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3D data visualization and biology: visualizing the invisible

Pisa, 21 Novembre 2019
Scientific and Large Data Visualization



Outline

Your speaker

What we visualize

The cell

Proteins

Tools and procedures

BioBlender

Visualization (Shape, MLP, EP)

Motion Calculation

Environment building (cellular landscape)

(Physical models – 3D soft prints)

But first, some special effects

[Link a Protein Expressions](#)

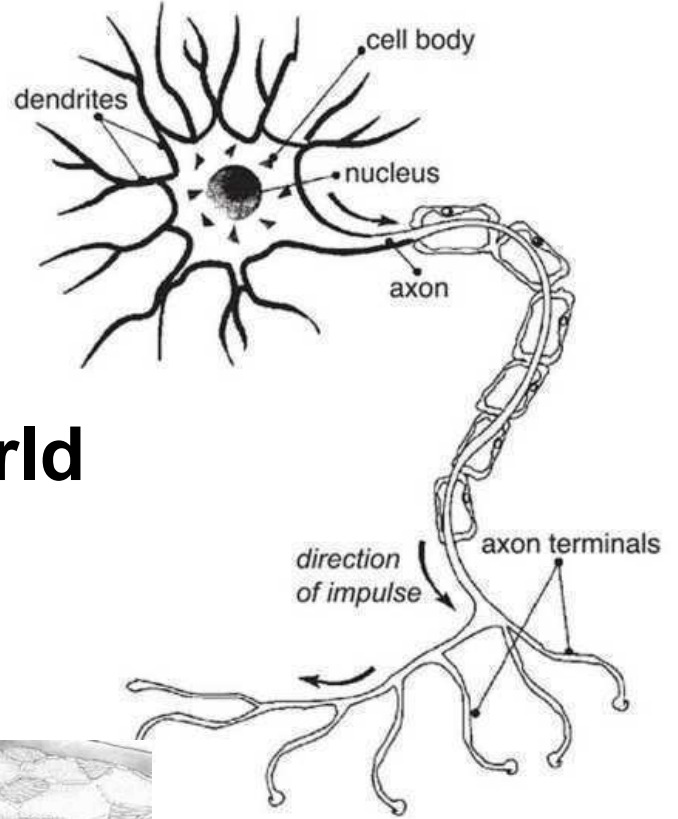
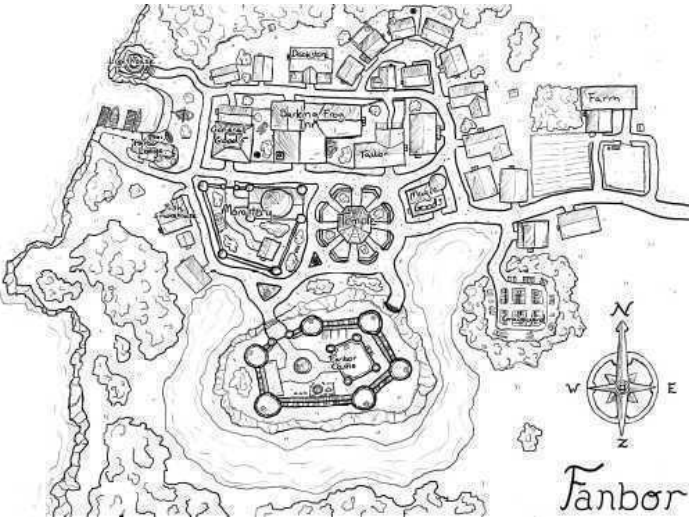


Your speaker

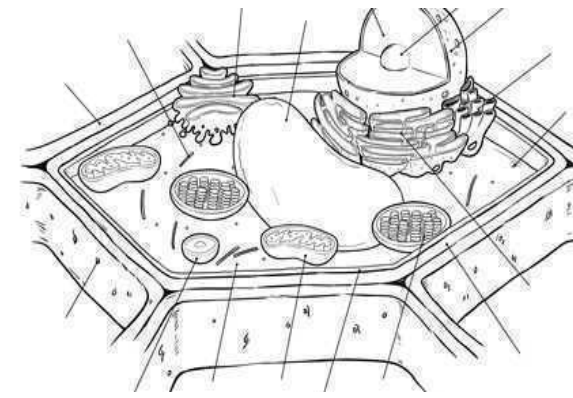
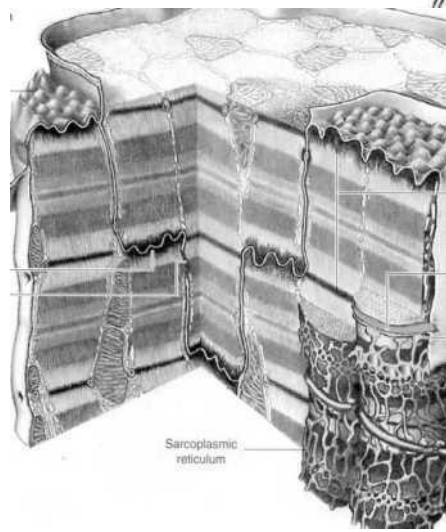
Biologist, worked in 'wet biology' since 1987

In 2003 switch to 'visual biology'

- Increasing complexity
- CG tools mature enough
- Need to visualize a different world



A different world THE CELL



A different world

THE CELL

Cells are the fundamental unit of all living systems

Common features

- Enclosed space (peripheral and internal membranes)
- DNA (Nucleus)
- Energy management (Mitochondria, chloroplasts)
- Transport systems (Skeleton)

ALL INVOLVING PROTEINS

Specific features

- Size
- Shape
- Internal organization
- Specific functions

...

The TenMillion Times perceptive scale

Direct perception mm to few km
Cellular scales nm to few μm

Major caveats:

- 2D vs 3D

- different forces

- non gravity

- different environmental features

How big (small) is a cell?

x 10 milions

<u>CELL</u>	5 – 50 μm	<u>TOWN</u>	50 – 500 m
Internal structures		Internal structures	
Nucleus	3 – 15 μm	Sports field, Major building	300 – 150 m
Golgi	1 – 5 μm	Building (3-6 floors), Airplane	10 – 50 m
Membrane (thickness)	5 – 7 nm	Internal wall, Door	5 – 7 cm
Ribosomes	30 nm	Cats	30 cm
Proteins			
GFP, Actin	3 – 4 nm	Apricot	3 – 4 cm
Spectrin	100 nm	Snake	1 m
NFkB complex	10 – 12 nm	Grapefruit	10 – 12 cm
DNA double helix	2 nm – 2 m	Water pipe – North to South pole	2 cm – 20000 km
Other molecules			
ATP	1,5 nm	Cherry	1,5 cm
Ca ⁺⁺ ion (naked)	0,2 nm	Small ant	2 mm
Ca ⁺⁺ ion (hydrated)	1,2 nm	Nut	1.2 cm
Water (H ₂ O)	0,28 nm	Mosquito	2.8 mm
Sugar (glucose)	0,6 nm	Pea	6 mm
Cholesterol	2 nm	Bee	2 cm
Virus (HIV)	100 nm	Kid 5 - 6 y human	1 m

Visualizing the cell

Sources of information

Microscopy (at ever increasing resolution)

Molecular data (X-ray crystallography, NMR and EM)

Molecular dynamics and theoretical models

Physico-chemical properties

Tools

Specific programs (VMD, pyMOL, S-PDBviewer, J-MOL)

CG tools (Mol-Maya, ePMV, BioBlender)



3D animation package

Free (no cost)

Open

Supported

Documented

Multitask

Multiplatform

Scriptable in Python

Internal and external render

32 or 64 bits (Linux and Windows)

Game Engine

Fast

Programmable
(Approximate)

MOLECULAR DATA PROTEINS

Proteins are the major operative structures of cells

DNA stores information, which is translated into proteins

Genes are stretches of DNA, each gene encodes one type of protein

There are about 30 thousands genes in human DNA

They generate about 300 thousands different proteins

Proteins are built as linear sequences of aminoacids

Upon synthesis they take up a specific shape (fold)

After production, proteins can be modified by many means

Most proteins work in assemblies of up to thousands units

MOLECULAR DATA PROTEINS

File PDB

atomic coordinates
chemical information

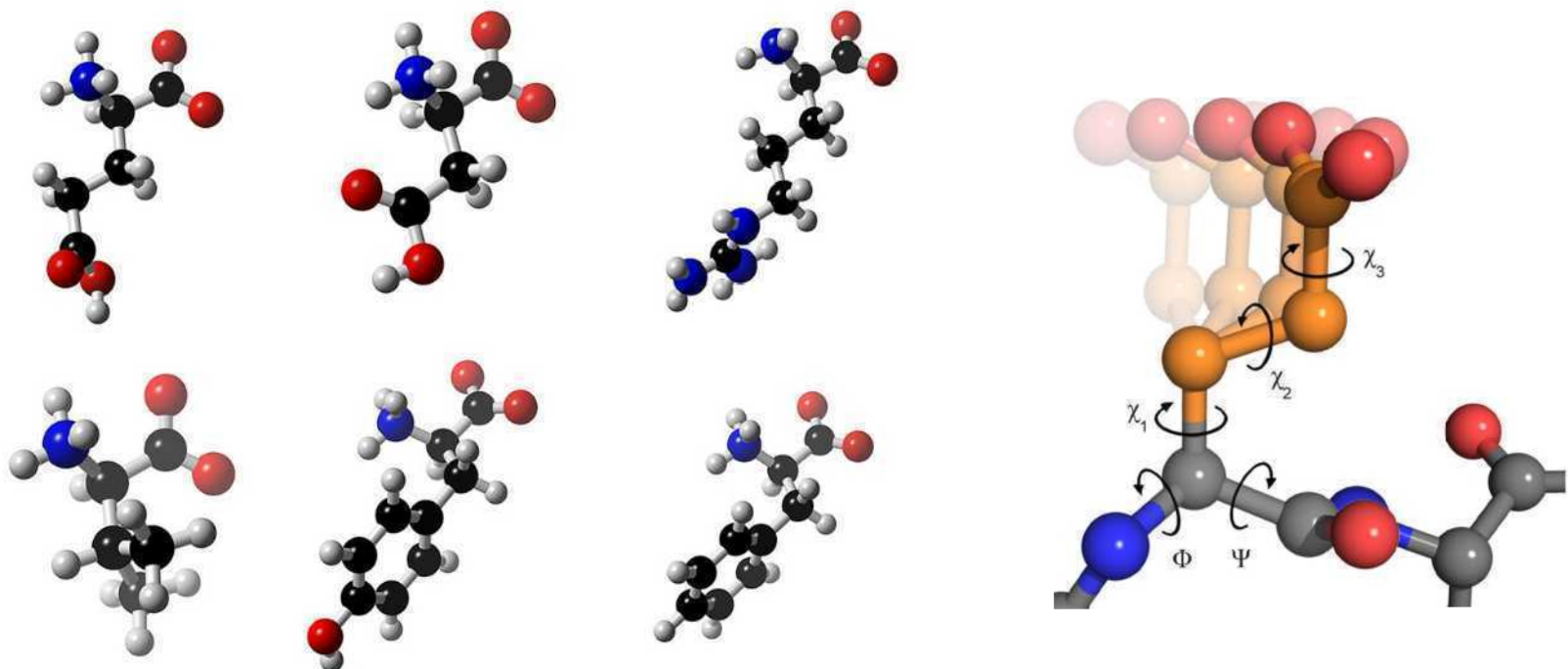
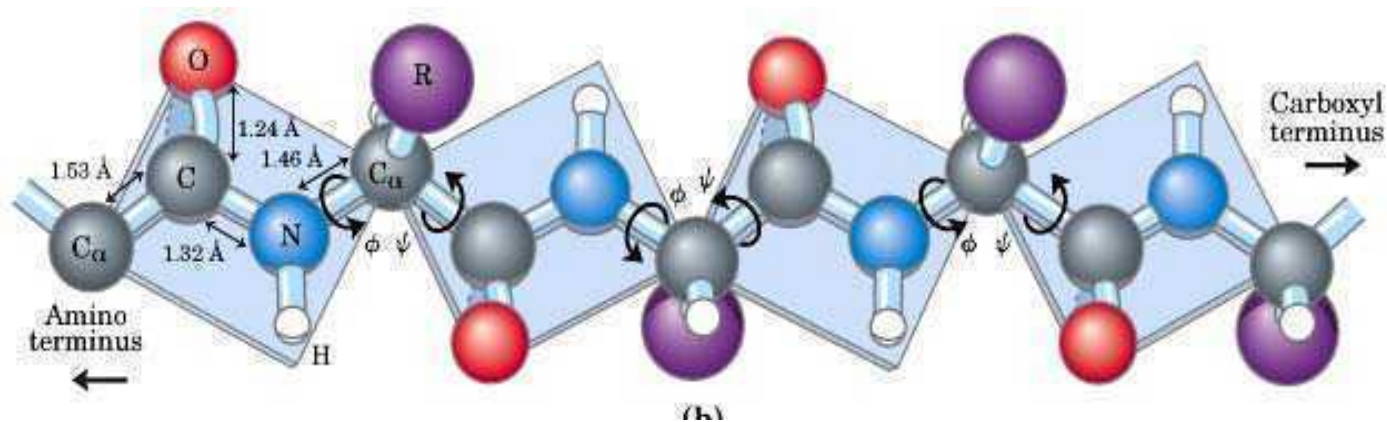
Libraries of

