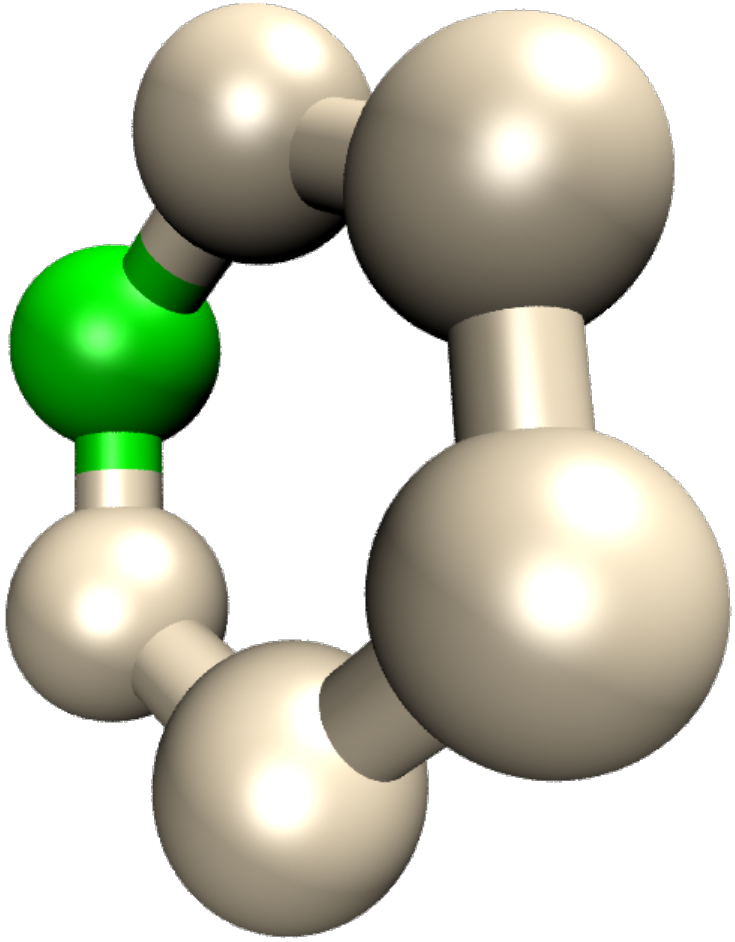
Molecular Simulation with OpenMM Zephyr



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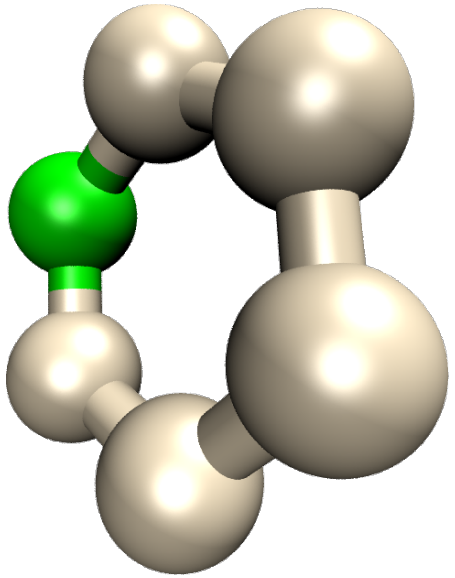
What is OpenMM Zephyr?

