A Tutorial for TIPSI, and How to Assemble Paths

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Introduction

Who am I?

- Dylan Goldsborough
- Student at the computational science master
- Attended the course on biomolecular simulation
- Enjoyed figuring out TIPSI in class
- Did a project to write a tutorial that introduces TIPSI over the past months!

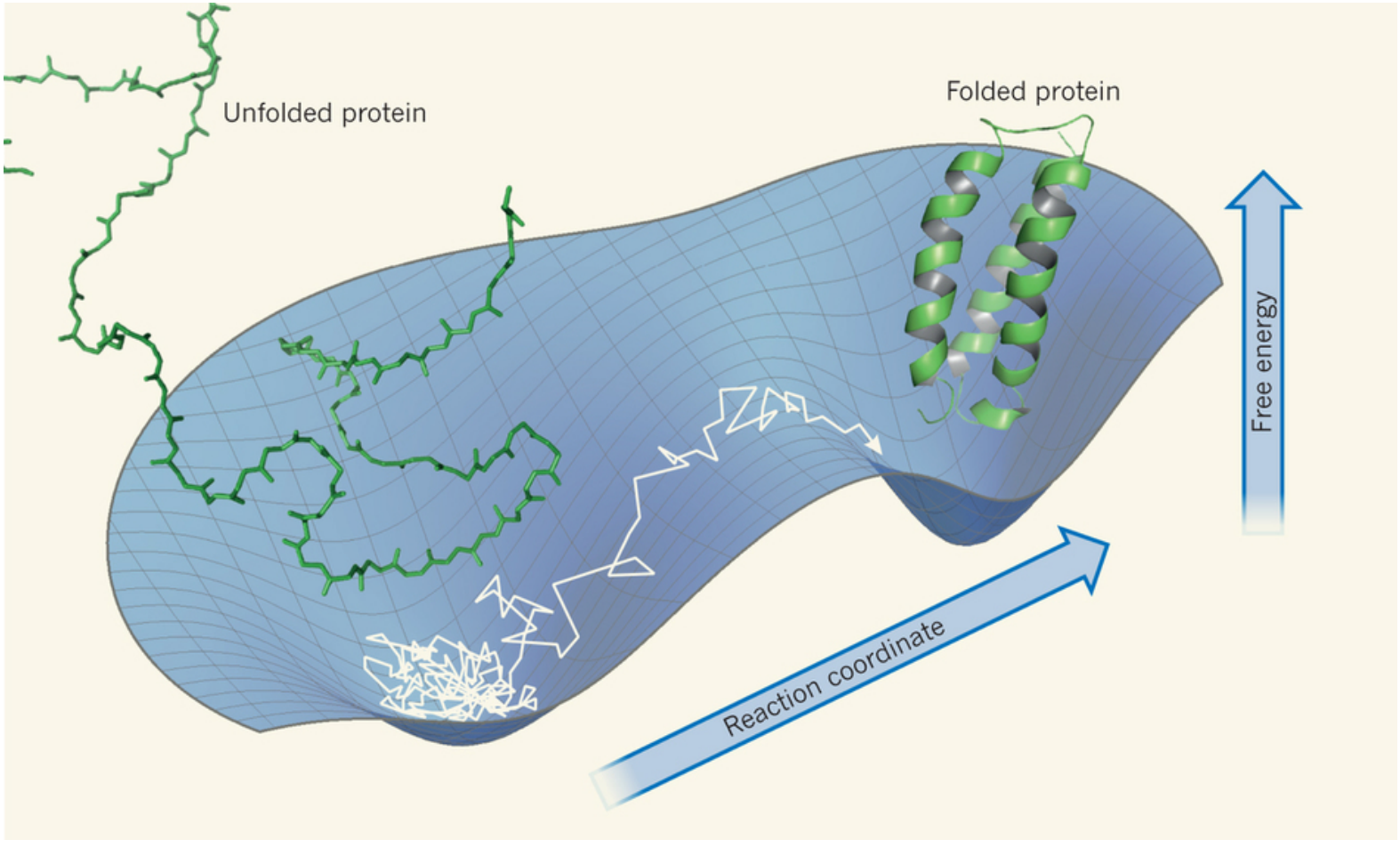
Outline

In this presentation I will:

- Give a brief recap of TPS
- Outline my contribution
- Discuss both the examples the tutorial offers
- Discuss the additional documentation

What is TPS?

Find trajectories of rare transitions:



(Chung and Eaton, 2013)

What is TPS?