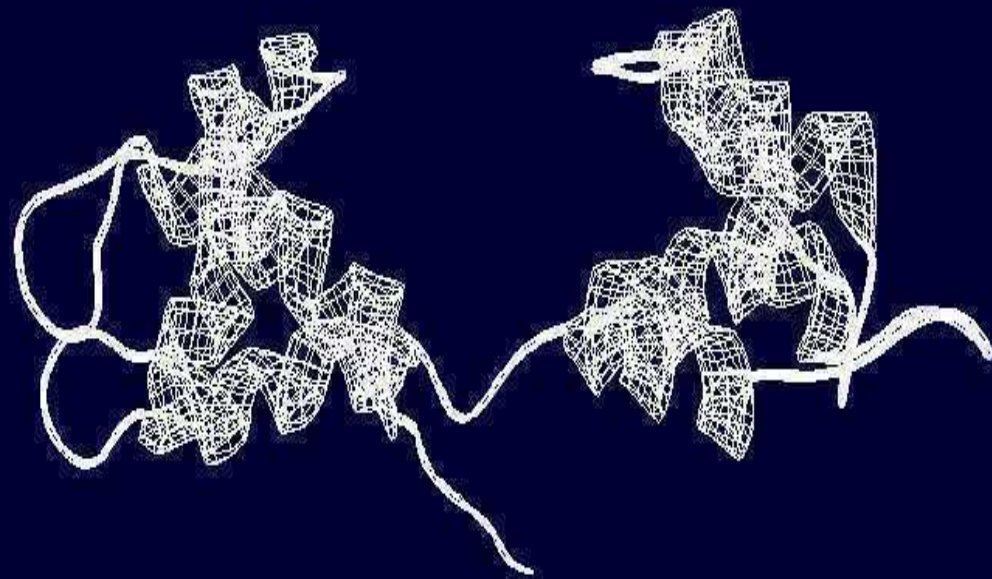
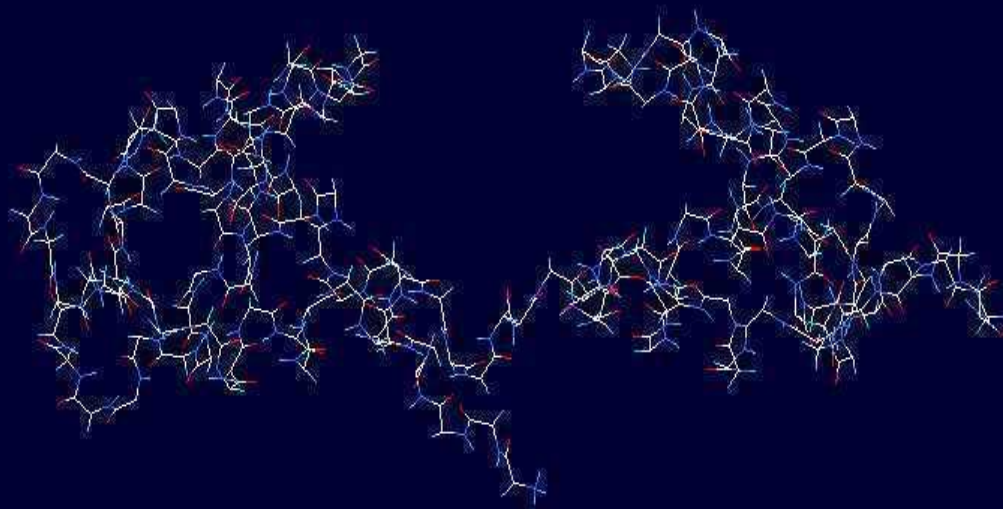
aminoacids
lipophilic potentials
electrostatic potentials

Motion data

ATOM	607	CD2	LEU	C	16	4.937	-19.723	12.773	1.00	31.92
ATOM	608	N	GLN	C	17	1.838	-21.040	8.630	1.00	33.32
ATOM	609	CA	GLN	C	17	0.446	-21.203	8.236	1.00	22.31
ATOM	610	C	GLN	C	17	0.102	-22.689	8.336	1.00	29.01
ATOM	611	O	GLN	C	17	-0.898	-23.067	8.933	1.00	55.36
ATOM	612	CB	GLN	C	17	0.264	-20.769	6.761	1.00	48.58
ATOM	613	CG	GLN	C	17	-1.204	-20.577	6.292	1.00	55.22
ATOM	614	CD	GLN	C	17	-1.700	-19.124	6.285	1.00	77.26
ATOM	615	OE1	GLN	C	17	-0.985	-18.161	5.899	1.00	60.75
ATOM	616	NE2	GLN	C	17	-2.964	-18.965	6.696	1.00	67.58
ATOM	617	N	ALA	C	18	0.990	-23.512	7.774	1.00	49.52
ATOM	618	CA	ALA	C	18	0.963	-24.980	7.788	1.00	41.06
ATOM	619	C	ALA	C	18	0.785	-25.541	9.190	1.00	39.24
ATOM	620	O	ALA	C	18	-0.268	-26.062	9.487	1.00	36.00
ATOM	621	CB	ALA	C	18	2.302	-25.468	7.246	1.00	31.16
ATOM	622	N	LEU	C	19	1.817	-25.389	10.037	1.00	43.58
ATOM	623	CA	LEU	C	19	1.831	-25.723	11.461	1.00	29.61
ATOM	624	C	LEU	C	19	0.609	-25.211	12.227	1.00	36.67
ATOM	625	O	LEU	C	19	0.020	-25.949	13.028	1.00	29.97
ATOM	626	CB	LEU	C	19	3.090	-25.133	12.094	1.00	28.85
ATOM	627	CG	LEU	C	19	4.332	-25.982	11.854	1.00	37.70
ATOM	628	CD1	LEU	C	19	5.411	-25.631	12.887	1.00	37.58
ATOM	629	CD2	LEU	C	19	3.987	-27.463	11.979	1.00	45.10
ATOM	630	N	GLU	C	20	0.234	-23.948	11.973	1.00	24.58
ATOM	631	CA	GLU	C	20	-0.953	-23.343	12.576	1.00	20.11
ATOM	632	C	GLU	C	20	-2.245	-24.007	12.119	1.00	35.63
ATOM	633	O	GLU	C	20	-3.206	-24.167	12.863	1.00	49.93
ATOM	634	CB	GLU	C	20	-1.011	-21.819	12.444	1.00	33.12
ATOM	635	CG	GLU	C	20	-2.311	-21.213	13.008	1.00	47.55
ATOM	636	CD	GLU	C	20	-2.448	-21.256	14.502	1.00	54.42
ATOM	637	OE1	GLU	C	20	-2.677	-22.299	15.090	1.00	48.91
ATOM	638	OE2	GLU	C	20	-2.359	-20.060	15.078	1.00	60.92
ATOM	639	N	LYS	C	21	-2.207	-24.517	10.911	1.00	31.49
ATOM	640	CA	LYS	C	21	-3.332	-25.246	10.432	1.00	34.26
ATOM	641	C	LYS	C	21	-3.463	-26.533	11.253	1.00	34.01
ATOM	642	O	LYS	C	21	-4.557	-26.852	11.740	1.00	51.77

MOLECULAR DATA PROTEIN STRUCTURE





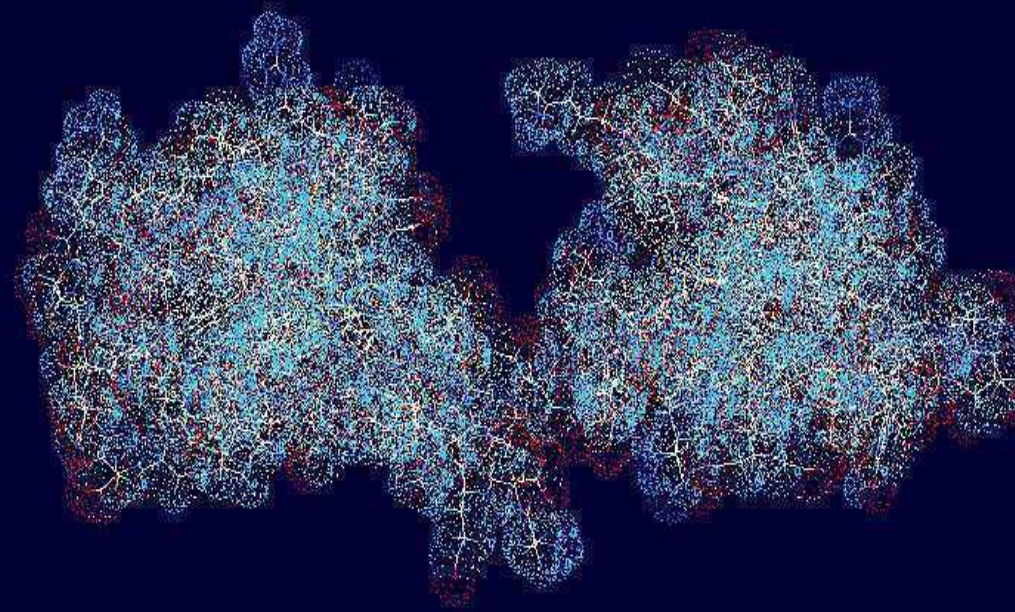
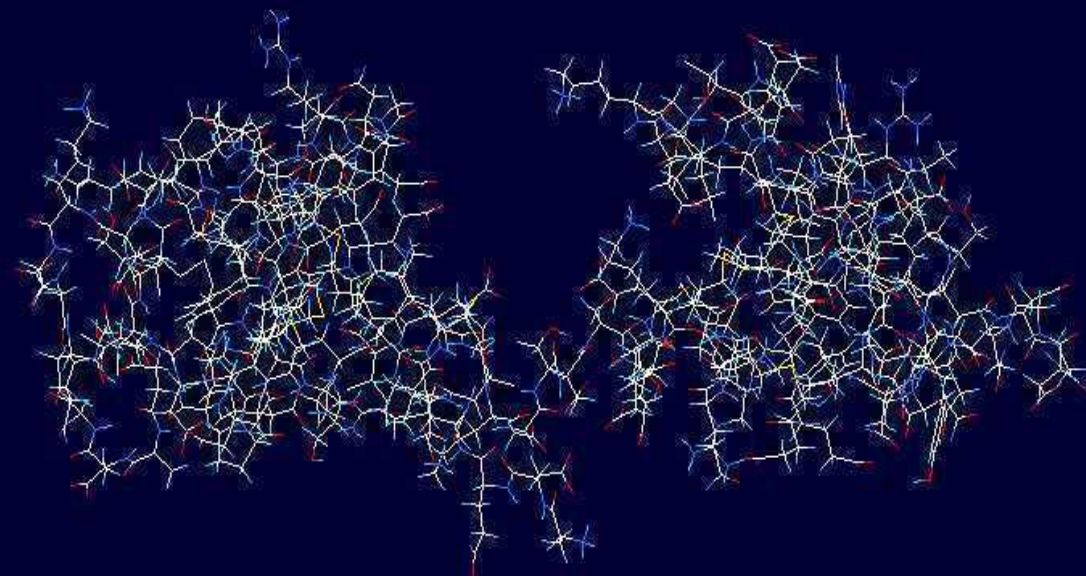
Standard representations

(PyMol, VMD, S-PDBviewer etc)

Atoms as stick, line or VdW

Color code by atom

Secondary structure



IMPORTER

Import PDB in Blender space (tmp file)

incl. molecular features (atom type, chemical bonds, charge)

VISUALIZATION in 3D viewport

Main Chain

All atoms

All + H

Surface

Atomic MLP

MOTION

Build Molecule (Atoms, bonds)

GE (Rigid Body Joint + collision)

Load NMA (ProDy)

Render Visualization

...

...

The screenshot shows the BioBlender interface within a Blender environment. The interface is organized into several vertical panels on the right side of the 3D viewport.

- BioBlender View Aminoacids list:** A panel for managing amino acid lists.
- BioBlender View Chains list:** A panel for managing chain lists.
- BioBlender View Proteins list:** A panel for managing protein lists, featuring an "Update Lists" button.
- BioBlender Select PDB File:** A panel for selecting a PDB file, showing the path `//sampleData\1CFC.pdb` and the name `protein0`.
- BioBlender Import:** A panel for configuring import options. It includes a list of model indices (2, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25) and a "Keyframe Inter: 20" dropdown. Below this, it states "File contains 25 PDB Models" and "File contains chains ['A']". A large "Import PDB" button is present. On the right, there are several checkboxes: Verbose, SpaceFill, Hydrogen, Make Bonds, High Quality, Single User, and Upload Errors.
- BioBlender View:** A panel for viewing the current model. It shows "Currently Selected Model:" with a small sphere icon. Below this is a navigation bar with tabs: `α Carbon`, `Main Chain`, `Side Chain`, `+ Hydrogen` (selected), and `Surface`. To the right of the tabs is a "Solve: 1.40" dropdown. Below the navigation bar are buttons for "Run in Game Engine", "Collision: 0", and "Radius: 0.70".
- BioBlender MLP Visualization:** A panel for Molecular Landscape Potential (MLP) visualization. It includes a "Formula:" dropdown set to "Testa". Below it are three sliders: "Grid Spacing: 1.00", "Contrast: 1.00", and "Brightness: 0.00". To the right are buttons for "Show MLP on Surface" and "Render MLP to Surface".
- BioBlender EP Visualization:** A panel for Electrostatic Potential (EP) visualization. It includes a "ForceField:" dropdown set to "amber". Below it are several sliders: "Ion concentration: 0.15", "Grid Spacing: 1.00", "Minimum Potential: 0.00", "n EP Lines*eV/Å²: 0.050", and "Particle Density: 1.00". To the right are buttons for "Show EP" and "Clear EP".
- BioBlender Output:** A panel for output settings. It shows a path `/tmp/` and a "Visualize:" dropdown set to "EP + MLP". To the right is a "Start Frame: 1" dropdown.