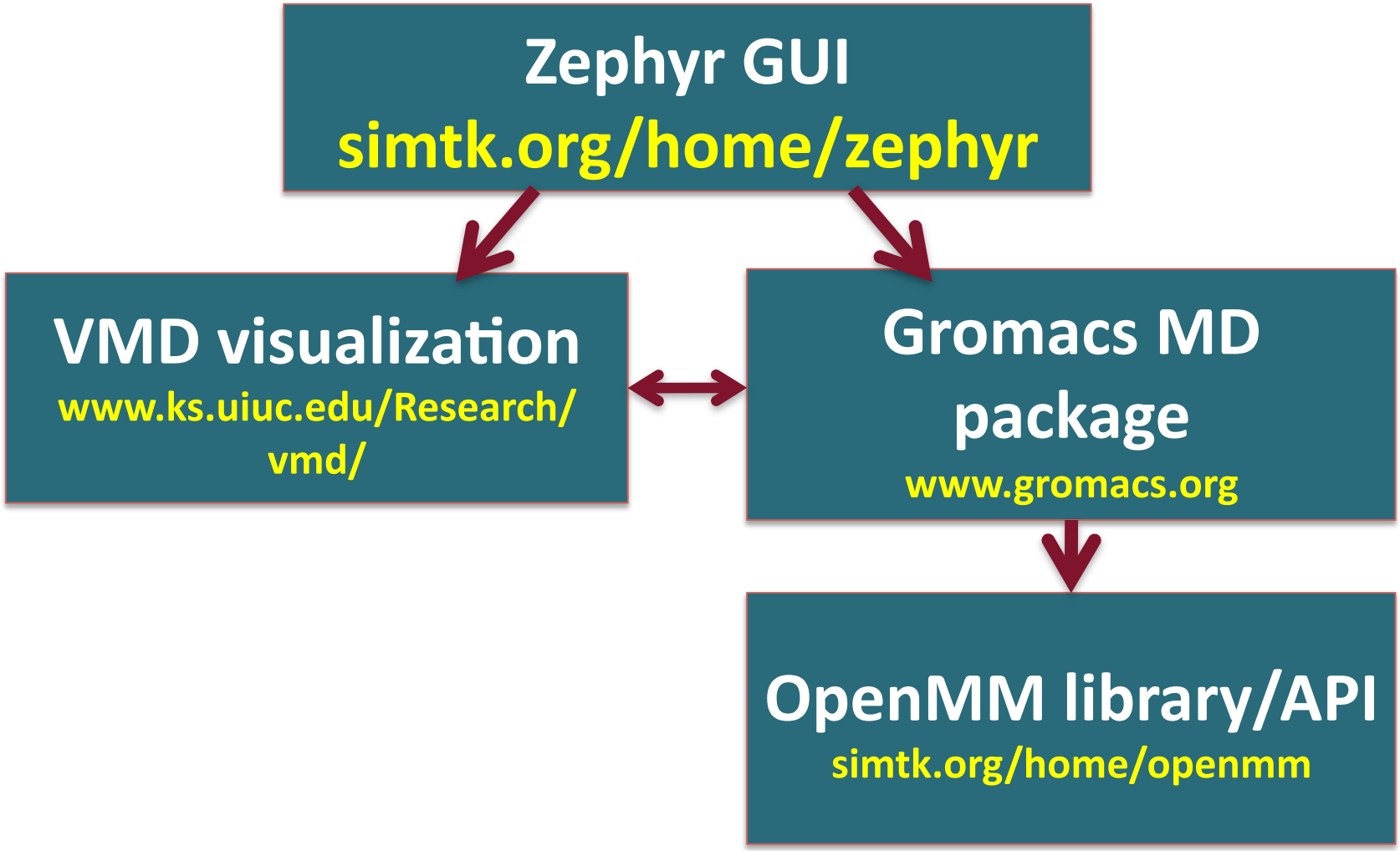
- Graphical user interface for running accelerated molecular dynamics simulations on high performance computer architectures, e.g., graphics processing cards (GPUs)

- Automates running of molecular dynamics programs, e.g., gromacs

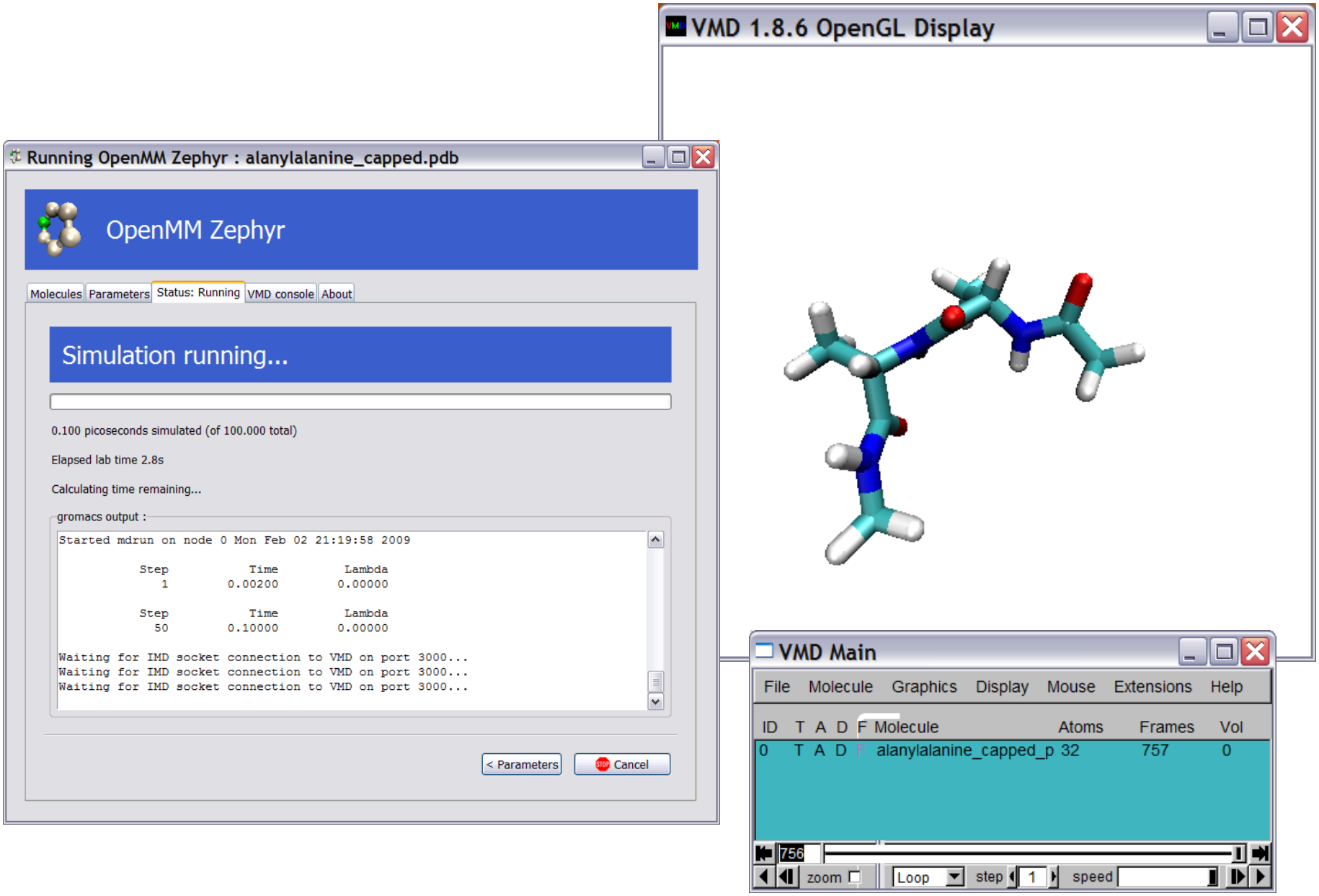
- Vision of OpenMM Zephyr being a learning tool



