MedicinalYoyos

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Intro

View the most up-to-date version of this doc here.

View it on GitHub here.

Steady-state assumptions and defining K_M.

$$\mathrm{E} + \mathrm{S} \underset{\mathrm{k_{-1}}}{\overset{\mathrm{k_1}}{\rightleftharpoons}} \mathrm{ES} \underset{\mathrm{k_{-2}}}{\overset{\mathrm{k_2}}{\rightleftharpoons}} \mathrm{EP} \underset{\mathrm{k_{-3}}}{\overset{\mathrm{k_3}}{\rightleftharpoons}} \mathrm{E} + \mathrm{P}$$

$$k_{cat} = \frac{k_2 k_3}{k_2 + k_3} \tag{1}$$

$$\begin{aligned} k_3 &>> k_2 \\ k_{cat} &= \frac{k_2 k_3}{\cancel{k_2} + k_3} \\ &= \frac{k_2 \cancel{k_3}}{\cancel{k_3}} \\ \implies k_{cat} &\approx k_2 \end{aligned}$$

Thus,

$$\mathrm{E} + \mathrm{S} \underset{\mathrm{k_{-1}}}{\overset{\mathrm{k_1}}{\rightleftharpoons}} \mathrm{ES} \xrightarrow{\mathrm{k_{cat}}} \mathrm{E} + \mathrm{P}$$

$$K_M = \frac{k_{-1} + k_{cat}}{k_1} \tag{2}$$

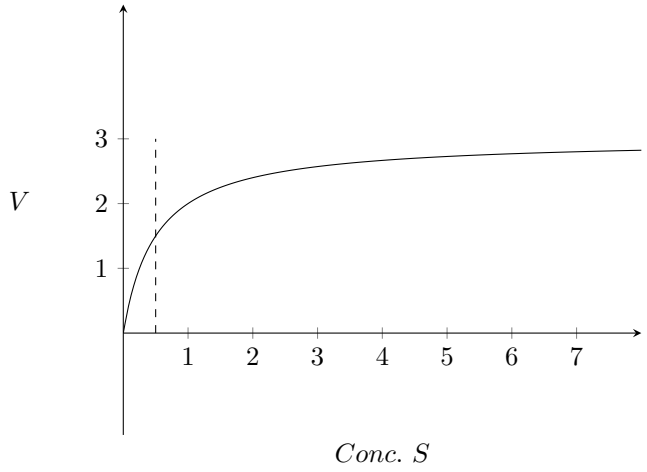
$$V = \frac{V_{max}[S]}{K_M + [S]} \tag{3}$$

$$V_{max} = k_{cat}[E_T] \tag{4}$$

$$E_T = [E] + [ES] \tag{5}$$

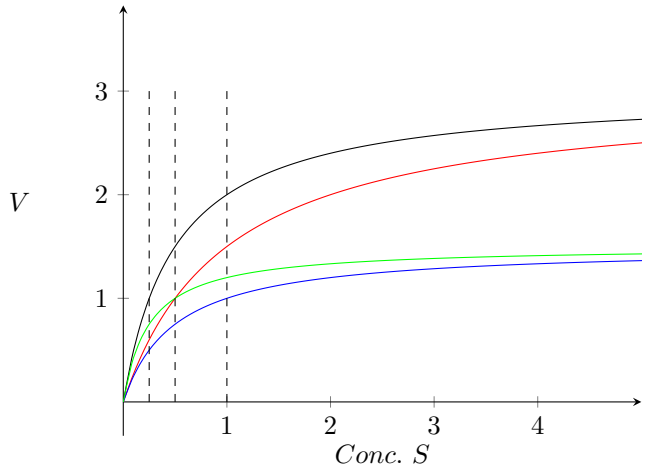
$$\text{Catalytic efficiency} = \frac{k_{cat}}{K_m} \tag{6}$$

M-M graph with the equation: $V = \frac{3[S]}{0.5+[S]}$



M-M graphs with the following parameters:

- In black: $V = \frac{3[S]}{0.5+[S]}$
- In red: $V = \frac{3[S]}{1+[S]}$, an example of competitive inhibition.
- In blue: $V = \frac{1.5[S]}{0.5+[S]}$, an example of noncompetitive inhibition.
- In green: $V = \frac{1.5[S]}{0.25+[S]}$, an example of uncompetitive inhibition.



