Physical Modelling of Complex Systems: Assignment 5

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Contents

1 The Goodwin model

The Goodwin model is one of the simplest models of biological oscillators. Below, we will focus mostly on the case of 3 components. Afterwards, we will sketch the generalization of the Goodwin model to N component systems.

1.1 Three components

The Goodwin model for a three component system is described by the following three differential equations (in non-dimensionalized form)

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \frac{1}{1+z^p} - bx \tag{1.1}$$

$$\frac{\mathrm{d}y}{\mathrm{d}t} = b(x-y) \tag{1.2}$$

$$\frac{\mathrm{d}z}{\mathrm{d}t} = b(y-z)\,, \tag{1.3}$$

where $b > 0$. We limit ourselves to $x, y, z > 0$, because we can imagine that x, y and z represent the concentration of mRNA, protein and end product, respectively (if we start from differential equations with correct dimensions, see for example [3]). Therefore, we can interpret b as the rate of transcription, translation, catalysis and degradation of the three species. Note that a more general version of the Goodwin model can be constructed by having a different rate b in each of the above equations, but this assumption of equal rates simplifies the analysis. There is only one non-linear term in the model describing repression of the variable z on x. Furthermore, we see that x is an activator for y, and y is an activator for z such that this network represents a negative feedback loop. Define F_1, F_2, F_3 to be the right hand sides of the above equations (i.e. $F_1(x, y, z) = \dot{x}$ et cetera). Below, we will use the lecture and the YouTube video by professor Carlon [1] as inspiration.

The above equations have a unique fixed point. From the second and third equation, we infer that a fixed point (x^*, y^*, z^*) of the system satisfies $x^* = y^* = z^* \equiv \xi$. From the first equation, we find that ξ has to be a solution of

$$1 - b\xi - b\xi^{p+1} = 0\,, \tag{1.4}$$

and we have to show there is only one solution to this equation. Let $f(x)$ denote the function at the left hand side of equation (1.4). Then

$$f'(x) = -b - b(p+1)x^p\,. \tag{1.5}$$

Since $f'(x) < 0$ for all $x > 0$ and all values of p, $f(x)$ is a strictly decreasing function in x. Since $f(0) = 1$, the graph of f will cross the x-axis a single time, such that $f(x)$ indeed has one zero in the half plane $x > 0$. Therefore, there is a unique fixed point $\Xi = (\xi, \xi, \xi)$. Note that ξ satisfies

$$b\xi = \frac{1}{1+\xi^p}\,, \tag{1.6}$$

from which we can derive the equation

$$\xi^p = \frac{1}{b\xi} - 1\,. \tag{1.7}$$

We now claim that the model fixed point undergoes a Hopf bifurcation for $p > 8$, while there is no Hopf bifurcation for $p < 8$. For this, we will investigate the Jacobian matrix evaluated at the unique fixed point. The only non-trivial entry in the Jacobian matrix will be the non-linear term. For this, define

$$\Phi \equiv -\frac{\partial F_1(x,z)}{\partial z}\Big|_{\Xi} = \frac{p\xi^{p-1}}{(1+\xi^p)^2}\,. \tag{1.8}$$

Using both equations (1.6) and (1.7), this can be written as

$$\Phi = \frac{p}{\xi}\xi^p b^2\xi^2 = \frac{p}{\xi}\left(\frac{1}{b\xi} - 1\right) b^2\xi^2 = \frac{p}{\xi}\left(\frac{1-b\xi}{b\xi}\right) b^2\xi^2 = pb(1-b\xi)\,. \tag{1.9}$$

The other entries of the Jacobian can be easily read off from the above differential equations. We find

$$J(\Xi) = \begin{pmatrix} -b & 0 & -\Phi \\ b & -b & 0 \\ 0 & b & -b \end{pmatrix} . \tag{1.10}$$

To find the eigenvalues of this Jacobian matrix, we start by writing down the characteristic polynomial $G(\lambda) \equiv \det(J(\Xi) - \lambda)$, which becomes

$$G(\lambda) = -(b+\lambda)^3 - b^2\Phi \,, \tag{1.11}$$

such that eigenvalues are solutions of

$$\lambda^3 + 3b\lambda^2 + 3b^2\lambda + b^3 + b^2\Phi \equiv \lambda^3 + A\lambda^2 + B\lambda + C = 0 \,. \tag{1.12}$$

