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. Available potentials include Amber *ff*94, *ff*96, *ff*98 and *ff*99, *ff99SB*, *ff14SB*, *ff19SB*, CHARMM19, CHARMM22, CHARMM27, CHARMM36m, Dang, MM2, MM3, MMFF94, MMFF94s, OPLS-UA, OPLS-AA, OPLS-AA/L and our AMOEBA, AMOEBA+ and HIPPO polarizable atomic multipole models. Other force fields can be added via new parameter files, and some are currently under consideration.

The Tinker programs perform many functions: (1) energy minimization over Cartesian coordinates, torsional angles or rigid bodies via conjugate gradient, variable metric or truncated Newton methods, (2) molecular, stochastic and rigid body dynamics with periodic boundaries and temperature/pressure control, (3) multiple time step RESPA integration for efficient MD simulation, (4) Shake, Rattle and Settle for holonomic constraints, (5) normal mode vibrational analysis, (6) distance geometry with efficient random pairwise metrization, (7) build protein and nucleic acid structures from sequence, (8) detailed analysis of single point potential energies, (9) verification of analytical derivatives of potential functions, (10) fast analytical alpha shapes-based surface area and volume with derivatives, (11) location of conformational transition states, (12) potential energy surface search via conformation scanning, (13) global optimization via simulated annealing, Monte Carlo minimization and potential surface smoothing methods, (14) free energy calculations via Bennett acceptance ratio (BAR), free energy perturbation or weighted histogram analysis, (15) analysis and comparison of electrostatic potentials, (16) fit intra- and intermolecular potential parameters to structural and thermodynamic data.

Analytical Cartesian derivatives through the Hessian and analytical torsional gradients are available. Energy minimization and vibrational analysis can be performed in either Cartesian or torsional space. The user can define atom groups and compute scaled energies between or within groups. Atomic multipoles through the quadrupole and induced dipole polarization are implemented for AMOEBA and other advanced force fields, as well as simpler electrostatic models. Restraint potentials may be included in all calculation types, and partial structures can be frozen in position. The molecular volume and surface area as well as their derivatives are available. Both replicative and image boundary conditions are supported for all unit cell types including truncated octahedra and rhombic dodecahedra. Nonbonded interactions can use splined distance windows, Method of Lights or pair neighbor lists. Particle mesh Ewald (PME) is available for partial charges and polarizable atomic multipoles. Poisson-Boltmann electrostatic calculations are available through an interface to the APBS package. Various continuum solvation models, such as GB/SA, GK and PB, are implemented. User-defined potentials are easily added.

The central component 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 developers welcome contributions of new modules for Tinker and is willing to consult, and serve as a resource and distribution center for such efforts.

A complete Java GUI for Tinker, Force Field Explorer or FFE, is available as an adjunct to the basic Tinker. FFE is tightly integrated with the Tinker code via a socket mechanism, and can setup, launch and visualize Tinker calculations. FFE allows interactive use on a single machine, as well as connection to jobs running on a remote server.

The Tinker package is written in a portable extended Fortran 95 dialect that makes use of dynamic memory allocation. OpenMP directives parallelize selected CPU intensive calculations on shared-memory multiple core systems. Program control is via an optional keyword file. Auxiliary programs are provided to convert Protein Data Bank files to and from the Tinker formats. Tinker coordinate files are directly supported by the VMD, PyMOL and MOLDEN modeling packages. Tinker structures are also compatible with the ChemDraw and ChemOffice programs.

Selected References:

(1) Tinker 8: Software Tools for Molecular Design, J. A. Rackers, Z. Wang, C. Lu, M. L. Laury, L. Lagardere, M. J. Schnieders, J.-P. Piquemal, P. Ren and J.W. Ponder, *J. Chem. Theory Comput.*, **14**, 5273-5289 (2018).

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(3) AMOEBA Polarizable Atomic Multipole Force Field for Nucleic Acids, C. Zhang, C. Lu, Z. Jing, C. Wu, J.-P. Piquemal, J. W. Ponder and P. Ren, *J. Chem. Theory Comput.*, **14**, 2084-2108 (2018).

(4) Polarizable Atomic Multipole Water Model for Molecular Mechanics Simulation, P. Ren and J. W. Ponder, *J. Phys. Chem. B*, ***107,*** 5933-5947 (2003).

(5) Analysis and Application of Potential Energy Smoothing for Global Optimization, R. V. Pappu, R. K. Hart and J. W. Ponder, *J. Phys. Chem. B,* ***102***, 9725-9742 (1998).

(6) Implicit Solvents for the Polarizable Atomic Multipole AMOEBA Force, R. A. Corrigan, G. Qi, A. C. Thiel, J. R. Lynn, B. D. Walker, T. L. Cassvant, L. Lagardere, J.-P. Piquemal, J. W. Ponder, P. Ren and M. J. Schnieders, *J. Chem. Theory Comput.*, **17**, 2323-2341 (2021).

(7) An Efficient Newton-like Method for Molecular Mechanics Energy Minimization of Large Molecules, J. W. Ponder and F. M. Richards, *J. Comput. Chem.,* ***8***, 1016-1024 (1987).

Availability:	Source Code at https://github.com/TinkerTools/Tinker/ Executables and Source at https://dasher.wustl.edu/tinker/
Version:	Tinker 26.1 and Force Field Explorer 26.1 of February 2026
Language:	Fortran 95 with common extensions and some C; FFE GUI in Java with Java 3D extensions
Lines of Code:	286,000 in Tinker Package (Fortran 95 and some C) 30,000 in Force Field Explorer (Java and some C)