MCell And DReAMM Simulations Of Catecholamine Release Detection Using a Patch Clamp Technique

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OUTLINE

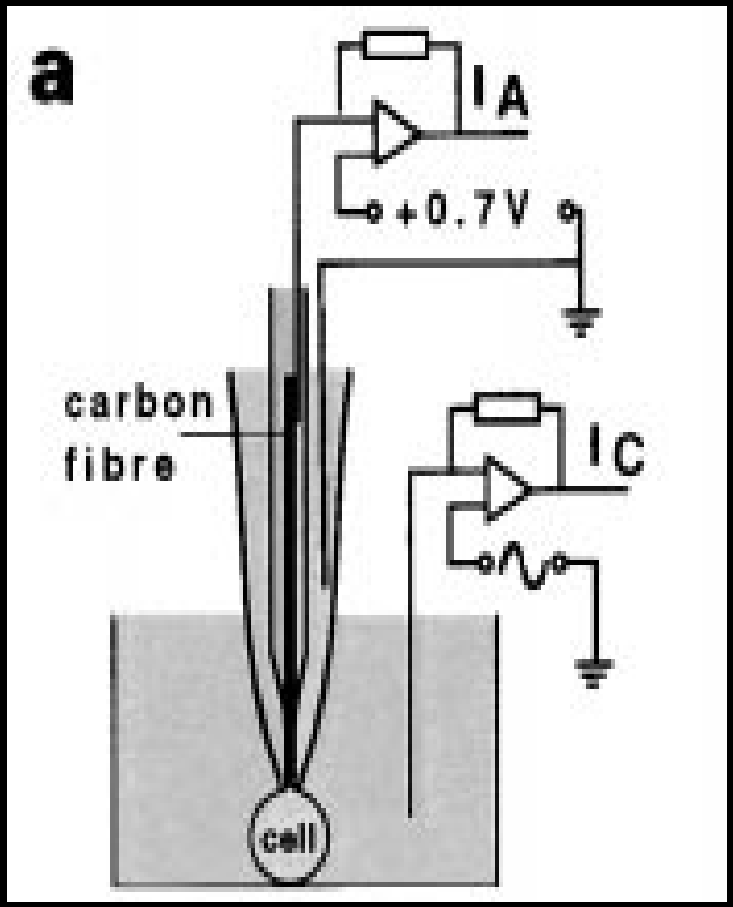
- Background :
  - Catecholamines
  - Patch Clamp
- Overview:
  - Blender
  - Mcell
  - DReAMM
- Results
- Difficulties
- Benefits

WHAT ARE CATECHOLAMINES?

- charged neurotransmitters
- released outside through a narrow fusion pore of a neuroendocrine cell ‘chromaffin’
- 1 catecholamine out = 2 electrons
- requires a charge compensation by other ions such as Ca^{2+} to maintain an osmotic balance of charges

PATCH CLAMP:

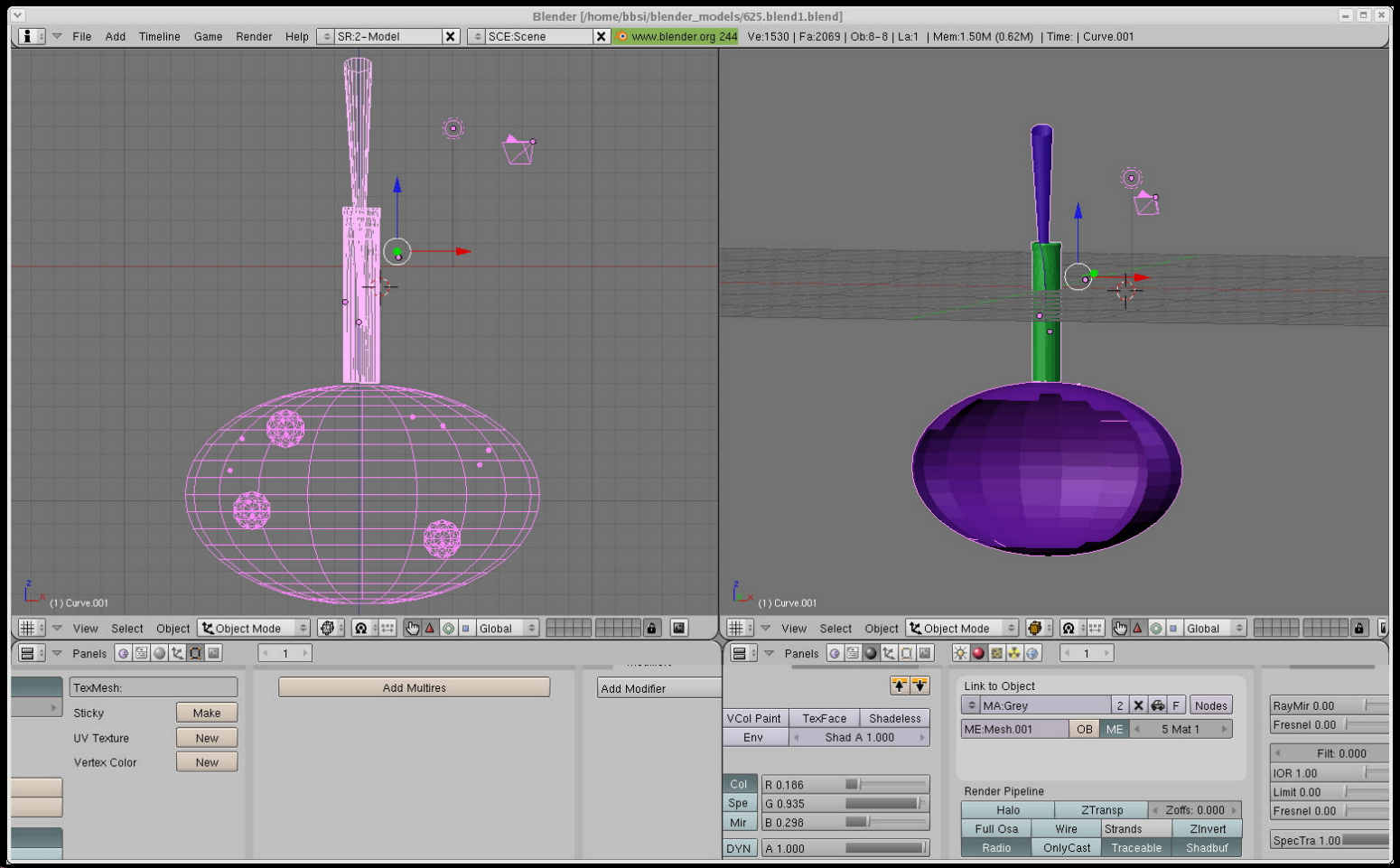
- A glass pipette with tip attached to surface of cell
- Contains a Carbon Fiber Electrode
- An external voltage
- Vesicles fuse into the Electrode



