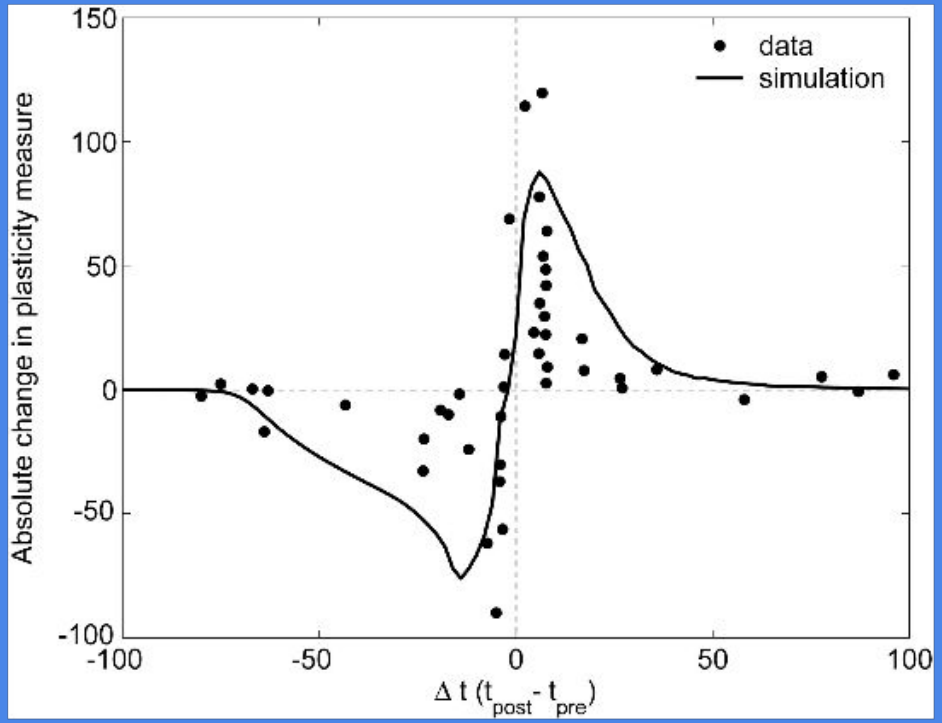
Collaboration and Validation in Models of Cells and Circuits

Richard (Rick) Gerkin, PhD
Arizona State University

Padraig Gleeson, PhD
University College, London

Parameter Consistency

Predictive Power



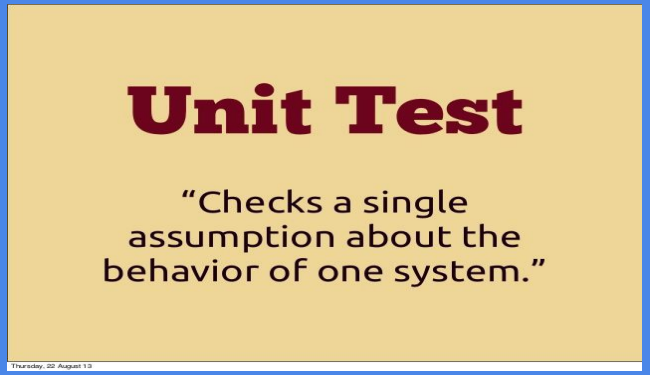
- Informality
- Inaccessibility
- Irreproducibility
- Incompleteness

