Skuld
User Manual

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Chapter 1

Introduction

Simulations of large neural networks can provide new insights in the workings of our brain and related disorders. Next to the modeling aspect of these projects, in which decisions have to be made regarding the structure of the network and values for the parameters, the computational part has to be considered carefully as well, especially if the network's size is too large to fit on a single desktop computer. But once these problems are overcome and desired networks can be evaluated without trouble, all data have to be analyzed in order to be useful for the research. This gives rise to a whole different problem: how should one interpret all the obtained results from these large network?

As some simulations generate hundreds of Megabytes of data easily, eyeballing is no more a feasible option. A very common way is to analyze the 'bulk statistics' of the network, e.g. mean membrane potential or a (simulated) microelectrode. However these quantities might be too bulky to reveal properties of cells and microcircuits within the large network and thereby negating the effects of *causality*. It could be the case that some behavioral changes of the network are caused by a small number of neurons only; too small to pop up in the bulk statistics of the network. For that reason, a convenient way has to be found to found that allows analysis of the causality within the network. Hence one should be able to see how the input from certain cells relates to their output and how other neurons are affected by this output.

The Skuld program described in this manual allows users to analyze simulations of large neural networks both on the level of individual neurons and their communications to other neurons as well as their relation with the higher level statistics. The user interface shows the physical position of all cells within the network, together with detailed information of the connections from and to other cells. Furthermore, time series of the membrane potentials can be plotted and raster plots can be made to analyze the behavior of a cell with respect to other cells.

This manual describes all the options and functions that can be used by Skuld to analyze simulations of large neural networks. An overview is given first of the requirements and installation of the program. Thereafter the tools for obtaining and loading data are described and in the end all functions to analyze the whole network, connections within the network and single neurons.

Chapter 2

Getting Started

2.1 Requirements

Skuld is developed as Matlab program, hence Matlab is required for execution. The program is originally built and tested on Matlab version 7.11.0.584 (R2010b) for Mac OS X. Full functionality of Skuld requires Matlab 7.6 (R2008a) or newer. Other versions of Matlab and other operating systems should not cause problems with Skuld, but exceptions may exist.

2.2 Installing and Starting Skuld

To install Skuld, extract all items from the archive to a single folder. Set the current directory in Matlab to the folder containing these files. Start the program by typing the command `Skuld`.

Chapter 3

Description

This chapter gives a detailed explanation of all functions of the Skuld program and how to use those.

> HINT   The data required by Skuld mostly exists of tab-delimited ASCII files. These files are easily made in Matlab using the `dlmwrite` command.

3.1 Loading Data

Data are required for Skuld to operate properly. To open the data window click either the icon in the toolbar or go to the menu *File>Load data*.

The window that shows up has several categories or tabs that can be navigated with the list on the left. The tabs and their corresponding features are:

3.1.1 Neurons

This is used to define the distinction between different cell types in the simulation program. For instance, different cell types can be represented with different colors or different symbols, making visual analysis of the network more attractive. The following settings can be made:

- *No distinction* all neurons are treated as if they are of the same type. They are visually represented with a blue dot.

- *Multiple types* The table at the bottom of the window contains information about the different cell types used in the simulation. Each row represents a population of a specific type of neurons, having the following properties:

  - *Show* determines whether that population is plotted or not.
  - *Name* is a string that represents the name of that population.
  - *#* is the number of neurons within the population.
  - *Symbol* is a single character that represents the shape of the plotted neurons. See Matlab Reference on the plot command for available symbols.
  - *Color* is an array of three elements, reprenting the RGB color used to plot the populations.

The order in which the cell types are entered in this table will be used throughout Skuld, e.g. the ordering of the membrane potentials should match with the numbers and types denoted in this table.

> NOTE   The option to plot only a subset of the populations is unavailable in the current version. All population will be plotted.

3.1.2   Positions

To visually represent the network, every neuron should be given a position. The following options are available:

- *Positions from file* a tab-separated ASCII file in which the ith line contains the x, y, z-position of cell i.

- *Structured positions* All neurons of a specific type are located on a layer. Different layers of different types are stacked in space.

- *Random positions* Every neuron is assigned a random position in space.

3.1.3   Network

The tab represents the connectivity between single neurons in a simulation.

- *No connectivity* Use this options if you do not know the individual connections between neurons.

