Full-scale biophysical modeling of hippocampal networks during spatial navigation

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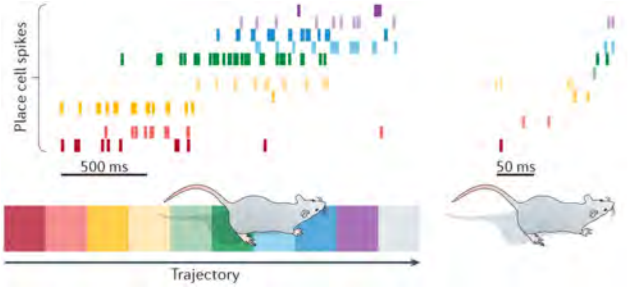
Towards Understanding of Episodic Memory

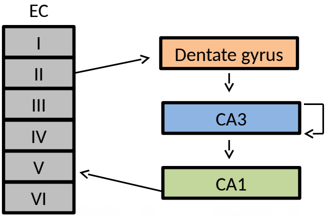


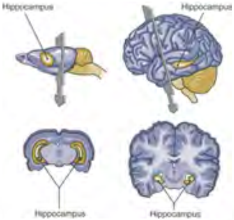
Colgin, Nat Rev Neuroscience, 2016

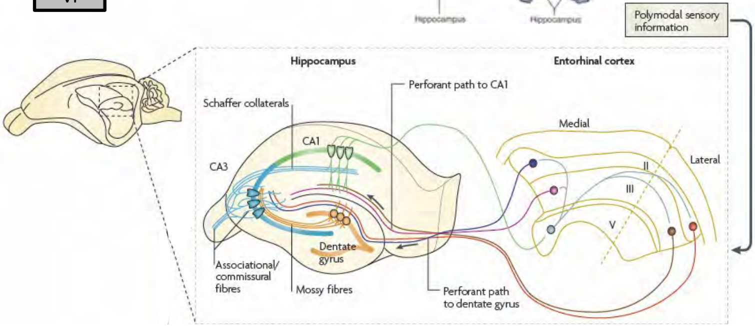
Computational models provide a framework for:

- understanding the sequences of neuronal activation;
- network oscillatory dynamics;
- hippocampal replay, a key mechanism for memory formation.

