BioBlender 2.1

Manual

2020-05-04

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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.

Resources

INFO
BioBlender website with general information about the project
SciVis website, where everything originated

FORUM
Users Forum: the place to ask questions, report bugs, post news or success stories

CODE
BioBlender is in continuous development. You can find the latest version on the **GitHub** dedicated page.
Please feel free to contribute if you can! :-)

Requirements

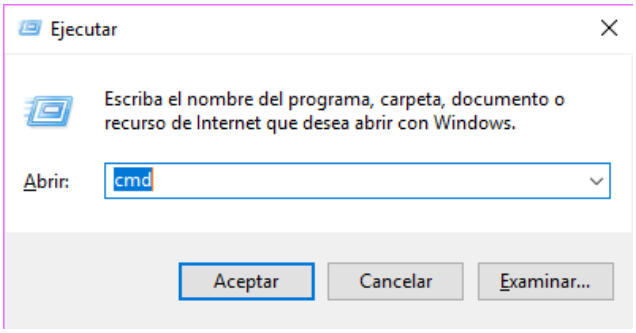
- Install Python 3.5.3 *Please use this version of Python. Newer versions may show problems in some BioBlender functions*

- Install Blender 2.79b

- Install PyMol

- Install the NumPy, SciPy and ProDy libraries:

  1. Open windows console (**Windows + R**)
  2. Type cmd

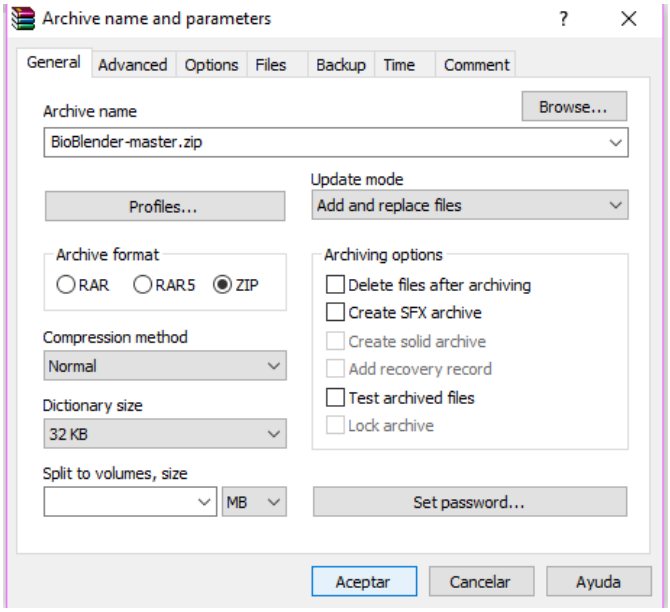


  3. Then in the Windows console type:
     ```
     pip install numpy
     ```
     and
     ```
     pip install scipy
     ```
  4. Once finished, proceed to install Prody:
     ```
     pip install Prody
     ```

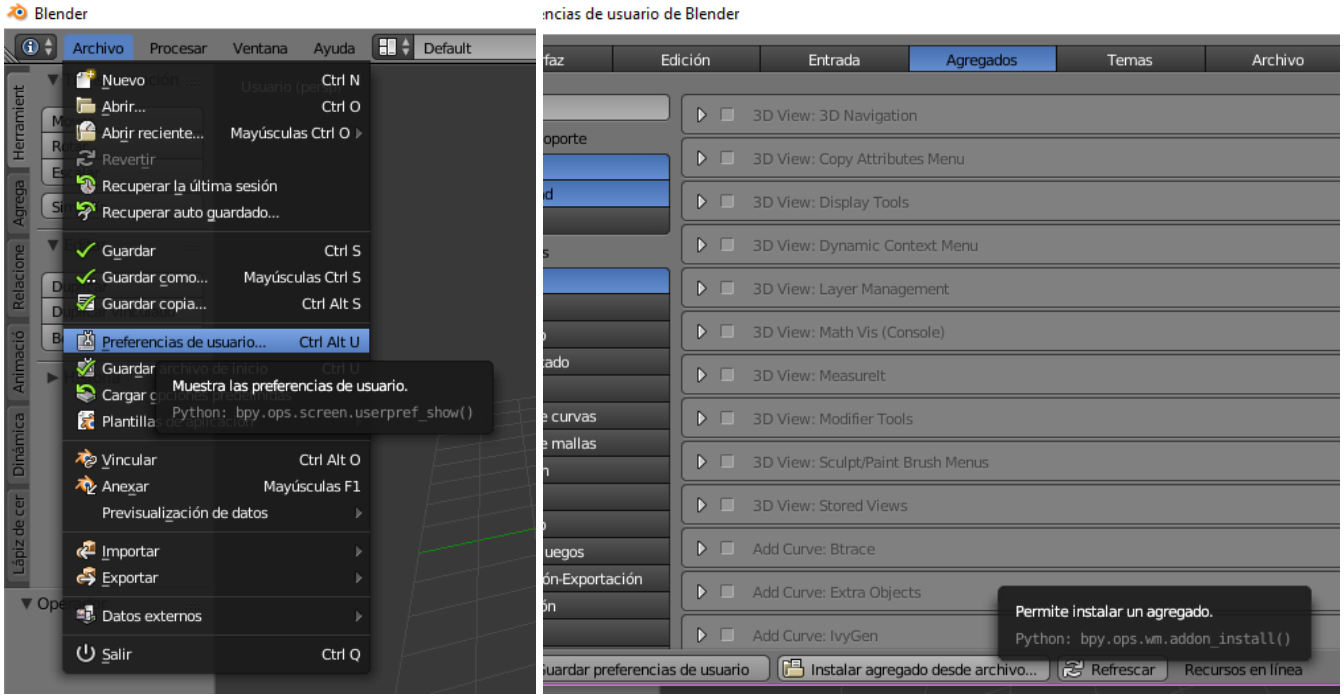
How to install BioBlender

Steps:

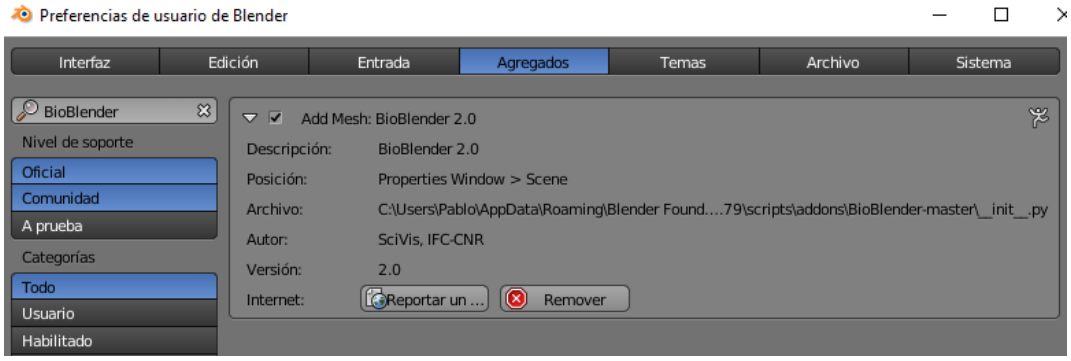
1. Use the compressed (.zip) BioBlender-master folder



2. Next, open Blender and add the BioBlender-master.zip file.
   Go to: File > User Preferences > Add-ons > Install Add-ons From File
   Here select the .zip file and press Install Add-ons From File



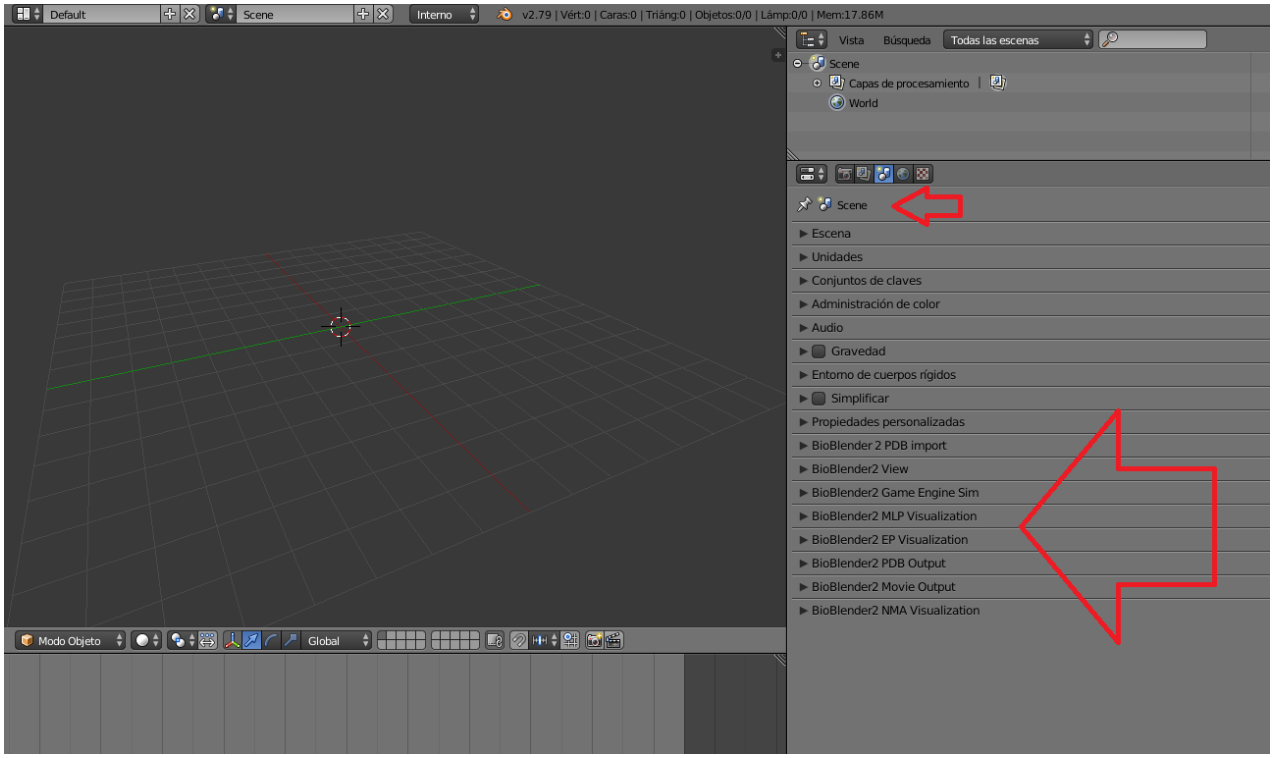
3. Once BioBlender has been added, it should be activated automatically, but in case it is not, go to:
   File > User Preferences > User. Here activate BioBlender by ticking the small square
   Then Save User Settings.



