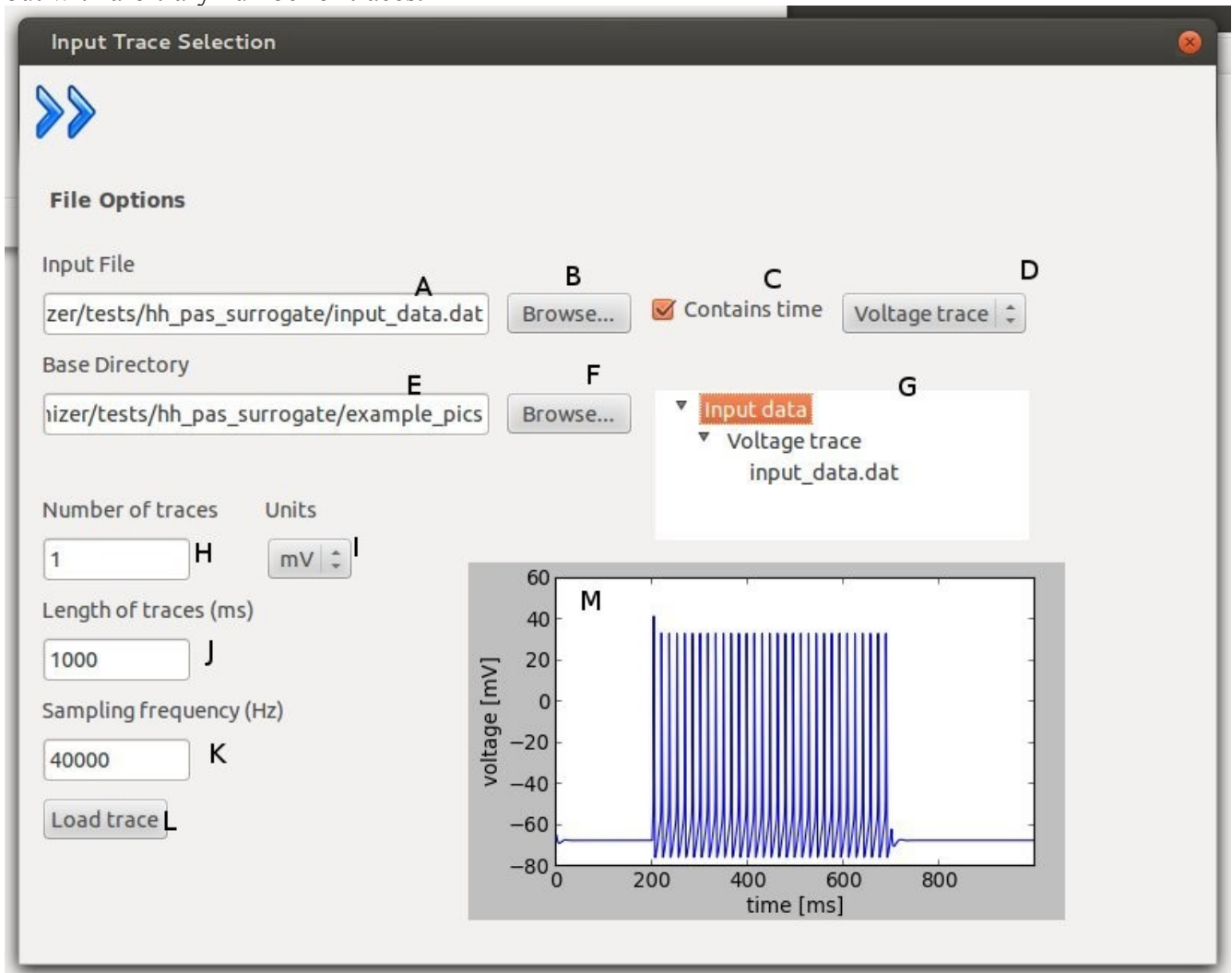


Optimizer tutorial

Layer 1

After the program started, the first layer will appear where the user can select the file containing the input trace(s). The user must specify the path to this file, and the working directory (base directory) where the outputs will be written. Apart from these the user must input the requested parameters of the trace set he/she wants to use. After loading the selected file, the user can check if the traces were loaded properly with the help of a plot which displays all the traces concatenated and with the help of a tree display. The concatenation only performed for displaying purposes, the traces are otherwise handled separately. The program only handles one input file (loading a new file will overwrite the existing one), but with arbitrary number of traces.