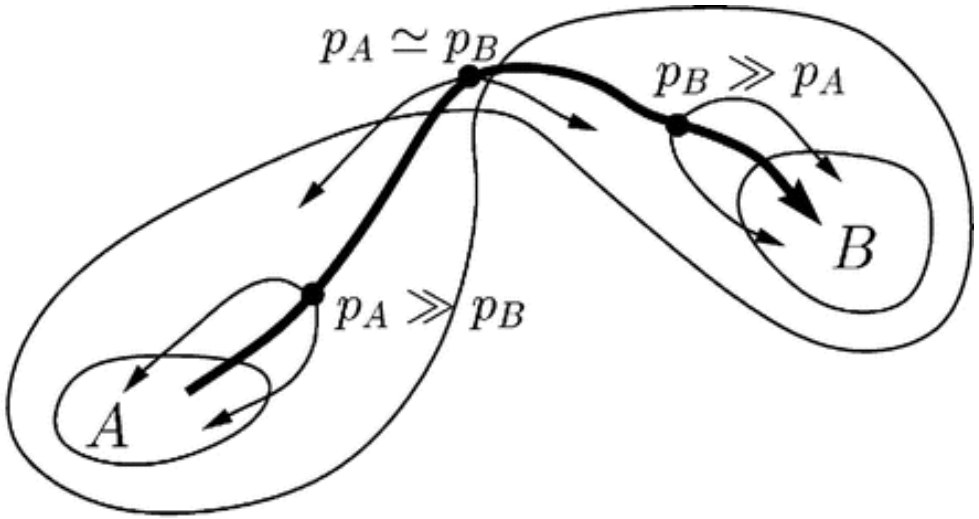
Algorithm:

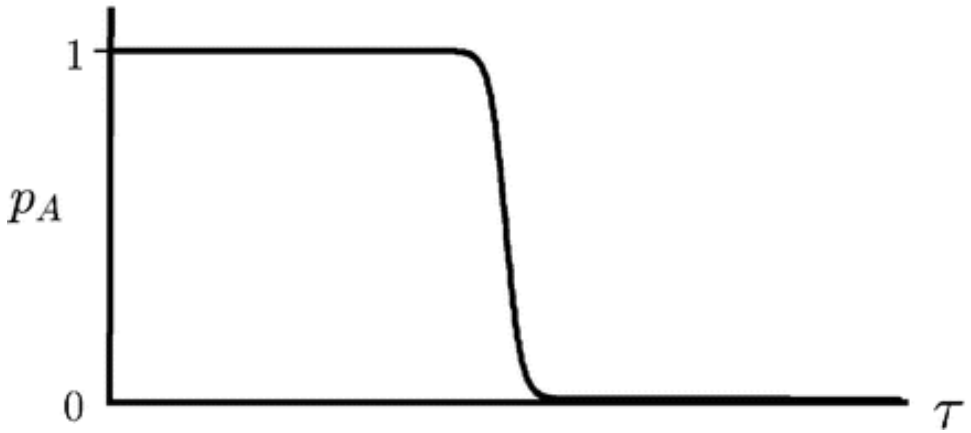
- Take existing path
- Choose random time slice t
- Change momenta slightly at t
- Integrate forward or backward in time to create new path
- Accept if state A or B is reached, otherwise reject and retain old path

Important: we assume that both states are stable, and that we have a transition trajectory ready!

What is TPS?

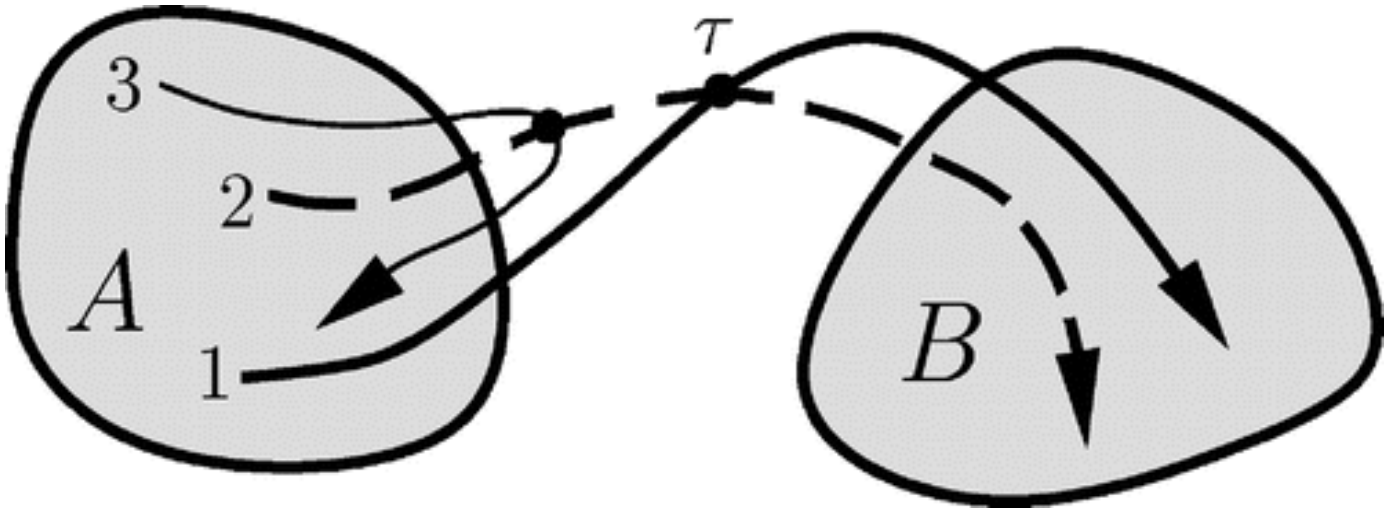
Committor probability:





