

Data-driven validation of neuroscience models

Richard (Rick) Gerkin, PhD
Arizona State University, USA

MODEL VALIDATION

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- A scientific model has high *validity* if:

MODEL VALIDATION

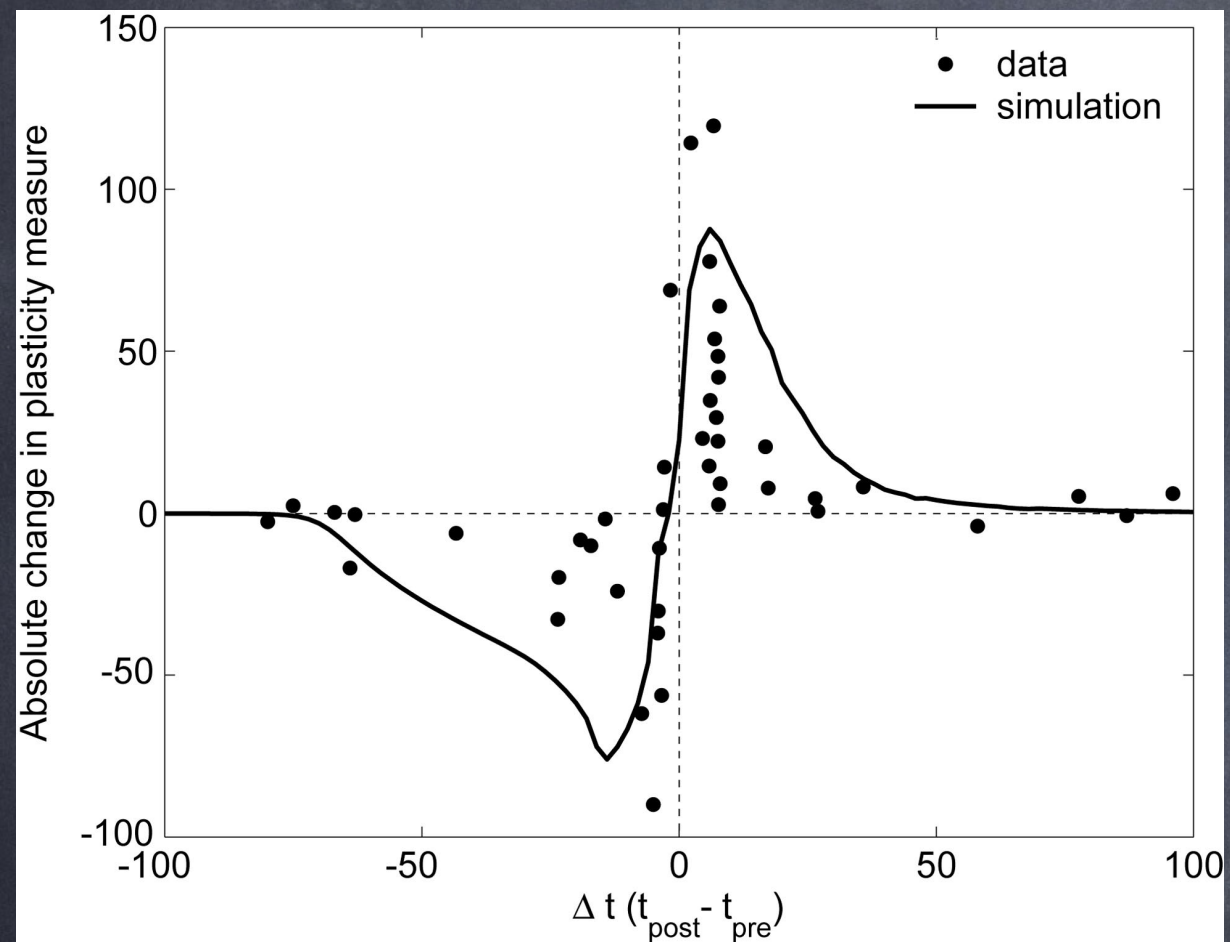
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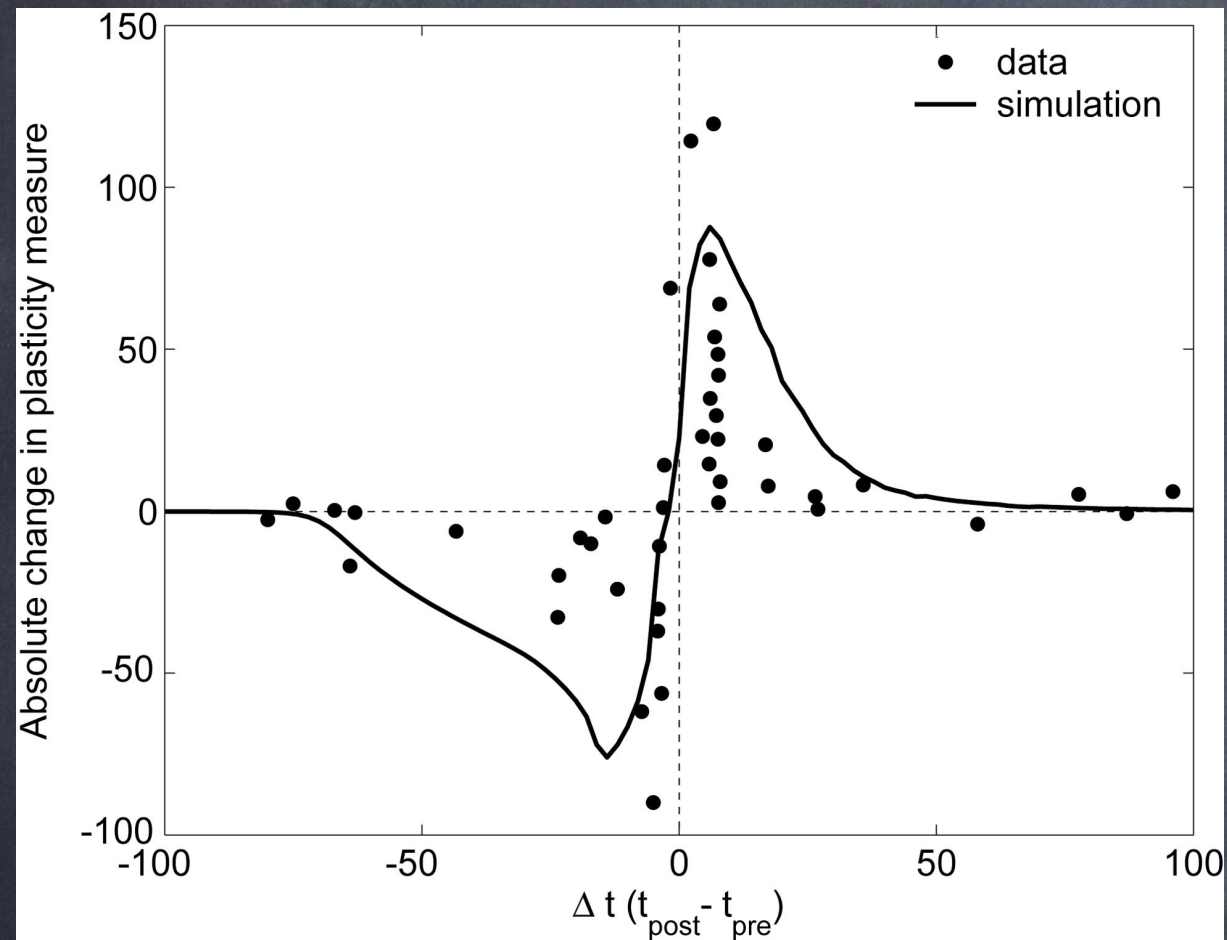
- A scientific model has high *validity* if:
 - It is *consistent with* a wide range of previously gathered data.
 - It can *predict* the results of many future experiments.

