# 3-Dimensional Agent-Based Model of Neural Activity in the Central Nucleus of the Amygdala During Pain

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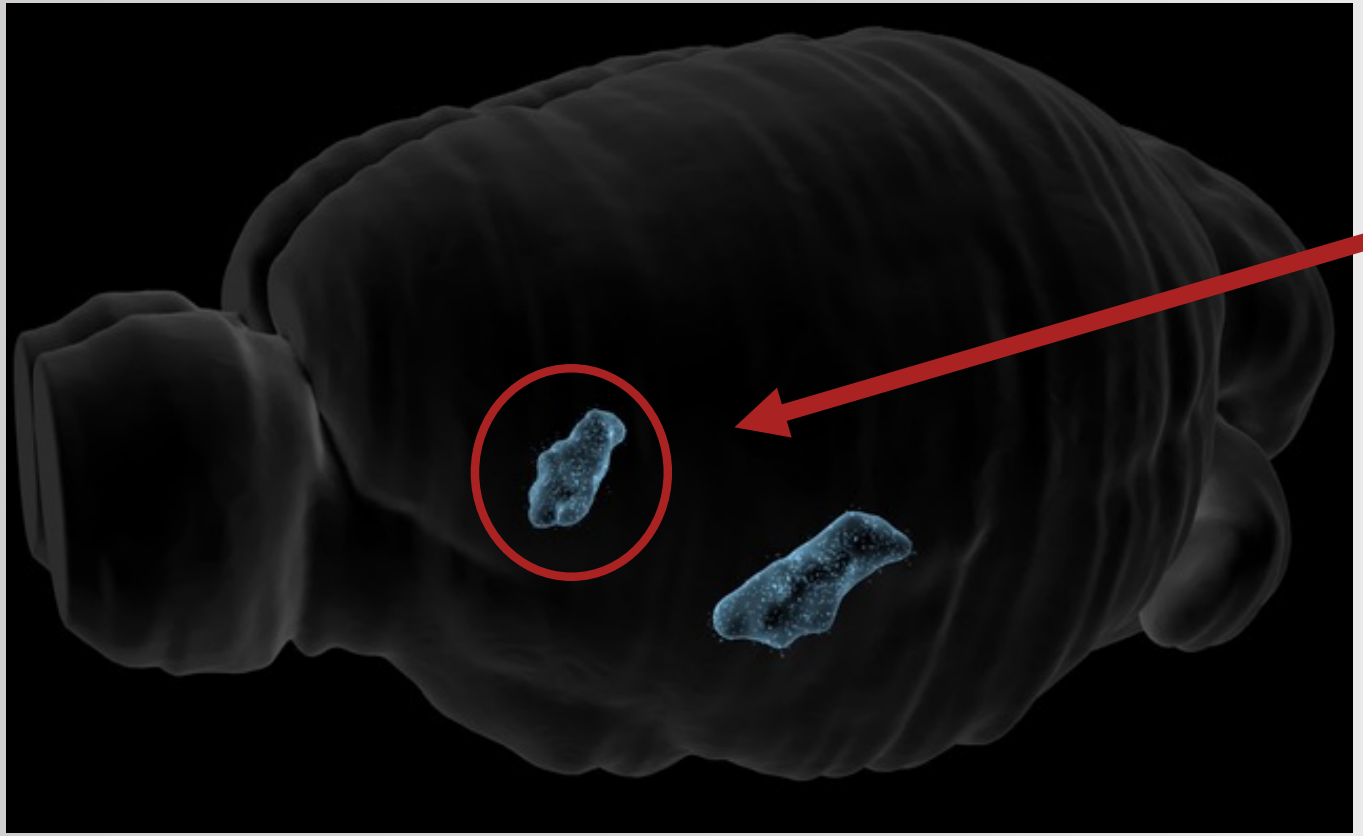
# Background



Central nucleus of the Amygdala (CeA)