What is TPS?

Shooting move:



Accepted if state A or B is reached.
(Bolhuis, 2002)

What is TIPSI?

TIPSI is a script by Tsjerk Wassenaar, which:

- Adaptation of a Perl script by Jarek Juraszek
- Written in Python
- It relies on GROMACS version 4.5.4 (a molecular dynamics engine)
- Does random shooting moves forward and backward
- Reverses time for backward shooting
- A "molecular calculator"

Contributions

I made several minor contributions to this project:

- Bash implementation to assemble paths
- Python script to analyze the paths
- Tutorial with a Python tool

Resulted in some surprises that had to be dealt with...

Assembling paths

TIPSI only saves the shooting moves to save space, so to view and analyze the transitions we need to assemble them.

The problem:

- TIPSI outputs shooting moves only
- Instructions on how the paths are made in `dat`-files
- Backward shooting moves are the wrong way around
- Negative timestamps

Result: assembling the paths is a minor nightmare...

TIPSI output

Example of Tipsi output:

```
DIR: tipsi-tutorial/output/jobname/DATA/9/1

9-1-BW.cpt   9-1-BW.out   9-1-BW.xtc   DONE
9-1-BW.dat   9-1-BW.top   9-1.dat      md-prod.mdp
9-1-BW.edr   9-1-BW.tpr   ACCEPTED     PARENT
9-1-BW.err   9-1-BW.trr   CMD          parent.dat
```

TIPSI output

```
REGEX: '[A-I]\s+(\S+)\s+[F-T][a-z]+\s+(\S+)\s+'

state    time      stop     file
A        -1325.0   True     ../../9/1/9-1-BW.trr
I        -1305.0   False    ../../9/1/9-1-BW.trr
I        -1285.0   False    ../../9/1/9-1-BW.trr
I        -1265.0   False    ../../9/1/9-1-BW.trr
...
I        465.0     False    ../../6/4/6-4-FW.trr
I        485.0     False    ../../6/4/6-4-FW.trr
I        505.0     False    ../../6/4/6-4-FW.trr
B        525.0     True     ../../6/4/6-4-FW.trr
```

Assembling paths

The solution:

- Bashscripts that searches for directories with `ACCEPTED`-file
- Scans `dat`-file using regular expressions
- Overwrites timestamps
- Creates each path by dumping and appending single frames
- Stores some metainformation in a `csv`-file

Takes a while to dump frames for long trajectories...

Metainformation paths

We can do some nice things with the metainformation, I wrote a script that:

