



## Analyzing and enhancing molecular dynamics simulations with PLUMED

Giovanni Bussi – Associate Professor, SISSA, Trieste Italy

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**Tuesday, May 22nd at 12:00pm EDT**

### Upcoming Webinars:

June 12<sup>th</sup>: Scipion with Jose Miguel de la Rosa Trevin

July: please send your suggestions

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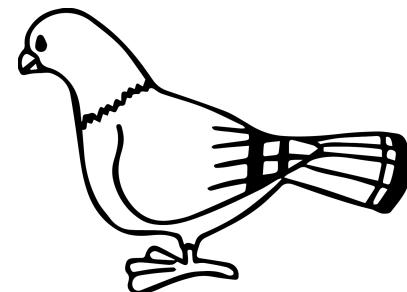
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# Systems Check

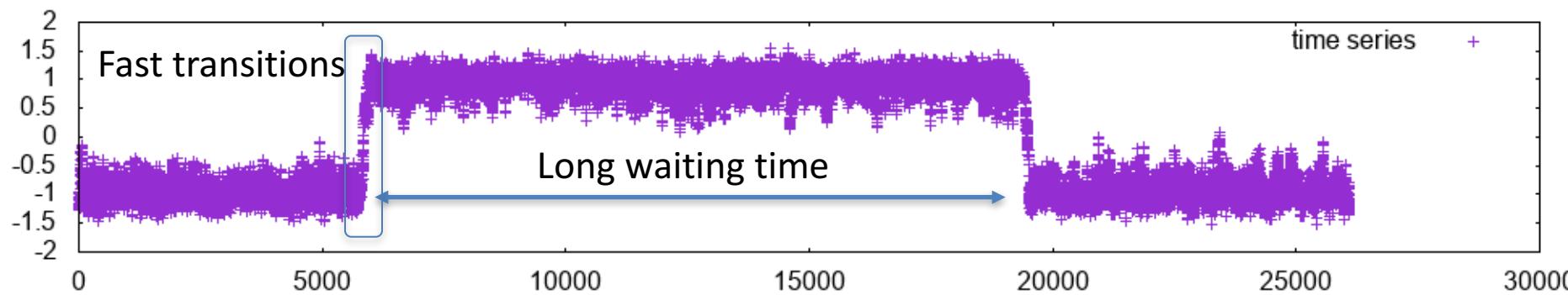
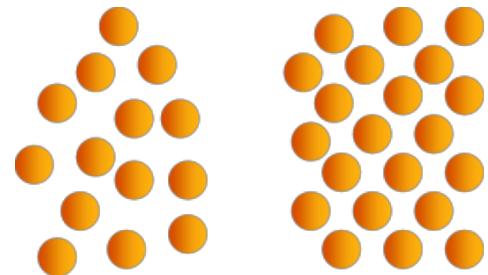
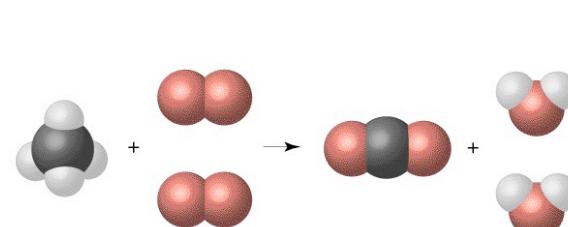
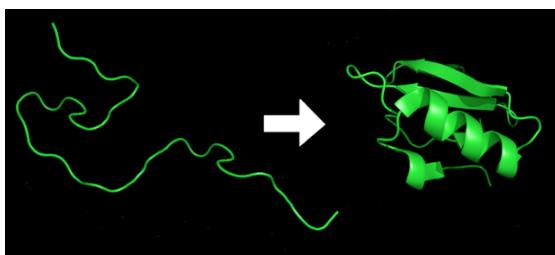
# Outline

- Rare events and collective variables
- PLUMED
- How to write a PLUMED input
- Practical tutorial with Max on a protein folding exercise



