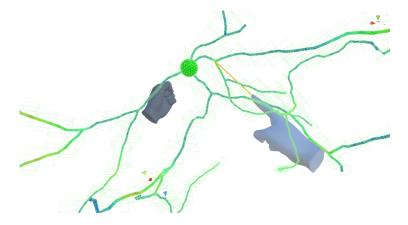
Neuro-VISOR

VISOR (Virtual Interactive Simulation Of Reality) is a research and software theme developed by Temple University's Center for Computational Mathematics and Modeling (C2M2), College of Science and Technology. The overarching long-term vision is to produce novel concepts and software that enable efficient immersed virtual reality (VR) visualization and real-time interaction with simulations of real-world processes described via principled mathematical equations. Unlike traditional high performance computing (HPC) applications, the philosophy of VISOR is that (a) the simulation runs while it is visualized in a virtual environment, and (b) the simulation continues even when the user affects and/or modifies the system state or its conditions.



Neuro-VISOR focuses on applications in computational neuroscience. Specifically, it provides a pipeline that (a) retrieves a wire-frame neuron geometry file from the public neuron database NeuroMorpho, and (b) generates a surface mesh from it. This mesh is then (c) visualized in VR, while an efficient numerical method approximates the Hodgkin-Huxley model on the given wire-frame neuron geometry. Finally, while the running simulation is fed to the VR environment in real time, (d) the user can interact with the surface mesh and affect the simulation while it is running via several methods outlined under controls.

A key use case of this framework is that is can rapidly accelerate scientific discovery by providing an immediate and very intuitive feedback to the user about how changes to the simulated system affect the system's behavior. This insight, obtained from the simple and fast models used for VISOR, can then enable the computational scientist to devise significantly more targeted (non-interactive) simulations on



large-scale HPC clusters of more complex models. In addition, in the context of neuroscience, the immersed 3D environment provides a more intuitive way to navigate and comprehend complex neuron geometries than traditional visualizations on computer screens.

The Neuro-VISOR software can be run in a VR version (currently only for Oculus), as well as via a desktop version (without VR headset). While the desktop version does not provide the 3D visualization of the VR version, it does provide all of the same interactive real-time simulation capabilities.

License

We use a modified version of the GNU LPGL v3. Our license can be found in LICENSE.txt

Research Team

This project is produced at the Center for Computational Mathematics and Modeling (C2M2) at Temple University.

Project Leads: Dr. Benjamin Seibold (Github), Dr. Gillian Queisser

Researchers and Developers: Rujeko Chinomona, Craig Fox (in), Calin Pescaru, Garret Quallet, James Rosado (in), Wayne Zheng

Code Documentation

Our code documentation is generated using Doxygen. The completeness of this documentation is dependent on code commenting, so there may be gaps and imperfections. If you notice issues with this documentation, please report it to seibold@temple.edu.

Other Code (Realted to this Project)

Stephan Grein maintains a separate project for generating neuron grids, as well as a project containing additional custom attributes which proved useful during development of Neuro-VISOR.

Connect with Us

Our blog goes into finer detail about some of our past and current code solutions. This blog contains interesting details about various areas of the project.

Inquiries about the project can be made to seibold@temple.edu.

Performance issues and code-related questions can be sent to craig.fox@temple.edu.

Use Guide

Recommended Hardware

- Oculus Rift, Rift S, or Quest Head Mounted Display (HMD) This project is currently tested on
 the Oculus Rift S and the Oculus Quest. It was previously developed on the original Rift headset.
 This project was developed using the Oculus SDK. We have not been able to run this project on
 other headsets, but have been working to make it more cross-compatible.
- We do not have rigorously tested minimum computer specs. We have listed our hardware setup below for convenience. Oculus has provided a list of VR-ready computers, but we do not necessarily endorse any computer recommended by them.