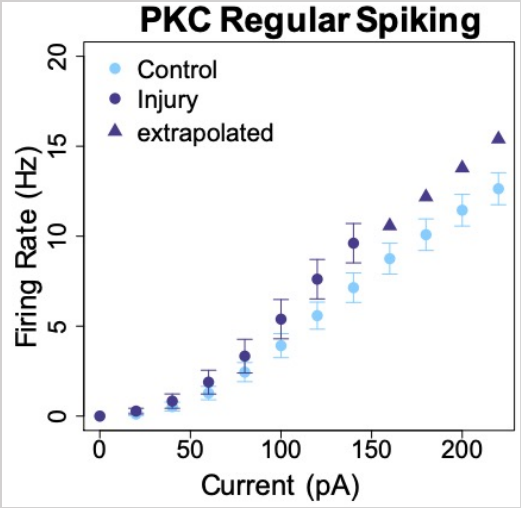
The CeA is a region of the brain important in **pain processing**

# Background

## Two pain-related neuron populations in the CeA:

### Protein kinase C-delta (PKC-δ) - increase pain.

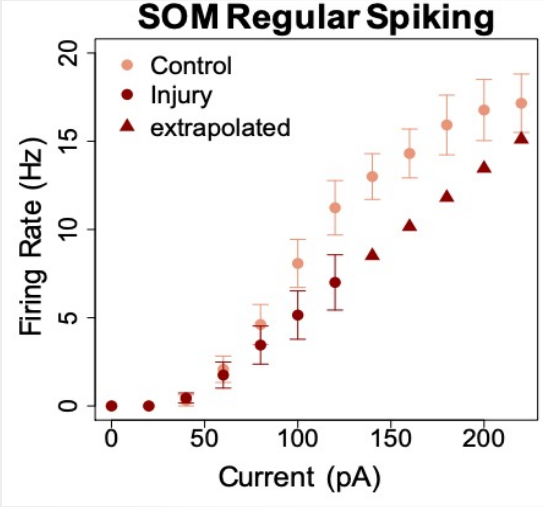
- Larger allocation: 682 (68%)
- Fire higher in the **presence of pain**[1]




- Fewer, longer connections[2]

### Somatostatin (SOM) - decrease pain.

- Smaller allocation: 317 (32%)
- Fire higher in the **absence of pain**[1]




- More, shorter connections[2]

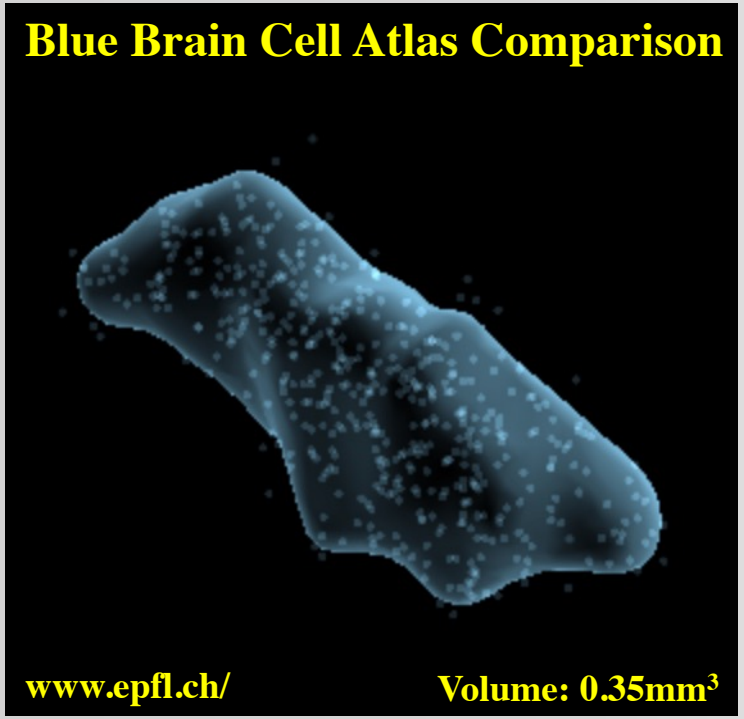

[1] Wilson et al., Dual and Opposing Functions of the Central Amygdala in the Modulation of Pain. Cell Rep. 2019.

