Parameter confidence estimation using the Monte Carlo bootstrap algorithm

Get some confidence estimates

1.1 Introduction

The Monte Carlo plugin is used to get estimates of a models parameters confidence limits. This is in the context where experimental data exists and a parameter minimization method, such as Levenberg-Marquardt or Nelder-Mead is used first in order to find a parameter minimum.

The Monte Carlo algorithm is used subsequently at this minimum and will give an estimate of parameter confidence limits corresponding to the variance in the original experimental data.

The plugin has properties such as the size of the Monte Carlo population, minimization algorithm to use (e.g. Nelder-Mead or Levenberg-Marquardt), and on output, confidence limits for each involved parameter. Currently, the plugin saves the generated Monte Carlo data sets to a Tellurium data file named, MCDataSets.dat (in current working directory).

Plugin properties are documented in more detail in the next section.

1.2 Plugin Properties

Available properties in the Monte Carlo plugin are listed in the table below.

Property Name	Data Type	Default Value	Description
SBML	string	N/A	SBML document as a string. Model to be used by the Monte Carlo plugin.
ExperimentalData	telluriumData	N/A	Input data.
InputParameterList	listOfProperties	N/A	Parameters to estimate confidence limits for.
MonteCarloParameters	listOfProperties	N/A	Parameters obtained from a Monte Carlo session.
ConfidenceLimits	listOfProperties	N/A	Confidence limits for each fitted parameter. The confidence limits are calculated at a 95% confidence level.
Experimental-DataSelectionList	stringList	N/A	Selection list for experimental data.
FittedDataSelectionList	stringList	N/A	Selection list for model data.
NrOfMCRuns	int	N/A	Number of Monte Carlo Data Sets
MinimizerPlugin	string	N/A	Minimizer used by the Monte Carlo Engine, e.g. "levenberg_marquardt".

Table 1.1: Plugin Properties

1.3 The `execute(bool inThread)` function

The `execute()` function will start the Monte Carlo algorithm. Depending on the problem at hand, the algorithm may run for a long time.

The `execute(bool inThread)`, do support a boolean argument indicating if the execution of the plugin work will be done in a thread, or not. Threading is fully implemented in the Monte Carlo plugin.

The inThread argument defaults to **false**.

1.4 Plugin Events

The Monte Carlo plugin are using all of a plugins available plugin events, i.e. the *PluginStarted*, *PluginProgress* and the *PluginFinished* events.

The available data variables for each event are internally treated as *pass trough* variables, so any data, for any of the events, assigned prior to the plugins execute function (in the assingOn() family of functions), can be retrieved unmodified in the corresponding event function.

Event	Arguments	Purpose and argument types
PluginStarted	void*, void*	Signal to application that the plugin has started. Both parameters are *pass trough* parameters and are unused internally by the plugin.
PluginProgress	void*, void*	Communicating progress of fitting. Both parameters are *pass trough* parameters and are unused internally by the plugin.
PluginFinished	void*, void*	Signals to application that execution of the plugin has finished. Both parameters are *pass trough* parameters and are unused internally by the plugin.

Table 1.2: Plugin Events

1.5 Python example

The following Python script illustrate how the plugin can be used.

```python
from telplugins import *
import matplotlib.pyplot as plt

try:
    #Load plugins
    modelP      = Plugin("tel_test_model")
    nP          = Plugin("tel_add_noise")
    chiP        = Plugin("tel_chisquare")
    lmP         = Plugin("tel_levenberg_marquardt")
    nmP         = Plugin("tel_nelder_mead")
    mcP         = Plugin("tel_monte_carlo_bs")

    #========== EVENT FUNCTION SETUP ===========================
    def myEventFunction(ignore):
        # Get the fitted and residual data
        experimentalData    = lmP.getProperty ("ExperimentalData").toNumpy
        fittedData          = lmP.getProperty ("FittedData").toNumpy
        residuals           = lmP.getProperty ("Residuals").toNumpy

        telplugins.plot(fittedData         [:,[0,1]], "blue", "-",    "",
              "S1 Fitted")
        telplugins.plot(fittedData         [:,[0,2]], "blue", "-",    "",
              "S2 Fitted")
        telplugins.plot(residuals          [:,[0,1]], "blue", "None", "x",
             "S1 Residual")
        telplugins.plot(residuals          [:,[0,2]], "red",  "None", "x",
             "S2 Residual")
        telplugins.plot(experimentalData   [:,[0,1]], "red",  "",     "*",
             "S1 Data")
        telplugins.plot(experimentalData   [:,[0,2]], "blue", "",     "*",
             "S2 Data")

        print 'Minimization finished. \n==== Result ===='
        print getPluginResult(lmP.plugin)
        telplugins.plt.show()

    #Communicating event
    myEvent =  NotifyEventEx(myEventFunction)

    #Uncomment the event assignment below to plot each monte carlo data set
    #assignOnFinishedEvent(lmP.plugin, myEvent, None)

    #This will create test data with noise. We will use that as '
        experimental' data
    modelP.execute()

    #Setup Monte Carlo properties.
    mcP.SBML                                 = modelP.Model
    mcP.ExperimentalData                     = modelP.TestDataWithNoise

    #Select what minimization plugin to use
    #mcP.MinimizerPlugin                       = "Nelder-Mead"
    mcP.MinimizerPlugin                      = "Levenberg-Marquardt"
    mcP.NrOfMCRuns                           = 1000
    mcP.InputParameterList                   = ["k1", 1.5]
```

```
    mcP.FittedDataSelectionList          = "[S1] [S2]"
    mcP.ExperimentalDataSelectionList    = "[S1] [S2]"

    # Start Monte Carlo
    mcP.execute()

    print 'Monte Carlo Finished. \n==== Result ===='
    print mcP.MonteCarloParameters.getColumnHeaders()
    paras = mcP.MonteCarloParameters.toNumpy
    print paras

    #Get mean (assuming normal distribution).
    print "The mean: k1= " + `np.mean(paras)`


    PropertyOfTypeListHandle = getPluginProperty(mcP.plugin, "
       ConfidenceLimits")
    print `getNamesFromPropertyList(PropertyOfTypeListHandle)`
    aProperty = getFirstProperty(PropertyOfTypeListHandle)
    if aProperty:
        print getPropertyValueAsString(aProperty)

    #Show MOnte Carlo parameters as a histogram
    plt.hist(paras, 50, normed=True)
    plt.show()

    #Plot Monte Carlo data sets
    #dataSeries =  DataSeries.readDataSeries("MCDataSets.dat")
    #dataSeries.plot()

    #Finally, view the manual and version
    mcP.viewManual()
    print 'Plugin version: ' + `mcP.getVersion()`


except Exception as e:
    print 'Problem.. ' + `e`
```

