

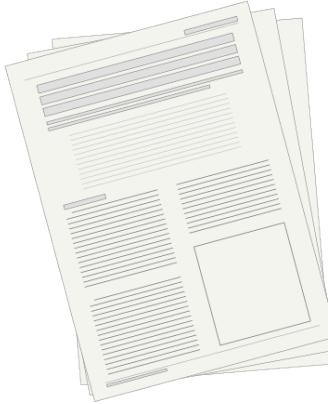
NeuroElectro.org: a window to the world's intrinsic electrophysiology data

<http://neuroelectro.org>

The goal of the NeuroElectro Project is to extract information about the intrinsic electrophysiological properties of diverse neuron types from the neuroscience literature and place it into a centralized database for widespread comparison, reuse, and reanalysis.

Database population

Neurophysiology articles



Algorithm-assisted
manual curation



Intrinsic ephys values

CA1 pyramidal cell

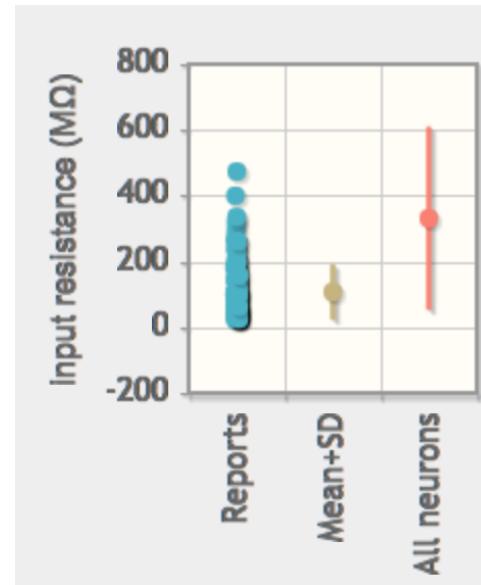
V_{rest}	-66.2 ± 1.1 mV
R_{input}	55.4 ± 3.7 MΩ
FR_{max}	140 ± 2.1 Hz

Experimental conditions

Species	Rat
Animal Age	14 - 63 days
Rec. Temp	$35.0 \pm 2.0^\circ\text{C}$
$Mg^{2+}_{\text{external}}$	2 mM
...	...

968 curated articles from ~100 neuron types
recorded under control conditions (as of 2016)

Visualization



Neuron search

"layer 2-3 fast-spiking cell"



32 hits from 19 articles

Methodology-based normalization

Curated NeuroElectro data

Ephys data	
Enhvs data	
Ephys data	
R_{input}	930 MΩ
AP_{hw}	1.65 ms
Exp conditions	
Animal age	17 days
Temp	22 °C
...	...

Statistical models

$$\text{neuron electrophys} = \text{fxn}(\text{Exp cond})$$

Normalized NeuroElectro data

Adjusted ephys data	
Adjusted enhvs data	
Adjusted ephys data	610 MΩ
R_{input}	1.16 ms
Normalized exp condns	
Animal age	27 days
Temp	30 °C
...	...

REST API for Applications

URL Request -> JSON containing a statistical summary of a neuron's ephys properties

Documentation: <http://neuroelectro.org/api/docs/>

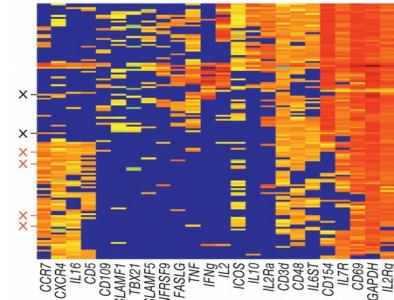
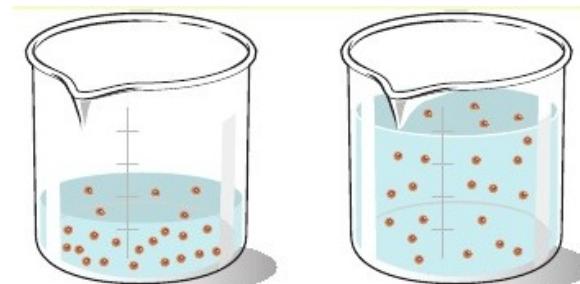
Used to create data-driven tests for model development and validation



```
import sciunit
from neuronunit import neuroelectro
from neuronunit.tests import InputResistanceTest, RestingPotentialTest

neuron = {'nlex_id': 'nifext_50'} # Layer V pyramidal cell
my_tests = []
for cls in (InputResistanceTest, RestingPotentialTest):
    observation = cls.neuroelectro_summary_observation(neuron)
    my_tests.append(cls(observation))
my_test_suite = sciunit.TestSuite("vm_suite", my_tests)
my_test_suite.judge(my_model)
```

How do academic lineage, experimental conditions, and gene expression determine reported physiological properties?

