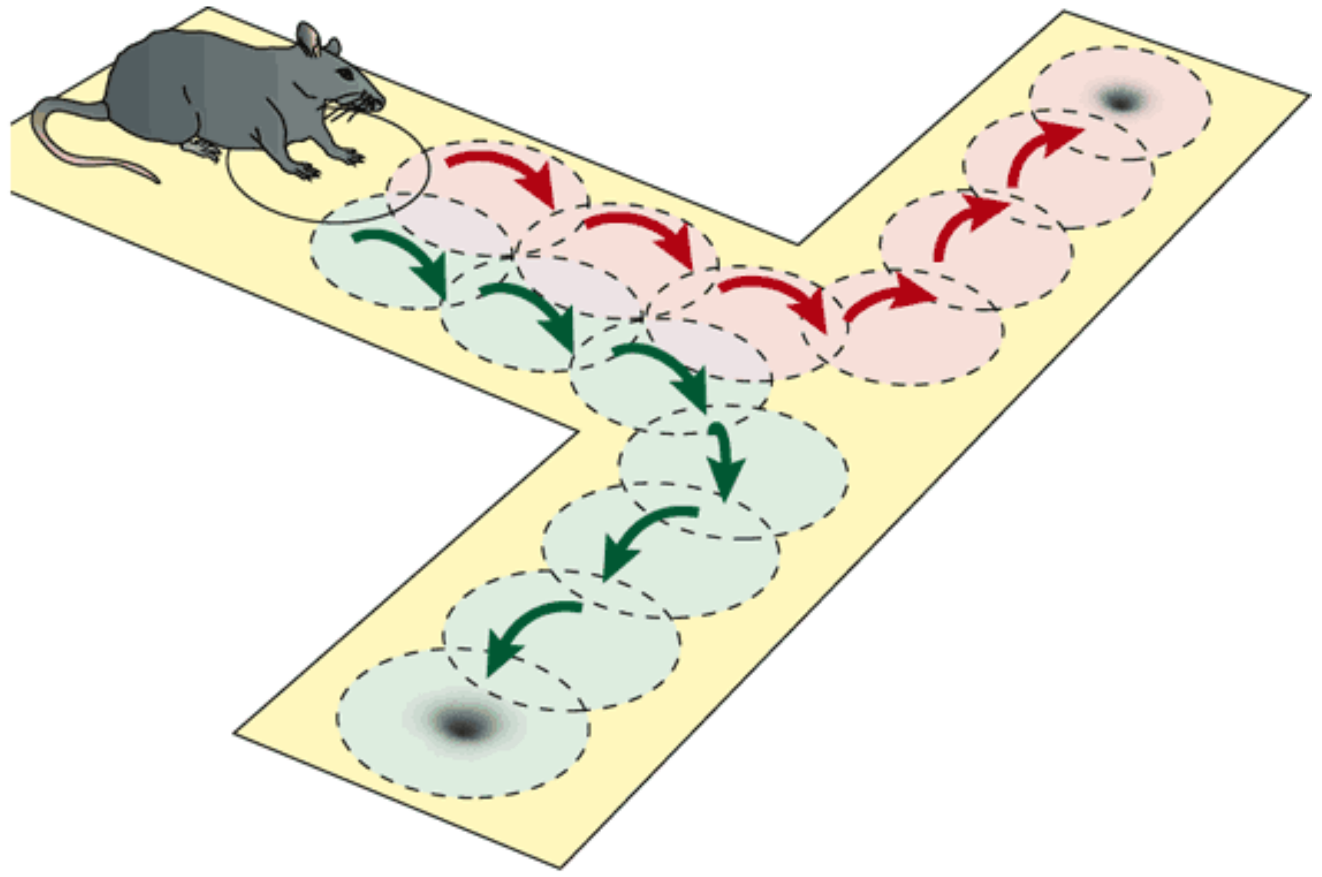
Full-scale biophysical modeling of hippocampal networks during spatial navigation



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Project PI: Ivan Soltesz

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Introduction

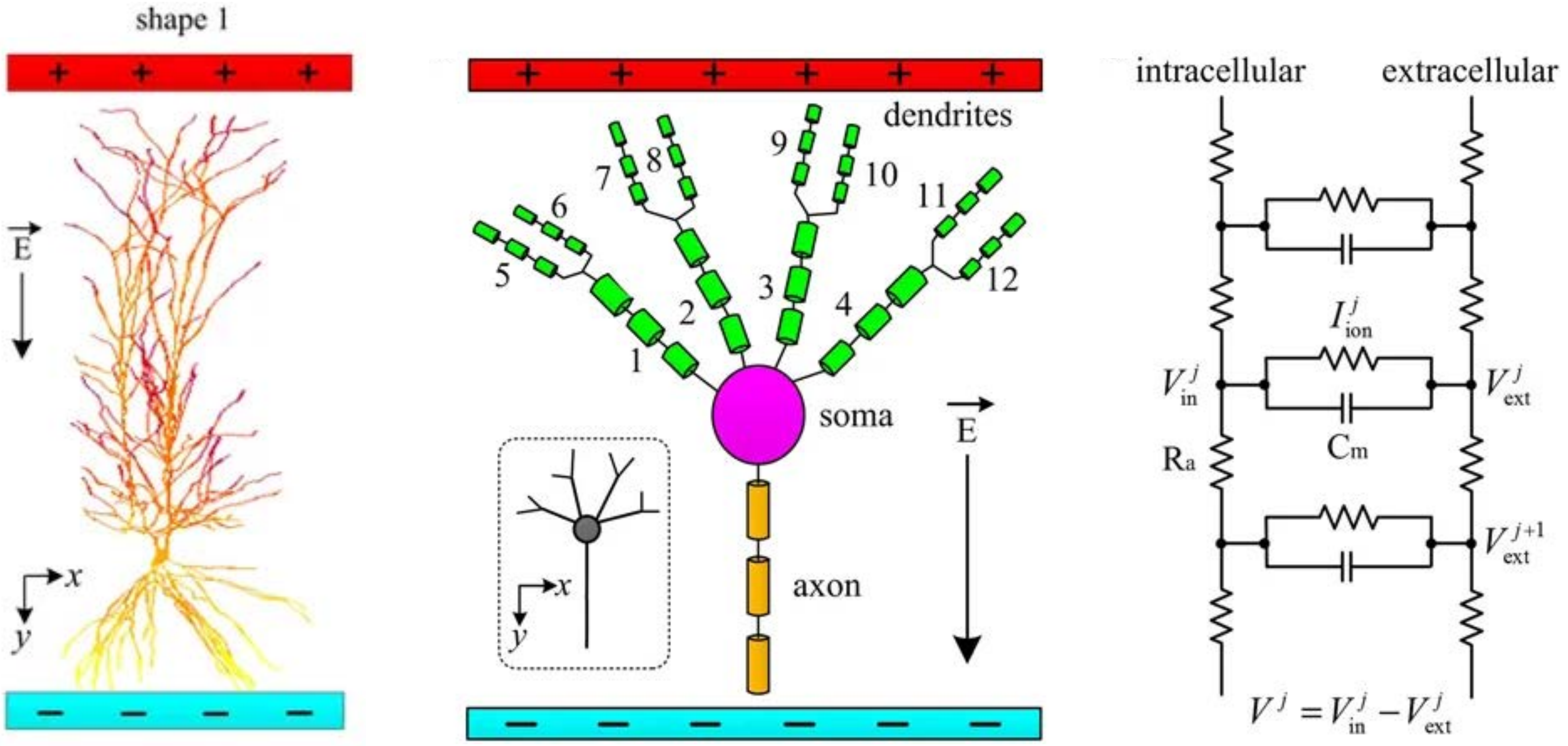
I use Blue Waters to construct, simulate and analyze full-scale biophysical computational models of the rodent hippocampus and understand the role of the neural circuitry in processing spatial information.

- **Full-scale**: 1:1 correspondence between model neurons and biological system (completed model will have approximately 2×10^6 neurons and 4×10^{10} connections)

- **Biophysical**: detailed neuronal morphology, synaptic connections, equations of ion channel and synapse currents (each model neuron can have thousands of state variables)

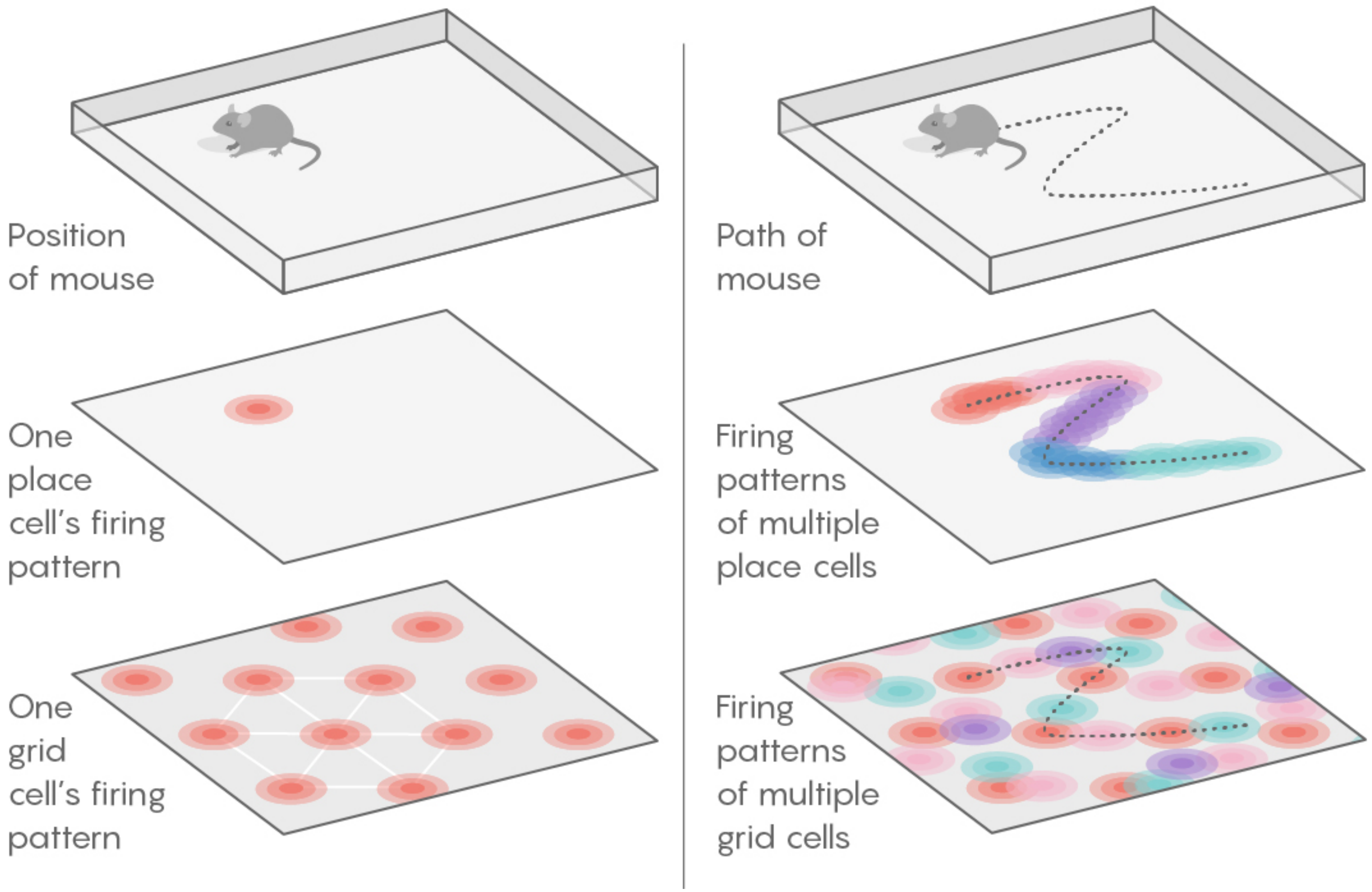
- **Hippocampus**: part of the brain responsible for learning, memory, and spatial navigation

