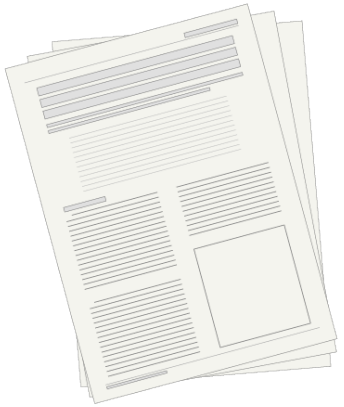
NeuroElectro.org: a window to the world's intrinsic electrophysiology data

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

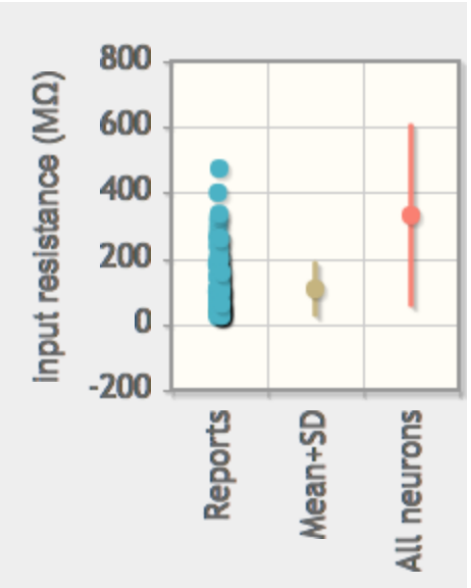
	CA1 pyramidal cell
V_{rest}	–66.2 ± 1.1 mV
R_{input}	55.4 ± 3.7 MΩ
FR_{max}	140 ± 2.1 Hz

Experimental conditions

Species	Rat
Animal Age	14 - 63 days
Rec. Temp	35.0 ± 2.0°C
$Mg^{2+}_{external}$	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

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

Statistical models

neuron electrophys = fxn(Exp conds)

Normalized NeuroElectro data

Adjusted ephys data

R_{input}	610 MΩ
AP_{hw}	1.16 ms
Normalized exp conds	
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

NeuronUnit

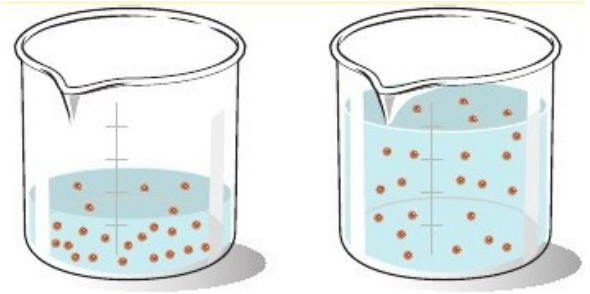
Data driven model validation for neuroscience

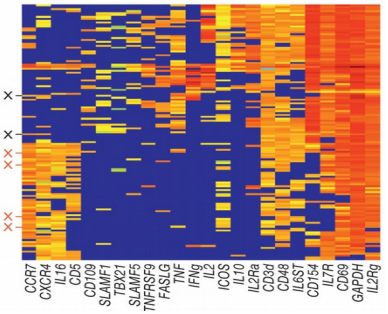
```
import sciunit
from neuronunit import neuroelectro
from neuronunit.tests import InputResistanceTest,RestingPotentialTest

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?

NeuroTree





Hippocampome.org: An open-access knowledge base of neuronal 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

Neuron Type	DG				CA1			
	SMo	SMi	SG	H	SLM	SR	SP	SO
CA1 Ivy						■	■	■
CA1 LMR					■	■		
CA1 LMR Projecting	■	■	■		■	■		
CA1 Neurogliaform					■			
CA1 Neurogliaform Projecting	■				■			

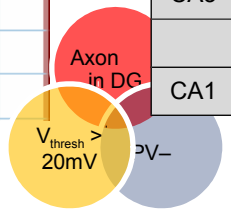
■ Axon present

■ Axon & Dendrite present

● Possible somata locations

Search by property

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



Search by author/PMID

Fuentealba P

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**

Neuron type page

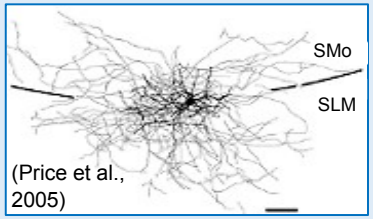
CA1 Neurogliaform Proj

Synonyms

List of articles

Morphology
- Soma: CA1 SLM
- Axons: DG SMo, CA1 SLM
- Dendrites: DG SMo, CA1 SLM

Representative figure



(Price et al., 2005)

Molecular markers
- Positive: CoupTFII, RLN, …
- Negative: CB, DYN, PV, VIP, …
- Mixed expression: CCK, CR, …

Electrophysiological Parameters
- V_{rest}, R_{in}, τ_m, V_{thresh}, AP_{width}, …

Connectivity
- Sources of input
- Targets of output

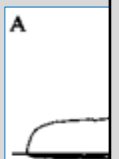
Evidence pages

CA1 Neurogliaform Proj
V_{thresh} Evidence Page

Interpretation: pa
Protocol: pa

Source: Pric
Kulik A, Lamb
Capogna M.
