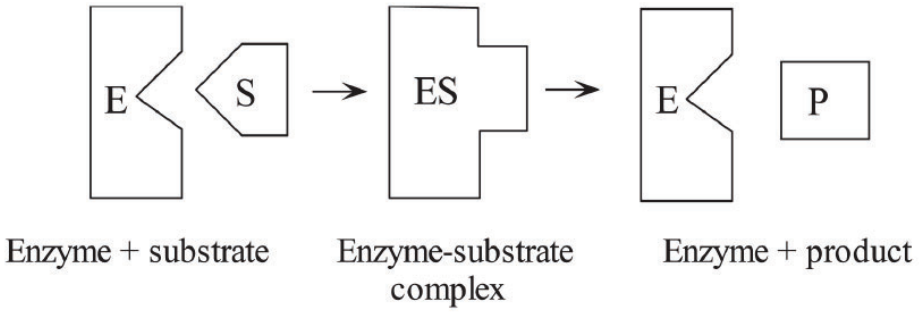
PLTL Calculus Session 7 – Enzyme Kinetics

Enzymes are catalysts that facilitate the biochemical reactions that occur within all living organisms. One of the fundamental laws of enzyme kinetics was proposed by Loenor Michaelis and Maud Menten in 1913. The law has been supported through laboratory experiments and explained through mathematical modeling; today, Michaelis-Menten kinetics are used in many biological models.

An enzyme molecule is designed to "fit" another molecule called a *substrate*. The substrate (S) and enzyme (E) form an intermediate complex (ES), which then dissociates to form the final end-product of the reaction (P) and the original enzyme. The enzyme can then be re-used.



Background Knowledge

- The rate of change of a function at a point is the derivative of the function there.
- Functions are increasing when they have positive slope and decreasing when they have negative slope. You can identify where a function is increasing and decreasing by finding where the derivative is zero, and then making a sign diagram for the intervals determined by those zeroes.
- Graphing functions requires manipulation of the graphing window so that you can see all the graph features, including end behavior.

An important question concerns the rate at which product molecules are formed. Under certain assumptions, Michaelis-Menton kinetics relates the rate of production of P to the amount of substrate present. In this project, we will explore these production rates, along with looking at how small changes in each variable changes the overall reaction over time. Let R be the rate of production of the final product P, and let s be the concentration of the substrate initially present. Both s and P are measured in units such as micro-moles μM, while R is measured in μM/s. The Michaelis-Menton law says that

$$R(s) = \frac{Vs}{K + s},$$

where $V > 0$ and $K > 0$ are constants that are specific to each enzyme.

1. Let $K = 5\ \mu$M and $V = 10\ \mu$M/s. Graph R as a function of s on the window $[0,35] \times [0,12]$. The graph looks to be increasing; prove that it actually is always increasing, using R', for this particular choice of V and K.

2. What does the function R mean biologically? As the initial concentration of the substrate s increases, what is the effect on the production rate P? (Remember, P is the actual amount of product produced, and R is the rate of change of P.)

Now let's interpret the constants V and K.

3. Evaluate the limit as $s \to \infty$ of $R(s)$. Explain why V is the maximum production rate. Is there any value of s for which the production rate equals V?

4. How does the shape of the graph of R change if V increases? How does it change if V decreases?

5. The constant K has the same units as s. Evaluate $R(K)$, the rate of production when $s = K$. Show that K is the initial enzyme concentration that gives a production rate of $V/2$ (so, half the maximum rate).

6. How does the shape of the graph of R change if K increases? How does it change if K decreases? Explain why a small value of K means that the enzyme has a high affinity for the substrate.

7. Evaluate $R'(0)$, which is the slope of the curve at the origin. How does the slope change if K is increased with V fixed? How does the slope change if V is decreased with K fixed?

8. Now suppose a particular enzyme obeys Michaelis-Menton kinetics, but we do not know the exact values of the parameters V and K. Now suppose that we measure two data points: (s_1, R_1) =(2 μM, 0.5 μM/s) and (s_2, R_2) =(5 μM, 1 μM/s). Find values of K and V that fit this data, and plot the points and the production rate function R in this case.

9. Occasionally, the Michaelis-Menton law is graphed with a semilog plot, which means that $\ln(s)$ is the variable for the horizontal axis. Mke a semilog plot of the Michaelis-Menton Law with $K = 5$ μM and $V = 10$ μM/s.