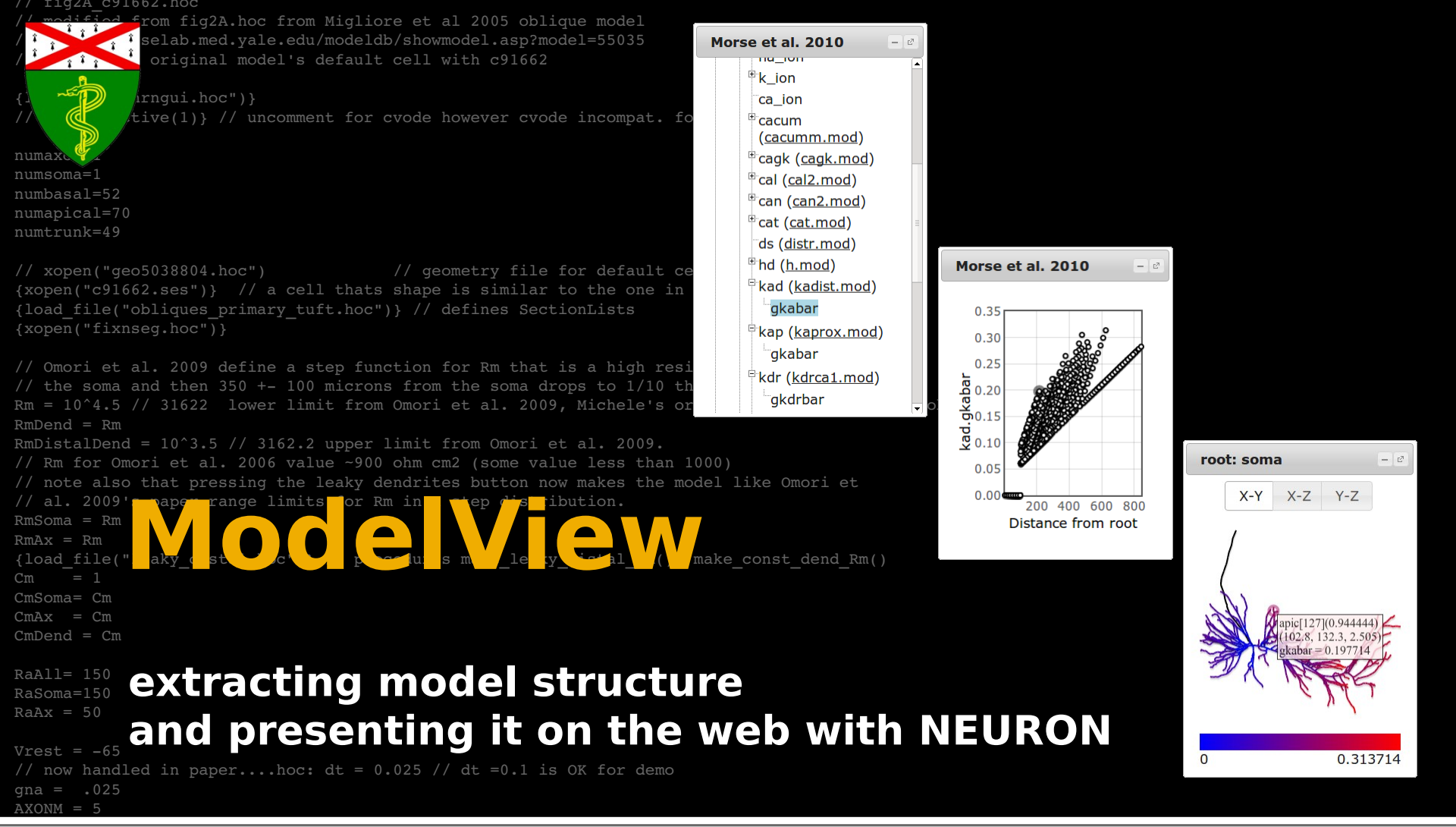


ModelView

extracting model structure and presenting it on the web with NEURON

14 May 2014
Open Source Brain
New Haven, CT

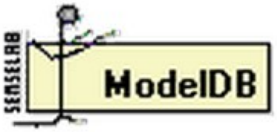
Robert A. McDougal
Postdoctoral Fellow
Neurobiology • Yale University

ModelDB

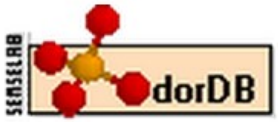
- 880 published computational neuroscience models
- 67 simulators
- Part of the SenseLab suite of databases

  modeldb.yale.edu

Neuronal Databases



Olfactory Databases



Disease Databases

What is needed for reproducibility?

What is needed for reproducibility?

Model

an approximation of the system of interest
e.g. in NEURON or NeuroML

What is needed for reproducibility?

Model

an approximation of the system of interest
e.g. in NEURON or NeuroML

Experimental protocol

what was done with the model to produce the data

What is needed for reproducibility?

