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Xolotl: An Intuitive and Approachable Neuron & Network Simulator in MATLAB

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An Intuitive Neuronal Simulator

2 ABSTRACT

xolotl is a free and open-source neuronal simulator written in C++ with MATLAB wrappers. Biophysically-detailed models of networks can be designed efficiently using an intuitive language tightly coupled to the object-based architecture of the underlying C++ code. Models can be specified by adding conductances to compartment objects. The structure is modular, serialized, and searchable, permitting high-level programmatic control over nearly all features of the models. C++ templates are provided for developing new conductances, compartments, and integration schemata. It also includes a customizable graphical user interface (GUI) for rapid prototyping and hand-tuning conductances in real-time. The modular structure and accessibility to all parameters, variables, and dynamics of the model network in MATLAB facilitate rapid construction and assessment of model networks. xolotl is freely available at https://github.com/marderlab/xolotl. This tool provides straightforward implementation and fast simulation of neuronal models while permitting full control over every aspect of the network and integration.

16 Keywords: simulator, MATLAB, C++, conductance-based, neuron, network, keyword

1 INTRODUCTION

xolotl (https://github.com/marderlab/xolotl) is a fast single-compartment and multicompartment simulator in C++ with MATLAB wrappers. Written with an emphasis on ease-of-use, xolotl can simulate single-compartment conductance-based models, networks of these, and detailed multi-compartment models. xolotl exploits a novel automatic type system, cpplab, which binds MATLAB code to C++ header files, creating objects and classes ad libitum in MATLAB which reflect the underlying object-oriented code. xolotl implements cpplab to represent the nested structure of conductance-based models, and exploits the computational efficiency of the low-level programming language to quickly integrate models. For this reason, models can be implemented entirely in MATLAB with a few lines of code.

Models are specified in MATLAB by a nested structure. The xolotl object contains compartments which themselves contain conductances. Synapses belong to the xolotl object and connect compartments together. The high-level specification supports arbitrarily large network and multi-compartment morphologies.

The software has been implemented in MATLAB due to its ease-of-use and popularity among neuroscientists. cpplab provides a powerful backend for specifying and integrating models without relying on the significantly slower and limiting MATLAB codegen. While automated C++ transpiling from MATLAB using the proprietary codegen can drastically improve performance over loops through strong typing and memory pre-allocation, supervenience of MATLAB over C++ prevents efficient use of low-level features, such as passing by reference and object-oriented programming. Minimal experience with MATLAB is required to use xolotl, and all equations and integration methods are provided transparently to the end user. No string parsing of equations is required (Sherfey et al. 2018; Stimberg, D F M Goodman, et al. 2014; Stimberg, D F Goodman, et al. 2013)

xolotl comes packaged with visualization functions and a graphical user interface (GUI) for realtime manipulation of model parameters. Plotting of voltage, intracellular calcium, conductance gating functions, and time constants is provided by built-in xolotl methods. The GUI permits real-time tuning of any network parameters using numerical sliders in a graphical interface which displays the resultant membrane potential and intracellular calcium traces. The ease-of-use of these tools lends them to pedagogical applications and rapid exploration of toy models. This tool aims to simplify the investigation of dynamics of complex neural network models, facilitate collaborative modeling, and complement other tools being developed in the neuroinformatics community.

2 DESIGN GOALS

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- 47 xolotl is designed to be easy-to-use without sacrificing speed.
- The software has been designed in MATLAB due to its popularity among neuroscientists for pedagogy and research. xolotl capitalizes on MATLAB's straightforward structure array syntax to permit rapid prototyping and experimentation, especially for small neuronal networks of complex models. Parameters of conductances, neuronal compartments, and simulations may all be edited in the structure before any calls to integration functions. The underlying code is written in C++ for speed and memory optimization, and while models can indeed be integrated using the compiled binary, symbolic manipulations can be readily performed in MATLAB without ever touching the foundational code.

