

Dynamics

EASILY INVESTIGATE AND VISUALIZE MOLECULAR STRUCTURE AND MOBILITY



Molecular dynamics simulations allow scientists to simulate molecular motion, explore conformational space, and provide insight into molecular structure and mobility. Molecular dynamics can generate an ensemble of conformers for a particular structure, or follow the evolution of a system over time. Molecular dynamics has been shown to be more efficient than Monte Carlo methods for simulation of complex molecules. Dynamics provides a number of techniques for producing such ensembles, as well as the graphical tools required for organizing and analyzing the resulting structures.

Dynamics' flexible setup, visualization, and statistical analysis tools make it a valuable addition to the SYBYL[®] expert molecular modeling environment.

Features

- Intuitive graphical interface for setup and results analysis
- User control of simulation parameters
- Extensive documentation, including detailed theory description and tips for better calculations
- Multiple options for solvent treatment
- Multiple methods of simulated annealing
- Tight integration with the Molecular Spreadsheet[™] for easy, detailed analysis

Easily Configurable

Dynamics runs are organized into intervals. While the settings are constant within a given interval, the number of intervals in a single run is virtually unlimited. The Dynamics default interval parameters are appropriate for most situations, but all are completely user-configurable.

Customizable Options

- Force field used for energy calculations (Tripos, AMBER, MM3[™], MMFF94....)
- Charge calculation method
- Dielectric constant treatment
- Simulation length
- Temperature
- Solvent treatment - droplet or periodic boundary conditions

Superior Statistical Analysis

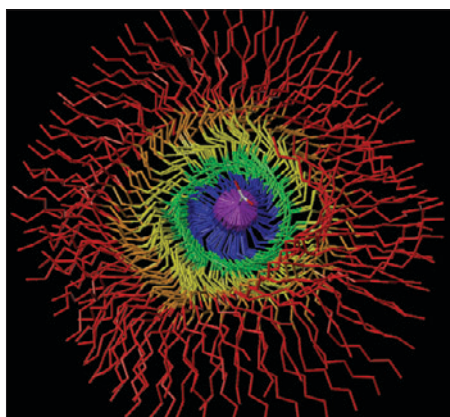
The results of Dynamics simulations are organized in the Molecular Spreadsheet, a powerful and intuitive tool for data analysis. As a spreadsheet, all the traditional statistical tools are available, including searching, sorting, filtering, and graphing. Data specific to analyzing dynamics simulations, such as kinetic energy, deformation, RMS movement, radius of gyration and others can also be calculated. User-defined columns can also be included. Graphs created from spreadsheet data are hyperlinked to the spreadsheet to provide convenient switching between graphical and tabular displays. The spreadsheet data can be exported to a file, printer or an HTML table.

Create Populations of Low Energy Structures

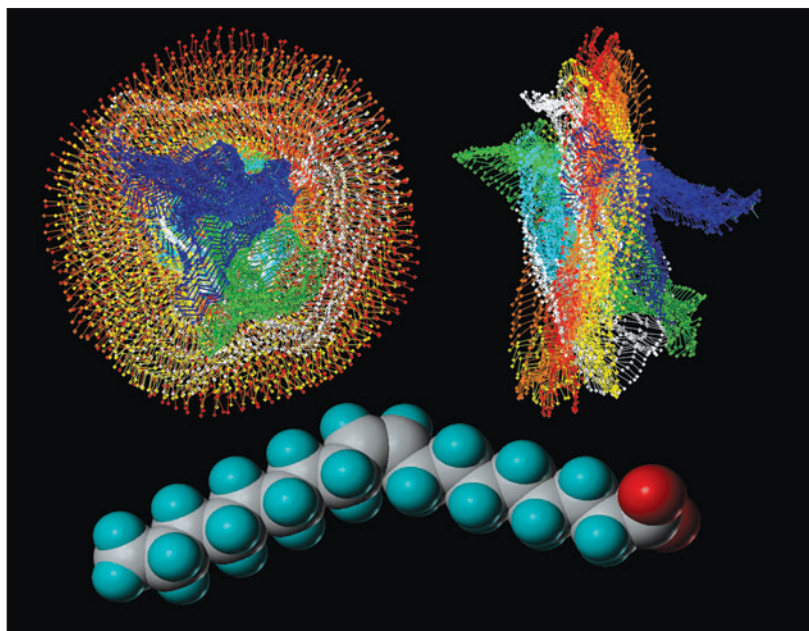
A special case of Dynamics, simulated annealing, is used to generate a number of different low energy conformations for a molecular structure, starting from a molecular model, crude X-ray, or NMR structure. In simulated annealing, the temperature of the system is cycled over time with the goal of widely sampling conformational space. Higher temperatures allow the system to overcome torsional and conformational barriers, and slow cooling brings the system back to a stable state. Repeating the cycle many times and collecting the low energy structures in the Molecular Spreadsheet results in a set of low energy conformations.

Calculate Macroscopic Properties

Classical statistical mechanics relate the microscopic features of a system to its macroscopic state functions. This can be done by randomly generating a large number of configurations for a particular system (ensemble). This ensemble is then used to calculate information about average structural quantities and values of state functions such as pressure, volume, energy, entropy, and temperature. With Dynamics, the ensemble consists of frames from a dynamics simulation. Average values of interesting macroscopic properties can be easily calculated from tables created from dynamics history files.



Radius of Gyration creates a "chrysanthemum" - a fatty acid is tethered at the carboxylate end of the molecule and followed for 50 picoseconds in a Dynamics run. The molecule is color-coded by the amount of local translation of the atoms.



The fatty acid shown at the bottom in CPK mode is used to study molecular motion. Positions of the heavy atoms are plotted as a sweep graph during a 500 picosecond dynamics simulation. Different colors highlight different phases of the simulation.

- **GASP™** for developing pharmacophore hypotheses using full conformational flexibility.
- **ProTable™** for analyzing and assessing the quality of protein structures.
- **SiteID™** for finding and visualizing protein binding sites.
- **Tuplets™** for pharmacophore-based virtual screening.

References

1. Northrup, S. H.; McCammon, J.A. *Biopolymers* **1980**, *19*, 1001.

Appropriate boundary conditions allow modeling of the important ensembles:

- microcanonical (constant volume and energy)
- canonical (constant temperature and volume)
- isobaric (constant pressure and temperature)

Hardware and Software Requirements

Dynamics is available in the Advanced Computation module and requires a separate Advanced Computation license. Dynamics and Advanced Computation run on workstations operating under IRIX® (SGI®) or Linux® (x86).

Complementary Software

- **Advanced Computation** for exploring the conformational properties of compounds.
- **AMPAC™** for calculating transition states and spectral properties using semiempirical quantum mechanical methods.
- **Biopolymer** for predicting, building, and visualizing macromolecular 3D structure.
- **Concord®** for generating accurate 3D coordinates.
- **Confort™** for generating sets of diverse, low energy conformers.
- **DISCOtech™** for elucidating pharmacophore models from precalculated conformers.



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