Question 2

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

8.1

The four equations for the rate of changes of the four species are as follows:

$$\begin{aligned}\frac{\mathrm{d}[E]}{\mathrm{d}t} &= -k_1[E][S]+k_2[ES]+k_3[ES]\\ \frac{\mathrm{d}[S]}{\mathrm{d}t} &= -k_1[E][S]+k_2[ES]\\ \frac{\mathrm{d}[ES]}{\mathrm{d}t} &= k_1[E][S]-k_2[ES]-k_3[ES]\\ \frac{\mathrm{d}[P]}{\mathrm{d}t} &= k_3[ES]\end{aligned}$$

8.2

Initial conditions are:
$E(0) = E_0 = 1\mu M, S(0) = S_0 = 10\mu M, ES(0) = 0$ and $P(0) = 0$.

In this reaction, the total amount of E_T and ES does not change, we have:

$$\frac{\mathrm{d}([E]+[ES])}{\mathrm{d}t} = 0 \implies [E]+[ES] = [E_0] \implies [E] = [E_0]-[ES]$$

Hence, the equations can be written as follows:

$$\begin{cases}\frac{\mathrm{d}[ES]}{\mathrm{d}t} = f_1(t,[ES],[S]) = \lambda S(t) - (k_2+k_3+k_1S(t))ES(t)\\ \frac{\mathrm{d}[S]}{\mathrm{d}t} = f_2(t,[ES],[S]) = -\lambda S(t) + (k_1S(t)+k_2)ES(t)\\ \lambda = k_1E_0\end{cases}$$

For E, $[E] = [E_0] - [ES]$.
For P, $V_p = \frac{\mathrm{d}[P]}{\mathrm{d}t} = k_3ES(t), [P] = \sum \frac{\mathrm{d}[P]}{\mathrm{d}t} \times h$

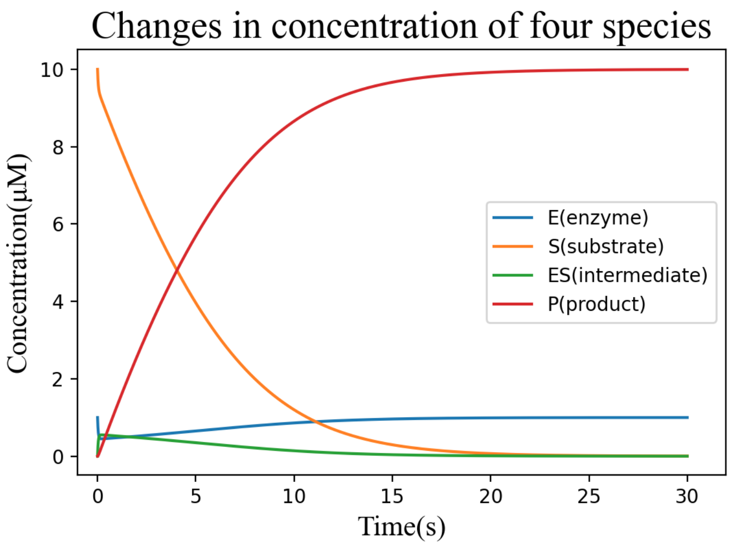
Using the fourth order Runge-Kutta method:

$$
\begin{cases}
y_{i+1} = y_i + \frac{h}{6}(m_1 + 2m_2 + 2m_3 + m_4) \\
m_1 = f(t_i, y_i) \\
m_2 = f(t_i + \frac{1}{2}h, y_i + \frac{1}{2}hm_1) \\
m_3 = f(t_i + \frac{1}{2}h, y_i + \frac{1}{2}hm_2) \\
m_4 = f(t_i + h, y_i + hm_3)
\end{cases}
$$

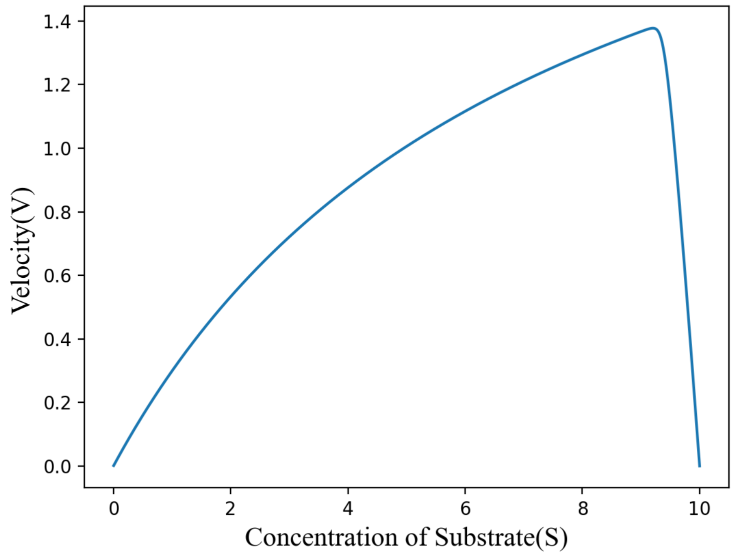
After 30s calculation with step-size 0.005s, the result of concentrations of four species is:

```
The concentration of E: 0.9995416729962799 μM
The concentration of S: 0.0033564265199168054 μM
The concentration of ES: 0.0004583270037201013 μM
The concentration of P: 9.996101121340393 μM
```