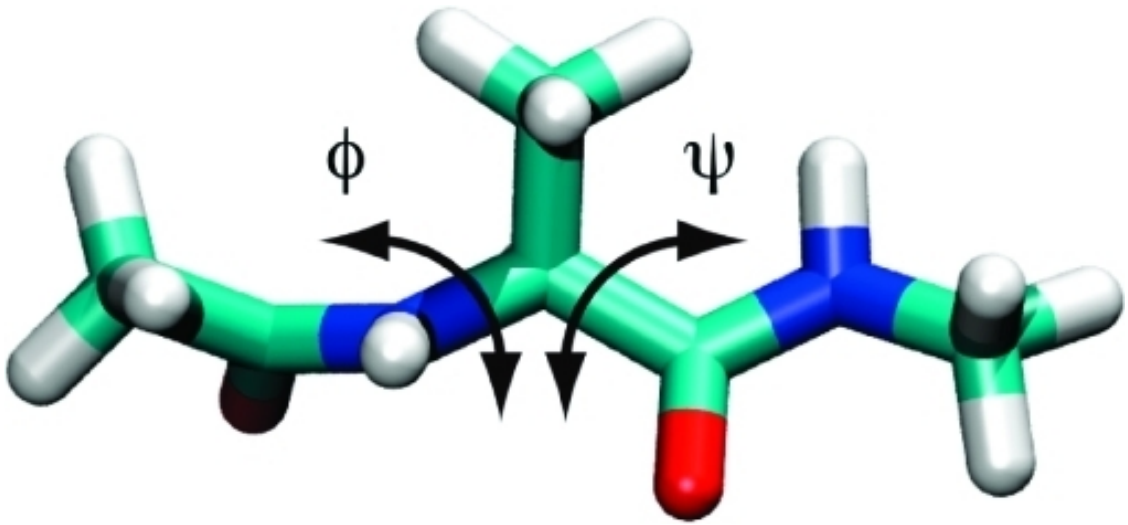
- Finds the average path length
- Finds the number of decorrelated groups of paths
- Ratio of FW:BW shooting moves
- Draws a tree of all shooting moves

Alanine Dipeptide

Our first example is **alanine dipeptide**:

- Extremely fast to run
- Very simple to understand, with simple order parameters (dihedrals)
- Has a nice transition between two distinct states
- Common example to use

Alanine Dipeptide



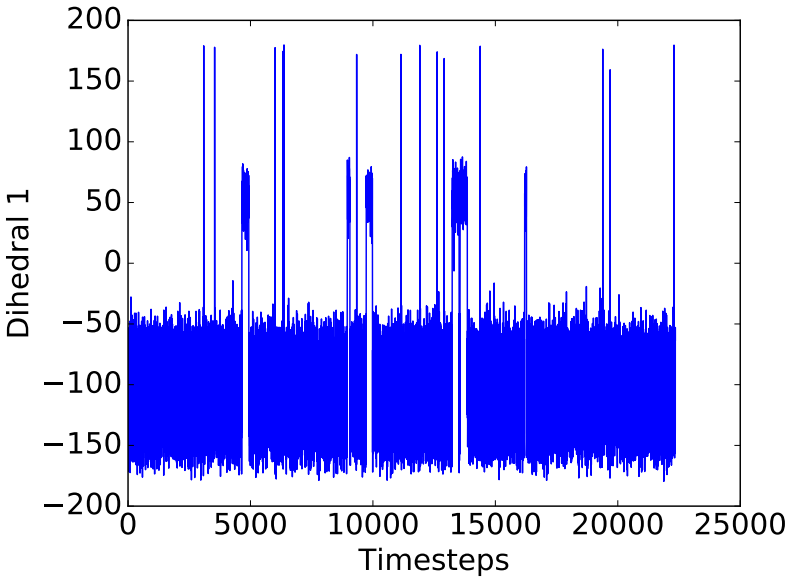
Preparing for TIPSI

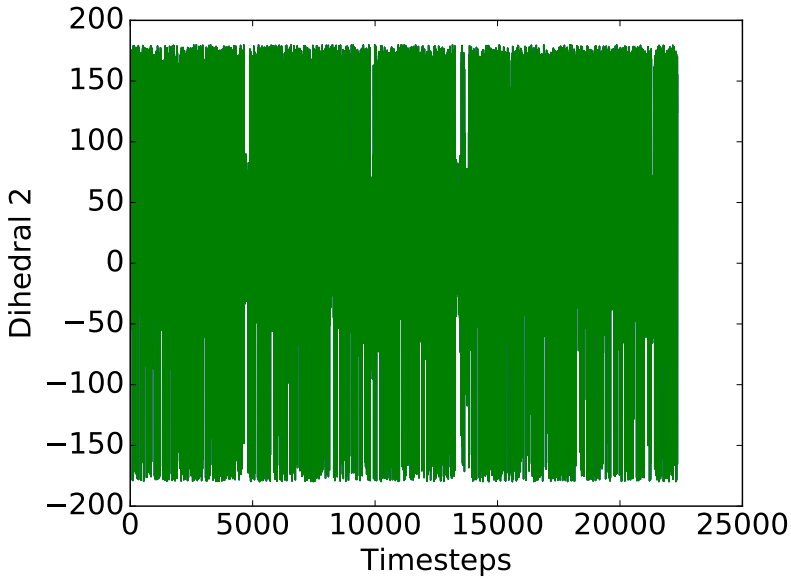
In this example we do everything from scratch:

