Enzyme Kinetics

Differential Equations Series

Instructor's Guide

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Intro

Chem 101

Resources

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Appendix A1

Developed by the Teaching and Learning Laboratory at MIT
for the Singapore University of Technology and Design

Introduction

Key Information

Duration: 16:56
Narrator: Prof. Krystyn Van Vliet
Materials Needed:
• Paper
• Pen/pencil

When to Use this Video

- In Chem 101, at home or in recitation, either before or after Lecture 36: More effects on reaction rates
- Prior knowledge: determining rate laws from experimental data, predicting rate laws from proposed reaction mechanisms, and understanding the effect of catalysts on reaction rate

Learning Objectives

After watching this video students will be able to:

- Explain how enzymes affect reaction rates.
- Derive a rate law for a general enzyme-catalyzed reaction.

Motivation

- The changing concentrations of species in a chemical reaction provides a nice context for students to practice writing differential equations. Even though students may not be able to solve the differential equations, understanding how to describe processes with differential equations is an important skill.
- Many chemistry textbooks invoke the steady-state approximation to simplify a system of differential equations without making it clear to the students what conditions need to be satisfied in order for the approximation to yield reasonable results. This video makes these conditions explicit.

Student Experience

It is highly recommended that the video is paused when prompted so that students are able to attempt the activities on their own and then check their solutions against the video.

During the video, students will:

- Derive a rate law for an enzyme-catalyzed reaction.
- Consider the mathematics behind the steady-state approximation.
- Think about how a proposed rate law might reveal useful information about a reaction mechanism.

Video Highlights

This table outlines a collection of activities and important ideas from the video.

Time	Feature	Comments
0:00	Video introduction - different processes catalyzed by enzymes are mentioned.	Some industrial processes that utilize enzymes are mentioned.
1:32	A short animation describes how enzyme inhibitors could help treat malaria.	This example provides students with one example of why understanding enzyme kinetics can be beneficial.
2:22	Biochemical terms (e.g., substrate, enzyme) are reviewed.	
2:47	How do enzymes work?	
5:55	Derivation of Michaelis-Menten equation begins.	
10:32	The justification for using the steady-state approximation is presented.	Numerical solutions for a system of differential equations are shown. The conditions where the steady-state approximation will hold are discussed.
14:42	The malaria example is revisited.	Students consider how kinetic data and a rate equation might help them understand how a enzyme inhibitor works.

Video Summary

Prof. Krystyn Van Vliet discusses the importance and utility of enzyme kinetics for drug development. Alongside the video, students derive a rate equation (the Michaelis-Menten equation) for a simple enzyme-substrate system. Returning to the drug development example, students see that rate equations can help them infer information about reaction mechanisms.

Chem 101 Materials

Pre-Video Materials

When appropriate, this guide is accompanied by additional materials to aid in the delivery of some of the following activities and discussions.

1. Rate laws from experimental data (Appendix A1)

Have students derive the rate law from the data given in Appendix A1. This should be a review for students.

2. Reaction mechanisms

Ask students if this mechanism

$$NO + Cl_2 \xrightarrow{k_1} NOCl_2$$

$$NOCl_2 + NO \xrightarrow{k_2} 2NOCl$$

is consistent with the rate law that they derived in the previous problem. Have students discuss which step might be rate determining. Why do they think so?

3. Catalysis

In small groups, have students discuss how a catalyst increases the rate of a reaction. Then, have students discuss whether or not a given reaction would have the same rate law in a catalyzed and uncatalyzed case. Students should explain their reasoning.

This question highlights the point that catalysts provide a different reaction pathway. Thus, the rate law would change because the reaction mechanism has changed.

Post-Video Materials

1. Enzyme-catalyzed reactions (Appendix A2)

Use this concept question to emphasize that enzymes, like synthetic catalysts, do not influence the thermodynamics of a reaction.

