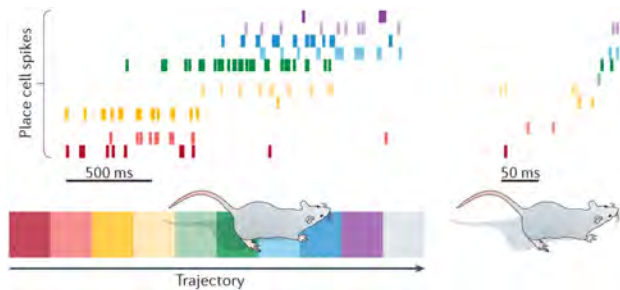


# Full-scale biophysical modeling of hippocampal networks during spatial navigation

I. Raikov   A. Milstein   M. Bezaire   I. Soltesz

Stanford University

# Towards Understanding of Episodic Memory

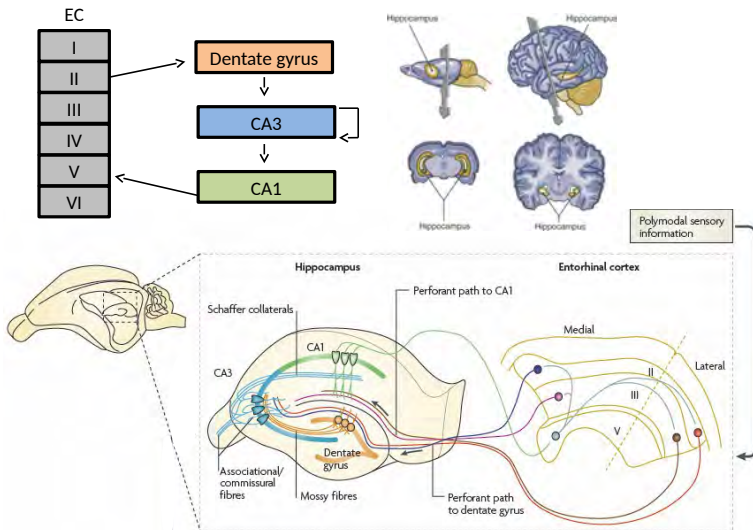


Colgin, Nat Rev Neuroscience, 2016

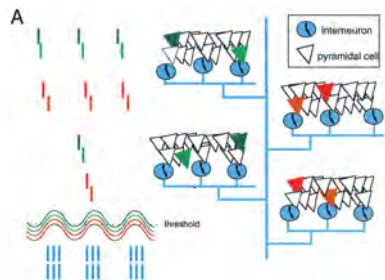
Computational models provide a framework for:

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

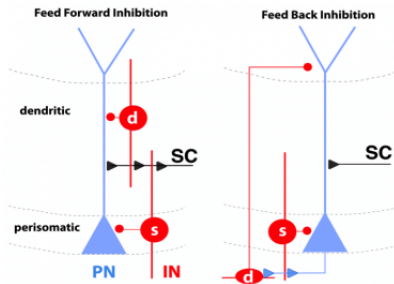
# Basis Circuitry of the Hippocampus



# Hippocampal Circuits and Timing



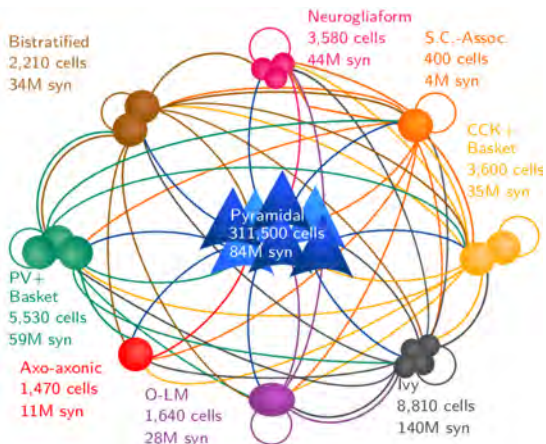
Buzsaki, 2002



Basu, 2016

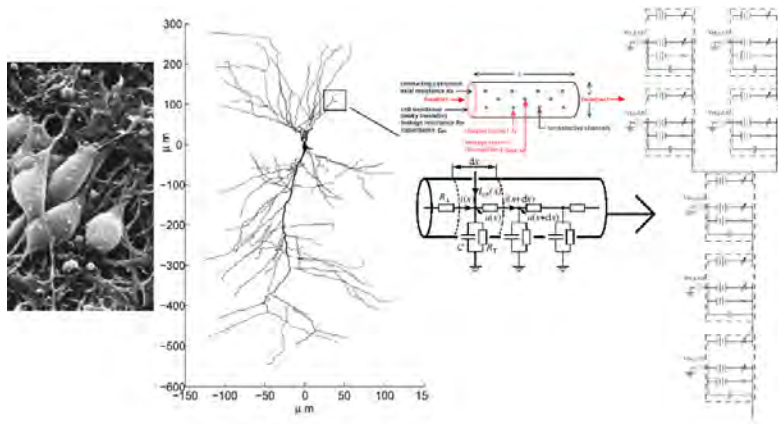
- Understanding the mechanisms of hippocampal information processing requires functional models of the underlying neural circuitry

# Neuronal Network Structure

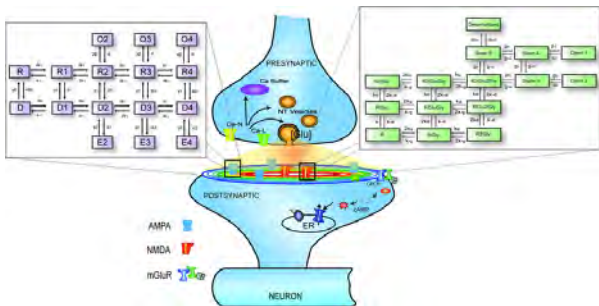


Bezaire et al., eLife 2016

# Neuronal Morphology and Ion Channels

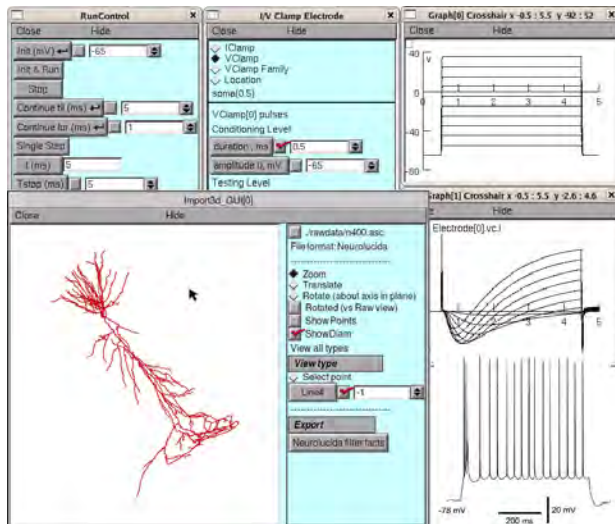


# Synapse Models



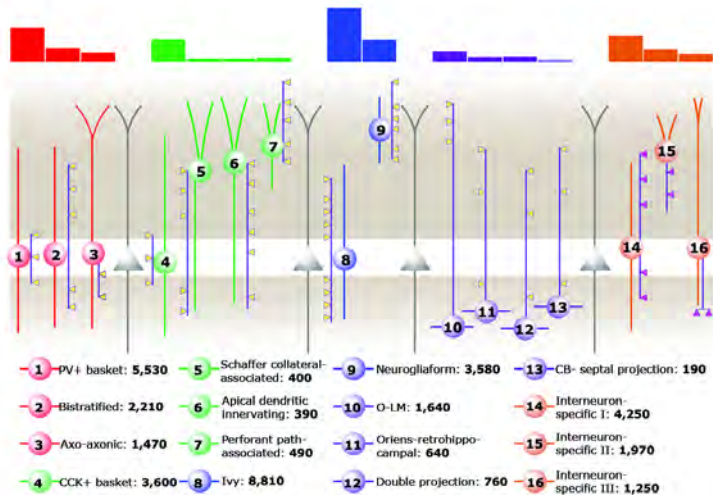
$$G = weight * factor * (e^{-\frac{t}{\tau_2}} - e^{-\frac{t}{\tau_1}})$$

