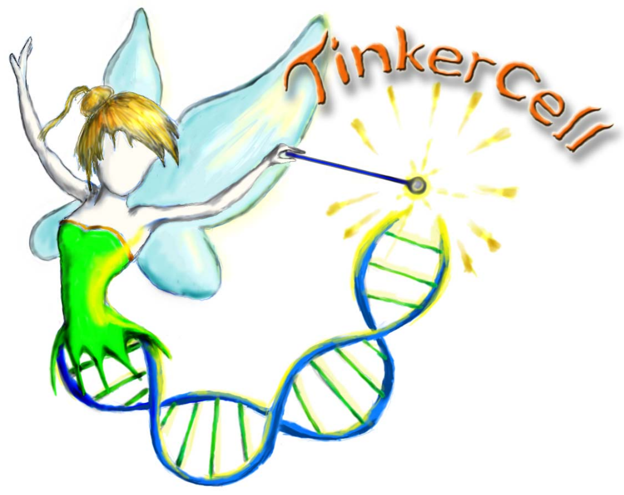

How to add Your Plug-in

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Introduction

The TinkerCell application is a graphical user interface that serves as a "host" to third-party programs written in the C programming language or other C-based languages such as Python, Perl, Ruby, and R. Currently, Python, Octave, and Ruby have been integrated, although only Python is fully tested in all major platforms. R and Perl have not been integrated at this point.

TinkerCell plug-ins and module files are stored in tinkercellextra.sf.net. Plug-ins from this repository are automatically made available to users when they start TinkerCell, so it is a convenient way to make a new program available to all TinkerCell users. The plug-in will automatically appear as a button inside TinkerCell. The author of the plug-in can update the code at any point in time; users will automatically get the updates.

The TinkerCell API uses C data structures (described here). For this reason, the functions do not return Python or Octave data structures. However, functions named "toTC" and "fromTC" are made available for converting between C data structures and the languages' data structures (see example code at the end of this document).

All TinkerCell functions begin with "tc_", e.g. tc_insert. For Ruby, the scripts would also need the module name in front, e.g. Tinkercell.tc_insert. In Python, this is not necessary if you use the import statement: from tinkercell import *

Submitting to the Repository

To submit a plug-in or module (model), you need: (1) a Sourceforge account and (2) install Subversion on your computer. Then contact someone who has access to tinkercellextra.sf.net so that you can be added to this group. Once you are part of the group, there are two ways to submit new plugins to the TinkerCell repository. Option 1 is to write the code inside TinkerCell and click the "save" button, which will ask you for the username and password for the Sourceforge account. Option 2 is described below:

Use the following command to download the existing plug-ins (for Windows, it might be easier using TortoiseSVN. See this video):

```
svn checkout https://tinkercellextra.svn.sourceforge.net/svnroot/tinkercellextra TinkerCellPlugins
```

The TinkerCellPlugins directory will be created with all the existing plug-ins and module files. Go into the folder. If you want to add a new Python plug-in, go into the "python" folder and add the new plug-in file there. If you want to add octave plug-in, add the file into the "octave" folder. For C plug-ins, you must also select the right folder for your operating system. After adding the new file, use the following commands to add and upload the new file to the repository:

```
svn add MyNewPluginFile
svn commit
```

Replace "MyNewPluginFile" with the name of your plug-in file. You must be inside the directory when executing these commands. Do the above two commands for each file you want to add to the repository. You can modify your code later and submit the modified code by doing:

```
svn commit
```