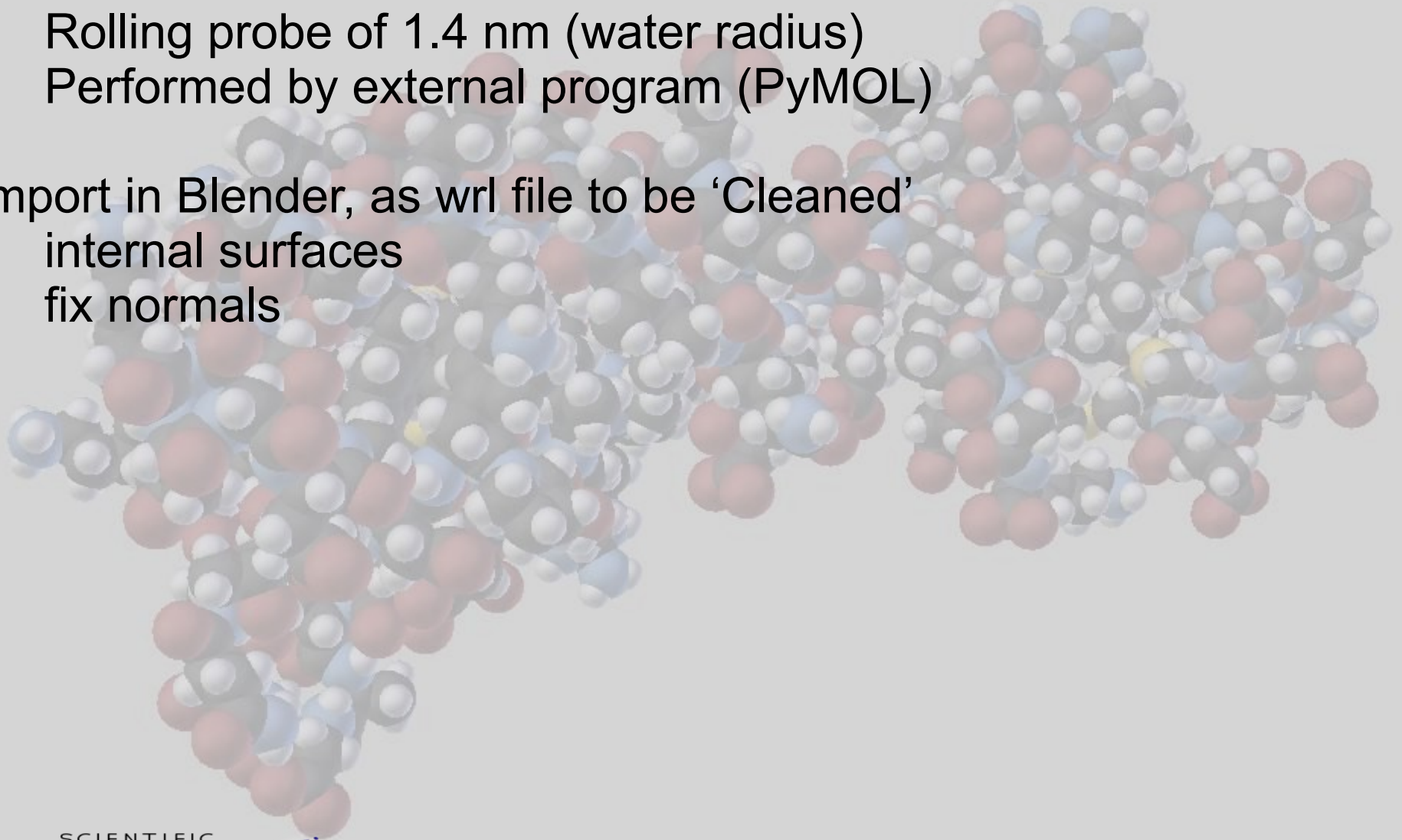
From atoms to shapes

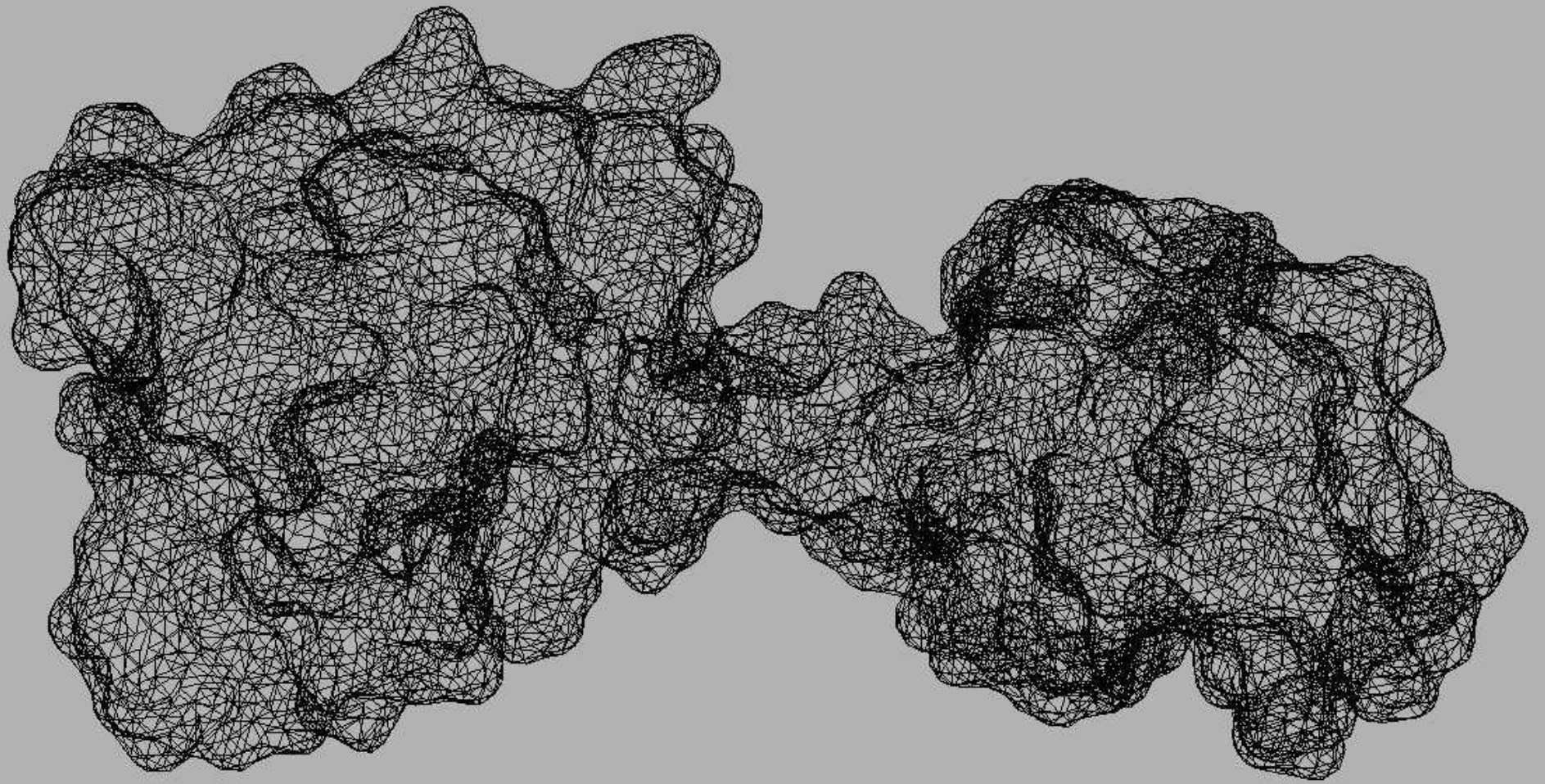
SES Solvent Excluded Surface

Rolling probe of 1.4 nm (water radius)

Performed by external program (PyMOL)

Import in Blender, as wrl file to be 'Cleaned'
internal surfaces
fix normals





From shapes to surfaces

Molecular Lipophilic Potential MLP

Electrostatic Potential

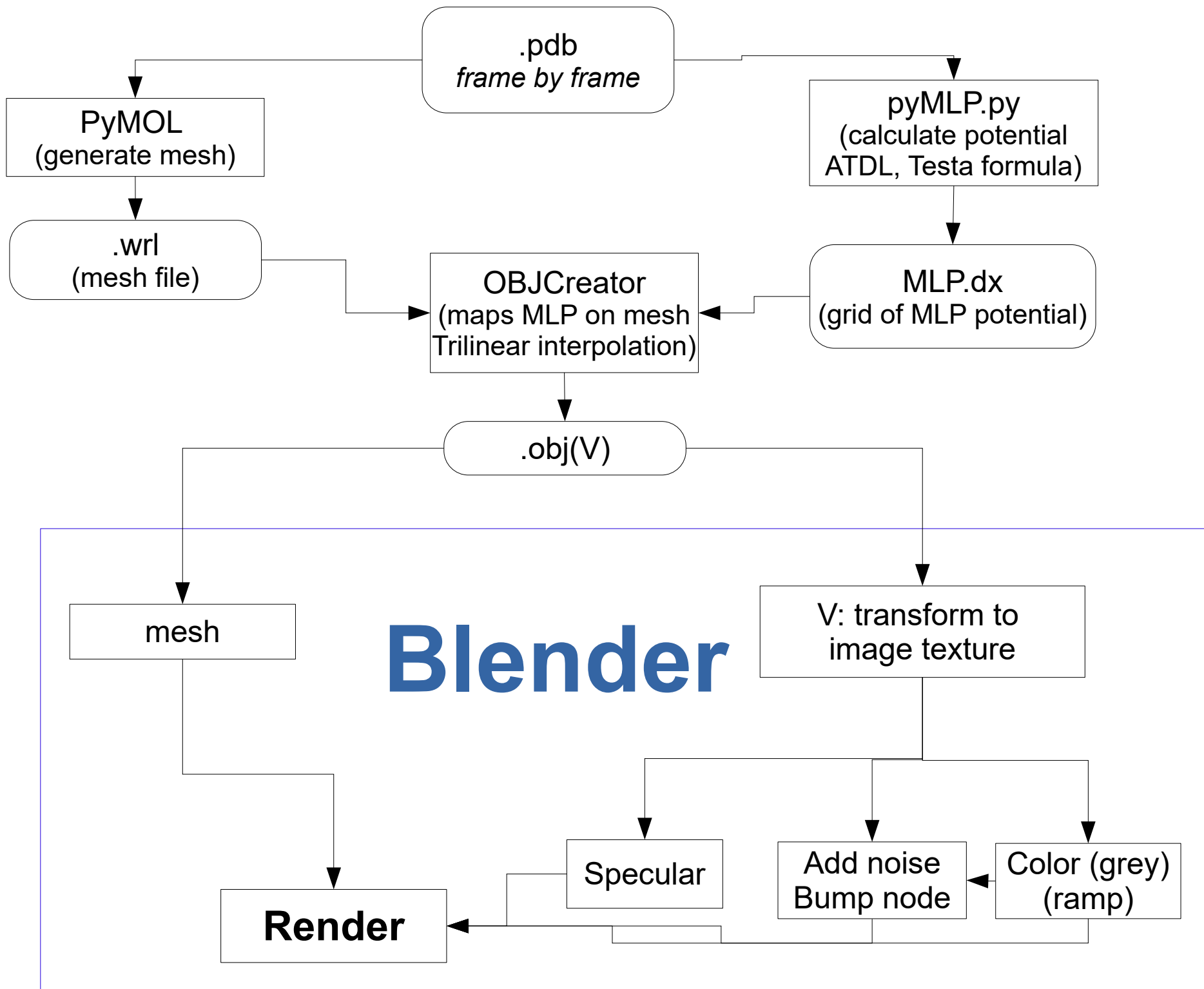
**representing physico/chemical properties that are
important for molecular behavior**

MLP processing

Molecular lipophilic potential

- determined by nature, position and chemical bonds of atoms
- affects the atomic interactions in the close neighborhood
- calculated as 'bulk' (by aminoacid) or on atomic basis
- integrated in volume, where few atoms influence each other

...it all starts with the PDB



pyMLP Molecular Lipophilic Potential evaluator by *Julien Lefeuvre*

128	☐	'LEU':	{ 'C': '-0.54',
129			'CA': '0.02',
130			'CB': '0.45',
131			'CD1': '0.63',
132			'CD2': '0.63',
133			'CG': '0.02',
134			'N': '-0.44',
135			'O': '-0.68' },
136	☐	'LYS':	{ 'C': '-0.54',
137			'CA': '0.02',
138			'CB': '0.45',
139			'CD': '0.45',
140			'CE': '0.45',
141			'CG': '0.45',
142			'N': '-0.44',
143			'NZ': '-1.08',
144			'O': '-0.68' },

Atomic MLP library

```
-9.757313e-006 -1.336629e-005 -1.823682e-005  
-2.478185e-005 -3.353776e-005 -4.519566e-005  
-6.063730e-005 -8.097459e-005 -1.075901e-004  
-1.421746e-004 -1.867539e-004 -2.436975e-004  
-3.156949e-004 -4.056869e-004 -5.167375e-004  
-6.518338e-004 -8.136077e-004 -1.003986e-003  
-1.223787e-003 -1.472308e-003 -1.746959e-003  
-2.043019e-003 -2.353599e-003 -2.669876e-003  
-2.981637e-003 -3.278125e-003 -3.549104e-003  
-3.786024e-003 -3.983069e-003 -4.137918e-003  
-4.252020e-003 -4.330270e-003 -4.380091e-003
```

.dx file

```
v -9.444720 -2.747547 7.548110  
vt 0.000000 -0.527086  
v -9.262868 -1.838463 7.646880  
vt 0.000000 -0.789033  
v -9.629772 -1.890827 7.310747  
vt 0.000000 -0.683912  
v -9.408696 -1.209171 6.871759  
vt 0.000000 -0.980798  
v -9.629772 -1.890827 7.310747  
vt 0.000000 -0.683912  
v -9.262868 -1.838463 7.646880  
vt 0.000000 -0.789033
```

.obj file

Location:

X: 0.000

Y: 0.000

Z: 0.000

Rotation:

X: 0°

Y: -0°

Z: 0°

XYZ Euler

Scale:

X: 1.000

Y: 1.000

Z: 1.000

Dimensions:

59.178

35.380

52.491

▼ Grease Pencil

New

Add New Layer

▼ View

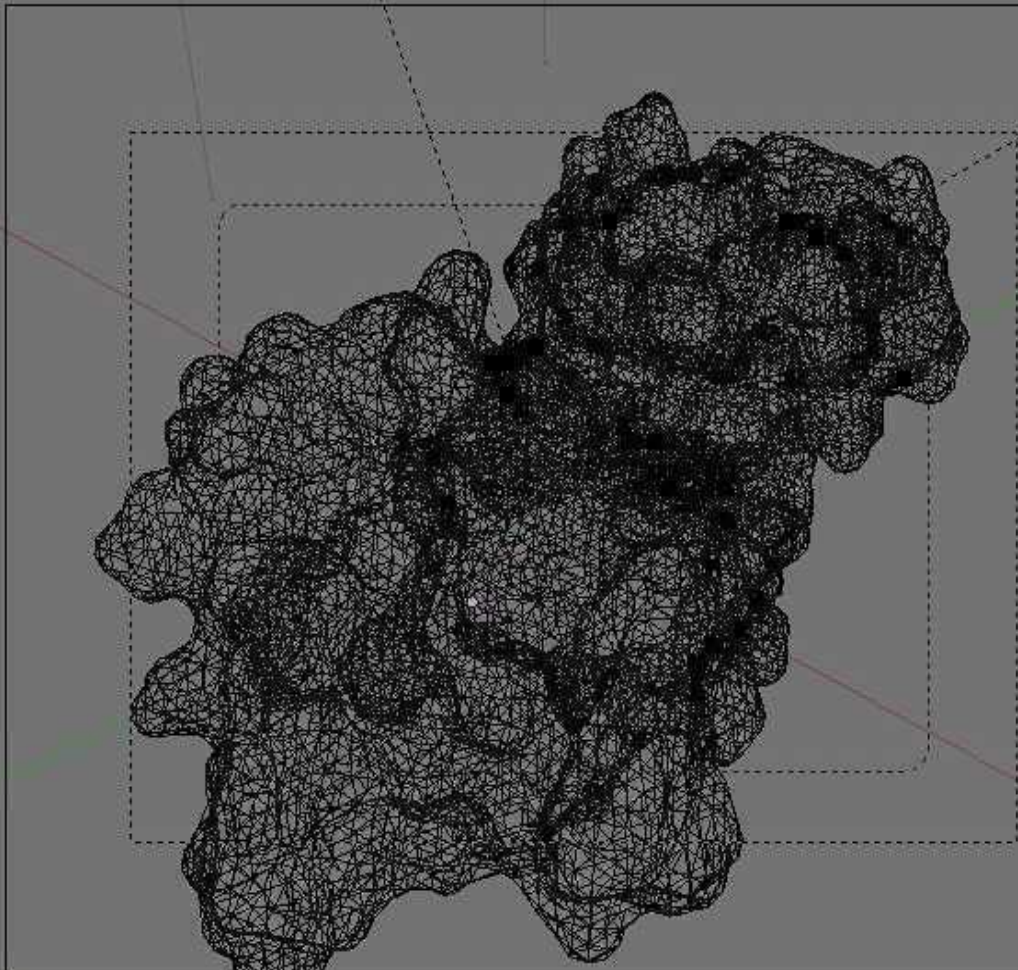
Lens: 35.000

Lock to Object:

Clip:

Start: 0.100

End: 5000.000



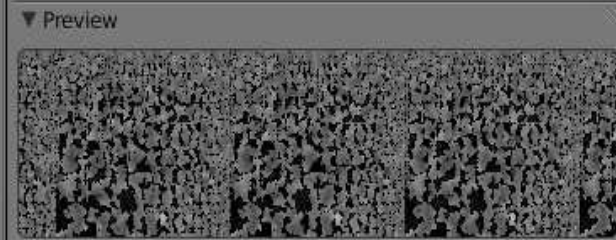
bump

specular

color

color + × Brush

Type: Image or Movie



Show Alpha

▼ Image

MLPBaked.001

Source: File

0-win32\blender\scripts\ui\bioBlender\MLP\data\MLPBaked

Image: size 1024 x 1024, RGB byte

Fields Premultiply

Upper First Lower First

► Image Sampling

► Image Mapping

► Colors

▼ Mapping

Coordinates: UV

Layer:

Projection: Flat

From Dupli X Y Z

Offset: X: 0.00 Y: 0.00 Z: 0.00

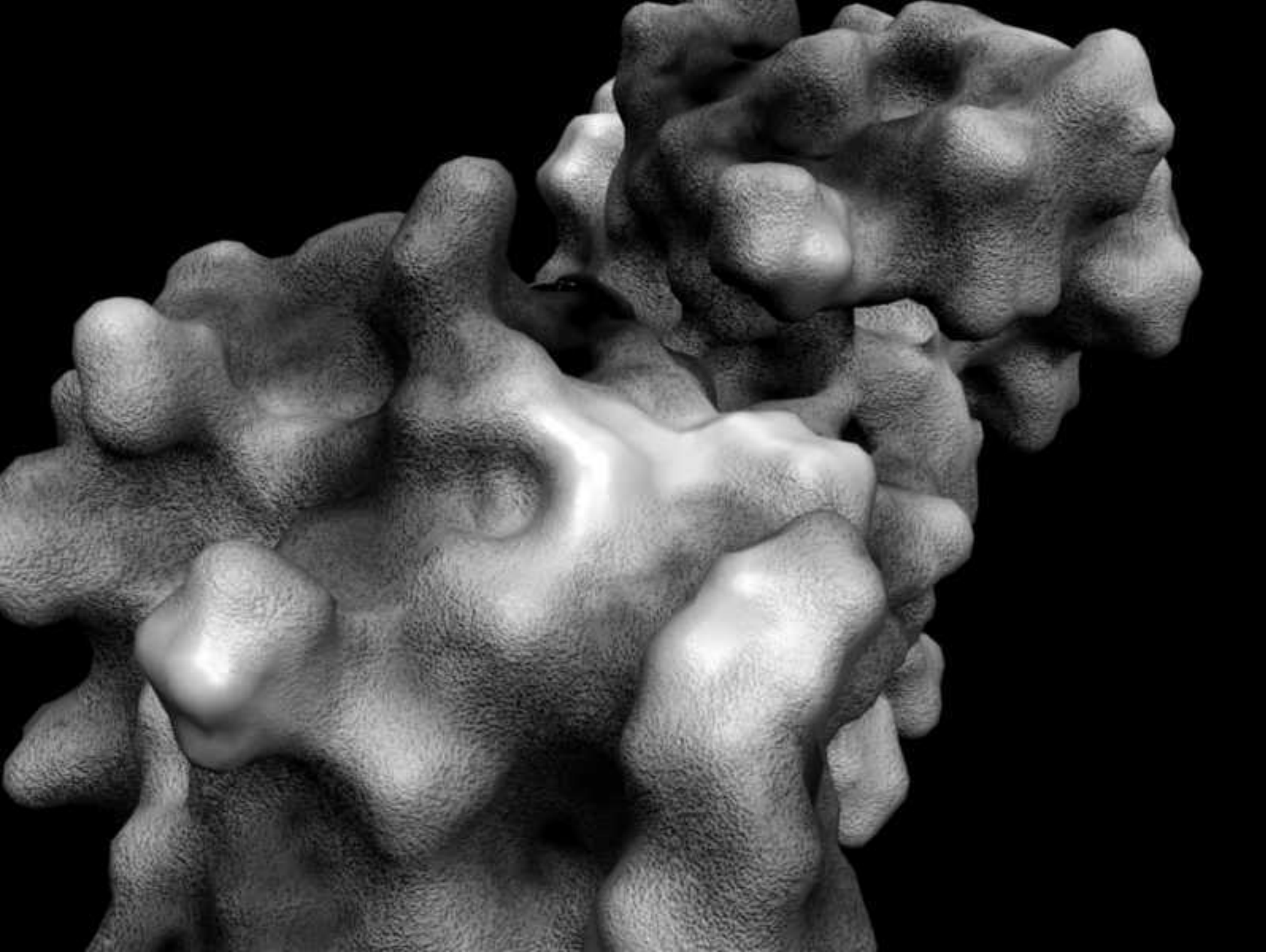
Size: X: 1.00 Y: 1.00 Z: 1.00

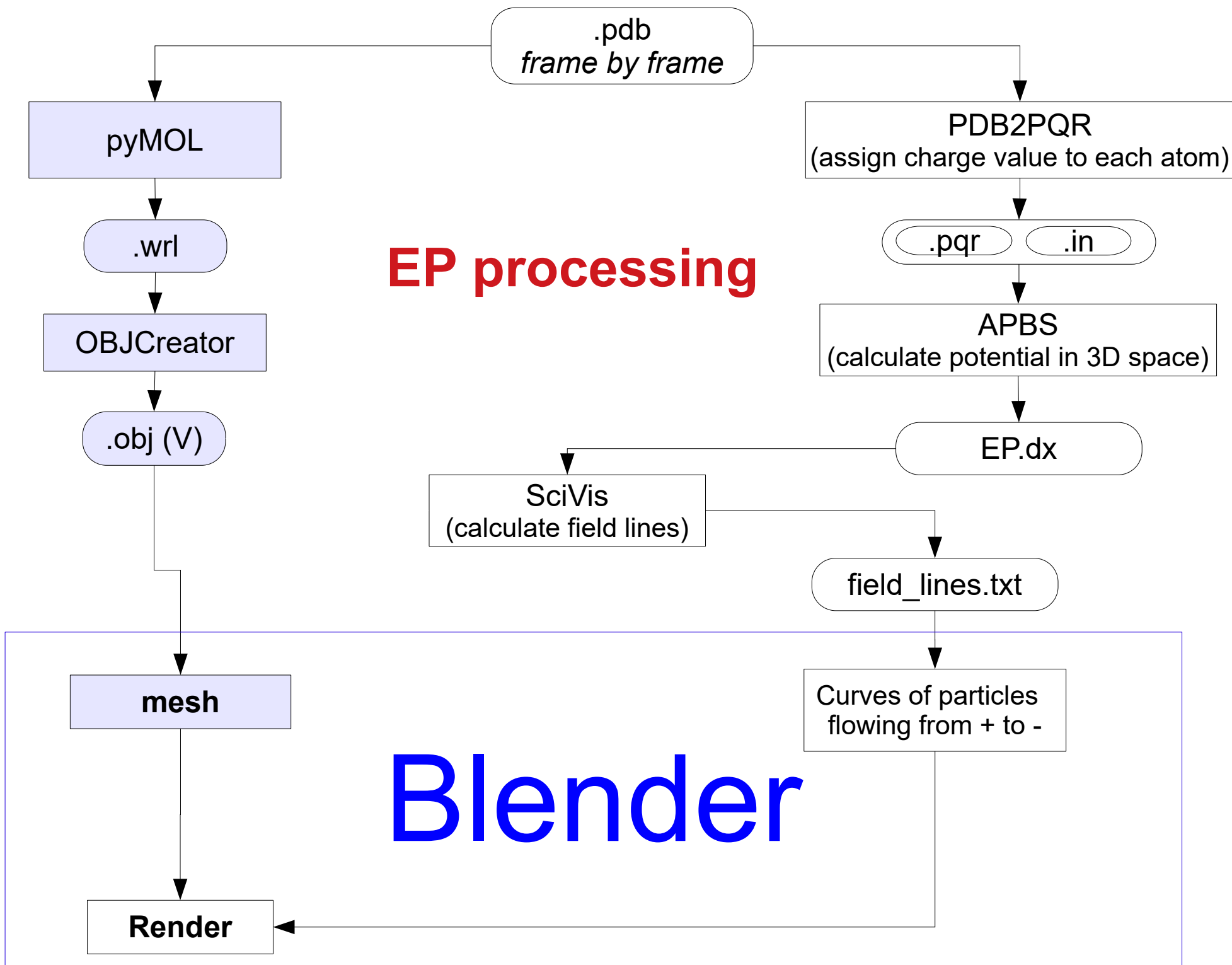
▼ Influence

Diffuse: Shading:

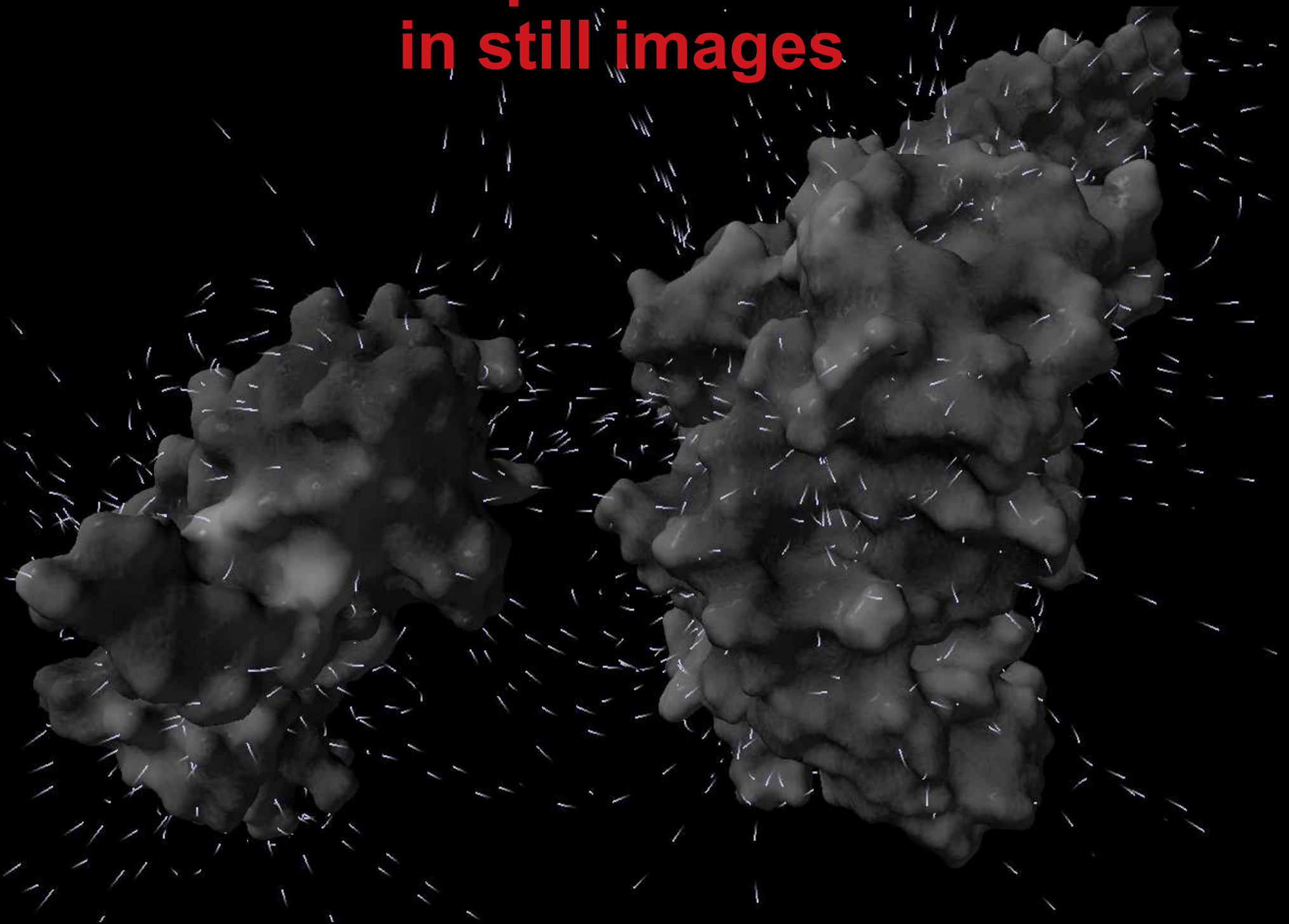
(1) Dggfi
(1) Mesh

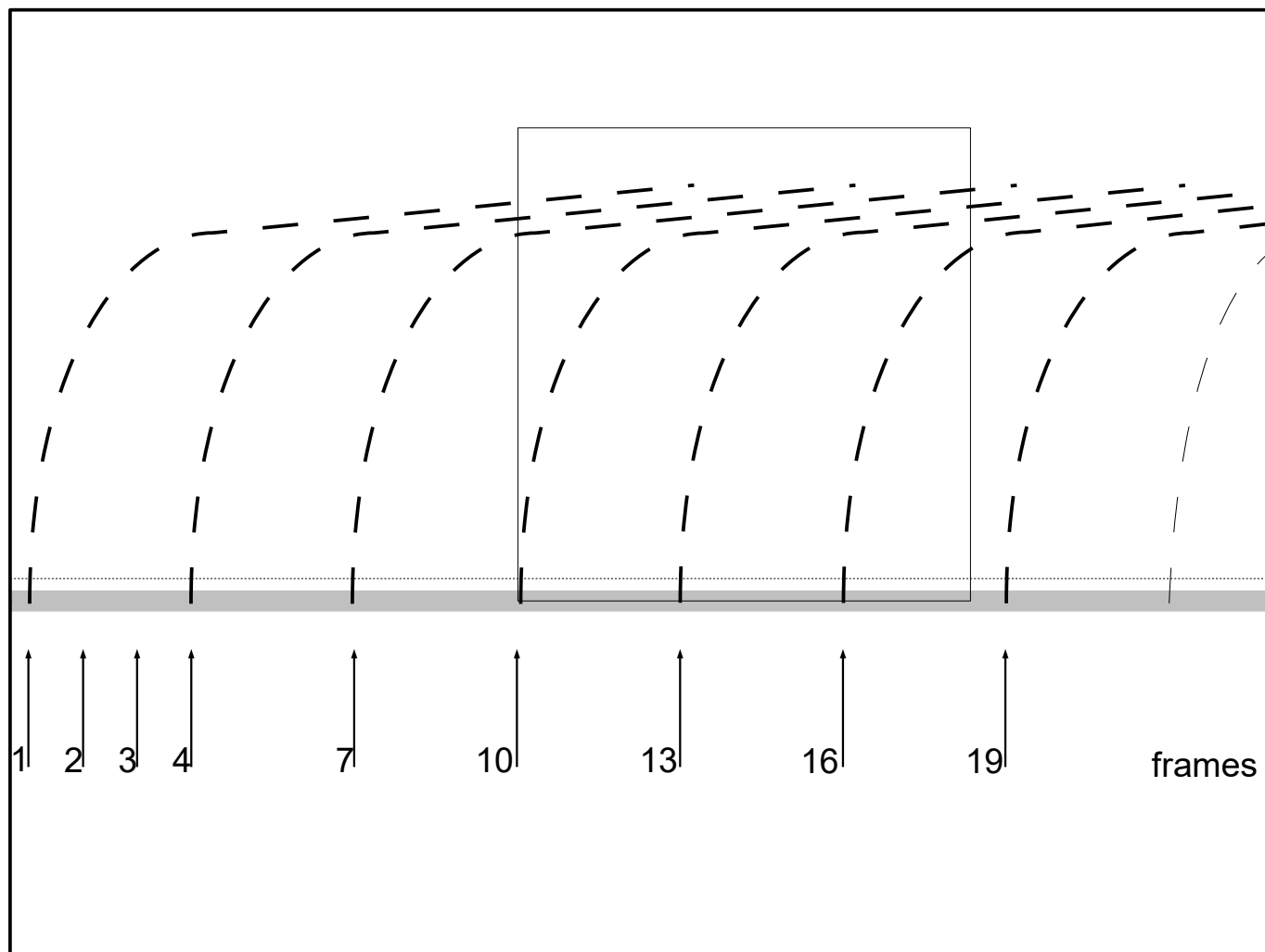
- Scene
- RenderLayers
- World
- Camera
- Mesh
- Point
- Point.001
- Point.002
- Point.003
- Point.004
- Point.005

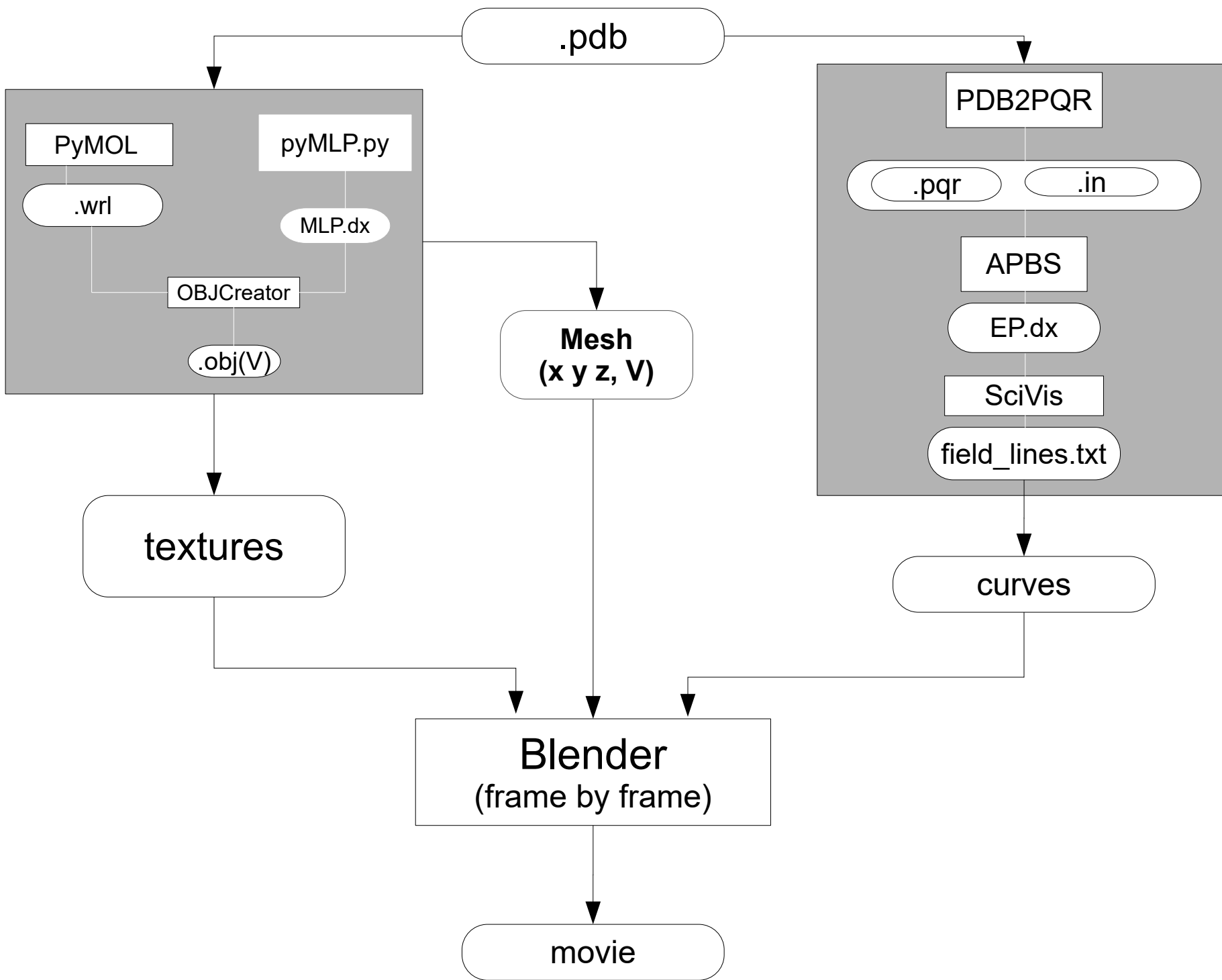




EP representation in still images







EP representation as movie

[Link to movie of EP](#)

Motion calculation

Sources of information

NMR series

X-ray in different conditions (conformations)

Molecular dynamics

Motion calculation

Sources of information

NMR series

X-ray in different conditions (conformations)

Molecular dynamics

... and their problems

only small molecules (up to 2-3 thousands atoms)

non corresponding atoms

vibration overwhelming

Molecular dynamics

BPTI Bovine Pancreatic Trypsin Inhibitor
468 atoms, 58 aminoacids

250 nanoseconds of simulated motion
sampled every 0.25 nanoseconds
transition between two known conformations, 1.97 Å RMSD

[Link to movie BPTI](#)

From Shaw et al. (Science, 2010, Vol. 330, pp. 341-346)
1 millisecond of MD simulation, with few

Motion calculation

Nuclear Magnetic Resonance

NMR series

20-50 conformations, in no specific order
MODEL 1, MODEL 2, ... in 1 single PDB file
Atoms consistent (except rotamers)

[Link to Calmodulin Atomic NMR](#)

Making (visual) sense of NMR data 1

Ordering NMR series

Fix rotamers

RMSD matrix

In Blender

Set GE (rotation, collision)

Set N frames (intermediates)