- *Verdandi* This option is most suitable for simulations of the Verdandi simulator (a newly developed, customizable C++ neuronal simulator). The files required have the following structure:

  - `ConnectionCount.nwk` is an ASCII file that holds a list of $nCell$ tab-separated integers. The ith element in the list is the total number of connections made by neuron i.
  - `ConnectionList.nwk` is a binary file specifying all connections in the network. The connections are ordered by the IDs of the source neuron, hence only the target is stored. Each connection is a 8-byte struct containing the following fields
    1. `unsigned short` containing the cell ID to which the connection is made (2 byte).
    2. `unsigned char (+ null character)` containing the channel ID on the cell to which the connection is made (1+1 byte).
    3. `unsigned short` containing the delay in µs between the generation of action potentials in the cell and activation of the synapse (2 byte).
    4. `unsigned short` containing the synaptic weight, scaled by the constant `WEIGHTSCALE` (2 byte).

  Binary files of this kind are sensitive to the machine-format of the hardware. In the accompanying drop-down list, the machine-format of these binary files can be selected. If unsure about the machine-format of your simulation, the "native" option always works for simulations performed on the same machine as Skuld is run.

- *Connectivity matrix* A tab-separated ASCII file that contains a square connectivity matrix. Element i, j represents the strength of the connection from neuron i to neuron j.

3.1.4 Spike data

This tab allows setting regarding the output of simulation:

- *No spike data* No data available for the neurons.

- *Membrane potentials* A tab-separated ASCII file containing in which element i, j represents the membrane potential of cell j at time step i. The sampling frequency denotes the number of timesteps per second of the simulation. Duration is the length of the simulation in seconds (possibly empty is uncertain). Spike threshold is the threshold value of the membrane potential to be exceeded in order to classify a spike.

- *Spike times* A tab-separated ASCII file in which each row represents a single action potential event. Required fields are the neuron ID and the time (in seconds) at which the neuron fired an action potential. Skuld allows users to indicate the columns numbers in which neuron IDs and corresponding spike times are denoted. Some simulators identify neurons starting at ID 0. In this case, check the corresponding box.

3.1.5 EEG/LFP data

Some simulations output, next to the individual cell behavior, a local field potential. In this manner, the effects of single neurons can be studied on such a macroscopic measure. The following settings are possible:

- *No EEG data* No data available.

- *Transmembrane currents* Similar to the membrane potentials. However, the transmembrane currents represent the local currents absorbed or generated each neurons. Nunez method of sinks and sources is used to estimate the local field potential measured at the top of the slice. Since not all neurons in the simulations might contribute to the local field potential or EEG (like thalamic cells, or interneurons due to their limited size), only the first n neurons are used for this calculation, as given by the field "Number of neurons".

- *Time series* Use this option if a single time series of the local field potential has already been generated by the simulation.

  HINT   Files can be selected in two ways: either entering the pathname to the file in the box or clicking the Edit button to open a dialog to browse for the file. A pathname that is colored red indicates that the given path does not exist and that is has to be changed.

  HINT   The entered duration for the files "Membrane potentials" and "Transmembrane currents" may be shorter than the length of the time series. In that case, the first part of the file is read only (until the given duration).

When all files are selected and the preferences for each population are set, the files can be loaded by pressing the Ok button in the lower-left corner. It might take a while for Skuld to read all the data files. The progress of reading files is printed in the Command Window in Matlab.

  NOTE   Depending on the data loaded, not all features of Skuld might be available; these features are "greyed out".

3.1.6 Saving and Loading Presets

If all the desired settings are made, the whole configuration can be stored and reused later. Before clicking the "Ok" button, choose the menu File >Save Settings. A save-file window shows up, allowing you to save the current configuration anywhere on your disk (as a *.mat file).

Loading an earlier made preset is done by choosing the menu option File >Load Settings. A file-browser shows up, allowing you to locate the formerly created file.

3.2 The Main Window

The main window of Skuld consists of several parts:

- main plot window, displaying the neurons in space and showing their connections to others,

- information panels on the right, showing information about the network as well as the selected neuron,

- a menubar and toolbar at the top of the window, allowing access to all functions of Skuld.

The plotted network can be rotated in 3d by selecting the *Rotate 3d* tool in the toolbar and dragging the cursor over the plot. This rotate tool should be deselected first (by cliking it again in the toolbar) before a neuron can be selected.

Neurons in the main plot window can be selected by clicking on them. The selected neuron will be plotted with a magenta edge. By default, all connections this cell makes to other neurons are indicated by black lines, whereas connections made onto the selected neurons are shown in light blue. This functionality will be described more elaborately later. The lower-right panel displays some general information about the selected neuron:

- the ID number of the cell,

- the type of the cell,

- the total number of connections that this cell receives from other neurons and corresponding to that a pie-chart that displays the distribution of the types of neurons responsible for these incoming connections,

- the total number of connections made by the selected neuron and a pie-chart showing the distribution of target cell types.