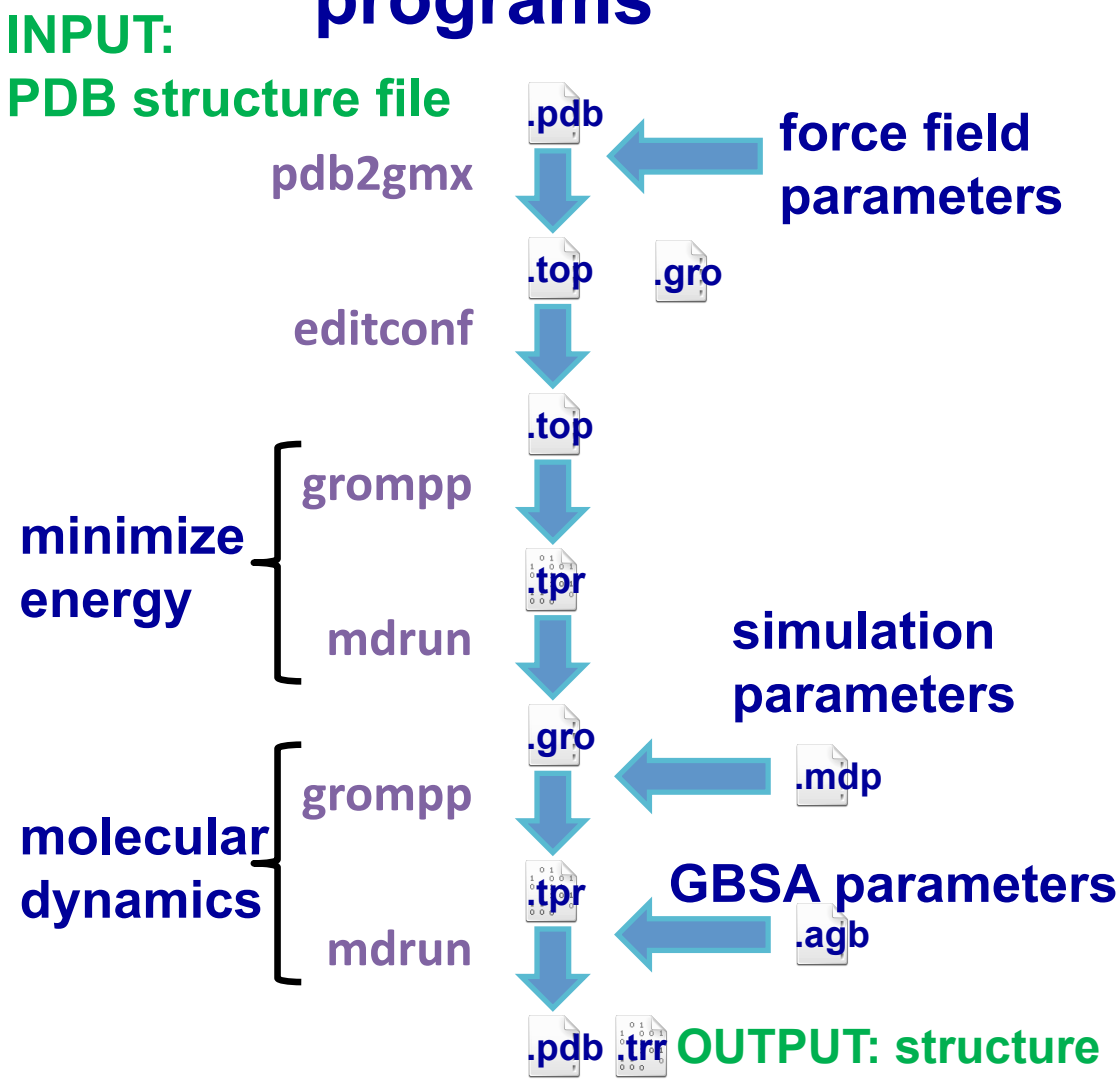
Zephyr is a GUI layer on OpenMM, Gromacs, and VMD



