Enzymes: Classification, Kinetics and Control

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References:

Lieberman, M; Marks, AD. Basic Medical Biochemistry: A Clinical Approach, 3rd Edition, 2009

Devlin, Thomas M. Textbook of Biochemistry with Clinical Correlations, 6th Edition, 2006

Nelson, DL; Cox, MM. Lehninger Principles of Biochemistry, 3rd Edition 2000

Bosquejo:

A) Introducción a las enzimas
B) ¿Cómo funcionan las enzimas?
C) Factores que afectan la actividad enzimática
D) Cinética enzimática
E) Inhibición de enzimas
F) Regulación de actividad enzimática

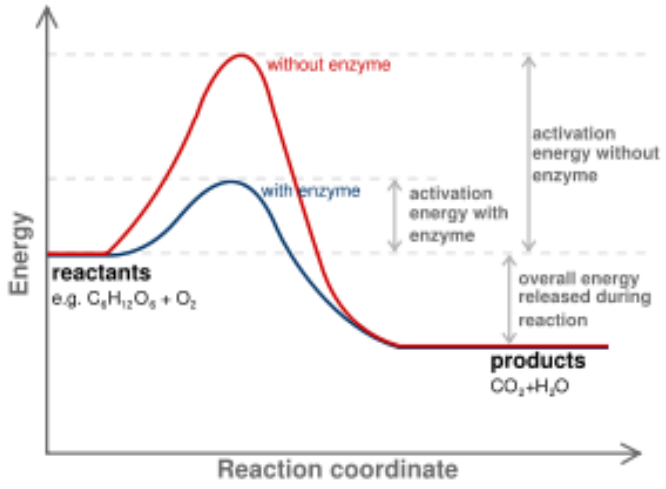
Introducción a las enzimas

Considere la siguiente reacción:

$$\text{Sucrose} + 6O_2 \longrightarrow 6CO_2 + 6\,H_2O$$

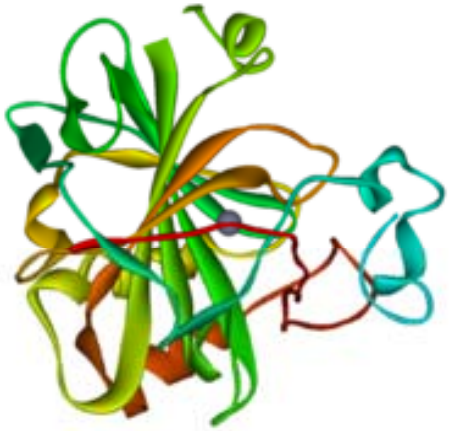
$$\Delta G = -2{,}840 \text{ kJ/mol}$$

- Es una reacción exergónica
- ¿Por qué razón el azúcar no se hace agua y CO_2 en la alacena?



Introducción a las enzimas

A. Las enzimas son mayormente proteínas.
B. La actividad enzimática fue descubierta por Eduard Buchner en la Universidad de Berlin (1897) – fermentación de azúcares sin células.
C. James Sumner (Cornell, 1926) – determinó que la enzima ureasa era una proteína



Anhidrasa Carbónica –
Convierte CO_2 en bicarbonato

$$CO_2 + H_2O \rightarrow^{\text{Carbonic anhydrase}} HCO_3^- + H^+$$

Enzyme Clasification

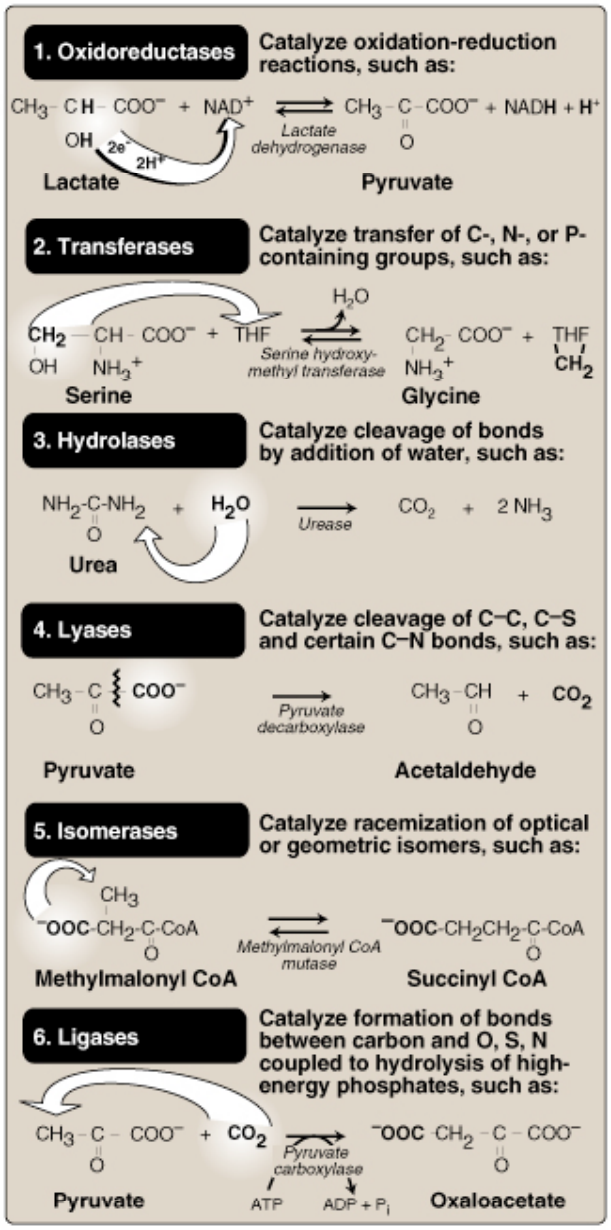
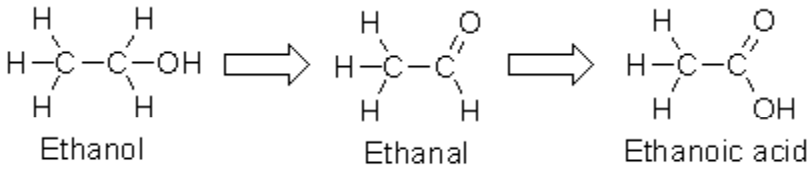
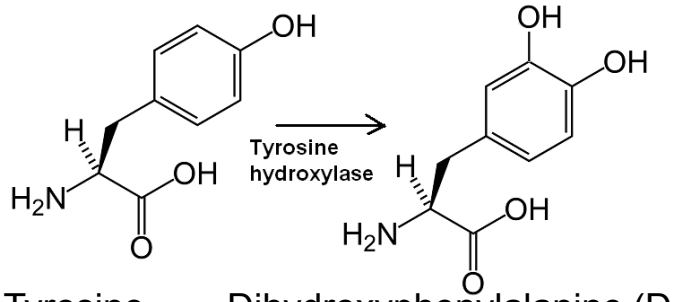


Figure 5.1
Examples of the six major classes of the international classification of enzymes (THF is tetrahydrofolate).

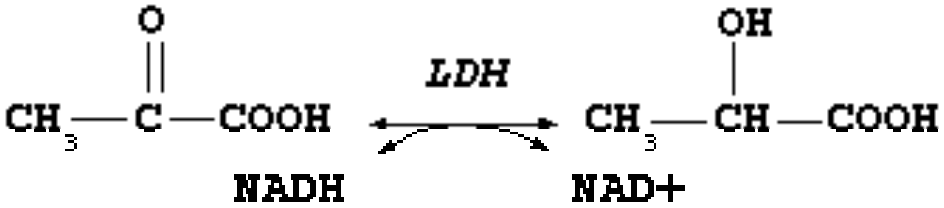


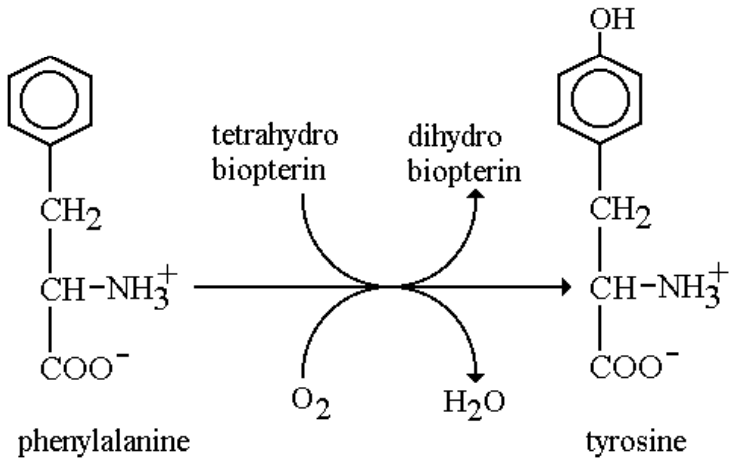
1. Oxidoreductase activity

Requires NAD/NADP or FAD/FMN for electron transfers



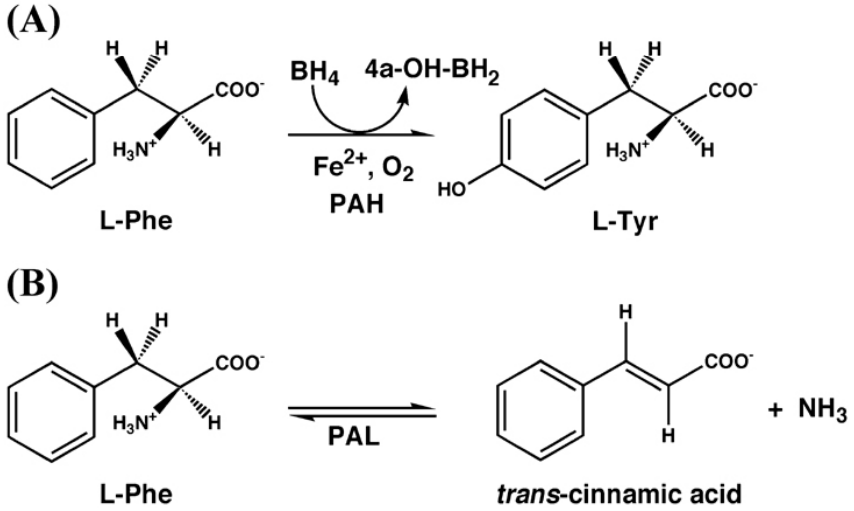
Tyrosine Dihydroxyphenylalanine (DOPA)





Phenylkenouria (1:16,000)

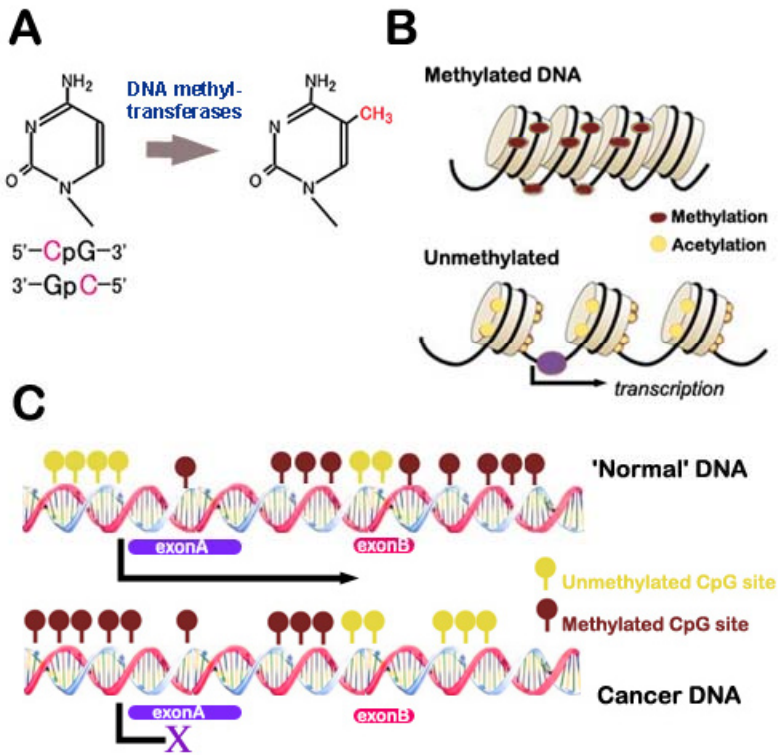
-Deficiency of Phenylalanine Hydroxylase (PAH) – (**in liver**)
-Current treatment consists of diet modification and tetrahydrobiopterin supplementation
-Enzyme replacement therapy is being explored as an alternative Treatment.



Cinnamic acid converted to benzoic acid and excreted in urine as hippurate.

- However, PAH has been found to be highly immunogenic
- PAL is a plant enzyme which has been found to lower plasma Phe

2. Transferase activity



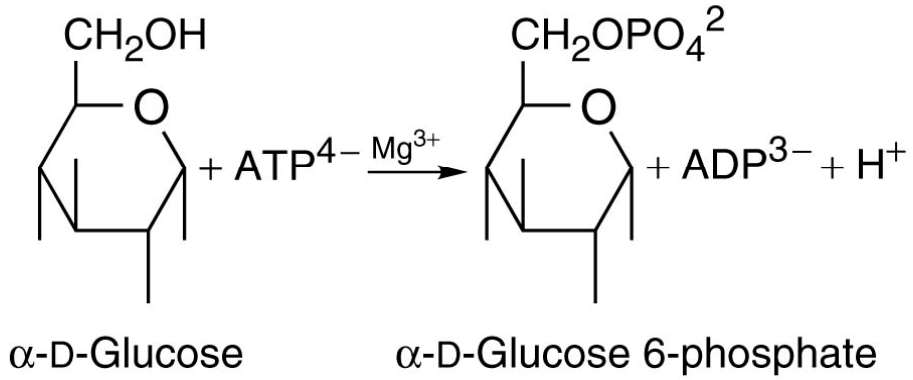
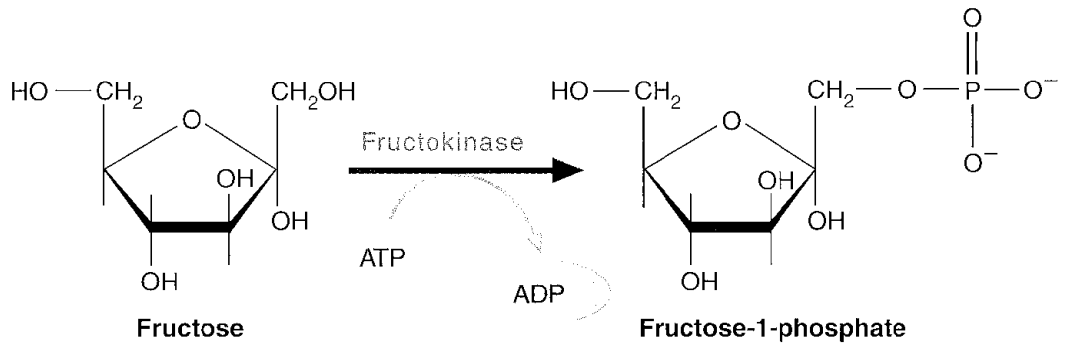


Figure 10.2. Phosphorylation reaction.

2. Transferase activity – Fructokinase (in **liver**)



Combined with aldolase B catalyze the formation of glycogen from fructose

Fructokinase deficiency results in **Frustosuria**, a rare but benign inherited disorder.

Diagnosed through detection of abnormal excretion of fructose in urine

2. Transferase activity – Galactose-1-phosphate uridyl transferase deficiency

This deficiency causes classic **galactosemia**.

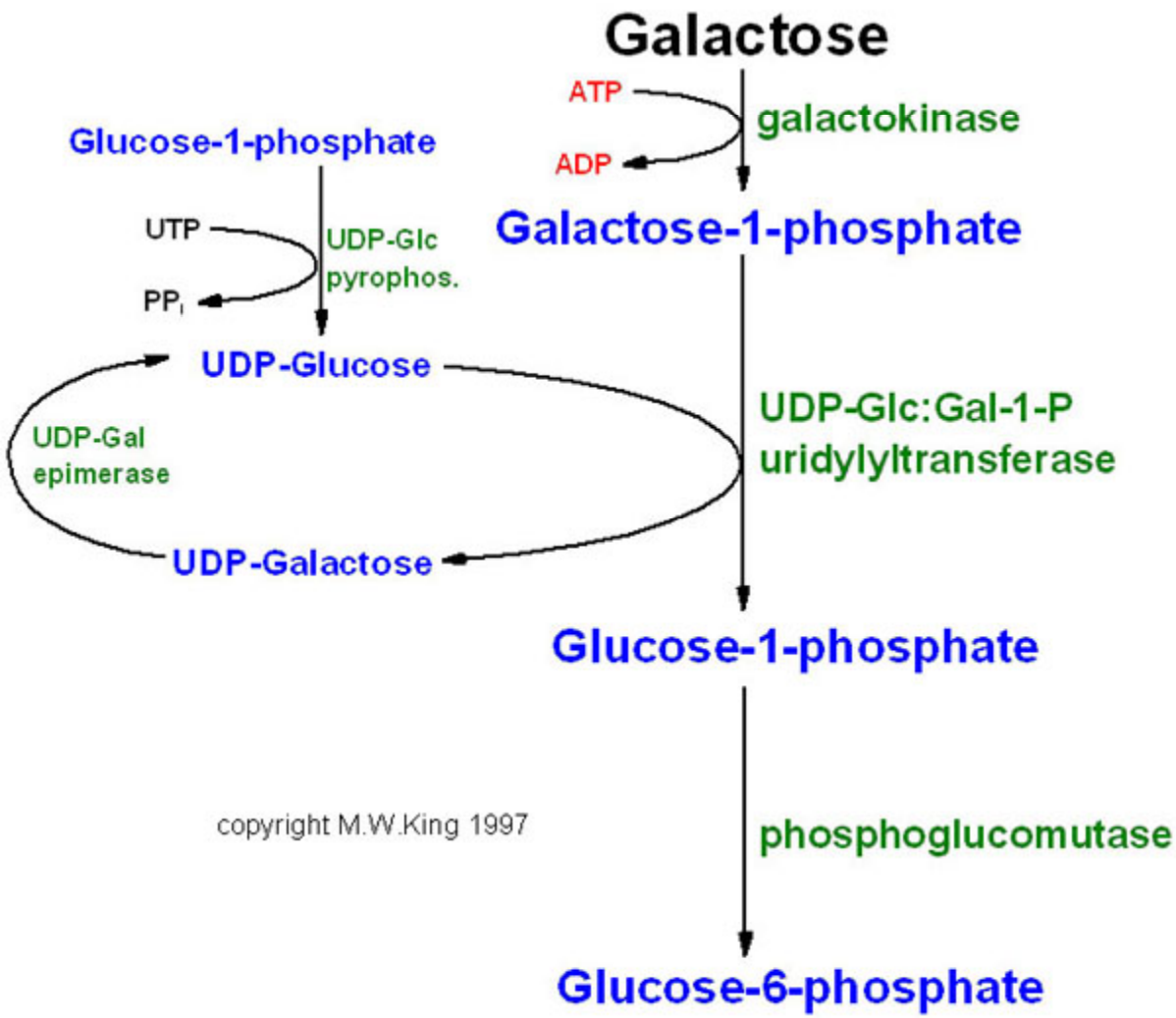
Incidence is 1/62,000 births; carrier frequency is 1/125.

Infants become anorexic and jaundiced within a few days or weeks of consuming breast milk or lactose-containing formula.

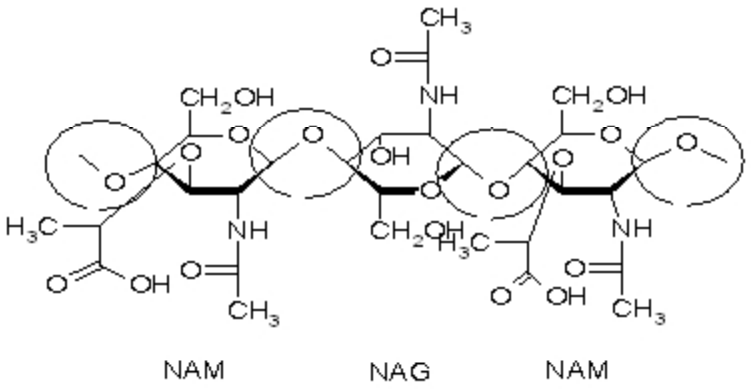
Vomiting, hepatomegaly, poor growth, lethargy, diarrhea, and septicemia (usually Escherichia coli) develop, as does renal dysfunction (eg, proteinuria, aminoaciduria, Fanconi syndrome), leading to metabolic acidosis and edema.

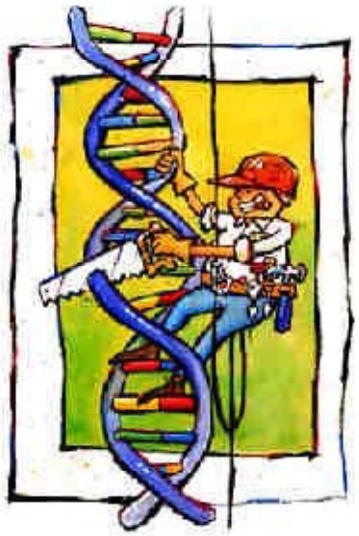
Hemolytic anemia may also occur. Without treatment, children remain short and develop cognitive, speech, gait, and balance deficits in their teenage years; many also have cataracts, osteomalacia (caused by hypercalciuria), and premature ovarian failure.

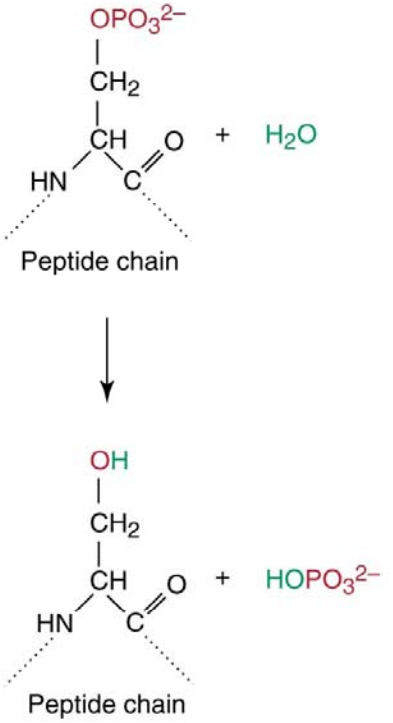
2. Transferase activity – Galactose-1-phosphate uridyl transferase deficiency



3. Hydrolase activity







5. Hydrolysis of a phosphorylated protein by a prote

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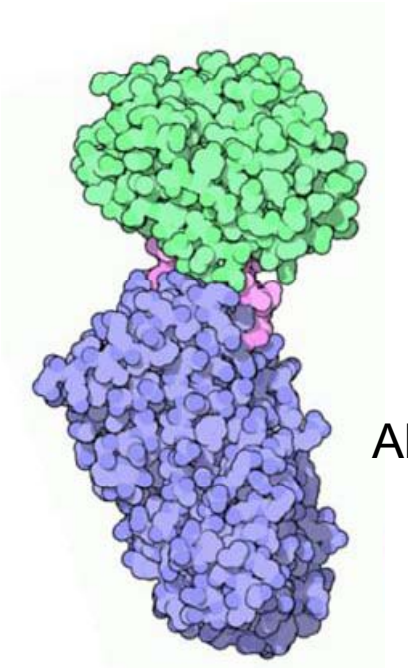
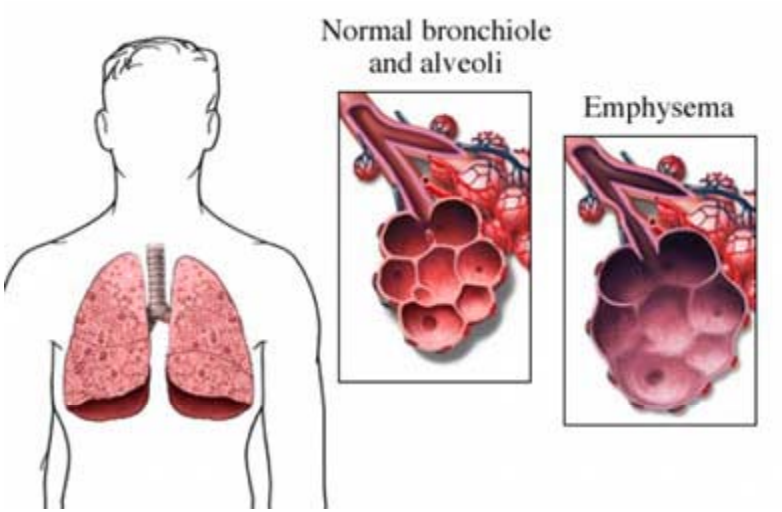
3. Hydrolase activity

Alpha-1-Antitrypsin is a protease inhibitor which regulates the elasticity In lung tissue



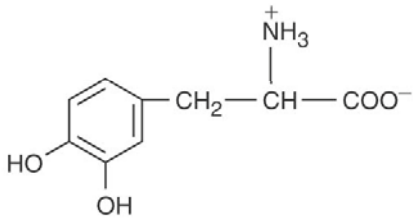
Trypsin

Alpha-1 AT

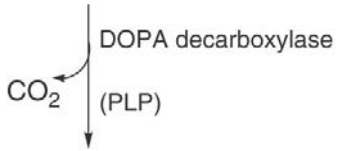


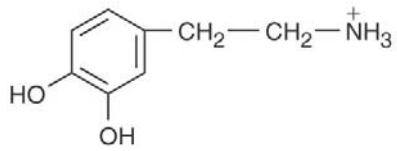
Alpha-1-Antitrypsin deficiency causes emphysema, COPD, and cirrhosis in Children.