BLENDER

- an open source, free of charge tool for 3D visualization
- creation of basic shapes- cell, vesicle, patch clamp, carbon fiber electrode- for mesh generation
- Varying the geometry of meshes
  - Exclusive for structural editing

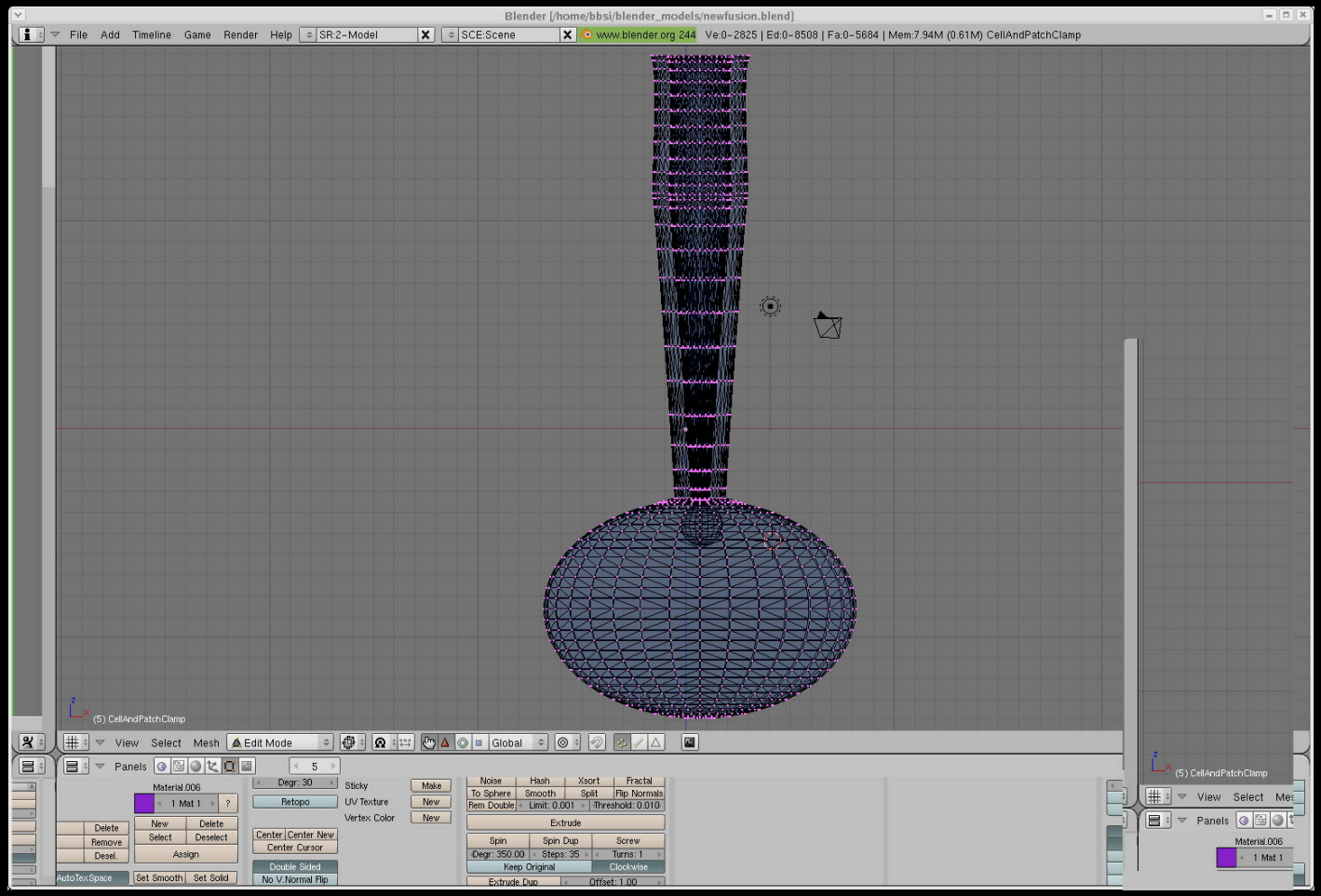
Early Blender Model



Understanding Blender

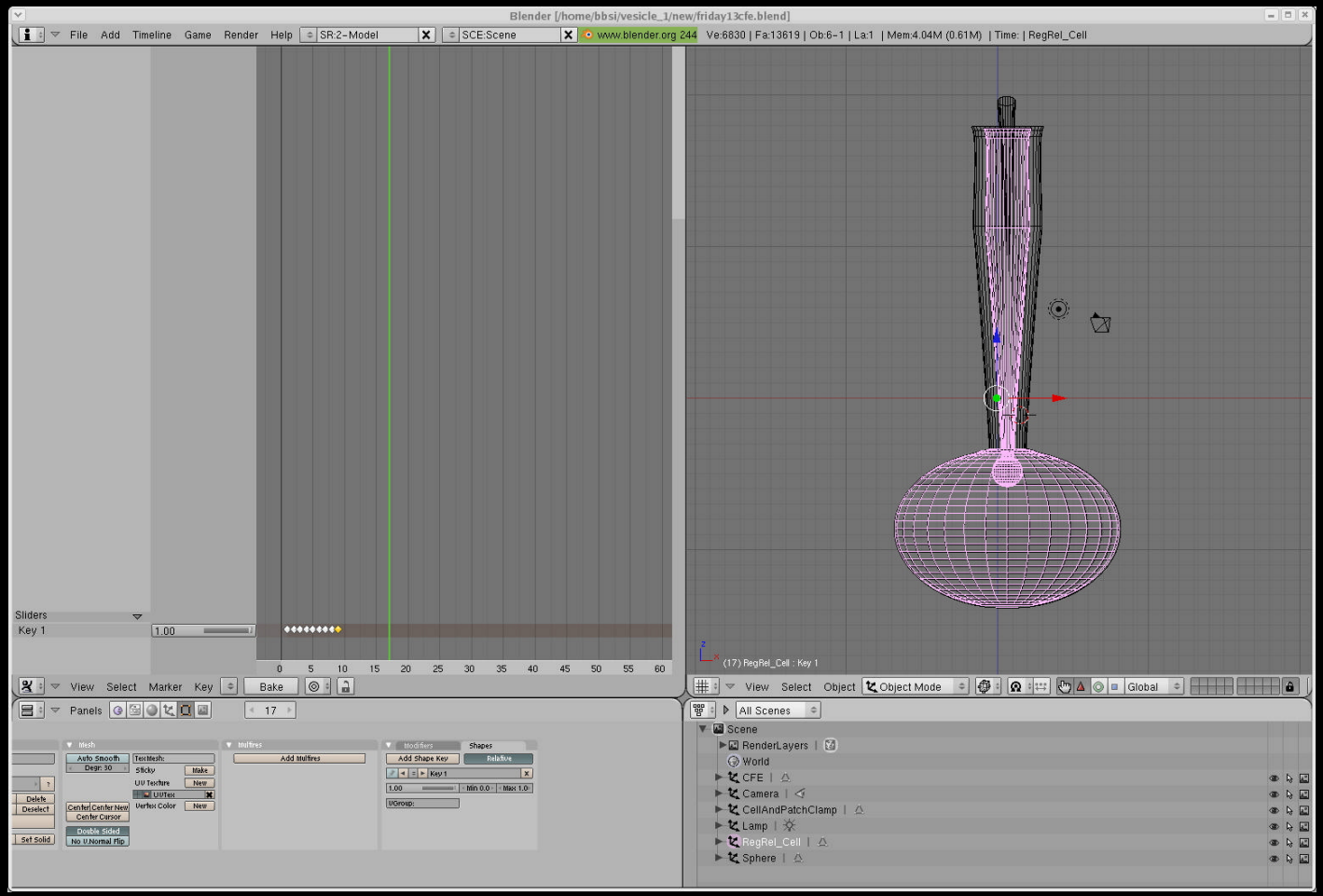
- Object Mode
  - objects are added, animation/ shape keys are added
- Edit Mode
  - vertices and faces of objects are edited (selected, erased…)
- Visual Example

Later blender model



- Regions/Objects created:
  - Cell
  - Patch Clamp
  - Carbon Fiber Electrode
  - Vesicle
  - Sphere
  - Inner Patch Clamp
  - Inner Cell

Creation of animation



Animation

- Action Editor
- Shape Keys defined in Object Mode
- manual shifting of objects and widening of fusion pore from the initial to the final position
- Use frames
- Run animation in Object Mode as well