TESTING VALIDITY

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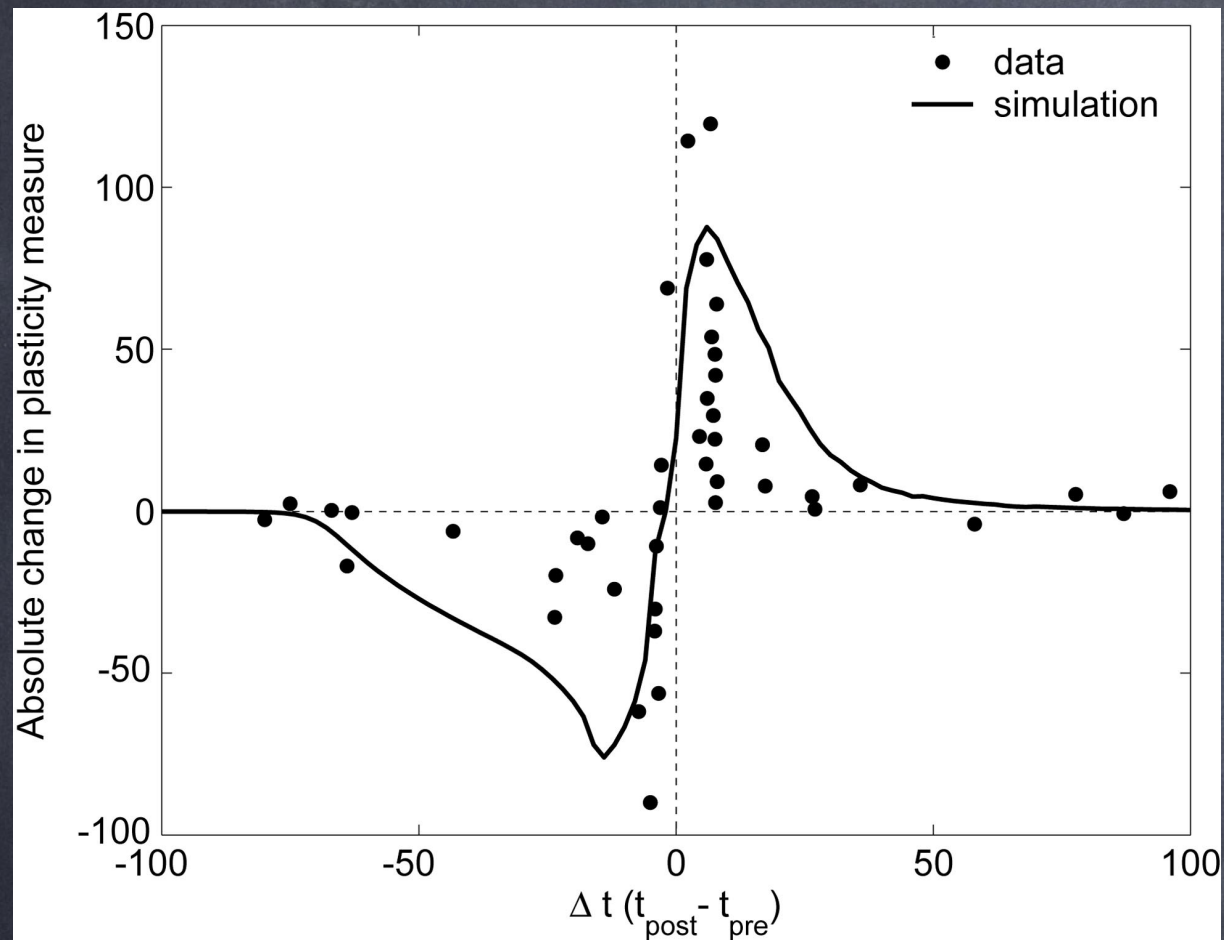