4. Lyase activity



3,4-Dihydroxyphenylalanine (DOPA)





Dopamine

gure 10.7. Dopamine synthesis involves a lyase reac

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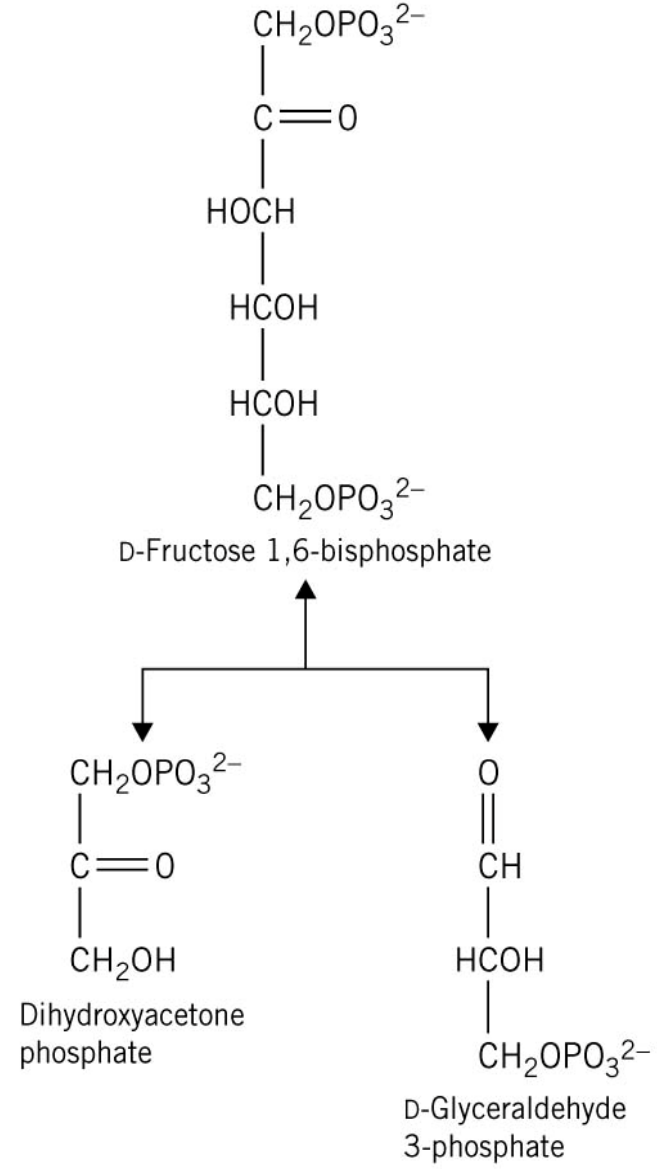

Figure 10.6. Lyase reaction catalyzed by aldolas

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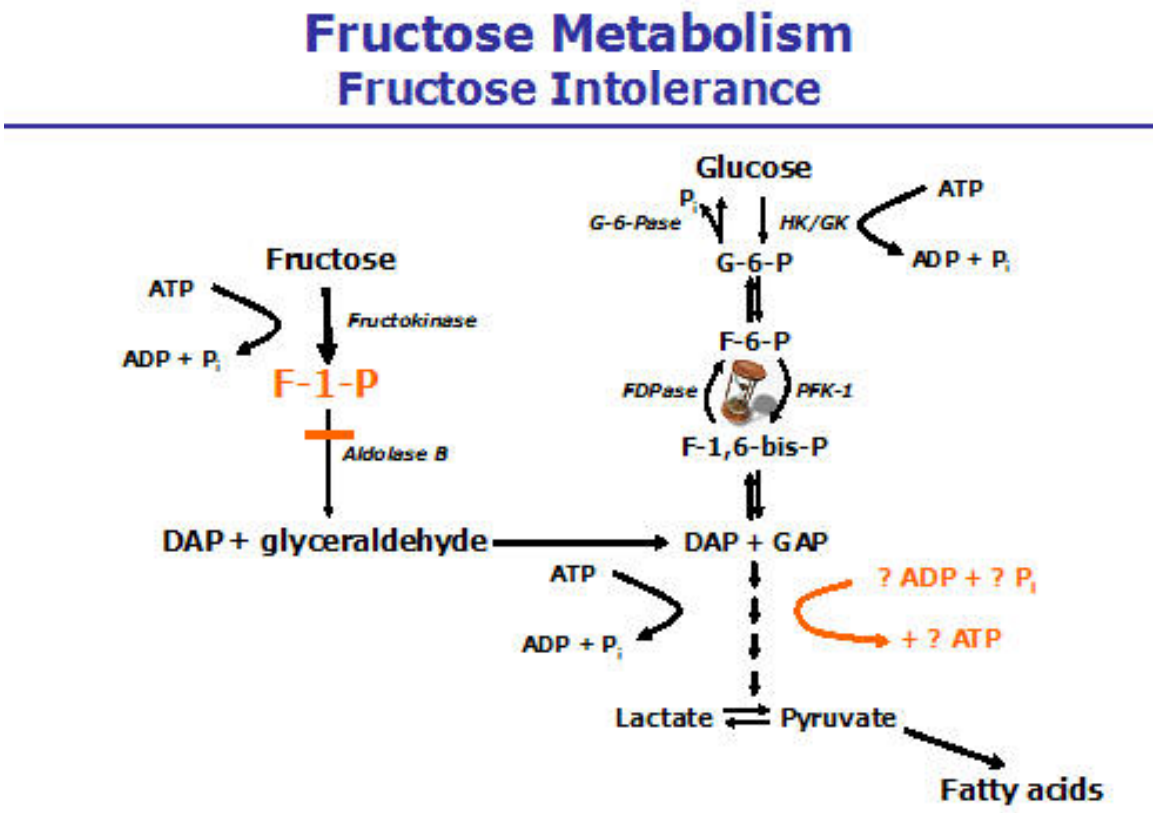
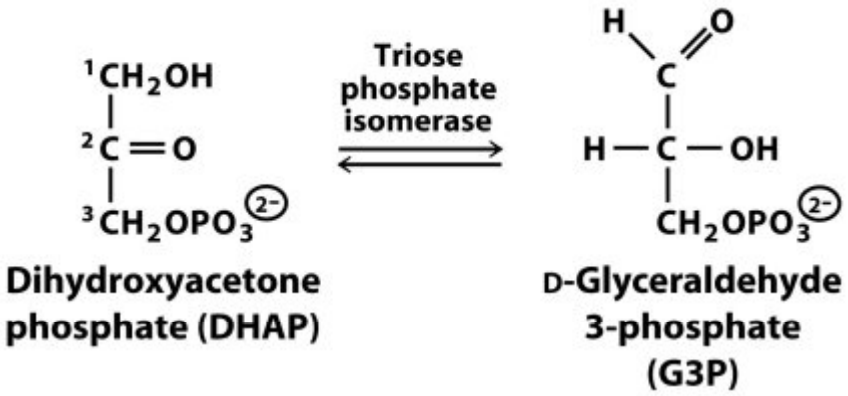
4. Lyase activity

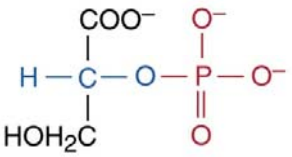
A defect in aldolase B causes Hereditary Fructose Intolerance

Accumulation of F-1-P leads to the inhibition of glycogen breakdown.



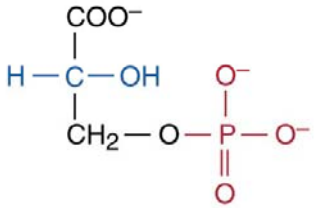
5.Isomerase activity





2-Phosphoglycerate

phosphoglyceromutase



3-Phosphoglycerate

Figure 10.8. Interconversion of 2- and 3-phosphoglycer

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6. Ligase activity

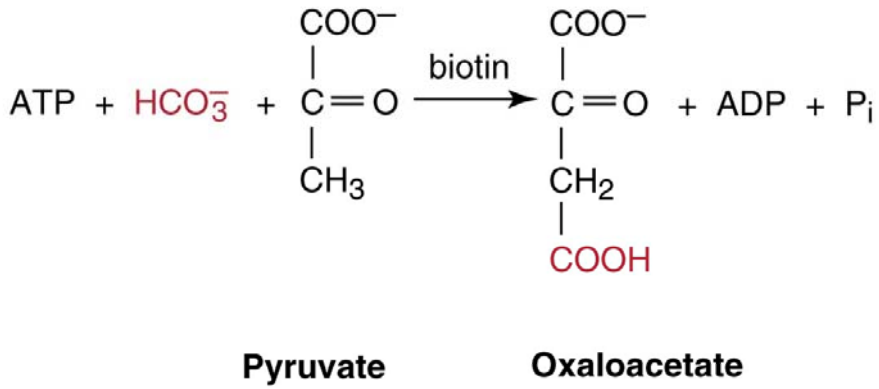
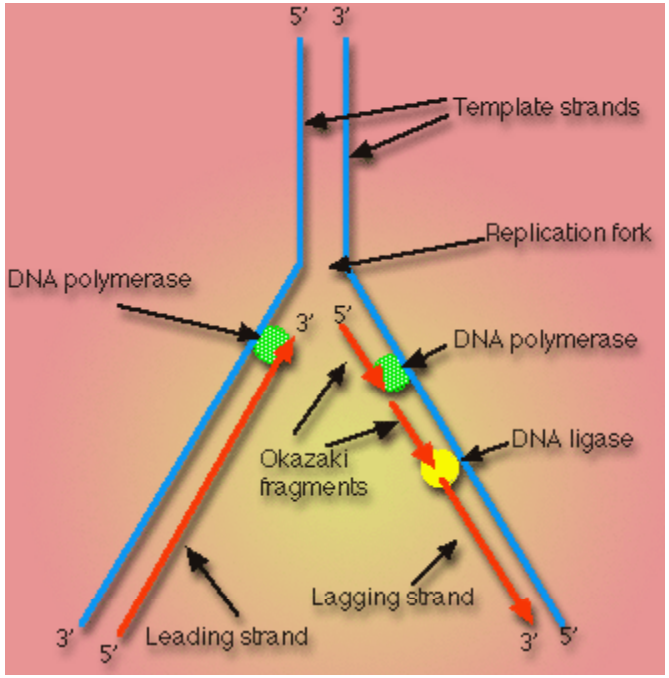


Figure 10.10. Pyruvate carboxylase reaction.



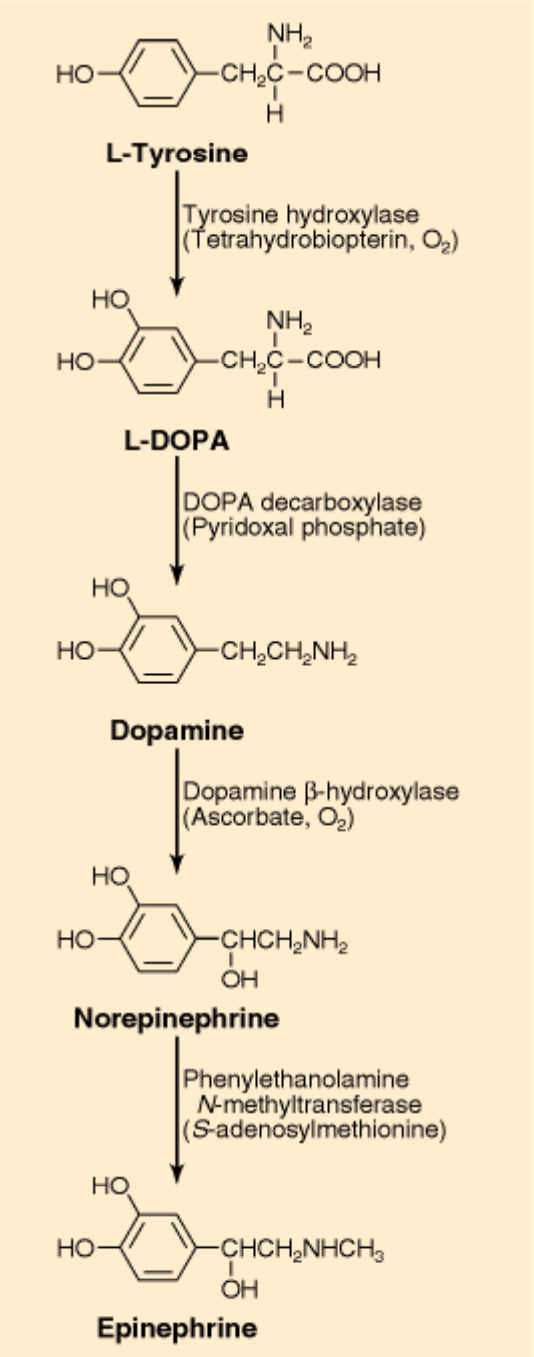
Biosynthetic pathways show a wide array of activities.

The conversion of dopamine to adrenaline involves four enzyme-catalyzed reactions

Tyrosine hydroxylase is the rate limiting step In the pathway.

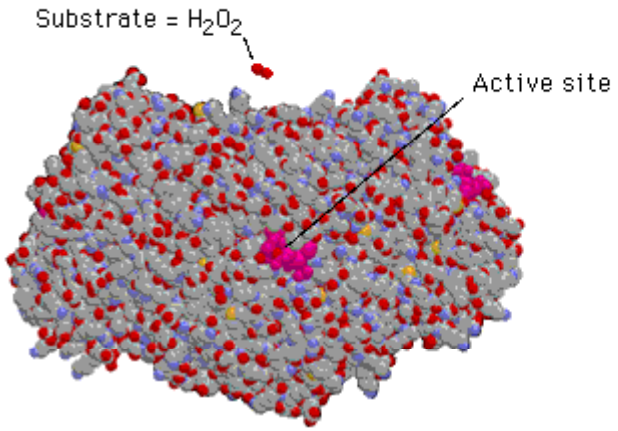
Tyrosine hydroxylase deficiency is a rare genetic disorder which results in impaired production of catecholamines.

Patients can be supplemented with L-DOPA

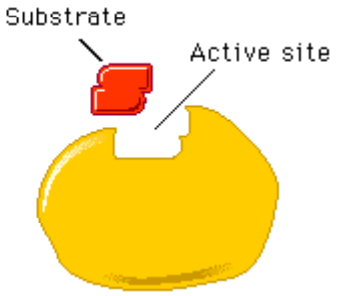


Introducción a las enzimas

A. Sitio activo
B. Especificidad exquisita
C. Algunas requieren cofactores
D. Aceleran reacciones que serían muy lentas sin catálisis.



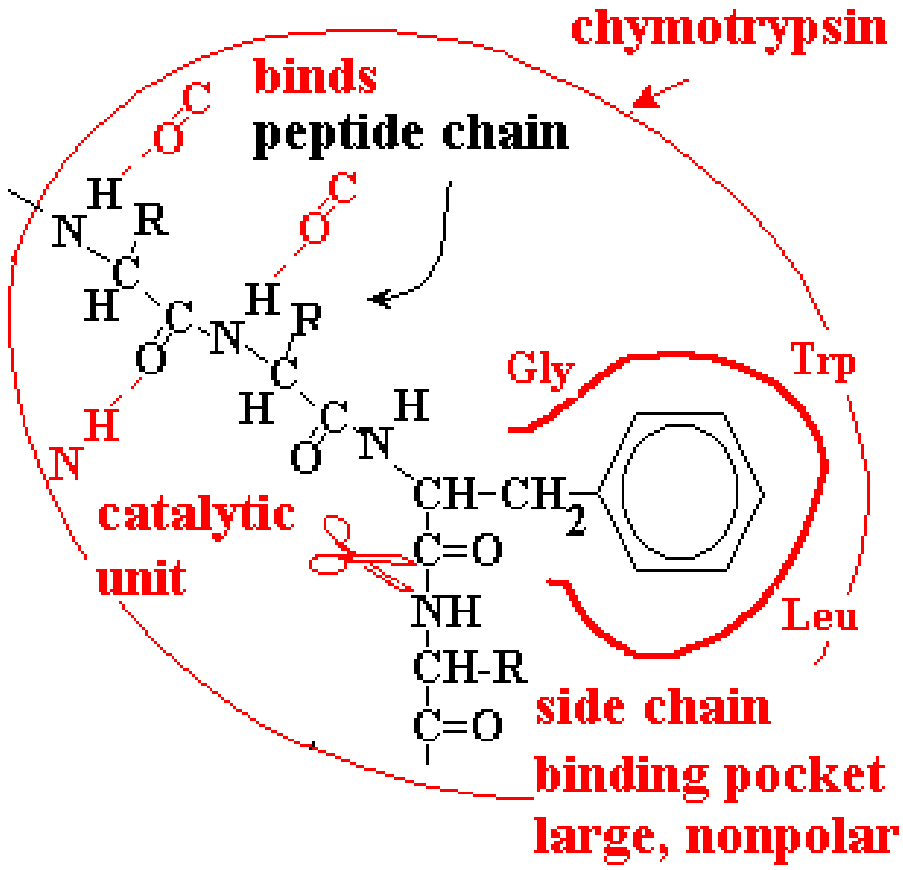
Molecular model of catalase



Schematic model of an enzyme

Substrate Specifictiy

Chymostrypsin:



Substrate Specifictiy

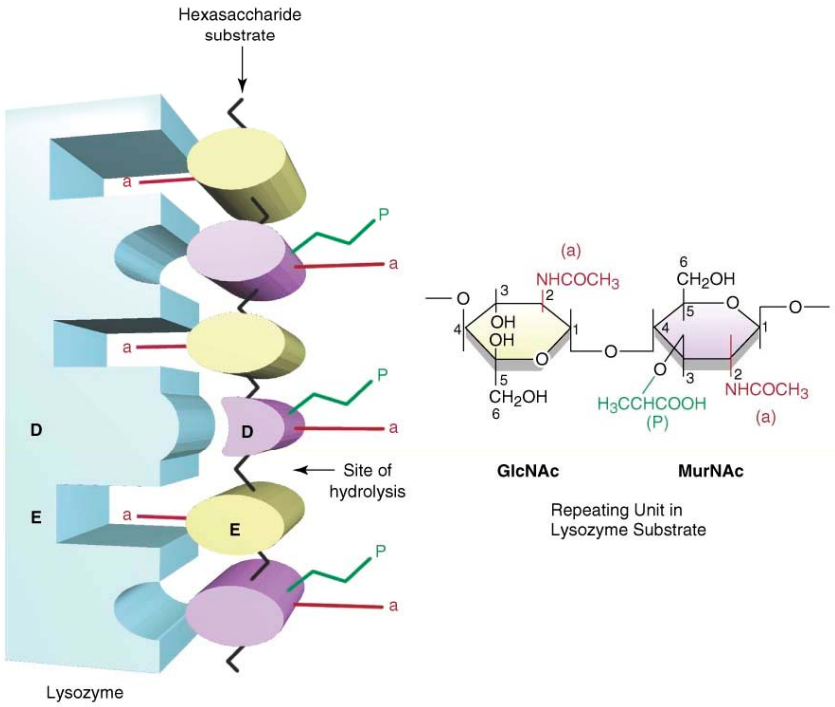


Figure 10.27. Hexasaccharide binding at active site of lysozyme. Redrawn based on model proposed by Imoto, T., et al. In: P. Boyer (Ed.), *The Enzymes*, Vol. 7, 3rd ed.NewYork: Academic Press, 1972, p. 713.

Stereoselectivity

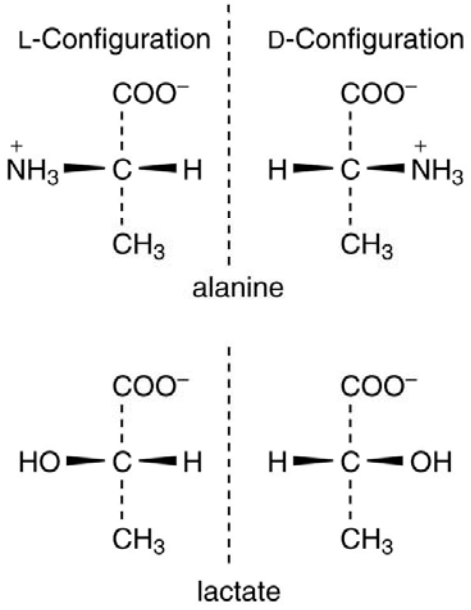
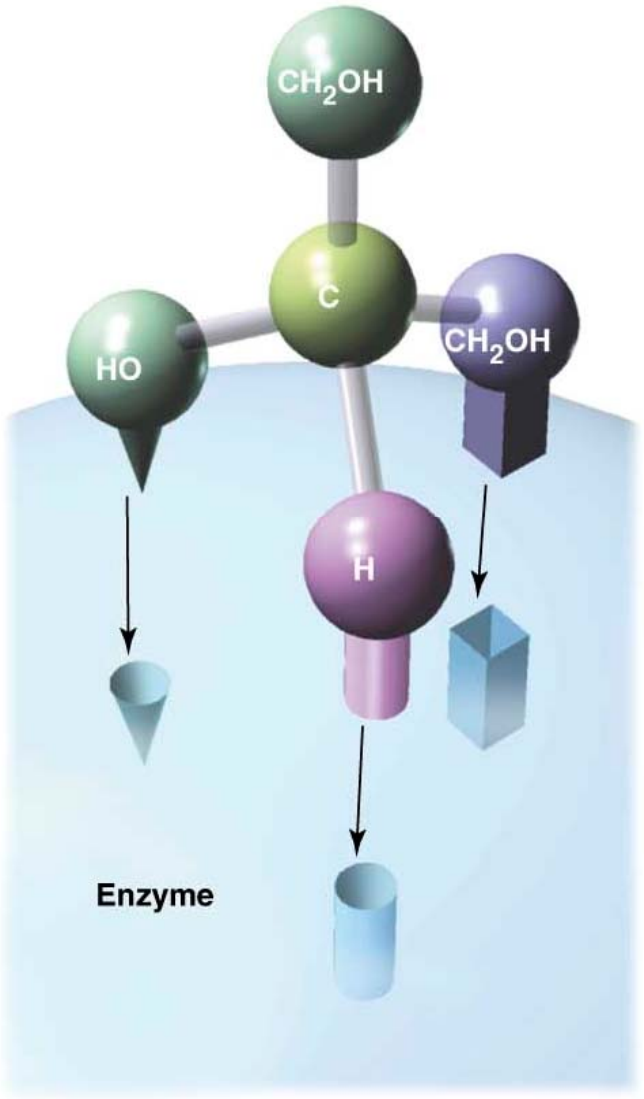


Figure 10.25. Enzymes can differentiate between optical isomers.



achment of a symmetrical substrate to an as

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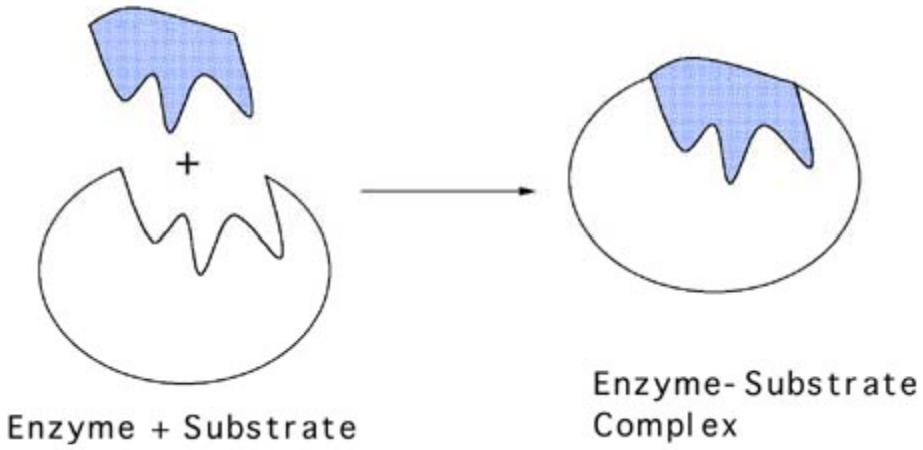
Models for substrate recognition



"Lock and Key"
(Fischer, 1894)

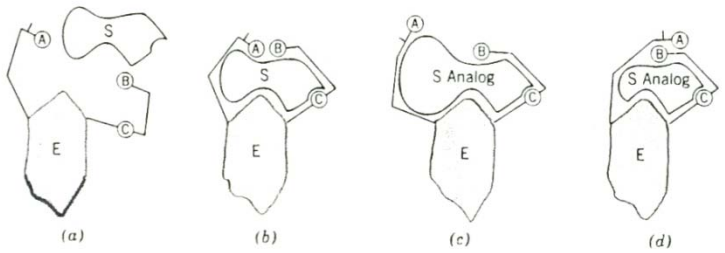
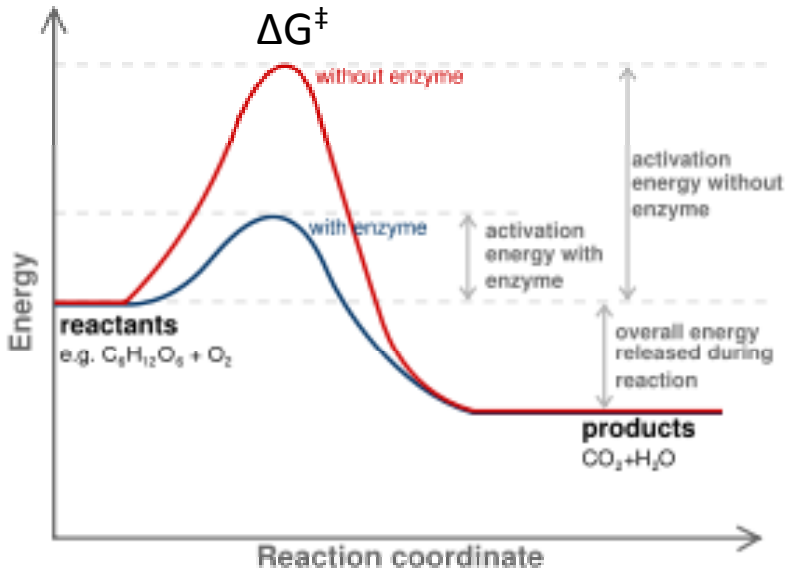


Figure 4-3 Induced-fit hypothesis of Koshland. (*a*) The substrate approaches the active site. (*b*) Substrate binding induces the proper alignment of the catalytic groups, A and B. (*c*) and (*d*) Substrate analogs (competitive inhibitors) bind to the enzyme (aided by group C) but the catalytic groups are not aligned properly. [Redrawn from D. E. Koshland, Jr., *Cold Spring Harbor Symposia on Quantitative Biology*, **28**, 473 (1963).]

"Induced Fit"
(Koshland, 1958)

¿Cómo funcionan las enzimas?

ΔG



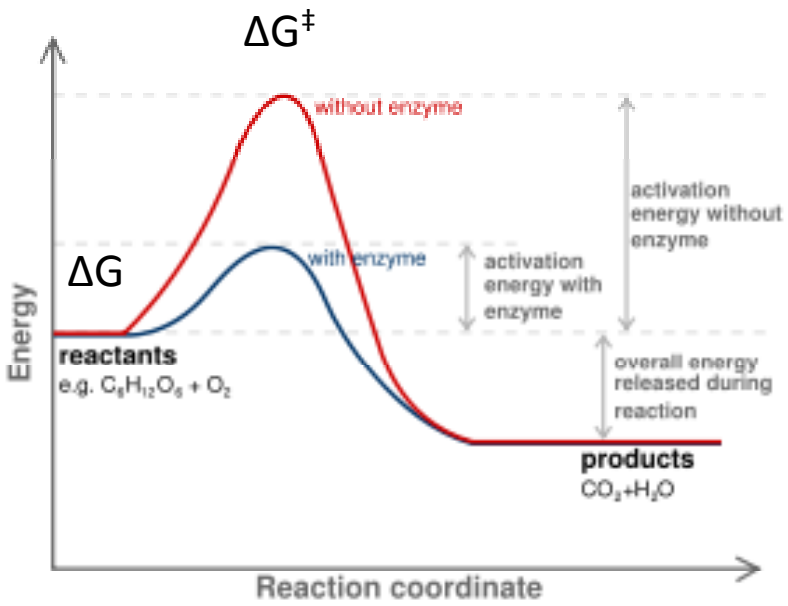
Las enzimas reducen la barrera de activación de las reacciones.