In the lectures, we saw that for a characteristic polynomial of this form, we have a Hopf bifurcation at $AB = C$, which, using equation (1.9) becomes

$$9b^3 = b^3 + pb^3(1 - b\xi) \,. \tag{1.13}$$

This condition can be further simplified to

$$b\xi = 1 - \frac{8}{p} \,. \tag{1.14}$$

Since $b > 0$ and $\xi > 0$ by assumption, we see that this condition can never be satisfied if $p < 8$, since in that case the right hand side is a negative number. However, if $p > 8$, then there is a Hopf bifurcation. By the Routh-Hurwitz theorem [3], if $b\xi > 1 - \frac{8}{p}$, the fixed point is stable, while if $b\xi < 1 - \frac{8}{p}$, the fixed point is unstable.

The condition $p > 8$ means the system must have an unrealistically high value for the cooperativity parameter p, and the degradation rates must be (nearly) equal to each other for the above analysis to hold: if this is not the case, the threshold value for p will be even larger [3]. Therefore, the Goodwin model is not easily realised in nature. A modified version of the Goodwin model which fixes these issues is the model by Bliss, Painter and Marr, which is discussed in [3]. We will not delve deeper into this model in this exercise.

Finally, we would like to remark that instead of exploiting the condition $AB = C$, we could also directly find the roots of $G(\lambda)$, which are

$$\lambda_1 = -b - \sqrt[3]{p(1 - b\xi)} < 0 \,, \tag{1.15}$$

$$\lambda_{2,3} = -b + \sqrt[3]{p(1 - b\xi)} \left[\cos\left(\frac{\pi}{3}\right) \pm i \sin\left(\frac{\pi}{3}\right) \right] . \tag{1.16}$$

The fixed point becomes unstable if $\mathrm{Re}(\lambda_{2,3}) > 0$, and some algebraic manipulations will then give the same condition as above. It is this second method that we will generalize to the case of multi-component systems in the next subsection.

We will now integrate the above differential equations of the Goodwin model, with parameter values $b = 1/4$ and $p = 12$. For this choice of parameters, the fixed point is unstable, as can easily be verified graphically by plotting the right hand side of $\mathrm{d}x/\mathrm{d}t$. For this, we plot the two terms of this function separately, defining $F_1(x) = F_+(x) - F_-(x)$ (we will substitute x for z since we are interested in the fixed point, which is symmetric). The fixed point lies at the intersection of these two curves. Since $F_-(x) = bx$, the plot allows us to quickly verify that the fixed point is unstable by comparing the y-coordinate of the fixed point (which is $b\xi$) with $1 - 8/p$, shown as a grey dashed line in Figure 1.1 below. Since $b\xi < 1 - 8/p$, the fixed point is indeed unstable.

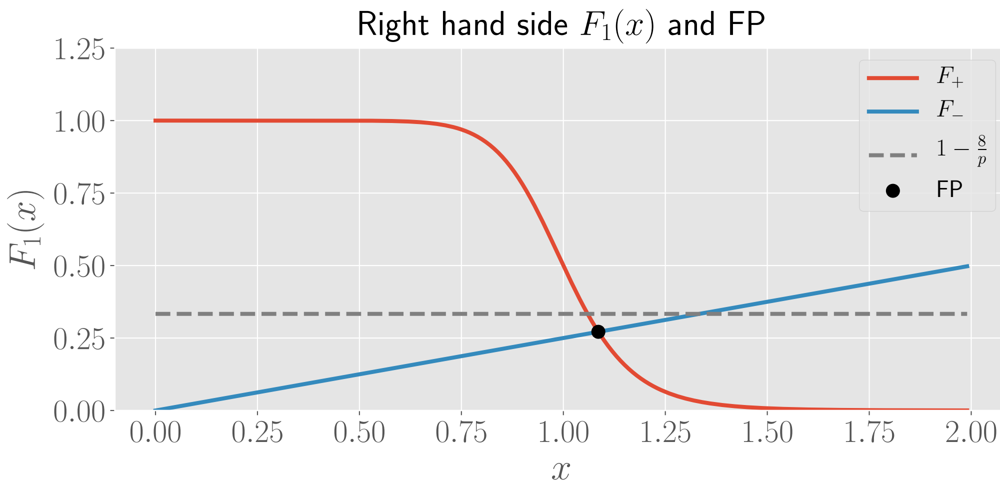

Figure 1.1: Plot of the two terms in $F_1(x)$, for $b = 1/4$ and $p = 12$, such that $\xi \approx 1.0858$. The fixed point lies at the intersection of the two curves, and is unstable for this choice of parameters.