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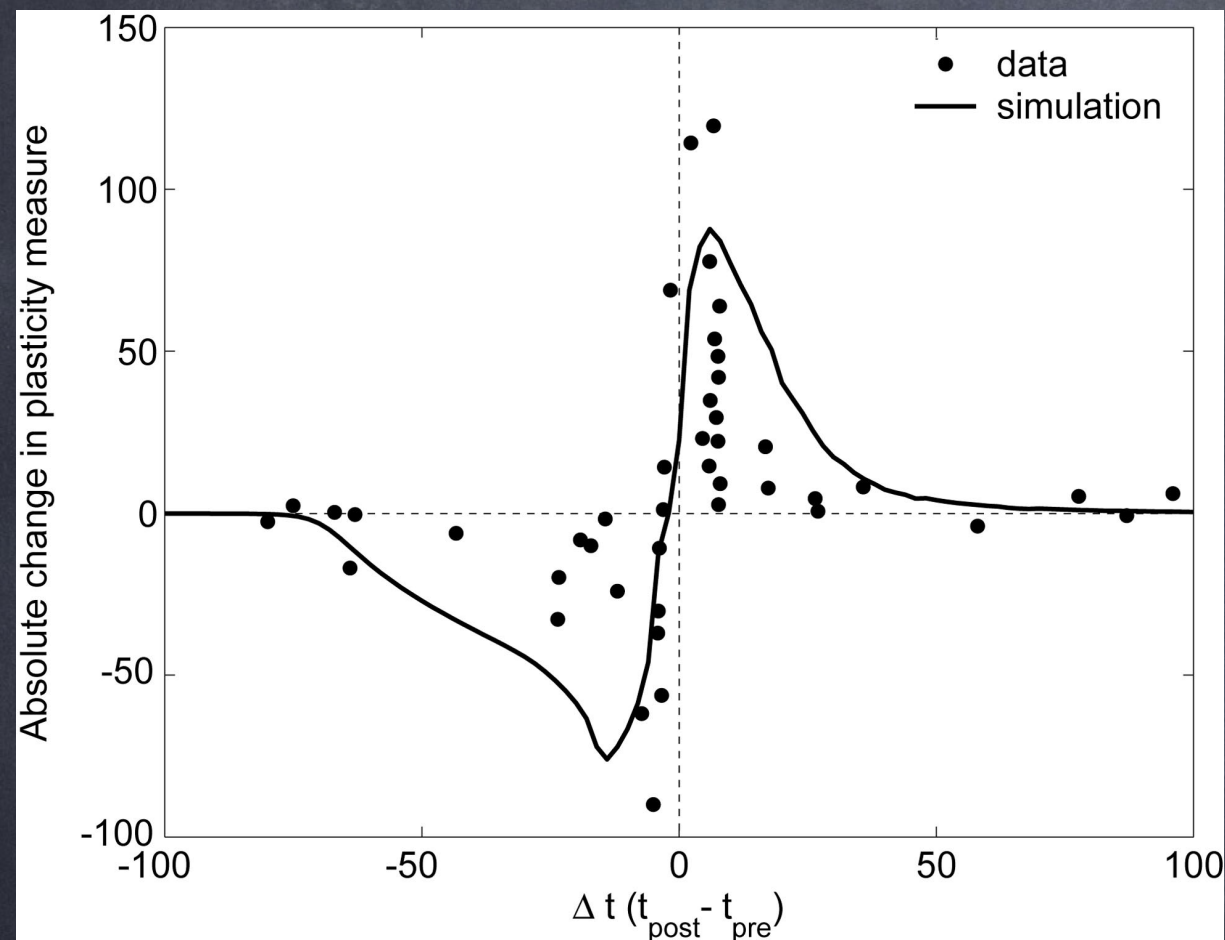
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