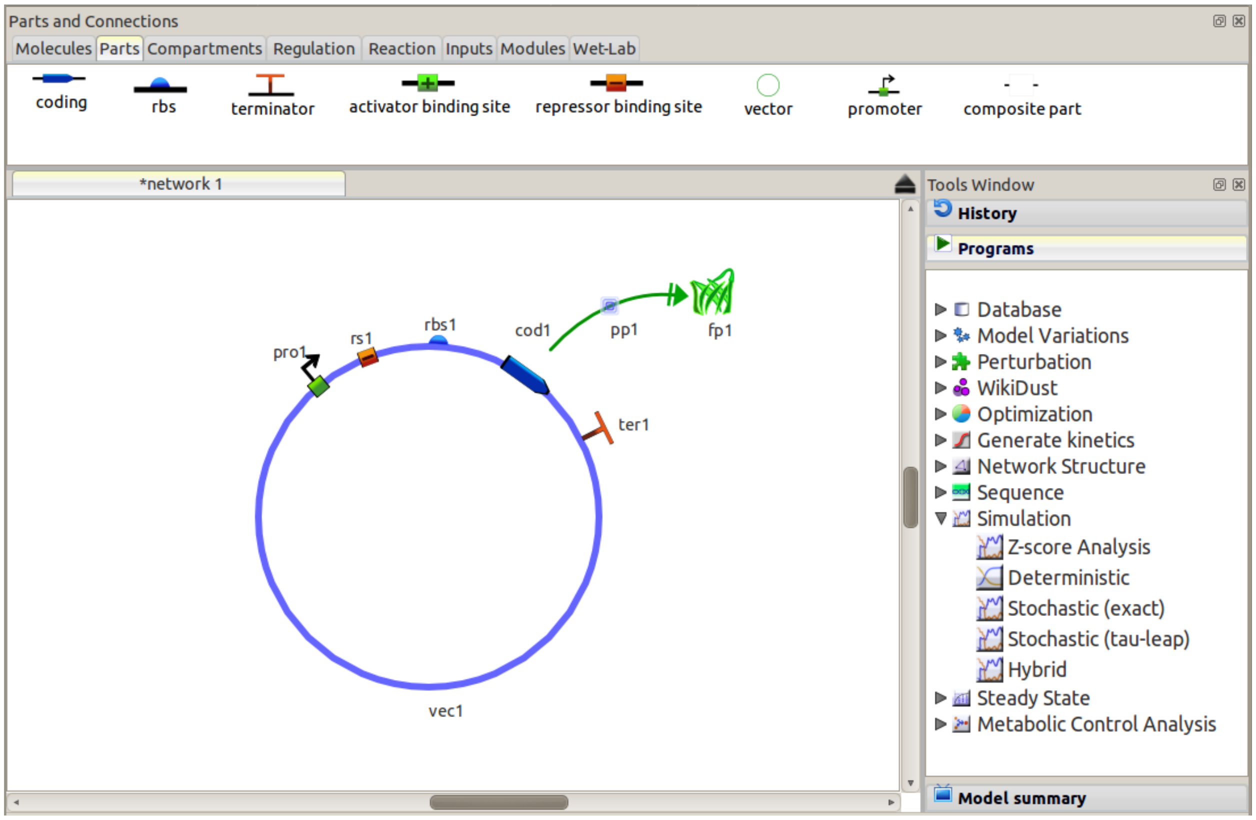
And you can use the following command to get all the updates from other plug-ins:

```
svn update
```

Note that all the above commands must be made inside the TinkerCellPlugins folder (or whatever folder name you are using). If you need to know more details, read about Subversion.

How do users get the plug-ins

TinkerCell simply performs an "svn update" on the <Documents>/TinkerCell folder every time TinkerCell starts. This will download all the new and updated plug-ins from the Sourceforge repository. To the users, this process is transparent. Then TinkerCell makes the plug-ins available inside the programs' menu on the right-hand side in the screenshot below.



