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Brownian dynamics

Simulation of ion throughput during cellular electroporation

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Presentation Outline

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- Introduction
- Geometry and boundary conditions
- Classical mechanics
- Initial conditions
- Algorithm
- Diffusion coefficient
- Conclusion

Introduction

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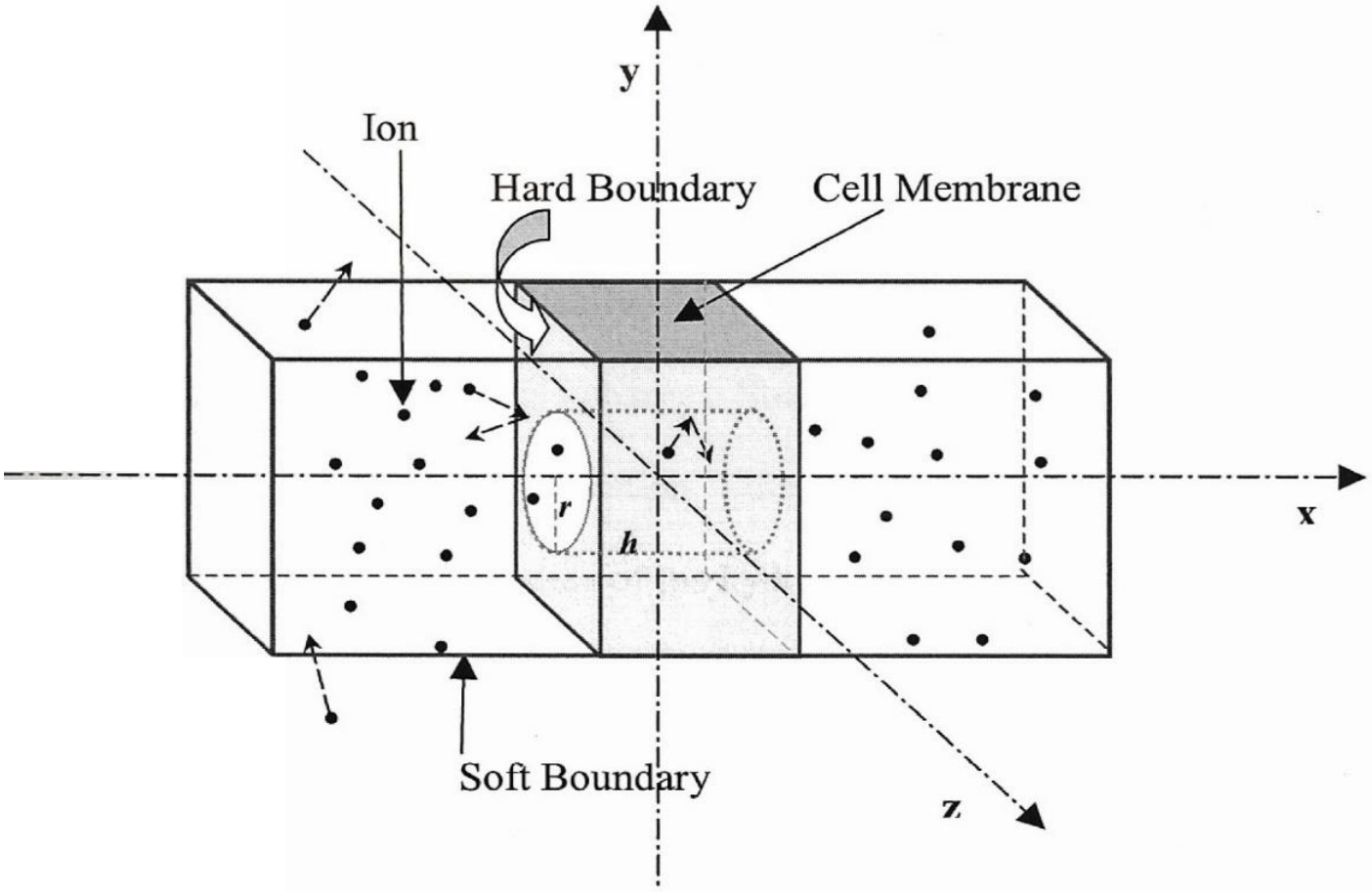
- Molecular dynamics (microscopic)
  - Simulation of all atoms and molecules
  - Involve a lot of computational power
  - Results in order of picoseconds
- Brownian dynamics (semi-microscopic)
  - Inter-atomic electrostatic forces treated microscopically
  - Treats water as a continuum with stochastic approximations
    - Friction forces
    - Random collision forces
- Macroscopic models
  - Cellular matter as continuum fluid
    - Charges and dielectric discontinues treated with voltage barriers
  - Results in microsecond time scale