Estabilizan el estado de transición

Estado de transición: inestable y fugaz

No afectan las concentraciones en equilibrio

Kinetics vs. Thermodynamics



Thermodynamics – Total energy involved in a reaction

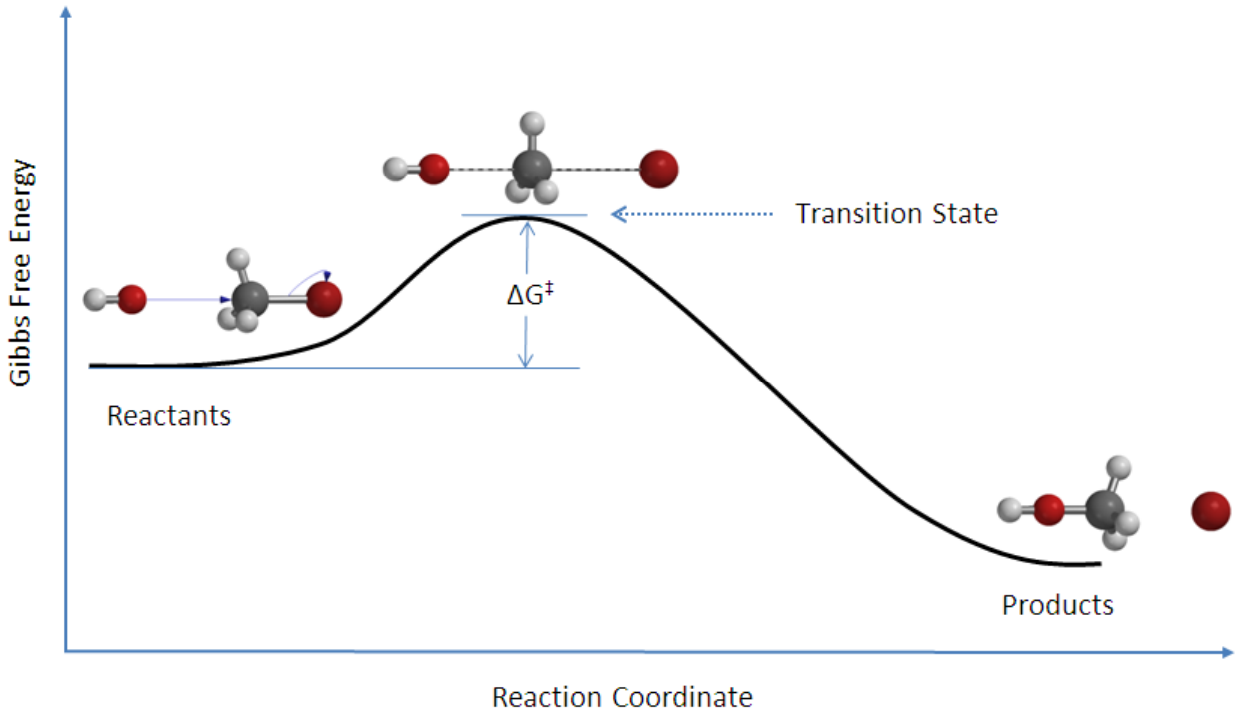
$$\Delta G = \Delta G^o + RT \ln Q$$

$$\Delta G^o = \Delta H^o - T\Delta S^o = -RT \ln K_{eq}$$

Kinetics – How quickly does a reaction reach equilibrium

$$k = Ae^{(-\Delta G‡/RT)}$$

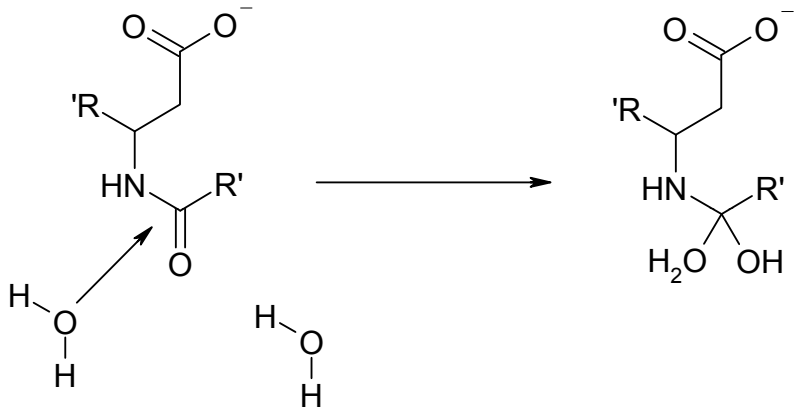
Transition state theory: “Every reaction has a transition state”



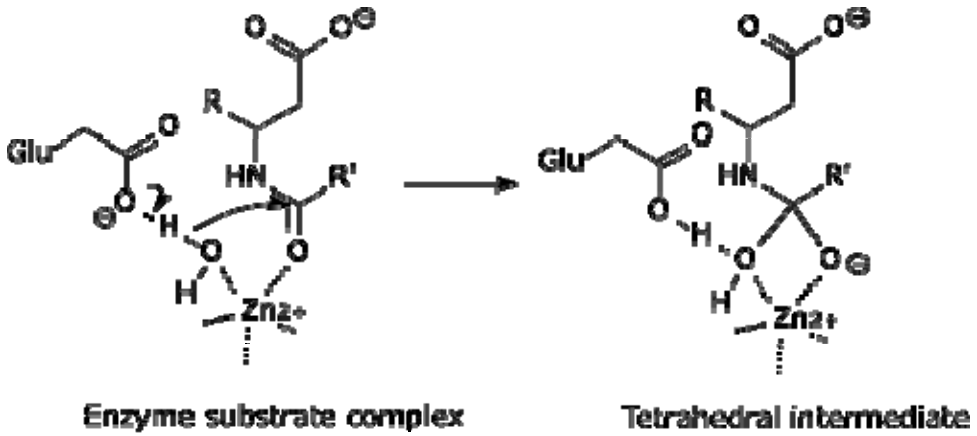
Reaction: $HO^- + CH_3Br \rightarrow [HO{-}{-}{-}CH_3{-}{-}{-}Br]^‡ \rightarrow CH_3OH + Br^-$

¿Cómo funcionan las enzimas?

No enzyme



Carboxypeptidase



ΔH of binding is maximal in the transition state

ΔS is less unfavorable
-orientational entropy
-desolvation

The decrease of unfavorable entropy of reaction results in:

Increased rates of reaction!

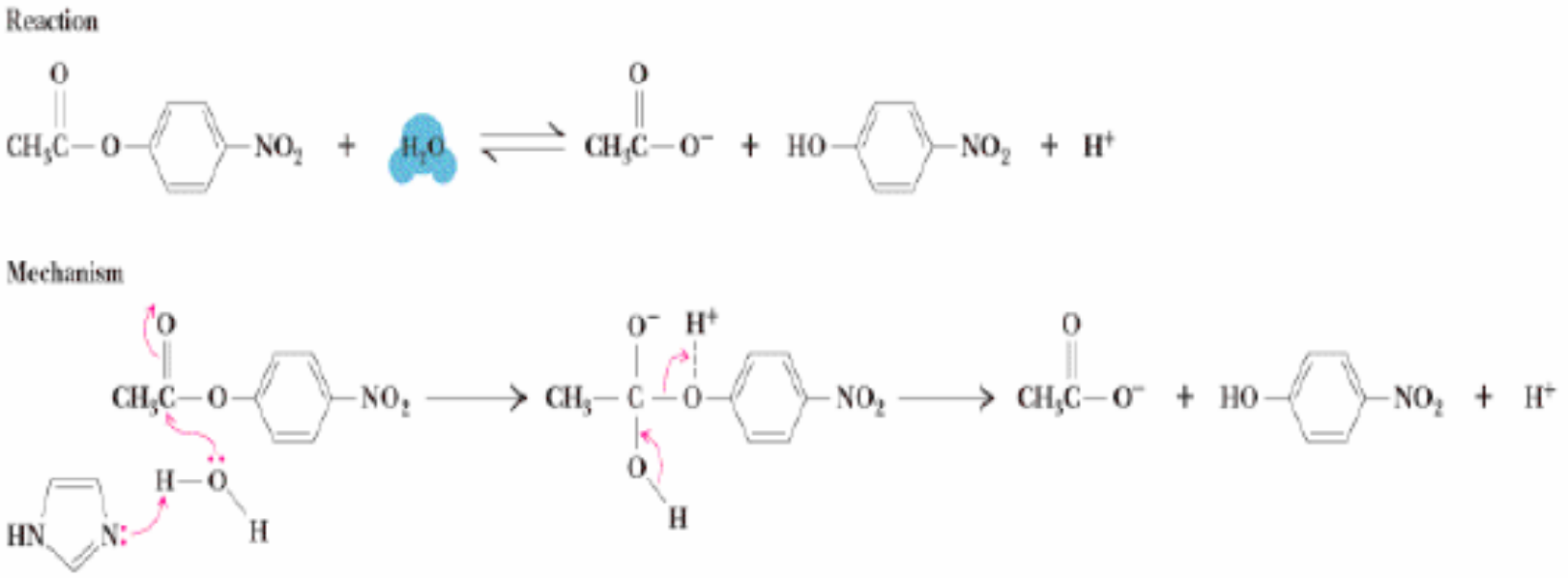
Types of Enzyme-catalyzed Reactions

Acid-Base Catalysis

Covalent Catalysis

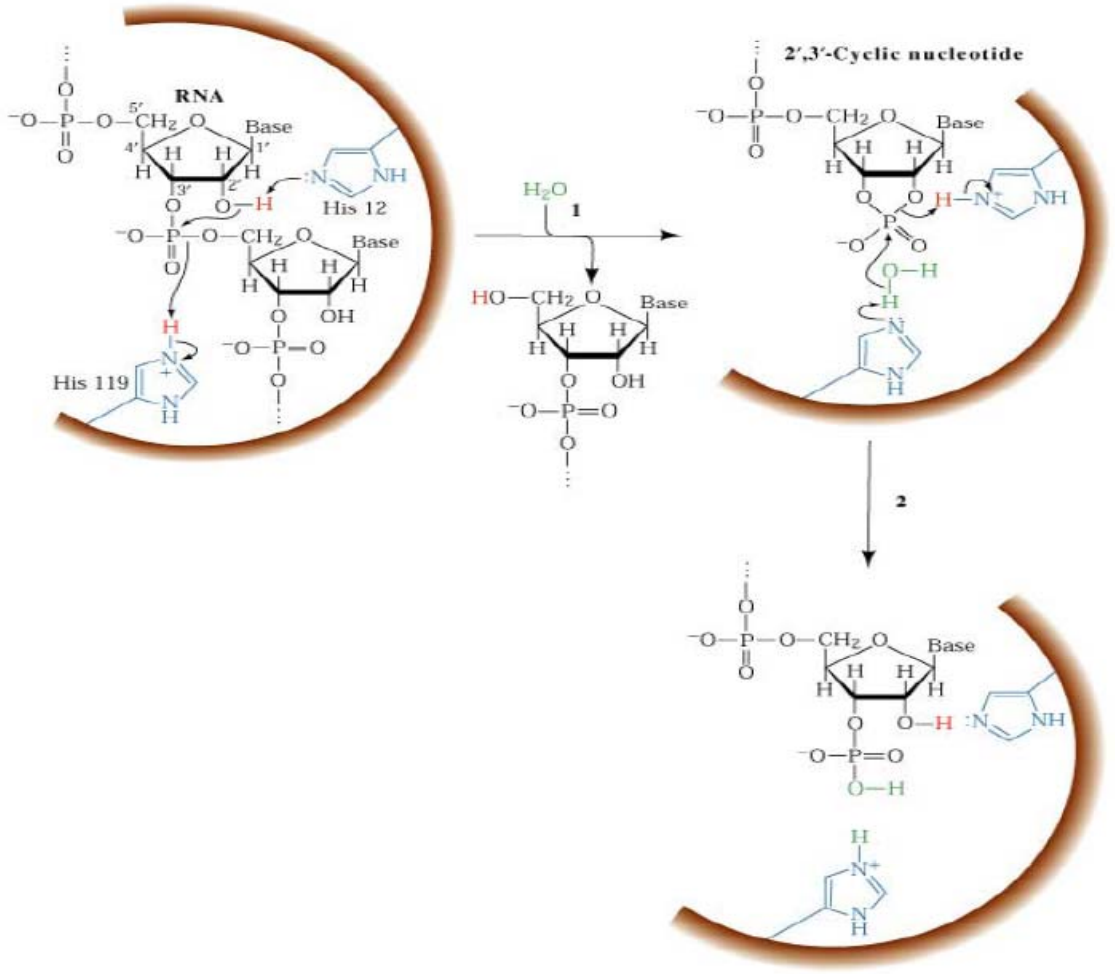
Metal Ion Catalysis

Acid-Base Catalysis

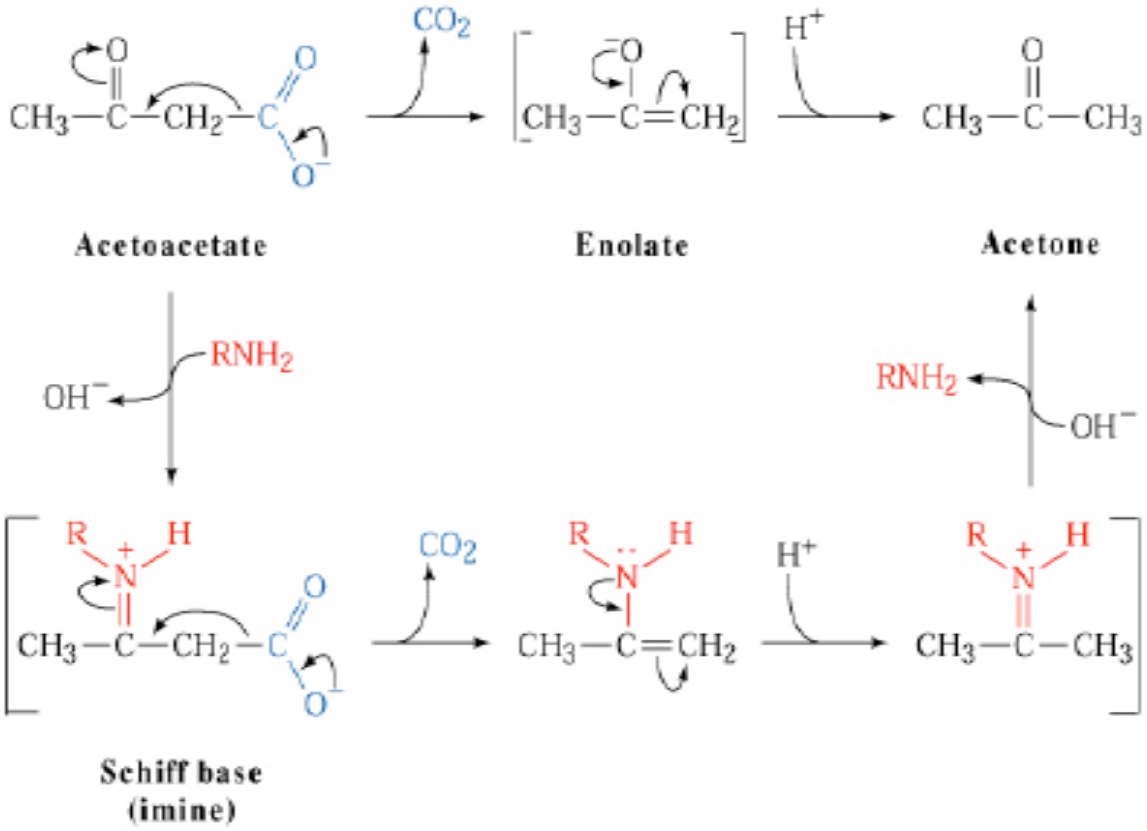


Garrett and Grisham: Biochemistry 2/e

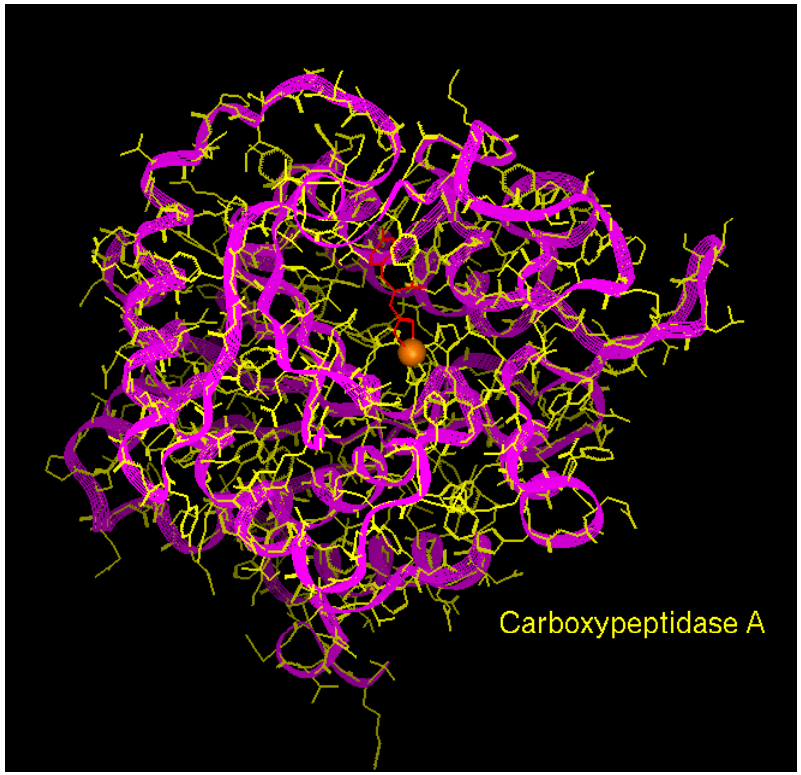
Acid-Base Catalysis

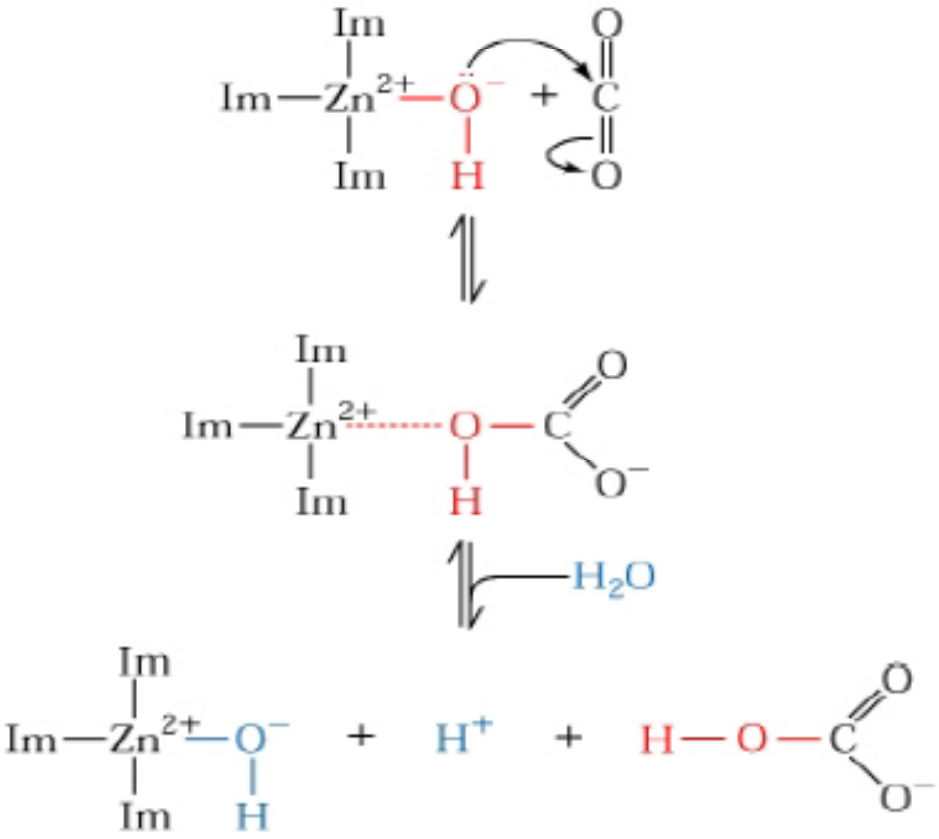


Covalent Catalysis



Metal Ion Catalysis





Im = imidazole

COFACTORES: forman parte del sitio activo y se regeneran con cada ciclo catalítico. Disociables reversiblemente de la enzima.

GRUPOS PROSTÉTICOS: cofactores no disociables que forman parte estable del sitio activo.

COENZIMAS: representan en realidad sustratos que pueden o no modificarse en la reacción y suelen ser regenerados mediante reacciones alternas.

APOENZIMA
HOLOENZIMA
ZIMÓGENO (proenzima)
ISO(EN)ZIMA

Enzyme Cofactors: inorganic

TABLE 6–1 Some Inorganic Elements That Serve as Cofactors for Enzymes

Cu^{2+}	Cytochrome oxidase
Fe^{2+} or Fe^{3+}	Cytochrome oxidase, catalase, peroxidase
K^{+}	Pyruvate kinase
Mg^{2+}	Hexokinase, glucose 6-phosphatase, pyruvate kinase
Mn^{2+}	Arginase, ribonucleotide reductase
Mo	Dinitrogenase
Ni^{2+}	Urease
Se	Glutathione peroxidase
Zn^{2+}	Carbonic anhydrase, alcohol dehydrogenase, carboxypeptidases A and B

Enzyme Cofactors: organic

TABLE 6–2 Some Coenzymes That Serve as Transient Carriers of Specific Atoms or Functional Groups

Coenzyme	*Examples of chemical groups transferred*	*Dietary precursor in mammals*
Biocytin	CO_2	Biotin
Coenzyme A	Acyl groups	Pantothenic acid and other compounds
5′-Deoxyadenosylcobalamin (coenzyme B_{12})	H atoms and alkyl groups	Vitamin B_{12}
Flavin adenine dinucleotide	Electrons	Riboflavin (vitamin B_2)
Lipoate	Electrons and acyl groups	Not required in diet
Nicotinamide adenine dinucleotide	Hydride ion ($:H^-$)	Nicotinic acid (niacin)
Pyridoxal phosphate	Amino groups	Pyridoxine (vitamin B_6)
Tetrahydrofolate	One-carbon groups	Folate
Thiamine pyrophosphate	Aldehydes	Thiamine (vitamin B_1)

Note: The structures and modes of action of these coenzymes are described in Part II.

Electron Donors Acceptors

NAD - NADP

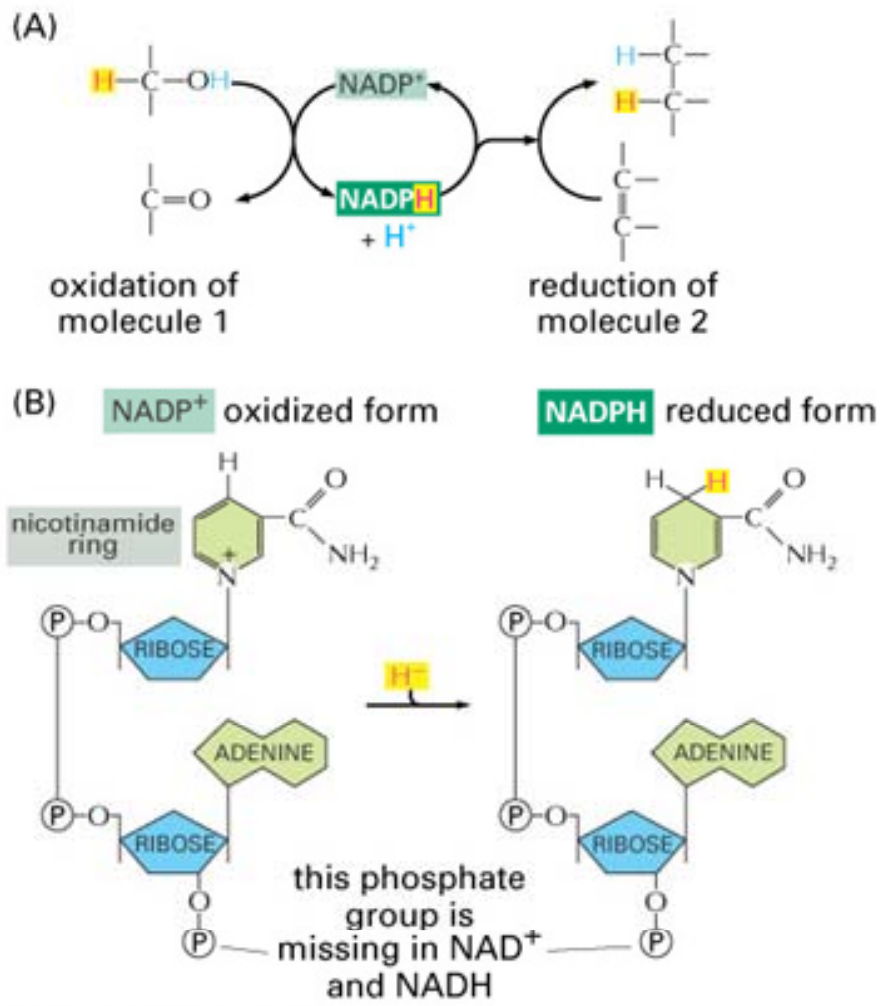
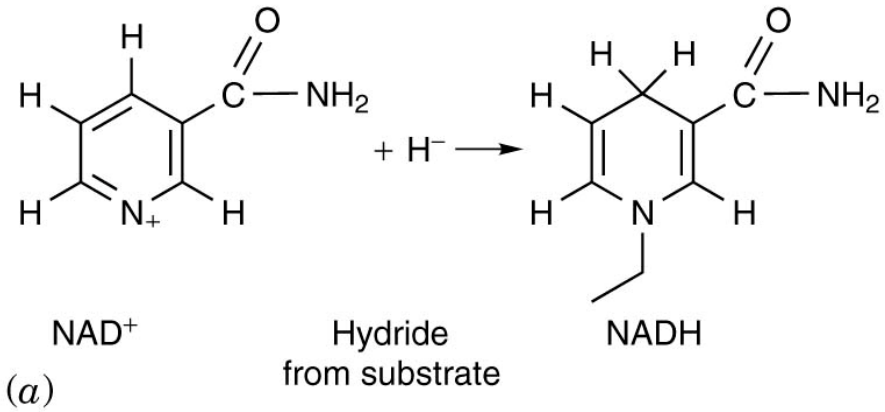


Figure 3-35 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Electron Donors-Acceptors

Nicotinamides



Electron donor or acceptor

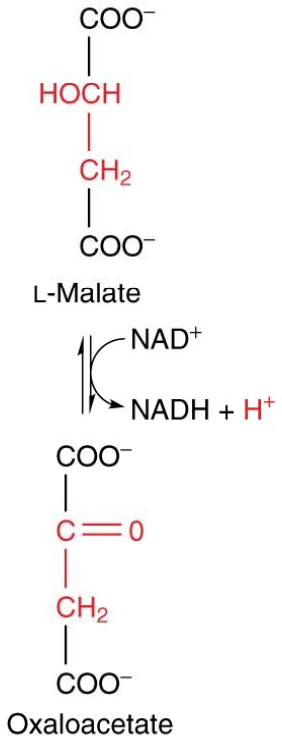
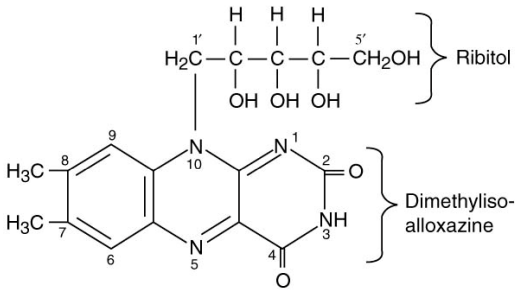


Figure 10.29. Reaction catalyzed by malate dehydrogenase.