Rubin et al, 2005

We need a framework for

– formally
– rapidly
– transparently
– continuously

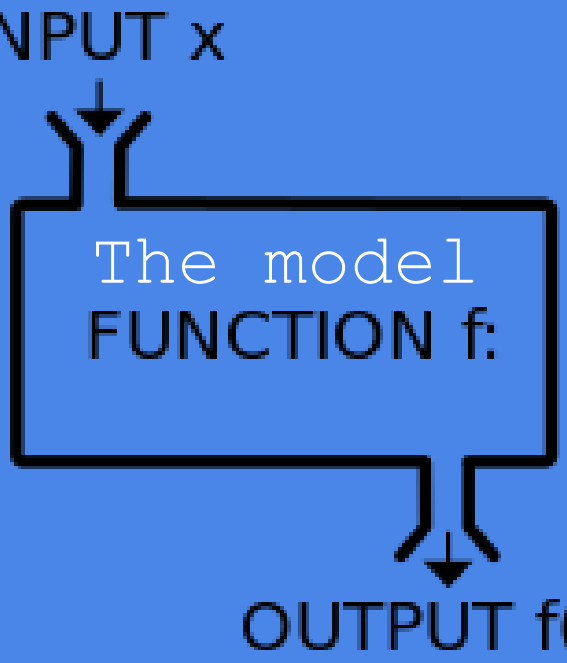
validating models



- *"... 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."*

http://en.wikipedia.org/wiki/Unit_testing

Experiments



Predicted observations

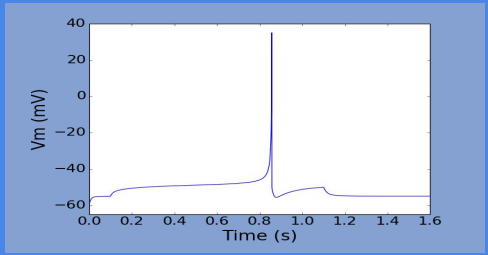
Inject a 100 pA, 500 ms, square wave into the soma

INPUT x

PVWL neuron model

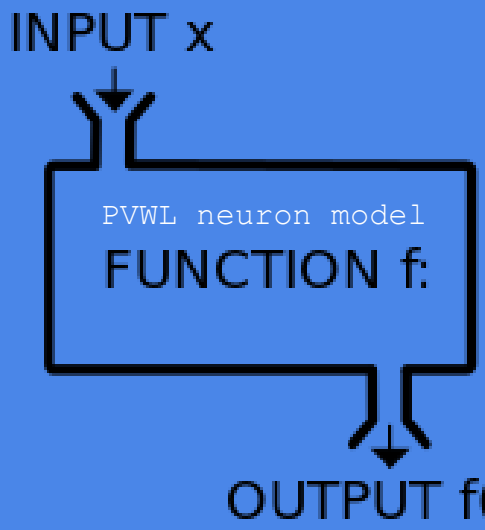
FUNCTION f:

OUTPUT f(x)



A predicted membrane potential waveform

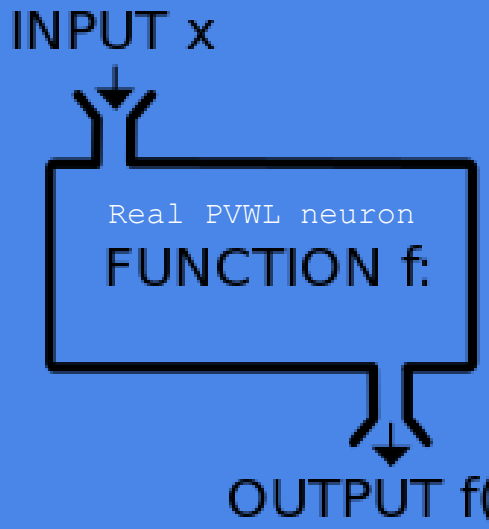
Inject a 100 pA, 500 ms, square wave into the soma



A *predicted* membrane potential waveform

= ?