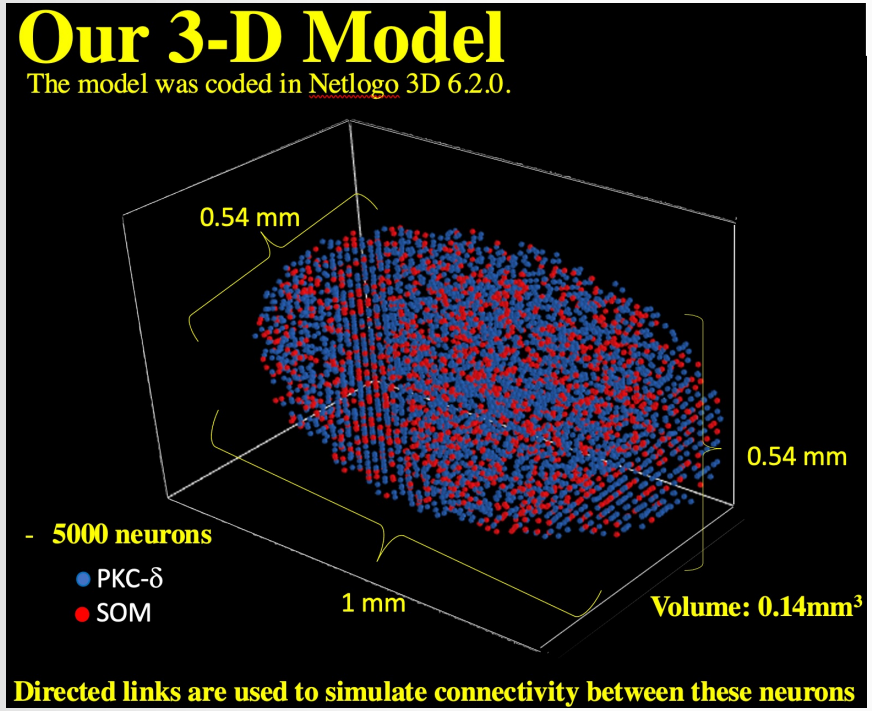
[2] Adke et al., Cell-Type Specificity of Neuronal Excitability and Morphology in the Central Amygdala. eNeuro. 2021.

# Objective

Design a 3-dimensional **agent-based model** of PKC-δ and SOM neurons in the CeA for the purpose of predicting pain.

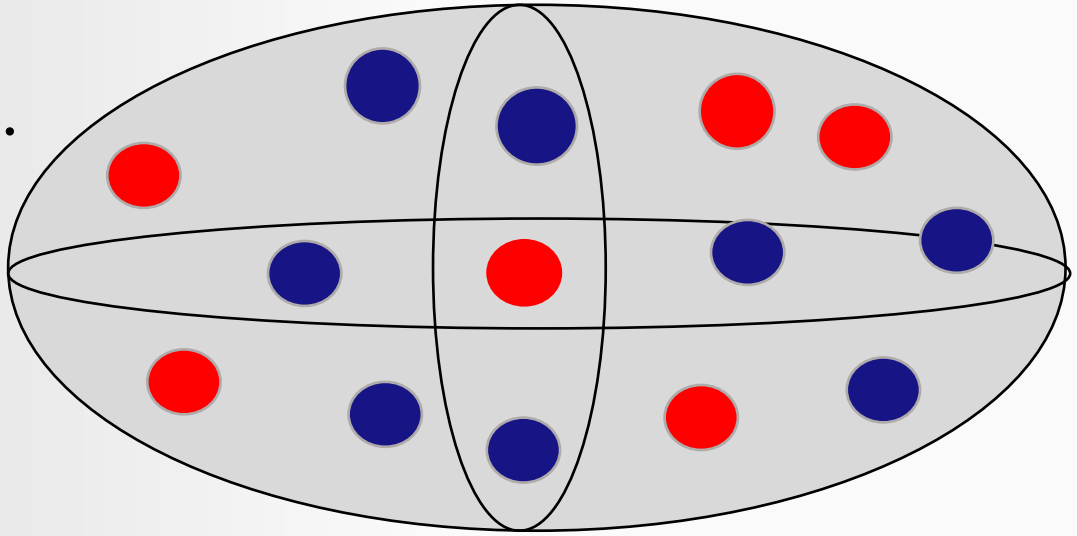
* An **agent-based model (ABM)** is a computational model for simulating the actions and interactions of autonomous agents in order to understand the behavior of a system.