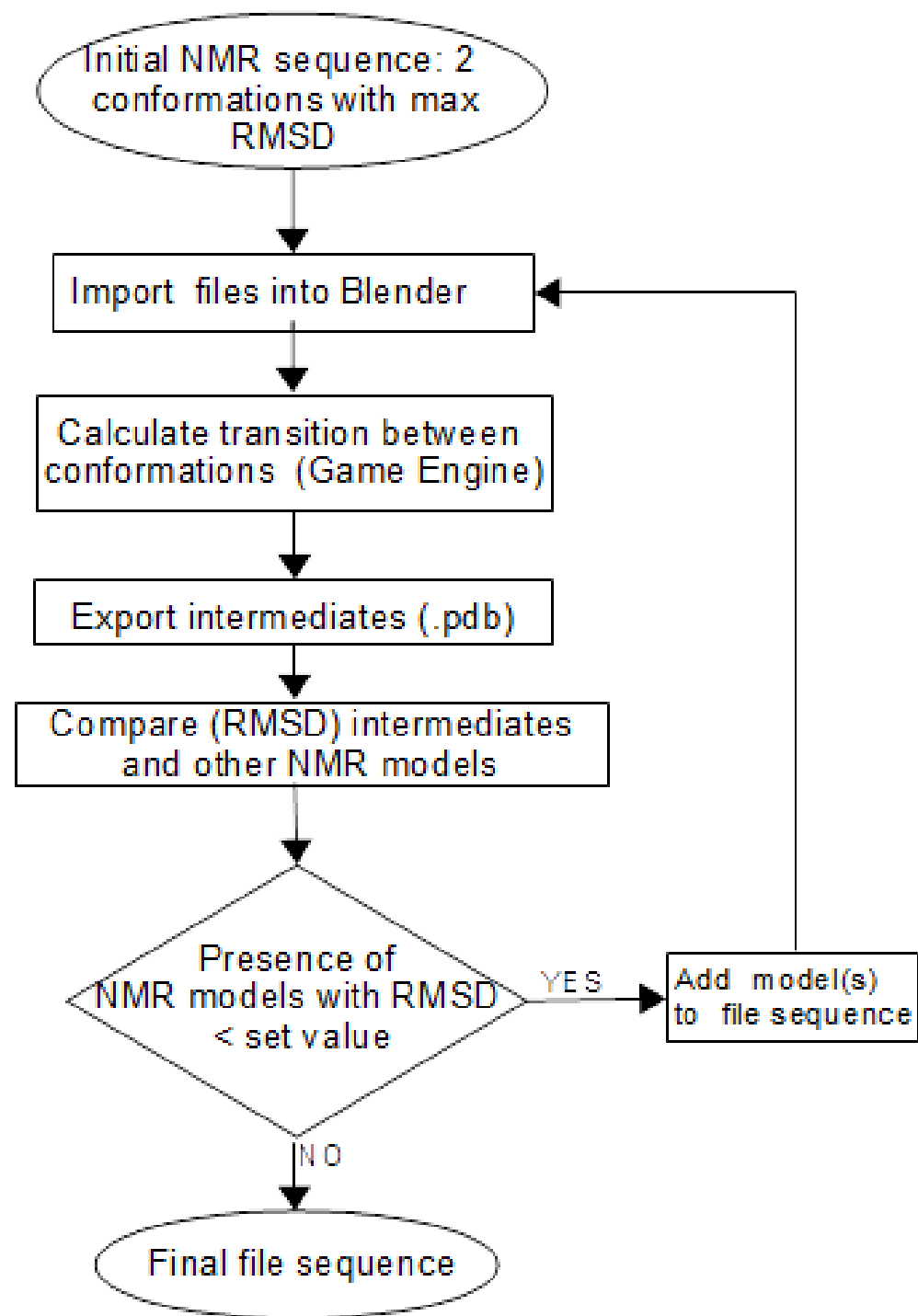
Run simulation

Record and export

Run procedure

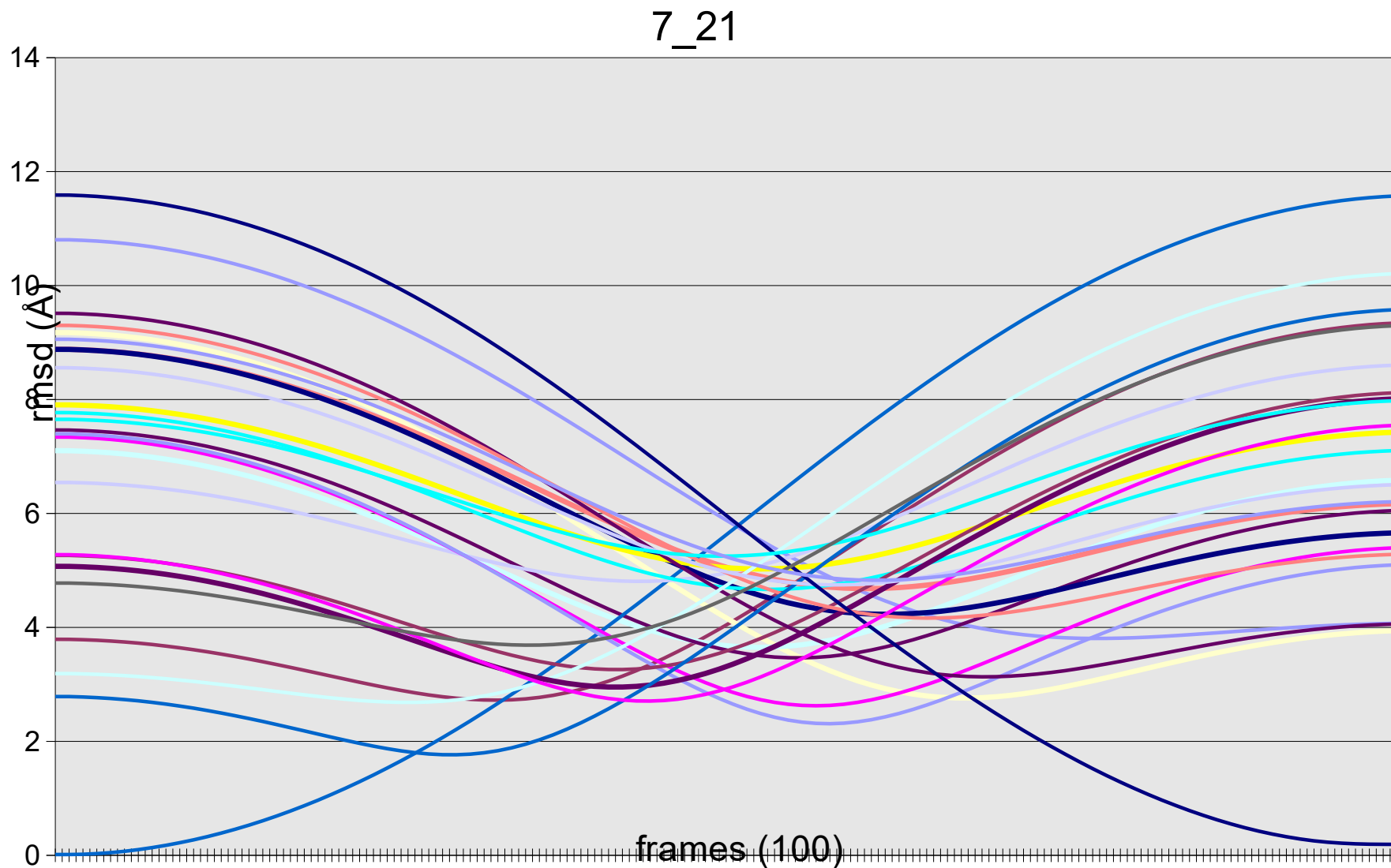
Making (visual) sense of NMR data 2

Conformations ordering procedure



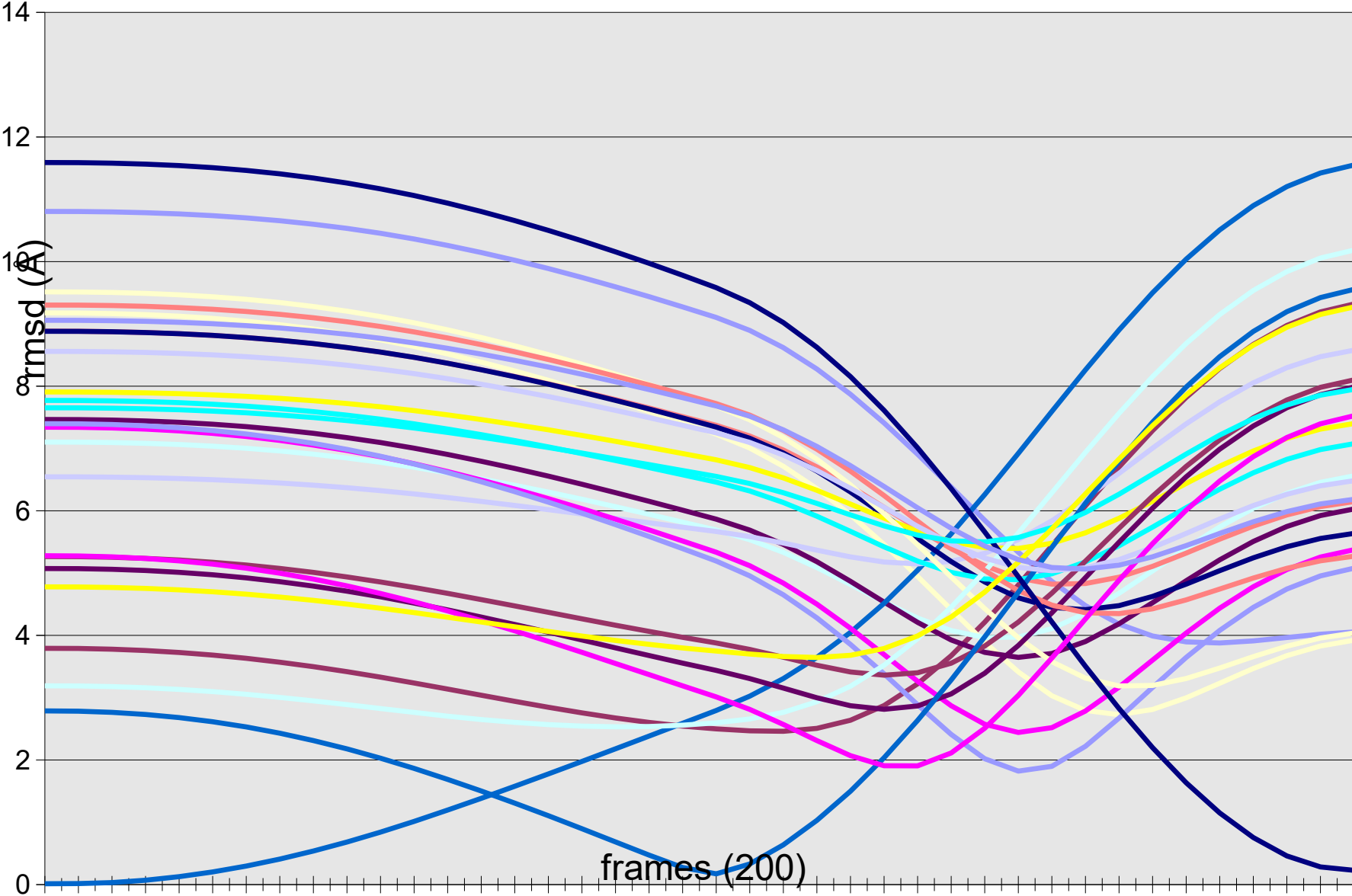
[Link to Calmodulin NMR ordered](#)

Making (visual) sense of NMR data



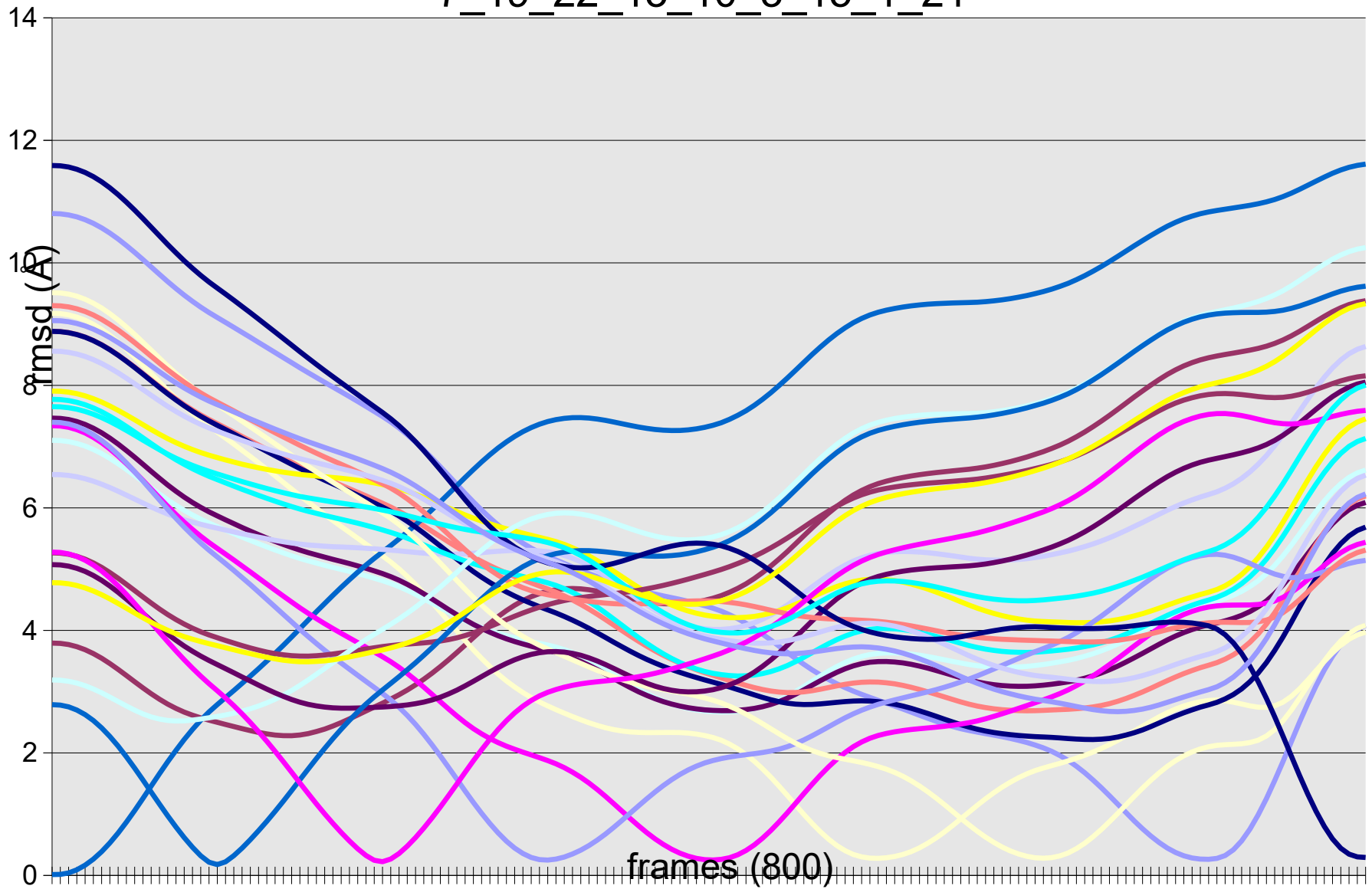
Making (visual) sense of NMR data

7_19_21



Making (visual) sense of NMR data

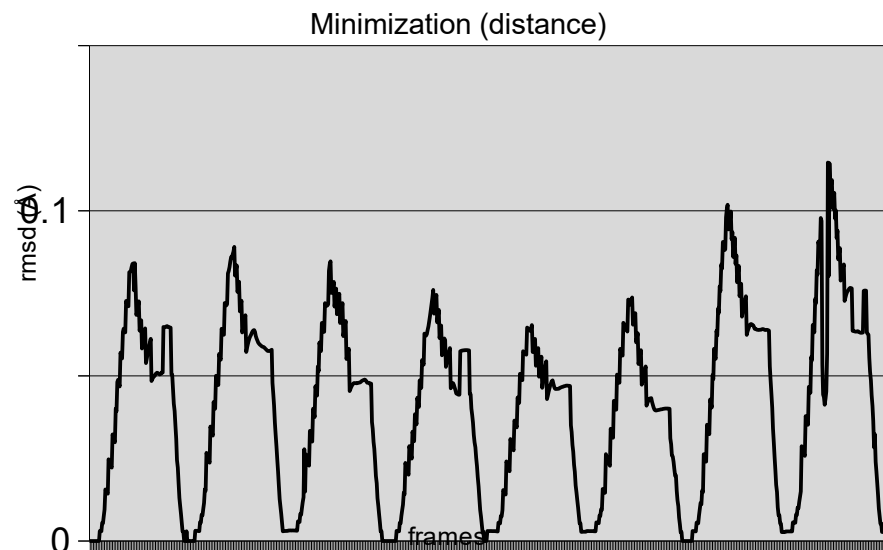
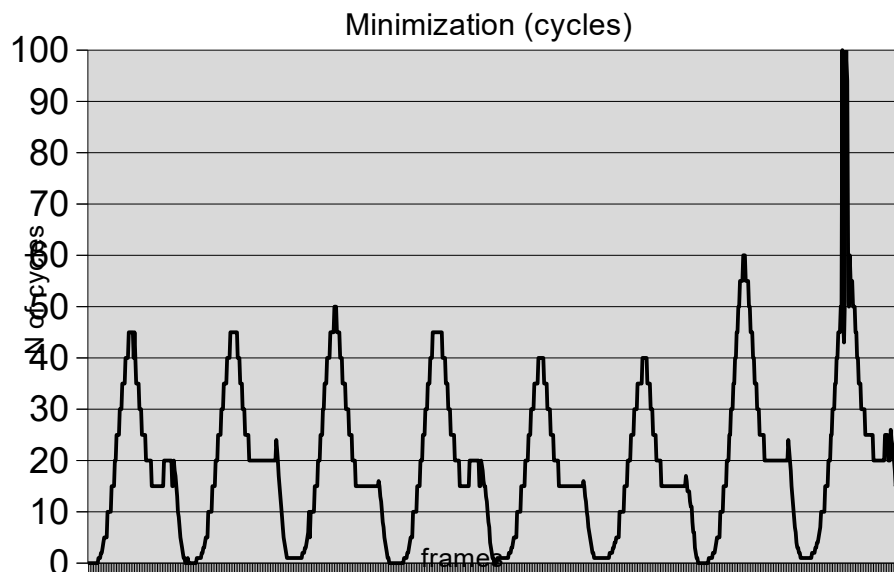
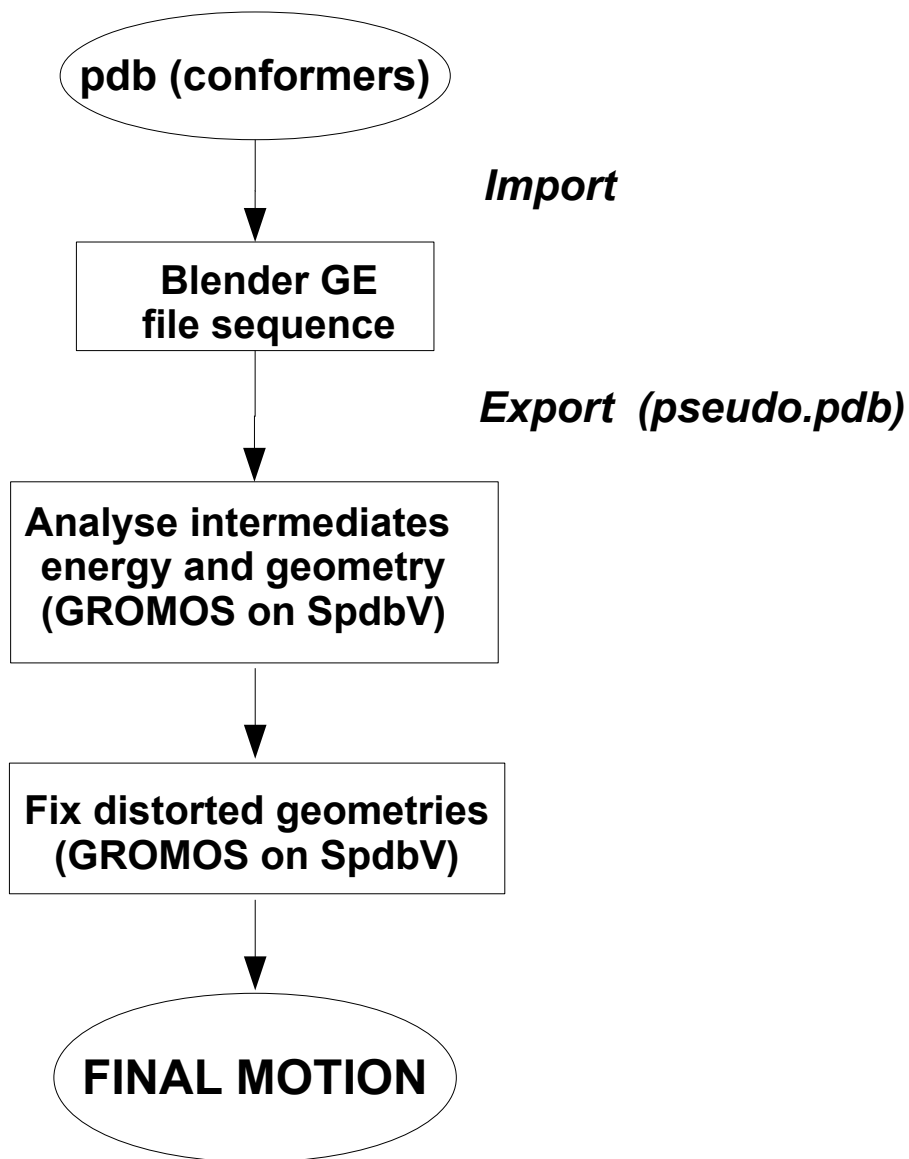
7_19_22_13_10_3_15_1_21



