

Collaboration and Validation in Models of Cells and Circuits

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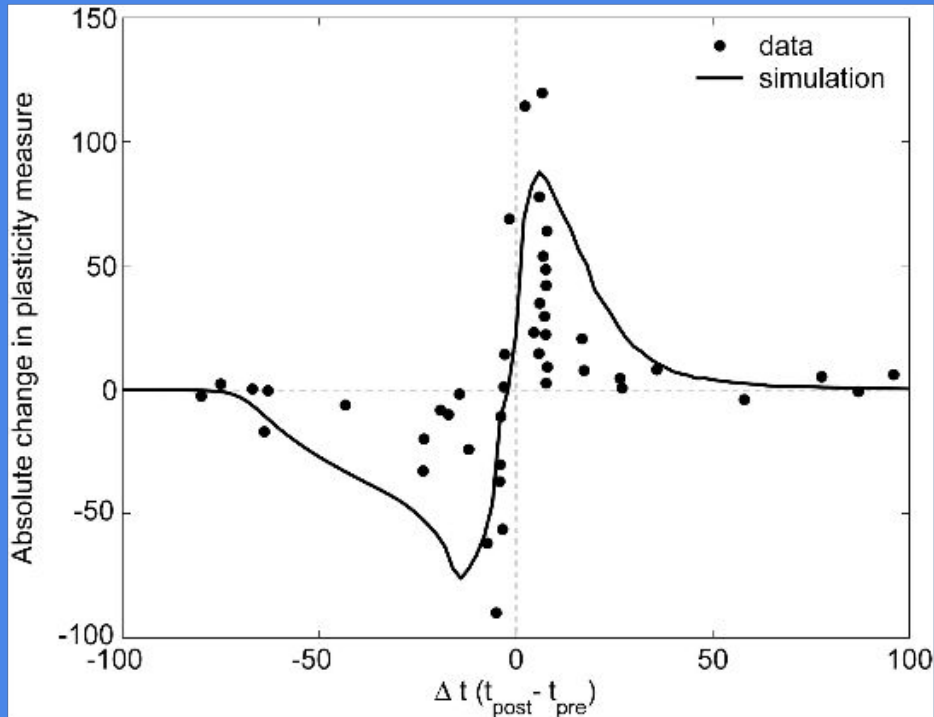


Parameter Consistency



Predictive Power





- Informality
- Inaccessibility
- Irreproducibility
- Incompleteness

We need a framework for

- formally
- rapidly
- transparently
- continuously

validating models



Unit Test

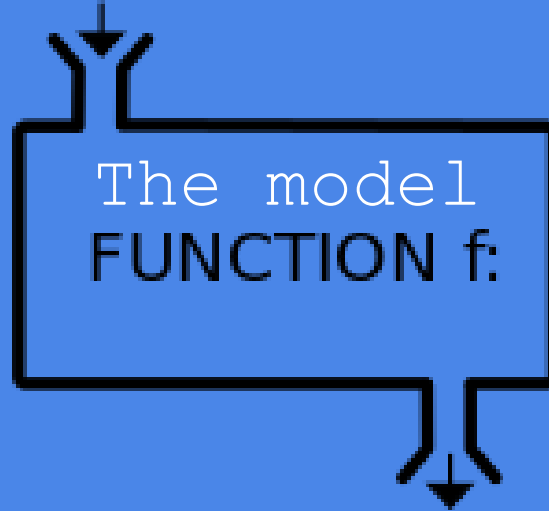
“Checks a single assumption about the behavior of one system.”

Thursday, 22 August 13

- *“... individual units of source code ... are tested to determine if they are fit for use.”*
- *“... the smallest testable part of an application.”*
- *“... a strict, written contract that the piece of code must satisfy.”*

