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## Probing retinal function with a multi-layered simulator

Evgenia Kartsaki, Bruno Cessac, Gerrit Hilgen, Evelyne Sernagor

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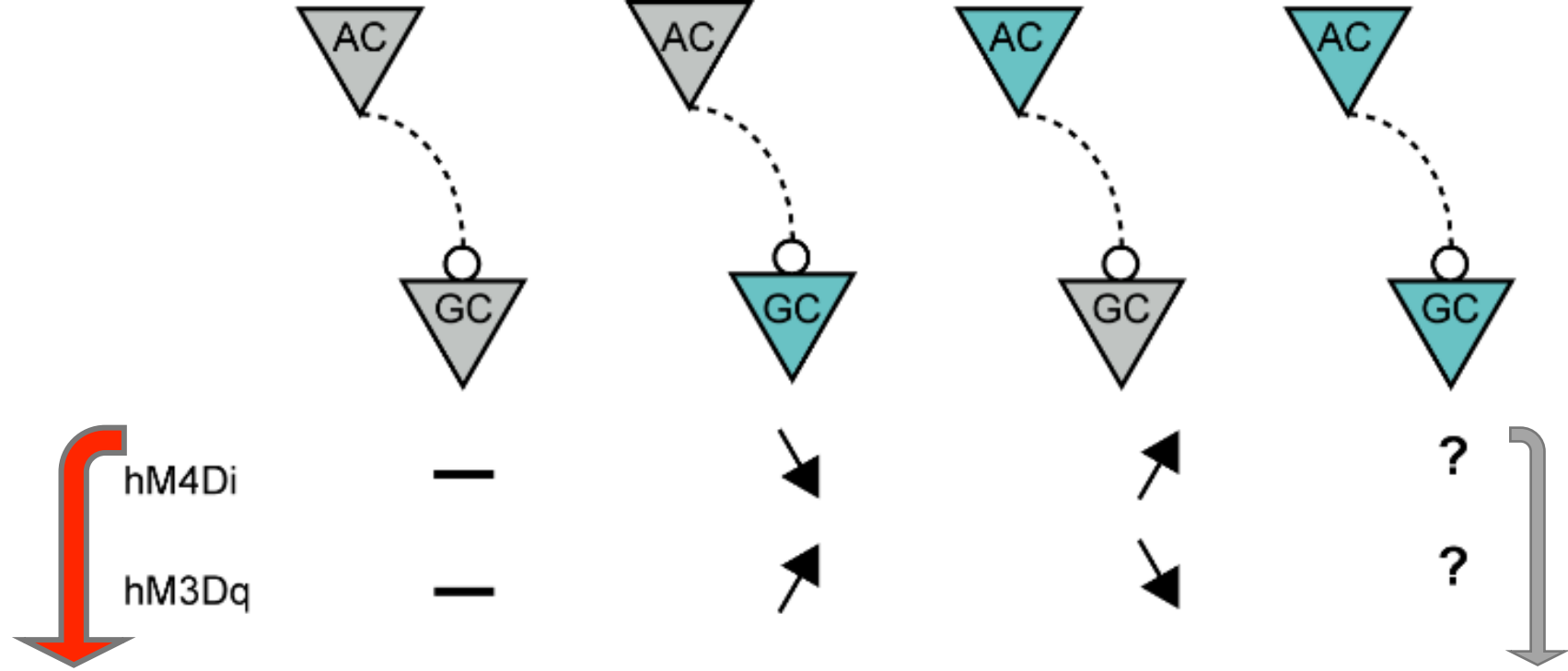


# Probing retinal function with a multi-layered simulator

Evgenia Kartsaki<sup>1,2</sup>, Bruno Cessac<sup>1</sup>, Gerrit Hilgen<sup>2</sup>, Evelyne Sernagor<sup>2</sup>

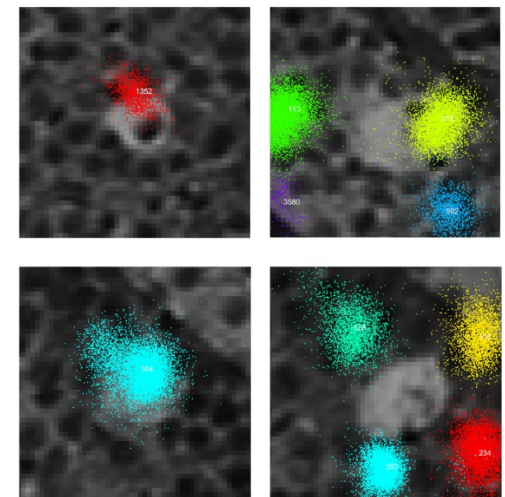
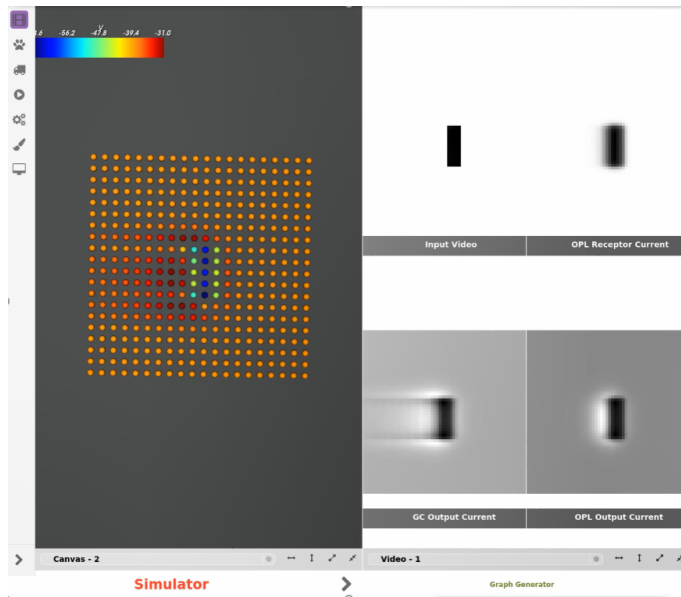
<sup>1</sup>Université Côte d'Azur, Inria, France