- Start with pdb-file (defines the structure) and MD settings
- We prepare make a periodic system with a solvent
- We do energy minimization followed by a constrained MD run
- We do runs at room temperature and high temperature

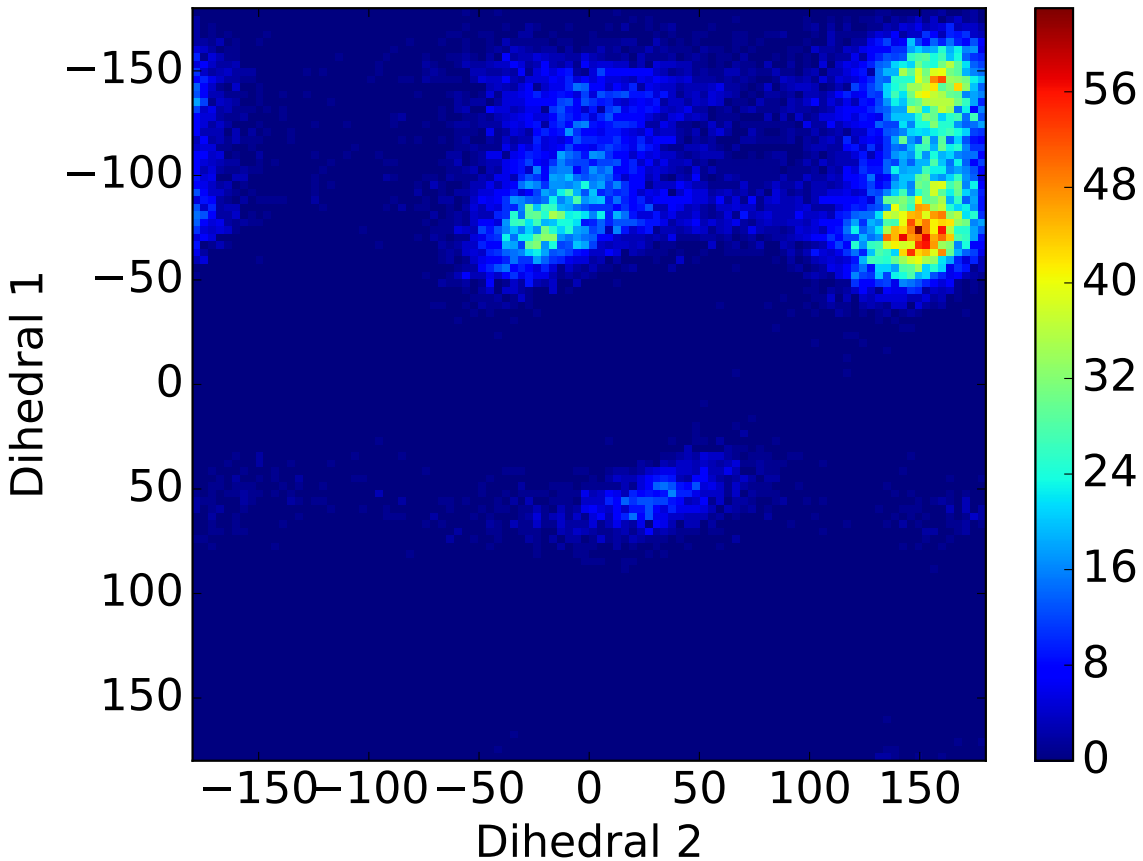
We look at the order parameters in the run using a Python script and GROMACS commands.