Dell Precision 5820 Tower		
CPU	Intel Xeon W-2125	
GPU	NVIDIA GeForce GTX 1080	
RAM	32 GB	

Recommended Software

Recommended for Running as a Standalone Application and in Unity Editor

- Windows 10 or 11 64-bit, or MacOS 64-bit This program may be functional on other operating systems, but its performance is not guaranteed. The emulator functions have been tested on Ubuntu 16.04 LTS.
- · Relevant HMD software and drivers

Recommended for Running in Unity Editor

- Unity 2019.4.26f1 (LTS)
- We use the Oculus Desktop 2.38.4 package
- Git version >= 2.7.0
- Git LFS version >= 2.10.0
- Note: Git users (versions < 2.23.0) should clone the repository by using git lfs clone. All other should use git clone. For users of older git versions this remedies the problem that every LFS versioned file will ask the user for their password.
- A pre-commit hook will block commits made with inappropriate versions of Git, Git LFS, or Unity.
 Users should install the hooks by calling ./install_git_hooks.sh from the root directory after cloning.

- git lfs: git lfs env in a terminal/console.
- git: git --version
- Unity: see UnityEditor

Starting the Program

Make sure that your HMD is set up and that you have gone through the first-time setup. Ideally you have tested several other programs on your headset before using this software.

Running as a Standalone Application

- 1. Download the latest build release.
- Place desired neuron cell files in Neuro-VISOR_Data/StreamingAssets/NeuronalDynamics/Geometries. Any cells found in this directory will be available at runtime.
- 3. Start the application by running Neuro-VISOR.exe.
- 4. Upon startup, the user is placed in a model of C2M2's lab. The application will detect a VR headset and launch in VR/keyboard emulator mode automatically.
- 5. Our control scheme is outlined below. Try moving around and looking at your hands.

Running in Unity Editor

- 1. Clone project to any location.
- 2. Ensure the correct version of the Unity Editor is installed
- Open project in Unity and open Assets/Scenes/MainScene
- 4. Place desired neuron cell files in Assets/StreamingAssets/NeuronalDynamics/Geometries . Any cells found in this directory will be available at runtime.
- 5. Start the application by pressing play in the editor.
- 6. Upon startup, the user is placed in a model of C2M2's lab. The application will detect a VR headset and launch in VR/keyboard emulator mode automatically.
- 7. Our control scheme is outlined below. Try moving around and looking at your hands.

Controls

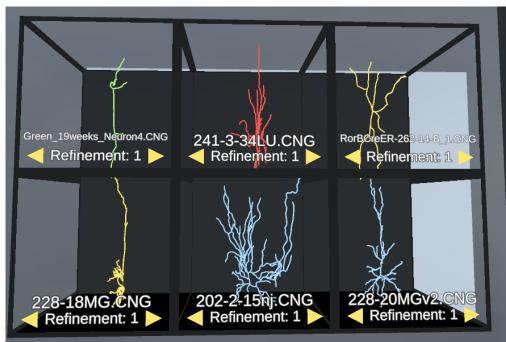
Oculus touch controller naming conventions can be found here. An instructional video demonstrating the controls can be found here. The term 'Hand Trigger' and 'Grip Trigger' are used analogously throughout the project, as are the terms 'Index Trigger' and 'Front Trigger'.

Action	Rift Touch Controllers	Keyboard/Mouse
Toggle raycasting	(P) Button one (A/X)	Always on
Interact	Raycast + (P/H) Index trigger	(P/H) Left mouse button
Grab	(H) Hand trigger	(H) Right mouse button
Reset Position	Grab + (P) Thumbstick	Raycast + 'X' key
Scale Object	Grab Ruler + Thumbstick up/down	Raycast Ruler + up/down arrow keys
Reset Scale	Grab Ruler + (P) Thumbstick	Raycast Ruler + 'R' key
Move Camera	Walk around!	WASD
Rotate Camera	Look around!	(H) Left-Ctrl + move mouse cursor
Quit	Oculus button	Escape key

Abbreviation	Meaning
(P)	Press button once
(H)	Hold button down

Selecting a Cell

1. A cell previewer stands against the whiteboard near the window. It attempts to render the 1D mesh of any neuron .vrn cell file archives found in StreamingAssets/Neuron alDynamics/Geometries . Six example cells are included with this repo. Several more cells can be found here.



