Don't reinvent the brain

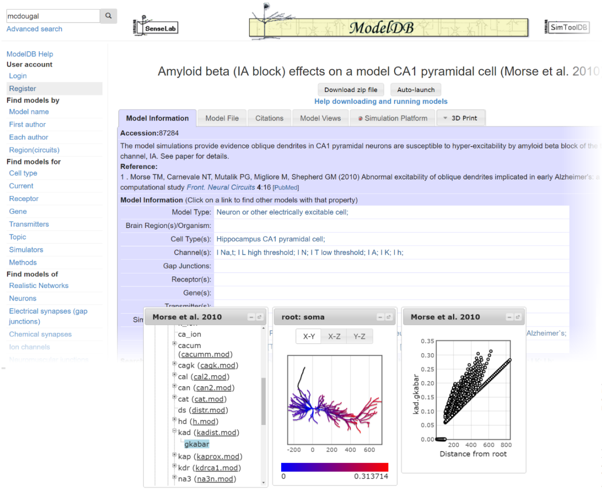
Using ModelDB and other archives for your research

Robert A. McDougal

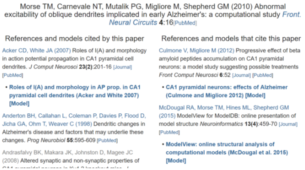
Yale School of Medicine

11 November 2016

What is ModelDB?




```
from neuron import h, rxd
import neuron.rxd.node as node
from matplotlib import pyplot
import time


h.load_file('stdrun.hoc')

soma = h.Section()
soma.L = 10
soma.diam = 10
soma.nseg = 11
dend = h.Section()
dend.connect(soma)
dend.L = 50
dend.diam = 2
dend.nseg = 51

def print_nodes():
    print ', '.join(str(v) for v in node._states)

print 'defining rxd'
region = rxd.Region(h.allsec(), nrn_region='i')
ca = rxd.Species(region, name='ca', d=1, charge=2, initial:
reaction = rxd.Rate(ca, -ca * (1 - ca) * (0.3 - ca))

print 'initializing'
h.finitialize()

print 'before:'
print_nodes()
print
```



modeldb.yale.edu

J Comput Neurosci
DOI 10.1007/s10827-016-0623-7

Twenty years of ModelDB and beyond: building essential modeling tools for the future of neuroscience

Robert A. McDougal[1] · **Thomas M. Morse**[1] · **Ted Carnevale**[1] · **Luis Marenco**[1,2,3] · **Rixin Wang**[3,4] · **Michele Migliore**[1,5] · **Perry L. Miller**[2,3,4] · **Gordon M. Shepherd**[1] · **Michael L. Hines**[1]

Received: 9 June 2016 / Revised: 17 August 2016 / Accepted: 30 August 2016

Abstract Neuron modeling may be said to have originated with the Hodgkin and Huxley action potential model in 1952 and Rall's models of integrative activity of dendrites in 1964.

groups (Allen Brain Institute, EU Human Brain Project, etc.) are emerging that collect data across multiple scales and integrate that data into many complex models, presenting new

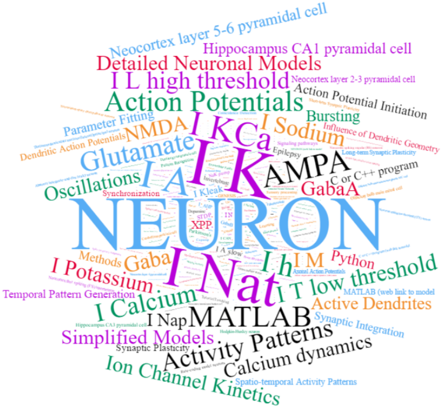
What is in ModelDB?

Models for:

- 178 cell types
- 16+ species
- 48 ion channels, pumps, etc
- 139 topics (Alzheimer's, STDP, etc)
- 25+ mammalian brain regions

1134 published models from 76 simulators

- 544 NEURON models
- 318 "realistic" networks
- 45 connectionist networks



Numbers are as of October 24, 2016

Why use ModelDB?

On reproducibility

"Non-reproducible single occurrences are of no significance to science."

– Karl Popper in *The logic of scientific discovery*, 1959.

What is needed for a model to be reproducible?

Model

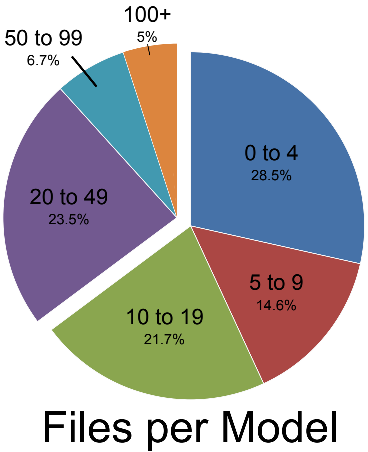
- an approximation of the system of interest
  e.g. a model organism or a complete statement of the properties of the model in mathematical or computable form

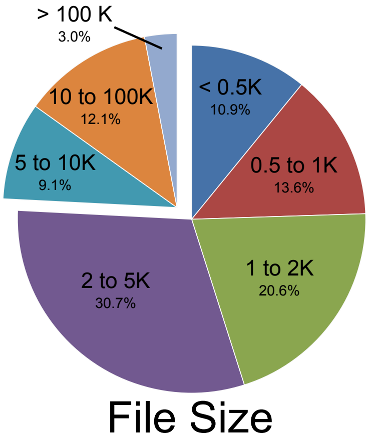
Experimental protocol

- what was done with the model to produce the data

Science builds upon previous work; in order to do that, the previous work needs to be reproducible.

