

Influence of enzyme concentration on the Michaelis-Menten constant: A new theory

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ABSTRACT:

This study proposes a novel theory that challenges the traditional view of the Michaelis-Menten constant (K_m) as a fixed value for a given enzyme-substrate pair. We explore the possibility that K_m can be modulated by enzyme concentration.

By analyzing the relationship between initial reaction velocity and substrate concentration at different enzyme concentrations, we observed a change in the apparent affinity constant (designated as K_{m1} and K_{m2}). This seemingly contradicts the established theory, and we have proposed a new theory to explain this variation.

INTRODUCTION:

In the context of enzyme kinetics, it has traditionally been argued that the Michaelis-Menten constant (K_m) is independent of enzyme concentration. This paradigm was based on the idea that, under standard conditions, K_m represents a specific constant for an enzyme, reflecting its affinity for the substrate. Thus, it was assumed that, regardless of changes in enzyme concentration, the value of K_m remains constant, representing an intrinsic characteristic of the enzyme-substrate relationship. (1)

In this communication, I will propose a theory suggesting that enzyme concentration influences the value of K_m .

This theory has the potential to open new avenues for research that could explain the Cytotoxicity of medication in more detail. In terms of applicability to allosteric enzymes, it allows us to consider the possibility of creating metabolic pathway blockers by increasing the enzyme concentration sufficiently so that $[S]$ cannot reach K_m .

Methodology :

This paper is based on a contradiction between two fundamental principles of biochemistry, namely:

1. When V_{max} increases, the fractional change in v is less than the fractional change in V_{max} .
2. K_m is constant regardless of the enzyme concentration.

According to the first principle, as V_{max} increases up to V_{max}' , $V_{max}/2$ will increase to less than $V_{max}'/2$, which means that the value of K_m increases with the enzyme concentration.

In this paper, we will attempt to explain why when the first principle is valid, the second one is not.

THEORY:

$$\frac{V_{MAX}}{a} = \frac{V_{MAX}'}{a} = a \Rightarrow \frac{K_m + [S]}{[S]} = \frac{K_M + [S]'}{[S]'} = a \Leftrightarrow K_{m1} = (a-1)[S] \text{ and } K_{m2} = (a-1)[S]'$$

- V_{MAX} represents the maximum velocity before the enzyme concentration increase.
- V_{MAX}' represents the maximum velocity after the enzyme concentration increase.
- $[S]$ represents the substrate concentration at V_{MAX}/a ,
- $[S]'$ represents the substrate concentration at V_{MAX}'/a ,
- a is a number greater than 1, belonging to the set of real numbers (\mathbb{R})

Since when v_{max} increase the fractional change in v is less than the fractional change in v_{max} , and v varies hyperbolically with the substrate concentration, it follows that $[s] < [s]'$.
 $\Rightarrow K_m$ increase with enzyme concentration.

For this mathematical model, I would like to propose this theory.

Let's consider, for simplicity, an ideal case: a sphere containing a solution of enzyme and substrate. On each substrate, a force acts equal to the sum of the attraction forces between each enzyme and its respective substrate, plus the sum of the repulsion forces between each substrate and its respective substrate. Since the solution is spherical, any deviation from the center of the sphere of the substrate's position will result in an increase in the repulsion and attraction forces acting on the substrate from the opposite side of the deviation, and a decrease in the repulsion and attraction forces from the same side with the deviation. Since the substrate concentration is much higher than the enzyme concentration, it means that the repulsion force dominates. Therefore, it follows that as

the substrate deviates more from the center of the sphere, the electrostatic force that drives it towards the periphery of the sphere increases, so the substrate will collide with an enzyme located closer to the periphery than the substrate. From here, we can conclude that with an increase in enzyme concentration, the forces opposing the substrate's trajectory increase, thus decreasing the enzyme's affinity for the substrate.

Fundamental biochemistry data supporting the theory:

1. When V_{max} increases, the fractional change in v is less than the fractional change in V_{max} ! This statement is consistent with the theory as it confirms that the activity of each enzyme decreases with an increase in enzyme concentration for the same substrate concentration.

2. The disproportion between the fractional change in v and the fractional change in V_{max} decreases with an increase in substrate concentration! This is another statement consistent with the theory as it confirms the decreasing relevance of the attraction forces between each enzyme and substrate, compared to the repulsion forces between each substrate and its reference substrate.

CONCLUSION:

This study demonstrates an unexpected relationship between enzyme concentration and K_m . Our observations suggest that K_m is not a fixed constant, but rather can vary depending on the amount of enzyme present.

This finding has significant implications for the interpretation of enzyme kinetic data. Traditionally, K_m has been considered an intrinsic characteristic of an enzyme, reflecting its affinity for its substrate. However, our findings indicate that K_m can be influenced by enzyme concentration, which must be taken into account when analyzing and modeling enzyme reactions

REFERENCES:

1. *The original Michaelis constant: translation of the 1913 Michaelis-Menten paper.* **Michaelis L, Menten ML, Johnson KA, Goody RS.** 2011, ACS Publication, p. 34.