Non-equilibrium Molecular Dynamics Of Ionic Channels: Pair Correlation Functions

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Ion Channel Permeation Simulated by Non-Equilibrium Molecular Dynamics

1. **Maintain necessary non-equilibrium condition: Biology happens in non-equilibrium**
2. **Obey long-range electrostatic interaction and boundary conditions**
3. **Invoke local atomistic interaction, particle-particle correlation effect, other necessary forces**

HOW TO CALIBRATE NEMD SIMULATIONS

NEMD & MONTE CARLO

- **Non-equilibrium Molecular Dynamics (NEMD)**

Dynamic properties: flux, time-correlation, density fluctuation, density distribution

- **Equilibrium Monte Carlo**

Equilibrium (steady-state) density distribution

Specifics of NEMD Simulations

- **Lennard-Jones for short-range local interaction**
- **P3M Method for long-range electrostatics**
- **Fourth order predictor-corrector for time propagation**

The pair distribution function is de¯ned as

$$g(r_{1;}r_2) = \frac{N(N\ \text{¡}\ 1)}{½^2 Z_{NVT}} \int dr_3 dr_4 ::: dr_N \exp(\text{¡}\ \beta E(r_1; r_2; :::; r_N));$$

where N is the number of the particles,
½ is the number density,
Z_{NVT} is the partition function (con¯guration integral),
$E(r_1; r_2; :::; r_N)$ is the total potential energy,
$\beta = k_B T$, k_B is the Boltzmann constant,
T is the temperature.

Any pair function is then

$$< a(r_i; r_j) > = \frac{1}{V^2} \int dr_i dr_j g(r_i; r_j) a(r_i; r_j)$$

The relationship between thermodynamic properties and the pair correlation function are

$$
\begin{aligned}
U &= U^{\circ} + 2\pi\rho N \sum_{ij} x_i x_j \int g_{ij} u(r_i; r_j) r^2 dr; \\
P &= \rho k_B T - \frac{2\pi\rho^2}{3} \sum_{ij} x_i x_j \int g_{ij} \frac{du(r_i; r_j)}{dr} r^3 dr \\
A &= A^{\circ} + \frac{2\pi N^2}{3} \sum_{ij} x_i x_j \int_1^V \left[g_{ij} \frac{du(r_i; r_j)}{dr} r^3 dr \right] \frac{dV}{V^2} \\
S &= \frac{U - A}{T} \\
G &= A + PV \\
\mu_i &= \mu_i^{\circ} + \frac{2\pi}{3} \left(\sum_{ij} n_i n_j \int_1^V \left[g_{ij} \frac{du(r_i; r_j)}{dr} r^3 dr \right] \frac{dV}{V^2} \right)_{T;V;n_{k \neq i}}
\end{aligned}
$$

where N is the number of the particles,
ρ is the number density,
Z_{NVT} is the partition function (con-guration integral),
$E(r_1; r_2; \ldots; r_N)$ is the total potential energy,
$\beta = k_B T$, k_B is the Boltzmann constant,
T is the temperature.

Reference: "Statistical Mechanics for Thermophysical Property Calculations", Richard L. Rowley, PTR P Jersey 1994 (ISBN 0-13-030818-8).

Origin Of The Code!