Geometry and boundary conditions



Classical mechanics

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Random Gaussian force (water molecules)

Friction force (ions with water)

Force due to applied Electric field

$$\vec{F}_{R,i} - \vec{F}_{fr,i} + \vec{F}_{E,i} + \vec{F}_{mem,i} + \vec{F}_{C,i} + \vec{F}_{\mathrm{r},i} = m_i \frac{d\vec{v}_i}{dt}$$

Short range repulsion force

Coulomb force (between ions)

Force from induced membrane charges

Classical mechanics - details

- Friction force

$$\vec{F}_r = m_i \gamma_i \vec{v}_i(t)$$

- Force from externally applied field

$$\vec{F}_{E,i=} q_i \left(\vec{E} + v_i \times \vec{B} \right)$$

$$V_a - V_b = -\int_b^a \vec{E} d\vec{l}$$

- Short range repulsion force

$$U(R) = Ae^{-bR}, R_l \leq R \leq R_{ii}$$

Classical mechanics - details

- Random Gaussian force

$$f(F_R) = \frac{1}{2\pi\sigma^2} e^{\frac{-|F_R - me|}{2\sigma^2}}$$

$$\sigma = \sqrt{\frac{2m_i k_B \gamma_i T}{\Delta T}}$$

- Coulomb force

$$\vec{F}_{Ci} = \frac{q_i}{4\pi\varepsilon_0} \sum_{\substack{k=0 \\ k\neq i}}^{n} \frac{q_k}{\left[\vec{r_i} - \vec{r_j}\right]^2}$$

- Image charge forces

Initial conditions

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- Initial velocities with Maxwell-Boltzmann distribution

$$f(v) = \frac{8\pi}{m_i}\left(\frac{m_i}{2\pi k_B T}\right)^{\frac{3}{2}} \varepsilon_i e^{\frac{-\varepsilon_i}{k_B T}}$$

- Initial positions with uniform distribution in extracellular space

Integration algorithms

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- Several algorithms have been developed to integrate the equations of movement
  - Verlet
  - Leap-frog
  - Velocity-verlet

- I) The algorithm must preserve energy and momentum
- ii) It must be computationally efficient
- iii) It has to allow a long time step for integration

Velocity-Verlet Algorithm

- Step 1: Calculate $\overrightarrow{v_i}\left(t_n + \frac{1}{2}\Delta t\right) = \overrightarrow{v_i}(t) + \frac{1}{2}\vec{a}_i(t)\Delta t$
- Step 2: Calculate $\vec{s}_i(t_n + \Delta t) = \vec{s}_i(t_n) + \vec{v}_i(t_n + \frac{1}{2}\Delta t)\Delta t$
- Step 3: Derive $\vec{a}_i(t_n + \Delta t)$ from the interaction potential using $\vec{s}_i(t_n + \Delta T)$
- Step 4: Calculate $\vec{v}_i(t_n + \Delta T) = \vec{v}_i\left(t_n + \frac{1}{2}\Delta t\right) + \frac{1}{2}\vec{a}_i(t_n + \Delta T)\Delta T$
- Step 5: Repeat steps 1 to 4 k times for k number of ions
- Step 6: Repeat steps 1 to 5 as many times as required until the end of the total simulation time interval