Experiments

INPUT x



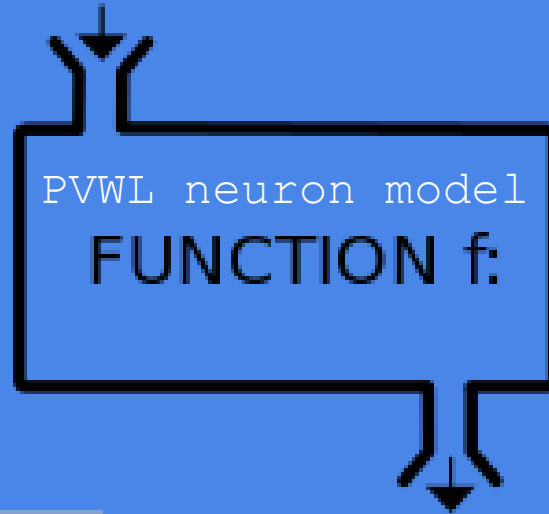
OUTPUT $f(x)$

Predicted observations

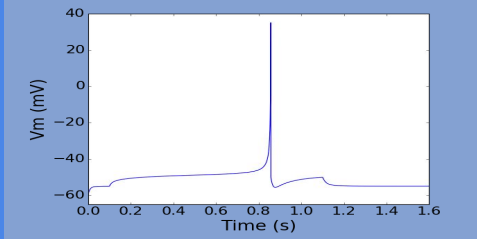
Inject a 100 pA, 500 ms,
square wave into the soma



INPUT x



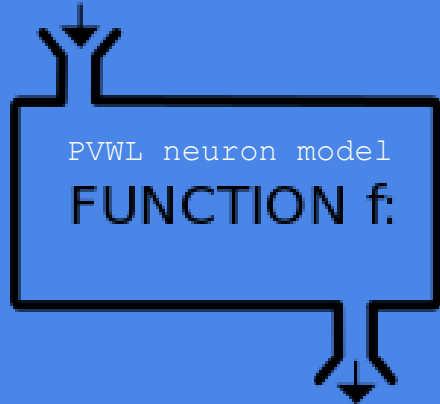
OUTPUT $f(x)$



A predicted membrane
potential waveform

Inject a 100 pA, 500 ms,
square wave into the soma

INPUT x

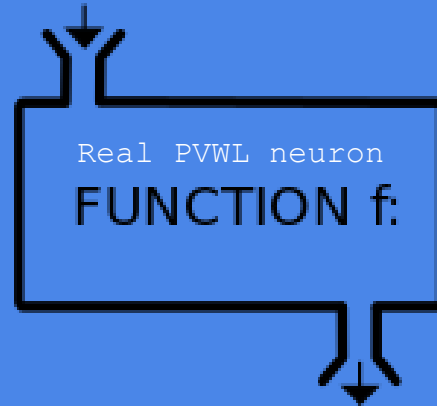


OUTPUT $f(x)$

A *predicted* membrane
potential waveform

Inject a 100 pA, 500 ms,
square wave into the soma

INPUT x



OUTPUT $f(x)$

A *recorded* membrane
potential waveform

= ?

- What if we built a **collaborative** collection of empirically-informed unit tests and **characterized models** by the **collection of tests that they pass**?
- `http://sciunit.scidash.org`



A synthesis of solar cycle prediction techniques

David H. Hathaway, Robert M. Wilson, and Edwin J. Reichmann

NASA Marshall Space Flight Center, Huntsville, Alabama

Tests

Table 3. Precursor Prediction Method Errors (Prediction - Observed) for Cycles 19-22

Prediction Method	19	20	21	22	RMS
Ohl's method	-55.4	19.1	21.8	4.4	31.3
Feynman's method	-42.8	9.6	26.9	3.6	25.8
Thompson's method	-17.8	8.7	-26.5	-13.6	17.9

Test Suite

Models

Goodness-of-Fit

Challenges

- **Q: How to interface with a wide range of scales, languages, and goals?**
A: *separate the implementation from the interface*
- **Q: How to minimize development time for writing tests?**
A: *domain standards and tools*
- **Q: How to adjudicate whether a test is fair?**
A: *collaborative development*

“Capabilities”

Test

I need you to have a soma, to receive somatic current injection, and to produce action potentials... can you do that?

Model1

Sorry, I'm a non-spiking model. I cannot produce action potentials.