2. Competitive and noncompetitive inhibition (Appendix A3-A5)

At the end of the video, a scenario is presented where a drug candidate is shown to decrease the apparent v_{max} of one of the proteases used by the malaria parasite to degrade hemoglobin. Two possible reaction mechanisms are proposed — competitive inhibition and noncompetitive inhibition. Have students derive a rate law from these mechanisms. Which rate law is supported by the data presented at the end of the video (replicated on page A3)?

3. If you have not done so already, introduce students to Lineweaver-Burk, Eadie-Hofstee, and Hanes-Woolf plots. What would a Lineweaver-Burk plot look like for a case of competitive inhibition, compared to the control? What would a Lineweaver-Burk plot look like for a case of noncompetitive inhibition, compared to control?

Additional Resources

Going Further

Biochemistry
The video discusses the use of enzyme inhibitors in the treatment of disease. Systematically designed competitive inhibitors can also be used to probe the geometry and chemical reactivity of the active site of an enzyme. This information, combined with information from X-ray crystallography and other experimental techniques, can lead to better understanding of enzyme chemistry and reaction mechanisms.

Kinetic experiments can also be used as a diagnostic to detect changes in physiological concentrations or activities of enzyme which might be indicative of disease.

Biochemical Engineering
An understanding of enzyme kinetics and the ability to formulate a rate law is essential for the modeling, design, and development of industrial processes that employ biocatalysts. In the design of these systems, conditions which may denature the enzyme will have to be considered. Temperature, exposure to mechanical forces, and the chemical environment (including pH) will have to be carefully considered. Rate data in the presence of possible denaturing conditions may need to be collected in order to more accurately predict substrate conversion.

References

The following chemical education articles discuss the motivation for and difficulties with teaching chemical kinetics.

- Campbell, J. A. (1984). Kinetics–Rates and Mechanisms. *Journal of Chemical Education. 61*(1), 40-42.
- Justi, R. (2002). Teaching and Learning Chemical Kinetics. In J. Gilbert, O. Jong, R. Justi, D. Treagust & J. Van Driel (Eds.), *Chemical Education: Towards Research-based Practice*. Dordrecht, The Netherlands: Kluwer Academic Publishers
- Lamb, W. G. (1984). Why Teach Kinetics to High School Students. *Journal of Chemical Education. 61*(1), 40-41.

The following MIT Open CourseWare lectures address enzyme kinetics.

- Drennan, Catherine, and Elizabeth Vogel Taylor. 5.111 Principles of Chemical Science, Fall 2008. (Massachusetts Institute of Technology: MIT OpenCourseWare), http://ocw.mit.edu (Accessed 12 Mar, 2012). License: Creative Commons BY-NC-SA
  –Video Lecture #35 discusses Enzyme Kinetics. Also see the Biology Related Example for Lecture #35, linked to from the 5.111 homepage of OCW
- Nelson, Keith A., and Moungi Bawendi. 5.60 Thermodynamics , Spring 2008. (Massachusetts Institute of Technology: MIT OpenCourseWare), http://ocw.mit.edu (Accessed 22 Mar, 2012). License: Creative Commons BY-NC-SA
  -Video Lecture #35 discusses Enzyme catalysis

The following textbook addresses the topic of enzyme catalysis from a biochemical engineering perspective.

- Bailey, J. E., and D. F. Ollis. (1986). *Biochemical Engineering Fundamentals*. (2nd ed.). New York, NY: McGraw-Hill.

What is the rate law?