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



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`

JOURNAL OF GEOPHYSICAL RESEARCH, VOL. 104, NO. A10, PAGES 22,375–22,388, OCTOBER 1, 1999

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*

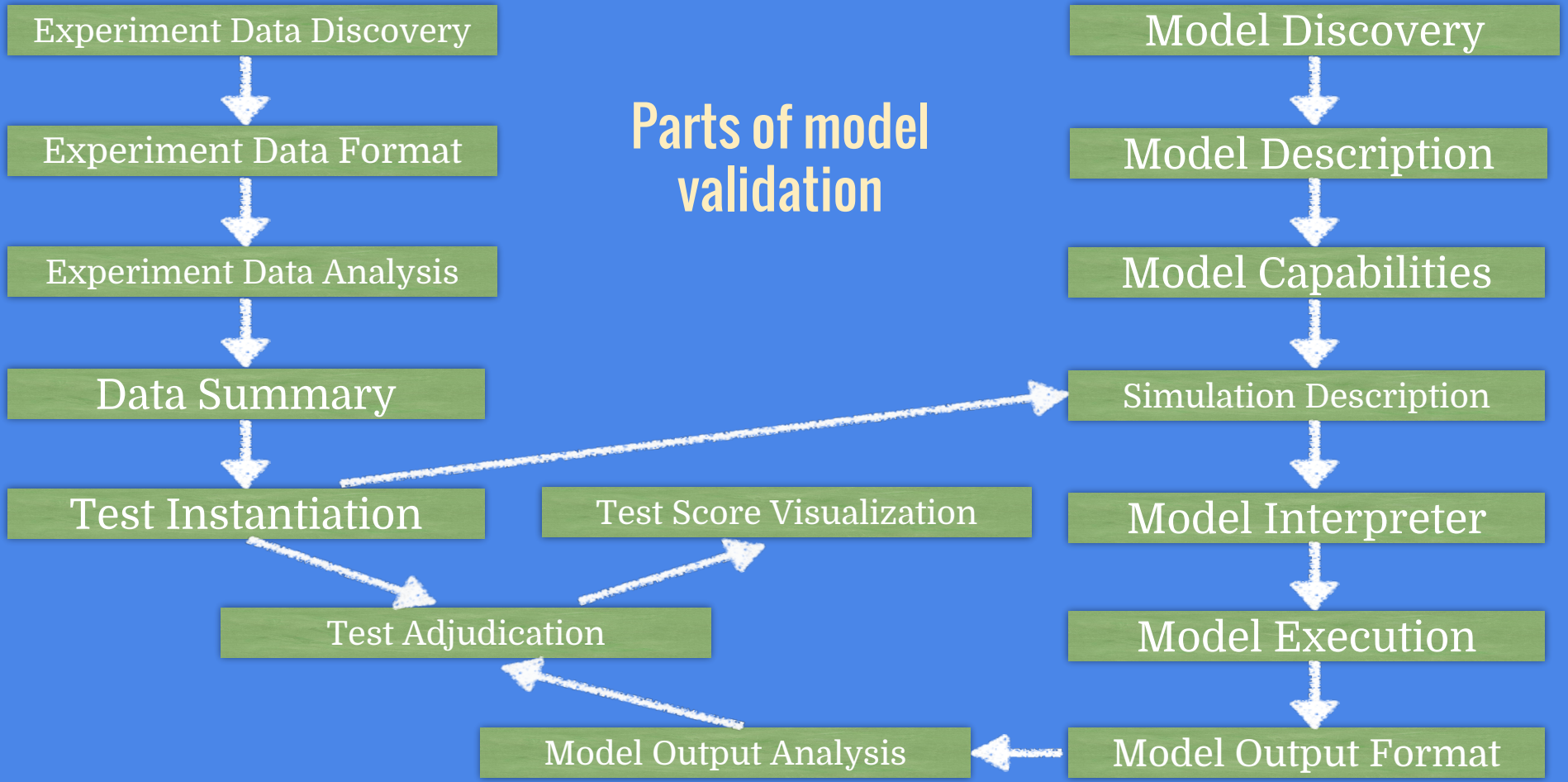
“Capabilities”

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

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

I can do all those things!

Model2, prepare to be tested!


