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Bioinformatics

Practice 3 - Trajectories in VMD

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1 Theoretical Framework

1.1 VMD's Trajectory Files

The time-evolving coordinates of a system are called a trajectory. They are most commonly obtained in simulations of molecular systems, but can also be generated by other means and for different purposes. Upon loading a trajectory, VMD can animate movies of system evolving with time and analyze various structural features throughout the trajectory [1].

Trajectory files are typically large binary files that contain the time varying atomic coordinates for the system. Each set of coordinates corresponds to one frame in time [1].

An example of a trajectory file is a DCD file. Trajectory files usually do not contain information structural information as found in protein structure files (PSF). Therefore, we must first load the structure file, and then add the trajectory data to the same molecule, so that VMD has access to both the structure and trajectory information [1].

1.2 Steered Molecular Dynamics Method

Steered Molecular Dynamics allows to explore biological processes on time scales accessible to molecular dynamics simulations. For instance, unbinding of ligands and conformational changes in biomolecules (like those explored using Atomic Force Microscopy, AFM) can be studied using this technique [2].

The basic idea behind any SMD simulation is to apply an external force to one or more atoms, which are referred to as SMD atoms. In addition, another group of atoms fixed can be kept and the behaviour of a protein can be studied under various conditions [2].

1.2.1 Pulling a Ubiquitin

The trajectory used for the section Using the pulling.dcd file is a simulation of an AFM (Atomic Force Microscopy) experiment pulling on a single ubiquitin molecule, performed using the Steered Molecular Dynamics (SMD) method (Isralewitz et al., Curr. Opin. Struct. Biol., 11:224, 2001) [1].

The behavior of the protein is looked as it unfolds while being pulled from one end, with the other end being constrained to its original position. Each frame step corresponds to 10ps [1].

Ubiquitin has many functions in the cell, and it is currently believed that some of these functions depend on the protein's elastic properties. Such elastic properties are usually due to hydrogen bonding between residues in β strands of the protein molecules [1].

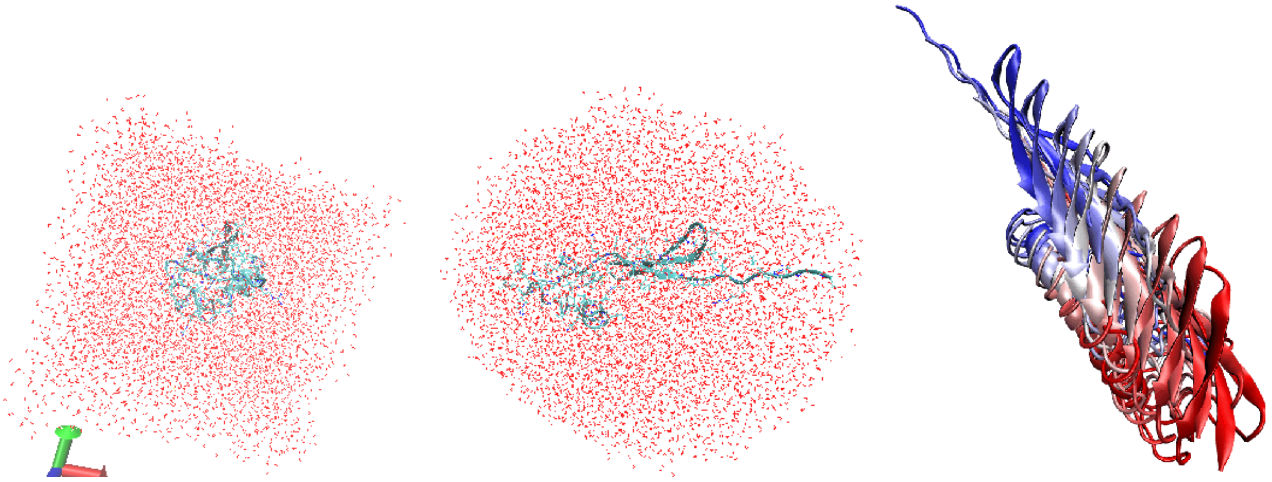
2 Material and Equipment

- VMD - Visual Molecular Dynamics Software.
- "Trajectories and Movie Making" tutorial from the VMD's official web page [1].
- Tutorial's files [3] provided by [1]:
  - **ubiquitin.psf**
  - **pulling.dcd**
  - **equilibration.dcd**
- Pro-apoptotic protein Bax model - 1F16 [4].