2. Enable raycast mode. The hand with raycast mode enabled should be constantly pointing forward.

3. With raycast mode enabled, hover over a cell preview window by pointing at it. A blue guide line should be drawn between your pointer finger and the preview window. Continue hovering to see more information about the cell, or press the Interact button to load the cell and launch solve code. The guide line should turn orange while pressing/holding if in VR. The geometry should render in the middle of the room, scaled to fit within the room.

Simple Cell Interaction

Grabbing

The cell can be grabbed by hovering your hand over the 3D geometry and pressing the hand trigger on that hand's controller. Once grabbed, you can move and rotate cells freely.

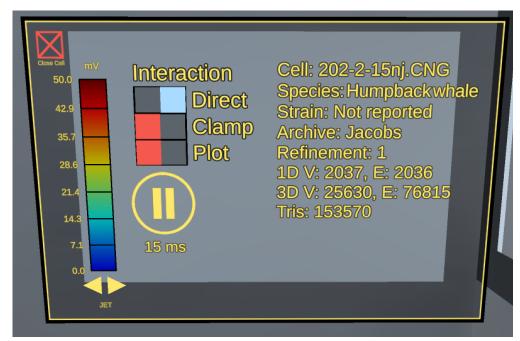
Resizing

While grabbing a cell, hold the thumbstick up or down on the hand that is being used to grab the cell to resize the cell in world space. Note: this does not affect the environment of the solver code: the cell can be scaled freely in world space without affecting the stored vertex positions of the 1D or 3D meshes.

Board Info and Controls

A large user interface is spawned upon selecting a cell. This board contains useful static information about the cell.

The board contains a color table that shows the current color gradient applied to the cell. The voltage value corresponding to different color values is diosplayed to the left of the color table. The user can change the value



corresponding to the top or bottom of the color scale by hovering their finger cursor over either number and holding up/down on the joystick (or the up/down arrow key). The user can also change the color scheme by interacting with the arrows beneath the color table.

The board contains a subpanel for selecting the type of interaction. The user can select any of these toggles to change the effect of directly interacting with the surface. See direct, clamp, synapse and plot interactions for explanations of each.

The board also contains a play/pause button. The user can use this to pause solver code at the current time step. Beneath is displayed the current simulation time.

Ruler controls

A ruler is spawned with every cell geometry. The ruler can be used to understand the length scale of the cell in its local space. While grabbing the ruler, resize it by moving the thumbstick up or down on the hand that is being used to grab the ruler.

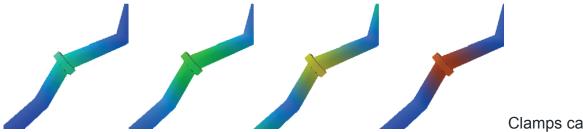
The measurements on the ruler will adapt to the world-space size of the geometry so that it can always act as a translator between the size of the cell in the user's space and the local length scales of the neuron.

Direct cell interaction

With raycast mode enabled, point at the surface of the geometry. A blue line should be drawn between your pointer finger and the surface of the geometry. Tap the geometry from up close, or press the Interact button from a distance to directly alter simulation value at the nearest 1D vertex to the point of interaction. The guide line should turn orange upon pressing, and the surface of the geometry should change color to reflect the affected potential at the nearest 1D vertex on the geometry.

-0 µm -2 -4 -6 -8 -10 -12 -14 -16 -18 -20 -22 -24 -26 -28 -30 -32 -34 -36 -38 -40 -42 -44 -

Clamp interaction



Clamps can be used to

continuously alter the value of a single vertex on the 1D mesh.

Enable Clamp Mode

With the cell loaded and raycast mode enabled, press the Clamp Mode button on the whiteboard. "Finger clamps" should appear on both of the user's pointer fingers whilst raycasting. The finger clamps should appear as cylinders on the user's pointer finger.