Models are complicated





- **38.5%** of ModelDB models have **over 20 files**; **24.2%** of files are **over 5K**.
- It is often hard to fully describe this complexity in a paper.
- Any bugs, typos, errors, or omissions might completely change the dynamics.

Distributions from ModelDB, Fall 2013. A model was counted as having 0 files if it was not hosted on ModelDB.

Model sharing helps, but only reuse what you understand

The easiest way to replicate someone else's results – a first step toward building on them – is to get their model code from a repository such as ModelDB.

But beware:

- They may be solving a different problem than you (with respect to species, temperature, age, etc).
- Their code may have bugs.

To reduce the risk of problems:

- **Read** the associated paper.
- **Compare** the model and results to other similar models.
- **Examine** the model with ModelView and/or psection.
- **Test** ion channels individually.
- **Collaborate** with an experimentalist.

Reproducibility in Computational Neuroscience Models and Simulations

Robert A. McDougal, Anna S. Bulanova, William W. Lytton

Abstract—**Objective: Like all scientific research, computational neuroscience research must be reproducible. Big data science, including simulation research, cannot depend exclusively on journal articles as the method to provide the sharing and transparency required for reproducibility.**

build novel theoretical frameworks. A century ago, work by Lapicque led to the development of integrate-and-fire models [4]. A half century later, Hodgkin and Huxley provided a detailed multiscale biophysical model of the squid axon [2],

- Simulators (NEURON, MCell, XPPAUT, NEST, etc)
- Multi-simulator interoperability (NeuroML, SWC, PyNN, NeuroConstruct, etc)
- Shared resources (Neuroscience Gateway, Simulation Platform)
- Sharing resources (ModelDB, OpenSourceBrain, NeuroMorpho.Org, etc)
- More: NSDF, NeuroLex, NIF, MIASE, licensing, etc

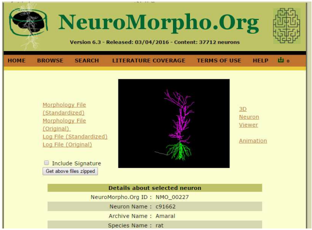
McDougal et al (2016) IEEE TBME 63(10):2021-2035; doi:10.1109/TBME.2016.2539602

Neurobiological context

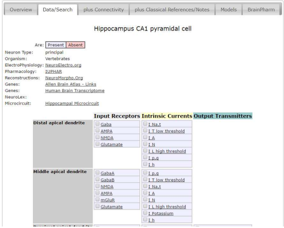
Metadata

cell types, channels, receptors, genes, transmitters, model topics, publication

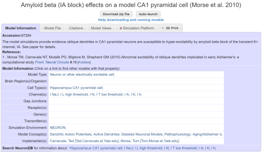
Morphology



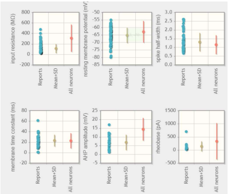
NeuronDB



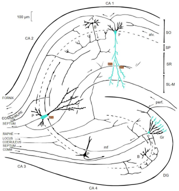
Model Entry



Electrophysiology



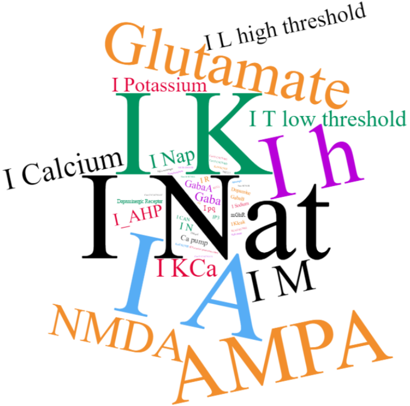
Microconnectome



ModelDB is a place to see what has been modeled in a cell type.

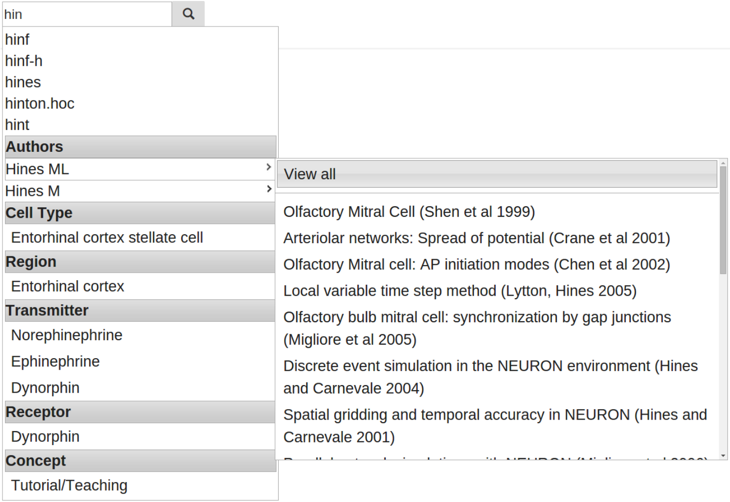
Not only can you get code, but by comparing models, you can see what mechanisms are considered critical by the community.