Defining the stable states





Defining the stable states



Running TIPSI

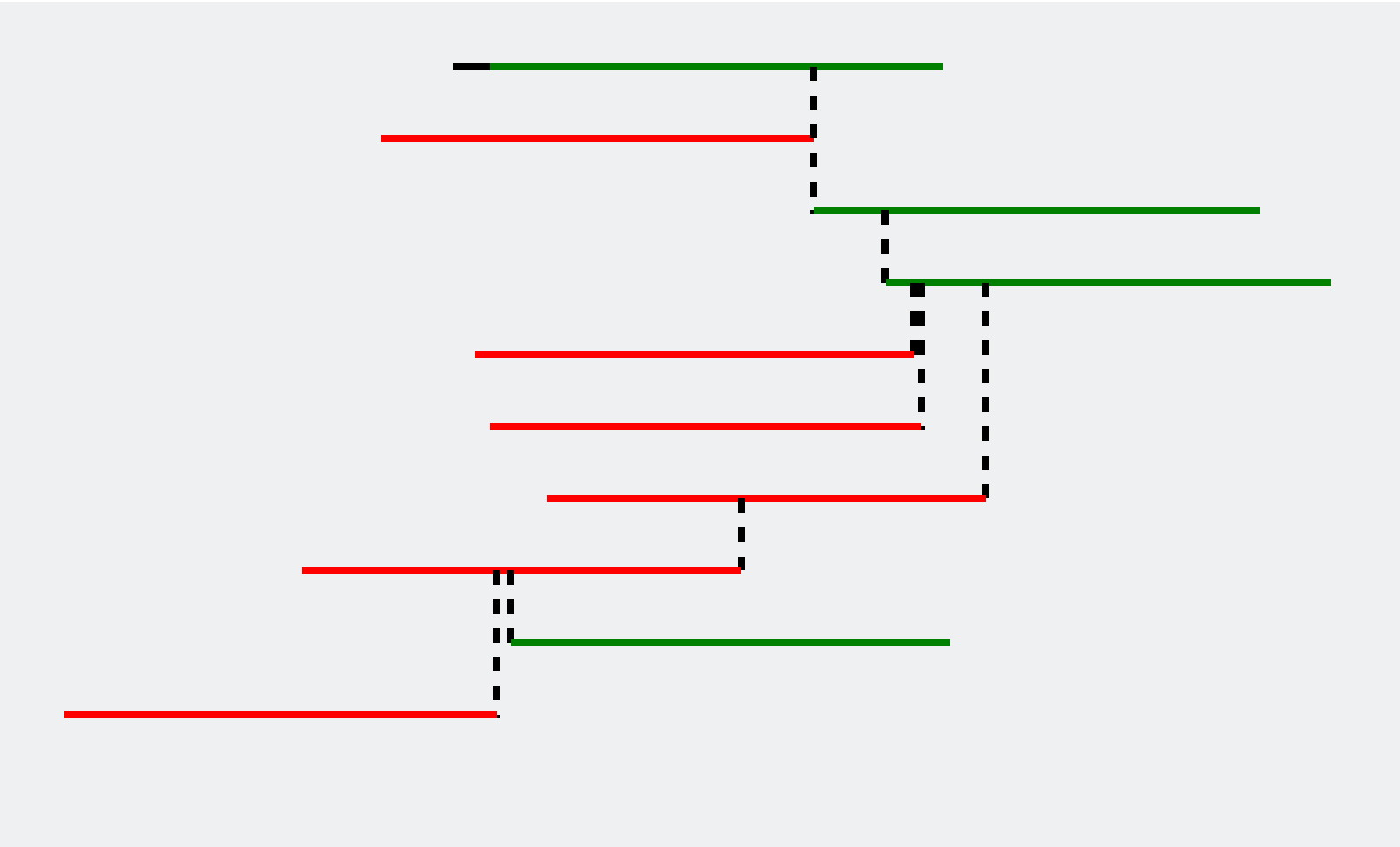
```
maxframes   = 2000

par dh1   = dihdeg(frame$Dihedral1)
par dh2   = dihdeg(frame$Dihedral2)

state A = (-150 < dh1 & dh1 < -50
         & 120 < dh2 & dh2 < 180)
state B = (-100 < dh1 & dh1 < -50
         & -50 < dh2 & dh2 < 20)

interface I = (!A) & (!B)
```

Analyzing TIPSI

I appended the bashscript to the end of the job, so that it puts all paths and the metadata in the `output/DATA` directory, now we can take a look at the trajectory in VMD!
We find that:

- Average length is 136.4 frames
- FW/BW ratio is 0.4
- Number of decorrelated groups of paths is 2