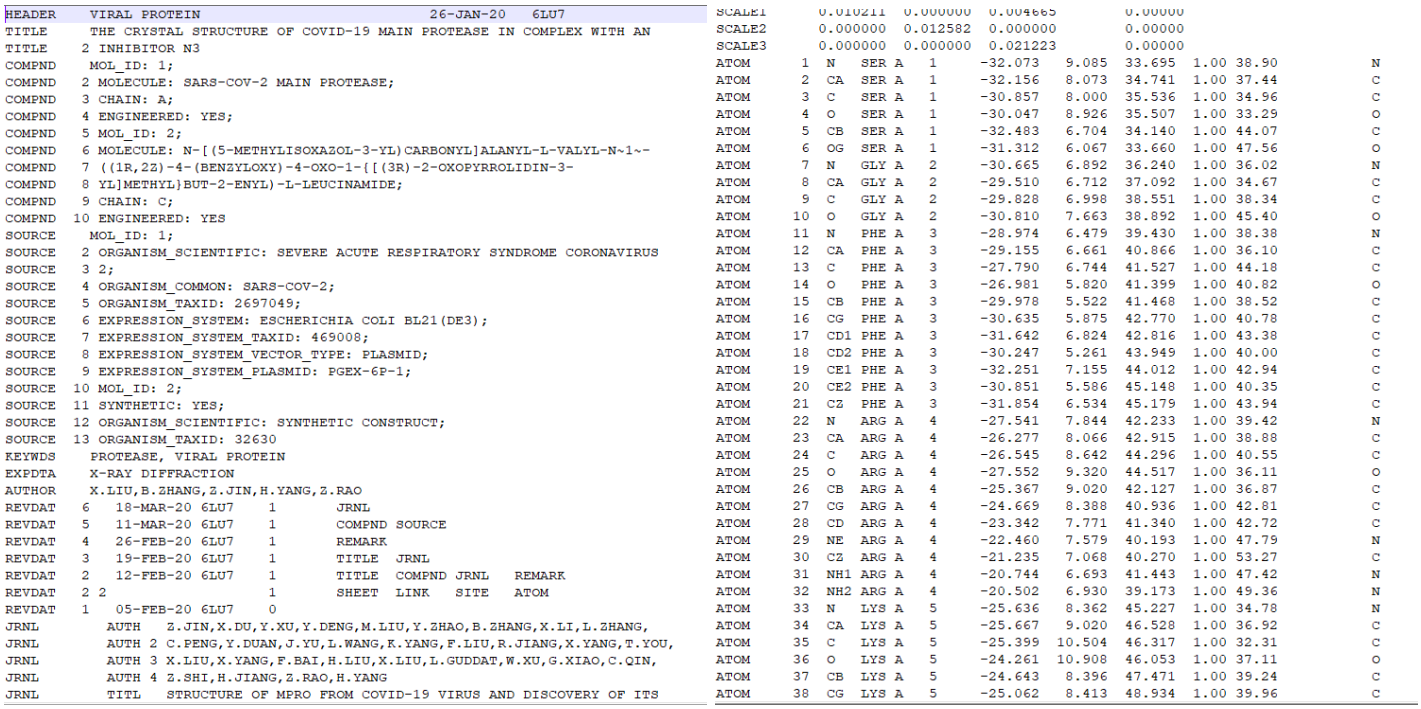
Import PDB file

Note: First of all, we suggest to delete all objects automatically loaded when you open Blender (cube, camera and light), by pressing **a**, then **x** and **Enter**. If you want Blender to always open with no objects in the scene, press **Ctrl** + **u**.

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, nucleic acids and other molecules. These data, generally obtained by X-ray crystallography, nuclear magnetic resonance, or Cryo-EM are deposited by biologists and biochemists around the world. They are in the public domain and can be freely used. All molecular data are stored in the PDB format, which is the format read by BioBlender to build the molecules in the 3D space.



```
HEADER    VIRAL PROTEIN                           26-JAN-20   6LU7
TITLE     THE CRYSTAL STRUCTURE OF COVID-19 MAIN PROTEASE IN COMPLEX WITH AN
TITLE    2 INHIBITOR N3
COMPND    MOL_ID: 1;
COMPND   2 MOLECULE: SARS-COV-2 MAIN PROTEASE;
COMPND   3 CHAIN: A;
COMPND   4 ENGINEERED: YES;
COMPND   5 MOL_ID: 2;
COMPND   6 MOLECULE: N-[(5-METHYLISOXAZOL-3-YL)CARBONYL]ALANYL-L-VALYL-N~1~-
COMPND   7 ((1R,2Z)-4-(BENZYLOXY)-4-OXO-1-{[(3R)-2-OXOPYRROLIDIN-3-
COMPND   8 YL]METHYL}BUT-2-ENYL)-L-LEUCINAMIDE;
COMPND   9 CHAIN: C;
COMPND  10 ENGINEERED: YES
SOURCE    MOL_ID: 1;
SOURCE   2 ORGANISM_SCIENTIFIC: SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS
SOURCE   3 2;
SOURCE   4 ORGANISM_COMMON: SARS-COV-2;
SOURCE   5 ORGANISM_TAXID: 2697049;
SOURCE   6 EXPRESSION_SYSTEM: ESCHERICHIA COLI BL21(DE3);
SOURCE   7 EXPRESSION_SYSTEM_TAXID: 469008;
SOURCE   8 EXPRESSION_SYSTEM_VECTOR_TYPE: PLASMID;
SOURCE   9 EXPRESSION_SYSTEM_PLASMID: PGEX-6P-1;
SOURCE  10 MOL_ID: 2;
SOURCE  11 SYNTHETIC: YES;
SOURCE  12 ORGANISM_SCIENTIFIC: SYNTHETIC CONSTRUCT;
SOURCE  13 ORGANISM_TAXID: 32630
KEYWDS    PROTEASE, VIRAL PROTEIN
EXPDTA    X-RAY DIFFRACTION
AUTHOR    X.LIU,B.ZHANG,Z.JIN,H.YANG,Z.RAO
REVDAT   6   18-MAR-20 6LU7    1       JRNL
REVDAT   5   11-MAR-20 6LU7    1       COMPND SOURCE
REVDAT   4   26-FEB-20 6LU7    1       REMARK
REVDAT   3   19-FEB-20 6LU7    1       TITLE  JRNL
REVDAT   2   12-FEB-20 6LU7    1       TITLE  COMPND JRNL   REMARK
REVDAT   2 2                    1       SHEET  LINK   SITE   ATOM
REVDAT   1   05-FEB-20 6LU7    0
JRNL        AUTH   Z.JIN,X.DU,Y.XU,Y.DENG,M.LIU,Y.ZHAO,B.ZHANG,X.LI,L.ZHANG,
JRNL        AUTH 2 C.PENG,Y.DUAN,J.YU,L.WANG,K.YANG,F.LIU,R.JIANG,X.YANG,T.YOU,
JRNL        AUTH 3 X.LIU,X.YANG,F.BAI,H.LIU,X.LIU,L.GUDDAT,W.XU,G.XIAO,C.QIN,
JRNL        AUTH 4 Z.SHI,H.JIANG,Z.RAO,H.YANG
JRNL        TITL   STRUCTURE OF MPRO FROM COVID-19 VIRUS AND DISCOVERY OF ITS
```

