BioBlender 2.1

Manual

2020-04-08

Index

What is BioBlender?

BioBlender is a software package based on open source Blender 3D modeling software.

Biology works at the nanoscale, with objects invisible to the human eye. With BioBlender it is possible to show some of the characters that populate our cells, based on scientific data and the highest level of 3D manipulation. Scientists from around the world study proteins at the atomic level and deposit information in the public Protein Data Bank repository, where each molecule is described as the list of its atoms and their 3D coordinates. With BioBlender, users can manage proteins in 3D space, display their surface in a photorealistic way, and construct protein motions based on known conformations.

BioBlender is an implementation of Blender, an open source, freely distributed, cross-platform, interoperable, and compatible 3D animation, visual effects, and video game.

The combination of 3D computer graphics, game engines and scientific programs make BioBlender a complete instrument for elaborating the movement of proteins and displaying their surface characteristics using visual code based on textures and special particle effects. In this way, it is possible to show the physical and chemical properties of a moving molecule.

Requirements

- Install Python 3.5.3

- Install Blender 2.79b

- Install Pymol

- Install the Numpy and Prody libraries

  To install these libraries:

  1. Open windows console (**Windows + R**)
  2. Type cmd
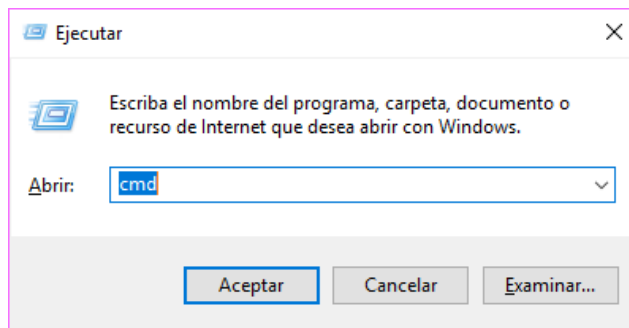
  3. Then in the Windows console type:
     ```
     pip install numpy
     ```
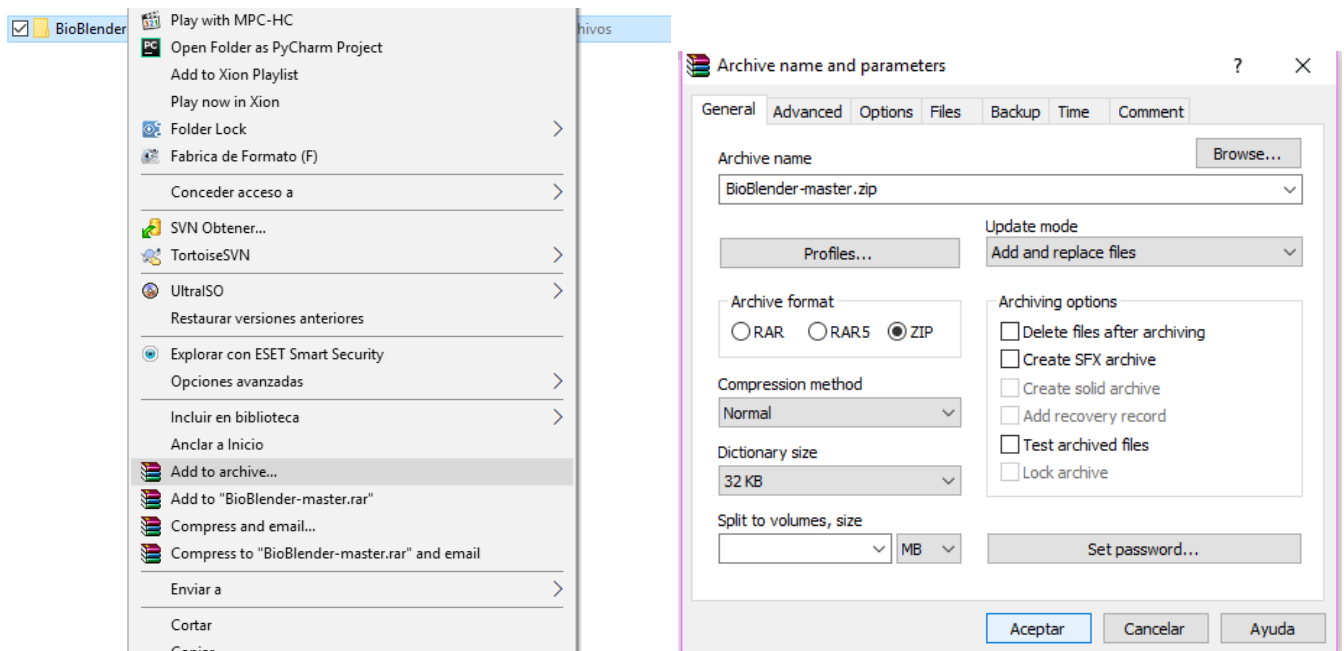
  4. Once finished, proceed to install Prody:
     ```
     pip install Prody
     ```

How to install BioBlender?

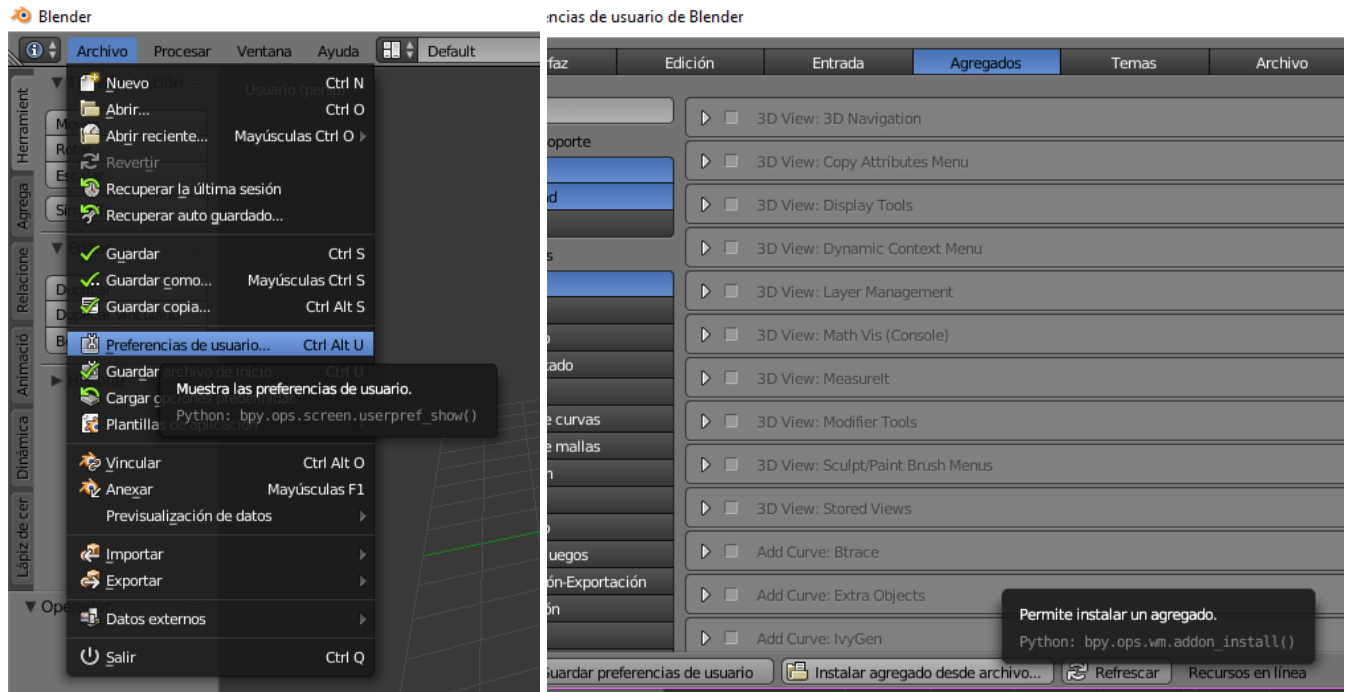- **Steps:**

  1. Compress the BioBlender-master folder in a .zip file (In case the folder is not compressed)

  2. Once the folder is compressed, open the Blender and add the BioBlender-master.zip file to Blender. For this you have to open:
     File > User Preferences > Add-ons > Install Add-ons From File (Here look for the directory, select the .zip file and press Install Add-ons From File)

