Russell talks about GRC Computational Chemistry 2004

mol_sims Discussion Group
GT Schools of Biology and Chemistry
et al
July 20, 2004

Requests

- **Philippe Hunenberger** (ETH) "New schemes for evaluating electrostatic interactions in molecular systems under periodic boundary conditions"

- Algorithms for GROMOS electrostatic force field determination, in next Rev. of that software

Hunenberger (p2)

The most straightforward algorithm to compute pairwise interactions within a given cutoff distance relies on a double loop over all unique atom pairs in the reference box, leading to a scaling of the computational cost as $\mathcal{O}[N(N-1)/2] \approx \mathcal{O}[N^2]$, where N is the number of atoms in the system. This computational effort may be reduced by application of the Verlet pairlist algorithm.[11] Here, the calculation of the pairwise interactions is performed in two successive steps: (1) generating a list of interacting atom pairs (i.e., pairs within the cutoff distance) by measuring the minimum-image distances between all unique pairs in the reference box, and (2) evaluating the nonbonded interactions for the atom pairs contained in the pairlist. The computational cost of the first step scales again as $\mathcal{O}[N^2]$, but that of the second step only scales as $\mathcal{O}[NR^3]$, where R is the cutoff distance. Time saving is achieved (at the expense of a limited loss of accuracy) if the pairlist is only updated every n (typically 5–10) timesteps, and assumed constant in between.
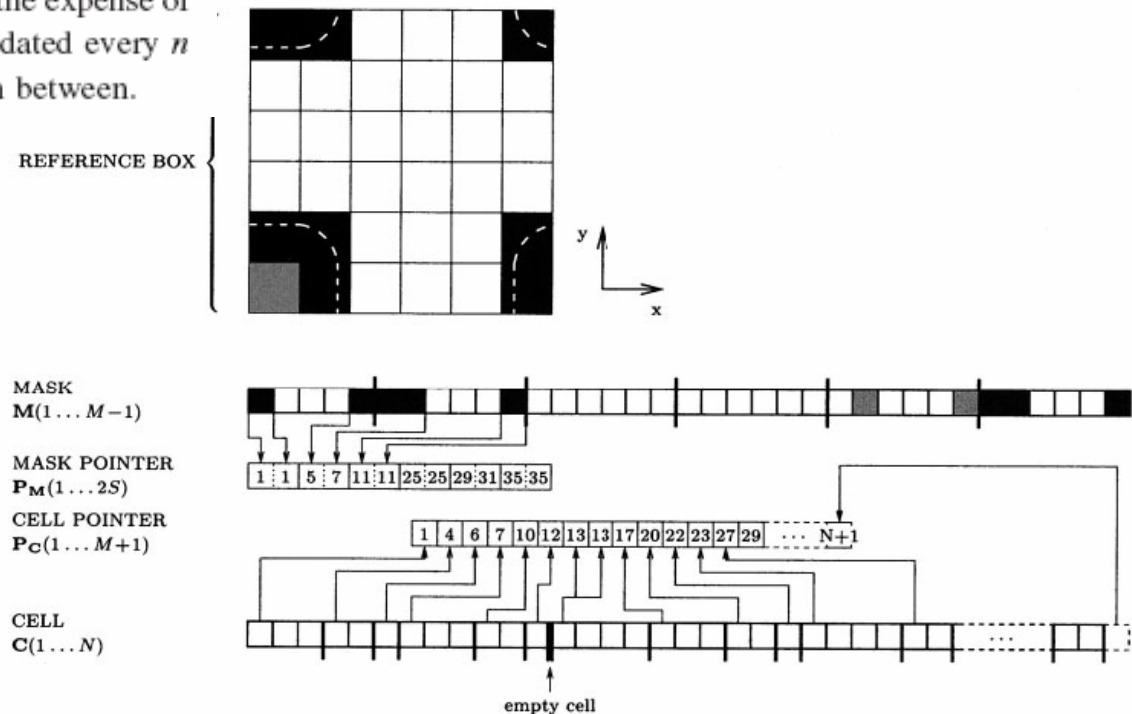

Figure 1. Schematic illustration of the principle underlying the present pairlist-construction algorithm, for a two-dimensional system with $L_x = L_y = L$, $N_x = N_y = N$ and $0 < R \leq L/6$. From top to bottom: reference box and its partition into grid cells, mask array, mask-pointer array, cell-pointer array, and cell array.

