

Química Medicinal



Mini-curso 17

62ª Reunião Anual SBPC - UFRN



27-30 julho de 2010



LASSBio

UFRJ

Eliezer j. Barreiro

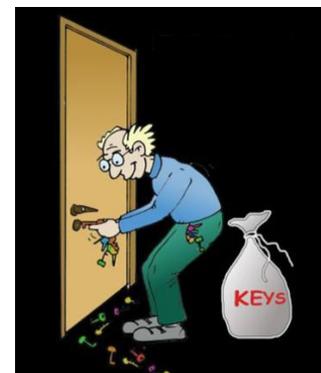
Professor Titular

Parte 2





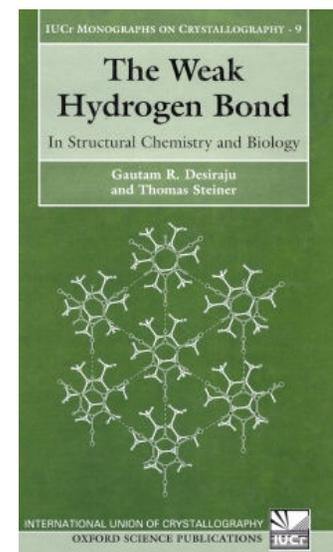
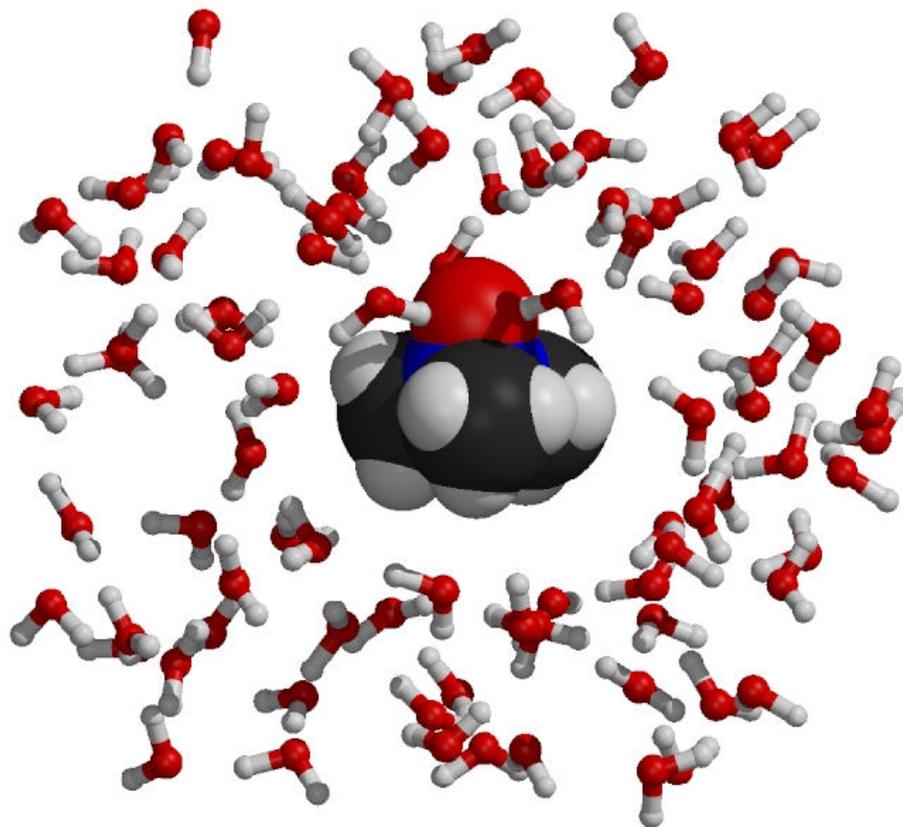
***A importância das
interações frágeis***



**Química
Medicinal**



A importância das “*ligações*” frágeis...



“*ligações*”
de hidrogênio ...

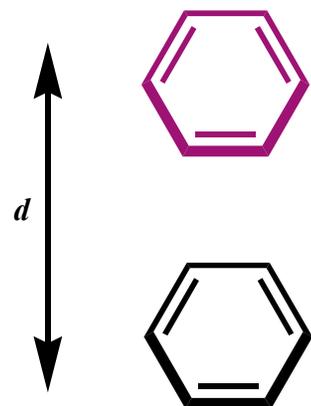


Linus Pauling, 1939

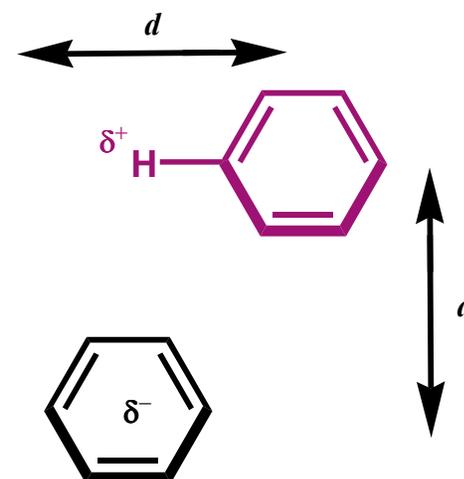




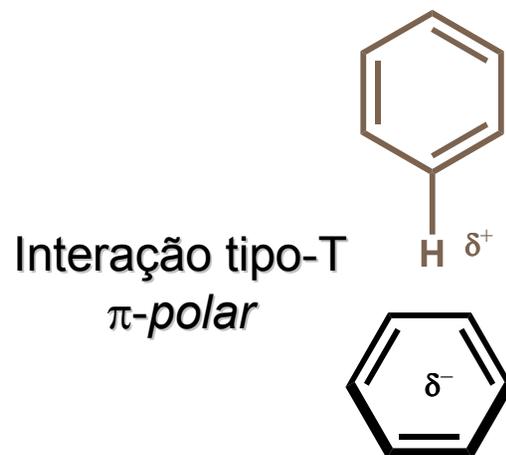
Interações π - π



Interação sanduíche
 π -stacking



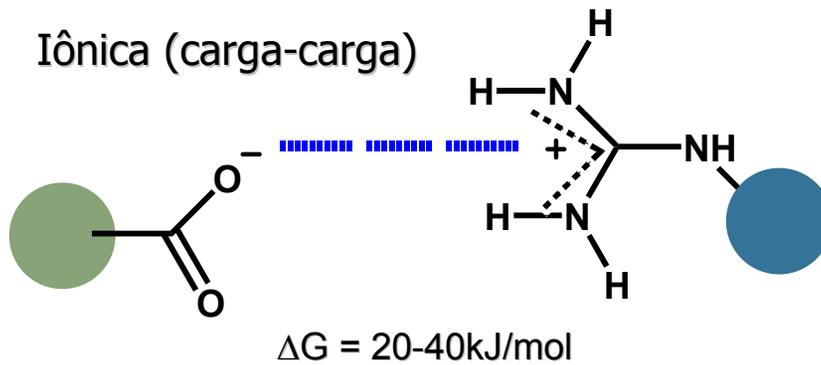
Interação paralela



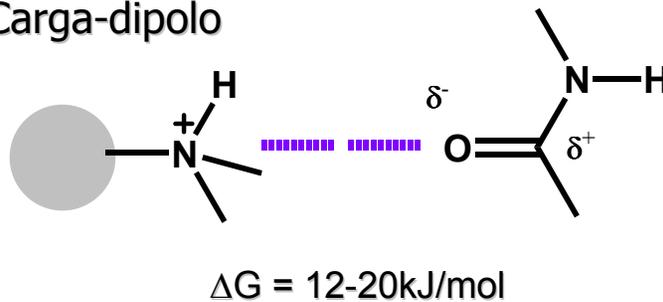


Tipos de interações

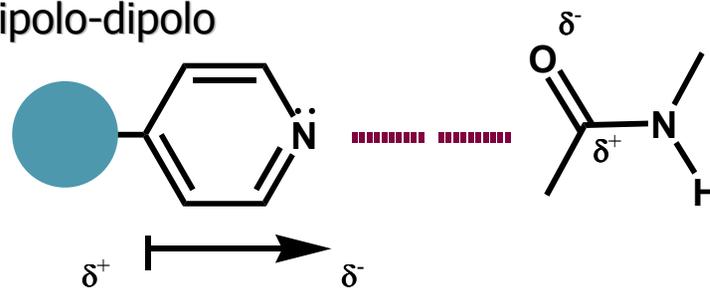
Iônica (carga-carga)