Parts of model validation
Experiment Data Discovery
Experiment Data Format
Experiment Data Analysis
Data Summary
Test Instantiation
Test Score Visualization
Test Adjudication
Model Output Analysis
Model Discovery
Model Description
Model Capabilities
Simulation Description
Model Interpreter
Model Execution
Model Output Format

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

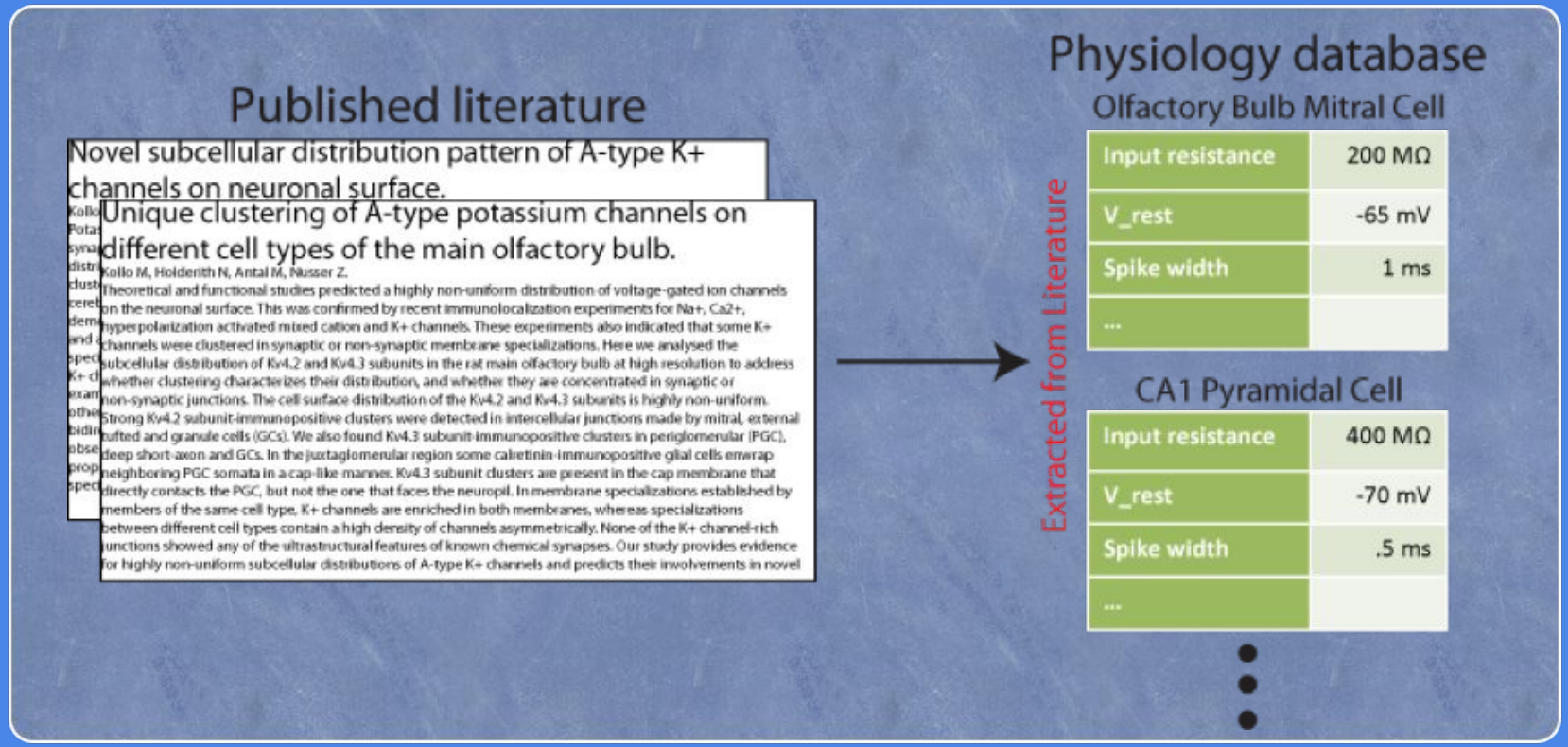
Model Output Format

- *SciUnit* is practical with *domain-specific* libraries for test construction and model execution that utilize *domain-specific standards*.