3. Once the BioBlender has been added, it should be activated automatically, but in case it has not been activated, go to: newline File > User Preferences > Added (Here activates BioBlender 2.0) newline Then save the preferences of user.
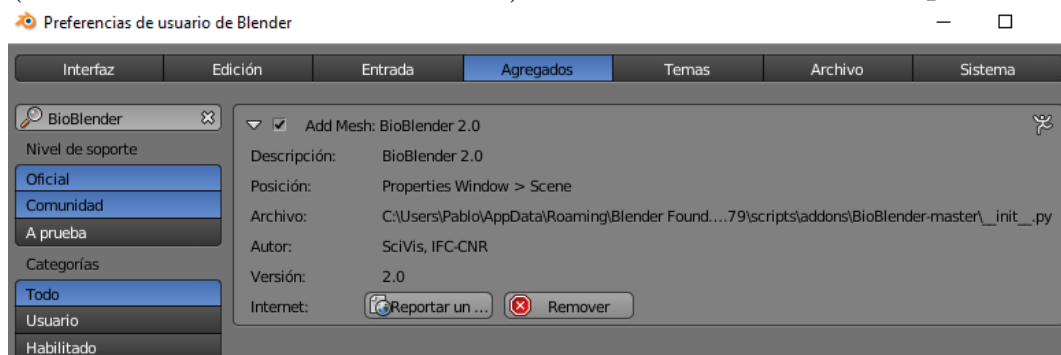
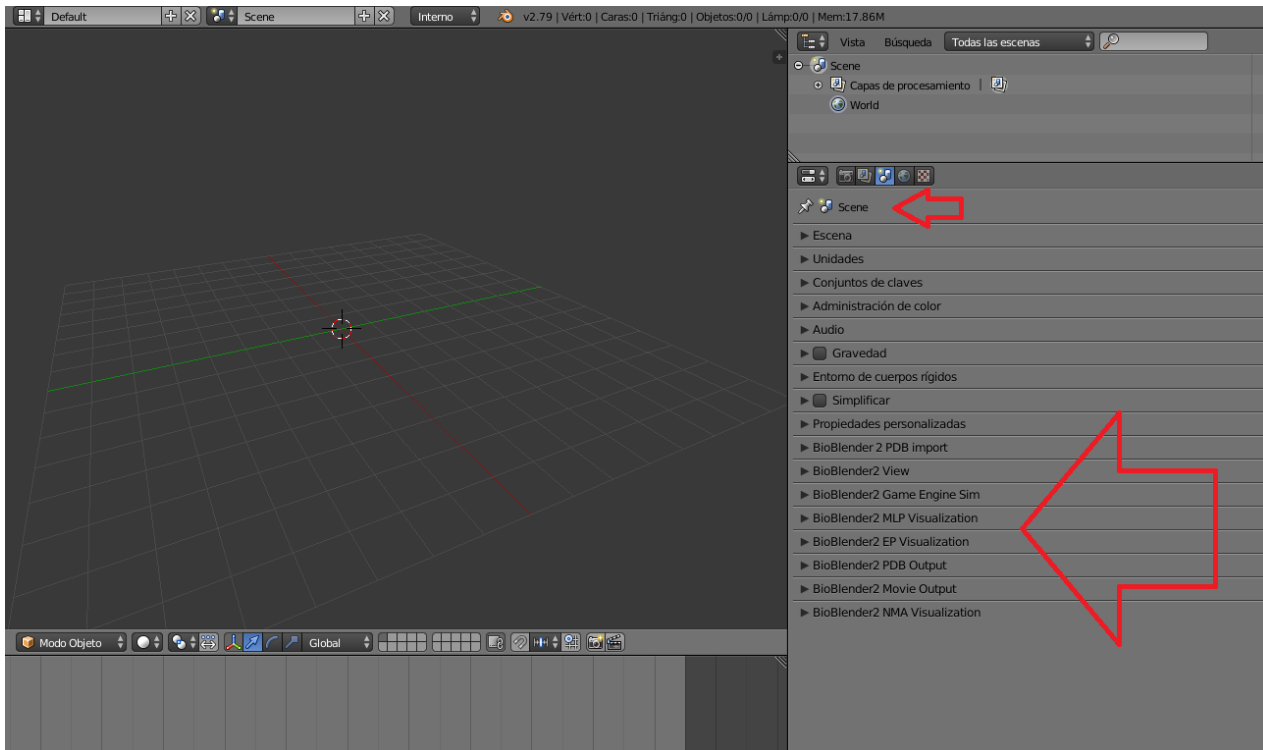# Import PDB file

Note: Well, first of all, if you want to delete all the objects that load automatically when you open Blender, press the **a** key, then the **x** key and **Enter**. If you want Blender to always open with no objects in the scene, press **Ctrl + u**, to save the scene you are in.

The BioBlender functions are found in the properties panel called **Scene**.

**Protein Data Bank (PDB)** it is a database of the three-dimensional structure of proteins and nucleic acids. These data, generally obtained by X-ray crystallography or nuclear magnetic resonance, are sent by biologists and biochemists around the world. They are in the public domain and can be freely used. The BioBlender has the possibility to read files in pdb format and obtain information about their atoms to represent them in space.

```
HEADER    VIRAL PROTEIN                           26-JAN-20   6LU7        SCALE1      0.010211  0.000000  0.004665        0.00000
TITLE     THE CRYSTAL STRUCTURE OF COVID-19 MAIN PROTEASE IN COMPLEX WITH AN    SCALE2      0.000000  0.012582  0.000000        0.00000
TITLE    2 INHIBITOR N3                                                         SCALE3      0.000000  0.000000  0.021223        0.00000
COMPND    MOL_ID: 1;                                                            ATOM      1  N   SER A   1     -32.073   9.085  33.695  1.00 38.90           N
COMPND   2 MOLECULE: SARS-COV-2 MAIN PROTEASE;                                  ATOM      2  CA  SER A   1     -32.156   8.073  34.741  1.00 37.44           C
COMPND   3 CHAIN: A;                                                            ATOM      3  C   SER A   1     -30.857   8.000  35.536  1.00 34.96           C
COMPND   4 ENGINEERED: YES;                                                     ATOM      4  O   SER A   1     -30.047   8.926  35.507  1.00 33.29           O
COMPND   5 MOL_ID: 2;                                                           ATOM      5  CB  SER A   1     -32.483   6.704  34.140  1.00 44.07           C
COMPND   6 MOLECULE: N-[(5-METHYLISOXAZOL-3-YL)CARBONYL]ALANYL-L-VALYL-N~1~-    ATOM      6  OG  SER A   1     -31.312   6.067  33.660  1.00 47.56           O
COMPND   7 ((1R,2Z)-4-(BENZYLOXY)-4-OXO-1-{[(3R)-2-OXOPYRROLIDIN-3-             ATOM      7  N   GLY A   2     -30.665   6.892  36.240  1.00 36.02           N
COMPND   8 YL]METHYL}BUT-2-ENYL)-L-LEUCINAMIDE;                                 ATOM      8  CA  GLY A   2     -29.510   6.712  37.092  1.00 34.67           C
COMPND   9 CHAIN: C;                                                            ATOM      9  C   GLY A   2     -29.828   6.998  38.551  1.00 38.34           C
COMPND  10 ENGINEERED: YES                                                      ATOM     10  O   GLY A   2     -30.810   7.663  38.892  1.00 45.40           O
SOURCE    MOL_ID: 1;                                                            ATOM     11  N   PHE A   3     -28.974   6.479  39.430  1.00 38.38           N
SOURCE   2 ORGANISM_SCIENTIFIC: SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS   ATOM     12  CA  PHE A   3     -29.155   6.661  40.866  1.00 36.10           C
SOURCE   3 2;                                                                   ATOM     13  C   PHE A   3     -27.790   6.744  41.527  1.00 44.18           C
SOURCE   4 ORGANISM_COMMON: SARS-COV-2;                                         ATOM     14  O   PHE A   3     -26.981   5.820  41.399  1.00 40.82           O
SOURCE   5 ORGANISM_TAXID: 2697049;                                            ATOM     15  CB  PHE A   3     -29.978   5.522  41.468  1.00 38.52           C
SOURCE   6 EXPRESSION_SYSTEM: ESCHERICHIA COLI BL21(DE3);                       ATOM     16  CG  PHE A   3     -30.635   5.875  42.770  1.00 40.78           C
SOURCE   7 EXPRESSION_SYSTEM_TAXID: 469008;                                     ATOM     17  CD1 PHE A   3     -31.642   6.824  42.816  1.00 43.38           C
SOURCE   8 EXPRESSION_SYSTEM_VECTOR_TYPE: PLASMID;                              ATOM     18  CD2 PHE A   3     -30.247   5.261  43.949  1.00 40.00           C
SOURCE   9 EXPRESSION_SYSTEM_PLASMID: PGEX-6P-1;                                ATOM     19  CE1 PHE A   3     -32.251   7.155  44.012  1.00 42.94           C
SOURCE  10 MOL_ID: 2;                                                           ATOM     20  CE2 PHE A   3     -30.851   5.586  45.148  1.00 40.35           C
SOURCE  11 SYNTHETIC: YES;                                                      ATOM     21  CZ  PHE A   3     -31.854   6.534  45.179  1.00 43.94           C
SOURCE  12 ORGANISM_SCIENTIFIC: SYNTHETIC CONSTRUCT;                            ATOM     22  N   ARG A   4     -27.541   7.844  42.233  1.00 39.42           N
SOURCE  13 ORGANISM_TAXID: 32630                                                ATOM     23  CA  ARG A   4     -26.277   8.066  42.915  1.00 38.88           C
KEYWDS    PROTEASE, VIRAL PROTEIN                                               ATOM     24  C   ARG A   4     -26.545   8.642  44.296  1.00 40.55           C
EXPDTA    X-RAY DIFFRACTION                                                     ATOM     25  O   ARG A   4     -27.552   9.320  44.517  1.00 36.11           O
AUTHOR    X.LIU,B.ZHANG,Z.JIN,H.YANG,Z.RAO                                      ATOM     26  CB  ARG A   4     -25.367   9.020  42.127  1.00 36.87           C
REVDAT   6   18-MAR-20 6LU7    1       JRNL                                     ATOM     27  CG  ARG A   4     -24.669   8.388  40.936  1.00 42.81           C
REVDAT   5   11-MAR-20 6LU7    1       COMPND SOURCE                            ATOM     28  CD  ARG A   4     -23.342   7.771  41.340  1.00 42.72           C
REVDAT   4   26-FEB-20 6LU7    1       REMARK                                   ATOM     29  NE  ARG A   4     -22.460   7.579  40.193  1.00 47.79           N
REVDAT   3   19-FEB-20 6LU7    1       TITLE  JRNL                              ATOM     30  CZ  ARG A   4     -21.235   7.068  40.270  1.00 53.27           C
REVDAT   2   12-FEB-20 6LU7    1       TITLE  COMPND JRNL   REMARK              ATOM     31  NH1 ARG A   4     -20.744   6.693  41.443  1.00 47.42           N
REVDAT   2 2                   1       SHEET  LINK   SITE   ATOM                ATOM     32  NH2 ARG A   4     -20.502   6.930  39.173  1.00 49.36           N
REVDAT   1   05-FEB-20 6LU7    0                                                ATOM     33  N   LYS A   5     -25.636   8.362  45.227  1.00 34.78           N
JRNL        AUTH   Z.JIN,X.DU,Y.XU,Y.DENG,M.LIU,Y.ZHAO,B.ZHANG,X.LI,L.ZHANG,   ATOM     34  CA  LYS A   5     -25.667   9.020  46.528  1.00 36.92           C
JRNL        AUTH 2 C.PENG,Y.DUAN,J.YU,L.WANG,K.YANG,F.LIU,R.JIANG,X.YANG,T.YOU, ATOM     35  C   LYS A   5     -25.399  10.504  46.317  1.00 32.31           C
JRNL        AUTH 3 X.LIU,X.YANG,F.BAI,H.LIU,X.LIU,L.GUDDAT,W.XU,G.XIAO,C.QIN,   ATOM     36  O   LYS A   5     -24.261  10.908  46.053  1.00 37.11           O
JRNL        AUTH 4 Z.SHI,H.JIANG,Z.RAO,H.YANG                                   ATOM     37  CB  LYS A   5     -24.643   8.396  47.471  1.00 39.24           C
JRNL        TITL   STRUCTURE OF MPRO FROM COVID-19 VIRUS AND DISCOVERY OF ITS   ATOM     38  CG  LYS A   5     -25.062   8.413  48.934  1.00 39.96           C
```

Steps to import the PDB:

1. Select the PDB file that you want to import, for this BioBlender has 2 options:

   - Search the local computer for the PDB file and select it.
   - Write only the name of the PDB you want to import. This is based on writing the PDB identifier with only 4 letters, which will be searched in the repository http://www.pdb.org/ (You need the Internet)

2. Read the PDB file, clicking **Make Preview**

3. Then a list of numbers appears, these numbers are the models that the PDB contains. This list you have the possibility to modify it and import the model that you want.