Introductory demonstration for Zephyr



A: Run these gromacs programs



A: Run these gromacs programs

INPUT:
PDB structure file

.pdb

pdb2gmx ← force field parameters

.top .gro

editconf

.top

minimize energy: grompp → .tpr → mdrun

simulation parameters: .mdp

.gro

molecular dynamics: grompp → .tpr → mdrun

GBSA parameters: .agb

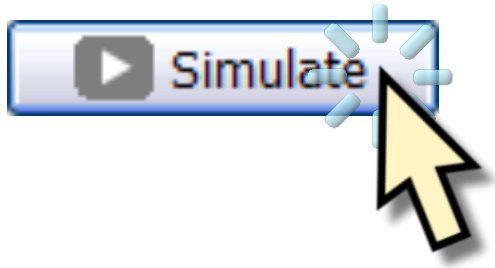
.pdb .trr OUTPUT: structure and trajectory

OR

B: Click "Simulate" button in Zephyr

INPUT:
PDB structure file

.pdb



.pdb .trr OUTPUT: structure and trajectory

Zephyr Design Principles

1. **Discoverability**
   - Not a black box
   - Learn molecular dynamics by investigating simulation interface
2. **Convention**
   - Harvest best practices of experts for default work flow
3. **Feedback**
   - Reveal when things go wrong
   - Reveal when things go right

Zephyr & Role in RNA Modeling

- Molecular dynamics
- Final step of a 3D structure modeling pipeline

Overview of exercises

1. Dinucleotide (adenylyladenylate) 2 residues
2. Tertaloop (GCAA) 12 residues
3. Minimize xtal + C2A tRNA structure
4. Minimize NAST tRNA structure (NAST + C2A)
5. Minimize PDB_00005 model

Exercise 1: RNA Dinucleotide

1. Launch Zephyr

2. Simulate adenylyladenylate.pdb for 40 picoseconds

Under Molecules tab:

Browse molecule (PDB) files… -> Select adenylyladnenylate.pdb

Parameters -> Change simulation length to 40.0ps

Select "View simulation live in VMD"

Simulate

Check estimated simulation time:

If more than 2 minutes, decrease simulation length

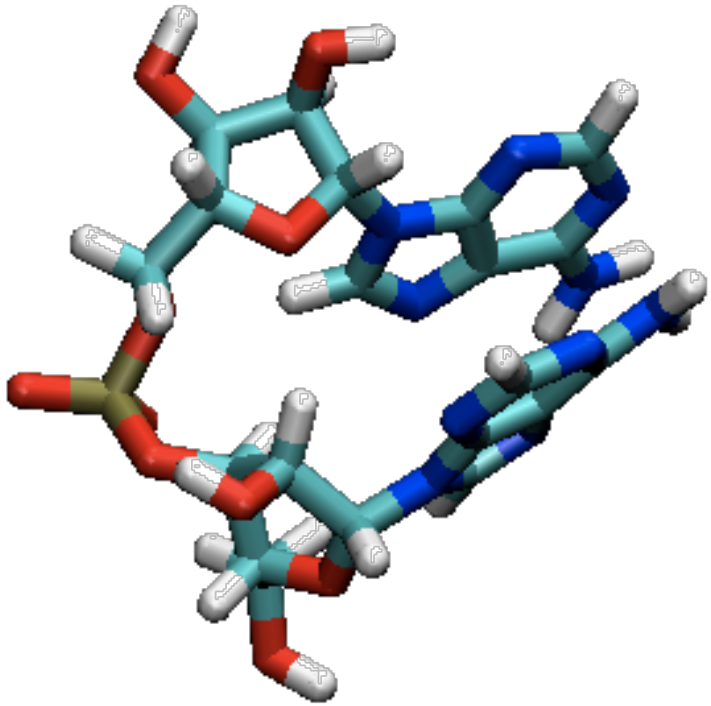
3. Raise solvent collision interval from 0.01099 to 1.0ps

What happens differently when you run this simulation?

