# Instruction of Dynamic Sensitivity Simulator

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# 1. Implementation of the DS simulator

* Download "DSsimulator.zip" and add the path on MATLAB.

* Install the following software.

1. libSBML

- ✓ Download “libSBML-5.10.0-win-matlab-fbc-x64.exe” from:
  http://sbml.org/Software/libSBML
- ✓ Execute “libSBML-5.10.0-win-matlab-fbc-x64.exe”.

2. SBMLToolbox

- ✓ Download “SBMLToolbox-4.1.0.zip” from:
  http://sbml.org/Software/SBMLToolbox
- ✓ Execute SBMLToolbox/toolbox/install.m on MATLAB.

3. SBToolbox2

- ✓ Download “SBPOP_PACKAGE_Rev_1278.zip” from:
  http://www.sbtoolbox2.org/main.php
- ✓ Execute SBPOP PACKAGE/ installSBPOPpackageInitial.m on MATLAB.
- ✓ Install a third-party C++ compiler from:
  http://www.mathworks.co.jp/support/compilers/R2014a/index.html

## 1.1 GUI

(1) Type "DSGUI" on the command window of MATLAB, the following window (Fig 1) appears.

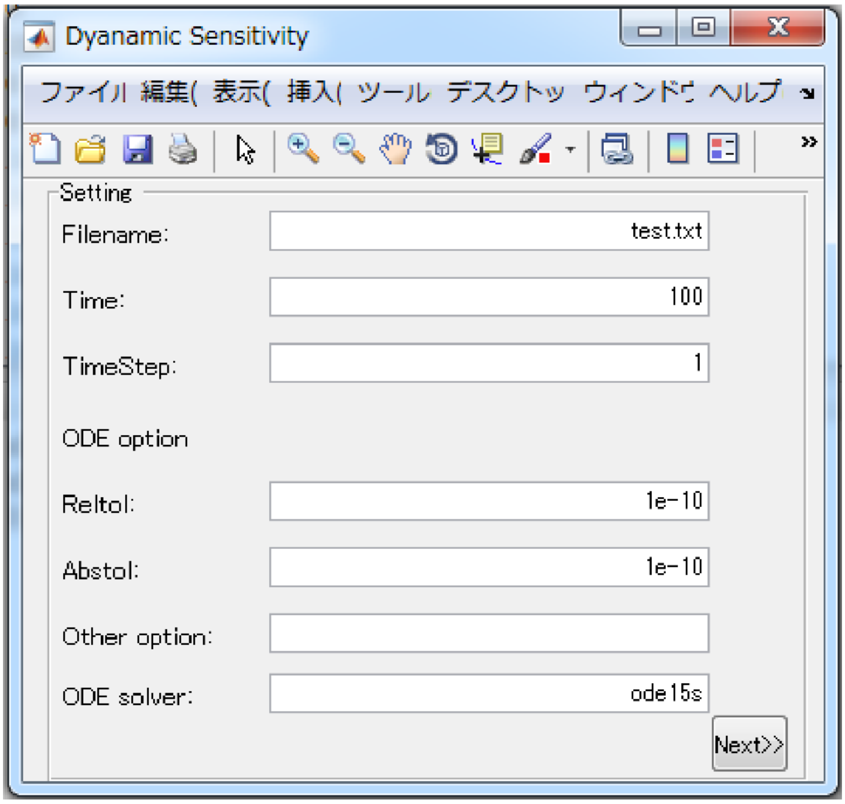



Fig 1: Setting window for simulation

Filename … a text file (".txt") or a SBML file (".xml")

Time … simulation time

TimeStep … time course from 0(s) to final time

Reltol, Abstol … relative and absolute tolerance

Other option … the other demanded options for ODE solver

ODE solver … ode15s, ode45, ode23, etc.

(2) Push the “Next>>” button, the following window (Fig 2) appears.