With clamp mode enabled, interacting with the surface of the cell should place a cylindrical potential clamp on the cell near the point of interaction. The clamp will snap to the nearest 1D vertex to the 3D point of interaction, and will effect that 1D vertex on the 1D mesh.

Toggling a clamp

Enable or disable the clamp by tapping it from up close or pressing the Interact button while pointing at it from a distance. The clamp is gray when it is disabled. It's color when enabled should reflect the clamp's current potential value.

Changing a clamp's power

While the clamp is enabled, the clamp's power can be changed by pointing at it, holding the Interact button, and moving the controller's joystick up or down.

Destroying a clamp

Clamps can be destroyed by holding the Interact button briefly while pointing at the clamp, and then releasing the Interact button.

Group clamp controls, clamp highlighting

Users can place many clamps on the geometry. Clamps cannot be placed too near to each other, but there is no set limit to the number of clamps that can be placed.

In addition to each clamp being individually interactable, the "finger clamps" mentioned in Enable Clamp Mode are also interactable, and act as controllers for all existing clamps. Any control that can be done to a single clamp (toggle, alter power, destroy), can be done to all existing clamps at once by interacting with the finger clamp in the same manner.

The user can highlight all clamps with a red sphere to clarify their position to the user. This is particularly useful on complicated geometries with many clamps attached. While pointing at the finger clamp and holding the Interact button, hold down the hand trigger to highlight all existing spheres.

Point-plotter interaction

The user is able to spawn line graphs that are attached to specific 1D vertices on the neuron cell. These graphs will show the voltage at that 1D point over time.

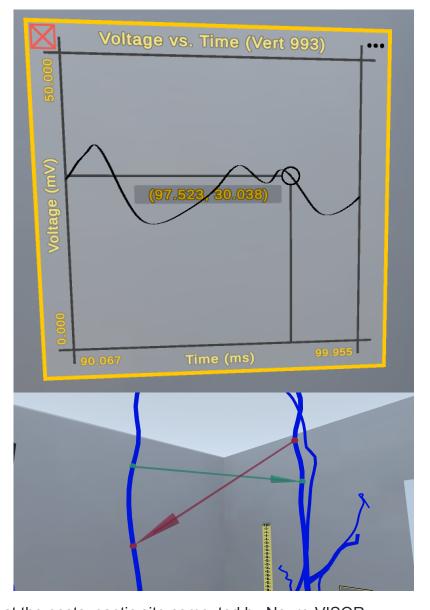
To spawn a graph panel, the user simply needs to toggle "Plot" on the board UI. At this point the user can raycast onto the surface of the mesh and press the index trigger (or click with the mouse) in order to spawn a graph attached to the nearest 1D vertex. Panels are grabbable and resizeable in the same way that the cell or the ruler is.

The user can hover over the graph-plane with their raycasting finger or the mouse in order to spawn a cursor at the point of hovering. The cursor will display the exact value of the graph at that point. The user can then press the index trigger (or click on the mouse) to lock the cursor at that position. Clicking again will free the cursor.

The number of samples in the graph can be altered by opening the "more info" panel (top-right corner of the graph), hovering over "number of samples", and holding up or down on the joystick (or holding the up or down arrows on the keyboard).

Synapse interaction

With the addition of principled synapse models into a multi-neuron network, one is now able to build a network of neurons and connect them via synapses, simulating transmission of electrical signals from one neuron to another. The project is equipped with two functional types of chemical synapse models found within the mammalian cerebellum. The two implemented synapse models are the excitatory NMDA-receptorbased and the GABAergic inhibitory synapse. The mathematical equation describing the NMDA receptor-based model is $I_{NMDAR} = G_{NMDAR} * a(t) * b(V_{postsyn}) *$ (V_{postsvn} – E_{NMDAR}). G_{NMDAR} is an experimental value for the conductance of