3 Practice Development

3.1 Using the pulling.dcd file

In the lab session, the "Trajectories and Movie Making" tutorial was followed up to the **Updating selections** section using the **ubiquitin.psf** and **pulling.dcd** files as example, that when loaded both together in VMD, looks like Figures 1a and 1b.



(a) First frame of the Ubiquitin model with the pulling.dcd file applied (NewCartoon style).

(b) Last frame of the Ubiquitin model with the pulling.dcd file applied. The protein now can be seen stretched.

(c) Image of every tenth frame showed at once, smoothed with a 20-frame window. Image taken from [1].

Figure 1: Pulling process simulation of the Ubiquitin protein model.

This dcd file "pulls" the Ubiquitin protein model, whose trajectory is showed in 100 frames. The simulated process is shown in Figure 1c. Additionaly, there is an option that can update the atoms of the selections as the trajectory advances. Figure 2 shows this.

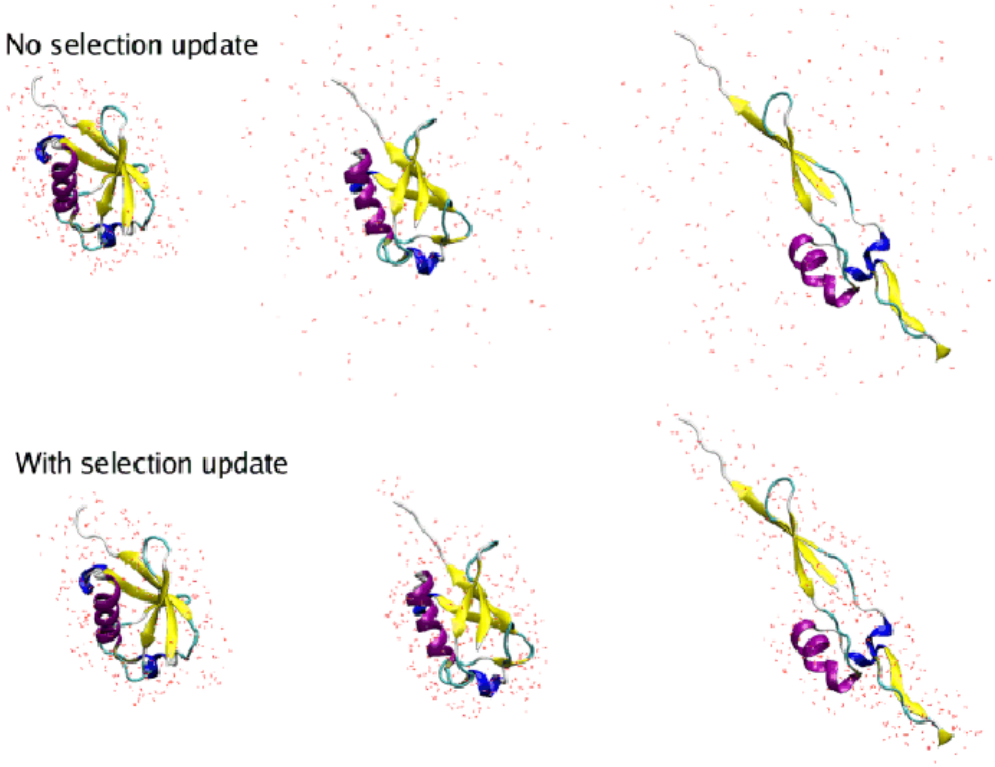


Figure 2: Water shown for a selection that is not updated and for the one that is updated each frame. The snapshots shown are (from left to right) for frames 0, 17, and 99. Image taken from [1].