4. You can modify the interval of the frames between each model where it says **Keyframe Interval**

5. Then a list of the strings that the PDB contains appears.

6. Where says **Import on Layer**, you select in which layer (layer) of Blender you want to import the molecule.

7. Also BioBlender gives you the possibility to import or not, the hydrogens.

8. Finally press the click **Import PDB**. The time it takes to import the PDB is proportional to the size of the molecule. If you want to represent a large molecule, the process will be delayed, since the import behaves exponentially.
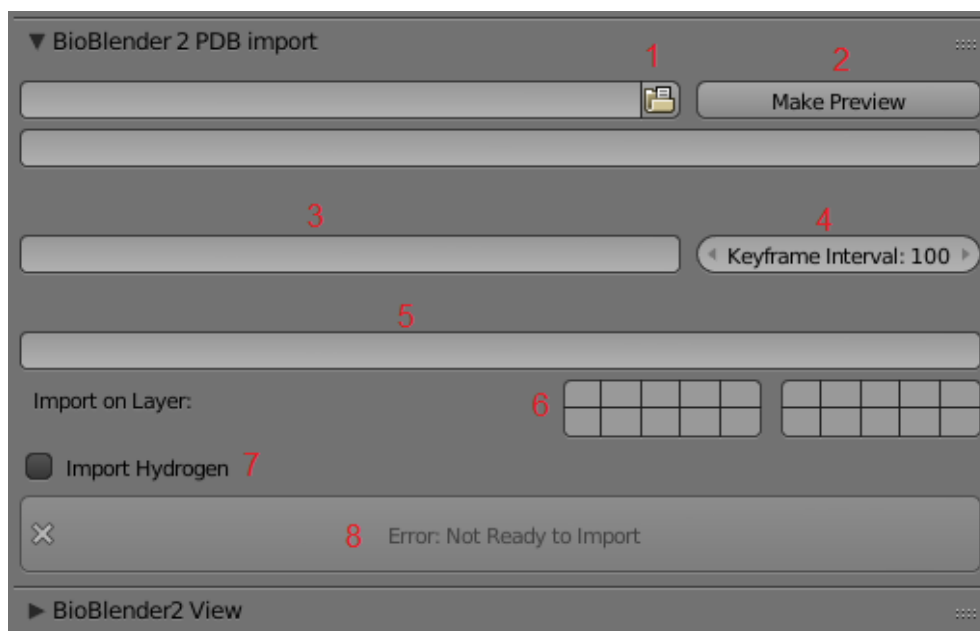
Once the PDB file is imported, you will be able to see:

1. The molecule represented on the scene.

2. The list of items that were created during your import.

3. In the list of elements you will find a Camera, which is located on layer 20.

   - If you press the key **Num 0**. You will be able to know what the camera is observing.
   - If you press the key **N** you can modify its location, you can rotate the camera and other options that Blender allows.

4. We can also find an element that contains the name of the imported PDB, which has as children (within it) all the imported atoms.

5. You can see the frames, which represent the animation of changing from one model to another in the PDB. In this example, the PDB contains 15 models and the frames reach 1401, this is because the first model is in frame 1, then the second is in frame 101, and so on until the end of the models is reached. (In this example an interval of 100 frames was chosen)
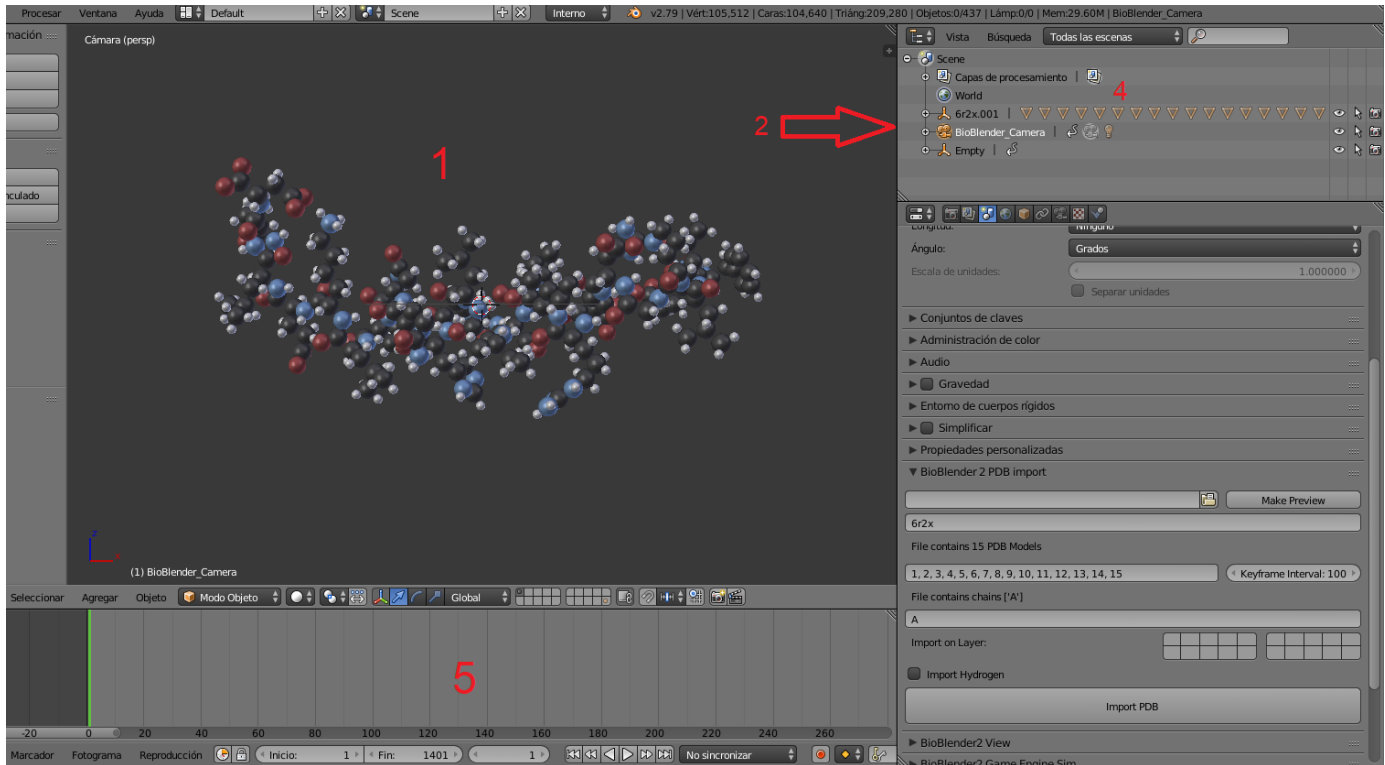
Change the views of the molecule

Once the PDB is imported you can change the view of the atoms of the molecule, for this BioBlender has several options:

Note: First you have to select the atoms you want to work with

- **Main Chain**: Show the main chain.
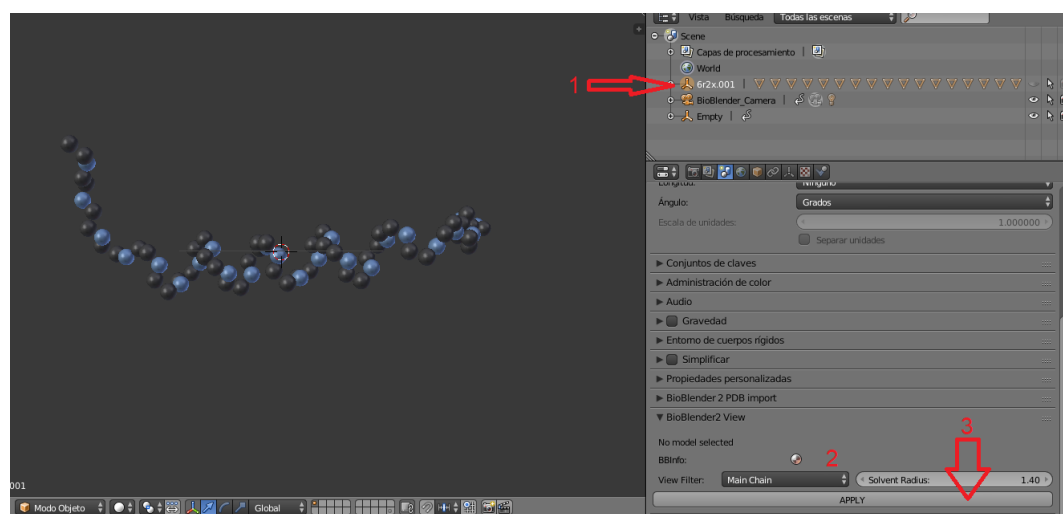
- **+ Side Chain**: Shows the main chain plus the atoms attached to it.
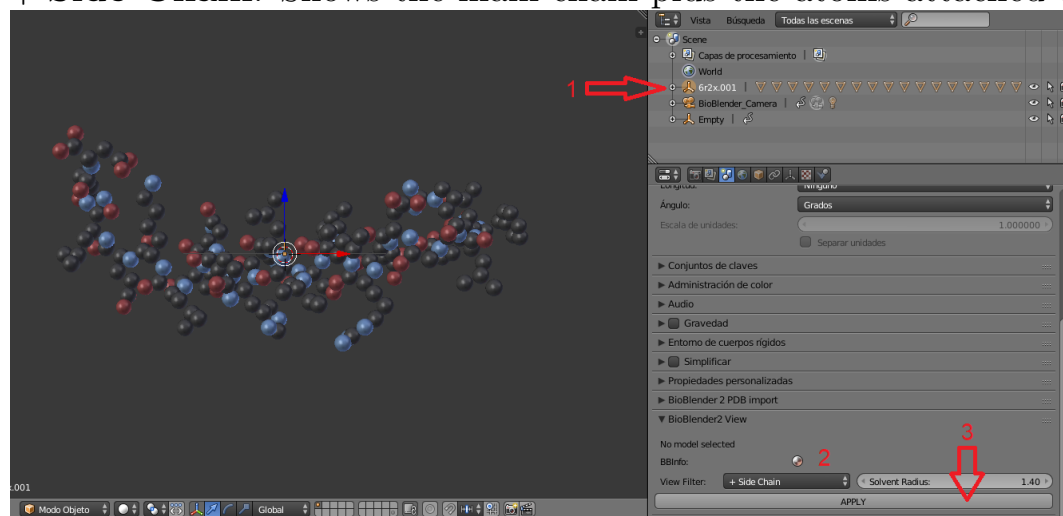
- **+ Hydrogen**: Shows all imported atoms plus hydrogens. (This only happens if you imported the hydrogens at the start)
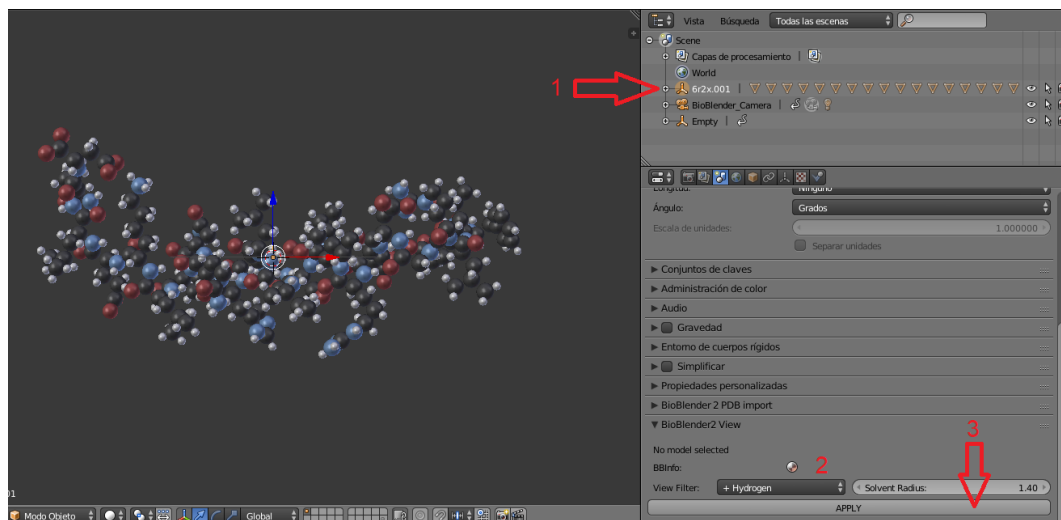
- **Surface**: Calculate the surface (through the external PyMol program) and show it on the scene. This option counts the property on the right **Solvent Radius**, which can be modified to calculate the surface of the molecule.

  - The property **Solvent Radius** property represents the radius of the water and defaults to 1.40. If this value is higher, you can calculate a good surface in less time.

  - Once the surface is calculated, an element is automatically added to the scene. This has the name: SURFACE, followed by the name of the PDB and then the frame number in which it is located.

  - If you have already calculated a PDB surface in the same number of frames, if you calculate the surface again, it will not calculate it because it will find the element already created.
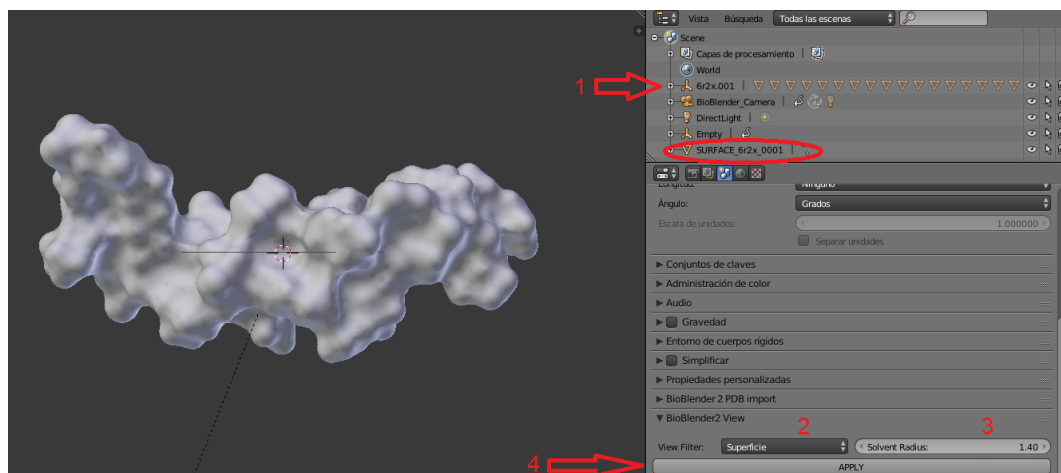
Molecule motion using Blender's physical engine

By importing the molecule into the scene and pressing **Alt** + **A** the animation of the molecule begins to play. In this case, only the atoms are moving from one location in one conformation to the other, but without taking into account their physical properties, therefore in order to calculate the transition of the protein between two conformations where its properties are taken into account, it is necessary to use the Blender Physics Engine.

Steps to run the Game Engine:

1. Click on **Refresh GE List**. This will automatically cause imported molecules to be selected and the name that identifies the molecule will be displayed below this button and the type of dynamic representation to its right (Default is **No Collisions**)

2. **Record Animation**: When selected, it allows recording the animation in F-Curves.

3. **Radius**: Represents the radius value for collisions in Blender's physical engine.

4. Click on **Run in Game Engine**. This operation once started can be canceled by pressing the key. **Esc**
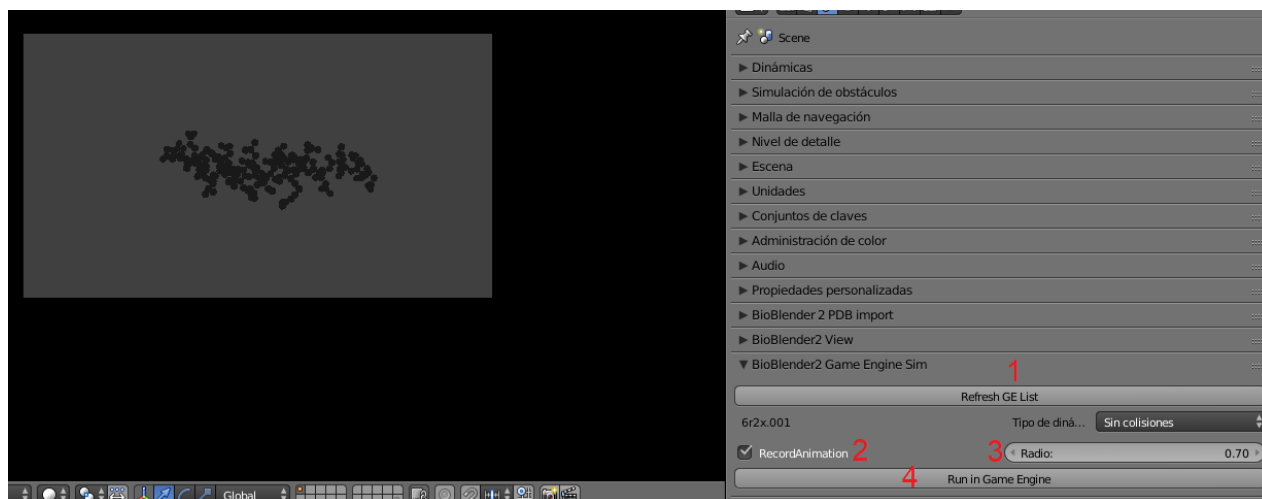
Calculate and visualize the Lipophilic Potential of the molecule (MLP)

BioBlender has the possibility of calculating the MLP, for this it is necessary to use the external Pymol software, which performs the calculations and then they are imported into the Blender.

Bioblender has two options:

- **Calculate the atomic MLP**: To do this you first have to select the atoms in the list of elements. (In this case the use of the external Pymol software is not necessary)
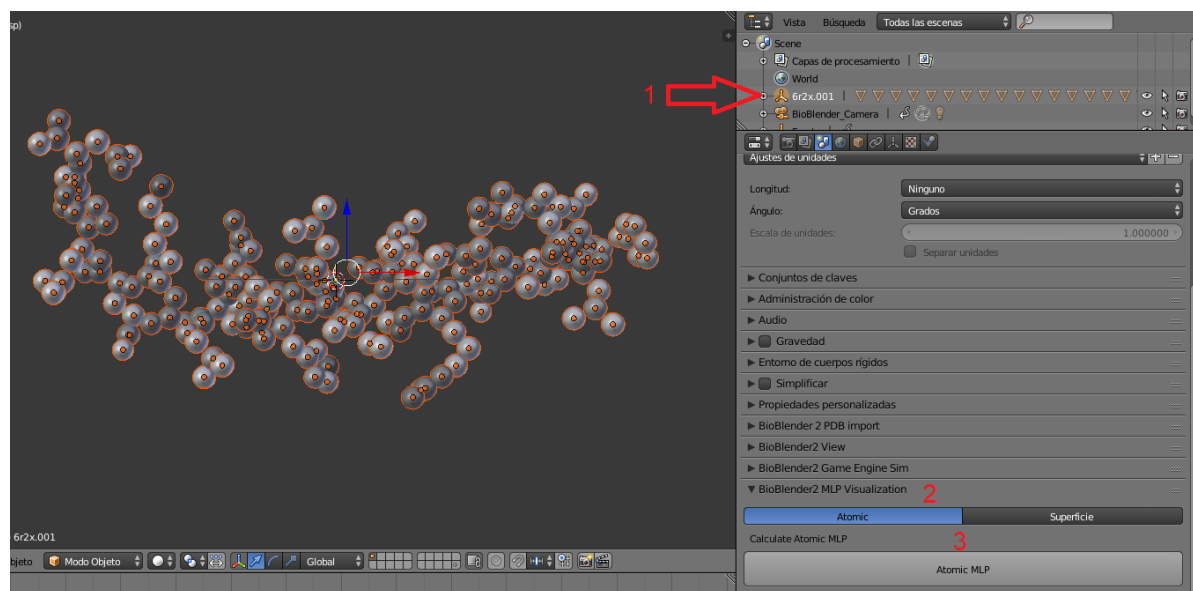
- **Calculate the MLP on the surface**: PyMLP is used to represent the surface, which obtains the values calculated by PyMol. For its correct operation it is necessary to follow a list of steps.