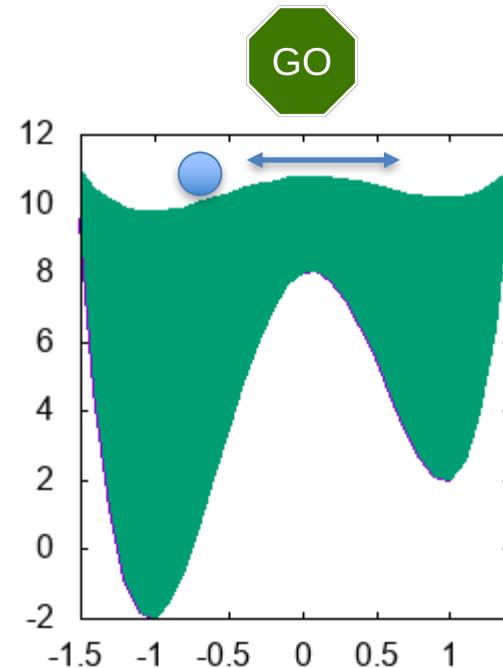
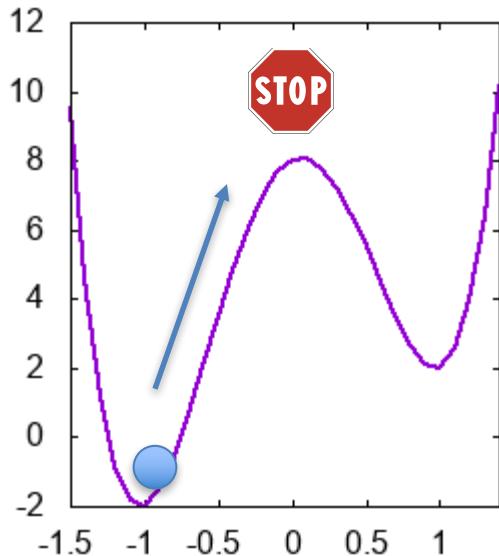
# Molecular dynamics & rare events

- MD as a “computational microscope”
- Quantitative tool to compute stabilities and rates.
- Typical timescales:  $\mu\text{s}$  (empirical potentials), 100ps (*ab initio*)
- Chemical reactions and conformational changes can take much longer! E.g.: protein/RNA folding ( $\mu\text{s-s}$ ), ligand unbinding ( $\mu\text{s-s}$ )



# Collective variables for analyzing and biasing MD simulations

- Functions of atomic coordinates:
  - Distances, torsional angles, RMSD, etc
- Analysis of MD simulations (detect events)
- Biasing (accelerate events)

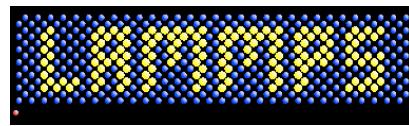


# What is PLUMED

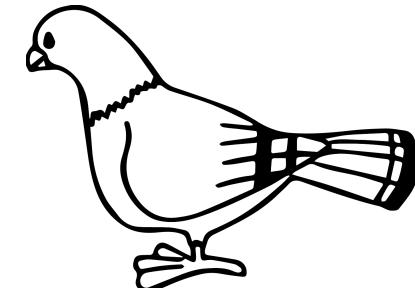
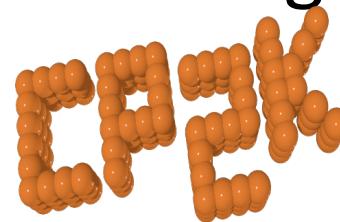
- An open source, portable plugin for biasing and analyzing MD
- Compatible with many MD engines (e.g. GROMACS, NAMD, LAMMPS, AMBER, OPENMM, CP2K, etc.)
- Implements many CVs and biasing methods