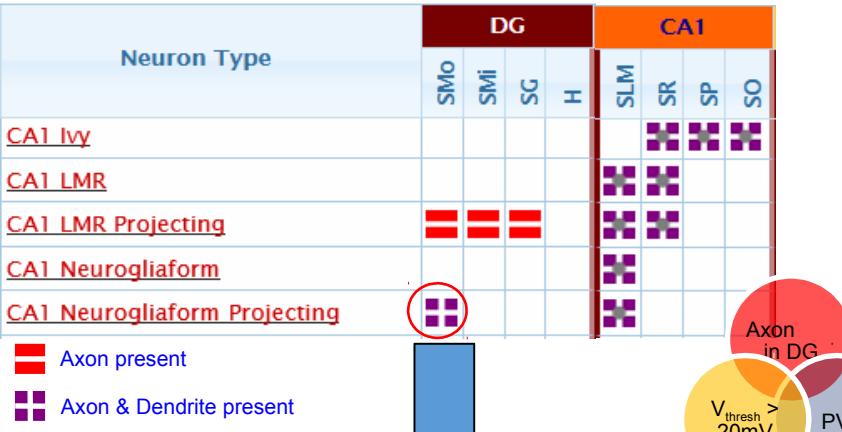


Hippocampome.org: An open-access knowledge base of neuron type properties for the rodent hippocampus

<http://hippocampome.org>

Hippocampome.org is a resource that combines approximately 21,000 pieces of experimental evidence about neuron types in the rodent hippocampus into a unified database. Analyzing these data has revealed about 10,500 different neuron properties and has identified over one hundred different neuron types.

Browse by morphology



Search by property

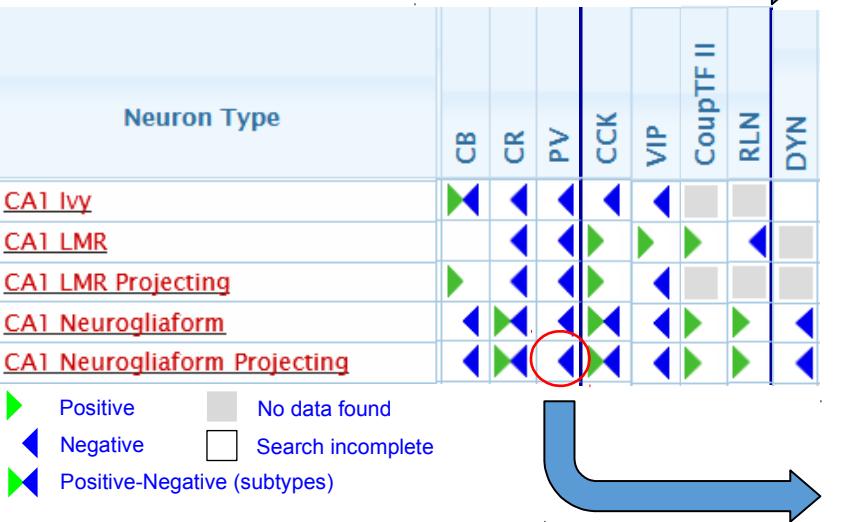
Neuron Types	
DG	Granule
	Mossy
CA3	Spiny Lucidum
	Mossy Fiber-Associated
CA1	CA1 Neurogliaform Proj

Search by author/PMID

Year	Journal	Neuron Types
2005	J Neurosci	Schaffer Collateral-Associated
2007	J Neurosci	CA1 Trilaminar
2008	Neuron	CA1 Neurogliaform CA1 Neurogliaform Proj
2008	J Neurosci	CA1 Hippocampo-Subicular Proj ENK+
2010	J Neurosci	CA1 Pyramidal CA1 Neurogliaform CA1 Neurogliaform Proj