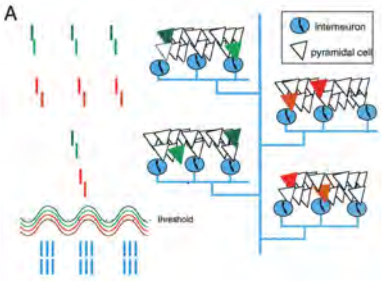
Basis Circuitry of the Hippocampus



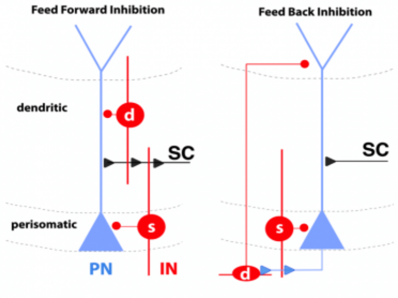




Hippocampal Circuits and Timing



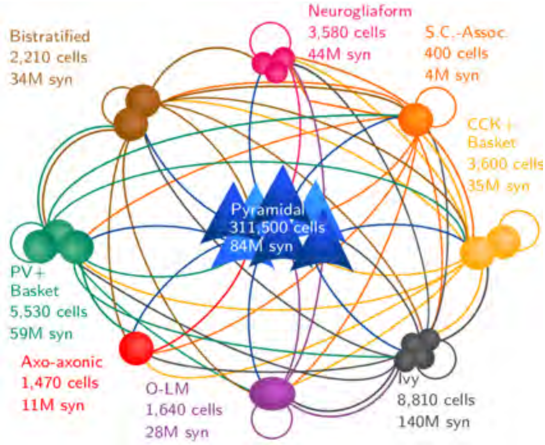
Buzsaki, 2002



Basu, 2016

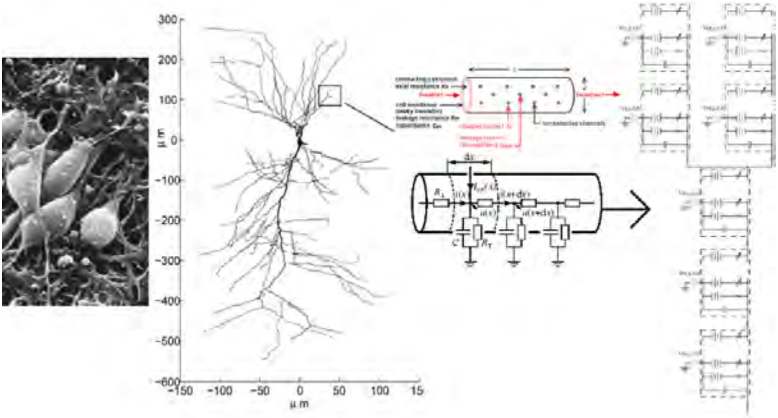
- Understanding the mechanisms of hippocampal information processing requires functional models of the underlying neural circuitry