- **Prof. Richard L. Rowley and his group**

  Department of Chemical Engineering
  Brigham Young University
  Provo, Utah

People doing the simulation

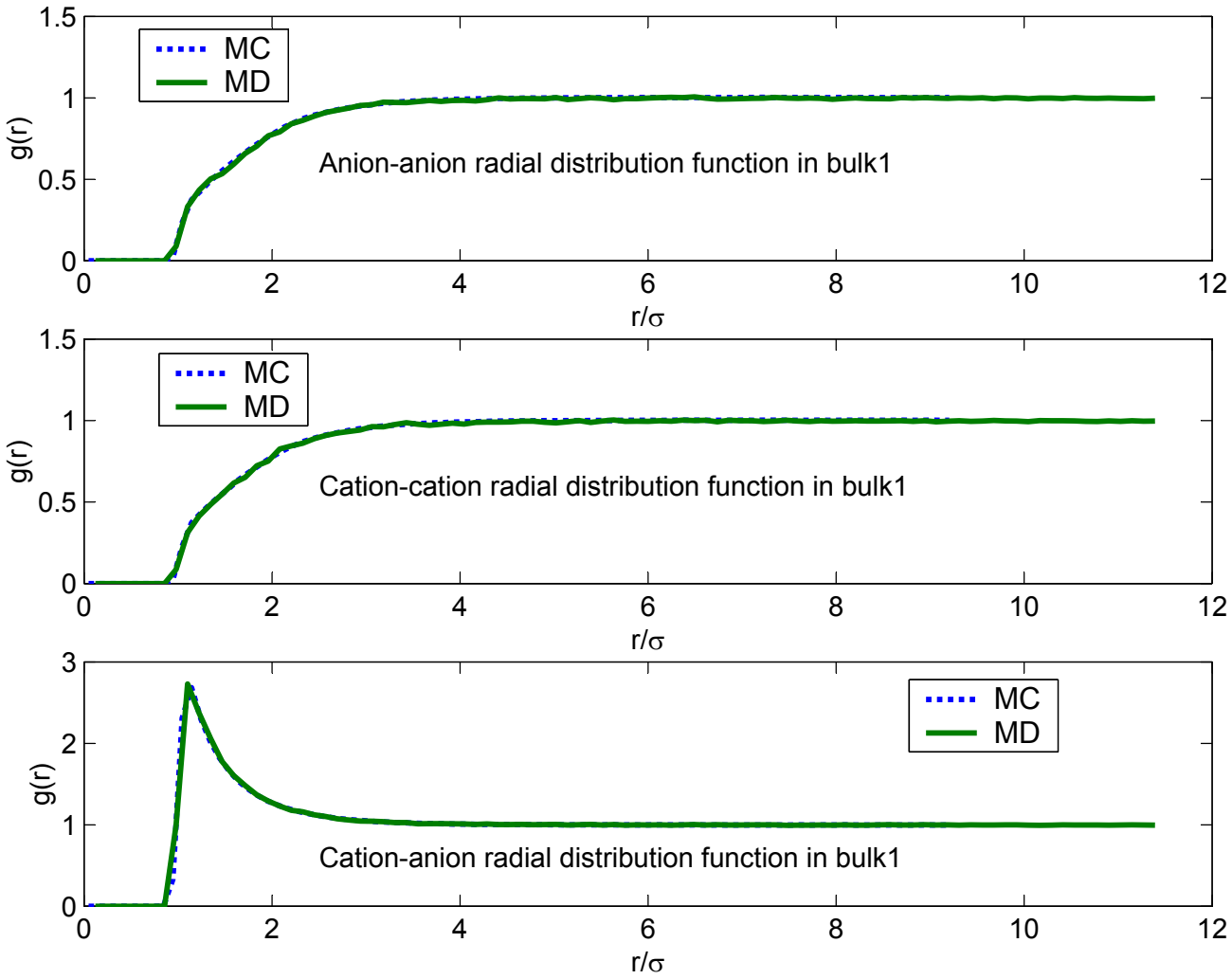
- **Brigham Young University**
  Doug Henderson
  Yan Yang