  1. Select the atoms in the item list.

  2. If you had previously created a surface through the options of the different views of the molecule, delete it.

  3. Select the formula by which to calculate the MLP

  4. Select the grid spacing.

5. Click on **Show MLP on Surface**.
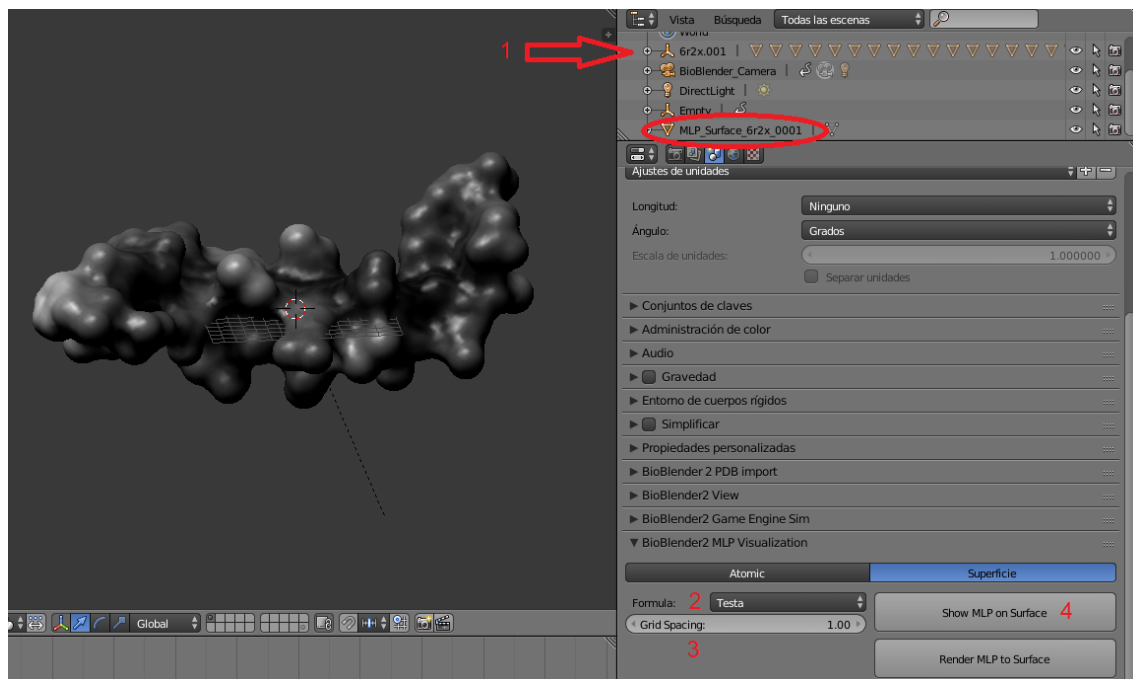
6. Once the surface is displayed, an element is automatically added to the scene. This has as name: MLP_Surface, followed by the name that identifies the PDB in the list of elements and then the number where the frame is located.
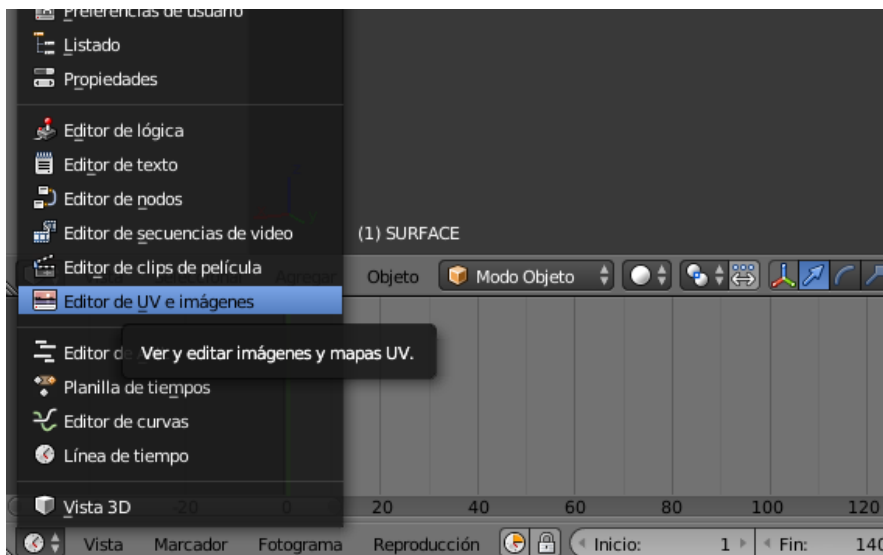
7. If you already calculated a PDB surface in the same number of frames, if you calculate the surface again, it will not calculate it because it will find the element already created.
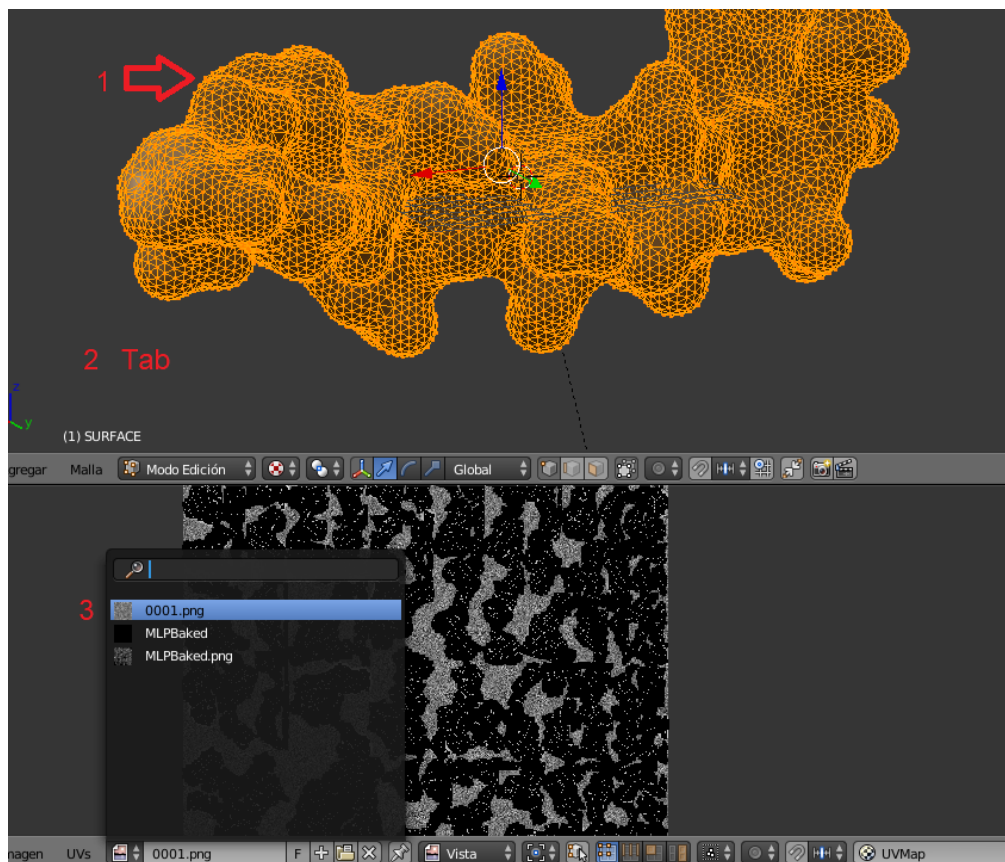
8. Select the created surface.

9. Click on **Render MLP to Surface**
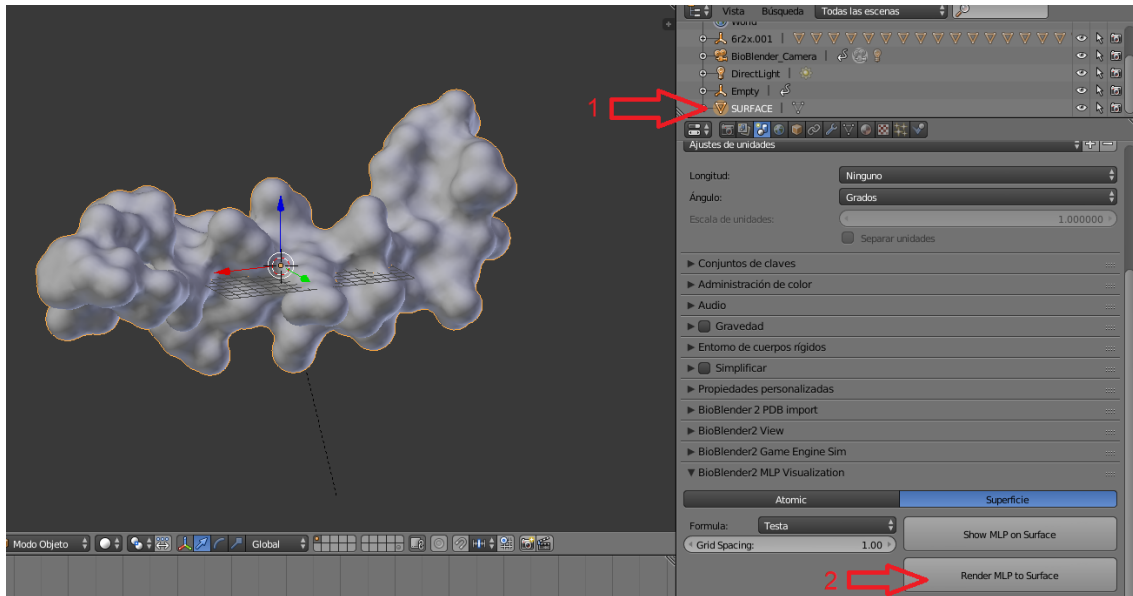
10. Once the texture is created go to **UV and Image Editor**

11. Select the surface and press the key **Tab**. Automatically all the vertices of the surface were rendered in the UV Editor.