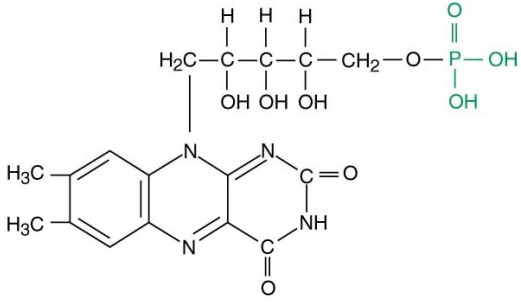
With Clinical Correlations, Sixth Edition, Edited by Thomas M. Devlin. Copyright © 200

Electron Donors-Acceptors

Flavins

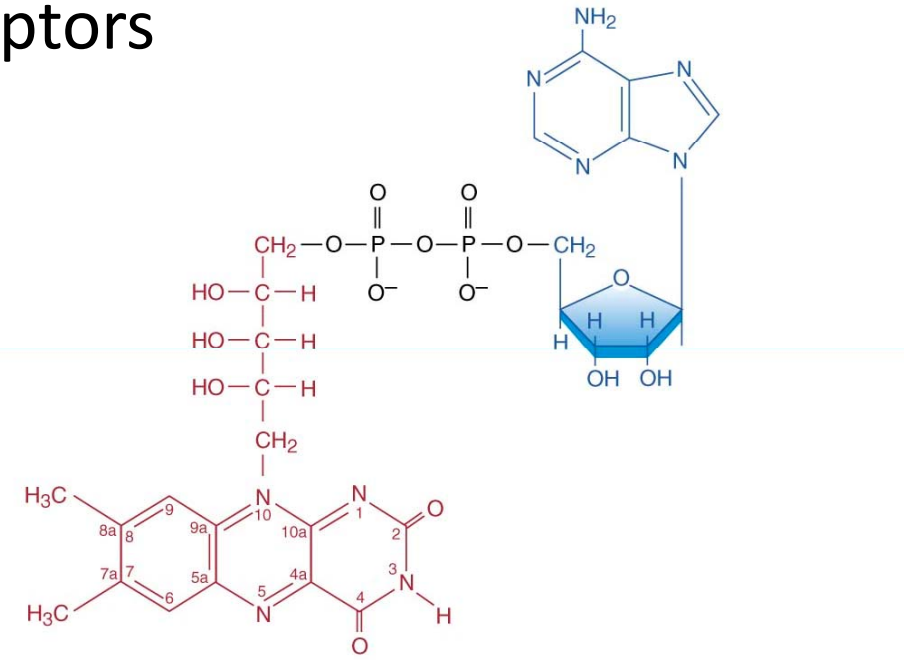


Riboflavin



Flavin mononucleotide (FMN)

Figure 10.32. Riboflavin and flavin mononucleotide.



Flavin adenine dinucleotide (FAD)

Figure 10.33. Flavin adenine dinucleotide (FAD).

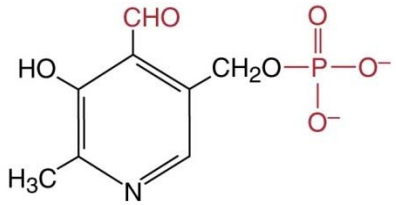
- 2-electron donors
- monoamino oxidase (MAO) – oxidizes serotonin and dopamine
- glutathione reductase

Amino Donors-Acceptors

Vitamine B6 – pyridoxine

Involved in amino acid reactions

Amino transferases – tranfers amino groups from one amino acid to the next



Pyridoxal phosphate

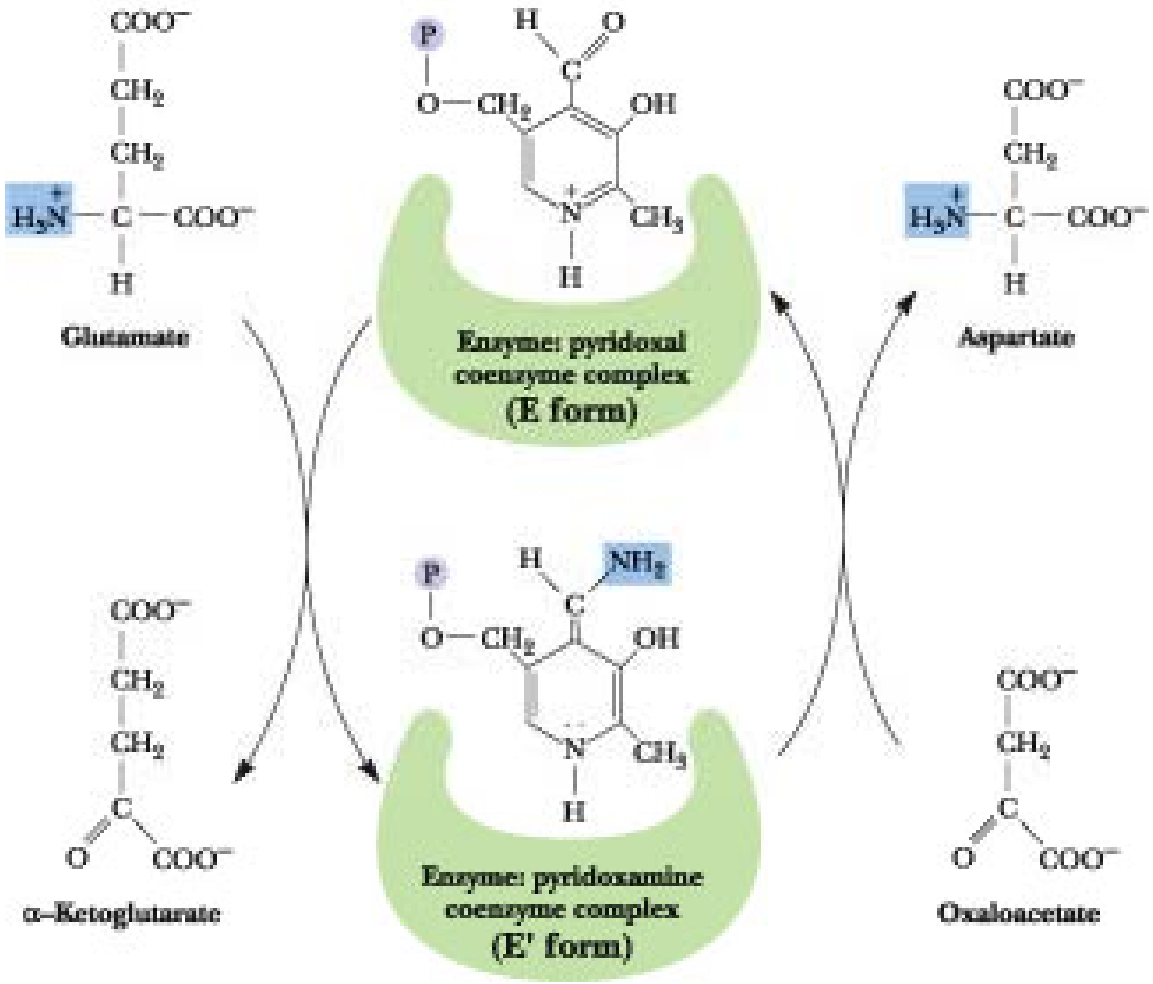
Figure 10.35. Pyridoxal phosphate.

Amino Donors-Acceptors

Vitamine B6 – pyridoxine

Involved in amino acid reactions

Amino transferases – tranfers amino groups from one amino acid to the next

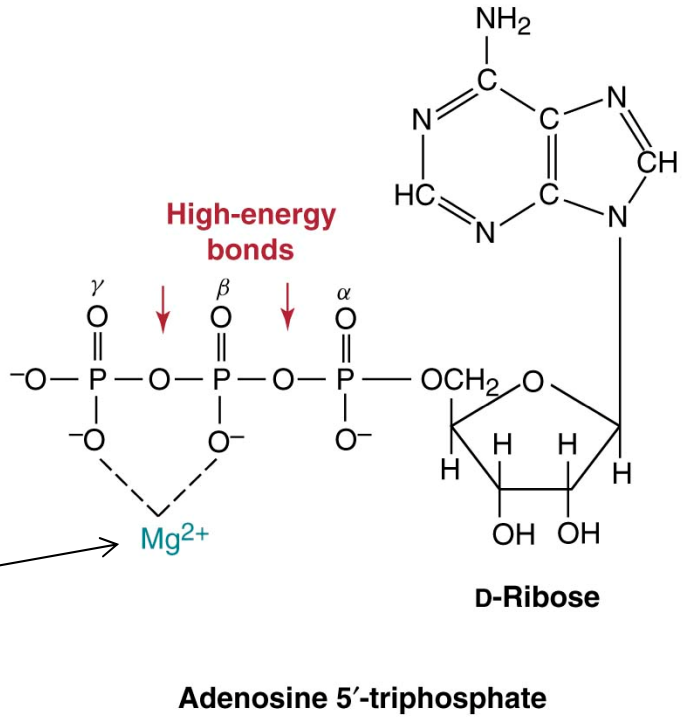


Phosphate Donors-Acceptors

ATP

Phosphate transfer reactions

Kinases



Metal ion

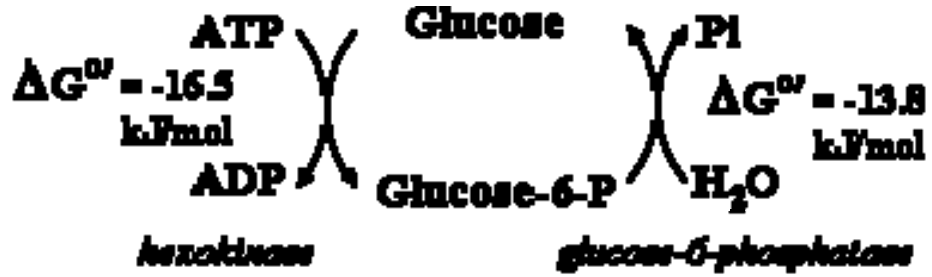
Figure 10.36. Structure of Mg^{2+}-ATP.

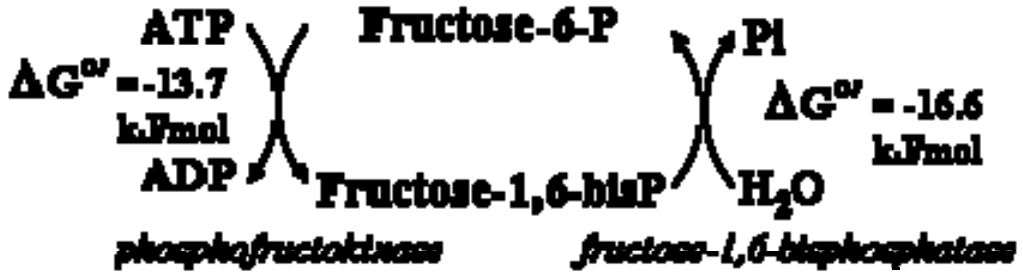
Phosphate Donors-Acceptors

ATP

Phosphate transfer reactions

Kinases





Metal Ions

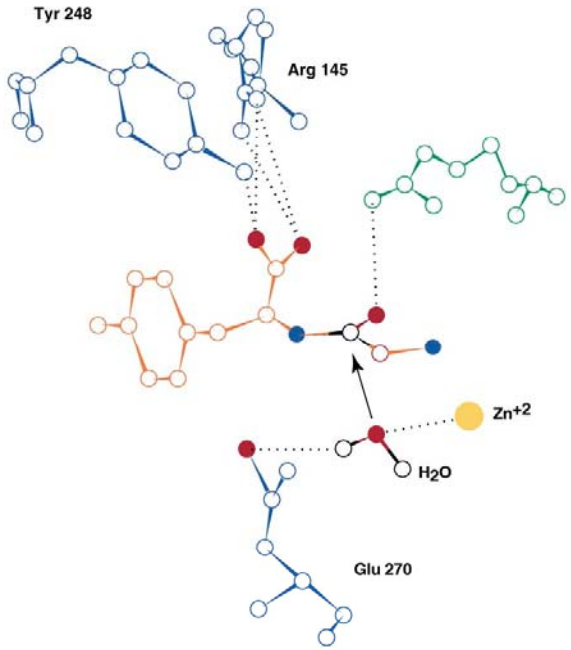


Figure 10.40. Zn^{2+} in the mechanism of reaction of carboxypeptidase A.

Metal ions:

-Structural role
- Lewis acids – binding unpaired electrons
- Directly as electron donors-acceptors

Enzyme Kinetics

Maud Menten

- PhD Universidad de Berlin 1916 con Leonor Michaelis
- El primer modelo conceptual cuantitativo de actividad enzimática.

Enzyme Kinetics

$$\text{Rate} = \frac{d[\text{product}]}{dt}$$

1 Enzyme Unit = amount of enzyme for v_o = 1 μmol/min

First Order	$A \rightarrow P$	$v = k[A]$
Second Order	$2A \rightarrow P$	$v = k[A]^2$
Second Order	$A + B \rightarrow P$	$v = k[A]\,[B]$

Pseudo-first order- one of the reactants is in huge excess
e.g. hydrolysis

Enzyme Kinetics

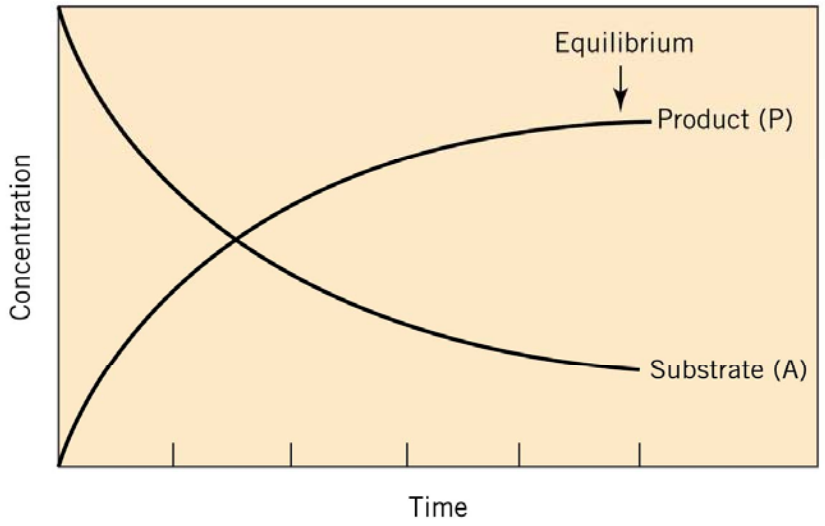


Figure 10.44. Plot of substrate disappearance and product formation.

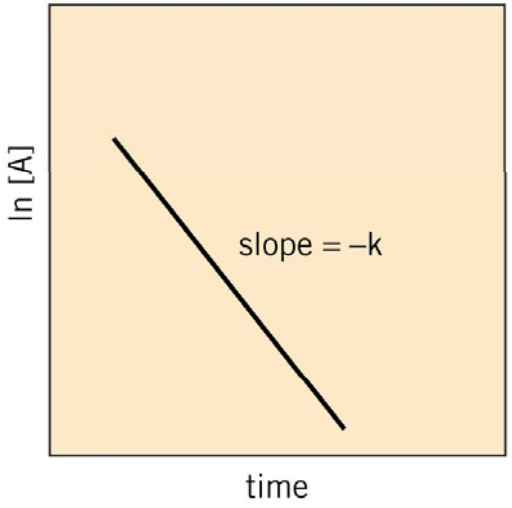


Figure 10.43. A plot of the ln[A] versus time for a first-order reaction.

Enzyme Kinetics

Reaction rate = slope of product v. time

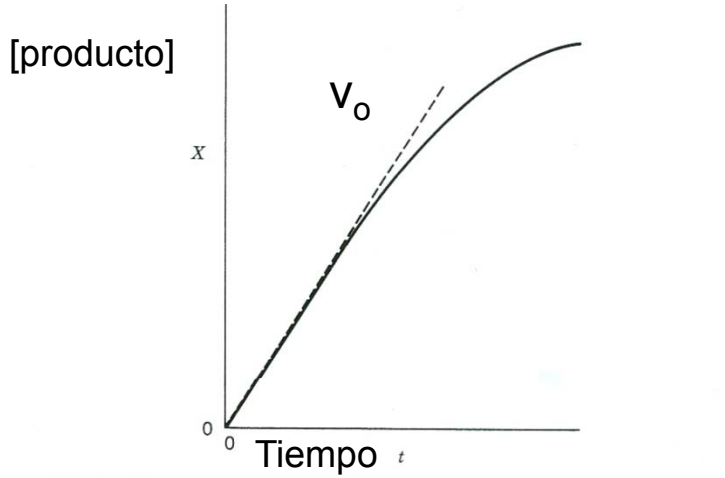
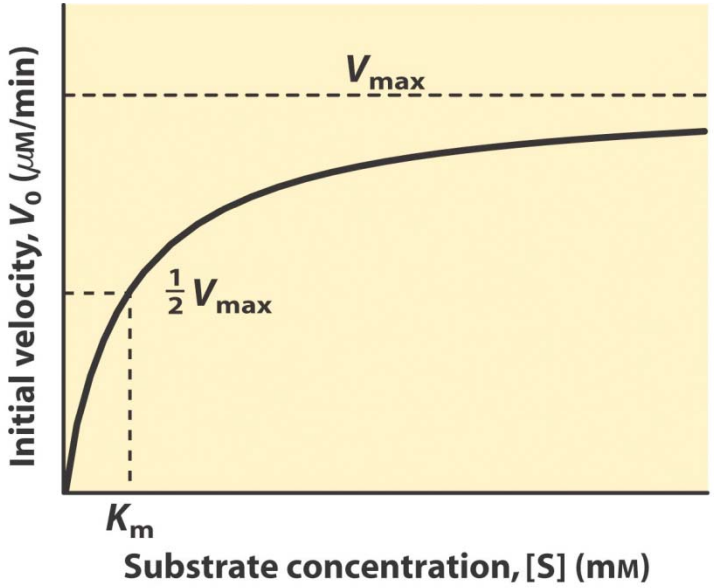
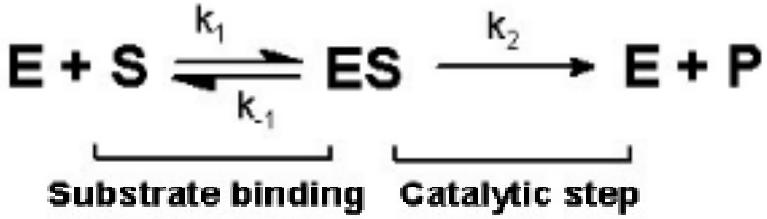


FIG. 2. Time course of enzyme-catalyzed reaction. The solid line shows the accumulation of product with time. The slope of the dashed line is the initial velocity, v_0.



- Es lineal
- Consumo mínimo de S (S=So)
- Evitar reacción inversa
- Evitar inhibición por productos
- Evitar denaturación de E

Enzyme Kinetics: Michaelis-Menten

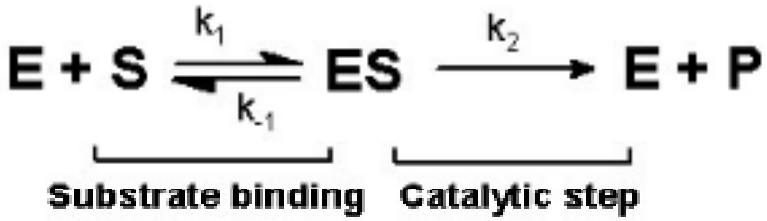


A k_2 también se le conoce como "k_{cat}" o "turnover number"

Se asume:

a) Que cantidad de sustrato [S] es mucho mayor que la cantidad de [E]
b) Que la reacción en reverso es descartable por considerarse velocidad inicial
c) Que la reacción está en estado estacionario =
la cantidad de [ES] no cambia con el tiempo (d[ES]/dt = 0)
Esta ultima condicion fue introducida por Briggs y Haldane en el 1925

Enzyme Kinetics: Michaelis-Menten



$v_o = k_2[ES]$

$$v_o = \frac{k_{cat}[S]\,[E]_{total}}{K_M + [S]} = \frac{V_{max}[S]}{K_M + [S]}$$

$$\frac{d[ES]}{dt} = k_1[E]\,[S] - k_{-1}[ES] - k_2\,[ES] = 0$$

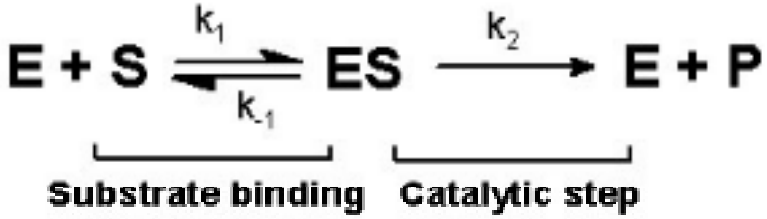
$$K_M = \frac{(k_{-1} + k_2)}{k_1}$$

$$V_{max} = k_{cat}\,[E]_{total}$$

$$\frac{(k_{-1} + k_2)}{k_1}[ES] = [E] = [E]_{total} - [ES]$$

$$[ES] = \frac{[E]_{total}}{\frac{(k_{-1} + k_2)}{k_1}\frac{}{[S]} + 1} = \frac{[S]\,[E]_{total}}{K_M + [S]}$$

Enzyme Kinetics: Michaelis-Menten

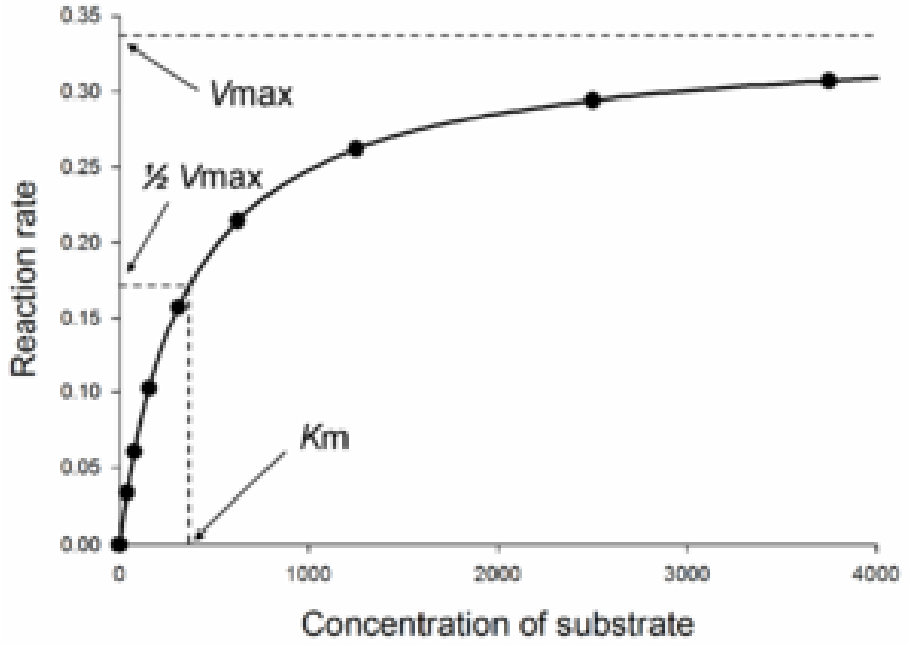


$$v_o = \frac{V_{max}[S]}{K_M + [S]}$$

donde:

$V_{max} = k_2[E]_{total}$

$$K_M = \frac{(k_{-1} + k_2)}{k_1}$$



Enzyme Kinetics Parameters

Phosphorylation of Hexoses

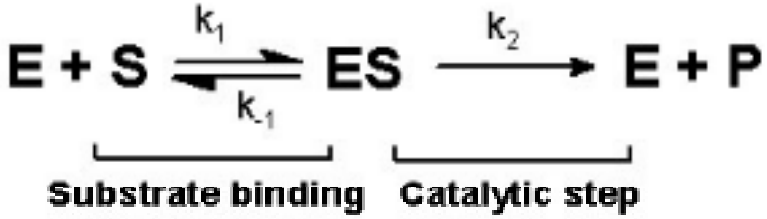
Enzyme	Km (glucose)	Km (fructose)	Km (galactose)	*Physiologic specificity*	Product	Found in
Hexokinase	~0.05mM	1.6 mM	1-2 mM	*Glucose*	G-6-P	All tissues (not ß-cell)
Glucokinase	~5.5 mM	-	-	*Glucose*	G-6-P	Liver, ß-cell, hypothalamus
Fructokinase	-	Low!	-	*Fructose*	F-1-P	Liver
Galactokinase	-	-	Low!	*Galactose*	Gal-1-P	Liver ,many other tissues

Enzyme Kinetics Parameters

TABLE 6–7 Turnover Numbers, k_{cat}, of Some Enzymes

Enzyme	*Substrate*	k_{cat} (s^{-1})
Catalase	H_2O_2	40,000,000
Carbonic anhydrase	HCO_3^-	400,000
Acetylcholinesterase	Acetylcholine	14,000
β-Lactamase	Benzylpenicillin	2,000
Fumarase	Fumarate	800
RecA protein (an ATPase)	ATP	0.4

Enzyme Kinetics Parameters

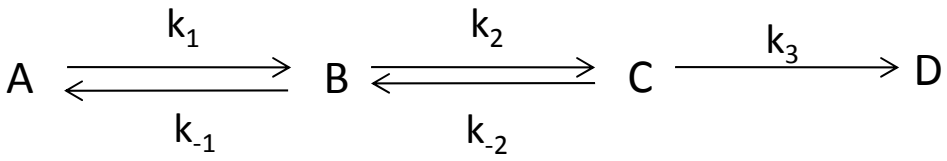


Eficiencia catalítica = "Constante de especificidad"

$$\frac{k_2}{K_M} = \frac{k_{cat}}{K_M}$$

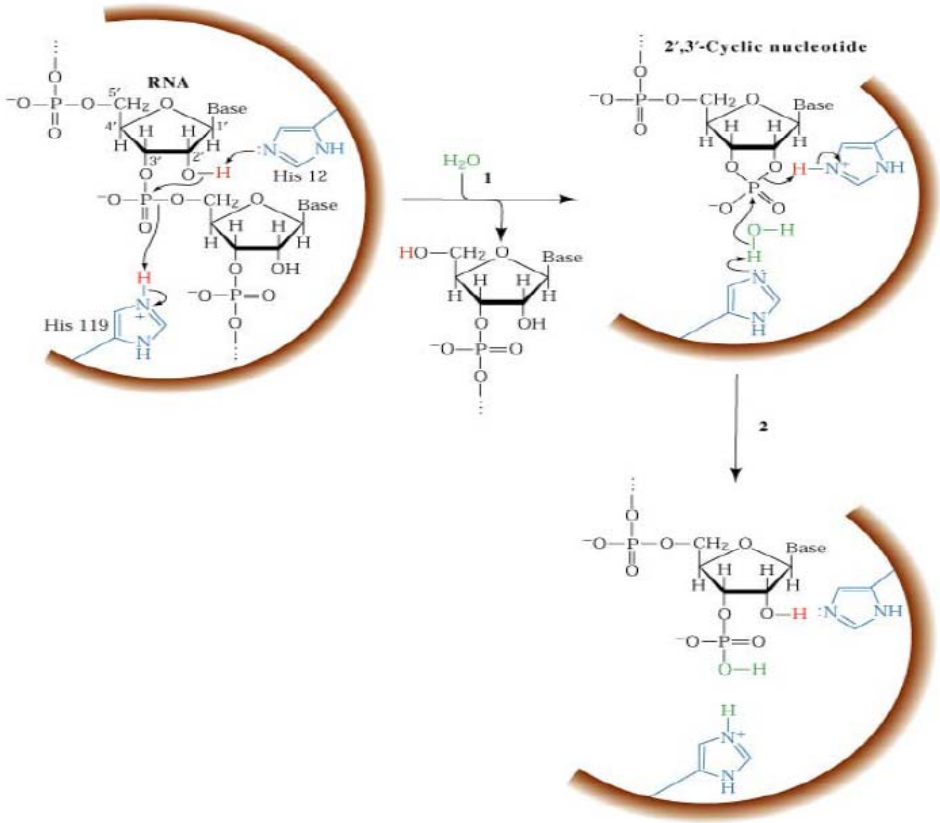
El parámetro más significativo al describir una enzima
Constante de segundo orden ($M_{-1}s_{-1}$)
Tiene una cota de 10^9 $M^{-1}s^{-1}$

Net Reaction Rates:

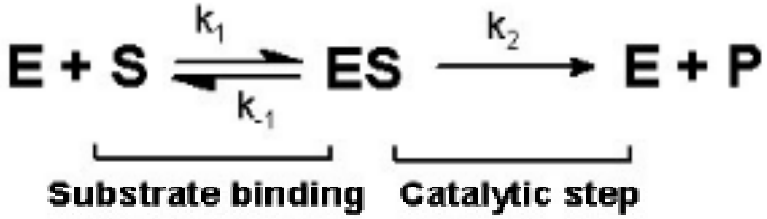


What is the rate-limiting step?