Fuentealba P

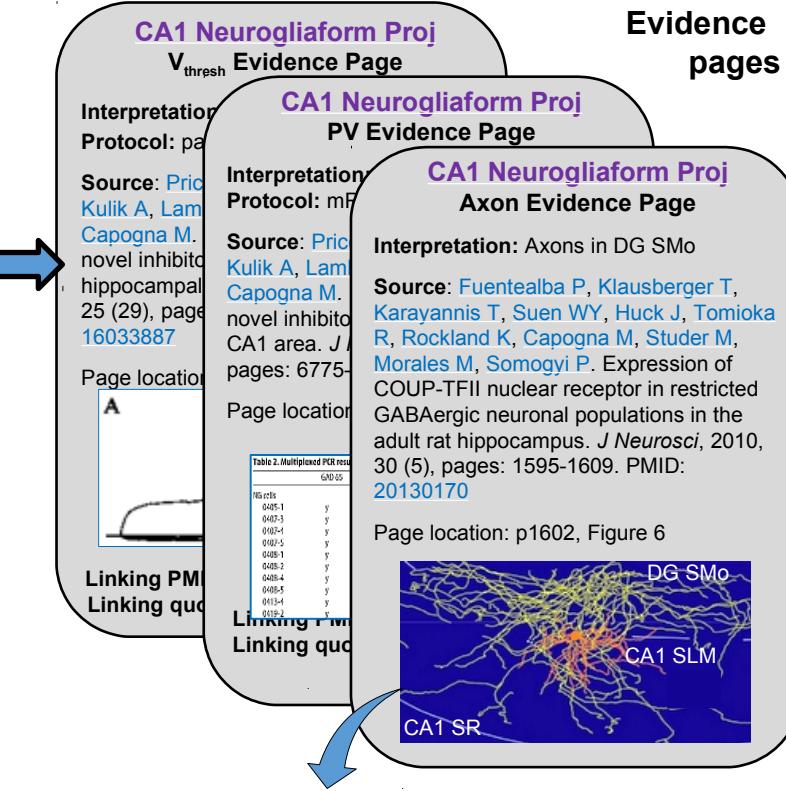
Browse by biomarker



Neuron type page

CA1 Neurogliaform Proj	
<u>Synonyms</u>	
<u>List of articles</u>	
<u>Morphology</u>	
-	Soma: CA1 SLM
-	Axons: DG SMO , CA1 SLM
-	Dendrites: DG SMO , CA1 SLM
<u>Representative figure</u>	
(Price et al., 2005)	
<u>Molecular markers</u>	
-	Positive: CoupTFII , RLN , ...
-	Negative: CB , DYN , PV , VIP , ...
-	Mixed expression: CCK , CR , ...
<u>Electrophysiological Parameters</u>	
-	Vrest , Rin , τm , Vthresh , APwidth , ...
<u>Connectivity</u>	
-	Sources of input
-	Targets of output

Evidence pages



Browse by electrophysiology

Neuron Type	V _{rest} (mV)	R _{in} (MΩ)	τ _m (ms)	V _{thresh} (mV)
CA1 Ivy	-71.0	72.8	7.6	30.1
CA1 LMR	-53.1	352.0	32.9	36.9
CA1 LMR Projecting				
CA1 Neurogliaform	-63.1	215.3	12.4	32.4
CA1 Neurogliaform Projecting	-63.1	215.3	12.4	44.4

"Axodendritic distribution and molecular profile of neurogliaform cells recorded in vivo. ... B, Partial reconstruction of the neurogliaform cell (T126c). Top: soma and dendrites complete (orange), axonal arborization (yellow) only from 5 coronal sections (60 μm). Note the dendrites biased to [SLM]."

Neuron Term Portal

Initial

Neuron Term - Selector

S

soma

Resource

Definition

Neurolex

The portion of a neuron that includes the nucleus, but excludes cell projections such as axons & dendrites.

CRISP

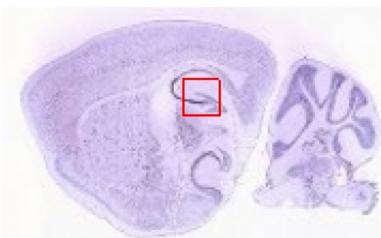
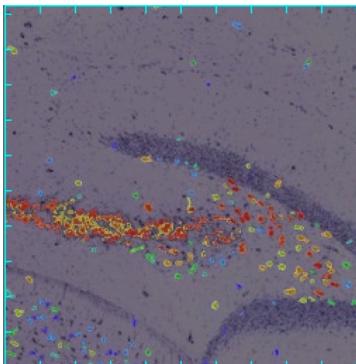
The cell body of a neuron.

Gene
Ontology

The portion of a cell bearing surface projections such as axons, dendrites, cilia, or flagella that includes the nucleus, but excludes all cell projections.