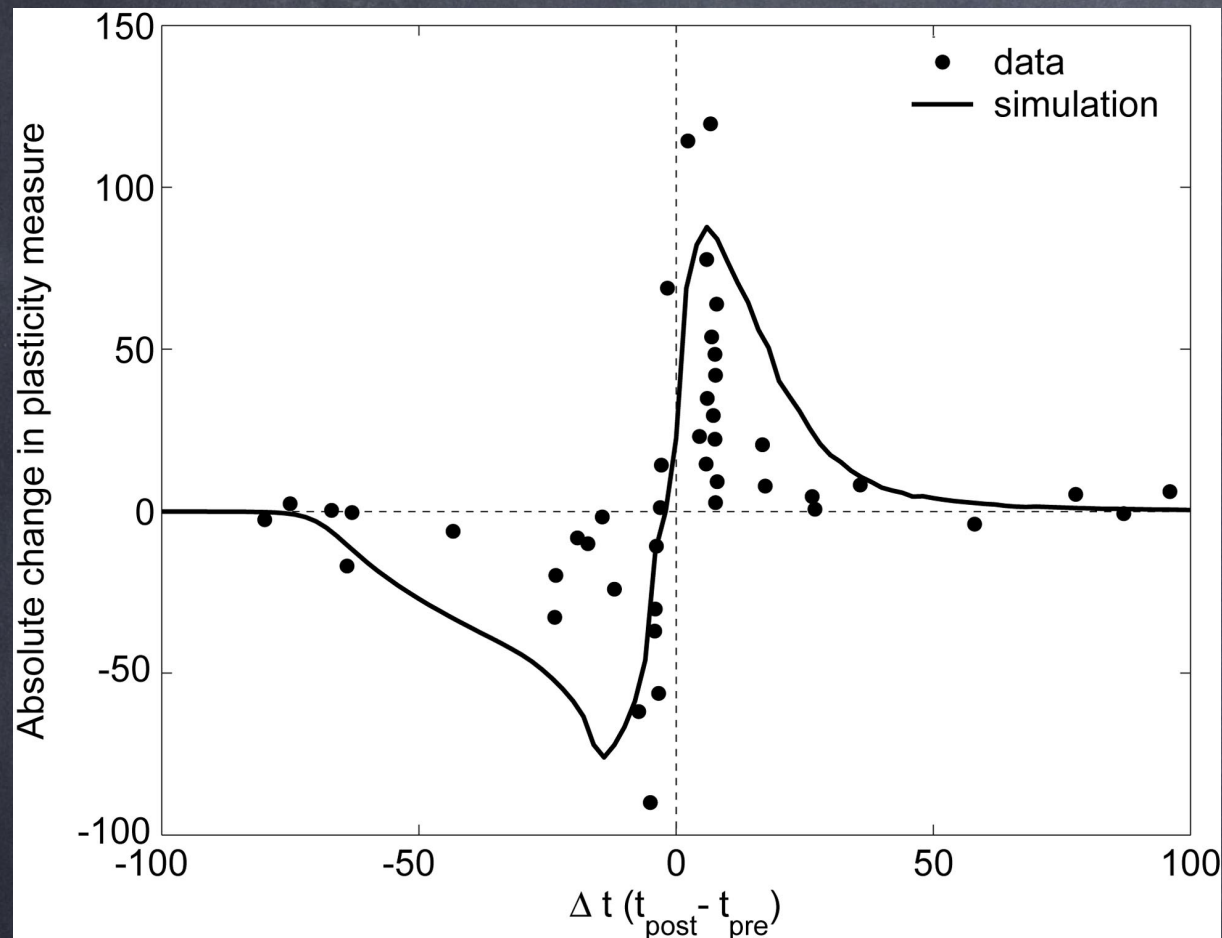
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