# Model Initialization

1. An ellipsoid is generated to represent CeA.



2. **5000 neurons** (i.e. agents) are generated.
   Each neuron is assigned
   - random location in the ellipsoid
   - expression type (PKC-δ or SOM)
   - firing type (Regular Spiking, Late Firing, or Spontaneous)
   - other variables relating to damage accumulation

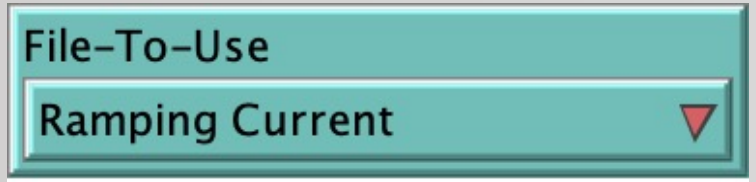
# Model Initialization

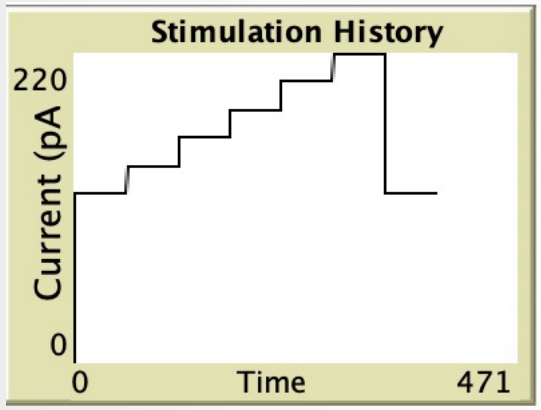
3. Neural Network is created with a switch


- Additional sliders and switches used for network specifications:
  - Number of PKC and SOM outgoing connections
  - Incoming signal threshold for silencing



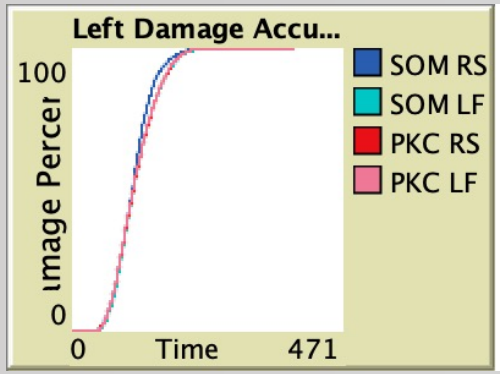
4. Stimulation history (pA) selected on Interface



# Model Procedures
# *At each time step*

1. Each neuron's damage level (d) is updated depending on each neuron's current damage variables.



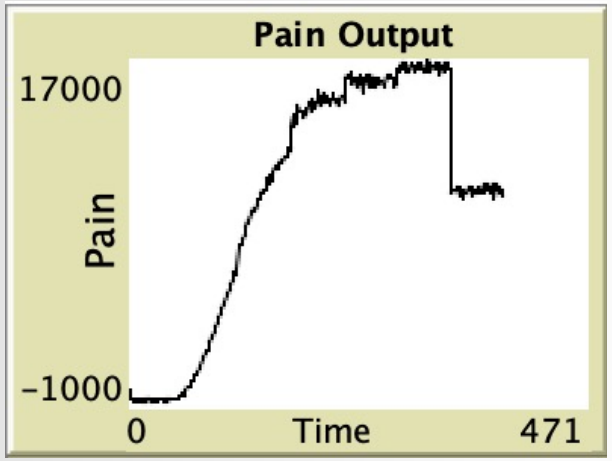

2. Each neuron's firing rate (FR) is stochastically updated using distributions estimated from lab data.

$$FR = \frac{100 - d}{100} * X + \frac{d}{100} * Y$$

*Firing rates are calculated using a linear combination of distribution X (from lab experiments on uninjured mice) and distribution Y (from lab experiments on injured mice).*

