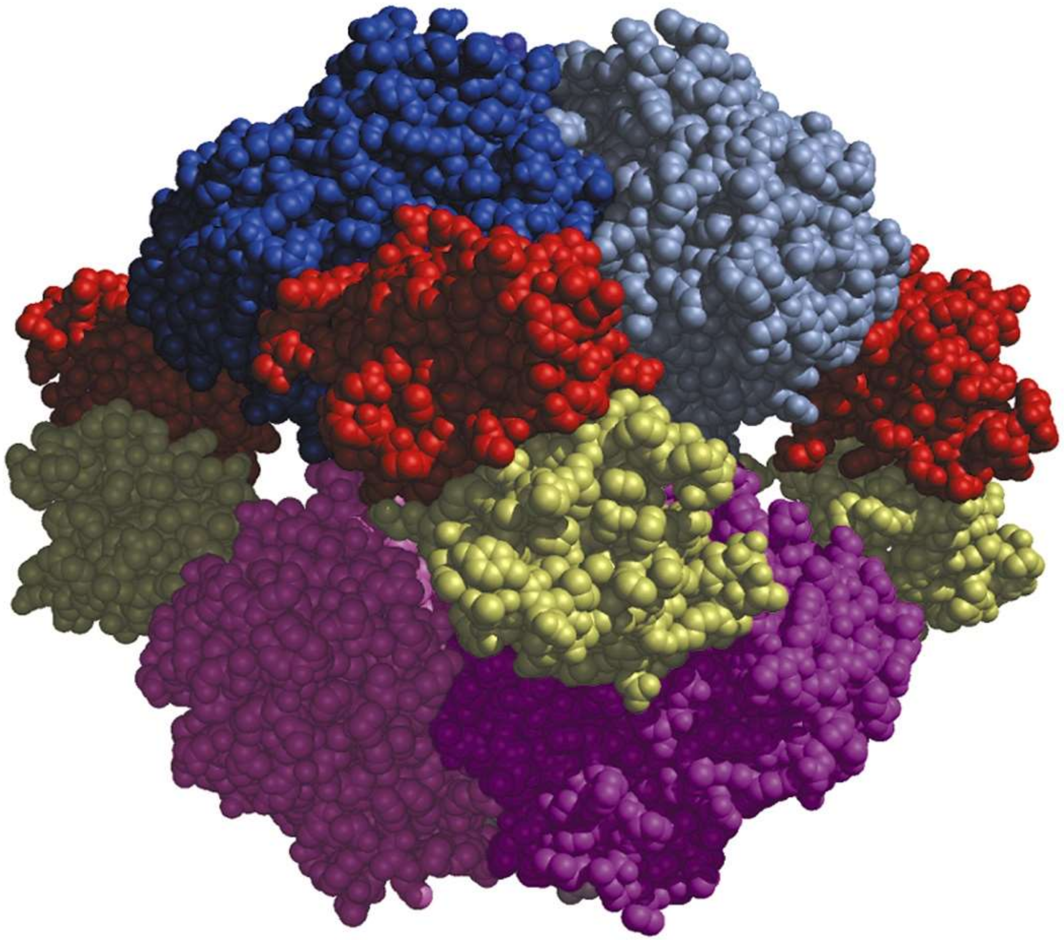
Enzimas

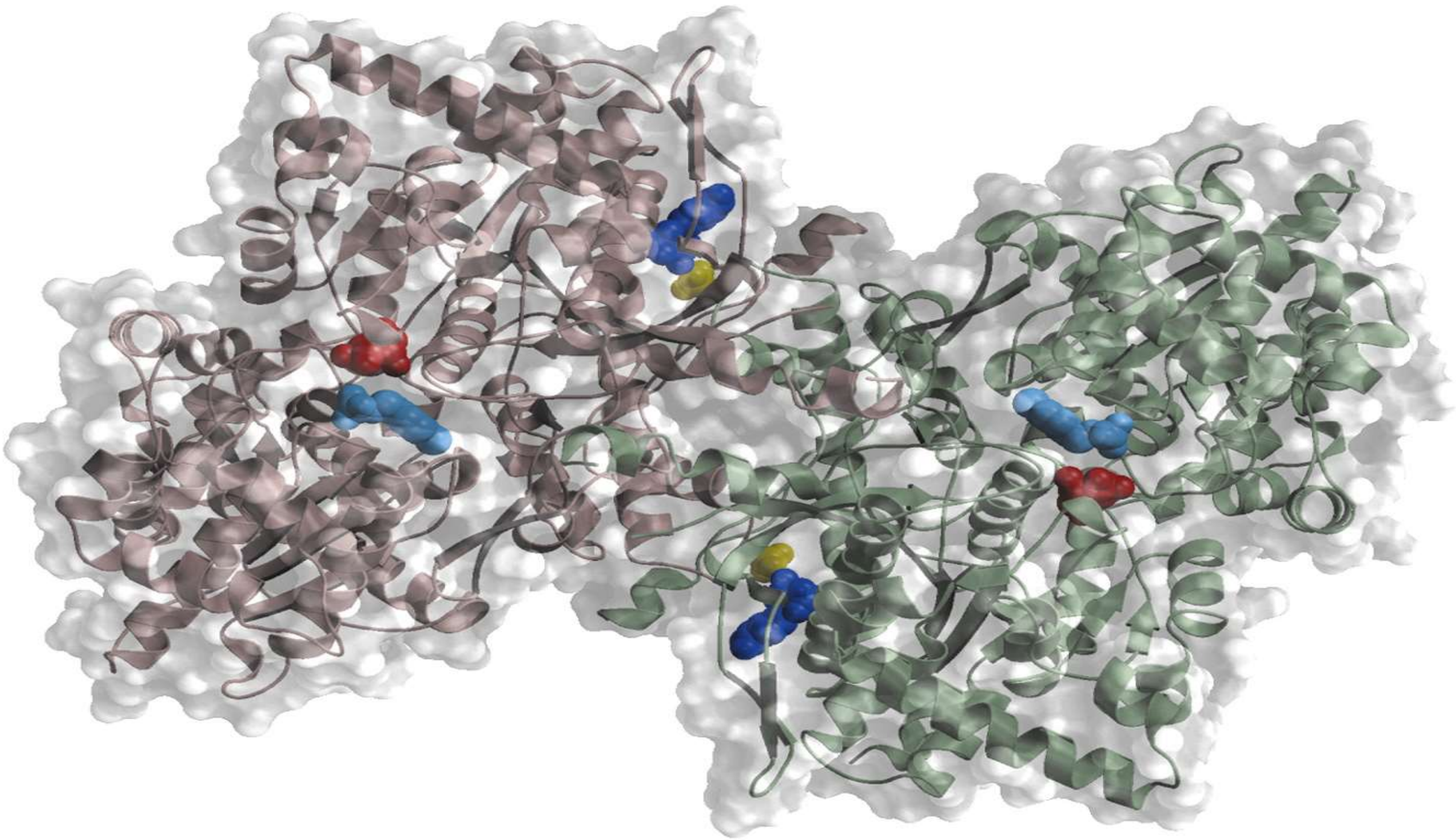


Introdução

Condições fundamentais para a vida:

1) capacidade de auto-replicar;

2) catalisar reações químicas eficiente e seletivamente. Ex: oxidação da sacarose.



A maioria das enzimas são proteínas

- Co-fator: **íons inorgânicos;**
- Coenzimas: **molécula orgânica complexa;**
- Grupo prostético: **coenzima ou íon metálico ligado covalentemente a enzima**

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

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)

Classificação das enzimas

- De acordo com as reações que catalisam

International Classification of Enzymes*

No.	Class	Type of reaction catalyzed
1	Oxidoreductases	Transfer of electrons (hydride ions or H atoms)
2	Transferases	Group-transfer reactions
3	Hydrolases	Hydrolysis reactions (transfer of functional groups to water)