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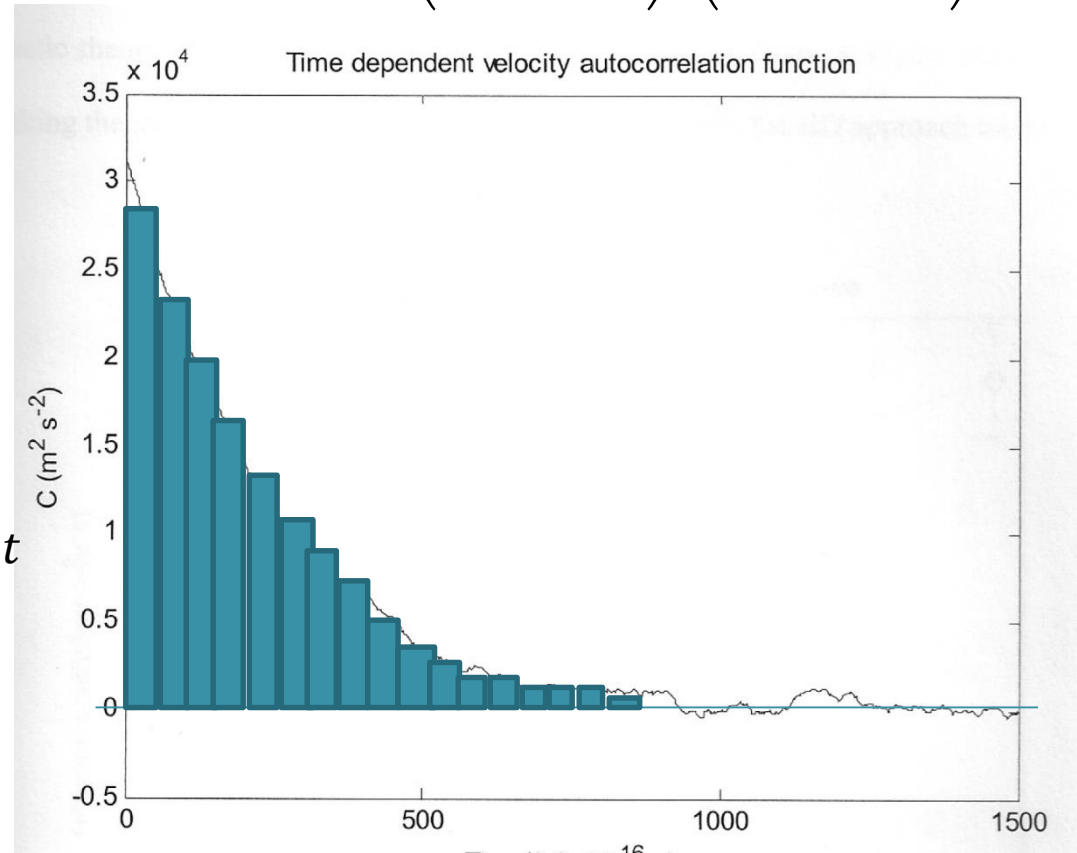
Diffusion coefficient