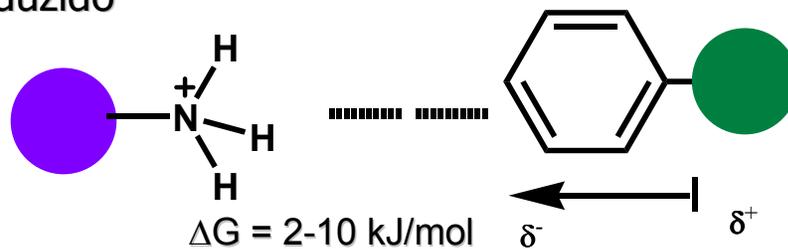
Carga-dipolo



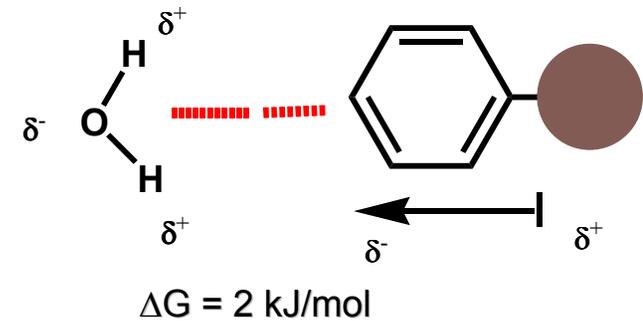
Dipolo-dipolo



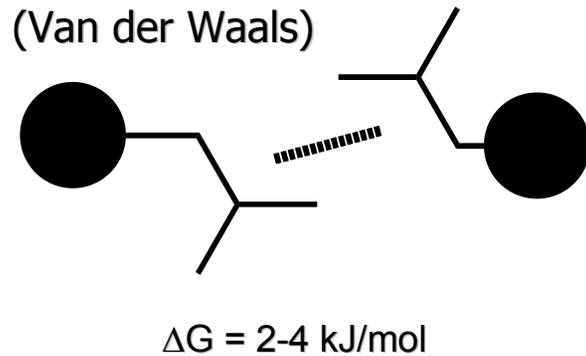
Carga-dipolo induzido



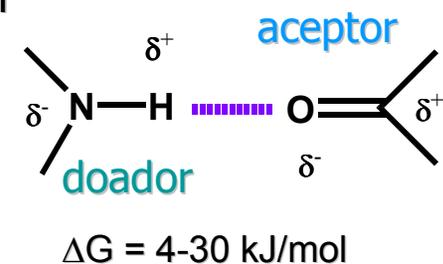
Dipolo induzido-dipolo



Dispersão (Van der Waals)



Ligação-H

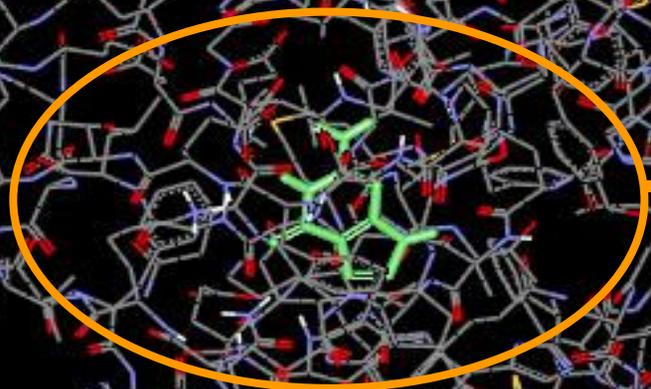




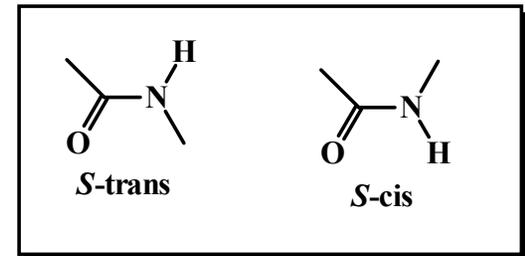
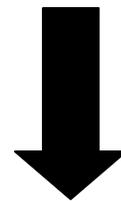
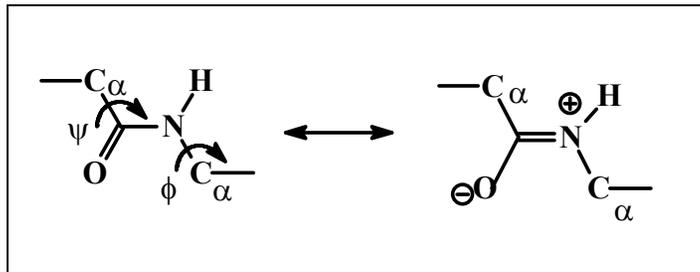
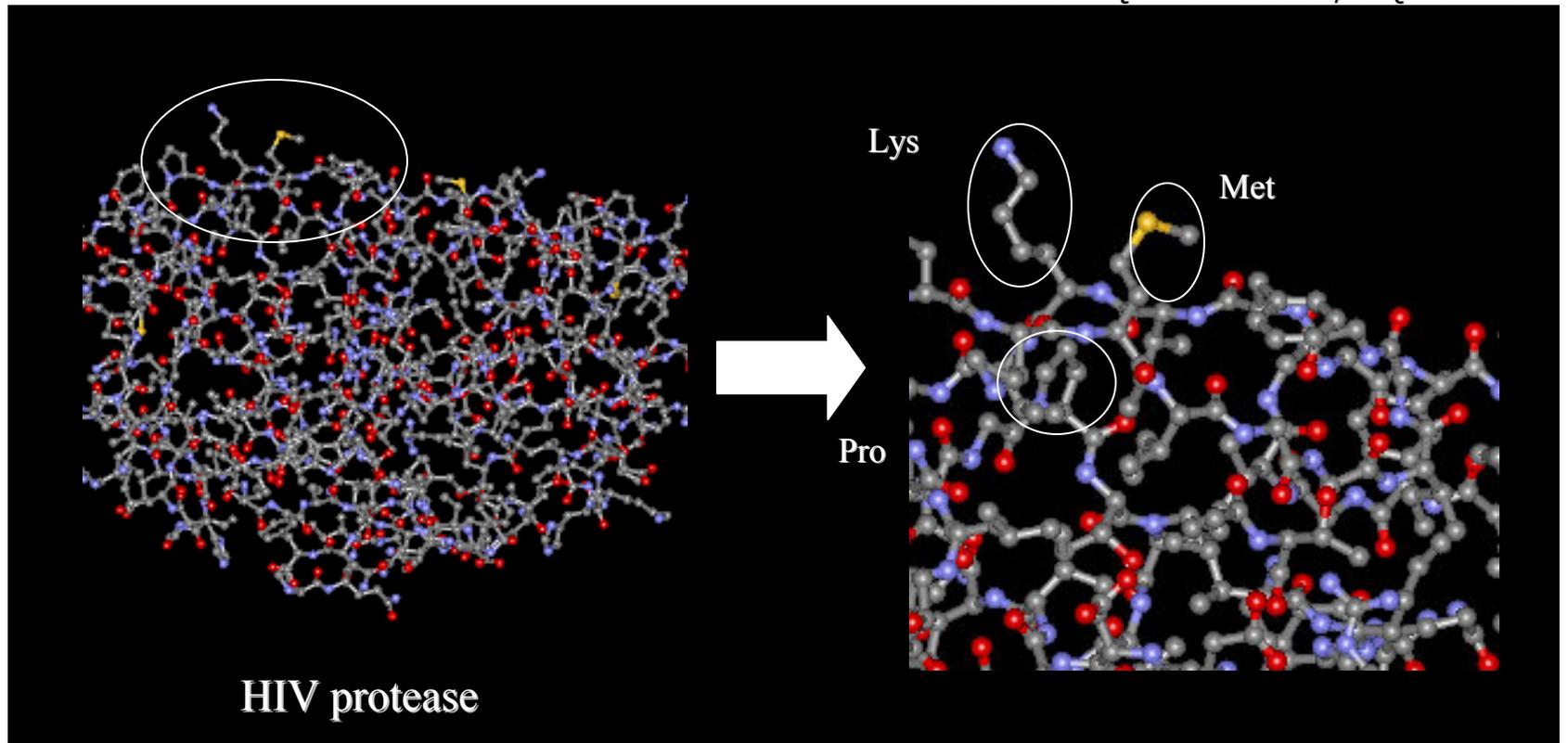
Biorreceptor