novel inhibito
CA1 area. *J*
pages 6775-

Page locatio



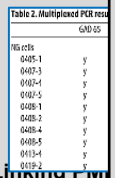
Linking PM
Linking quc

CA1 Neurogliaform Proj
PV Evidence Page

Interpretation:
Protocol: mR

Source: Pric
Kulik A, Lamb
Capogna M.
novel inhibito
CA1 area. *J*
pages: 6775-

Page locatio



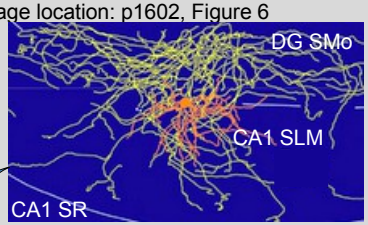
Linking PM
Linking quc

CA1 Neurogliaform Proj
Axon Evidence Page

Interpretation: Axons in DG SMo

Source: Fuentealba P, Klausberger T, Karayannis T, Suen WY, Huck J, Tomioka R, Rockland K, Capogna M, Studer M, Morales M, Somogyi P. Expression of COUP-TFII nuclear receptor in restricted GABAergic neuronal populations in the adult rat hippocampus. *J Neurosci*, 2010, 30 (5), pages: 1595-1609. PMID: 20130170

Page location: p1602, Figure 6



"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]."

Browse by biomarker

Neuron Type	CB	CR	PV	CCK	VIP	CoupTF II	RLN	DYN
CA1 Ivy	◀▶	◀	◀	◀	◀	■	■	
CA1 LMR		◀	◀	▶	▶	▶	◀	■
CA1 LMR Projecting	▶	◀	◀	▶	◀	■	■	■
CA1 Neurogliaform	◀	◀▶	◀	◀▶	◀	▶	▶	◀
CA1 Neurogliaform Projecting	◀	◀▶	◀	◀▶	◀	▶	▶	◀

▶ Positive ■ No data found

◀ Negative □ Search incomplete

◀▶ Positive-Negative (subtypes)

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

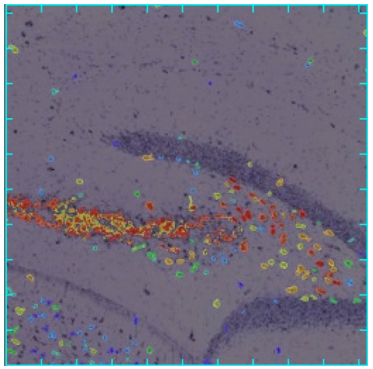
Neuron Term Portal

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.