<sup>2</sup>Institute of Neuroscience, University of Newcastle, UK

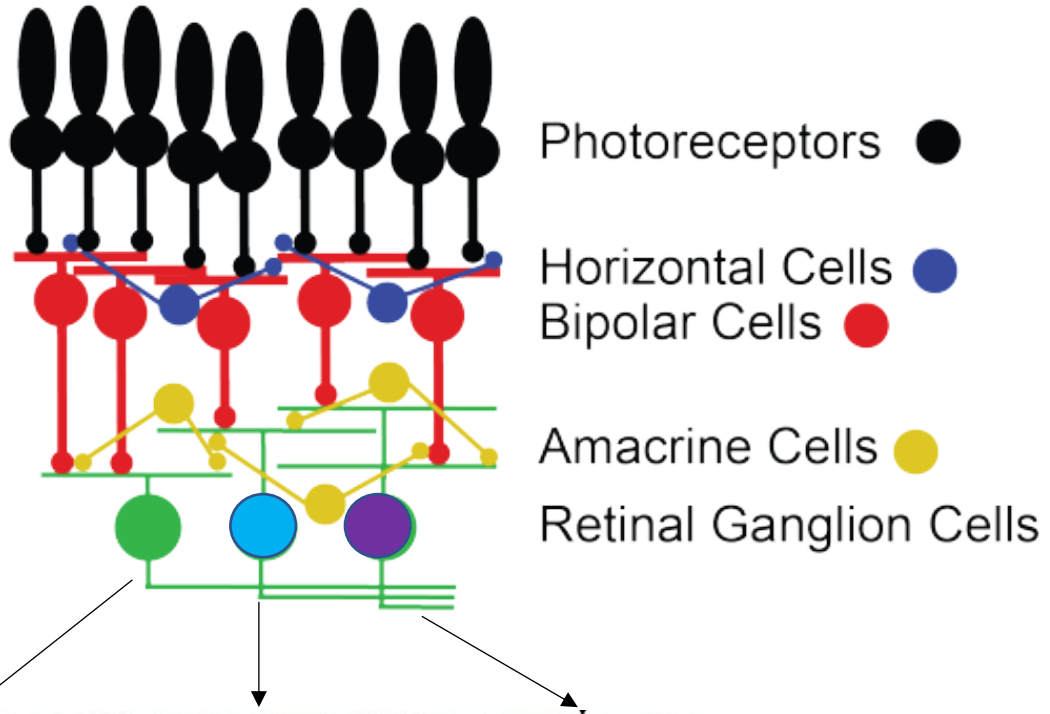


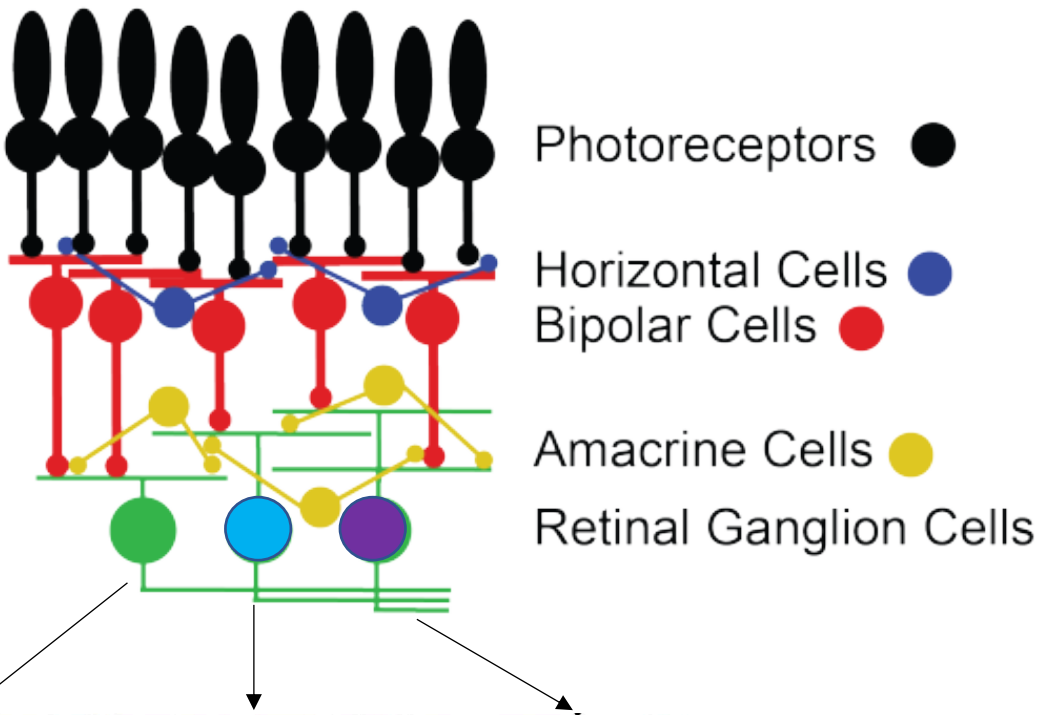
Retinal Simulator

Electrophysiology & IHC



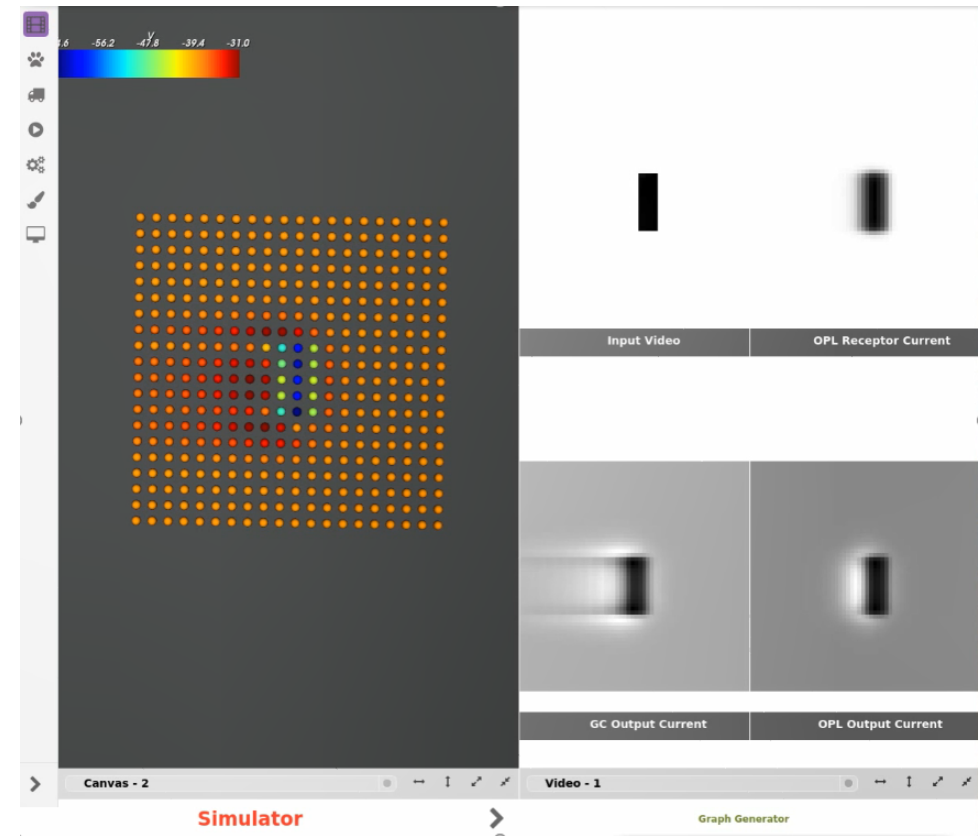
Gerrit Hilgen



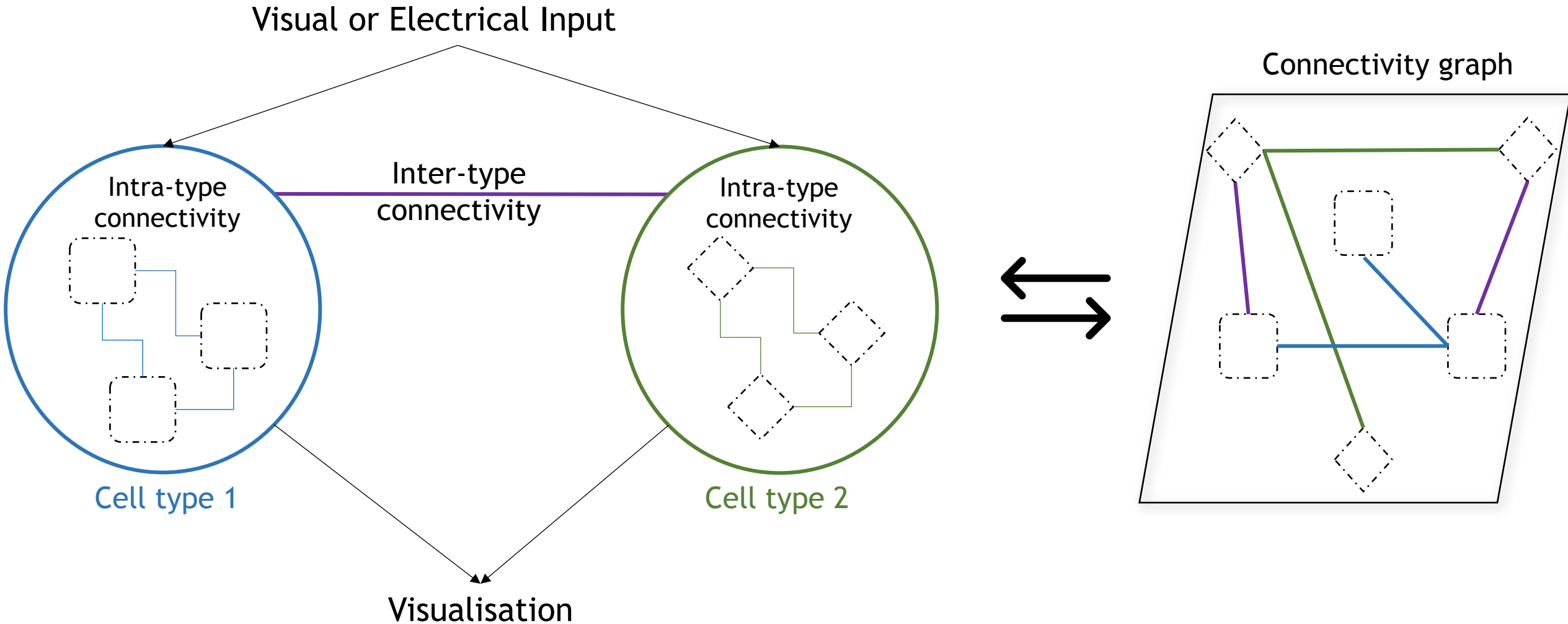


$$\frac{dy}{dx}$$

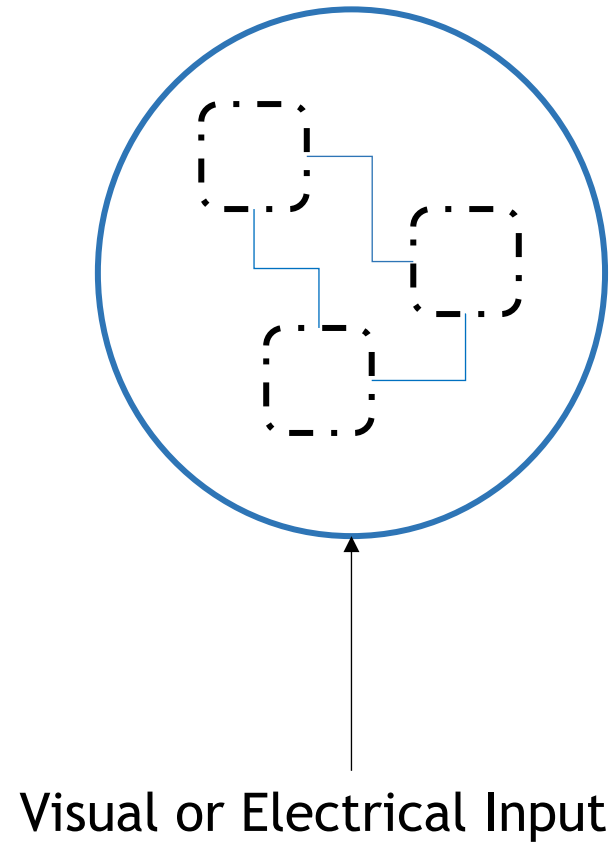
## Macular



# General structure

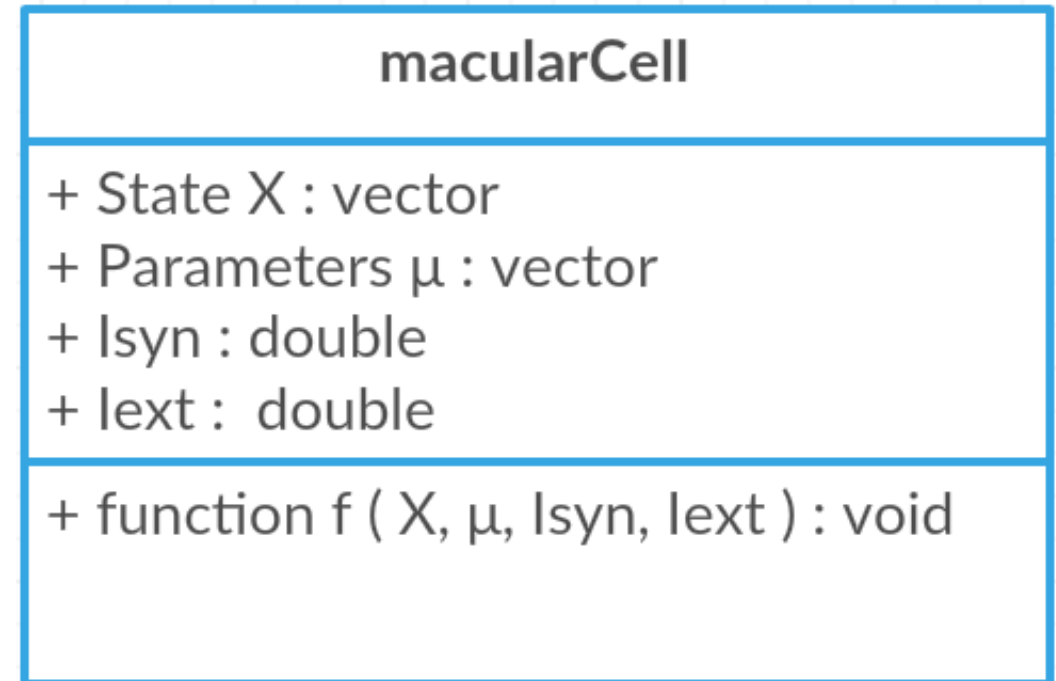


# Basic building blocks - cell



# Cell

- ✓ A set of **variables** evolving in time and characterizing the cell's evolution : e.g. membrane potential, probability that a ionic channel of a given type is open etc.





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- ✓ A set of **variables** evolving in time and characterizing the cell's evolution : e.g. membrane potential, probability that a ionic channel of a given type is open etc.
- ✓ A set of **parameters** that constrain the cell's evolution : e.g. conductance, reversal potential, membrane capacitance, characteristic time of a channel's activity

macularCell
+ State $X$ : vector
+ Parameters $\mu$ : vector
+ $I_{syn}$ : double
+ $I_{ext}$ : double
+ function $f ( X, \mu, I_{syn}, I_{ext} ) : void$

# Cell

- ✓ A set of **variables** evolving in time and characterizing the cell's evolution : e.g. membrane potential, probability that a ionic channel of a given type is open etc.
- ✓ A set of **parameters** that constrain the cell's evolution : e.g. conductance, reversal potential, membrane capacitance, characteristic time of a channel's activity
- ✓ A function controlling the cell's evolution with a differential equation

macularCell
+ State $X$ : vector
+ Parameters $\mu$ : vector
+ $I_{syn}$ : double
+ $I_{ext}$ : double
+ function $f ( X, \mu, I_{syn}, I_{ext} ) : void$

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- ✓ A function controlling the cell's evolution
- ✓ **Isyn** : A synaptic input corresponding to synaptic connections with other cells