Deriving Lineweaver-Burk

$$V = \frac{V_{max}[S]}{K_M + [S]}$$

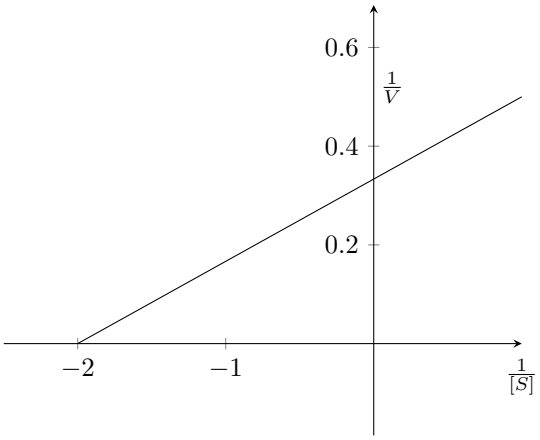
Inverse:

$$\frac{1}{V} = \frac{K_M + [S]}{V_{max}[S]} \tag{7}$$

$$= \frac{K_M}{V_{max}[S]} + \frac{[S]}{V_{max}[S]} \tag{8}$$

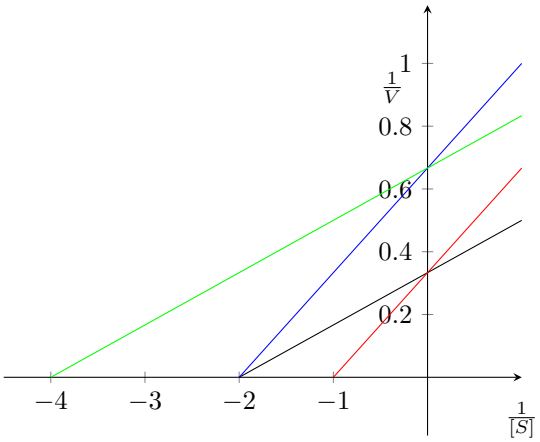
$$= \frac{K_M}{V_{max}}(\frac{1}{[S]}) + \frac{1}{V_{max}} \tag{9}$$

This is just a fancy $y = mx + b$!



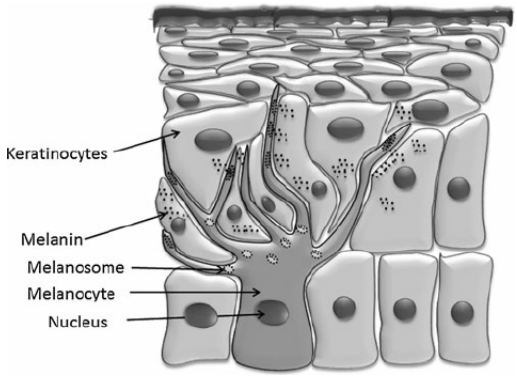
These are the same equations as earlier, translated to Lineweaver-Burk.

- In black: $\frac{1}{V} = \frac{0.5}{3}(\frac{1}{[S]}) + \frac{1}{3}$ (M-M: $V = \frac{3[S]}{0.5+[S]}$)
- In red: $\frac{1}{V} = \frac{1}{3}(\frac{1}{[S]}) + \frac{1}{3}$ (M-M: $V = \frac{3[S]}{1+[S]}$) - competitive inhibition.
- In blue: $\frac{1}{V} = \frac{0.5}{1.5}(\frac{1}{[S]}) + \frac{1}{1.5}$ (M-M: $V = \frac{1.5[S]}{0.5+[S]}$) - noncompetitive inhibition.
- In green: $\frac{1}{V} = \frac{0.25}{1.5}(\frac{1}{[S]}) + \frac{1}{3}$ (M-M: $V = \frac{1.5[S]}{0.25+[S]}$) - uncompetitive inhibition.



Passage (Question 1-6)

Melanin is a pigment produced by melanocytes in the basal layer of the epidermis. It is the primary determinant of skin color in humans. Melanocytes are dendritic in shape and produce and store melanin in melanosomes. Melanosomes are phospholipid-bound organelles that transport and deposit melanin throughout the epidermis. An image of this process is shown below.



Tyrosinase is an important oxidase in the production of melanin. Tyrosine is oxidized by tyrosinase to form L-DOPA. L-DOPA is further oxidized by tyrosinase to form Dopaquinone. Dopaquinone undergoes a series of reactions to form melanin.

A group of researchers were interested in whether citrus essential oils have an effect on tyrosinase. From the oils of 13 citrus fruits, they found three inhibitory extracts, citral, myrcene, and kojic acid. The results of an enzyme assay for tyrosinase on the substrate L-DOPA are shown below.