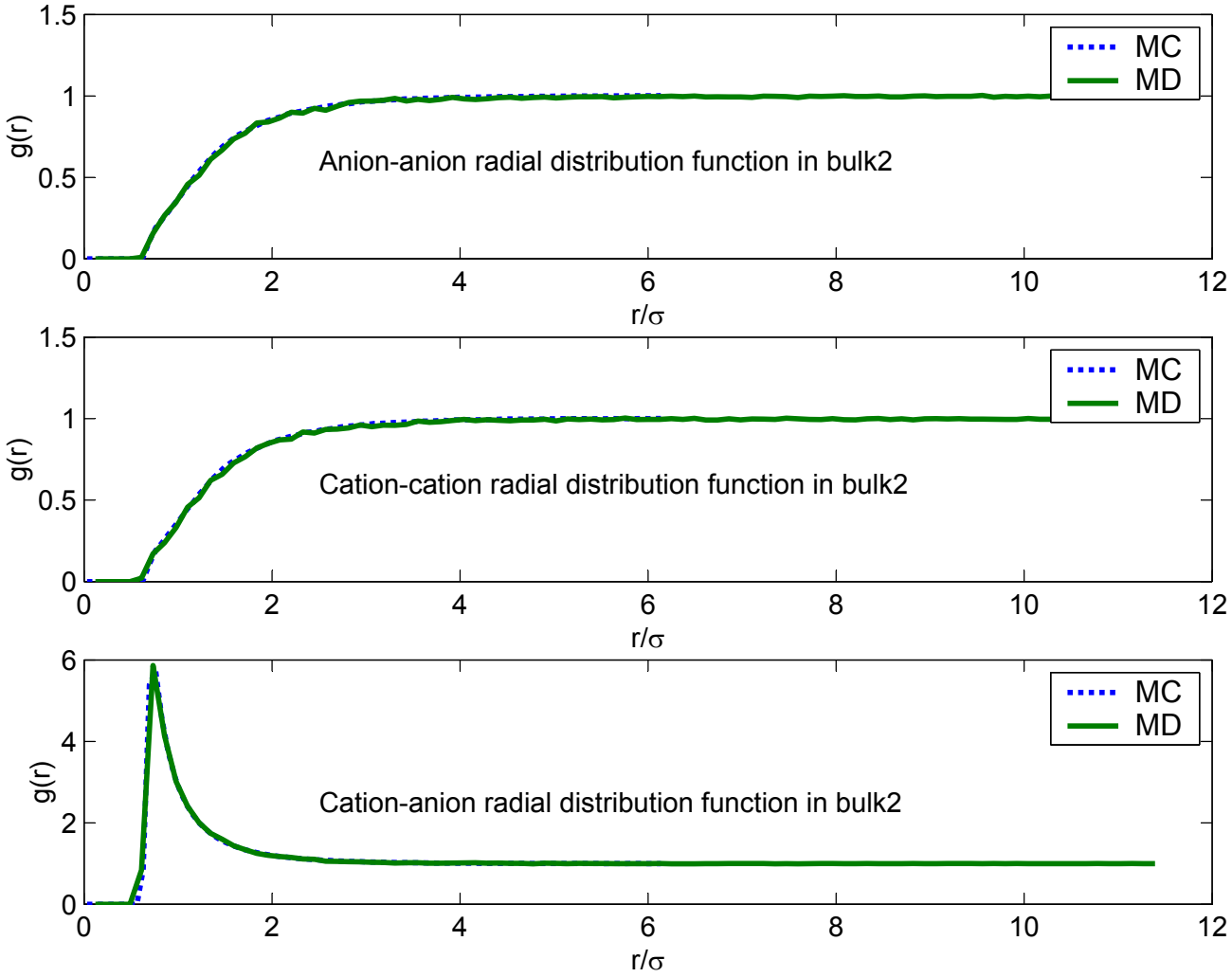
- **Rush University**
  Zhifeng Kuang
  Bob Eisenberg
  Duan Chen

