



# SysMIC Workshop: Working with Models

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## Activities

Welcome

Introduction: **The Goodwin Model**

Exercise: **Setting up a model of a linear chain or reaction without and with feedback**

Exercise: **Numerical Simulations of a set of differential equations**

Tasks:

- **State Space**
- **Parameter Space**
- **Parameter Protocol**

## Group Work Topics

### - Group 1: State Space

A model that has more than one variable can be studied and understood in the so called *state space*: this is the space of all possible outcomes. The state space has as many axis as there are variables, i.e. it is high-dimensional if there are many variables. For the Goodwin model the state space is 3-dimensional.

In state space, the state of all variables is depicted as a single points. A steady state is therefore also represented as a single point. Time is not an axis in state space but the temporal evolution can be seen as the values of the variables change. This is called a trajectory. State space plots illustrate the dynamics of non-steady state solutions and of transients following a perturbation. Any set of initial conditions can be thought of as a perturbation.

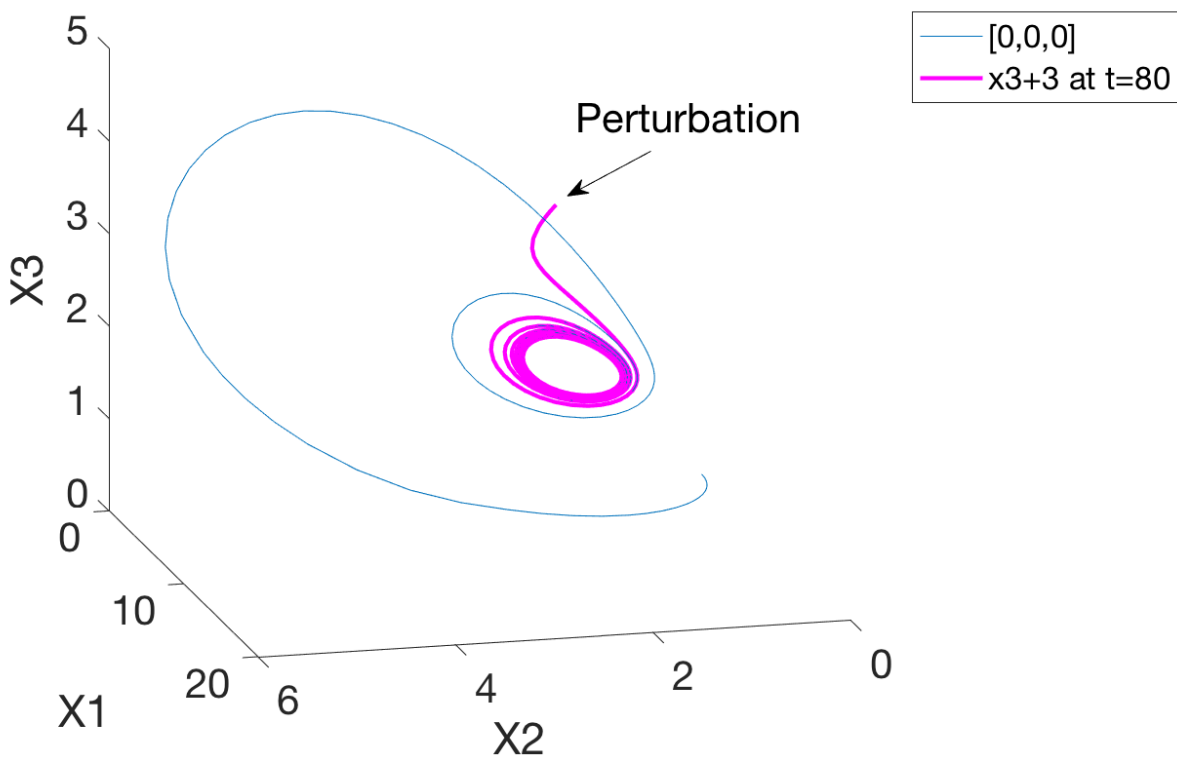
(i) Fix parameters and initial conditions of the 3 variable Goodwin model and run simulations. Plot a 3D state space composed of the three variables using MATLAB function *plot3*. Figure out in which direction the trajectory evolves. Describe the effect of picking different sets of initial conditions. What happens if all variables are initially set to zero? Check the state space graph against the display of the variables as a function of time.

(ii) Pick the final state of a simulation as the initial conditions for a second simulation and introduce a “perturbation” to one of the variables. E.g using MATLAB code like

```
x_ini(1) = x(end,1) - 3; % Perturbation
x_ini(2) = x(end,2);
x_ini(3) = x(end,3);
```

The plots are reproducible only if you start from the same initial condition.

Rerun the simulation and plot in the same figure as previously using another plot colour.