Estrutura 3D do alvo terapêutico

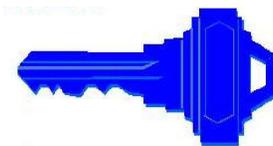
Sítio de reconhecimento molecular



Fármaco

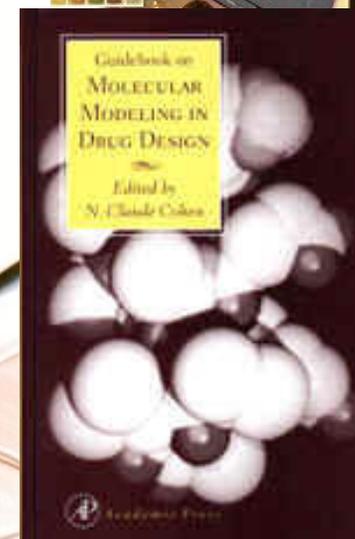
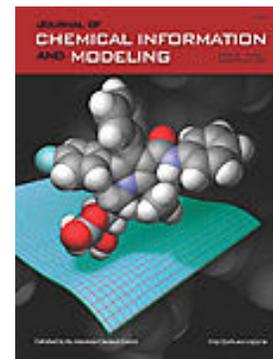


proteínas
enzimas
biorreceptores





Modelagem Molecular





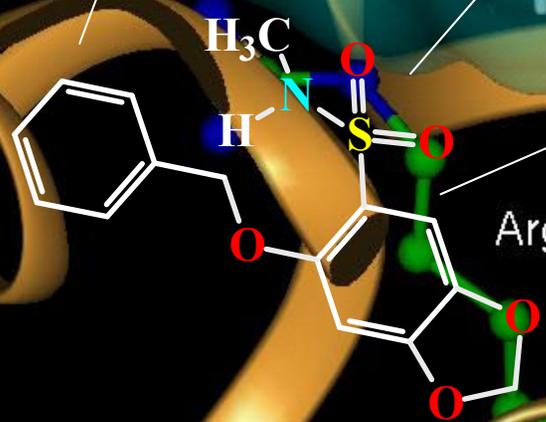
Arg513

Phe518

Tyr385

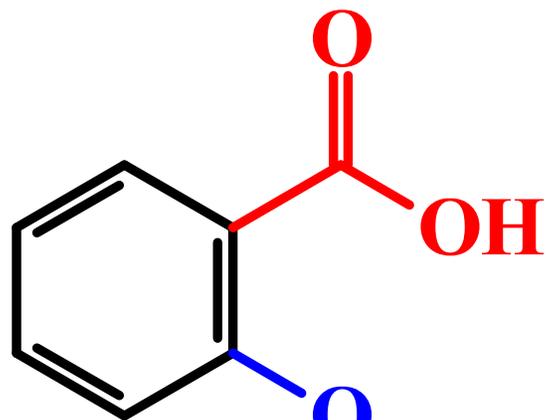
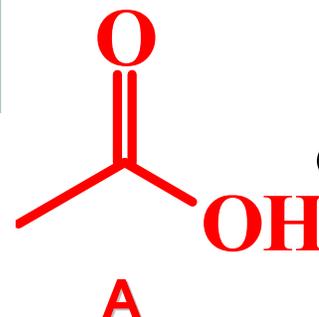
Ser530

Arg120

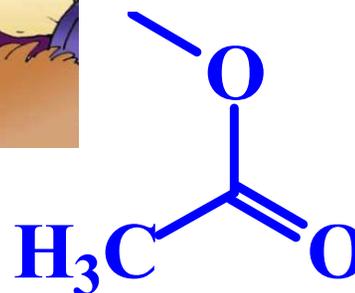
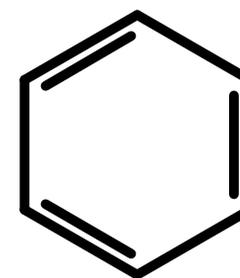
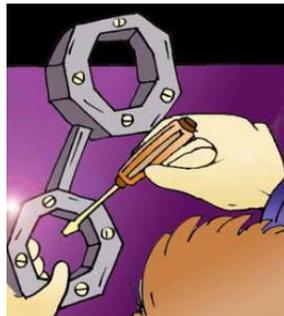




Dissecação Molecular

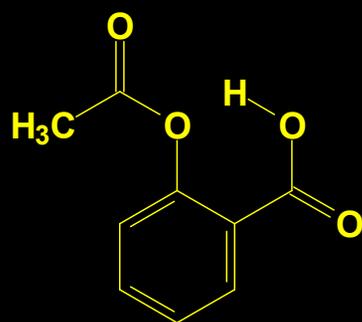
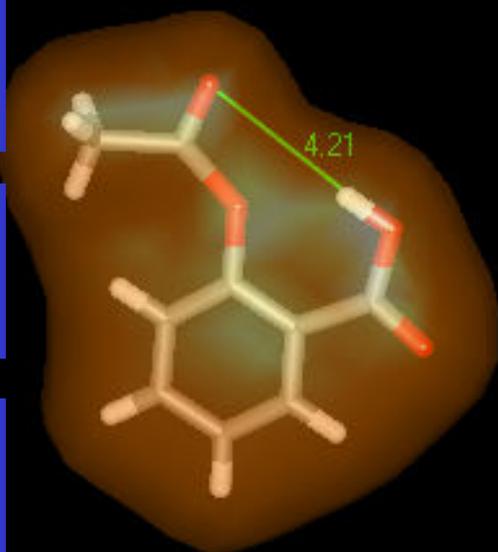