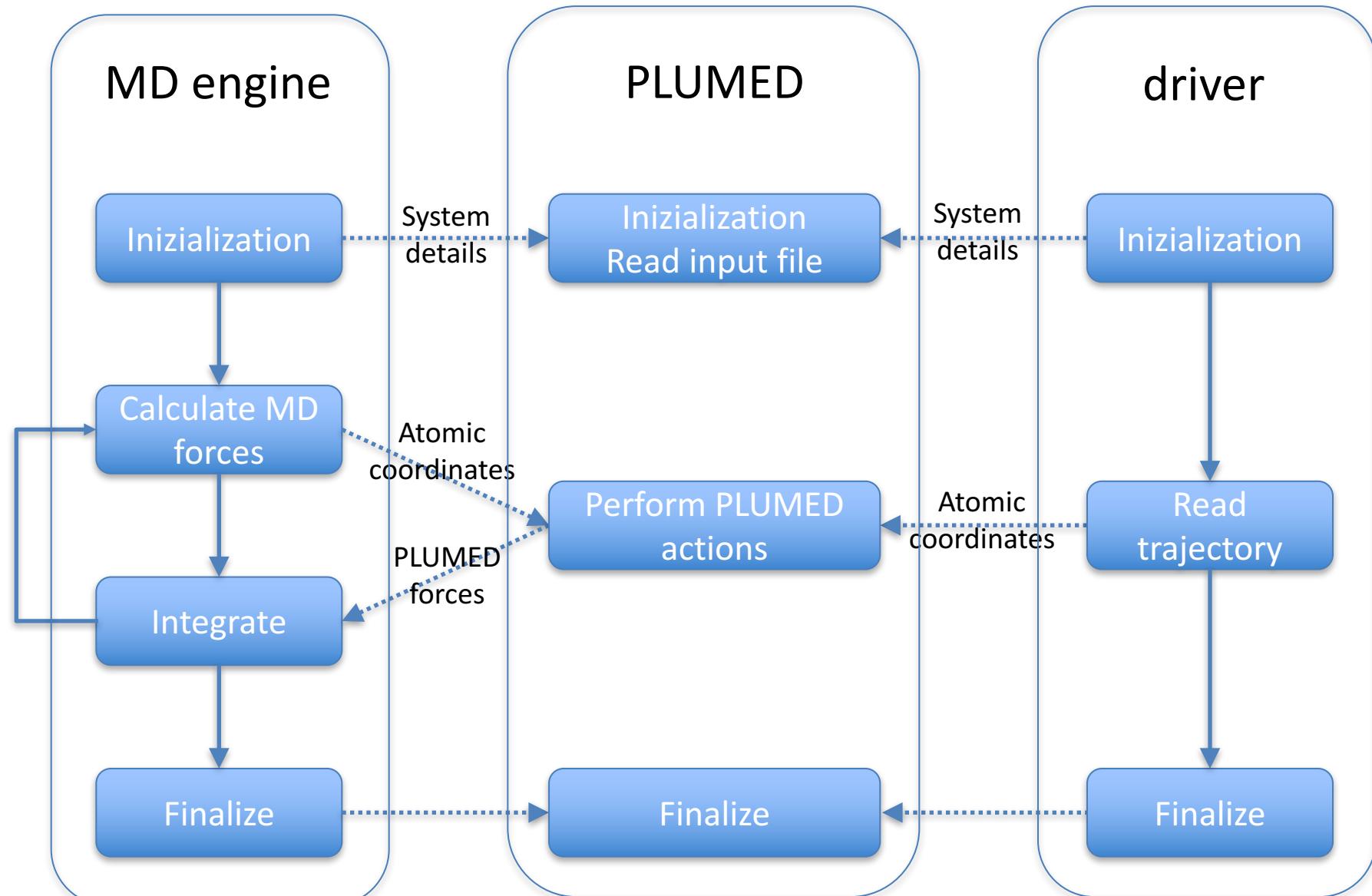
**NAMD**  
Scalable Molecular Dynamics



OpenMM



# Workflow

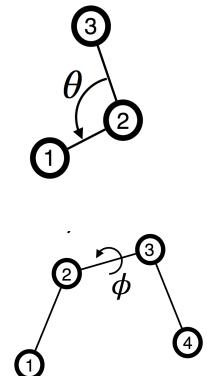


`gmx mdrun -plumed plumed.dat`

`plumed driver --igro traj.gro`

# A typical PLUMED input

```
# define distance between atoms 1 and 3
# later we will refer to this as `dist`
dist: DISTANCE ATOMS=1,3
# define angle between atoms 5, 6, and 10
ang: ANGLE ATOMS=5,6,10
# define torsion between atoms 5, 6, 10, and 11
tor: TORSION ATOMS=5,6,10,11
# print on file `colvar` every 10 steps
PRINT ARG=dist,ang,tor FILE=colvar STRIDE=10
```



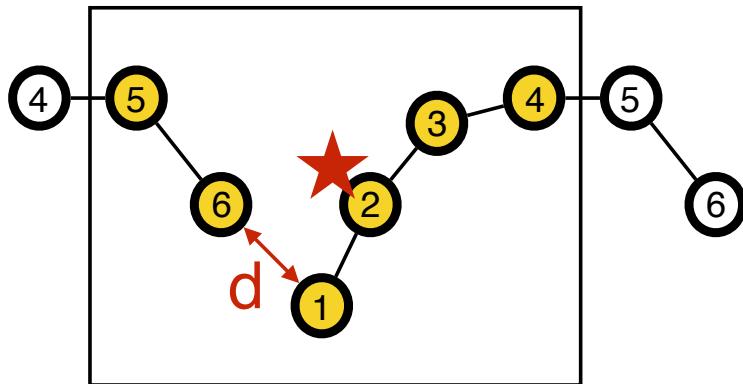