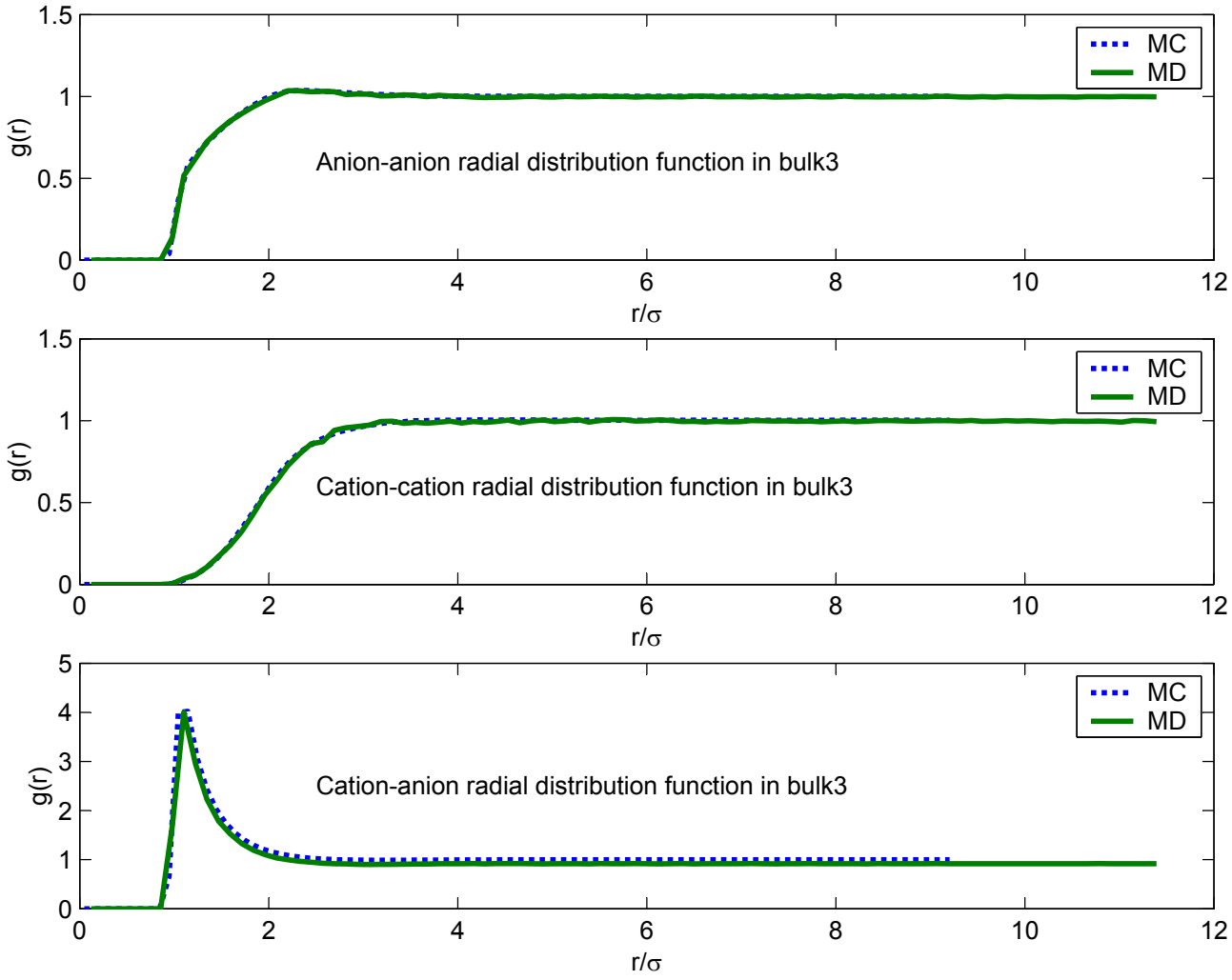
Solutions simulated in comparison of NEMD with equilibrium Monte Carlo

