \geq 0 \\ \Delta \psi & \text{for } \psi_E \approx \Delta \psi < 0 \end{cases} \]

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Nanoelectropulse-Driven Phosphatidylserine Externalization and Small Molecule Permeabilization

**FM1-43 Fluorescence Intensification After Phosphatidylserine Externalization**

FM1-43 equilibrium distribution shifts after phosphatidylserine externalization:
- **Aqueous medium** (non-fluorescent) ↔ **lipid membrane** (fluorescent)

Translocation of phosphatidylserine to the external face of the membrane with the associated additional electrostatic attraction for the quaternary ammoniums of FM1-43, permits more dye binding per unit area and thus an increase in fluorescence.

- **FM1-43**
- **Phosphatidylserine**
- **Phosphatidylcholine**

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**Multi-channel UPSET Microchamber — Gold Electrodes on Photoresist on Standard Microscope Slide**

- **SU-8 photoresist** (10–30 μm)
- **Cell in suspension**
- **Au/Ti film** (0.15 μm)
- **Channel cross-section**

**Channel Dimensions**
- **Width:** 25–100 μm
- **Height:** 10–30 μm
- **Length:** 12,000 μm

**Medium**

- **Translocation of phosphatidylserine to the external face of the membrane, with the associated additional electrostatic attraction for the quaternary ammoniums of FM1-43, permits more dye binding per unit area and thus an increase in fluorescence.**