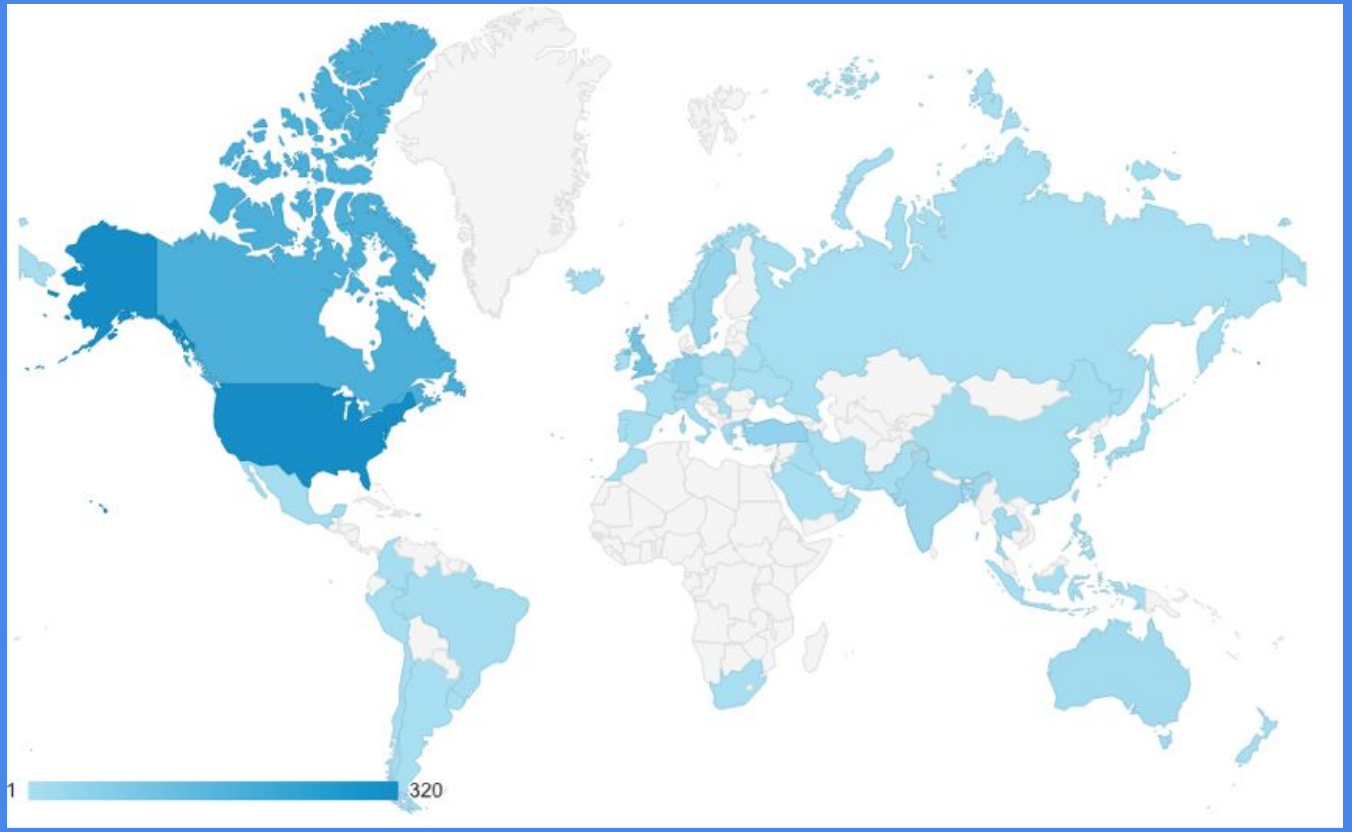
- Is there such a library for neuron and ion channel physiology?