Velocity autocorrelation function

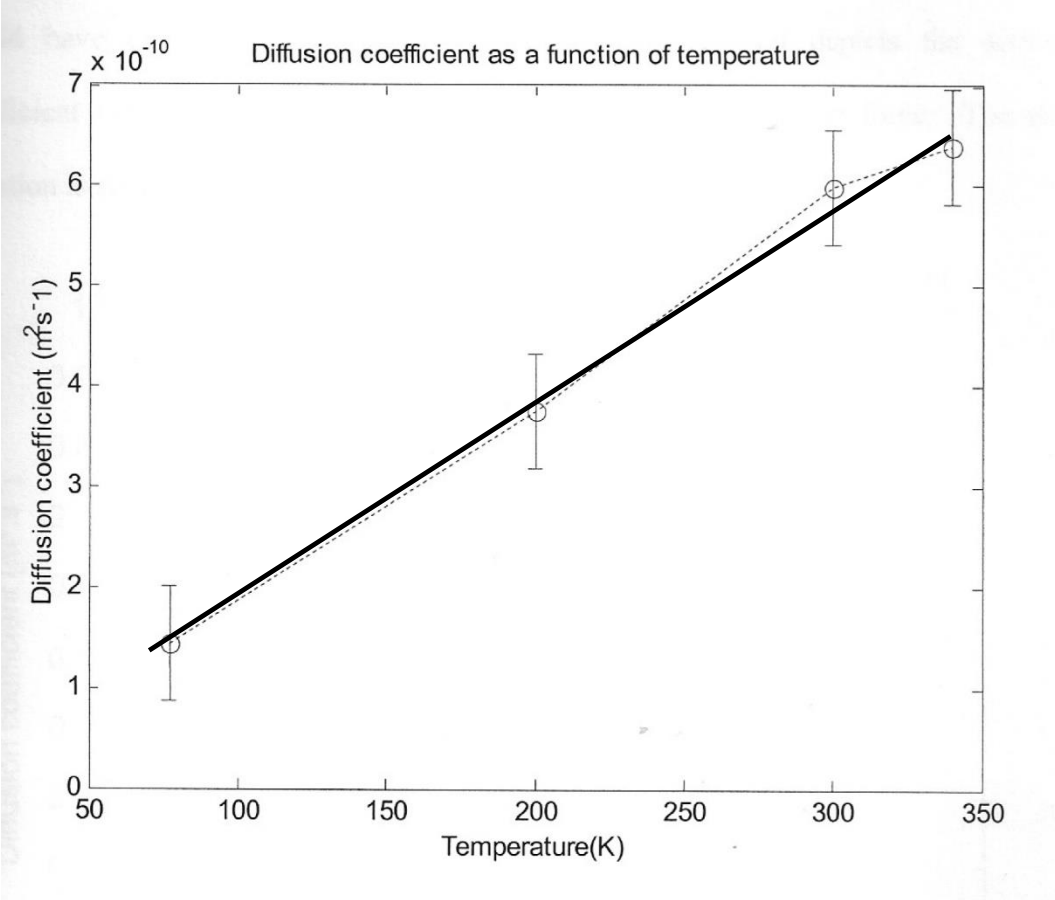
$$C(t) = < v_i(t)v_i(t_0) > - < v_i(t) >< v_i(t_0) >$$

$$C(t) = \frac{1}{N}\sum_{i=1}^{N}[v_i(t)v_i(t_0)] - \left(\frac{1}{N}\sum_{i=1}^{N}v_i(t)\right)\left(\frac{1}{N}\sum_{i=1}^{N}v_i(t_0)\right)$$

