Problem set 6: Computational Molecular Physics and Methods of Molecular Simulations

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Please hand in by: 17th June, 2014 (4pm)

1. PCCA

(25 points) The task is to analyze the metastable sets of a reversible transition matrix. You will find the ascii file for the matrix on Prof. Petra Imhof's webpage in the teaching section: http://tinyurl.com/mok6p98.
Choose your favorite programming langugage and do a metastability analysis of the transition matrix:

(a) Determine the eigenvalues of the matrix and plot them.
(b) Based on (a) decide how many eigenvectors you want to look at and plot these eigenvectors in such a way that you can determine the simplex structure for PCCA.
(c) Find the linear transformation that will map the vertices of the simplex on unit vectors (hint use the inverse)
(d) Define the membership vectors and plot them.
(e) Why was no Schur decomposition required in the procedure unlike what was discussed in the lecture?

For further reading on PCCA and PCCA+ see Deufelhard and Weber in Linear Algebra and its Applications, 398, 2005, 161-184 DOI: 10.1016/j.laa.2004.10.026

2. Electrostatic Interactions

(only students who attend Thursday's classes) (25 points)
Figure 1 lists the topology and charges of two amino acid residues, Aspartate (ASP) and Glutamate (GLU) as used in the CHARMM force field. Aoms that are directly connected by bonds are explicitely listed. Angles and dihedral are implicitely defined as all sets of three/ atoms that are connected by bonds (via two/three bonds), respectivley. Bonds, angles and dihedrals are called "bonded interactions". All atoms that are not interactiong via bonded interactions contribute pairwise non-bonded interactions by Lenard-Jones terms $E_{i,j}^{LJ}$ and electrostatic terms $E_{i,j}^{elec}$.

(1) Energies

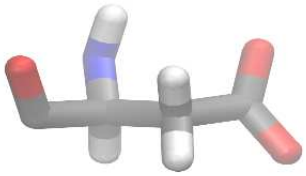
The total energy is calculated as

$$E = \sum_{bonds} E_{bond} + \sum_{angles} E_{angles} + \sum_{dihedrals} E_{dihedrals} + \sum_{i,j} E_{i,j}^{LJ} + \sum_{i,j} E_{i,j}^{elec}$$

(a)How many bonded terms contribute to the total energy in Aspartate and in Glutamate with the topologies shown in Figure 1?
(b) How many Lennard-Jones terms contribute in Aspartate and in Glutamate, respectively ?
(c) How many terms for electrostatic interaction contribute in Aspartate and in Glutamate, respectively?

```
RESI ASP      -1.00
GROUP
ATOM N    NH1    -0.47 !       |
ATOM HN   H       0.31 ! HN-N
ATOM CA   CT1     0.07 !       |   HB1    OD1
ATOM HA   HB      0.09 !       |    |    //
GROUP                  ! HA-CA--CB--CG
ATOM CB   CT2    -0.28 !       |    |    \
ATOM HB1  HA      0.09 !       |   HB2   OD2(-)
ATOM HB2  HA      0.09 !  O=C
ATOM CG   CC      0.62 !       |
ATOM OD1  OC     -0.76
ATOM OD2  OC     -0.76
GROUP
ATOM C    C       0.51
ATOM O    O      -0.51

BOND CB CA
BOND  CG CB
BOND OD2 CG
BOND N  HN
BOND N  CA
BOND C   CA
BOND CA HA
BOND CB HB1
BOND CB HB2
BOND O   C
BOND CG  OD1
```



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RESI GLU      -1.00
GROUP
ATOM N     NH1    -0.47 !       |
ATOM HN    H       0.31 !   HN-N
ATOM CA    CT1     0.07 !       |   HB1 HG1   OE1
ATOM HA    HB      0.09 !       |    |    |     //
GROUP                   ! HA-CA--CB--CG--CD
ATOM CB    CT2    -0.18 !       |    |    |     \
ATOM HB1   HA      0.09 !       |   HB2 HG2   OE2(-)
ATOM HB2   HA      0.09 !    O=C
GROUP              !    |
ATOM CG    CT2    -0.28
ATOM HG1   HA      0.09
ATOM HG2   HA      0.09
ATOM CD    CC      0.62
ATOM OE1   OC     -0.76
ATOM OE2   OC     -0.76
GROUP
ATOM C     C       0.51
ATOM O     O      -0.51

BOND CB CA
BOND CG CB
BOND CD CG
BOND OE2 CD
BOND N  HN
BOND N  CA
BOND C   CA
BOND CA HA
BOND CB HB1
BOND CB  HB2
BOND CG  HG1
BOND CG HG2
BOND O  C
BOND CD  OE1
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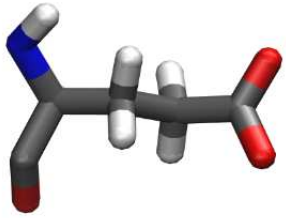

Figure 1: Topology and Charges of top: Aspartate and bottom Glutamate in the CHARMM Force Field. Atomic charges are defined as "ATOM atomlabel atomtype charge". Bonds that connect atoms are listed as "BOND atom1 atom2". In addition the schematic drawing (afer the "!" signs) shows a single or double line for atoms connected by a bond. (Remark:These are not the full amino acids but the parts that appear in a peptide chain.)

(2)Electrostatics and polarisation
Aspartate and Glutamate differ by Glutamate being one CH2-group longer. Example coordinates for each of the wo are given in he files Asp.dat and Glu.dat (in columns 1-3) together with the atomic charges and Radii.
(a) Calculate the electrostatic interaction energy

$$E^{elec} = \sum_{ij} \frac{q_i q_j}{\varepsilon r_{ij}}$$

of the non-bonded atoms in Aspartate and Glutamte, respectively, for $\varepsilon = \epsilon_{vac} = 1$ and $\varepsilon = \epsilon_w = 80$.
(b) Calculate the polarisation (electrostatic) part of the solvation free ΔG^{pol} energy for Aspartate and Glutamate when changing from vacuum, $\epsilon_{vac} = 1$ to water $\epsilon_w = 80$ according to the Born formula

$$\Delta G^{pol}_{Born} = -\frac{q^2}{2a}\left(\frac{1}{\varepsilon_{vac}} - \frac{1}{\varepsilon_w}\right) .$$

Treat the molecules as spheres with q as the net charge and the radius given by half the CG – CA distance.
(c) Calculate the polarisation part of the solvation free energy according to the generalised Born formula

$$\Delta G^{pol}_{GB} = -\frac{1}{2}\left(\frac{1}{\varepsilon_{vac}} - \frac{1}{\varepsilon_w}\right)\sum_{i,j} \frac{q_i q_j}{f_{GB}\left(r_{ij)}\right)}$$

with $f_{GB}\left(r_{ij}\right) = \left[r_{ij}^2 + R_i R_j \exp\left(\frac{-r_{ij}^2}{4R_i R_j}\right)\right]^{\frac{1}{2}}$.
(d) Repeat task a) and b) for a super-molecule, that consists of both Aspartate and Glutamate.
(e) Now shift the Glutamate by 2; 5; 10 Angstrom in x-direction (adding 2; 5; 10 to the x-coordinates of the Glu atoms), and recalculate the energies from d). What do you observe?