4	Lyases	Addition of groups to double bonds, or formation of double bonds by removal of groups
5	Isomerases	Transfer of groups within molecules to yield isomeric forms
6	Ligases	Formation of C—C, C—S, C—O, and C—N bonds by condensation reactions coupled to ATP cleavage

*Most enzymes catalyze the transfer of electrons, atoms, or functional groups. They are therefore classified, given code numbers, and assigned names according to the type of transfer reaction, the group donor, and the group acceptor.

Exemplo:

ATP + glicose → ADP + glicose 6-fosfato

Nome trivial: Hexocinase

Nome sistemático: ATP-glicose fosfotransferase

Número na Comissão de Enzimas (EC): 2.7.1.1

Primeiro dígito: (2) classe da enzima ➡ Transferase;

Segundo dígito: (7) subclasse ➡ fosfotransferase;

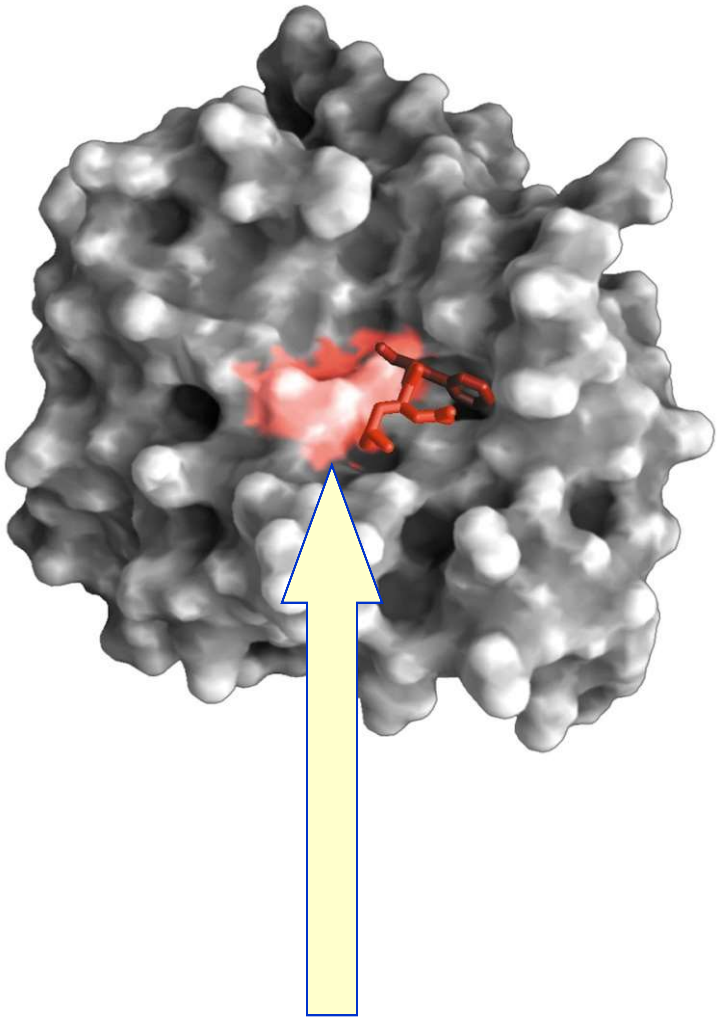
Terceiro dígito: (1) fosfotransferase que possui um grupo hidroxila aceptor de fosfato;