The different menus in the menubar contain the following features:

3.2.1 Cell Menu

All features in this menu are related to single cell activity in the loaded simulation.

NOTE   Selecting a neuron might be required to enable all features in this menu.

Select Cell

This brings up a dialog box asking you to enter the cell ID number of the cell that you want to select. Use this option if you want to study a particular cell.

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Vm Trace

This option opens up a secondary plot window showing the time series of the membrane potential of the selected neuron. Next to the default Matlab function (like zoom/pan) some additional features are available as well:

- *Listen to the time series* by clicking the green "play" button in the toolbar.

- *Apply high/low pass filters* by selecting the desired option in the Skuld menu in the menu bar on top.

  HINT   The time-axes of all plot windows shown are by default linked to each other. Zooming in on a plot will cause other plots to zoom to the same range as well. If desired this function can be toggled on/off for each plot individually by selecting the menu item *Skuld>Link view*.

ISI Distribution

Shows the distribution of the inter-spike intervals of the selected neuron. Furthermore, it calculates the mean of distribution and the coefficient of variation (cv).

Auto Spectrum

Calculates the power spectrum of the spike train using Welch's method.

Raster Plot

Generates a raster plot for the selected neuron itself and for all incoming and outgoing neurons. All neurons that connect to the selected neuron are plotted on positive values on the vertical axis, the selected neuron itself is plotted on the line $y = 0$ and all neurons to which the selected cell connects are plotted for negative values on the vertical axis.

   Because the transmission delay of action potentials is unique for all connections, one might be more interested in the time at which the post-synaptic potential (PSP) is delivered to the selected neuron. Furthermore, the study the effects of the action potentials sent by the selected cells, one would be most interested in the PSP timing with respect to the AP time of the receiving neuron.

   The *Skuld >Delay correction* menu option does two things to study the effectiveness of specific action potentials. First it shifts all the spikes in the positive y-plane (the ones that represent neurons making connections to the selected neuron) to the right by an amount equal to the characteristic delay of that the connections. Hence, 'spikes' in the positive plane represent the initiation of PSPs. Secondly, all spikes in the negative plane (the that represent neurons receiving input from the selected neuron) are shifted to the left by an amount equal to the connection delay. This allows the user to see the effectiveness of the selected neuron to the neurons in connects to.

   HINT   In any raster plot the cell ID of a spike train can be requested by right clicking on the spike train.

Visualization option

The remaining options in the menu regard the visual representation of the selected neuron and the connection neurons:

- *Incoming connections* plots a cyan line from every neuron that makes a connection onto the selected neuron.

- *Incoming cells* outlines all neurons that make a connection onto the selected neuron with cyan.

- *Outgoing connections* plots a black line to every neuron to which a connection is made by the selected neuron.

- *Outgoing cells* outlines all neurons that receive a connection from the selected neuron with black.

NOTE   A known bug in Skuld arises when neurons make reciprocal connections ($A \to B$ and $B \to A$). If both the options Incoming cells and Outgoing cells are selected, a cell is given only a single outline instead of two. Furthermore, if one of the view options is switched off, the outline of that neuron vanishes rather than switching to the other color (because that option is still active). No such problems exist for the options Incoming connections and Outgoing connections.

3.2.2 Population Menu

Several global features of specific cell types can be viewed in this menu.

Mean Vm

This shows a list dialog that prompts the populations to be shown. Once a selection is made, a plot is made that shows the mean membrane potential of all neurons of that type.

Firing Rates

Shows time series of the normalized (with respect to population size) instantaneous firing rates of the selected populations. This is determined by the following formula:

$$\text{Instantaneous firing rate} = \frac{\text{\# of spikes of population in a bin}}{\text{Population size} \times \text{Bin-size}}$$

A dialog shows up with a list of available populations, select the desired population(s) and press Ok. Another dialog shows to request the size of the bins (in ms).

Raster Plot

This options makes a raster plot of the selected populations. Contrary to the raster plot of the single cell, this one does not allow for correction of time lags between neurons.

3.2.3 Network Menu

Show EEG/LFP

Selecting this option plots a time series of a recording as would be made by an extracellular electrode placed in the proximity of the network.

Background

The program's name, Skuld, is taken from Nordic myhtology. She represents a fairy that, together with Urd and Verdandi, reigns the fates of mankind. Often pictured as three old ladies beneath a gargantuan tree (the Tree of Life), their task consists of controling a spinning wheel. Every fate is thought of as a wire that is spun into a large thread, representing the interaction between and strengthening of individuals. Whenever such a wire breaks, the life of that person passes away.

The logo of Skuld refers not only to the wires spun, but also to the Tree of Life. In the context of this program the Tree of Life refers also to the complex dendritic structure that is found in the brain.