

FUNDAMENTOS DE QUÍMICA

MedChem

Parte 3

MEDICINAL - COMO NASCEM OS FÁRMACOS

26ª Semana da Química do Instituto de Química da UFRJ
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Professor Titular



Resumo

Universidade Federal do Rio de Janeiro

Neste curso-curto apresentaremos os fundamentos da **Química Medicinal**, para o desenho molecular de novos candidatos a fármacos. A introdução abordará o histórico e a cronologia da disciplina, com ênfase ao seu caráter interdisciplinar. O processo de descoberta de fármacos ilustrará como “nascem” os fármacos. Apresentaremos alguns aspectos da inovação farmacêutica radical, em especial para os fármacos sintéticos. Em conclusão, alguns exemplos selecionados do trabalho realizado no Laboratório de Avaliação e Síntese de Substâncias Bioativas (LASSBio) do ICB da UFRJ, criado e coordenado pelo apresentador, serão apresentados.



A invenção do propranolol

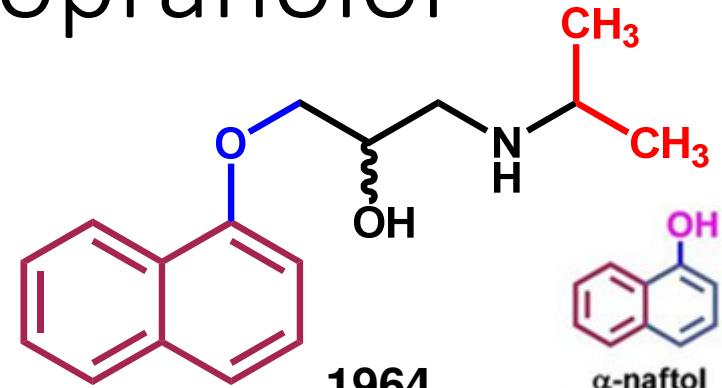
1988



James W. Black
(1924-2000)

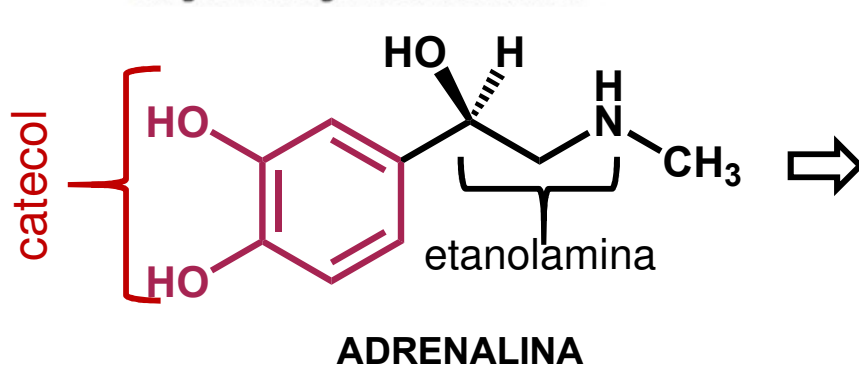
J. Black et al., *Br. J. Pharmacol. Chmother.* 1965, 25, 577

James W. Black, 1988 - "Pronethalol always seemed to us to be a prototype drug, good enough to answer questions of principle, but not good enough to be marketable"

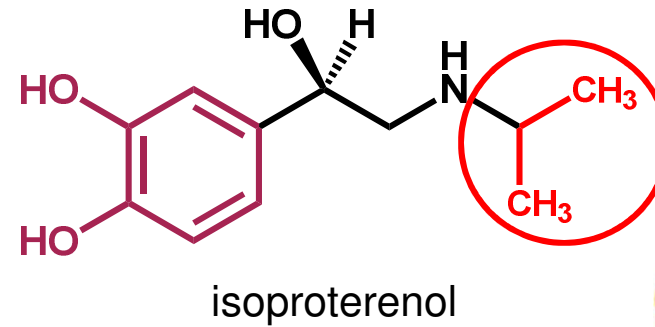


1964

1° β -bloqueador seletivo

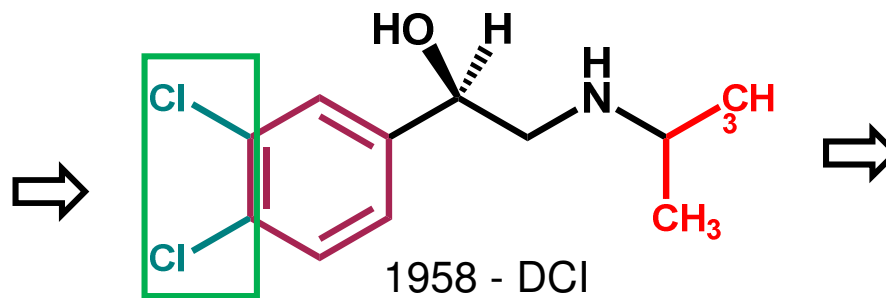


ADRENALINA

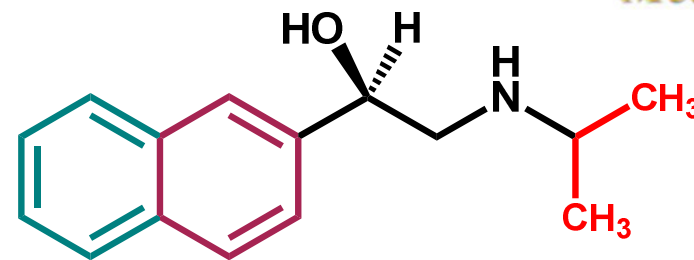


isoproterenol

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chem
Medicinal



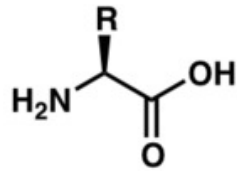
1958 - DCI



1959 - pronetalol

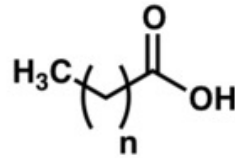
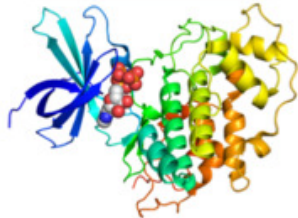


Os alfabetos bioquímicos



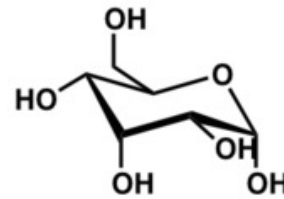
amino ácidos

proteínas



ácidos graxos

fosfolipídeos

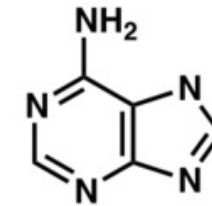
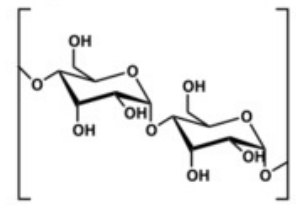


carboidratos

glicerol

mono
sacarídeos

poli-
sacarídeos



bases nucleícas

nucleotídeos

DNA/RNA



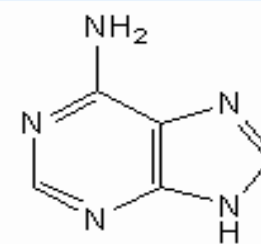
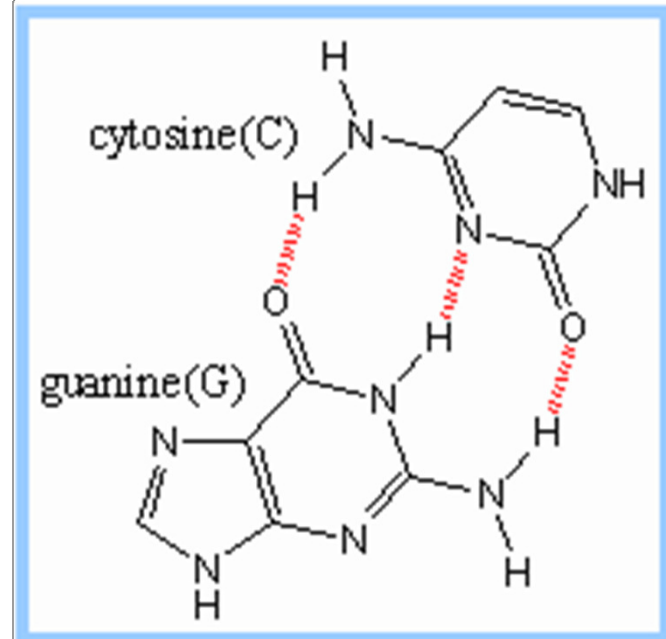


Proteínas, carboidratos, DNA, lipídeos, canais iônicos

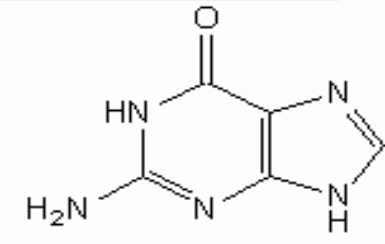


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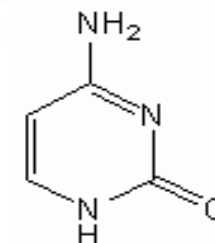
H



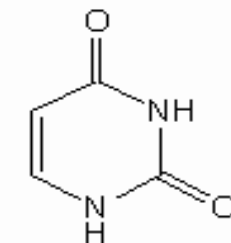
adenine (A)



guanine (G)