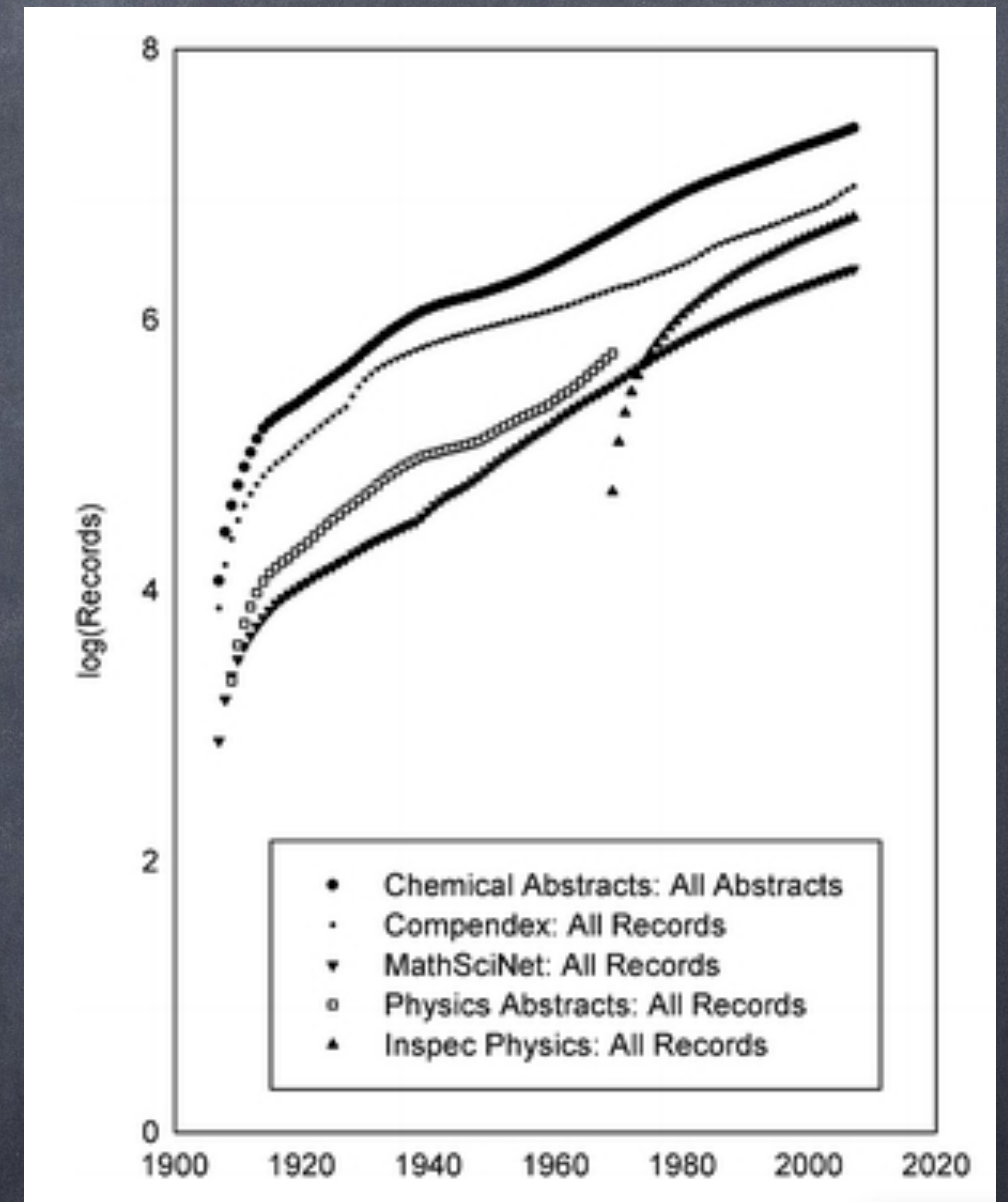
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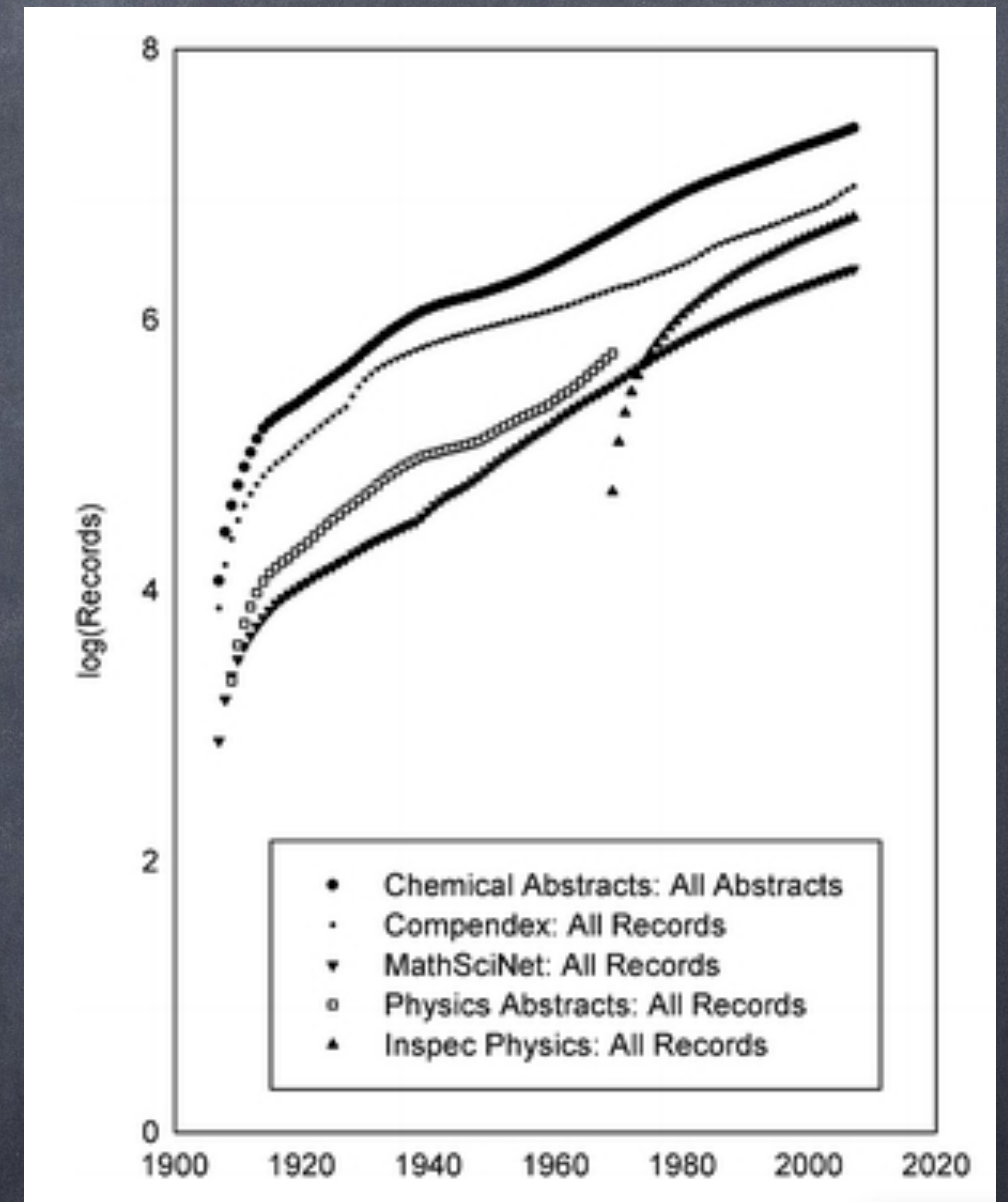