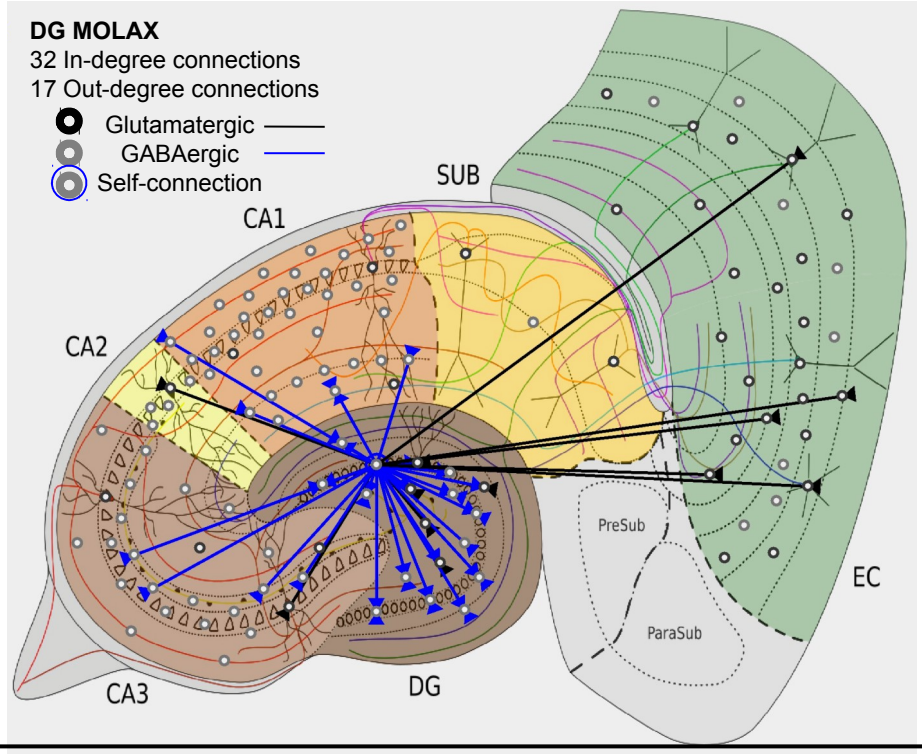
Allen Mouse Brain Atlas data

- 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



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

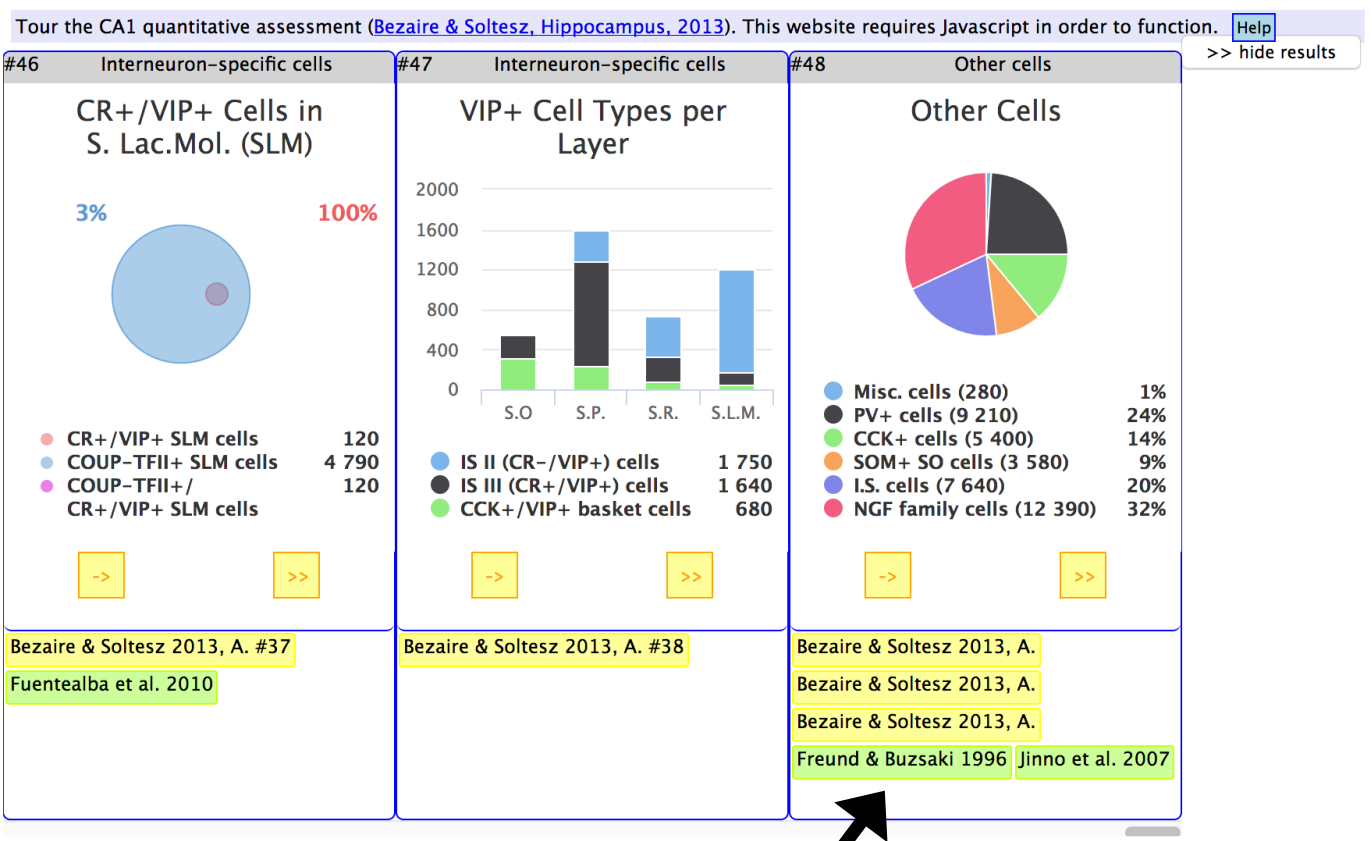
An interactive anatomical database, graphical representation and full scale model of hippocampal area CA1

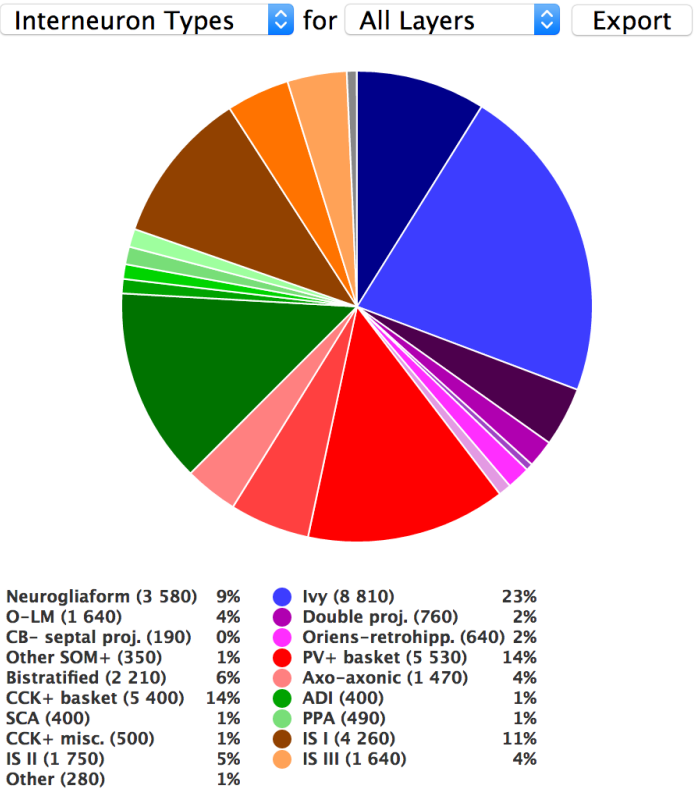
Estimation of cell numbers:
http://mariannebezaire.com/qagraphic/myQA.html

Graphical description of model:
http://mariannebezaire.com/ca1_graphic/mymodel.html

Model code:
http://mariannebezaire.com/models/ca1/

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





- 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. Pyramidale