2.1 FEATURES

- 55 MATLAB provides a high level programmatic and graphical interface for implementing, manipulating, and visualizing models without sacrificing the enhancements of the underlying C++ code.
- 57 *Modular structure.* Models are specified by adding compartments and synapses to the xolotl object.
- 58 Conductances are added to compartments and controllers can be added to conductances. This modular
- 59 structure recapitulates the biophysics of the Hodgkin-Huxley formalism and obviates the need to explicitly
- 60 write out equations, which in xolotl are contained within the conductance header files.
- 61 Interface between C++ and MATLAB. xolotl relies on cpplab constructions, which allow the user
- 62 to exploit the efficiency of low-level C++ code. MATLAB treats cpplab objects as fully-typed variables
- 63 allowing for symbolic manipulation using only the high-level programming language and graphical inter-
- 64 faces. xolotl is fast because all time-intensive code is written in C++. While automated C++ transpiling
- 65 from MATLAB using the proprietary codegen can drastically improve performance over loops through
- 66 strong typing and memory pre-allocation, supervenience of MATLAB over C++ prevents efficient use of
- 67 low-level features, such as passing by reference and object-oriented programming. C++ provides speed

- 68 improvements beyond the benefits of translating MATLAB features into low-level code. For this reason,
- 69 cpplab has been designed to provide an interface for constructing, transpiling, and compiling C++ code
- 70 to be called from within MATLAB. xolotl simulations are run entirely from C++ executables.
- 71 Automatic and efficient compiling. xolotl automatically handles transpiling and compiling MATLAB
- 72 code into C++. The MD5 algorithm hashes the network to compile a new binary and MEX bridge file only
- 73 if needed and to confirm that the correct binary fetched during execution.

2.2 SYNTAX

- MATLAB can easily control the cpplab objects using the standard, flexible data structure notation popular in high-level scripting languages.
- 76 Adding features. The add function creates a compartment, conductance, or controller and affixes it as
- 77 a field in the xolotl network structure. This function generates a MATLAB struct that faithfully
- 78 represents the underlying C++ code. Compartments add to the xolotl object and conductances add to
- 79 compartments. Specific properties can be specified using key-value pair arguments (e.g. Figure 1A).
- 80 Finding features. cpplab comes with several features which simplify the handling of complexly-nested
- 81 models. The find function acquires a cell array of all properties of the network which satisfy a search
- 82 condition. For example, one can find all paths to maximal conductances within the 'HH' compartment
- 83 by:
- 84 x.find('HH*gbar');
- 85 To extract a vector of the maximal conductances:
- gbars = x.get('HH*gbar');
- 87 To set the maximal conductances all at once:
- x.set('HH*qbar', qbars)
- 89 Compartments. A model neuron consists of one or more compartments, each representing a section of
- 90 membrane with capacitance and surface area. Isopotential models require one compartment, whereas
- 91 models with multiple neurons, units, or non-trivial morphology require multiple compartments. All
- 92 specifiable properties of compartments are shown in Supplementary Table 1.
- 93 Synapses. xolotl provides some features for generating complex models. Synapses can be added
- 94 with the connect function. At minimum synapses possess identifiers to presynaptic and postsynap-
- 95 tic compartments and default to electrical synapses. All specifiable properties of synapses are shown in
- 96 Supplementary Table 2. To create axons or transport chains, the slice function splits a compartment
- 97 into *n* discrete segments and adds these compartments to the network connected by electrical synapses.
- 98 Conductances and controllers. All conductances contain fields for maximal conductance and reversal
- 99 potential. Conductances with activation and inactivation variables include them as m and h respectively.
- 100 Gating functions and their respective time constants are contained within the conductance header file.
- 101 xolotl comes packaged with conductances from several dozen papers (Supplementary Table 3).
- 102 Creating custom cpplab objects. xolotl contains template header files for producing custom con-
- 103 ductances. The template contains instructions on how to design novel conductances with arbitrary
- 104 specifications.