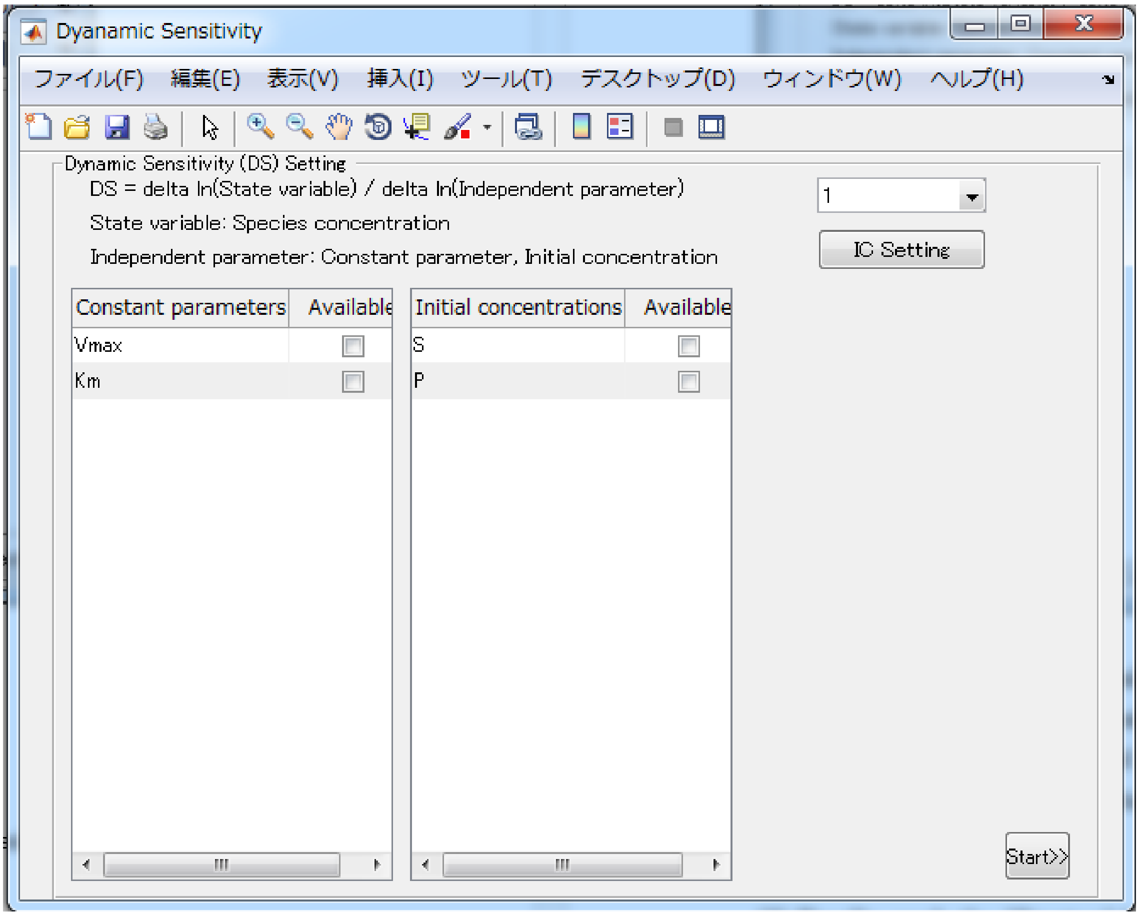


Fig 2: Dynamic sensitivity (DS) setting

Constant parameters … DS is calculated for the specified constant parameters

Initial concentrations … DS is calculated for the specified initial concentrations

IC Setting … DS is calculated under some initial conditions.

(3) Finally, push the “Start>>” button, the simulator starts calculating the DS for the identified file.

## 1.2 Character User Interface (CUI)

Output = DSsensitivity (Input)

This function calculates the DS from mathematical model (".txt" or ".xml").

% [data] = DSsensitivity (filename, timevector)

% [data] = DSsensitivity (filename, timevector, options)

% [data] = DSsensitivity (filename, timevector, options, ode)

% [data] = DSsensitivity (filename, timevector, options, ode, species)

% [data] = DSsensitivity (filename, timevector, options, ode, species, parameters)

% [data] = DSsensitivity (filename, timevector, options, ode, species, parameters, independents)

% [data] = DSsensitivity (filename, timevector, options, ode, species, parameters, independents, initial)

% [data] = DSsensitivity (filename, timevector, options, ode, species, parameters, independents, initial, InH1, InH2, InH3)

% [data] = DSsensitivity (filename, timevector, options, ode, species, parameters, independents, initial, bebug)

**filename**: The file is used by SBMLmodel and SBmodel in the SBTOOLBOX2.

**timevector**: When the simulation time is set to 100, set timevector = 100 or [0:100].

**options**: ODE options

**ode**: ODE solver

**species**: the initial parameters to be perturbed for DS calculation. When the DS is calculated with respect to an initial value of E, set species = {'E'};

**parameters**: the kinetic parameters to be perturbed. When the DSs are calculated for all the parameters, use { }.

**independent**: the independent parameters to be perturbed.

**initial**: the initial values of species. Multiple sets of the initial values are used.

For example,

initial(1).name = 'E'; initial(1).value1 = 1; initial(1).value2 = 2;

initial(2).name = 'S'; initial(2).value1 = 10.3; intial(2).value2 = 92.4;

**InH1**: Inhibitor concentration (InH1:ERK inihibitor)

**InH2**: Inhibitor concentration (InH1:Akt inihibitor)

**InH3**: Inhibitor concentration (InH1:ErbB inihibitor)

*These function can be used for MCF7.txt only.