Model

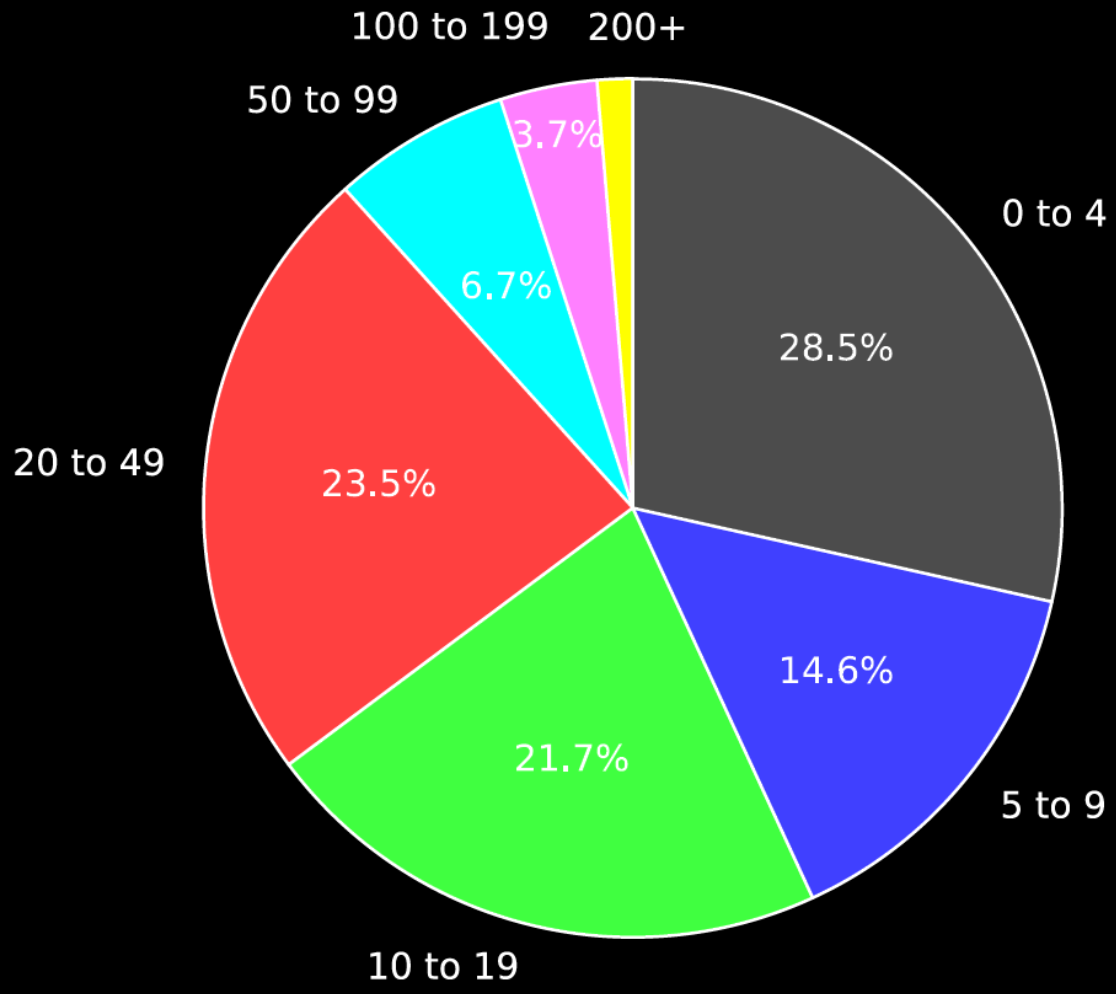
an approximation of the system of interest
e.g. in NEURON or NeuroML

Experimental protocol

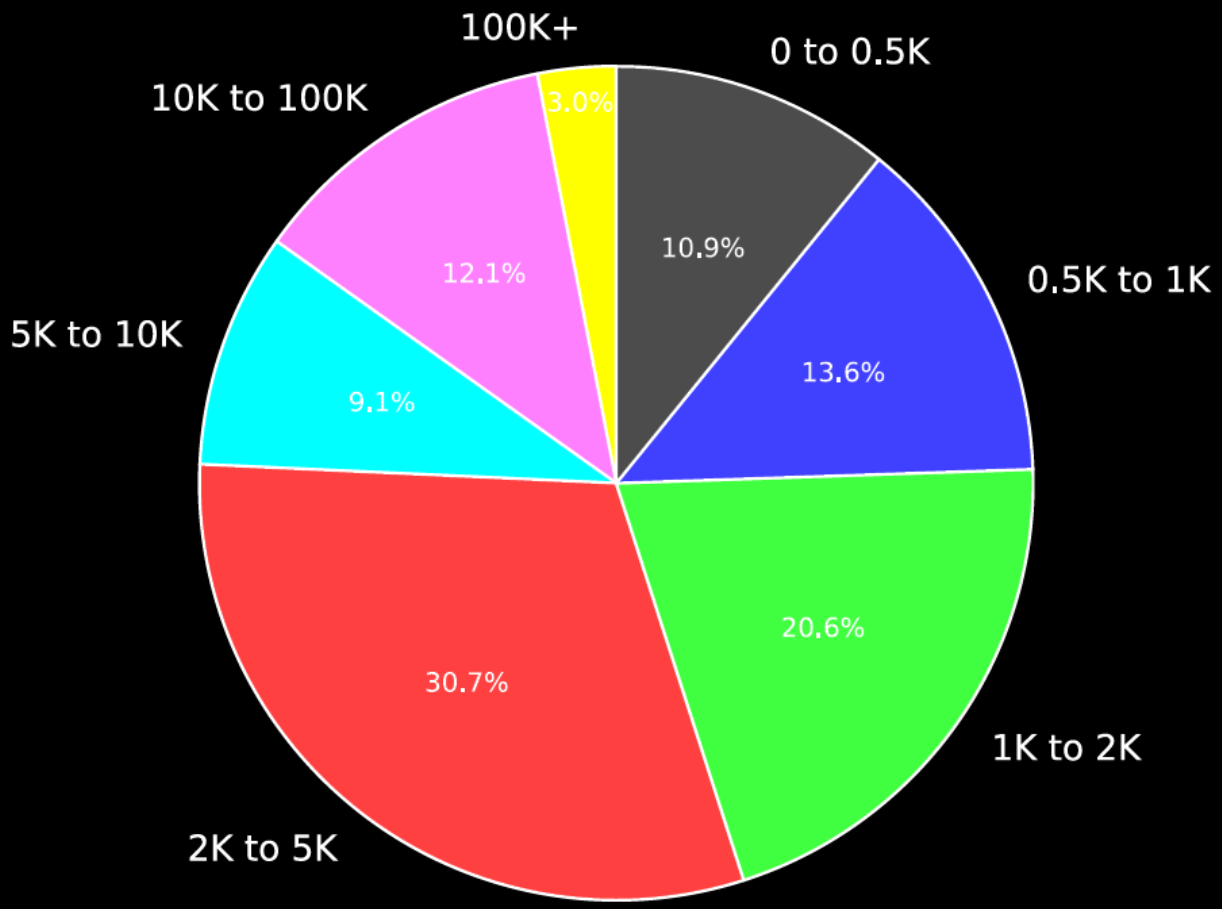
what was done with the model to produce the data

in every ModelDB entry

Models May Contain Many Files



Model Files May Be Large



Model Files Might Be Structured...

```
<cell name = "SimpleCell">

    <segments xmlns="http://morphml.org/morphml/schema">
        <segment id ="0" name="Soma"  cable="0">
                <proximal x="0" y="0" z="0" diameter="10"/>
                <distal x="10" y="0" z="0" diameter="10"/>
        </segment>
        <segment id ="1" name="Dendrite" parent="0" cable="1">
                <proximal x="10" y="0" z="0" diameter="3"/> <!-- Note 3D point
                        same as parent, diam different-->
                <distal x="20" y="0" z="0" diameter="3"/>
        </segment>
    </segments>

    <cables xmlns="http://morphml.org/morphml/schema">
        <cable id="0" name="SomaCable" />
        <cable id="1" name="DendriteCable" />
    </cables>

</cell>
```

http://neuroml.org/NeuroMLValidator/ViewNeuroMLFile.jsp?localFile=NeuroMLFiles/Examples/MorphML/SimpleNeuroML.xml