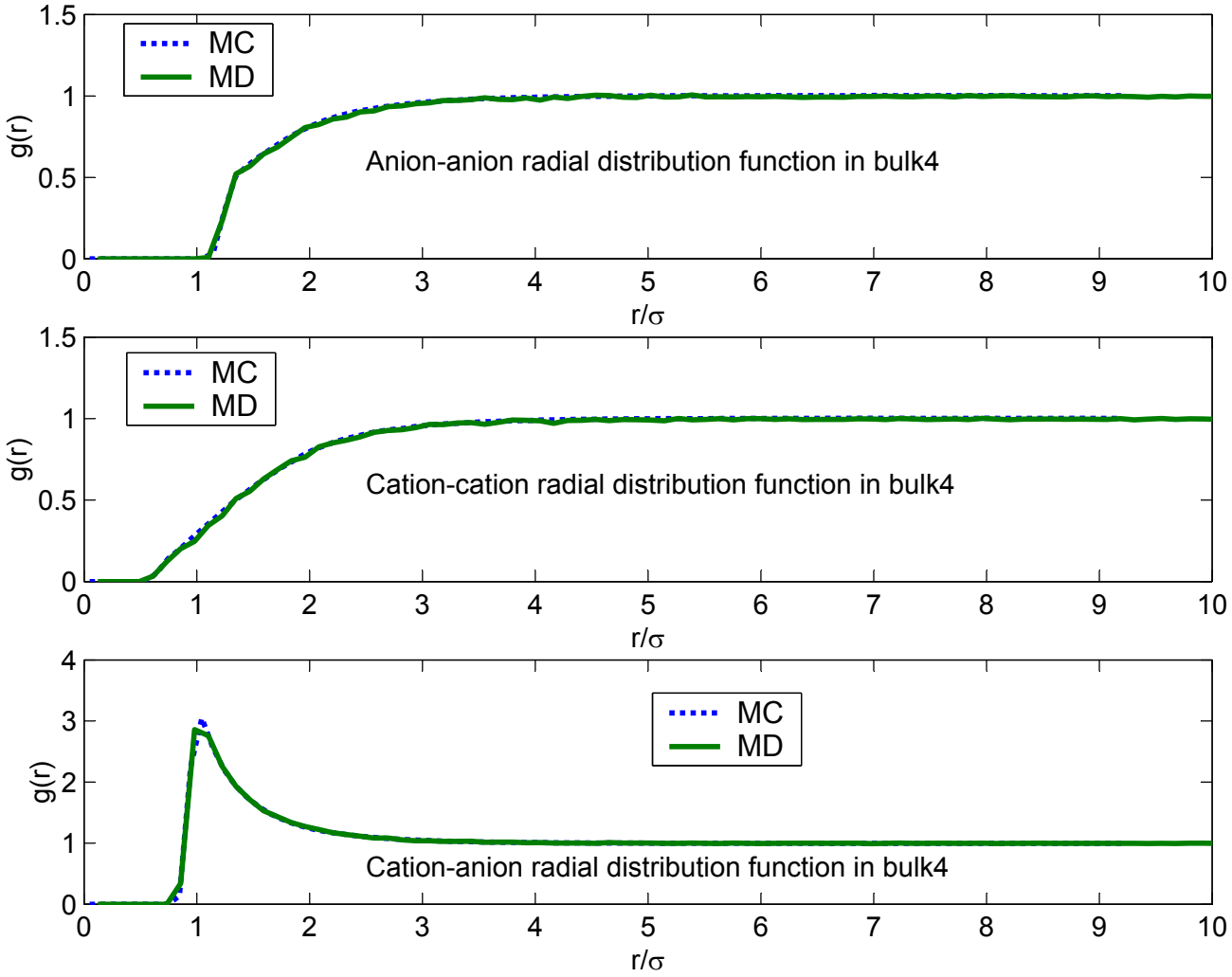
	Bulk1		Bulk2		Bulk3		Bulk4		Bulk5	
	Cation	Anion	Cation	Anion	Cation	Anion	Cation	Anion	Cation	Anion
N	200	200	200	200	200	400	200	200	150	300
Q[e]	1.00	-1.00	1.00	-1.00	2.00	-1.00	1.00	-1.00	2.00	-1.00
d[Å]	3.00	3.00	2.00	2.00	3.00	3.00	1.90	3.62	1.90	3.62
T[K]	298.15		298.15		298.15		298.15		298.15	
L[Å]	69: 251		69: 251		69: 251		69: 251		62: 919	

