Michaelis-Menten Model Analysis

Introduction

- In our real world, it is impossible to have infinite exponential growth
- In our pseudo Lotka-Volterra system, we use Michaelis-Menten to model our production of prey.

Michaelis-Menten Equation

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} ES \overset{k_2}{\longrightarrow} E + P \qquad \frac{d[P]}{dt} = k_2[E_0]\frac{[S]}{K_m + [S]} = V_{max}\frac{[S]}{K_m + [S]}$$

- Michaelis-Menten kinetics describes the kinetics of many enzymes
- V – Reaction rate/Velocity, Km – Michaelis Constant
- Valid only when the concentration of enzyme is much less than the concentration of substrate

Objective:

- To study and understand the dynamics of modified Lotka-Volterra system

Assumption made by using Michaelis-Menten

- The behaviours of promoter and activator are exactly the same as enzyme and substrate except that activator is not used up as substrate. (Hence, the Km should be Kd, the equilibrium constant).
- The LuxR concentration reaches steady state much faster than any others, hence it is assumed to be a constant in our rate equation.
- Although the actual product of prey cell is not AHL (but LuxI), we assume AHL to be our final product, since LuxI is directly responsible for AHL production. Hence AHL can be treated as being reproduced itself exponentially.

ODE (Ordinary Differential Equation):

$$\frac{dx}{dt} = \frac{Vx}{x + k_d} - bxy$$

$$\frac{dy}{dt} = cxy - dy$$

x	The population of prey at time t
y	The population of predator at time t
V	Maximum Speed of prey production
k_d	Equilibrium Constant
b	Rate constant on how fast prey killed by predator
c	Rate constant on how fast predator reproduce when fed from prey
d	Rate constant on how fast predator die

- The prey (AHL) production is limited by the limited number of promoters. This is modeled by Michaelis-Menten kinetics. The rate of production becomes linear when number of promoters is saturated.
- The rest parts of the equation are still behaving the same as the original Lotka-Volterra equation.

Stationary Points

- By setting ODEs to 0, i.e. dx/dt=0 & dy/dt=0, there are two stationary points found.

[0, 0]
[d/c, V*c/b/(k*c+d)]

Jacobian Analysis

- The Jacobian matrix of ODEs is

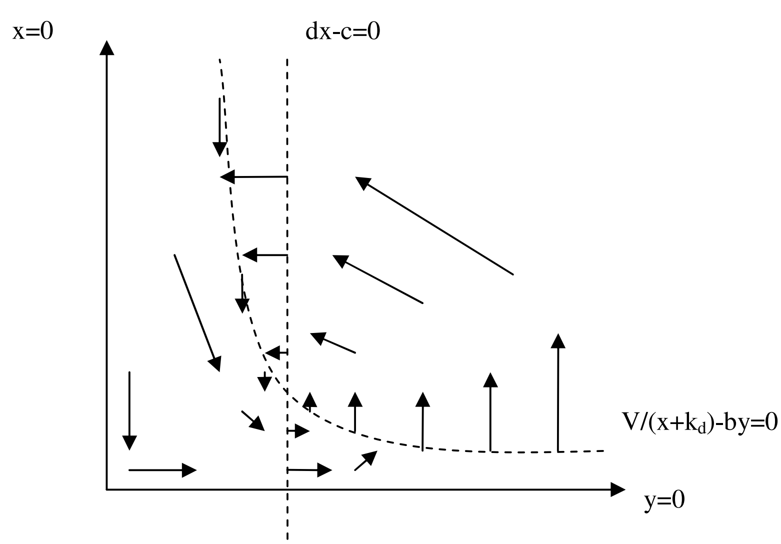
[-b*y+V/(k+x)-x*V/(k+x)^2, -x*b]
[y*c, -d+c*x]

Stability analysis (eigenvalue)