Because of this, the steps of the tutorial for this specific dcd file won't be reported. Instead of that, the remaining dcd file **equilibration.dcd**, alongside the **1F16** protein model will be shown and analyzed in this paper.

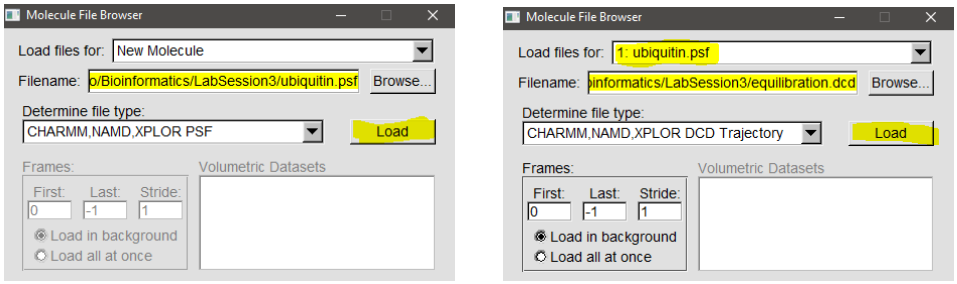
3.2 Using the equilibration.dcd file

3.2.1 Loading Trajectories

Start VMD. In the VMD Main window, choose File > New Molecule and load the **ubiquitin.psf** file through the File Browser window as shown in Figure 3a.

There won't be anything displayed in VMD, so now again try to load another molecule, but this time in the File Browser window make sure that **ubiquitin.psf** is selected in the *Load Files for* option, then load the **equilibration.dcd** file. The File Browser window should look like Figure 3b.

Figure 4 shows how it looks the protein with its trajectory displayed in VMD. It's necessary to create two representations: protein selection with NewCartoon style and Secondary Structure color, and water selection with Lines style and Name color.



(a) Loading ubiquitin.psf file.

(b) Loading equilibration.dcd for the ubiquitin molecule.

Figure 3: Loading frames for a molecule in VMD.

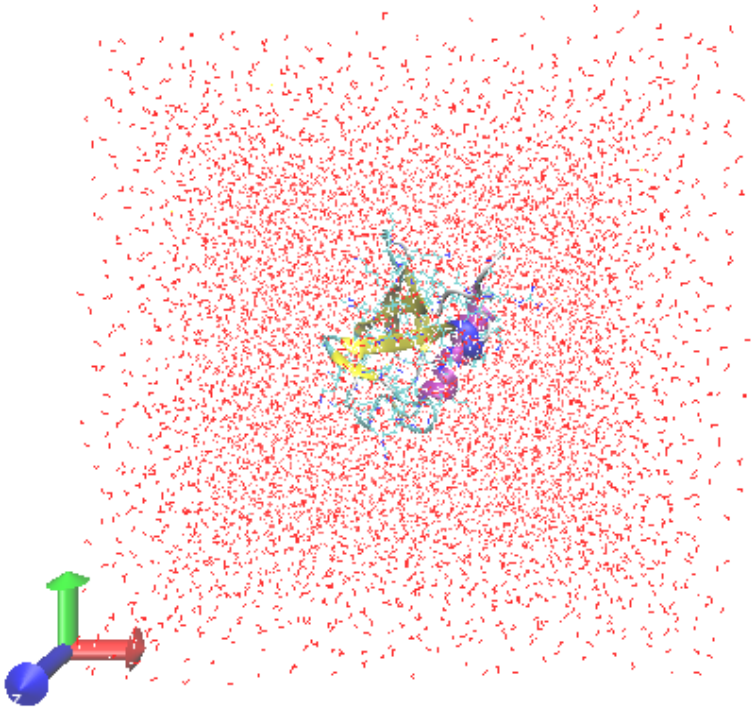


Figure 4: 1UBQ model with an equilibration trajectory (last frame).