12. Select the image 001.png

13. The molecule already presents the surface with the MLP and its texture, ready for rendering.
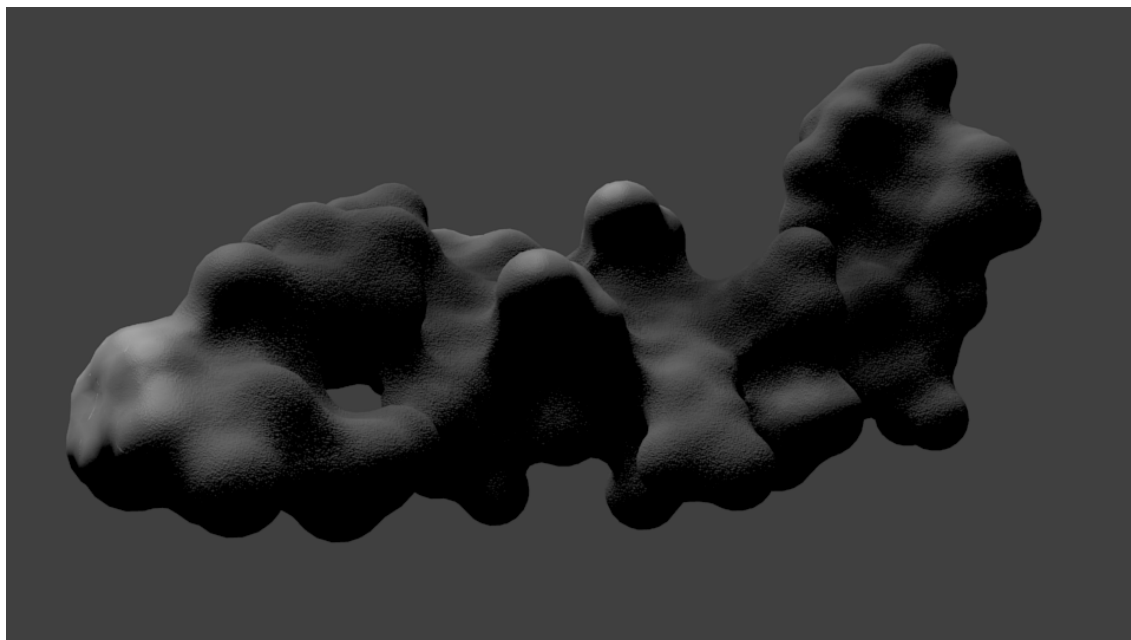
Calculate and visualize the Electrostatic Potential (EP)

BioBlender has the possibility of calculating the electrostatic potential of the molecule and showing its potential lines on the scene. For this BioBlender needs the use of external software **apbs** for carrying out calculations of potential and energy; and the software **SCIVIS** to calculate the lines and export them in a .txt file that BioBlender will later read and make possible their visualization on the scene.

Steps to calculate the EP

1. Select the atoms you want to work with.

2. This function has various properties which can be modified according to what you want to work with.

   - **ForceField**: It allows the selection of the force fields with which you want to work.
   - **Ion concentration**: Allows you to choose the ion concentration of the solvent. Default is 0.15
   - **Grid Spacing**: Allows you to choose the grid spacing. Smaller is much better, but the calculation is slower.
   - **Minimum Potential**: It allows choosing the minimum potential from which the lines of the force field start in absolute value.
   - **n EP Lines**: Represents the concentration of the lines.
   - **Particle Density**: Represents the density of the particles.

3. Click on **Show EP** to calculate the potential.

4. Once the EP is calculated, the lines shown in the scene present animation, which you can see since when calculating the EP, the animation automatically plays. (These only go up to approximately 270 frames)

Note: If you want to remove the potential lines from the scene you can click on **Clear EP**, which will remove all the lines not only from the scene, but from the item list as well.
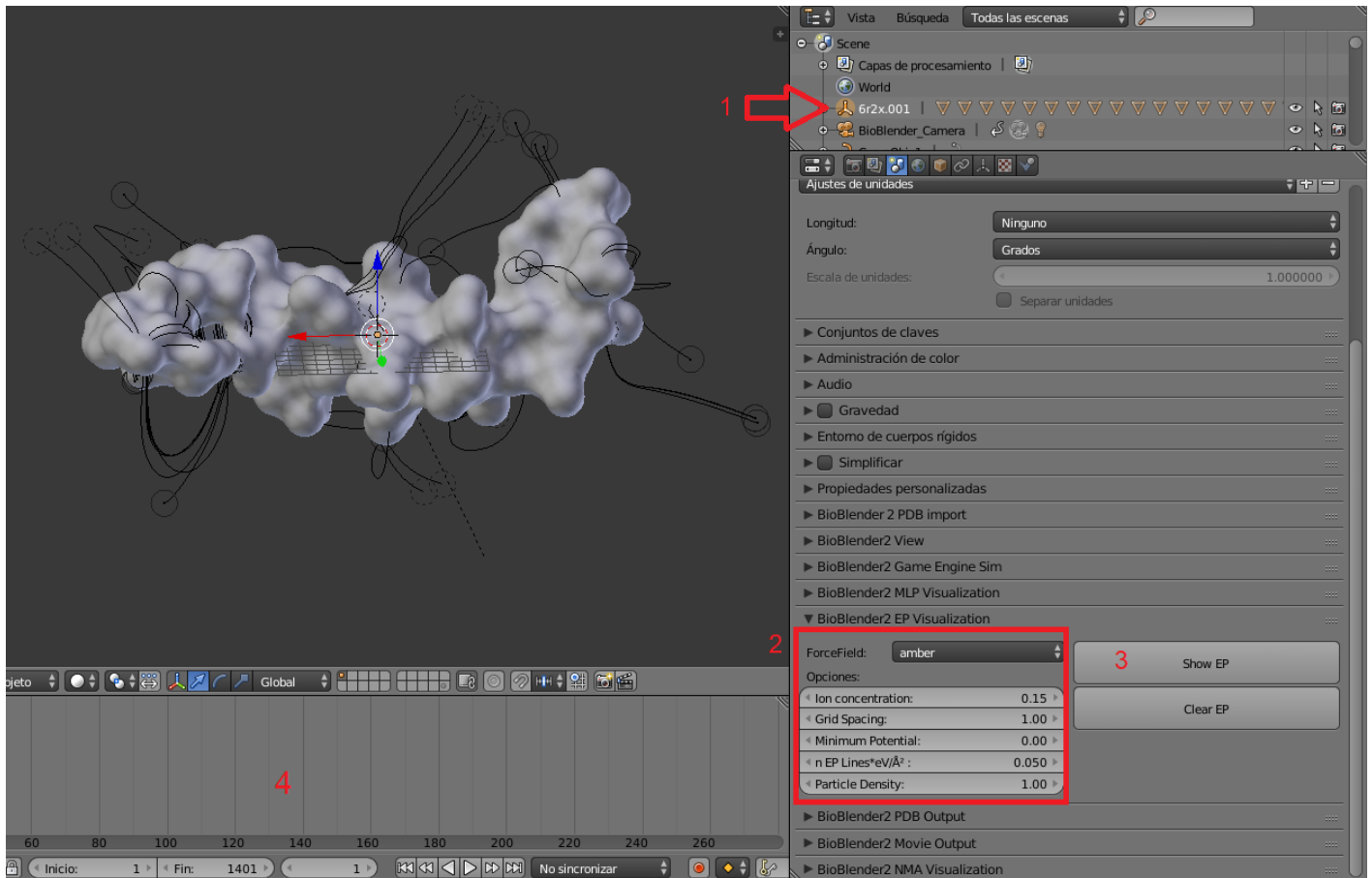
Export PDB file

BioBlender gives the user the possibility of exporting a PDB file according to the location of the molecule in the scene, that is, when exporting the PDB file, it will take the position of all the atoms for each frame of the animation, therefore Keep in mind that if you have 1000 as the final frame, the PDB file generated by the BioBlender will contain 1000 models, since one model is created for each frame.

Steps to export a new PDB file:

1. Select the atoms you want to work with.

2. Search local storage for the address where you want to save the PDB file.

3. Select the starting frame from which you want to start obtaining the position of the atoms to generate your PDB file.

4. Select the final frame where you want to stop getting the position of the atoms to generate your PDB file.

5. Select the jumps between the frames, by default it is 1. This means that it will increase the frames by 1 until reaching the end of the selected frames.

6. Click on **Export PDB**
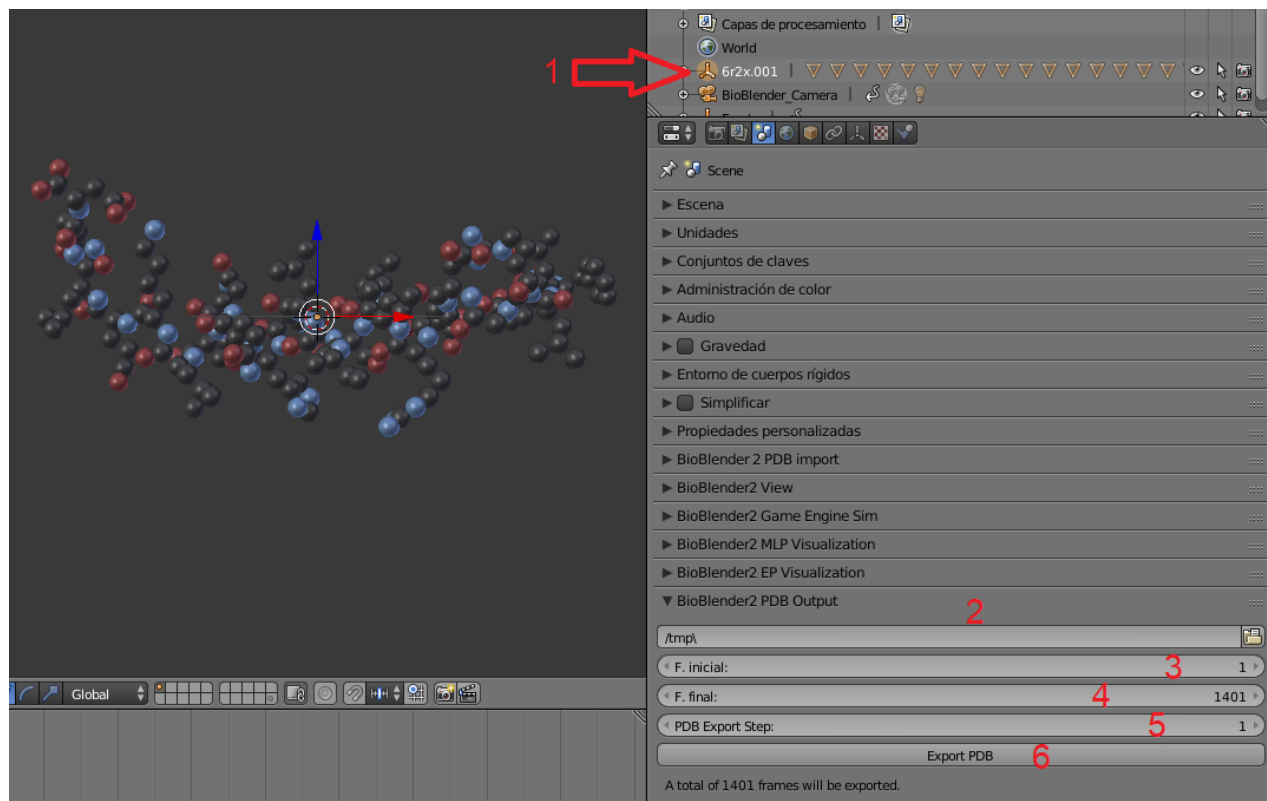
Export Movie

BioBlender offers the possibility of exporting all the frames you want, as well as choosing how you want to observe the molecule in these images. This works through the Blender Render.