# The NEURON Simulator



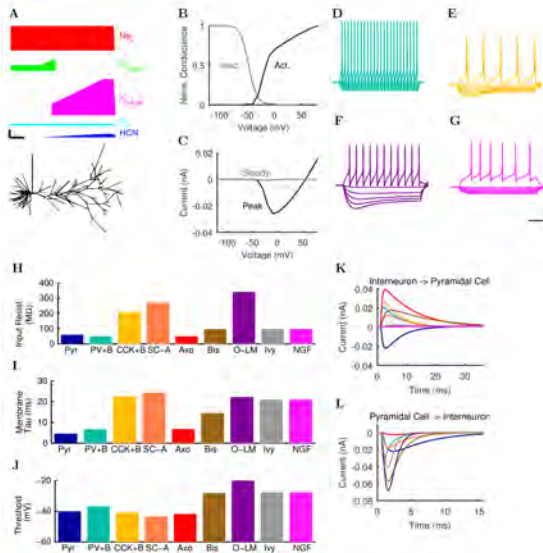


# Diversity of Neuronal Species in CA1



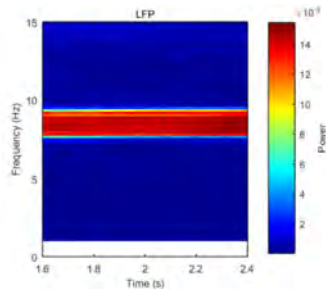
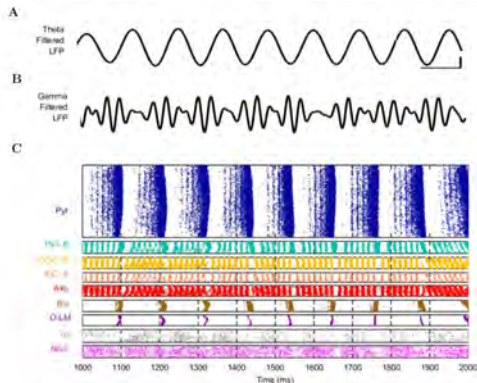
Bezaire and Soltesz, 2013

# CA1 Biophysical Characteristics



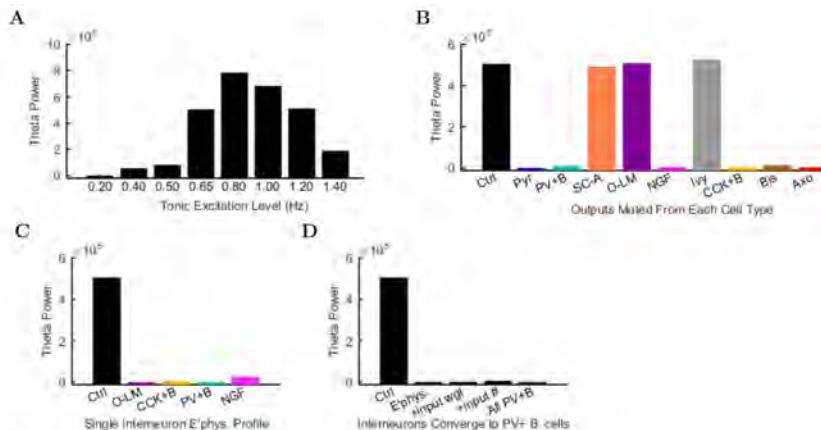
# Spontaneous Theta Oscillations in CA1

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



# Factors Affecting Theta Oscillations in CA1

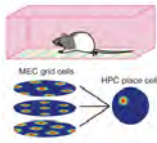
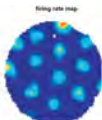
Narrow solution space for theta highlights importance of excitation level and interneuronal diversity.