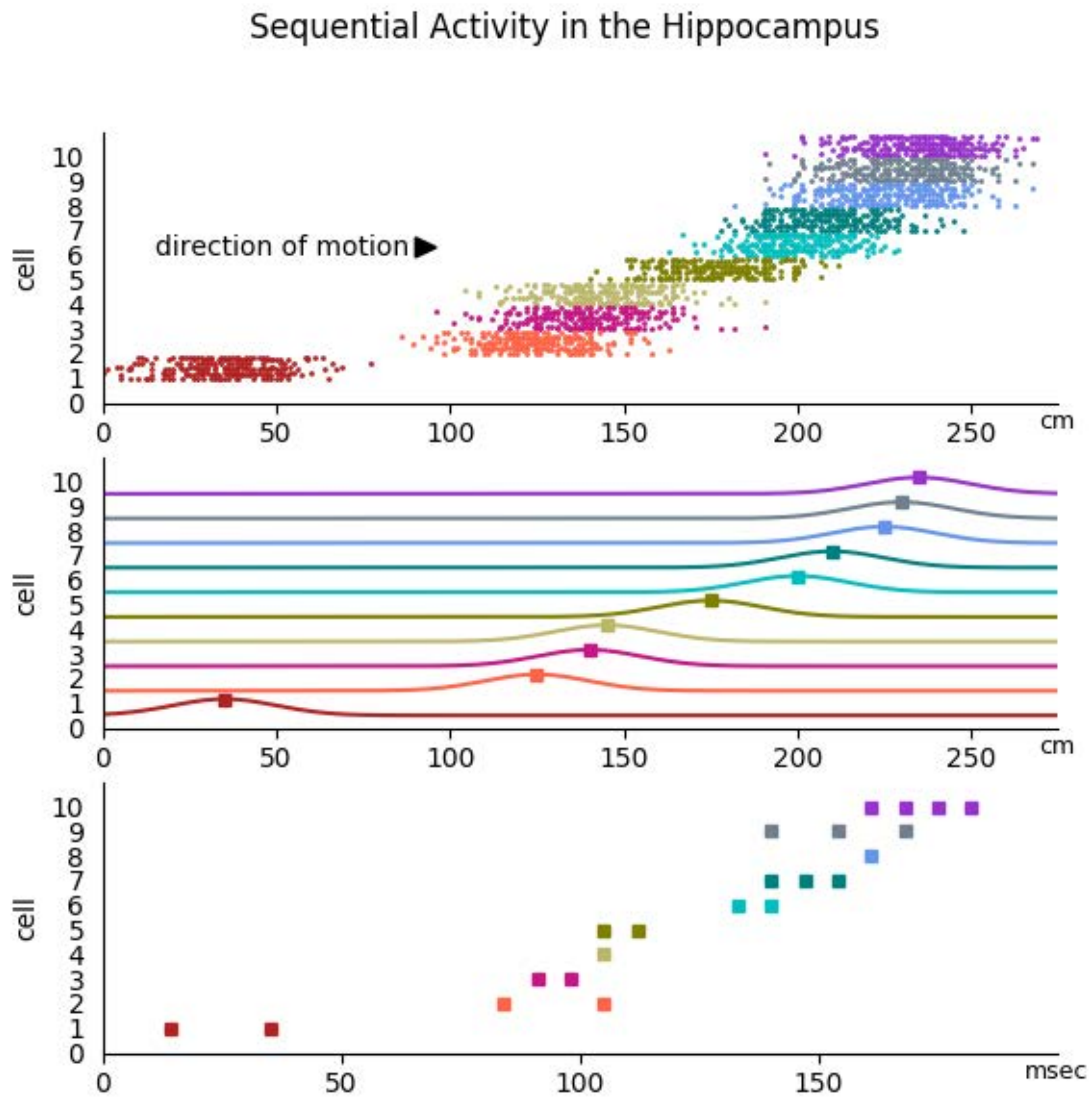
Introduction



Yi et al., 2016

The brain's navigational system

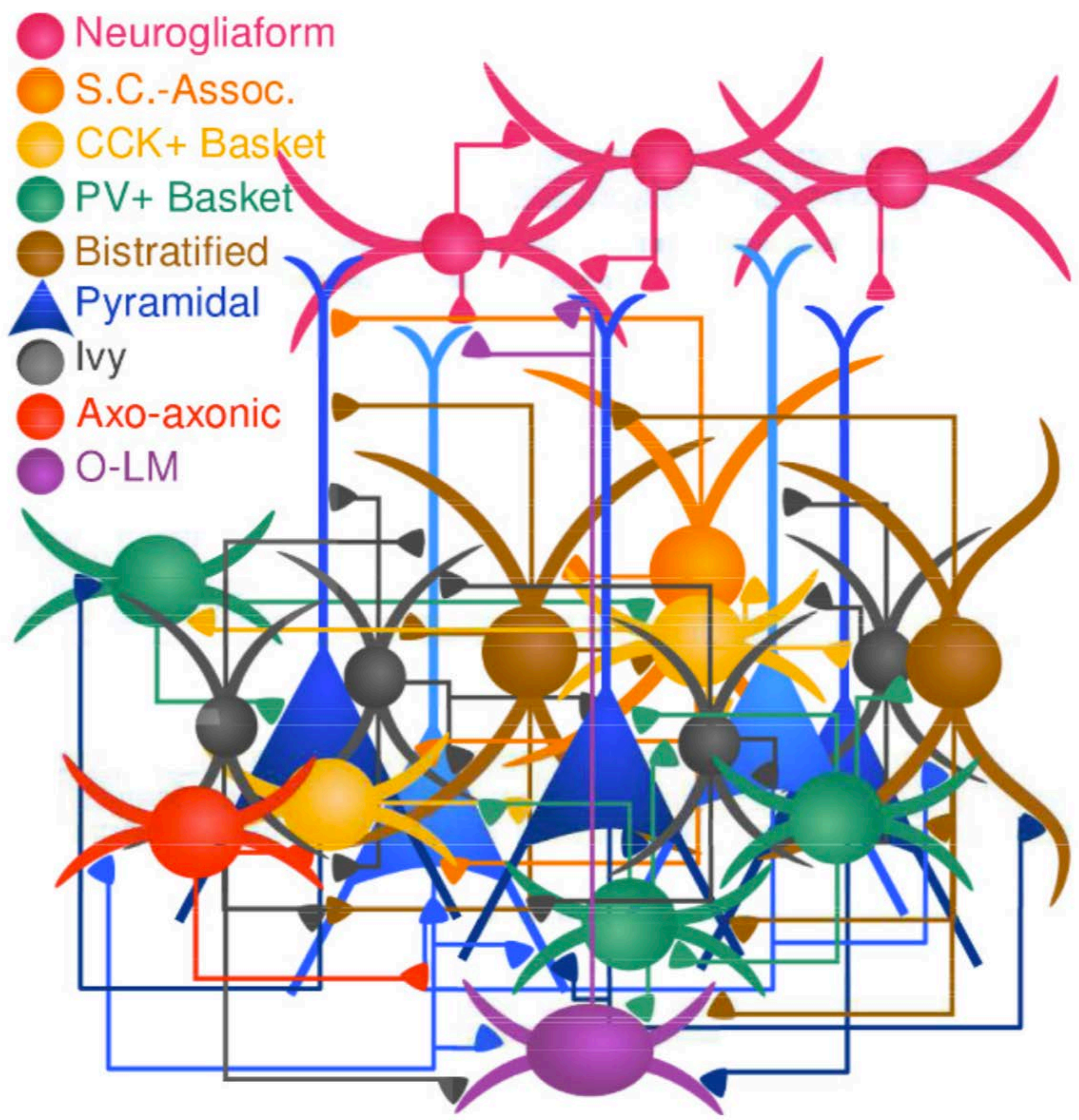


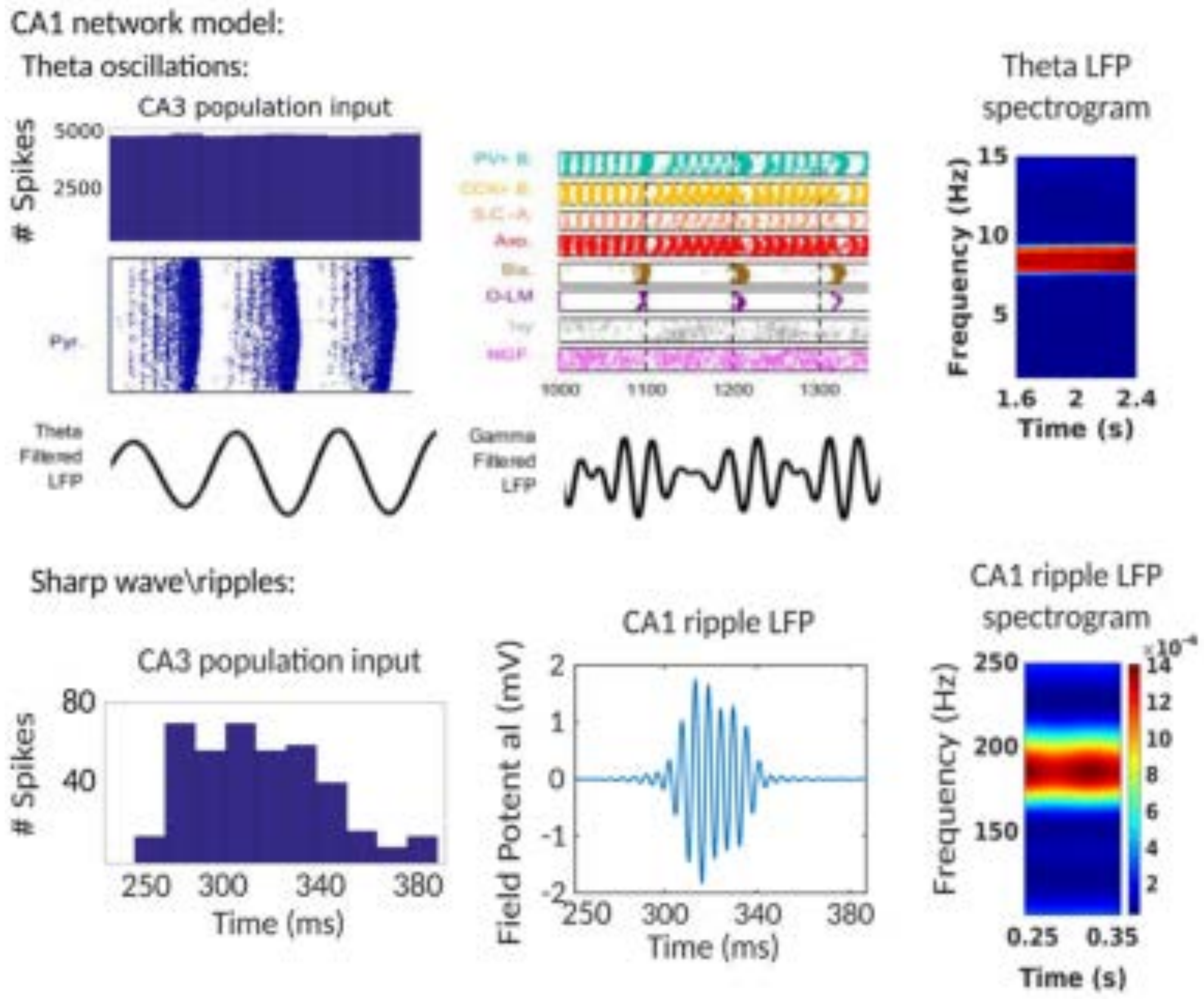


Cellular diversity and recurrent connectivity enable rhythm generation in a full scale model of CA1

Biological realism:	
	High
	Intermediate
	Low

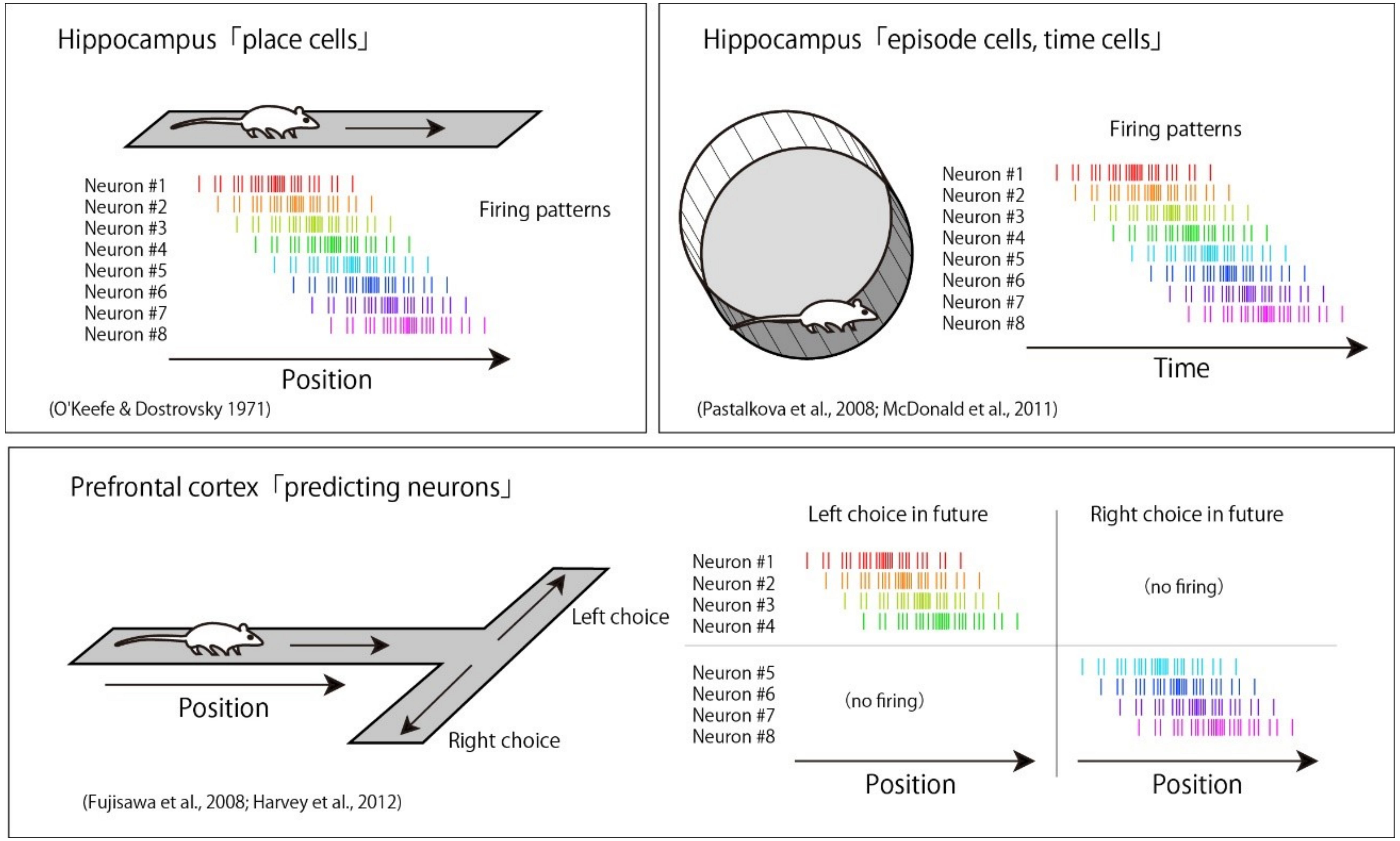
	Previous work
Model:	Bezaire, Raikov & Soltesz, 2016
Network configuration:	CA1
# of principal cells	>300,000
# of synapses / principal cell	~20,000
Cell excitability model	Biophysical