Allen Mouse Brain Atlas data

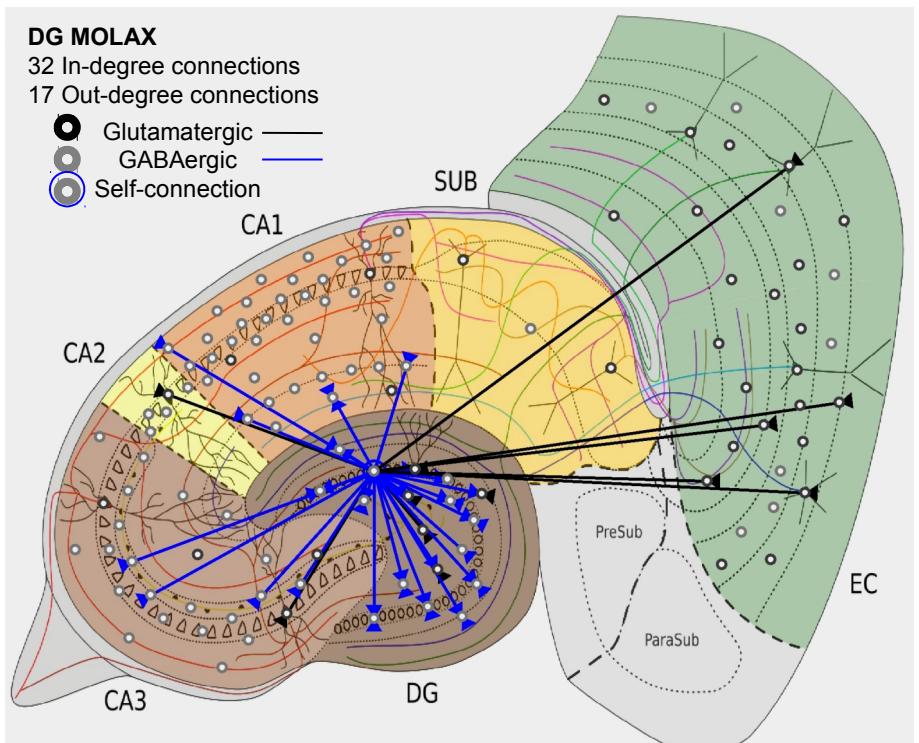
- Focus on principal cell layers of DG, CA3, CA2, CA1.
- Mouse *in situ* hybridization data.
- Increases the biomarker pieces of knowledge (PoK) from ~1100 to more than ~6800.



Acetylcholinesterase (Ache) is expressed in CA3c Pyramidal cells and not expressed in DG Granule cells.

Interactive connectivity navigator

DG MOLAX
32 In-degree connections
17 Out-degree connections
● Glutamatergic
● GABAergic
● Self-connection



Forthcoming additions

Biomolecular marker inferences

- Relational expression inferences supplement direct expression evidence.
- Contrapositive inferences.

Firing pattern phenotypes

- 9 firing pattern elements.

Modeling firing patterns

- Firing patterns simulated using Izhikevich models (IEEE Trans Neural Netw 14:1569-1572 (2003)).

New neuron types

- Splitting of CA1 Pyramidal cells into Superficial and Deep types.
- Inclusion of Adult-Born Immature Granule cells.

CA1 anatomy and model

An interactive anatomical database, graphical representation and full scale model of hippocampal area CA1

Estimation of cell numbers:

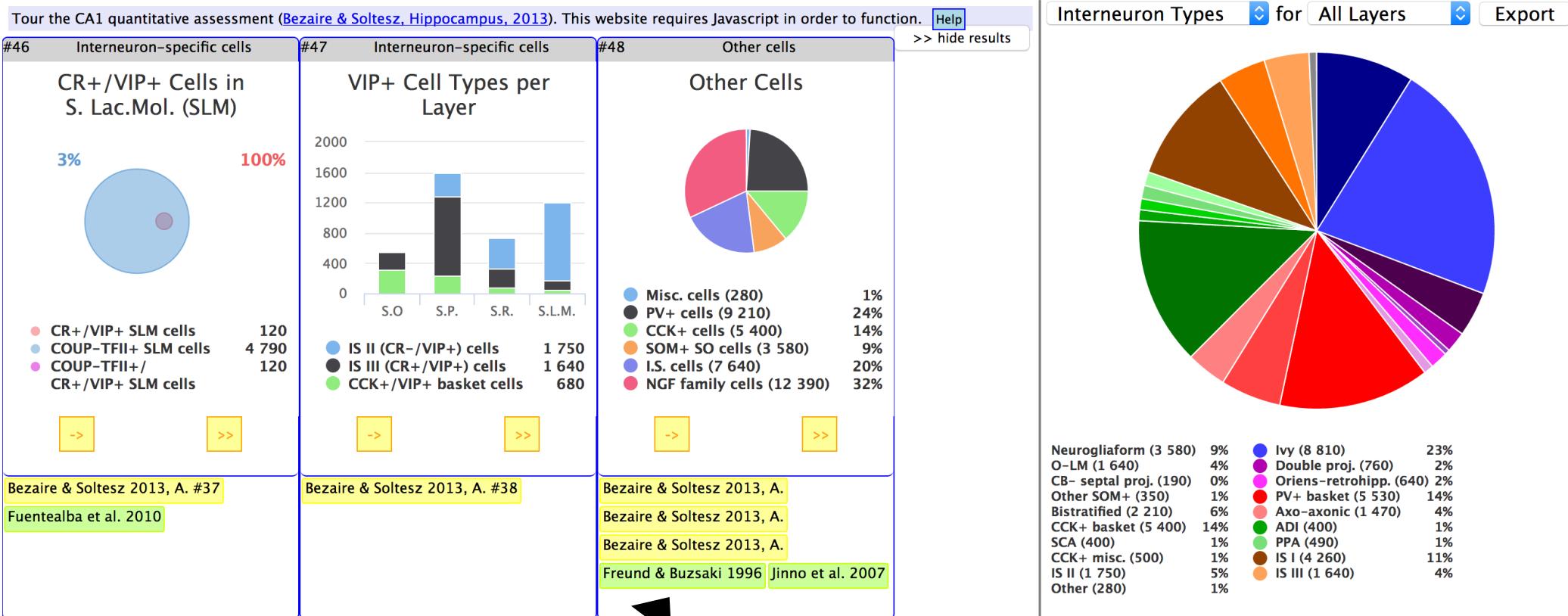
<http://mariannebezaire.com/qagraphic/myQA.html>

Graphical description of model:

http://mariannebezaire.com/ca1_graphic/mymodel.html

Model code:

<http://mariannebezaire.com/models/ca1/>



- Each box represents a calculation towards cell number estimates, from Bezaire & Soltesz, 2013.
- The green & yellow references can be clicked to show details:
- Under development is the ability to edit assumptions or data and then recalculate estimates

Fuentealba et al. 2010

Coexpression of nNOS/NPY with COUP-TFII, in S. Pyramide

Expression of COUP-TFII nuclear receptor in restricted GABAergic neuronal populations in the adult rat hippocampus.

See Supplemental Table 2, section "Testing for putative ivy cells: immunoreaction with antibodies to NPY/nNOS/COUP-TFII" in article.

Bezaire & Soltesz 2013

nNOS+/NPY+ cells are always ivy or neurogliaform cells

Quantitative Assessment of CA1 Local Circuits: Knowledge Base for Interneuron-Pyramidal Cell Connectivity

Quote: "All nNOS+/NPY+ cells are either ivy cells or neurogliaform cells"

See assumption #7 in Table 2 of article.

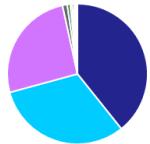
Interneuron	Fraction (%)	Total	Layer			
			Oriens	Pyramide	Radiatum	Lac.Mol.
Neurogliaform Family	32.2	12390	980	5410	3030	2970
Ivy	22.9	8810	980	5410	2420	0
Neurogliaform	9.3	3580	0	0	610	2970
SOM expressing	9.3	3580	3580	0	0	0
O-LM	4.3	1640	1640	0	0	0
Double proj.	2.0	760	760	0	0	0
CB- septal proj.	0.5	190	190	0	0	0
Oriens-retrohipp.	1.7	640	640	0	0	0
Other SOM+ cells	0.9	350	350	0	0	0
PV expressing	23.9	9210	2200	6460	550	0
PV+ Basket	14.4	5530	1320	3870	330	0
Bistratified	5.7	2210	530	1550	130	0
Axo-axonic	3.8	1470	350	1030	90	0
CCK expressing	14.0	5400	1150	1080	1970	1200
CCK+ Basket	9.4	3610	790	950	1170	710
ADI	1.0	400	0	0	400	0
SCA	1.0	400	0	0	400	0
PPA	1.3	490	0	0	0	490

Welcome to the ca1 model!

http://mariannebezaire.com/ca1_graphic/mymodel.html

Network Details:

Neurons in the Model: 793543



Pyramidal	311500 (39.3%)
EC	250000 (31.5%)
CA3	204700 (25.8%)
Ivy	8810 (1.1%)
PV+ basket	5530 (0.7%)
CCK+ basket	3600 (0.5%)
Neurogliaform	3580 (0.5%)
Bistratified	2210 (0.3%)
O-LM	1640 (0.2%)

