Research by Wilfred F. van Gunsteren since 1972

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Since 1972 Wilfred van Gunsteren (WFvG) has been active in research, till 1976 in computational nuclear physics at the Free University of Amsterdam, after that year in computer simulation of bio-molecular systems at the University of Groningen (1976-1978, 1980-1990), at Harvard University (1978-1980), and at the ETH in Zürich (Swiss Federal Institute of Technology) since 1990. His major research interest is the development of methodology to simulate the behaviour of bio-molecular systems, in particular proteins [e.g. paper 402]. By applying the developed methodology to bio-molecular systems of practical interest, for which ample experimental data are available, deficiencies of current methodology can be identified and new ideas may emerge. Simulation of bio-molecular systems per se leads to enhanced insight into bio-molecular processes at the atomic level, which are often inaccessible to experimental probes. Below the major research activities are briefly sketched. The references to publications are coded according to the publication list of WFvG.

1. Molecular dynamics simulation: general algorithmic developments

- Molecular dynamics (MD) time integration algorithms for harmonic versus non-harmonic forces [10].
- MD simulation at constant temperature and pressure [34].
- A method to simulate molecular systems at constant chemical potential [176].
- A method to simulate molecular systems at constant pH [326].
- Use of bond, bond-angle or dihedral-angle constraints in large molecules [10,14,15,16,19,28,294,407,609,611,616].
- A method to impose flexible (adiabatic) constraints in MD simulation [388,427].
- Searching neighbour particles in simulations of macromolecular systems [32].
- Multiple-time-step algorithms for MD simulation [54,99,337,612,615].
- Time integration algorithms for stochastic dynamics (SD) simulation [21,22,27,71].
- An improved leap-frog kinetic energy expression [437].
- MD simulation in four dimensions [147,165].
- Methods to calculate the dielectric permittivity of liquids [306,504].
- Multi-graining: an algorithm for simultaneous fine-grained and coarse-grained simulation [409].
- Use of weak-coupling in replica-exchange simulation [590].
- An algorithm for flexible boundaries in multi-resolution simulation [594].

2. Atomic-level (GROMOS) force-field development for bio-molecular systems

- Force-field parametrisation using the weak-coupling method [181,191].
- Force-field parametrisation using quasi-Newtonian dynamics for the parameters [227].
- Force-field parameters for protein-water interactions [29].
- GROMOS force field 43A1 for bio-molecular simulation [243,254].
- GROMOS force field 43A2 for bio-molecular simulation [284].
- GROMOS force field 45A3 for bio-molecular simulation [304,339].
- GROMOS force field 45A4 for bio-molecular simulation [371].
- GROMOS force field 53A5 and 53A6 for bio-molecular simulation [358].
- GROMOS force field 54A7 and 54B7 for bio-molecular simulation [470,507].

- GROMOS force field 54A7_ß and 54B7_ß for beta-peptides [505,570].
- Flexible versus rigid models of liquids [213].
- A simple point-charge model (SPC) for liquid water [18,324,340,497,581].
- Model for chloroform [173,487,527].
- Model for dimethyl sulfoxide [189,349,527,577].
- Model for carbon tetrachloride [223,496].
- Model for methanol [276,406,527].
- Model for urea [348,586].
- Model for acetonitrile [393].
- Model for ethylene glycol [432].
- Model for dimethyl sulfone [516].

3. Treatment of (long-range) electrostatic interactions in molecular simulation

- Inclusion of the (stochastic and delayed) electrostatic reaction-field in simulations [12,192,230].
- Analysis of the P3M method to calculate long-range electrostatic interactions [177,196].
- Method to calculate non-periodic long-range electrostatic interactions using P3M [211].
- Different schemes to incorporate long-range forces in MD simulation [245,300,342].
- Method to calculate dielectric permittivity and relaxation [504].

4. Mean-solvation force-field terms

- Stochastic and frictional forces representing the omitted solvent degrees of freedom [78].
- Mean-solvation models for simulation of proteins in water [214,500,545,617].

5. Introduction of polarisability into molecular force fields

- Development of a charge-on-spring (COS) model for polarisability in MD simulation [436,465,579].
- A polarisable model for liquid water [338,365,465,579,581].
- A polarisable model for liquid methanol and methanol-water mixtures [406].
- A polarisable model for liquid ethylene glycol and ethylene glycol-water mixtures [432].
- A polarisable model for chloroform [487].
- A polarisable model for carbon tetrachloride [496].
- A polarisable model for liquid hydrocarbons [574].
- A polarisable model for dimethyl sulfoxide and dimethyl sulfoxide-water mixtures [577].
- A polarisable model for urea-water mixtures [586].
- A polarisable model for acetone [597].