# of cell types	9
Cell-type-specific connectivity	Distance-dependent
Input pattern	Constant
Input strengths	Equal
Long-term plasticity	None
Network output:	
Rhythmicity	Theta, gamma, ripple
Output selectivity	None
Output fraction active (%)	~100%
Key insight:	Cellular and circuit mechanisms of rhythm generation





Bezaire, M. J., Raikov, I., Burk, K., Vyas, D., & Soltesz, I. *eLife*, 2016.

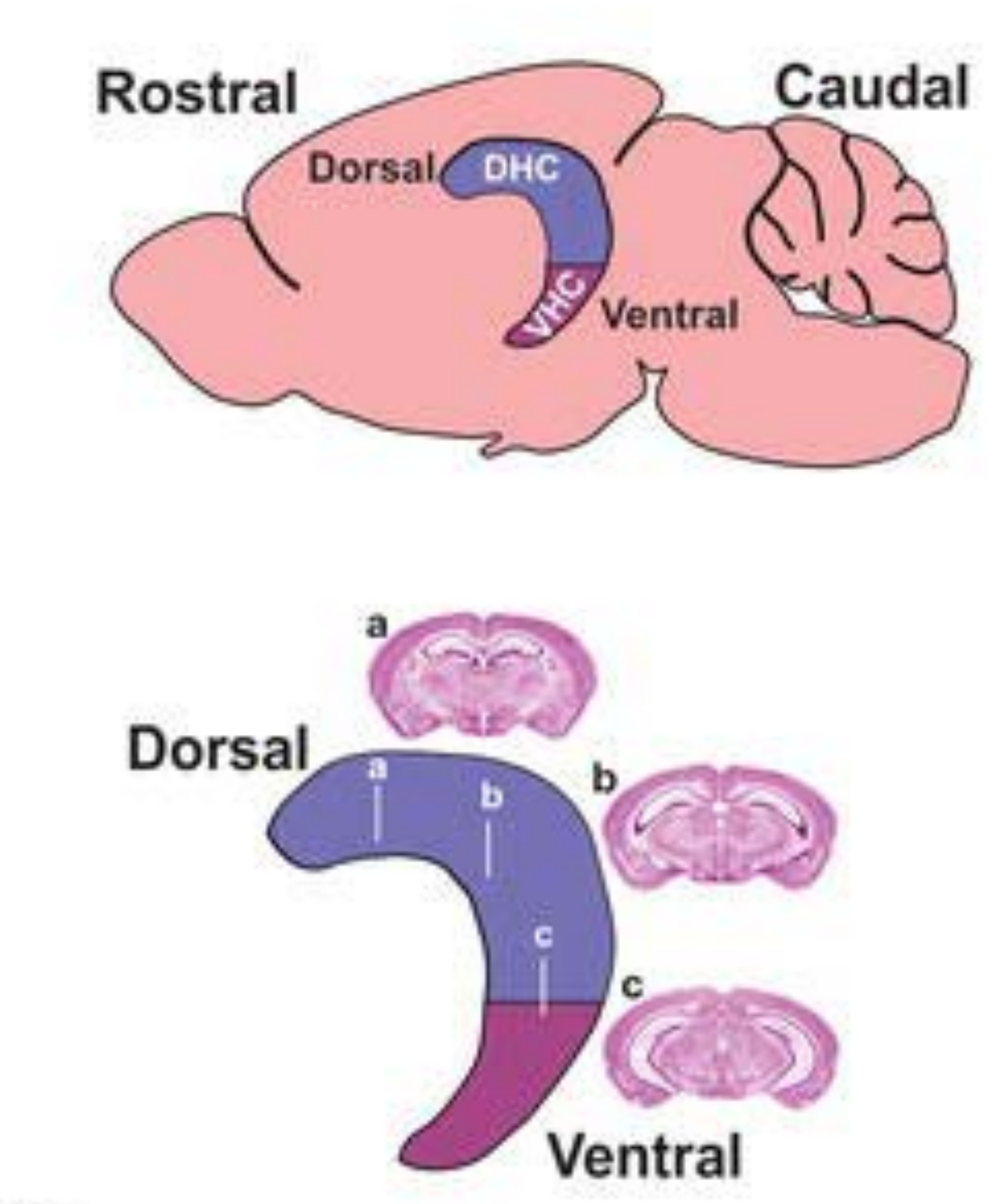
Diversity of information representation in the hippocampus and cortex

