Exercise 1. Analysis of different non-covalent interaction types

a) We are now going to analyze different systems that you already know. Describe the different interactions you see, identifying them with what you expected:

- Water dimer
- Benzene dimer (parallel conformation)
- Bicyclooctene

b) With what you have learnt in the previous exercise, describe the interactions you find in more complex situations:

- Adenine-thymine
- Phenol dimer
- Formic acid dimer
- Peptide – note that you can change the cutoff for a better visualization with the following keyword, where you can play with the RDG value (`xx`):
  `CUTPLOT xx 0.5`

c) Charge the adenyn and thymine residues separately in order to visualize intermolecular interactions only. This can be done easily with the following input:
```
2
A.xyz
T.xyz
INTERMOLECULAR
```

Exercise 2. Delocalized vs localized

This exercise will enable you to see the difference between localized and delocalized interactions. Whereas localized interactions are mainly between two atoms, delocalized one are between several atoms (so the surface spreads out).

a) Calculate CH_4 dimer, $CH_4 \cdots H_2O$, $CH_4 \cdots HF$ and $CH_4 \cdots NH_3$ and visualize NCI. Which interactions are local (mainly between two atoms) or delocalized?

b) We will see how localized and delocalized interactions vary with size. We will analyze NCI for benzene, naphthalene and anthracene. These systems have one, two and three fused rings.

Calculate NCI. Since in this case we are using rather big systems, we will choose promolecular densities, faster to calculate. We will further accelerate the calculation with an adaptive grid:

```
2
MonomerA.xyz
MonomerB.xyz
INTERMOLECULAR
CG2FG 3 4 2 1
```

Visualize the non-covalent interactions in the parallel conformation (P) and the T-shape conformation (T) for benzene and classify them as delocalized or localized. Visualize now naphthalene and anthracene P and T conformations. What happens as the size increases for each interaction type?

You can quantify the size effect with NCIPLOT4.0. Use the following input type to obtain the volume of the non-covalent interactions the parallel and T-shape series with respect to the number of units.

```
2
BenzeneA.xyz
BenzeneB.xyz
INTERMOLECULAR
RANGE 3
-0.07 -0.01
-0.01 0.01
0.01 0.07
```

Plot the charge (n=1) with respect to the benzene units (1 to 3). What interaction becomes favored with size?

# Benzene units	Parallel conformation volume	T-shape conformation volume
1		
2		
3		

Exercise 3. Biomolecules (NCIweb)
We will analyze interactions in biosystems using nciweb:
https://nciweb.dsi.upmc.fr/index.php

a) Upload the β-sheet file and analyze which interactions keep the sheets together.

b) Upload the file 3NIR (pdbs can be uploaded directly by its name) and analyze the intermolecular interactions with what you have learnt. Do not forget to add the hydrogens!

c) In order to quantify the interactions you can carry out an integration of the charge within the NCI region. We will look at a dimer (monomers A and B) of the Aβ40 extracted from the fibril structure. We can for example look at the three coloring ranges, attractive (-0.1< ρ <0.02), repulsive (0.02< ρ <0.1) and van der Waals (-0.02<ρ<0.02) with the following input:

```
2
abeta40dimerA.xyz
abeta40dimerB.xyz
INTERMOLECULAR
CUTOFFS 0.2 1.0  ! following intervals for s=0.1 and ρ=0.2
CG2FG 4 8 4 2 1
INCREMENTS 0.2 0.2 0.2 !smaller number of points
OUTPUT 1  !dont print the cube files
RANGE 3
-0.1 -0.02
-0.02 0.02
0.02 0.1
```

Take the values for n=1, which correspond to the charge enclosed by the intermolecular interactions up to s=1.0 and fill in this table:

Interaction type	Charge (n=1)
Atractive	
vdW	
Repulsive	

**Exercise 4. MD trajectory**

a) Now we are going to focus in a classical MD. The test system is a dimer (A and B) of the Aβ42 extracted from the fibril structure of PDB 2NAO.

The initial geometry of the dimer is that of the fibril; a 1μs dynamics in explicit solvent (water) simulation is run to observe the folding (the yellow pieces in the figure represent the β-sheet secondary structure). What interactions do you expect from the intra and intermolecular point of view at the following steps?

Folding around the hydrophobic sequence

0 ns   500 ns   1000 ns
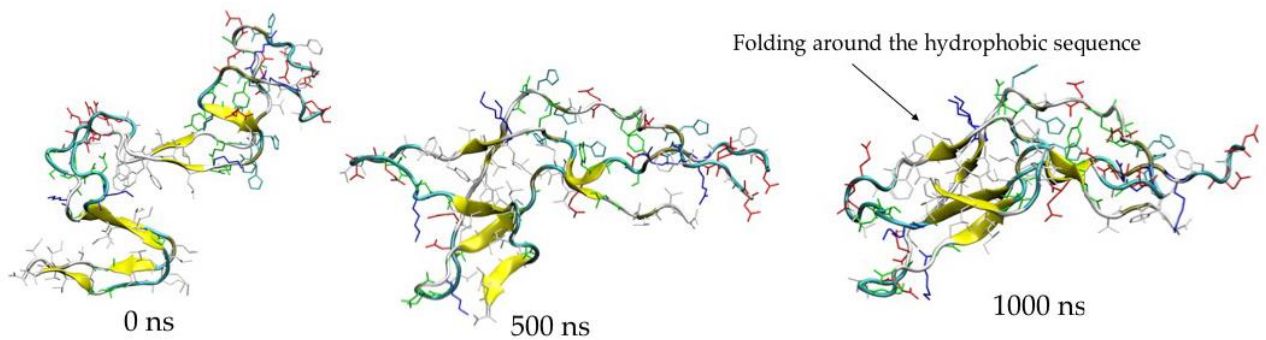
b) We will focus in the intramolecular van der Waals interactions of the monomer B hydrophobic residues (17 to 20 and 30 to 42) (`abeta42dimerB_1micros_apolar_n.xyz`, n=timestep) in order to see the intramolecular folding. We will look at steps every 10 snapshots. Evaluate the evolution of the integrals along the MD What do you observe?