How TinkerCell loads C programs

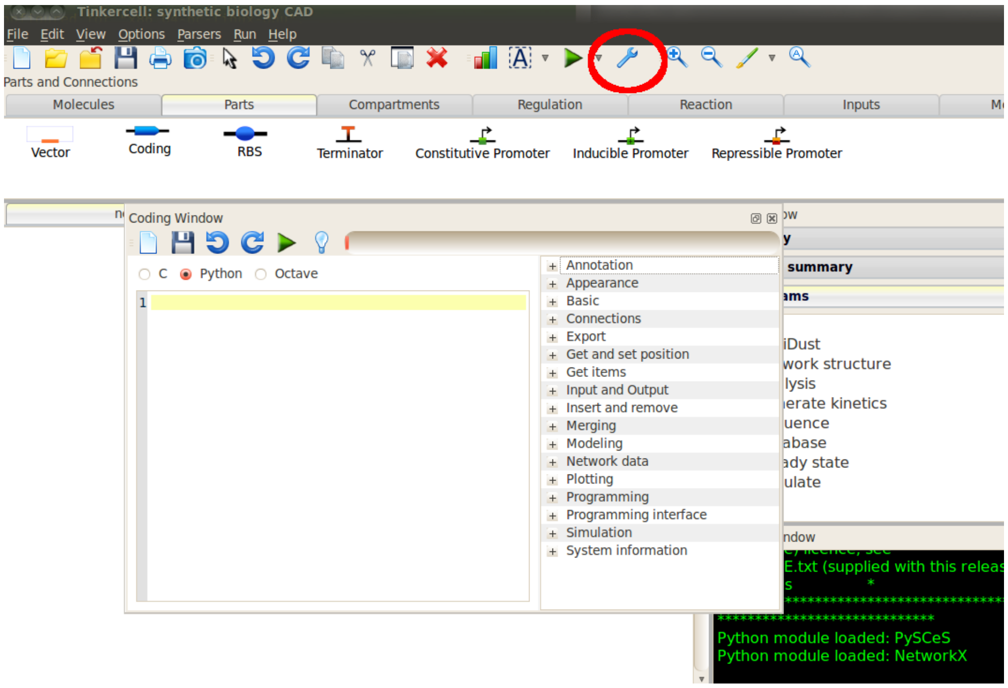
All C programs that are loaded into TinkerCell must be dynamic libraries. The dynamic libraries must be placed in the Plugins/c of the TinkerCell directory. TinkerCell will look for the void tc_main() function in the library and call that function.

void tc_main() is the main entry point. If it is not defined, nothing will happen when the library is loaded, unless the library has an accompanying C++ plug-in that is already loaded into TinkerCell. For example, the flux balance analysis plug-in in TinkerCell is a combination of a C++ plug-in, which provides the graphical user interface, and a C library, which provides the linear optimization function. The graphical interface knows which functions exist in the C library and calls those functions specifically; therefore tc_main does not have to be defined in such cases.

Available C functions

The C application programmer interface (API) is located at: http://tinkercell.sourceforge.net/CAPI/index.html

Another resource for studying is the API is to run TinkerCell and open the "Coding Window" (image shown to the right). The Coding Window contains a list of all the functions available in the C API, organized by categories. Double-clicking on one of the functions will place an example call to the function on the text editor.



C [✓ Python] Octave

```
E.txt (supplied with this releas
s                    *
**************************************
Python module loaded: PySCeS
Python module loaded: NetworkX
```

Integrating C programs in TinkerCell

Suppose we are interested in integrating the following trivial function into TinkerCell:

```
double function(double a, double b)
{
    return (a + b);
}
```

There are four options for integrating the function into the user interface:

1. The user will drag and drop the file into TinkerCell. TinkerCell will run the function and the unload the library. It will not remain loaded in TinkerCell.
2. The function will appear as a button in TinkerCell. The library will remain loaded until TinkerCell exists.
3. The library uses callback functions to interact with TinkerCell, i.e. no buttons are available for the user to click. The library will remain loaded until TinkerCell exists.
4. The library has an accompanying C++ plug-in in TinkerCell. The C++ plug-in manages all the calls to the C library.

Most of these options can be used in combination as well. For example, a library can have callback functions as well as buttons for user interaction.