A	Path to input data.
B	Browse the location of the input data.
C	Input contains time or not.
D	Type of input (voltage or current trace).
E	Path to base directory (resulting files will be stored here).
F	Browse the base location.
G	Input data browser (the loaded file is displayed under it's type).
H	Number of traces in file (trace set).
I	Units of the data.
J	Length of trace(s). (in case of multiple traces, they must have the same length)
K	Sampling frequency (in case of multiple traces, they must have the same).
L	Loads the trace(s) from the given file.
M	Displays the loaded trace (if given file contains more, the trace will be concatenated for displaying).

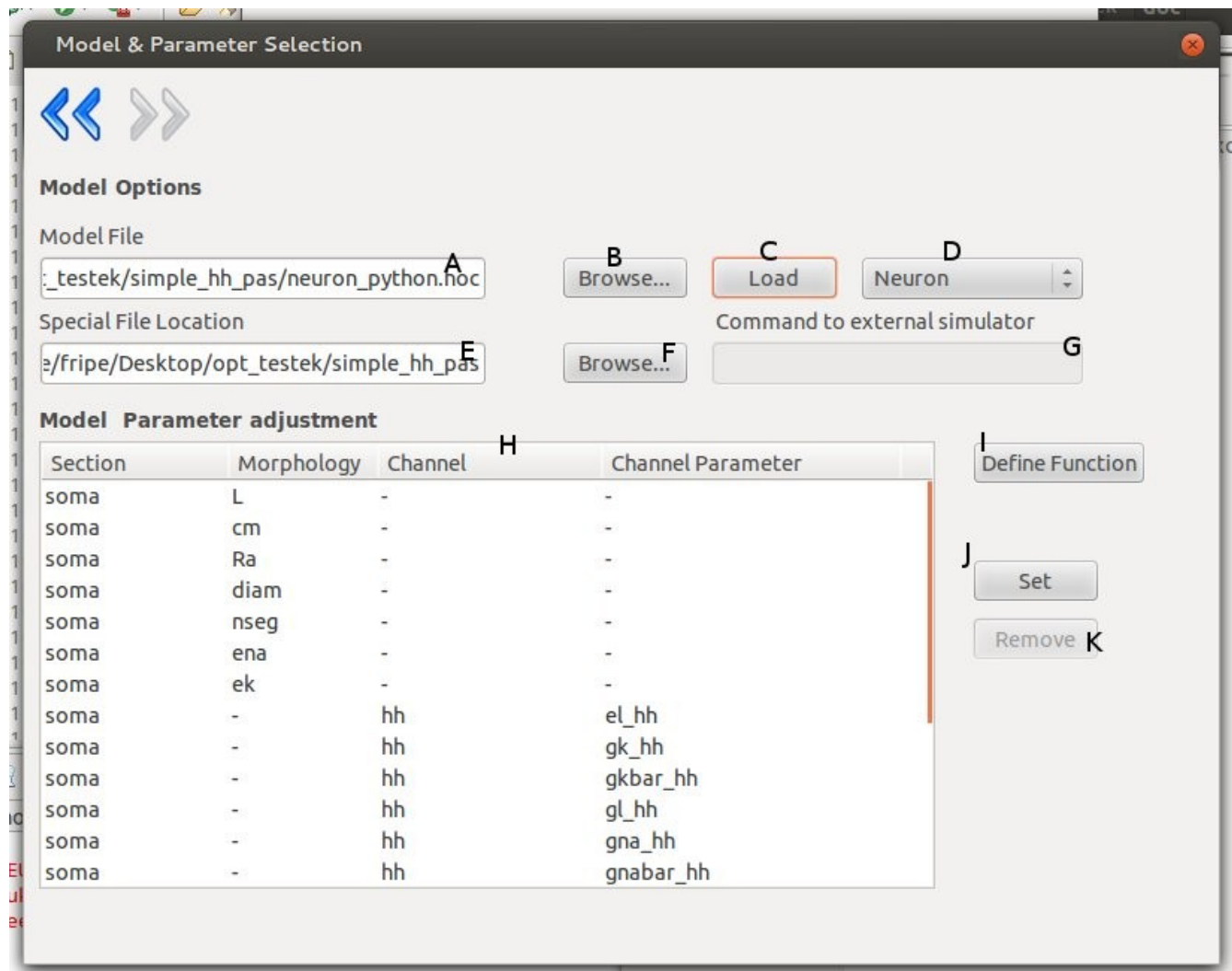
Layer 2

On the second layer the user can specify the simulator which can be Neuron or external.

If the user decided to use Neuron as the simulator then the model file must contain only the necessary structure and mechanisms. The model can be loaded simply after selecting the model file and the special folder where the necessary .mod files are located (optional).

As Neuron can not load it's .dlls after startup, if the special files were not found, the software must be restarted. Once the model is loaded successfully, the content of the model will be displayed, and the user can select the parameters by picking them into the list and pressing the “set” button. Removing a parameter is done in a similar fashion.

At this point the user can load or define a special function which carries out different tasks during the optimization.



A	Path to model file.
B	Browser for model file.
C	Loads the specified model.
D	Simulator type selection (Neuron or external)
E	Path to special files (the compiled mod files for Neuron), this should point to a folder, which contains the folder of the compiled files (e.g.: to a folder which has an x86-64 directory)
F	Browser for special file location.
G	<p>Here you can give the command which invokes the external simulator. The given command must consists of the following:</p> <ul style="list-style-type: none"> -the command that calls the simulator -the name of the model -options to the simulator (optional) -as the last parameter, the number of parameters subject to optimization
H	Displays the recognized parameters. These can be selected for optimization. If the parameters you need, are missing, you can create a user defined function.
