Project 3: due on June 10 (by end of the day)

Glycolysis is the biochemical process by which living cells break down sugars to release energy, which is used to form Adenosine Triphosphate (ATP). The complete glycolytic pathway is a complex series of ten enzyme-catalyzed reactions, involving intermediates that are derivatives of common sugars like fructose and glucose. Here, we wish to examine **glycolytic oscillations** that arise is one of these intermediate processes that relate ATP and Fructose-6-phosphate (F6P).

By measuring the concentrations of ATP and F6P in yeast and muscle extracts, scientists have demonstrated that their rates of change depend nonlinearly on the current concentration of the other. A simplified model for this part of glycolysis is:

$$\frac{d[ATP]}{dt} = -[ATP] + a[F6P] + [ATP]^2[F6P] \qquad \frac{d[F6P]}{dt} = b - a[F6P] - [ATP]^2[F6P]$$

where square brackets denote concentrations (typically detected by proxy using fluorescence). Here, a and b are kinetic constants that depend on other intermediates and external factors like the temperature. For simplicity, we will assume that <u>all terms are in dimensionless units</u>.

(a) Numerically solve the system of ODEs for $a = 0.05$ and $b = 1.2$ until $t = 100$ if the initial concentrations are $[ATP] = 1$ and $[F6P] = 1$. Plot this solution with correct labels. Does the eventual steady state concentration depend on initial conditions?

(b) Experiments often observe the so-called 'glycolytic oscillator' where the concentrations oscillate for several minutes. Use the same initial conditions as part (a) with constant $a = 0.05$. However, $b = 1.2$ in the beginning like before but changes to $b = 0.8$ at $t = 30$. Solve and plot the concentrations up to $t = 100$.

(c) The kinetic parameters are often not constant, and change continuously depending on the surrounding environment, temperature, and other intermediate products. In a particular case, let's say you discover that while a is mostly a constant, the parameter b changes continuously with time as follows:

$$\frac{db}{dt} = -0.1[F6P][ATP]e^{-1/b}$$

Now solve and plot the concentrations of ATP and F6P up to $t = 200$ if $a = 0.05$ and the initial values are $[ATP] = 1$, $[F6P] = 1$ and $b = 1$.