The slowest step in a reaction that determines the overall rate



Lineweaver-Burke Plot



Ecuación Hiperbólica

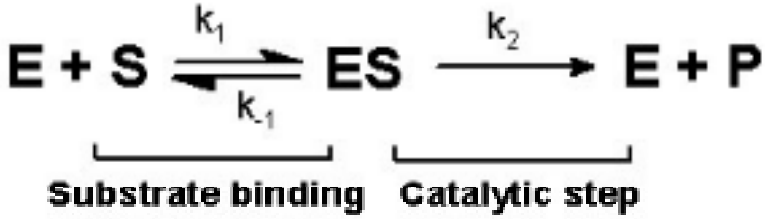
$$v_o = \frac{V_{max}[S]}{K_M + [S]}$$

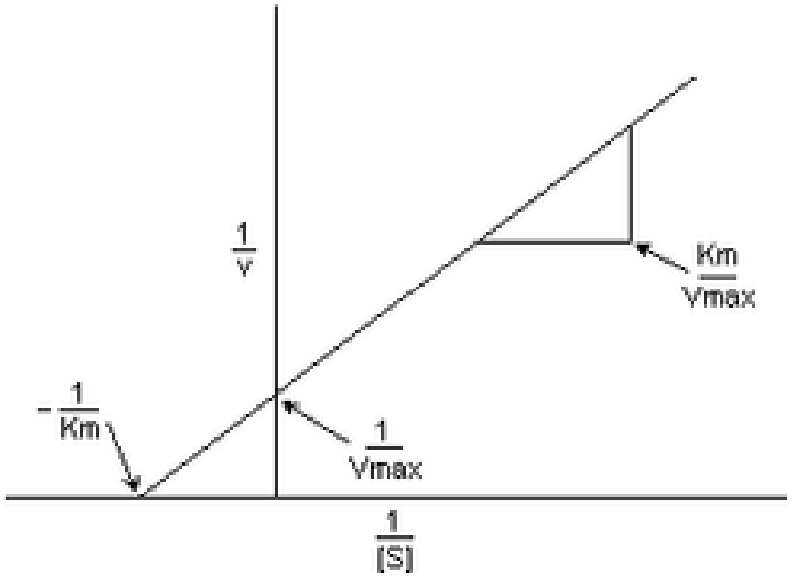
Ecuación lineal

$$\frac{1}{v_o} = \frac{K_M + [S]}{V_{max}[S]} = \frac{K_M}{V_{max}} * \frac{1}{[S]} + \frac{1}{V_{max}}$$

$$y = m * x + b$$

Lineweaver-Burke Plot



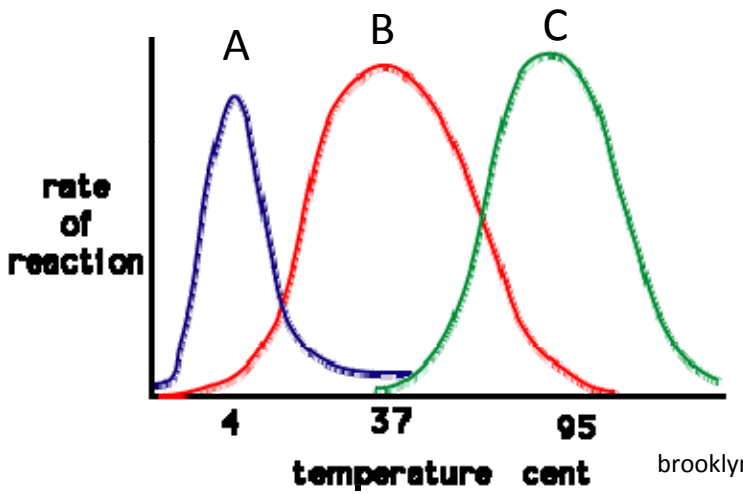


Gráfica de Lineweaver-Burke

$$\frac{1}{v_o} = \frac{K_M}{V_{max}} * \frac{1}{[S]} + \frac{1}{V_{max}}$$

Factores que afectan la función de las enzimas:

Temperatura:



brooklyn college - cuny

Todas las enzimas tienen una temperatura óptima propia.

Cuál de estas tres proteínas es humana?
De dónde provienen las otras dos?

Factores que afectan la función de las enzimas:

pH:

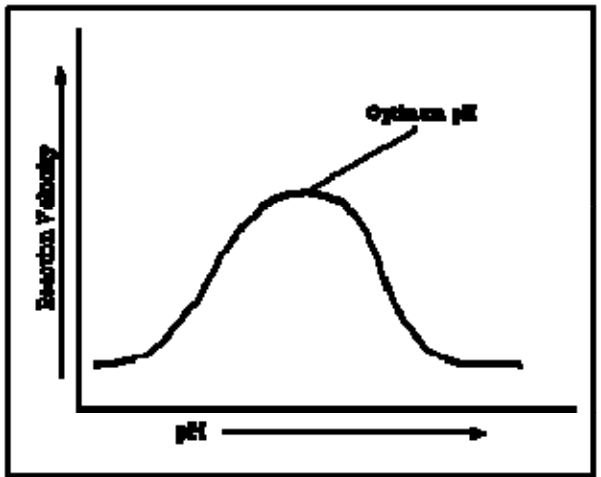


FIGURE 14
Effect of pH on reaction rate

pH for Optimum Activity

Enzyme	**pH Optimum**
Lipase (pancreas)	8.0
Lipase (stomach)	4.0 - 5.0
Lipase (castor oil)	4.7
Pepsin	1.5 - 1.6
Trypsin	7.8 - 8.7
Urease	7.0
Invertase	4.5
Maltase	6.1 - 6.8
Amylase (pancreas)	6.7 - 7.0
Amylase (malt)	4.6 - 5.2
Catalase	7.0

Factores que afectan la función de las enzimas:

Fuerza Iónica:

La concentración de sales en solución también afecta la actividad de una enzima. Cada enzima tiene una fuerza iónica óptima para su funcionamiento.

Cinética de dos sustratos:

Concerted mechanism

Many ligases exhibit a concerted two-substrate mechanism

Some kinases exhibit a ping-pong mechanism

Usually involves temporary covalent modification

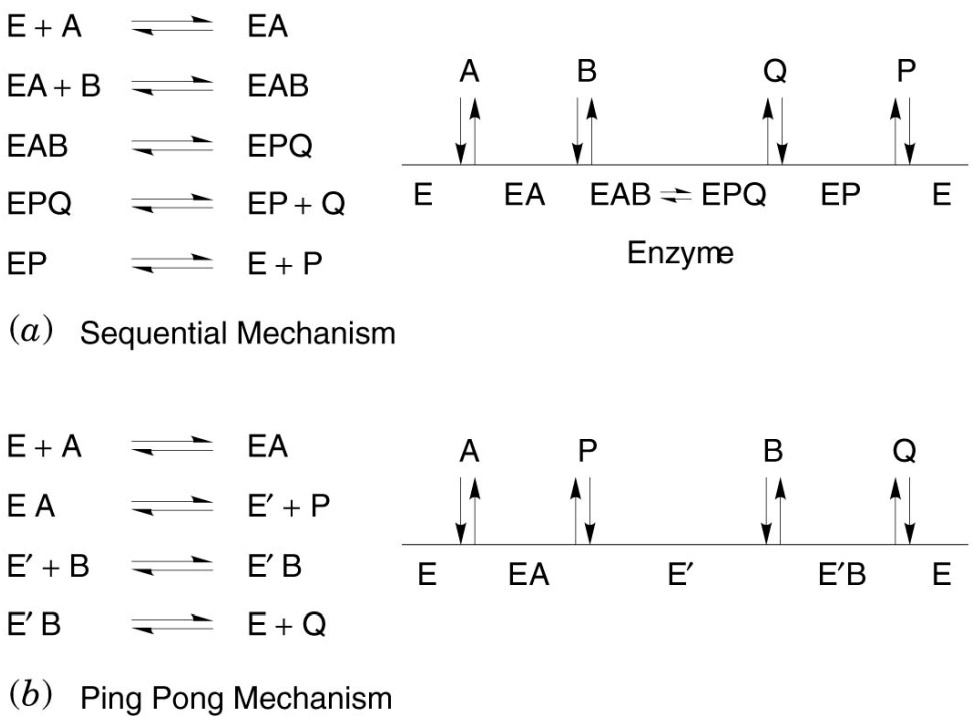


Figure 10.53. Mechanisms of interaction for two substrate reactions.

Cinética de dos sustratos:

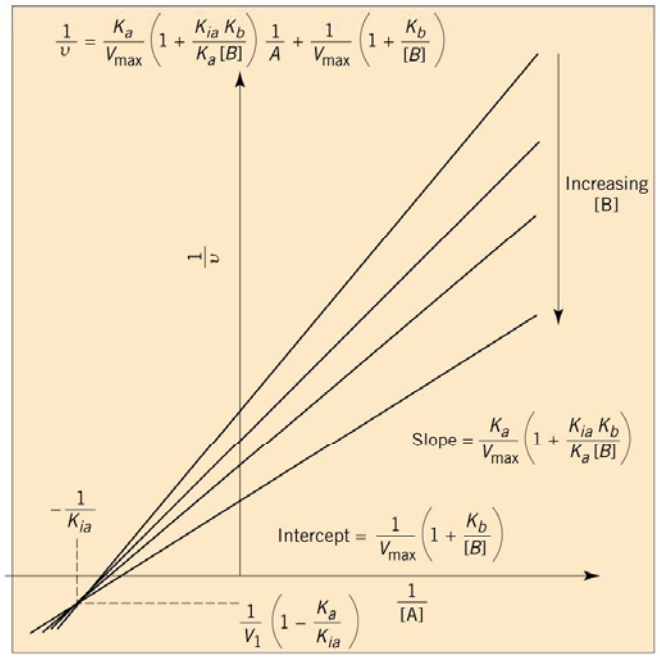


Figure 10.54. Double reciprocal plot of initial velocity for a sequential reaction.

Sequential mechanism

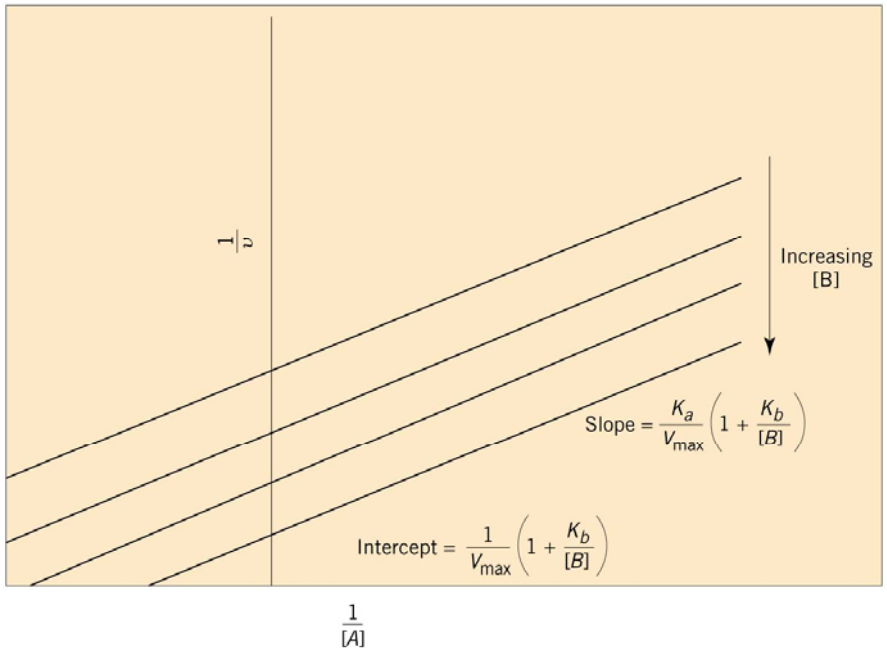
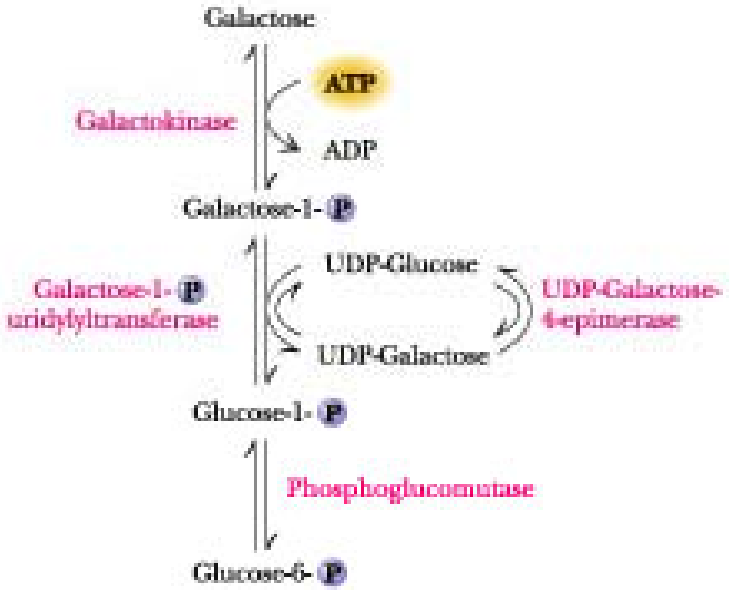
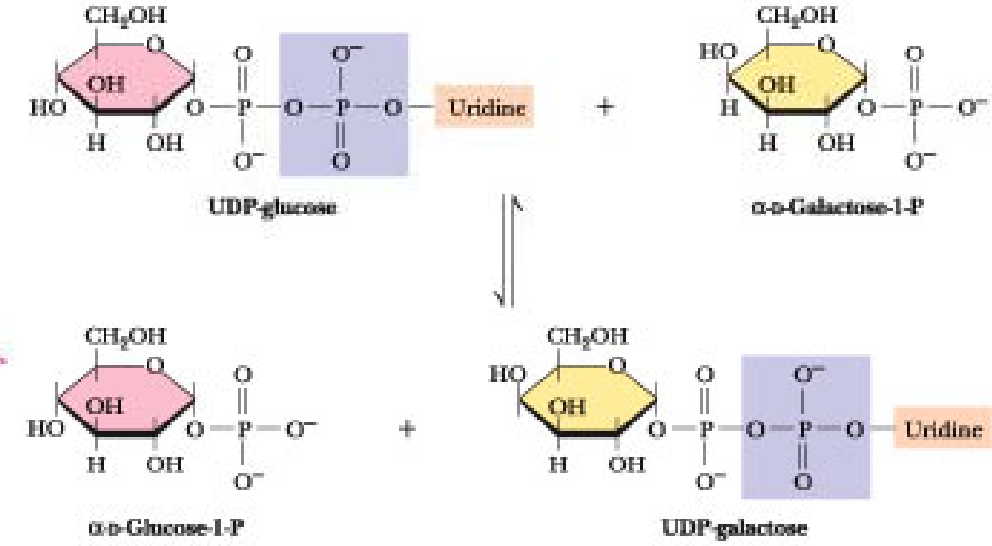


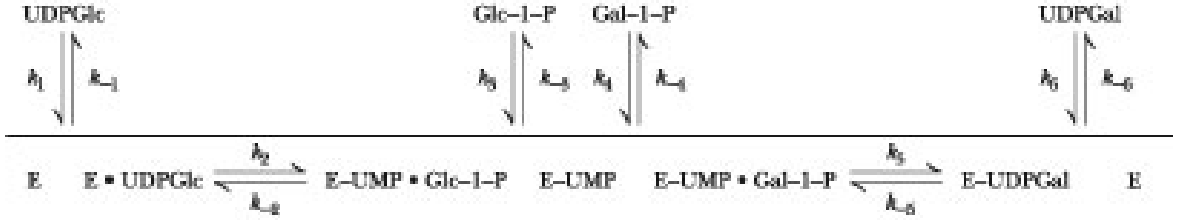
Figure 10.55. Double reciprocal plot of initial velocity for a ping-pong reaction.

Ping-pong mechanism

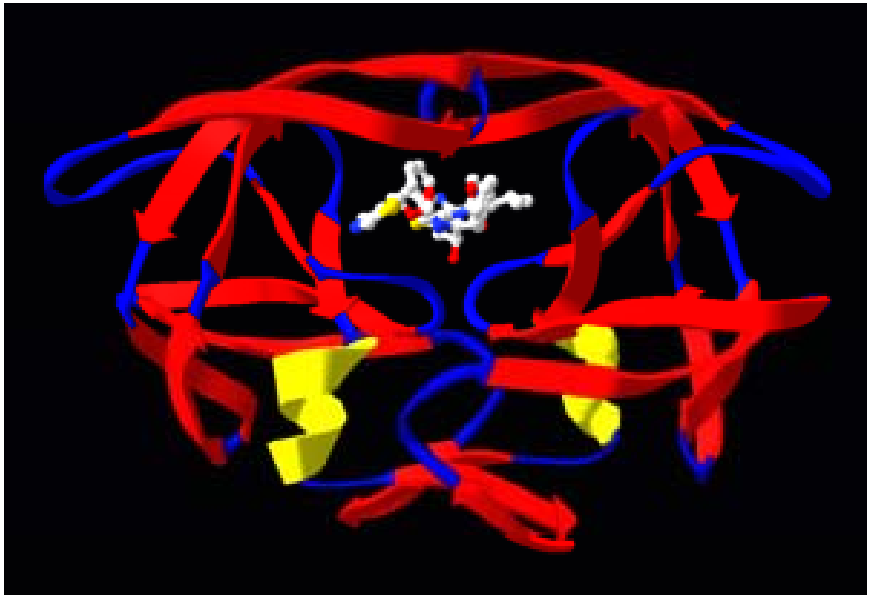
Galactose Epimerase -







Inhibición de enzimas:



Proteasa de HIV con su inhibidor ritonavir

Importante en la industria farmacéutica

Pesticidas – inhibidores de acetilcolina esterasa

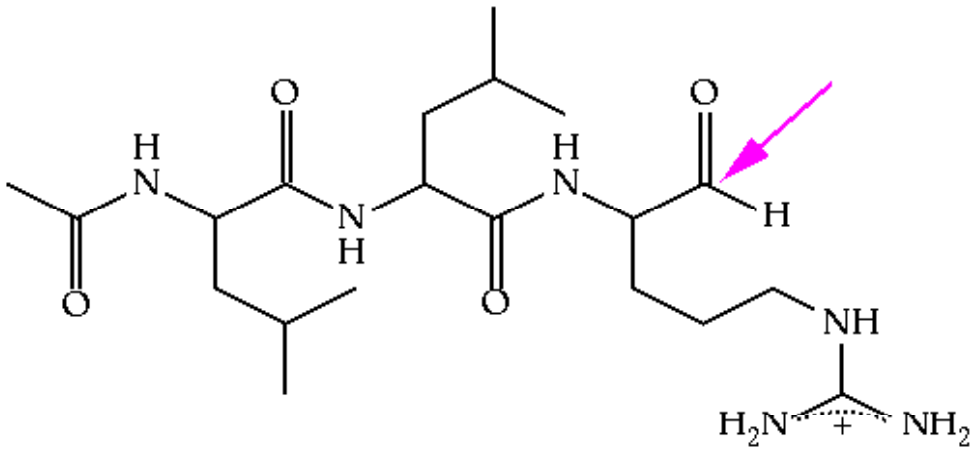
Toxinas -

Inhibición de enzimas:

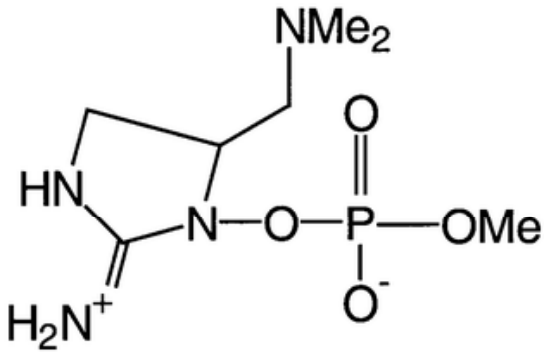
I. Inhibición irreversible
   a. Covalente
   b. Suicida
II. Inhibición reversible
   a. Inhibición competitiva
   b. Inhibición no-competitiva (“non-competitive”)
   c. Inhibición acompetitiva (“uncompetitive”)

Inhibición de enzimas:

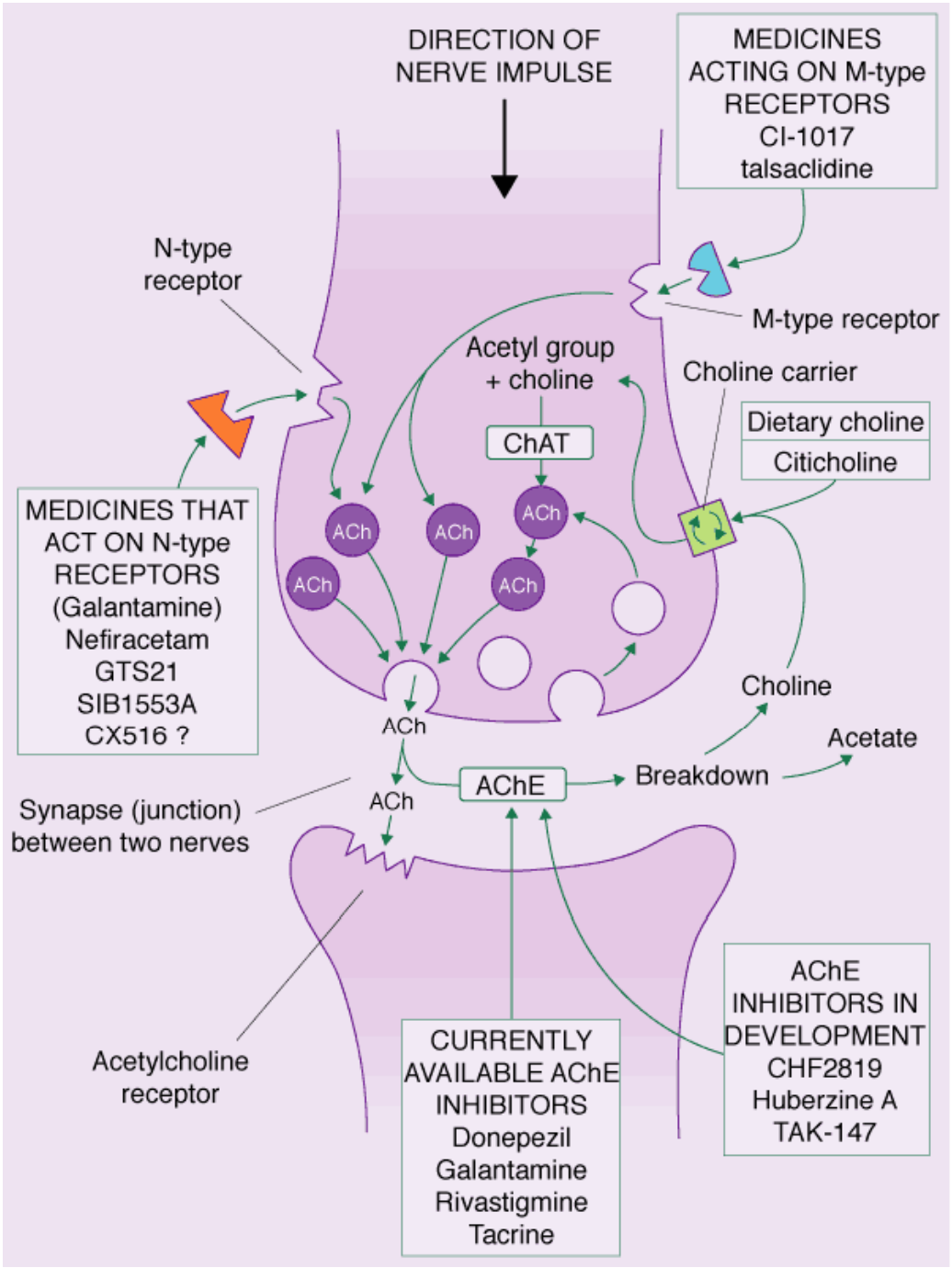
I. Inhibición irreversible
   a. Covalente



Leupeptina es un inhibidor covalente
de proteasas de serina

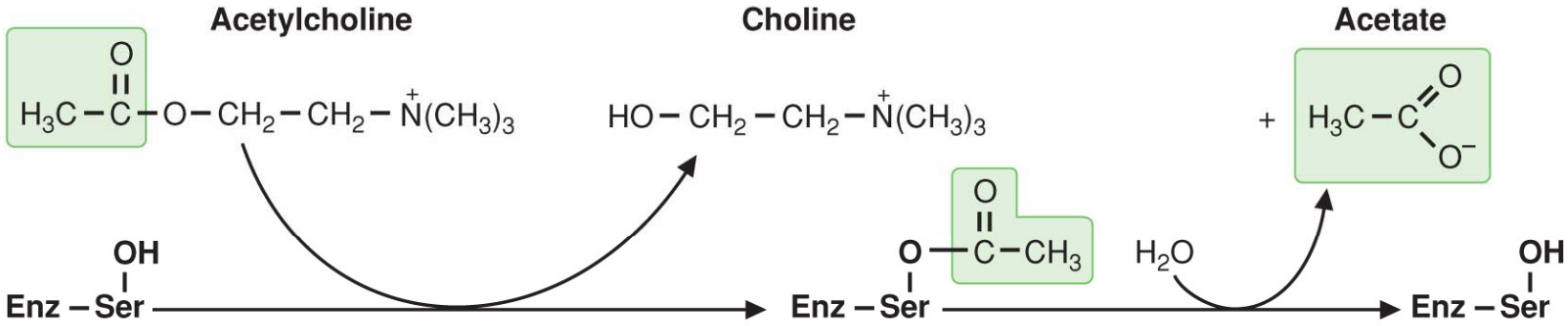


Anatoxina es un inhibidor covalente de
Acetylcolina esterasa

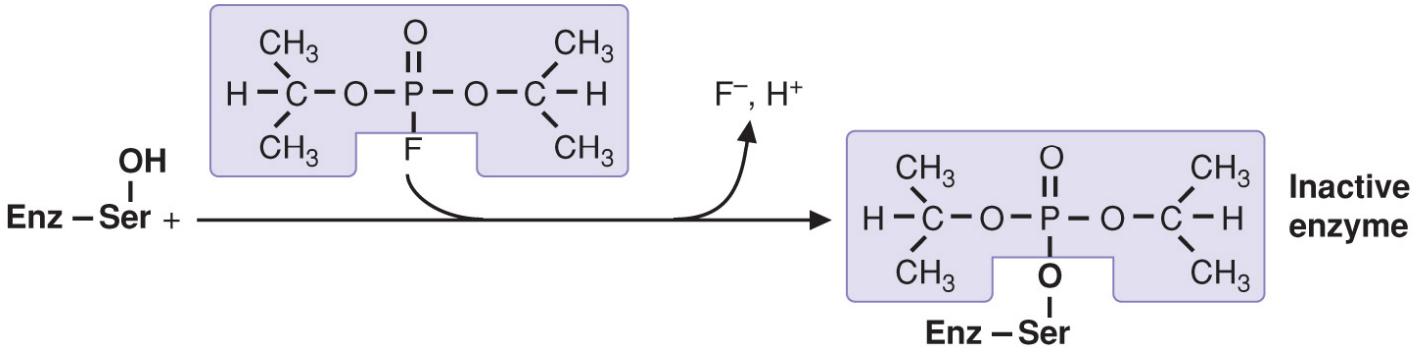


Acetylcholine esterase in the neuromuscular junction

A. Normal reaction of acetylcholinesterase

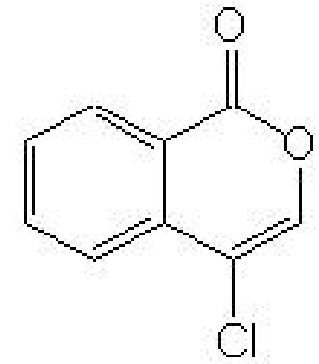


B. Reaction with organophosphorus inhibitors

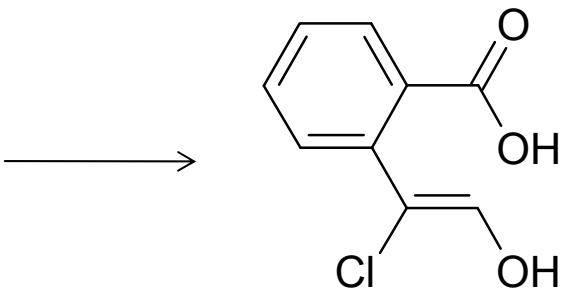


Inhibición de enzimas:

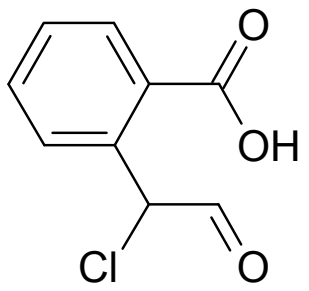
I. Inhibición irreversible
   a. Covalente
   b. Suicida



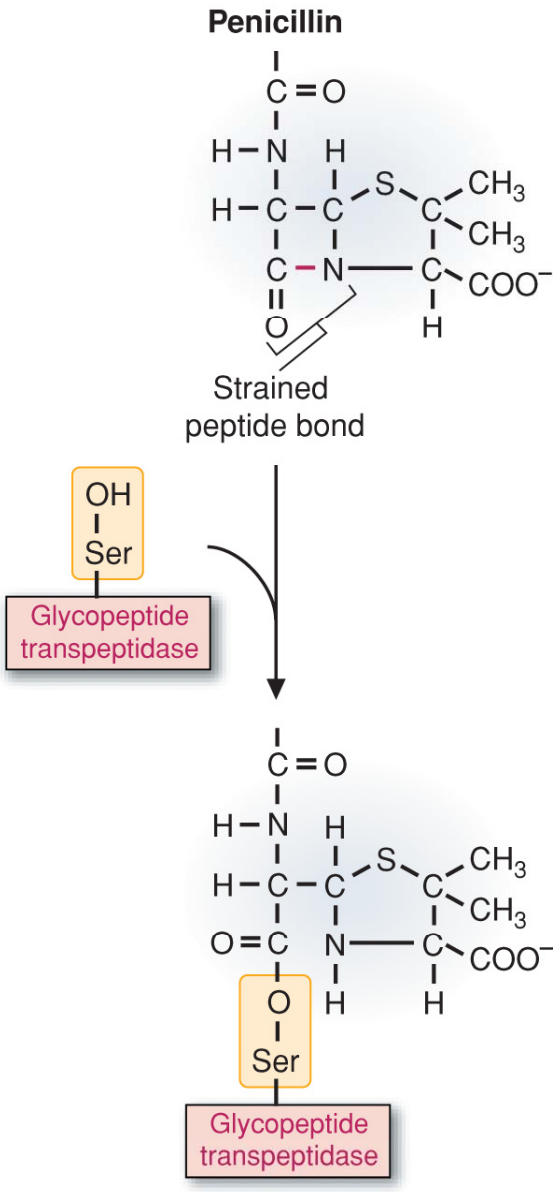
Inhibidor suicida de proteasas



α– halo-enol

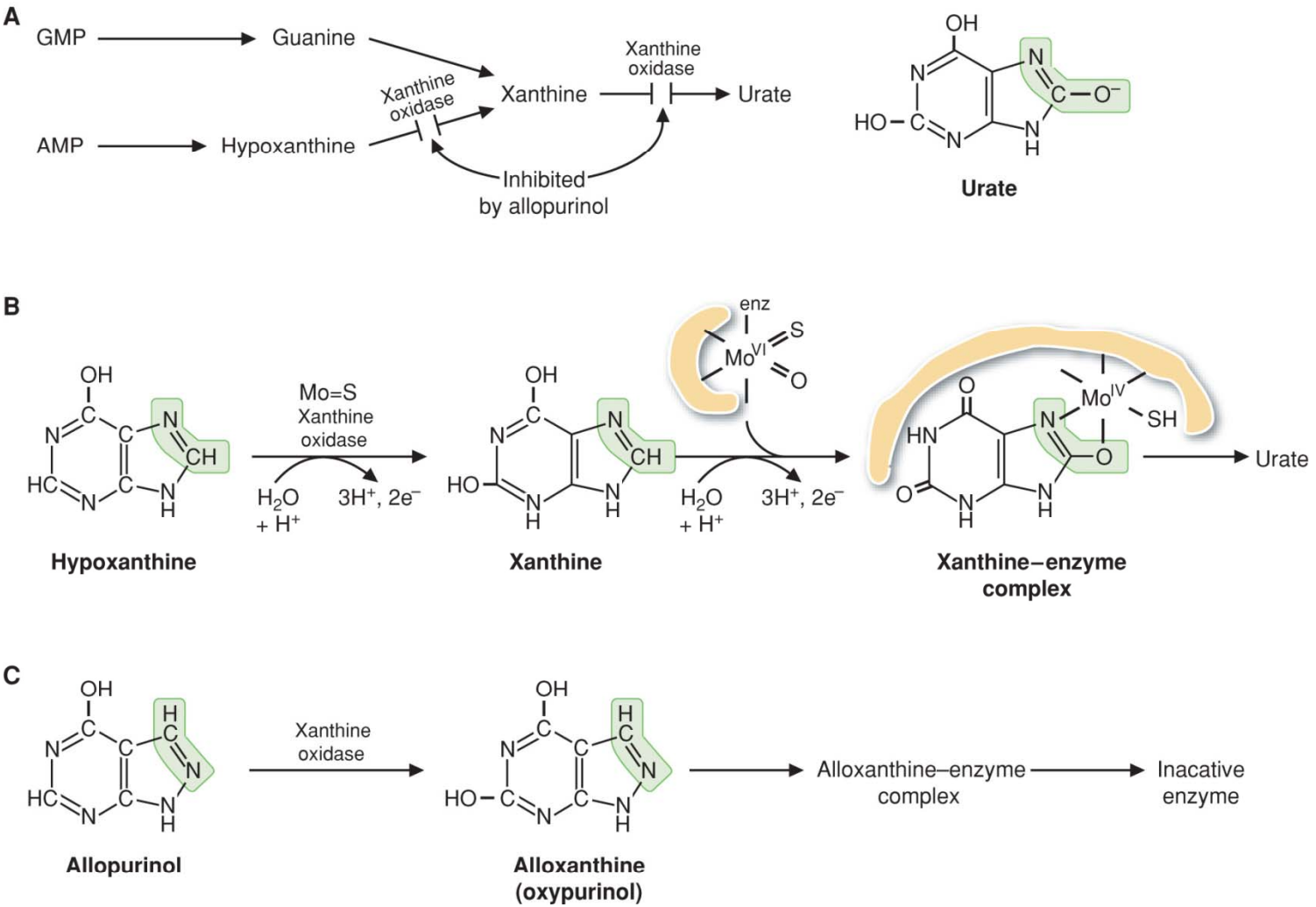


α– halo-aldehyde

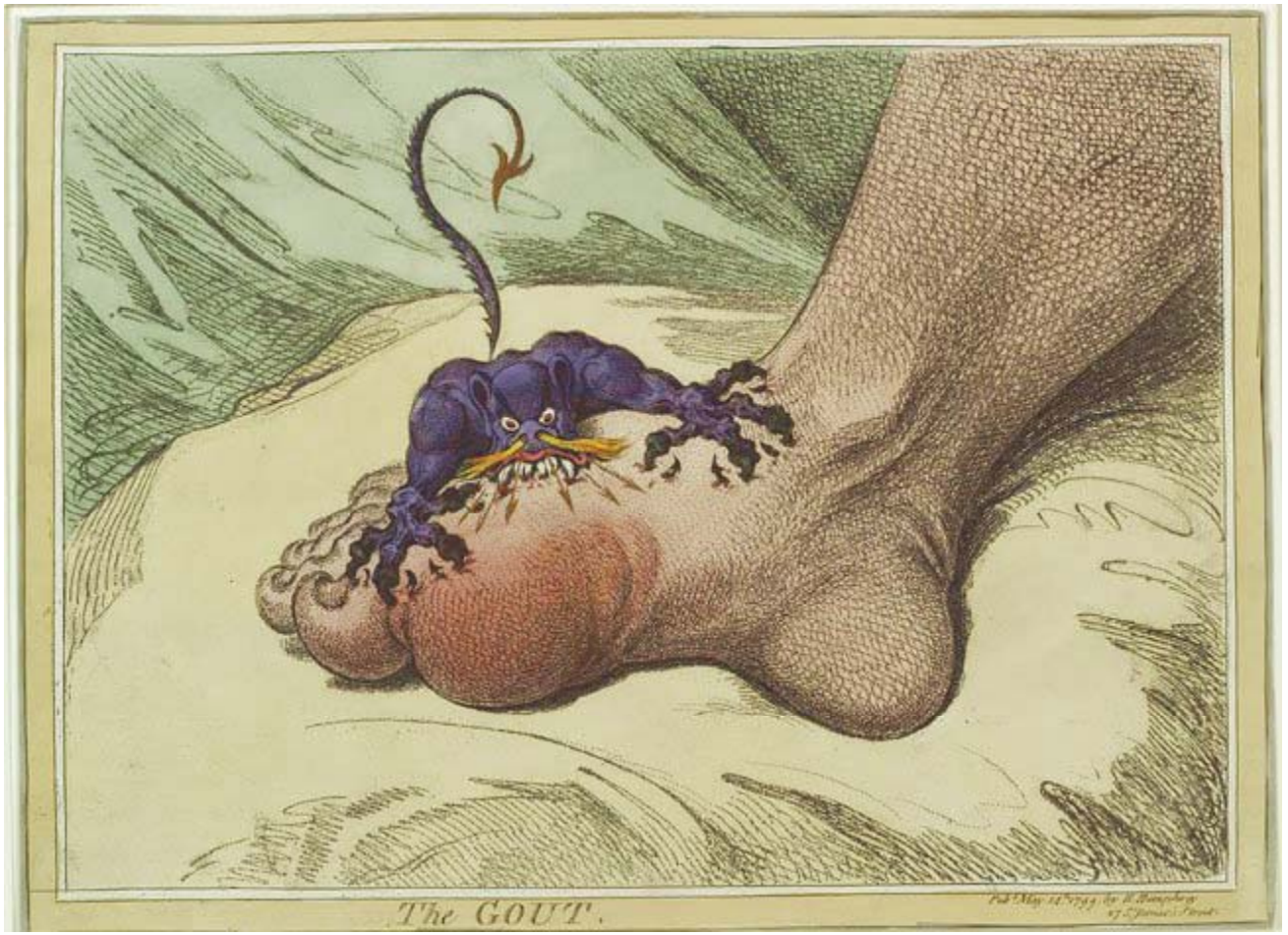


Penicillin is a covalent inhibitor of glycopeptide transpeptidase

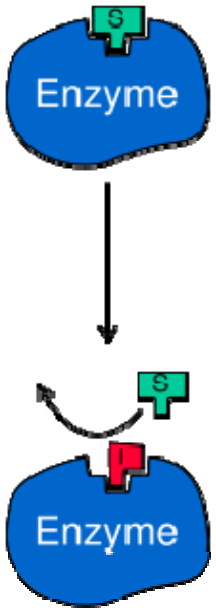
Allopurinol is a suicide inhibitor of xanthine oxidase



The Gout by James Gillgray (1799)



Inhibición competitiva

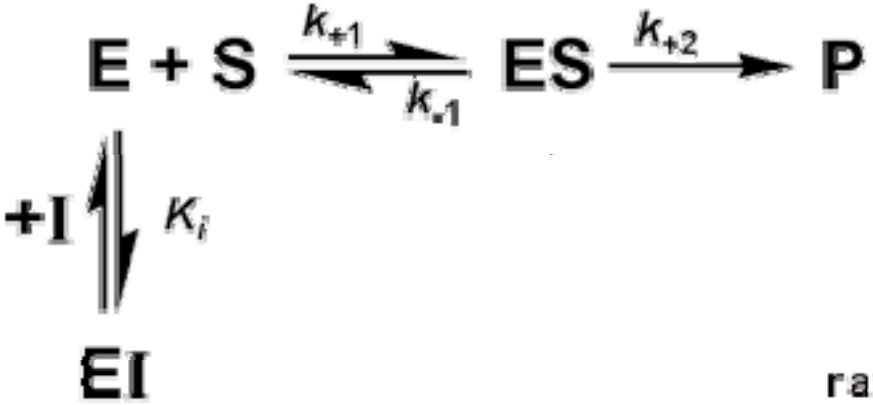


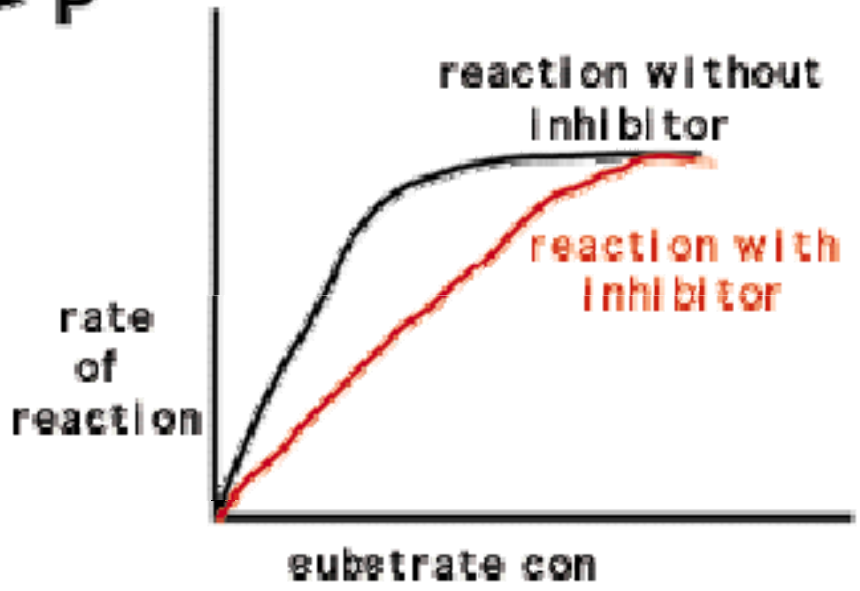
$$E + S \underset{k_{-1}}{\overset{k_{+1}}{\rightleftharpoons}} ES \xrightarrow{k_{+2}} P$$

$$+I \rightleftharpoons K_i$$

$$EI$$

Inhibición competitiva





$$v_o = \frac{V_{max}[S]}{\left(1 + \frac{[I]}{K_i}\right) K_M + [S]}$$

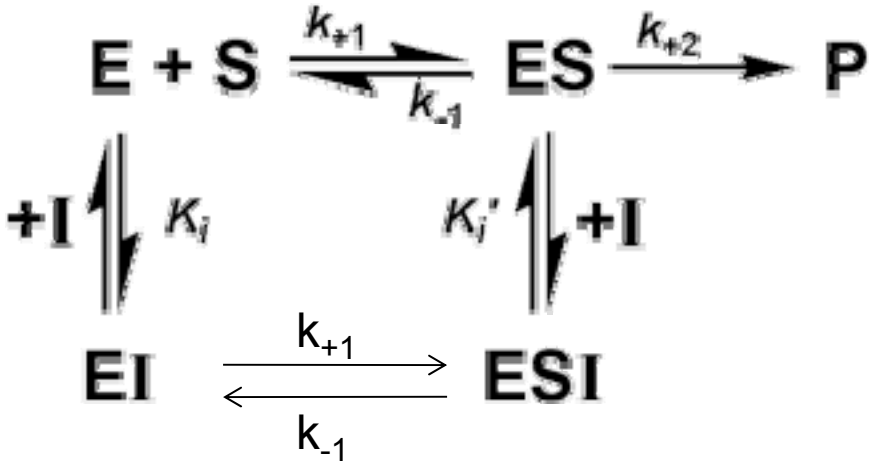
Inhibición competitiva

Afecta el proceso de asociación del sustrato

K_m aparente es mayor

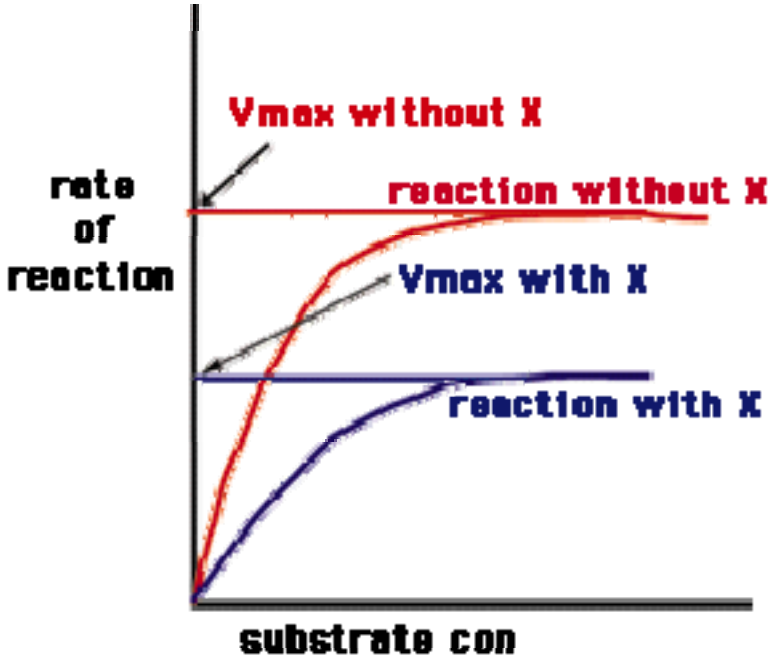
V_{max} no se afecta

Inhibición no-competitiva



Inhibición no-competitiva

$$v_o = \frac{\frac{V_{max}}{(1 + \frac{[I]}{K_i})} * [S]}{K_M + [S]}$$

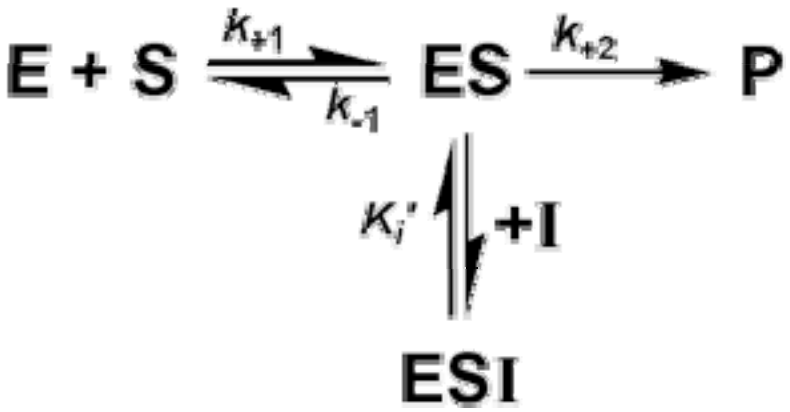


Inhibición no-competitiva (“non-competitive”)

K_m no se afecta

V_{max} disminuye – hay menos enzima disponible

Inhibición acompetitiva (“uncompetitive”)



$$v_o = \frac{\dfrac{V_{max}}{\left(1 + \dfrac{[I]}{K_i}\right)} * [S]}{\dfrac{K_M}{\left(1 + \dfrac{[I]}{K_i}\right)} + [S]}$$

Inhibición acompetitiva (“un-competitive”)

Afecta V_{max} y K_m por exactamente el mismo factor

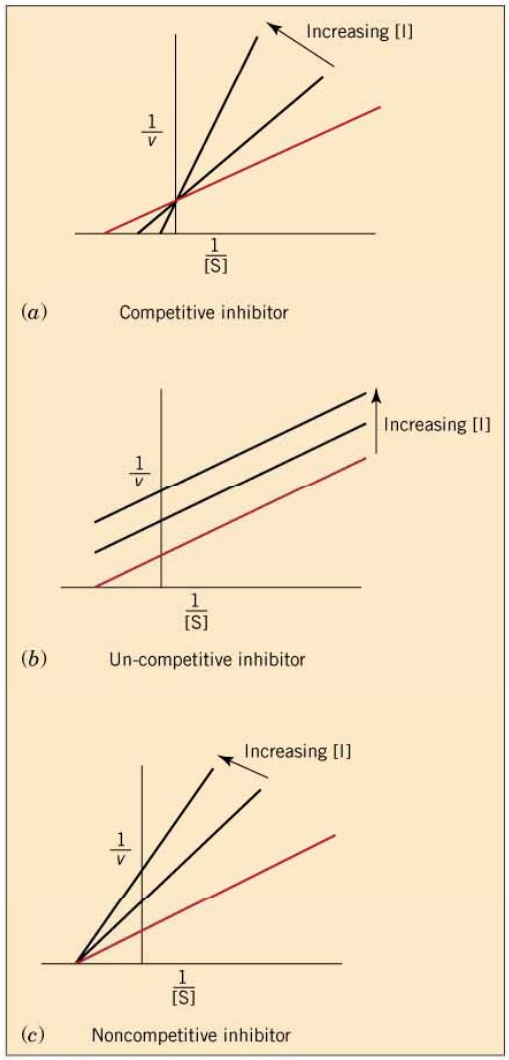


Figure 10.60. Double-reciprocal plots for competitive, uncompetitive, and reversible noncompetitive inhibition.

Inhibitors as drugs:

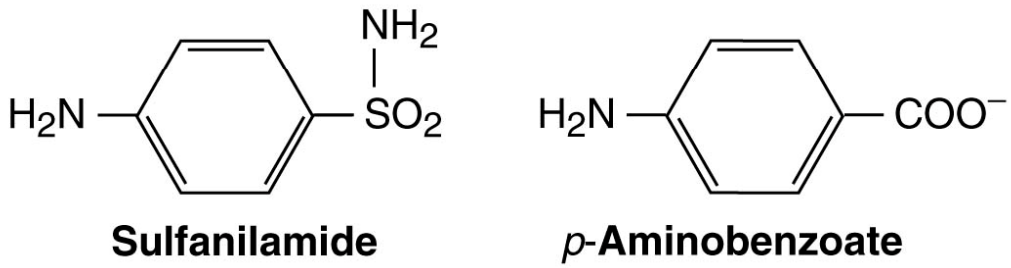


Figure 10.64. Structure of *p*-aminobenzoate and sulfanilamide, a competitive inhibitor of a bacterial enzyme involved in the synthesis of folic acid.

Sulfa antibiotics block the conversion of p-aminobenzoate to folic acid in bacteria.

Regulación de actividad enzimática:

Modos de regulación de actividad enzimática:

a. Alosterismo
b. Retroregulación (feedback inhibition)
c. Activación proteolítica de zimógenos
d. Modificación covalente
e. Regulación de la síntesis de enzimas

Regulación de actividad enzimática: Alosterismo

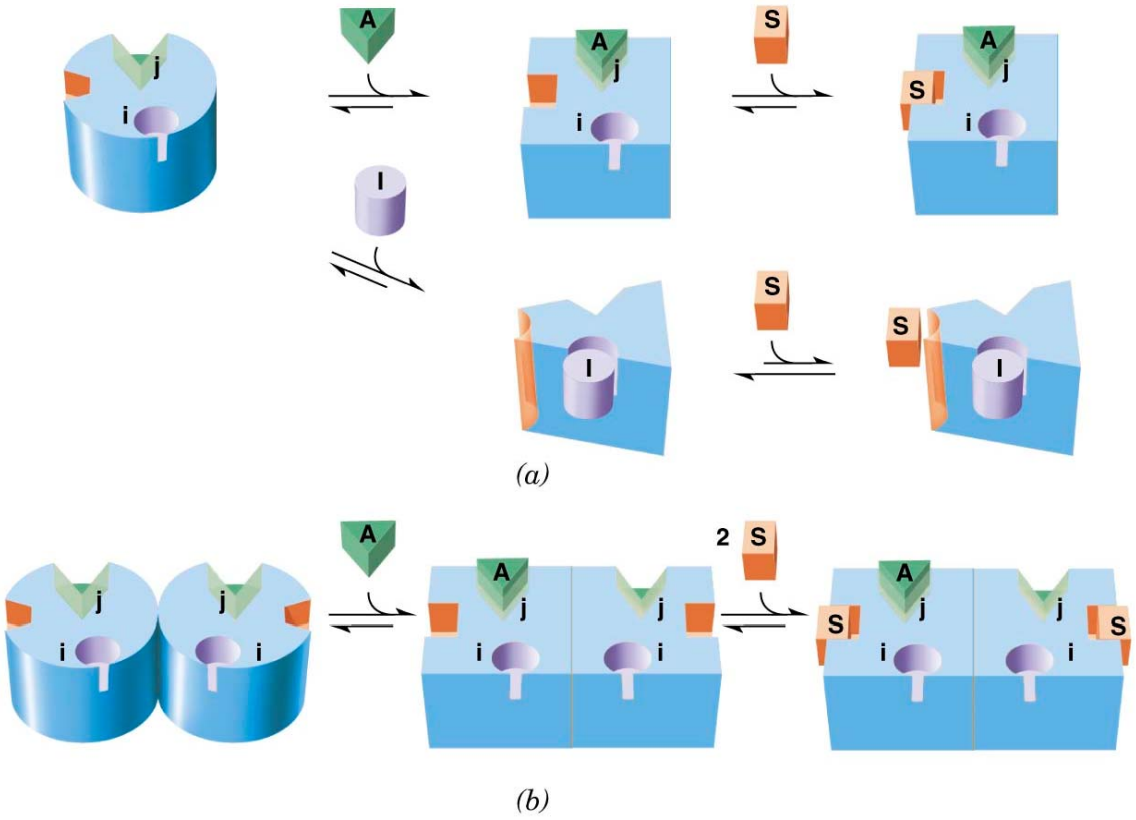
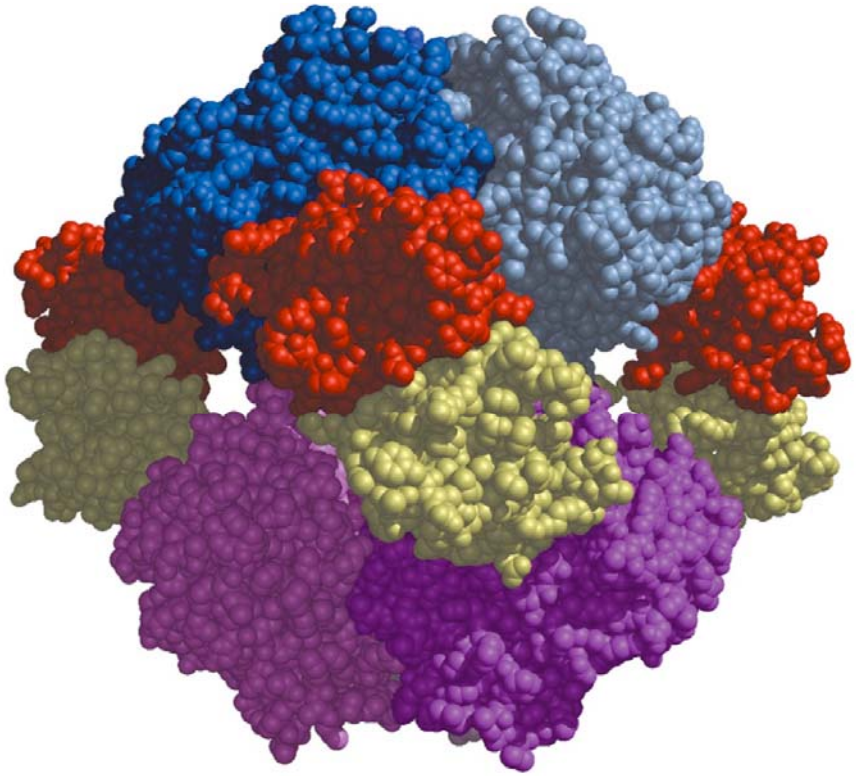
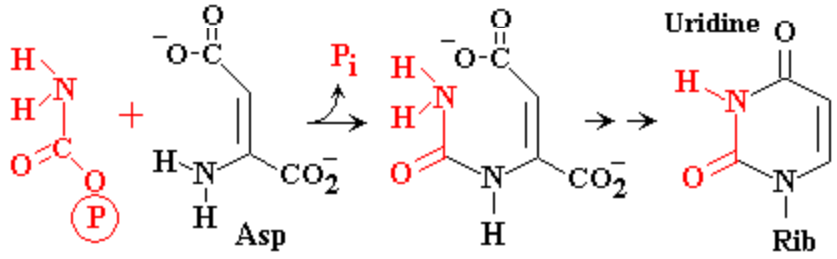


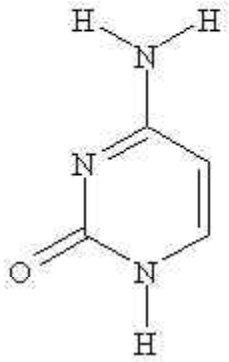
Figure 10.65 Models of allosteric enzyme systems.