Metadata associated with
CA1 Pyramidal Cell Models ($n = 71$)



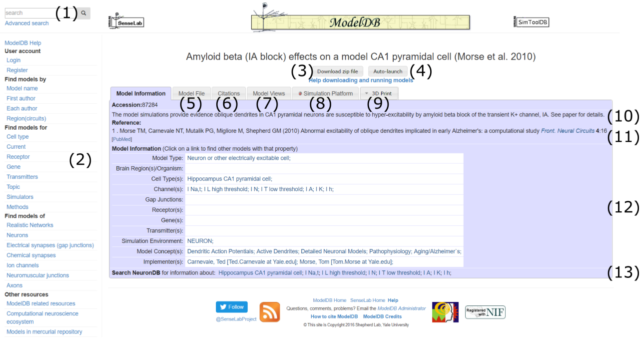
How to use ModelDB

Finding models



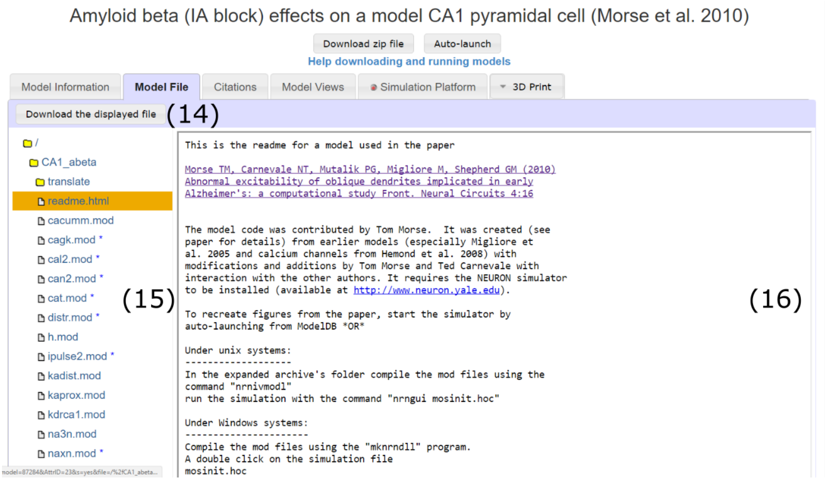
- **Search box** on the top-left of every page.
- Do **full text** or **attribute** searches.
- Word completions (based on ModelDB entries not English) and attribute results **updated as you type**.
- **Advanced search** and **browsing** are also available.

ShowModel features



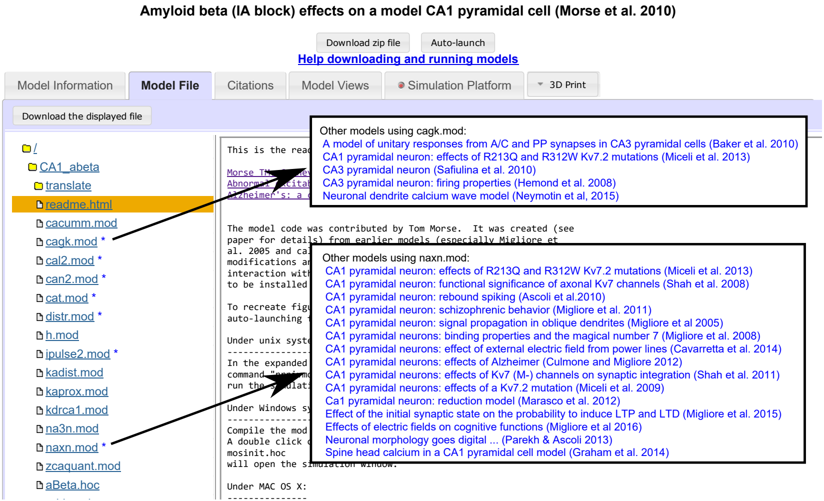
(1) Search models. **(2)** Browse models. **(3)** Link to download the entire model code. **(4)** Auto-launch a NEURON simulation (requires browser configuration). **(5)** View model files. **(6)** Find models and papers cited by this model's paper, or that cite this model. **(7)** ModelView: visualize model structure. **(8)** Simulation platform (5 minutes of remote desktop access to experiment with the model). **(9)** 3D printable versions of cells from the model (in 3DModelDB). **(10)** Description of model. **(11)** Paper(s) describing or using model. **(12)** Searchable metadata. **(13)** Links to NeuronDB (channel distributions etc within cell types).

ShowModel features



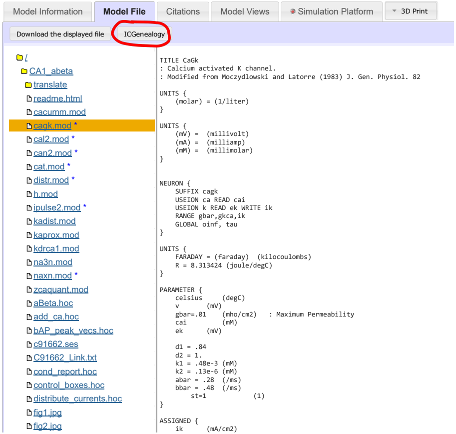
(14) Download the currently selected file. **(15)** Directory browser, showing model files. **(16)** View pane for the currently selected file.