▲ 1/2 ▼

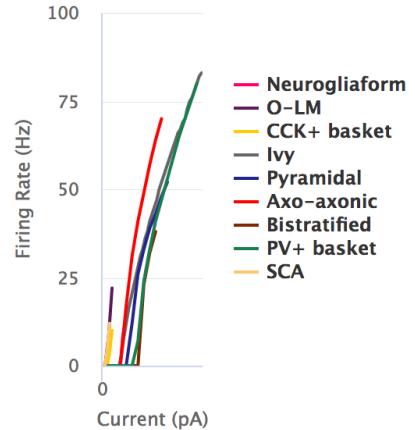
Synapses in the Model: 5.142e+9



remote excitatory → local excitatory	4.537e+9 (88.2%)
local inhibitory → local excitatory	3.330e+8 (6.5%)
remote excitatory → local inhibitory	1.661e+8 (3.2%)
local excitatory → local excitatory	6.137e+7 (1.2%)
local inhibitory → local inhibitory	

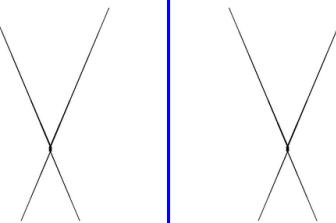
▲ 1/2 ▼

Cell Electrophysiology in the Model

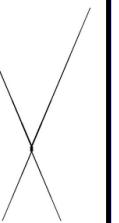


Cell and Connection Details:

Axo-axonic

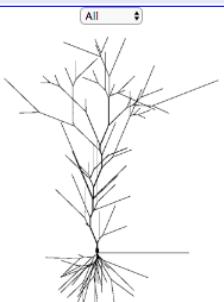


Bistratified

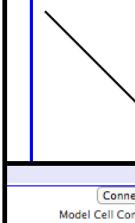


Morphology:

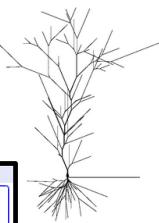
Part	Surface Area (μm^2)	Length (μm)	Average diameter (μm)
all	17074.3	10313.6	1.1
soma	421.0	18.4	6.3
axon	706.9	300.0	0.8
dendrite	15946.5	9995.2	0.7
apical	11674.8	6723.0	0.8
basal	4271.6	3272.2	0.5



O-LM



Pyramidal



PV+ basket

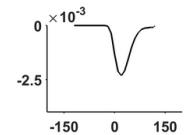


SCA

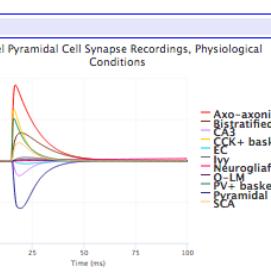
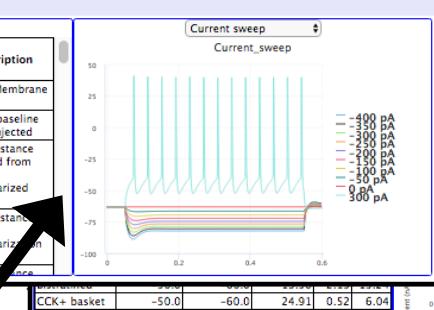
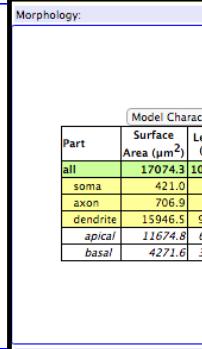
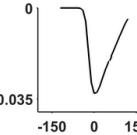


Ion Channel Details:

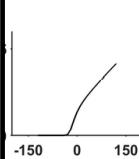
$\text{Ca}_{v,L}$ (CavL)
L-type Calcium



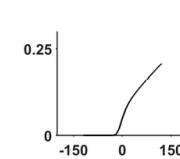
$\text{Ca}_{v,N}$ (CavN)
N-type Calcium



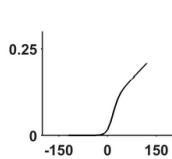
$K_{dr,fast}$ (Kdrfast)
Delayed Rectifier Potassium (fast)



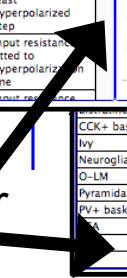
$K_{dr,fast,ngf}$ (Kdrfastngf)
Delayed Rectifier Potassium (fast)



$K_{dr,p}$ (Kdrp)
Delayed Rectifier Potassium



- Click each cell or channel for additional information:



IonChannelGenealogy

<https://icg.neurotheory.ox.ac.uk>

The ICG database provides a comprehensive and quantitative assay of ion channel models currently available in the neuroscientific modeling community, all browsable in interactive visualizations.