I	Opens the window to define/load your own function for the optimization.
J	Ads the currently selected parameter to the list of parameters subject to optimization.
K	Removes the parameter from the aforementioned list.

Layer 3

On the second layer the user can specify the simulator which can be Neuron or external.

If the user decided to use Neuron as the simulator then the model file must contain only the necessary structure and mechanisms. The model can be loaded simply after selecting the model file and the special folder where the necessary .mod files are located (optional).

As Neuron can not load it's .dlls after startup, if the special files were not found, the software must be restarted. Once the model is loaded successfully, the content of the model will be displayed, and the user can select the parameters by picking them into the list and pressing the “set” button. Removing a parameter is done in a similar fashion.

As mentioned earlier the functionality of the GUI can be extended by the usage of external files.

At this point the user can load or define a special function which carries out different tasks during the optimization.

On the next layer the settings regarding stimulation and simulation can be made. The user can select the stimulation protocol which can be either current clamp or voltage clamp (the voltage clamp is implemented as a SEClamp from Neuron). The stimulus type also can be selected, either step protocol or custom waveform. If the step protocol is selected the properties of the step can be specified. In case of multiple stimuli, only the amplitude of the stimuli can vary, no other parameter (position of stimulus, duration, delay, etc) can be changed. Via the GUI the user can specify up to ten stimuli amplitude.

The user can make use of external files here as well by selecting the custom waveform as stimulus type. After the stimulation parameters are selected, the user must choose a section and a position inside that section to stimulate the model.

In the second column the parameters regarding the simulation and the recording process can be given. The user must give an initial voltage parameter, the length of the simulation and the integration step used for calculations (variable time step methods are not supported yet). After these settings are done, the user can select the parameter to be measured (either current or voltage), the section and the position where the measurement takes place.

