Question 2: Enzyme Kinetics

Enzymes are catalysts that help convert molecules that we will call substrates into other molecules that we will products. They themselves are not changed by the reaction. Within cells, enzymes are typically proteins. They can speed up biological reactions, sometimes by up to millions of times. They are also regulated by a very complex set of positive and negative feedback systems. Computational biologists are painstakingly mapping out this complex set of reactions. In this problem, we will model and simulate a simplified enzyme reaction.

An enzyme *E* converts the substrate *S* into the product *P* through a two-step process. First, *E* forms a complex with *S* to form an intermediate species *ES* in a reversible manner at the forward rate *k1* and reverse rate *k2*. The intermediate *ES* then breaks down into the product *P* at a rate *k3*, thereby releasing *E*. Schematically, we write

$$E + S \underset{k_2}{\overset{k_1}{\rightleftharpoons}} ES \overset{k_3}{\rightarrow} E + P$$

8.1. Using the law of mass action, write down four equations for the rate of changes of the four species, *E*, *S*, *ES*, and *P*.

By the law of mass function, we have that

rate of change of E: $\frac{d[E]}{dt} = (k_2+k_3)[ES] - k_1[E][S]$

rate of change of S: $\frac{d[S]}{dt} = k_2[ES] - k_1[E][S]$

rate of change of ES: $\frac{d[ES]}{dt} = k_1[E][S] - (k_2+k_3)[ES]$

rate of change of P: $\frac{d[P]}{dt} = k_3[ES]$

8.2. Write a code to numerically solve these four equations using the fourth-order Runge-Kutta method. For this exercise, assume that the initial concentration of *E* is 1 μM, the initial concentration of *S* is 10 μM, and the initial concentrations of *ES* and *P* are both 0. The rate constants are: *k1*=100/μM/min, *k2*=600/min, *k3*=150/min.