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

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

Citations Citation Browser

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;

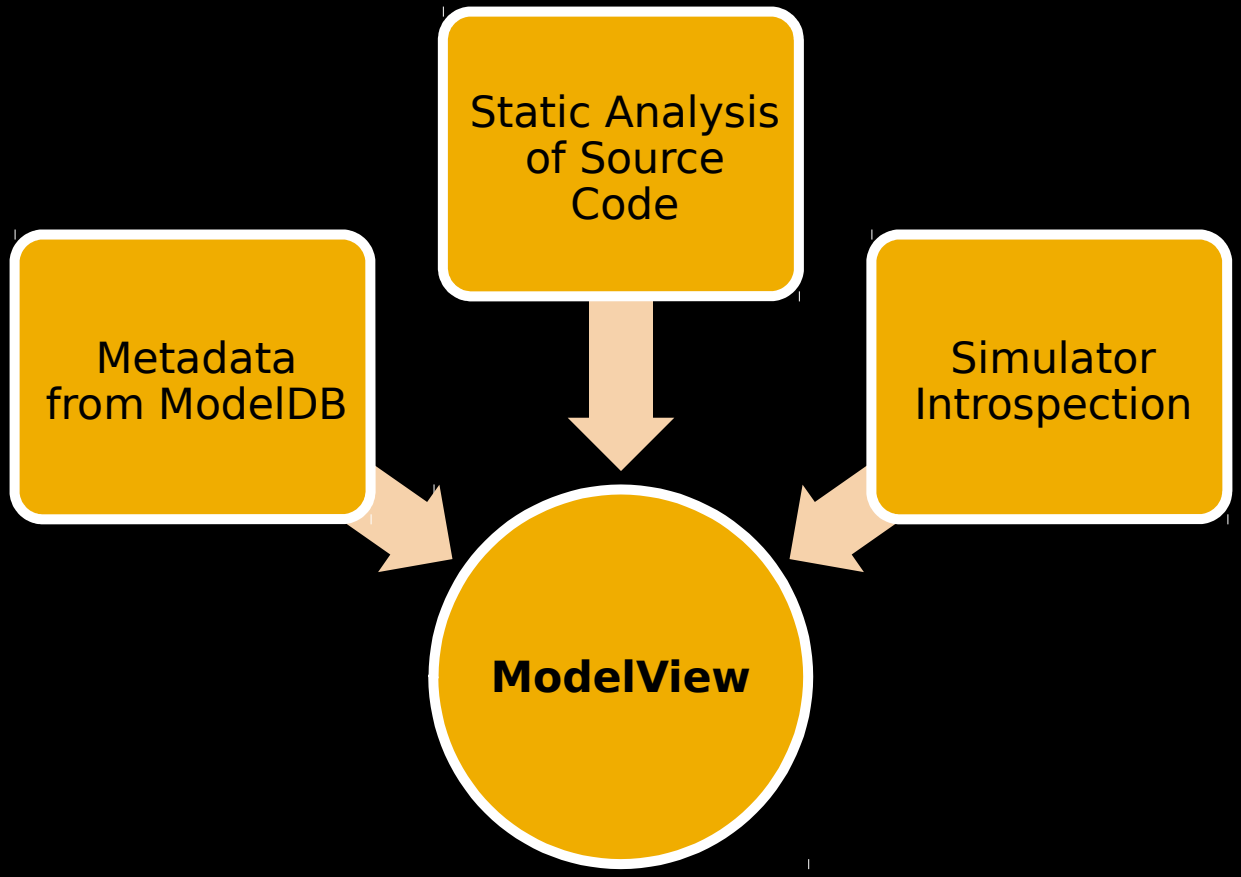
Model files Download zip file | Auto-launch | Download the displayed file | Simulation Platform | ModelView | Help downloading and running models