- `http://neuronunit.scidash.org`

NeuroElectro.org



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

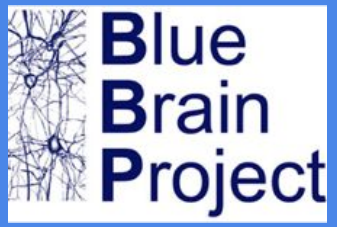
Richard Naud[1*], Thomas Berger[1], Brice Bathellier[2], Matteo Carandini[3] and Wulfram Gerstner[1]

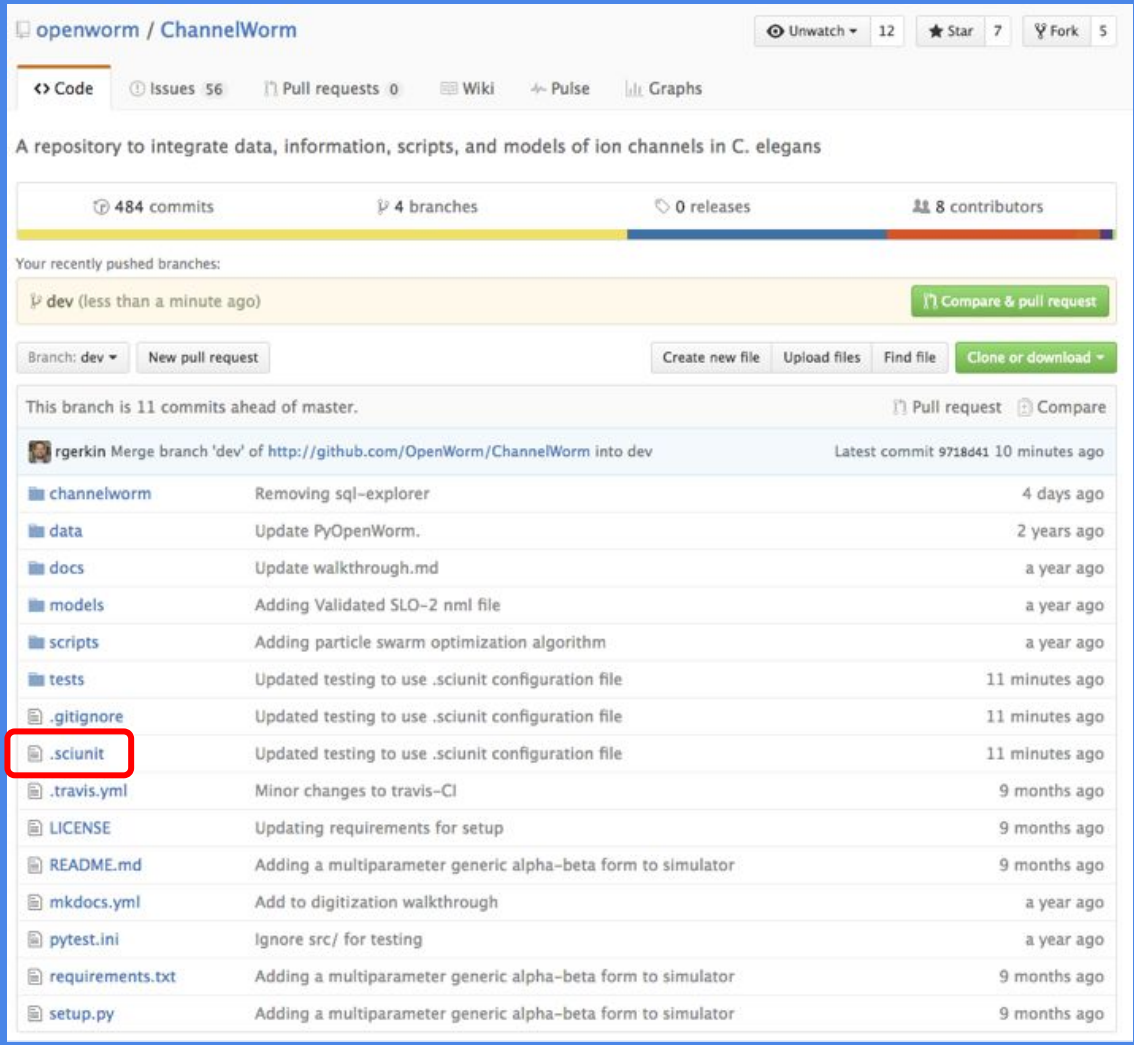
1 Ecole Polytechniqe Federal de Lausanne (EPFL), Switzerland
2 University of Bern, Switzerland
3 University College London, United Kingdom

