OpenMM-Gromacs from Command-line

Motivation

- Not all parameters/scenarios that you may want to pursue are available through Zephyr
- Gentle introduction to Gromacs
  - Gromacs is a large suite of programs:

    Build input files, energy minimization, molecular dynamics, analysis
  - Lots of parameters, arguments to programs, …

Goals

- Outline the steps required to generate the input file for a molecular dynamics (md) simulation and then run the simulation
- Point out potential pitfalls
- View resulting trajectories in VMD

Gromacs MD Input File

- Input for Gromacs md simulation is a single file with a .tpr suffix
- File encapsulates all information & data needed for a md run
  - Initial coordinates of molecules [.gro file]
  - Force-field parameters, topology of molecules, … [.top file]
  - md parameters (number of time steps, step size, temperature, …) [.mdp file]
- Is a binary file, but …
- Gromacs program grompp generates tpr file

Strategy for Generating tpr File

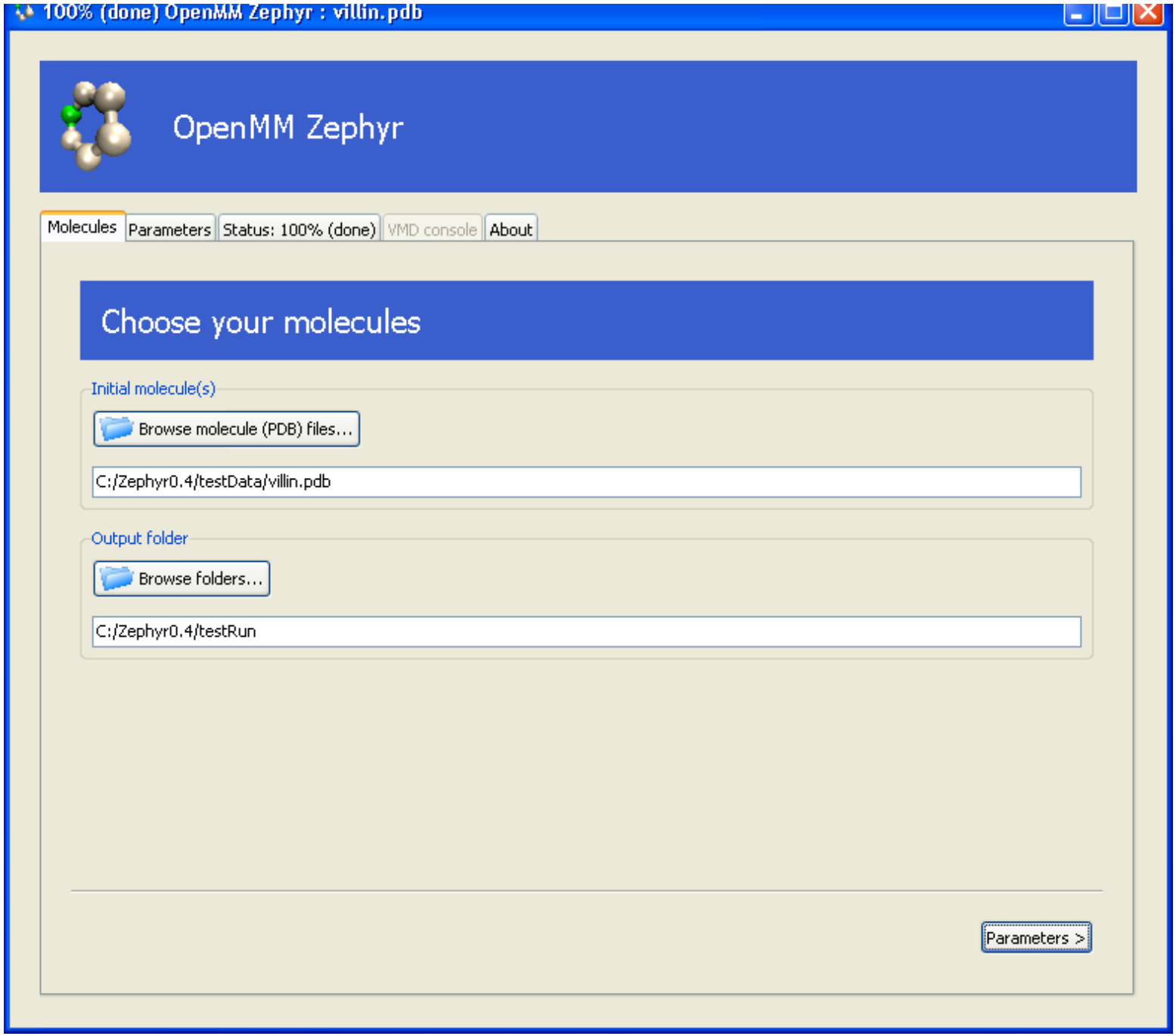
- Run Zephyr using molecule of interest for only a small number of timesteps
- Reuse the gro and top files generated by Zephyr as input to grompp
- Edit the mdp file output by Zephyr to change the md simulation parameters
- Set required environment variables