105 Simulation. Models are simulated in xolotl with the integrate function which outputs as time series

- 106 the membrane potentials, intracellular calcium concentrations, controller states, intrinsic currents, and
- 107 synaptic currents. The integrate function also accepts an argument which specifies injected current or
- 108 clamped voltage.
- 109 Numerical integration. xolotl uses the exponential Euler method for single compartment models, for-
- 110 ward Euler for gating variables, and a Crank-Nicholson regime for electrically-coupled compartments
- 111 (Butcher 2016; Dayan and Abbott 2001; Oh and French 2006) These defaults provide a mix of speed,
- 112 accuracy, and stability, and are built into the cpplab header files. Custom cpplab header files can
- 113 be customized with any iterative integration method. The simulation time-resolution can be specified to
- target arbitrary precision, and an output time step can be selected to support automatic down-sampling for
- 115 memory considerations.
- 116 'Closed-loop' vs. 'open-loop.' Simulations can be run in 'closed-loop' mode where each simulation be-
- gins by resetting all dynamical variables to their initial conditions at instantiation, or 'open-loop' mode
- 118 which begins simulation with the current network state.
- 119 Using the graphical interface to manipulate parameters. xolotl comes packaged with a graphical user
- 120 interface for visualizing parameter changes in real-time. The manipulate function opens the GUI,
- 121 which displays a figure plotting the membrane potential and intracellular calcium concentration of all
- 122 compartments as time series, and a dialog box with customizable sliders for all parameters of the model,
- much like the Manipulate function in Wolfram Mathematica. Moving the sliders integrates the model in 'open-loop' mode with the new parameters. The parameters available in the sliders can be cus-
- model in 'open-loop' mode with the new parameters. The parameters available in the sliders can be customized by passing a cell array to manipulate. For example, to only see sliders for maximal conductances
- 126 of the HH compartment, call x.manipulate ('HH*gbar'). Closing the GUI saves the network state
- of the model to the xolotl object. This is particularly helpful for rapid prototyping of models.
- 128 Optimizing parameters. xolotl can use the Global Optimization toolbox for MATLAB to optimize any
- 129 accessible xolotl parameters. The toolbox is algorithm-agnostic and accepts any function in MATLAB
- 130 with a scalar first output as the objective function. Simulations run on multi-core processors or high-
- 131 performance computing clusters using the Parallel Computing toolbox.

2.3 LIMITATIONS

- The focus on ease-of-use and speed means some features were elided in the streamlining process.
- 133 Reliance on compiled C++ code. While MATLAB comes with robust features for compiling C and C++
- 134 code, xolotl cannot run without C++ compilation. For users, this necessitates the additional step of
- 135 setting up the mex compiler which can be problematical, especially for nonstandard (e.g. Arch-based
- 136 Linux). Secondly, compilation adds a small amount to total processing time. Longer simulations (> 1000
- 137 time-steps) minimizes this effect. Adding new conductances also requires writing some C++ code. For
- model conductances in the Hodgkin-Huxley formalism (Dayan and Abbott 2001; Hodgkin, Huxley, and
- 139 Katz 1952) adjustments consist of changing default values in a template C++ header file. Implementing a
- 140 new integration scheme requires much more in-depth usage of C++.
- 141 Limited to conductance-based models. xolotl has been developed specifically for conductance-based
- models. It does not currently support rate- or current-based models.
- 143 Limited numerical integration strategies. While the exponential Euler method performs well in neuronal
- models (Dayan and Abbott 2001; Oh and French 2006) it may be desirable to use other methods un-
- 145 der certain conditions. xolotl does not currently support other integration schemes for its built-in
- 146 conductances, nor does the software support error-sensitive variable step-sizes 'out-of-the-box.'

- *Inefficient tools for handling large networks.* While xolotl can integrate large networks (> 1000 com-
- 148 partments), xolotl uses string-based comprehension for labeling compartments which is suited to
- 149 descriptive naming, but prohibits vector operations over compartments.

USAGE EXAMPLES

- 150 In MATLAB, users create a xolotlobject and populate it with cpplab-generated objects which describe
- compartments, conductances, synapses, and controllers. The model is integrated with the integrate 151
- function where the membrane potential, intracellular calcium concentration, controller states, intrinsic 152
- currents, and synaptic currents can be outputs. 153
- 154 xolotl comes packaged with a library of pre-existing conductance and synapse objects which greatly
- 155 simplify the task of constructing model neurons. These objects can be referenced by name and added
- directly to a compartment. Novel conductance dynamics can be easily written by modifying a template 156
- header file contained in the xolotl distribution, or designed entirely from scratch. 157