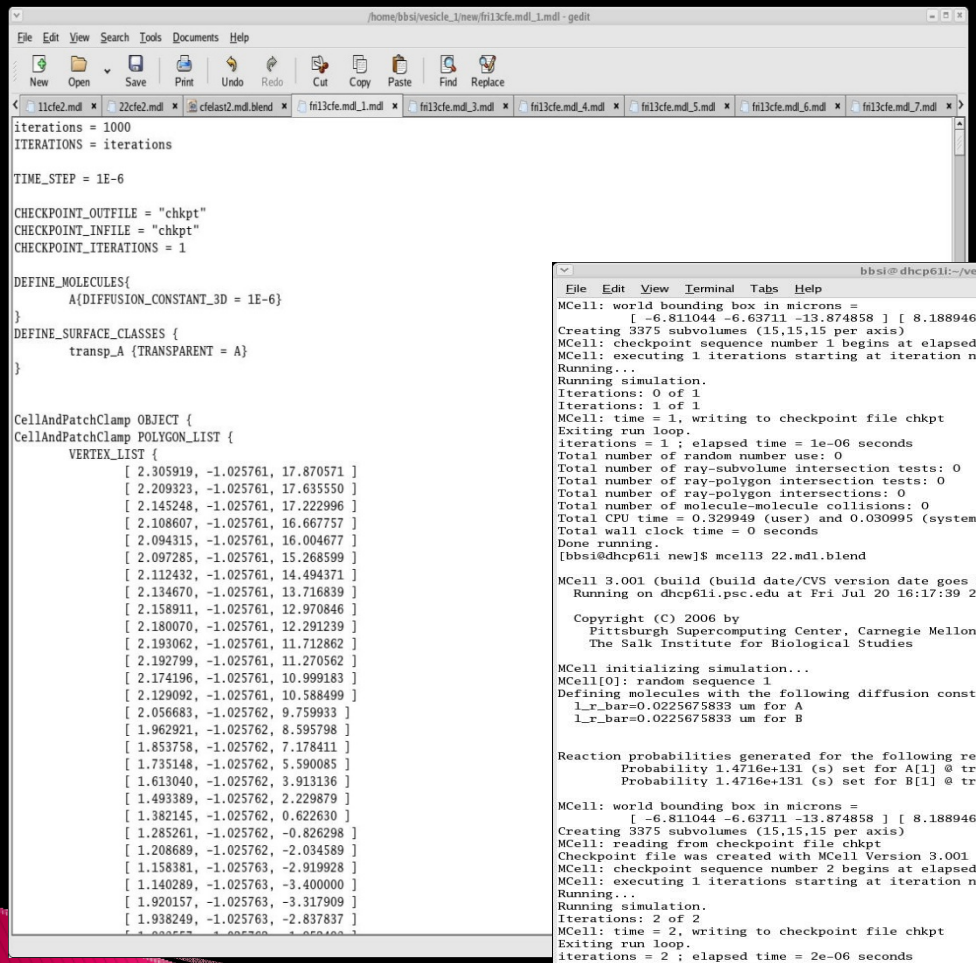
Exporting in Blender

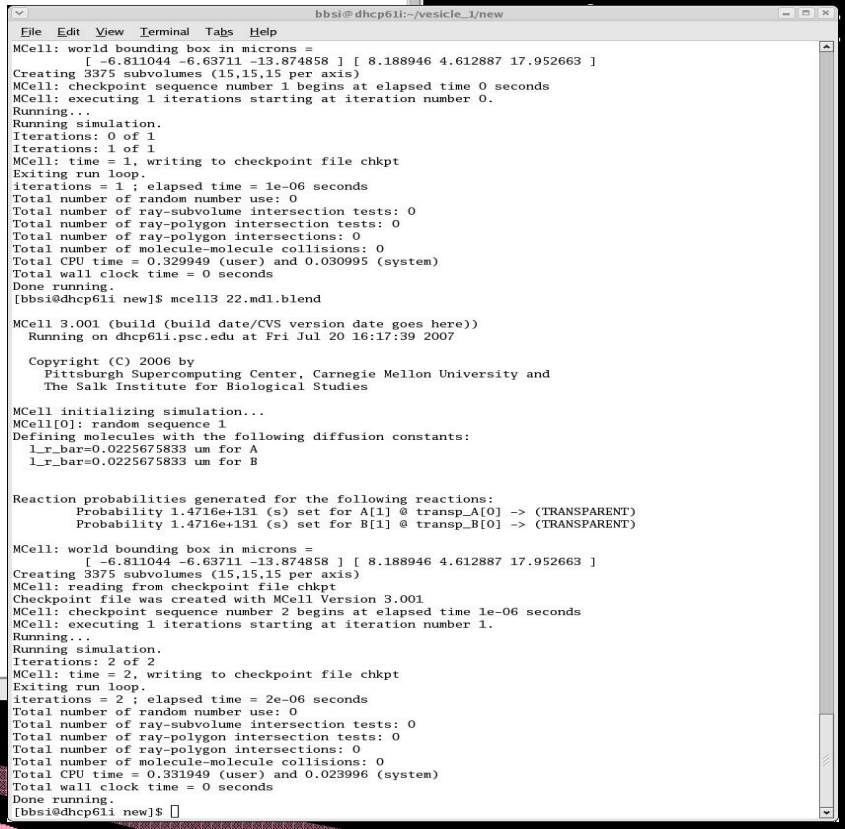
- Export to MCell
  - Filename.blend → Filename.mdl
  - Animations :
    - Define number of frame files else by default : 250
- Export to DReAMM
  - Filename.blend → Filename.dx

MCell3 (Monte Carlo Cell)

- Simulations run in Mcell by reading MDL files
- Specialized Monte Carlo Algorithms used for simulation
- Separate MDL files created for each frame (total: 16) used in the animation

An MDL File





- Beginning of an MDL File
- Length of file can vary ~20,000 lines
- Iterations, molecules, ices defined

MDL Commands

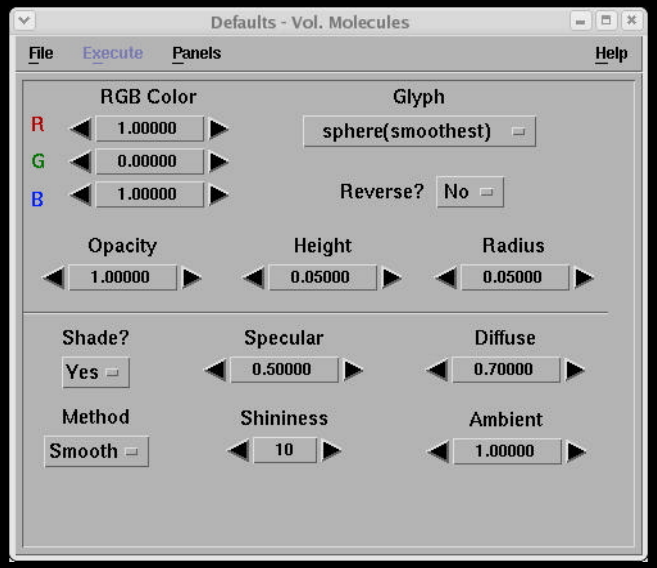
```
DEFINE_MOLECULES {
        A {DIFFUSION_CONSTANT_3D = 1E-6}
        }

DEFINE_SURFACE_CLASSES {
         transp_A {TRANSPARENT = A}
        }

A_RELEASE_SITE
{
SHAPE = world.Sphere [whole_mesh]
MOLECULE = A
NUMBER_TO_RELAESE = 200
}
```

Varying numbers in an MDL file

- Iterations
- Checkpoints
- Region Release
- Surface Classes
- Diffusion Constants

DReAMM (Design, Render & Animate Mcell Models)

- A computer aided design software
- Final visualization of Mcell simulations
  - Imports variety of mesh objects
- Variables such as opacity, shape, size can be altered
- Different 3D rotations and views (x, y, z axis)