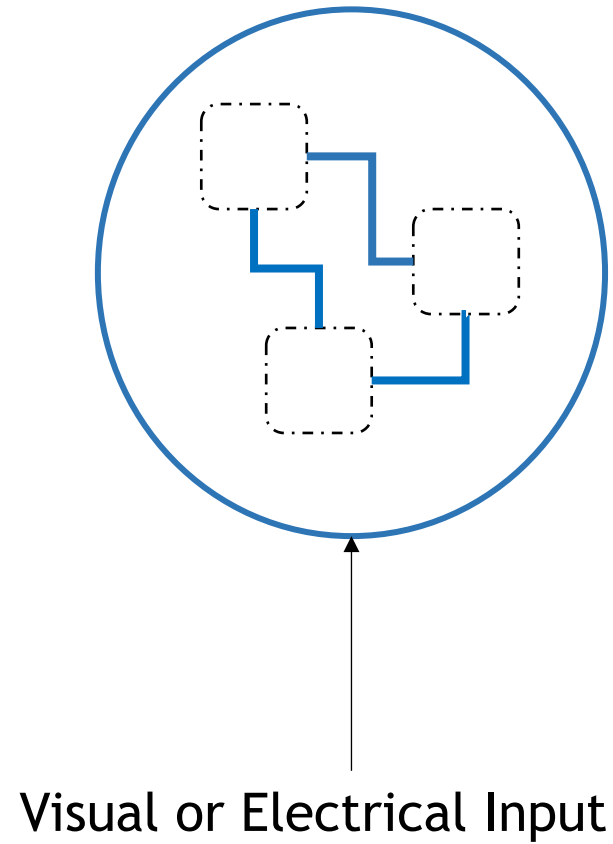
macularCell
+ State $X$ : vector + Parameters $\mu$ : vector + Isyn : double + Iext : double
+ function $f ( X, \mu, Isyn, Iext ) : void$

# Cell

- ✓ A set of **variables** evolving in time and characterizing the cell's evolution : e.g. membrane potential, probability that a ionic channel of a given type is open etc.
- ✓ A set of **parameters** that constrain the cell's evolution : e.g. conductance, reversal potential, membrane capacitance, characteristic time of a channel's activity
- ✓ A function controlling the cell's evolution
- ✓ **Isyn** : A synaptic input corresponding to synaptic connections with other cells
- ✓ **Iext** : An external input corresponding either to a visual input or the electric current provided by an electrode

macularCell
+ State $X$ : vector
+ Parameters $\mu$ : vector
+ Isyn : double
+ Iext : double
+ function $f ( X, \mu, Isyn, Iext ) : void$

# Basic building blocks - synapse



# Synapse

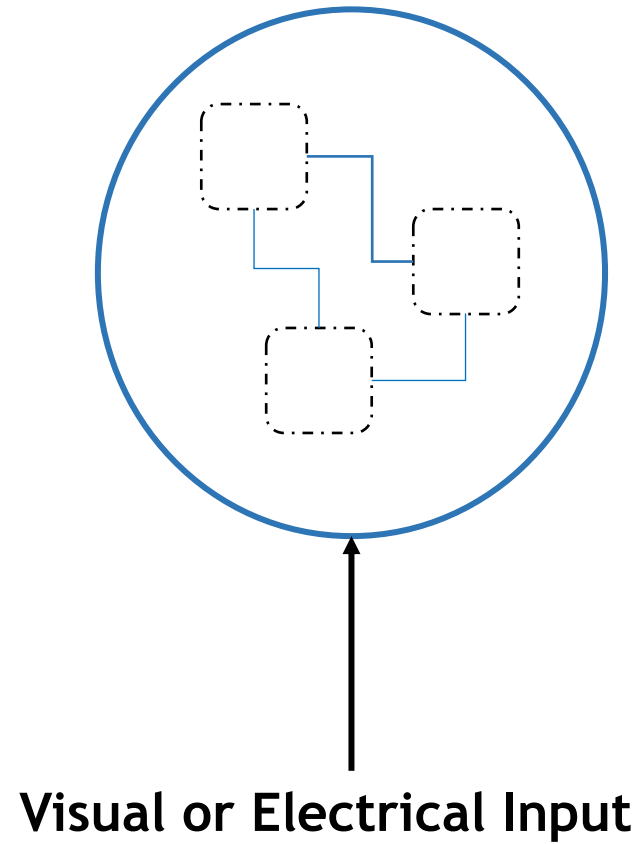
## macularSynapse

+ Variables  $X$  : vector  
+ Parameters  $\mu$  : vector

+ computeSynapticCurrent ( $X$ ,  $\mu$ , pre, post) : void

- ✓ Chemical or electrical (gap junction)
- ✓ A set of variables that evolve in time : e.g. conductance
- ✓ A set of parameters : e.g. synaptic weight