Ácido acetilsalicílico

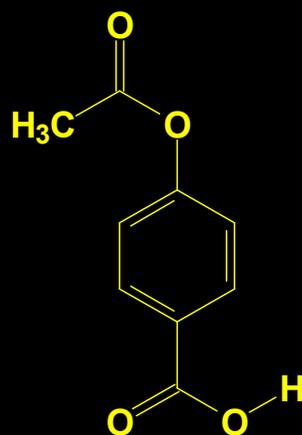
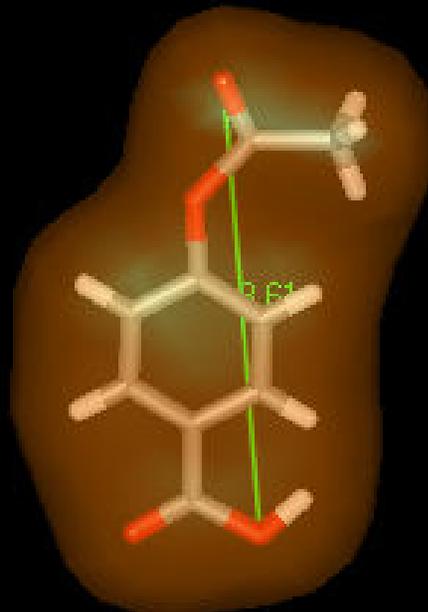




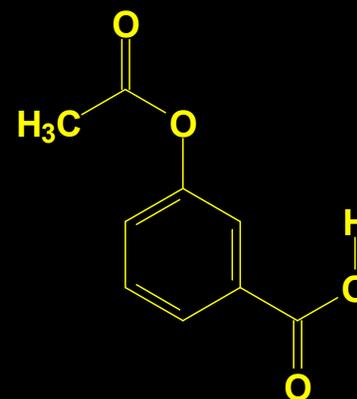
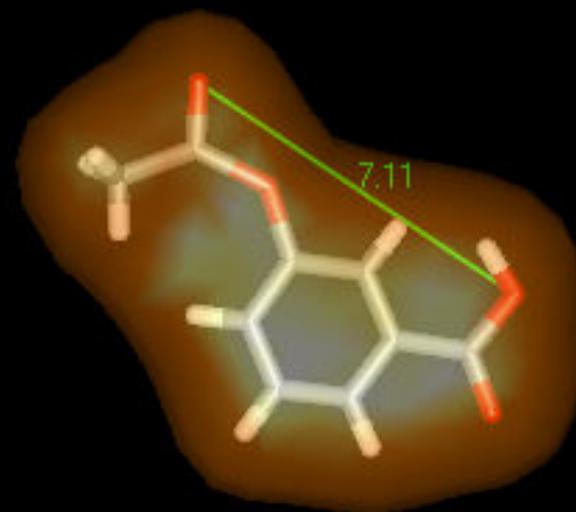
Regioisomêros do ácido acetil salicílico (AAS)



orto



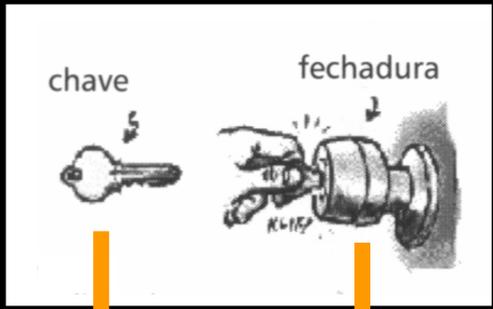
para



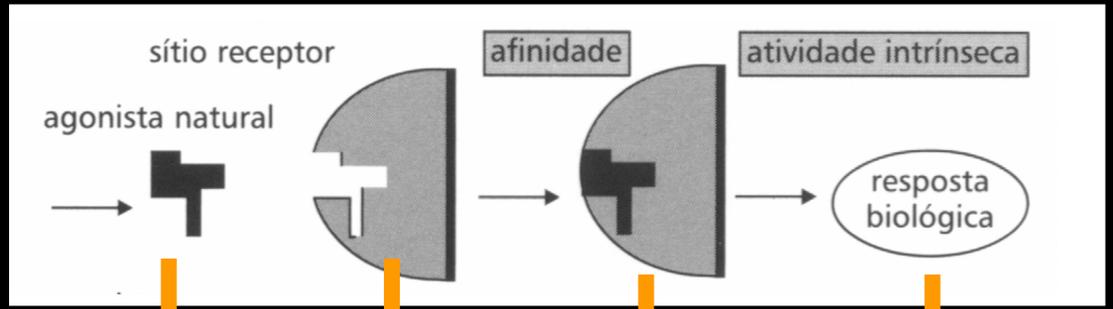
meta



O Centenário Modelo "Chave-Fechadura"

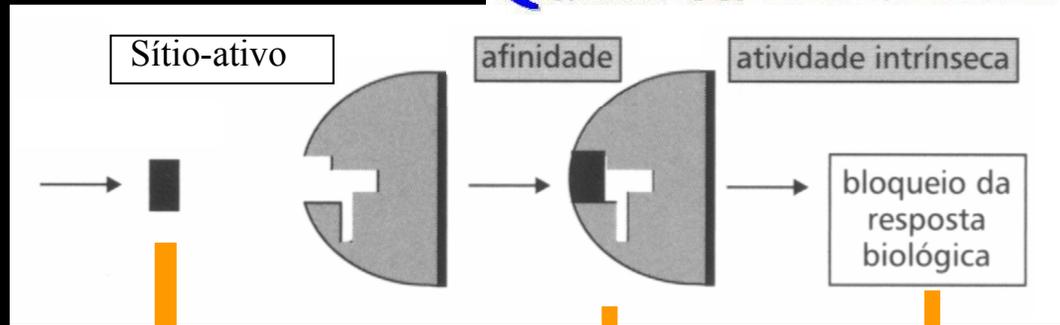


Fármaco
Substrato natural
Enzima
= Alvo terapêutico

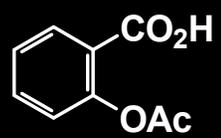


Ácido araquidônico
PGHS-1
PGHS-2
PGE₂ icosanóide
inflamação

Química Medicinal



Inibidor: AAS
PGHS-2
PGHS-1
NSAI



NSAI = antiinflamatórios não-esteróides



A maioria dos biorreceptores dos fármacos contemporâneos são enzimas ...