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ATOM      1  N   SER A   1     -32.073   9.085  33.695  1.00 38.90           N
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ATOM      7  N   GLY A   2     -30.665   6.892  36.240  1.00 36.02           N
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ATOM     35  C   LYS A   5     -25.399  10.504  46.317  1.00 32.31           C
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ATOM     38  CG  LYS A   5     -25.062   8.413  48.934  1.00 39.96           C
```

Steps to import a PDB file:

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

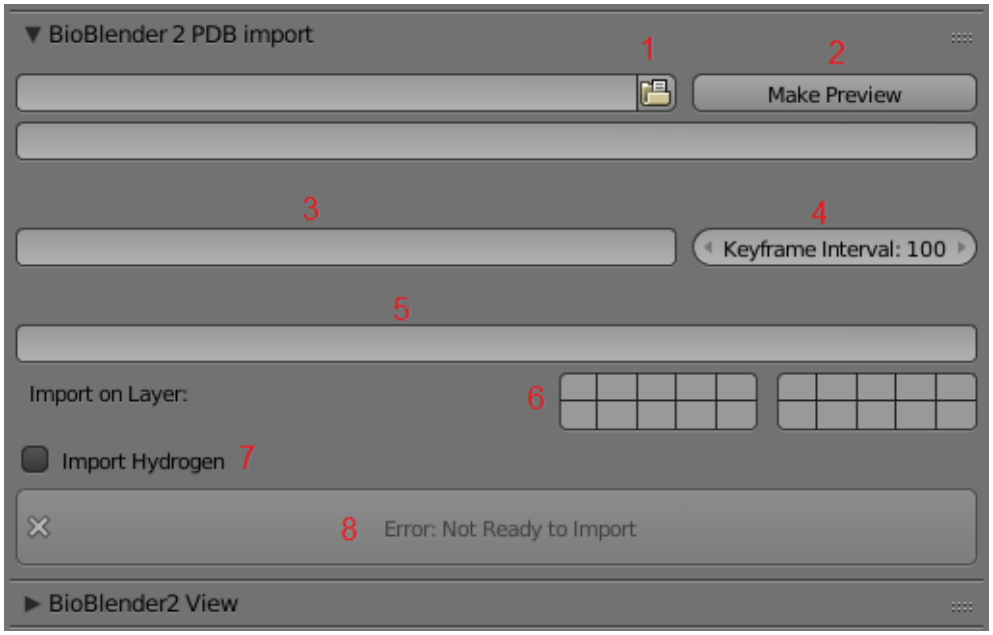
   - Search the local computer for the PDB file and select it.
   - Write only the 4 letter code (identifier) of the PDB you want to import. (You need the Internet)
   - ***Note.*** *In some cases, users have experienced a problem when fetching the file from PDB. In this case, please download the file on your PC and then upload it using the first option.*

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

3. A list of numbers may appear, if the PDB contains ¿1 models. In this window you have the possibility to modify the list, selecting which models to import and in which order.

4. You can modify the interval (in frames) between each model **Keyframe Interval**

5. A list of letters may appear, if the PDB contains ¿1 molecules.
6. Where says **Import on Layer**, you may select in which layer of Blender to import the molecule.
7. If the PDB file contains them, you may decide to import (or not) hydrogen atoms (using this option will make the import process much longer).
8. Finally click **Import PDB**. The time to import the PDB depends on the size of the molecule. For very large molecules, the process may take several minutes, since the import behaves exponentially.