# Basic building blocks - External Input



# External Input



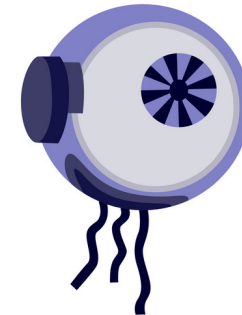
Visual Input



Virtual Retina module

- ✓ Emulate the outer plexiform layer (OPL) current

A.Wohrer et al., 2009

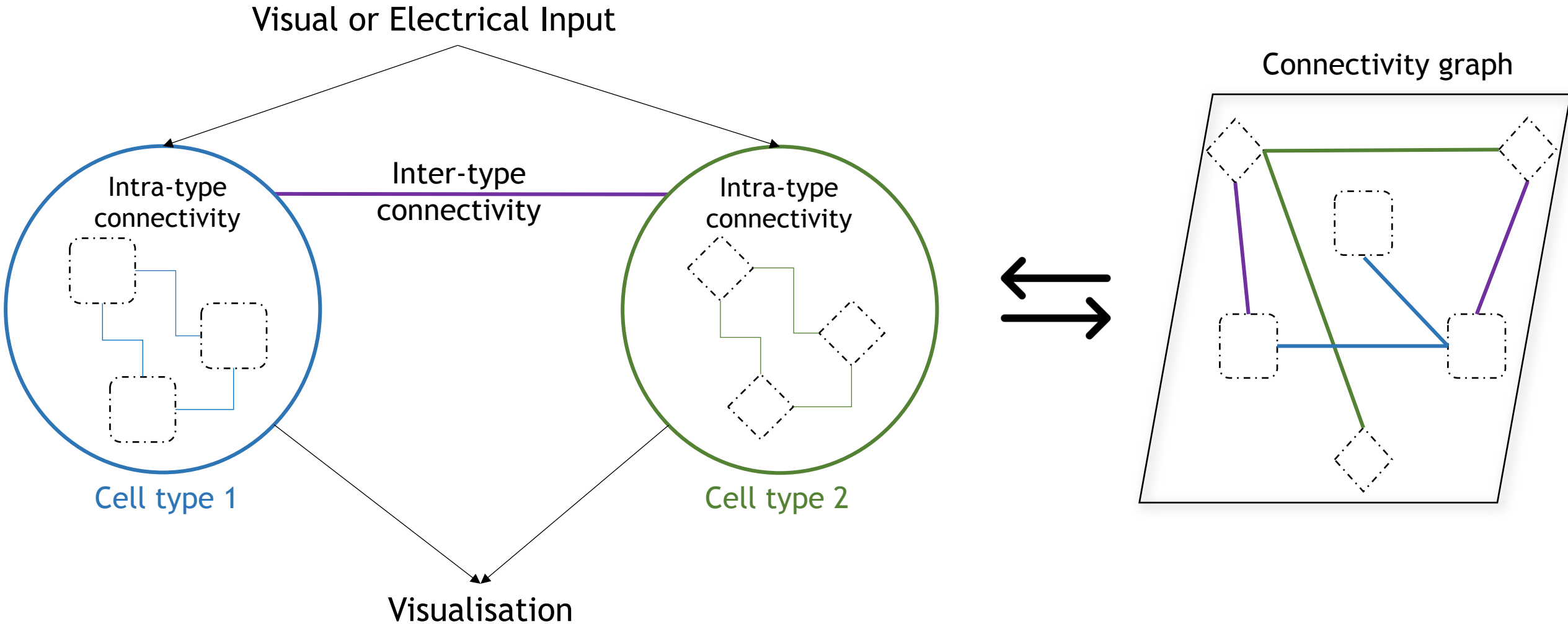


Retinal prosthesis

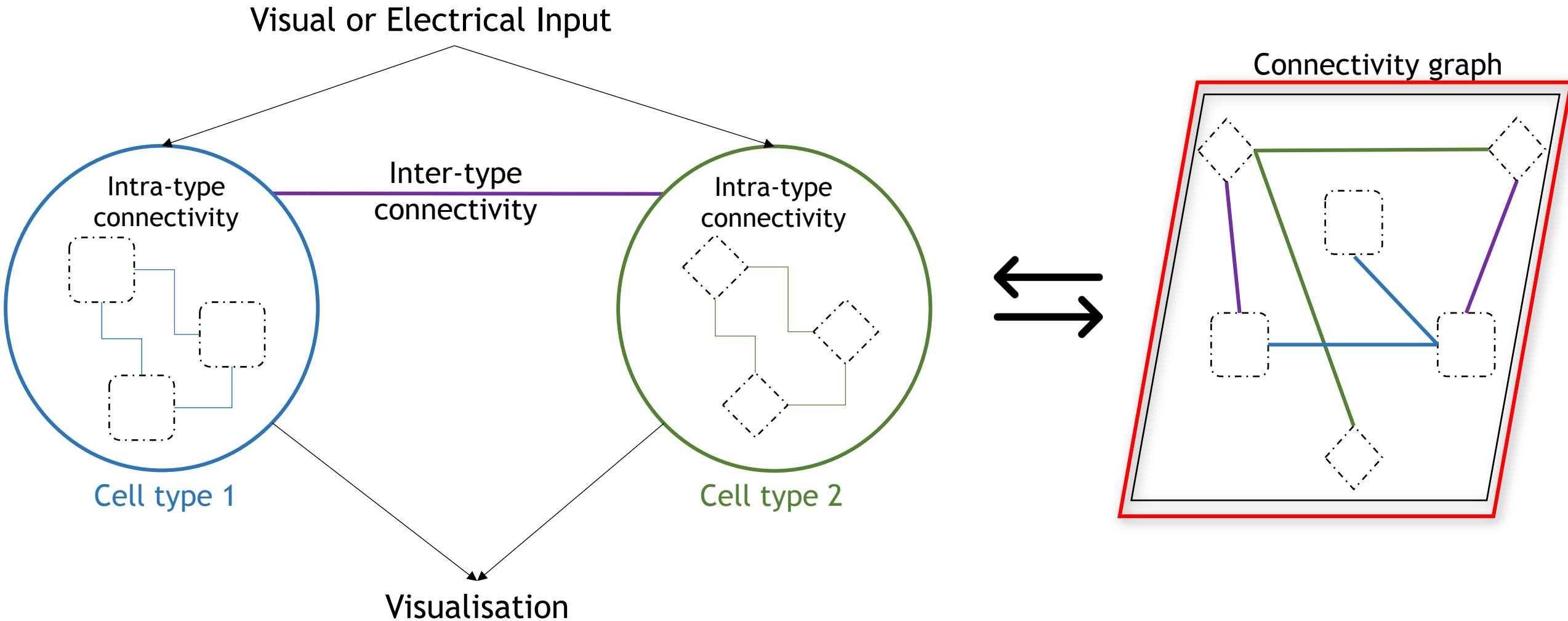
- ✓ Emulate the electric current provided by an electrode



# General structure



# General structure



# Graph

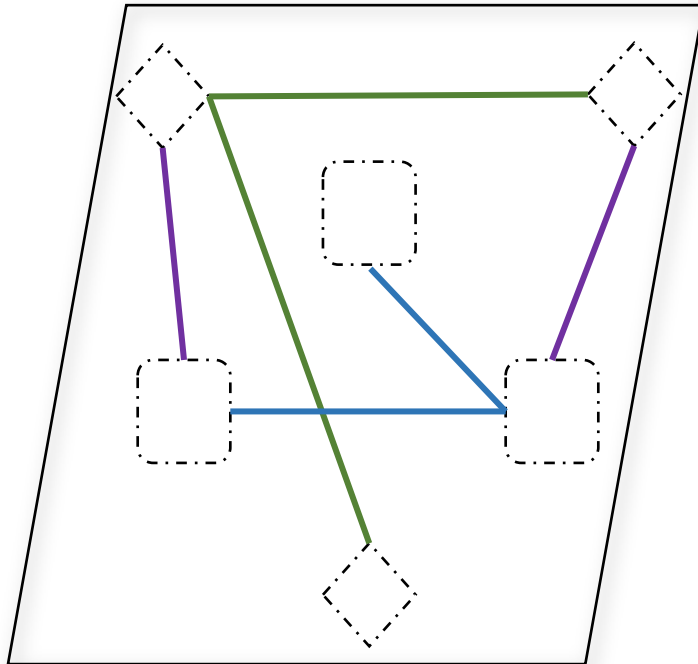
## macularGraph

+ cells : macularCell  
+ synapses : macularSynapse  
+ CellCoordinates: vector  
+ SynapseIndices: vector

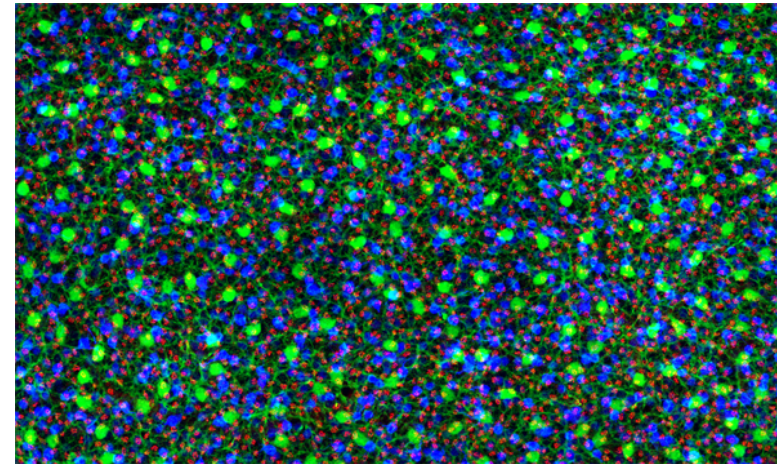
- ✓ Cell types
- ✓ Synapse types
- ✓ Cell coordinates
- ✓ Synapse indices