Identifying existing reuse



Asterisks in the file browser indicate that the file is reused in other models; click the asterisk to see a list of the other models.

ICGenealogy: ion channel metadata



General data

- **ICG id:** 2464
- **ModelDB id:** 87284
- **Reference:** *Morse TM, Carnevale NT, Mutalik PG, Migliore M, Shepherd GM (2010)*: Abnormal Excitability of Oblique Dendrites Implicated in Early Alzheimer's: A Computational Study.

Metadata classes

- **Animal Model:** rat
- **Brain Area:** hippocampus, CA1
- **Classes:** KCa
- **Ion Type:** K
- **Neuron Region:** unspecified
- **Neuron Type:** pyramidal cell
- **Runtime Q:** Q4 (slow)
- **Subtype:** not specified

Metadata generic

- **Age:** 7-14 weeks old.
- **Comments:** Calcium activated k channel, modified from moczydlowski and latorre (1983). From hemond et al. (2008), model no. 101629, with no changes (identical mod file). Animal model taken from chen (2005) which is used to constrain model. Channel kinetics from previous study on hippocampal pyramidal neuron (hemond et al. 2008)
- **Runtime:** 76.722

When viewing most `mod` files describing an ion channel, an ICGenealogy button appears. Clicking this button loads the corresponding page of the ICGenealogy database which shows curated information about the channel model (how it was derived, information about the underlying data, etc) and response curves.

ModelView

Amyloid beta (IA block) effects on a model CA1 pyramidal cell (Morse et al. 2010)

Download zip file | Auto-launch

Help downloading and running models

Model Information | Model File | Citations | Model Views | Simulation Platform | 3D Print

Accession:87284

The model simulations provide evidence oblique dendrites in CA1 pyramidal neurons are susceptible to hyper-excitability by amyloid beta block of the transient K+ channel, IA. See paper for details.

Reference:

1 . Morse TM, Carnevale NT, Mutalik PG, Migliore M, Shepherd GM (2010) Abnormal excitability of oblique dendrites implicated in early Alzheimer's: a computational study *Front. Neural Circuits* **4**:16 [PubMed]

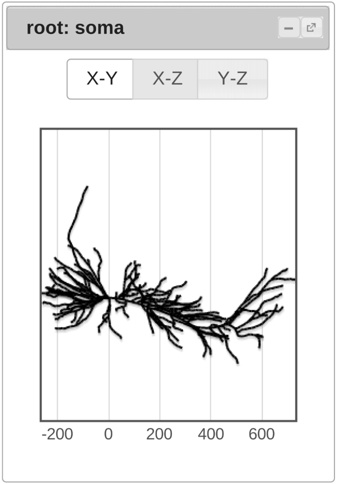
Model Information (Click on a link to find other models with that property)

Model Type:	Neuron or other electrically excitable cell;
Brain Region(s)/Organism:	
Cell Type(s):	Hippocampus CA1 pyramidal cell;
Channel(s):	I Na,t; I L high threshold; I N; I T low threshold; I A; I K; I h;
Gap Junctions:	
Receptor(s):	
Gene(s):	
Transmitter(s):	
Simulation Environment:	NEURON;
Model Concept(s):	Dendritic Action Potentials; Active Dendrites; Detailed Neuronal Models; Pathophysiology; Aging/Alzheimer`s;
Implementer(s):	Carnevale, Ted [Ted.Carnevale at Yale.edu]; Morse, Tom [Tom.Morse at Yale.edu];

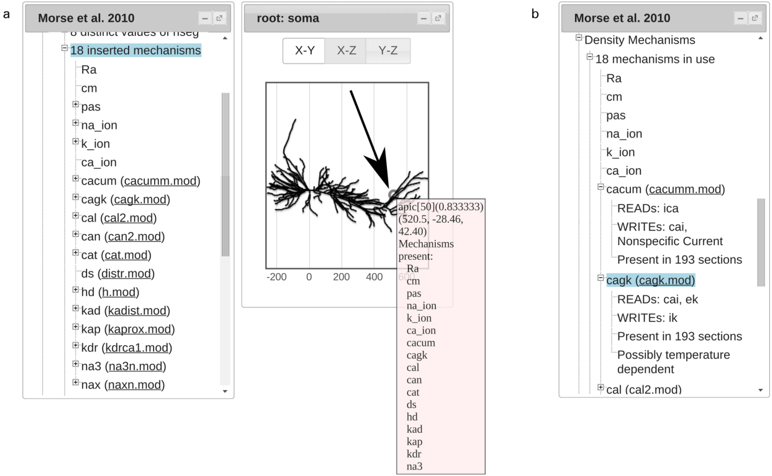
Search NeuronDB for information about: Hippocampus CA1 pyramidal cell; I Na,t; I L high threshold; I N; I T low threshold; I A; I K; I h;