- Most claims about model validity are informal.
- These claims cannot be formally evaluated.
- Claims are difficult to locate.
- Falsifiable claims spanning many data sets are rare.

TESTING VALIDITY



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Huge amounts of data!
Even *informal validation* is becoming difficult.

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- Not testing models rigorously leaves a field with an **unclear** view of:
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 - What needs explaining.
- Needed: a **framework** for validating scientific models, based on established techniques for **formally validating** software.

THE UNIT TEST

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- “one can view a unit as the **smallest testable part** of an application.”
- “A unit test provides a **strict, written contract** that the piece of code must satisfy.”

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- Example: A *complete* model of a given neuron type should produce spikes that, given a specified description of the stimulus, **match physiologically observed features** such as spike shapes, rates, interval distributions, etc.
- Each such feature can be encoded in a unit test.

SCIUNIT

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- <http://github.com/scidash/sciunit>

VISUALIZING VALIDITY

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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

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
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Test Suite

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

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

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Model2

I can do all those things.

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Model2

I can do all those things.

Test

Model2, bring it on!

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NEUROELECTRO

<http://www.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 puffed 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

```
In [1]: from neuronunit.neuroelectro import NeuroElectroSummary
```

```
In [2]: summary = NeuroElectroSummary(neuron={'name': 'Hippocampus CA1 Pyramidal Cell'},  
...:                                  ephysprop={'name': 'spike width'})
```

```
In [3]: observation = summary.get_observation(show=True)
```

Getting data values from neuroelectro.org

http://www.neuroelectro.org/api/1/nas/?e__name=spike+width&n__name=Hippocampus+CA1+Pyramidal+Cell

```
{u'e': {u'definition': u'Duration of AP, not explicitly referred to as half-width',  
        u'id': 23,  
        u'name': u'spike width',  
        u'nlex_id': None,  
        u'norm_criteria': u'Values are unchanged from those reported. Values currently lump multiple measures of spike width which do not  
explicitly denote spike half-width. Refer to individual articles for definition and calculation methodology.'},  
        u'n': {u'id': 85,  
                u'name': u'Hippocampus CA1 pyramidal cell',  
                u'neuron_db_id': 258,  
                u'nlex_id': u'sao830368389'},  
        u'num_articles': 6,  
        u'num_nedms': 10,  
        u'value_mean': 2.6020833333333333,  
        u'value_sd': 0.766070080381394}}
```

```
In [4]: from neuronunit.tests import SpikeWidthTest
```

```
In [5]: ca1_pyramidal_spike_width_test = SpikeWidthTest(observation = observation)
```


NEUROELECTRO

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In [1]: from neuronunit.neuroelectro import NeuroElectroSummary

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```

- Uses the NeuroElectro API (and NeuroLex) to get collated data about a named *neuron type* for a specified *electrophysiological property* in order to *parameterize a test*.

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SCIUNIT: TESTS



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Fork it!



COMPETITION

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

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

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

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<https://github.com/incf/qsnmc>

COMPETITION

SciUnit can also provide a common evaluation and visualization framework for competitions between *algorithms or methods*:

- Spike-sorting algorithms
- Spike time extraction from fast calcium imaging.
- Neural system prediction and identification challenge (*nuSPIC*)
- Brain computer interface (BCI, PhyPa (<http://www.phypa.org>))
- Seizure prediction (Sejnowski)