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

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

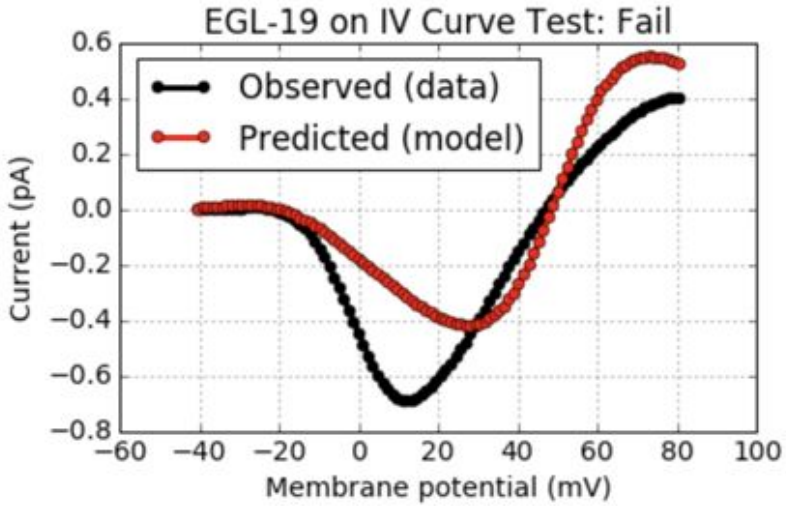
- **Open Source Brain**
  - biophysically detailed neuron/microcircuit models
  - *http://www.opensourcebrain.org*
- **The Blue Brain Project**
  - biophysically detailed cortical microcircuit models
- **OpenWorm**
  - simulation of an entire organism
  - *http://www.openworm.org*
  - tested using data from neuron to behavior