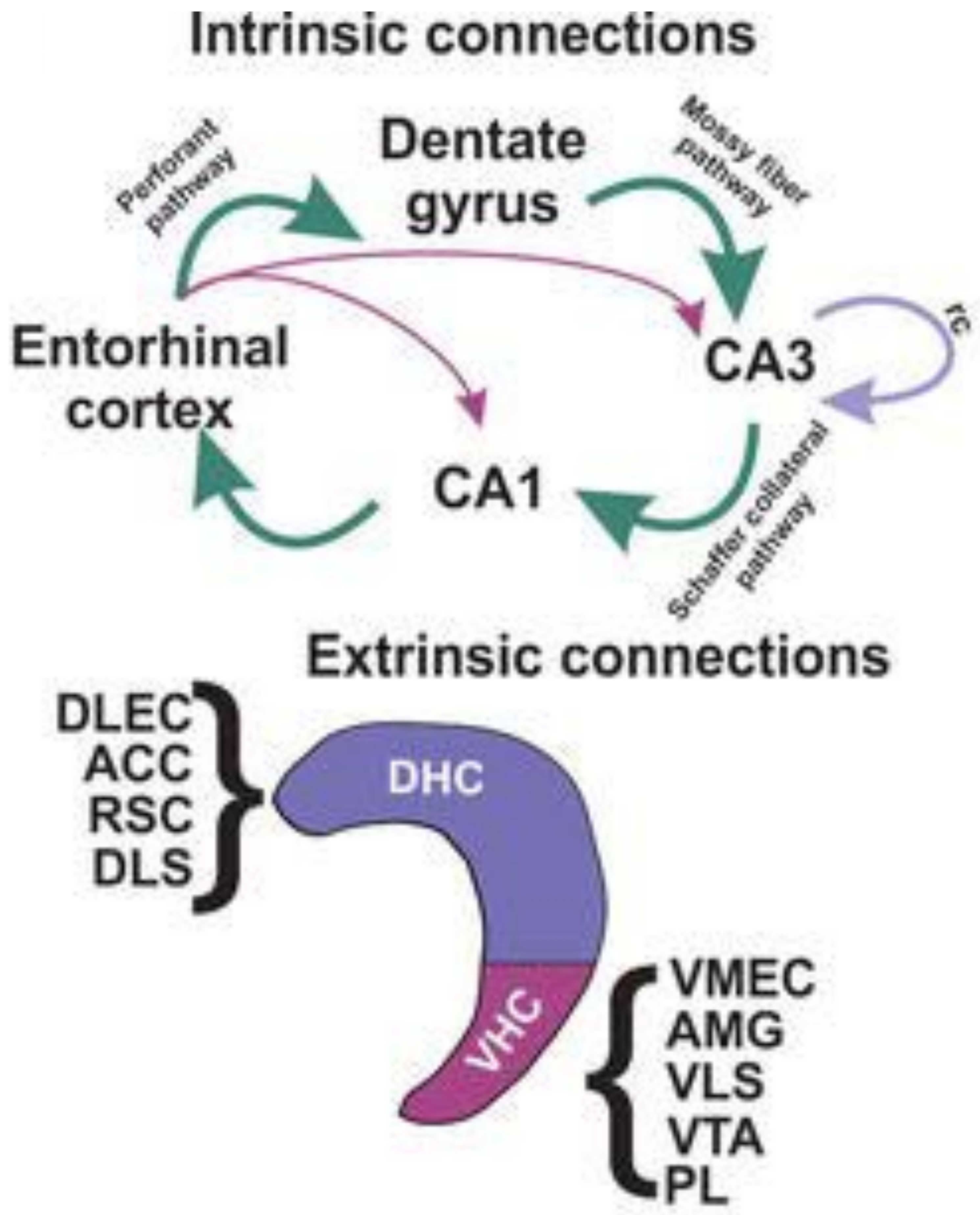


Fujisawa et al., 2017

- neuronal sequences are organized internally and do not require sensory inputs or motor outputs
- the internally organized sequences can represent spatial and temporal information and planned behaviors corresponding to the near future.
- The aim of this project is to decipher the cellular and network mechanisms of the formation of population activity sequences that represent spatiotemporal information.