Setup

- Create new folder C:\Zephyr0.4\testRun
- Start Zephyr (double-click OpenMMZephyr.tcl)

Molecules tab

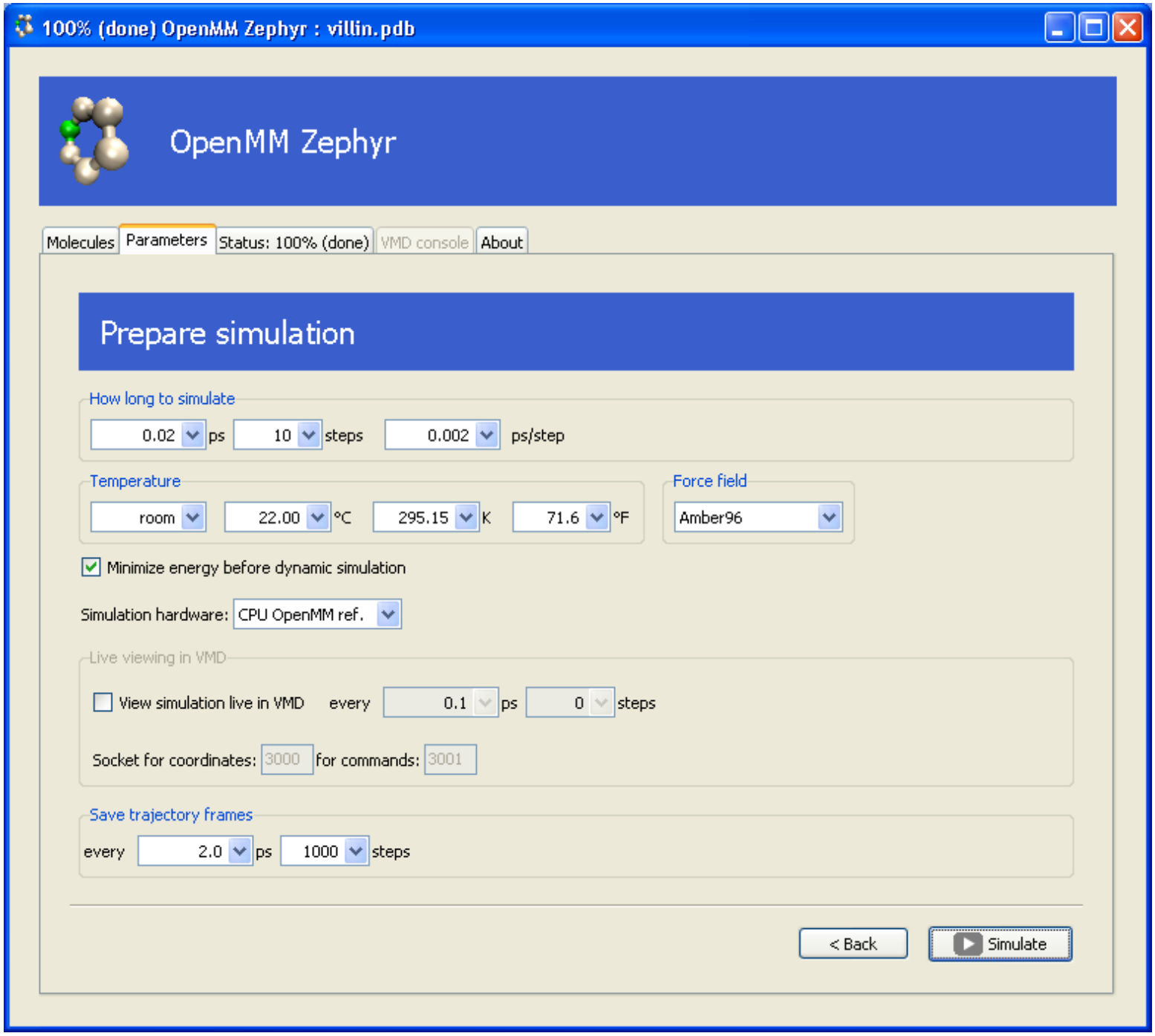
- Select a molecule (villin.pdb) in Initial Molecule(s)
- Set testRun folder as the Output folder