The trend of four species is as follows:



8.3



From the plot the Vm is around $1.4\mu M/s$.
Use Python to find the exact maximum value of V: at $1.38\mu M/s$, when the concentration of S is $9.20\mu M$.

```
The maximum value of Velocity: 1.3774629318788003
The concentration of S when velocity reaches Vmax:
9.20469388036423
```

References

[1] Barazandeh, Y., & Ghazanfari, B. (2018). Numerical Solution for Fuzzy Enzyme Kinetic Equations by the Runge–Kutta Method. *Mathematical and Computational Applications*, *23*(1), 16. https://doi.org/10.3390/mca23010016
[2] University of Oxford, Enzyme Kinetics. Chapter 2. https://courses-archive.maths.ox.ac.uk/node/view_material/52366

Codes

Please refer to the 'Question_2.py' project to check the entire codes.

```
import math
import matplotlib.pyplot as plt

# Known values
```

```
k1 = 100/60
k2 = 600/60
k3 = 150/60
E0 = 1

# Define functions of ES and S
def f1(time, ES, S):
    function = k1 * E0 * S - (k2 + k3 + k1 * S) * ES
    return function

def f2(time, ES, S):
    function = - k1 * E0 * S + (k1 * S + k2) * ES
    return function

# Input the initial conditions
ES = [0]
S = [10]
h = 0.005 # define a step size
n = int(30/h) # define the time range to be 30s
t = []
# To create the time list
for i in range(n+1):
    t_add = i * h
    t.append(t_add)

# The Runge-Kutta method
def main():
    for i in range(n):
        m_1 = f1(t[i], ES[i], S[i])
        q_1 = f2(t[i], ES[i], S[i])
        m_2 = f1(t[i] + h/2, ES[i] + h/2 * m_1, S[i] + h/2 * q_1)
        q_2 = f2(t[i] + h/2, ES[i] + h/2 * m_1, S[i] + h/2 * q_1)
        m_3 = f1(t[i] + h/2, ES[i] + h/2 * m_2, S[i] + h/2 * q_2)
        q_3 = f2(t[i] + h/2, ES[i] + h/2 * m_2, S[i] + h/2 * q_2)
        m_4 = f1(t[i] + h, ES[i] + h * m_3, S[i] + h * q_3)
        q_4 = f2(t[i] + h, ES[i] + h * m_3, S[i] + h * q_3)

        ES_add = ES[i] + (m_1 + 2 * m_2 + 2 * m_3 + m_4) * h / 6
```

```
        S_add = S[i] + (q_1 + 2 * q_2 + 2 * q_3 + q_4) * h / 6
        ES.append(ES_add)
        S.append(S_add)

main()

E = []
P = []
Pv = [] # the velocity of enzyme reaction (rate of change of P)
ES_sum = 0
# To get the value of E, P, and P velocity
for i in ES:
    Ei = E0 - i
    P_velo = k3 * i
    ES_sum += i
    Pi = k3 * ES_sum * h
    E.append(Ei)
    Pv.append(P_velo)
    P.append(Pi)

# Output the result at 30s range
print('The concentration of E: '+ str(E[n]) + ' µM')
print('The concentration of S: '+ str(S[n]) + ' µM')
print('The concentration of ES: '+ str(ES[n]) + ' µM')
print('The concentration of P: '+ str(P[n]) + ' µM')

# Visualization 8.2: changes in concentration of four species
plt.figure()
plt.title('Changes in concentration of four species', family =
'Times New Roman', size = 20)
plt.xlabel('Time(s)', family = 'Times New Roman', size = 15)
plt.ylabel('Concentration(µM)', family = 'Times New Roman', size
= 15)
plt.plot(t, E, t, S, t, ES, t, P)
plt.legend(labels=['E(enzyme)', 'S(substrate)',
'ES(intermediate)', 'P(product)'])
plt.show()
```

```
# Visualization 8.3: Plot the velocity as a function of the
concentration of the substrate
plt.figure()
plt.xlabel('Concentration of Substrate(S)', family = 'Times New
Roman', size = 15)
plt.ylabel('Velocity(V) ', family = 'Times New Roman', size = 15)
plt.plot(S, Pv)
plt.show()

# To find exact Vm in the Pv list
print('The maximum value of Velocity: ' + str(max(Pv)))
index_Vm = Pv.index(max(Pv)) # To find the location of Vm in the
list
# To find the exact concentration of S at Vm
print('The concentration of S when velocity reaches Vmax: ' +
str(S[int(index_Vm)]))
```