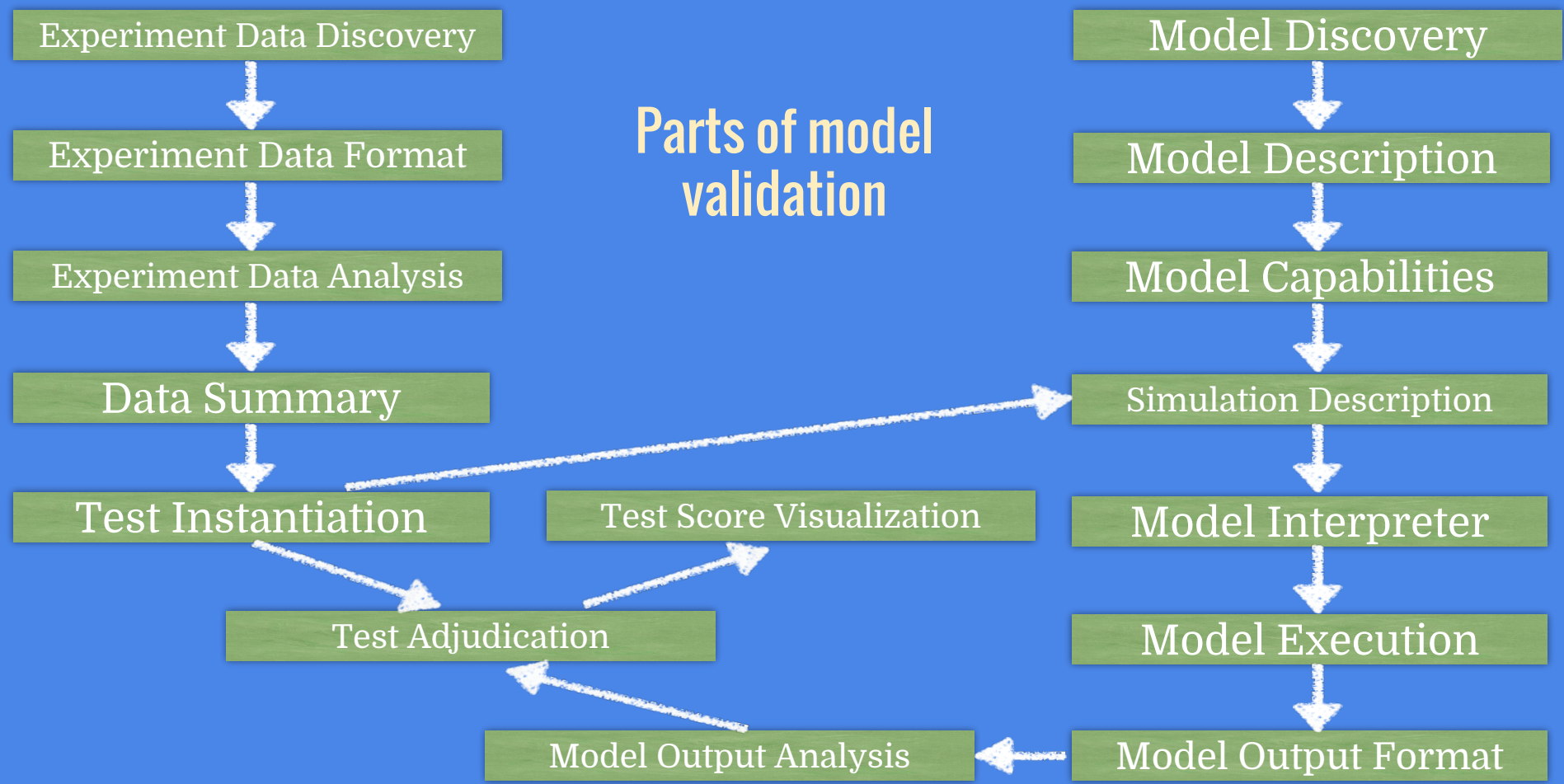
Model2

I can do all those things!

Test

Model2, prepare to be tested!

Parts of model validation



Experiment Data Discovery

Experiment Data Format

NWB

Experiment Data Analysis

Data Summary

NeuroElectro.org

Test Instantiation

NeuronUnit

Test Adjudication

SciPy

Model Output Analysis

Parts of model validation

Corresponding domain standards

Test Score Visualization

Model Discovery
OpenSourceBrain

Model Description
NeuroML

Model Capabilities

Simulation Description
SED-ML

Model Interpreter

Model Execution
NEURON

Model Output Format

- *SciUnit* is practical with *domain-specific* libraries for test construction and model execution that utilize *domain-specific standards*.
- Is there such a library for neuron and ion channel physiology?
- <http://neuronunit.scidash.org>



NeuronUnit

NeuroElectro.org

Published literature

Novel subcellular distribution pattern of A-type K⁺ channels on neuronal surface.