Now we will plot the trajectories of the solutions of the Goodwin model for various initial conditions (which can be found in the Jupyter Notebook) in the xy, yz and xz planes. The result is shown in Figure 1.2 below. The figure shows that the solutions tend towards a limit cycle. This limit cycle appears more clearly if we restrict the plots to the second half of the datapoints of the numerically obtained solutions shown in Figure 1.2, which is shown in Figure 1.3. The limit cycle lies somewhere in the thin region between the two disconnected regions where the solutions lie. Indeed, in the outer part, the solutions spiral inwards towards the limit cycle, while in the inner part, the solutions will spiral outwards tending towards the limit cycle. Since the solutions tend towards the limit cycle from both sides (inside and outside), we can conclude the limit cycle is stable.

We remark that we can rigorously motivate the existence of the limit cycle by invoking the Poincaré-Bendixson theorem [2, p.203]. Indeed, if we look at each of the three projections, and take a large enough region R surrounding the fixed point, but not containing an arbitrarily small neighbourhood of the fixed point, then the plots show various possible trajectories that are confined in R. The Poincaré-Bendixson theorem then shows that there exists a closed orbit inside R. Since the plots show that the closed orbit is an isolated one, this shows there exists a limit cycle.

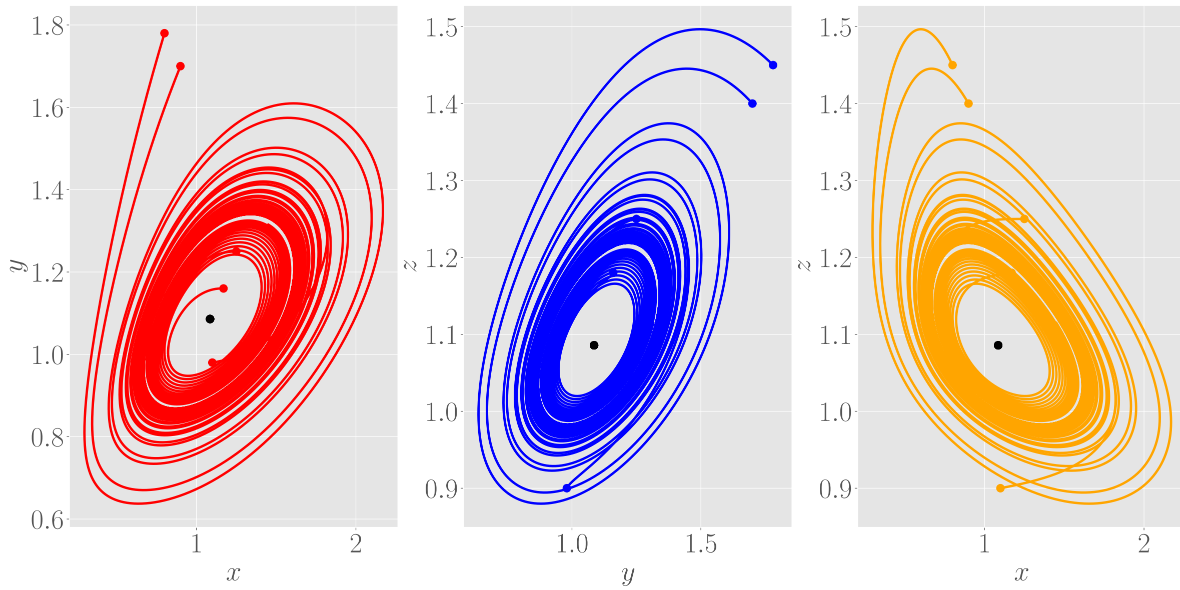

Figure 1.2: Solutions of the Goodwin model for various initial conditions (denoted as coloured dots), for parameters $b = 1/4$, $p = 12$, such that $\xi \approx 1.0858$ and the fixed point (black dot) is unstable. The solutions tend towards a limit cycle.