3.2.2 Main Menu Animation Tools

The movie of the loaded trajectory can be played back and forth, using the animation tools shown in Figure 5.

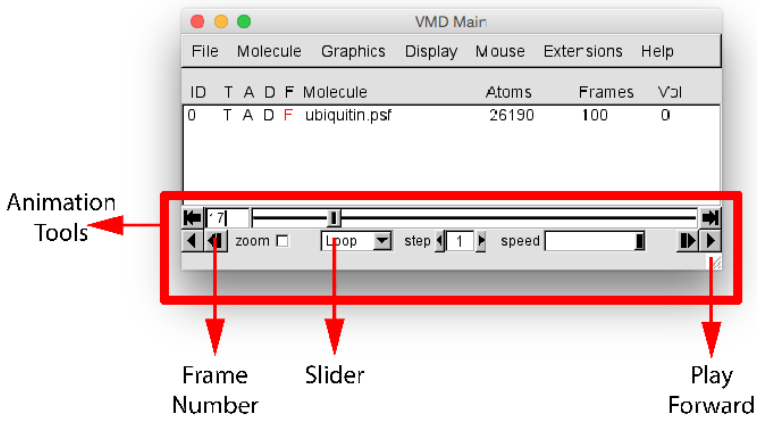
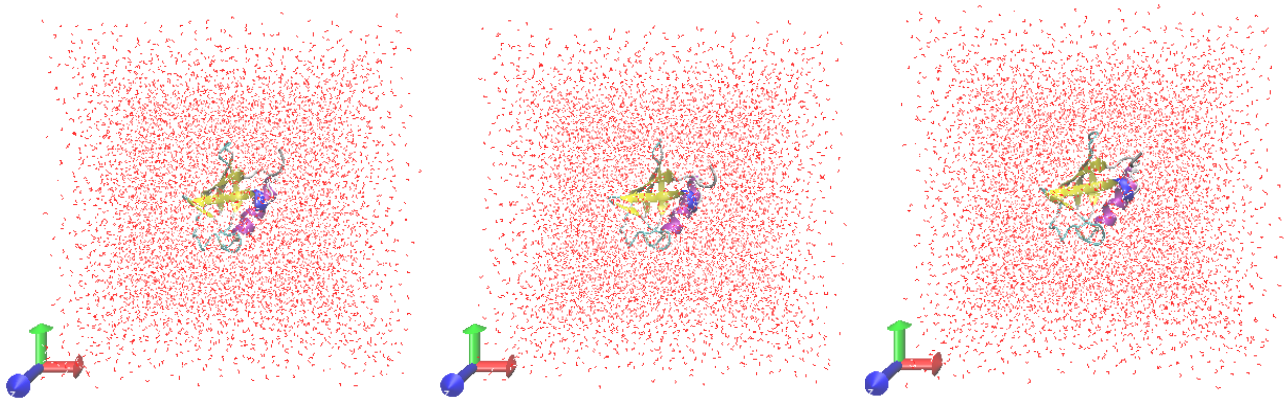


Figure 5: Animation tools in the main menu of VMD. Image taken from [1].

These tools allows to go over frames of the trajectory (e.g., using the slider) and to play a movie of the trajectory in various modes (Once, Loop, or Rock) and at an adjustable speed [1]. Figure 6 shows the protein in different moments of the trajectory, using the slider bar. As can be seen, the protein is not so drastically altered, it is only stabilized.