- \
  - CA1_abeta
    - translate
    - readme.html
    - fig1.jpg
    - fig2.jpg
    - fig3.jpg
    - fig4.jpg
    - fig5.jpg
    - fig6b.jpg
    - cal2.mod *
    - can2.mod *
    - cat.mod *
    - distr.mod *
    - cacumm.mod
    - cagk.mod *
    - h.mod
    - ipulse2.mod *
    - kadist.mod
    - kaprox.mod
    - kdrca1.mod
    - na3n.mod
    - naxn.mod *
    - zcaquant.mod
    - control_boxes.hoc
    - cond_report.hoc
    - figs.hoc
    - find_averages.hoc
    - fixnseg.hoc
    - generate_conc_graph.hoc
    - gka_averager.hoc
    - graph_na3_kinetics.hoc
    - distribute_currents.hoc
    - init_and_run_and_graph.hoc
    - add_ca.hoc
    - bAP_peak_vecs.hoc
    - fig2A_c91662.hoc
    - leaky_distal.hoc
    - maxica.hoc
    - mosinit.hoc
    - na3_shifter.hoc

```
// fig2A_c91662.hoc
// modified from fig2A.hoc from Migliore et al 2005 oblique model
// http://senselab.med.yale.edu/modeldb/showmodel.asp?model=55035
// to replace original model's default cell with c91662

{load_file("nrngui.hoc")}
// {cvode_active(1)} // uncomment for cvode however cvode incompat. for calcium analysis

numaxon=1
numsoma=1
numbasal=52
numapical=70
numtrunk=49

// xopen("geo5038804.hoc")            // geometry file for default cell
{xopen("c91662.ses")}  // a cell thats shape is similar to the one in Chen C et al. 2005
{load_file("obliques_primary_tuft.hoc")} // defines SectionLists
{xopen("fixnseg.hoc")}

// Omori et al. 2009 define a step function for Rm that is a high resistance, RmDend nea
// the soma and then 350 +- 100 microns from the soma drops to 1/10 that value, RmDistal
Rm = 10^4.5 // 31622  lower limit from Omori et al. 2009, Michele's original value: 2806
RmDend = Rm
RmDistalDend = 10^3.5 // 3162.2 upper limit from Omori et al. 2009.
// Rm for Omori et al. 2006 value ~900 ohm cm2 (some value less than 1000)
// note also that pressing the leaky dendrites button now makes the model like Omori et
// al. 2009's paper range limits for Rm in a step distribution.
RmSoma = Rm
RmAx = Rm
{load_file("leaky_distal.hoc")} // procedures make_leaky_distal_Rm(), make_const_dend_Rm
Cm    = 1
CmSoma= Cm
CmAx  = Cm
CmDend = Cm

RaAll= 150
RaSoma=150
RaAx = 50

Vrest = -65
// now handled in paper....hoc: dt = 0.025 // dt =0.1 is OK for demo
gna =  .025
AXONM = 5
gkdr = 0.01
celsius = 35.0
KMULT =  0.03 // Michele suggests that changing these to 0.04 from 0.03
KMULTP = 0.03 // is within the physiological range
ghd=0.00005
// the below 2 get reset later but must be defined to show up in gui text editors
gc=0  // used for setting the T, L, and N Ca2+ currents max conductance
gKc=0 // used for setting the Ca2+ sensitive K current max conductance
gt=0  // used for setting the T-type Ca current max cond. to a particular value

alzheimers_flag=0 // flag turns true when simulating alzheimers
current_marker_color=3 // starts out blue (3), red is 2
apic_resize_factor=1 // default value doesn't change anything, 10, 1/10 typical choices
apic_comp_index=0 // selects in text box which compartment is specifically changed, 0-12
marker_graph=1 // 1 for marker graphs
line_graph=1 // 1 for line graphs
strdef current_marker_style
current_marker_style="O"
current_marker_size=3
current_cai_marker=3 // peak internal Ca2+ concentration graphs:  3=triangle 2=square
current_cai_marker_color=1 // 1=black, 2=red
aBeta_concentration_factor=1 // this is used to model smaller concentrations of aBeta
                             // than were measured experimentally.  The assumption is
// that the blocking due to a smaller value of aBeta would be linearly proportional to
// the full blocking as a factor of the ratio of the model concentration divided by the
// experimentally measured concentration (1 uM aBeta).
scale_ka=1 // used to scale the A-type current gmax's in the Migliore distribution
scale_obliques=1 // used to scale the A-type current gmax's on the relative distrib. in
objref g, b1, b2, c, d, stim, distrx, distry, distrt, cdistry
objref peak_ca_graph, peak_optical_graph

objref distrca, distr_cai_t // store the maximum cai values and times those max's occurr
objref tmp_vecx, tmp_vecy
objref b3
objref obliquex, obliquey, primaryx, primaryy, tuftx, tufty
objref obliqueca, primaryca, tuftca
objref obliqueoptical, primaryoptical, tuftoptical
objref p, chen_c_bpAP_peaks
objref soma_v_vec, dend_v_vec
objref obdend_v_vec, healthy_obdend_v_vec, abeta_obdend_v_vec

forsec "axon" {insert pas e_pas=Vrest g_pas = 1/RmAx Ra=RaAx cm=CmAx}
forsec "soma" {insert pas e_pas=Vrest g_pas = 1/RmSoma Ra=RaSoma cm=CmSoma}

// the union of dendrites in dendrite and user5 in the original model are
// analagous to the union of the dendrites in basal and apic in c91662

// forsec "dendrite" {insert pas e_pas=Vrest g_pas = 1/RmDend Ra=RaAll cm=CmDend}
forsec "basal" {insert pas e_pas=Vrest g_pas = 1/RmDend Ra=RaAll cm=CmDend}
// forsec "user5" {insert pas e_pas=Vrest g_pas = 1/RmDend Ra=RaAll cm=CmDend}
forsec "apic" {insert pas e_pas=Vrest g_pas = 1/RmDend Ra=RaAll cm=CmDend}

access soma

freq=50
geom_nseg()
// chance here to change the nseg for compartments if want to study effect of that
// high resolution for middle oblique of interest:


// for apicindex=73,79 {
//  apic[apicindex] nseg*=27

//forall { nseg*=27 }
/**/

tot=0
forall {tot=tot+nseg}
distance()  // establishes soma (still accessed) as origin for distance(x) function

tstop=20

load_file("control_boxes.hoc")

p = new PlotShape()
p.exec_menu("Shape Plot")
p.size(-194.658,304.758,-223.667,609.667)
p.variable("v")
p.show(0)

rel=0.5
soma {
  stim= new IClamp(rel)
  stim.amp=0 // was 2.5 in original Migliore et al. 2005 model
  stim.dur=1.5
  stim.del=1
```

How can we present this information in a human accessible way?

Part I:
extracting model structure

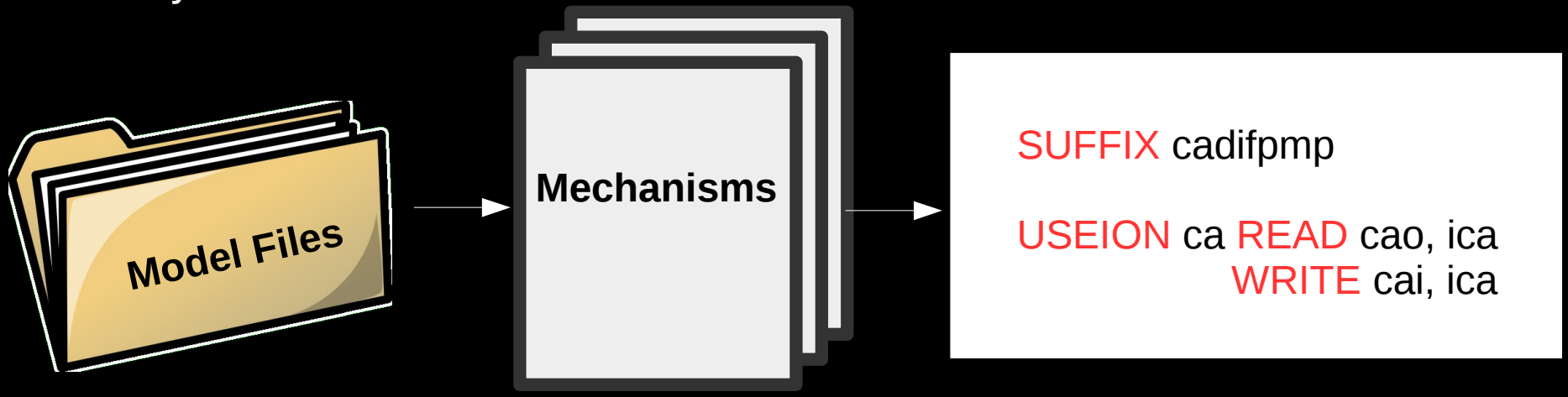

Static Analysis of Source Code
Metadata from ModelDB
Simulator Introspection
ModelView

Metadata

- The single most important piece of metadata is the simulator type, because that affects how everything else is interpreted.
- Run protocols describe how to run a simulation.
- Metadata may be static or dynamic.
- Static metadata, such as the doi of the paper that describes the model, is read only once, at preprocessing.
- To facilitate automated extracting metadata from a model's ModelDB page, we introduced ids for each of the named fields in the HTML.
- Dynamic metadata, such as component reuse, is loaded at display time by querying a web service.