Once the PDB file is imported, you will see:

1. The molecule represented as Atoms in the 3D scene.
   In the Outliner, there are now the items created during import: the molecule and a Camera aimed at the molecule.

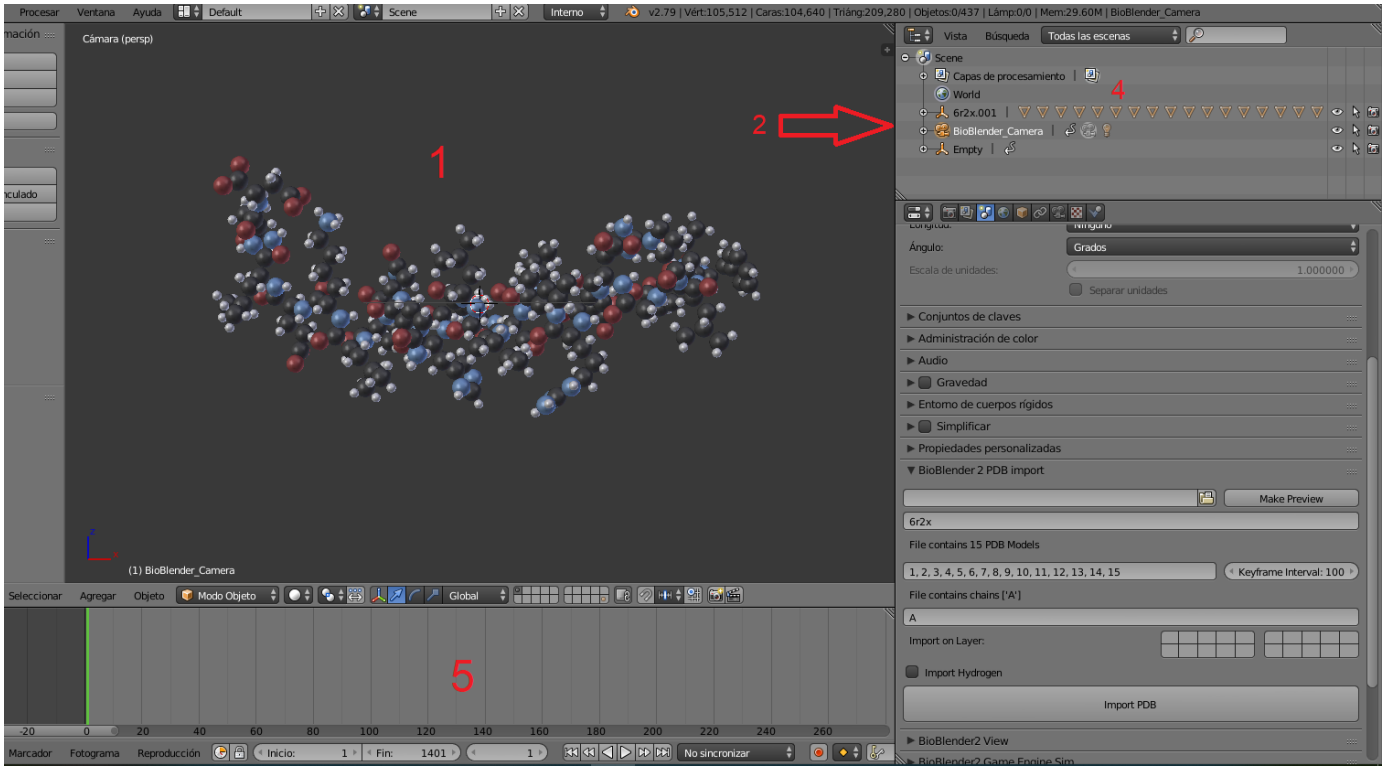
2. The Camera is located on layer 20.

   - Pressing the key **Num 0** the camera view is activated.
   - Press the key **N** to modify its location and rotation, or to access other Blender options.

3. The imported PDB, named with the last 4 characters of the file, which contains

4. all its atoms as children and

5. all the frames and keyframes in the Timeline. In this example, the PDB contains 15 models and the frames reach 1401: the first model is in frame 1, then the second is in frame 101, and so on until the last model. (In this example an interval of 100 frames was selected)

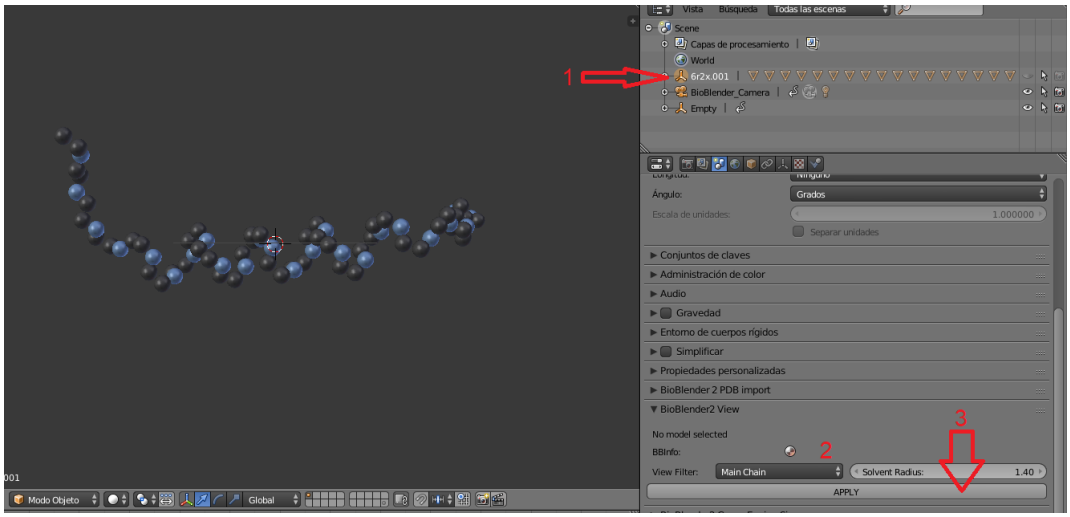


Changing the view of the molecule

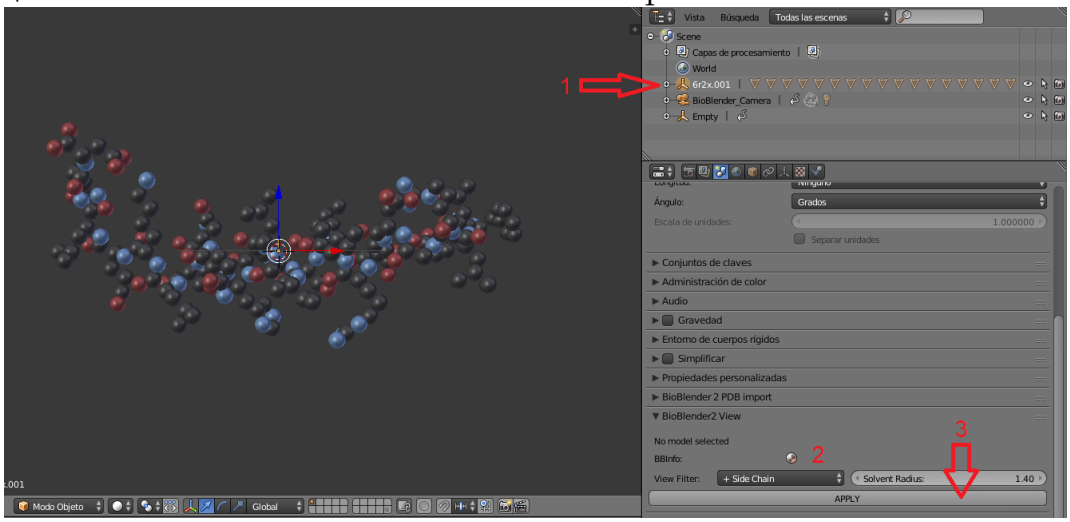
BioBlender can show the molecule(s) according to several options:

Note: First you have to select the molecule in the Outliner (1)

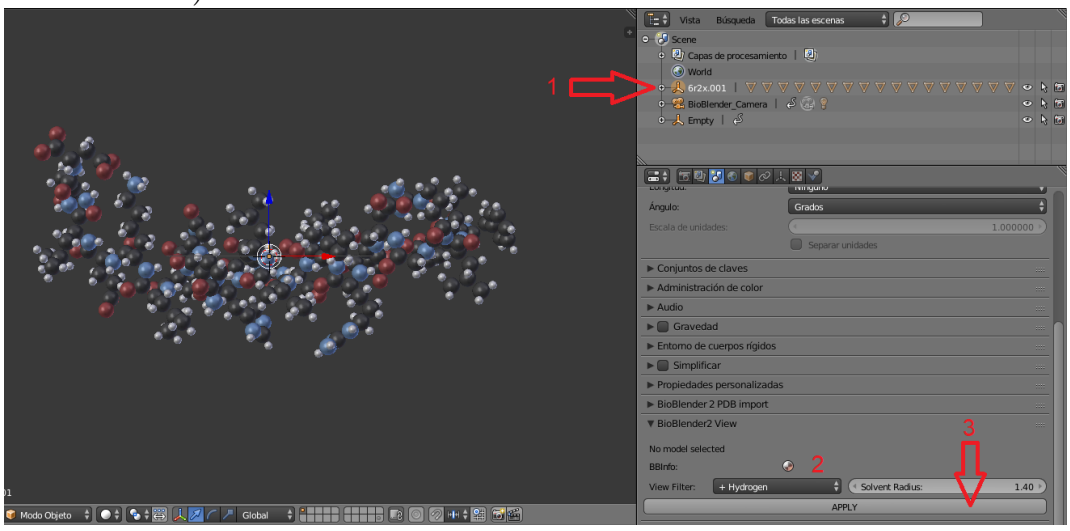
- **Main Chain**: Show the main chain.



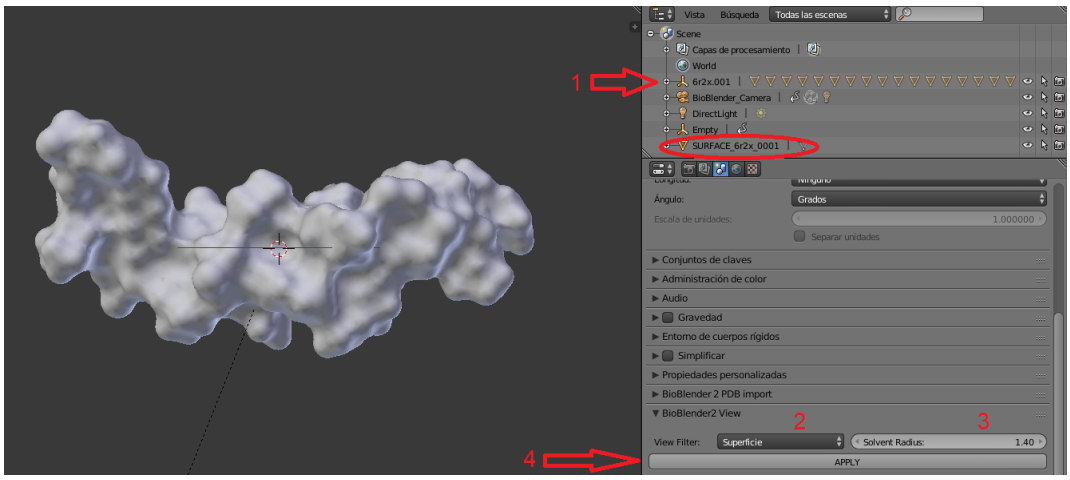
- + **Side Chain**: Shows the main chain plus the atoms attached to it.



- + **Hydrogen**: Shows all imported atoms including Hydrogen. (If H were imported at the start)



- **Surface**: Calculate the surface (through the external PyMol program) and show it on the scene. With this option, you are prompted to select some properties:
  - **Solvent Radius** defines the radius of the probe (defaults is water, 1.40). Setting higher values, up to 2.5 or 3, allows faster calculation, while still providing a good surface.