Option 1: drag and drop

When a C dynamic library file is dropped on the TinkerCell main window, TinkerCell will look for "void tc_main()" and call that function. So, in this case, the C code would be as follows:

```
#include "TC_API.h"

double function(double a, double b)
{
    return (a + b);
}

TCAPIEXPORT void tc_main()
{
    double d, x=10.0, y = 5.0;
    char c[100];
    sprintf(c,"answer = %lf\0", function(x,y));
    tc_print(c);
}
```

Compile the above code as a shared (dynamic) library (wikipedia has a nice article on shared libraries if needed). Be sure to list the Tinkercell/API directory in your set of include directories when compiling. That is where TC_api.h is located. TC_api.h includes all the other header files form the API folder, so all the other header files are also necessary.

Option 2: button and menu item

Use the tc_addFunction(&f, "name of function", "short description", "category", "icon file", "restrictions", int, int, int);

The "restrictions" argument can be used so that this function only shows up when items of that family are selected. For example, if "promoter" is used for the "restrictions" argument, then this function will only appear when promoter nodes are selected.

The last three arguments are either 1 or 0 for answering the following:
insert button in functions list? insert button in menu? make this the primary function?

See runcvode.c for example. Look at the tc_main function.

Option 3: callback functions

Use tc_callback(void (*f)(void)) to assign a function as the callback function. The function f will get called whenever the model is altered, i.e. when items are inserted, deleted, renamed, or when data within items are changed.
...more documentation to come...

Option 4: interfacing via a C++ plug-in

This is primarily done using a C++ class that inherits from AbstractInputWindow class, one of the TinkerCellCore classes. AbstractInputWindow can provides interface for loading a library and connecting signals to functions in that library. The C++ class would setup its widgets so that the buttons or other interfaces in the widgets trigger functions in the library. All calls will be done using a CThread (i.e. multi-threaded). See the OtherTools/LPSolveInput.cpp for a simple example of a C/C++ combined plug-in.

Available Python functions

The set of Python functions is the same as the set of C functions, which is located at: http://tinkercell.sourceforge.net/CAPI/index.html

Using the "Coding Window" (same image shown previously) is another good option for learning all the available functions and testing a new script. The Coding Window contains a list of all the functions available in the Python API. Double-clicking on one of the functions will place an example call to the function on the text editor.The pressing the "Play" button on top of the editor will run the script.

Two important functions are fromTC and toTC. These functions are used to convert from and to TinkerCell data types. For example:

```
a = tc_allItems()
m = tc_getStoichiometry(a)
M = fromTC(m)  #get python 2D list
```

Integrating Python scripts

Integrating a Python code requires two things:
1. adding TinkerCell header on top of the Python script
2. copying the .py file inside <Documents>**/TinkerCell/python** folder or <TinkerCell installed directory>**/python** folder

The TinkerCell header looks like this:

```
"""
category: category for the new python script
name: name of the python function
description: description of python function
icon: location of icon relative to <TinkerCell installed directory>
menu: yes or no, indicating whether or not to place the function in the functions menu
specific for: optional entry to indicate whether this function is specific for a type of objects
tool: yes or no indicating whether or not a tool button should appear when the specific objects are selected
"""
```