Stimuli & Recording Settings



Stimulation Settings

Stimulation protocol

IClamp

A

Stimulus Type

Step Protocol

B

Amplitude(s)

C

Delay (ms)

D

Duration (ms)

E

Section

soma

F

Position inside the section

0.5

G

Run Control

Initial Voltage (mV)

-65

H

tstop (ms)

1000

I

dt

0.05

J

Parameter to record

v

K

Section

soma

L

Position

0.5

M

A	Stimulation protocol (Vclamp or Iclamp).
B	Type of the stimulus (Step protocol or Custom Waveform).
C	Opens the window for specifying step amplitudes or loading custom waveform (depending on the previous options).
D	Delay of stimulus onset.
E	Duration of stimulus.
F	Section which receives stimulus.
G	Point of stimulation inside the section.
H	Initial membrane potential.
I	Length of the recording.
J	Integration step size.
K	The parameter to be recorded.
L	The section where the recordings takes place.
M	Position inside the recording section.

Layer 4

On the next layer the combination of fitness functions can be selected with the desired weights. Optimizer offers weight normalization with the press of a button, but not normalized values are acceptable as well. The user can fine tune the behavior of the functions by giving parameters to them (the value of the same parameter should be the same across the functions).

Fitness Function Selection

Fitness Functions **A**

- ☒ Average Squared Error
- ☒ Spike Count
- ☐ Averaged Squared Error
- ☐ Spike Rate
- ☐ ISI Differences
- ☐ Latency to 1st Spike
- ☐ AP Overshoot
- ☐ AHP Depth
- ☐ AP Width
- ☐ Derivative Difference
- ☐ PPTD

Weights **B**

0.5
0.5

Function Parameters **C**

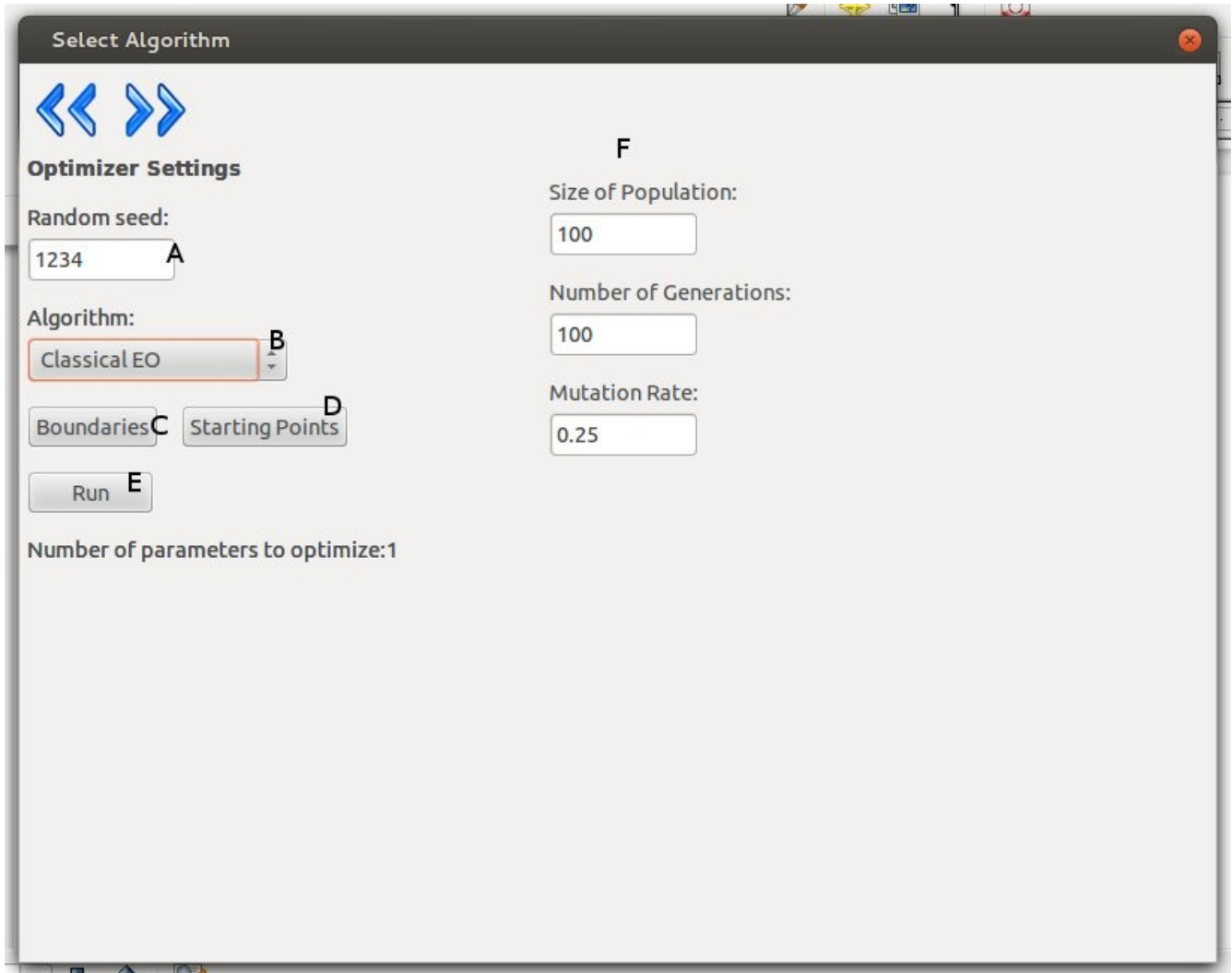
Spike Detection Thres. (mv) 0.0
Spike Detection Thres. (mv) 0.0
Spike Window (ms) 1.0