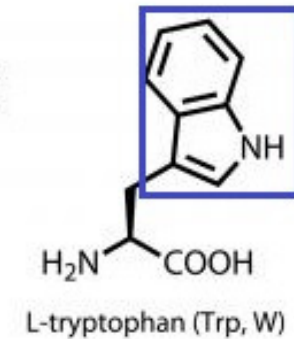
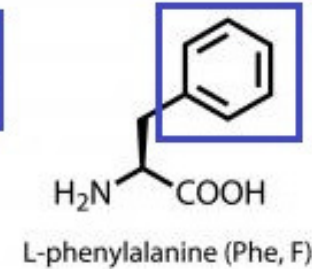
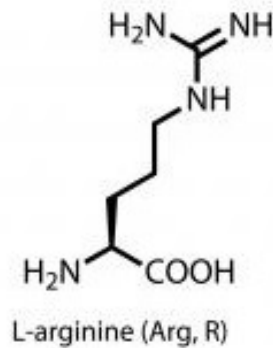
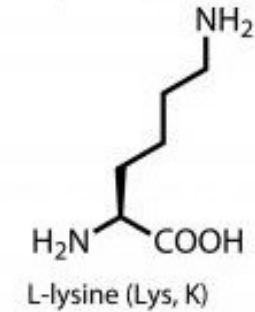
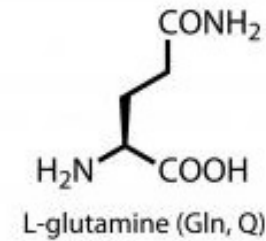
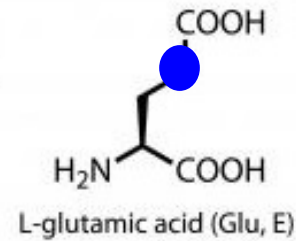
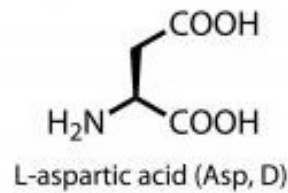
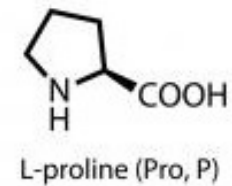
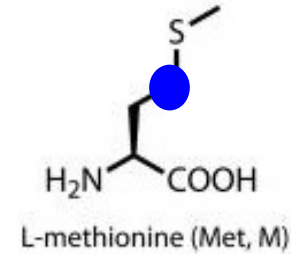
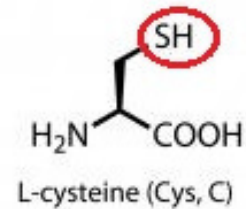
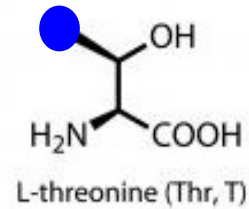
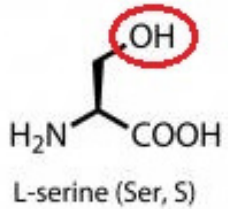
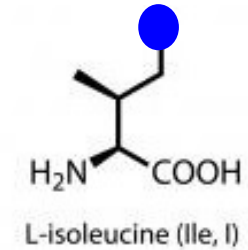
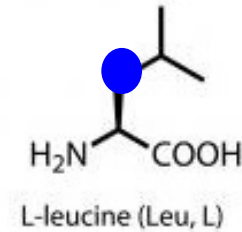
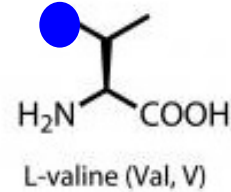
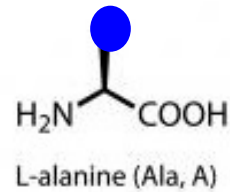
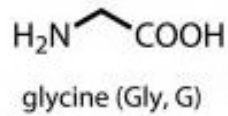
cytosine (C)



uracil (U)