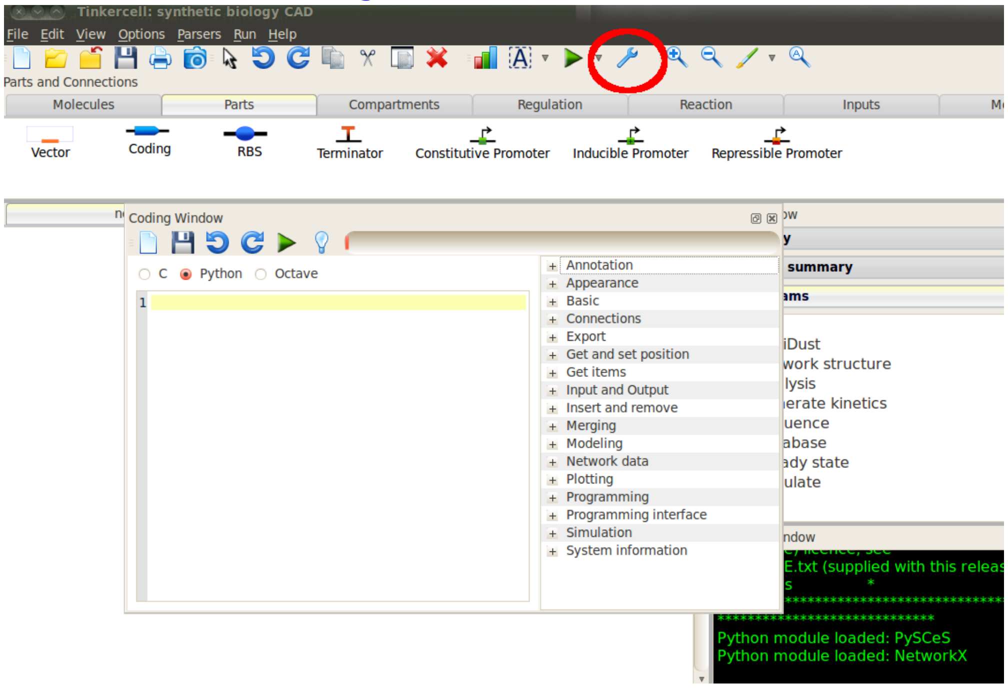
Here is an example from the hillEquations.py script, which is a function that specifically works on "CDS" type objects.

```
"""
category: Generate kinetics
```

```
name: Hill equations
description: automatically generate the equilibrium rate equation for
transcript
ion
icon: plugins/c/hillequation.png
menu: yes
specific for: CDS
tool: yes
"""
```

Available Octave functions

The set of Octave functions is the same as the set of C functions, which is located at: http://tinkercell.sourceforge.net/CAPI/index.html



```
E.txt (supplied with this releas
s                *
*****************************
*****************************
Python module loaded: PySCeS
Python module loaded: NetworkX
```

Using the "Coding Window" (image shown to the right) is another good option for learning all the available functions and testing a new script. The Coding Window contains a list of all the functions available in the Octave API. Double-clicking on one of the functions will place an example call to the function on the text editor.

Pressing the "Play" button on top of the editor will run the script.

Integrating Octave script

Integrating Octave code requires two things:
1. adding TinkerCell header on top of the Octave script
2. copying the **.m** file inside <Documents>**/TinkerCell/octave** folder or <TinkerCell installed directory>**/octave** folder

The TinkerCell header looks like this:

```
%category: category for the new python script
%name: name of the python function
%description: description of python function
%icon: location of icon relative to <TinkerCell installed directory>
%menu: yes or no, indicating whether or not to place the function in the functions menu
%specific for: optional entry to indicate whether this function is specific for a type of objects
%tool: yes or no indicating whether or not a tool button should appear when the specific objects are selected
```

An important function is fromTC , which is used to convert from TinkerCell data types. For MS Windows, fromTC will only work on tc_matrix.

Available Ruby functions

The set of Ruby functions is the same as the set of C functions, which is located at: http://tinkercell.sourceforge.net/CAPI/index.html

Integrating Ruby script

Integrating Ruby code requires two things:
1. adding TinkerCell header on top of the Ruby script file
2. copying the **.rb** file inside <Documents>**/TinkerCell/ruby** folder or <TinkerCell installed directory>**/ruby** folder

Ruby integration works the same way as Octave and Python integration mentioned above