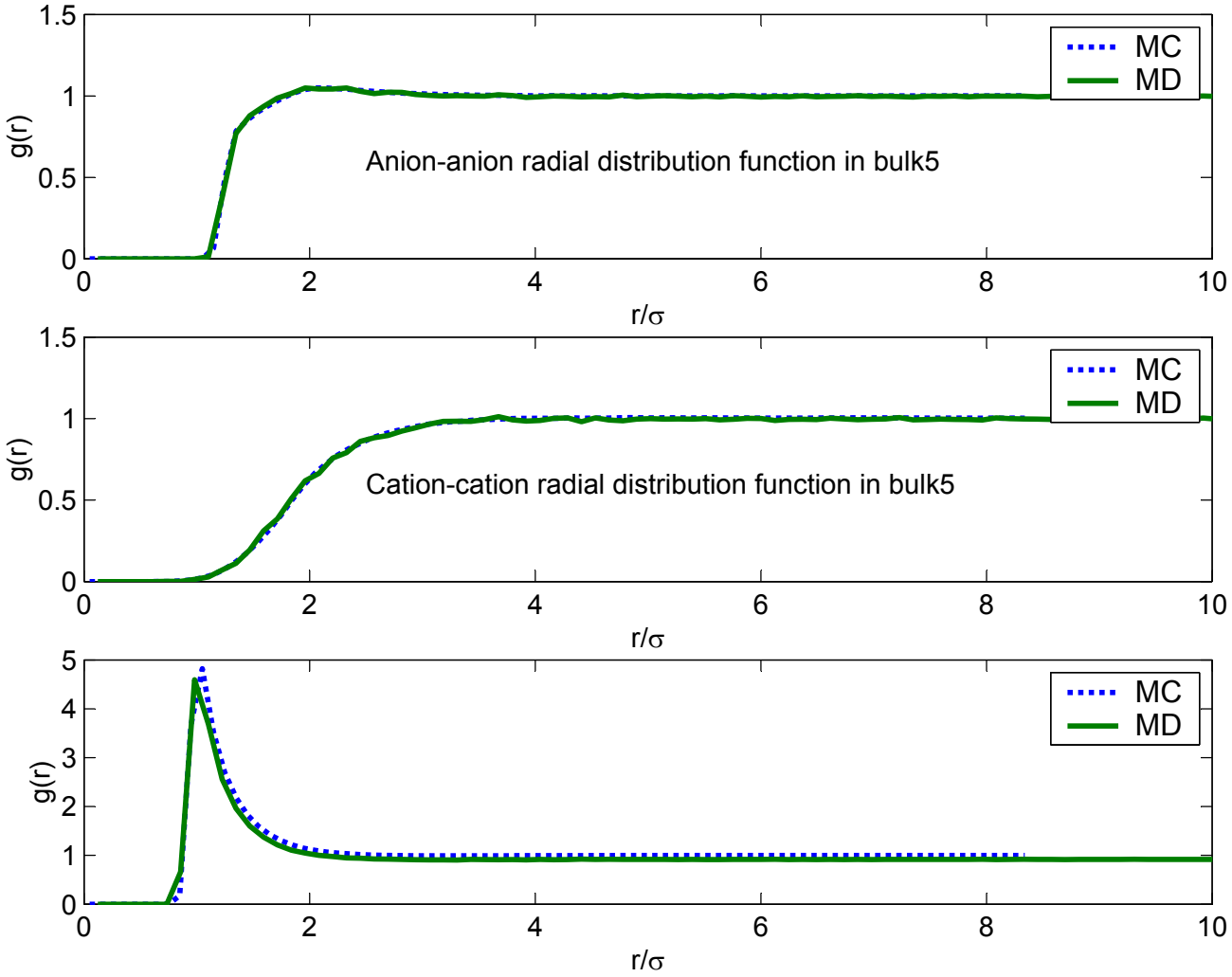
Notations: N = number of particles; Q = charge of particles; d = diameter of particles; T = temperature; L = length of the simulation cubic box.


MC
MD
Anion-anion radial distribution function in bulk1
g(r)
r/σ
MC
MD
Cation-cation radial distribution function in bulk1
g(r)
r/σ
MC
MD
Cation-anion radial distribution function in bulk1
g(r)
r/σ


1.5
1
0.5
0
g(r)
MC
MD
Anion-anion radial distribution function in bulk2
0
2
4
6
8
10
12
r/σ
1.5
1
0.5
0
g(r)
MC
MD
Cation-cation radial distribution function in bulk2
0
2
4
6
8
10
12
r/σ
6
4
2
0
g(r)
MC
MD
Cation-anion radial distribution function in bulk2
0
2
4
6
8
10
12
r/σ


MC
MD
Anion-anion radial distribution function in bulk3
g(r)
r/σ
MC
MD
Cation-cation radial distribution function in bulk3
g(r)
r/σ
MC
MD
Cation-anion radial distribution function in bulk3
g(r)
r/σ


MC
MD
g(r)
Anion-anion radial distribution function in bulk4
r/σ
MC
MD
g(r)
Cation-cation radial distribution function in bulk4
r/σ
MC
MD
g(r)
Cation-anion radial distribution function in bulk4
r/σ


Anion-anion radial distribution function in bulk5
Cation-cation radial distribution function in bulk5
MC
MD
g(r)
r/σ
0
0.5
1
1.5
2
3
4
5
6
8
10

Current Status of NEMD

- **Adapting the code for electrochemistry for ion channel permeation**
- **Applying NEMD in equilibrium condition**
- **Comparing NEMD in equilibrium condition with equilibrium Monte Carlo, experiment, and other published work**

A good agreement!

Improvement and Future Directions

- **Numerical Algorithm**
  - **Use better Poisson solver**
  - **Investigate better propagator solver**
- **Applications**
  - **Study ion-ion correlation effects**
  - **Study ion selectivity**
  - **Study permeation: application of NEMD to non-equilibrium conditions**