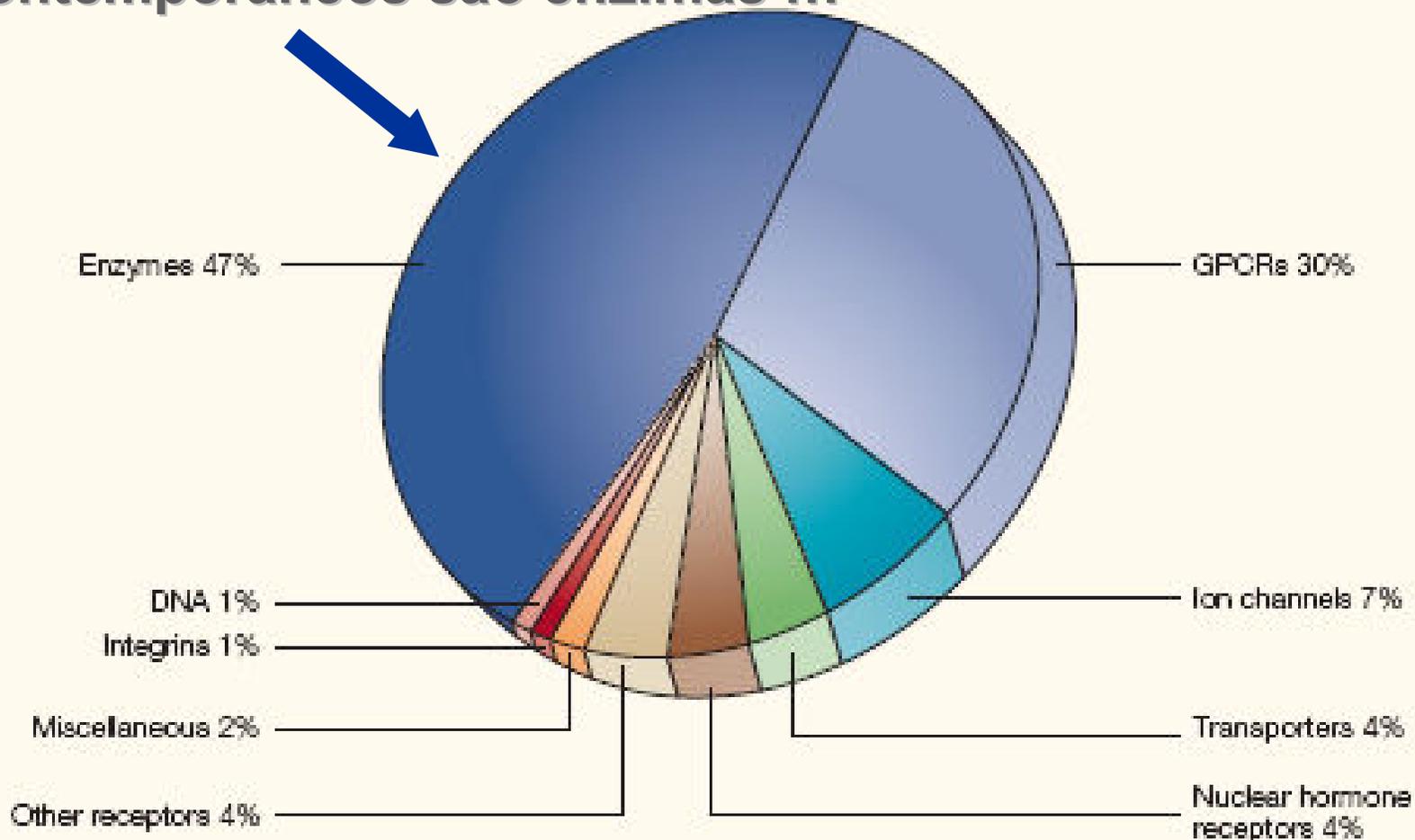
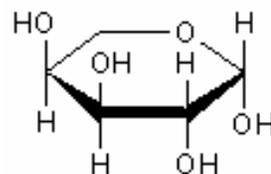
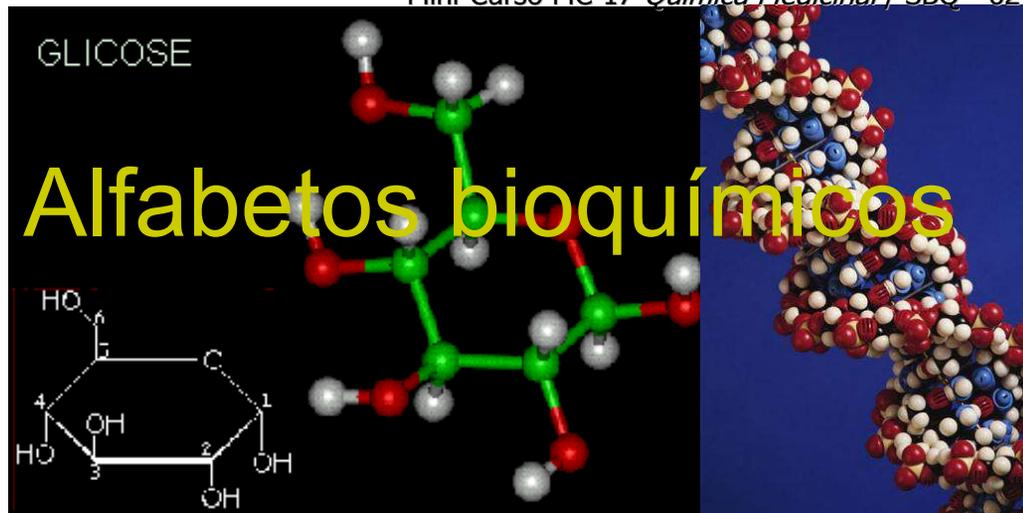
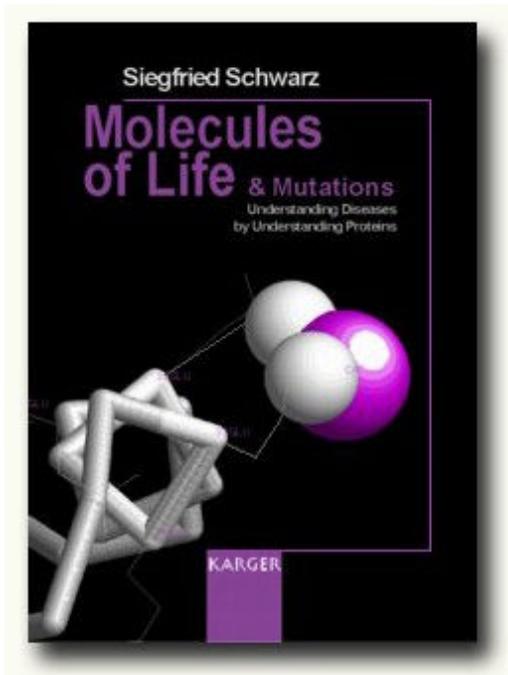


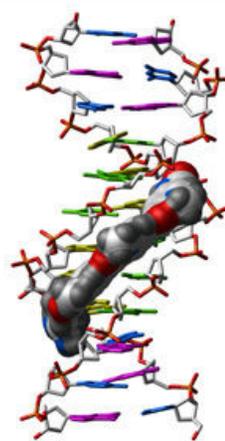
Figure 4 | Marketed small-molecule drug targets by biochemical class. GPCR, G-protein-coupled receptor.

...de apenas 130 famílias distintas de proteínas !