Example Code

Perturb all RBS's in the model (using *python)*

```
from tinkercell import *

#get all RBS parts
rbs_parts_c = tc_itemsOfFamily("RBS")
rbs_names_c = tc_getUniqueNames(rbs_parts_c)

#get just RBS related parameters
rbs_params = tc_getParameters(rbs_parts_c)
```

```
#rbs perturbation
for n in range(0, rbs_params.rows):
    tc_showProgress("mRNA Perturbation", int(100 * n /
rbs_params.rows))
    x = tc_getMatrixValue( rbs_params , n , 0)
    tc_setMatrixValue(rbs_params, n, 0, 0.2 * x)
    tc_updateParameters(rbs_params) #temporary update (faster
than setParameters)
    sim = tc_simulateDeterministic(0,500,500)
    s = ""
    for j in range(0, sim.cols):
        col = str(tc_getColumnName(sim, j))
        if (j == 0):
            s += col
        else:
            p = tc_find(col)
            if tc_isA(p, "mRNA") == 1:   #only output mRNA data
                s += "\t" + str(tc_getColumnName(sim, j))
    s += "\n"
    for i in range(0,sim.rows):
        for j in range(0, sim.cols):
            col = str(tc_getColumnName(sim, j))
            if (j == 0):
                s += str(tc_getMatrixValue(sim, i, j))
            else:
                p = tc_find(col)
                if tc_isA(p, "mRNA") == 1:   #only output mRNA data
                    s += "\t" + str(tc_getMatrixValue(sim, i, j))
        s += "\n"
    filename = str(tc_getRowName(rbs_params, n)) +
"_5x_down.tab"
    FILE = open(filename,"w")
    FILE.write(s)
    FILE.close()
    tc_setMatrixValue(rbs_params, n, 0, x)
```

```
tc_showProgress("mRNA Perturbation", int(100))
#open files
for n in range(0, rbs_params.rows):
    filename = str(tc_getRowName(rbs_params, n)) +
"_5x_down.tab"
    tc_openUrl(filename)
```

Testing for non-monotonic input/output response (using *Octave*)

```
target = [0 0.3 1 0.3 0]';
inputs = [0 0.1 0.3 0.5 1]';
outputs = zeros(5,1);
ic = tinkercell.tc_getInitialValues(tinkercell.tc_allItems());
k = tinkercell.tc_getRowIndex(ic, "INPUT");
for i = 1:5
    x = inputs(i);
    tinkercell.tc_setMatrixValue(ic, k, 0, x);
    tinkercell.tc_updateParameters(ic);
    ss = tinkercell.tc_getSteadyState();
    j = tinkercell.tc_getRowIndex(ss, "OUTPUT");
    if (j > -1)
        outputs(i) = tinkercell.tc_getMatrixValue(ss, j, 0);
    end
end
m = [ inputs outputs ];
m2 = toTC(m);
tinkercell.tc_plot(m2, "input-output");
score = corrcoef( target, outputs )
```

Optimize for non-monotonic input/output response (using *python*)

```
from tinkercell import *
from tc2py import *
from numpy import *
from PSO import *  #particle swarm optimization (included with
TinkerCell)

nameOfInput ="INPUT" #name of input variable in the model
nameOfOutput ="OUTPUT" #name of output variable in the model

params = tc_createMatrix(1,1)
tc_setRowName(params,0,nameOfInput)
def Objective():
    tc_setMatrixValue(params, 0, 0, 0.1)
    tc_updateParameters(params)
    ss = tc_getSteadyState()
    i = tc_getRowIndex(ss, nameOfOutput)
    x1 = tc_getMatrixValue(ss, i, 0)
    tc_setMatrixValue(params, 0, 0, 2)
    tc_updateParameters(params)
    ss = tc_getSteadyState()
    x2 = tc_getMatrixValue(ss, i, 0)
    tc_setMatrixValue(params, 0, 0, 5)
    tc_updateParameters(params)
    ss = tc_getSteadyState()
    x3 = tc_getMatrixValue(ss, i, 0)
    if x3 > x1: x1 = x3
    return (x2 - x1)

optimizer = ParticleSwarm()
#minimize or maximize?
```

```
optimizer.numpoints = 50
optimizer.maxiter = 10
optimizer.minimize = False
optimizer.title = "Nonmonotic test"
g = optimizer.run(Objective,10)
```