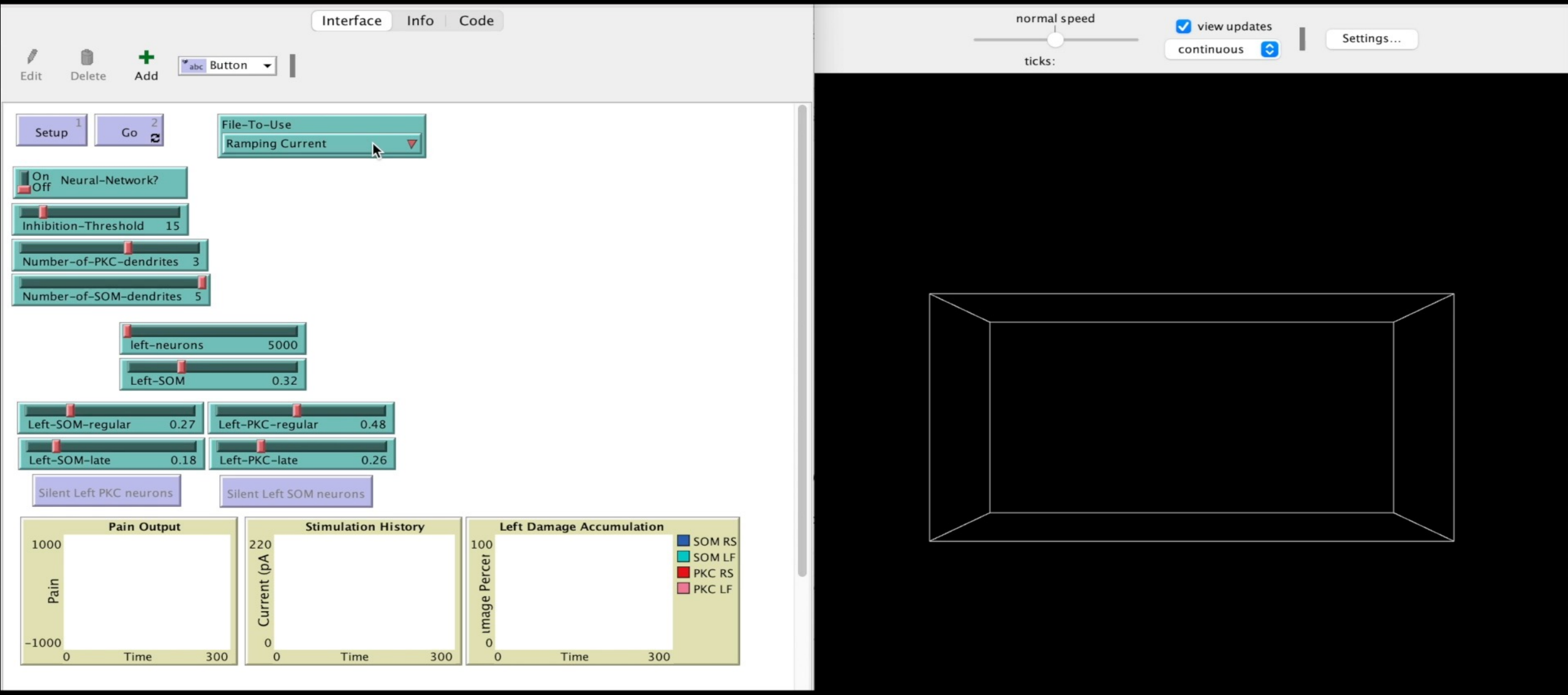
3. If neural network is turned on, neurons send inhibitory signals through directed links. For each neuron, if sum of incoming signals exceeds 15 Hz, then neuron is silenced (FR = 0).

4. System-level measure of pain (P) is calculated as difference in the cumulative firing rates of PKC neurons and cumulative firing rates of SOM neurons.




