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Lab VI: Advanced SASSIE-web

Torsion Angle Monte Carlo (BETA)

Performs molecular Monte Carlo simulations on protein, and B-DNA. Move sets for single-stranded nucleic acids, carbohydrates and polymers are in development.

Accessibility

The Torsion Angle Monte Carlo module is accessible from the Beta section of the main menu.

While we test our prototypes, this module will remain in "Beta", and may not always be accessible and/or stable as new features are added and tested. Refer to the SASSIE-web Google Group for support, watch the GitHub page for current developments, and use the feedback mechanism to report bugs and feature requests.

Basic Usage

The purpose of the module is perform a molecular simulation by sampling torsion angles. Facilities to incorporate new torsion move-sets are available for developers. Currently, backbone protein, double-stranded nucleic acid are working. One can combine multiple move-set sampling in a single molecular simulation.

Notes

- The input definitions flexible regions differs from the Monomer Monte Carlo and Complex Monte Carlo modules. This difference enables additional types of move sets and complicated topologies often present in hybrid systems. When defining the inputs for simple systems, this new method may require slightly more complicated definitions. An advantage of the new system is that the input definitions for complicated systems are much simpler than the previous method. Additionally, the new input system follows the notation used in VMD (excluding shortcuts and generic options such as 'backbone', 'sidechain', 'nucleic', 'water', 'protein', etc). This allows one to copy-and-paste input

definition between VMD and TAMC to verify region definitions.

- The starting structure must be a complete structure without missing residues. Atom and residue naming must be compatible with those defined in the CHARMM force field. See the pages on Structures and Force Fields and PDB Scan for further details.
- A PSF topology file of the entire system is required to use this module.
- Only protein and B-DNA move sets are incorporated. Your system can include other molecular types, but these must be part of the rigid pre or post regions. No internal Monte Carlo sampling can be done on them.
- Several standard and exploratory implicit solvent models will be available for use.
- The output file format is DCD since in most cases many structures are generated. There is no option to save the output files in PDB format. One can use Extract Utilities to convert DCD files to multi-frame PDB files.
- Structures are generated by Metropolis Monte Carlo sampling of molecular structures. Energetics of protein backbone torsion angles are determined using CHARMM force field parameters. Energetics of B-DNA moves are discussed further in this publication.
- Typically, between 10,000 to 50,000 structures are required to sample adequate configuration space for most problems.
- Parameters are supplied to help guide the Monte Carlo sampling such as temperature, control of single move angle sampling per region, and directed Monte Carlo options to guide the radius of gyration (Rg) to a user supplied value.
- Several options are offered to check for atomic overlap: heavy atoms, all, backbone, and atom name. 1 If one chooses the atom name option, then the user will be prompted to supply an atom name that should exist in all residues and a overlap distance cutoff value. Other options set the cutoff distance automatically.
- In Advanced Input, options are provided to reject structures based on Rg value, position of atoms in the Z-direction, and via atomic constraints provided as a list in a text file (described in the page on Using Atomic Constraints). These options are not mutually exclusive and can be used in the same run as needed.
- Typical workflows involve generating an ensemble of structures using this module, then energy minimizing the ensemble using Energy Minimization, then calculating scattering from the ensemble using modules in Tools, and finaly comparing results to experimental data using modules in Analyze.
- In many situations, multiple runs need to be carried out to find structures that cover configuration space and have scattering profiles that are in agreement with experimental data. One can use Merge Utilties to combine both the structures (DCD files) and SAS profiles into a single new DCD file and SAS directory, where the SAS profiles will be

renumbered to correspond with the frames in the new DCD file. Please note that for large systems, the combined DCD files may become excessively large, in which case a more custom approach must be taken.

- To simulate long random coil regions, usually at the ends of globular proteins, it is often neccessary to sub-sample accepted structures as adjacent structures can be correlated. To obtain adequate power-law scaling, one can sub-sample a trajectory using the periodic option of Extract Utitilies.

Demonstration

	Protein Backbone	B-DNA	Single-Stranded Nucleic Acid Backbone	Isopeptide Bond
HIV-1 Gag Matrix Protein	X			
Linear strand of B-DNA		X		

Exercises

The following table links examples using the each type of flexible region currently available. Please work through each of these examples noting the differences between the different move types. The Torsion Angle Monte Carlo documentation contains additional examples, and will be updated as future move sets are added.

	Protein Backbone	B-DNA	Single-Stranded Nucleic Acid Backbone	Isopeptide Bond
Nucleosome Core Particle	X	X		
rpoS mRNA			X	
Diubiquitin				X
Tetranucleosome	X	X		

Limitations

The program is written so that linear polymers of proteins, single-stranded nucleic acids, and B-DNA are simulated over a specific selection of residues in a single direction.

Reference(s) and Citations

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1. Linkage-specific conformational ensembles of non-canonical polyubiquitin chains, C. A. Castaneda, J. E. Curtis, S. Krueger, D. Fushman, Phys. Chem. Chem. Phys., 18, 5771-88 (2016).
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