Neuronal Network Structure

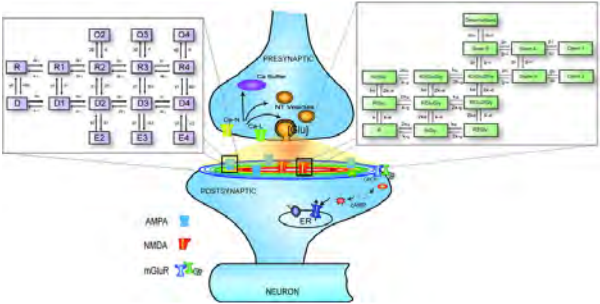


Bezaire et al., eLife 2016

Neuronal Morphology and Ion Channels

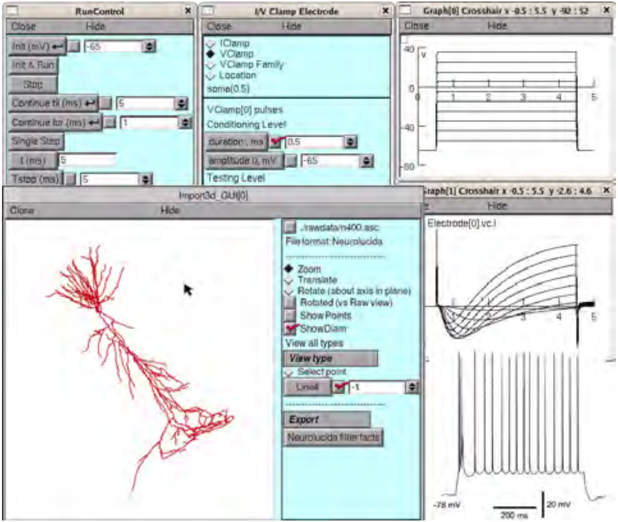


Synapse Models

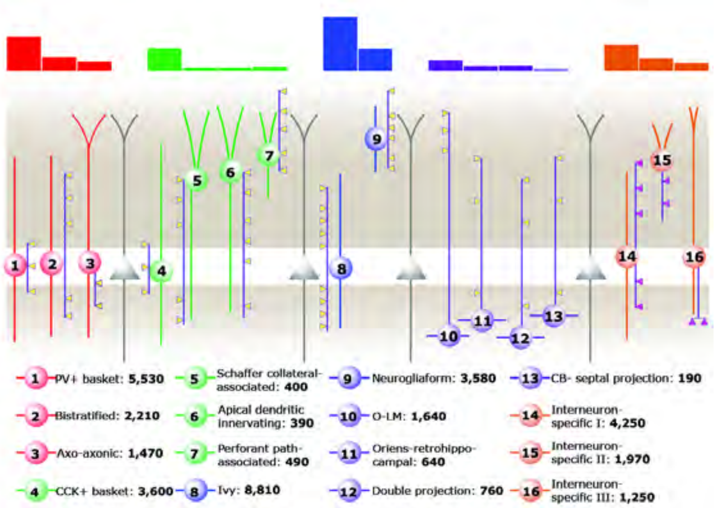


$$G = weight * factor * (e^{\frac{-t}{\tau_2}} - e^{\frac{-t}{\tau_1}})$$

The NEURON Simulator

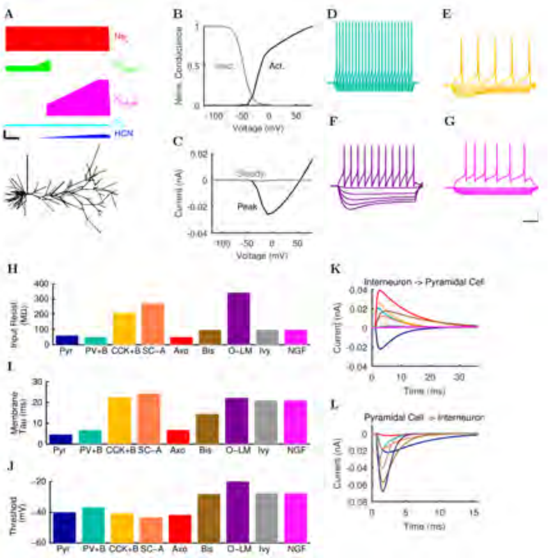


Diversity of Neuronal Species in CA1



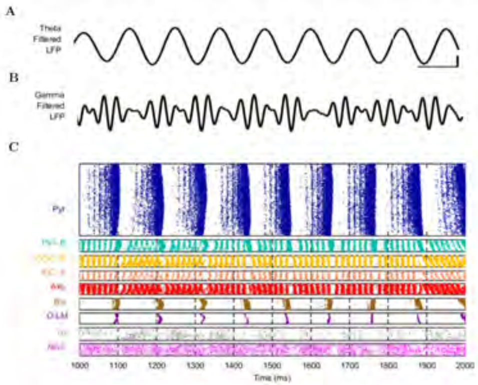
Bezaire and Soltesz, 2013

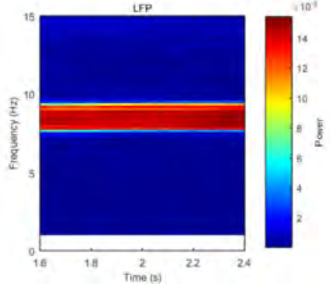
CA1 Biophysical Characteristics



Spontaneous Theta Oscillations in CA1

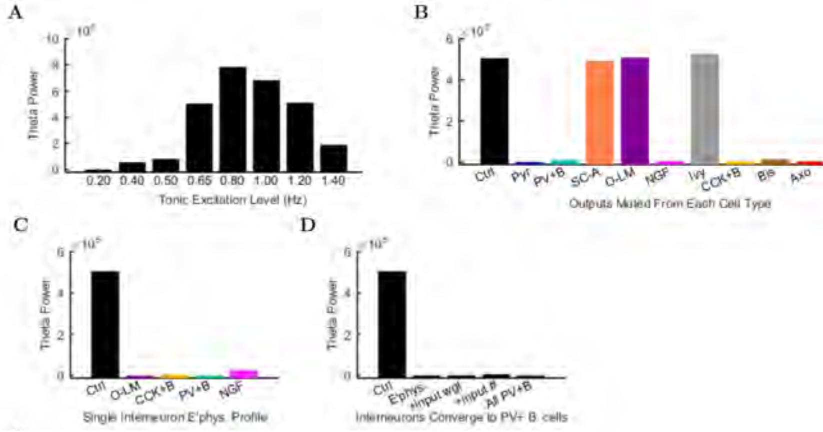
Spontaneous oscillatory behavior of the CA1 network in response to homogeneous Poisson input.



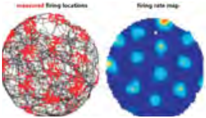


Factors Affecting Theta Oscillations in CA1

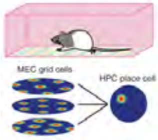
Narrow solution space for theta highlights importance of excitation level and interneuronal diversity.