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Hunenberger (p3)

Computer "Experiments" on Classical Fluids. I. Thermodynamical Properties of Lennard-Jones Molecules*

LOUP VERLET†

This potential is cut at $r_v = 2.5\sigma$ in most of our experiments, or, in some of them at $r_v = 3.3\sigma$. The problem is to integrate the equation of motion

$$m\frac{d^2\mathbf{r}_i}{dt^2} = \sum_{j \neq i} \mathbf{f}(r_{ij}).$$

(2)

To integrate (2), we use the very simple algorithm

$$\mathbf{r}_i(t+h) = -\mathbf{r}_i(t-h) + 2\mathbf{r}_i(t) + \sum_{j \neq i} \mathbf{f}(r_{ij}(t))h^2,$$

(4)

where h is the time increment which we take equal to 0.032. This is practically the value chosen by Rahman (i.e., 10^{-14} sec in the case of argon). We have checked that this time increment is adequate and even superfluously small in most cases. For instance, for $T = 1.38$, $\rho = 0.55$ (i.e., temperature just above critical, density almost twice critical), we have performed two integrations up to the time $t = 4$. In one case we have taken $h = 0.032$, in the other $h = 0.016$, with the same initial

Requests

- **Anthony Stone** (Cambridge University) "*Ab initio* calculation of intermolecular potential energy surfaces"

Jiali Gao

- **Jiali Gao** (U. Minn.) [Michael Zerner Memorial Lecture] "Dynamics of Enzymatic Reactions from Combined QM/MM Simulations"

Jiali
Gao

Dynamics of QMMM

$$K(T) = \gamma(T) \frac{k_B T}{h} e^{-\Delta G^*/N_A k_B T}$$

Consider Reaction Coord

$$R_c = \frac{1}{(m_a + m_o)} \left\{ M_{ce} R(\alpha - C) - m_o R(O - C) \right\}$$

↖ difference of mass-weighted term

For enzyme catalysis, interested in

   I) Dynamics Contributions

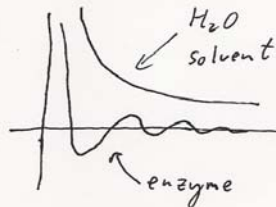$$K = (\ldots) \text{ Big Eqn}$$

   II) Calculated Transmission Coefficient

Generalized Langevin Eqn (GLE)

$$m\ddot{g}(t) = -m \int_0^t d\tau \, \partial(\cdots) \text{ Big Eqn}$$

   III) Time Correlation Function (TCF)

$$TCF = \frac{\langle \delta F_{RC}(t) \, \delta F_{RC}(0) \rangle}{\langle \delta F_{RC}(0) \, \delta F_{RC}(0) \rangle}$$

H₂O solvent / enzyme

   ┌─────────────────────────────────┐
   │ 3 Methods for Vibrational Modes │
   └─────────────────────────────────┘

   I) Normal Mode

   II) Fourier Transform

$$I(\omega) = \int \langle \quad \rangle d\omega$$

   III) Schrödinger Eqn

Calculation of T_1, T_2 relaxation times
from quantum mechanical time correlation function

Compare T_1 relaxation time
to Quantum Correction Factor (QCF)

	QCF		T_1 (ps)	
re-parametrized semi-empirical for each system	H₂O	CA-II	H₂O	CA-II
	expt			

Semi-empirical gives you: → Doesn't Work For:
Potential E Surface for   1) Transition matter
Breaking Chemical bonds, etc.   2) Redox
                                 3) (⋯)   AM1, MP2 result
Refs: Garcia-Viloca, Karplus, Science (2004);   (PNAS 2000, v97, p 9937)

Protein Phenomena Session

- Joan Shea: "Role of Frustration in Chaperonin-Mediated Protein Folding":
  - How cellular environments affect protein folding
  - Effects on protein folding: pH, temp, crowding
  - Aggregates of mis-folded proteins in diseases like Parkinson's
  - Chaperonins recognize misfolded proteins by exposed hydrophobic patches
  - GroEL:
    - 10sec time for ATP hydrolysis

Joan Shea (p2)

- Three theories to how chaperone
  - 1) Populating trapped states
  - 2) Passive mechanism (inefficient b/c protein aggregates; "Folding in the cage")
  - 3) Non-cycling single GroEL, prot. outside cavity, no confinement effects
- $T_m > T_f$:
  - Temp of min folding time greater than folding temp

Matthew Tirrell

- **Matthew Tirrell** (U. Calif. Santa Barbara) "Frontiers of Computational Chemistry: Ideas from the National Research Council Report"

- Edited two books:
  - Beyond the Molecular Frontier
  - National Security and Homeland Defense: Challenges for the Chemical Sciences in the 21st Century (2002)

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End Requests
… now for the good stuff

Maria Kurnikova

- **Maria Kurnikova** (Carnegie-Mellon University)
  "Hierarchical Methods for Modeling Membrane Protein Structure and Function"

Maria
Kurnikova

Ion current through open channel

MD / Continuum Electrostatics / Drift-diffusion

Modeling of α-hemolysin, β-cyclodextrin

Electrolyte ions treated as continuous charge dist. characterized by concentrations $\{c_i(\vec{r})\}$ of involved ionic species. Dist. of concentrations governed by drift-diffusion eqns.