Source code

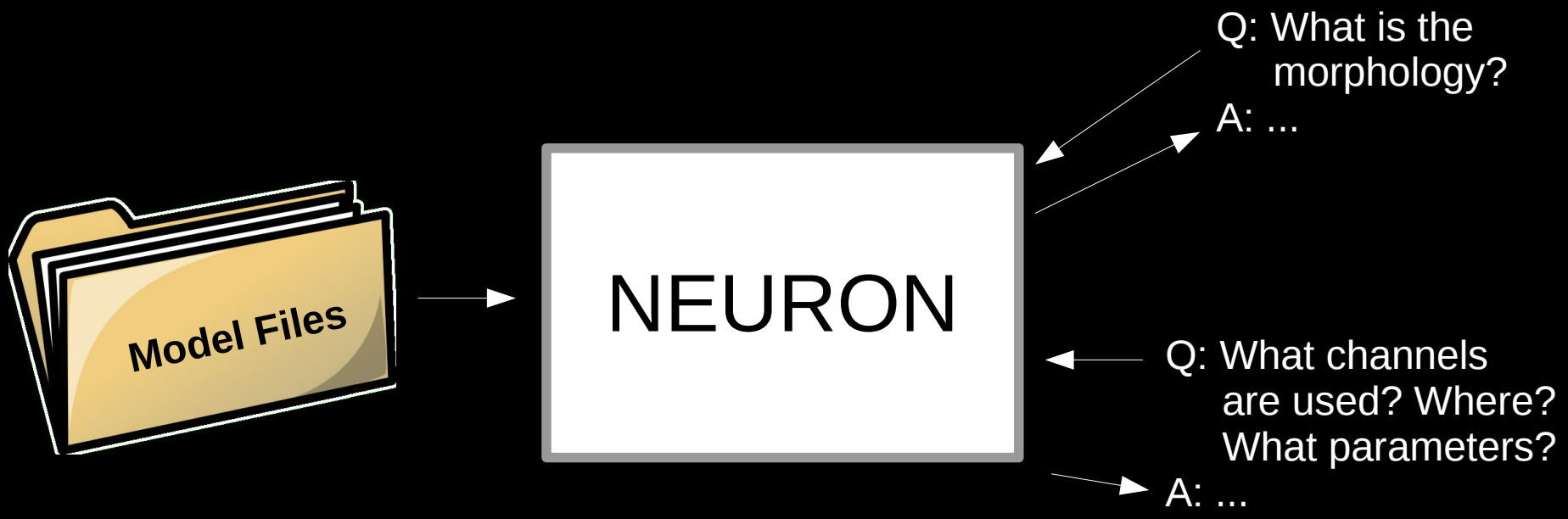
- Easy to extract information that the simulator requires to be expressed in a structured way (e.g. SUFFIX and POINT_PROCESS designations in NEURON).
  - We use this to map specific inserted mechanisms to the source code that defines them.
- Comments and flow control statements (e.g. if) complicate this analysis.



http://www.clker.com/cliparts/9/3/b/9/11949844132328857 55folder_01.svg.hi.png

Simulator introspection

- Gold standard: run the model. Ask the simulator what it did.
- This is used for most of the data in our model view tool (morphology, mechanism localization, parameters, etc...)
- Requires simulator support.



JSON data structure

```
{
  'title': 'Long title for page',
  'short_title': 'Migliore et al 2004',
  'neuron': [{
    'title': 'Pyramidal Cell',
    'morphology': [[[x1, y1, z1, d1], ...]]
  }, {... another neuron ...}],
  'colorbars': [
    {'type': 'css', 'css': ...}, ...
  ],
  'tree': [{
    'text': 'row text',
    'children': [...],
    'action': [{kind=...}],
    'noop': true or false or omitted
    'include': url or omitted
  }]
}
```

Part II:
Web presentation

ModelView web app

http://senselab.med.yale.edu/modeldb/modelview/modelview.html#87284_1

SenseLab ModelDB

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

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: 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]

Citations Citation Browser

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;