  - Once the surface is calculated, an element is automatically added to the scene and in the Outliner. 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 surface in the same frame, if you calculate the surface again, it will not calculate it because it will find the element already created. To re-calculate, delete the old surface before.

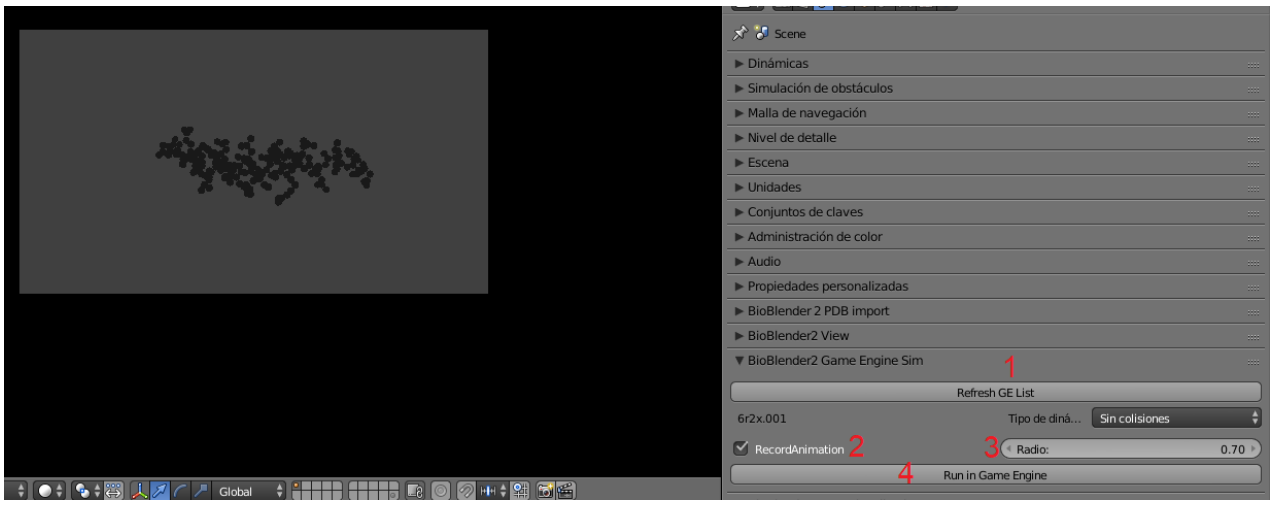


Molecule motion using Blender's physical engine

If the molecule imported contains more than 1 MODELs, by pressing **Alt** + **a** the animation of the molecule begins to play. In this case, atoms move from the location in one conformation to the net, without taking into account their physical properties: you may see impossible motion, like atoms compenetrating. In order to calculate the transition of the protein between two conformations taking into account their physical properties, BioBlender uses the Blender Physics Engine.

Steps to run the Game Engine:

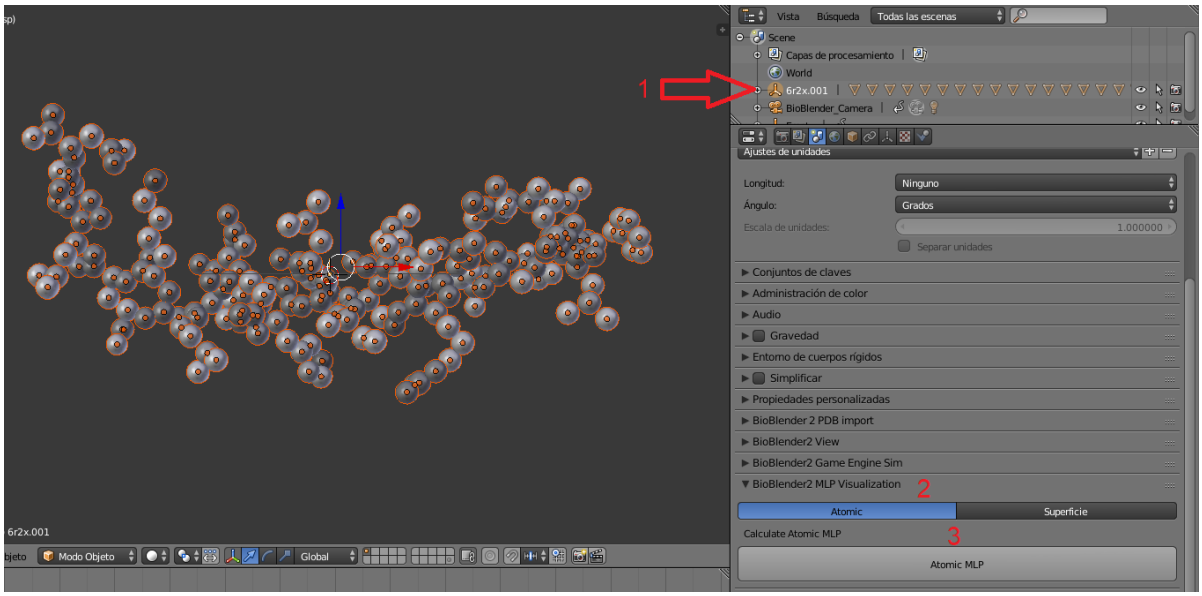
1. Click on **Refresh GE List**. With this imported molecules will automatically be selected, and its name will be displayed.
2. Select the Physics Type to **Rigid Body** (Default is **No Collisions**)
3. **Record Animation**: When selected, it allows recording the animation in F-Curves.
4. **Radius**: Represents the radius value for collisions in Blender's physical engin.
5. 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)

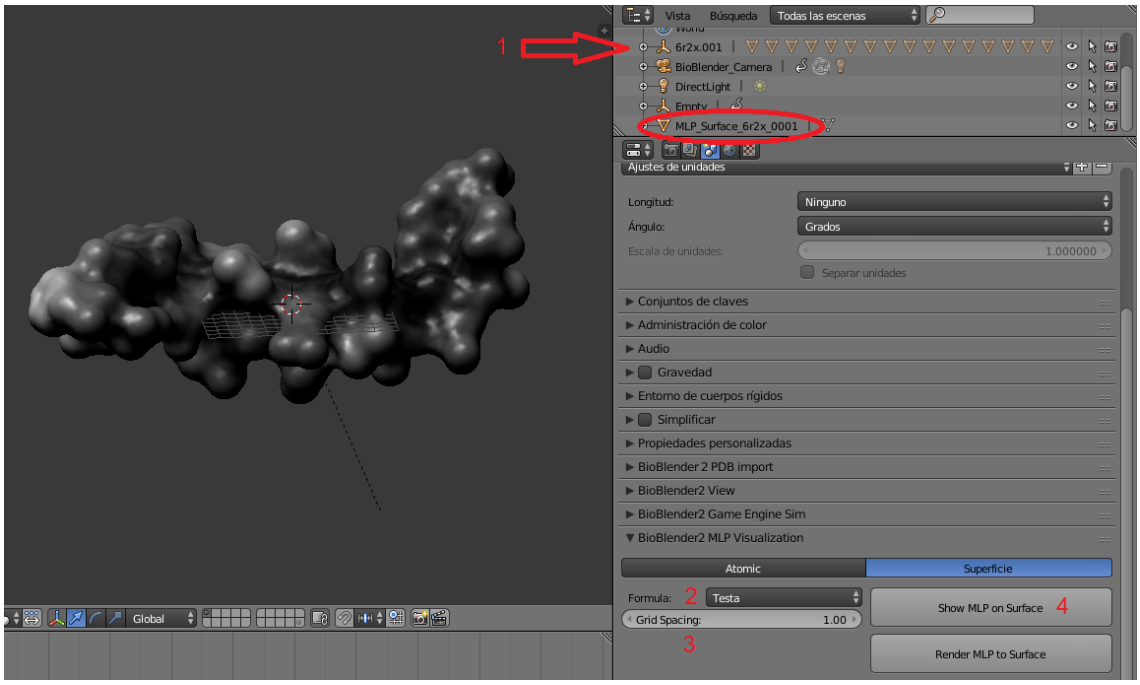
To calculate the MLP, BioBlender usse the external PyMLP software, which performs the calculations that then are imported into Blender.
Bioblender has two options:

- **Calculate MLPon atomic basis**: First select the molecule in the Outliners. (In this case the external software is not necessary)



- **Calculate MLP and display on the surface**: PyMol is used to calculate the surface, PyMLP calculates values and . For its correct operation it is necessary to follow a list of steps.