The reaction

$$2NO(g) + Cl_2(g) \quad > \quad 2NOCl\ (g)$$

was studied at -10°C. The following data were obtained where

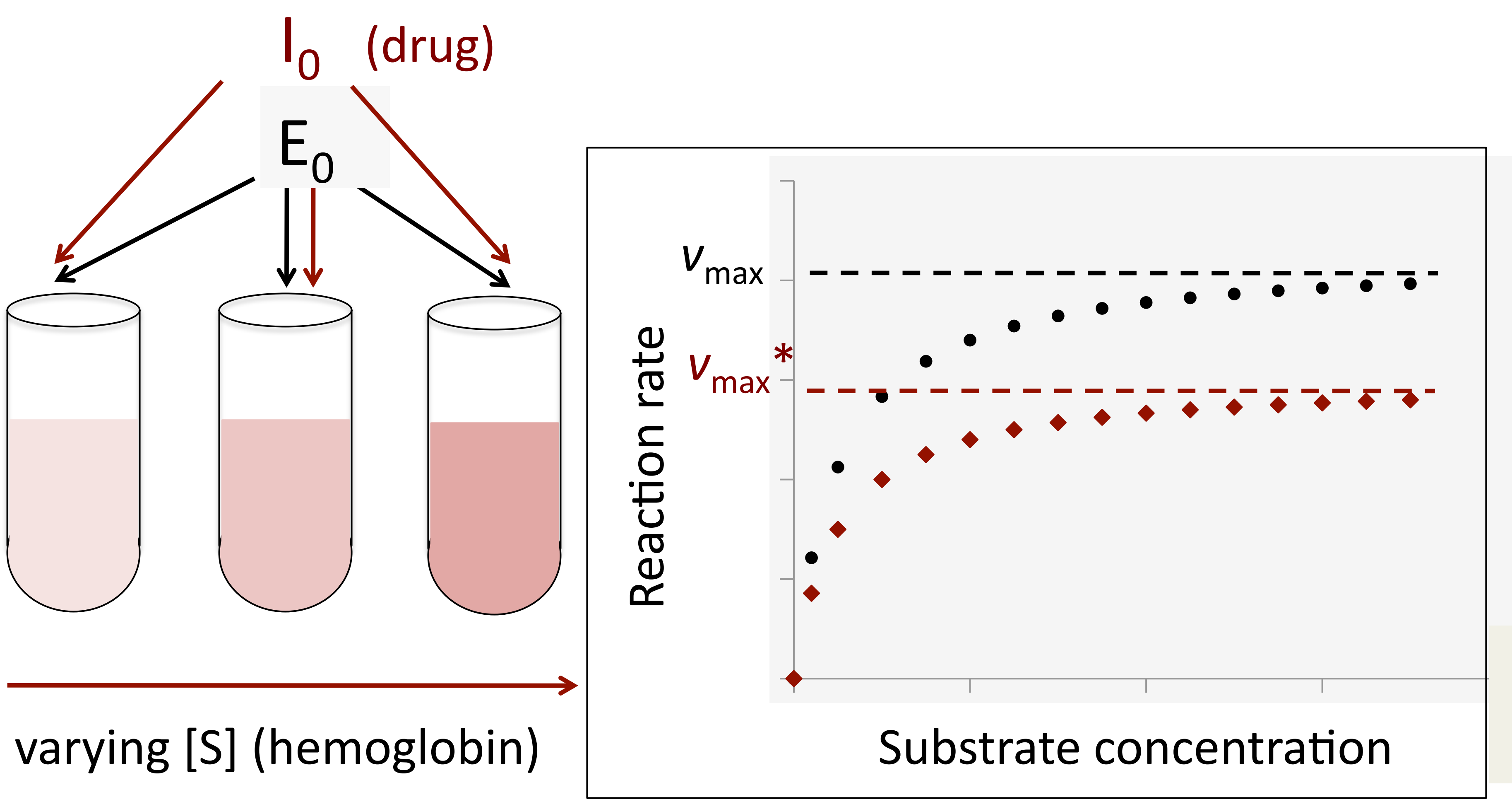
$$Rate = -\frac{\Delta[Cl_2]}{\Delta t}$$

$[NO]_0$ (mol/L)	$[Cl]_0$ (mol/L)	Initial rate (mol/L min)
0.10	0.10	0.18
0.10	0.20	0.35
0.20	0.20	1.45