Mapping the function of neuronal ion channels in model and experiment

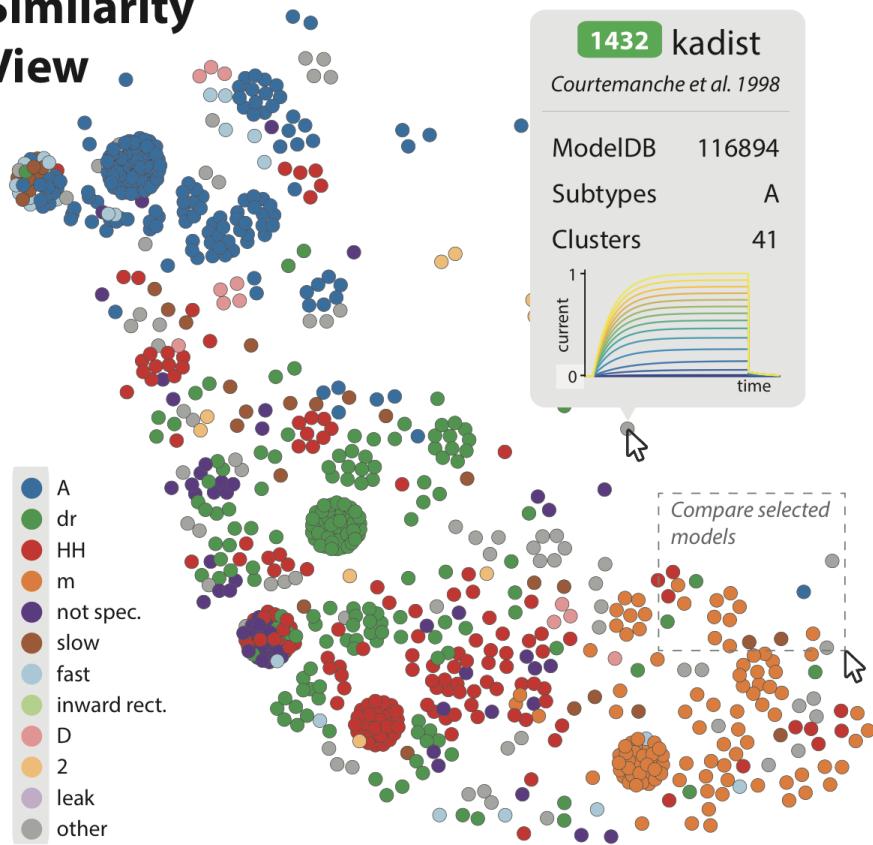
William F Podlaski, Alexander Seeholzer, Lukas N Groschner, Gero Miesenböck, Rajnish Ranjan, Tim P Vogels

icg.neurotheory.ox.ac.uk

The ICG website

(1) Browse database through four interactive views:

Similarity View



TYPE ► Similarity Family

FAMILY ► Kv Nav
Cav KCa Ih

COLOR ► Subtype Date ...

FILTERS ► Text ... Cluster

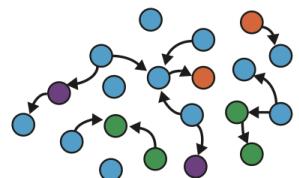
CHANNEL DETAILS

1432 kadist

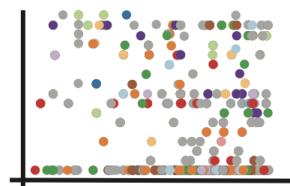
MODELDB 279

ION TYPE	K
SUBTYPE	HH
NEURON TYPE	TCR cell
RUNTIME Q	Q2
TEMPERATURE	model fit at...
COMMENTS	model from...
	⋮

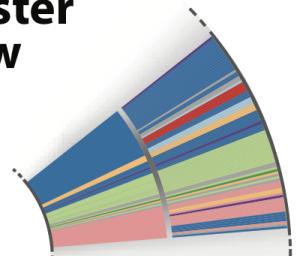
Hierarchy view



XY view



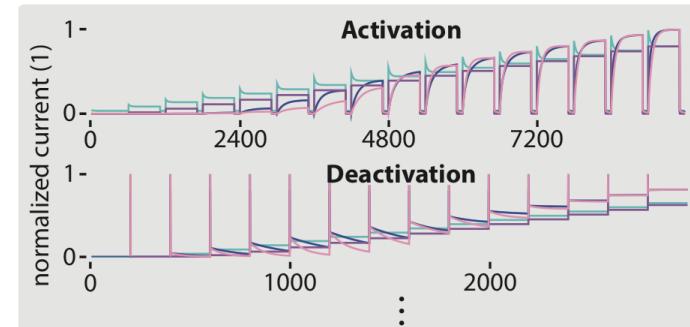
Cluster view



(2) Compare ion channel metadata and kinetics side by side:

Channel Comparison

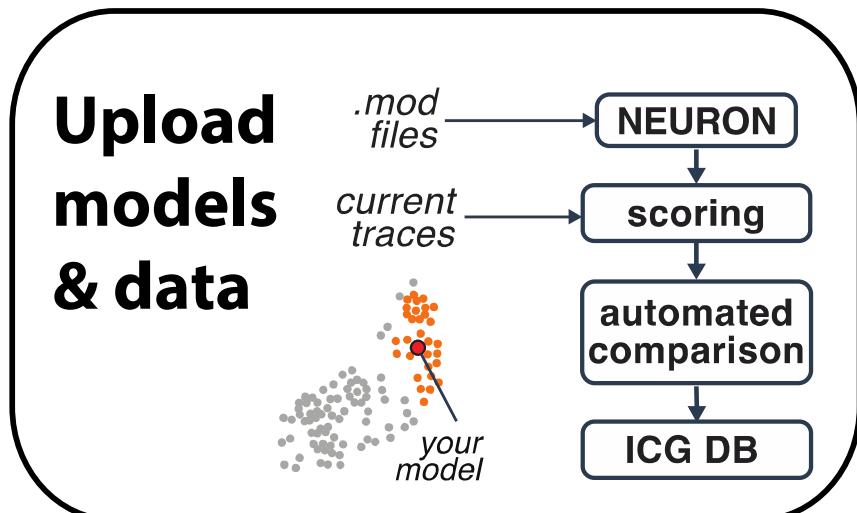
Model	Ion Type	Subtype	Neuron Type	...
2568 97860_kv4hh	K	4	dopaminergic	
276 116094_kM	K	m	mitral	
970 136715_hh	K	HH	pyramidal	
12 101629_km	K	m	pyramidal	
		⋮		



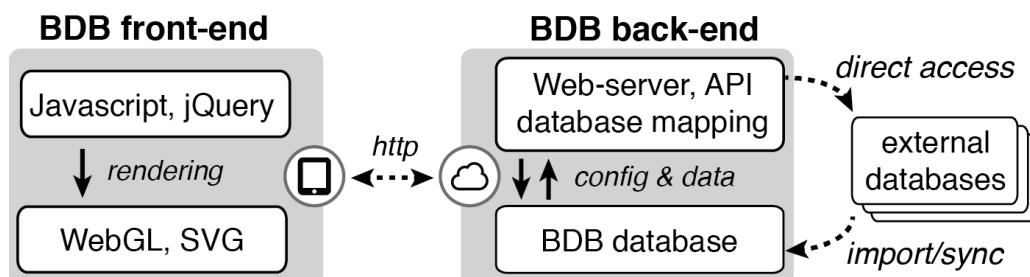
For more details on methods and analyses, refer to our publication in eLife!

Current and future work

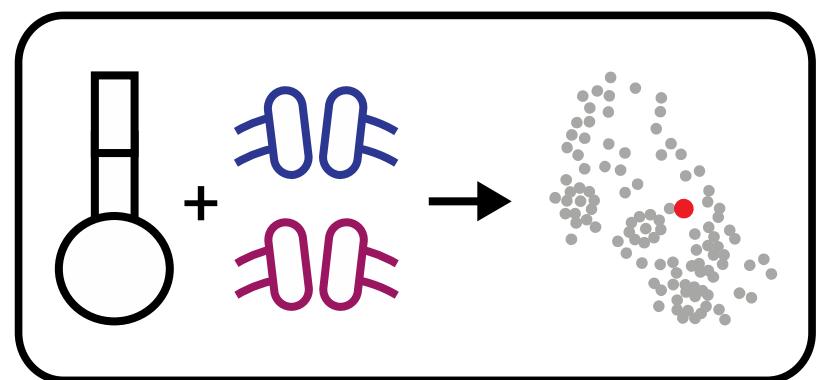
- Maintenance of database with new models & collection of experimental traces



- Generalisation of the database and visualisation software



- Addition of models in other programming languages & channel types
- Integration with existing resources (ModelDB, NeuroML, etc.)
- Extension to combinations of ion channel models, morphology, and other neuroscience datasets



- Continued support thanks to funding from the BBSRC