100% (done) OpenMM Zephyr : villin.pdb
OpenMM Zephyr
Molecules
Parameters
Status: 100% (done)
VMD console
About
Choose your molecules
Initial molecule(s)
Browse molecule (PDB) files...
C:/Zephyr0.4/testData/villin.pdb
Output folder
Browse folders...
C:/Zephyr0.4/testRun
Parameters >

Setup Continued

Parameters tab

- Set to run for 1 or 10 steps in Parameters tab
- Uncheck View Simulation live in VMD box
- Run by clicking Simulate


100% (done) OpenMM Zephyr : villin.pdb
OpenMM Zephyr
Molecules
Parameters
Status: 100% (done)
VMD console
About
Prepare simulation
How long to simulate
0.02
ps
10
steps
0.002
ps/step
Temperature
room
22.00
°C
295.15
K
71.6
°F
Force field
Amber96
Minimize energy before dynamic simulation
Simulation hardware:
CPU OpenMM ref.
Live viewing in VMD
View simulation live in VMD
every
0.1
ps
0
steps
Socket for coordinates:
3000
for commands:
3001
Save trajectory frames
every
2.0
ps
1000
steps
< Back
Simulate

Edit mdp File

- Copy file testRun\md.out.mdp to testRun\villinMod.mdp
- Open testRun\villinMod.mdp with favorite editor (WordPad, Notepad, …)

MD Parameters

Text after ';' is ignored (comments)

~ Line 17

```
; Start time and timestep in ps
t_init                  = 0
dt                       = 0.0020        ;(step size)
nsteps                  = 10000         ;(time steps --
   smaller if
                                        ; not GPU accelerated)
```

Change Viscosity

Find tau_t in the mdp file (~ line 141)

```
------------------------------------------------------------
; OPTIONS FOR WEAK COUPLING ALGORITHMS
; Temperature coupling
tcoupl                  = No
; Groups to couple separately
tc-grps                 = system
; Time constant (ps) and reference temperature (K)
; tau_t                       = 0.01099 ;( =1/91 = water collision
    frequency)
tau_t                    = 1.0
ref_t                    = 295.15
; Pressure coupling
Pcoupl                  = No
Pcoupltype              = Isotropic

------------------------------------------------------------
```

Note

- The parameter bd-fric is for Brownian dynamics – does not change stochastic (Langevin) dynamics viscosity -- contrary to what mdp file documentation might suggest:

```
; LANGEVIN DYNAMICS OPTIONS
; Friction coefficient (amu/ps) and random
   seed
bd-fric                  = 0
```

VMD Output Parameter

If you see these messages when running simulation and program is slow:

Waiting for IMD socket connection to VMD on port 3000...
Waiting for IMD socket connection to VMD on port 3000...
Waiting for IMD socket connection to VMD on port 3000...

then you need to modify to the parameter nstvmdout

This is a Zephyr parameter, not a Gromacs parameter (not in Gromacs documentation)

```
; VMD live visualization
; nstvmdout              = 50
nstvmdout              = 0
vmdSocketNumber        = 3000
blockUntilVmdConnected  = 1
```