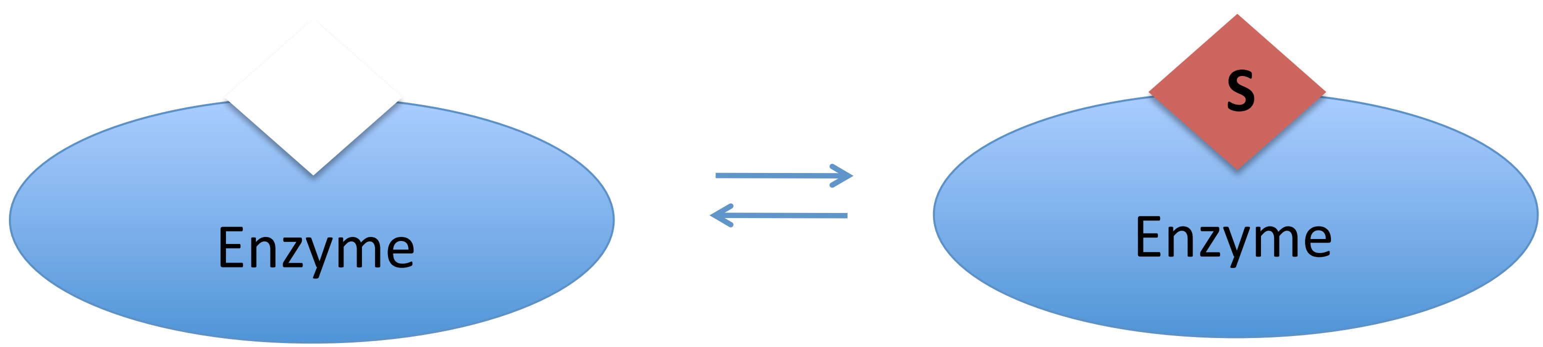
Which of the following is NOT changed in an enzyme catalyzed reaction?

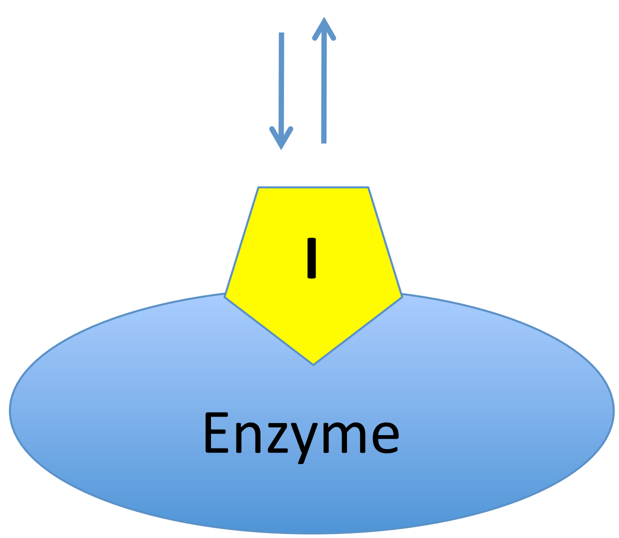
a. The equilibrium constant, K
b. The rate of reaction
c. The reaction mechanism
d. The rate law