β -L-Arabinose



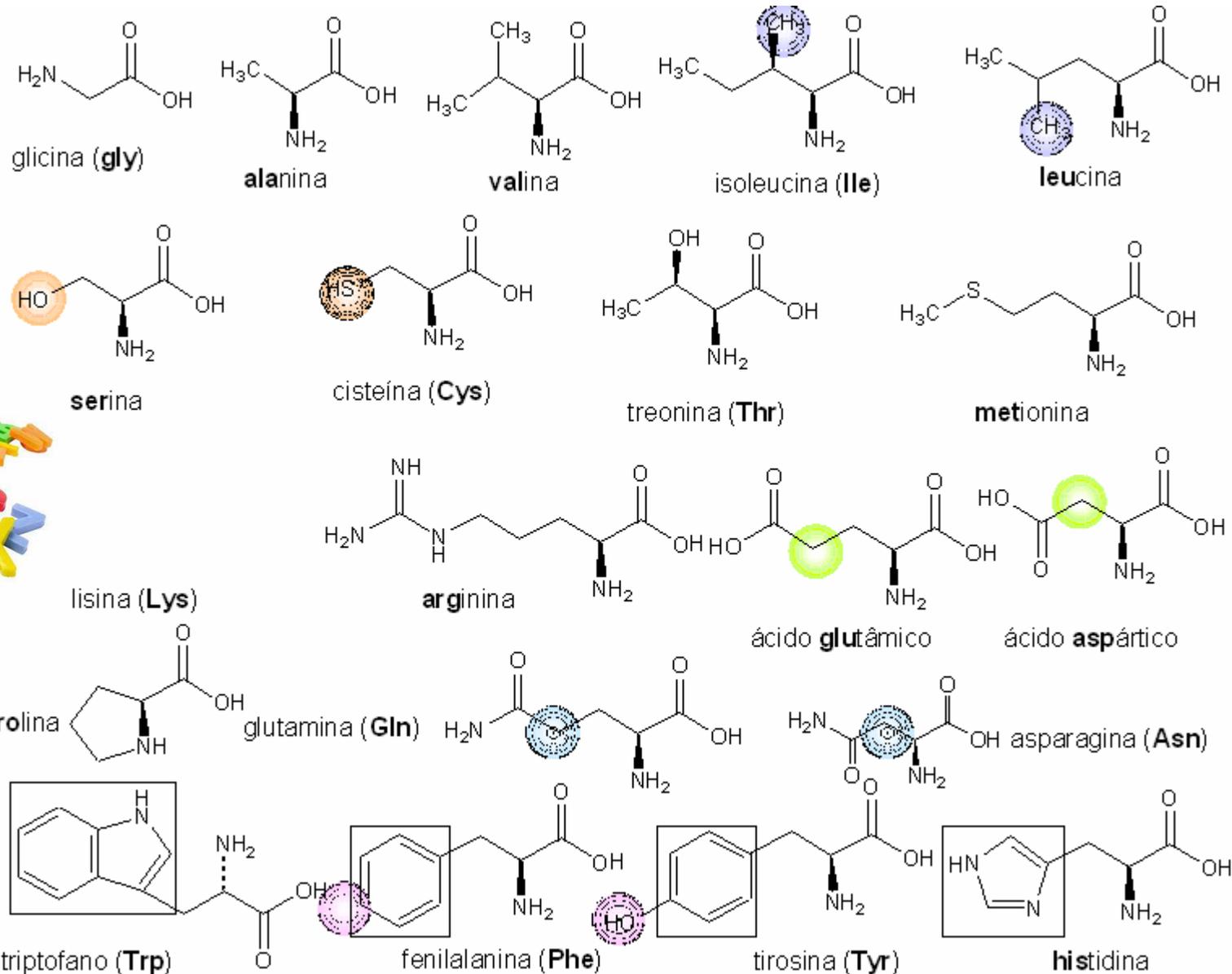
Model Compound Bound to the Minor Groove of a DNA Molecule

Carboídratos
Lipídeos
ácidos nucleícos
proteínas



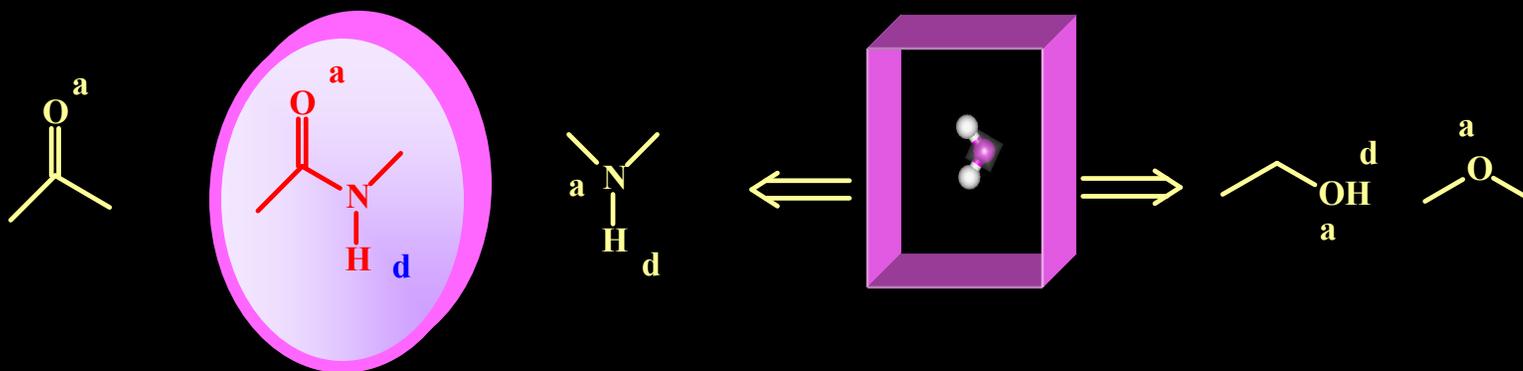
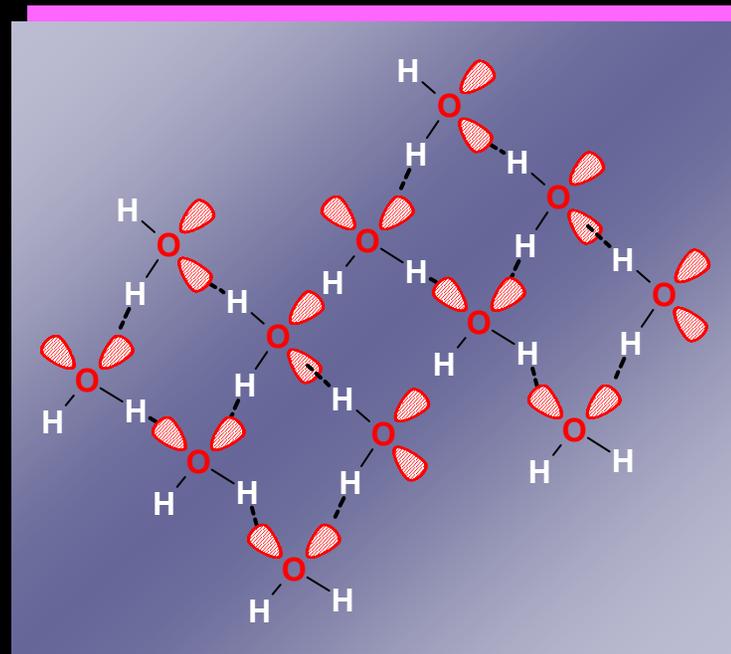
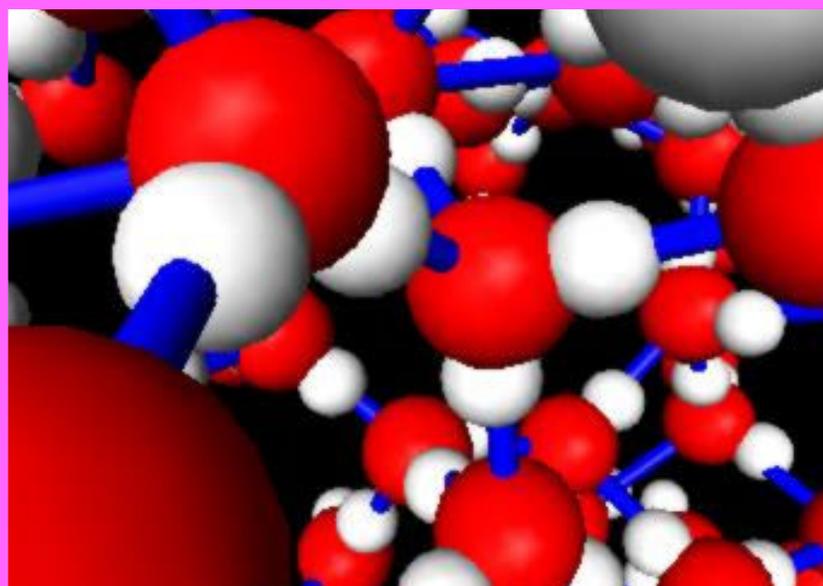
“ligações” de hidrogênio ...