$$P = \sum_{Type=PKC-\delta} \frac{d}{100} FR - \sum_{Type=SOM} FR$$

# User Interface



# Results

**The model's neural network preserves key connectivity properties:**

- Link Percentages

| % SOM->SOM | % PKC->SOM |
|---|---|
| 51.975 | 10.284 |
| **% SOM->PKC** | **% PKC->PKC** |
| 14.95 | 20.52 |

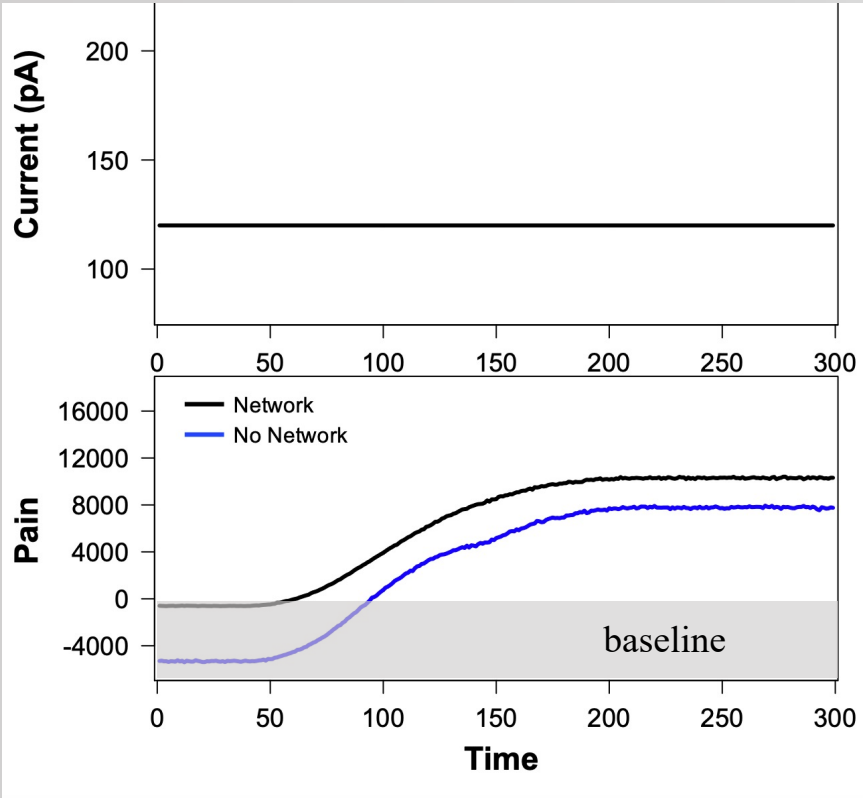
- Link Lengths

| Mean SOM link length (μm) |
|---|
| 62.998 |
| **Mean PKC link length (μm)** |
| 122.549 |