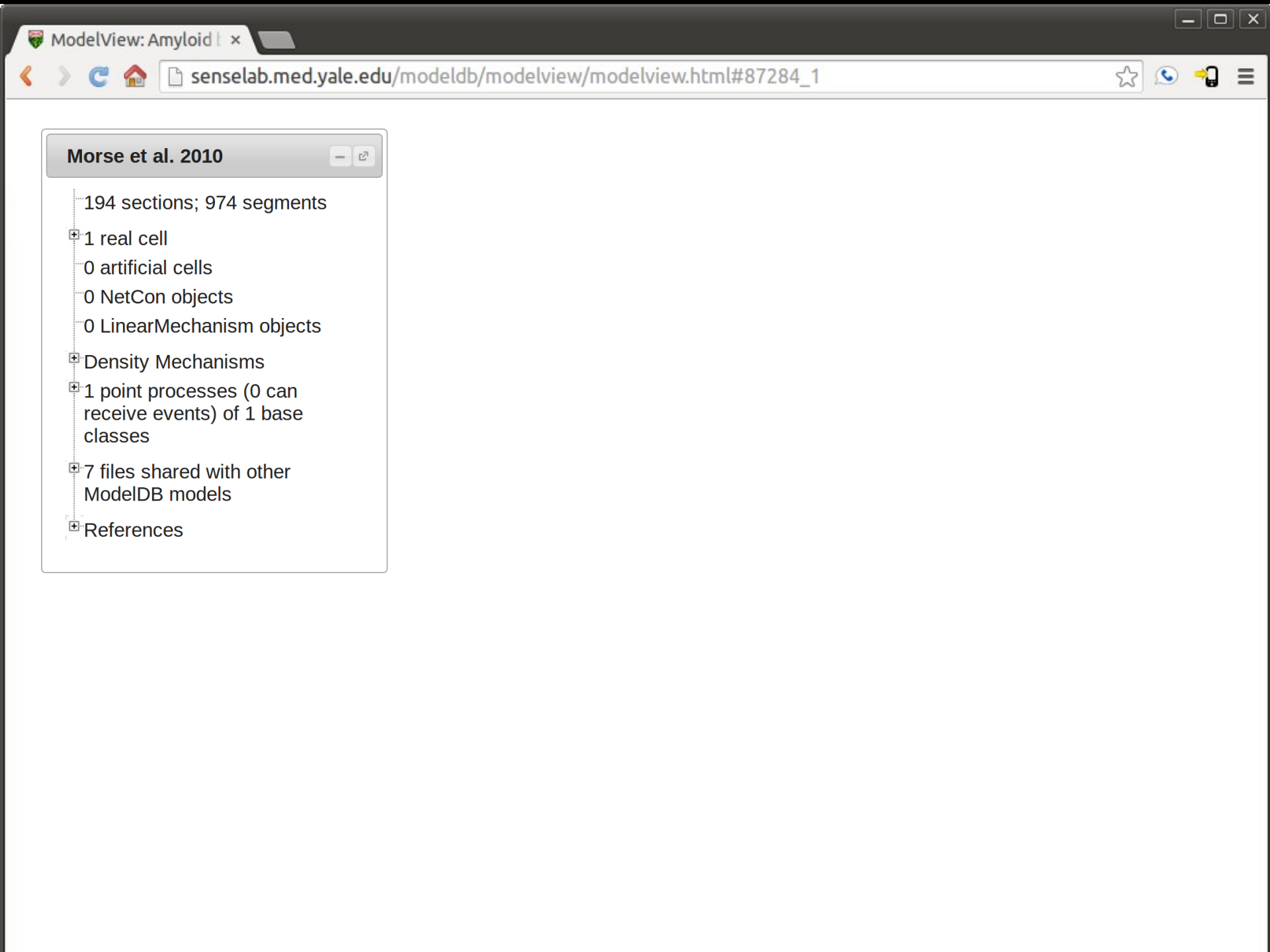
Model files Download zip file | Auto-launch | Simulation Platform | ModelView | Help downloading and running models

- \
  - CA1_abeta
    - translate

This is the readme for a model paper

Morse TM, Carnevale NT, Mutalik e M, Shepherd GM (2010) Abnormal excitability of obliqu implicated in early

Figure 1, 2
Figure 3
Figure 4


ModelView: Amyloid
senselab.med.yale.edu/modeldb/modelview/modelview.html#87284_1
Morse et al. 2010
194 sections; 974 segments
1 real cell
0 artificial cells
0 NetCon objects
0 LinearMechanism objects
Density Mechanisms
1 point processes (0 can receive events) of 1 base classes
7 files shared with other ModelDB models
References

ModelView: Amyloid

senselab.med.yale.edu/modeldb/modelview/modelview.html#87284_1

Morse et al. 2010

- nseg
- 19 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)

root: soma

X-Y | X-Z | Y-Z

apic[66](0.7)
(350.1, -47.93, -32.50)
Mechanisms present:
Ra
cm
pas
na_ion
k_ion
ca_ion
cacum
cagk
cal
can
cat
ds
hd
kad
kap
kdr
na3
caquant

ModelView: Amyloid

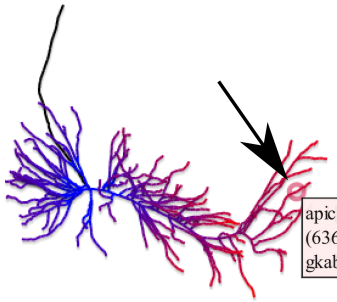
senselab.med.yale.edu/modeldb/modelview/modelview.html#87284_1

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)