# Simplify atom selection (MOLINFO and GROUP)

```
# load a PDB with atom names
# atoms should be numbered as in the MD input
MOLINFO STRUCTURE=reference.pdb
# select phi angle of third residue
tor: TORSION ATOMS=@phi-3
# define your own group
solute: GROUP ATOMS=100-200
# compute its gyration radius
gyr: GYRATION ATOMS=solute
# print on file `colvar` every 10 steps
PRINT ARG=dist,ang,tor,gyr FILE=colvar STRIDE=10
```

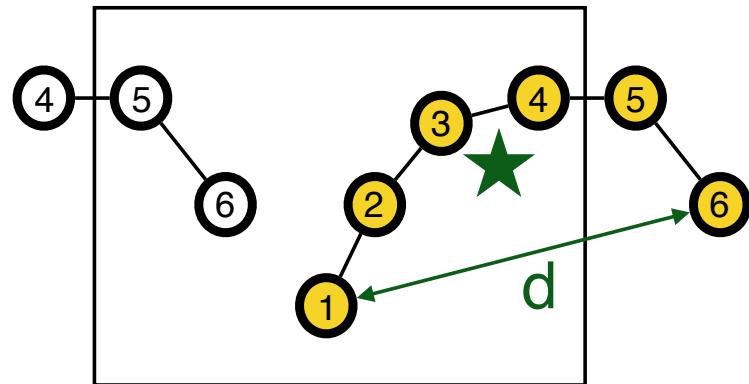
See the manual for other shortcuts (torsions for proteins/RNA/DNA etc).

# Check periodic boundary conditions!

a)



b)