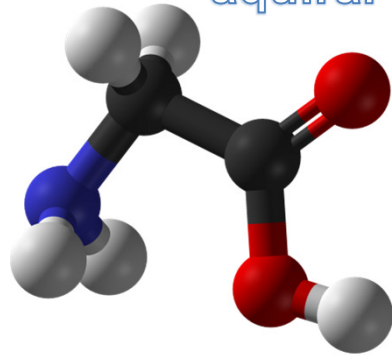


Os 20 amino-ácidos essenciais

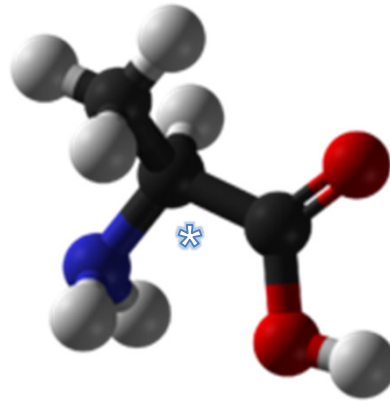




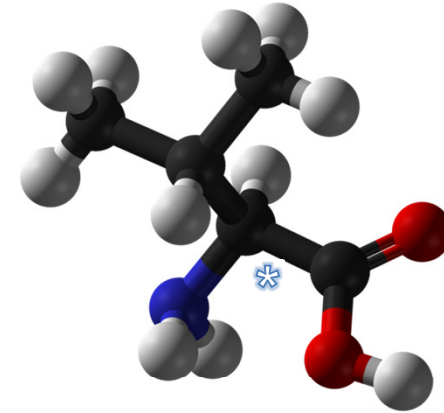
aquiral



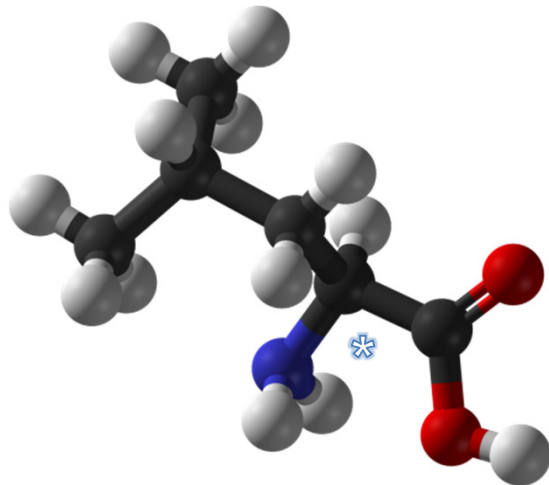
Glicina



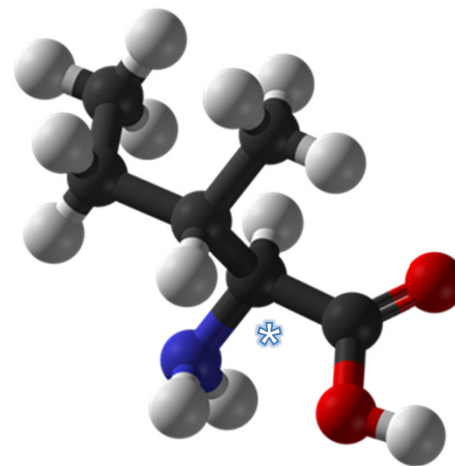
Alanina



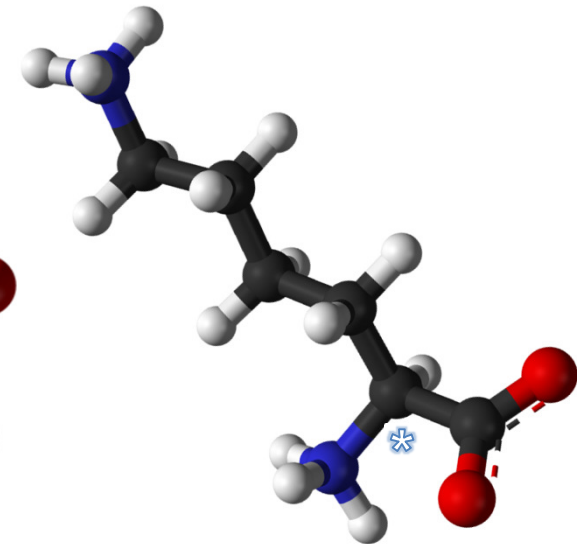
Valina



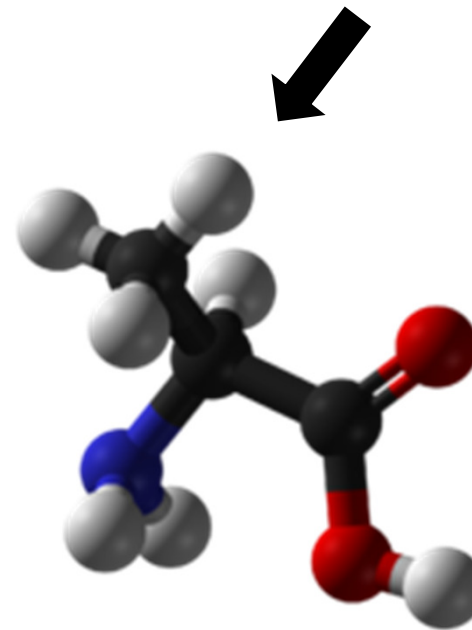
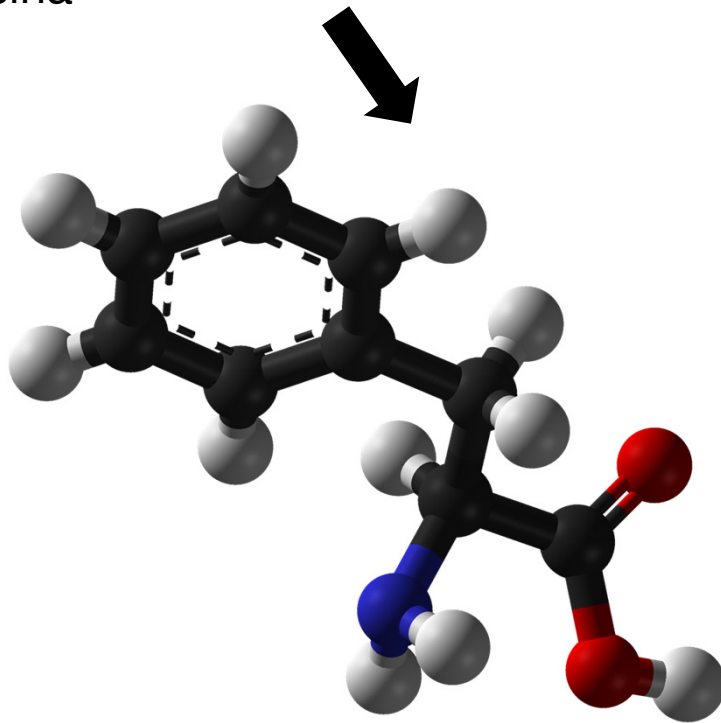
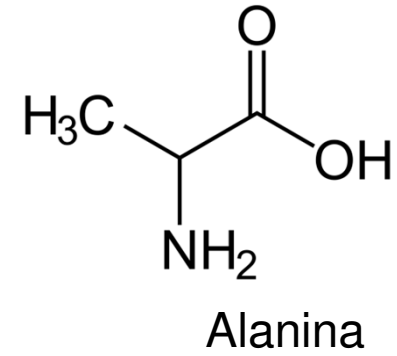
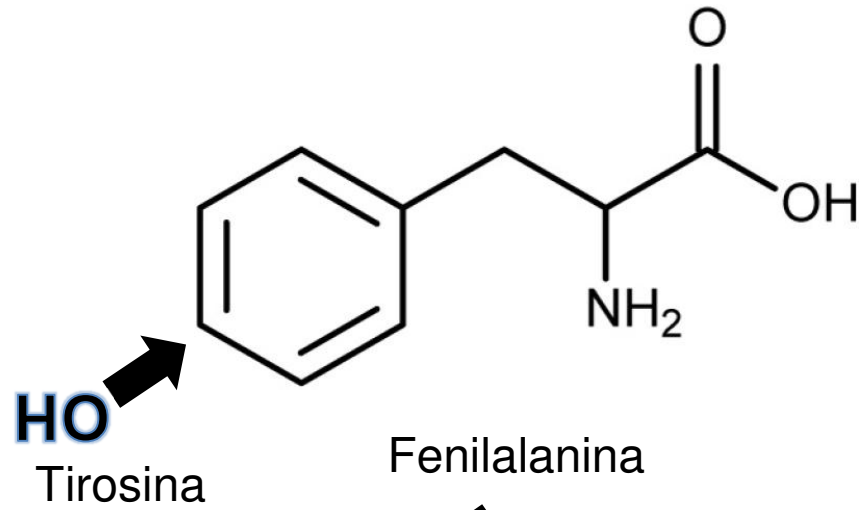
Leucina