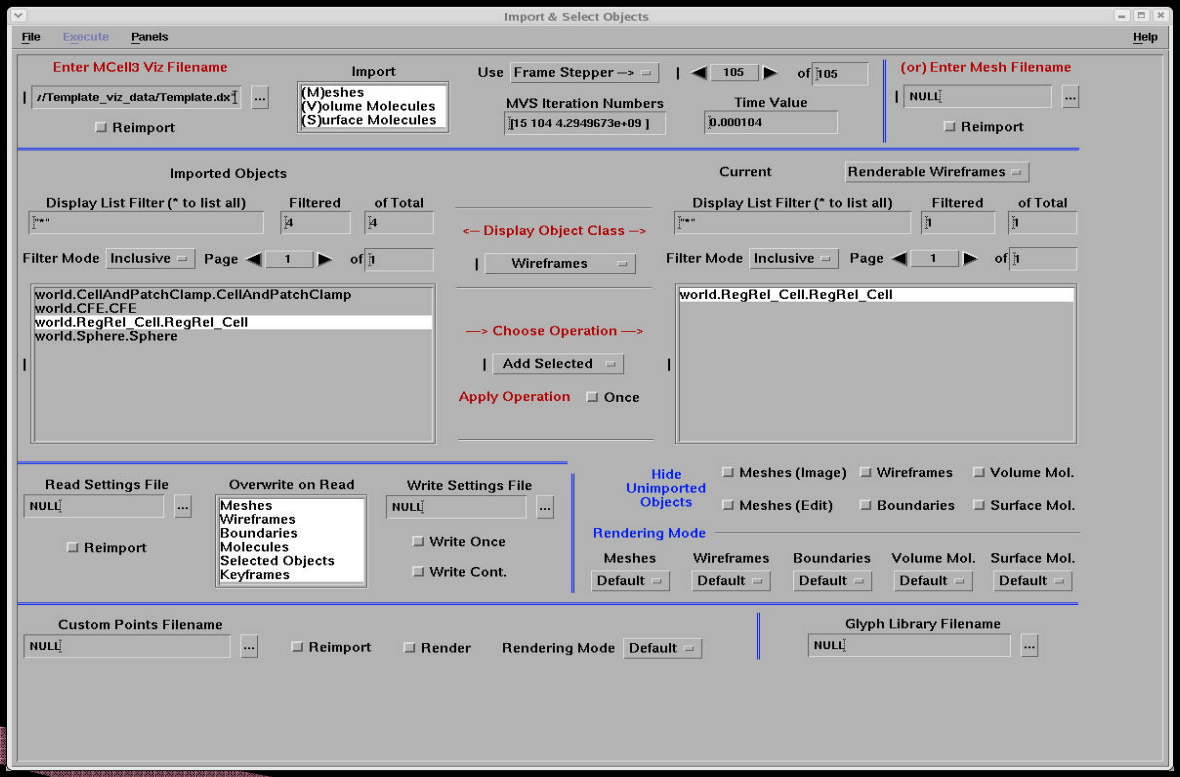


Import & Select Objects Menu

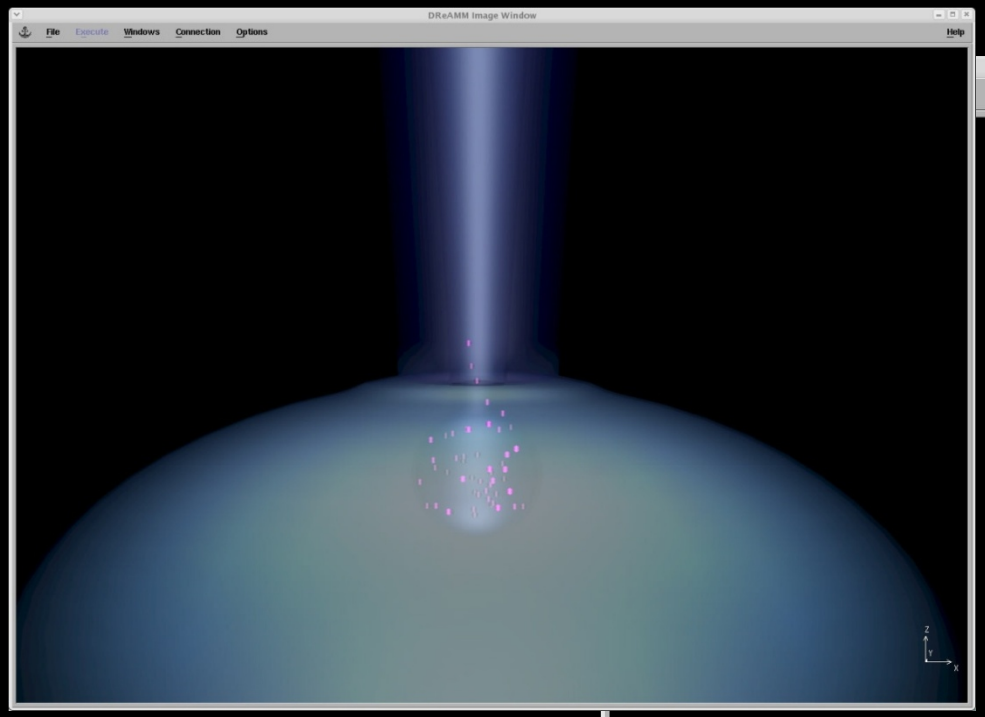
- Import viz data
- Select objects for editing
- Step through frames
- Edit meshes