Quarto dígito: (1) glicose é o aceptor de fosfato.

Como as enzimas funcionam?

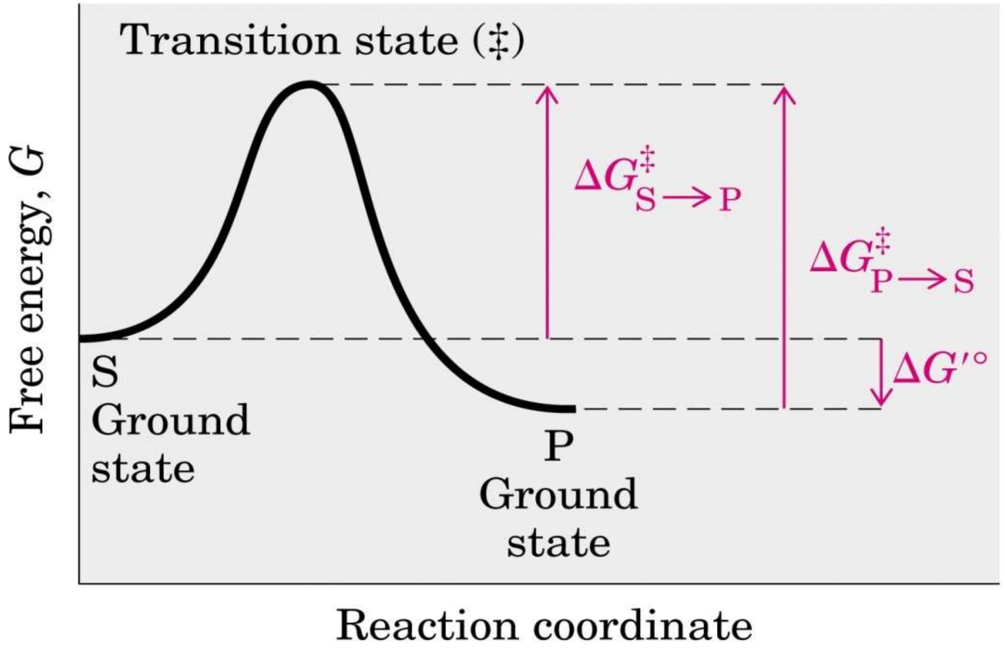
As enzimas afetam a velocidade mas não o equilíbrio químico das reações

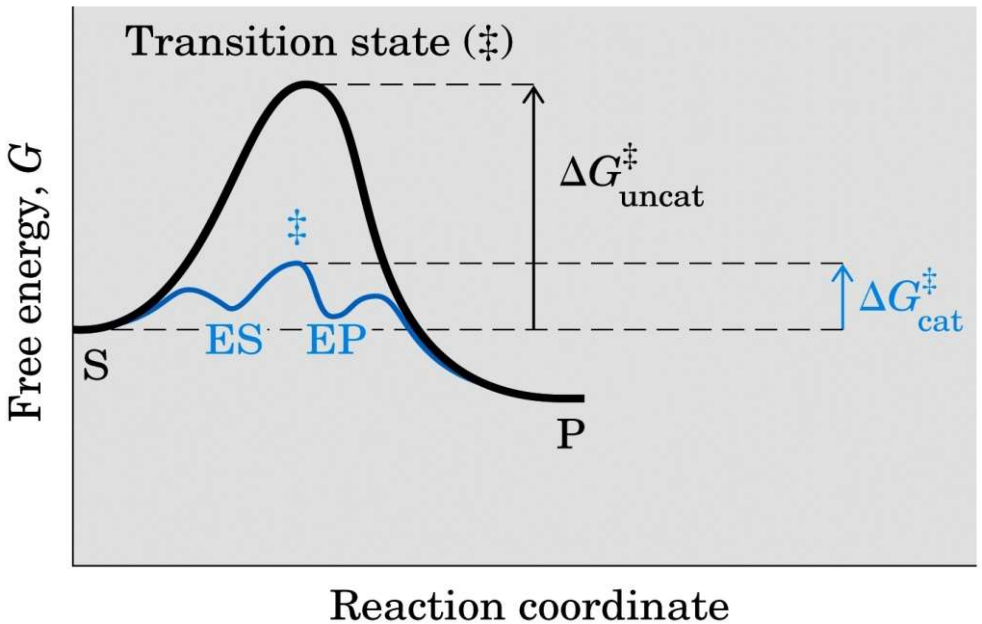
$$A \underset{10^{-6}}{\overset{10^{-4}}{\rightleftharpoons}} B$$