Create input dialogs for calling custom functions (using *python)*

```
from tinkercell import *

#callback function
def myFunc(w,h,output):
print "width = " + str(w) + " height = " + str(h) + " output = " +
output

#create the input window with 3 rows and 1 column
inputWindow = tc_createMatrix( 3, 1 )
tc_setMatrixValue(inputWindow, 0, 0, 0)
tc_setMatrixValue(inputWindow, 1, 0, 0.0)
tc_setMatrixValue(inputWindow, 2, 0, 0.0)

#given row names to display
tc_setRowName(inputWindow, 0, "Width")
tc_setRowName(inputWindow, 1, "Height")
tc_setRowName(inputWindow, 2, "Output")
tc_createInputWindowForScript(inputWindow, "Screenshot",
"myFunc")

#make the last row a set of options
list = ["Wiki code","HTML code"]
tc_addInputWindowOptions("Screenshot", 2, 0, toTC(list))
```

Here is the screenshot. When the user clicks the ok button, the callback function is called with the arguments 55, 12, "Wiki code"

Perturb all parameters with a specific prefix (using *python*)

```
# we are just going to change all the parameters that begin with the phrase 'synthconst'

items = tc_allItems()
params = tc_getParameters(items)

p = ""   #parameter name

#just count how many there are

total = 0
for i in range(0,params.rows):
    p = tc_getRowName(params, i)
    if p.count('synthconst') > 0:
    total += 1

#for each parameter
j = 0
for i in range(0,params.rows):
    p = tc_getRowName(params, i)
    if p.count('synthconst') > 0:   #check parameter name
```

```
        tc_showProgress("steady state perturbation", int((100.0 * j)/
total))  #progress meter
        j += 1
        #perturb
        s = ""
        FILE = open(p + '.perturb.txt','w+')  #save to file
        p0 = tc_getMatrixValue(params, i, 0)  #original parameter
value
        for q in [100, 10, 2, 1]:        #perturbations
            tc_setMatrixValue(params, i, 0, p0/q)
            tc_setParameters(params,0)
            m = tc_getSteadyState() #steady state
            s += str(p0/q)
            for i in range(0,m.rows):  #for each output value
                if tc_getRowName(m,i).count('m') > 0: #if name starts
with m
                    s += "\t"
                    s += str(tc_getMatrixValue(m, i, 0))
                    s += "\n"
            FILE.write(s)
            FILE.close()
#done
tc_showProgress("steady state automation", 100)  #close
progress meter
```

Set global parameters (using *python* or *octave*)

```
#for octave add tinkercell. in front of all the tc_ commands
p = tc_find("_")  #get global item
tc_setParameter(p,"k1" ,0.00022)
tc_setParameter(p,"k2" ,0.19)
tc_setParameter(p,"k3" , 0.2)
tc_setParameter(p,"k4" , 0)
tc_setParameter(p,"k5" , 0.0015)
tc_setParameter(p,"k6" , 0.2)
tc_setParameter(p,"k7" , 0.005)
tc_setParameter(p,"k8" , 0.0001)
tc_setParameter(p,"k9" , 0.005)
tc_setParameter(p,"k10" , 0.0001)
tc_setParameter(p,"k11" , 2e-06)
tc_setParameter(p,"k12" , 0.05)
tc_setParameter(p,"k13" , 4.5e-06)
tc_setParameter(p,"k14" , 4e-05)
tc_setParameter(p,"k11n" , 0.0005)
tc_setParameter(p,"k13n" , 5e-05)
tc_setParameter(p,"kk" , 5000)
tc_setParameter(p,"ks" , 833)
tc_setParameter(p,"n" , 2)
tc_setParameter(p,"p" , 5)
```