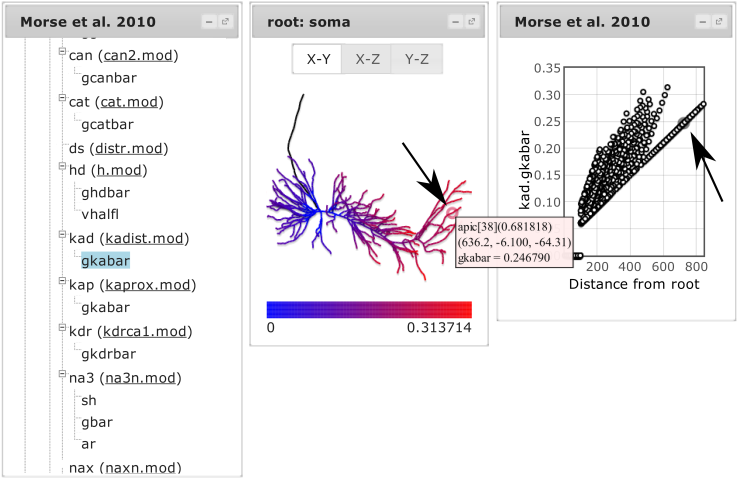
Morse et al. 2010

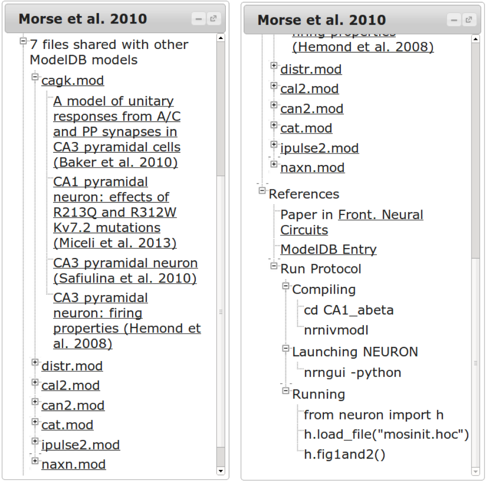
- 194 sections; 974 segments
- 1 cell with morphology
- 0 artificial cells
- 0 NetCon objects
- 0 LinearMechanism objects
- Temperature: 35°C
- Density Mechanisms
- 1 point processes (0 can receive events) of 1 base classes
- 7 files shared with other ModelDB models
- References



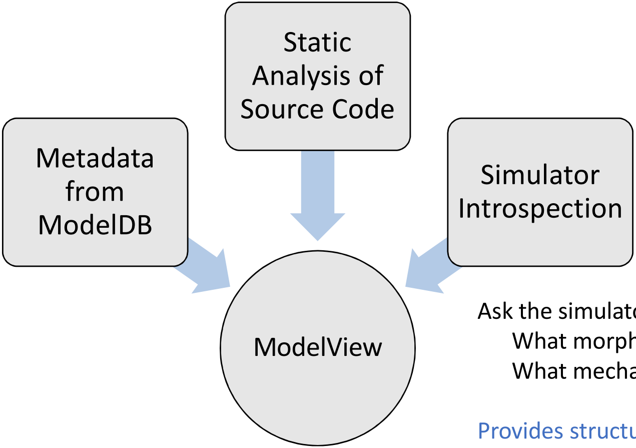
McDougal et al, *Neuroinformatics* 2015


a
Morse et al. 2010
8 distinct values of nseg
18 inserted mechanisms
Ra
cm
pas
na_ion
k_ion
ca_ion
cacum (cacumm.mod)
cagk (cagk.mod)
cal (cal2.mod)
can (can2.mod)
cat (cat.mod)
ds (distr.mod)
hd (h.mod)
kad (kadist.mod)
kap (kaprox.mod)
kdr (kdrca1.mod)
na3 (na3n.mod)
nax (naxn.mod)
root: soma
X-Y
X-Z
Y-Z
-200
0
200
400
600
apic[50](0.833333)
(520.5, -28.46, 42.40)
Mechanisms present:
Ra
cm
pas
na_ion
k_ion
ca_ion
cacum
cagk
cal
can
cat
ds
hd
kad
kap
kdr
na3
b
Morse et al. 2010
Density Mechanisms
18 mechanisms in use
Ra
cm
pas
na_ion
k_ion
ca_ion
cacum (cacumm.mod)
READs: ica
WRITEs: cai, Nonspecific Current
Present in 193 sections
cagk (cagk.mod)
READs: cai, ek
WRITEs: ik
Present in 193 sections
Possibly temperature dependent
cal (cal2.mod)


Morse et al. 2010
can (can2.mod)
gcanbar
cat (cat.mod)
gcatbar
ds (distr.mod)
hd (h.mod)
ghdbar
vhalfl
kad (kadist.mod)
gkabar
kap (kaprox.mod)
gkabar
kdr (kdrca1.mod)
gkdrbar
na3 (na3n.mod)
sh
gbar
ar
nax (naxn.mod)
root: soma
X-Y
X-Z
Y-Z
apic[38](0.681818)
(636.2, -6.100, -64.31)
gkabar = 0.246790
0
0.313714
Morse et al. 2010
0.35
0.30
0.25
0.20
0.15
0.10
kad.gkabar
200
400
600
800
Distance from root