D
Normalize

A	List of available fitness function.
B	Weight assigned to the selected function.
C	Parameters passed to the fitness functions.
D	Normalizes the weights (not necessary).

Layer 5

On the next layer, the user can select the desired algorithm from the current list and tune the parameters of it. Since optimizing neuron models is a bounded optimization problem the program requires boundaries for the parameters. The user can give a set of values as starting points to the algorithm which will be interpreted differently, depending on the used algorithm. In the case of the global algorithms the given set of values will be included in the initial set of parameters. In the case of the local algorithms the algorithm will start from the point specified by the parameters.

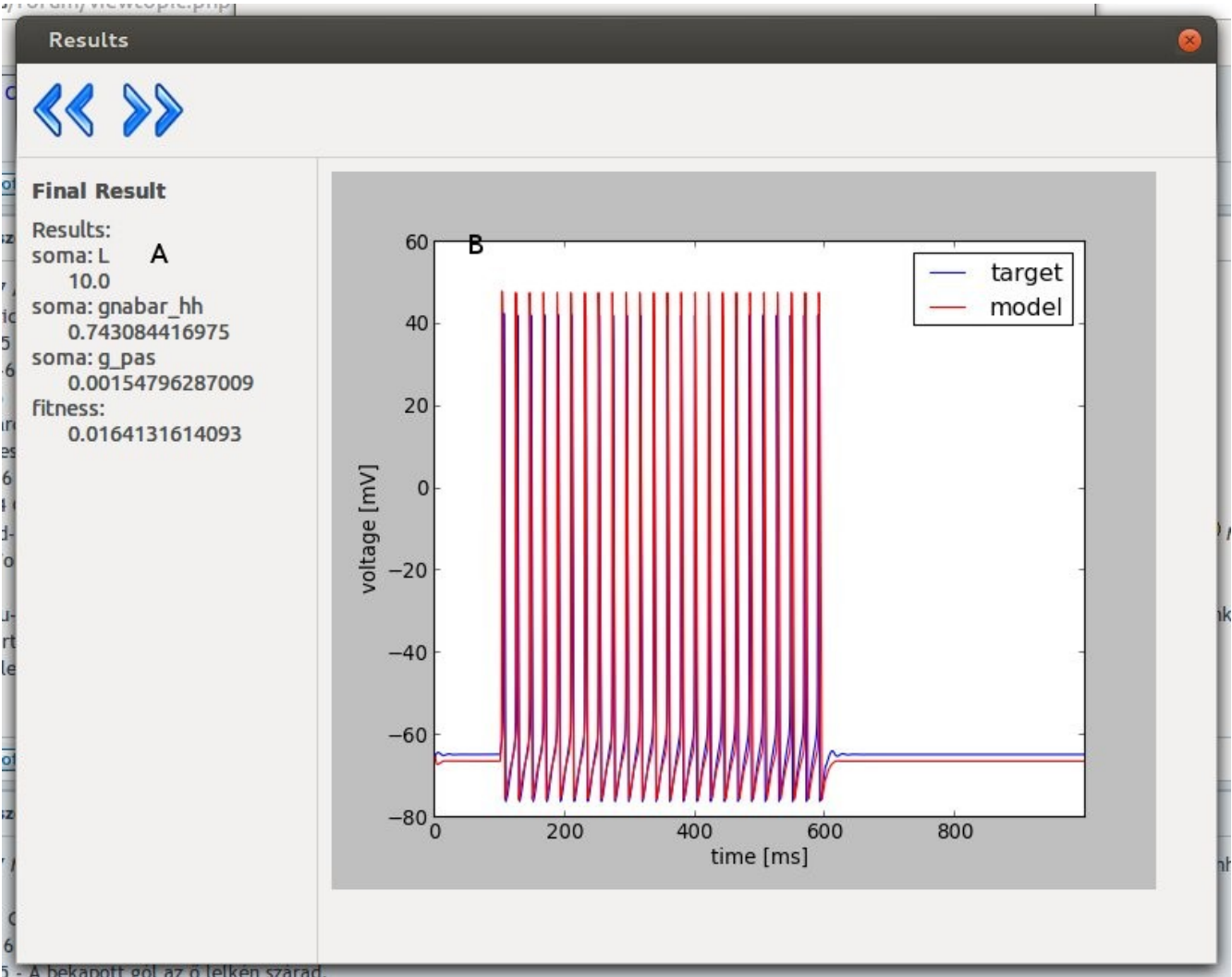


The screenshot shows a 'Select Algorithm' dialog box with the following elements:

- Navigation:** Two blue arrow icons (left and right) at the top left.
- Section Header:** 'Optimizer Settings' in bold.
- Random seed:** A text input field containing '1234', labeled with a red 'A'.
- Algorithm:** A dropdown menu showing 'Classical EO', labeled with a red 'B'.