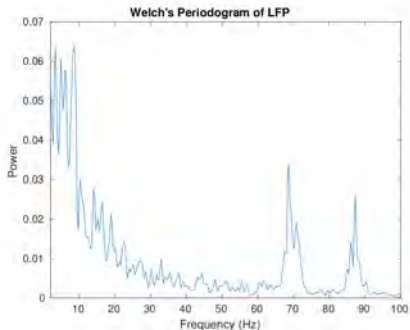
# CA1 Network Dynamics During Spatial Navigation



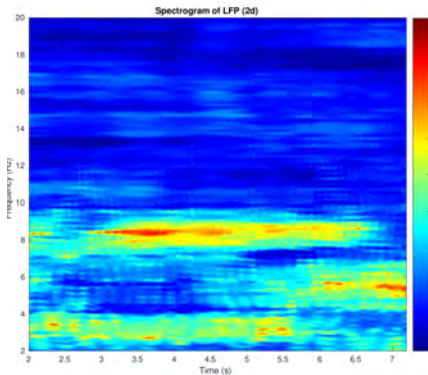
Sargolini et al., Science 2006



Sasaki et al., 2016

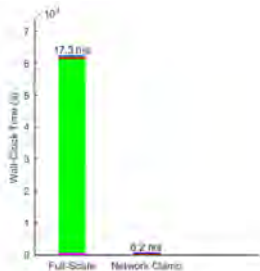


Simulation of realistic MEC grid cell activity reveals theta oscillations with frequency bands that shift with progression through the grid.



# Simulation Performance on Blue Waters

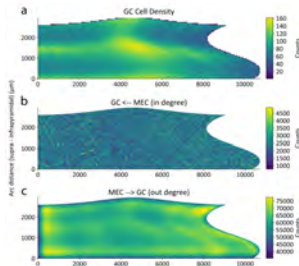
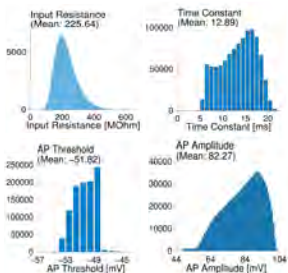
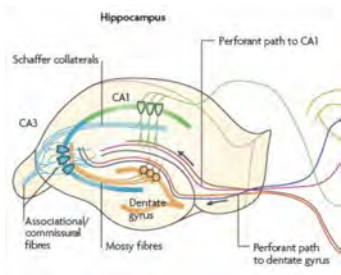
Spatial navigation simulations are only possible on Blue Waters.



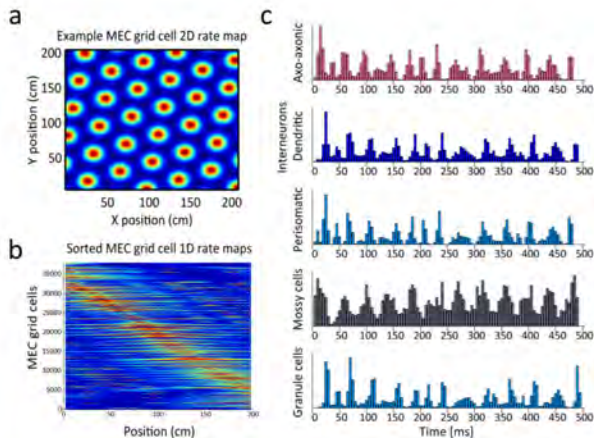
Simulation run times on Blue Waters (16384 cores)	
Simulation type	Duration
Homogeneous Poisson input (4000 ms)	11348 s (3.2 hours)
Spatial input (10000 ms)	46160 s (12.8 hours)
Control simulation 100 ms	450 s

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

# 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>

The screenshot shows the CRCNS website interface. At the top, the site title is "CRCNS - Collaborative Research in Computational Neuroscience - Data sharing". Below this is a navigation menu with links for Home, News, Data Sets, Download, Marketplace, Forum, About, Publications, Other Resources, Hosted Projects, NWB project, and Course. A breadcrumb trail indicates the current location: "You are here: Home -> Data Sets -> Simulations -> sim-1 -> About sim-1".