Unique clustering of A-type potassium channels on different cell types of the main olfactory bulb.

Kollo M, Holderith N, Antal M, Nusser Z.

Theoretical and functional studies predicted a highly non-uniform distribution of voltage-gated ion channels on the neuronal surface. This was confirmed by recent immunolocalization experiments for Na⁺, Ca²⁺, hyperpolarization activated mixed cation and K⁺ channels. These experiments also indicated that some K⁺ channels were clustered in synaptic or non-synaptic membrane specializations. Here we analysed the subcellular distribution of Kv4.2 and Kv4.3 subunits in the rat main olfactory bulb at high resolution to address whether clustering characterizes their distribution, and whether they are concentrated in synaptic or non-synaptic junctions. The cell surface distribution of the Kv4.2 and Kv4.3 subunits is highly non-uniform. Strong Kv4.2 subunit-immunopositive clusters were detected in intercellular junctions made by mitral, external tufted and granule cells (GCs). We also found Kv4.3 subunit-immunopositive clusters in periglomerular (PGC), deep short-axon and GCs. In the juxtglomerular region some calretinin-immunopositive glial cells envelop neighboring PGC somata in a cap-like manner. Kv4.3 subunit clusters are present in the cap membrane that directly contacts the PGC, but not the one that faces the neuropil. In membrane specializations established by members of the same cell type, K⁺ channels are enriched in both membranes, whereas specializations between different cell types contain a high density of channels asymmetrically. None of the K⁺ channel-rich junctions showed any of the ultrastructural features of known chemical synapses. Our study provides evidence for highly non-uniform subcellular distributions of A-type K⁺ channels and predicts their involvements in novel

Physiology database

Olfactory Bulb Mitral Cell

Input resistance	200 MΩ
V _{rest}	-65 mV
Spike width	1 ms
...	