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	Pyramidale	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

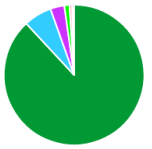
Network Details:

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 ▼

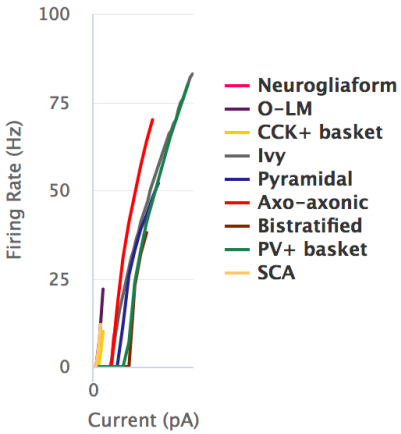
Synapses in the Model: 5.142e+9



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	

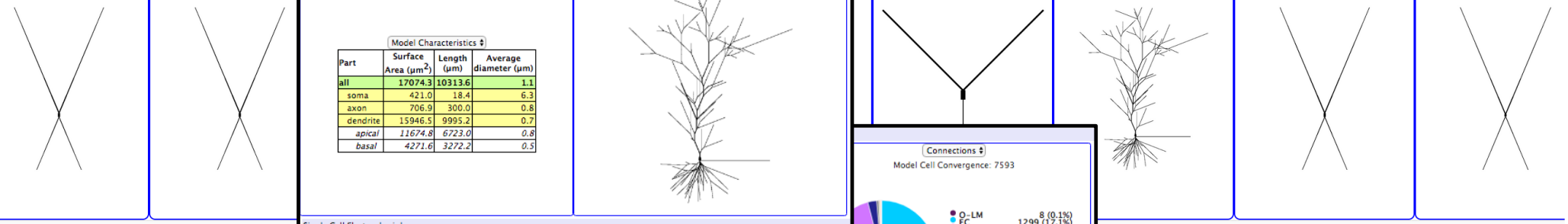
▲ 1/2 ▼

Cell Electrophysiology in the Model



Cell and Connection Details:

Axo-axonic | Bistratified | O-LM | Pyramidal | PV+ basket | SCA



Morphology:

Model Characteristics

Part	Surface Area (μm²)	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*

Single Cell Electrophysiology:

Model Char. (diff. from Exp.)