  1. Select the molecule in the item list (Outliner).
  2. If you had previously created a surface, delete it.
  3. Select the formula by which to calculate the MLP
  4. Select the grid spacing (larger value, faster computation).
  5. Click **Show MLP on Surface**.

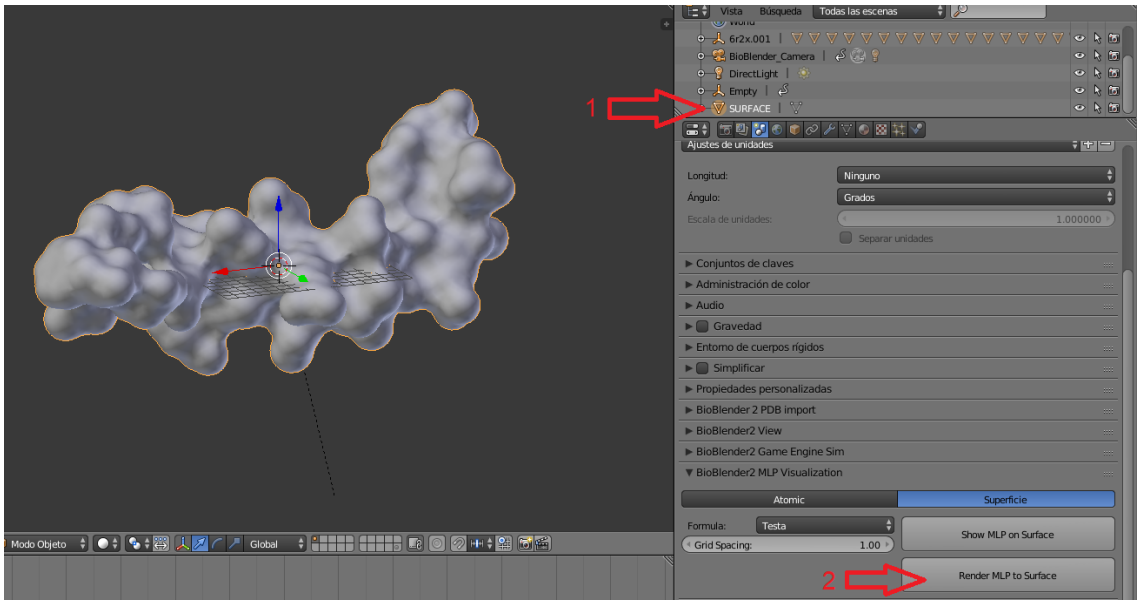


6. Once the surface is displayed, an element is automatically added to the scene (see in the OUtliner), with name: MLP_Surface_name of the PDB_number of the frame.

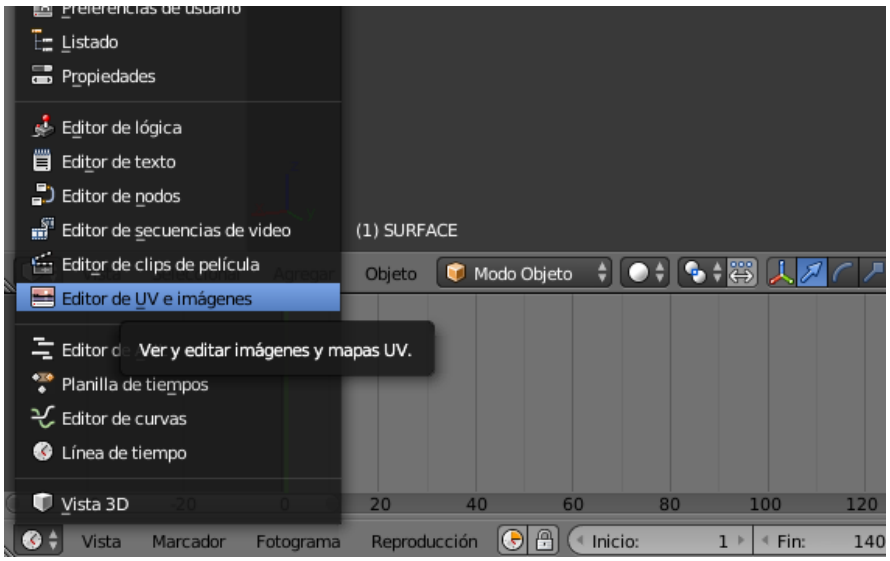
7. If you already calculated a surface in the same frame, if you calculate the surface again, it will not calculate it because it will find the element already created.

8. Select the newly created surface.

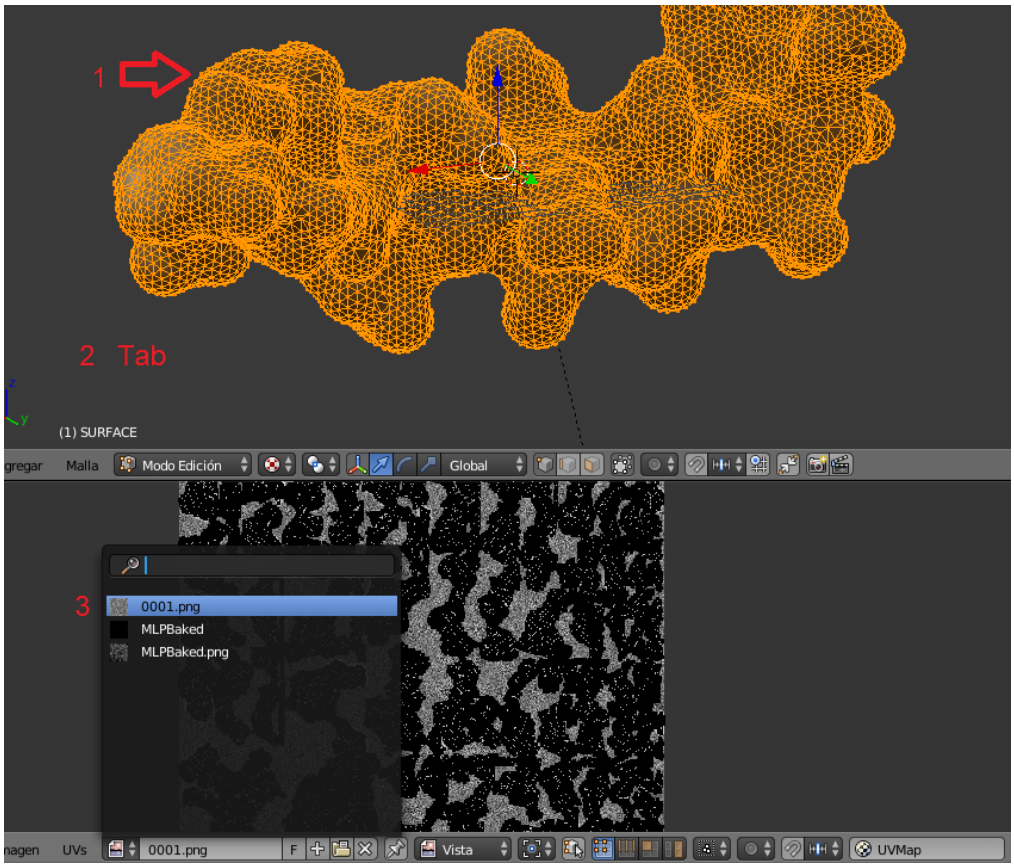
9. Click **Render MLP to Surface**



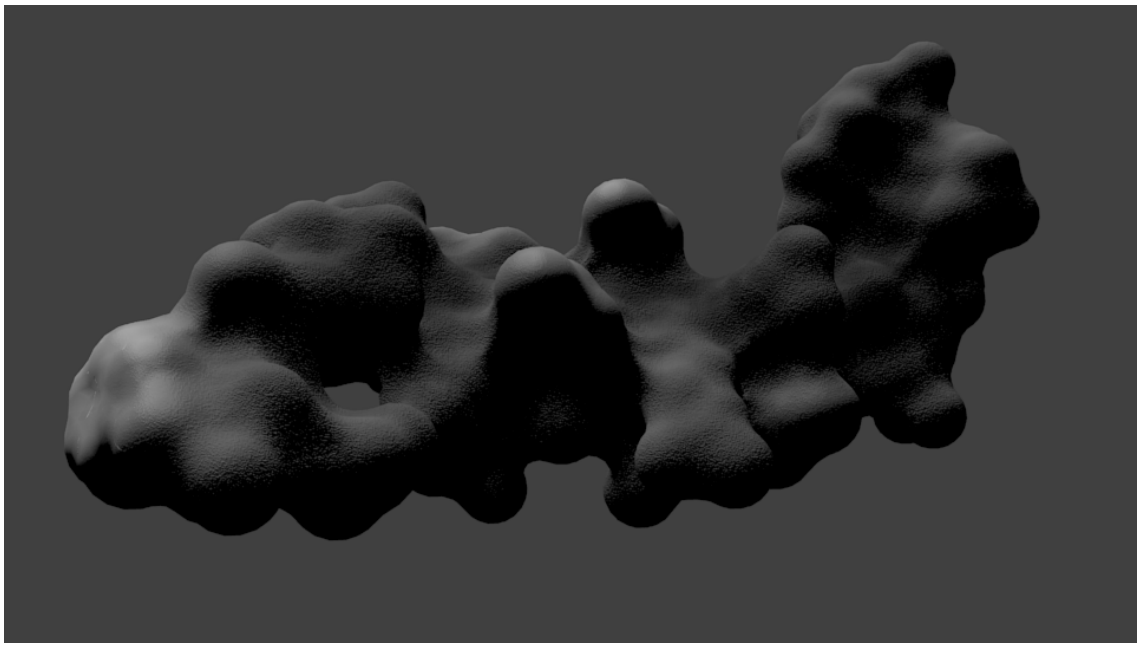
10. Once the texture is created open a **UV and Image Editor** panel



11. Select the surface and press **Tab**, to enter Edit Mode. All the vertices of the surface are displayed 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)

As the EP is among the major determinants of molecular behavior, in BioBlender we have developed the possibility of calculating and showing it in the form of field lines and particles flowing in the scene. For this BioBlender needs the external software **apbs** and **PDB2PQR**, to calculate potential and energy; and the software **SCIVIS** to calculate the lines and export them in a .txt file that BioBlender will finally read and render on the scene.

Steps to calculate the EP

1. Select the molecule you want to work with from the Outliner.

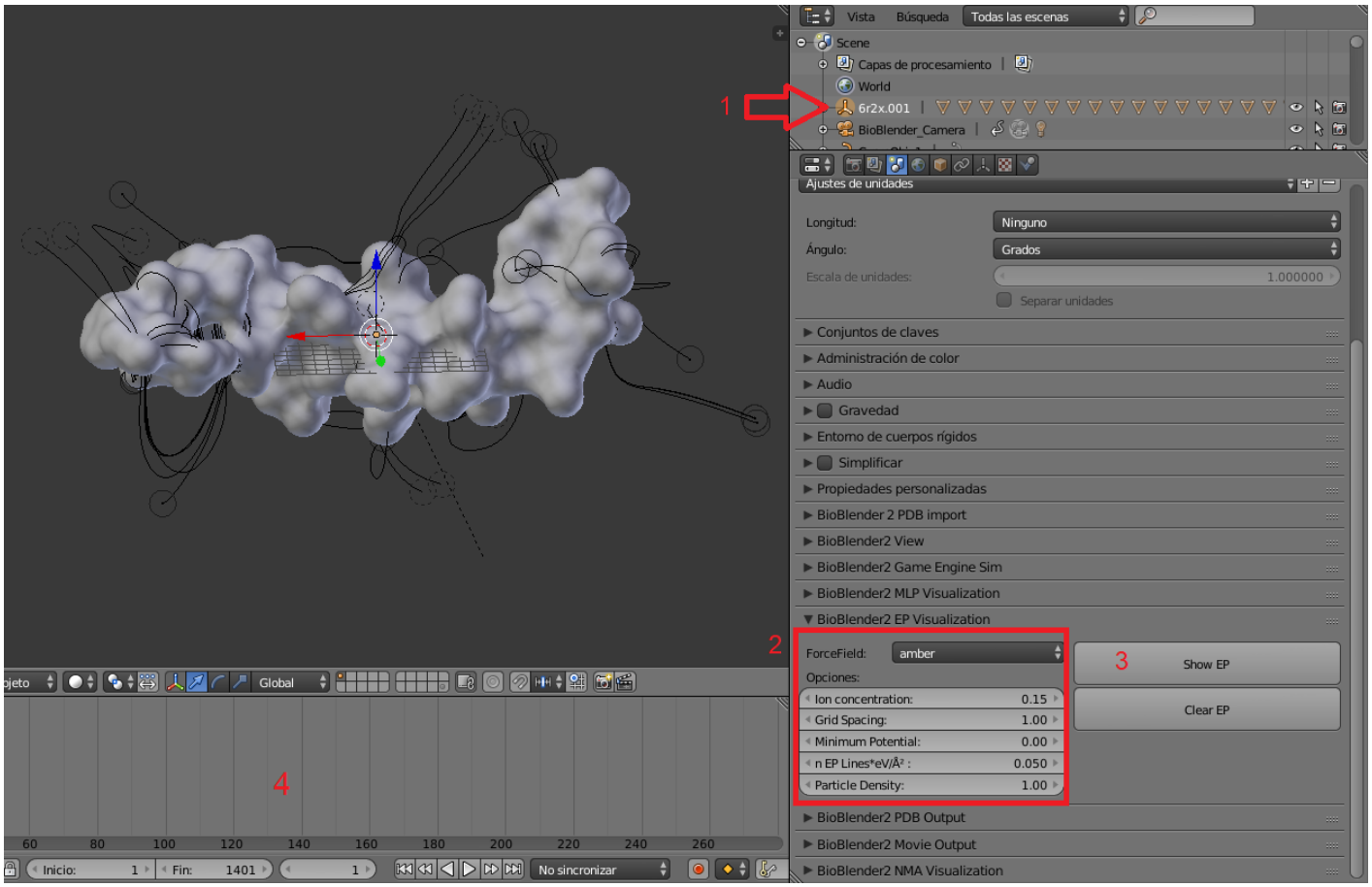
2. In the EP Visualization panel, select the specific values for

   - **ForceField**: selection of the force field among those available (default is Amber)