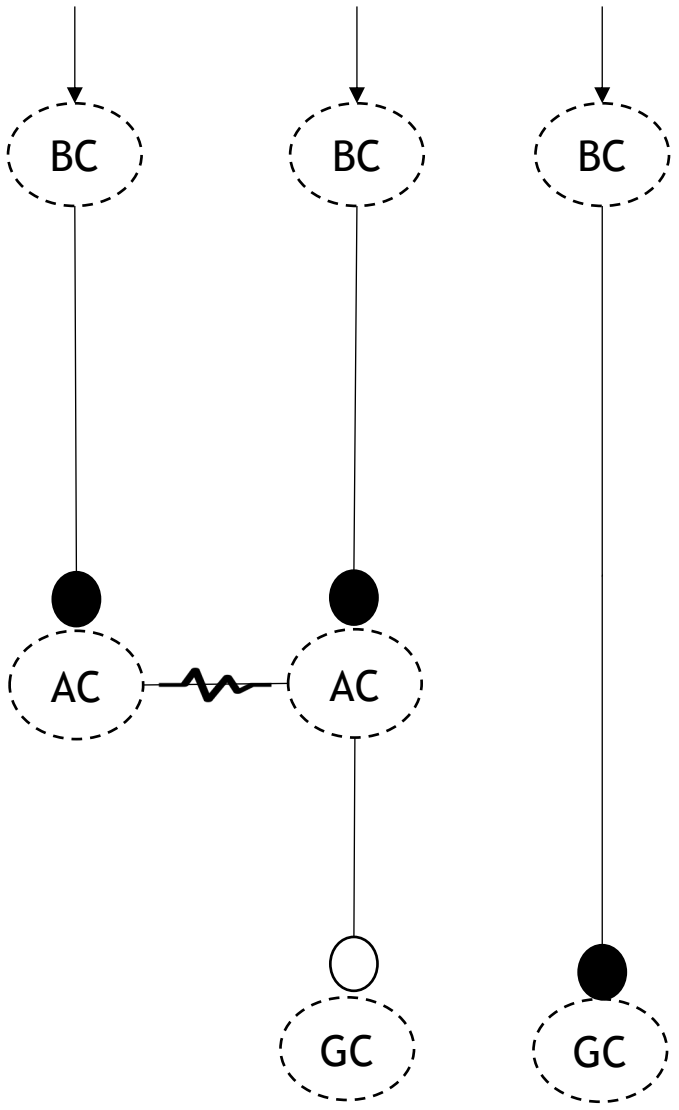
# Graph

Connectivity graph

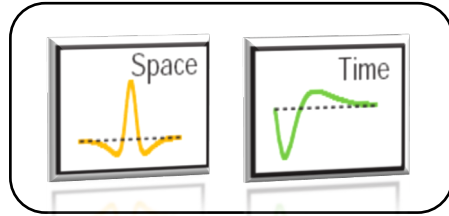
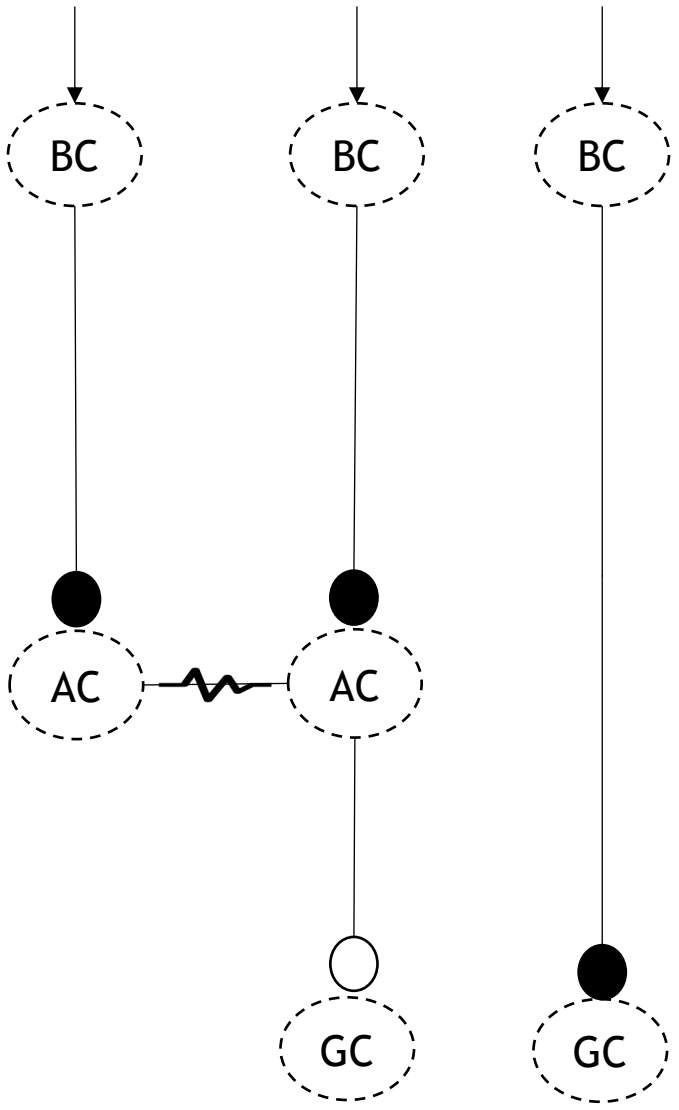


- Design a local circuit with specific connectivity patterns
- Deploy it to the whole retina



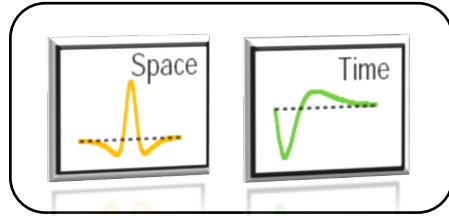
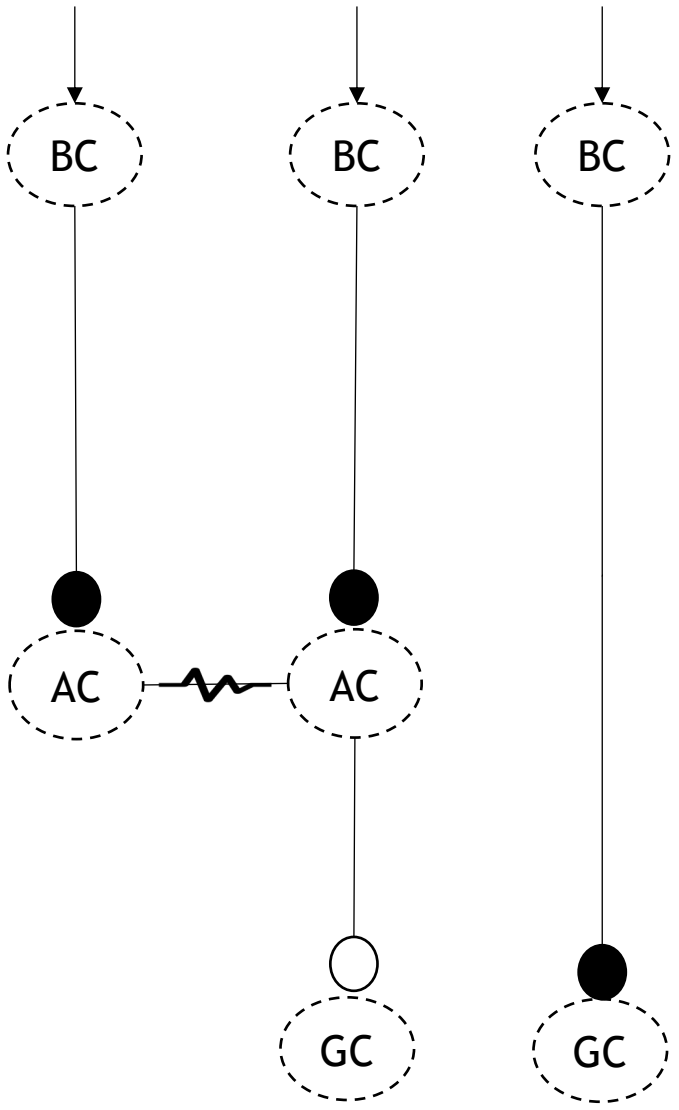