Making (visual) sense of NMR data 1

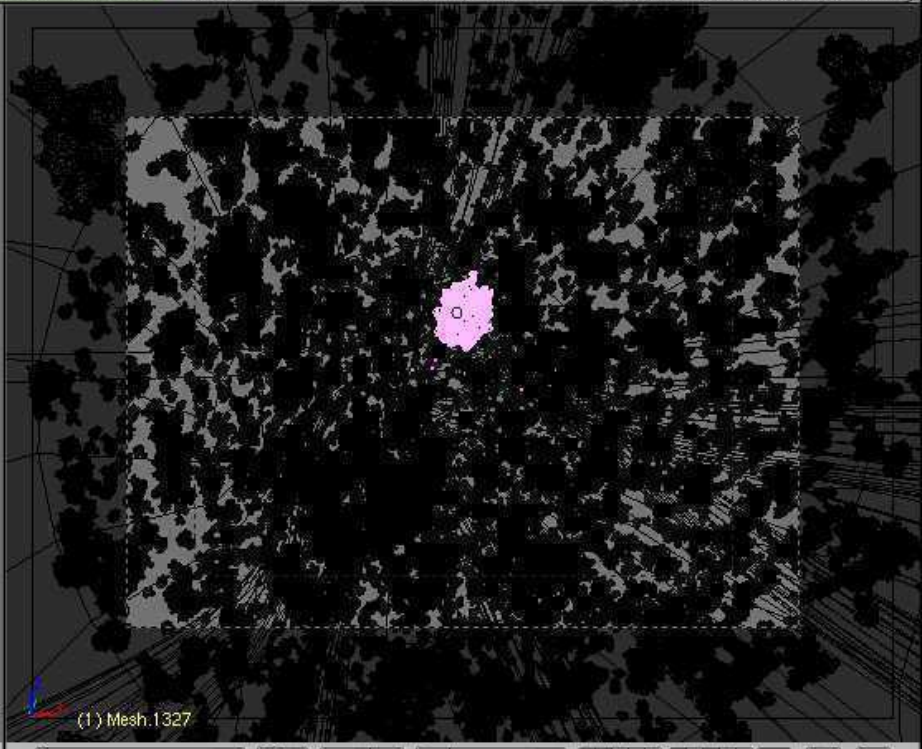
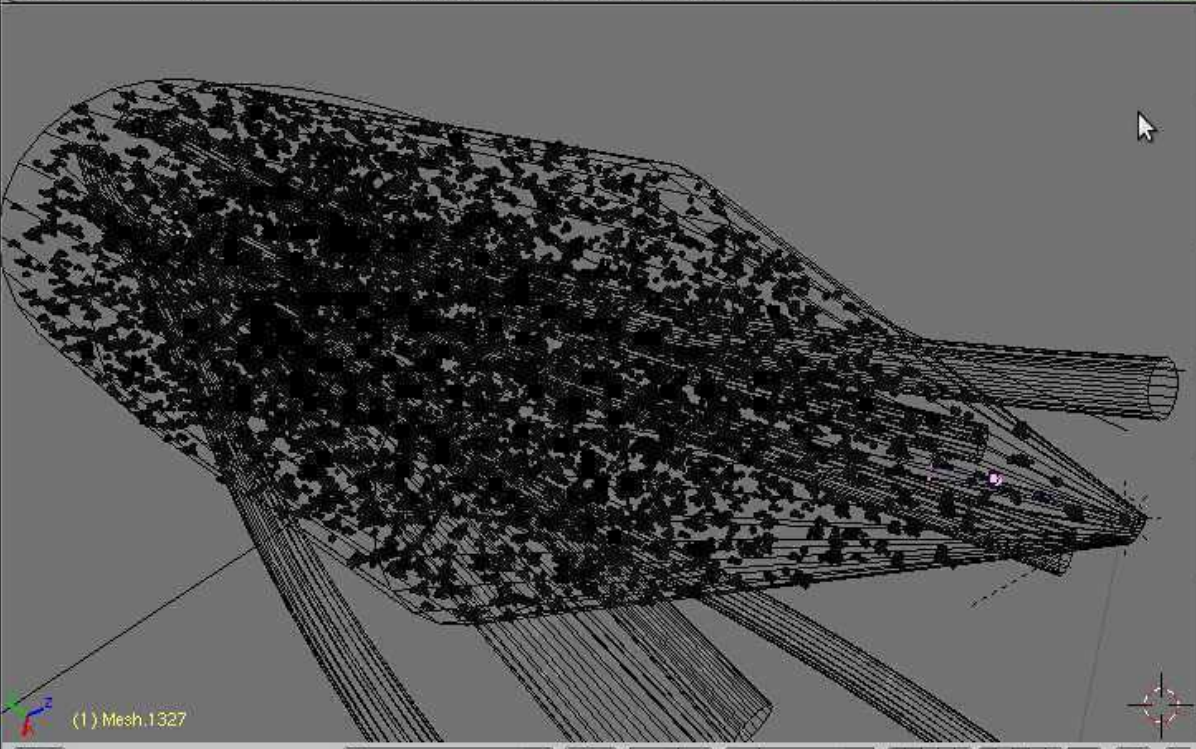
[Link to Calmodulin NMR ordered](#)

Validation of method and refinement



Some details of movie production

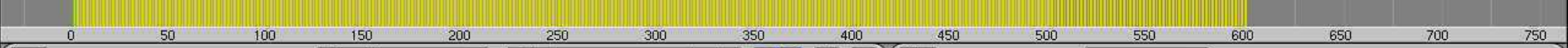




View Select Object Object Mode Local

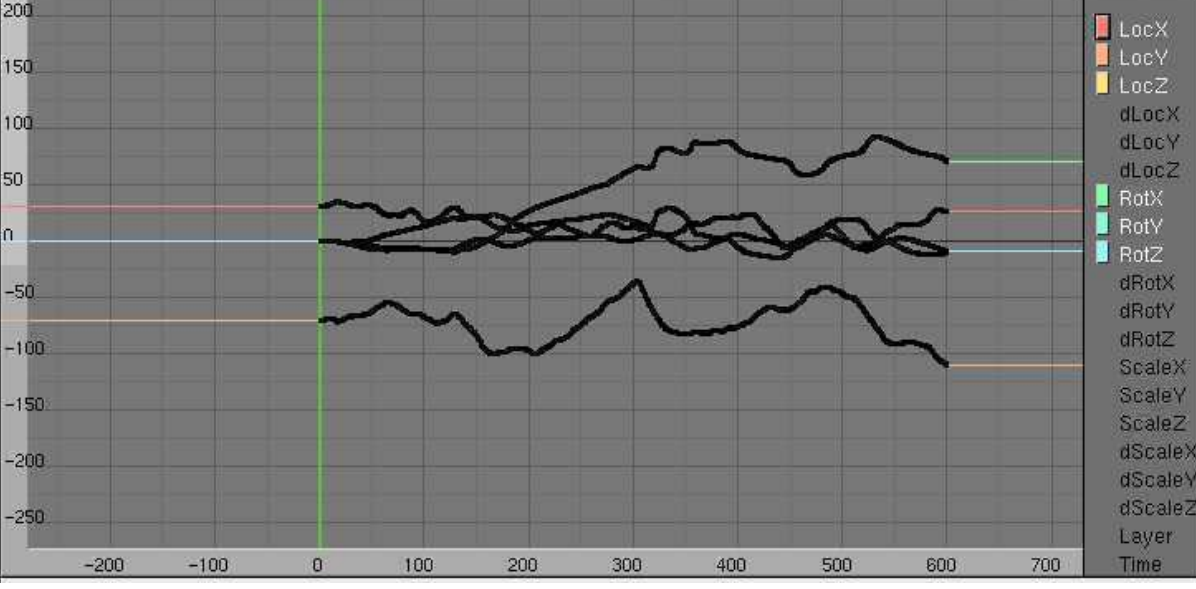
Object Mode Global

View Frame Playback Pr Start: 1 End: 500 1

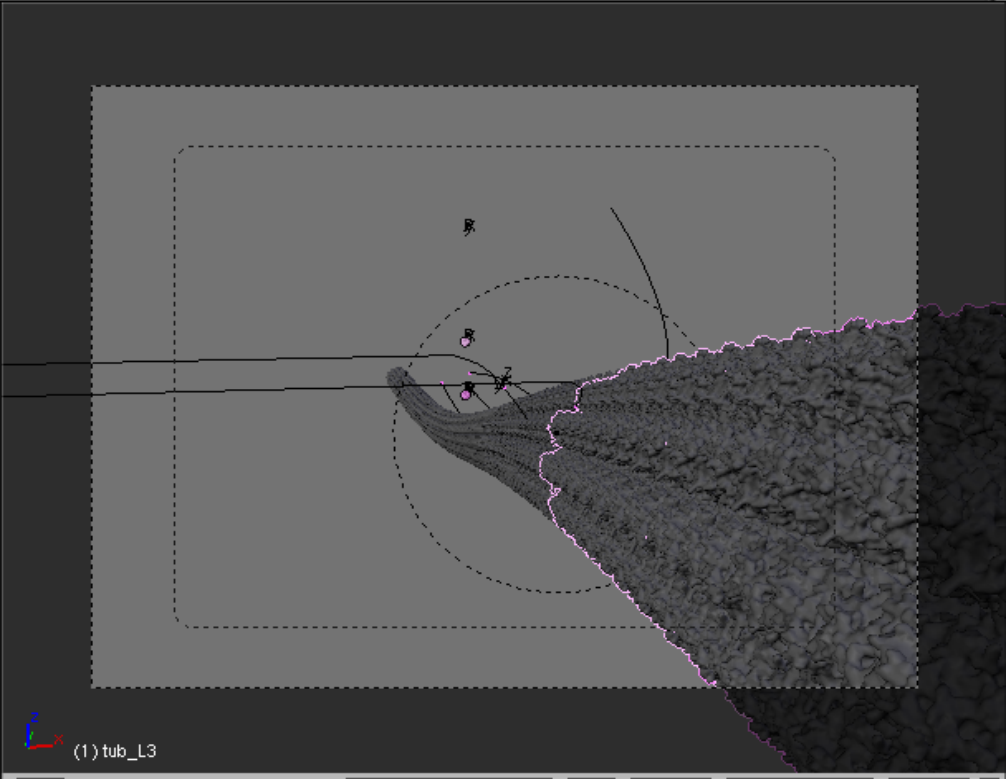
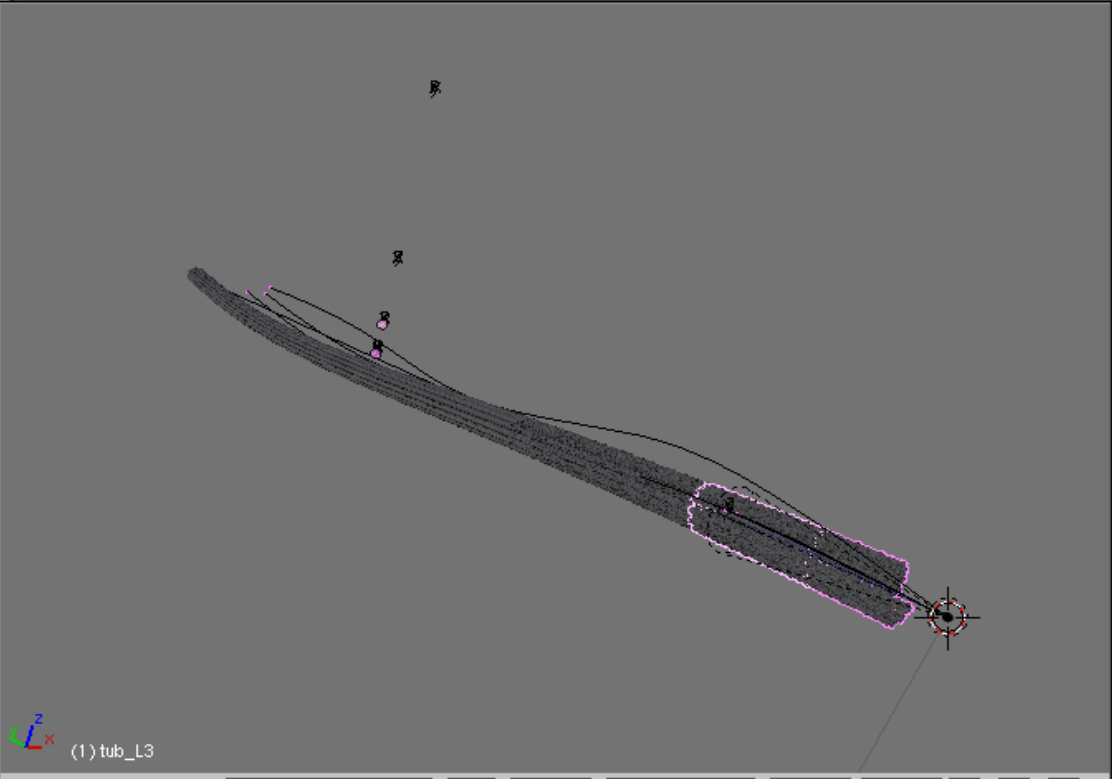