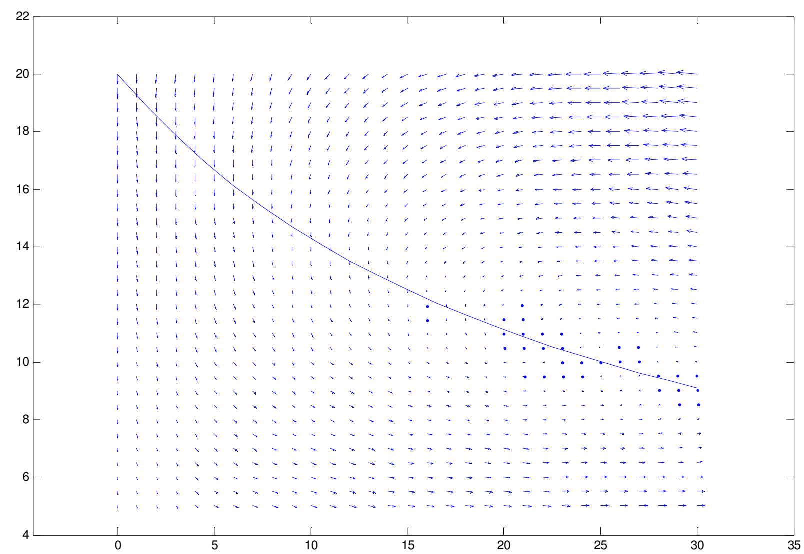
- For the first stationary point [0, 0], the Jacobian matrix is
  [V/k, 0]
  [0, -d]
- Trace = V/k – d, Determinant = -Vd/k < 0
  → The first stationary point is **unstable**.
- For the second stationary point [d/c, V*c/b/(k*c+d)], the Jacobian matrix is
  [-d*V*c/(k*c+d)^2, -d/c*b]
  [V*c^2/b/(k*c+d), 0]
- Trace = -d*V*c/(k*c+d)^2 < 0, Determinant = d*c*V/(k*c+d) > 0
  → The second stationary point is **stable**.

Vector Field Representation

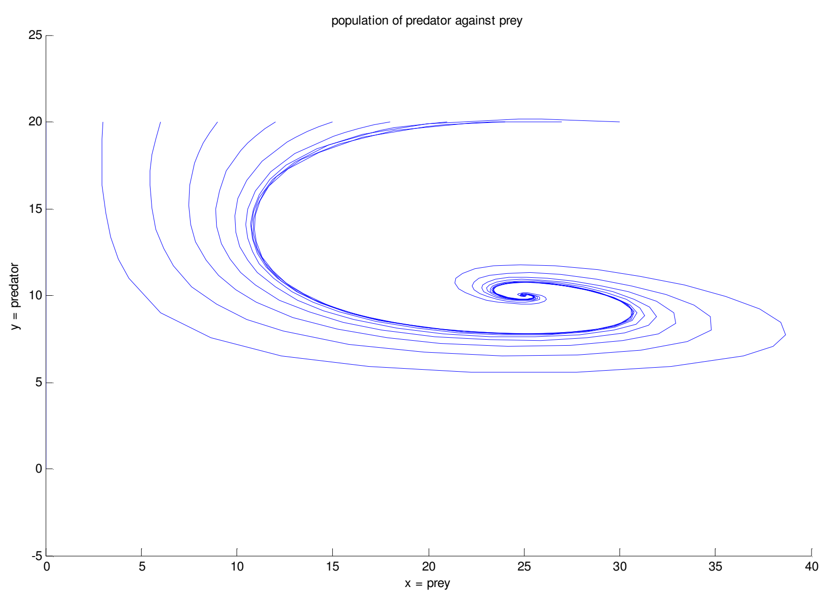
- Nulclines are x=0, V/(x+k_d)-by=0, y=0, dx-c=0



- From the vector field, we could identify the intersection of the two dashed lines (second stationary point) is a stable stationary point.
- Vector Field plot generated by Matlab with parameters V = 50 k_d = 25 b = 0.1 c = 0.02 d = 0.5. The parameters is a random set since the value of parameters will not change the stability of the stationary points. The graph is shown below:



- The general trend of "stable" characteristic stationary point is indeed the same as we predicted
- The contour of the Predator against Prey is plotted by Matlab. The following graph, which uses the same values of parameter given above with the initial population of predator of 20, is generated by increasing the initial prey population from 0 to 30 by 3 each time.



- From the graph above, we could see that the contour is attracted to the stable stationary point.