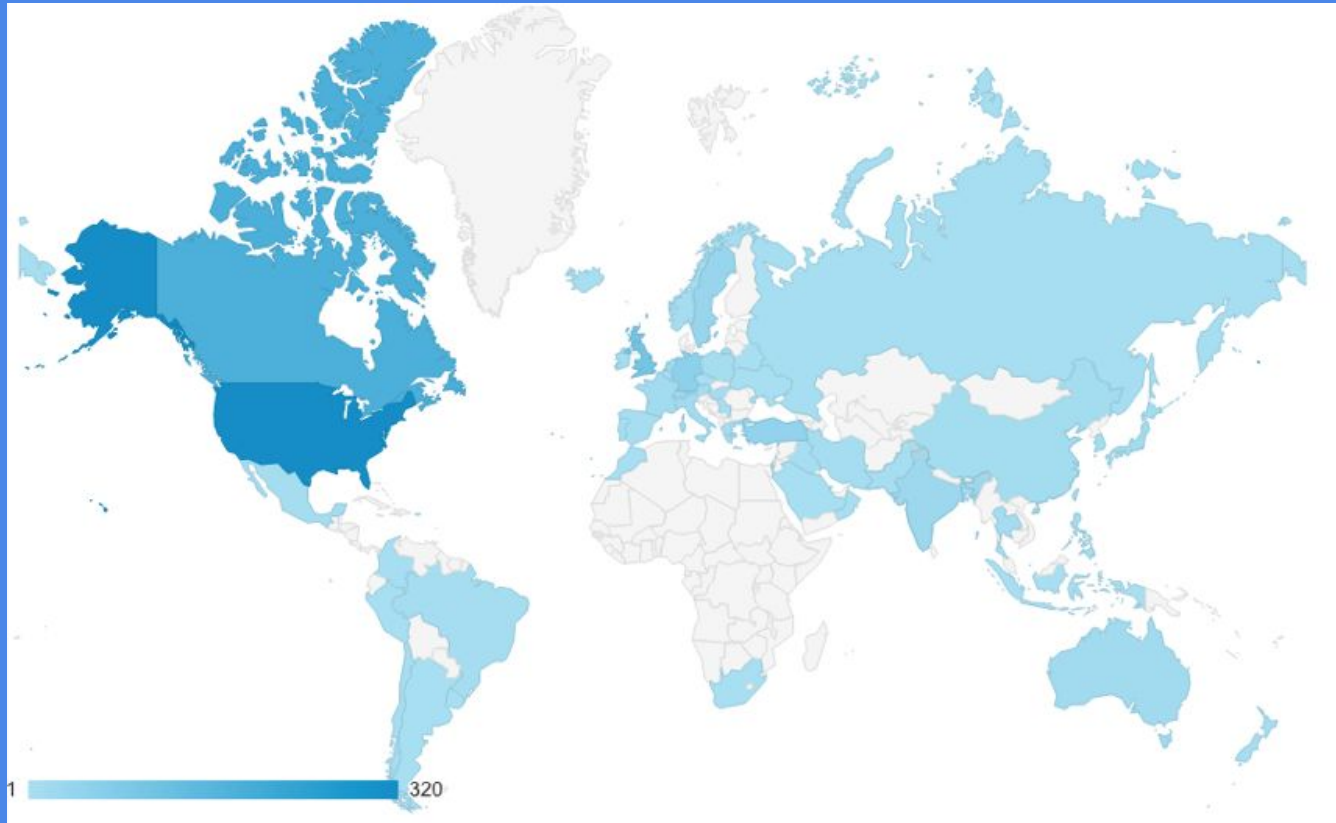
CA1 Pyramidal Cell

Input resistance	400 MΩ
V _{rest}	-70 mV
Spike width	.5 ms
...	

Extracted from Literature



NeuroElectro.org





GitHub



rgerkin Testing works with sciunit command line tools

Latest commit 3e9cf6f 28 days ago

capabilities	Substantial update of CosmoSuite test repository	2 months ago
models	Testing works with sciunit command line tools	28 days ago
records	Initial commit	3 years ago
suites	Testing works with sciunit command line tools	28 days ago
tests	Testing works with sciunit command line tools	28 days ago
.gitignore	Initial commit	3 years ago
.sciunit	Testing works with sciunit command line tools	28 days ago
README.md	Initial commit	3 years ago

Quantitative Single-Neuron Modeling: Competition 2009

Richard Naud^{1*}, Thomas Berger¹, Brice Bathellier², Matteo Carandini³ and
Wulfram Gerstner¹

¹ Ecole Polytechnique Federal de Lausanne (EPFL), Switzerland

² University of Bern, Switzerland

³ University College London, United Kingdom

```
from QSNMC.tests import tests
from QSNMC.models import models

for model in models:
    for test in tests:
        score = test.judge(model)
        score.summarize()
```

- **Open Source Brain**

- biophysically detailed neuron/microcircuit models
- <http://www.opensourcebrain.org>



- **The Blue Brain Project**

- biophysically detailed cortical microcircuit models



- **OpenWorm**

- simulation of an entire organism
- <http://www.openworm.org>
- tested using data from neuron to behavior



[Code](#) [Issues 56](#) [Pull requests 0](#) [Wiki](#) [Pulse](#) [Graphs](#)A repository to integrate data, information, scripts, and models of ion channels in *C. elegans*

484 commits

4 branches

0 releases

8 contributors

















Your recently pushed branches:

dev (less than a minute ago)

[Compare & pull request](#)Branch: dev [New pull request](#)[Create new file](#)[Upload files](#)[Find file](#)[Clone or download](#)

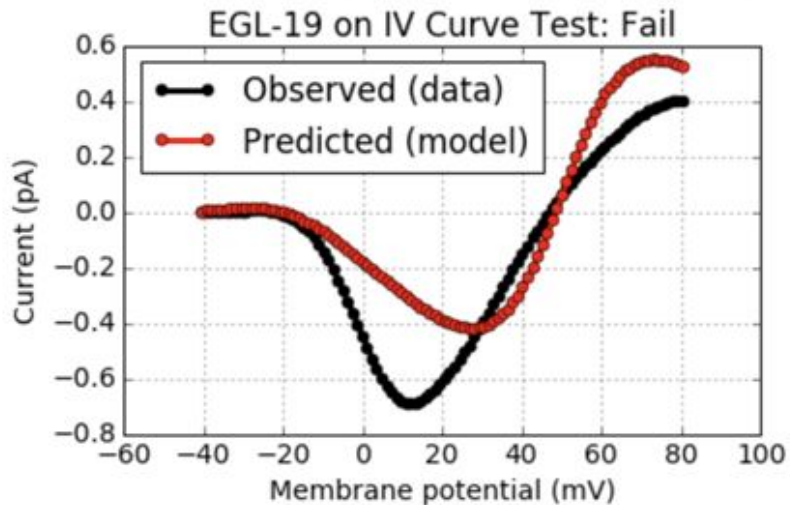
This branch is 11 commits ahead of master.