- Buttons:** Two buttons labeled 'Boundaries' (labeled with a red 'C') and 'Starting Points' (labeled with a red 'D').
- Run Button:** A button labeled 'Run', labeled with a red 'E'.
- Parameters:** Three text input fields on the right:
 - 'Size of Population:' containing '100', labeled with a red 'F'.
 - 'Number of Generations:' containing '100'.
 - 'Mutation Rate:' containing '0.25'.
- Status:** A label at the bottom left reads 'Number of parameters to optimize:1'.

A	Seed for the random generator.
B	Selected algorithm.
C	Boundaries of the parameters subject to optimization.
D	Starting points
E	Run the optimization.
F	Depending on the selected algorithm, different settings will appear here.


Layer 6



A	The resulting parameters.
B	The trace(s) obtained with the resulting parameters.

Layer 7

Analysis



Analysis

Results: **A**

soma: gkbar_hh
0.25472535557

soma: gnabar_hh
0.805018060607

soma: el_hh
0.503315247391

fitness:
0.0172600765972

Fitness statistics **B**

Best: 0.0172600765972
Worst: 0.176114745016
Mean: 0.0244876963855
Median: 0.0173369097168
Std:0.0179892977677

Fitness Components: **C**

name	value	weight	weighted value
calc_ase	0.034	0.5	0.017
calc_spike	0.0	0.5	0.0
weighted sum: 0.017			