Isoleucina

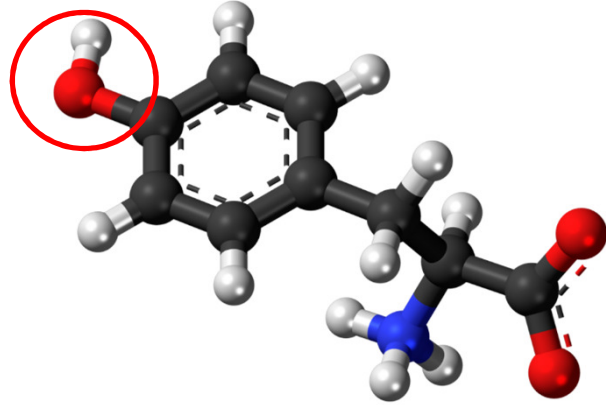


Lisina



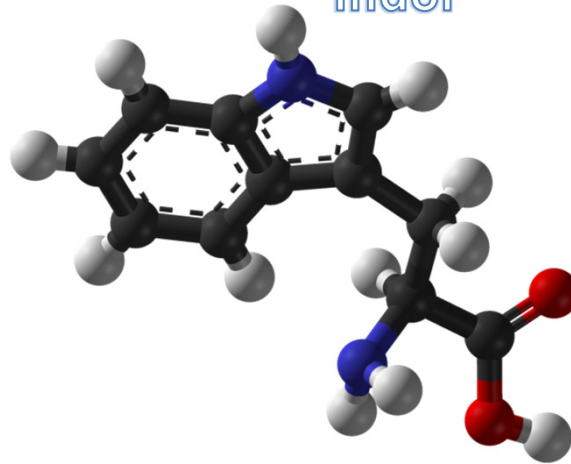


fenol



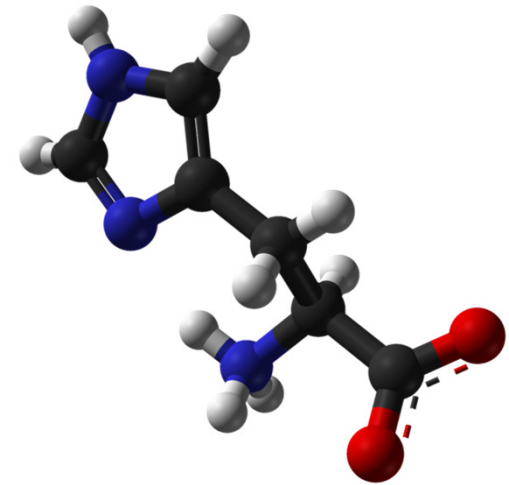
Tirosina

indol

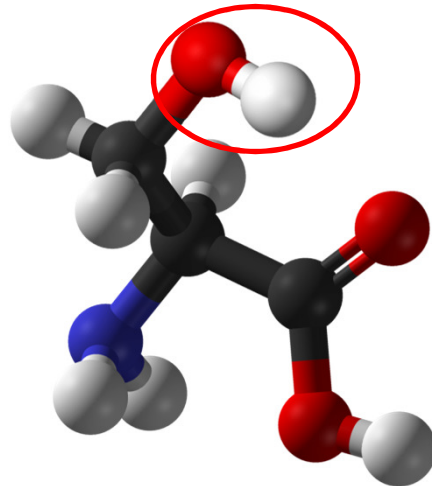


Triptofano

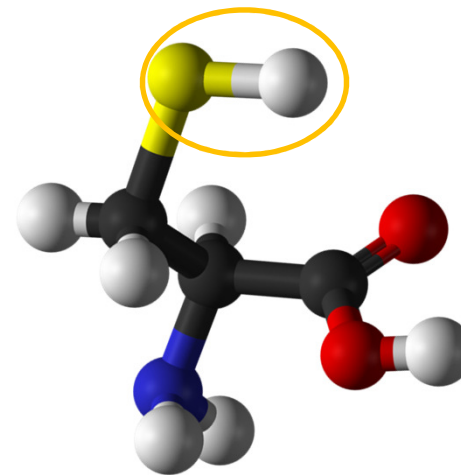
imidazol



Histidina



Serina



Cisteína



Tabela Periódica

The Periodic Table of the Elements

period 1 group 1 18

| | | | | | | | | | | | | | | | | | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1.00794 1312.0 2.20 1s ¹ H Hydrogen | | | | | | | | | | | | | | | | | 4.002602 2372.3 1s ² He Helium |
| 6.941 520.2 0.98 1s ² 2s ¹ Li Lithium | 9.012182 899.5 1.57 1s ² 2s ² Be Beryllium | | | | | | | | | | | 10.811 800.6 2.04 1s ² 2s ² 2p ¹ B Boron | 12.0107 1096.5 2.65 1s ² 2s ² 2p ² C Carbon | 14.0067 1402.3 3.04 1s ² 2s ² 2p ³ N Nitrogen | 15.9994 1313.9 3.44 1s ² 2s ² 2p ⁴ O Oxygen | 18.998403 1681.0 3.98 1s ² 2s ² 2p ⁵ F Fluorine | 20.1797 2080.7 1s ² 2s ² 2p ⁶ Ne Neon |
| 22.98976 495.8 0.93 1s ² 3s ¹ Na Sodium | 24.3050 787.7 1.31 1s ² 3s ² Mg Magnesium | | | | | | | | | | | 26.98153 577.5 1.61 1s ² 3s ² 3p ¹ Al Aluminium | 28.0855 786.5 1.90 1s ² 3s ² 3p ² Si Silicon | 30.97696 1011.8 2.19 1s ² 3s ² 3p ³ P Phosphorus | 32.065 399.6 2.58 1s ² 3s ² 3p ⁴ S Sulfur | 35.453 1251.2 3.16 1s ² 3s ² 3p ⁵ Cl Chlorine | 39.948 1620.6 1s ² 3s ² 3p ⁶ Ar Argon |
| 39.0983 418.8 0.82 1s ² 3s ² 3p ⁶ 4s ¹ K Potassium | 40.078 589.8 1.00 1s ² 3s ² 3p ⁶ 4s ² Ca Calcium | 44.95591 633.1 1.96 1s ² 3s ² 3p ⁶ 4s ² 4d ¹ Sc Scandium | 47.867 658.8 1.54 1s ² 3s ² 3p ⁶ 4s ² 3d ² Ti Titanium | 50.9415 650.9 1.63 1s ² 3s ² 3p ⁶ 4s ² 3d ³ V Vanadium | 51.9962 652.9 1.66 1s ² 3s ² 3p ⁶ 4s ² 3d ⁴ Cr Chromium | 54.93804 717.3 1.55 1s ² 3s ² 3p ⁶ 4s ² 3d ⁵ Mn Manganese | 55.845 762.5 1.83 1s ² 3s ² 3p ⁶ 4s ² 3d ⁶ Fe Iron | 58.93319 760.4 1.91 1s ² 3s ² 3p ⁶ 4s ² 3d ⁷ Co Cobalt | 58.93319 757.1 1.88 1s ² 3s ² 3p ⁶ 4s ² 3d ⁸ Ni Nickel | 63.546 745.5 1.90 1s ² 3s ² 3p ⁶ 4s ² 3d ⁹ Cu Copper | 65.38 900.4 1.65 1s ² 3s ² 3p ⁶ 4s ² 3d ¹⁰ Zn Zinc | 69.723 578.8 1.81 1s ² 3s ² 3p ⁶ 4s ² 3d ¹⁰ 4p ¹ Ga Gallium | 72.64 762.0 2.01 1s ² 3s ² 3p ⁶ 4s ² 3d ¹⁰ 4p ² Ge Germanium | 74.92160 947.0 2.18 1s ² 3s ² 3p ⁶ 4s ² 3d ¹⁰ 4p ³ As Arsenic | 78.96 941.0 2.55 1s ² 3s ² 3p ⁶ 4s ² 3d ¹⁰ 4p ⁴ Se Selenium | 79.904 1159.9 3.00 1s ² 3s ² 3p ⁶ 4s ² 3d ¹⁰ 4p ⁵ Br Bromine | 83.798 1350.8 3.00 1s ² 3s ² 3p ⁶ 4s ² 3d ¹⁰ 4p ⁶ Kr Krypton |
| 85.4678 493.0 0.82 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ¹ Rb Rubidium | 87.62 589.8 0.95 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² Sr Strontium | 88.90585 600.0 1.22 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹ Y Yttrium | 91.224 640.1 1.33 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ² Zr Zirconium | 92.90638 652.1 1.60 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ³ Nb Niobium | 95.96 664.3 2.16 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ⁴ Mo Molybdenum | (98) 702.0 1.90 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ⁵ Tc Technetium | 101.07 710.2 2.20 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ⁶ Ru Ruthenium | 102.9055 719.7 2.28 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ⁷ Rh Rhodium | 106.42 804.4 2.20 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ⁸ Pd Palladium | 107.8682 791.0 1.93 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ⁹ Ag Silver | 112.441 907.8 1.89 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ Cd Cadmium | 114.818 588.4 1.78 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ¹ In Indium | 118.710 706.0 1.96 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ² Sn Tin | 121.760 854.0 2.06 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ³ Sb Antimony | 127.60 959.3 2.10 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁴ Te Tellurium | 126.9044 1099.0 2.06 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁵ I Iodine | 131.293 1097.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ Xe Xenon |
| 132.9054 375.7 0.79 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ¹ Cs Caesium | 137.327 502.9 0.89 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² Ba Barium | 174.9668 523.5 1.27 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹ Lu Lutetium | 178.49 658.5 1.30 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ² Hf Hafnium | 180.9478 761.0 1.50 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ³ Ta Tantalum | 183.84 770.0 2.36 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ⁴ W Tungsten | 186.207 760.0 1.90 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ⁵ Re Rhenium | 190.23 840.0 1.90 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ⁶ Os Osmium | 192.227 880.0 2.20 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ⁷ Ir Iridium | 195.084 870.0 2.28 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ⁸ Pt Platinum | 196.9665 890.1 2.54 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ⁹ Au Gold | 200.59 1007.1 2.00 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ Hg Mercury | 204.3833 589.4 1.62 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ¹ Tl Thallium | 207.2 703.0 2.33 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ² Pb Lead | 208.9804 703.0 2.02 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ³ Bi Bismuth | (210) 812.1 2.00 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁴ Po Polonium | (210) 890.0 2.20 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁵ At Astatine | (220) 1097.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ Rn Radon |
| (223) 380.0 0.70 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ¹ Fr Francium | (226) 509.3 0.90 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² Ra Radium | (252) 470.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ¹ Lr Lawrencium | (261) 580.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ² Rf Rutherfordium | (262) 580.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ³ Db Dubnium | (266) 580.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ⁴ Sg Seaborgium | (264) 580.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ⁵ Bh Bohrium | (277) 580.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ⁶ Hs Hassium | (268) 580.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ⁷ Mt Meitnerium | (271) 580.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ⁸ Ds Darmstadtium | (272) 580.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ⁹ Rg Roentgenium | (285) 580.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ¹⁰ Cn Copernicium | (284) 580.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ¹¹ Uut Ununtrium | (289) 580.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ¹² Fl Flerovium | (288) 580.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ¹³ Uup Ununpentium | (292) 580.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ¹⁴ Lv Livermorium | 117 589.3 1.25 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ¹⁴ 6d ¹ Uus Ununseptium | (294) 580.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁰ 6p ⁶ 7s ² 5f ¹⁴ 6d ² Uuo Ununoctium |

atomic mass
or most stable mass number
1st ionization energy
in kJ/mol

55.845 26

762.5 1.83

chemical symbol
Fe

name
Iron

electron configuration
[Ar] 3d⁶ 4s²

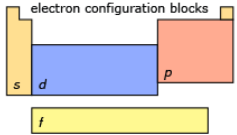
atomic number

electronegativity

oxidation states
most common are bold

+6
+5
+4
+3
+2
+1
-1
-2

- alkali metals
- alkaline metals
- other metals
- transition metals
- lanthanoids
- actinoids
- metalloids
- nonmetals
- halogens
- noble gases
- unknown elements
- radioactive elements have masses in parentheses

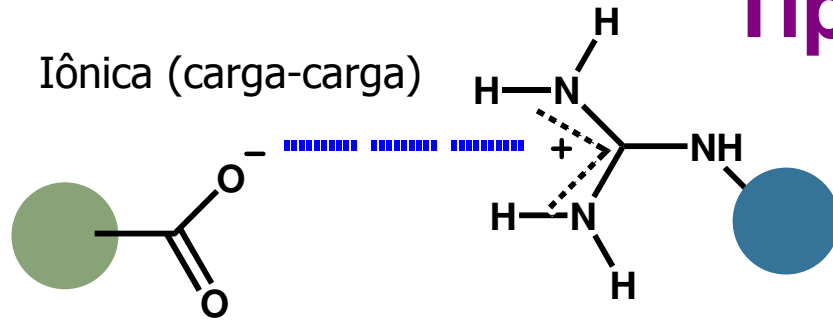


- notes
- as of yet, elements 113,115,117 and 118 have no official name designated by the IUPAC.
 - 1 kJ/mol ≈ 96.485 eV.
 - all elements are implied to have an oxidation state of zero.

| | | | | | | | | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 138.9054 538.1 1.10 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁴ La Lanthanum | 140.116 584.4 1.12 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁴ Ce Cerium | 140.9076 527.0 1.13 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁴ Pr Praseodymium | 144.242 533.1 1.14 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁴ Nd Neodymium | (145) 540.0 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁴ Pm Promethium | 150.36 544.5 1.17 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁴ Sm Samarium | 151.964 547.1 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁴ Eu Europium | 157.25 589.4 1.20 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁴ Gd Gadolinium | 158.9253 589.6 1s ² 3s ² 3p ⁶ 4s ² 4p ⁶ 5s ² 4d ¹⁰ 5p ⁶ 6s ² 4f ¹⁴ Tb Terbium |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