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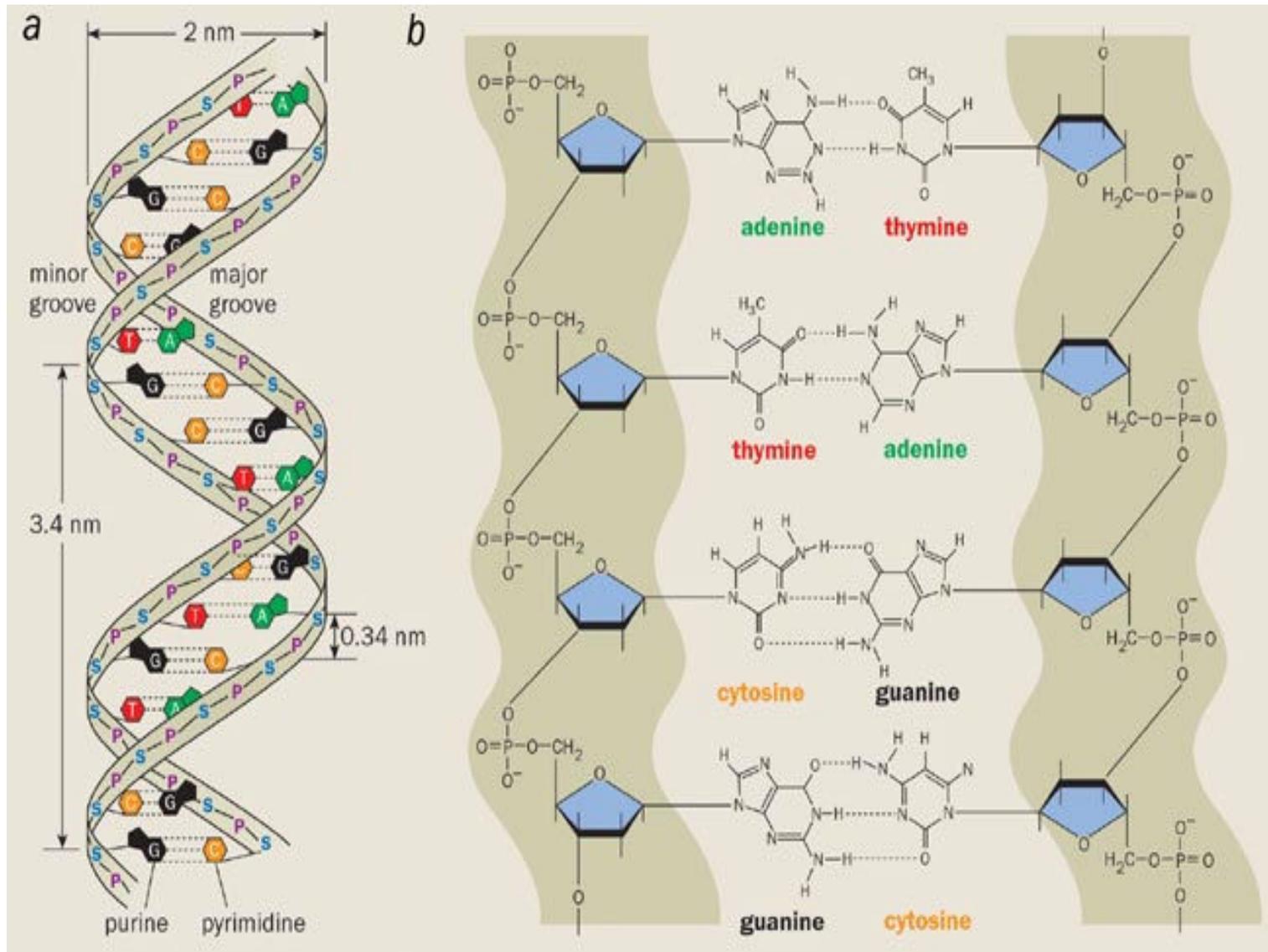


A ligação de hidrogênio





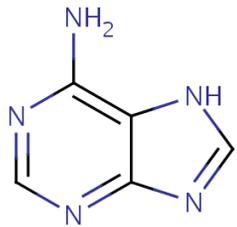
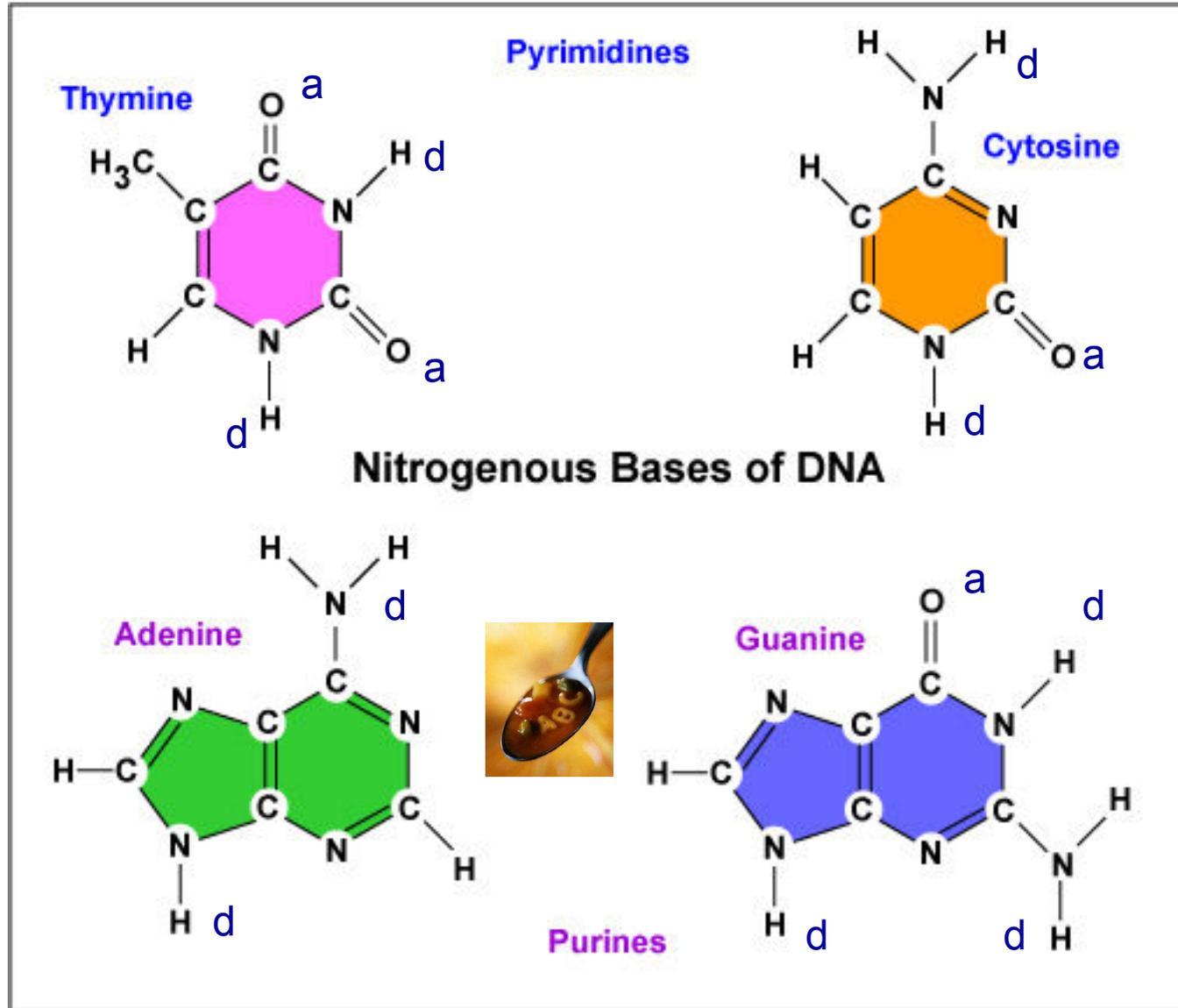
A Importância da Ligação de Hidrogênio