Other MD Parameters

~Line 52:

```
; OUTPUT CONTROL OPTIONS
; Output frequency for coords (x), velocities (v) and forces (f)
nstxout      = 1000 ;(print coords every 1000 steps to .trr
    file[Zephyr])
nstvout      = 1000 ;(print velocities every 1000 steps to .trr file)
nstfout      = 0      ;(do not print forces, but output would go .trr
    file)
nstxtcout  = 2000  ;(print coords every 2000 steps to .xtc file)
                          ; xtc compressed, portable xdr format
xtc_precision = 1000 ;( precision of coordinates in .xtc file 3
    digits?)
```

Start Command Prompt window

Start Menu →All Programs →Accessories
→Command Prompt

Or

Start Menu →Run… → cmd

grompp Needs Location of Force-Field Parameters, Topology, … Files

- Example: #include "ffamber96.itp" in top file
- The required files are all located in folder: C:\Zephyr0.4\bin\gmxlib\
- The location is implicitly provided to grompp through the environment variable GMXLIB

Environment Variables

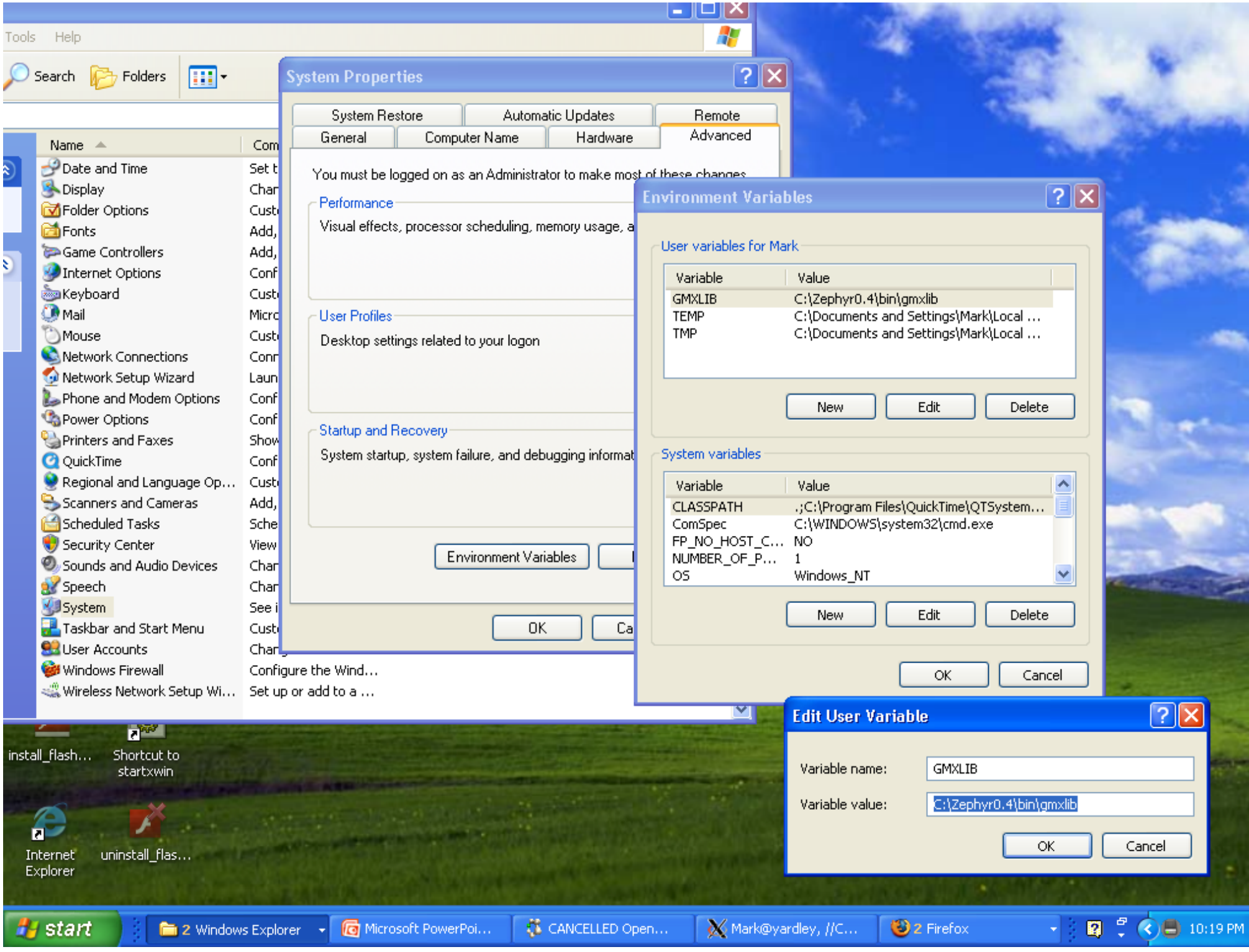
- Provide location of auxiliary files, directories, libraries or control behavior of program
- Environment variables can either be set
  - temporarily for the lifetime of the Command Prompt window
  - permanently
    - Warning: may need to be changed if you later install a new version of Zephyr or are using non-Zephyr versions of Gromacs