   - **Ion concentration**: choose the ionic strength of the solvent (default 0.15 M)
   - **Grid Spacing**: choose the grid spacing. Smaller is better, but the calculation is slower.
   - **Minimum Potential**: the minimum value (abs) of potential from which the lines of the force field start.
   - **n EP Lines**: Represents the concentration of the lines.
   - **Particle Density**: Represents the density of the particles flowing along the lines.

3. Click **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. 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 molecule in the Outliner.

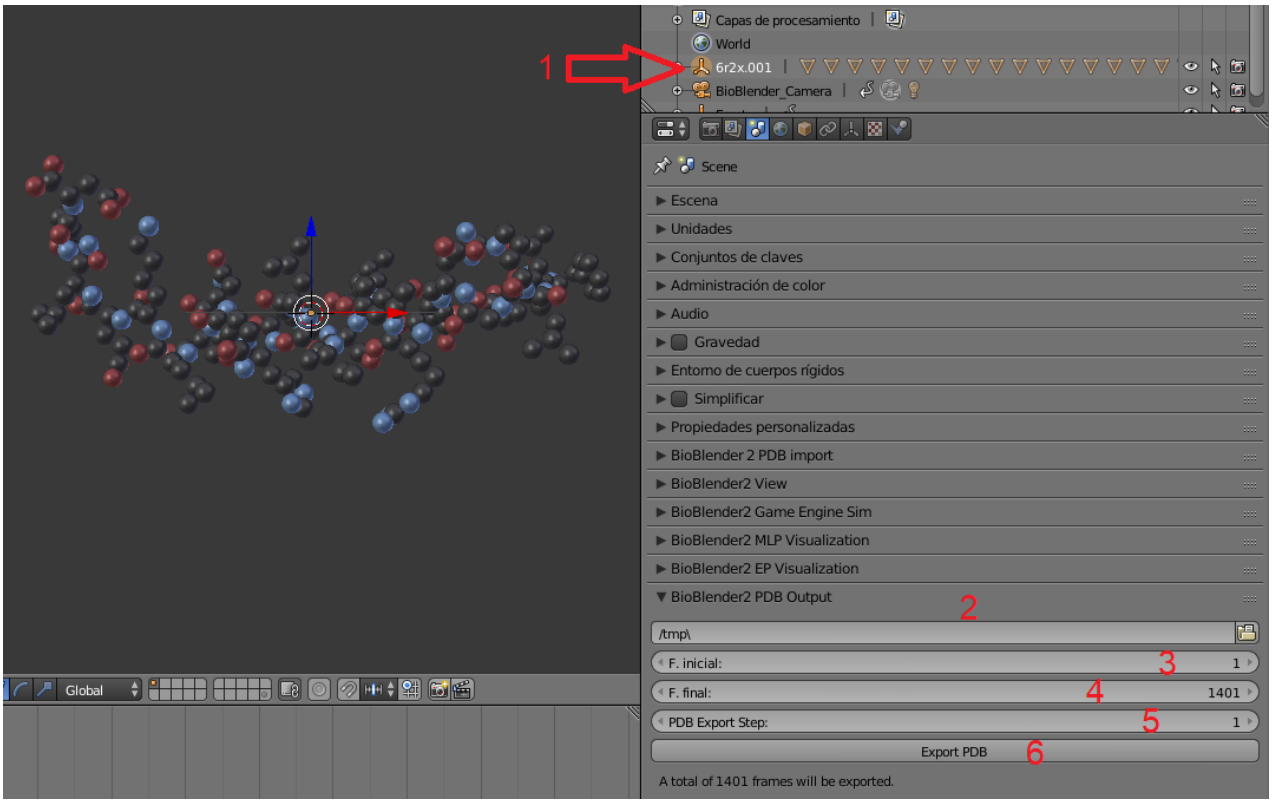
2. Select the local storage where you want to save the PDB file.

3. Select the starting frame.

4. Select the final frame .

5. Select the interval between 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**


1
Capas de procesamiento
World
6r2x.001
BioBlender_Camera
Scene
Escena
Unidades
Conjuntos de claves
Administración de color
Audio
Gravedad
Entorno de cuerpos rígidos
Simplificar
Propiedades personalizadas
BioBlender 2 PDB import
BioBlender2 View
BioBlender2 Game Engine Sim
BioBlender2 MLP Visualization
BioBlender2 EP Visualization
BioBlender2 PDB Output
2
/tmp\
F. inicial:
1
3
F. final:
1401
4
PDB Export Step:
1
5
Export PDB
6
A total of 1401 frames will be exported.
Global

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.

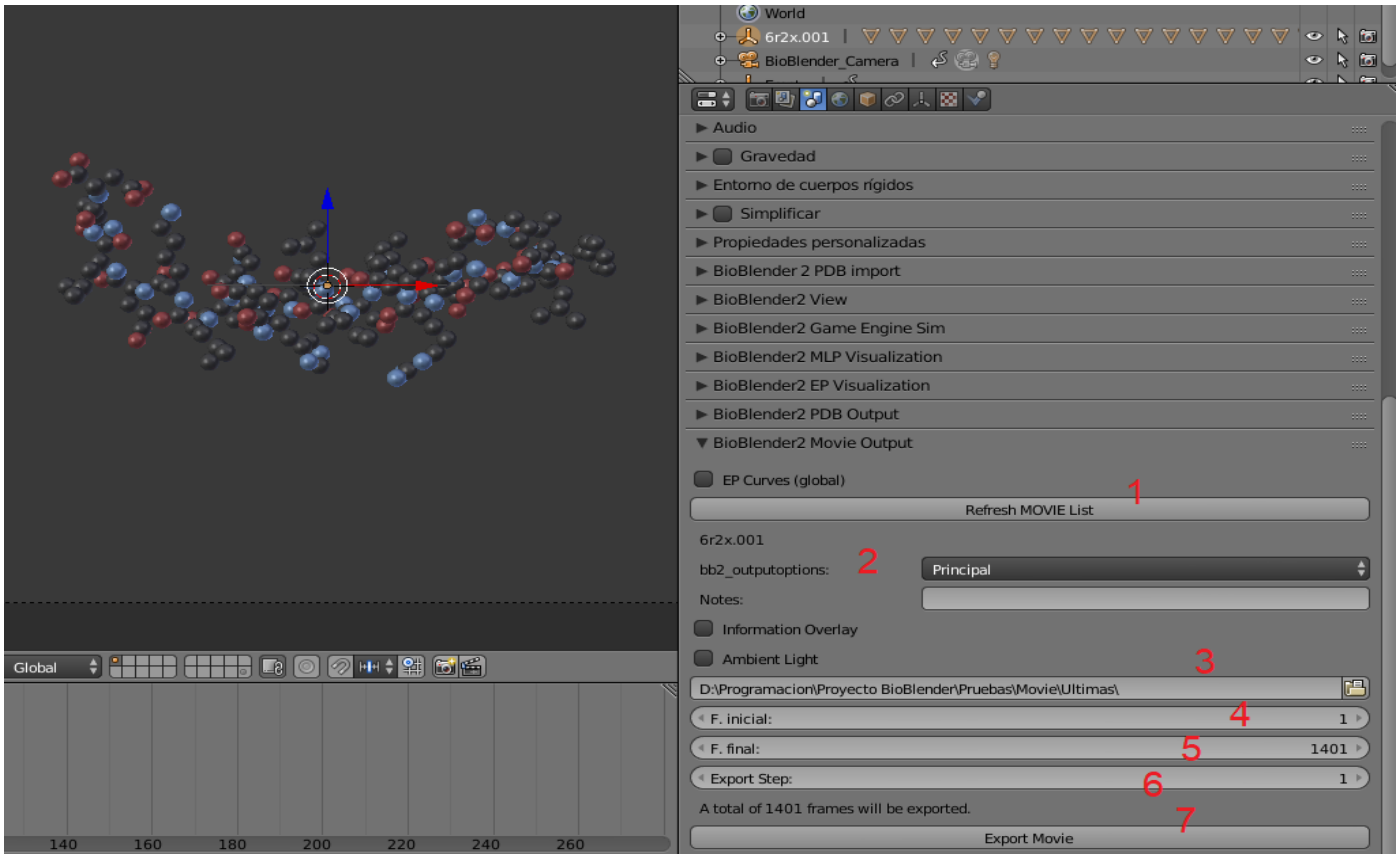
3. Select in the local storage the address where you want to save the movie.

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.

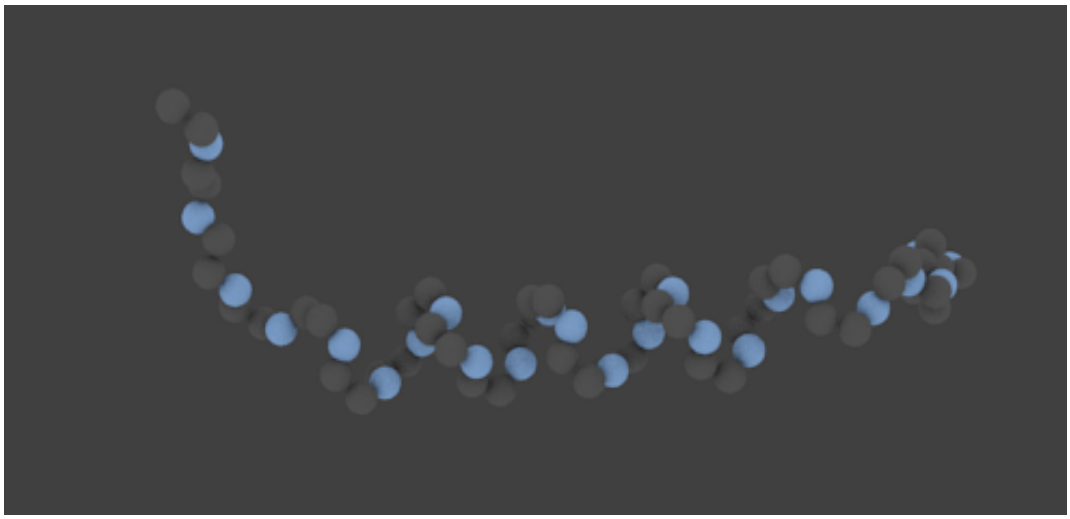
6. Select the jumps between the frames, by default it is 1. This means that it will increase the frames by 1 until reaching the end of the selected frames.

7. Click on **Export Movie**