the receptor. $V_{postsyn}$ is the membrane voltage at the postsynaptic site computed by Neuro-VISOR. E_{NMDAR} is an experimental value for the reversal potential assigned to the synapse. The other terms in the equation, a(t) and b(V_m), are probability functions. The a(t) term describes the time course of the conductance and takes two variables, time of the presynaptic action potential as well as the postsynaptic membrane voltage. The other term, b(V_m) is a simple Boltzmann function that describes the fraction of NMDA receptors left unblocked. The term is used to simulate the magnesium ion block of the NMDA receptor which prevents excessive activation. When a given voltage threshold is reached on the presynaptic membrane the voltage of the postsynaptic membrane will be increased. The GABAergic synapse model is described by $I_{GABAR} = G_{GABAR} * a(t) * (V_{postsyn} - E_{GABAR})$. Like the NMDA Receptor model, the GABA current has many of the same terms, just with differing constants and conductance. The GABAergic synapse model doesn't include the Boltzmann function. The chemical signal received when using the GABAergic model will activate the GABA receptor, which will polarize the postsynaptic cell and produce an inhibitory effect. In the simulation, when the user seeks to employ the GABAergic model, the voltage at the postsynaptic membrane will decrease until it reaches a designated voltage threshold.

- 1. To interact with synapses in the simulation, select and place neurons to be worked with into the main scene.
- 2. Left click in desktop mode or raycast in the VR environment onto the mode titled "Synapse" and select a vertex on the cell. The selected vertex will be the presynaptic membrane.
- 3. Next select a vertex on another neuron to be the postsynaptic site (It is possible to select a different vertex on the same cell to be the postsynaptic site, however the action potential propagation is clearer when there are synapses connecting two neurons).
- The same synapse mode allows a user to switch between two different types of synapse models, namely excitatory or inhibitory.
- 5. To switch between these two modes, select the presynaptic site the same way as before and the mode will change from either excitatory to inhibitory or vice versa. If using the headset, raycast to select the presynaptic site, however if using the desktop mode left click on the postsynaptic site. Which synapse model is active is denoted by the synapse color displayed by the pre and postsynaptic sites as well as the arrow that points in the direction from these two membranes.
- 6. Note that the GABA receptor in our simulation is colored red as to distinguish between the NMDA receptor which is colored green. The two types of synapse models, combined with the neuron signaling, represent the key ingredients needed to build micro-circuits with realistic signal processing capabilities.

Known Issues Log

- The programs freezes while a new neuron loads in
- Adding in a neuron while the simulation is paused, makes it appear white and buggy (resuming the simulation will fix this)
- Changing the color scale introduces various bugs

Branches

Master: The latest stable version of the project

Development: The active beta, contains the latest features but at a higher risk of bugs

multiHeadsetsSupport: Based off of 2.0.0, adds rudimentary support for all headsets

Changelog

Contributors: Rujeko Chinomona, Craig Fox (in), Calin Pescaru, Garret Quallet, James Rosado (in), Wayne Zheng.

- Both excitatory and inhibitory synapses can now be added
- Synapses accutarely model real-world behavior
- Simulation configurations can be saved and loaded in
- · Various performance improvements and consistence improvements were made

2.0.0

Contributors: Michael Bennett, Rujeko Chinomona, Craig Fox (in), James Rosado (in), Jacob Wells (in), Noah Williams, Wayne Zheng.

Beta Testers: Calin Pescaru, Garret Quallet

- · More than one neuron can now be added
- Synapses can now be added NOTE: This is still a proof of concept feature and is not physically
 accurate
- Significant performance improvements were made
- · Desktop mode now has all the features of VR
- MacOS is now supported

1.0.1

Fixes group clamp control issue

1.0.0

Contributors: Craig Fox (in), Stephan Grein (in), Bogdan Nagirniak, James Rosado (in), Jacob Wells (in), Noah Williams.

Beta Testers: Marcus Bingenheimer, Rouying Tang

- Allows the creation of one, physically-accurate neuron
- Designed for VR, but a limited capability desktop version exists
- The neuron can have a voltage directly applied to it, can be clamped with a continuous voltage, and can have point plotters displaying voltage over time applied to it
- A ruler provides a length reference point
- A board displays cell information, controls the controls, sets the color information, and pauses, resumes, and quits the simulation