**Navigation**

- Visual cortex
- Auditory cortex
- Frontal cortex
- Prefrontal Cortex (PFC)
- Parietal cortex
- Motor cortex
- Somatosensory cortex
- Orbitofrontal cortex (ofc)
- Hippocampus
- Thalamus
- Basins
- LGN
- Brainstem
- Avian
- Insect

**About sim-1**

**Information about the sim-1 data set.**

**Summary**

The CRCNS.org sim-1 data set contains simulation results from the publication:

Marianne J. Bezaire, Ivan Raikov, Kelly Burk, NEURON Developers, Dhruvil Vyas, and Ivan Soltesz. From full scale to rationally reduced small network models: application related firing of the isolated CA1 subfield. (In Preparation).

**Format of the data**

Results of 48 simulations are included. The results from each simulation are stored in a separate directory and packaged using a compressed tar archive (extension 'tar.gz' document linked to at the end of this page lists the simulations and described the files generated from them.

**How to download the data**

Data may be downloaded from:

<https://portal.nersc.gov/projects/crcns/download/sim-1>

A CRCNS.org account is required. See the download link for more instructions.

**Getting help using the data.**

If you have questions about using the data, post them on the forum for using data sets.

**How to cite the data**

Publications created through usage of the data should cite the publication given above and also cite the data set in the following recommended format:

Marianne J. Bezaire, Ivan Raikov, Kelly Burk, Dhruvil Vyas, Ivan Soltesz. (2015) Simulation results from full scale and rationally reduced network models of the isolated hippocampal CA1 subfield in rat. CRCNS.org

# Model code on ModelDB

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



## 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 connections 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 scalable 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 be 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://mariennebezaire.com/modeldb>

### 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. [Epilepsia](#) [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.

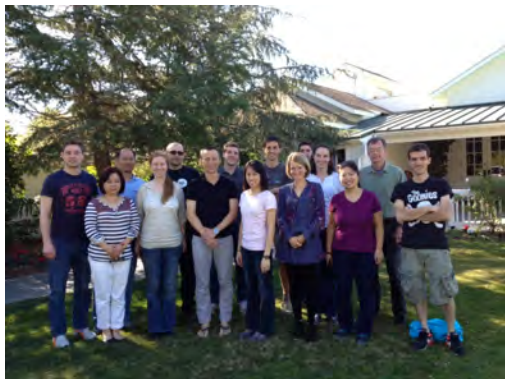
**Model information** (Click on a link to find other models with that property)

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 CA1 basketed cell; Hippocampus CA1 axo-axonic cell; Hippocampus CA1 PV+ fast-spig interneuron
Channel(s):	I <sub>Na</sub> ; I <sub>K</sub> ; I <sub>K</sub> (Leak); I <sub>h</sub> ; I <sub>K</sub> ; Ca; I <sub>Calcium</sub>
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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Gergely Szabo  
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Mattia Maroso  
Aaron Milstein  
Barna Dudok  
Ivan Raikov

Marianne Bezaire, Calvin Schneider, Mark Plitt, Grace Ng

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- NSF Petascale Computing Resource Allocations (PRAC)
- NSF Extreme Science and Engineering Discovery Environment (XSEDE), NSF grant ACI-1053575
- NEURON developers Michael Hines and Ted Carnevale (NIH NINDS grant R01-NS11613 and NSF grant 1458495)
- San Diego Supercomputing Center (SDSC)