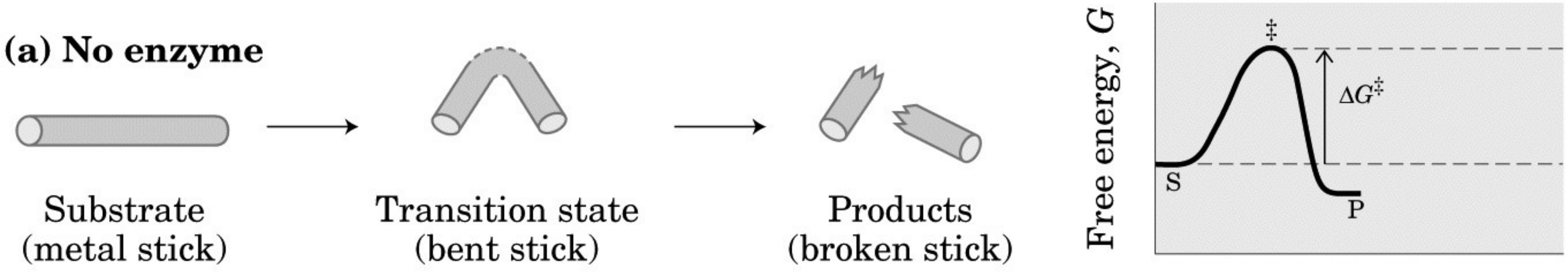
Sítio ativo

Diagramas de coordenadas de uma reação química

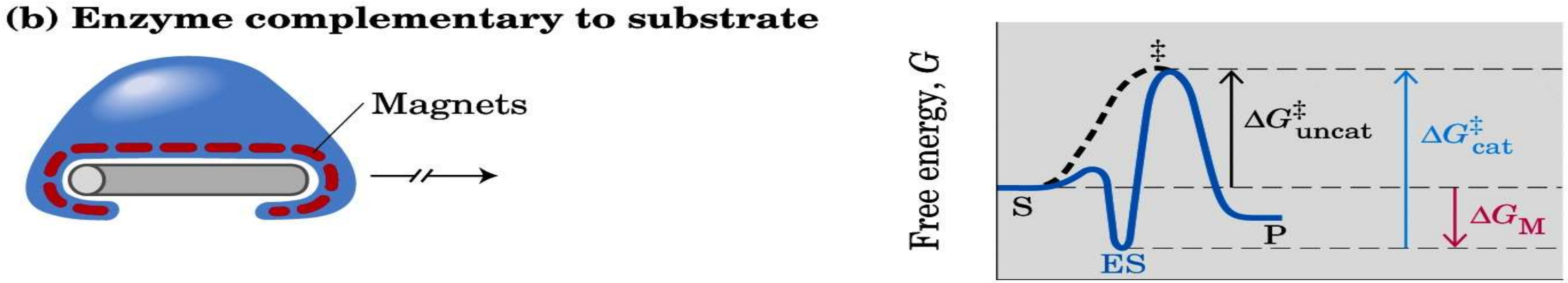




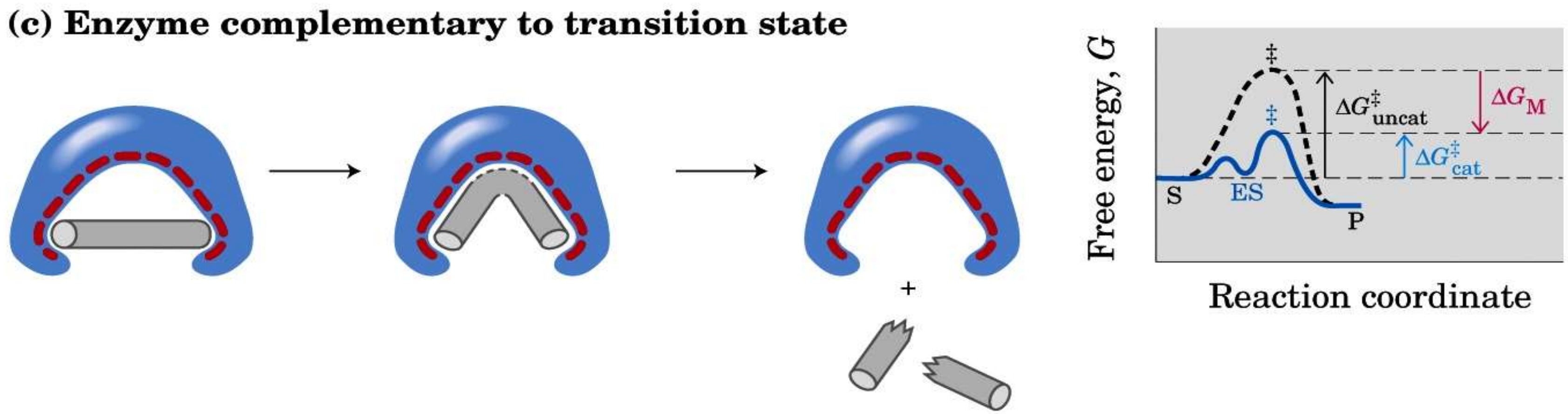
Otimização da interações fracas no estado de transição