6. Supra-atomic/molecular-level (GROMOS) force-field development for bio-molecular systems

- Using a too large time step in MD simulation of supra-atomic coarse-grained models [457,473].
- A supra-molecular polarisable model for liquid water [497,533].
- Supra-molecular polarisable models for dimethyl sulfoxide, chloroform and methanol [527].
- Mixed fine-grained (atomic) and coarse-grained (supra-molecular) systems [533,534,536,555,575,583].

- A supra-atomic polarisable model for alkanes [588,591].

7. Searching and sampling the (vast) configuration space of large bio-molecules

- Conformational search by potential energy annealing [112].
- Local-elevation: a method to improve the searching of conformational space [174].
- Conformational search using a Boltzmann-weighted mean-field approach [219].
- Conformational search by cooperative MD simulation [249].
- Sampling rare events using hidden restraints [407].
- Adiabatic decoupling of degrees of freedom to enhance configurational sampling [502,510,513,529].
- Enhanced conformational sampling using EDS [569].

8. Structure determination or refinement of proteins based on experimentally derived data

- Determination of protein structure from NMR data using restraining MD simulation [35,37,40,44].
- Time-dependent NOE distance restraints in protein structure determination by NMR [89,96].
- Time-dependent restraints in protein structure determination by X-ray diffraction [98,140,180,265].
- Time-dependent ^{3}J-coupling restraints in protein structure determination by NMR [127,600,614].
- Determination of protein structure from chemical-shift NMR data using MD simulation [136,241].
- Structure refinement using MD simulation in four dimensions [147].
- Structure refinement using a Boltzmann-weighted conformational ensemble [199].
- Structure refinement using weak-coupling NOE distance restraining [224].
- Structure optimisation using soft-core interactions and the diffusion-equation approach [235].
- Use of time-dependent or time-averaging restraints in MD simulation [253,266,299,362,417].
- Structure refinement based on adaptive restraints [439].
- Structure refinement based on time-averaged order-parameter restraints [580,613].
- Structure refinement based on Residual Dipolar Couplings and rotational sampling [618].

9. Calculation of free energy and entropy in bio-molecular systems

- Thermodynamic cycles to compute free energy differences [63,84,132].
- Calculation of relative free energy via indirect pathways [103].
- One-step perturbation technique to calculate free energy differences [137,150,159,209,217,269,313,341,346,373,378,553,565].
- Pathway effects in free energy calculations [151,157,193,317,410,411,595].
- Decomposition of relative free energies in terms of interactions or amino acids [162,175].
- MD relative free energy calculations in four dimensions [165].
- Calculation of entropy from MD simulation [286,296,316,347,351,352,400,403,404,405,416,444,585].
- Calculation of free energy of deprotonation in solution [312].
- Method of enveloping distribution sampling (EDS) to compute relative free energies [424,448,456,466,508,519,526,535,556,557,564,571,576].
- Calculation of the free energy of polarisation [441] and quantisation [452].
- A method to compute the free enthalpy of replacing water molecules in a binding pocket [546].

10. Combining classical (MD) and quantum-mechanical treatments in bio-molecular systems

- Proton transfer using density-matrix (QM) evolution [149].
- Application of path-integral QM to water [156].
- Analysis of QM/MM simulations [182,210,221,237,246,247,267,268,293,438,523].
- Integration of the time-dependent Schrödinger equation [208].
- Non-adiabatic proton transfer in solution [239,248,274].
- Methodological aspects of QM/MM simulations [435].

11. Software development for bio-molecular simulation

- Adaptation of the implementation of MD simulation algorithms to supercomputers [33,124].
- Molecular dynamics on a multi-signal-processor system [123, 125,131].
- Groningen Molecular Simulation (GROMOS) software development [206,262,386].
- Molecular dynamics using Graphical Processor Units (GPU) [477].
- Description of the GROMOS software: architecture [525], functionalities [524,579], structure refinement [512], free energy calculation [517], analysis of trajectories [514], tutorial [610].
- Interfacing the GROMOS simulation software to quantum-chemical software [540].