CA1 Network Dynamics During Spatial Navigation

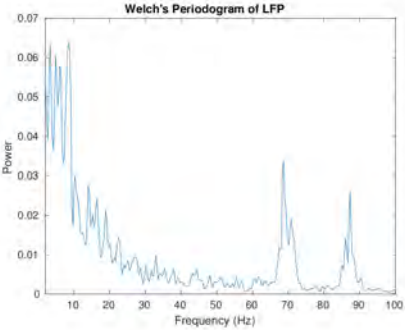


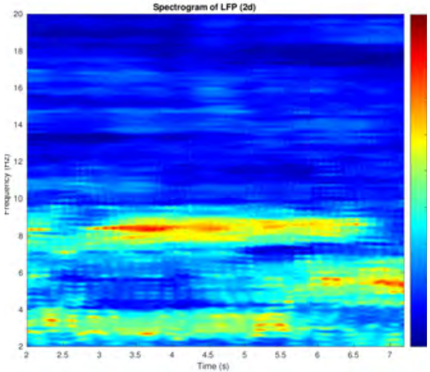
Sargolini et al., Science 2006



Sasaki et al., 2016

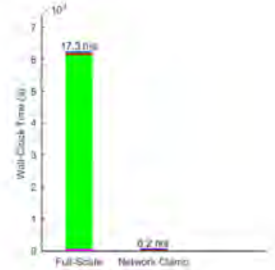
Simulation of realistic MEC grid cell activity reveals theta oscillations with frequency bands that shift with progression through the grid.





Simulation Performance on Blue Waters

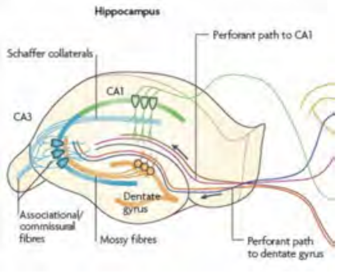
Spatial navigation simulations are only possible on Blue Waters.

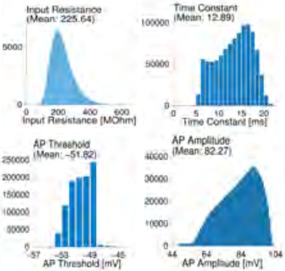


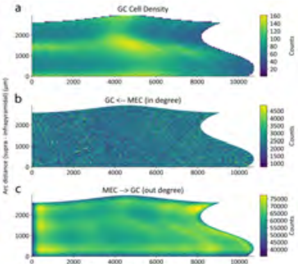
Simulation performance on SDSC Comet (1680 cores; 4000 ms run)

Simulation run times on Blue Waters (16384 cores)	
Simulation type	**Duration**
Homogeneous Poisson input (4000 ms)	11348 s (3.2 hours)
Spatial input (10000 ms)	46160 s (12.8 hours)
Control simulation 100 ms	450 s

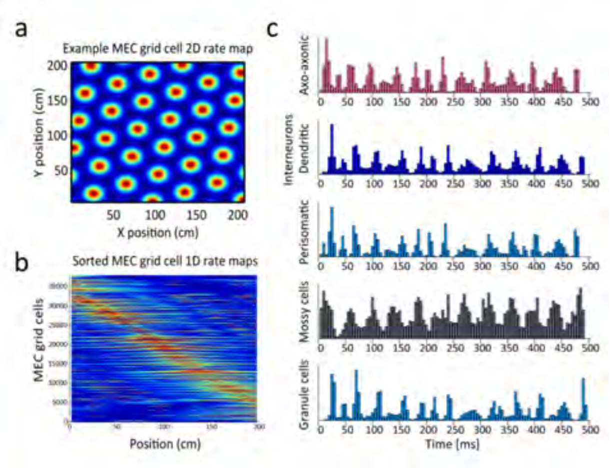
Dentate Gyrus Connectivity Structure and Function







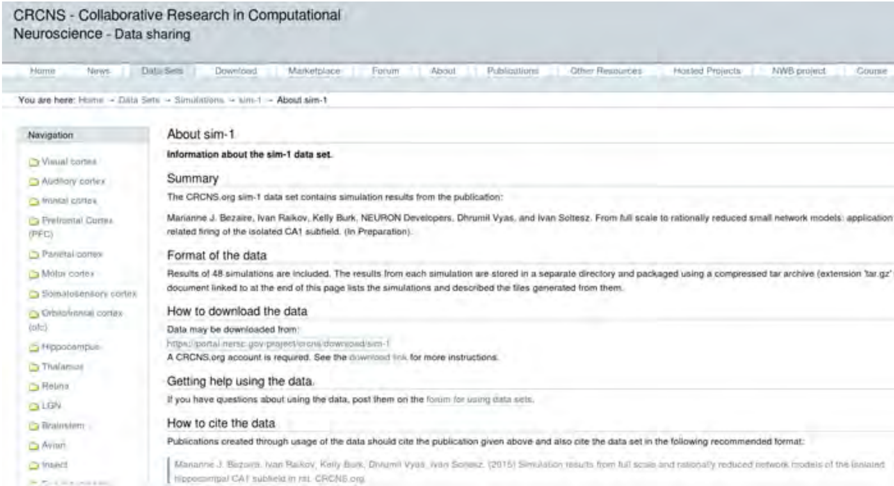
Dentate Gyrus Network Dynamics During Simulated Spatial Navigation