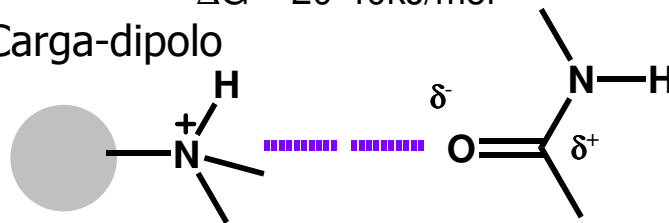


Tipos de interações F-R



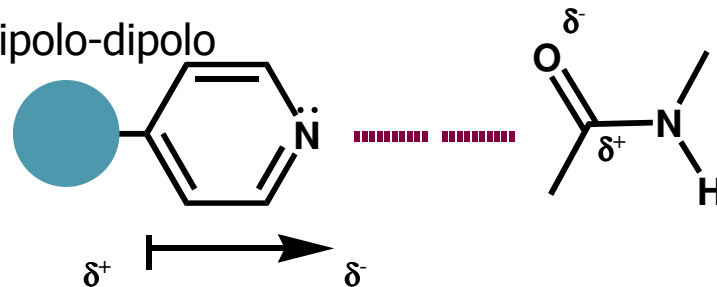
$$\Delta G = 20-40 \text{ kJ/mol}$$

Carga-dipolo



$$\Delta G = 12-20 \text{ kJ/mol}$$

Dipolo-dipolo



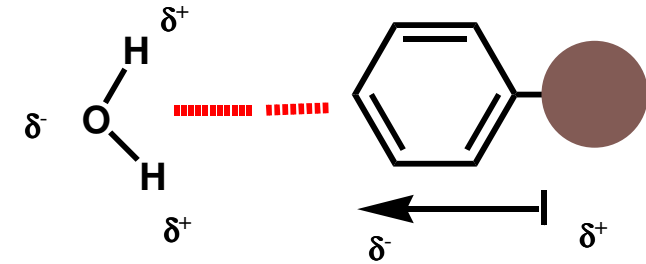
Carga-dipolo induzido

$$\Delta G = 4-12 \text{ kJ/mol}$$



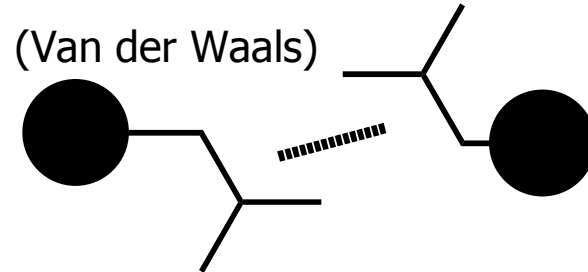
$$\Delta G = 2-10 \text{ kJ/mol}$$

Dipolo induzido-dipolo



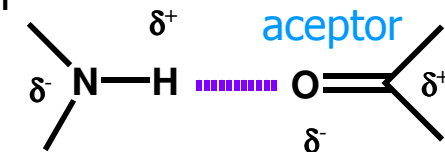
$$\Delta G = 2 \text{ kJ/mol}$$

Dispersão (Van der Waals)



$$\Delta G = 2-4 \text{ kJ/mol}$$

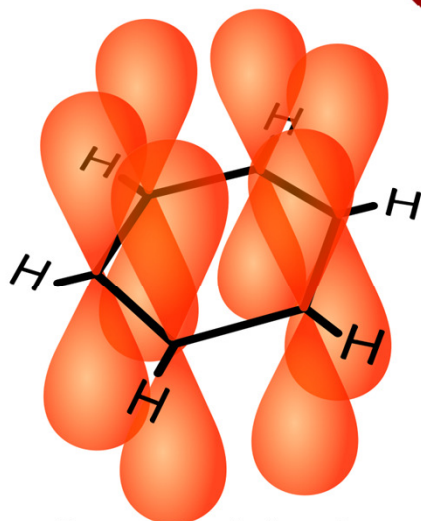
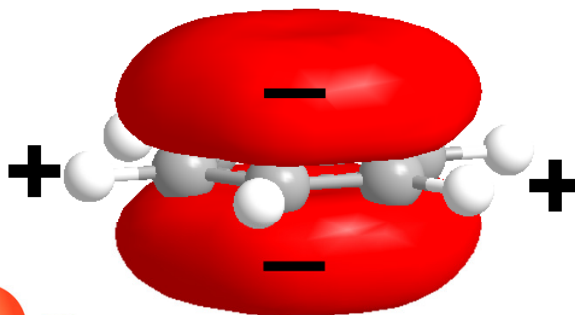
Ligação-H



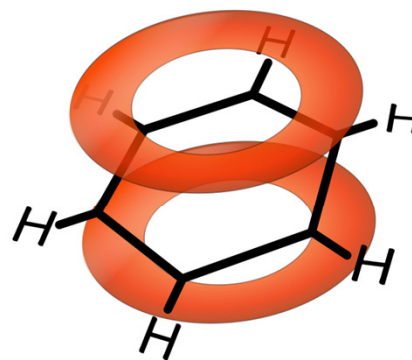
$$\Delta G = 4-30 \text{ kJ/mol}$$



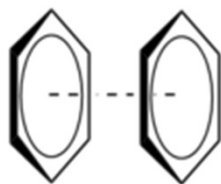
Interações π



6 p-orbitals



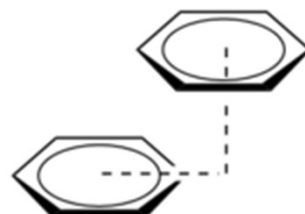
delocalized



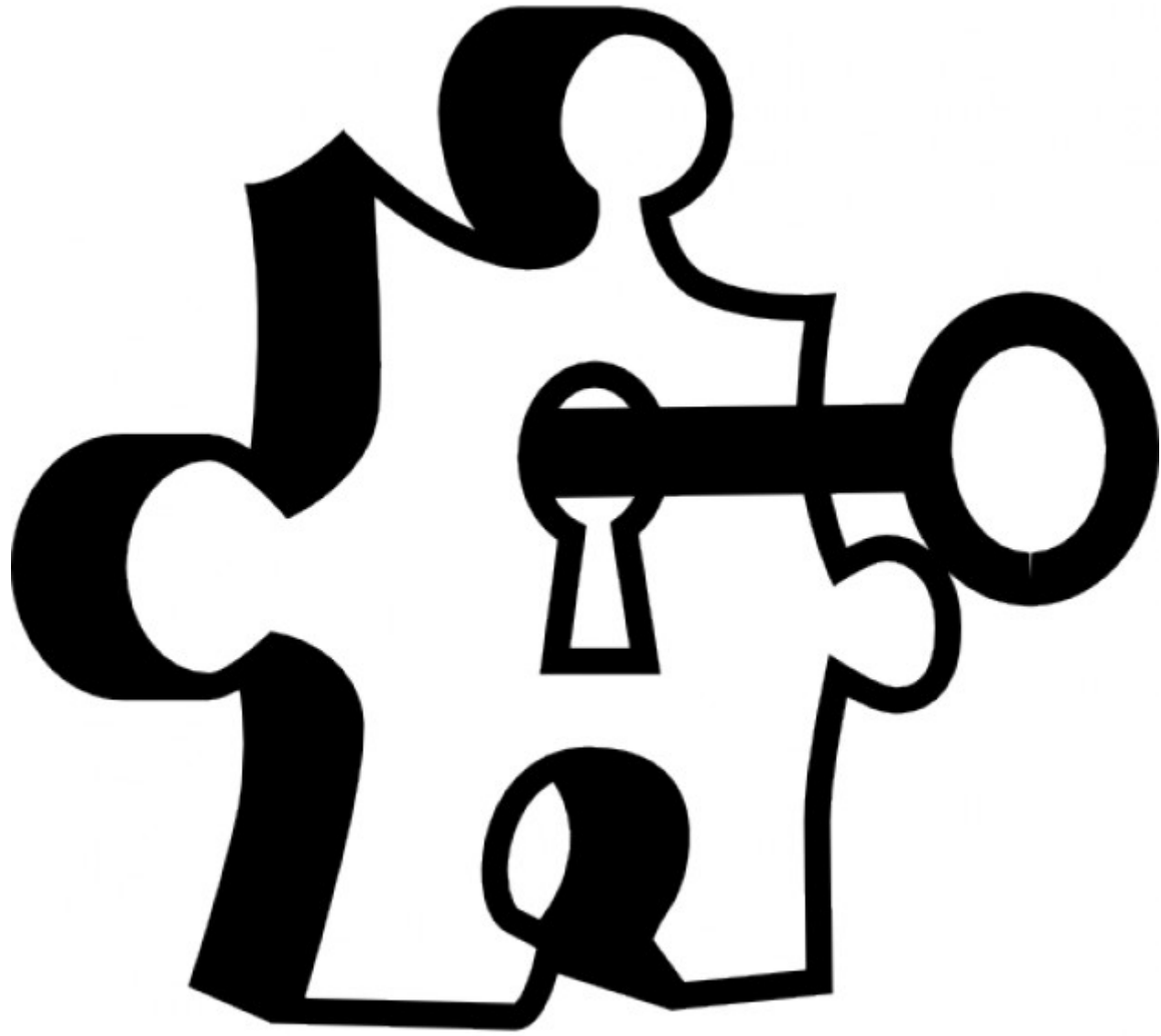
Sandwich



T-shaped

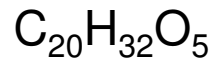
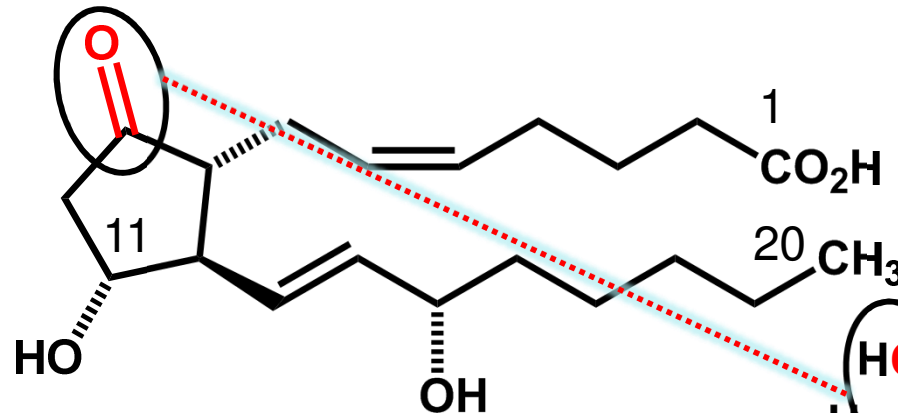