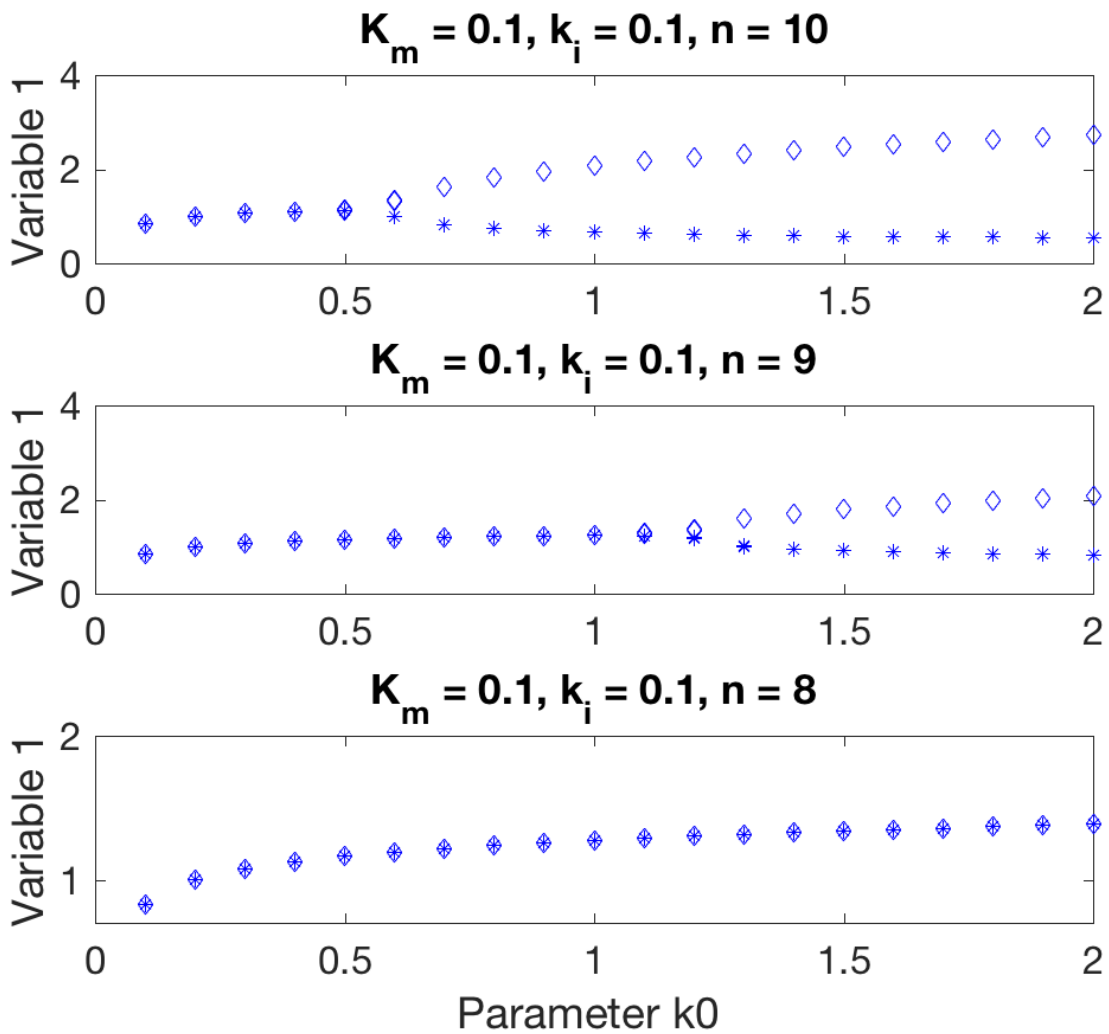
(iii) Describe the outcomes for the situation when the model parameters are fixed to yield a steady state.

(iv) Describe the outcomes for the situation when the model parameters are fixed to yield an oscillation. In this case, the outcome depends on the phase of the oscillation at the moment the perturbation is applied.

## - Group 2: Parameter Space

We have seen that the Goodwin model allows for different types of outcome depending on the specific setting of the kinetic parameters. The results might be very peculiar observations. Your task is to explain, what type of outcome to expect for combinations of two parameters. The technique is to explore and classify the *parameter space*, the space of all possible parameter sets. The parameter space has as many dimensions as there are parameters, i.e. it is high-dimensional if there are many of them. In the case of the Goodwin model it is 7-dimensional.

- (i) Pick two parameters to find the organisation of a subset of parameter space (e.g.  $k_0$  and  $k_i$ ). Run simulations and take notes of your results. You can explore the state space manually by changing the values of two parameters. Or you let can Matlab do a scan of different combinations and record the results (i.e. instruct MATLAB do do a set of simulations in one go). The important thing to observe is that the classification of state space is done on the asymptotic solution, i.e. after the transients caused by an arbitrary choice of initial conditions have disappeared.
- (ii) Experiment with ways of presenting the results in a table or in a graph. You need to decide how long to simulate before you record what is considered to be the asymptotic state, and what to record if the final state is not a steady state. Results that are only found for individual points or lines in parameter space are considered singular. For a behaviour to be considered robust it should be found in a volume of parameter space.



- (iii) Try to speculate what the results might look like if a third parameter is included into the picture: will the border between steady state and oscillation shift? Test it with some simulations.