SIMULATING A HODGKIN-HUXLEY MODEL

- 158 The seminal Hodgkin-Huxley model of action potentials in the squid giant axon (Hodgkin and Huxley
- 159 1952; Hodgkin, Huxley, and Katz 1952) contains a fast inactivating sodium conductance (NaV), a non-
- inactivating delayed rectifier (Kd), and a passive leak current (Figure 1A). A compartment, HH, with 160
- membrane capacitance (Cm) and surface area (A) can be specified by Figure 1B. Network properties can 161
- be set during construction or afterwards using dot-notation in MATLAB (e.g. x.HH.Cm). Figure 1C shows 162
- 163 the MATLAB command prompt after invoking the xolotl object x, displaying the hierarchical structure
- 164 inherent in conductance-based treatments of neurodynamics.
- 165 This model was constructed using conductances from Liu et al. 1998 based on electrophysiological
- recordings from the lobster stomatogastric ganglion (Turrigiano, LeMasson, and E. Marder 1995) In 166
- the absence of applied positive current, the model is quiescent. When 0.2 nA is injected, the model 167 168 tonically spikes (Figure 1D). The integrate function takes the applied current as an argument (e.g.
- x.integrate(Iapp)), so that the xolotl object is agnostic to integration-specific perturbations.
- 169
- The plot function generates voltage and intracellular calcium traces, where the voltage trace is colored 170
- by the dominant current. If the membrane potential is increasing, the strongest instantaneous inward cur-171
- rent colors the trace. Conversely, if the membrane potential is decreasing, the strongest outward current 172 colors the trace instead. Figure 1F-I display the results of the show function. Activation and inactivation
- 174
- steady-states and the voltage-dependent time constants of these gating variables describe the conductance
- 175 dynamics in absence of other channel types.

3.2 PERFORMING A VOLTAGE CLAMP EXPERIMENT IN-SILICO

- xolotl can recapitulate the results of voltage clamp experiments (Destexhe and Bal 2009; Swensen and 176
- E. Marder 2000, 2001; Turrigiano, LeMasson, and E. Marder 1995) Figure Figure 2 displays steps in the 177
- 178 procedure to clamp the membrane potential of a cell with delayed rectifier potassium conductance. Dur-
- ing an *in-vitro* experiment, confounding currents would be pharmacologically-blocked and two-electrode 179
- voltage clamp used to record tail currents at fixed membrane potential (Connor and Stevens 1971a,b) 180
- A single-compartment model with a delayed-rectifier conductance is simulated at stepped membrane 181
- potentials. The model is simulated using the integrate function. The second argument determines the 182
- 183 clamped voltage and the fourth output is the current trace.
- 184 [V, Ca, ~, I] = x.integrate([], clamped_voltage)

185 Currents under voltage clamp approach the steady-state holding current (Figure 2D-E). The currentvoltage relation is the steady-state current over the clamped voltage, and the effective conductance is the 186 187 derivative of that relation (Figure 2F-G). Since the effective conductance is the product of the maximal conductance and the gating variables (Dayan and Abbott 2001; Turrigiano, LeMasson, and E. Marder 188 1995) and the tail current is monotonically-increasing with time under voltage clamp, the current can be represented as non-inactivating. Fitting a sigmoid to various powers yields a model for the current dy-190 namics (Figure 2H-I). These figures describe graphically the theoretical underpinnings of current analysis 191 through voltage clamp and can serve as an effective pedagogical tool for computational and quantitative 192 193 neuroscience.

3.3 SIMULATING NETWORK MODELS

Network models in xolotl consist of compartment objects connected by synapses. Synapses are stored in a vector array as a field of the xolotl object in MATLAB. Presynaptic and postsynaptic labels indicate the connectivity of the synapse. Figure Figure 3 implements a model of the triphasic pyloric rhythm in the stomatogastric ganglion of crustaceans. The pyloric model contains three compartments and seven synapses (Figure 3A). This structure is reciprocated in the hierarchy of the xolotl object, where conductances are contained within compartments (Figure 3B).

Representing the network in xolotl requires constructing three compartments and eight conductances in each using the add function.

```
202 x.add('AB', 'compartment', 'Cm', 10, 'A', 0.628, ...)
203 x.AB.add('prinz/NaV', 'gbar', 1000, 'E', 50)
204 ...
```

Synapses are upper-level properties of the network which point between two compartments (Figure 3C). This exploits vectorized operations in MATLAB and does not require each synapse to possess a unique name. The connect function adds synapses to the network. The first two arguments specify the presynaptic and postsynaptic compartments. The third dictates the type of synapse. All others follow the 'keyword', value paradigm and preset parameters of the synapse.

```
x.connect('AB', 'LP', 'Chol', 'gbar', 30)
```

3.4 SIMULATING INTEGRAL CONTROL

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211 xolotl can implement homeostatic tuning rules as integral control. The controller computes an error 212 signal (typically a function of intracellular calcium concentration), and adjusts the conductance or synapse 213 it controls accordingly (O'Leary et al. 2013) In xolotl, integral controllers are cpplab objects added 214 to the conductance or synapse they regulate.

