TINKER − *Software Tools for Molecular Design*

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TINKER is a complete package for performing empirical force field molecular mechanics and dynamics calculations. It is intended to serve as a platform for algorithm development and parameterization, while still being efficient enough for most production work. The available potentials include AMBER-95, CHARMM22, MM2(1991), MM3(2000), OPLS-AA, OPLS-UA and our TINKER potential. Other force fields can be added via new parameter files; ENCAD, MMFF and UFF are under consideration for future addition.

Programs are provided to perform many functions including the following: (1) energy minimization over Cartesian coordinates, torsional angles or rigid bodies via conjugate gradient, variable metric or our truncated Newton method, (2) molecular, stochastic and rigid body dynamics with periodic boundaries and control of temperature and pressure, (3) normal mode vibrational analysis, (4) distance geometry including an efficient random pairwise metrization, (5) building protein and nucleic acid structures from sequence, (6) simulated annealing with various cooling protocols, (7) analysis and breakdown of single point potential energies, (8) verification of analytical derivatives of standard and user defined potentials, (9) location of a transition state between two minima, (10) full energy surface search via our Conformation Scanning method, (11) a simple free energy perturbation facility, (12) fitting of intermolecular potential parameters to structural and thermodynamic data, and (13) global optimization via energy surface smoothing including our own Potential Smoothing and Search (PSS) method.

Analytical Cartesian derivatives through the Hessian and analytical torsional derivatives through the gradient are available. Energy minimization and vibrational analysis can be performed in either Cartesian or torsional spaces. The user can define rigid bodies and compute scaled energies between or within bodies. Atomic multipoles through the quadrupole and induced dipole polarization, as well as simpler electrostatic models, are implemented. Restraint potentials may be included in all types of computations or partial structures can be frozen in space. Both replicative and image boundary conditions are supported for all unit cell types and for truncated octahedra. Nonbonded interactions can be cutoff using smoothing windows via double loop searches or the Method of Lights. Particle mesh Ewald (PME) is available for partial charges, and standard Ewald for polarizable atomic multipoles. The molecular volume and surface area as well as their derivatives are included. Various continuum solvation models, such as GB/SA, are implemented. User-defined potentials can be easily added.

The heart of the TINKER package is a modular set of callable routines which allow the manipulation of coordinates and evaluation of potential energy and derivatives in a straightforward fashion. The author welcomes development by others of new modules for TINKER and is willing to serve as a resource and distribution center for such development efforts.

The TINKER package is written in a portable Fortran dialect that makes use of some common extensions to the Fortran-77 standard. Program control is via an optional Keyword Parameter file. A modified version of RasMol for TINKER is available for viewing molecular structures. A complete GUI in Java is currently under active development and planned for future release. TINKER coordinate input files are also compatible with Cambridge Scientific Software's CHEMDRAW & CHEM3D programs and with the gOpenMol, MOLDEN and ReView molecule viewers. Auxiliary programs are provided to convert Brookhaven Protein Data Bank files to and from the TINKER formats. Output can also be generated in formats compatible with the Tripos Sybyl, Accelrys InsightII, and Xmakemol programs.

Selected References:

1. J. W. Ponder and F. M. Richards, An Efficient Newton-like Method for Molecular Mechanics Energy Minimization of Large Molecules, *J. Comput. Chem.*, ***8***, 1016-1024 (1987).
2. C. E. Kundrot, J. W. Ponder and F. M. Richards, Algorithms for Calculating Excluded Volume and Its Derivatives as a Function of Molecular Conformation and Their Use in Energy Minimization, *J. Comput. Chem.*, ***12***, 402-409 (1991).
3. M. J. Dudek and J. W. Ponder, Accurate Modeling of the Intramolecular Electrostatic Energy of Proteins, *J. Comput. Chem.*, ***16***, 791-816 (1995).
4. Y. Kong and J. W. Ponder, Reaction Field Methods for Off-Center Multipoles, *J. Chem. Phys.*, ***107***, 481-492 (1997).
5. M. Dudek, K. Ramnarayan and J. W. Ponder, Protein Structure Prediction Using a Combination of Sequence Homology and Global Energy Minimization II. Energy Functions, *J. Comput. Chem.*, ***19***, 548-573 (1998).
6. R. V. Pappu, R. K. Hart and J. W. Ponder, Analysis and Application of Potential Energy Smoothing for Global Optimization, *J. Phys. Chem. B*, ***102***, 9725-9742 (1998).

Availability:	http://dasher.wustl.edu/tinker/
Version:	TINKER 3.9 of June 2001
Language:	Fortran-77 with common extensions, C translation via f2c available, Fortran-90 version under development
Lines of Code:	Approximately 118,000 including comments