Parallel-displaced





A seletividade dos biorreceptores



PGE₂

Similaridade molecular

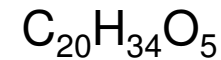
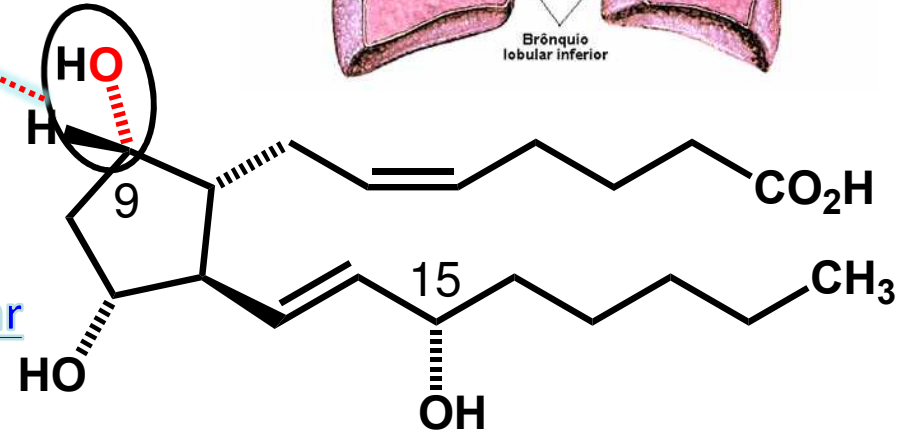
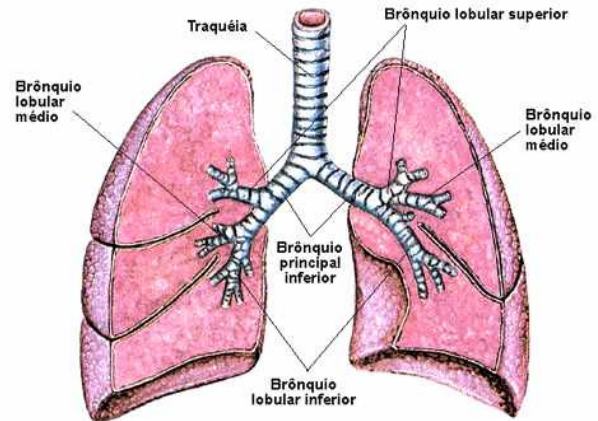
PGF_{2α} em cães provoca
intensa broncodilatação



EPr

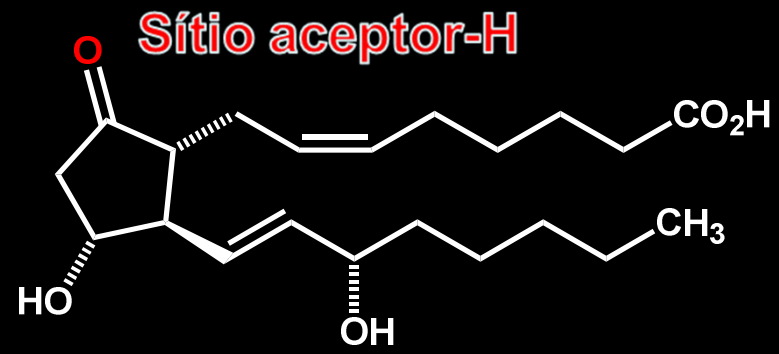
FPr

Reconhecimento Molecular

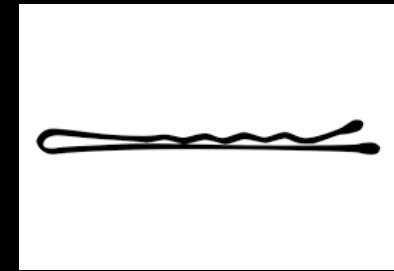
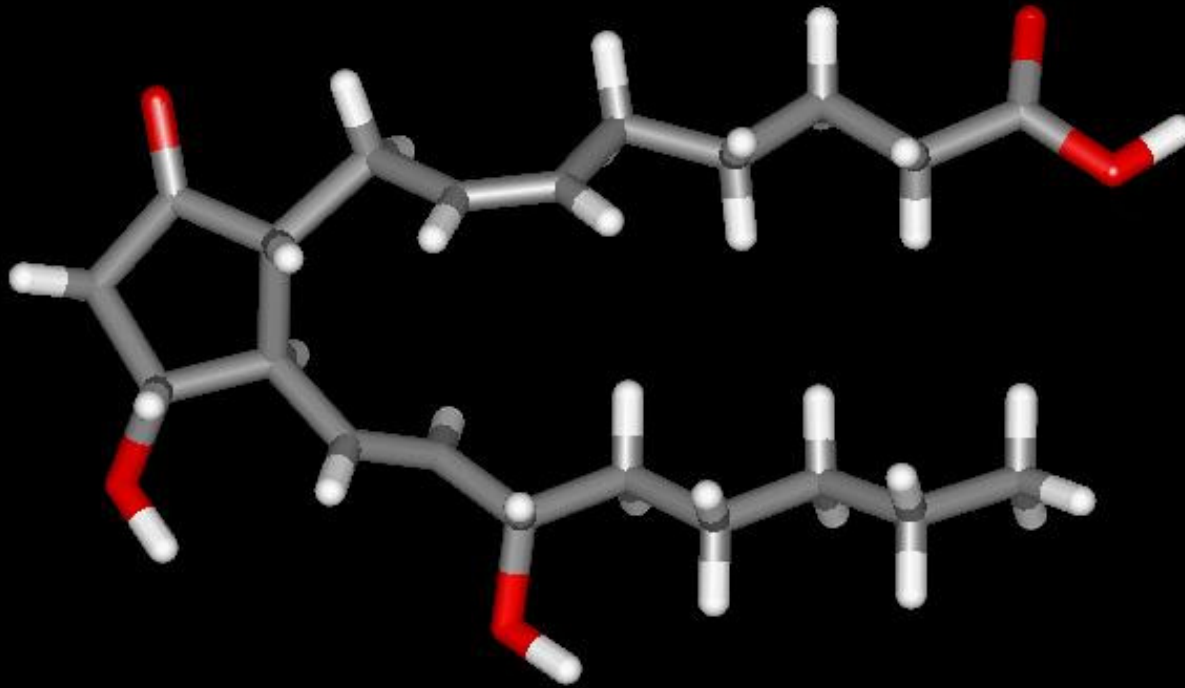


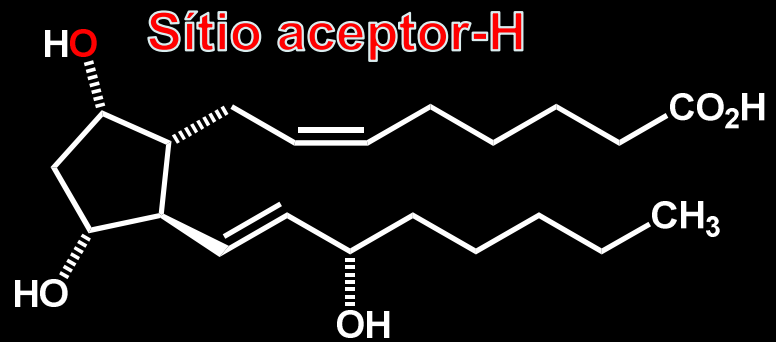
PGF_{2α}

PGF_{2α} em cães provoca
severa broncoconstricção

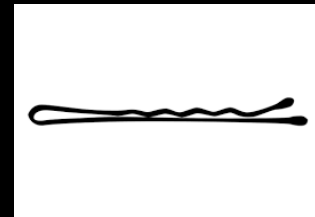
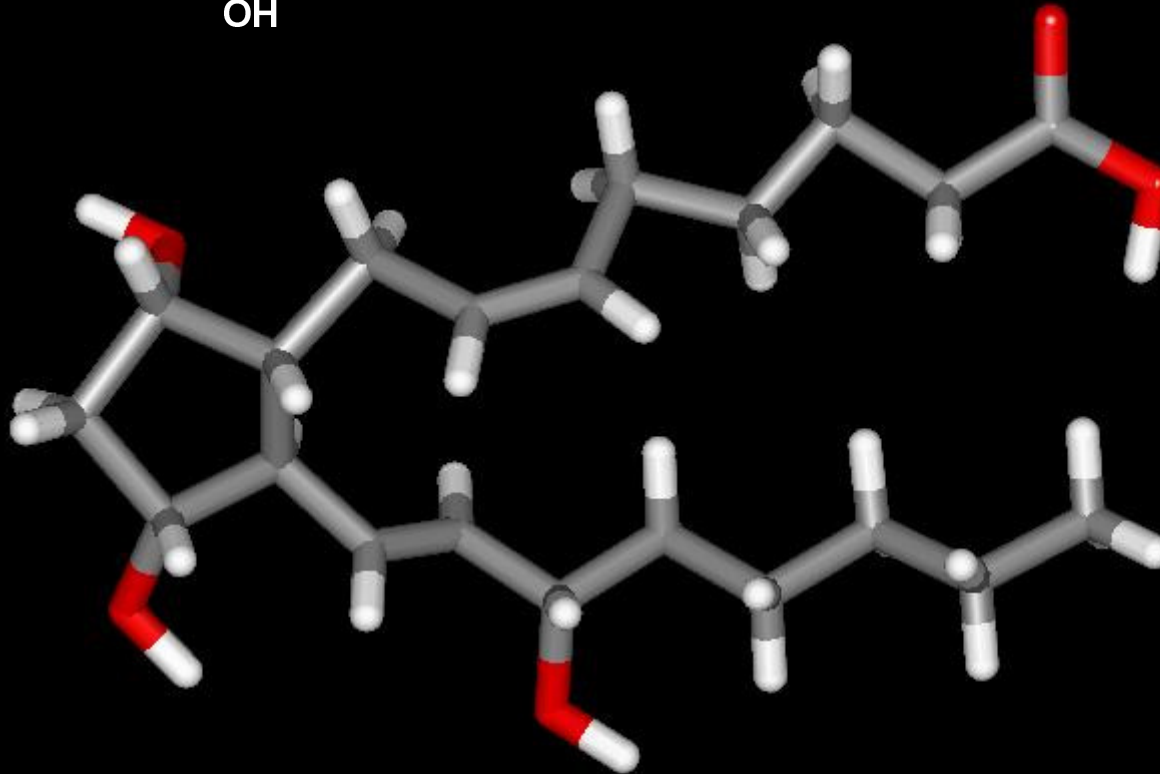


