Simulating Steady-State Transport through Channels and Nanopores with Local Equilibrium Monte Carlo

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Goal: simulating steady-state diffusion of particles between two reservoirs through membranes/pores/channels on the basis of a molecular model.

**Examples:** ion channels in biological membranes, synthetic nanopores, silicate membranes (zeolite, silicalite, kaolinite)

**Phenomena of interest:** selectivity, permeation, rectification

**Models:** from all-atom to coarse-grained (reduced)

**Motivation:** technology, biology
Tasks associated with the goal

- **Computing flux in the transport region**
  - Simulating dynamics directly
    - Molecular Dynamics (MD)
    - Langevin (or Brownian) Dynamics (LD)
    - Dynamic Monte Carlo (DMC)
  - Using a transport equation – Nernst-Planck (NP) equation

- **Handling boundary conditions** – fixing the properties of the baths
  - Concentration (chemical potential)
  - Electrical potential (voltage)
  - These two together: electrochemical potential
  - Pressure

The difference (gradient) of the quantities provides the **driving force** of the transport.
Boundary conditions in control cells

**Basic task:** particle reinjection/annihilation to reach steady-state

- **Fixing concentration:**
  Dual Control Volume (DCV) method - use Grand Canonical Monte Carlo (GCMC) simulations
  – the control cells are in equilibrium separately

- **Fixing electrical potential:**
  using electrodes with Dirichlet boundary conditions *(on average or on the fly)* and solve Poisson
  – practically, charge reinjection.

- **Fixing pressure:**
  a new method of Tamás Kristóf and Zoltán Ható (for dilute gas):
  Tuned Boundary Driven MD (tBDMD): pressure is controlled by particle insertion/deletion at the boundaries of the control cells (ask Zoli!)
Simulating transport

Players of the game

**Sure thing:** dynamics (Newton)

- **Flux:** output of the calculation – $j^\alpha(r)$
- **Concentration:** availability of the transported particles – controlled by the simulation – $c^\alpha(r)$
- **Diffusion coefficient:** mobility of the transported particles – $D^\alpha(r)$
  - Inherently included in MD
  - Implicitly included in LD (coupling with water) and DMC (maximum displacement)
  - Explicitly included in NP (input parameter of the equation)
- **Driving force:** difference/gradient of the electrochemical potential – $\mu^\alpha(r)$
  - **Handling the transport between control cells with MD, LD, or DMC:** the difference is enough – the resulting methods: MD+DCV, LD+DCV, DMC+DCV
  - **Handling the transport with NP:** we need the gradient everywhere
    NP+DCV is not enough
Electrodiffusion: the Nernst-Planck equation

The equation that makes the connection between the players.

\[ j^\alpha(r) = -\frac{1}{kT} D^\alpha(r) c^\alpha(r) \nabla \mu^\alpha(r) \]

- What is \( \mu^\alpha(r) \) in the transport (non-equilibrium) region?
- Chemical potential is defined by equilibrium statistical mechanics.
- General solution: divide the system into volume elements and assume local equilibrium (LE) in them
- Use the procedures of equilibrium statistical mechanics in the volume elements.
  - Poisson-Boltzmann: old method called Poisson-Nernst-Planck (PNP) theory
  - Dynamic Density Functional (Tarazona, Gillespie)
  - Simulation (our suggestion): perform a GCMC simulation for the whole system, but using different electrochemical potentials in the volume elements – Local Equilibrium Monte Carlo (LEMC)
The algorithm:

\[ \mu_i^\alpha[n] \xrightarrow{\text{LEMC}} c_i^\alpha[n] \xrightarrow{\text{NP}} j_i^\alpha[n] \xrightarrow{\nabla \cdot j^\alpha = 0} \mu_i^\alpha[n + 1]. \]

LEMC provides the \( c^\alpha(r) \) profile for a given \( \mu^\alpha(r) \) profile.

