Molecular Moeling -- lecture 11 exercises

Test your knowledge

Question: Given the following alignment, what will MOE's automated homology modeling tool try to do?

Answer: "Loop search will try to find a loop of length **N** that fits into the space between anchor residues **x** and **y**, currently spanned by **M** residues." Fill in the blanks.

alignment	x	y	N	M
target ACDTGFW template LMN..YI				
target AC.DTGFW template LMN...YI				
target LMN..YI template ACDTGFW				
target LMN....YI template AC.DTGF.W				

Exercise 11

Adding waters to a protein structure:

Part one: Solvate

Download 1csk from **File | Protein database**
Delete all chains except **A**.
Load energy function **Amber12EHT** (lower left corner). Fix Hydrogens and charges if necessary.
Compute | Prepare | Structure preparation (correct any errors)
Protonate3D (Add protons or take them away)
Compute | Simulations | Dynamics
Forcefield setup : **Amber12EHT**. (If problems are found at this point, choose a different protein!)
Solvent setup: Salt: NaCl, Margin:4, Layer. Delete far. OK.
Solvent layer appears. NA+, Cl- and water.
Cancel | Dynamics. (don't run MD)
Select | solvent, Edit | potential | unfix, Select | invert, Edit | potential | fix
Minimize

Part two: Freeze dry

In **SEQ** window, select water and salt ions chains. (single **left-click** on chain labels, don't double click)
In **MOE** window**, Select | Selector.. (**Click **UI** button on menu bar**)**
Check "**selected chains**".
Operation "**Or**"

Connectivity I pull down to **Accessibility**.
Probe radius: **5.0**

In **SEQ** sindow: Check how many waters are left.
Return to Atom Selector.
Click **Exposed**.
Click **Extend**: **Residue**. (just to the right in Atom Selector window)
Go to **MOE** window: **Delete**. Exposed waters disappear.
Go back to Atom Selector.

Repeat these three steps until only ~20-30 waters are left:

Part three: Equilibrate

Select I Solvent
Atoms I spacefill
Edit I Potential I Unfix
Select I Invert
Edit I Potential I Fix
Select I clear
Minimize. (Only waters move.)
Compute I Simulations I Dynamics
Uncheck "Rigid water"
Change file name to **water.mdb**
OK.
Do any waters fly away? Does the simulation "explode"?
Which waters are moving the most? Least? Why?
After a few minutes, **Cancel I Dynamics**

Part four: Find stable waters

Load movie: **File I Open**, water.mdb
In database window,
File I Browse, Hit the "play" button. Use slider to set speed.
In MOE window, watch animation. **Hide** all protein atoms. Make waters **spacefill**.
Hide I Receptor
Select I solvent, **Atoms I** spacefill

Waters that are sitting in deep energy wells move very little in a MD simulation. Waters that are sitting on an energy slope, or in a shallow energy well, move around. By looking the at the movie, select five waters that are in deep energy wells. **Color them light blue**.

While movie is still playing. Select individual waters in **SEQ**, and click **Siteview** in **MOE.**

Is the water's motion correlated with the number of hydrogen bonds?

Save MOE file with and Upload to the homework site, as Exercise 11