Regulación de actividad enzimática: Alosterismo

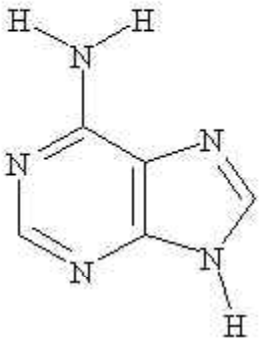


Aspartate Transcarbamoylase





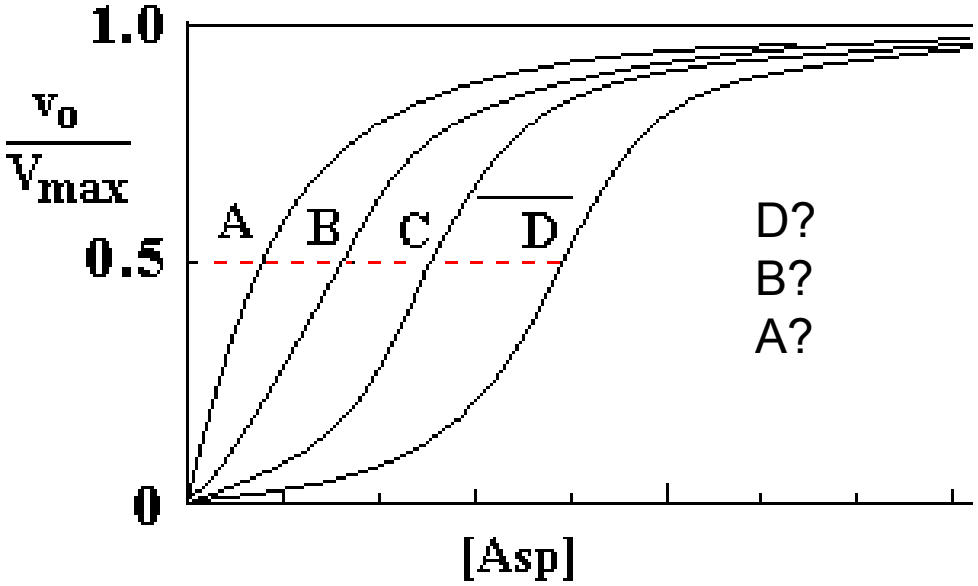
cytosine



adenine

CTP – negative allosteric effector
ATP – positive allosteric effector

Regulación de actividad enzimática: Alosterismo



Curva C: describe la actividad de ATCase por sí sola.

Actividad sigmoidea: un indicador de regulación alostérica

Cinética sigmoidea: mayor control de la velocidad

Regulación de actividad enzimática: Alosterismo

Concerted

Sequential

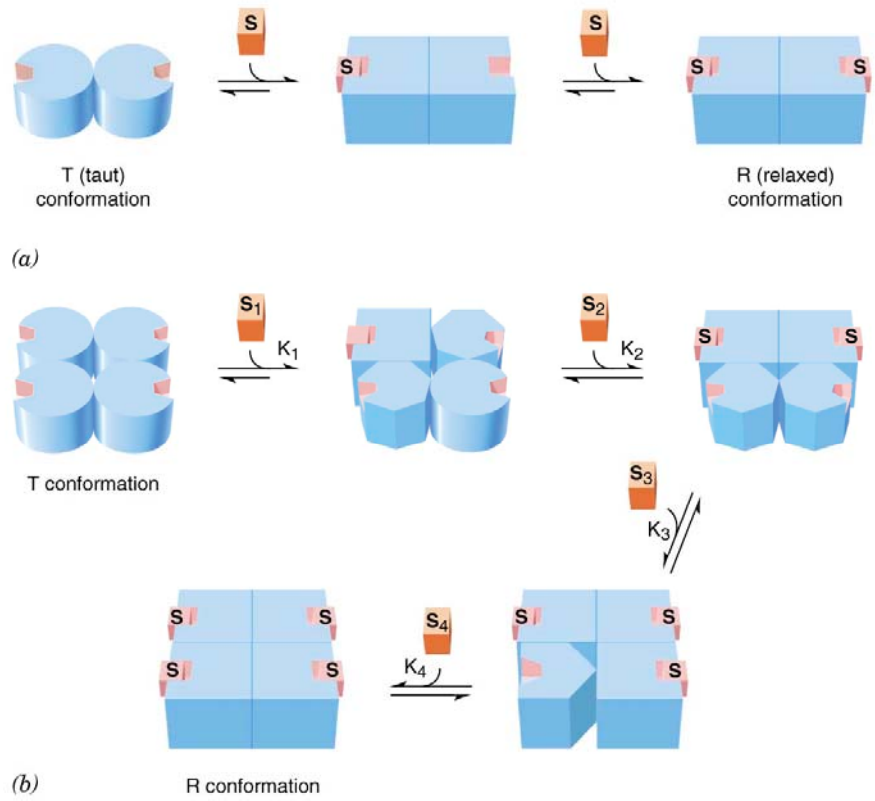


Figure 10.68. Models of cooperativity.

Regulación de actividad enzimática: Alosterismo

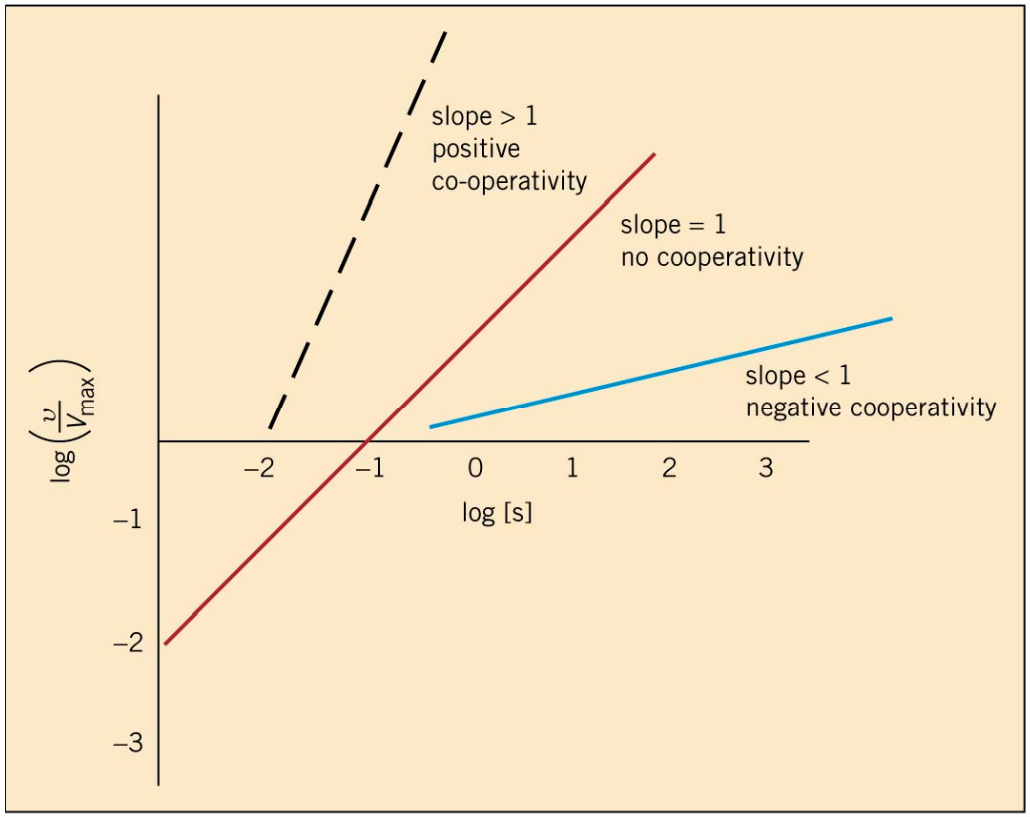
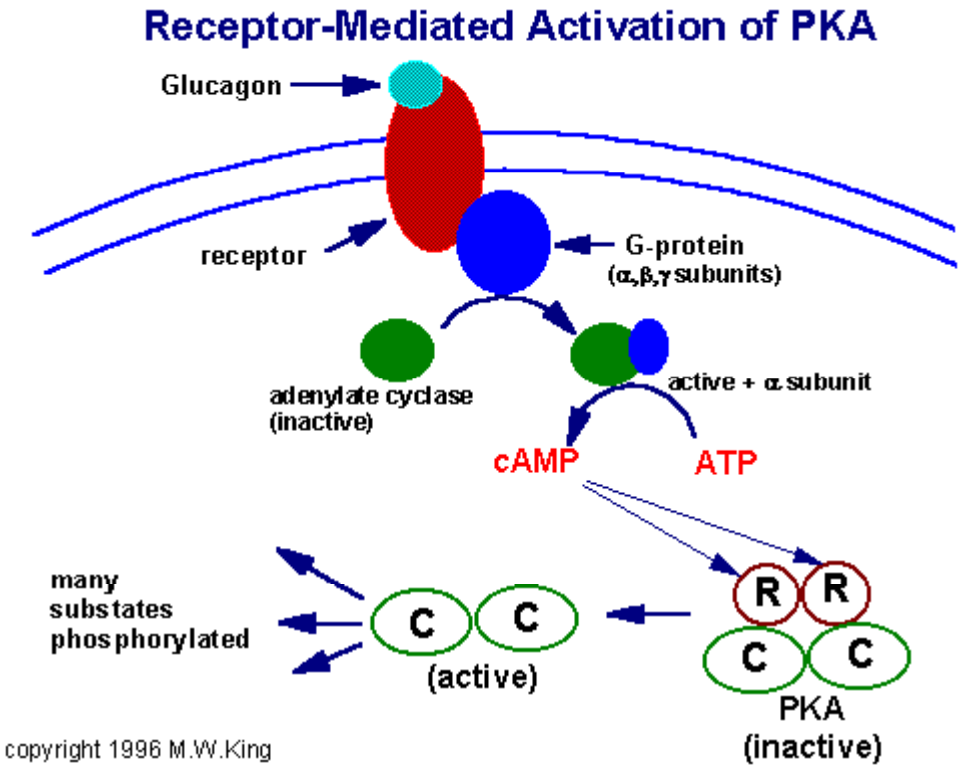


Figure 10.67. Hill plot for an allosteric enzyme.

Regulación de actividad enzimática: Alosterismo

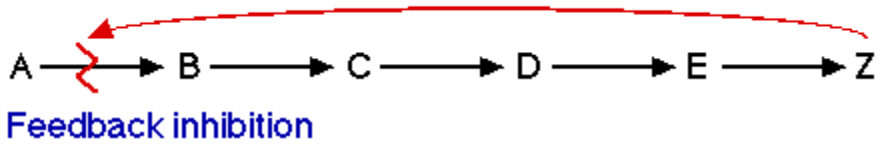


La actividad de algunas enzimas está modulada por efectores alostéricos

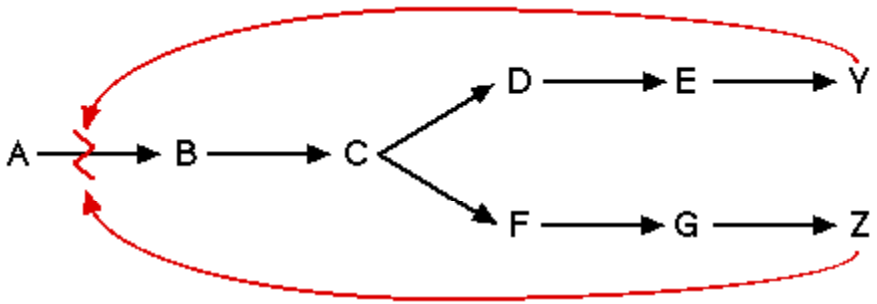
Estos efectores alostéricos pueden tener un efecto inhibidor o activador

Estos efectores pueden ser homotrópicos o heterotrópicos.

Regulación de actividad enzimática: Retroregulación (“Feedback Inhibition”)



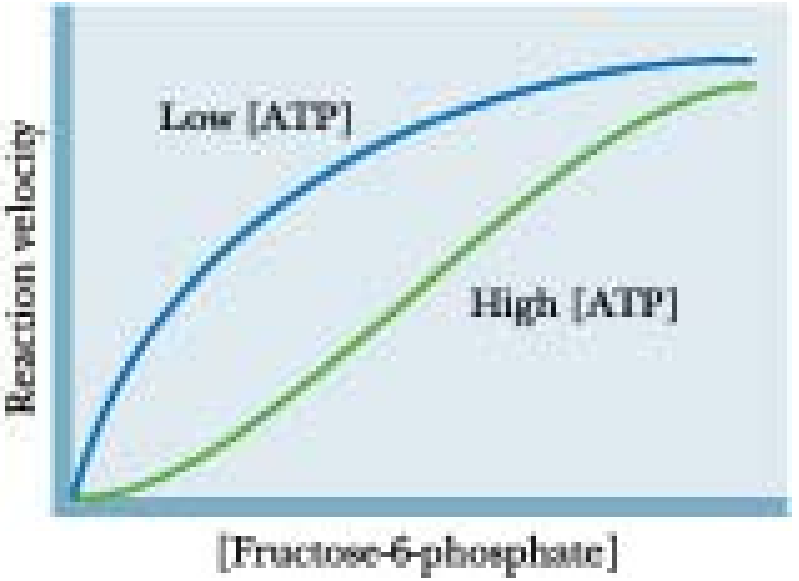
Feedback inhibition



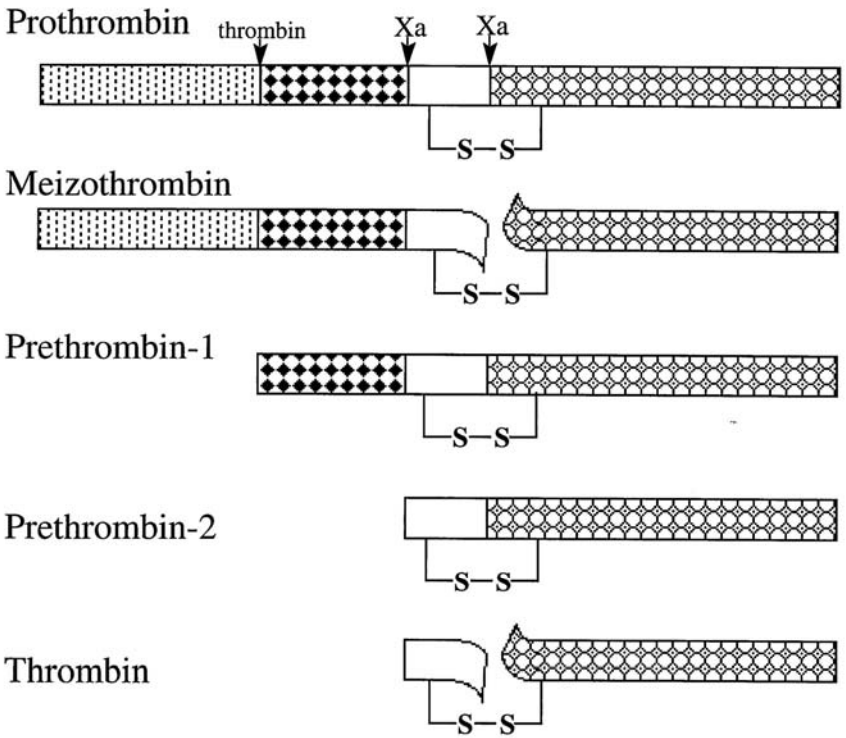
Cumulative feedback inhibition

Hamline University

fosfofructokinasa es inhibida por citrato



Regulación de actividad enzimática: Proteólisis de zimógenos

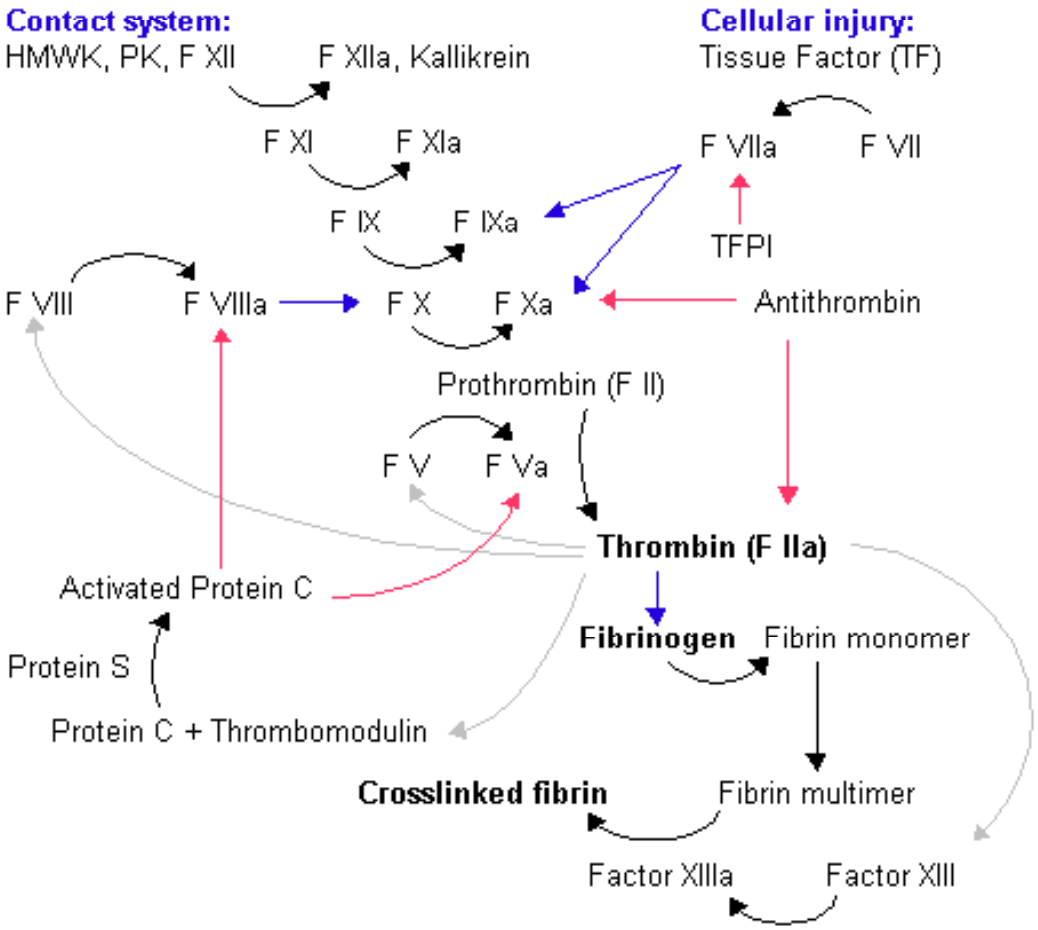


(DiBella, Maurer and Scheraga, 1995)

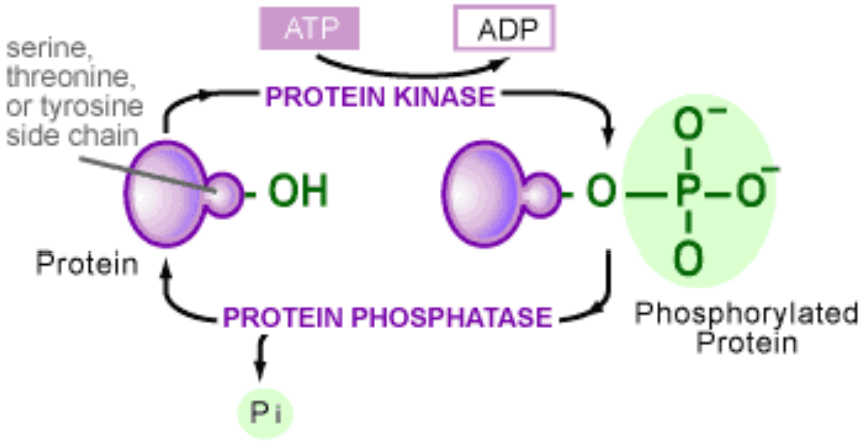
Zimógeno: precursor inactivo que es activado por proteólisis

Trombina: enzima final en la cascada de coagulación sanguínea

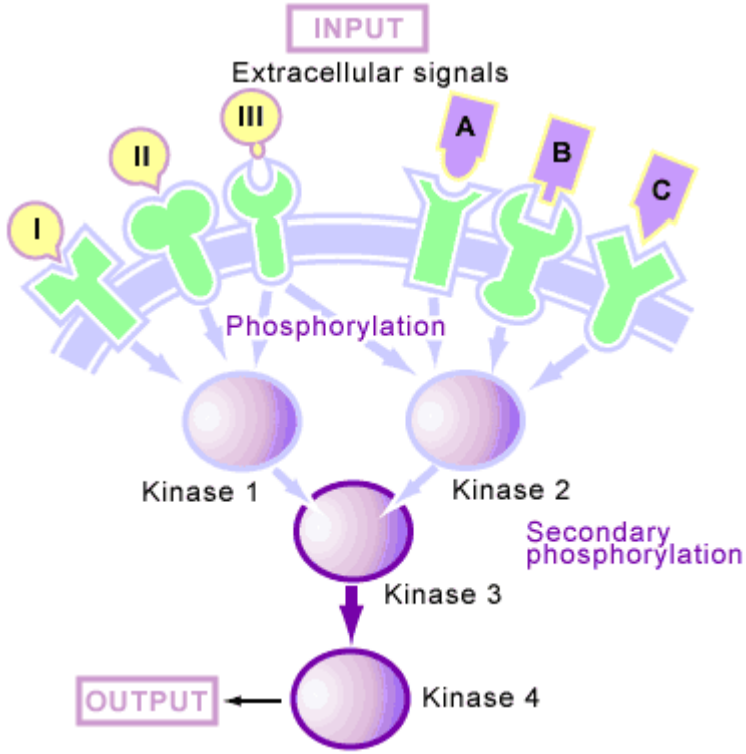
Regulación de actividad enzimática: Cascada de coagulación



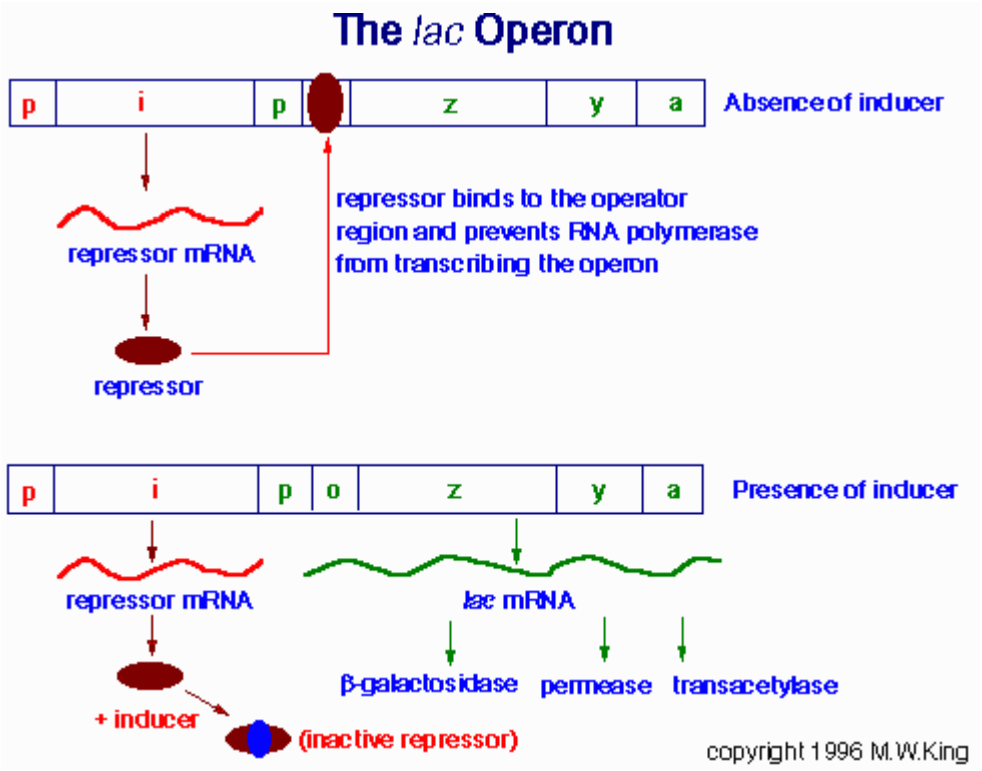
Regulación de actividad enzimática: Fosforilación



Science Creative Quarterly
University of British Columbia



Regulación de actividad enzimática: Síntesis de enzimas



Utilidad diagnóstica:

- La presencia de algunas enzimas indica que ha ocurrido dano celular
- ELISA
- PCR

Utilidad diagnóstica:

Cuando ocurre daño celular, se liberan enzimas a la sangre

Estas enzimas pueden ser específicas a los tejidos y podrían indicar el organo donde ocurre el daño.

- ALT (Alanine aminotransferase) abunda en el hígado

- La presencia de esta enzima en la sangre significa que el hígado ha sufrido daño.