### - **Group 3: Parameter Protocol**

Once the outcome of a model simulation is known (its asymptotic behaviour) one tries to find out how it will respond to stimulations.

“Stimulation” here stands for any type of external impacts that might be expected in an in vivo or in vitro situation. This could be a set-up where at some point the experimental conditions are changed.

Implement a protocol where after some time of simulation one of the parameters is altered. Some possibilities are:

- the parameter step, where one parameter assumes two different but constant values during a simulation;
- the parameter ramp, the continuous increase or decrease of one parameter as a function of time;
- the parameter pulse, one parameter is set to a different value for some time and then reversed to the original value.

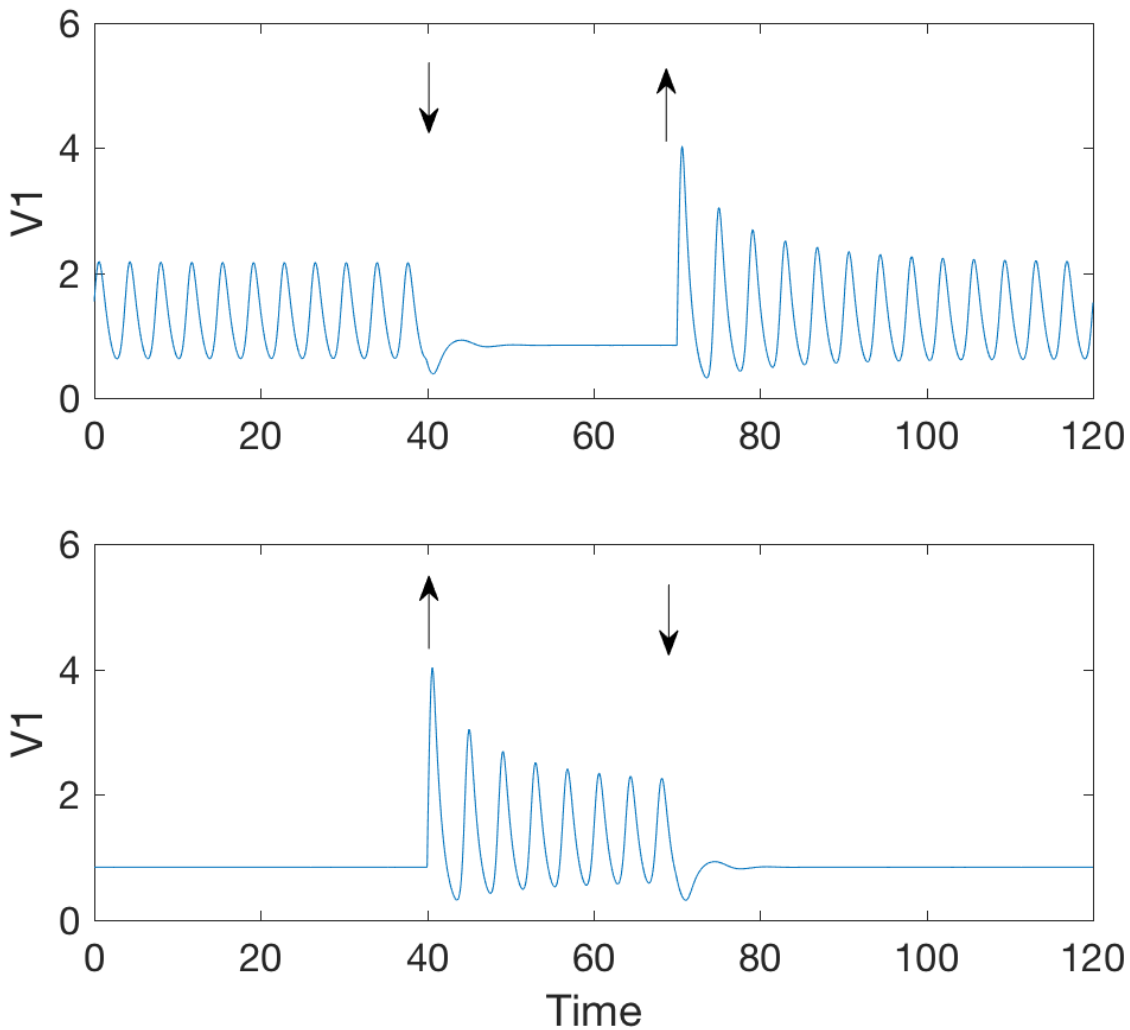
Investigate in more detail the latter case, parameter pulse. You can vary the size of the step and the duration of the step. Note that when the unperturbed behaviour is oscillatory, the response will also vary depending on the moment in which you apply the pulse.

This code can be applied in the model function:

```
% Stimulation Protocol, example code
```

```
k0 = 0.1;  
if t>20 && t<21  
    k0=k0+1;  
end
```

These simulations show a pulse perturbation of 30 time units in the oscillatory and in the steady state settings of the Goodwin model:



For any stimulation protocol consider what interpretation it might have in an experimental setting. Try to think of ways to present the results comprehensively.