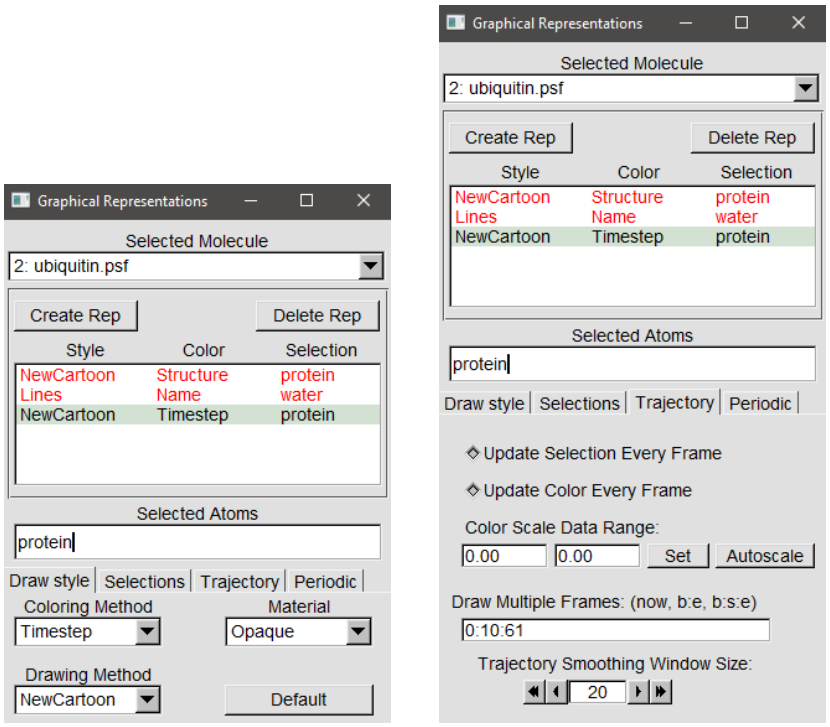
(a) Frame 10. (b) Frame 25. (c) Frame 40.

Figure 6: Behavior of the water around the 1UBQ protein in different moments of the equilibration trajectory.

3.2.3 Displaying multiple frames

In the Graphical Representations window hide the protein and water representations and create a new representation with the next characteristics: protein selection, NewCartoon style and Trajectory > Timestep coloring (as shown in Figure 7a).

Then, go to the Trajectory Tab, where the trajectory motion smooth can be changed and multiple frames of the trajectory can be drawn at once [3].



(a) Representation values. (b) Trajectory Tab values.

Figure 7: Configuration for displaying multiple frames at once.

Enter *0:10:61* on the Draw Multiple Frames input, which selects and displays every tenth frame from the range 0 to 61, and set the smoothing window to 20. Figure 7b shows how it should look the Trajectory Tab in the Graphical Representations window, and the resulted display should be similar to Fig 8.

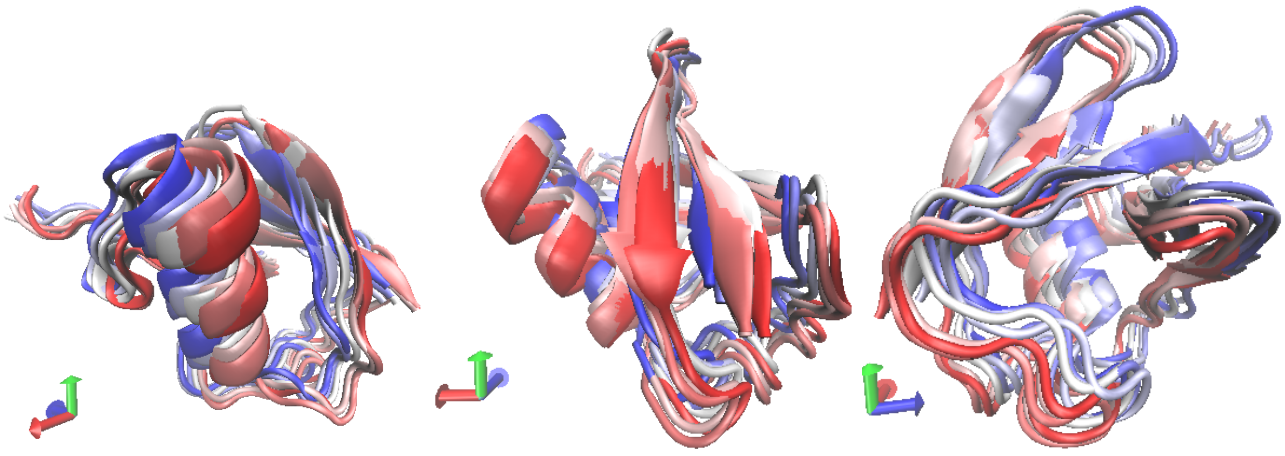


Figure 8: Every tenth frame showed at once, smoothed with a 20-frame window.

