Homework 8: Oscillations in life

1. Plot the *Hill function*:

$$v = \frac{V_{\max}([S]/K_m)^2}{1 + ([S]/K_m)^2}$$

and the function for *substrate inhibition*:

$$v = \frac{V_{\max}[S]/K_m}{1 + ([S]/K_m)^2}$$

both describing cooperative binding of two substrates to an enzyme. Pick up any value for $V_{\max}$ and K_m.

2. Hill function: How would you make the reaction reach (get very close to) its maximum rate $V_{\max}$ at lower/higher concentration of the substrate $[S]$, changing parameters of the curve?

3. Substrate inhibition function has a clear peak, corresponding to the maximum substrate $[S]$ concentration, after which the rate of reaction starts decreasing with $[S]$. How would you move this peak to lower/higher concentrations of $[S]$, changing the parameters of the curve?

4. How would you make the peak correspond to the higher rate values?

5. (**extra: +2 points**) Consider a model of the glycolitic oscillations:

$$\begin{cases} \dfrac{dx}{dt} = 1 - xy \\ \dfrac{dy}{dt} = \alpha y \left(x - \dfrac{1+r}{1+ry} \right) \end{cases}$$

The steady state of the system is: $\bar{x} = \bar{y} = 1$. We aim at plotting the Hopf bifurcation curve (2D bifurcation analysis).

We know that the eigenvalues $\lambda_{1,2} = \dfrac{\tau \pm \sqrt{\tau^2 - 4\Delta}}{2}$, where τ and Δ are trace and determinant of the linearization matrix (A), respectively. τ and Δ are functions of α and r, i.e. parameters of the system. Let us define:

$$F(\alpha, r) = \tau$$
$$G(\alpha, r) = \tau^2 - 4\Delta$$

We know that if there is an imaginary part for λ_i, it comes from $G(\alpha, r)$, being negative. Moreover, we know that in this case real part of λ_i will be determined by $F(\alpha, r)$.

So, if we plot $F(\alpha, r) = 0$ and determine the sign of the function on the two half planes demarcated by the line corresponding to $F(\alpha, r) = 0$, we can find potential area for the limit cycle oscillations.

Which of the half planes corresponds to the limit cycle?

Finally, we just need to find an intersection of the potential oscillatory region and the region, where $G(\alpha, r) < 0$ to make sure we have imaginary eigenvalues.

Hints:

(a) use Matlab's `contour` command that can plot the levels of a function on a plane.

(b) define area of plotting in the $\alpha - r$ plane using `meshgrid` ($\alpha \in [0, 10]$ and $r \in [0, 1]$ is enough, make sufficient resolution with `meshgrid`).

(c) define the values of the functions $F(\alpha, r)$ and $G(\alpha, r)$ at the points of the generated mesh of α and r values.

(d) zero level of a function can be drawn as:

```
contour(alpha,r,F,[0 0]);
```

similarly for any other level.

You should get something like the figure below:

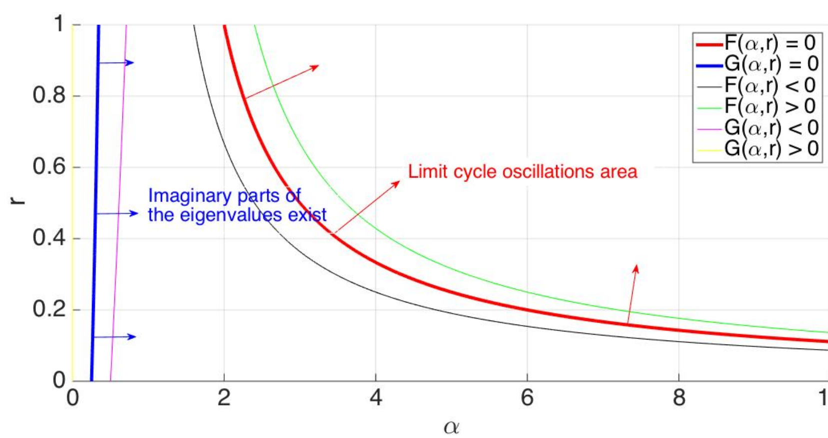

Figure 1: The parametric region to the right of the red curve (Hopf bifurcation) corresponds to the limit cycle oscillations.

You can also simulate the system for any particular parameter pair $\{\alpha, r\}$ in any of the found regions to confirm your findings. If you succeed, congratulations! The diagram above is called two dimensional bifurcation diagram, which is a quite non-trivial task to compute even for the specialized bifurcation analysis software.