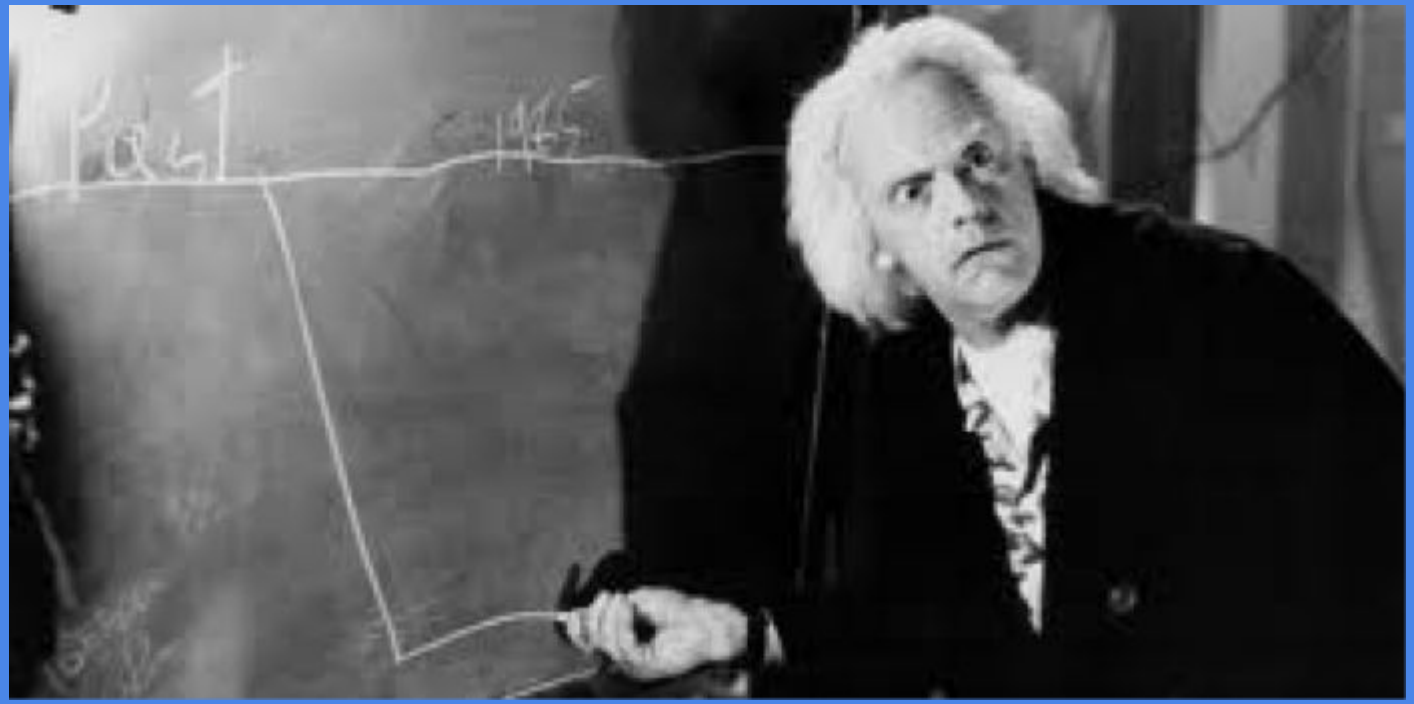



openworm / ChannelWorm
Unwatch 12
Star 7
Fork 5
Code
Issues 56
Pull requests 0
Wiki
Pulse
Graphs
A repository to integrate data, information, scripts, and models of ion channels in C. elegans
484 commits
4 branches
0 releases
8 contributors
Your recently pushed branches:
dev (less than a minute ago)
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!

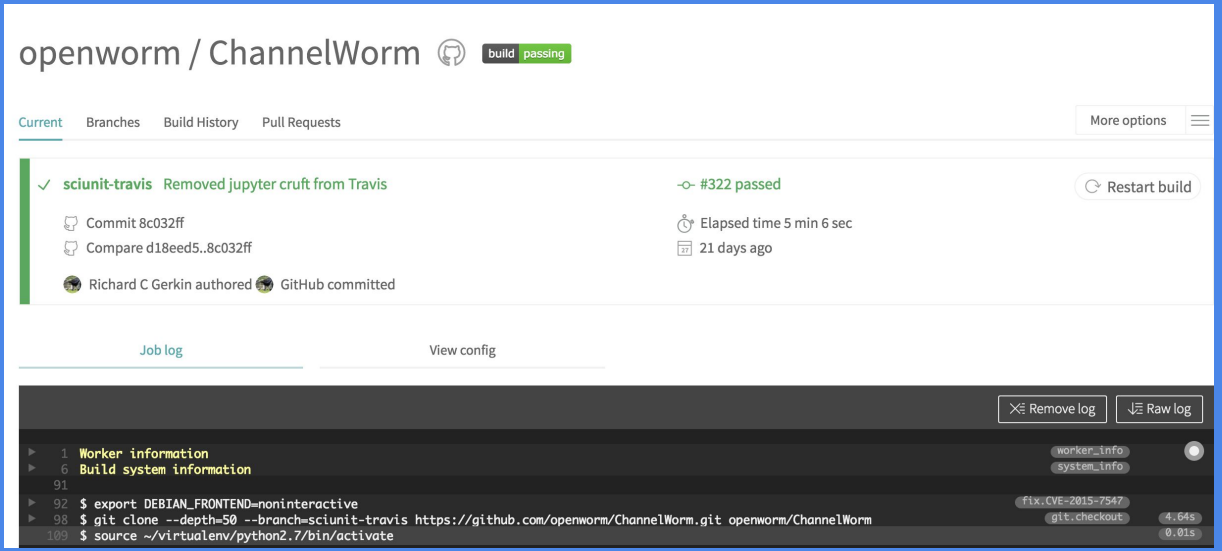
GitHub

- 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



```
1125 Suite SLO-2 IV Curves:
1126        SLO-2 IV
1127 EGL-19  Unknown
1128 SLO-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

NeuronUnit