Listing 1.1: Monte Carlo plugin example.

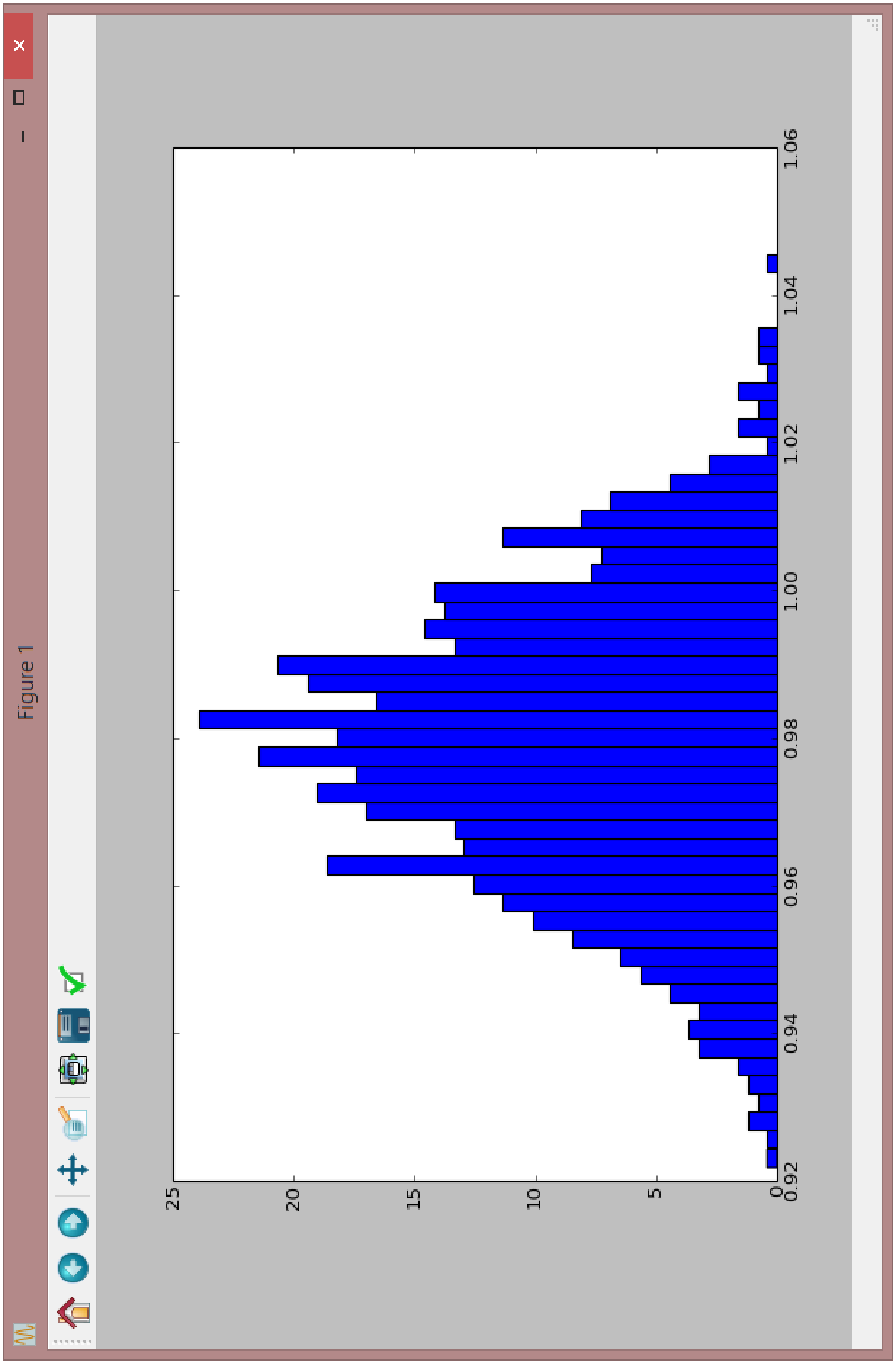

Figure 1.1: Output for the example script above, using 1000 Monte Carlo runs. The histogram shows the distribution for the model parameter, 'k1'. The mean for the distribution was 0.980 and obtained confidence limits were +/- 0.001.