In a demonstration adapted from O'Leary et al. 2013, integral control changes maximal conductances to bring a neuron from quiescence into a bursting regime. Calcium sensors supervene on maximal conductance density (Figure 4) to change neuronal activity. Each conductance in the xolotl structure contains a calcium-sensitive controller (Figure 4B-C). Maximal conductances increase from random initial conditions to a set which elicits the desired network output by minimizing the error signal (Figure 4D-F).

3.5 USING THE GUI TO MANIPULATE PARAMETERS

The manipulate function opens the GUI which permits visualization of changing parameters in realtime. Moving sliders representing the values of network parameters updates a plot (Figure 5B). By default, the function opens a figure displaying the results of the plot function, which shows the voltage and

intracellular calcium traces for each compartment (Figure 5A). manipulate grants slider control over all xolotl parameters by default, but specific ones can be selected by passing them as arguments. For 225 example, to manipulate only the maximal conductances and visualize using the myPlot function 226

```
227
            x.manipulate('*gbar', @myplot)
```

BENCHMARKS

- To assess speed and accuracy, xolotl, DynaSim (Sherfey et al. 2018) and NEURON (Hines and 228 Carnevale 1997) were compared in simulations over varied time resolution, simulation time, and number 229
- of compartments (Figure 6). 230
- Single-compartment Hodgkin-Huxley-like models were generated using conductance dynamics from 231
- Liu et al. 1998 in the simulation environments. xolotl uses the exponential Euler method for in-232
- tegrating membrane potential (Dayan and Abbott 2001) DynaSim was implemented with a 2nd-order 233
- Runge-Kutta integration scheme as recommended for high-performance in the documentation. NEURON 234
- 235 used an implicit Euler regime (Hines and Carnevale 1997)
- To compare the integration methods, models were simulated for 5 s at varying time-resolution (Figure 236
- 6A). The ratio between 'simulated' time and actual runtime was defined as the speed factor. Higher values 237
- 238 indicate faster simulations. The coincidence factor determines the correlative overlap between two spike
- trains (Jolivet et al. 2008) To assess accuracy over decreasing time-resolution for the three simulation 239
- environments, spike trains at each resolution were compared to a 'canonical' spike train (exponential 240
- Euler at a time-step of dt = 0.001 ms). 241
- To assess the performance of the simulators in absence of set-up overhead, models were simulated with 242
- a time-resolution of 0.1 ms over increasing simulation time (Figure 6B). The speed factor was defined as 243
- 244 the ratio between time represented in the simulation and actual runtime (simulation-time). Therefore, the
- speed factor represents how many times faster the simulation is than a real-time observation. 245
- Many simulators perform well in simulations of many compartments (Brette et al. 2007; Delorme 246
- and Thorpe 2003; Sherfey et al. 2018; Vitay, Dinkelbach, and Hamker 2015) Networks of up to 1,000 247
- Hodgkin-Huxley cells were simulated for 5 s at a time-resolution of 0.1 ms (Figure 6C). 248
- DESCRIBE BENCHMARK RESULTS 249

DISCUSSION

REPRODUCIBILITY 5.1

- xolotl fosters reproducibility in science. While the availability of hosting sites with version control (viz. 250
- GitHub (https://github.com), GitLab (https://gitlab.com/), and Open Science Frame-251
- work (https://osf.io/)) and the push for reproducibility in computational science (Baker 2016; 252
- Eklund, Nichols, and Knutsson 2016; Stodden et al. 2016) has resulted in the availability of source code, 253
- much of this code base is bespoke and difficult to implement (Sedano 2016; W Xu, D Xu, and Deng 2017) 254
- To this end, xolotl provides an environment with readability and reproducibility in mind. Each net-255
- work is hashed to provide a unique alphanumeric identifier. Conductance header files are easily viewed in 256
- the xolotl source files; conductances in MATLAB contain links to the full path of the generating file.