...alfabeto de 4 letras apenas... para 20 AA essenciais

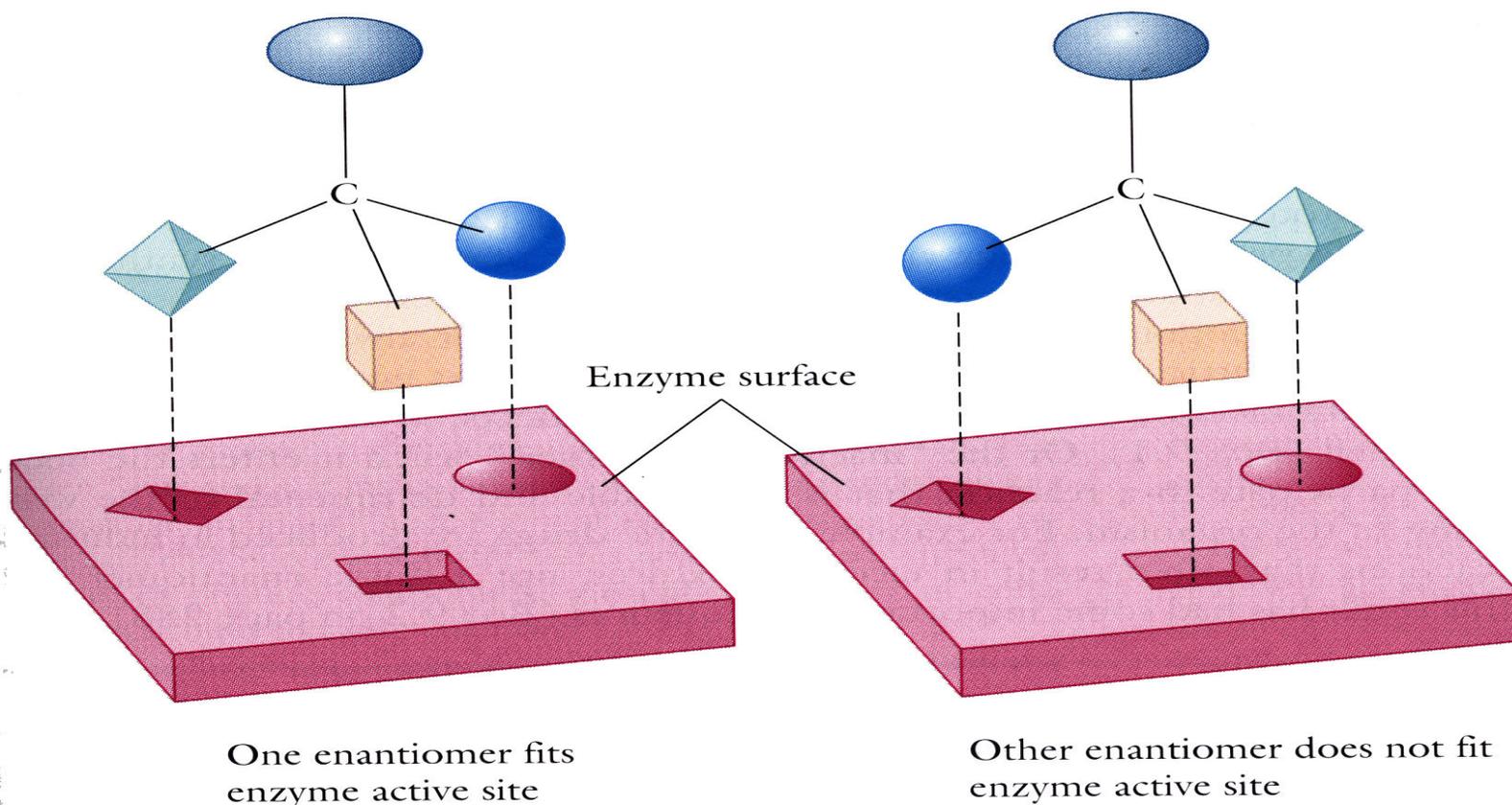


“ligações” de hidrogênio ...



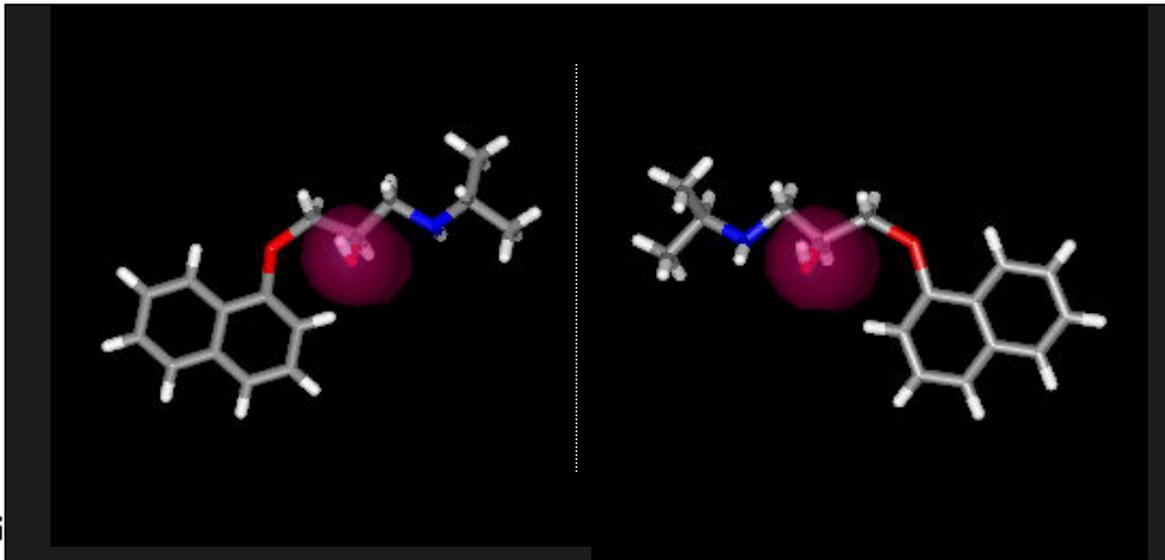


A quiralidade da vida...



Modelo dos três pontos

Modelo de Easson-Stedman



Eutômero
Distômero

Interação hidrofóbicas

