

Computational Biology > Paper Discussions

Course: CSE 498/598K
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- **Validation of molecular dynamics simulation**

- Wilfred F. van Gunsteren (Oxford University)

- Alan E. Mark (Swiss Federal Institute of Technology)

- **Assessing Equilibration and Convergence in Biomolecular Simulations**

- Lorna J. Smith (Oxford University)

- Xavier Daura (Oxford University)

- Wilfred F. van Gunsteren (Oxford University)

- Introduction
- Five Validation Issues
 - First Issue: Quality of theory or model
 - Second Issue: Accuracy of inter-atomic interaction function or force field
 - Third Issue: Degree of sampling, statistics, and convergence
 - Fourth Issue: Quality of the simulation software
 - Fifth Issue: How competently the simulation software is used
- Enabling and improving validation of simulation results
- Review

- **Introduction**

- Importance of simulations
- Complexity
- Analysis of simulations: New phenomenon or Error

- **Five Validation Issues**

- Quality of theory or model
- Accuracy of inter-atomic function or force field
- Degree of sampling, statistics, and convergence reached in simulation
- Quality of simulation software
- How competently software is used

- **First Issue: Quality of theory or model**

- Approximations of Electrostatic interactions for ionic and non-ionic systems
- Decomposition of free energy differences into components
- Incorrect formulation of Hamiltonian mechanics
- Determining Biomolecular structure.

- **Second Issue: Accuracy of inter-atomic interaction function or force field**
 - Involve as many different properties (structural, energetic, dynamical) as possible
 - Carried out using equilibrated systems and comparing converged average values of properties
- **Third Issue: Degree of sampling, statistics, and convergence**
 - Length of MD simulation is the central question
 - $T_{\text{equilibrium}} > T_{\text{relaxation}}$
 - $T_{\text{sampling}} \gg T_{\text{relaxation}}$
- **Fourth Issue: Quality of the simulation software**
 - Elementary algorithmic tests
 - Reproduce well-known standard benchmark systems
 - Practical research projects
 - Documentation

- **Fifth Issue: How competently the simulation software is used**
 - Careful consideration of physical laws and physical & chemical characteristics of molecular system
- **Enabling and improving validation of simulation results**
 - Software suppliers : specify software including algorithms, force fields, source code, model etc.
 - Software users: specify chosen input parameters.
 - Publishers, Reviewers: Enforce guidelines for the suppliers and the users
- **Review**
 - Nice introductory paper on Molecular Dynamics simulations
 - Awareness as Software user, Software developer, and Reviewer
 - Little short on implementation details

- Introduction
- Methods
- Results
- Conclusions
- Review

- **Introduction**

- Reliable assessment of equilibration & convergence
- System I: 7 residue β -peptide in methanol (962).
Two 50ns trajectories & Four 5ns trajectories (340K & 360K)
- System II: 11 residue α -peptide in water (2105)
Four 5ns trajectories (300K & 400K)
- Compare the trajectories & calculate the convergence and equilibrium of different quantities.

- **Methods**

- GROMOS96 software & GROMOS96 43A1 force field with periodic boundary conditions
- Time step of 2fs performed at 1atm
- Bond lengths were constrained to ideal values with 10^{-4} accuracy
- Non bonded interactions treated using twin range method
short range cutoff 0.8nm
long range cutoff 1.4nm
- Reaction field applied beyond 1.4nm

- **Results**

- Intra-molecular energy of the peptide
- Main chain atom positional RMS deviation w.r.t initial structure
- Number of clusters present
- Number of different intra-molecular H bonds populated in the peptide
- Atom positional RMS fluctuations
- Total number of torsion angle transitions and the number of chain torsion angle transitions

- **Conclusions**

- Important to probe conformational and dynamical properties of the peptide
- Peptide interaction energy and atom positions RMSD is used as criteria for convergence
- Number of clusters populated is much more informative quantity for assessing convergence
- Very long simulation times required for adequate sampling

- **Review**

- Nice follow up paper to the previous one
- In depth coverage of experiments