Temporarily Setting GMXLIB Environment Variable

C:\Zephyr0.4> set GMXLIB=C:\Zephyr0.4\bin\gmxlib

Permanently Setting GMXLIB Environment Variable

- Start Menu → {Control Panel} → System → Advanced → Environment Variables → New (under 'User variables for XXX)
- Variable Name: GMXLIB
- Variable Value: C:\Zephyr0.4\bin\gmxlib


Tools Help
Search Folders
Name
Date and Time
Display
Folder Options
Fonts
Game Controllers
Internet Options
Keyboard
Mail
Mouse
Network Connections
Network Setup Wizard
Phone and Modem Options
Power Options
Printers and Faxes
QuickTime
Regional and Language Op...
Scanners and Cameras
Scheduled Tasks
Security Center
Sounds and Audio Devices
Speech
System
Taskbar and Start Menu
User Accounts
Windows Firewall
Wireless Network Setup Wi...
Configure the Wind...
Set up or add to a ...
System Properties
System Restore
Automatic Updates
Remote
General
Computer Name
Hardware
Advanced
You must be logged on as an Administrator to make most of these changes
Performance
Visual effects, processor scheduling, memory usage, a
User Profiles
Desktop settings related to your logon
Startup and Recovery
System startup, system failure, and debugging informat
Environment Variables
OK
Environment Variables
User variables for Mark
Variable
Value
GMXLIB
C:\Zephyr0.4\bin\gmxlib
TEMP
C:\Documents and Settings\Mark\Local ...
TMP
C:\Documents and Settings\Mark\Local ...
New
Edit
Delete
System variables
Variable
Value
CLASSPATH
.;C:\Program Files\QuickTime\QTSystem...
ComSpec
C:\WINDOWS\system32\cmd.exe
FP_NO_HOST_C...
NO
NUMBER_OF_P...
1
OS
Windows_NT
New
Edit
Delete
OK
Cancel
Edit User Variable
Variable name:
GMXLIB
Variable value:
C:\Zephyr0.4\bin\gmxlib
OK
Cancel
install_flash...
Shortcut to startxwin
Internet Explorer
uninstall_flas...
start
2 Windows Explorer
Microsoft PowerPoi...
CANCELLED Open...
Mark@yardley, //C...
2 Firefox
10:19 PM

GPU Board Type

- Start Menu → {Control Panel} → System → Hardware → Device Manager → Display adapters
  - ATI Radeon HD 2600 XT
  - NVIDIA GeForce 8800M GTS

Setting OPENMM_PLUGIN_DIR Environment Variable

- Used by Zephyr to find GPU platform-specific libraries
- Not a Gromacs environment variable like GMXLIB
- Setting depends on whether you have ATI or NVIDIA GPU card

Temporarily Setting OPENMM_PLUGIN_DIR Environment Variable

```
C:\Zephyr0.4>
 set OPENMM_PLUGIN_DIR=C:\Zephyr0.4\bin\win32\lib\openmm
    \ati
```

```
C:\Zephyr0.4> set OPENMM_PLUGIN_DIR=C:\Zephyr0.4\bin
    \win32\lib\openmm\nvidia
```