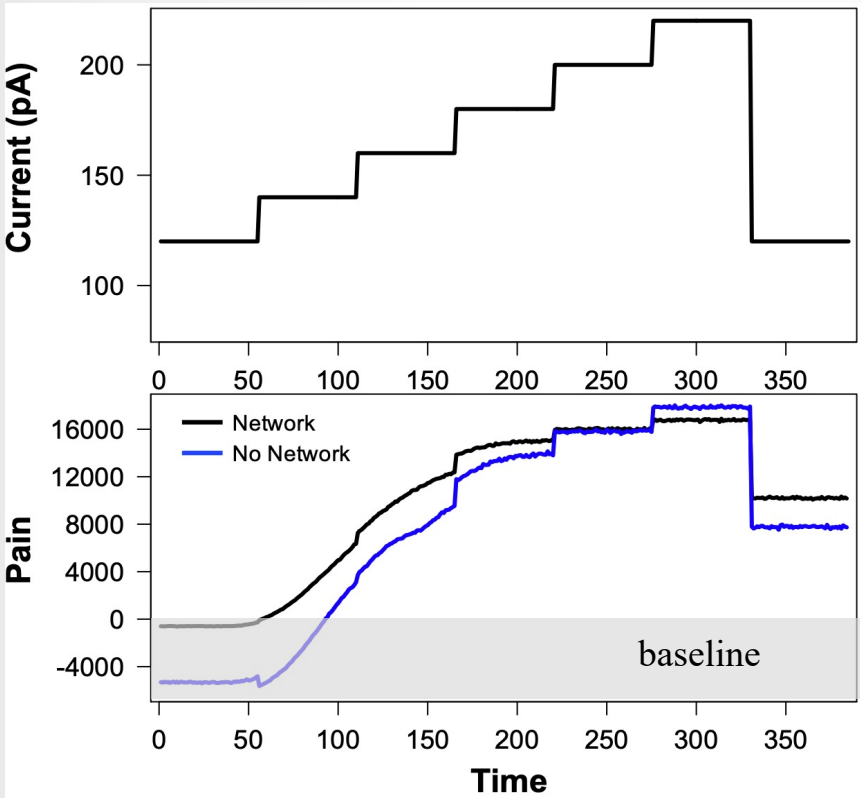
# Results

## Model output replicates both (A) spontaneous and (B) evoked pain

A Scenario 1: Constant 120 pA Current



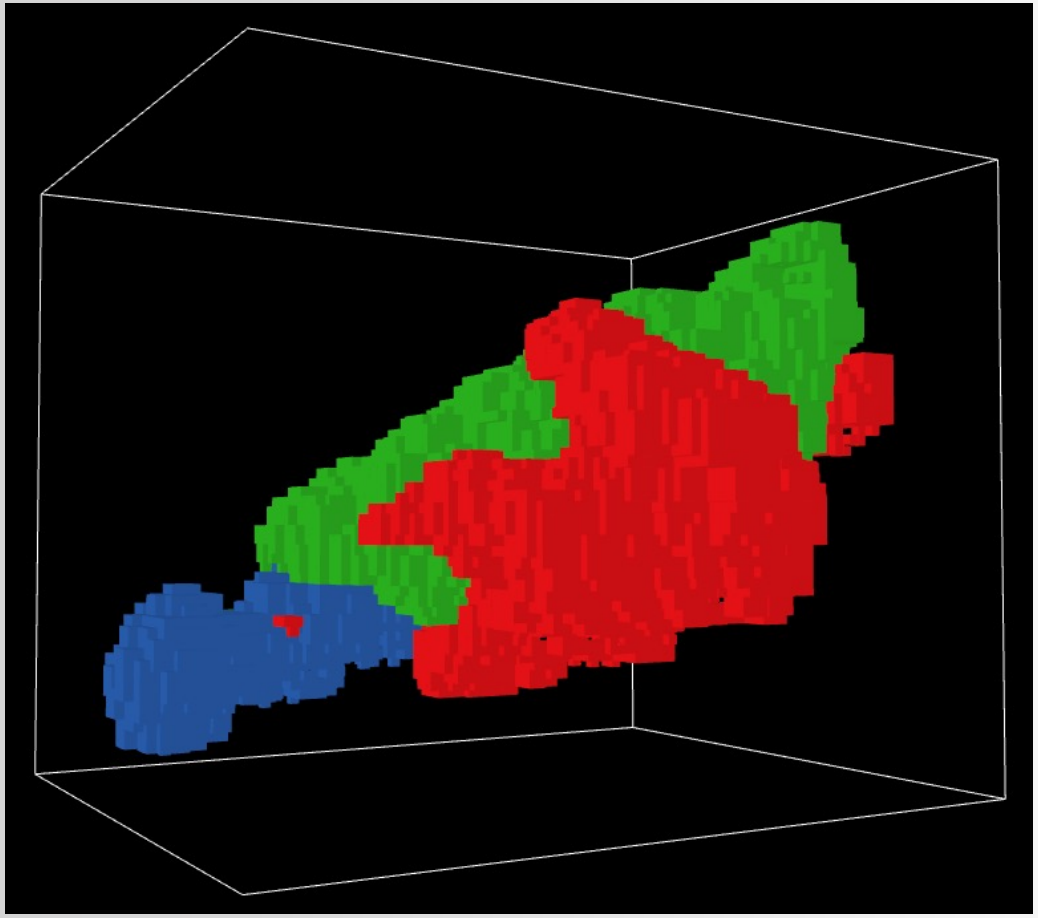

B Scenario 2: Ramping Current



# Ongoing Work

- Refine model to capture the correct anatomical shape of the CeA and its sub-nuclei.

***Spatial domain indicating the subnuclei of the CeA***



***Lateral division (CeL), Medial division (CeM), Capsular division (CeC)***

# Conclusions

- We designed an agent-based computational model of pain-related neurons in the CeA and simulated the behavior and interactions of these neurons under various conditions.

- Results indicate the neural activity and pain output from the model accurately reflect observations made in the real world.

- The computational model provides a framework for exploring parameters and network settings without committing time and resources to additional laboratory experiments.

# Acknowledgements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