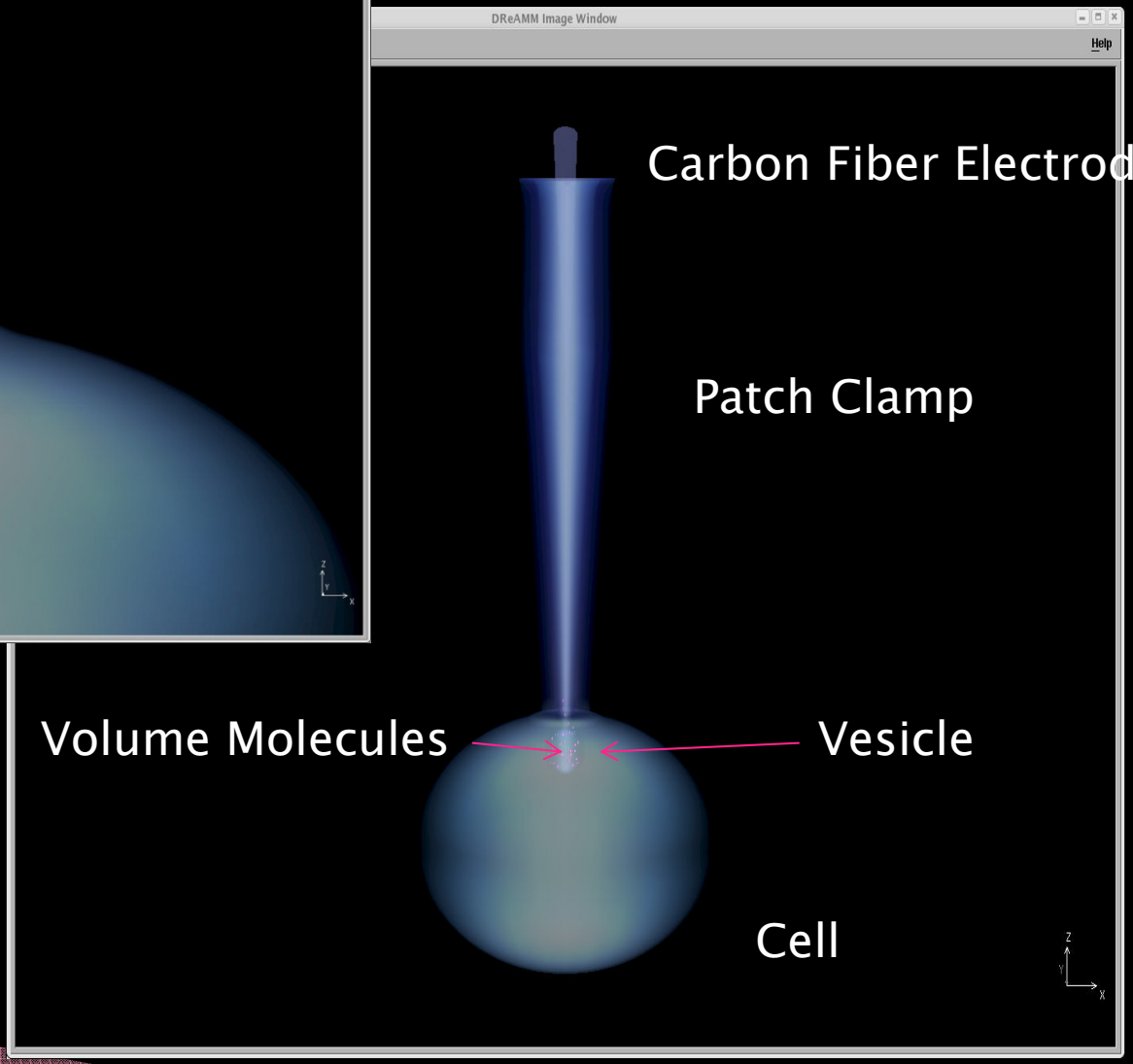
Editing Volume Molecules

- color (red, blue, green)
- Shape
- Size
- opacity

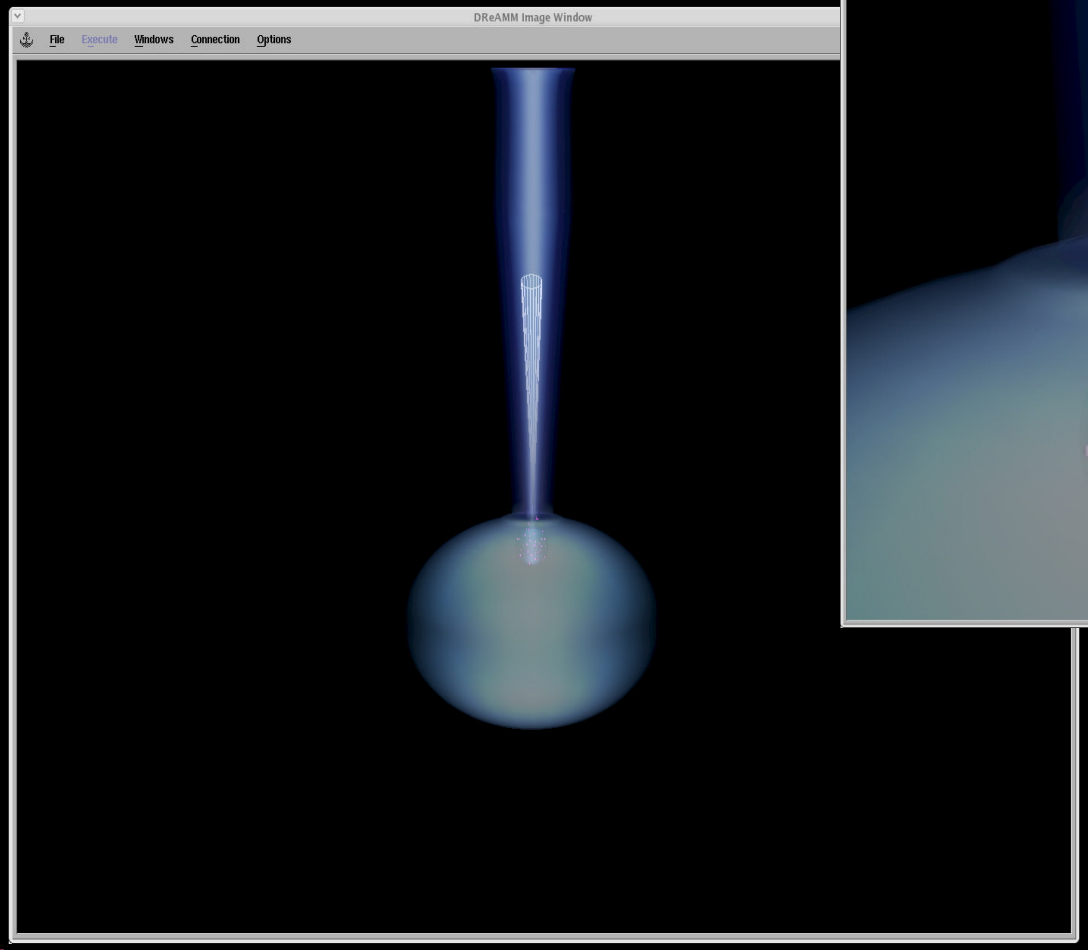


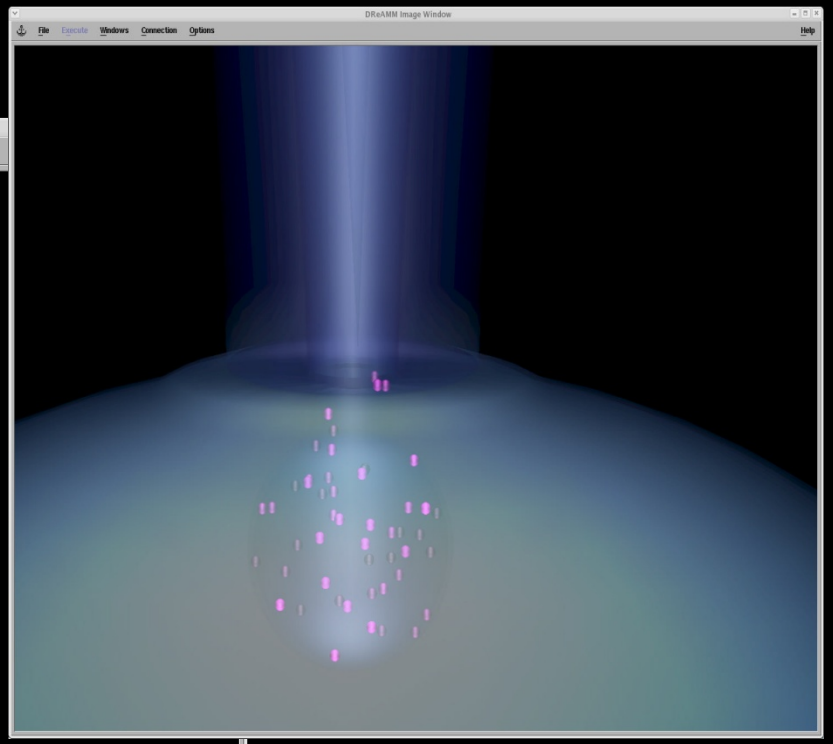
Catecholamine Detection





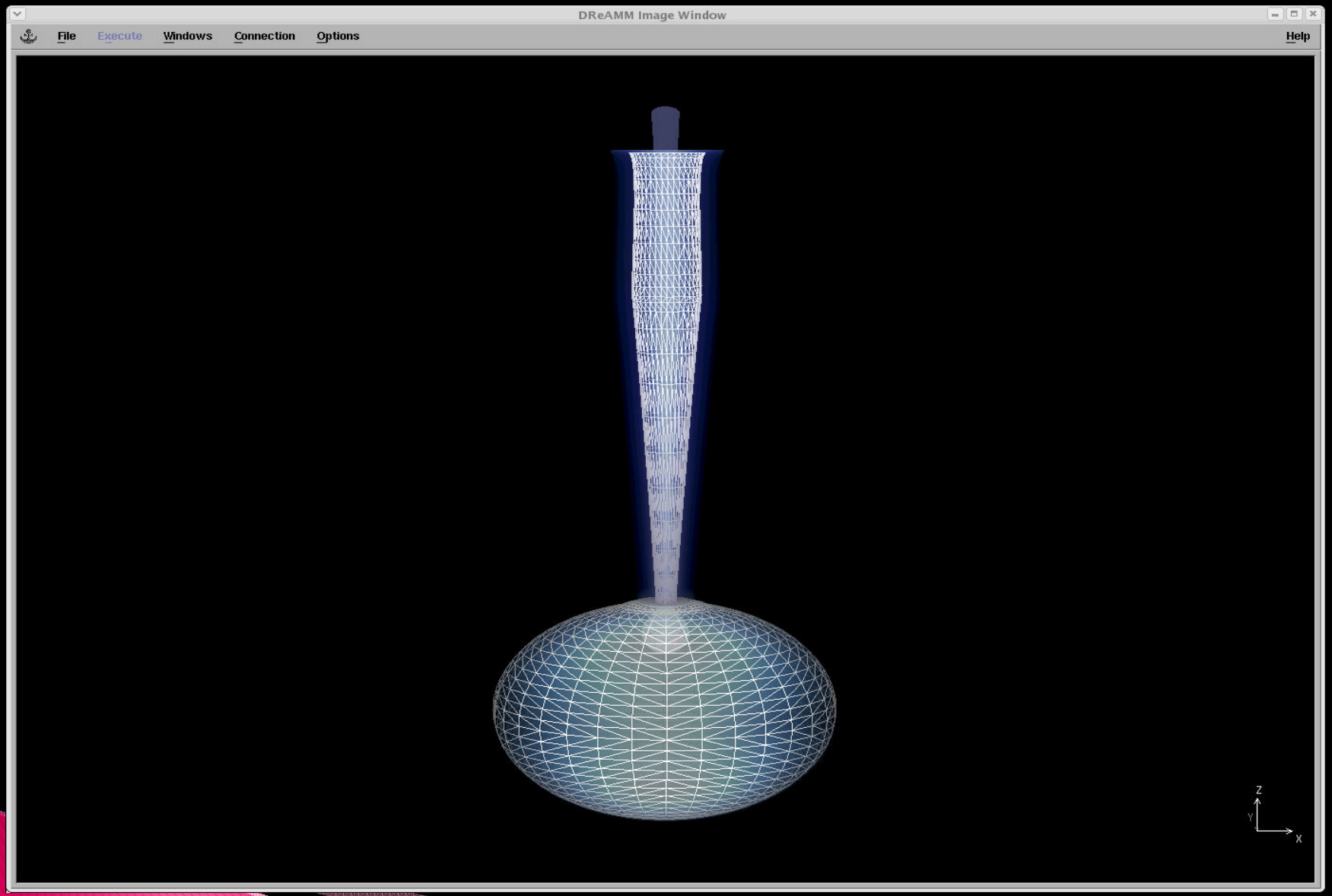
Carbon Fiber Electrode Varied

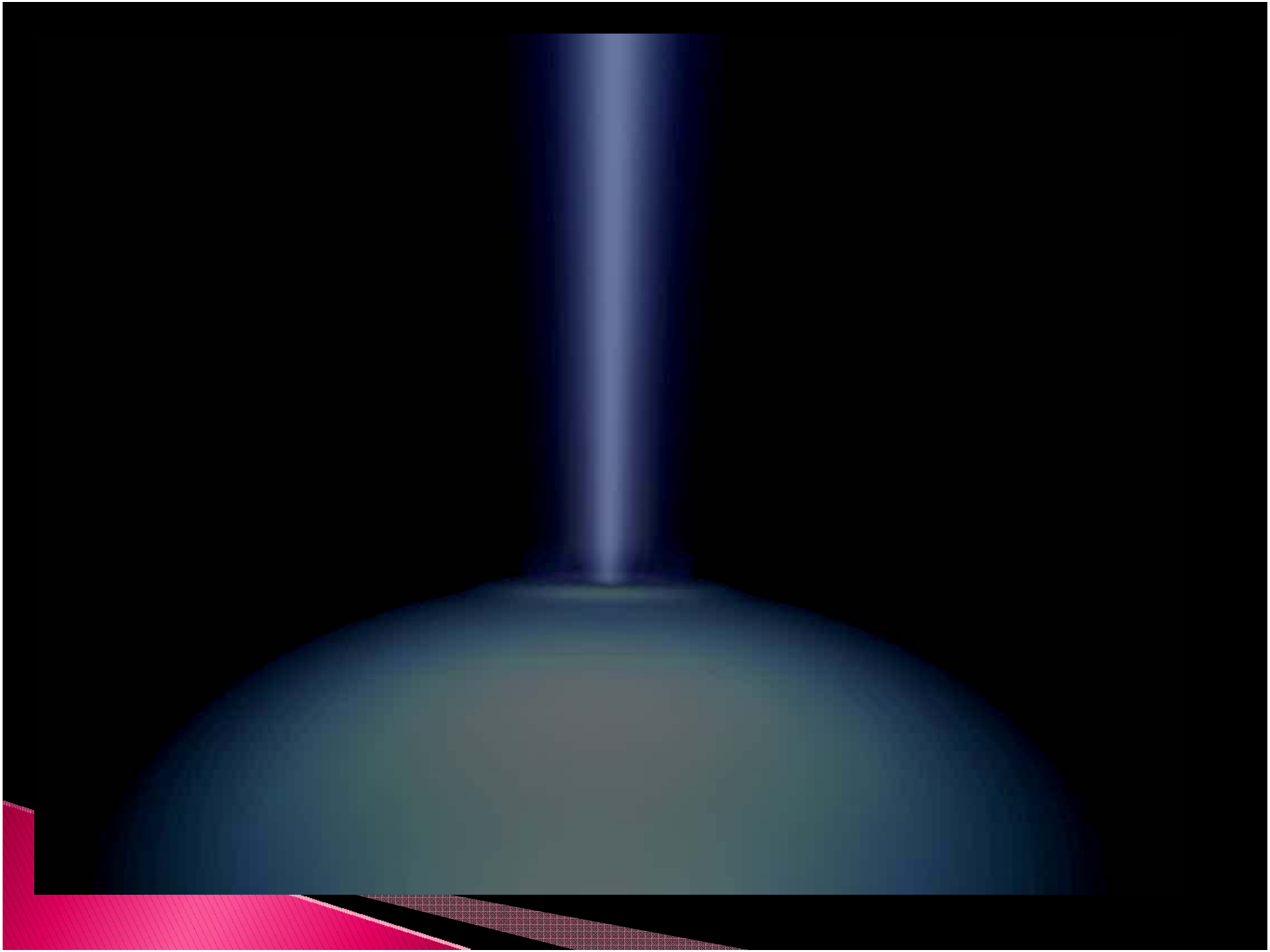




Number of molecules detected increases when the carbon fiber electrode is closer to membrane

Wireframes


DReAMM Image Window
File
Execute
Windows
Connection
Options
Help
Z
Y
X



Difficulties

- Blender/MCell
  - Releasing on an unclosed region
  - Syntax Errors
  - Experimenting with number of iterations
  - Undefined objects
  - CANNOT join meshes once animation is defined
  - EXTREMELY tedious
- DReAMM
  - If errors in MDL file, no images displayed

Benefits

- Familiarity with the concept of patch clamp amperometry
- Knowledge of UNIX expanded
- Learned to work with the three new softwares: Blender, Mcell and DReAMM
- Used MDL which is similar to ‘Object Oriented Programming’
- Acquired the art of having Patience !!!

Thank You!

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