Property	Value	Diff. from Exp.	Units	Description
RMP	-63.0	-10.8%	mV	Resting Membrane Potential
Baseline	0.0	NaN%	pA	Average baseline current injected
Input Resistance #1	76.1	-45.5%	MegaOhm	Input resistance calculated from least hyperpolarized step
Input Resistance #2	62.2	-34.8%	MegaOhm	Input resistance fitted to hyperpolarization line

Connections

Model Cell Convergence: 7593

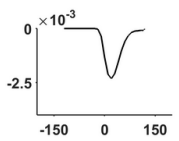
O-LM	8 (0.1%)
EC	1299 (17.1%)
CA3	5985 (78.8%)
Pyramidal	197 (2.6%)
Ivy	42 (0.6%)
PV+ basket	17 (0.2%)
Neurogliaform	14 (0.2%)
CCK+ basket	13 (0.2%)
Bistratified	10 (0.1%)
Axo-axonic	6 (0.1%)
SCA	2 (0%)

Model Pyramidal Cell Synapse Recordings, Physiological Conditions

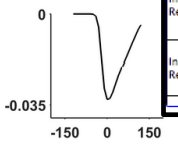
CCK+ basket	-50.0	-60.0	24.91	0.52	6.04
Ivy	-50.0	-60.0	1.64	3.62	15.36
