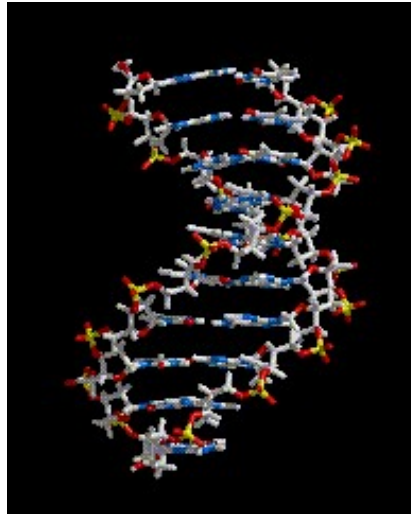


DNA polyA–polyT decamer tutorial

1) Introduction



Pictured above is the average structure from a 1 nanosecond molecular dynamics simulation of a 10 base pair poly(A)–poly(T) DNA duplex. The calculation was run in explicit solvent using periodic boundaries and the particle mesh Ewald method of treating long range electrostatics. The average structure was generated using *ptraj* by RMS fitting all of the DNA atoms in 1,000 snapshots at 1 ps intervals and then averaging the coordinates.

The purpose of this tutorial is to demonstrate how to use the tools provided with the AMBER suite of molecular dynamics (MD) programs to set up a standard decamer poly(A)–poly(T) duplex DNA model structure, run MD simulations using this structure and then analyse the results. This tutorial is based on version 8.0 of the AMBER software.

In this tutorial we will first figure out how to generate a starting structure and then use this structure to construct the necessary input files required for running *sander*, the main molecular dynamics engine supplied with AMBER. The basic files required for running a simulation using *sander* (using their default filenames) are:

- ◆ `prmtop` – an file containing a description of the molecular topology and the necessary force field parameters.
- ◆ `inpcrd` (or a `restrt` from a previous run) – a file containing a description of the atom coordinates and optionally the velocities and current periodic box dimensions.
- ◆ `mdin` – the *sander* input file consisting of a series of namelists and control variables than determine the options and type of simulation to be run.

After we have constructed the required `prmtop` and `inpcrd` files, for both *in vacuo* and explicitly solvated systems, we will then run *sander* to perform minimisation followed by molecular dynamics and eventually get to the point where we can create the picture shown above.

Since running these calculations with explicit solvent can be rather expensive, we will also use some models that include solvent implicitly (i.e. a gas phase calculation with solvent effects added implicitly). These types of simulations are more tractable to the timescale of this tutorial and can be run in a few minutes to give a picture of the system dynamics.

For the various simulations this tutorial will provide a description of a suitable approach to minimisation and equilibration of the system and will then discuss performing "production" molecular dynamics runs.

All of the simulations in explicit solvent will be run using the *particle mesh Ewald* (PME) [J. Chem. Phys. **103**, 8577–8593 (1995)] method for treating long range electrostatics, implemented within *sander 8.0*. Although information is provided on how to run these simulations yourself they can take a considerable amount time to run (> 1 hour) and so trajectories are provided that will allow you to continue with the analysis section of the tutorial without waiting for the explicit solvent simulations to finish.

The approximate ordering of this tutorial is as follows:

1. Create the `prmtop` and `inpcrd` files: This is a description of how to generate the initial structure and set up the molecular topology/parameter and coordinate files necessary for performing minimisation or dynamics with *sander*.
2. An introduction to minimisation and molecular dynamics: Run short MD simulations *in-vacuo*. Perform basic analysis such as calculating the root-mean-squared deviations (RMSd) and plotting various energy terms as a function of time. Visualising the results with VMD.
3. Minimisation and molecular dynamics in implicit solvent: Setting up and running equilibration and production minimisation and molecular dynamics simulations for our DNA model using the Born implicit solvent model.
4. Minimisation and molecular dynamics in explicit solvent: Setting up and running equilibration and production minimisation and molecular dynamics simulations for our DNA model using TIP3P explicit water.

Throughout this tutorial filenames and command line switches will be written in *courier* or an equivalent monospace font while program names such as *sander* will be written in the same font but *italicised*. Input files will be coloured in **red** and output files in **green**.

The tutorial will introduce the AMBER programs/tools required to set-up, minimise, perform molecular dynamics on, and partially analyse the results for a 10-mer polyA–polyT DNA duplex. The programs that will be introduced during the course of this tutorial include:

- **LEaP**: A program that reads in force field, topology and coordinate information and produces the files necessary for production calculations (i.e. minimisation, molecular dynamics, analysis, ...). There are two versions of this program, a graphical interface called *xleap* and a terminal interface called *tleap*. Since we want to "see" graphical representations of our models as we build them, this tutorial will use *xleap*.
- *sander*: The main minimisation and molecular dynamics engine. We will highlight the generalised Born implicit solvent model and particle mesh Ewald simulations in periodic boundary simulations.
- *ptraj*: Trajectory analysis program.

In addition to these programs, pointers will also be provided to other programs for molecular visualisation and graph plotting (not supplied with AMBER).

A summary page containing links to all of the files referenced in each chapter of this tutorial is available [here](#). This is particularly useful if you intend to print this tutorial and follow it on paper and want easy access to the various input and output files that are linked to.