Kinetic Data Collection



Competitive Inhibition

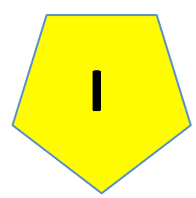




$$E + S \rightleftharpoons ES$$

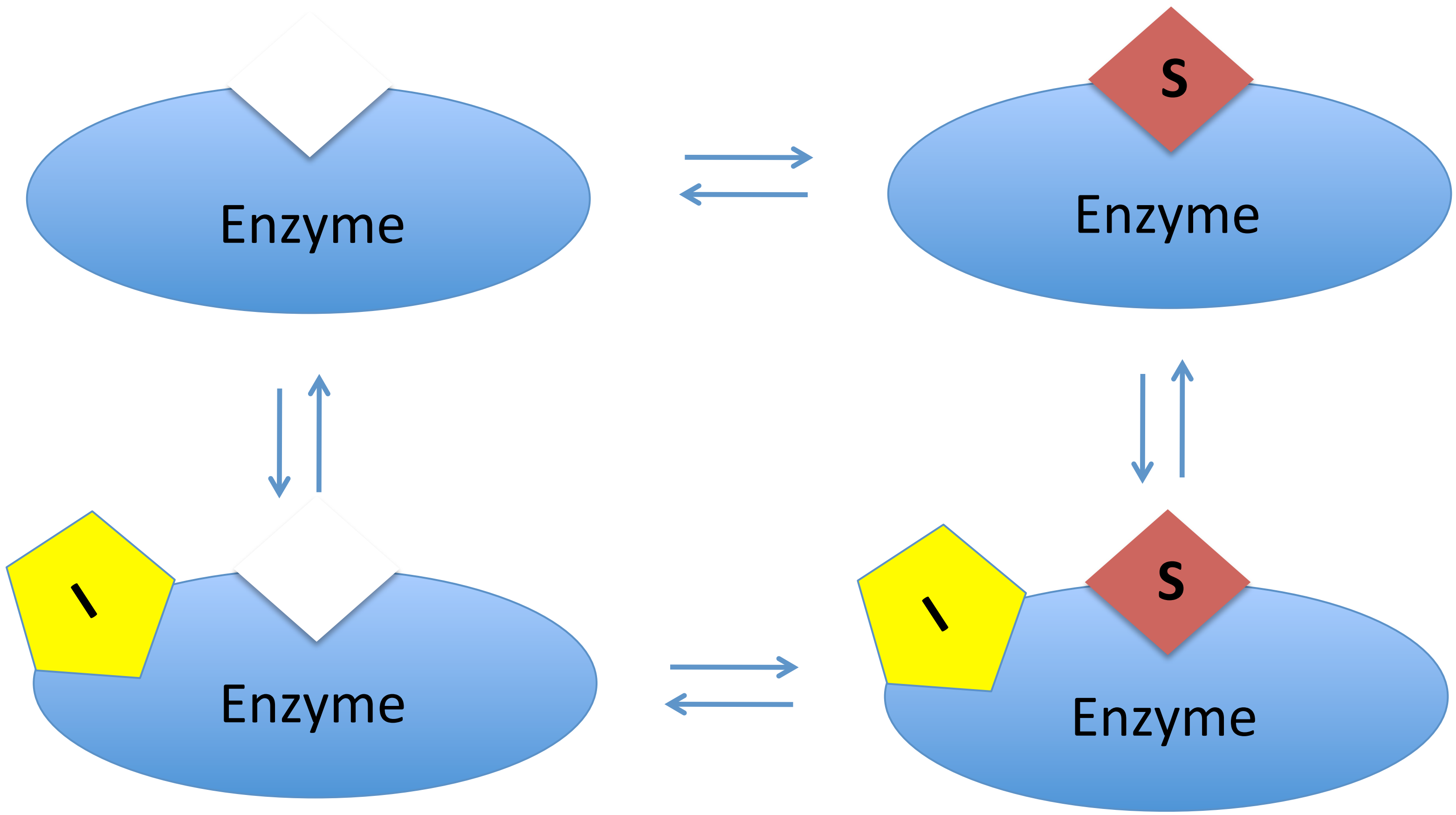
$$E + I \rightleftharpoons EI$$

$$ES \longrightarrow E + P$$



= inhibitor (drug)

Noncompetitive Inhibition



$$E + S \rightleftharpoons ES$$

$$EI + S \rightleftharpoons ESI \qquad ES + I \rightleftharpoons ESI$$

$$ES \longrightarrow E + P$$