# WRONG!

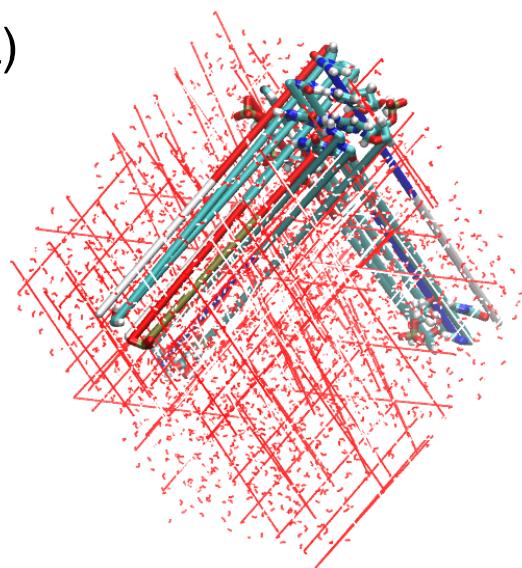
```
dist: DISTANCE ATOMS=1,6
```

# RIGHT!

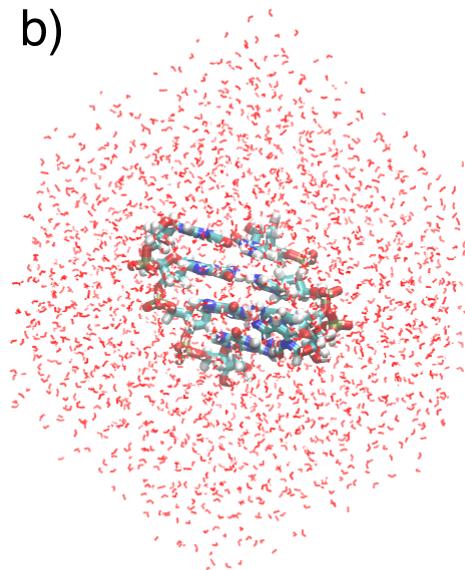
```
# DUMPATOMS ATOMS=1-6 FILE=out2.xyz  
WHOLEMOLECULES ATOMS=1-6  
# check the effect  
DUMPATOMS ATOMS=1-6 FILE=out.xyz  
dist: DISTANCE ATOMS=1,6 NOPBC
```

# Reconstruct molecules

a)

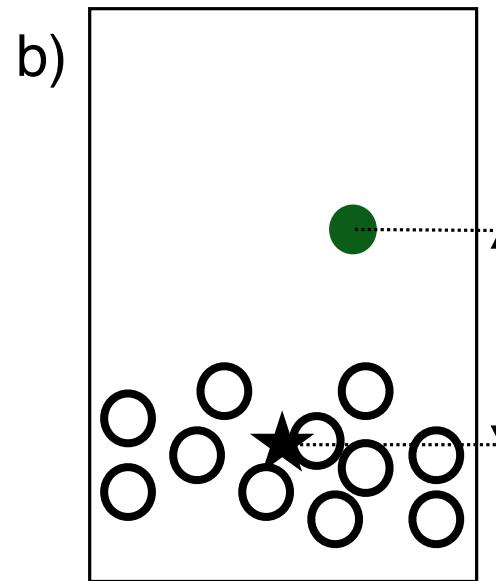
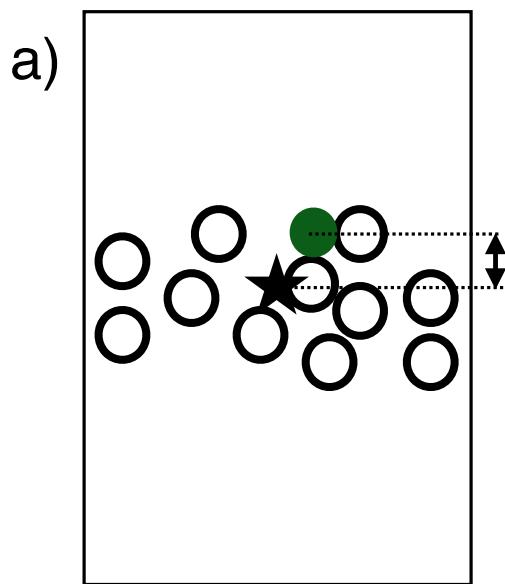


b)