3.2.4 Updating selections

Hide the timestep representation and show the previous two representations (protein NewCartoon and water Lines). Change the water selection to *water and within 3 of protein*, and change the style to Licorice, as shown in Figure 9.

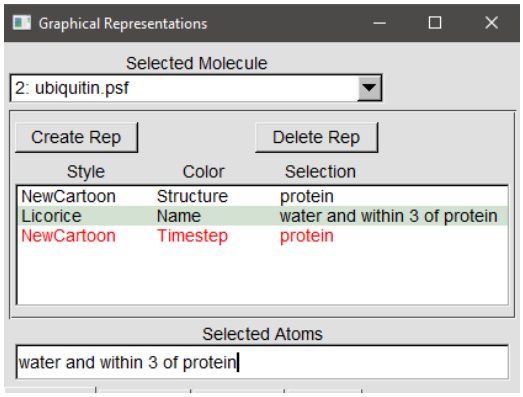


Figure 9: Selection of all water atoms within 3 Armstrongs of the protein.

Although the displayed water atoms may be near the protein for a little while playing the trajectory, they soon wander off, and are still shown despite no longer meeting the selection criteria (see Figure 10) [1].

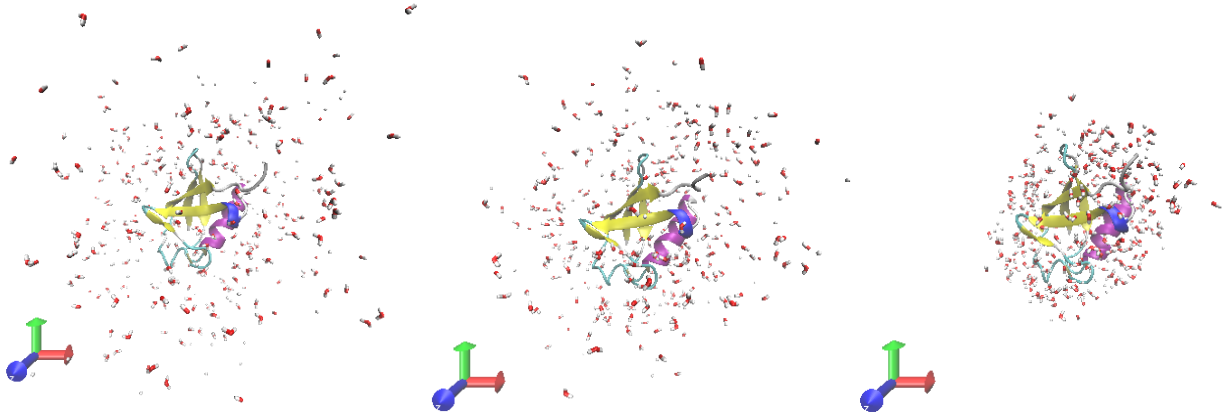


Figure 10: Trajectory with no selection update. Frames are (left to right) 20, 40 and 60.

The *Update Selection Every Frame* option in the Trajectory tab of the Graphical Representations window remedies this. If the option box is checked, the selection is updated every frame (see Figure 11) [1].