Modelo chave e fechadura

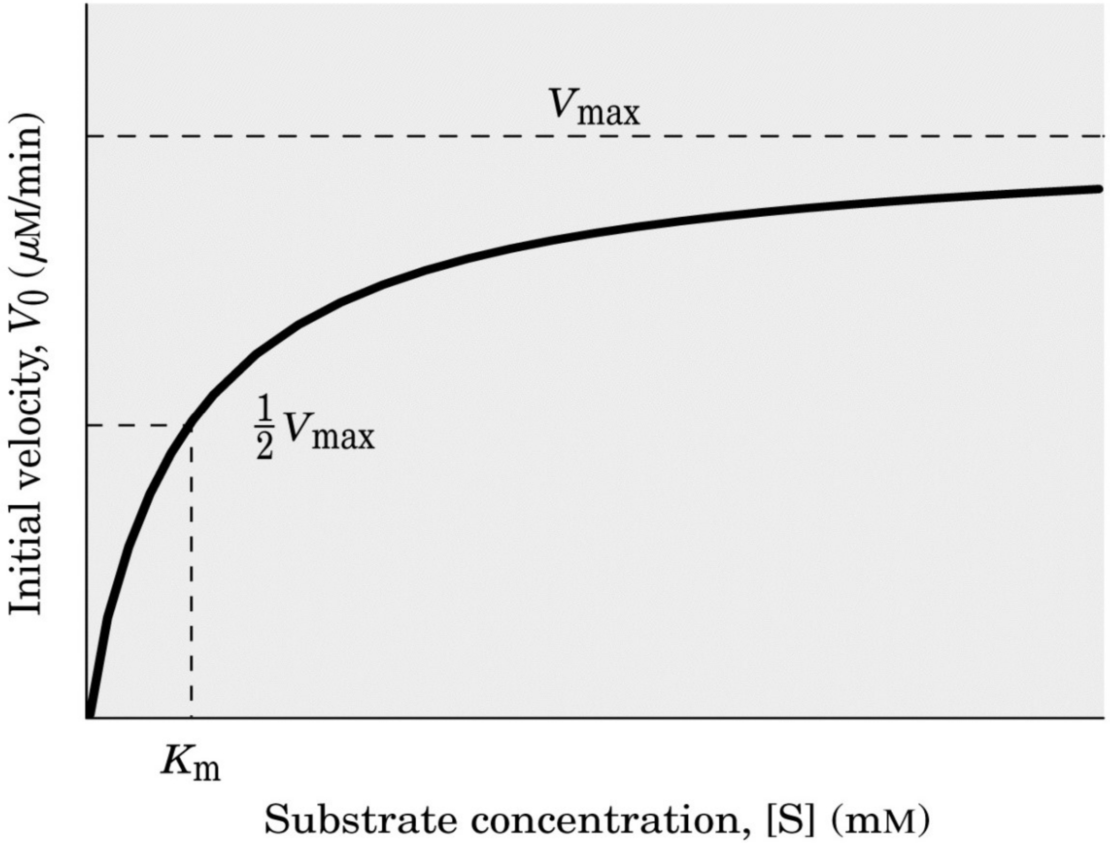


Modelo encaixe induzido



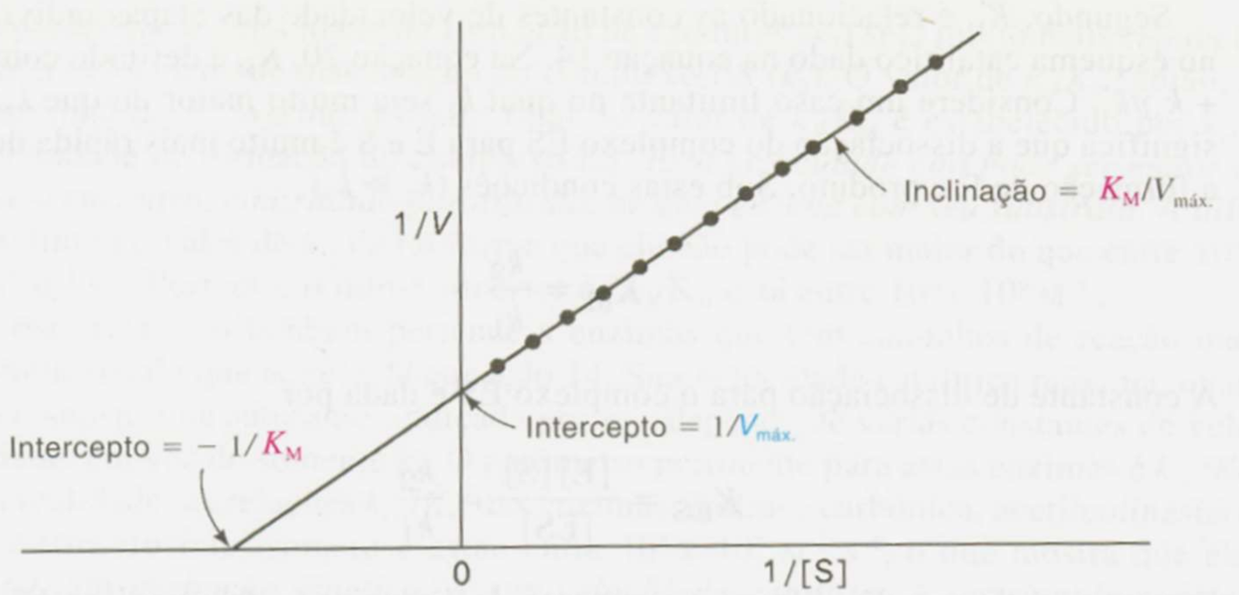
O Modelo de Michaelis-Menten

$$E + S \underset{K_2}{\overset{K_1}{\rightleftharpoons}} ES \xrightarrow{K_3} P + E$$