Analyzing TIPSI



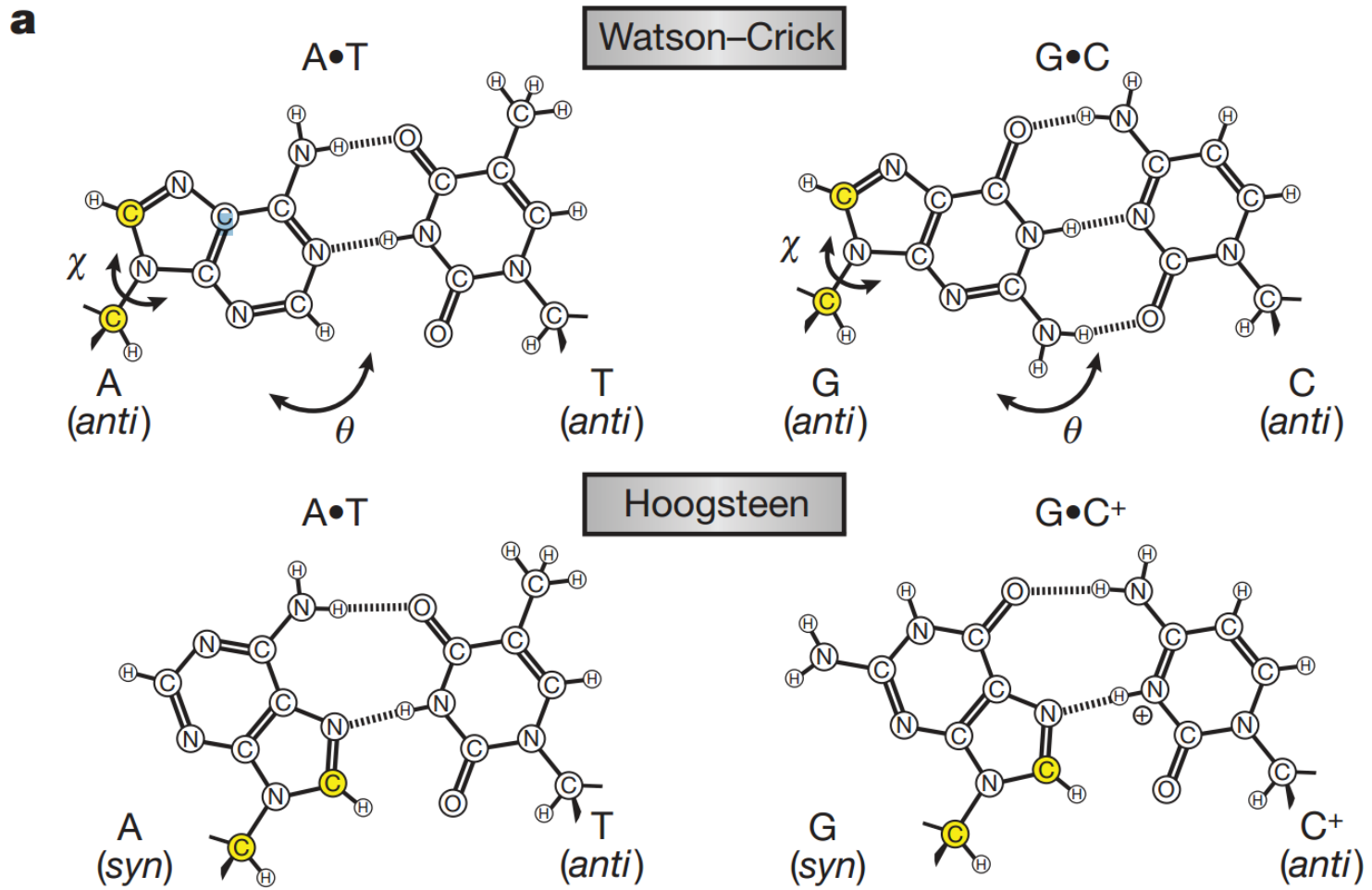
DNA baseroll

Second example is the DNA baseroll:

- Project by Jocelyne Vreede and David Swenson
- Concerns the transition from the WC- to the HG-pairing
- An actual rare event (microsecond range), unlike example 1

Metadynamics simulation has been done, so there is a trajectory available that contains the transition!

DNA baseroll



Preparing for TIPSI

In this example we start with a trajectory and state definitions:

- We import the custom topology
- We create a `tpr`-file (containing the simulation settings) to suit our MD-needs
- We set up a parameter file that include the state definitions (H-bonds)
- We run TIPSI with this `tpr` and the provided trajectory

We look at the order parameters in the run using a Python script and GROMACS commands.

Analyzing TIPSI

(Same slide as with dipeptala, when carbon is up again...)

Cheatsheets

As an appendix, I included:

- A Linux cheatsheet, for students who are unfamiliar
- A GROMACS cheatsheet (which I caught myself use often too)
- A TIPSI cheatsheet

The last adresses the documentation problem with TIPSI.