**debug**: At debug=1, model information is saved.

# 2. The specification of a text file

A text and SBML file are used for describing a mathematical model.
Fig 3 is an example of a mathematical model described on a text file.

## 2.1.1 Model name

The model name is identified from "********** MODEL NAME" to the next identifier line.

Ex)

********** MODEL NAME

Test model

## 2.1.2 Model notes

The model notes (explanation) are identified from the "********** MODEL NOTES" line to the next identifier line.

Ex)

********** MODEL NOTES

It is an explanation of the model.

## 2.1.3 Model states

The ODEs and the initial value are described as follows. d/dt(X) is the ODE and X is the time-dependent variable. X(0) is the initial value. The Model states are identified from "********** MODEL STATES" to the next identifier line.

Ex)

********** MODEL STATES

d/dt(A) = -R % comment

d/dt(B) = +R

A(0) = 0

B(0) = 0

## 2.1.4 Model parameters

The values of the parameters are set. The DSs are calculated for the parameters listed on the model parameters. The model parameters are identified from "********** MODEL PARAMETERS" to the next identifier line.

Ex)

```
********** MODEL PARAMETERS
k1 = 0.1
k2 = 1
k3 = 0
k4 = 0
k5 = 0
```

## 2.1.5 Model variables

The model variables are identified from "********** MODEL VARIABLES" to the next identifier line.

Ex)

```
********** MODEL VARIABLES
v1 = k1+3
```

## 2.1.6 Model reactions

The model reactions are identified from "********** MODEL REACTIONS" to the next identifier line.

Ex)

```
********** MODEL REACTIONS
R = (k1+k2+k3+k4+k5)*A    %comment
```

## 2.1.7 Model functions

The model functions are identified from "********** MODEL FUNCTIONS" to the next identifier line.

Ex)

```
********** MODEL FUNCTIONS
f(x,y) = x+y
```

## 2.1.8 Model events

The model events are identified from “********** MODEL EVENTS” to the next identifier line. The MATLAB functions, lt and gt, can be used.

Ex)

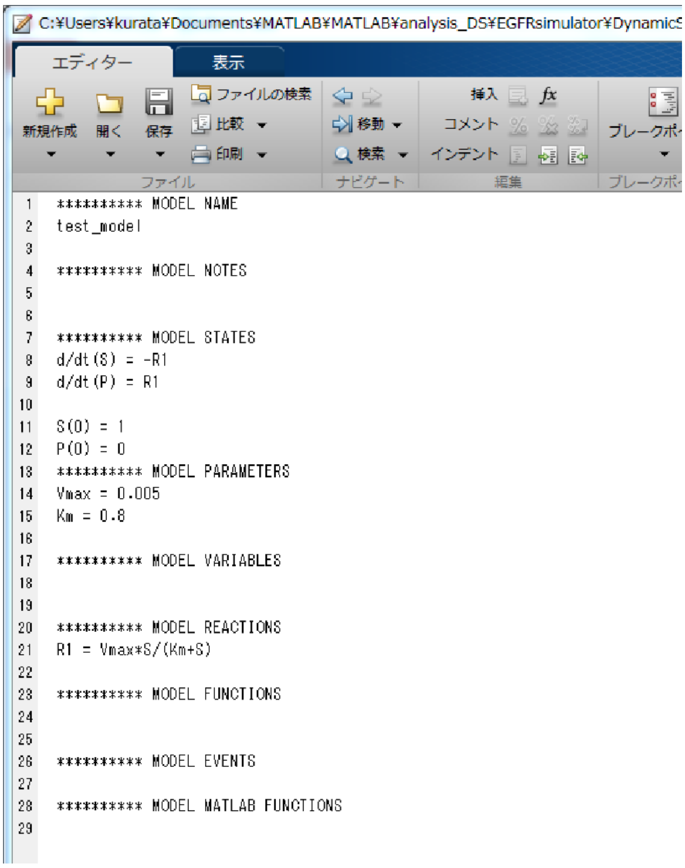
********** MODEL EVENTS

event = lt(A,0.3), A, 1, B, 0 %OK

event = lt(A,0.3), A, 2*B, B, 0 %NG

## 2.1.9 Model MATLAB functions

The model MATLAB functions are identified from “********** MODEL MATLAB FUNCTIONS” to the next identifier line.



```
********** MODEL NAME
test_model

********** MODEL NOTES


********** MODEL STATES
d/dt(S) = -R1
d/dt(P) = R1

S(0) = 1
P(0) = 0
********** MODEL PARAMETERS
Vmax = 0.005
Km = 0.8

********** MODEL VARIABLES


********** MODEL REACTIONS
R1 = Vmax*S/(Km+S)

********** MODEL FUNCTIONS


********** MODEL EVENTS

********** MODEL MATLAB FUNCTIONS

```

Fig 3: Example of a text file