Permanently Setting OPENMM_PLUGIN_DIR Environment Variable

- Name: OPENMM_PLUGIN_DIR
- Values:

  C:\Zephyr0.4\bin\win32\lib\openmm\ati

  or

  C:\Zephyr0.4\bin\win32\lib\openmm\nvidia

Confirm Environment Variables Set

Enter

```
>set GMXLIB
>set OPENMM_PLUGIN_DIR
```

in Command Prompt window to confirm variables set correctly

- If not set (you went the permanent route), then try starting new Command Prompt window

Confirm Input Files Present

In Command Prompt window navigate to the folder:

```
C:\Documents and Settings\friedrim>cd C:\Zephyr0.4\testRun
C:\Zephyr0.4\testRun>dir /OD *gro
C:\Zephyr0.4\testRun>dir /OD *top
C:\Zephyr0.4\testRun>dir /OD *mdp
```

Should see in listing:

```
02/05/2009  01:47 PM            27,473 villin_processed.box.em.gro
02/05/2009  01:47 PM           184,801 villin_processed.top
02/05/2009  03:40 PM            10,319 villinMod.mdp
```

Want the villin_processed.box.em.gro file since contains energy-minimized coordinates

Run grompp

Command:

C:/Zephyr0.4/bin/win32/grompp

-f villinMod.mdp

-c villin_processed.box.em.gro

-p villin_processed.top

-o villinMod.tpr

-po villinMod.out.mdp

-debug 1

> out.log 2> err.log

Run grompp & Confirm OK

- Optional (ultimately less typing): place command in gromppRun.bat file and run bat file from command line:

  C:\Zephyr0.4\testRun>gromppRun.bat

- grompp messages and other output will be in out.log, err.log and grompp.log
- Confirm tpr generated by checking time:

```
C:\Zephyr0.4\testRun>dir /OD *tpr
02/05/2009  01:47 PM           156,292 villin_processed.box.em.tpr
02/05/2009  01:47 PM           156,260 villin_processed.box.em.md.tpr
02/06/2009  05:46 PM           156,260 villinMod.tpr
```

Checking Parameter Values

- Most mdp parameter values echoed near top of md.log file generated when simulation run
- Or to echo contents of tpr file run C:/Zephyr0.4/bin/win32/gmxdump –s villinMod.tpr > tprContents.txt
  - gmxdump used to view contents of various Gromacs binary files
  - http://www.stanford.edu/~friedrim/gmxdump.exe
  - File tprContents.txt will contain all parameters, initial coordinates, velocities, …

Running Gromacs-OpenMM

C:\Zephyr0.4\testRun> C:\Zephyr0.4\bin\win32\mdrun_openmm.exe -s villinMod.tpr

mdrun_openmm.exe is OpenMM/Zephyr equivalent of Gromacs mdrun.exe

- Includes VMD connection code
- GPU acceleration calls

Checking For Gpu Accleration

Screen Output:

Back Off! I just backed up ener.edr to ./ #ener.edr.4#

OpenMM Platform: Reference *(CPU)*

OpenMM Platform: Brook *(ATI board)*

OpenMM Platform: Cuda *(NVIDIA board)*

Confirm Run Completed Successfully

- C:\Zephyr0.4\testRun>dir /OD
  - Check output files (md.log, traj.trr, state.cpt ener.edr, …) exist with expected date/times
  - md.log log file
  - traj.trr trajectory file
  - state.cpt checkpoint file
  - ener.edr energy stats
    - Not populated with mdrun_openmm

View md.log To Check For Problems

If message

'Could not read agb file. GBSA is being omitted'

Present in md.log, implicit solvent not active

- this is an error!
- params.agb file contains atomic radii for GBSA algorithm
- Needed since current version (4.03) of Gromacs does not support GBSA

View md.log To Check For Problems

Check that all steps completed:

Step	Time	Lambda
9000	18.00000	0.00000
Step	Time	Lambda
10000	20.00000	0.00000

Program C:\Zephyr0.4\bin\win32\mdrun_openmm.exe, VERSION 4.0.3pre_zephyr

Source code file: ..\..\..\src\gmxlib\checkpoint.c, line: 872

File input/output error:

Cannot rename checkpoint file; maybe you are out of quota?

