NMA-RRT PRACTICALS GUIDE

1- Preparing Input Files

1.1- PDB files

NMA-RRT computes the transition path between two conformations of a protein provided as input in PDB files. Homolog proteins or mutants can also be used, but the current version requires the same number of amino acid residues for both proteins.

1.2- AMC files

AMC files are simple text files that contain information about the "mechanistic" representation of the proteins. The required input files for NMA-RRT can be generated using the programs `build_amc` and `make_tripep`
AMC files for the EIA example can be generated as follows:

```
> cd NMARRT_tests/EIA/
> ../../binaries/build_amc -b -s 1EIA-amb.pdb   (generates 1EIA-amb.amc)
> ../../binaries/make_tripep   (follow instructions to generate a new file, e.g. 1EIA-amb_tri.amc)
```

2- Running NMA-RRT

2.1- Parameter setting

The values of most parameters of the NMA-RRT algorithm can be specified in a *parameters file*, which is used to run the application. This file also specifies the location of input and output files. A template file for EIA could be:

```
initial_pdb_filename = "1EIA-amb.pdb"
target_pdb_filename = "2EIA-amb.pdb"
initial_amc_filename = "1EIA-amb_tri.amc"
target_amc_filename = "2EIA-amb_tri.amc"
output_folder = "Test1"
errlog_filename = "NMARRT_err"
diag_filename = "NMARRT_diag"
vdW_scaling_factor = float 0.70
RRT_NFailMax = int 100
result_resolution = float 0.1
```

In this case, values are specified only for two parameters. The other parameters will take default values.
The accessible parameters are (default valuers are indicated between brackets):

```
initial_pdb_filename
initial_amc_filename
target_pdb_filename
target_amc_filename
errlog_filename
diag_filename
output_folder
fixed_residues  (OPTIONAL. See KPO for example. MUST FIT THE TRIPEPTIDE-BASED DECOMPOSITION)

max_nb_RRTnodes [1000]      (Maximum number of RRT nodes)
max_nb_RRTiter [3000]       (Maximum number of RRT iterations)
RRT_NFailMax [100]          (Maximum number of consecutive failures permitted for node expansion)
RRT_StepSize [0.025]        (RRT validation step size)
vdW_scaling_factor [0.7]    (vdW radii scaling factor)
perturb_maxPChange [0.03]   (Maximum position perturbation of particles)
perturb_maxQChange [0.02]   (Maximum orientation perturbation of particles)
perturb_maxDChange [0.03]   (Maximum bond torsion perturbation)
min_particle_move [0.005]   (Minimum particle move)
rrt_min_move [0.01]         (Minimum particle RMSD value to consider an RRT run as successful)
backtracking_step [2]       (Number of RRT cycles to go back after an unsuccessful RRT run)

result_prefix ["conformation_"]  (Prefix of the output files of the algorithm)
result_resolution [0.05]    (Particle RMSD between two consecutive conformation in the output path)
stop_condition [0.5]        (Particle RMSD to target conformation at which the NMA-RRT algorithm stops)
```

2.2- Running the program

```
> ../../binaries/NMA_RRT_Test params.txt
```

If you want to (brutally) stop before the end of the simulation : `Control+C`

3- Results

3.1- Transition path

The result of NMA-RRT is a sequence of PDB files at: *`output_folder`*`/path`
To visualize a movie of the conformational transition:

```
> cd output_folder/path
> cp ../../../load_mov.py .
> pymol load_mov.py
```

3.2- Performance

Information about the performance of NMA-RRT is provided in: *`output_folder`*`/info.txt`

IMPORTANT NOTE: This is a simplified version of the software that does not consider protein side-chains. Therefore, results are not very accurate.