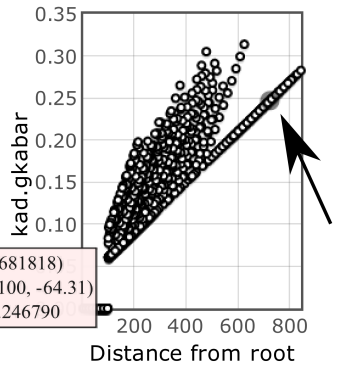
root: soma

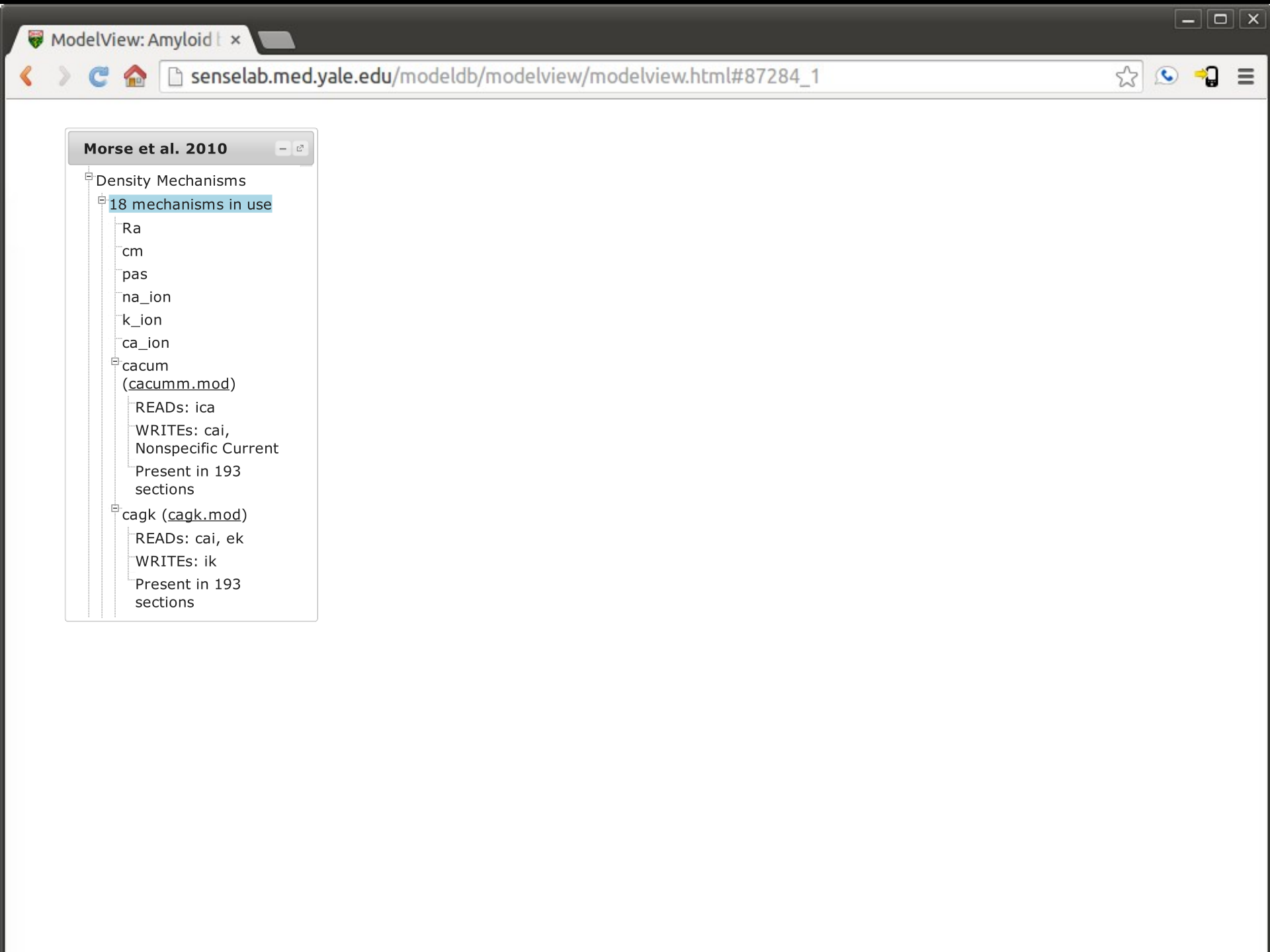
X-Y | X-Z | Y-Z



0 0.313714

Morse et al. 2010




ModelView: Amyloid
senselab.med.yale.edu/modeldb/modelview/modelview.html#87284_1
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

ModelView: Amyloid

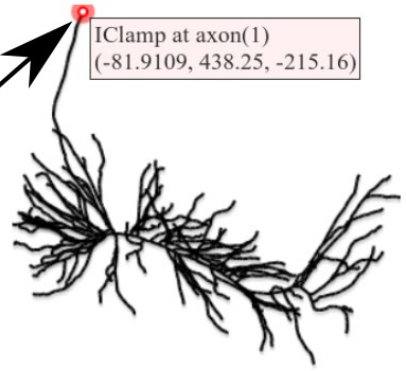
senselab.med.yale.edu/modeldb/modelview/modelview.html#87284_1