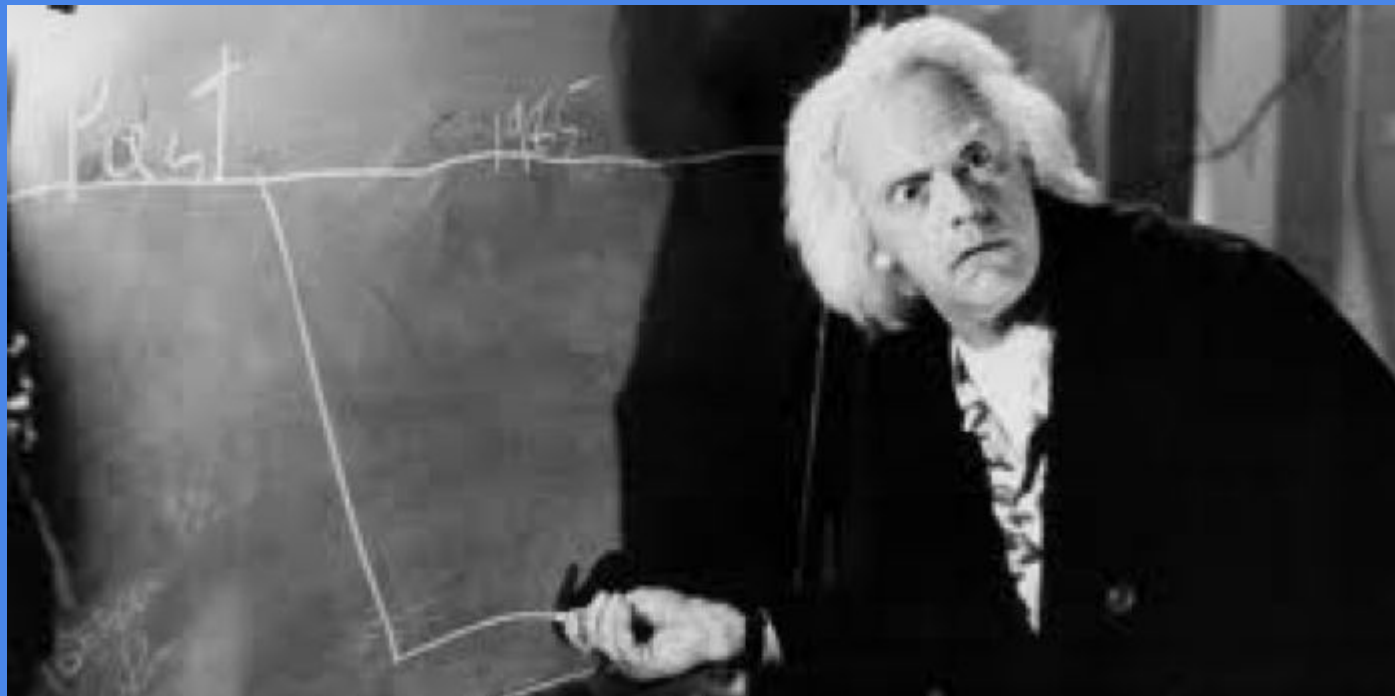
[Pull request](#) [Compare](#)

 rgerkin	Merge branch 'dev' of http://github.com/OpenWorm/ChannelWorm into dev	Latest commit 9718d41 10 minutes ago
 channelworm	Removing sql-explorer	4 days ago
 data	Update PyOpenWorm.	2 years ago
 docs	Update walkthrough.md	a year ago
 models	Adding Validated SLO-2 nml file	a year ago
 scripts	Adding particle swarm optimization algorithm	a year ago
 tests	Updated testing to use .sciunit configuration file	11 minutes ago
 .gitignore	Updated testing to use .sciunit configuration file	11 minutes ago
 .sciunit	Updated testing to use .sciunit configuration file	11 minutes ago
 .travis.yml	Minor changes to travis-CI	9 months ago
 LICENSE	Updating requirements for setup	9 months ago
 README.md	Adding a multiparameter generic alpha-beta form to simulator	9 months ago
 mkdocs.yml	Add to digitization walkthrough	a year ago
 pytest.ini	Ignore src/ for testing	a year ago
 requirements.txt	Adding a multiparameter generic alpha-beta form to simulator	9 months ago
 setup.py	Adding a multiparameter generic alpha-beta form to simulator	9 months ago