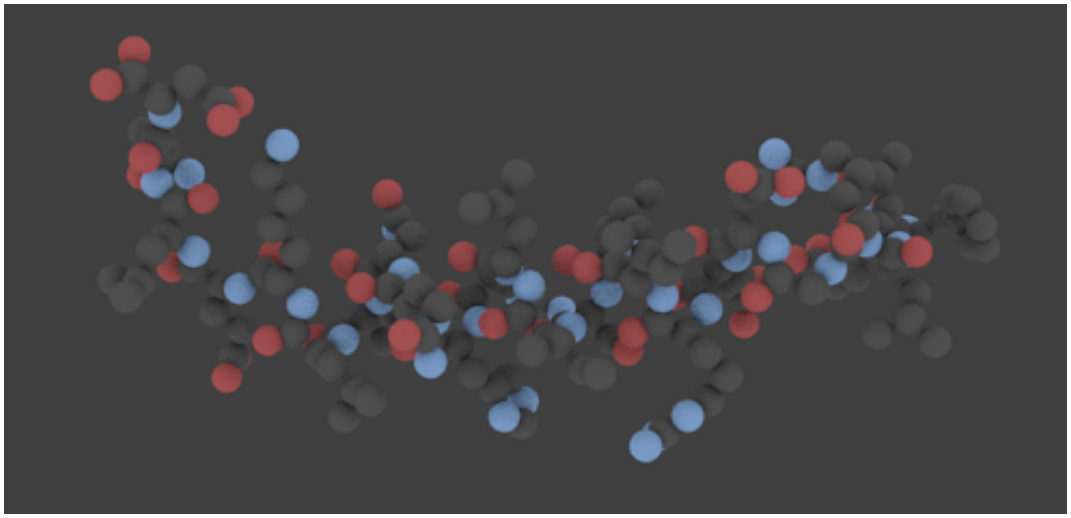


Example of different views of the molecule:

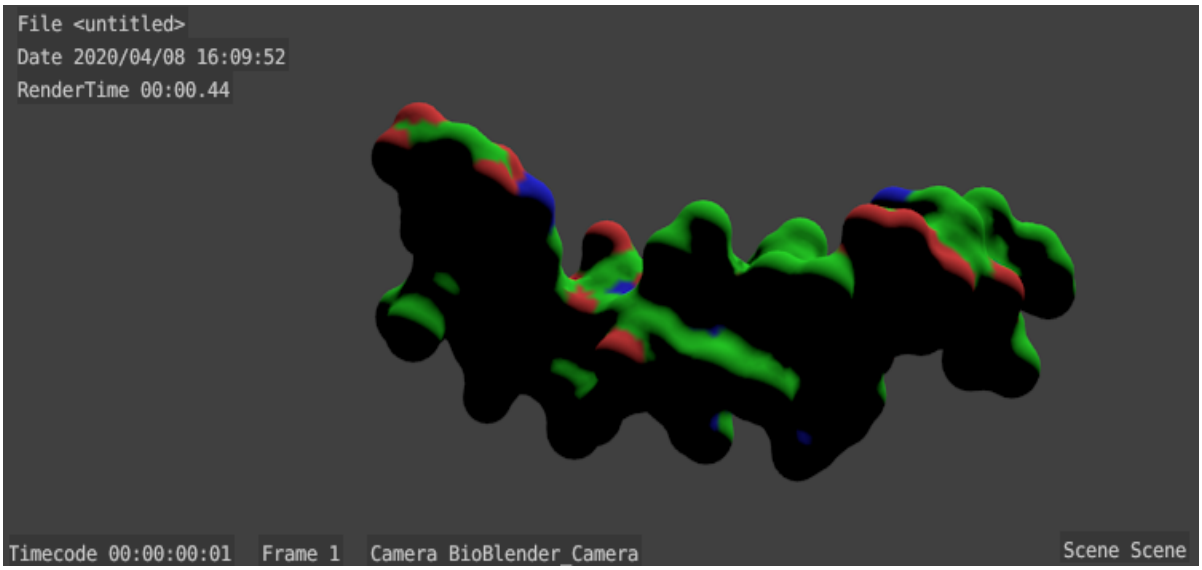
1. View selection **Main** only.



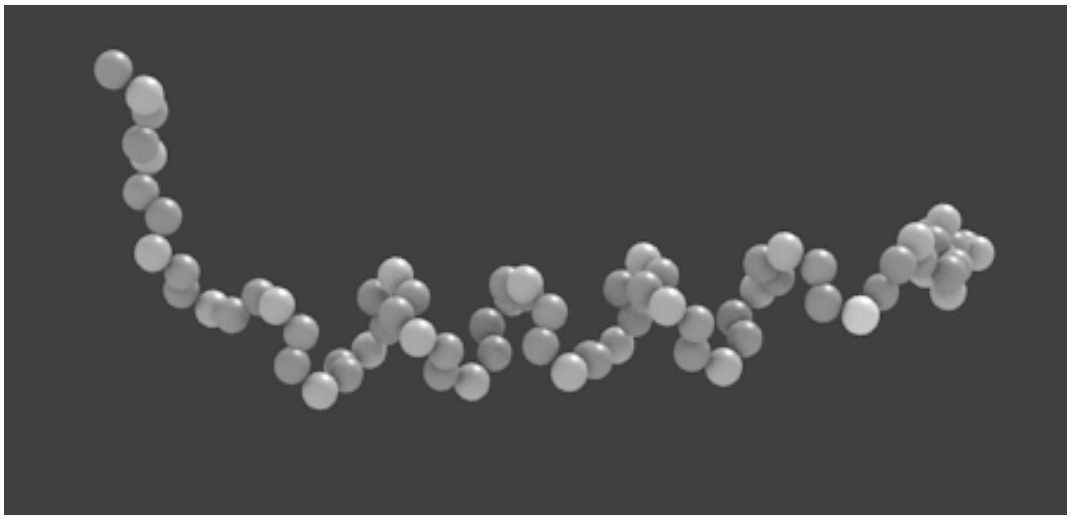
2. Selecting the view + **Side** only.



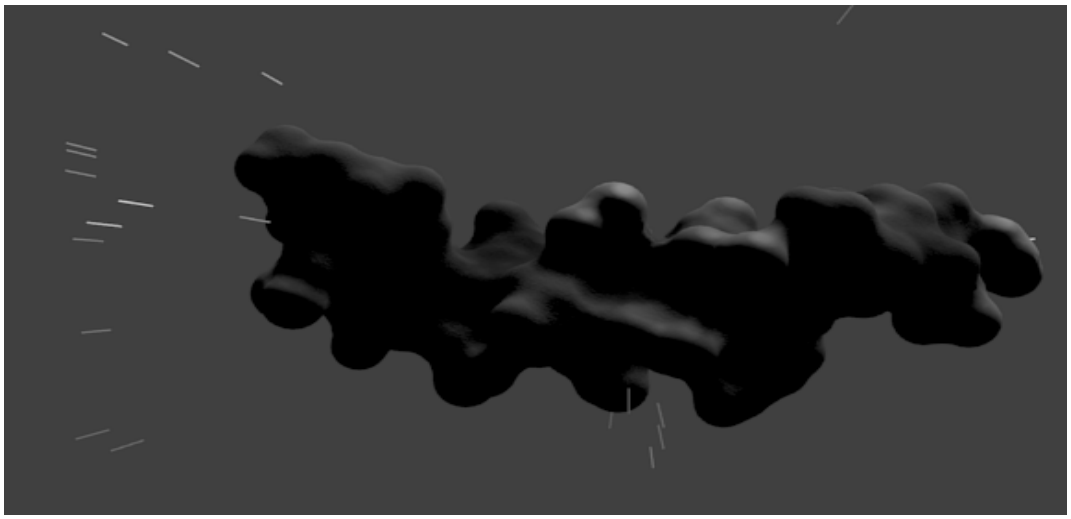
3. Selecting the view **Superficie** and of **Information Overlay**

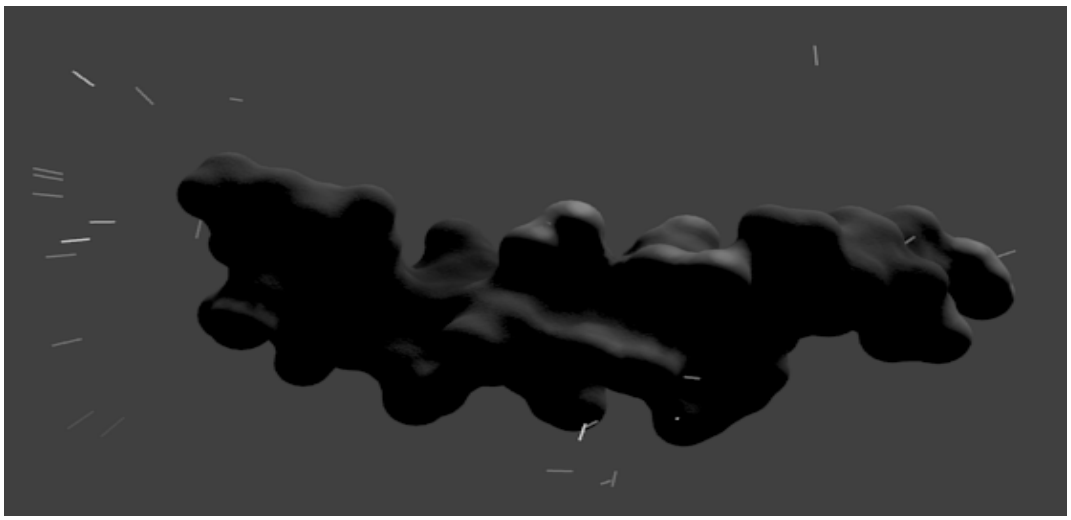


4. Selecting the view **MLP Main**:



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





Calculate the NMA

In BioBlender it is possible to calculate the path of the **Normal Mode Analysis**, using the **Prody** library. 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.

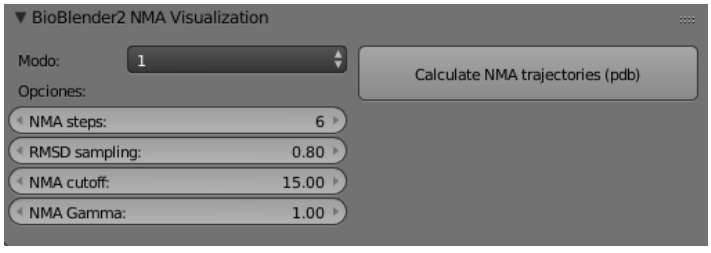
Options provided by the calculation of the NMA:

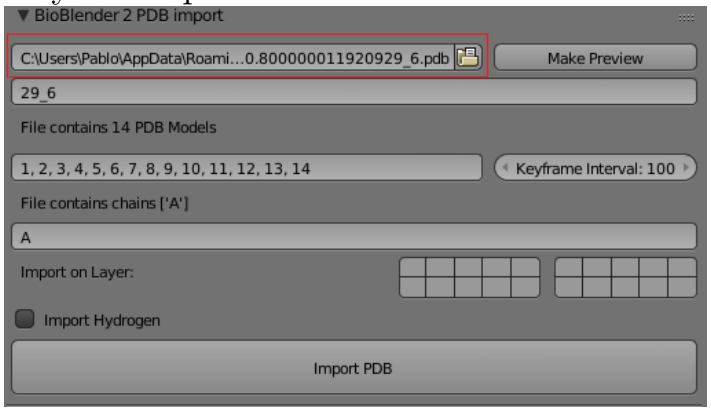
- **Modo**: Select a normal mode analysis to show.
- **NMA Steps**: Represents the Number of conformations to be calculated in each direction.
- **RMSD sampling**: RMSD between the given and the farthest conformation.
- **NMA cutoff**: NMA cutoff distance $(\overset{\hat{A}^{o}}{A})$ for pairwise interactions.
- **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.





Important notes

Many processes in BioBlender export files to be used in other operations; these files can be 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\BioBlender-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 MLP for display on Surface:
  - original.pdb
  - surface.pml
  - tmp.pdb
  - tmp.wrl
  - tmp.dx

- **BioBlender2 MLP Visualization**: When calculating the texture of the MLP, it generates images to wrap the texture:
  - 0001.png
  - MLPBaked.png
  - noise.png
  - composite.blend This is a Blender file, which contains the nodes for texture composition.

- **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