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

Transformações da equação de Michaelis-Menten



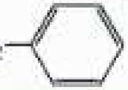
$$\frac{1}{V} = \frac{1}{V_{max}} + \frac{K_M}{V_{max}} \cdot \frac{1}{[S]}$$

Perfeição cinética na catálise enzimática

$$E + S \underset{K_2}{\overset{K_1}{\rightleftharpoons}} ES \xrightarrow{K_3} P + E$$

O critério Kcat/KM

QUADRO 8.7 Preferências de Substrato da Quimotripsina

Aminoácido em Éster	Cadeia Lateral do Aminoácido	k_{cat}/K_M ($s^{-1}M^{-1}$)
Glicina	$-H$	$1,3 \times 10^{-1}$
Valina	$-CH(CH_3)_2$	2,0
Nor-valina	$-CH_2CH_2CH_3$	$3,6 \times 10^2$
Nor-leucina	$-CH_2CH_2CH_2CH_3$	$3,0 \times 10^3$
Fenilalanina	$-CH_2-$ 	$1,0 \times 10^5$

Fonte: Segundo A. Fersht, *Structure and Mechanism in Protein Science: A Guide to Enzyme Catalysis and Protein Folding* (W. H. Freeman and Company, 1999), Quadro 7.3.

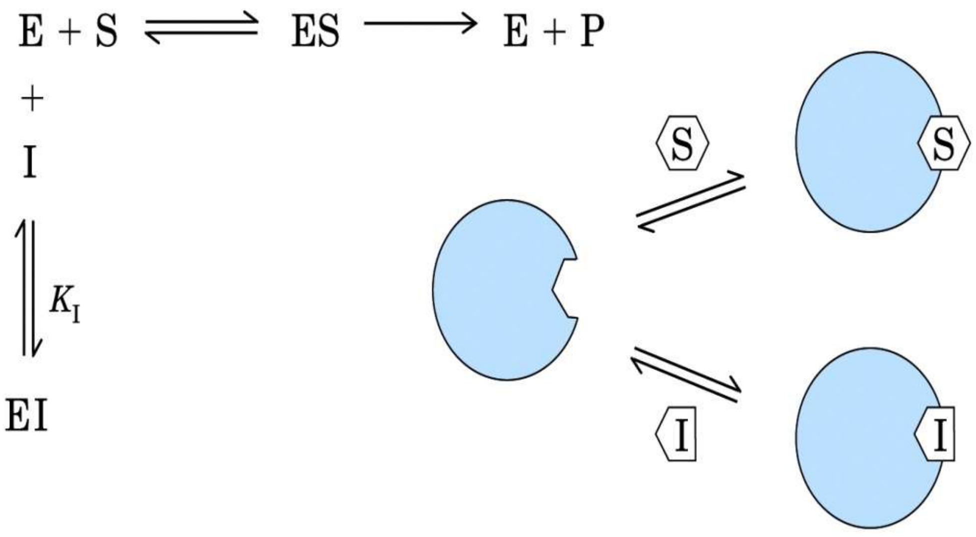
QUADRO 8.6 Números de Renovação Máximos de Algumas Enzimas

Enzima	Número de Renovação (por segundo)
Anidrase carbônica	600.000
3-Ceto esteróide isomerase	280.000
Acetilcolinesterase	25.000
Penicilinase	2.000
Lactato desidrogenase	1.000
Quimotripsina	100
DNA polimerase I	15
Triptofano sintase	2
Lisozima	0,5