PGE₂





$\text{PGF}_{2\alpha}$

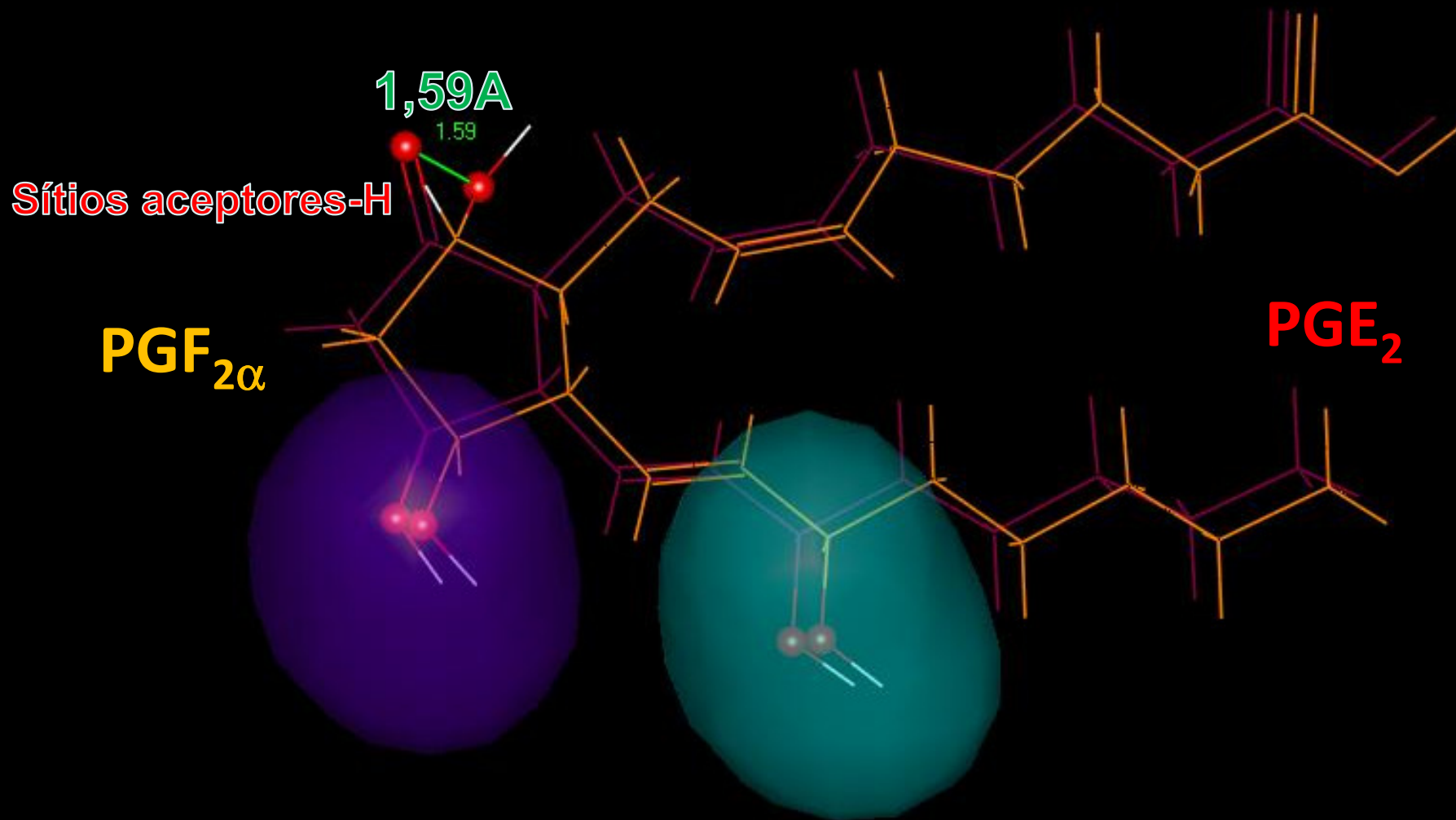


Grampo-de-cabelo

Conformação estável



Sobreposição molecular



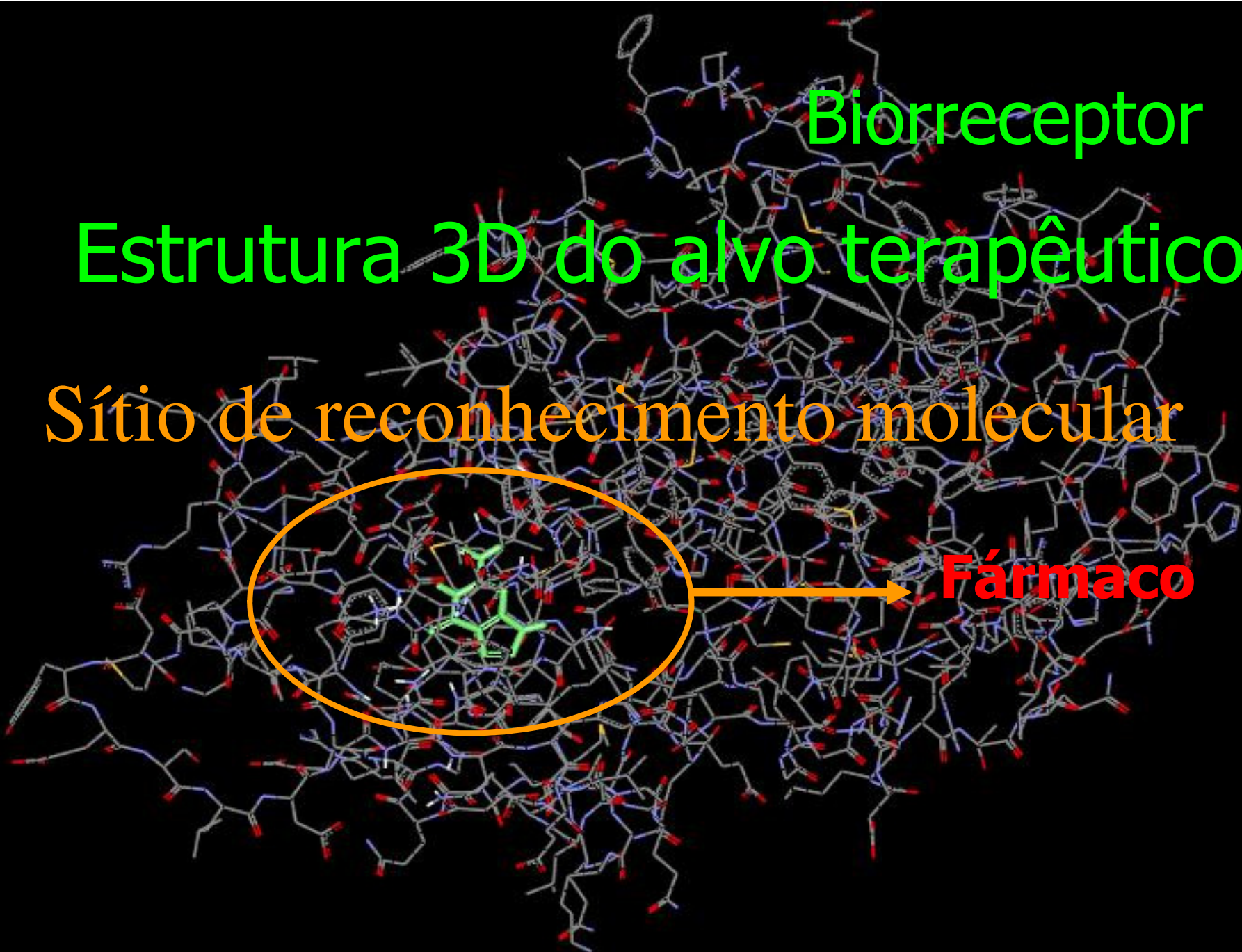