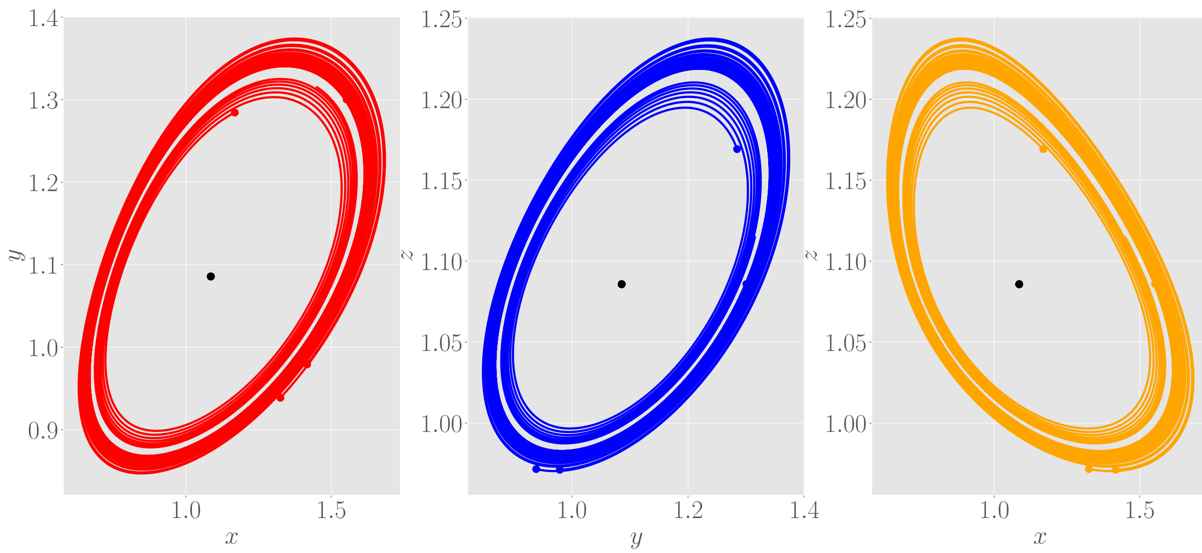

Figure 1.3: Second half of the solutions plotted in Figure 1.2, which makes it easier to spot the limit cycle. Note that the coloured dots now denote the starting location, after we have discarded the first half of the solutions.

1.2 Generalization to N components

We consider now a generalized Goodwin model with N components.

$$\frac{\mathrm{d}x_1}{\mathrm{d}t} = \frac{1}{1+x_N^p} - bx_1 \tag{1.17}$$

$$\frac{\mathrm{d}x_2}{\mathrm{d}t} = b(x_1 - x_2) \tag{1.18}$$

$$\frac{\mathrm{d}x_3}{\mathrm{d}t} = b(x_2 - x_3) \tag{1.19}$$

$$\dots$$

$$\frac{\mathrm{d}x_N}{\mathrm{d}t} = b(x_{N-1} - x_N)\,. \tag{1.20}$$

In this case, too, there is a unique fixed point. As before, fixed points should satisfy $x_1 = x_2 = \cdots = x_N = \xi$. Requiring that $\dot{x}_1$ equals zero then gives the same equation as in the three component case as condition on ξ. As shown there, there is one solution to this equation, such that the fixed point is unique and given by $\Xi = (\xi, \xi, \dots, \xi)$ as before. The Jacobian of this system, evaluated at the fixed point, is

$$J(\Xi) = \begin{pmatrix} -b & 0 & 0 & \dots & -\Phi \\ b & -b & 0 & \dots & 0 \\ \vdots & \ddots & \ddots & \ddots & \vdots \\ 0 & \dots & b & -b & 0 \\ 0 & \dots & \dots & b & -b \end{pmatrix}, \tag{1.21}$$

where Φ is identical to Φ for the three component system, since Φ only depends on the coefficients in the $\dot{x}_1$ equation, which is independent of N. To find the eigenvalues of the above matrix, we need to find the zeroes of the characteristic polynomial. Therefore, the eigenvalues are solutions of

$$G(\lambda) = (b+\lambda)^N + pb^N(1-b\xi) = 0\,, \tag{1.22}$$

where we again made use of equation (1.9) to rewrite the factor Φ. Taking the N-th root then gives N different complex eigenvalues

$$\lambda_n = -b + bp^{1/N}\left(1-b\xi\right)^{1/N} e^{i\frac{\pi}{N}(2n+1)} \qquad n = 0, 1, \dots, N-1\,. \tag{1.23}$$