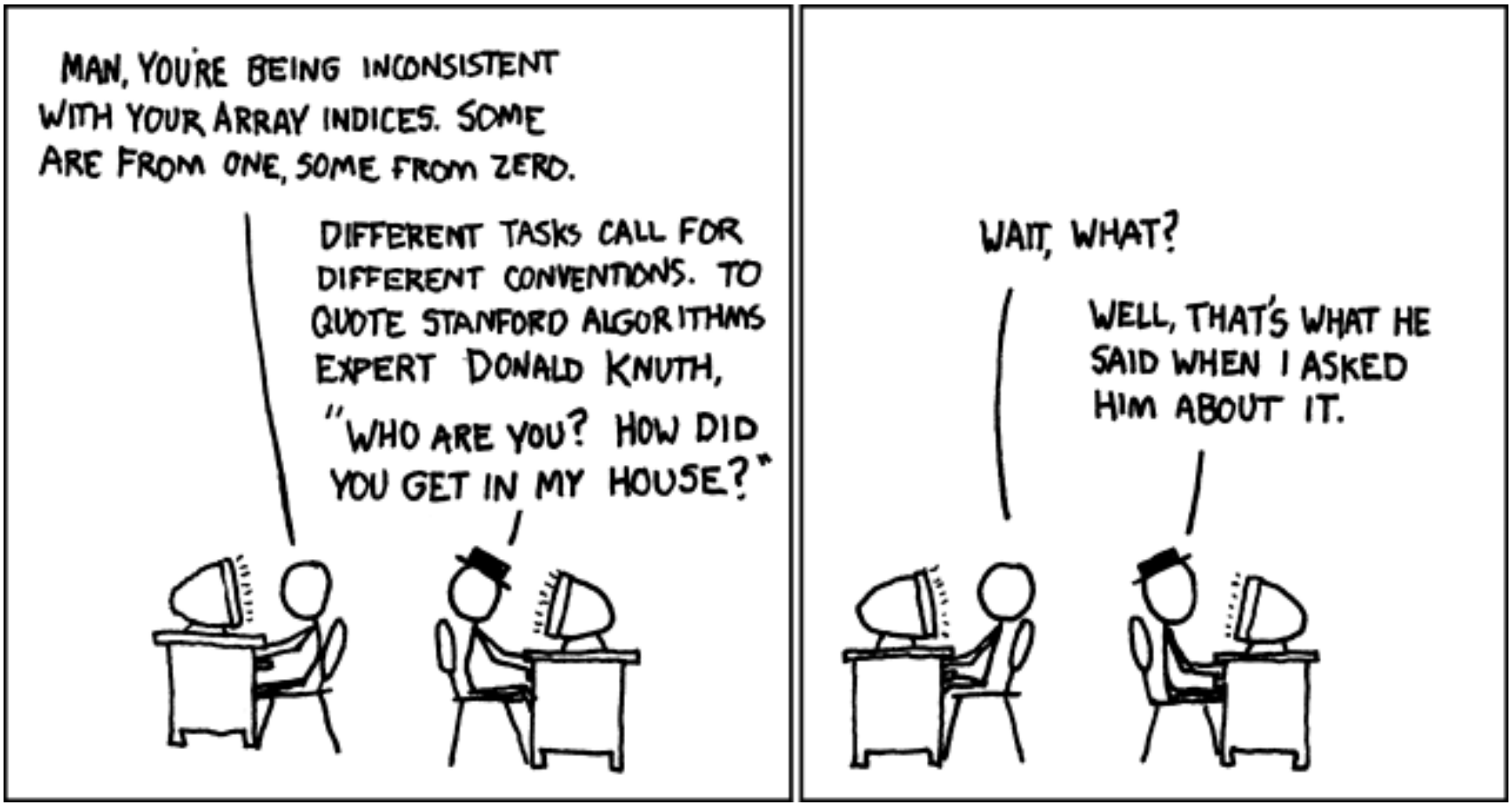
Cheatsheets

TIPSI cheatsheet includes:

- How to set up a parameter file
- All calculator options
- Several ways to define groups of atoms
  - Numpy arrays
  - Groups from GROMACS `ndx`-files (defines groups of atoms by their number)

There are **indexing problems**...

Relevant XKCD



Running TIPSI

Calculator options are:

- `com`: center of mass
- `dist`: distance (several options)
- `angle`: angle of 3 atoms
- `dihrad`/`dihdeg`: dihedral in rads/degrees
- `rgyr`: radius of gyration, incompatible with GROMACS
- `rmsd`: root-mean-square-deviation
- `hbonds`: number of hydrogen bonds, specific or non-specific

Summary

- I wrote a tutorial for students/people interested in TIPSI with a fast and uninteresting example, and a more computationally demanding but actually interesting example
- Added a bash script that finishes the output to make it fit for further analysis
- Added a basic script that helps understand the shooting moves made
- Compiled all calculator options, and how to set up a parameter file for TIPSI

Future changes?

There might be some things to change down the line:

- Include OPS as an analysis tool (no time now, and still being developed)
- Append to the possibilities in the parameter file (non-calculator options)
- Any other changes...

The project is on GIT and should be public:
`https://github.com/dgoldsb/tipsitutorial.git`