4. Restore the solvent collision interval to 0.01099

Lessons from exercise 1: RNA Dinucleotide

- Increased collision interval means low viscosity.
- Lower viscosity permits faster exploration of conformational space.
- Zephyr provides a rich environment for exploring molecular simulations.



Exercise 2: Using VMD to view and convert trajectories

1. Load the Zephyr trajectory from the previous simulation into VMD

VMD Main -> File -> New Molecule

Molecule File Browser -> Browse

Navigate to Output folder ({…}/zephyr_sims/adenylyladnylate)

Select adenylyladenylate_processed.box.em.md.gro

Load

Browse (again, to load trajectory on top of .gro file)

Select adnylyladenylate_processed.box.em.md.trr

Load

2. Save trajectory in PDB format from VMD

Select trajectory in VMD Main window

File -> Save Coordinates

File type: pdb, Selected atoms: all -> Save adenylyladenylate_processed.box.em.md.pdb

Exercise 3: Tetraloop hairpin

1. Begin simulating gcaa.pdb

Use default parameters.

How long would it take to complete? Press "Cancel" to halt the simulation.

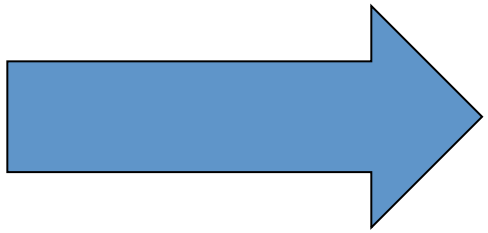
(On Mac you may need to close VMD and/or Zephyr to halt.)

2. Set "Simulation Hardware" to "GPU Nvidia". Simulate Again.

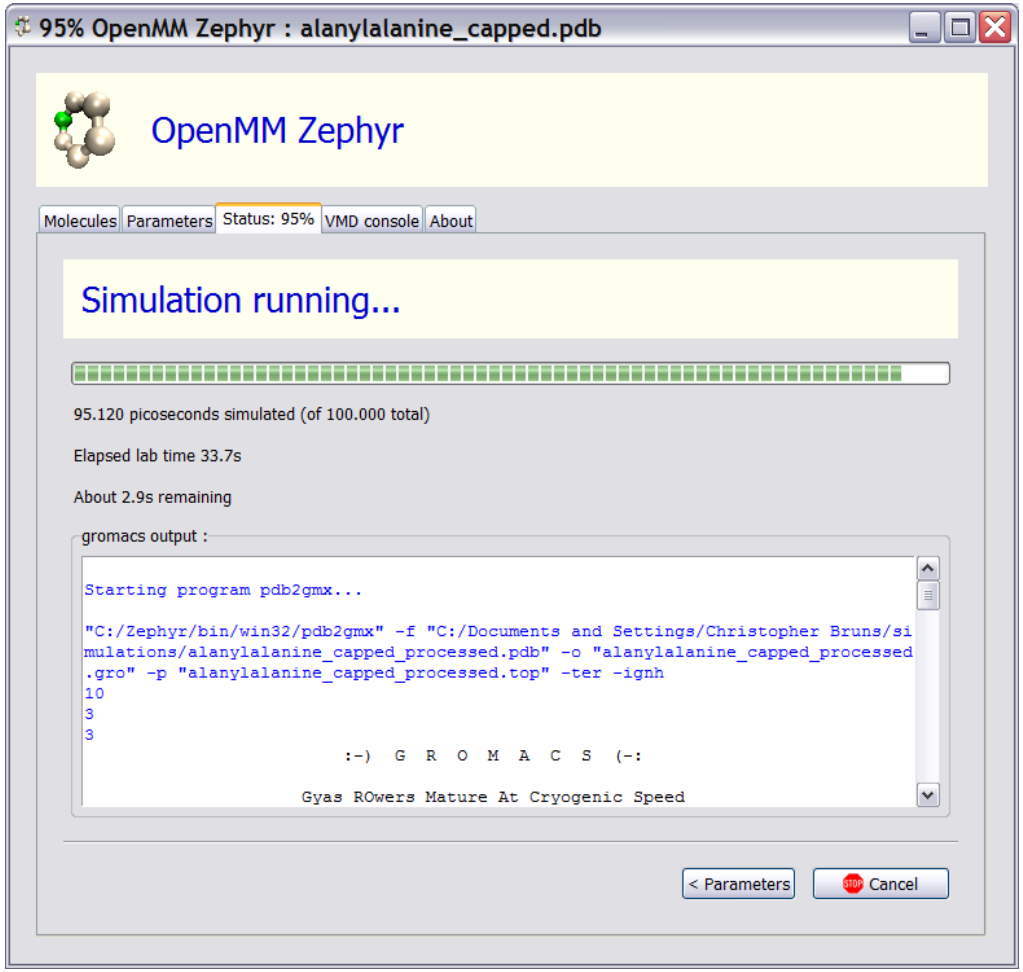
What happens?