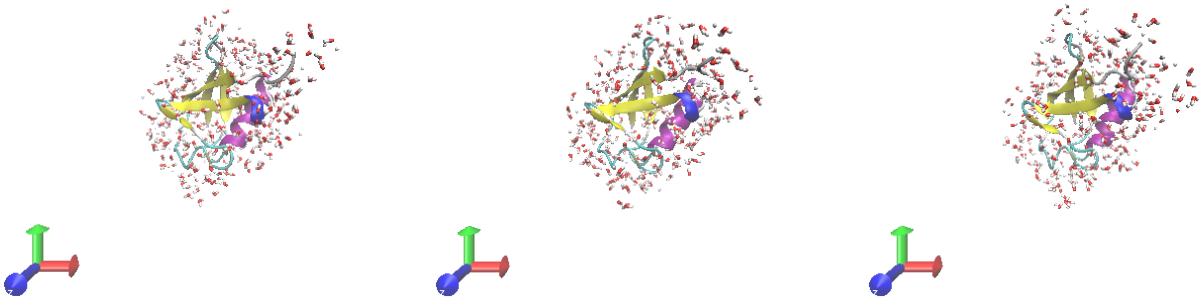


Figure 11: Trajectory with selection update. Frames are (left to right) 20, 40 and 60.

3.3 Using the 1F16 protein model

In this section the frames of the 1F16 solution structure of a Pro-apoptotic protein Bax model are explored and analyzed.

First, when the PDB file is loaded in VMD, this already has 20 frames on it. Figure 12 shows how the last frame of this protein model looks displayed with VMD's default settings.

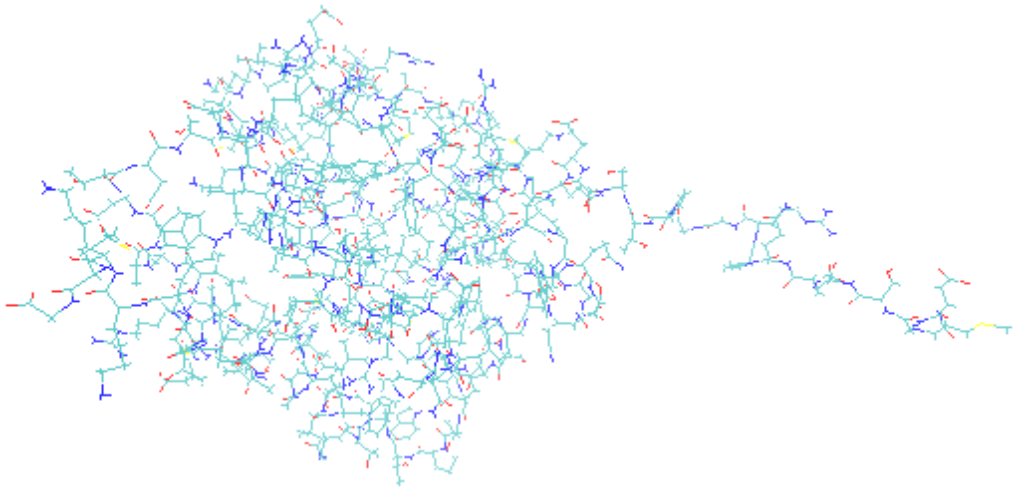
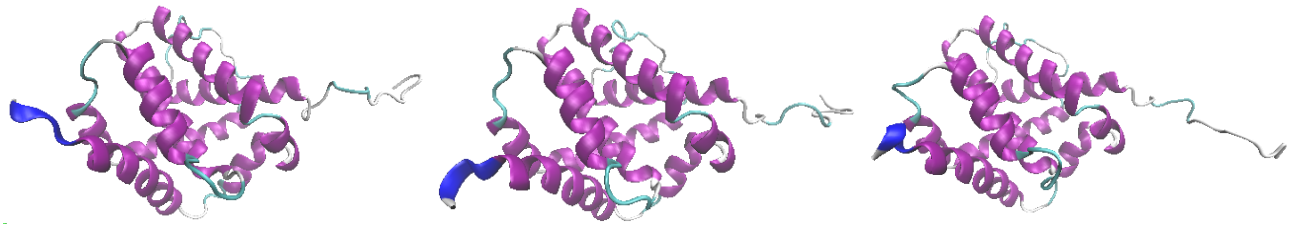


Figure 12: Last frame of the 1F16 Bax model.