Topographical connectivity in the hippocampus



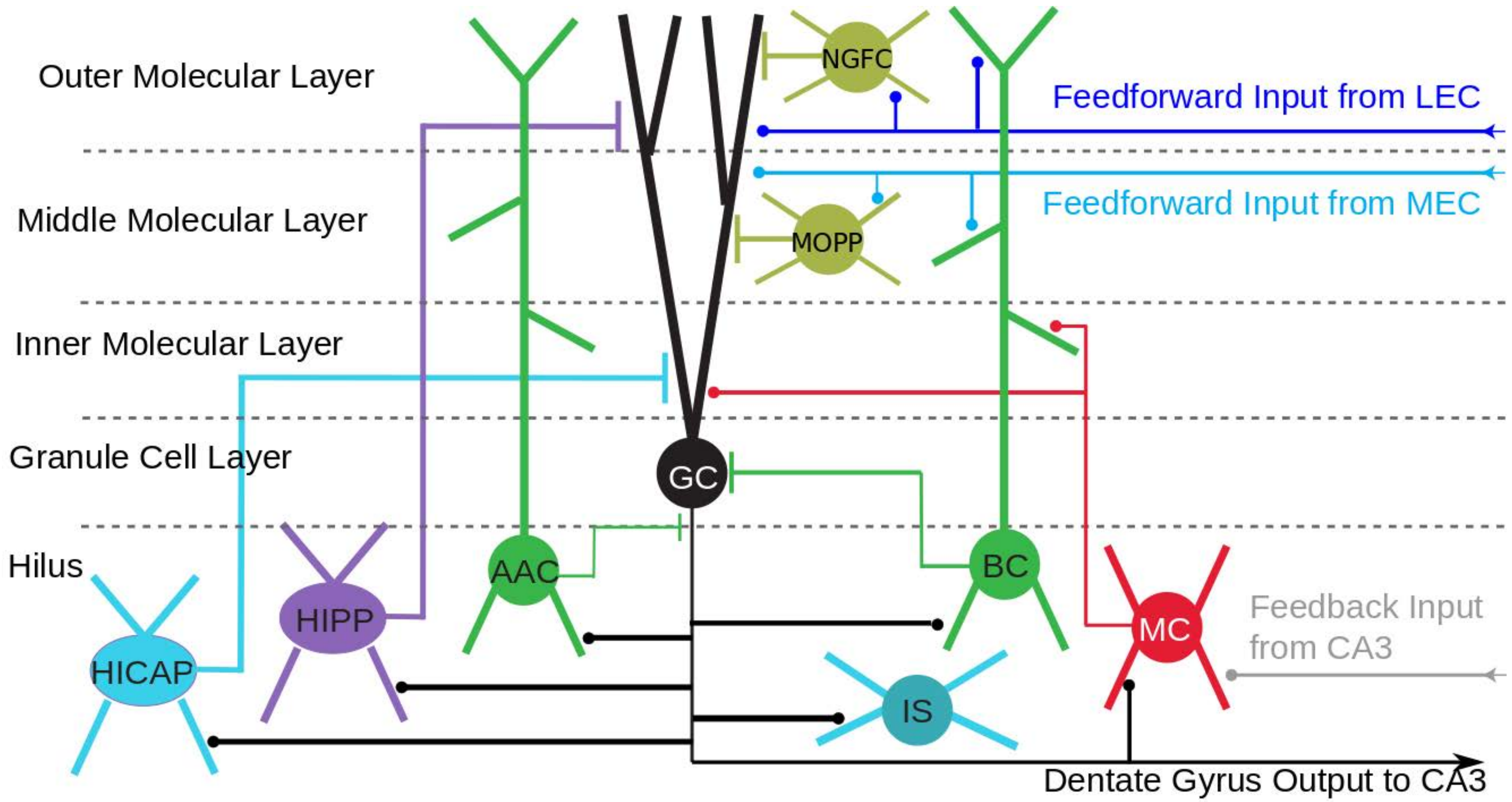


Harland, Contreras and Fellous, 2017

Large-scale biophysical model of spatial coding in the hippocampal dentate gyrus

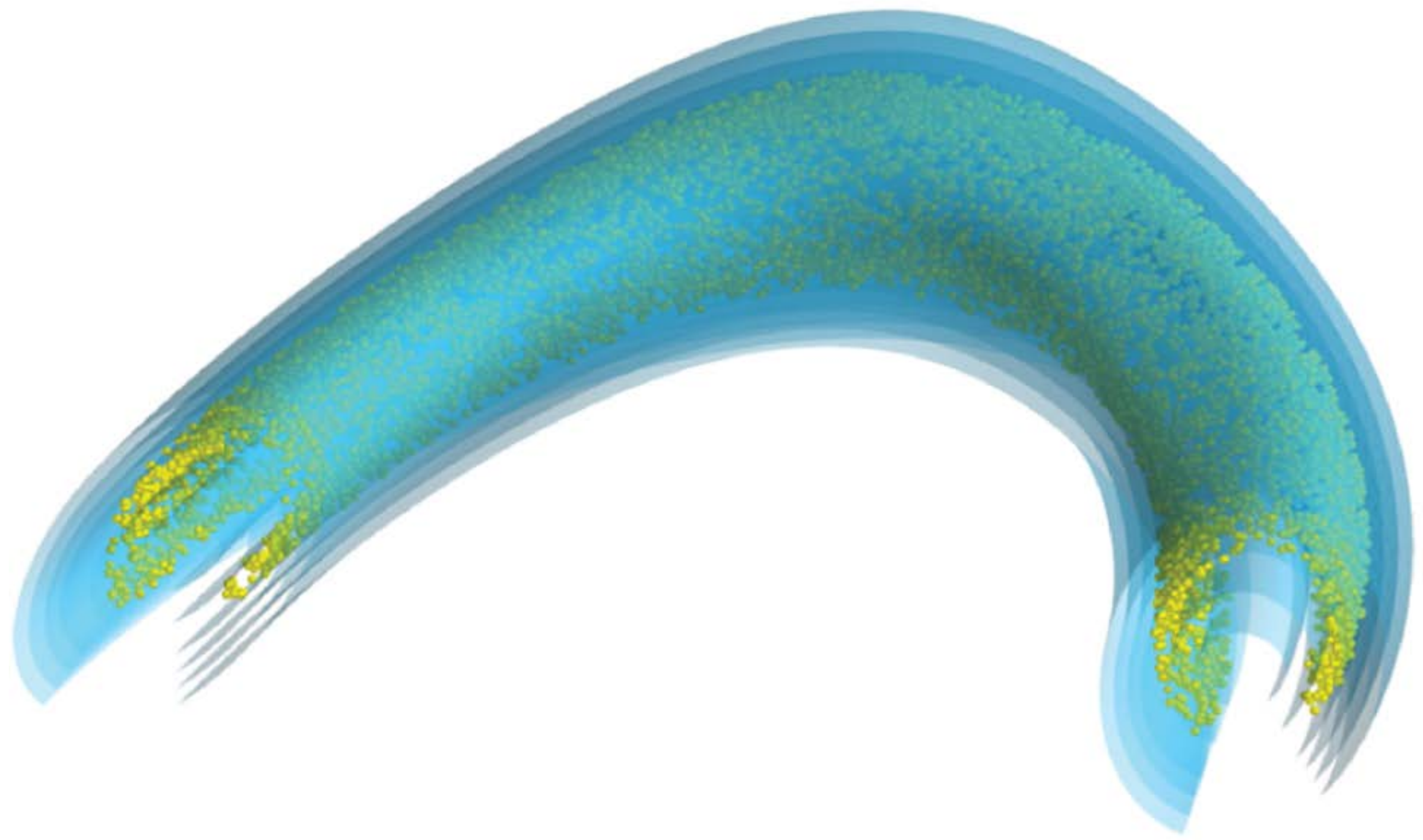
Biological realism:	
High	* In progress
Intermediate	
Low	

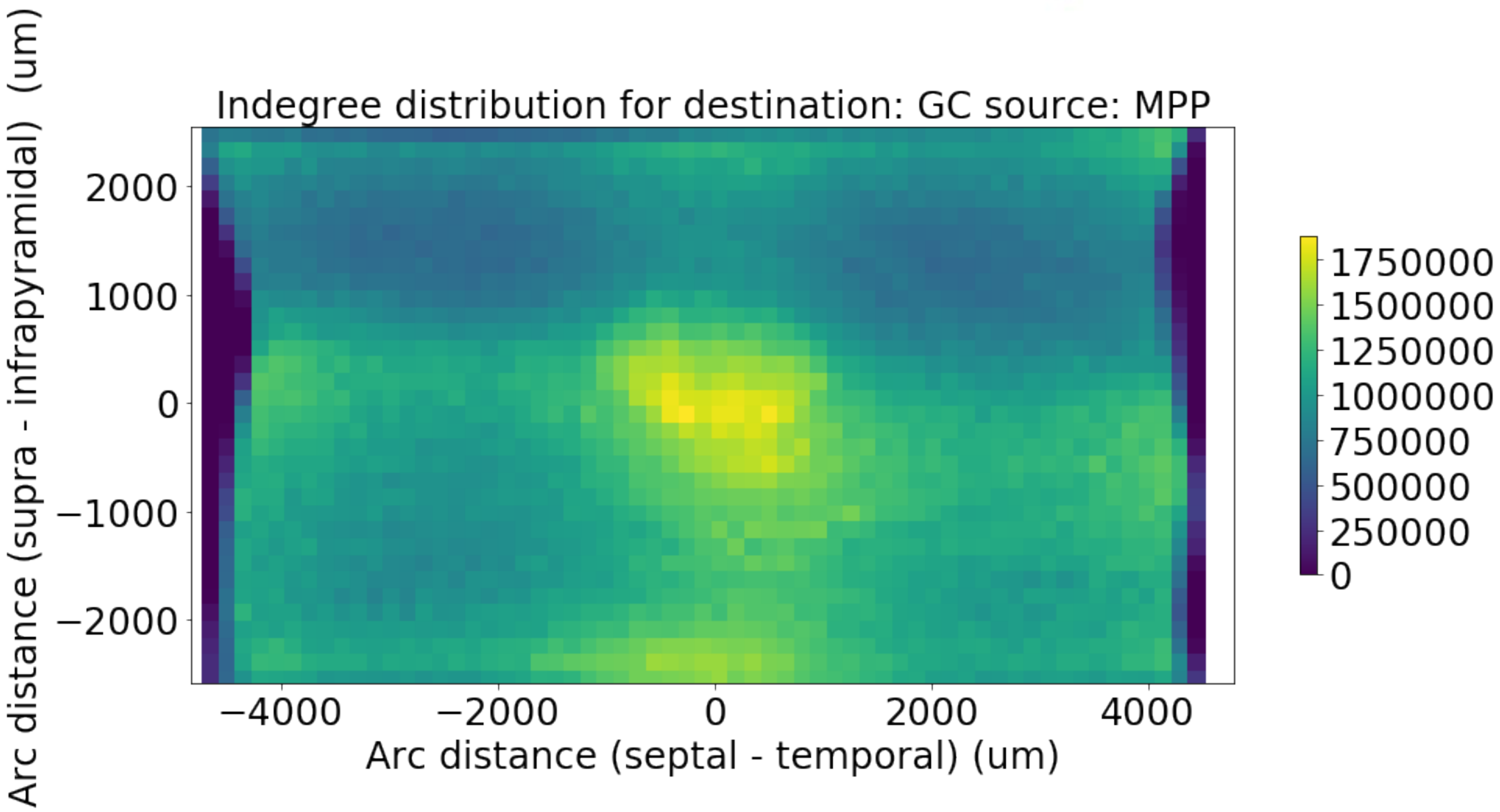
	Previous work
Model:	Raikov, Milstein & Soltesz
Network configuration:	DG
# of principal cells	1,000,000
# of synapses / principal cell	~10,000
Cell excitability model	Biophysical
# of cell types	9
Cell-type-specific connectivity	Distance-dependent
Input pattern	Selective (grid + place)
Input strengths	* History-dependent
Long-term plasticity	None
Network output:	
Rhythmicity	Theta, gamma
Output selectivity	* Realistic anatomical gradient of field widths
Output fraction active (%)	* <2% GC, >15% MC
Key insight:	Role of feedback excitation from mossy cells in regulating sparsity and selectivity in the dentate gyrus.