If GPU acceleration is unavailable: Restore hardware to "CPU OpenMM ref."

Read the blue lines to learn to run Gromacs-OpenMM on the command line



see also zephyr.log file



Exercise 4: Minimizing C2A output

1. Simulate 6TNA-0-fixed.pdb from the C2A exercise

Navigate to 6TNA_c2a example folder to select file 6TNA-0-fixed.pdb

Change parameters:

Simulate 10 steps

Output frequency every 1 steps

The minimization process minimized most gaps in the full atomic structure. Additional simulation steps help further reductions, but are time-expensive.

2. Run a similar simulation with T2-M1-0.pdb

What happens if the C2A model has very large gaps?

Both NAST and C2A have stochastic components, good to run many times as some models will be better than others.

Quality of C2A model depends on quality of NAST model.

Quality of minimized model depends on quality of C2A model.

3. Run a similar simulation with your PDB_00005 model

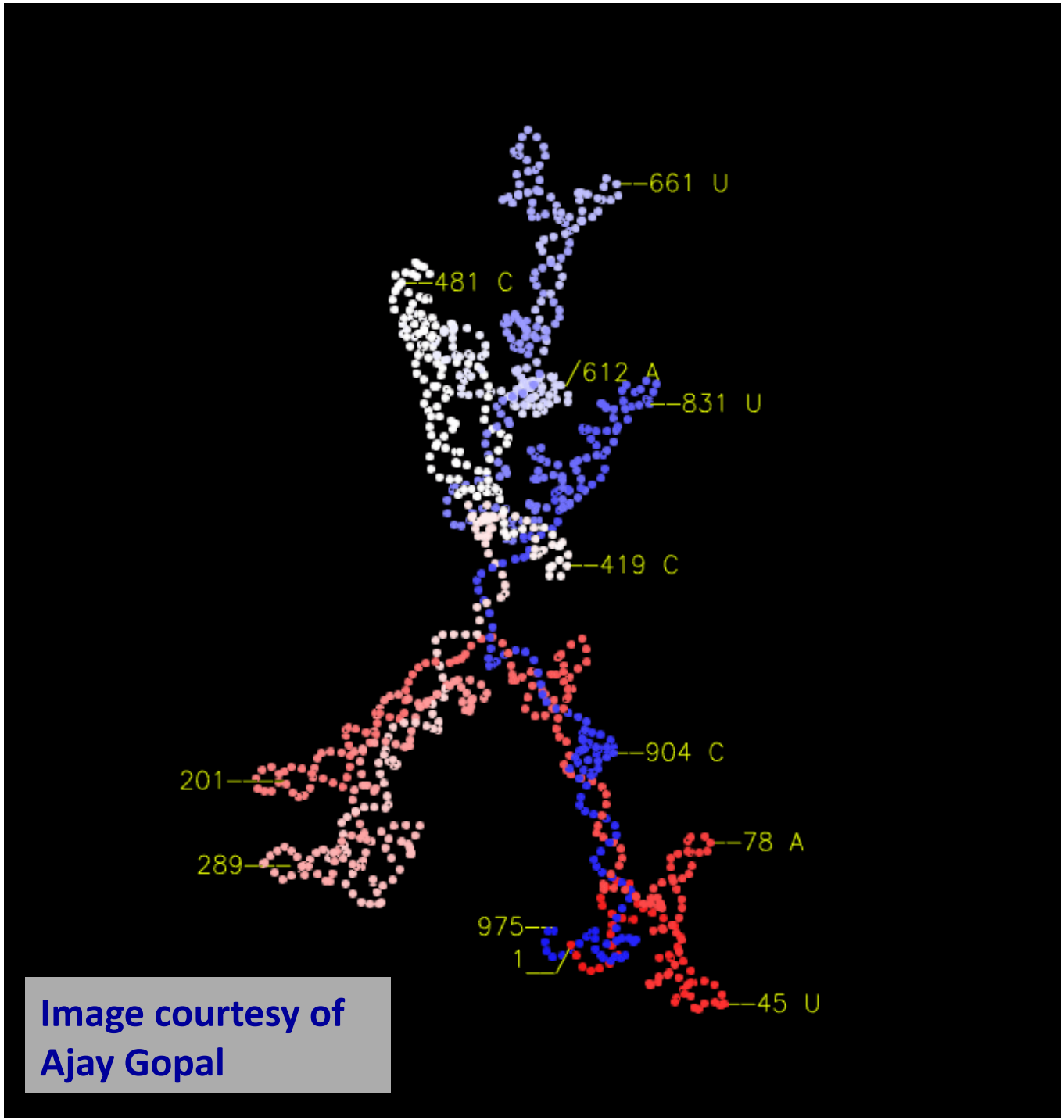
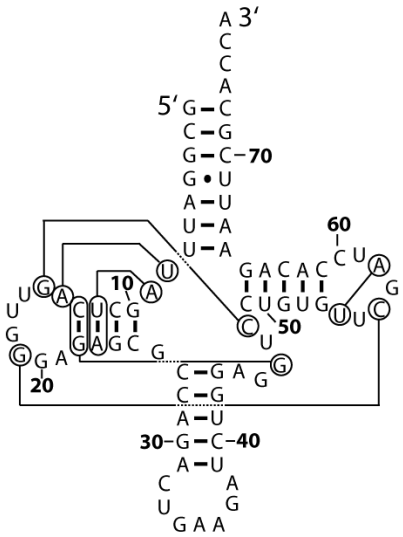
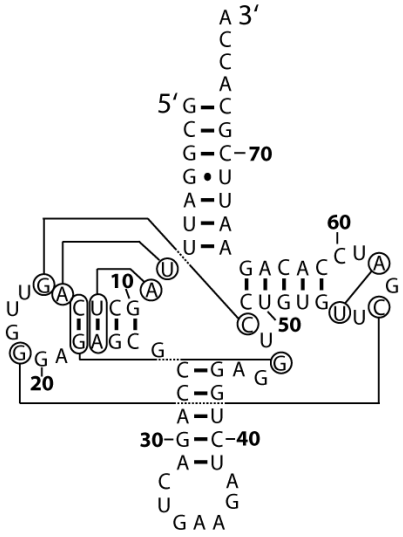