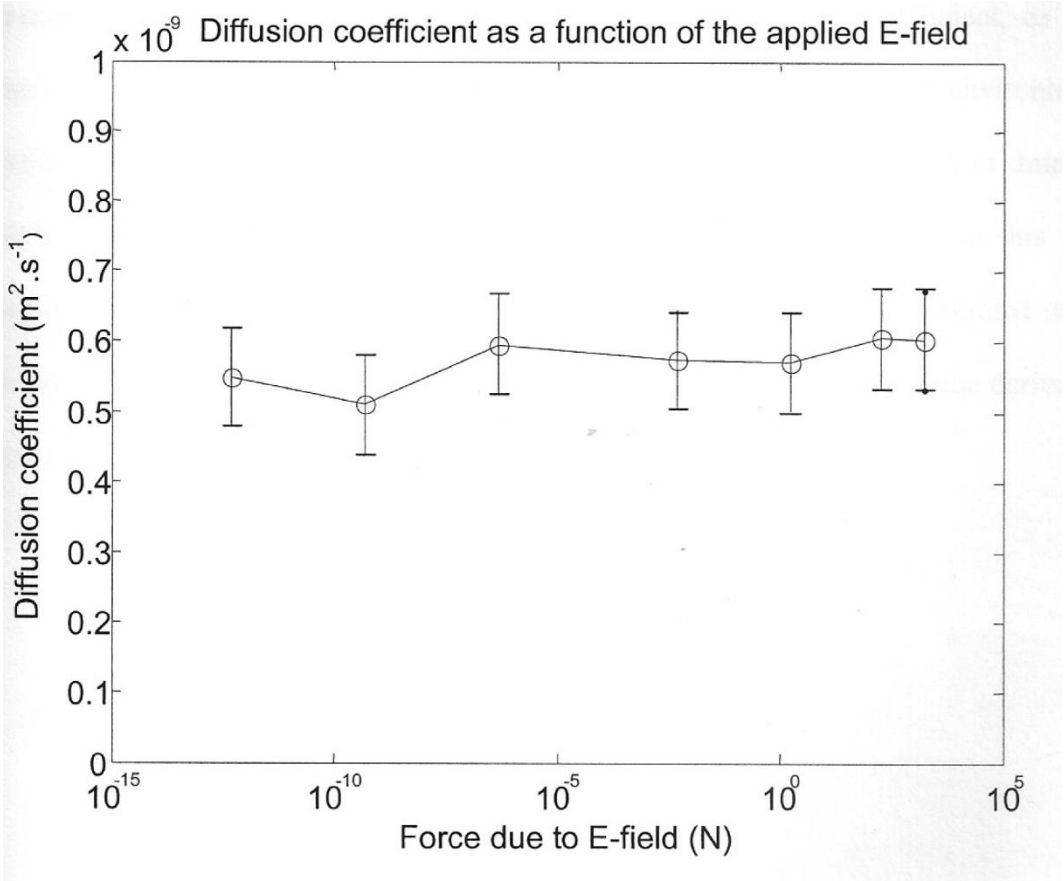
$$D = \int_0^\infty C(t)dt$$



Diffusion coefficient vs. temperature



Diffusion coefficient vs. E-field



Parallelized Simulation

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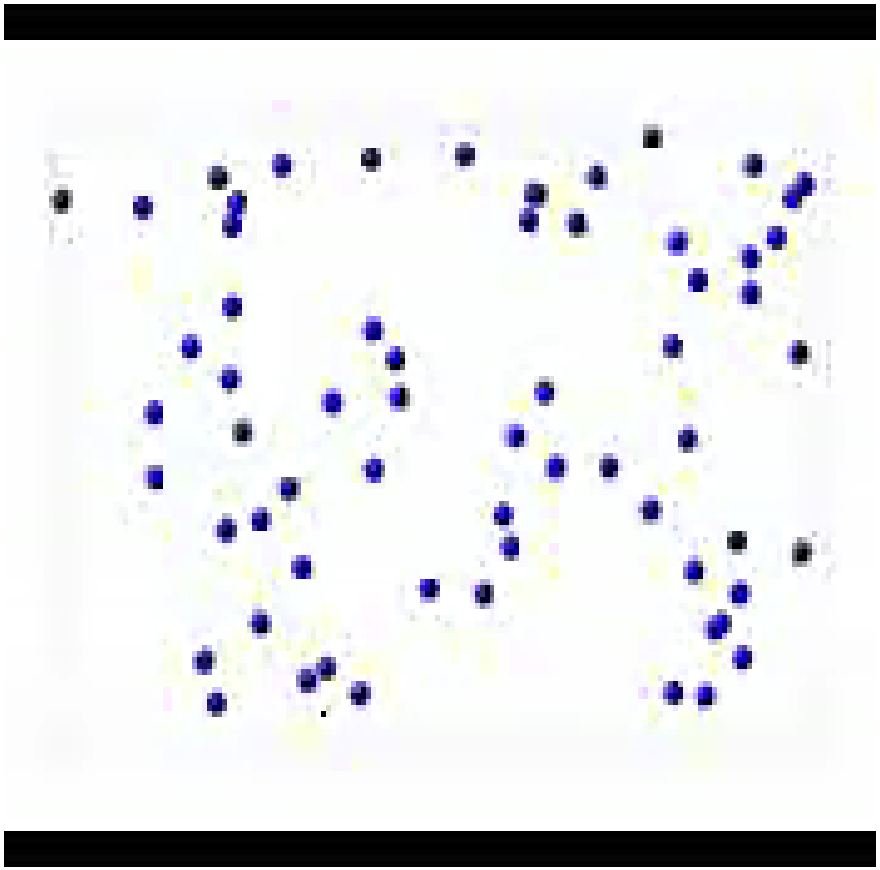

CENTRO DE COMPUTACION DE LA FIUNA
Prof. Dr. Sergei Nikolaevich Sispanov
DIRECCION DE INVESTIGACION

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Concluding remarks

- Model developed to calculate throughput of ions during electroporation
- Model time step calibrated comparing computed and measured Ca^{2+} diffusion in bulk
- Study of diffusion coefficient relation to temperature and E-field
- Main driving force due to E-field, while random collisions decrease throughput