Jupyter

```
In [6]: import matplotlib as mpl
import matplotlib.pyplot as plt
mpl.rcParams.update({'font.size':14, 'lines.linewidth':3})
score.plot()
plt.tight_layout()
plt.savefig('/Users/rgerkin/Desktop/iv_curves.eps', format='eps')
```





Fork it!



- Every time the model is updated:
 - all tests are run
 - results are stored and visualized
 - overall performance is summarized

Out[5]: Show 10 entries

Search:

	Mean	Rheobase	Resting potential	Input resistance	Injected current AP width	Injected current AP amplitude
V_rest=-70mV	0.701	Ratio = 1.00	Z = -0.24	Z = -0.81	Z = -0.40	Z = -0.54
V_rest=-65mV	0.653	Ratio = 1.51	Z = 0.48	Z = -0.68	Z = -0.36	Z = -0.53
V_rest=-75mV	0.561	Ratio = 0.72	Z = -0.96	Z = -0.91	Z = -0.44	Z = -0.54
V_rest=-60mV	0.560	Ratio = 2.51	Z = 1.20	Z = -0.49	Z = -0.30	Z = -0.54
V_rest=-55mV	0.519	Ratio = 4.97	Z = 1.92	Z = -0.20	Z = -0.25	Z = -0.54
V_rest=-50mV	0.445	Ratio = 13.84	Z = 2.64	Z = 0.28	Z = -0.20	Z = -0.54

Showing 1 to 6 of 6 entries

◀ Previous Next ▶

✓ **sciunit-travis** Removed jupyter cruft from Travis

→ #322 passed

 Restart build

 Commit 8c032ff

 Elapsed time 5 min 6 sec

 Compare d18eed5..8c032ff

 21 days ago

 Richard C Gerkin authored  GitHub committed

[Job log](#)

[View config](#)

```
> 1 Worker information
> 6 Build system information
91
> 92 $ export DEBIAN_FRONTEND=noninteractive
> 98 $ git clone --depth=50 --branch=sciunit-travis https://github.com/openworm/ChannelWorm.git openworm/ChannelWorm
109 $ source ~/virtualenv/python2.7/bin/activate
```

 Remove log

 Raw log

worker_info

system_info

fix: CVE-2015-7547

git_checkout

4.64s

0.01s



Travis CI

1125 Suite SL0-2 IV Curves:

1126 SL0-2 IV

1127 EGL-19 Unknown

1128 SL0-2 Fail

1129

1130

1131

1132 The command "sciunit run" exited with 0.

1133 \$ sciunit make-nb

1134 Created Jupyter notebook at:

1135 /home/travis/build/openworm/ChannelWorm/tests/scidash/scidash.ipynb

1136

1137

1138 The command "sciunit make-nb" exited with 0.

1139 \$ sciunit run-nb

1140

1141

1142 The command "sciunit run-nb" exited with 0.

1143

1144 Done. Your build exited with 0.

Benefits for Modelers

- Know what other models can and can't do, and what a new model (if needed) should explain in order to be better.
- The ability to continuously test your model against the data it is supposed to explain/predict.
 - Accelerates model development (towards some goal of realism).
- Gives you bragging rights in the arena of model competition.
- Address reviewers who demand that your model pass formal tests.
- Post-publication review of your model, *even as new data come to light*.
- Look your child in the face when they ask if you, an alleged scientist, used the scientific method in the development of your model.

Benefits for Experimentalists

- The ability to put your observations in context.
 - Is there a model that explains my data?
 - Which model best explains my data?
 - What other data does it explain?
- Pre-experiment, grant stage discovery of hypothesis implications.
 - If I do experiment E and get result Y, it will support model A.
 - If I do experiment E and get result Z, it will support model B.
- Increased community awareness of the data you collected.
 - It could become the gold standard by which models are judged!

<http://sciunit.scidash.org>



<http://neuronunit.scidash.org>