Image courtesy of Ajay Gopal

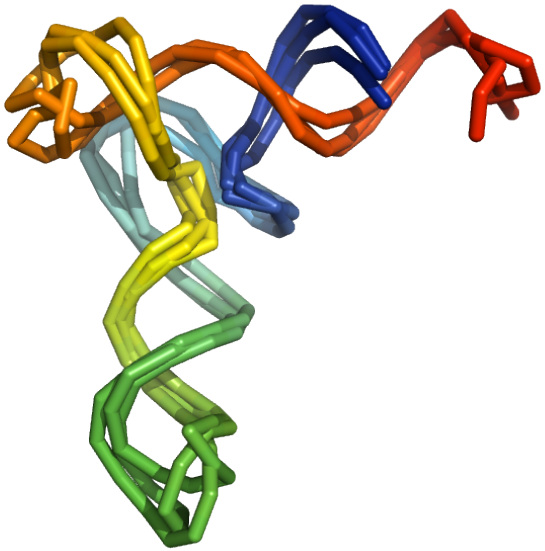

A 3′
C
C
A
5′ G–C
C–G
G–C–70
G•U
A–U
U–A
U–A
60
C U
A
G
G A C A C
C U G U G
U U C
50
U
10
A
U
G A
20
C–G A G
G
C–G
A–U
30–G–C–40
A–U
C A
U G
G A A