Steps to export the movie:

1. Click on **Refresh MOVIE List**

2. Configure the various options it provides:

   - **EP Curves (global)**: When selected, when exporting the molecule in the frame, it also introduces the Electrostatic Potential (EP) into the image.
   - **bb2_outputoptions**: It allows the selection of the view of the molecule that you want to export in the image.
   - **Notes**: Allows you to add custom text to the image.
   - **Information Overlay**: Provides detailed information for each frame in the image.
   - **Ambient Light**: Add light from the environment.

3. Select in the local storage the address where you want to save the movie.

4. Select the starting frame from which you want to start generating the movie.

5. Select the final frame up to where you want to generate the movie.

6. Select the jumps between the frames, by default it is 1. This means that it will increase the frames by 1 until reaching the end of the selected frames.
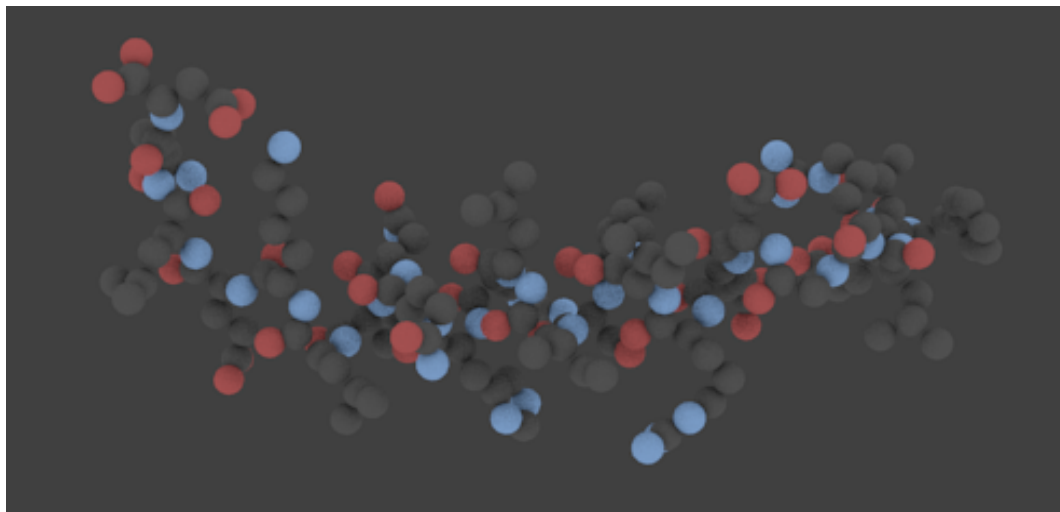
7. Click on **Export Movie**
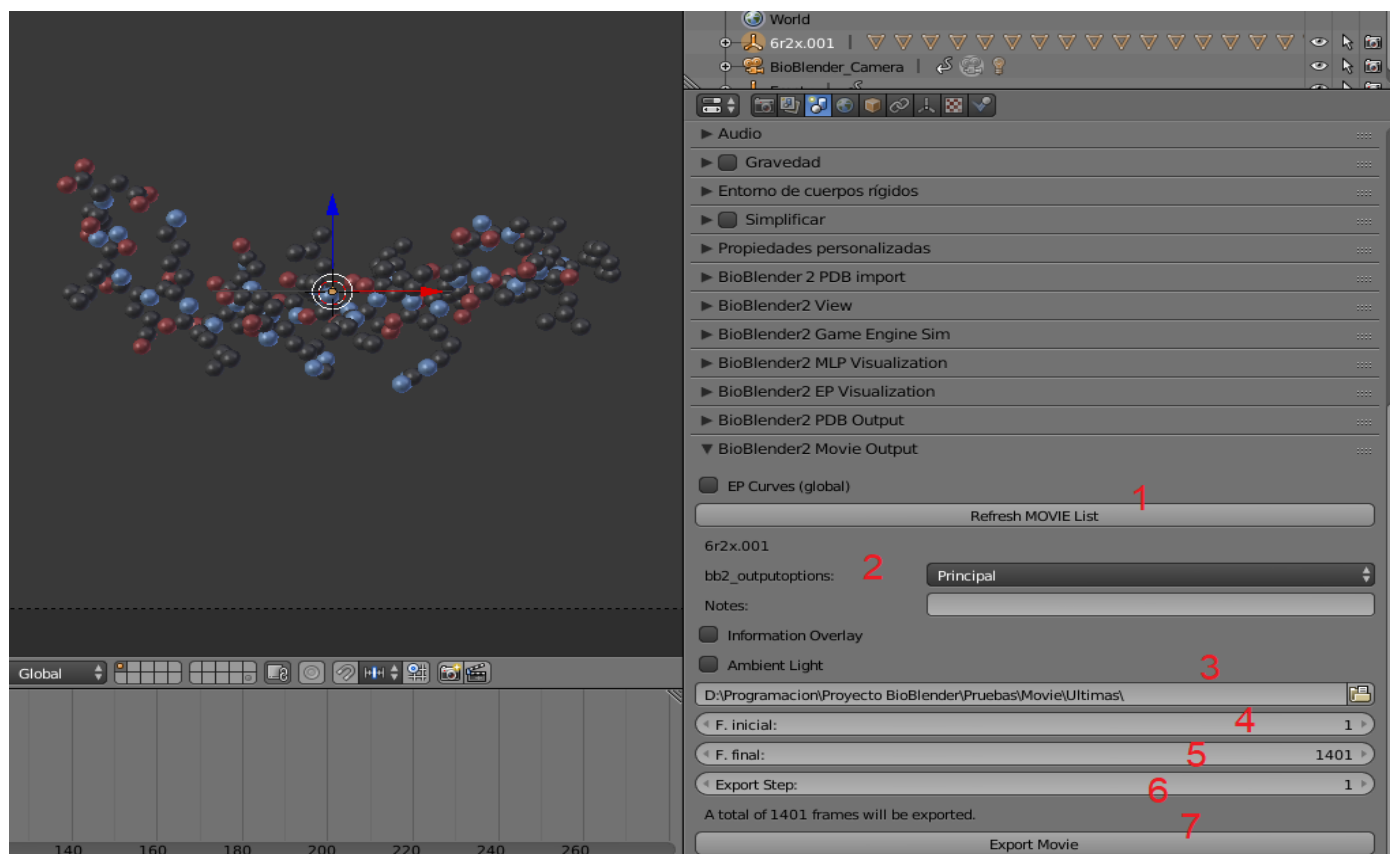
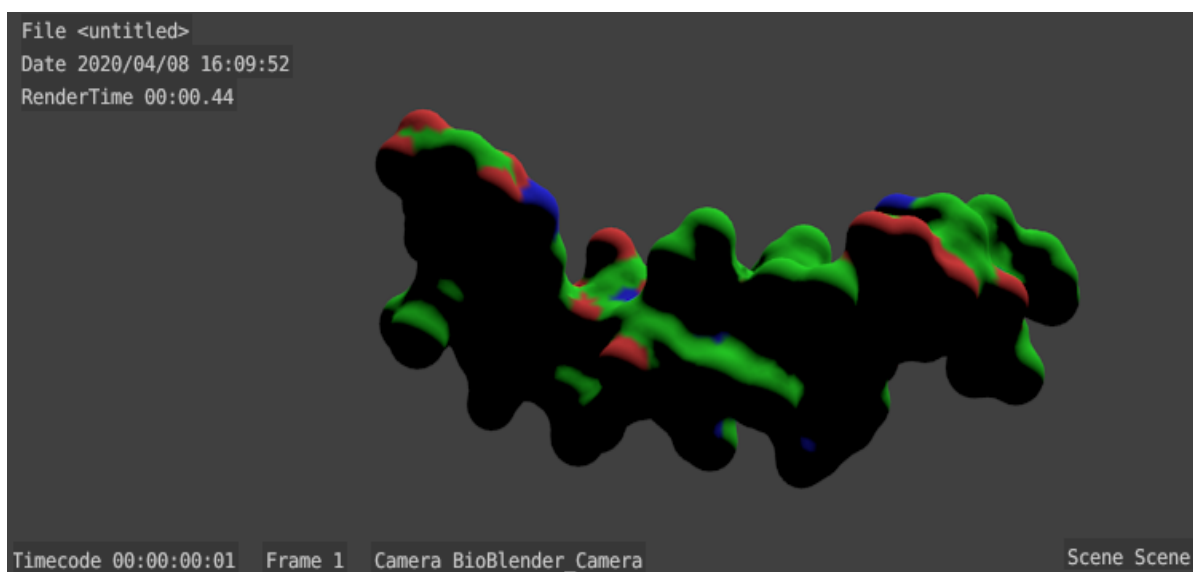**Example of different views of the molecule**:

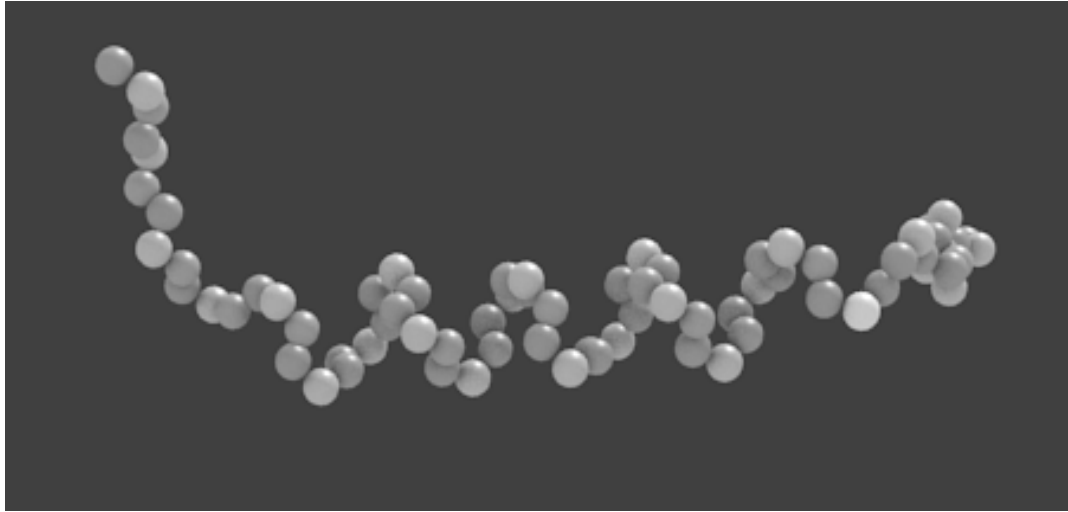1. View selection **Main** only.
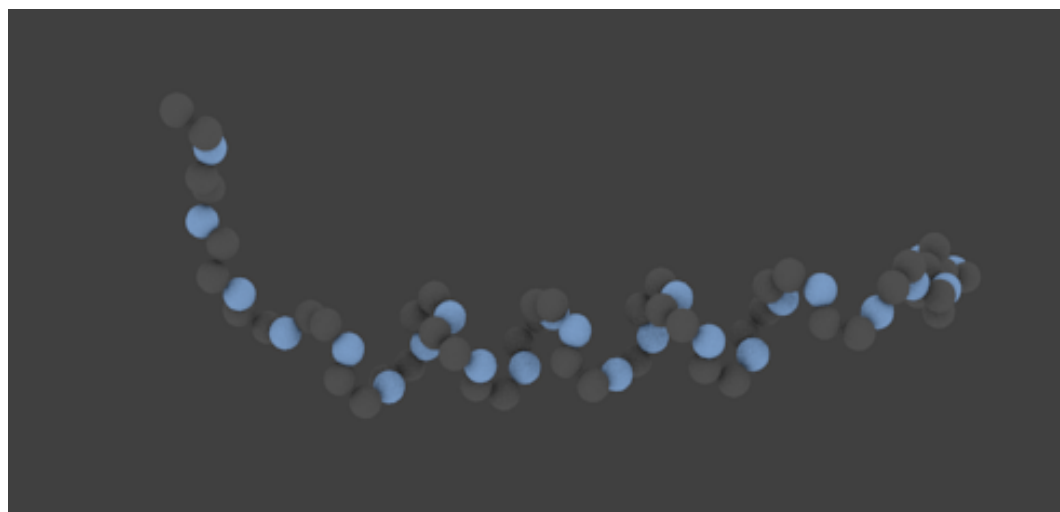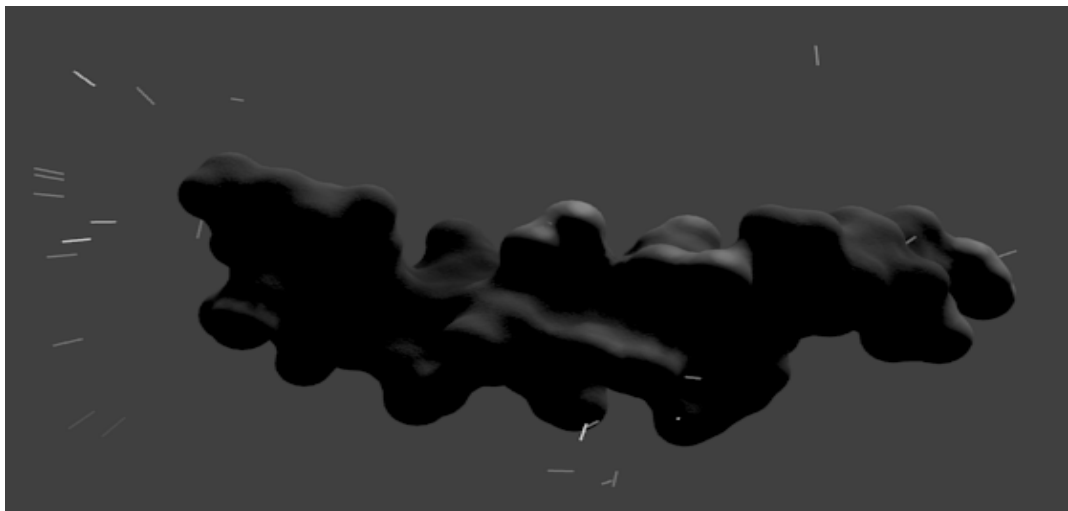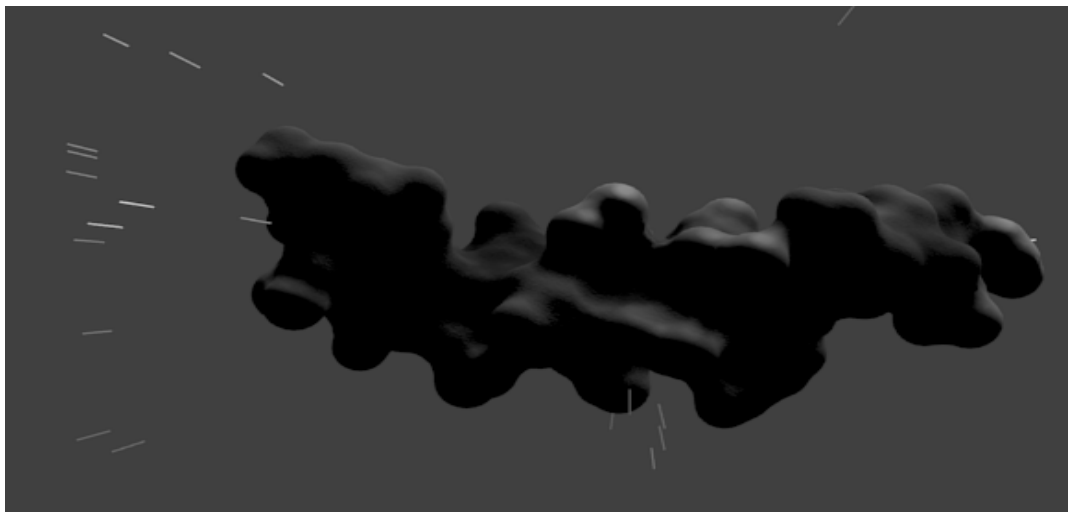
2. Selecting the view + **Side** only.

3. Selecting the view **Superficie** and of **Information Overlay**

4. Selecting the view **MLP Main**:

5. Selecting the view **MLP Surface** and **EP Curves (global)**

Calculate the NMA

BioBlender has the possibility of calculating the path of the **Normal Mode Analysis**, for this the use of the **Prody** library is required, which allows the analysis to be carried out. The NMA is only calculated for the first model in the PDB file that was imported at startup, so if you only want to calculate the NMA when working with BioBlender, you will not need to import all other models from the PDB.

To calculate the NMA, it is not necessary to select the atoms with which you want to work.

Options provided by the calculation of the NMA:

- **Modo**: Select a normal mode analysis to show.

- **NMA Steps**: Represents the Number of conformations to be calculated in each direction.

- **RMSD sampling**: RMSD between the given and the farthest conformation.

- **NMA cutoff**: NMA cutoff distance $(\overset{o}{A})$ for pairwise interactions.

- **NMA Gamma**: Represents the NMA spring constant

Note: When calculating the NMA a PDB file is exported in the folder

C:\Users\ **Username**\AppData\Roaming\Blender Foundation\Blender\2.79\scripts\addons master\fetched

This file contains the calculated path and the address where it is located is automatically entered in the Import function, ready for import.

▼ BioBlender2 NMA Visualization

Modo: 1

Opciones:

Calculate NMA trajectories (pdb)

◄ NMA steps: 6 ►

◄ RMSD sampling: 0.80 ►

◄ NMA cutoff: 15.00 ►

◄ NMA Gamma: 1.00 ►

▼ BioBlender 2 PDB import

C:\Users\Pablo\AppData\Roami...0.800000011920929_6.pdb   Make Preview

29_6

File contains 14 PDB Models

1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14   ◄ Keyframe Interval: 100 ►

File contains chains ['A']

A

Import on Layer:

☐ Import Hydrogen

Import PDB

Important notes for your knowledge

The vast majority of processes in BioBlender export files of vital importance to their operation, which can be very useful for personal use apart from BioBlender. These files are located in the folder:

C:\Users\ **Username**\AppData\Roaming\Blender Foundation\Blender\2.79\scripts\addons master\tmp

Functions that generate files in this folder:

- **BioBlender2 View**: When calculating the **Surface**.:

    - original.pdb
    - surface.pml
    - tmp.pdb
    - tmp.wrl

- **BioBlender2 MLP Visualization**: When calculating the MLP on the Surface:

    - original.pdb
    - surface.pml
    - tmp.pdb
    - tmp.wrl
    - tmp.dx

- **BioBlender2 MLP Visualization**: When calculating the texture of the MLP on the Surface, it generates the necessary images to carry out the texture:

    - 0001.png
    - MLPBaked.png
    - noise.png

– composite.blend   This file is typical of Blender, which keeps the composition of the texture with it.

- **BioBlender2 EP Visualization**: When calculating the EP:
  - scenewide.obj
  - scenewide.in
  - scenewide.pqr
  - scenewide.wrl
  - scenewide.pdb
  - scenewide-input.p
  - surface.pml
  - io.mc
  - tmp.txt
  - pot.dx
  - apbs.exe