● ○ Chemical synapse  
— Electrical synapse



$$K(x, y, t) = K_S(x, y)K_T(t)$$

$$\int (S * K)(x, y, t)$$



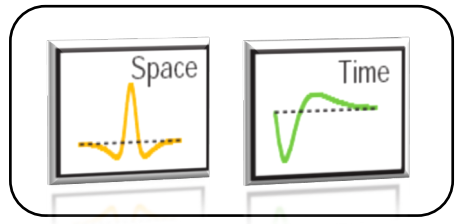
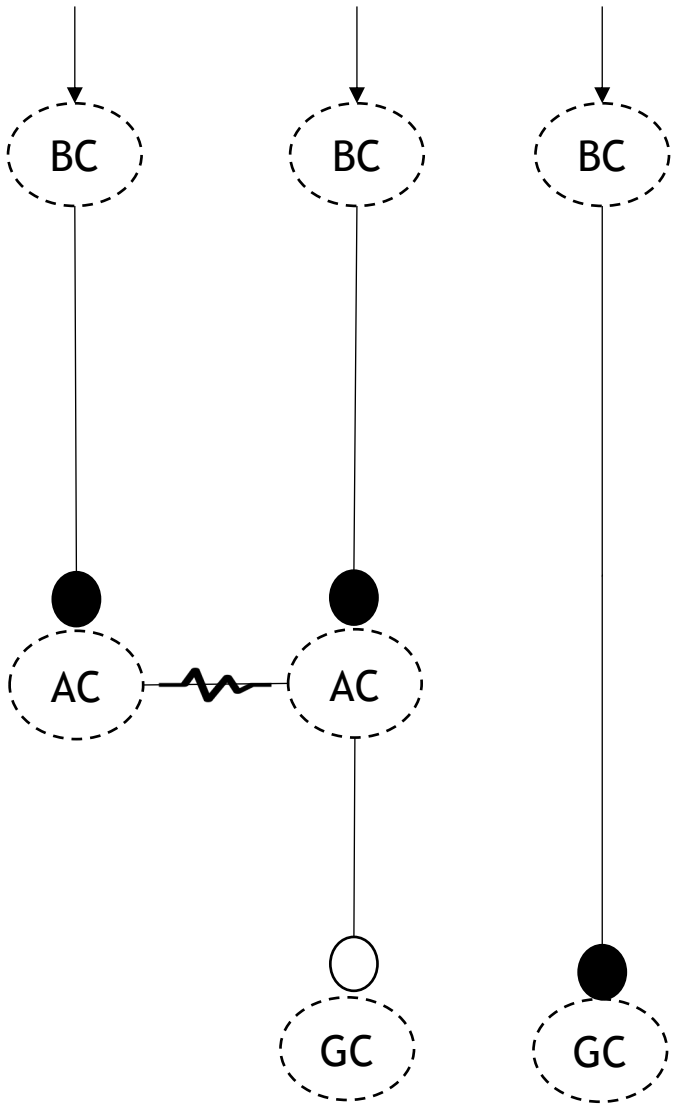
● ○ Chemical synapse  
 ~~~~~ Electrical synapse

$$K(x, y, t) = K_S(x, y)K_T(t)$$

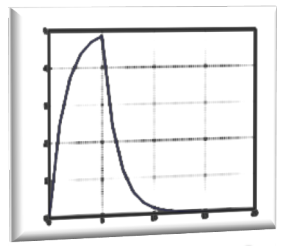
$$\int (S * K)(x, y, t)$$

$$I_{syn} = -g_{syn} (V_{post} - E_{syn})$$

$$I_{GAP} = -g_{GAP} (V_{post} - V_{pre})$$



● ○ Chemical synapse  
 ~~~~~ Electrical synapse



$$K(x, y, t) = K_S(x, y)K_T(t)$$

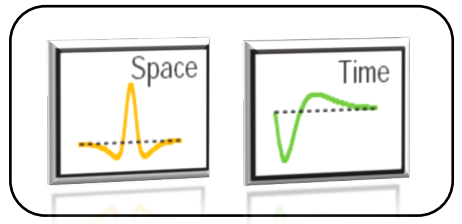
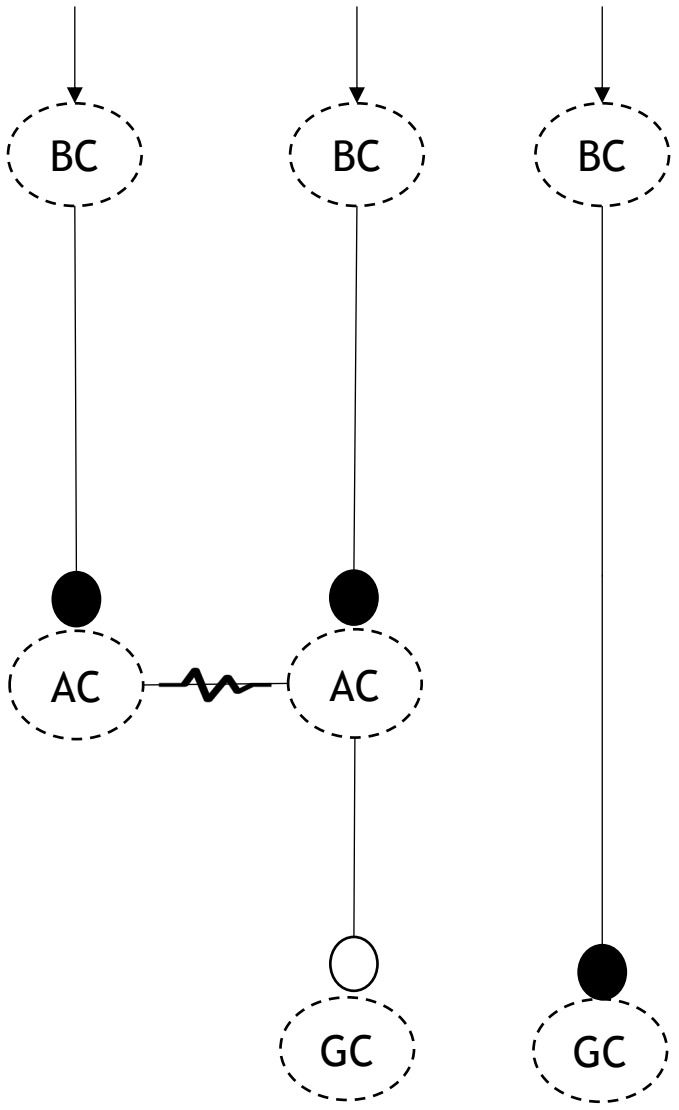
$$\int (S * K)(x, y, t)$$

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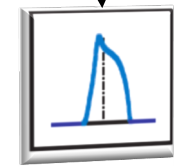
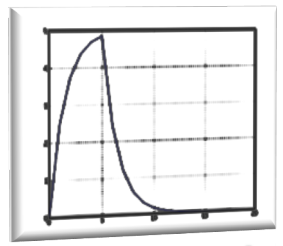
$$I_{GAP} = -g_{GAP} (V_{post} - V_{pre})$$