Neurogliaform	-50.0	-60.0	1.03	65.50	0.00
O-LM	-50.0	-60.0	0.58	3.30	13.78
Pyramidal	-50.0	0.0	23.00	1.57	9.75
PV+ basket	-50.0	-60.0	20.56	0.51	6.73
	-50.0	-60.0	8.78	1.70	8.35
	-50.0	0.0	7.20	1.86	7.14
	-50.0	0.0	1.41	3.25	13.67

Ion Channel Details:

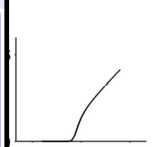
$Ca_{v,L}$ (CavL) L-type Calcium



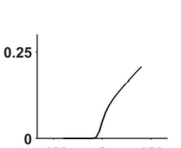
$Ca_{v,N}$ (CavN) N-type Calcium



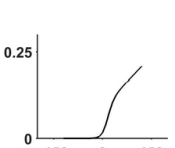
$K_{dr,fast}$ (Kdrfast) Delayed Rectifier Potassium (fast)



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



$K_{dr,p}$ Delayed Rectifier Potassium



- Click each cell or channel for additional information:

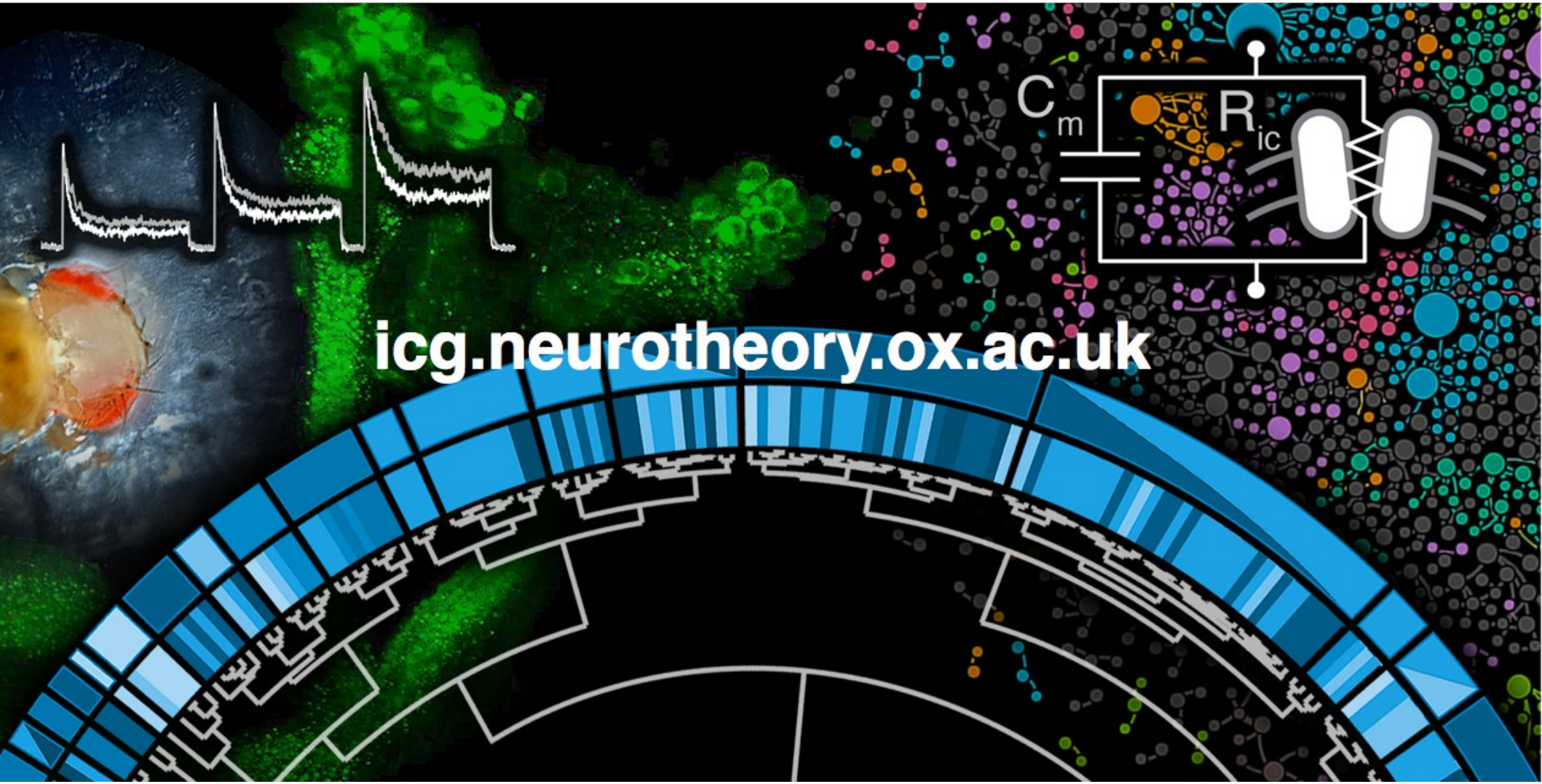
IonChannelGenealogy

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.

