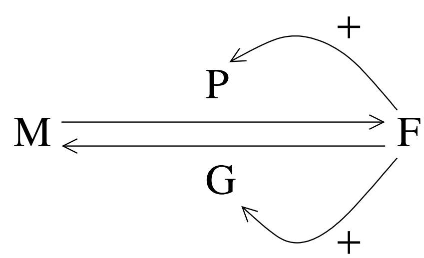
Chemistry 4010 Fall 2019 Assignment 4

Due: Oct. 22, 6:00 p.m.

Total marks: 15

This assignment will have you studying a biochemical model due to Berry [1] for the remodeling of the extracellular matrix:



The model describes the conversion of insoluble extracellular matrix proteins (M) to soluble proteolysis fragments (F) catalyzed by a proteinase (P). The reverse reaction is catalyzed by a transglutaminase (G). The soluble fragments activate the export of both enzymes to the extracellular medium. The proteinase degrades all proteins in the system: M, F, P and G. The fact that P can degrade itself leads to a quadratic degradation term.

The dimensionless rate equations for this model are the following:

$$\begin{aligned}
\frac{dm}{dt} &= \frac{k_g f g}{M_G + f} - \frac{mp}{1+m} + r, \\
\frac{df}{dt} &= -\frac{k_g f g}{M_G + f} + \frac{mp}{1+m} - \frac{fp}{1+f}, \\
\frac{dp}{dt} &= \frac{\alpha f^n}{M_R^n + f^n} - k_a p^2, \\
\frac{dg}{dt} &= \frac{\beta f^q}{M_S^q + f^q} - \frac{k_d g p}{M_d + g}.
\end{aligned}$$

The following parameter values should allow you to observe some interesting behavior: $M_R = 4.5$, $M_S = 1$, $\alpha = 0.026$, $\beta = 7.5 \times 10^{-4}$, $n = q = 4$, $M_G = 0.1$, $M_d = 1.1$, $k_g = 0.05$, $k_d = 0.05$, $k_a = 0.046$. You will be varying the value of r, which represents the rate of *de novo* synthesis of extracellular matrix proteins.

1. As usual, you need a starting point for a bifurcation analysis, preferably a stable equilibrium point. Look for a stable equilibrium for $r = 0.005$ using the following initial data: $m(0) = 10$, $f(0) = 1$, $p(0) = 0.01$, $g(0) = 0.1$.

   Obtain a bifurcation diagram over the range $r \in [0.005, 0.04]$. Find at least three pairs of period-doubling points. (You will find that each branch of limit cycles starts and ends at well-defined bifurcation points.) Your report should include your bifurcation diagram as well as a table listing the values of r at the Andronov-Hopf and period-doubling bifurcations. [10 marks]

   Hints:

   - You will find that the equilibrium point is approached very slowly. Set large values of `Total` and of `Dt` in the numerics menu.
   - Don't forget to set both `Par Min` and `Par Max` in the `Numerics` menu of AUTO.
   - You may find it advantageous to decrease `Dsmax` to 0.05 or less in AUTO's `Numerics` menu. Don't forget to adjust `Ds` is you push `Dsmax` too low. Also, as you decrease `Dsmax`, it may be useful to increase `Nmax` and `NPr`. Experiment to find numerical parameters that give you a good result.
   - If you notice AUTO running back-and-forth over ground it has previously covered, you can stop it by hitting the escape key.

   Note: The bifurcation diagram is much more complicated than what you will be computing. It includes branches that can only be found using techniques not discussed in this course.

2. Using your bifurcation diagram, you can take a reasonable guess as to where it might be possible to find a chaotic solution. Do so. In your report, display the attractor, and give the value of r at which it was found. [5 marks]

References

[1] H. Berry. Chaos in a bienzymatic cyclic model with two autocatalytic loops. *Chaos Solitons Fractals*, 18:1001–1014, 2003.