$$C \frac{dV}{dt} = -g_L (V - V_L) + I_{syn} + I_{ext} + I_{CNO}$$





● ○ Chemical synapse  
 ~~~~~ Electrical synapse



$$K(x, y, t) = K_S(x, y)K_T(t)$$



$$\int (S * K)(x, y, t)$$


$$I_{syn} = -g_{syn} (V_{post} - E_{syn})$$

$$I_{GAP} = -g_{GAP} (V_{post} - V_{pre})$$

$$C \frac{dV}{dt} = -g_L(V - V_L) + I_{syn} + I_{ext} + I_{CNO}$$

$$N_G(V) = \begin{cases} 0, & \text{if } (V \leq 0) \\ \alpha(V - \theta), & \text{if } (\theta \leq V \leq \frac{N_{max}}{\alpha + \theta}) \\ N_{max}, & \text{otherwise} \end{cases}$$


 **All Items**

Identifier Acetylcholine  
 Settings  
 Extend


**Macular repository** macular

Model functions

gAch(A, gA, gammaA)

doc Actylcholine conductance for nicotinic receptors


format SymPy


 Edition  $gA * A^{**2} / (gammaA + A^{**2})$   
 Formula


All

Acetylcholine


+ New

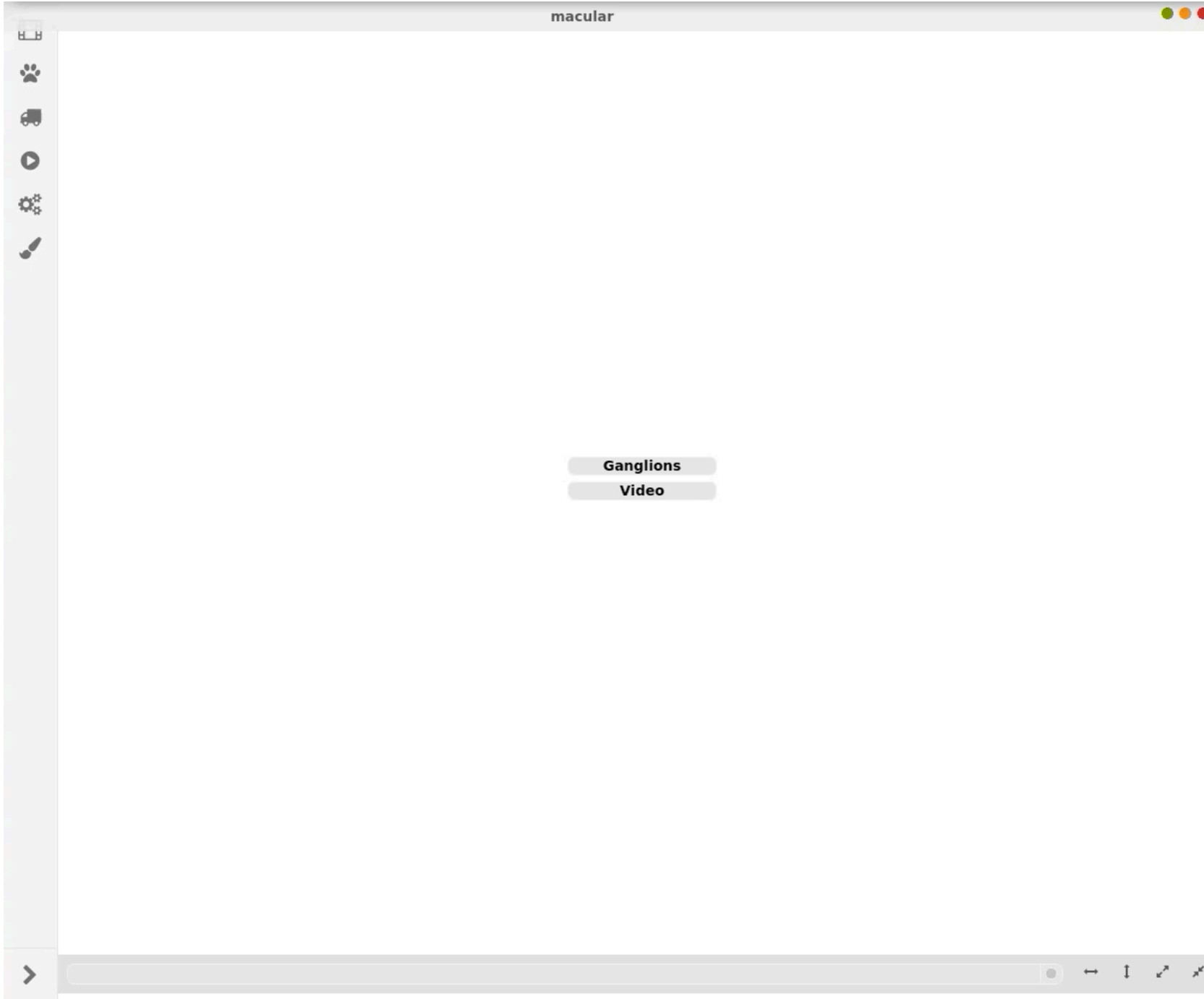
 File

 Themes

 Choose Theme >

Model synaptic current

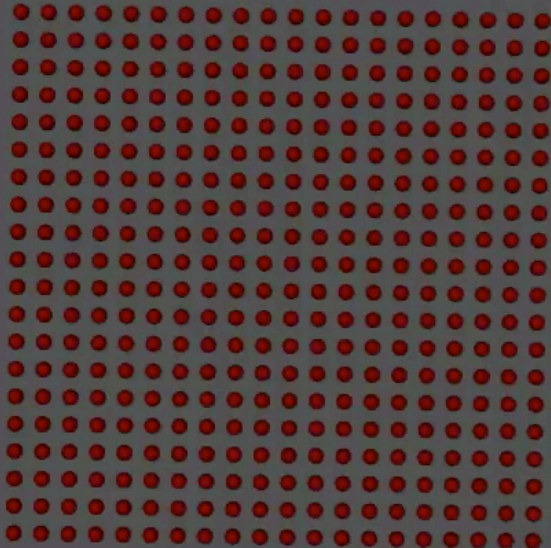
 Cancel Save



**Simulator**

Graph Generator

0.00 0.00 0.00 0.00 0.00



Canvas - 2

Simulator



| Input Video       | OPL Receptor Current |
|-------------------|----------------------|
|                   |                      |
| GC Output Current | OPL Output Current   |
|                   |                      |

Video - 1

**All Items**

Video Input

Browse Video **test\_small**

Graph Input

**object\_motion\_graph3**

Worker settings

Cone Bipolar On >

Cone Bipolar Off >

Rod Bipolar On >

Prosthesis >

Controls

Run Simulation **Run**

Reset Simulation **Run**

Frame Rate **10**

Integration timestep **105000**

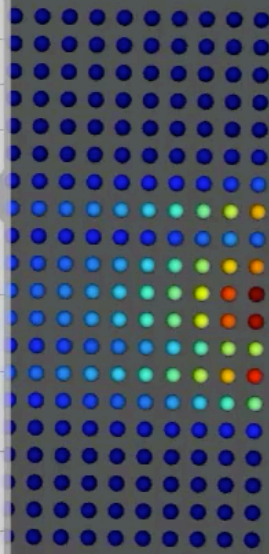
Save/Restore parameters

Save frequency **0**

Model **Prosthesis**

Parameters

- MorrisLecar >
- HodgkinHuxley >
- SAC >
- BipolarGainControl >
- MorrisLecarAch >



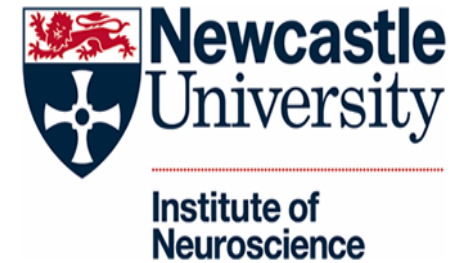
| Input Video       | OPL Receptor Current |
|-------------------|----------------------|
|                   |                      |
| GC Output Current | OPL Output Current   |
|                   |                      |

Video - 1

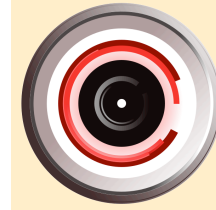
Simulator

# Acknowledgements

Prof. Evelyne Sernagor  
Dr. Gerrit Hilgen



Biovision team



Dr. Bruno Cessac  
AMDT team

LEVERHULME  
TRUST \_\_\_\_\_

The background features several microscopy images of cells expressing green fluorescent protein (GFP). The cells are shown in various stages of division or growth, with bright green spots indicating the nuclei and a network of fine green lines representing the cytoskeleton. The images are arranged in a hexagonal pattern on a black background. A dark grey rectangular box with rounded corners is overlaid on the right side of the image, containing the text 'Thank you!' and 'Questions?' in white.

**Thank you!**

**Questions?**