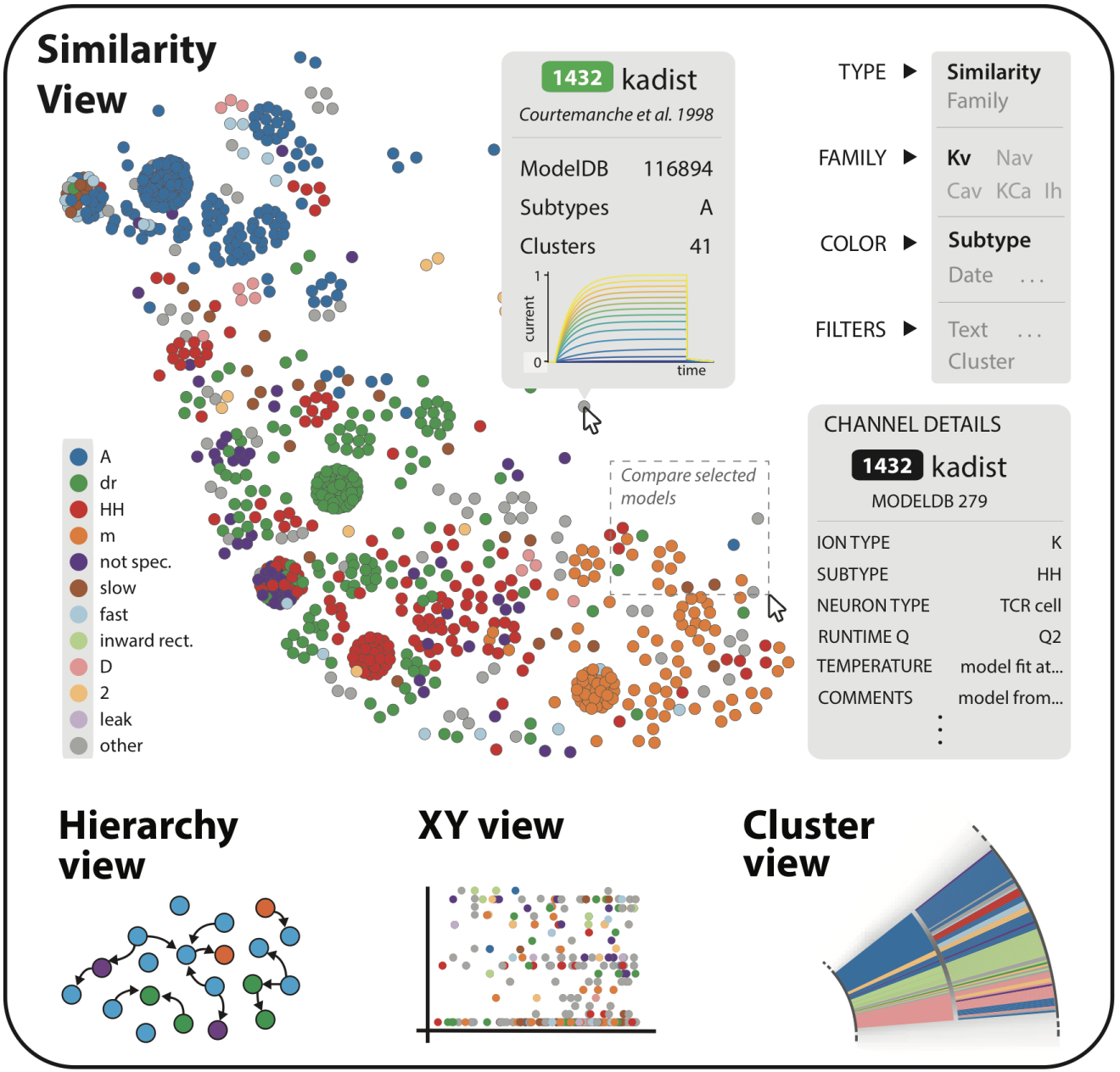
Mapping the function of neuronal ion channels in model and experiment

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

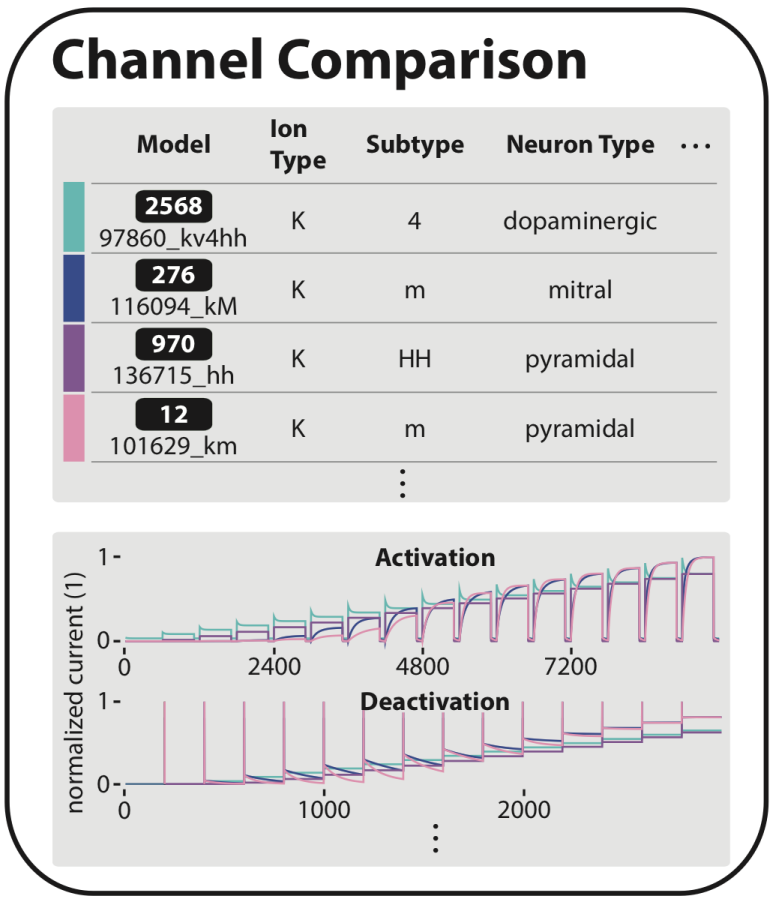


The ICG website

(1) Browse database through four interactive views:



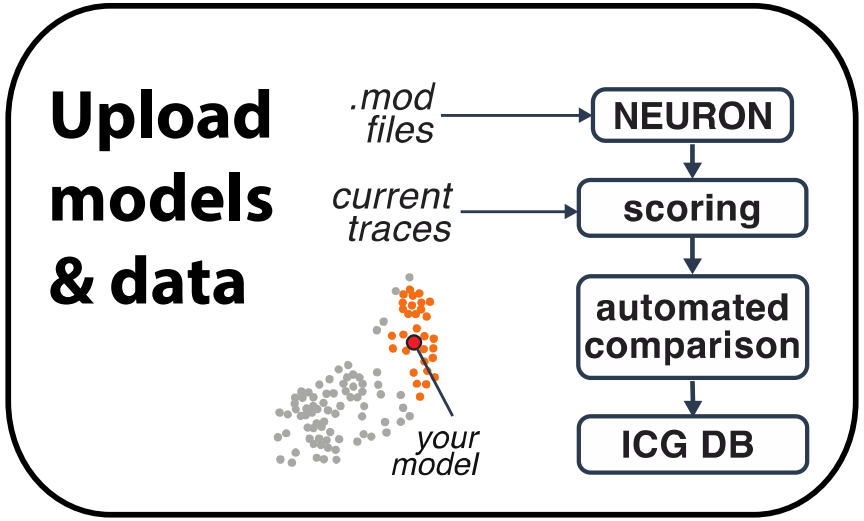
(2) Compare ion channel metadata and kinetics side by side:



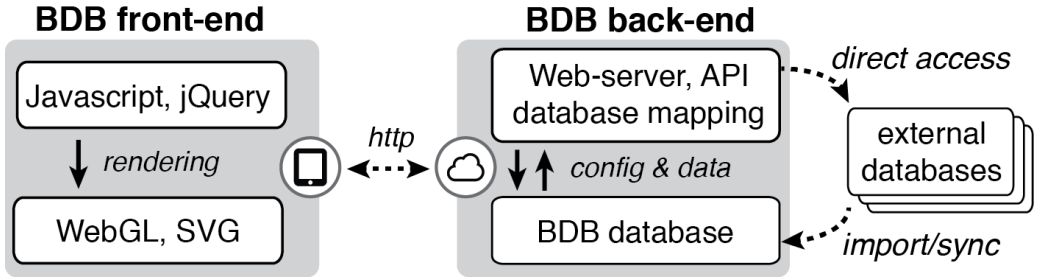
For more details on methods and analyses, refer to our publication in eLife!

Current and future work

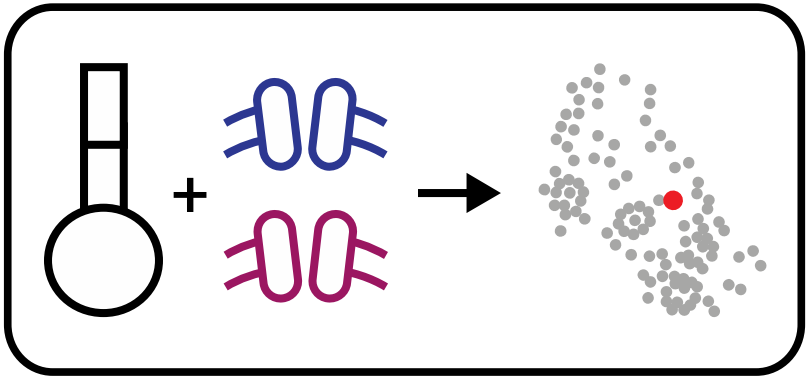
- *Maintenance of database with new models & collection of experimental traces*



- *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*

BBSRC bioscience for the future