5.2 CIRCUMVENTING LANGUAGE TRADEOFFS

- 258 Executing C/C++ code in higher-level languages such as MATLAB or Python often provides speed
- 259 improvements for iterative code in algorithms.
- 260 C is statically-typed, with procedural syntax that provides low-level access to memory (Kernighan and
- 261 Ritchie 1978) providing significant advantages for time-intensive computations. Unfortunately, automatic
- 262 code-generation is limited by the supervening language. MATLAB, for instance, cannot use pointers or pass
- by reference, which limits the efficiency of C code automatically generated from MATLAB. Conversely,
- 264 custom C/C++ code provides significant increases in performance and memory conservation, but lacks
- 265 the ease-of-use and flexibility of scripting languages.
- 266 xolotl handles this problem through symbolic manipulation of C++ objects in MATLAB. Built from
- 267 the ground up in C++, xolotl maintains all the advantages of custom compiled code, but can run in
- 268 MATLAB without the user having to touch the C++ code. xolotl represents compartment, conductance,
- 269 synapse, and controllers as cpplab objects, which map to underlying C++ header files. In this way,
- 270 properties of the xolotl network can be examined and changed using object-oriented paradigms. The
- 271 object specifies the integrate function, not the other way around.

5.3 APPLICATIONS OF CPPLAB

272 NEED TO WRITE THIS

CONFLICT OF INTEREST STATEMENT

- 273 The authors declare that the research was conducted in the absence of any commercial or financial
- 274 relationships that could be construed as a potential conflict of interest.

AUTHOR CONTRIBUTIONS

- 275 SG-S designed and implemented the core of the xolotl toolbox. AH contributed to the code base,
- 276 created the online user documentation, and wrote the manuscript. EM supervised the project. All authors
- 277 reviewed the paper.

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SUPPLEMENTAL DATA

Tables including all conductances packaged with xolotl should be put in the supplementary material.

DATA AVAILABILITY STATEMENT

283 The code to generate all figures is available at (https://github.com/marderlab/284 xolotl-paper). xolotl is frely available at (https://github.com/marderlab/xolotl).

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FIGURE CAPTIONS

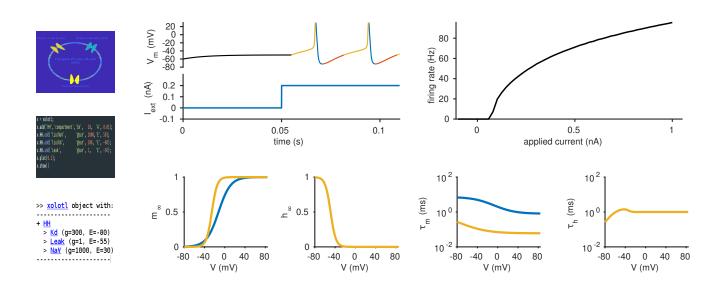


Figure 1: xolotl can quickly set up and simulate conductance-based models. (A) Cartoon of a Hodgkin-Huxley single-compartment neuron model with fast sodium, delayed rectifier, and leak currents. (B) Code snippet in MATLAB used to implement D, F-I. (C) xolotl schematic displayed in the MATLAB command prompt. (D) Simulated voltage trace of a Hodgkin-Huxley model with three conductances and 0.2 nA of injected current. Colors indicate the dominant current (gold is fast sodium, blue is delayed rectifier, red is leak). (E) Firing rate-input relation displaying firing rate as a function of injected current current. (F-G) Steady-state gating functions for activation (m) and inactivation (h) gating variables. (H-I) Voltage-dependence of time constants for activation (m) and inactivation (h) gating variables.

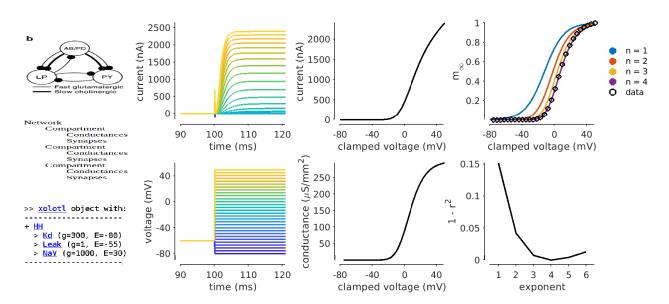


Figure 2: Simulating a voltage-clamp experiment. (A) Cartoon of a cell with delayed rectifier potassium conductance (Liu et al. 1998) with experimentally-fixed voltage. (B) Structure of xolotl object in A. (C) Code snippet depicting integration under voltage clamp. (D-E) Current response to steps in voltage from a holding potential of $V_m = -60$ mV. (F) Current-voltage relation of the steady-state current (t = 400 ms) indicating a reversal potential of E = -80 mV and no inactivation. (G) Conductance-voltage relation at steady-state takes the form of a sigmoid. (H) Sigmoids m fit to the model as m^n data indicating that n = 4 is the best fit. (I) Goodness of fit vs. exponent n, suggesting n = 4 as the best fit to the data.