Part 2: Verlet Integrator Without Solvent ~ Vacuum

C:\Zephyr0.4\testRun>copy villinMod.mdp villinMod2.mdp

Edit villinMod2.mdp

; integrator = sd ; Langevin

integrator = md ; Verlet algorithm

; dt = 0.002 ; step size

dt = 0.001

; implicit_solvent = GBSA

implicit_solvent = No

Run grompp As Before

Command:

C:/Zephyr0.4/bin/win32/grompp

-f villinMod2.mdp

-c villin_processed.box.em.gro

-p villin_processed.top

-o villinMod2.tpr

-po villinMod2.out.mdp

-debug 1

> out2.log 2>&1

Confirm tpr Generated Successfully

C:\Zephyr0.4\testRun>dir /OD *tpr

```
02/09/2009  05:19 PM           156,292 villin_processed.box.em.tpr
02/09/2009  05:19 PM           156,260 villin_processed.box.em.md.tpr
02/09/2009  05:32 PM           156,260 villinMod.tpr
02/09/2009  05:41 PM           156,260 villinMod2.tpr
```

Confirm tpr Generated Successfully

C:\Zephyr0.4\testRun>dir /OD *tpr

```
02/09/2009  05:19 PM           156,292 villin_processed.box.em.tpr
02/09/2009  05:19 PM           156,260 villin_processed.box.em.md.tpr
02/09/2009  05:32 PM           156,260 villinMod.tpr
02/09/2009  05:41 PM           156,260 villinMod2.tpr
```

Run Gromacs-OpenMM

C:\Zephyr0.4\testRun>

C:\Zephyr0.4\bin\win32\mdrun_openmm.exe -deffnm villinMod2 > out.log 2>&1

With –deffnm all files will have villinMod2 as base name w/ appropriate suffix

C:\Zephyr0.4\testRun>dir villinMod2*

```
02/05/2009  05:16 PM            15,320 villinMod2.cpt
02/05/2009  05:16 PM               544 villinMod2.edr
02/05/2009  05:16 PM            41,777 villinMod2.gro
02/05/2009  05:16 PM            31,074 villinMod2.log
02/05/2009  04:30 PM            10,318 villinMod2.mdp
02/05/2009  04:36 PM            10,289 villinMod2.out.mdp
02/05/2009  04:36 PM           156,260 villinMod2.tpr
02/05/2009  05:16 PM            72,720 villinMod2.trr
```

View Trajectory in VMD

- VMD needs both gro & trr file
  - atom and residues names in gro file used bond info
- Start VMD (Start Menu → University of Illinois)
- In VMD Main window, File → New Molecule
- Molecule File Browser → Browse C:\Zephyr0.4\testRun\villinMod2.***gro***
- Load
- Repeat for C:\Zephyr0.4\testRun\villinMod2.***trr***

Removing Backup (#) Gromacs Files

```
02/05/2009  10:04 AM         4,536 #alanylalanine_capped_processed.box.em.m.trr.1#
02/05/2009  10:04 AM           504 #traj.trr.1#
02/05/2009  10:56 AM         7,272 #traj.trr.2#
02/05/2009  10:57 AM         1,356 #traj.trr.3#
02/05/2009  10:58 AM         9,216 #traj.trr.4#
02/05/2009  06:08 PM           504 #traj.trr.5#
02/05/2009  06:08 PM         4,536 alanylalanine_capped_processed.box.em.md
```

```
C:\Zephyr0.4\simulations>del   #*trr*#      #*mdp*#     #*gro*#
```

Or

```
C:\Zephyr0.4\simulations>del   #*#
```

Final Notes

- tpr file generated with Zephyr version of grompp will not work with non-Zephyr mdrun
  - same gro & top files should work
  - mdp file contains Zephyr parameters not recognized by 'pure' Gromacs
- Gromacs Documentation

  http://www.gromacs.org/