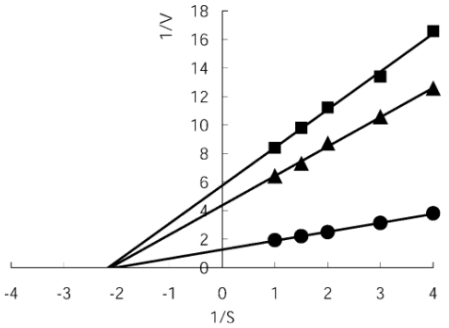


Figure 6. Lineweaver–Burk plots of tyrosinase and L-DOPA with 0 (●), 1.0 (▲), and 1.2 mM (■) citral.

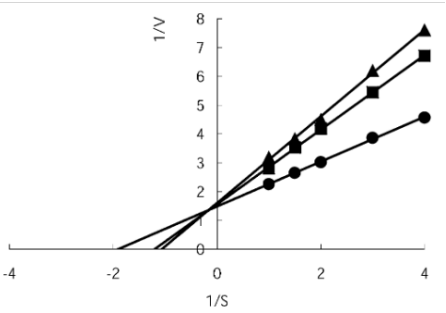


Figure 7. Lineweaver–Burk plots of tyrosinase and L-DOPA with 0 (●), 0.1 (■), and 2 mM (▲) myrcene.

Study and figures pulled from *Matsuura, R. et al.* [1]. Please note details of the study were altered. to suit the passage.

Questions

1. What are the likely reactants for the first step of melanin production mentioned in the passage?
   (a) L-tyrosine + water
   (b) L-tyrosine + an electron source
   (c) D-tyrosine + water
   (d) L-tyrosine + $NADH^+ + H^+$
2. Which of the following are likely to cause depigmented skin?
   I. An autoimmune disease where melanocytes are destroyed by macrophages.
   II. An ointment that increases the production of L-DOPA.
   III. A medicine that reduces the Vmax of all oxidases.
   (a) I only
   (b) I and II
   (c) I and III
   (d) I, II, and III
3. What type of inhibitor is citral?
   (a) competitive inhibitor
   (b) uncompetitive inhibitor
   (c) noncompetitive inhibitor
   (d) allosteric inhibitor
4. Tinea versicolor is a disease where a yeast that produces azelaic acid grows on the skin. Azelaic acid is a competitive inhibitor of tyrosinase. Which of the following is true?
   (a) K_M of tyrosinase would increase as the concentration of azelaic acid increases.
   (b) Tyrosinase will have a lower catalytic efficiency in the presence of azelaic acid.
   (c) V_{max} of tyrosinase will decrease due to azelaic acid.
   (d) Azelaic acid will cause negative cooperativity in tyrosinase.
5. What is the likely mechanism for the transport of melanin?
   (a) Kinesin-mediated anterograde transport.
   (b) Actin-mediated anterograde transport.
   (c) Kinesin-mediated retrograde transport.
   (d) Actin-mediated retrograde transport.
6. Kojic acid is found to be a mixed inhibitor. Assuming there is unlimited large supply of subtrate, will the reaction velocity of tyrosinase be faster in the presence of myrcene or kojic acid?
   (a) Kojic acid because V_{max} is decreased by myrcene.
   (b) Kojic acid because V_{max} is increased by kojic acid.
   (c) Myrcene because K_M of tyrosinase is lowered by myrcene.
   (d) Myrcene because V_{max} of tyrosinase is lowered by kojic acid.

Answer Key

1. B
2. C
3. C
4. A
5. A
6. D

Explanations

Alas, it is summer and the days are long. Yet somehow my time is short, and I have not found the time to write out answer explanations.

Discussion on tyrosine hydroxylase vs tyrosinase https://jn.nutrition.org/article/S0022-3166(22)15174-6/fulltext

Bonus Questions

These are ideas for questions I have not finished, so maybe come back here once I finish them!

1. Mutations in the gene that encodes tyrosinase is a common cause for albinism and is inherited in an autosomal recessive manner. Suppose a mutation alters the open reading frame of the TYR gene, which produces tyrosinase. How would this affect the
2. Mut on ORF of TYR, something about destruction in ERAS
3. Something about Malassezia Furfur
4. Something about dopamine vs melanin
5. T. gondii affect on tyrosine hydroxylase efficiency or vaccination https://pubmed.ncbi.nlm.nih.gov/32244791/
6. Tinea versicolor is a disease where a yeast that produces azelaic acid grows on the skin. Azelaic acid is a competitive inhibitor of tyrosinase. Which of the following is true?
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   (c) V_{max} of tyrosinase will decrease due to azelaic acid.
   (d) Azelaic acid will cause negative cooperativity in tyrosinase.

References

[1] R. Matsuura, H. Ukeda, and M. Sawamura. "Tyrosinase inhibitory activity of citrus essential oils". In: *J Agric Food Chem* 54.6 (Mar. 2006), pp. 2309–2313.