The final result is: *The code is at the end*

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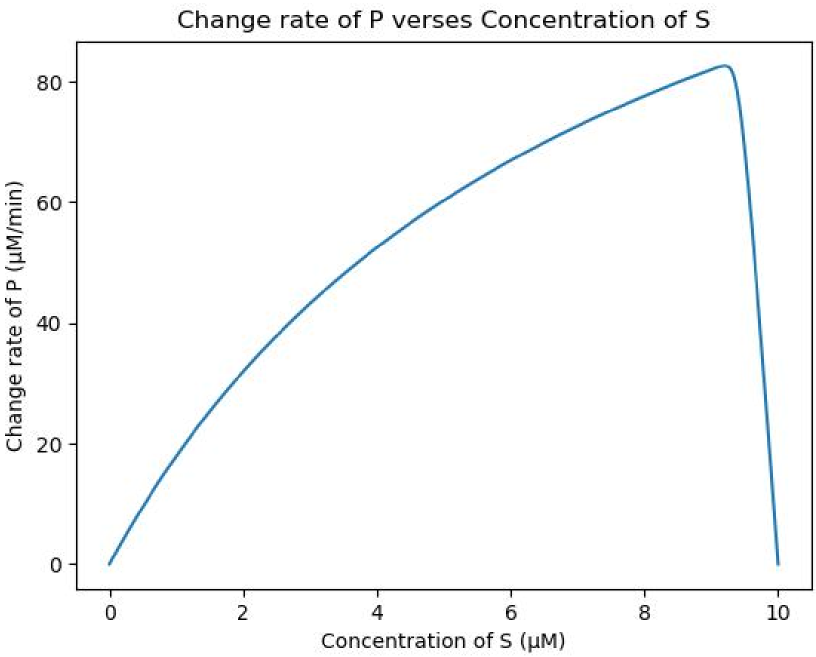
After 10000 iterations, set 0.0001 as time step, the results are shown as:
E: 0.9999999441180305 μM
S: 4.090395657009357e-07 μM
ES: 5.5881969762389094e-08 μM
P: 9.999999535078526 μM
```

8.3. We define the velocity, V, of the enzymatic reaction to be the rate of change of the product P. Plot the velocity V as a function of the concentration of the substrate S. You should find that, when the concentrations of S are small, the velocity V increases approximately linearly. At large concentrations of S, however, the velocity V saturates to a maximum value, Vm. Find this value Vm from your plot.



When the concentration of S is smaller than 9 μ M, the velocity V increases approximately linearly. When the concentration of S is around 9 μ M, however, the velocity V saturates to a maximum value Vm. From this graph, Vm is approximately equal to 80 μ M/min.

Appendix

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import numpy as np
import matplotlib.pyplot as plt

#define constant rate
k1 = 100
k2 = 600
k3 = 150

#define four equations
def Ve(E, S, ES):
    df = (k2 + k3) * ES - k1 * E * S
    return df

def Vs(E, S, ES):
    df = k2 * ES - k1 * E * S
    return df

def Ves(E, S, ES):
    df = k1 * E * S - (k2 + k3) * ES
    return df

def Vp(E, S, ES):
    df = k3 * ES
    return df


def RK4(y1, y2, y3, y4, h, n):
    """
    :param y1: Initial value of y1
    :param y2: Initial value of y2
    :param y3: Initial value of y3
    :param h: time step
    :return: New iterative solution
    """
    E, S, ES, P, vp= [], [], [], [], []

    for i in range(n):

        E.append(y1)
        S.append(y2)
        ES.append(y3)
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        P.append(y4)


        K_1 = Ve(E[i], S[i], ES[i])
        L_1 = Vs(E[i], S[i], ES[i])
        M_1 = Ves(E[i], S[i], ES[i])
        N_1 = Vp(E[i], S[i], ES[i])

        K_2 = Ve(E[i] + h / 2 * K_1, S[i] + h / 2 * L_1, ES[i] + h / 2 * M_1)
        L_2 = Vs(E[i] + h / 2 * K_1, S[i] + h / 2 * L_1, ES[i] + h / 2 * M_1)
        M_2 = Ves(E[i] + h / 2 * K_1, S[i] + h / 2 * L_1, ES[i] + h / 2 * M_1)
        N_2 = Vp(E[i] + h / 2 * K_1, S[i] + h / 2 * L_1, ES[i] + h / 2 * M_1)

        K_3 = Ve(E[i] + h / 2 * K_2, S[i] + h / 2 * L_2, ES[i] + h / 2 * M_2)
        L_3 = Vs(E[i] + h / 2 * K_2, S[i] + h / 2 * L_2, ES[i] + h / 2 * M_2)
        M_3 = Ves(E[i] + h / 2 * K_2, S[i] + h / 2 * L_2, ES[i] + h / 2 * M_2)
        N_3 = Vp(E[i] + h / 2 * K_2, S[i] + h / 2 * L_2, ES[i] + h / 2 * M_2)

        K_4 = Ve(E[i] + h * K_3, S[i] + h * L_3, ES[i] + h * M_3)
        L_4 = Vs(E[i] + h * K_3, S[i] + h * L_3, ES[i] + h * M_3)
        M_4 = Ves(E[i] + h * K_3, S[i] + h * L_3, ES[i] + h * M_3)
        N_4 = Vp(E[i] + h * K_3, S[i] + h * L_3, ES[i] + h * M_3)

        y1 = y1 + (K_1 + 2 * K_2 + 2 * K_3 + K_4) * h / 6
        y2 = y2 + (L_1 + 2 * L_2 + 2 * L_3 + L_4) * h / 6
        y3 = y3 + (M_1 + 2 * M_2 + 2 * M_3 + M_4) * h / 6
        y4 = y4 + (N_1 + 2 * N_2 + 2 * N_3 + N_4) * h / 6

        vp.append (Vp(E[i],S[i],ES[i]))

    return E, S, ES, P, vp


def main():
    h = 0.0001
    n = 10000
    E, S, ES, P, vp= RK4(1, 10, 0, 0, h, n)
    print ("After", n, "iterations, set",h,"as time step, the results are shown as:")
    print ("E:",E[n-1],"μM")
    print ("S:",S[n-1],"μM")
    print ("ES:",ES[n-1],"μM")
    print ("P:", P[n-1],"μM")

    #plot question 8.3
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```
    plt.title("Change rate of P verses Concentration of S")
    plt.xlabel("Concentration of S (μM)")
    plt.ylabel("Change rate of P (μM/min)")
    plt.plot(S, vp)
    plt.show()

if __name__ == '__main__':
    main()
```