Morse et al. 2010
7 files shared with other ModelDB models
cagk.mod
A model of unitary responses from A/C and PP synapses in CA3 pyramidal cells (Baker et al. 2010)
CA1 pyramidal neuron: effects of R213Q and R312W Kv7.2 mutations (Miceli et al. 2013)
CA3 pyramidal neuron (Safiulina et al. 2010)
CA3 pyramidal neuron: firing properties (Hemond et al. 2008)
distr.mod
cal2.mod
can2.mod
cat.mod
ipulse2.mod
naxn.mod
Morse et al. 2010
(Hemond et al. 2008)
distr.mod
cal2.mod
can2.mod
cat.mod
ipulse2.mod
naxn.mod
References
Paper in Front. Neural Circuits
ModelDB Entry
Run Protocol
Compiling
cd CA1_abeta
nrnivmodl
Launching NEURON
nrngui -python
Running
from neuron import h
h.load_file("mosinit.hoc")
h.fig1and2()

What described where?
Beware: comments, if statements.



Simulator?
Papers?
Species?
Channels?
Context?

Ask the simulator what it did.
    What morphology?
    What mechanisms?

Provides structured data from unstructured code.

How do people use ModelDB?

- Find a model described in a paper, download it, and experiment to understand the model's predictions.
- Find a model described in a paper. Use ModelView to understand the model's structure.
- Locate models and modeling papers on a given topic.
- Locate model components (e.g. L-type calcium channel) for potential reuse.
- Search for simulator keywords (e.g. FInitializeHandler) to find examples of how to use them.

You can help by sharing your model code on ModelDB after publication.

Sharing your models

McDougal, Dalal, Shepherd in preparation

Sharing your models

search
Advanced search

SenseLab ModelDB SimToolDB

- ModelDB Help
- **User account**
  - Login
  - Register
- **Find models by**
  - Model name
  - First author
  - Each author
  - Region(circuits)
- **Find models for**
  - Cell type
  - Current
  - Receptor
  - Gene
  - Transmitters
  - Topic
  - Simulators
  - Methods
- **Find models of**
  - Realistic Networks
  - Neurons
  - Electrical synapses (gap junctions)
  - Chemical synapses
  - Ion channels
  - Neuromuscular junctions
  - Axons
- **Other resources**
  - ModelDB related resources
  - Computational neuroscience

Submit New Model

Required information:

Your full name: Modeler or Contributor name

Your email address: Email

Zip file of model code: Choose File No file chosen

Read-Write access code (15 character max): Access code
Used as a password to only access this model

PubMed ID(s) or citation(s) associated with the model:
Only required for publicly shared models.
Citation(s) can be in any bibliographic format.

You may Submit with just the above information, but **to make your model more discoverable, please fill out as much of the next section as you can.** *Note: Your model will remain private until you request the ModelDB administrator make it public.*

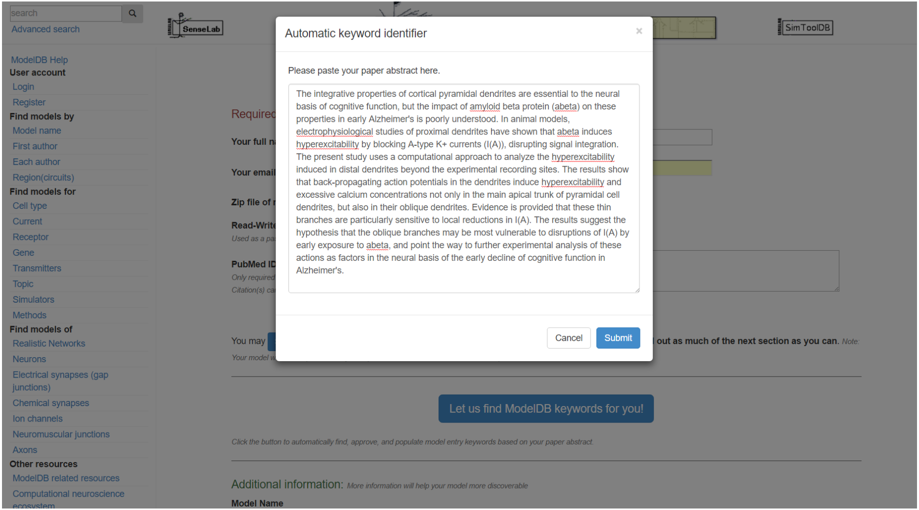
Let us find ModelDB keywords for you!

Click the button to automatically find, approve, and populate model entry keywords based on your paper abstract.