\( \mu^\alpha(r) \) is iterated until the flux satisfies the \textit{continuity equation} (conservation of mass): \( \nabla \cdot j^\alpha(r) = 0 \)

Advantages:
- NP is fast
- LEMC provides „correct” statistical mechanical closure between \( c^\alpha(r) \) and \( \mu^\alpha(r) \)
- Handling boundary conditions is obvious

Disadvantage:
- Dynamics is hidden in the diffusion coefficient – at the end, \( D^\alpha(r) \) is an adjustable parameter fitted to experiments

Solution: simulate flux directly with MD, LD, or DMC (with all their disadvantages)
RyR calcium-release ion channel

- CaV (voltage gated) L-type Ca channel
- $\text{Ca}^{2+}$-release Ryanodine Receptor (RyR) Ca channel
Models of the RyR Ca\(^{2+}\)-release channel

1-D model of Dirk Gillespie for NP+DFT

Our 3-D model for NP+LEMC based on Dirk’s model
Results for ion channels

I-V curves for NaCl

Symmetric 250 mM NaCl (basis of fit of $D^{\alpha}$ in the channel).

Non-symmetric NaCl - non-symmetric I-V curve. Requires non-symmetric channel model.
I-V curve for NaCl-CaCl$_2$ mixture

-200 -150 -100 -50 0 50 100 150
U / mV
-20 0 20 40 60 80
I / mA

Exp.
NP+LEMC
NP+DFT
250mM NaCl | 250mM NaCl
4µM CaCl$_2$ | 50mM CaCl$_2$
Anomalous mole fraction effect for the RyR channel

CaCl$_2$ is added to 100 mM NaCl

CaCl$_2$ is added to 100 mM CsCl
Anomalous mole fraction effect for the RyR channel

**Na\(^+\) vs. Cs\(^+\) competition**

![Graph showing Na\(^+\) vs. Cs\(^+\) competition](image)

- **Exp.**
- **NP+DFT**
- **NP+LEMC**

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Rectifying ion channel

Motivation: pont mutation experiments by Miedema

- The negative/positive amino acids of a non-rectifying ion channel (OmpF porin) were exchanged to form a P-N „diode”.
- The mutated ion channel (RREE) rectifies.

Rectifying ion channel

Reduced model

- Simulations with an all-atom model by Kristóf Tamás and Ható Zoltán did not show rectification.
- What about a reduced model that grabs only the crucial features (PN junction) of the channel?
Rectifying ion channel

Results

- The rectifying property is reproduced
- The all-atom model fails, the reduced model succeeds. Why????????????????????
Other direction: coupling DMC with LEMC

- Use a direct dynamical simulation method in the transport region
  - We tried DMC.
  - We are working on LD.
  - MD is difficult.

- Use GCMC everywhere, not only in the control cells: DMC+LEMC


- An **iteration** procedure is still needed to satisfy conservation of mass.
- **Advantage**: dynamics is simulated directly; it is not buried in the diffusion coefficient
- **Disadvantage**: particles popping out of hyperspace need to be handled (no problem in DMC, big problem in MD)
Diffusion of LJ particles through a Powles-membrane

- **Powles-membrane**: cut&shifted LJ particles at fixed positions
- **Diffusing particles**: mixtures of cut&shifted LJ particles
- **Driving force**: concentration difference (simple diffusion)
Diffusion coefficient profile deduced from DMC+LEMC and used in NP+LEMC

- Fine details of $d\mu^\alpha/dx$ and $c^\alpha$ profiles are determined by the intermolecular forces, NOT by the diffusion coefficient profiles.

- It is a good approximation to use stepwise constant $D^\alpha(x)$ profiles.
Application of the tBDMD method:
Selective diffusion through Silicalite-1 membrane

- Results of Tamás Kristóf and Zoltán Ható (ask him for details)
- $S_E$: equilibrium selectivity (simulated by GCMC)
- $S_P$: permeation selectivity (simulated by MD+DCV)
- $S_{Pn}$: permeation selectivity (simulated by tBDMD)
- 1:1 CO$_2$-H$_2$ gas mixture at different feed pressures ($\sim$ vacuum at the permeate side)
Ambitions for the future

- Coupling LD with LEMC
- Go for systems comparable to experimental situation in length and time scale

**Example:** swelling and exfoliation of kaolinite (T. Kristóf and Z. Ható)

Initial configuration → after 2ns MD simulation → after more time (experiment)

100 nm × 100 nm × 10 nm, **6.5 million atoms**, Gromacs, **768 cores**, **3 months** – Ask Zoli for details!

- Simulate nanopores of various properties, especially, rectification

**Thanks for your attention!**