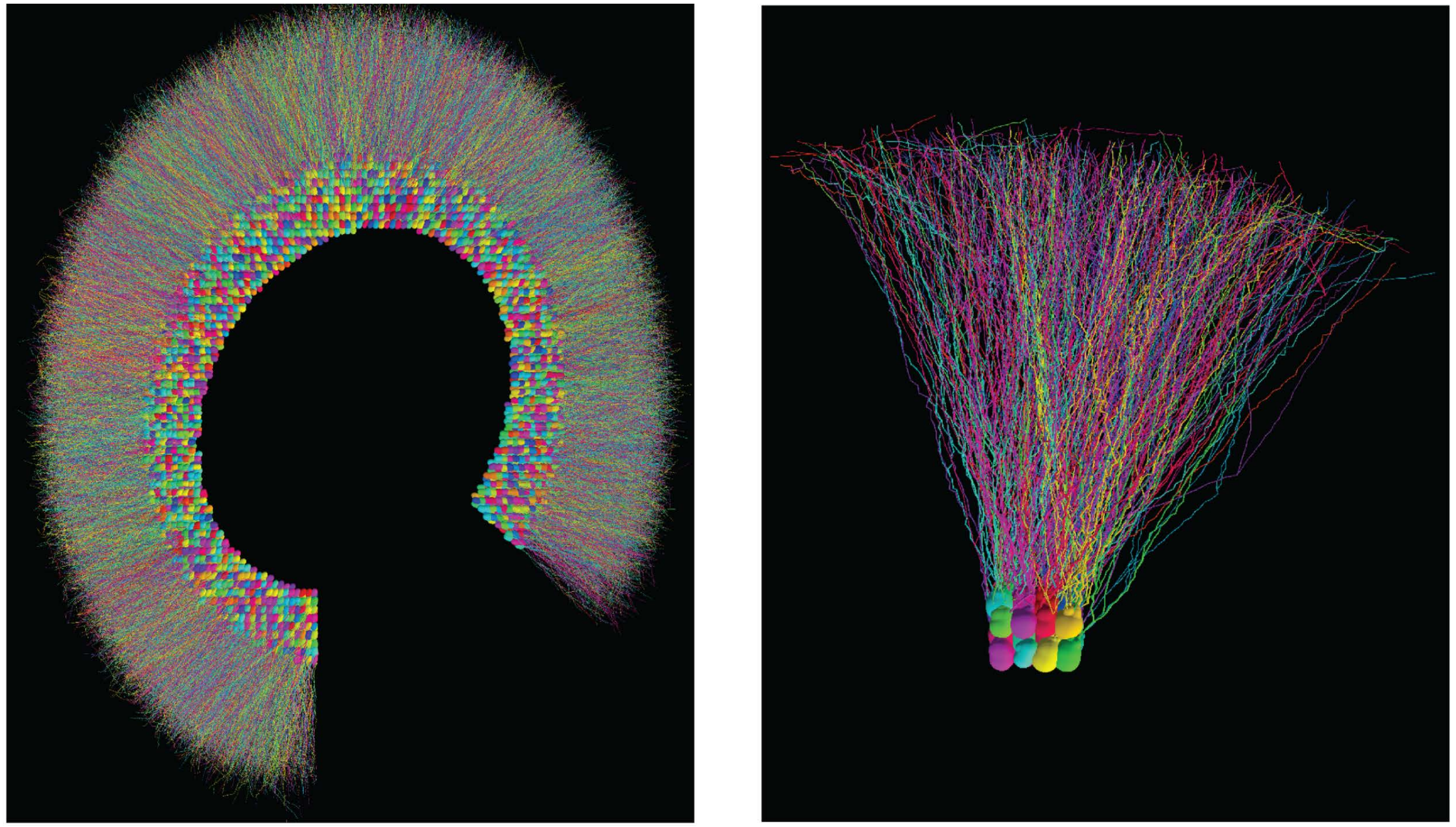


Raikov, I., Milstein, A. D., Ng G., Hadjiabadi, D. & Soltesz, I. *Unpublished*, 2019.

Realistic geometry in a full scale model of the dentate gyrus



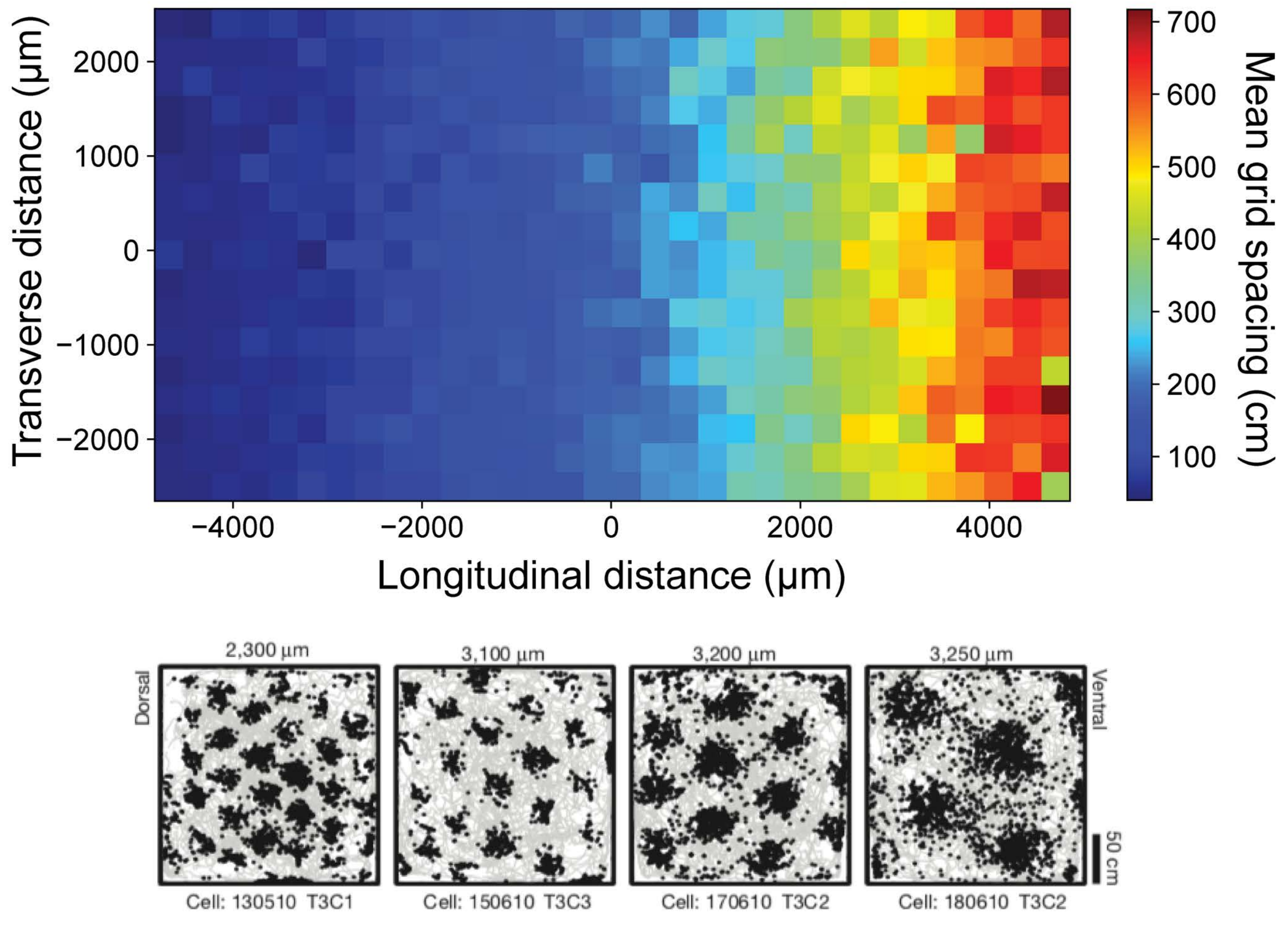




Schneider et al., *PloS Comp Biol*, 2014

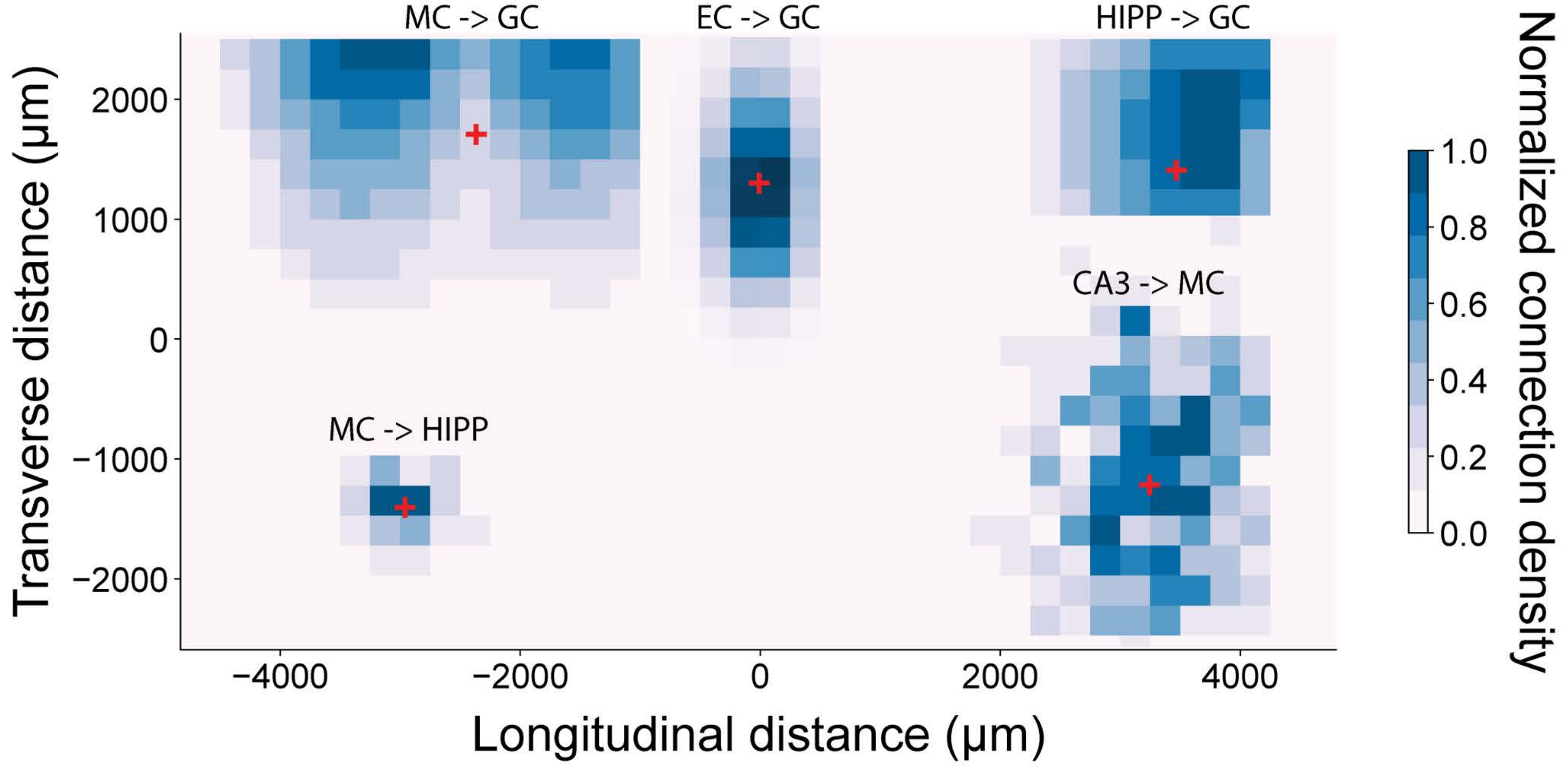
large-scale biophysical model of the hippocampal dentate gyrus

Topography of spatial inputs to the hippocampus from entorhinal grid cells



From Stensola et al., *Nature*, 2012.