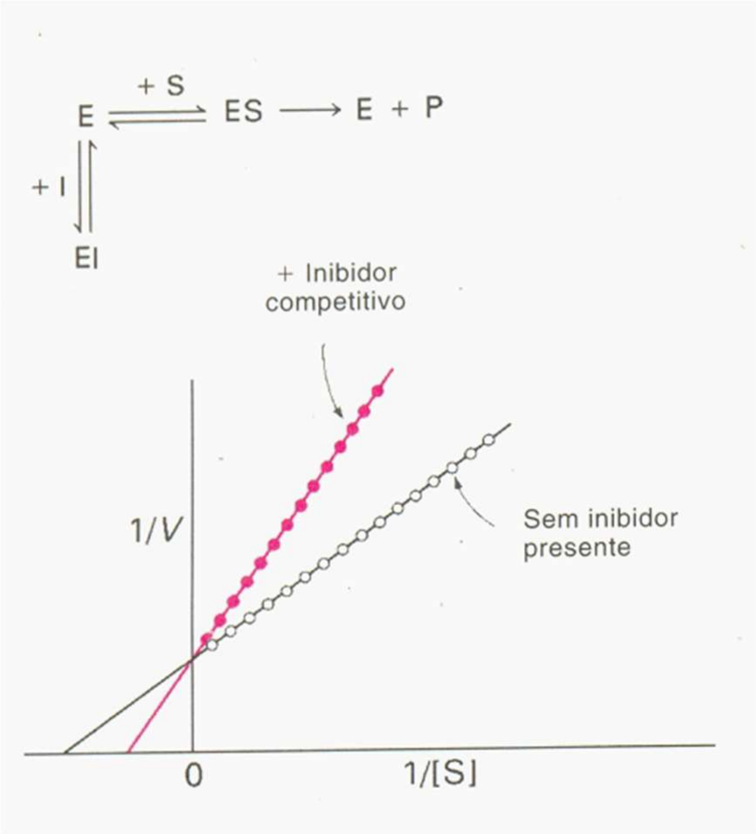
Inibição enzimática

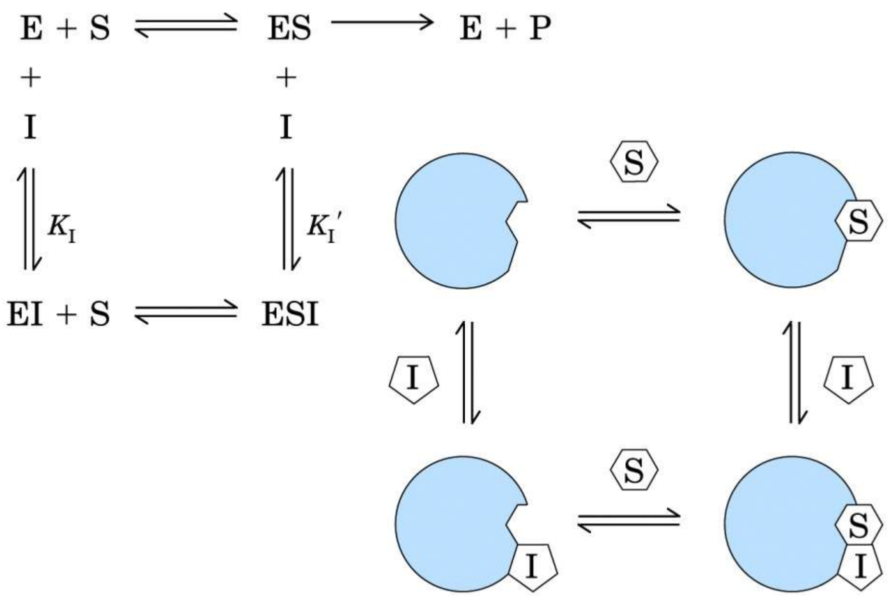
1 - Irreversível

2- Reversível
- competitiva
- não competitiva

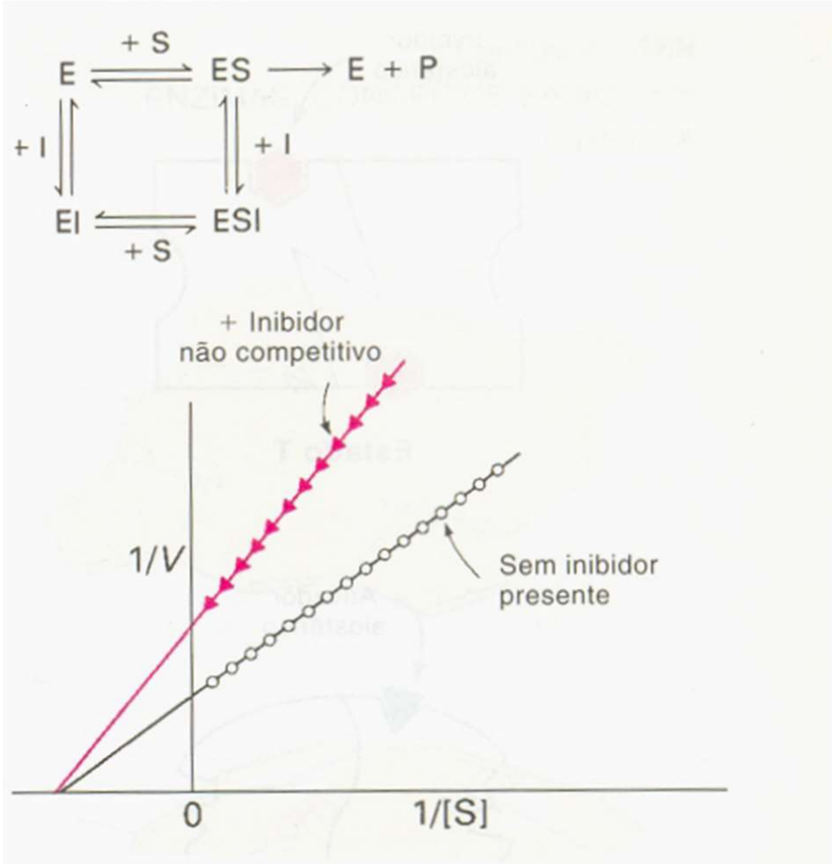


(a) Competitive inhibition



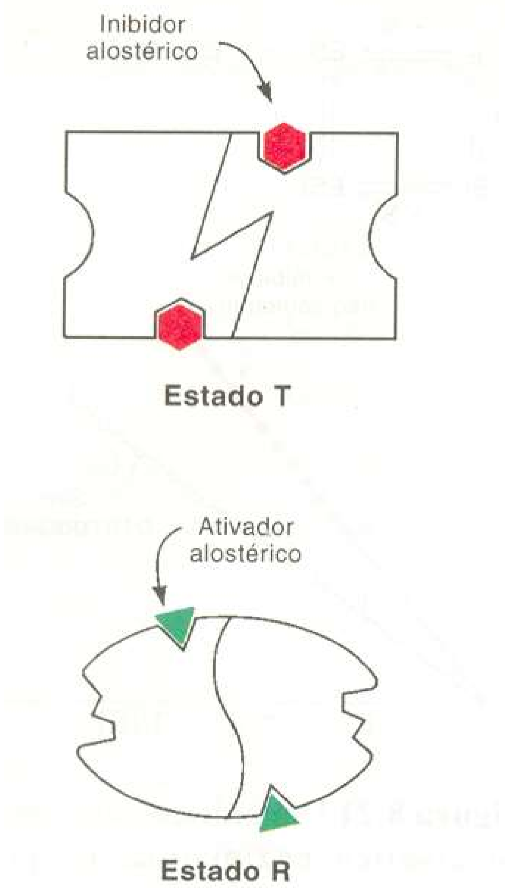


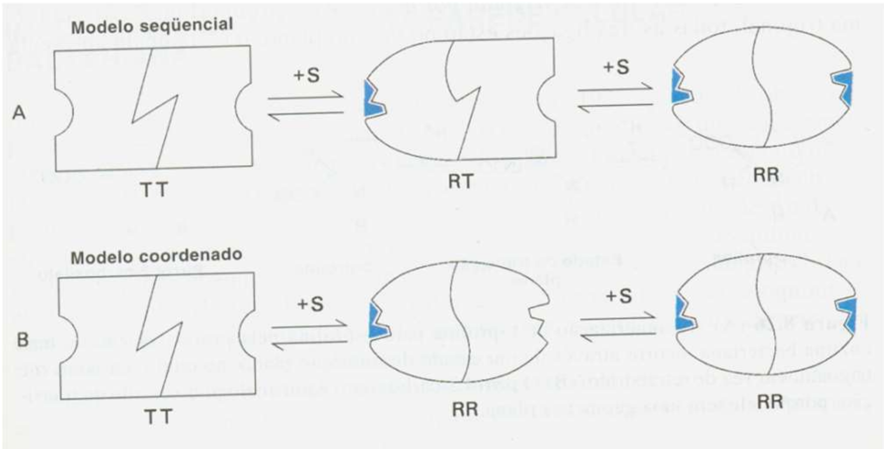
(c) Mixed inhibition



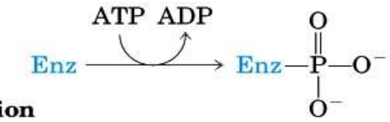
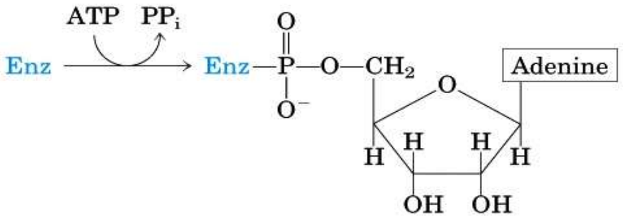
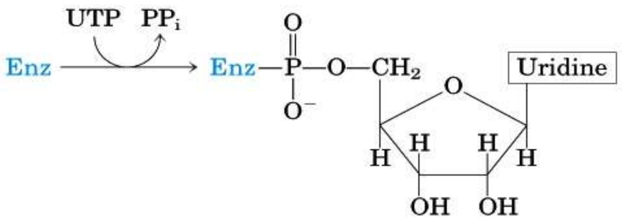