12. Reviews

- Computer simulation: Methodology, applications, perspectives [99,302,402,445].
- Computer simulation: Overview of time-saving techniques [105].
- Taking account of solvation [161].
- Computer simulation of protein motion [200].
- Empirical interaction functions for molecular simulation [238,255].
- Validation of molecular dynamics simulation [244,446,605].
- Accounting for polarisation in molecular simulation [385].
- On searching, sampling and moving through conformational space [431].
- Basic ingredients and practical aspects of free energy calculations [471,578].
- Developing coarse-grained models for bio-molecular simulation [538].
- Thirty-five years of bio-molecular simulation: 1977 – 2012 (-2019) [544,607].
- Multi-resolution simulation of bio-molecular systems: methodological issues [554].
- Deriving structural information from experimentally measured data [601].
- Effects of assumptions and approximations in molecular simulation [612].

13. Protein and polypeptide folding

- Polypeptide folding [236,250,257,259,270,273,288,291,295,314,334,335,359,361,363,370,387, 392,395,399,426,434,459,463,472,478,479, 491,495,498,505,562,583,584].

14. Simulation of membranes

- MD simulation of n-dodecyl phosphate bilayers and micelles [309].
- MD simulation of lipid bilayers [315,322,357,375,382,391,394].
- MD simulation of the outer membrane protein X in a lipid bilayer and in a micelle [490].

15. Ethical issues in science

- Seven sins in the natural sciences [549].
- Pitfalls of peer review [593].
- Going for a PhD: Joys and pitfalls [598].
- Publication of research results: Use and abuse [602].
- Surfing versus drilling in fundamental research [606].

16. Proteins, peptides, DNA, sugars simulated

- bovine pancreatic trypsin inhibitor (BPTI)
  [17,20,24,25,31,55,98,129,133,139,153,168,183,198,203,615,616].
- lac repressor DNA binding domain [37,40,58,79,92,108].
- L7/L12 protein [39].
- avian pancreatic polypeptide hormone [49].
- eight-base-pair DNA [54].
- retinol-binding protein [57,59].
- insulin [60,72,107].
- cyclosporin A [64,86,97,148}.
- cyclodextrins [67,68,70,75,76,126,163,493].
- polypeptide cardiac stimulant anthopleurin-A [83].
- phospholipase A2 [85,90].
- carboxypeptidase A [88].
- bacteriophage T4 glutaredoxin [101].
- hen egg white lysozyme [118,129,153,185,195,203,277,283,303,366,483,522,539,559,613,614,617].
- subtilisin BPN' [121,138].
- antamanide [134].
- dihydrofolate reductase [137].
- flavodoxin [154].
- histidine-containing phosphocarrier protein HPr [160].
- chymotrypsin inhibitor 2 [171].
- surfactant protein C [187].
- 434 repressor DNA-binding domain [207].
- HIV-protease [221].
- antamanide [225].
- plasmodium falciparum circumsporoite surface protein [229].
- 16 base-pair DNA [252].
- alpha-lactalbumin [260,263,303,316,368,455].
- factor Xa [278,289].
- murine V_H domain [282].
- beta domain of metallothionein [285].
- estrogen receptor ligand binding domain [287].
- p-hydroxybenzoate hydroxylase [293].
- alpha-helical surfactant-associated polypeptide C [301].

- llama antibody heavy-chain variable domain [303].
- fatty acid binding protein [303,323,325].
- ubiquitin [305,425,469].
- photoactive yellow protein [336].
- quercetinase [364].
- azurin [372,530].
- bee venom mellitin [391].
- arc repressor protein [408].
- cyclophilin [414].
- cytochrome c [415].
- human interleukin-4 [440,604].
- ccß-Met amyloid [442].
- ASC and NALP1 pyrin domains [443].
- ankyrin repeat protein [454].
- HET-s(218-289) prion [460,596].
- TRP-cage mini protein TC5b [467].
- GFP chromophore [482].
- outer membrane protein X [490].
- plasmepsin II [503].
- phenylethanolamine N-methyltransferase [508].
- french bean plastocyanin [531].
- p53 core domain {541].
- chorismate mutase [542].
- barley and maize lipid transfer protein [550].
- AppA BLUF domain [558].
- isochorismate pyruvate lyase [560].
- protein G [563].
- bacteriophage lambda lysozyme [587].
- protein hGH [603].

17. Liquids, solvents simulated

- water [18,202,324,338,340,365,465,497,579,581].
- chloroform [171,487,527].
- dimethyl sulfoxide [189,349,527,577].
- carbon tetrachloride [223,496].
- methanol [276,406,527].
- urea [348,586].
- acetonitrile [393].
- ethylene glycol [432].
- dimethyl sulfone [516].
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