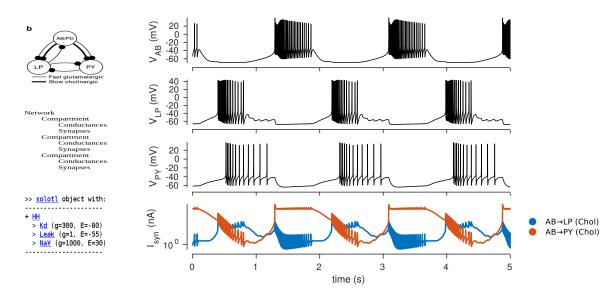


Figure 3: Simulating a network of conductance-based model neurons. (A) Diagram of a network model of the pyloric rhythm in the crustacean stomatogastric ganglion (Prinz *et al.* 2004). (B) Each neuron is modeled as a single compartment with 7-8 intrinsic conductances and 1-3 post-synaptic conductances. (C) xolotl implements conductances as fields of compartments and synapses as connections between compartments. (D-F) Simulated voltage trace of a model network for the three compartments. (G) Time series of synaptic currents in the simulated network can be obtained from the integration.

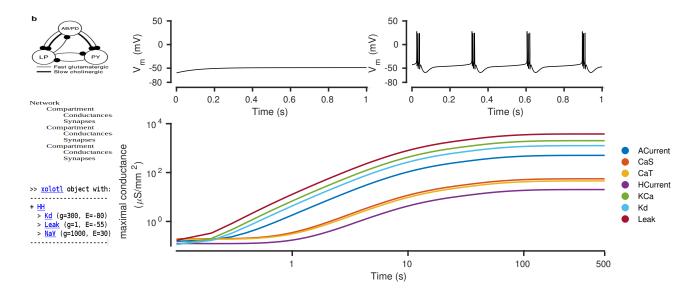


Figure 4: Simulating neurons under homeostatic regulation. (A) Cartoon of a model neuron (Liu et al. 1998) with integral control (O'Leary et al. 2013) (B) Hierarchical structure of a neuronal network considers controllers as components of compartments which act on conductances. (C) xolotl implements controllers as properties of conductances and synapses. (D) Calcium sensors change maximal conductances to move a neuron from quiescence to a bursting state. (E) Voltage trace shows regular bursting activity after integral control.

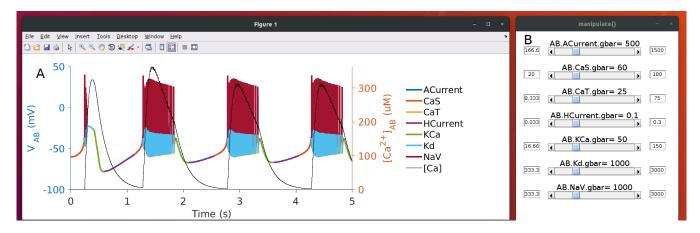


Figure 5: Using the GUI to manipulate neuron parameters. (A) Real-time output of the plot function displaying voltage (colored) and intracellular calcium (black) traces of a bursting neuron model (Prinz, Billimoria, and Eve Marder 2003; Prinz, Bucher, and Eve Marder 2004) Colors indicate the dominant current. (B) Sliders control the maximal conductances, which updates on the figure.

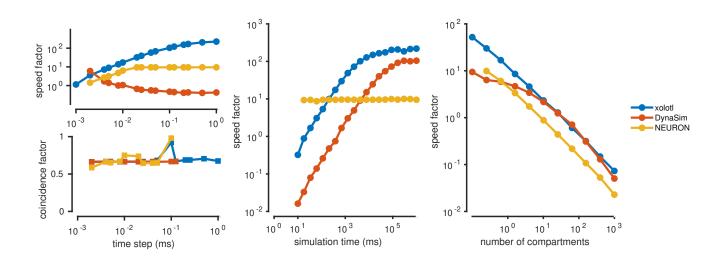


Figure 6: xolotl benchmarked against DynaSim and NEURON. (A) Ratio of 'simulated' time to runtime (speed factor) and accuracy, measured by spike train coincidence plotted against decreasing time-resolution. (B) Speed factor for models at increasing simulation times. (C) Speed factor over number of compartments.