Cell-type-specific distance-dependent connectivity



Raikov, I., Milstein, A. D., Ng G., Hadjiabadi, D. & Soltesz, I. *Unpublished*, 2019.

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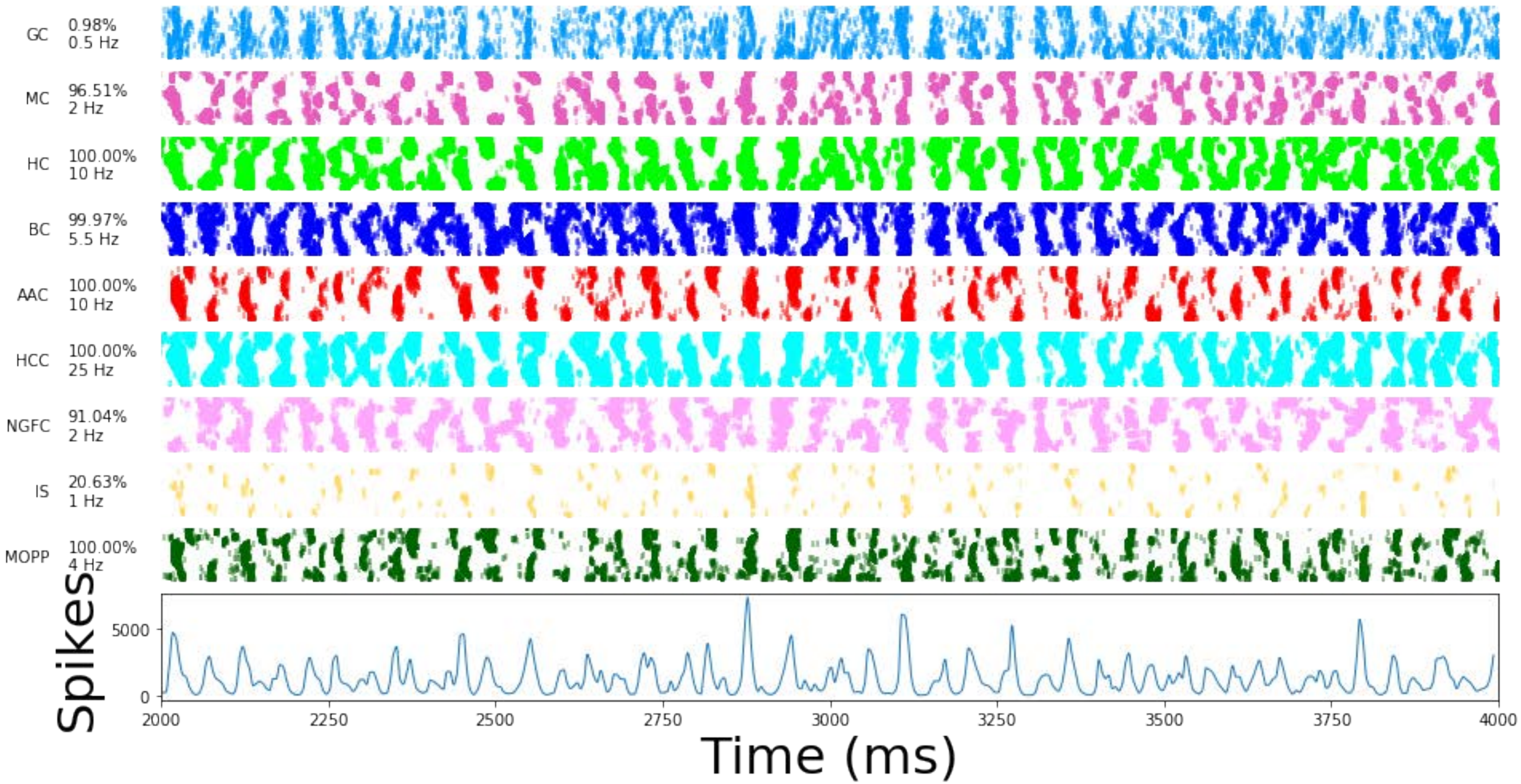
Spatial selectivity and sparsity of dentate gyrus model



Raikov, I., Milstein, A. D., Ng G., Hadjiabadi, D. & Soltesz, I. *Unpublished*, 2019.

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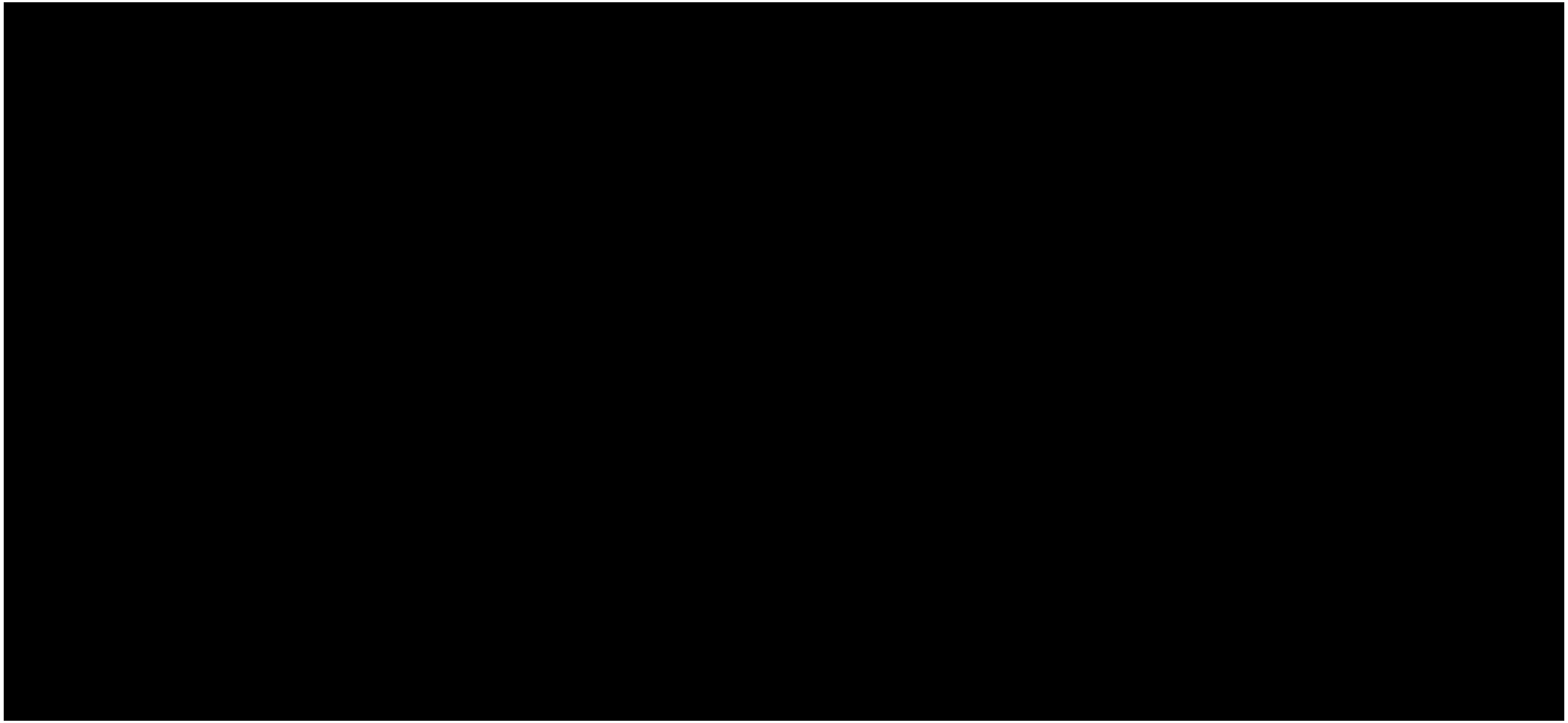