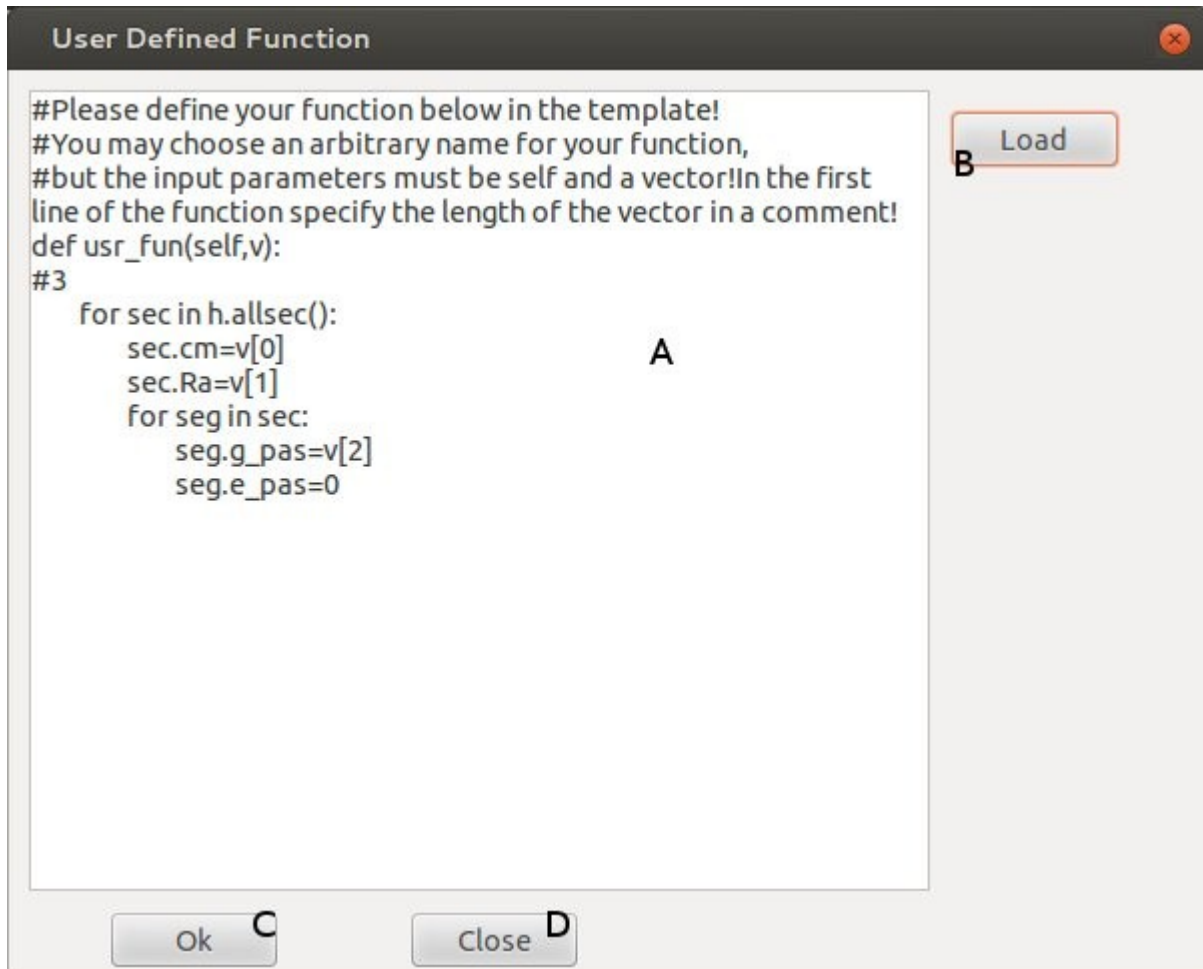
Generation Plot **D**

Allele Plot **E**

Grid Plot **F**

A	The obtained parameters.
B	Fitness statistics (only in case of inspyred algorithms: Classical EO, SA)
C	Fitness components: name of fitness function; fitness value, calculated by the function; weight assigned to the function; the weighted fitness value; the resulting cumulated fitness value.
D	Displays the “state” of the population during the evolution. (only for inspyred algorithms)
E	Displays the alleles (only for inspyred algorithms), only useful for single parameter tasks.
F	Displays the given proximity of the optimum.

Other windows and layers



A	Entry field for function definition.
B	Load a previously defined function from a txt.
C	Done editing, save function and continue.
D	Discard function and go back.

Set Amplitude(s) ✕

Number of stimuli: **A** **B**

Amplitude1 (nA): **C**

A	Number of stimuli.
B	Create the specified number of stimuli.
C	Specify the amplitude of the stimuli.

Boundaries

L	A	B	C
		10	50
	gnabar_hh	0.01	1
	g_pas	1e-06	0.01

D Set

A	The list of selected parameters.
B	Lower bounds.
C	Upper bounds.
D	Boundaries are set, continue.