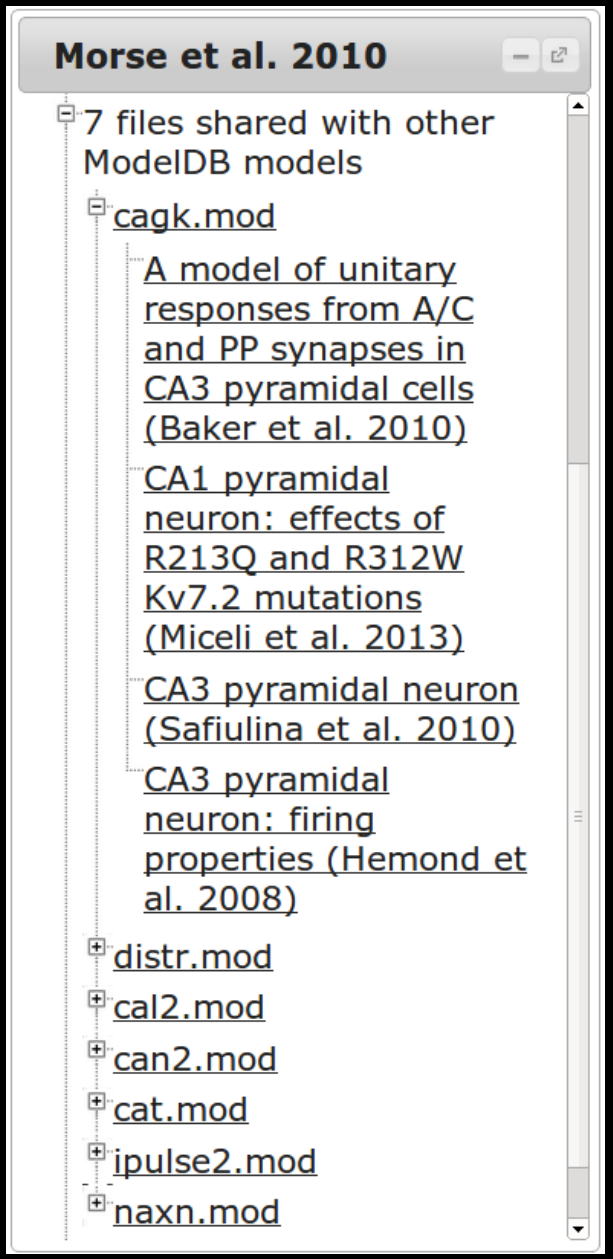
Morse et al. 2010

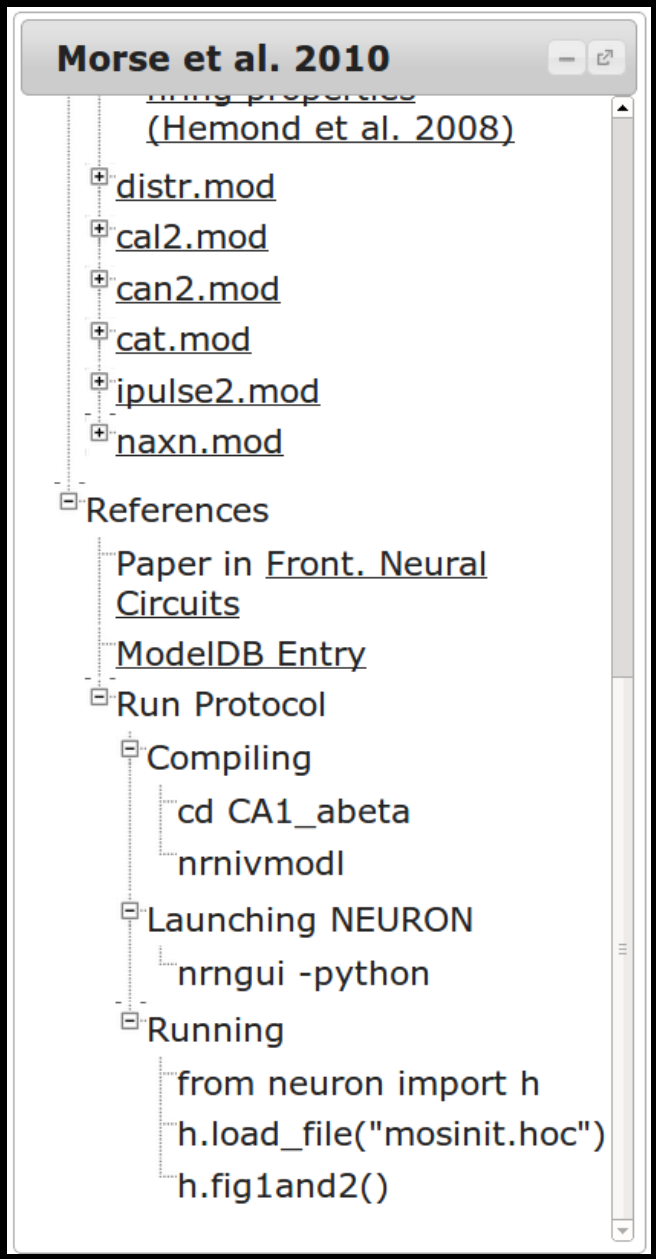
- 194 sections; 974 segments
- 1 real cell
- 0 artificial cells
- 0 NetCon objects
- 0 LinearMechanism objects
- Density Mechanisms
- 1 point processes (0 can receive events) of 1 base classes
  - 1 IClamp (builtin: ref)
    - del = 0
    - dur = 0.2
    - amp = 0.1
  - Global parameters for Point Processes
  - KSChan definitions for Point Processes
- 7 files shared with other ModelDB models

root: soma

X-Y | X-Z | Y-Z

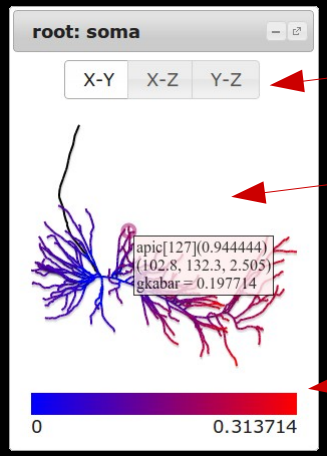



Morse et al. 2010
7 files shared with other ModelDB models
cagk.mod
A model of unitary responses from A/C and PP synapses in CA3 pyramidal cells (Baker et al. 2010)
CA1 pyramidal neuron: effects of R213Q and R312W Kv7.2 mutations (Miceli et al. 2013)
CA3 pyramidal neuron (Safiulina et al. 2010)
CA3 pyramidal 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()

NeuronWeb

- A general purpose library for presenting scientific information online.
- Uses JavaScript to dynamically rewrite the DOM to add and remove elements from the web page.
- Native elements, JQueryUI, Flot charts provide the core widgets.



JQueryUI Button Set

Flot Chart

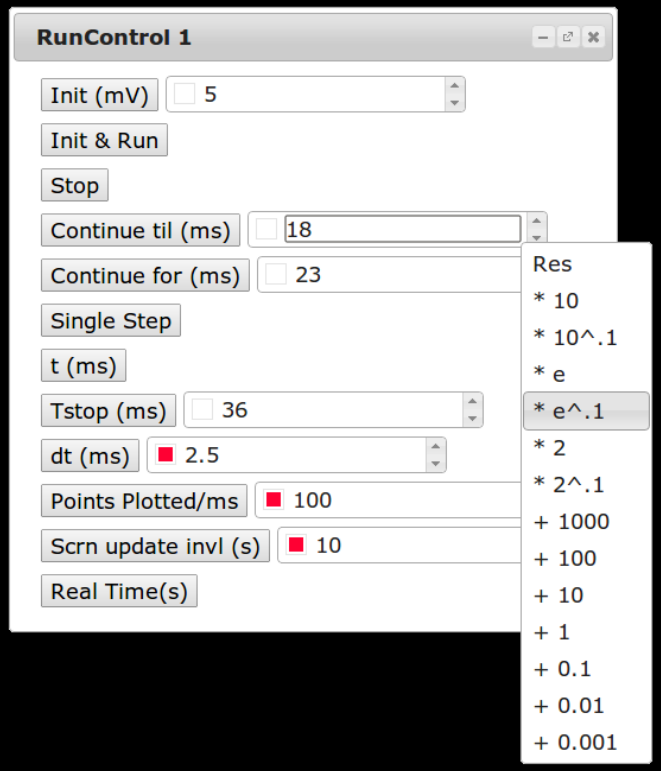
NeuronViewer widget

SVG Graphics

JQueryUI Dialog

NeuronWeb

- A general purpose library for presenting scientific information online.
- Level I: JavaScript layer for stand-alone web apps.
    - e.g. create a dialog with one function call, a graph with another.
    - Supports automatic layout adjustments.
- Level II: Interface controlled via websockets.
- Level III: Python library for controlling the interface.

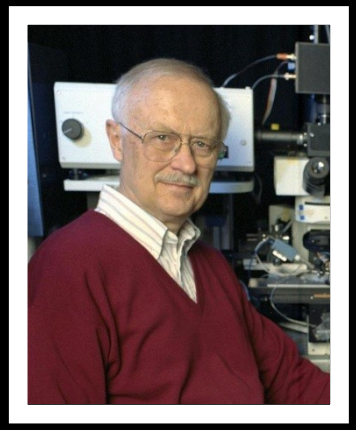


Conclusions

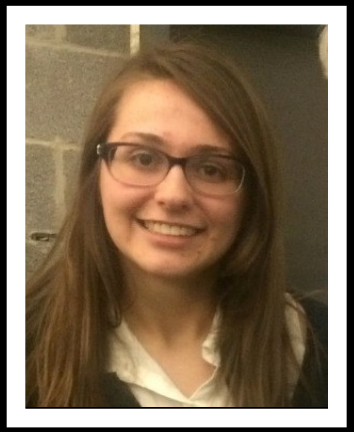
- Computational neuroscience models may be complicated.
- The source code is not human interpretable.
- Developed a web-based visualization tool that combines information from ModelDB metadata, source code text-mining, and introspection.
- The web viewer is simulator independent; general clickable tree and graph support is provided. Data is loaded from pre-generated JSON or dynamically generated JSONP.
- Model View should facilitate the interpretation and reuse of computational models.
- Model View could potentially be used to convert models to work with other simulators and for identification and analysis of repeated modeling motifs.

Acknowledgements

Michael Hines



Gordon Shepherd



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