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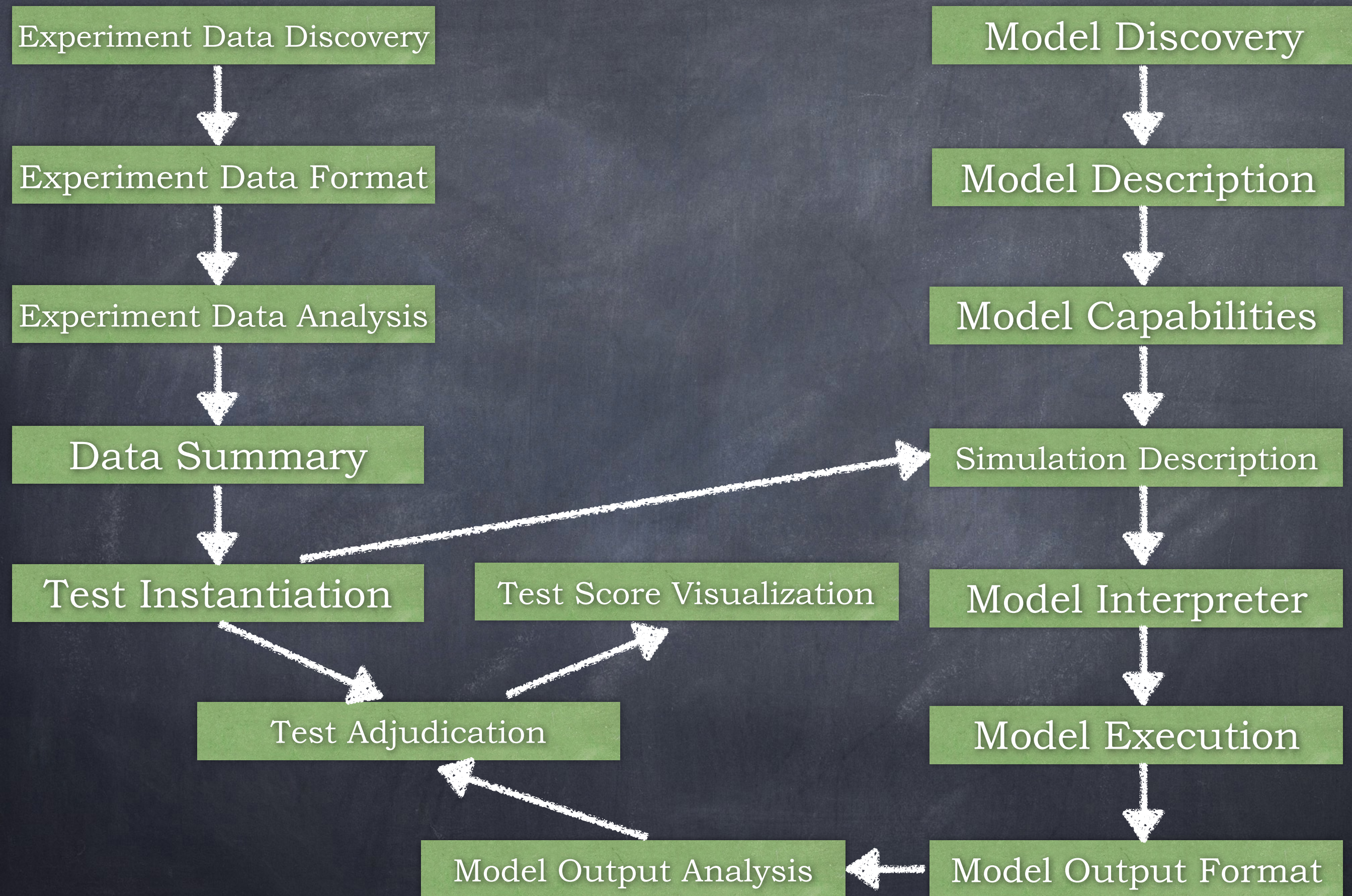
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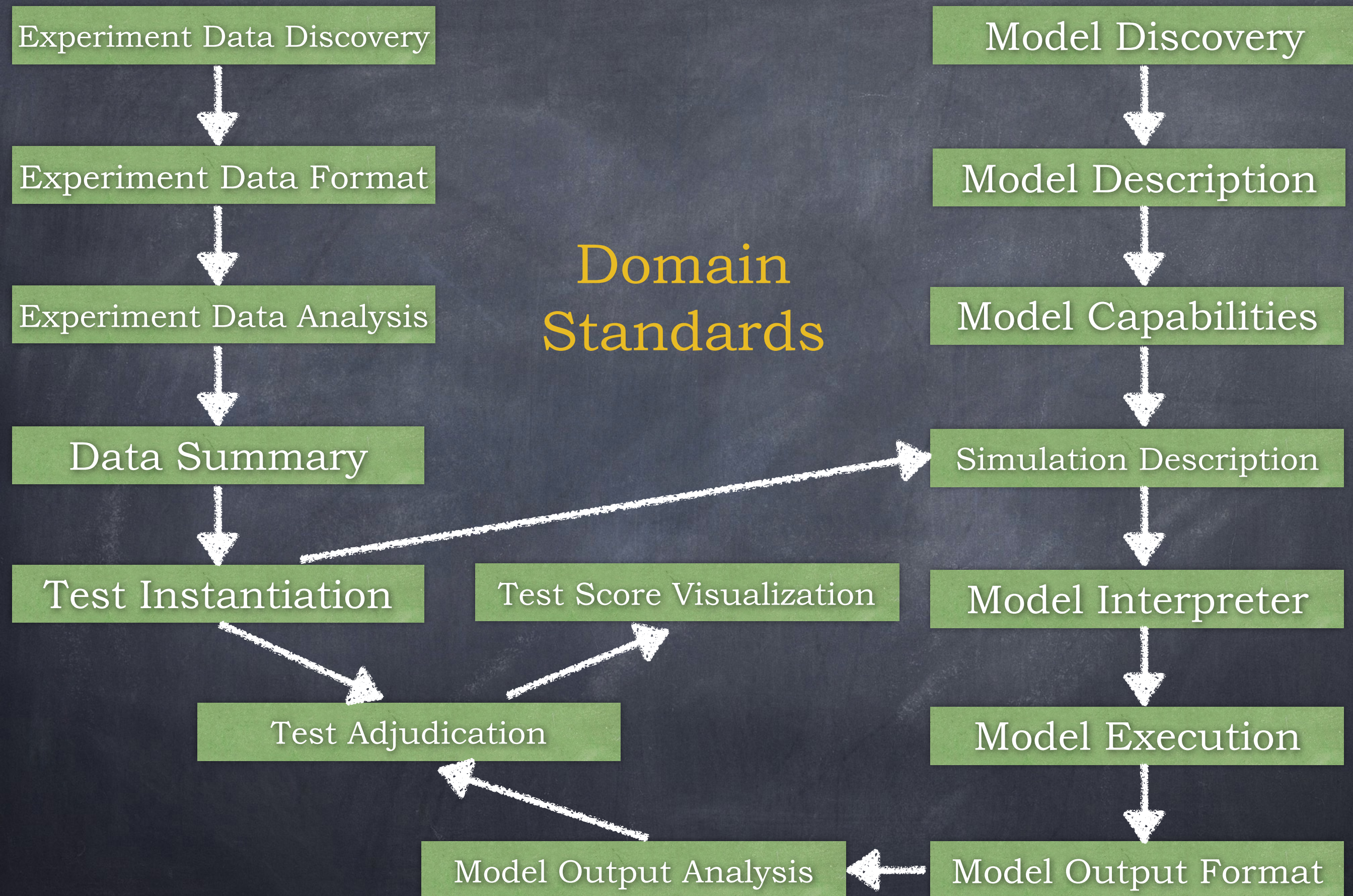
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 - tested using data from NeuroElectro
- OpenWorm
 - simulation of an entire organism
 - <http://www.openworm.org>
 - tested using data from neuron to behavior





Domain Standards

Experiment Data Discovery

CRCNS.org

Experiment Data Format

NIX

Experiment Data Analysis

NEO/NeuroTools

Data Summary

NeuroElectro

Test Instantiation

NeuronUnit

Test Adjudication

NumPy/SciPy

Test Score Visualization

SciDash

Model Output Analysis

NEO/NeuroTools

Model Discovery

Open Source Brain

Model Description

NeuroML

Model Capabilities

Comp. Neuroscience Ontology

Simulation Description

SED-ML

Model Interpreter

NeuroConstruct

Model Execution

NEURON

Model Output Format

NSDF

Linking Domain Standards

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- Look your child in the face when they ask if you, an alleged scientist, used the scientific method in the development of your model.

