***Part 2: Goodwin Oscillators***

In this exercise we will examine the behaviour of the following system.

In this system X, Y and Z are proteins that interact and regulate each others production rates.

This system is an example of a *Goodwin Oscillator* which can exhibit limit cycle oscillations as a result of non-linearity, negative feedback, and delay. This type of model is based on the work of the mathematical biologist Brian Goodwin who first discussed them in a 1965 paper *Oscillatory behavior in enzymatic control processes* (Adv Enzyme Regul 3: 425–438).

The aim of the model was an attempt to propose a potential mechanism by which the observation of periodic/rhythmic behaviour in cellular processes could be explained.

**Task 2a.**

Examine the model equations above.

1. Which terms are associated with production?
2. Which terms are associated with loss?
3. The proteins in the system have interactions which act either enzymatically or as transcription factors to activate production of the other proteins. The general model for such processes where protein S activates production of protein P is a production rate term like:

Under what conditions can this model be simplified and reduced to the model of activation used in the model equations above, i.e.

1. Describe the relationships between
2. X and Y
3. Y and Z
4. X and Z
5. Draw a diagram of this system

use an arrow like this ----| to identify a inhibiting relationship

use an arrow like this ----> to identify an activating relationship

vi) Explain which features of the model provide the necessary conditions for limit cycle oscillations (non-linearity and delay).

1. Suppose the system is initially in a state where the no proteins are present (i.e. the concentrations of X,Y and Z are all zero).

Try to use the model to predict how the system will behave from this point, and describe in words what you might expect to find.

**Task 2b.**

i) Code the system using the template code file oscillator\_template.py to get you started.

Run the system with parameters:

k1=1.0=k2=k4=k6=KI=1.0

k3=k5=10.0

n=1.0

and initial conditions:

X=Y=Z=0.0

ii) Describe the behaviour observed in the timeseries.

iii) Add code to draw the phase plot showing X on the x-axis and Z on the y-axis.

**Task 2c.**

If you increase **n** while holding the other parameters constant you can make the system produce limit cycle behavior. Find the minimum integer value of **n** required for the system to limit cycle behaviour and analyse the oscillations you observe.

i) How can you demonstrate that a limit cycle has been reached?

ii) Use the plots generated to determine the amplitude and period of the cycles.

*Think about how could you make more accurate measurements of these parameters using the values in the t\_obs and s\_obs arrays?*

iii) How does the limit cycle change as n is increased, e.g. to 20?

**Task 2d.**

The model we use assumes a chain in which:

X activates Y

Y activates Z

Z inhibits X.

Adjust your model to add an additional species into the chain such that:

X activates Y1

Y1 activates Y2

Y2 activates Z

Z inhibits X.

i) Investigate how this changes the minimum value of n required for oscillations.

ii) Explain this change in reference for the requirements for a Goodwin oscillator.