Simulation run times on Blue Waters (16384 cores)	
Simulation type	**Duration**
Spatial input (250 ms)	9725 s (2.7 hours)
Control simulation 100 ms	3890 s (1.08 hours)

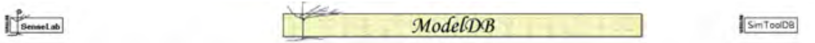
Simulations datasets on CRCNS

`https://crcns.org/data-sets/sim/sim-1`



Model code on ModelDB

`https://senselab.med.yale.edu/modeldb/ShowModel.cshtml?model=187604`



SenseLab ModelDB SimToolDB

Hippocampal CA1 NN with spontaneous theta, gamma: full scale & network clamp (Bezaire et al 2016)

Download zip file Auto-launch
Help downloading and running models

- Model Information
- Model File
- Citations
- Model Views

Accession:187604

This model is a full-scale, biologically constrained rodent hippocampal CA1 network model that includes 9 cells types (pyramidal cells and 8 interneurons) with realistic proportions of each and realistic conne… between the cells. In addition, the model receives realistic numbers of afferents from artificial cells representing hippocampal CA3 and entorhinal cortical layer III. The model is fully scaleable and parallelized … it can be run at small scale on a personal computer or large scale on a supercomputer. The model network exhibits spontaneous theta and gamma rhythms without any rhythmic input. The model network can … perturbed in a variety of ways to better study the mechanisms of CA1 network dynamics. Also see online code at http://bitbucket.org/mbezaire/ca1 and further information at http://mariannebezaire.com/model…

Reference:

1 . Bezaire MJ, Raikov I, Burk K, Vyas D, Soltesz I (2016) Interneuronal mechanisms of hippocampal theta oscillation in a full-scale model of the rodent CA1 circuit. Elife [PubMed]

2 . Bezaire M, Raikov I, Burk K, Armstrong C, Soltesz I (2016) SimTracker tool and code template to design, manage and analyze neural network model simulations in parallel NEURON *eLife*, *in press*

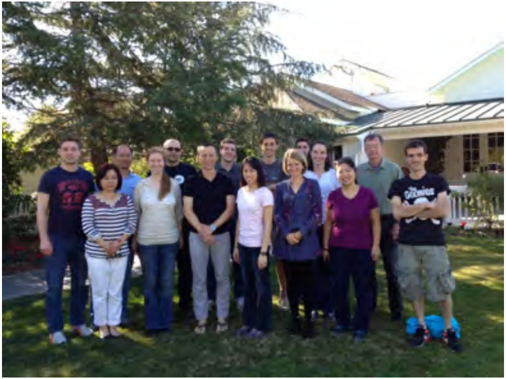
Model Information (Click on a link to find other models with that property)

Model Type:	Realistic Network;
Brain Region(s)/Organism:	Hippocampus;
Cell Type(s):	Hippocampus CA1 pyramidal cell; Hippocampus CA1 interneuron oriens alveus; Hippocampus CA1 basket cell; Hippocampus CA1 stratum radiatum interneuron; Hippocampus C… bistratified cell; Hippocampus CA1 axo-axonic cell; Hippocampus CA1 PV+ fast-firing interneuron;
Channel(s):	I Na,t; I K; I K,leak; I h; I K,Ca; I Calcium;
Gap Junctions:	
Receptor(s):	GabaA; GabaB; Glutamate; Gaba;

Conclusions

- Blue Waters has made possible neural simulations at unprecedented scale and level of detail.
- Completed CA1 model exhibits robust and realistic oscillatory dynamics in response to both random inputs and simulated spatial inputs from EC.
- Work-in-progress DG model shows promising results in spatial navigation simulations.
- Technical assistance provided by Blue Waters team and PAID program has dramatically improved our HPC workflow.

The Soltesz Lab



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- San Diego Supercomputing Center (SDSC)