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(EXPERIMENTALIST'S/TESTER'S PERSPECTIVE)

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 - What other data does it explain?

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 - 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.

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 - Is there a model that explains my data?
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- Pre-experiment, grant stage discovery of hypothesis implications.
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BENEFITS

(EXPERIMENTALIST'S/TESTER'S PERSPECTIVE)

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- Increased community awareness of the data you collected.

BENEFITS

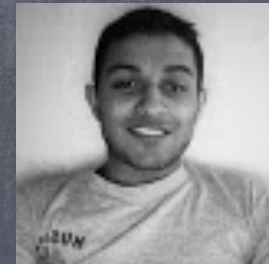
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 - It could become the gold standard by which models are judged!

ACKNOWLEDGEMENTS

- **Cyrus Omar**

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Univ. of British Columbia, Canada



- **Sharon Crook**

Arizona State University, USA



- **Padraig Gleeson**

University College, London, UK



Appendix

SCIUNIT: CAPABILITIES

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- Each **model** declares its capabilities via inheritance, and satisfies them via implementation.
- Each **test** lists its *required capabilities*.

SCIUNIT: CAPABILITIES

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class ProducesSpikes(Capability):  
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    """  
  
    def get_spikes(self):  
        """Gets computed spike times from the model.  
  
        Arguments: None.  
        Returns: a NeuroTools SpikeTrain object.  
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- Capabilities are *implemented* by those who understand the model being tested.

SCIUNIT: TESTS

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class SpikeWidthTest(sciunit.Test):

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- The *sciunit.Test* base class has a *judge* method which takes a model, checks capabilities, and invokes all of the above to return a score.

SCIUNIT: MODELS

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```
class LIFModel(sciunit.Model, ProducesMembranePotential, ProducesSpikes):  
    """A leaky integrate and fire model."""  
  
    def get_spikes(self):  
        # Get membrane potential.  
        membrane_potential = self.get_membrane_potential()  
        # Extract spike times.  
        spike_times = membrane_potential.threshold(0)  
        return spike_times  
  
    def get_membrane_potential(self):  
        # Create membrane potential object from model attribute.  
        membrane_potential = AnalogSignal(self.v_m, self.dt)  
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    def simulate(self, ...):  
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- *SciUnit* models *implement* capabilities to match the design of the underlying real model.

SCIUNIT: CAPABILITIES

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```
class ProducesActionPotentials(ProducesSpikes):
    """Indicates the model produces action potential waveforms.
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    """

    def get_action_potentials(self):
        """Gets action potential waveform chunks from the model.

        Returns
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        NeuroTools.signals.AnalogSignalList
            A list of spike waveforms
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- Tests are inherently **subjective**.

NEURONUNIT: MODELS

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 - Model description: *NeuroML* (<http://neuroml.org>)
 - Simulation description: *SED-ML* (<http://sed-ml.org>)
 - Simulation execution: ... whatever reads NeuroML (neuroConstruct, NEURON, etc.)

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from neuronunit.models import OSBModel

# Purkinje Cell model from OSB at cerebellum/cerebellar_purkinje_cell/PurkinjeCell""
PurkinjeCell = OSBModel.make_model("cerebellum",
                                   "cerebellar_purkinje_cell",
                                   "PurkinjeCell")

# Initialize (parameterize) the model with some initialization parameters.
model = PurkinjeCell(population_name="OrigChansCellGroup_0")
```


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from neuronunit.models import OSBModel

# Purkinje Cell model from OSB at cerebellum/cerebellar_purkinje_cell/PurkinjeCell""
PurkinjeCell = OSBModel.make_model("cerebellum",
                                   "cerebellar_purkinje_cell",
                                   "PurkinjeCell")

# Initialize (parameterize) the model with some initialization parameters.
model = PurkinjeCell(population_name="OrigChansCellGroup_0")
```

... followed by many interactions with this model via its capabilities, in the course of test execution.

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class InjectedCurrentSpikeWidthTest(SpikeWidthTest):  
    """Tests the full widths of spikes at their half-maximum under current injection."""  
  
    def __init__(self,  
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```
def injection_params(amplitude):  
    return {'injected_current':{'ampl':amplitude}}:  
  
width_test_1 = InjectedCurrentSpikeWidthTest(observation, injection_params(25.0))  
width_test_2 = InjectedCurrentSpikeWidthTest(observation, injection_params(50.0))  
width_test_2 = InjectedCurrentSpikeWidthTest(observation, injection_params(75.0))  
  
width_suite = sciunit.TestSuite([width_test_1,width_test_2,width_test_3])
```


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VISUALIZING VALIDITY

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A synthesis of solar cycle prediction techniques

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2009a test now runs against hand-coded LIF model		
 rgerkin authored 7 days ago	latest commit e73962fd32 	
 capabilities	2009a test now runs against hand-coded LIF model	7 days ago
 comparators	2009a test now runs against hand-coded LIF model	7 days ago
 docs	Added documentation for spike train similarity metric	23 days ago
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 suites	Year 2009 Test A now works for simple models	23 days ago
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 .gitignore	Ignoring pickled files (too big for GitHub	21 days ago
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