Note that minus sign is taken inside the exponential factor. To find the Hopf-bifurcation point, we have to require that the complex eigenvalues with the largest real part satisfy $\mathrm{Re}(\lambda) = 0$. Indeed, if all eigenvalues have negative real part, the fixed point is stable, whereas if there are eigenvalues with positive real part, the fixed point becomes unstable. The real part of an eigenvalue is

$$\mathrm{Re}(\lambda_n) = -b + bp^{1/N}(1-b\xi)^{1/N}\cos\left(\frac{\pi}{N}(2n+1)\right)\,. \tag{1.24}$$

This is largest for $n = 0$ (so also for $n = N - 1$). We now determine when this eigenvalue crosses the imaginary axis, so

$$-b + bp^{1/N}(1 - b\xi)^{1/N} \cos\left(\frac{\pi}{N}\right) = 0\,. \tag{1.25}$$

Using some straightforward algebraic manipulations, we can derive

$$b\xi = 1 - \frac{1}{p\cos^N\left(\frac{\pi}{N}\right)}\,, \tag{1.26}$$

which is the generalization of the condition that we found earlier. We can check the above equation for $N = 3$, and since $\cos^3\left(\frac{\pi}{3}\right) = 1/8$, this indeed agrees with the result that we obtained in the previous subsection.

As was the case for the three component system, the above equation implies a constraint on p in order to have Hopf-bifurcation. As before, since $b\xi > 0$, p should be large enough such that the right hand side is positive as well, and this gives the requirement

$$p > \frac{1}{\cos^N\left(\frac{\pi}{N}\right)} \equiv p^N_{\min}\,. \tag{1.27}$$

In Figure 1.4 below, we plot $p^N_{\min}$ as a function of N. We see that for increasing N, the threshold value of p decreases. Therefore, if we have a larger number of components, we can use lower values of the cooperativity parameter (if we want to have Hopf bifurcation), which allows for a more realistic situation compared to the three component system.

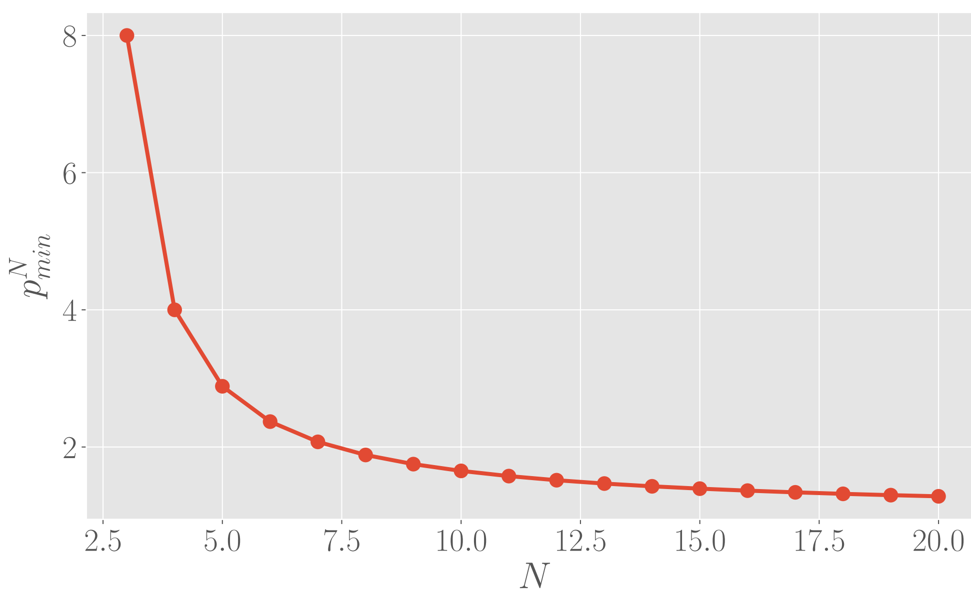

Figure 1.4: Plot of $p^N_{\min}$ as a function of N (for $N \geq 3$), showing that the threshold value for p decreases for an increasing number of components in the system.

References

[1] Enrico Carlon. Goodwin oscillator. `https://www.youtube.com/watch?v=yY4wZTJM74g&ab_channel=ECarlon`.

[2] Steven H Strogatz. *Nonlinear dynamics and chaos with student solutions manual: With applications to physics, biology, chemistry, and engineering*. CRC press, 2018.

[3] John J Tyson. Biochemical oscillations. In *Computational cell biology*, pages 230–260. Springer, 2002.