Flux: $\quad \vec{j}_i(\vec{r}) = -D_i(\vec{r})\left[\dfrac{\partial c_i(\vec{r})}{\partial \vec{r}} + c_i(\vec{r})\dfrac{d}{d\vec{r}}\left(\beta \psi_i(\vec{r})\right)\right]$

Nernst-Planck
Eqns (NPE)

$\psi_i(\vec{r}) :=$ free energy of ions of species i in solution

Potential-of-Mean-Force-Poisson-Nernst-Planck approach to ion current calculation $\quad$ (PMF PNP) through channel.

No current, NPE simplify to Poisson-Boltzmann Eqn

Use Poisson-Nernst-Planck to study influence of membrane surface charge density and interfacial dipole potentials on the conductance of gramicidin A (GA) channel embedded in lipid bilayers.

Diffusion eqn of pore defined by

geometry: 1) Influences Parameterization

2) Relate to flux eqns above.

Stark Effect: Only observed at the <u>ligand</u> not
Two Models: the <u>channel</u>

Model 1)-two-level atom, vacuum and exciton coupling
- anisotropic vacuum to exciton coupling is
exactly compensated by anisotropic couplings between
the exciton and two-pair states ∴ whole effect
does not depend on the probe polarization

Model 2)-energy levels shift by the quantity

$$\delta w = 2 \frac{|\mu_{cv} \varepsilon_p|^2}{\hbar^2 \Delta w}$$

μ_{cv} := dipolar matrix element
between Valence and
conduction bands
ε_p := pump electric field
amplitude
Δw := detuning
i.e. freq. difference b/w
transition and pump

- Model 2 is distinguished from Model 1
since two levels are not vacuum and
exciton, but any Coulomb-free valence and
conduction states of the same wave vector.
- for transient case, i.e. w/o steady-state pump field,
pump intensity is introduced as function of time
but either in <u>Coulomb-free</u> or <u>Hartree — Fock</u>
frameworks.

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Ref: Joffre, M et al, IEEE Quantum Electronics (1989)

Yuko Okamoto

- **Yuko Okamoto** (Institute for Molecular Science, Okazaki, Aichi, Japan) "Protein Force Fields: Comparisons and Improvements"

- Replica-Exchange MD (REMD)
  - MUCAREM, REMUCA

Yuko Okamoto

New Protein Energy Function

$$F = \sum_{m>1}^{N} \frac{1}{N_m} \sum_{im=1}^{Nm} |\vec{f}_{im}|^2 \quad \left(Kcal^2/mol^2 \mathring{A}^2 \right)$$

$N := $ # prot mols
$N_m := $ # in math. model

seek to optimize
this function $F(\ ,\ )$

Trouble #1 / Amber 94, 96, 98
have same functional form which was
already fit empirically when those force
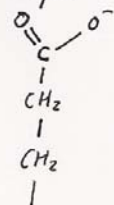fields were parameterized
⟹ should have re-derived those parameters
(some guy: Amber 96 has other factors)

Trouble #2: Fit force field params to PDB, no protons

┌─────────────────────────────────────┐
│ ∃ different protonation states │
└─────────────────────────────────────┘

e.g. histidine ⟵ ambiguous protonation
glutamic acid ⟵ also ambiguous

$O=C\overset{O^-}{\diagdown}$
|
CH_2
|
CH_2
|

Trouble #3: His force field assumed
net force on AA's $= \varnothing$, in PDB structure
have time-averaged ensemble coordinates, in
reality must re-equilibrate (i.e. to state where
net forces on AA's is far from zero)

Refs: Yoda, Chem Phys Lett (2004)
Sakae, Theor Comput Chem (2004)

Trouble #4: Uses objective function for optimization
... forces are not whole story; dihedral angles; etc.

Martin Head-Gordon

Martin Head-Gordon (U. Calif. Berkeley)
"Localized orbitals and fast correlation methods"

- Faster methods for electron correlation? New MP2 methods?

- Pulay-Saebo Model

- BSSE – Basis Set Superposition Error

- Resolution of Identity function smaller than all possible products

- DFT does not do dispersion

$$E_{mp2} = -\sum_{\alpha} \frac{|\langle \psi_\alpha | \ddot{v}^{(i)} | \psi^{(o)} \rangle|^2}{(E_\alpha^{(o)} - E^{(o)})}$$

Questions

- Can Density Functional Theory (DFT) fold proteins?

- Self-interaction of DFT is hopeless?

- Fast Multipole vs. Ewald?

- GAMESS-US vs. GAMESS-UK?

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