Additional information: *More information will help your model more discoverable*

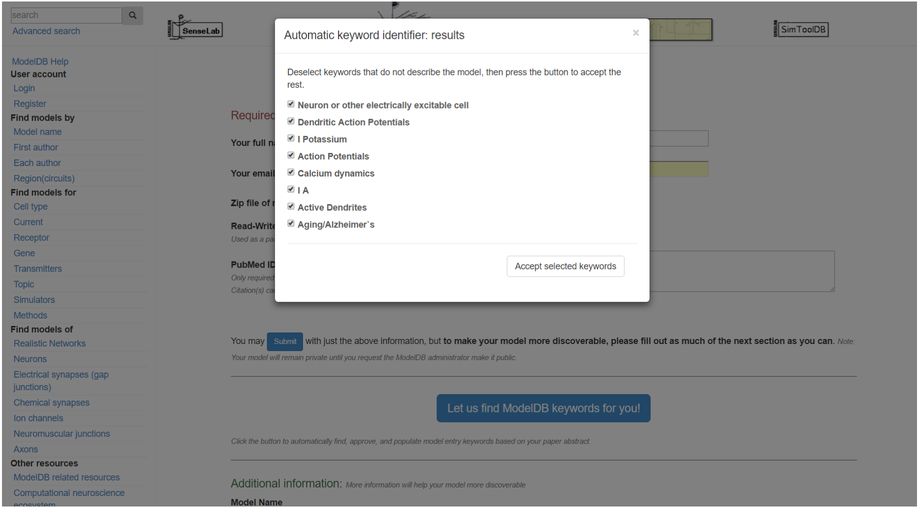
McDougal, Dalal, Shepherd in preparation

Sharing your models



McDougal, Dalal, Shepherd in preparation; abstract from Morse et al, 2010.

Sharing your models



McDougal, Dalal, Shepherd in preparation

Sharing your models

search
Advanced search

SenseLab

ModelDB

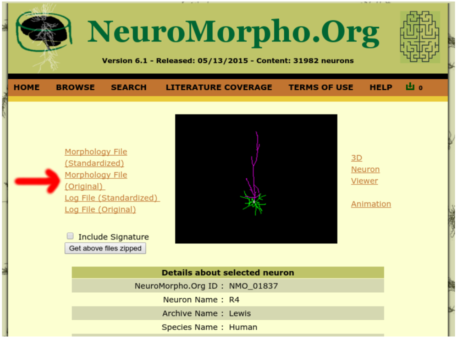
SimToolDB

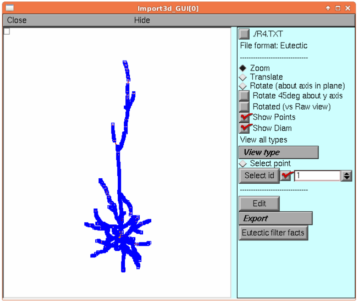
Other Neuron	
Model Neurotransmitters	
Other Neurotransmitter	
Model Receptors	
Other Receptor	
Model Currents	x I Potassium x I A
Other Current	
Gap Junctions	
Gene	
Other Gene	
Model Type	x Neuron or other electrically excitable cell
Other Model Type	
Model Concept	x Dendritic Action Potentials x Action Potentials x Calcium dynamics x Active Dendrites x Aging/Alzheimer`s
Other Concept	
Simulator software	
Other Simulator	
Region Organism	
Implemented by	

McDougal, Dalal, Shepherd in preparation

Other resources

NeuroMorpho.Org

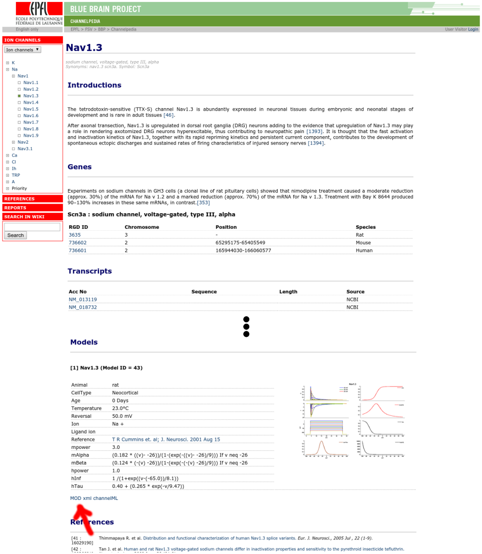




Tools ▶ Miscellaneous ▶ Import 3D

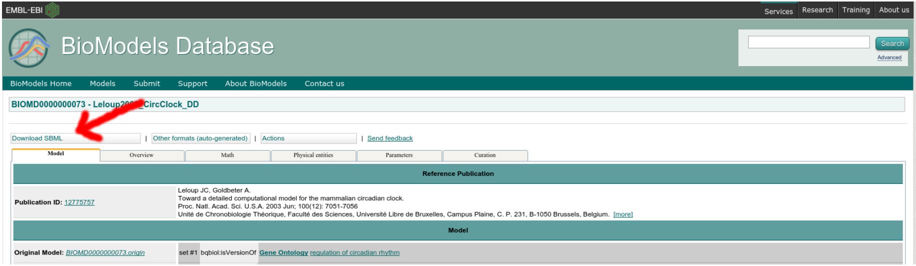
- NeuroMorpho.Org is home to 50,356 reconstructed neurons from 212 cell types and 37 species as of October 24, 2016.
- Warning: not every morphology was reconstructed with the intent of being in a simulation. Before using: rotate to check for z-axis errors, check to make sure the diameters are not all equal.
- Use the Import 3D tool to import morphologies into NEURON. For details, see: neuron.yale.edu/neuron/docs/import3d

Channelpedia (Channelpedia.epfl.ch)



- Home to information about ion channels.
- Many channels have one or more associated models (e.g. different species or cell types); all are downloadable as MOD files.
- Shows gating variable and channel response to voltage clamp for each model.