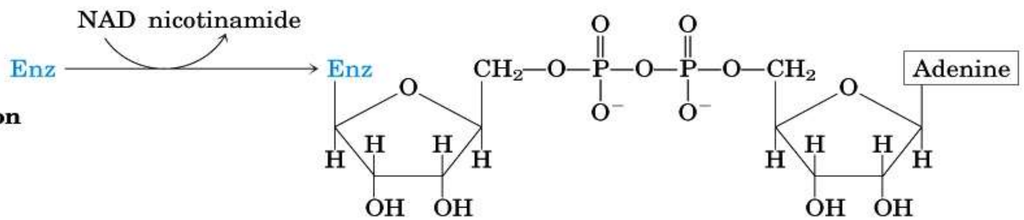
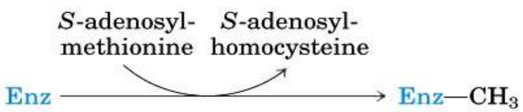
Enzimas reguladoras

1 – Enzimas alostéricas





2- Enzimas reguladas por modificação covalente reversível

Covalent modification		Amino acid residues known to accept covalent modification
Phosphorylation		Tyr, Ser, Thr, His
Adenylylation		Tyr
Uridylylation		Tyr
ADP-ribosylation		Arg, Gln, Cys, diphthamide (a modified His)
Methylation		Glu

Inibição por retroalimentação