Second, the included trajectory of the model is explored through the slider bar of the Animations Tools (see subsection Main Menu Animation Tools). In the Graphical Representations window edit the drawing method of the representation to NewCartoon and the coloring method to Secondary Structure. Figure 13 shows the protein in different moments of its own trajectory. As can be seen, only a few of its secondary structures and coils are altered.



(a) Frame 7. (b) Frame 14. (c) Frame 19.

Figure 13: Behavior of the 1F16 protein in different moments of the trajectory.

Finally, apply the same configuration as the 1UBQ multiple frames display for 1F16, seen in section Displaying multiple frames, but now entering *0:3:19* on the Draw Multiple Frames input, to select and display every third frame from the range 0 to 19. Figure 14 shows the results of this.

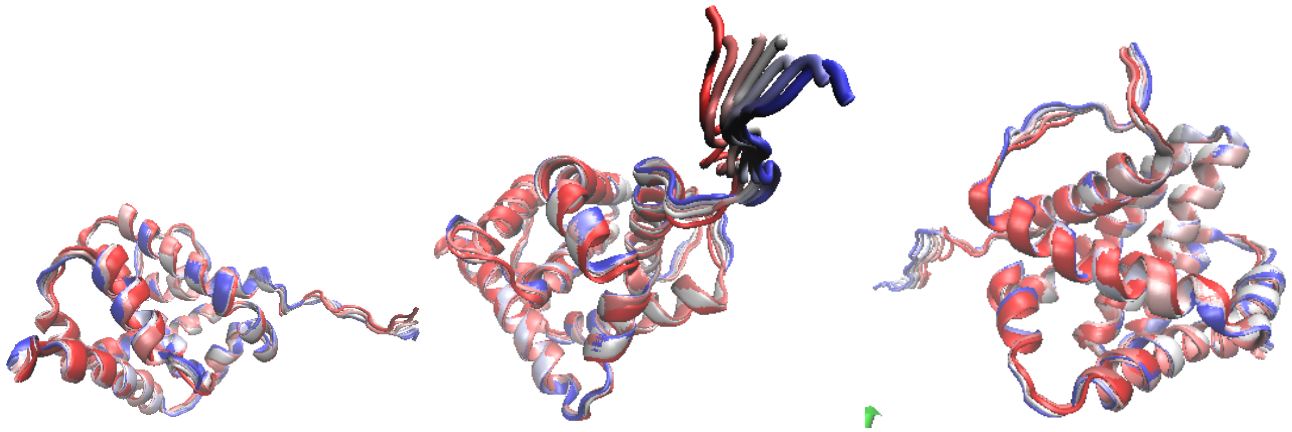


Figure 14: Every third frame showed at once, smoothed with a 20-frame window.

4 Conclusions and recommendations

It's highly recommended that select the correct drawing methods in a molecule while running their trajectory through the Main Menu Animation Tools, in order to appreciate and watch correctly the parts of interest. On the other hand, it's very interesting those proteins that have already in them a trajectory by default, such as the 1F16, reviewed in this practice. This depends on the protein's nature itself. Finally, the performance of the animation is controlled by the computational power of our workstation.

5 References

[1] Theoretical and Computational Biophysics Group, "Trajectories and Movie Making," https://www.ks.uiuc.edu/Training/Tutorials/vmd/tutorial-html/node3.html, [Online; last access October 19, 2020].

[2] ——, "Steered Molecular Dynamics," https://www.ks.uiuc.edu/Training/Tutorials/namd/namd-tutorial-unix-html/node16.html, [Online; last access October 20, 2020].

[3] ——, "Index of /Research/vmd/vmd-1.8.2/tutorial/vmd-tutorial-files," https://www.ks.uiuc.edu/Research/vmd/vmd-1.8.2/tutorial/vmd-tutorial-files/, [Online; last access October 19, 2020].

[4] R. PDB, "1F16 SOLUTION STRUCTURE OF A PRO-APOPTOTIC PROTEIN BAX." https://www.rcsb.org/structure/1F16, [Online; last access October 19, 2020].