Biomodels (www.ebi.ac.uk/biomodels-main)



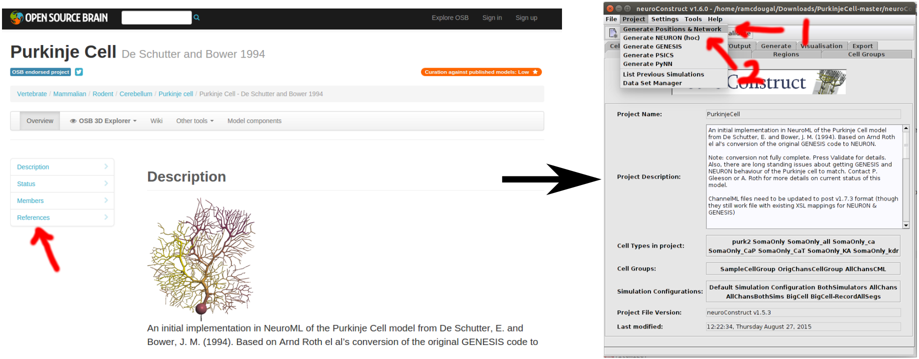
`jnml BIOMD0000000073_LEMS.xml -neuron`

Biomodels model (SBML) ⟶ LEMS model ⟶ MOD file

`jnml -sbml-import BIOMD0000000073.xml 1000 5`

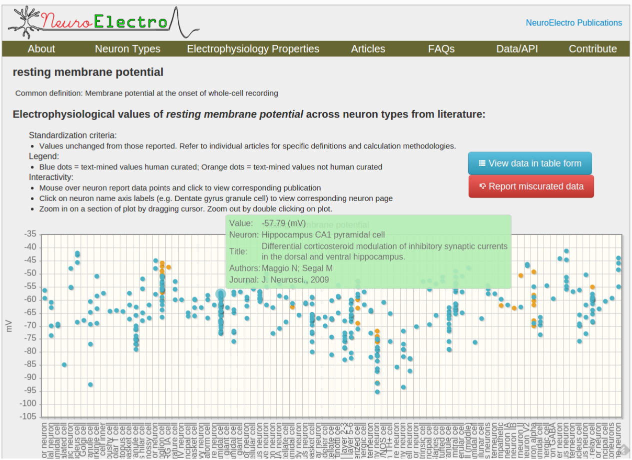
- Biomodels is a systems biology model repository.
- Models are in SBML but can be converted to MOD files via e.g. jNeuroML (github.com/NeuroML/jNeuroML). Test converted models before using in a larger model. Edits will likely be necessary to get them to interoperate with other mechanisms.
- A native SBML importer for NEURON's rxd module is under development.

Open Source Brain (OpenSourceBrain.org)



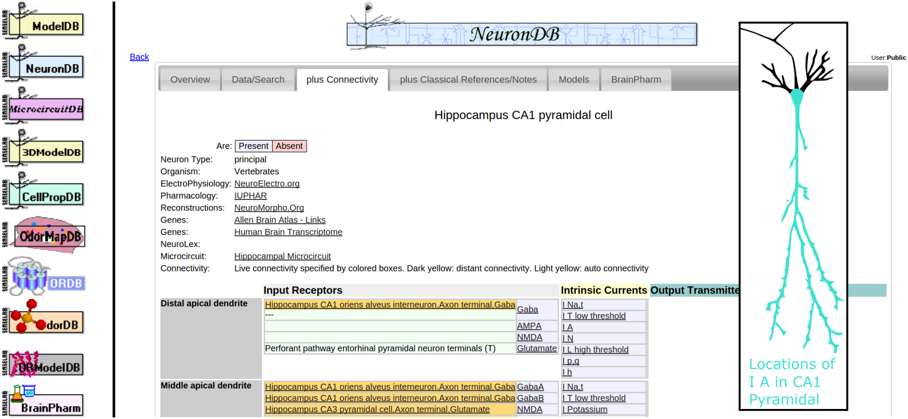
- Open Source Brain promotes collaborative model development via github.
- Models are typically in NeuroML or neuroConstruct format; neuroConstruct (neuroConstruct.org) converts both formats to NEURON.
- The conversion process places different ion channels in different MOD files, which allows extracting model components.

NeuroElectro (NeuroElectro.org)



- NeuroElectro archives experimentally measured electrophysiology values for different cell types; it shows the spread and allows comparing values across different cell types.
- Read the paper associated with a value to understand: species, experimental conditions, etc.

SenseLab (senselab.med.yale.edu)



- SenseLab is a suite of 10 interconnected databases (listed at left).
- ModelDB and NeuronDB (at right) are the most useful for modeling.
- NeuronDB shows what channels are present and the inputs and outputs *by cell region* (e.g. distal apical dendrite vs proximal apical dendrite).

Stay up to date

Twitter

Many groups announce new developments on Twitter, including:

- SenseLab (including ModelDB): @SenseLabProject
- Open Source Brain: @OSBTeam
- NeuroMorpho.Org: @NeuroMorphoOrg
- ICGenealogy Project: @ICGenealogy
- Int. Neuroinformatics Coordinating Facility (INCF): @INCForg