View Select Marker Curve Object :ORIG_BBOX.2673 F

View Search All Scenes



- Curve.022
- Curve.024
- Curve_forLVLs
- Lamp
- Mesh
- Mesh.001
- Mesh.002
- Mesh.003
- Mesh.004
- Mesh.005
- Mesh.006
- Mesh.007
- Mesh.008
- Mesh.009
- Mesh.010
- Mesh.011
- Mesh.012



Select Object Object Mode Global View Select Object Object Mode Global

Start: 1 End: 600 1

0 50 100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900

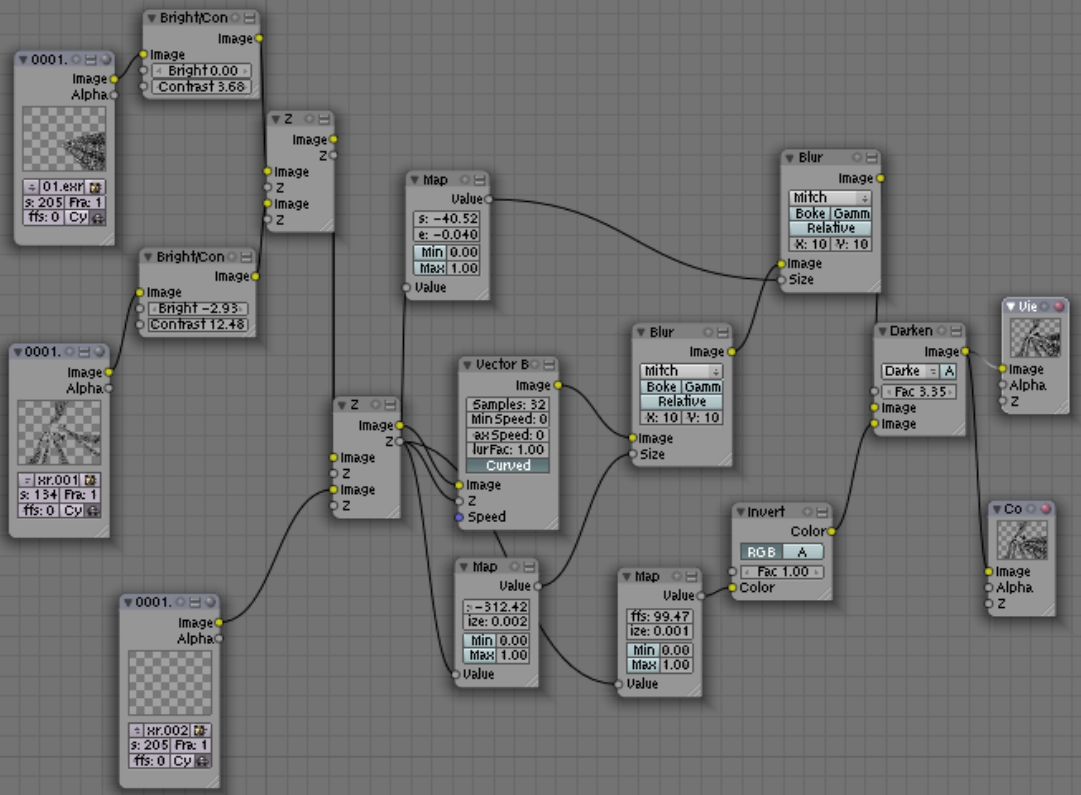
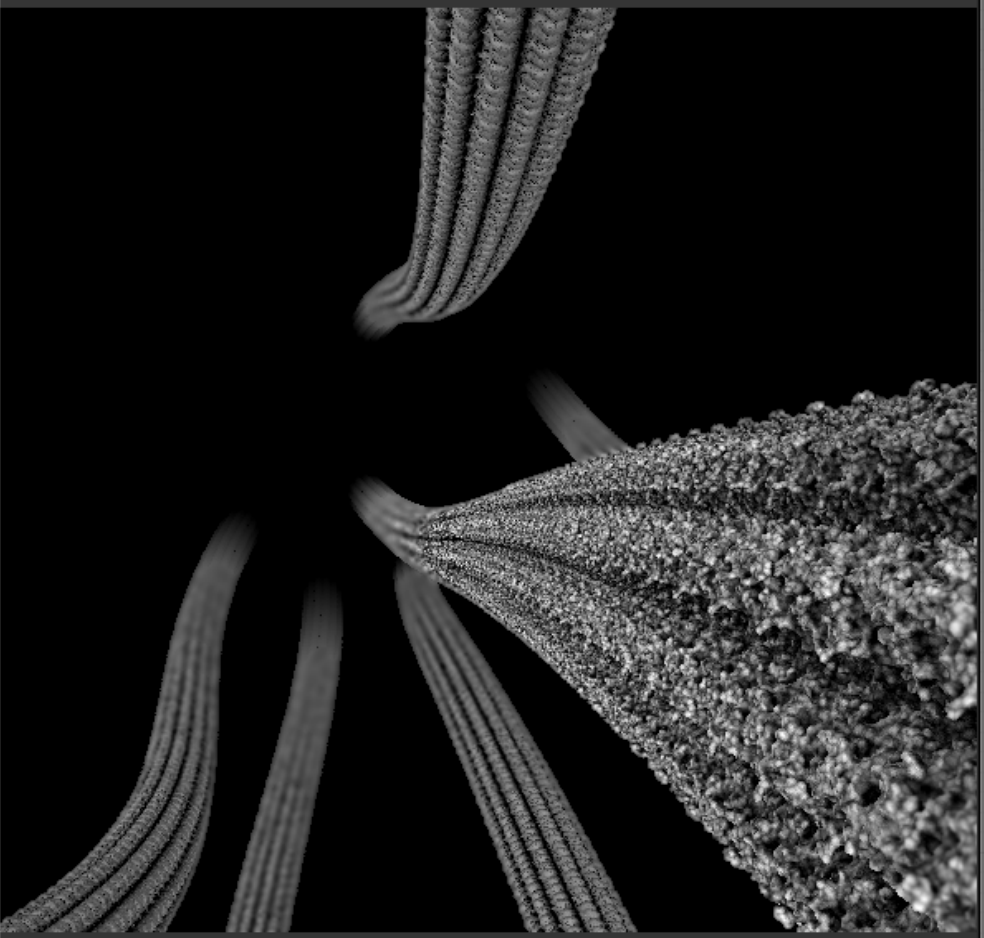
Sticky Make
UV Texture New
UVTex X
Vertex Color New

Array
 Fixed Count: Count: 8
 Constant Offset: X: 0.000, Y: 0.000, Z: 8.000
 Relative Offset: X: 0.000, Y: 0.000, Z: 8.000
 Merge: First Last, Limit: 0.0100
 Object Offset: Ob:
 Start cap: End cap:

Array
 Fixed Count: Count: 13
 Constant Offset: X: 0.000, Y: 0.000, Z: 0.600
 Relative Offset: X: 0.000, Y: 0.000, Z: 0.000
 Merge: First Last, Limit: 0.0100
 Object Offset: Ob: empty_L3
 Start cap: End cap:

View Search All Scenes

- MasterCTRL
- ORIG
- PathAim
- PathAim.001
- PathCam
- PathCam.001
- PathSpot
- Sphere
- TubulinDimer
- TubulinDimer.001
- empty_L2
 - tub_L2
- empty_L3
 - tub_L3
- empty_L4
 - tub_L4
- empty_L5
 - tub_L5



View Image IM:Viewer Node View Select Add Node Use Nodes Free Unused Backdrop

View Frame Playback Pr Start: 1 End: 134 2

-20 -10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230 240 250 260 270 280 290 300 310 320 330

Panels 2

Output

Render Layers

- /comp_071
- /backbuf

Extensions Touch No Overwrite

No Set Scene

Dither: 0.000 Edge Edge Settings

Threads: 2 Disable Tex Free Tex Images

Save Buffers Full Sample

Render Window

Render

RENDER

Shado SSS Pano
Env Ma Ray Radi

FSA MBLUR 100%
5 8 11 16 Bf: 0.50 75% 50% 25%

Xparts: 4 Yparts: 4
Fields Odd X
Gauss < 1.00

Sky Premul Key 128 Border

Anim

Bake

ANIM

Do Sequence
Do Composite

PLAY rt: 0

Sta: 1 End: 134
Step: 1

Format

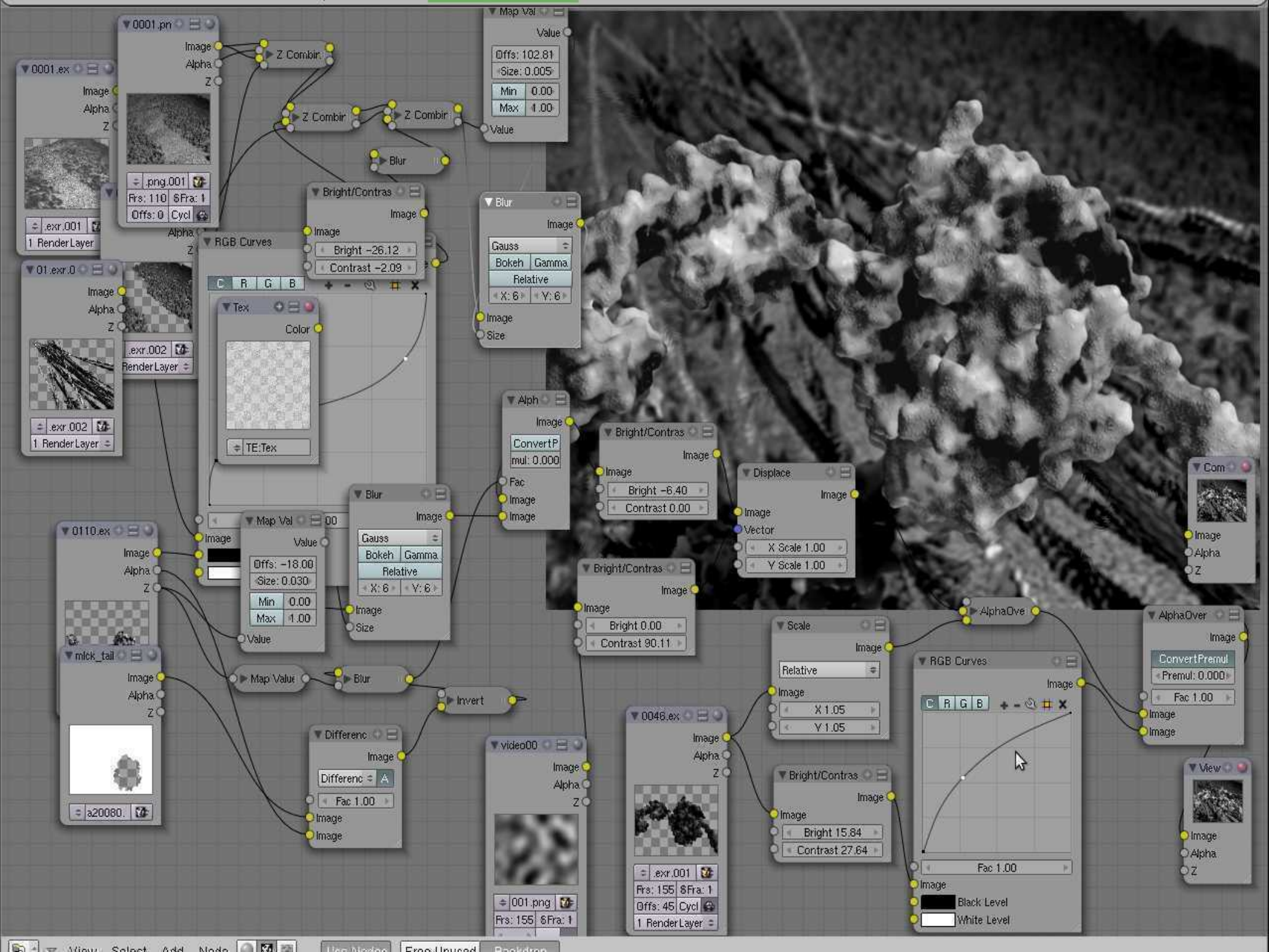
Stamp

Game framing settings

SizeX: 720 SizeY: 576
AspX: 54.00 AspY: 51.00

PNG Crop
Q: 100 FPS: 25 / 1.000
BW RGB RGBA

PAL
NTSC
Default
Preview
PC
PAL 16:9
PANO
FULL
HD



Links and References

Movies by SciVis

www.scivis.it/videos include Explanatory notes
other info on SciVis project www.scivis.it

Other Molecular movies

<https://clarafi.com/showcase/>

Drew Berry 'classical' www.wehi.edu.au/wehi-tv

Blender

www.blender.org

Molecular graphics

BioBlender www.bioblender.org

Molecular Flipbook

Papers

BB and related, on scivis.it/publications

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THANKS!

:)

Questions?

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