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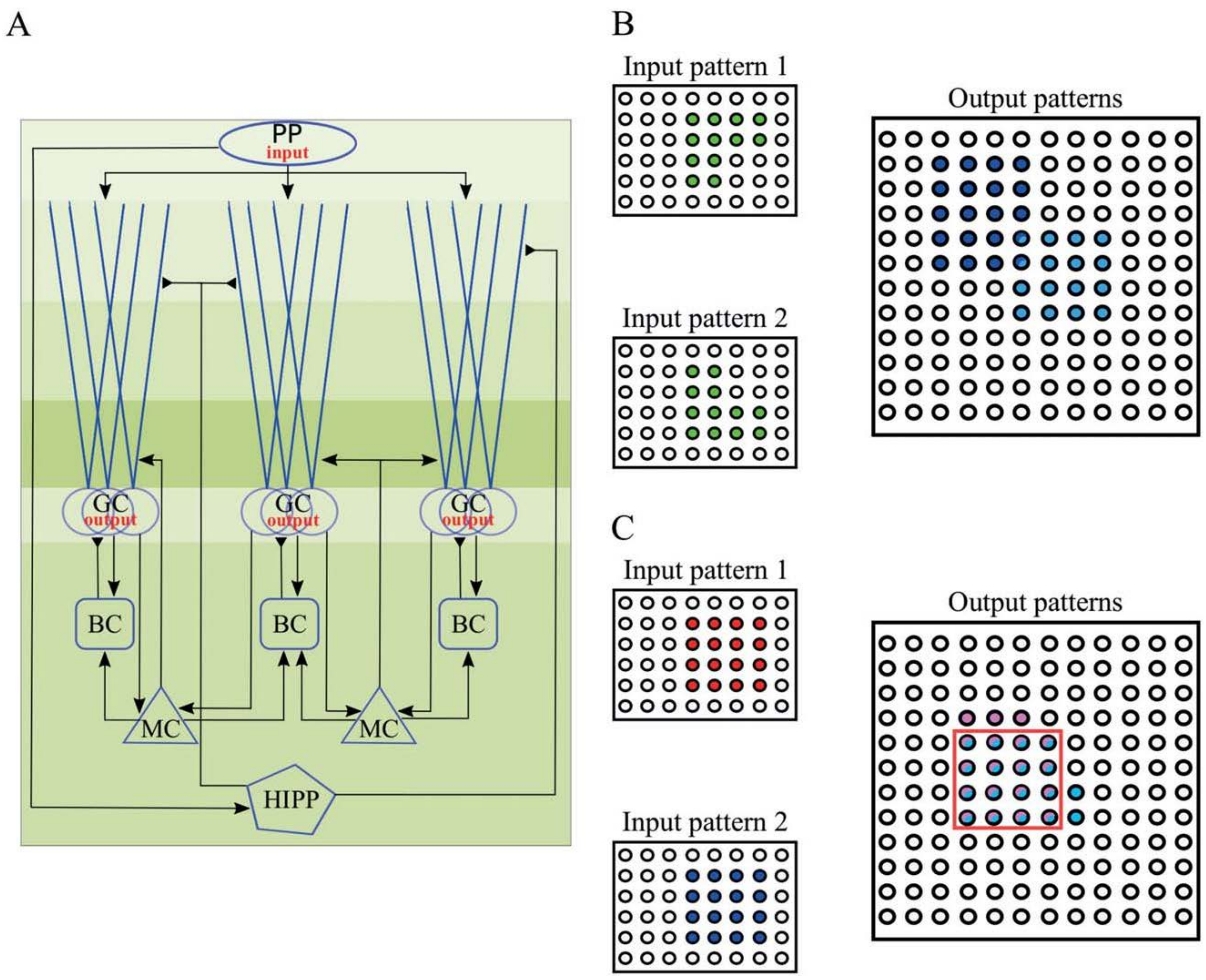
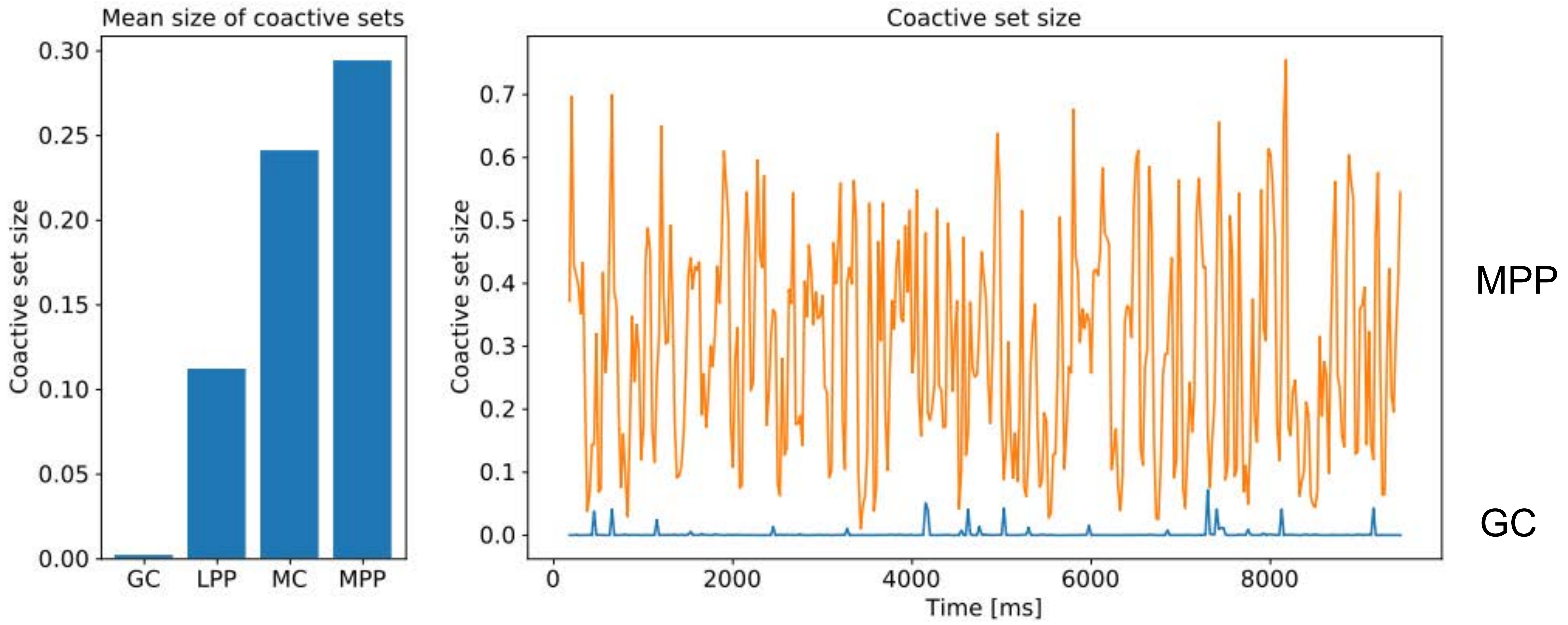
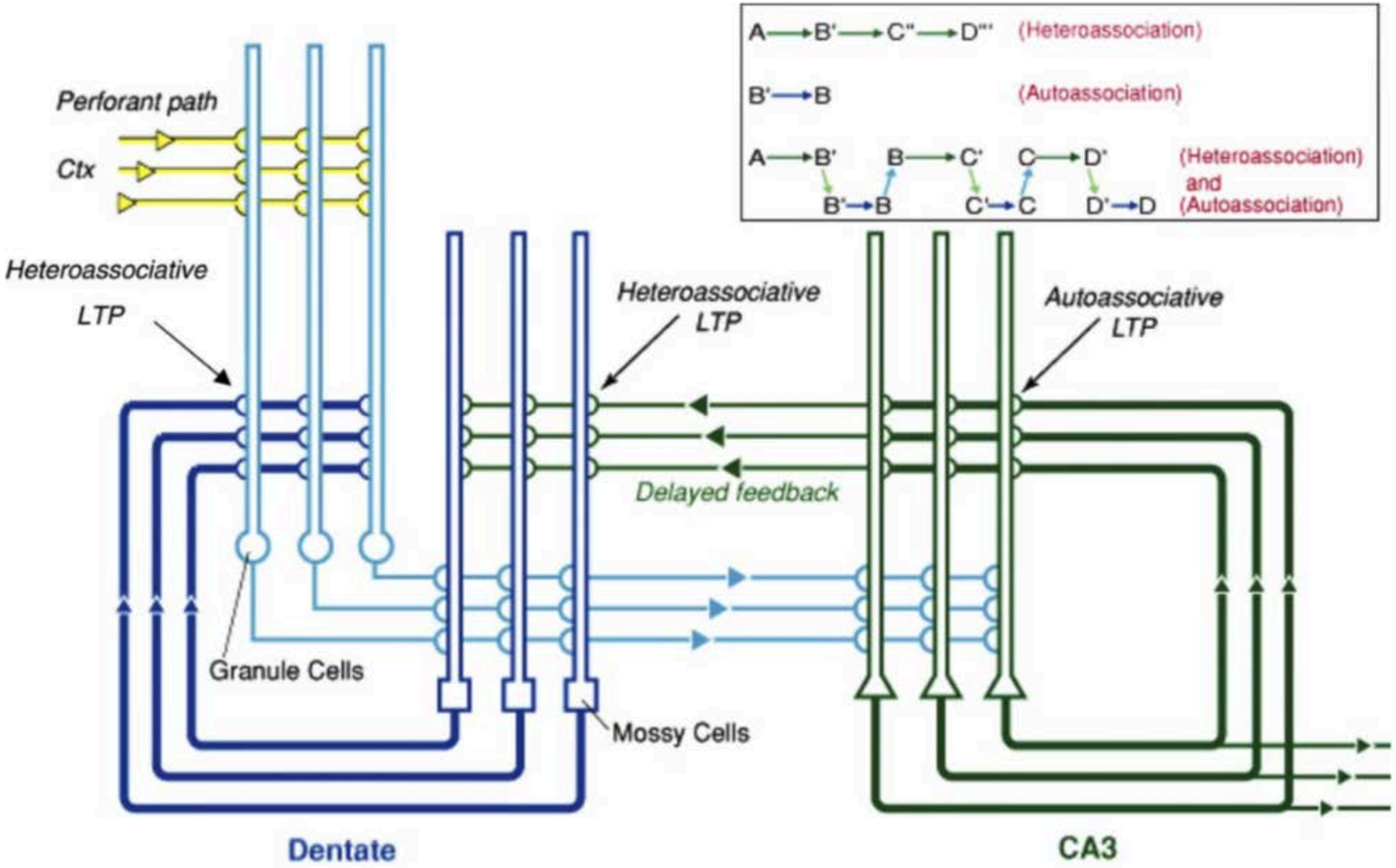


Spatial selectivity and sparsity of dentate gyrus model



Raikov, I., Milstein, A. D., Ng G., Hadjiabadi, D. & Soltesz, I. *Unpublished*, 2019.

Testing a theory for hippocampal interactions in sequence generation



Lisman, J. E., Talamini, L. M., & Raffone, A. *Neural Networks*, 2005.

Conclusions

- We have made significant progress developing a full-scale, biophysical model of the rodent hippocampus

- Model comprised of realistically diverse cell types, cell-type-specific connectivity, realistic anatomical distribution of cells, and non-uniform distributions of synaptic input strengths

- The dentate gyrus (DG) model generates sparse, selective, and sequential population activity that matches in vivo experimental data

- Prototype to develop general software infrastructure to specify, simulate, optimize, and analyze large-scale biophysically-detailed neuronal network models

- Scalable across tens of thousands of processors on Blue Waters

Simulation run time on Blue Waters

Model	Number of Nodes	Simulated time	Run time
Dentate gyrus	2048	10 s	7.5 hours
Dentate gyrus	4096	10 s	6.1 hours
CA1	1024	10 s	12.8 hours
CA1	2048	10 s	6.2 hours

Acknowledgments

Soltesz lab members:

- Aaron Milstein
- Grace Ng
- Sarah Tran
- Darian Hadjiabadi
- Raymond Liou

External collaborators:

- Cesar Renno-Costa (Digital Metropolis Institute, Brazil)
- Sandro Romani (Janelia)

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XSEDE Extreme Science and Engineering Discovery Environment

NEURON for empirically-based simulations of neurons and networks of neurons

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