Summary

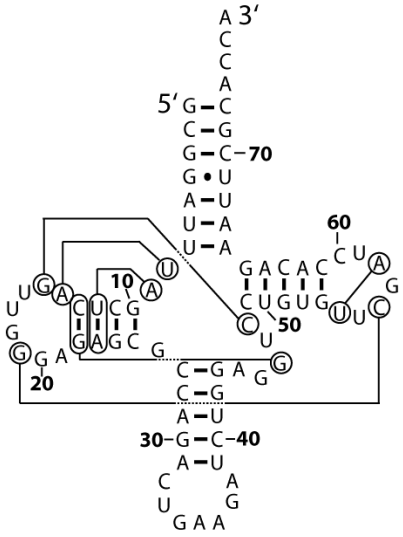
Summary



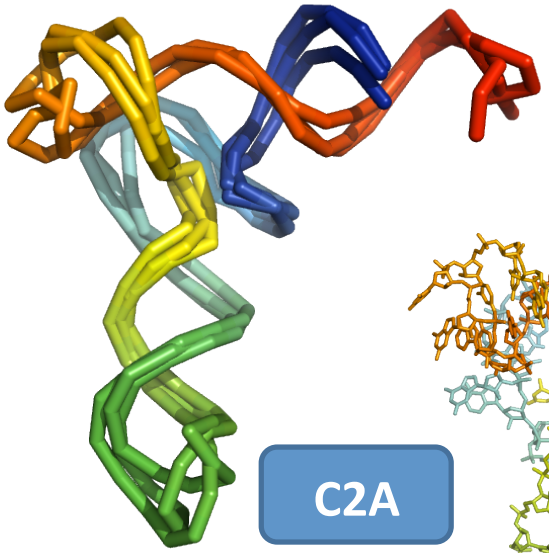
NAST



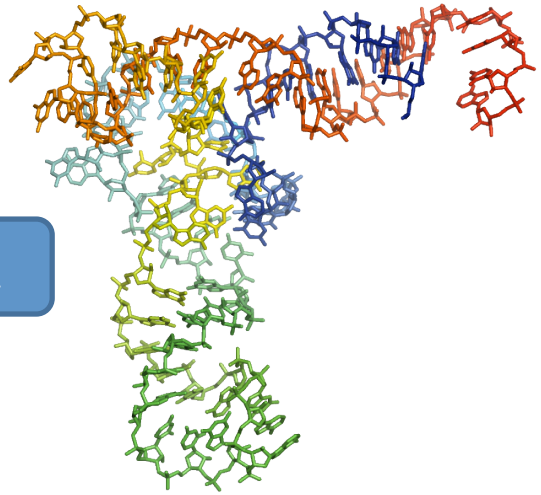
Summary



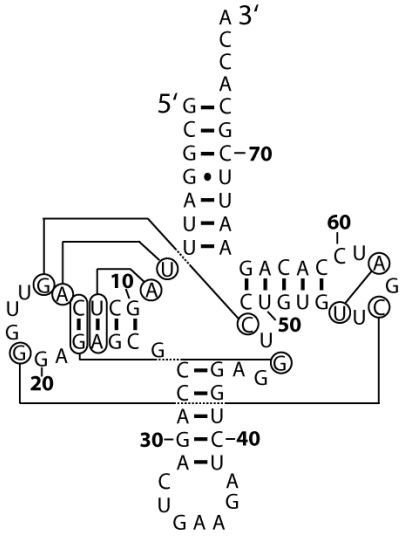
NAST



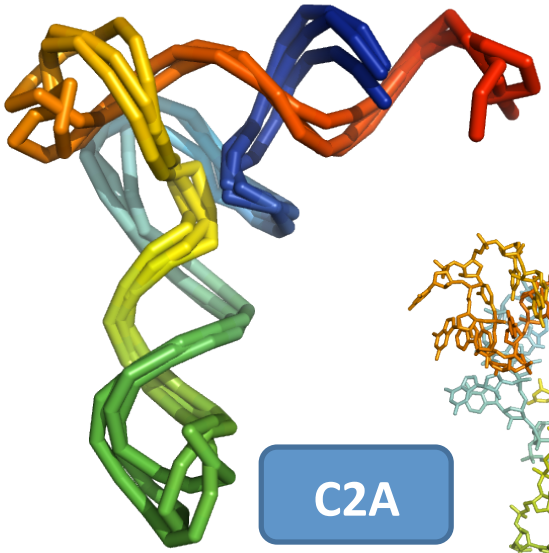
C2A



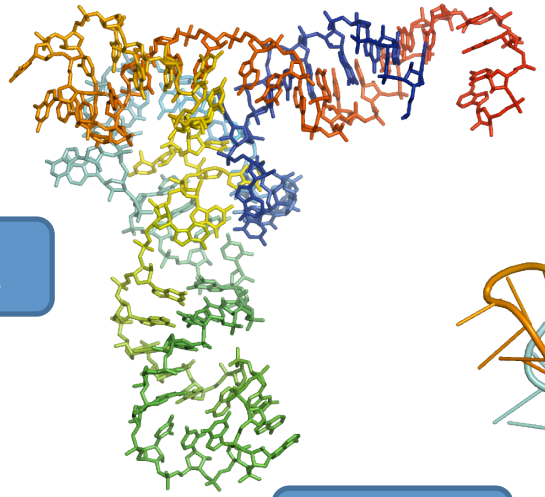
Summary



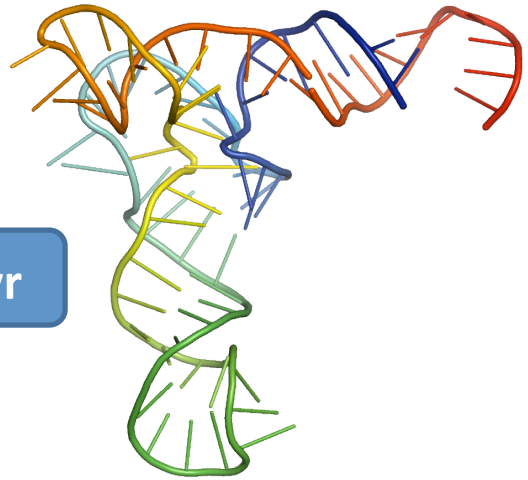
NAST



C2A



Zephyr



Downloads

NAST (includes C2A):	www.simtk.org/home/nast
C2A (stand alone):	www.simtk.org/home/c2a
Zephyr:	www.simtk.org/home/zephyr

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Thank You!

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