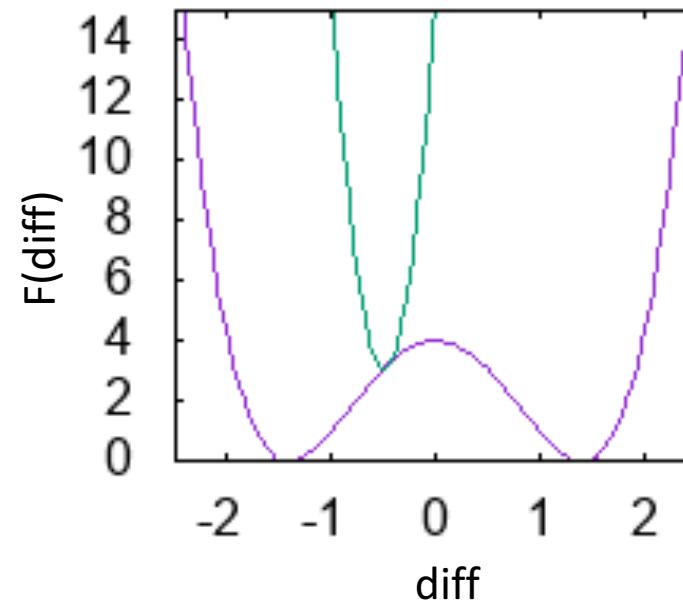
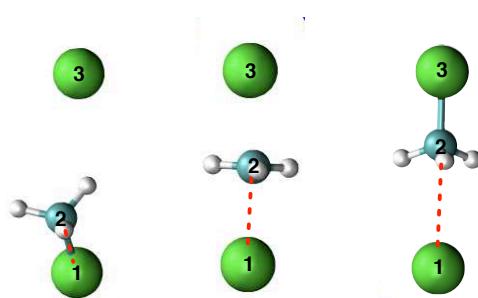
```
MOLINFO STRUCTURE=ref.pdb
rna: GROUP ATOMS=1-258
wat: GROUP ATOMS=259-6579
WHOLEMOLECULES ENTITY0=rna
FIT_TO_TEMPLATE REFERENCE=ref-rna.pdb TYPE=OPTIMAL
center: CENTER ATOMS=rna
WRAPAROUND ATOMS=wat AROUND=center GROUPBY=3
DUMPATOMS ATOMS=rna,wat FILE=rna-wrap.gro
```

# Do not use atom positions directly!



```
# very bad idea
pos: POSITION ATOM=1001
# better first compute center of membrane
# notice that membrane could be broken... CENTER should implicitly
# make it whole (but you should check!)
center: CENTER ATOMS=1-1000
DUMPATOMS ATOMS=1-1000,center FILE=checkme.gro STRIDE=100
# then compute its distance from the ion (atom n 1001)
dist: DISTANCE COMPONENTS ATOMS=1001,center
PRINT ARG=pos.z,dist.z
```