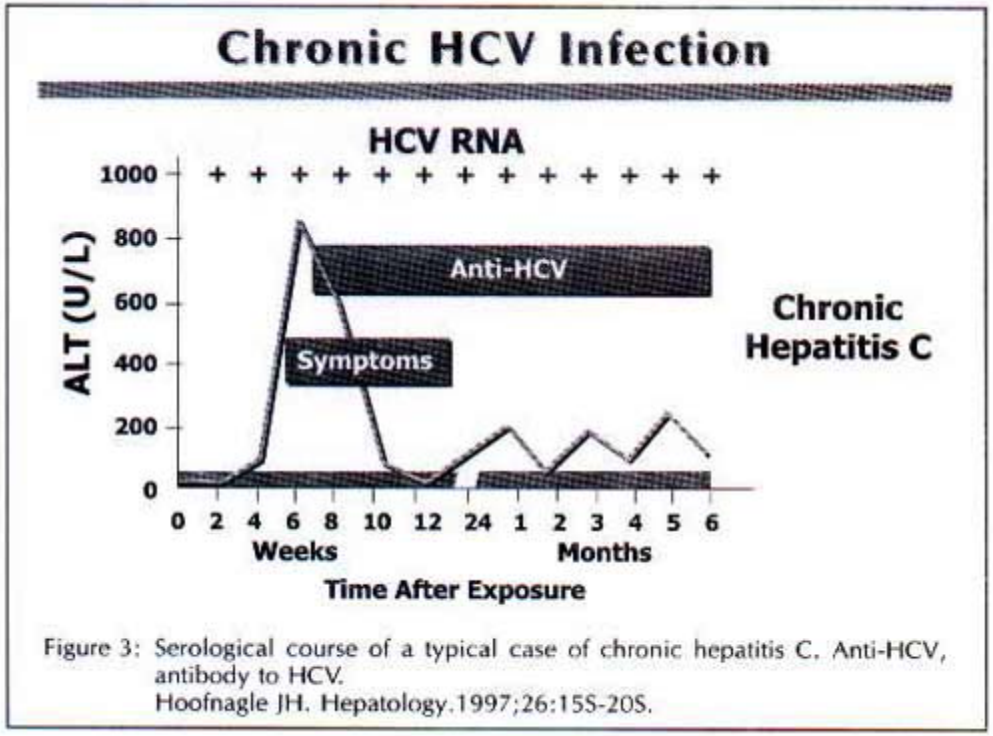


Figure 3: Serological course of a typical case of chronic hepatitis C. Anti-HCV, antibody to HCV.
Hoofnagle JH. Hepatology.1997;26:15S-20S.

TABLE 1
Conditions associated with elevated ALT levels in blood donors

Conditions	ALT levels elevated only at first blood donation (n=15)		ALT levels elevated during follow-up (n=101)		All donors with elevated ALT* (n=116)	
	n	(%)	n	(%)	n	(%)
Obesity	5	33	48	47.5	53	45.6
Alcohol abuse	5	33	24	23.8	29	25.0
Obesity and alcohol abuse	-	-	19	18.9	19	16.3
Exposition to solvents/ paints	-	-	3	2.9	3	2.6
Hyperlipidemia	1	7.0	1	1.0	2	1.7
Use of hepatotoxic drugs	1	7.0	-	-	1	0.9
Hipothyroidism	-	-	1	1.0	1	0.9
Diabetes mellitus	-	-	1	1.0	1	0.9
Reactive liver	-	-	3	2.9	3	2.6
Chronic hepatitis	-	-	1	1.0	1	0.9
Unknow	3	20	-	-	3	2.6

* ALT normal = 40 IU/L

Lactate Dehydrogenase

LDH-1 (4H) - in the heart

LDH-2 (3H1M) - in the reticuloendothelial system

LDH-3 (2H2M) - in the lungs

LDH-4 (1H3M) - in the kidneys

LDH-5 (4M) - in the liver and striated muscle

LDH is a tetramer composed of subunits termed M and H

Utilidad diagnóstica:

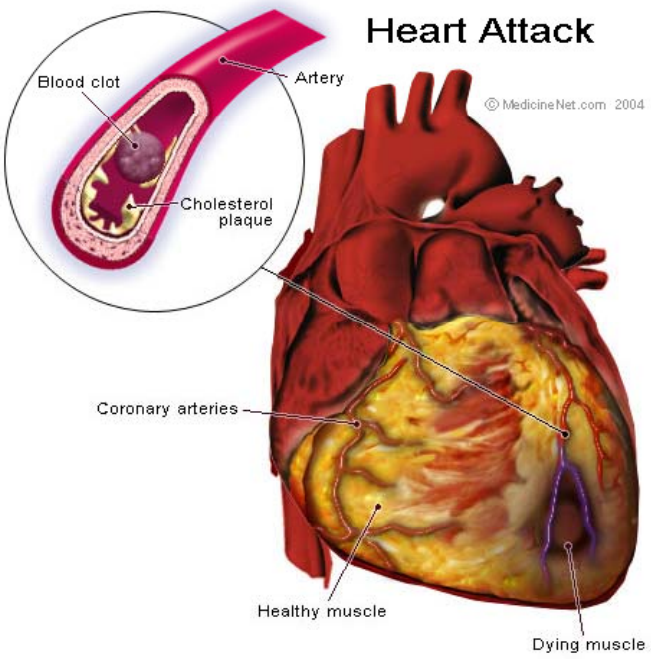
Dehidrogenasa de lactato (LDH)

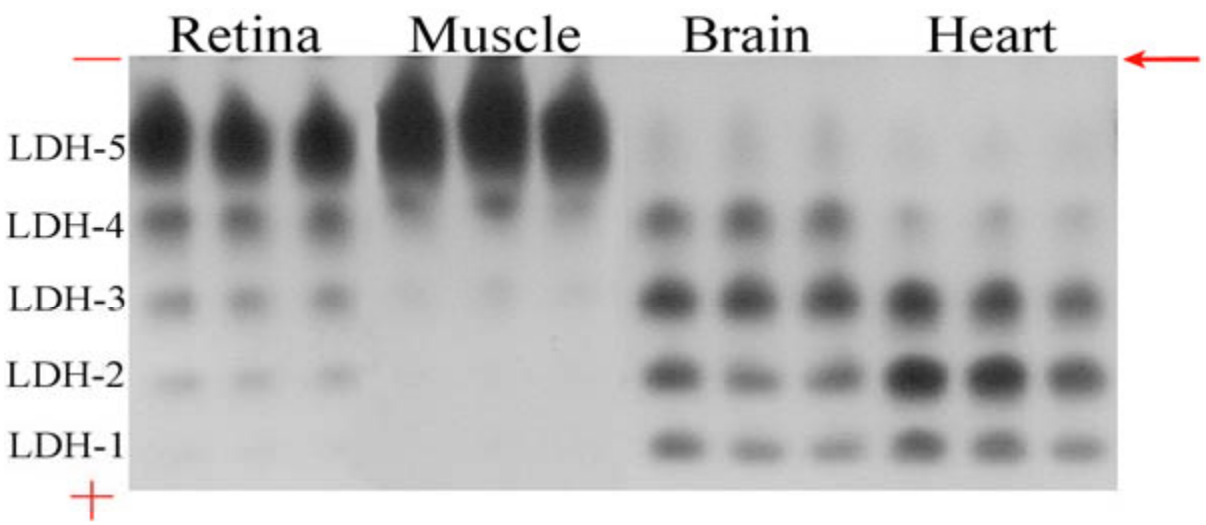
LDH 1 – Corazon y globulos rojos - 17% - 27% del suero normal

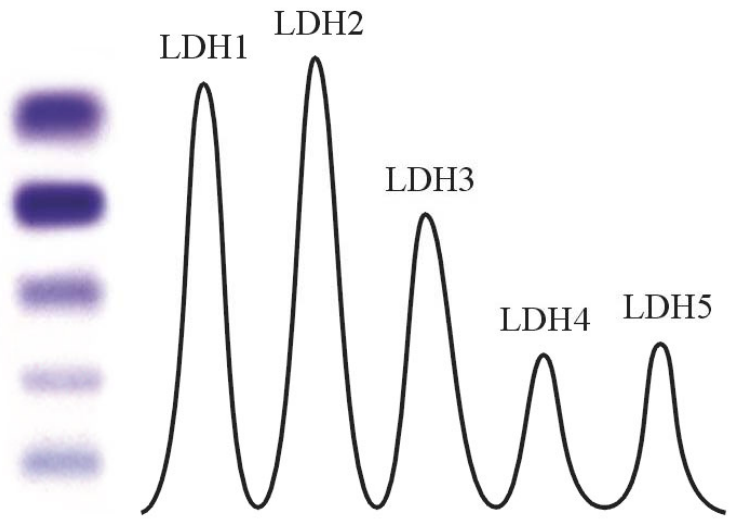
LDH 2 – Predomina en suero- 27% - 37% del suero normal

$$\frac{LDH1}{LDH2} < 1$$ Normal

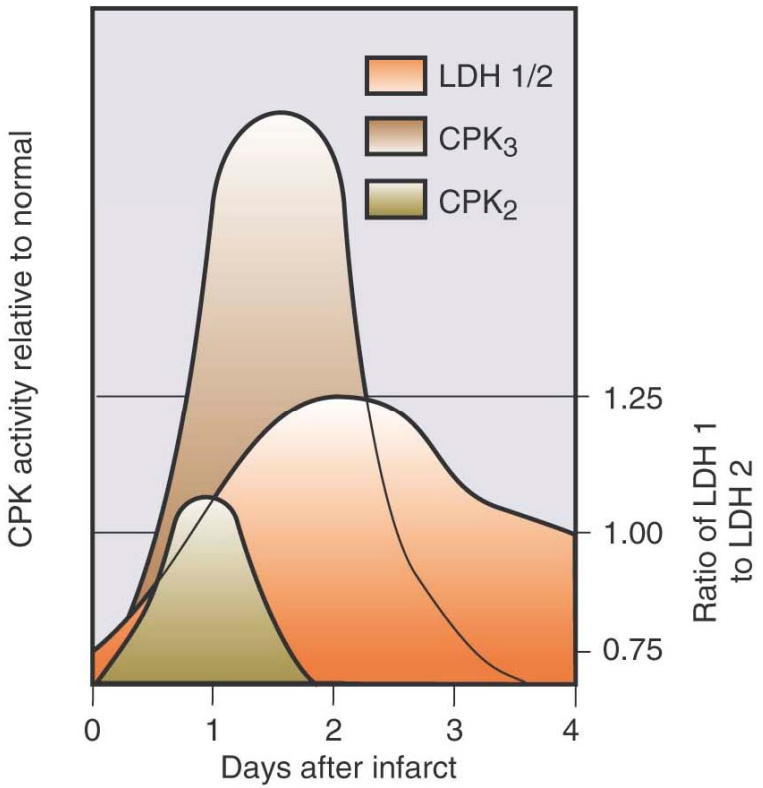
$$\frac{LDH1}{LDH2} > 1$$ 24-48 hrs despues de un infarto




Retina
Muscle
Brain
Heart
LDH-5
LDH-4
LDH-3
LDH-2
LDH-1

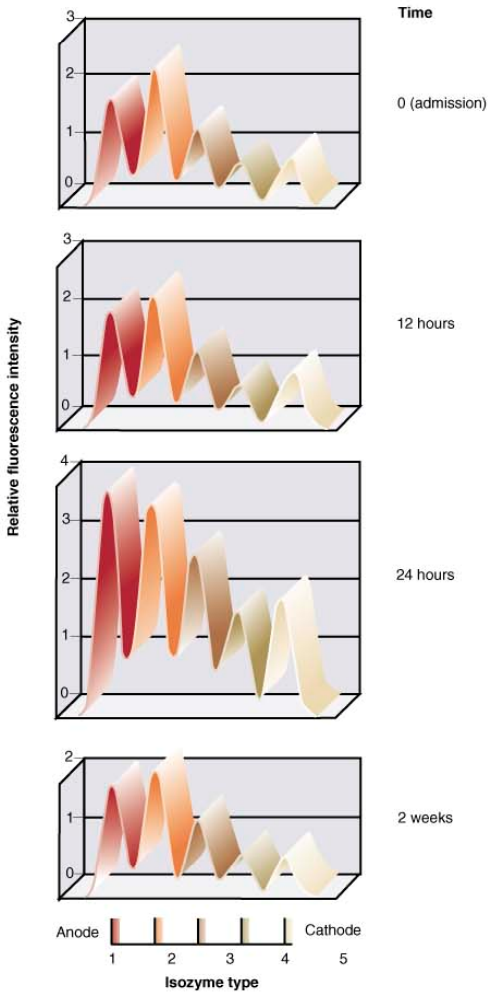

LDH1
LDH2
LDH3
LDH4
LDH5

Utilidad diagnóstica: LDH Isozymes



Characteristic changes in serum CPK and LDH isozymes following a myocard

Biochemistry With Clinical Correlations, Sixth Edition, Edited by Thomas M. Devlin. Copyright © 2006 John Wiley &



meter scans of LDH isozymes at time intervals fo

al Laboratories, University of Arkansas for Medical

cal Correlations, Sixth Edition, Edited by Thomas M. Devlin. Copyrigh

Utilidad diagnóstica:

Dehidrogenasa de lactato (LDH)

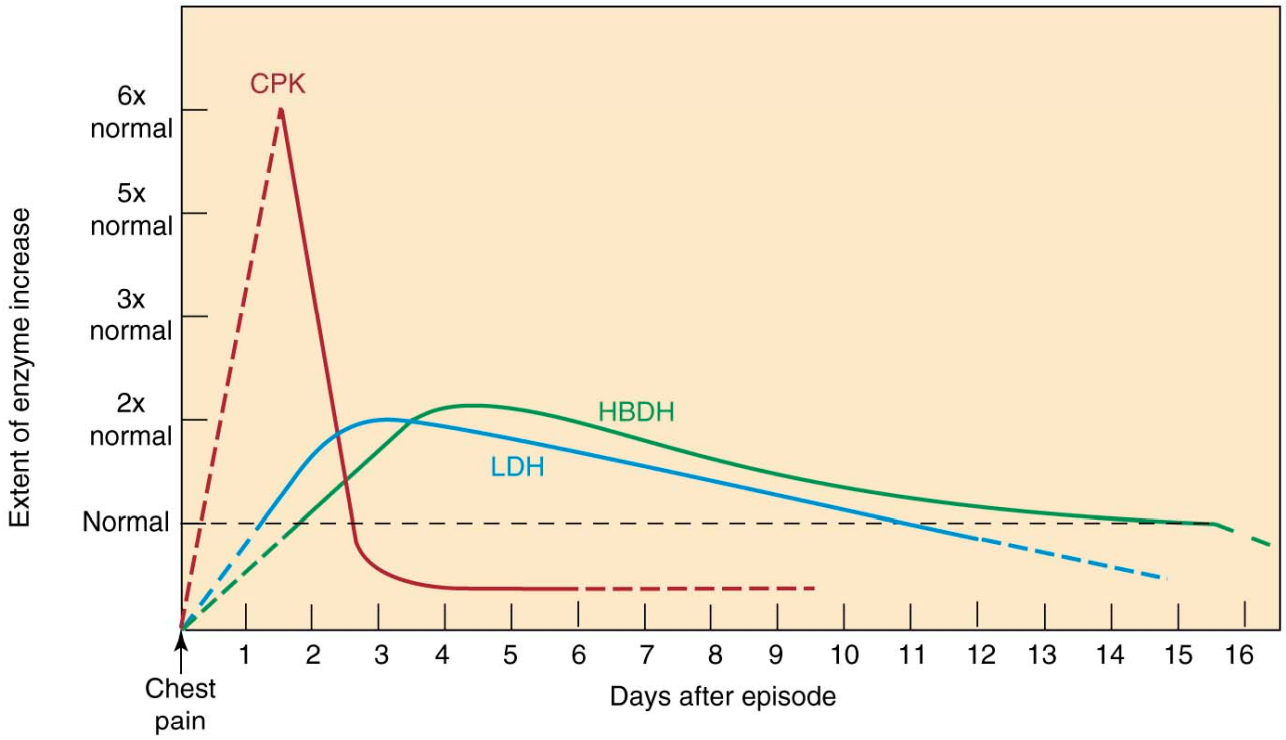
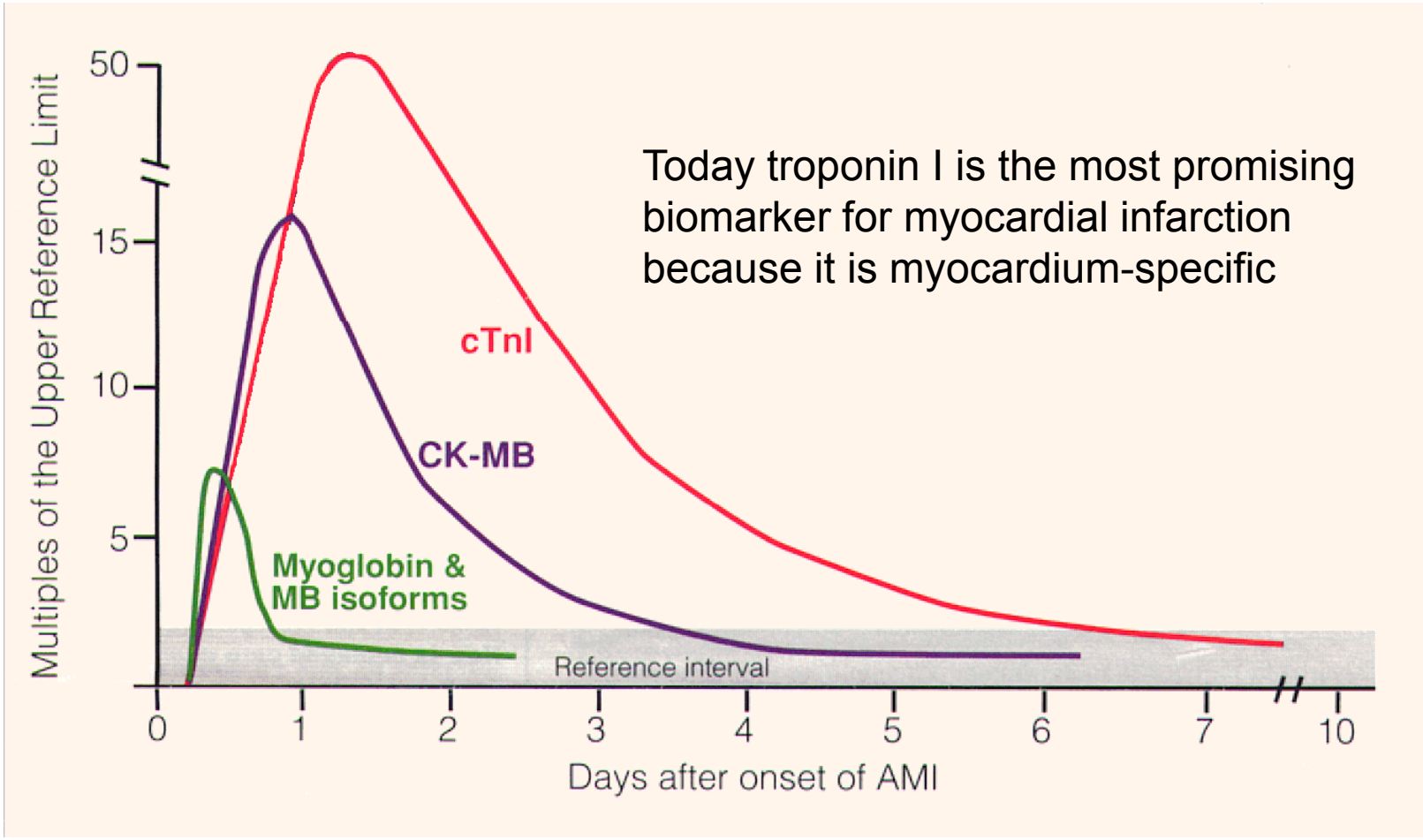


Figure 10.71. Kinetics of release of cardiac enzymes into serum following a myocardial infarction. Reprinted with permission from Coodley, E. L. *Diagnostic Enzymes.* Philadelphia: Lea & Febiger, 1970, p. 61.



Today troponin I is the most promising biomarker for myocardial infarction because it is myocardium-specific

Utilidad diagnóstica: ELISA

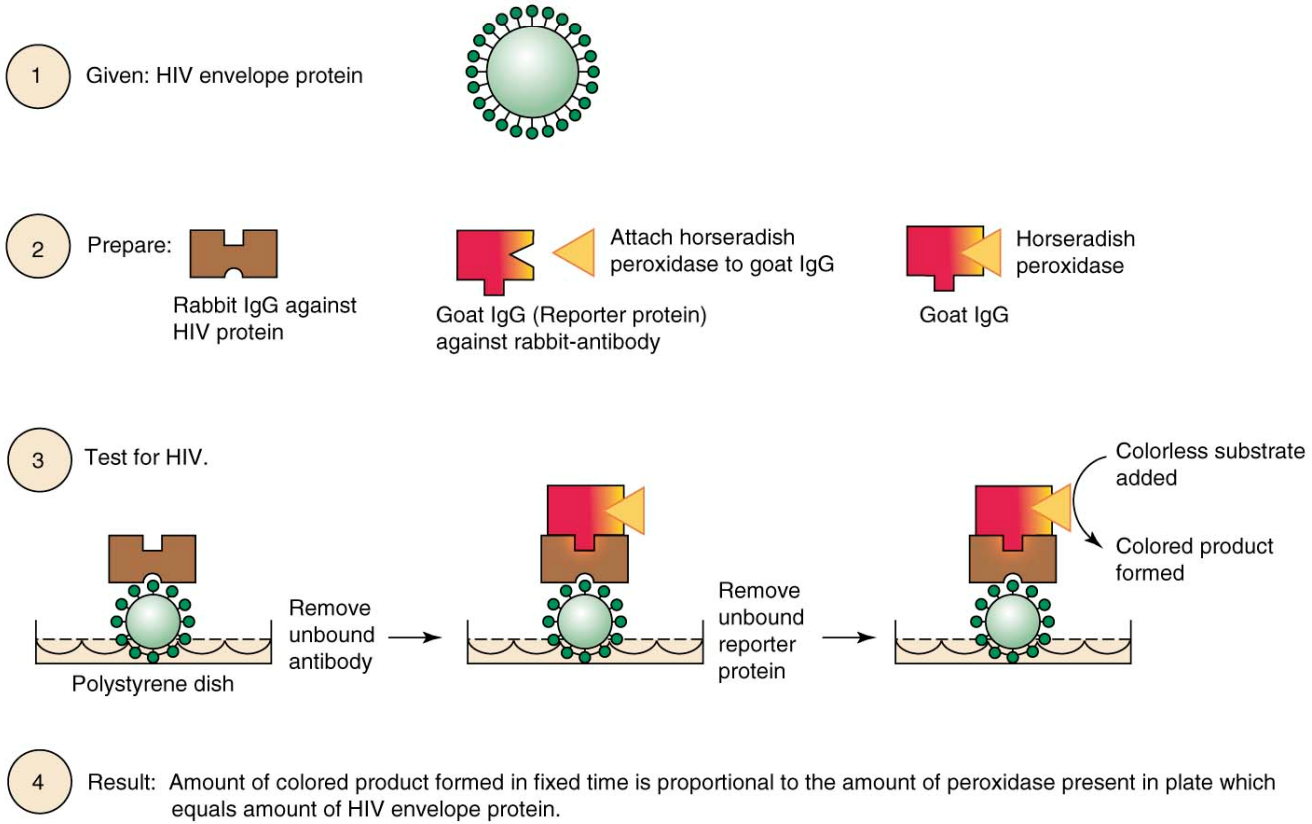
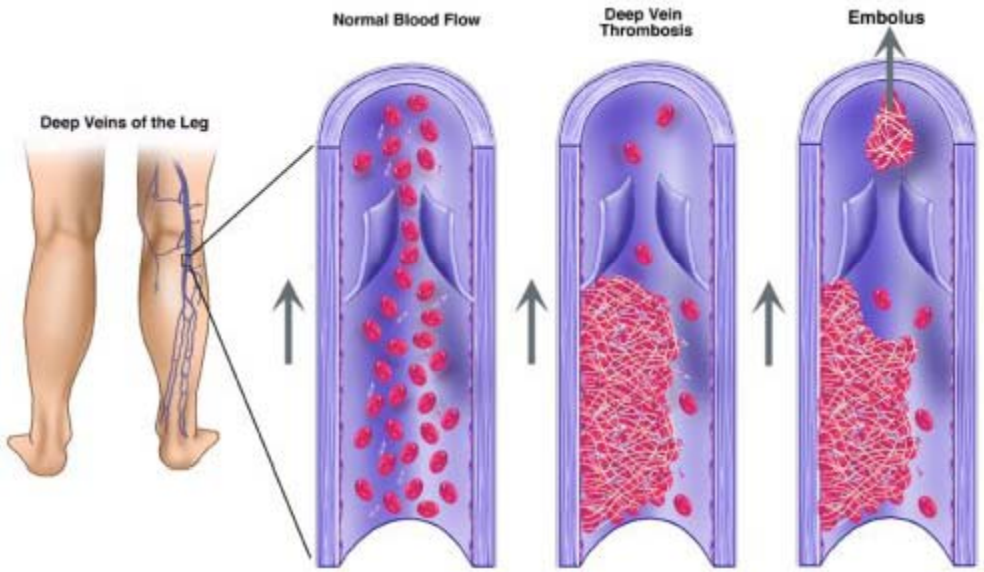
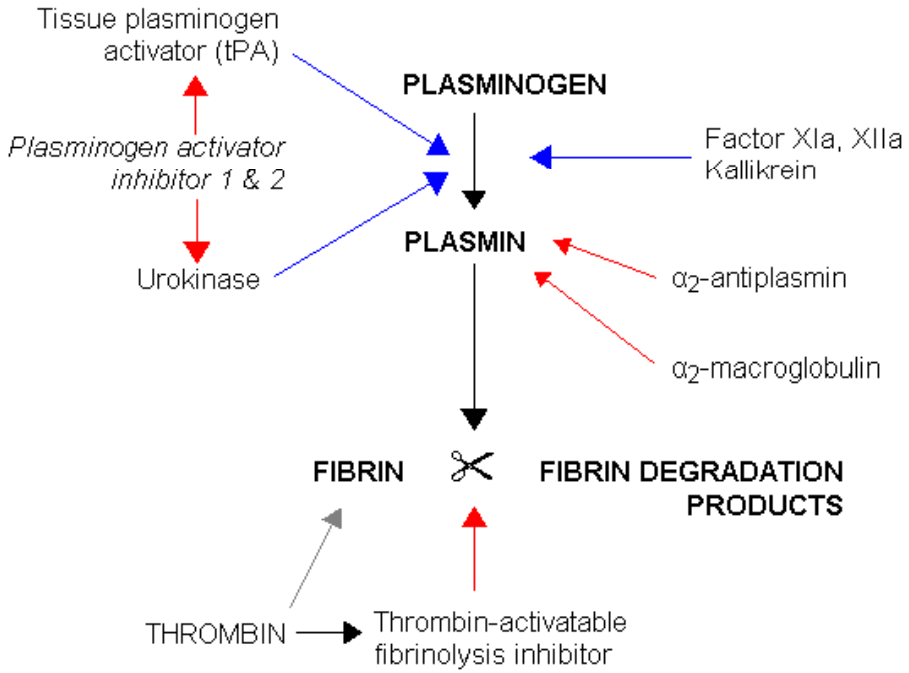


Figure 10.72. Schematic of ELISA (enzyme-linked immunoadsorbent assay) for detecting the human immunodeficiency virus (HIV) envelope proteins.

Utilidad diagnóstica: Urokinasa para coágulos





Industrial applications of enzymes:

Detergent additives – starch degrading enzyme
Food additives
- pet foods – easier to digest
- cattle and poultry feeds – easier to turn to fertilizer

Organic waste degradation –
Oil degradation - lipases
Paper recycling
Food preparation
- -turns trans fats to saturated fats
- -lactose-free milk

Leather processing
Chemical synthesis