Exercise 5
Ab-initio structure prediction
The Procedure

1. Low-resolution step \((fast)\)
   – Identify potential minima

2. Cluster analysis
   – Identify broadest basins in landscape.

3. High-resolution step \((slow)\)
   – Identify lowest energy minimum in the basins
Low-resolution step

- Conducted via the *AbinitioRelax* protocol
- Centroid representation, ideal bonds & angles
- “Rough” scoring function – less terms, mainly for compact structures, long range interactions

**Employs:**
- Fragment insertion
- Monte Carlo sampling of different perturbations
  (small move, shear move, chuck move, gunn move, wobble move, crank shaft)
Cluster analysis

- Optional step, run via the *cluster* protocol
- Motivation:
  - Low resolution step less accurate – need different starting structures for high resolution step
  - Native conformation theoretically in broad, easily reachable energy basin
High resolution step

- Can be employed via the *AbinitioRelax* protocol (using the "-abinitio:relax" flag), or as a stand-alone application - *Relax*

- More sensitive score function

- Full atom representation (ideal bonds & angles)

**Employs:**

- small & shear moves (under increasing weight for VdW repulsive)
Currently recommended command

```bash
AbinitioRelax.linuxgccrelease \   
   -database rosetta_database \   
   -in:file:fasta input_files/1elwA.fasta \   
   -in:file:native input_files/1elw.pdb \   
   -in:file:frag3 input_files/aa1elwA03_05.200_v1_3 \   
   -in:file:frag9 input_files/aa1elwA09_05.200_v1_3 \   
   -abinitio:relax \   
   -relax:fast \   
   -abinitio::increase_cycles 10 \   
   -abinitio::rg_reweight 0.5 \   
   -abinitio::rsd_wt_helix 0.5 \   
   -abinitio::rsd_wt_loop 0.5 \   
   -use_filters true \   
   -psipred_ss2 input_files/1elwA.psipred_ss2 \   
   -kill_hairpins input_files/1elwA.psipred_ss2 \   
   -out:file:silent 1elwA_silent.out \   
   -nstruct 100000
```

Today it's a two step protocol:
1. Low resolution step
2. High resolution step
   * brute force sampling

https://www.rosettacommons.org/docs/latest/abinitio-relax.html