# Harmonic restraint

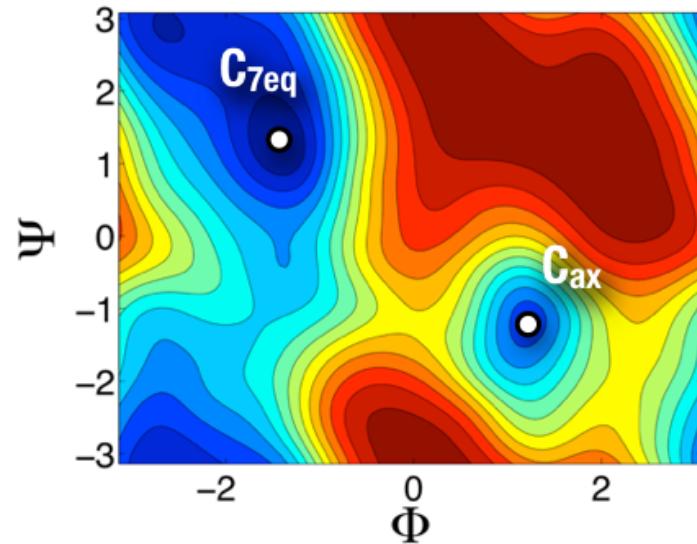
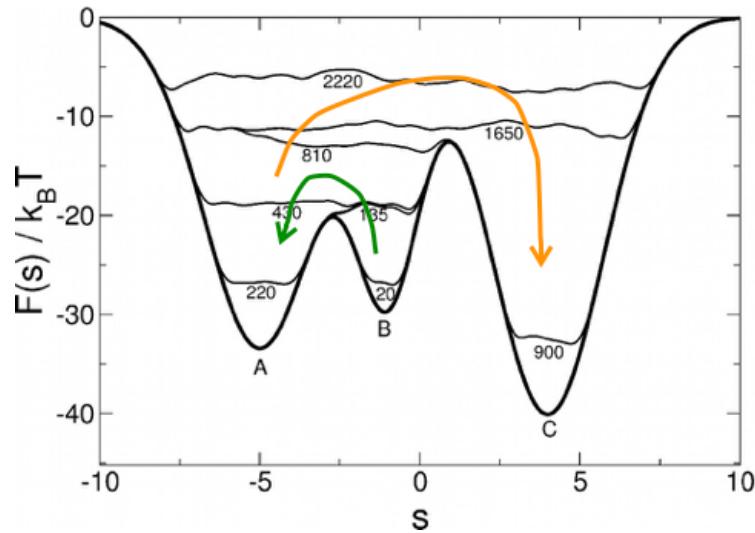


```
# define a distance
d1: DISTANCE ATOMS=1,2
# define another distance
d2: DISTANCE ATOMS=2,3
# compute the difference between the two distances
diff: CUSTOM ARG=d1,d2 FUNC=y-x
# apply a restraint
# this is implicitly applied at every step (STRIDE=1)
rr: RESTRAINT ARG=diff AT=-0.5 KAPPA=100
# print the distance and the value of the bias potential
PRINT ARG=diff,rr.bias FILE=colvar
```

E.g. for umbrella sampling, Torrie and Valleau 1977

# Metadynamics

Laio and Parrinello PNAS 2002



```
# define collective variables (CVs)
```

```
phi: TORSION ATOMS=5,7,9,15
```

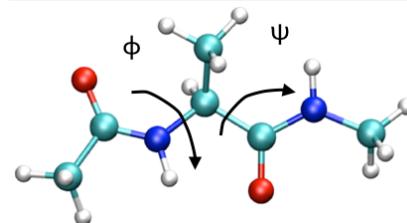
```
psi: TORSION ATOMS=7,9,15,17
```

```
# activate metadynamics
```

```
metad: METAD ARG=phi,psi PACE=500 HEIGHT=1.2 SIGMA=0.35,0.35
```

```
# print CVs values and metadynamics bias
```

```
PRINT STRIDE=10 ARG=phi,psi,metad.bias FILE=COLVAR
```



# To learn more

- Home: <http://www.plumed.org>
- Code: <http://github.com/plumed/plumed2>
- Google group: plumed-users
- Original papers:
  - PLUMED: A portable plugin for free-energy calculations with molecular dynamics.  
Comput. Phys. Commun. 2009
  - PLUMED 2: New feathers for an old bird. Comput. Phys. Commun. 2014
- Workshops (tutorial+meeting): Belfast (2014), Trieste (2017), TBA (2019)
- Online tutorials (most recent: Manual -> Tutorials -> Trieste tutorials)
- Material for the present webinar: <http://github.com/plumed/sbgrid2018>

# Acknowledgements

- Current developers:
  - Max Bonomi (University of Cambridge, UK)
  - Giovanni Bussi (SISSA, Trieste, Italy)
  - Carlo Camilloni (Università di Milano, Italy)
  - Gareth Tribello (Queen's University, Belfast, UK)
- Past developers:
  - Davide Branduardi (Schroedinger, UK)
- Other contributors: see <http://github/plumed/plumed2>



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