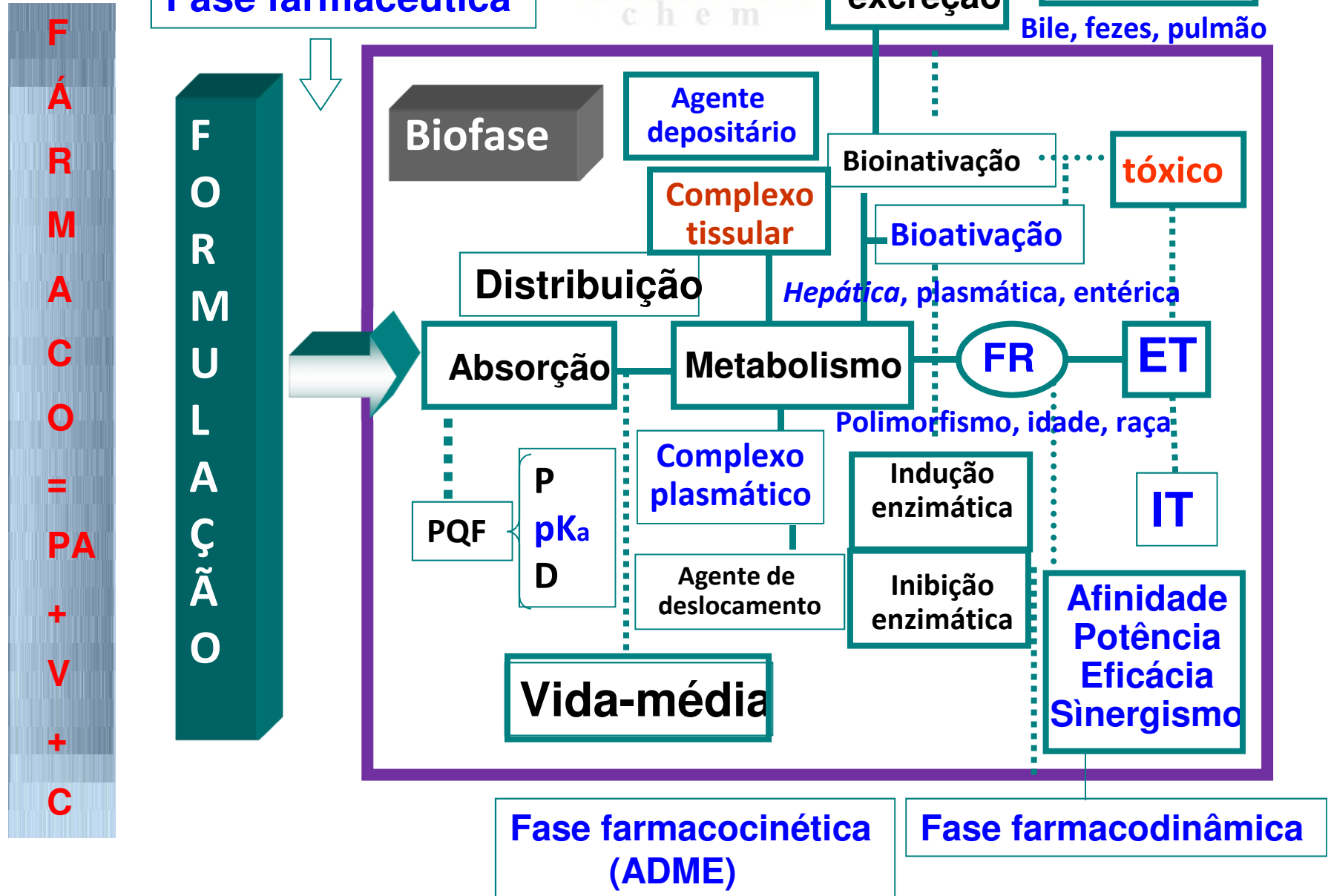
Biorreceptor

Estrutura 3D do alvo terapêutico

Sítio de reconhecimento molecular

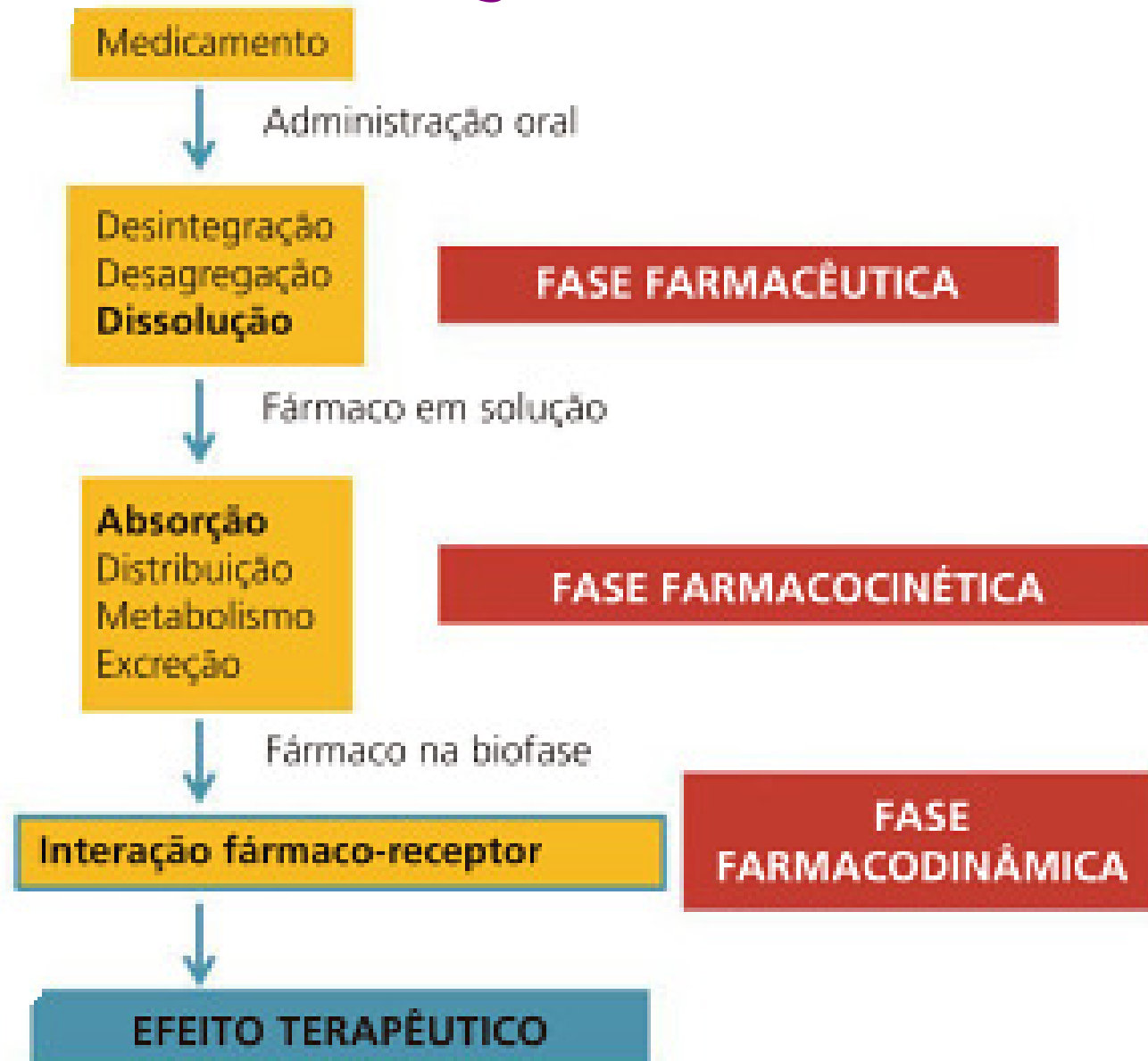
Fármaco





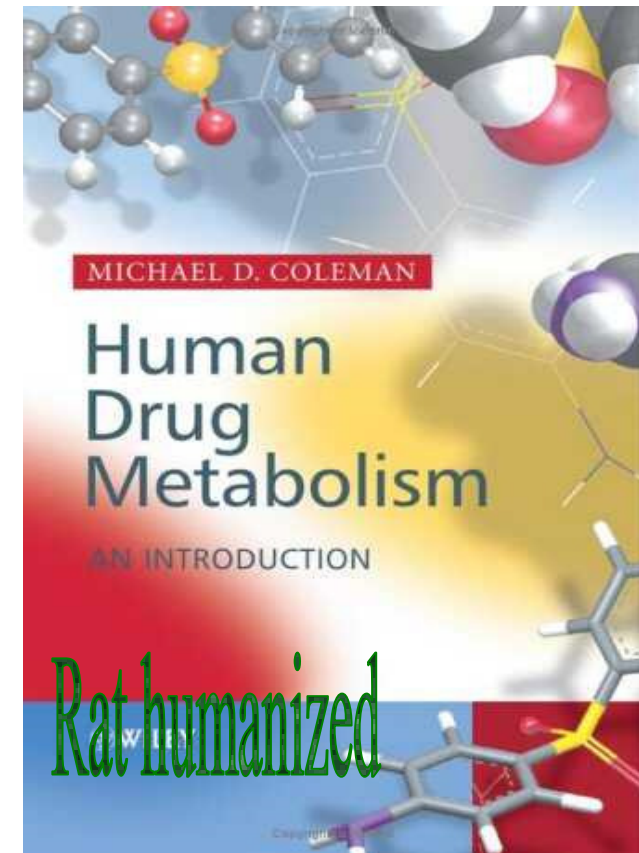
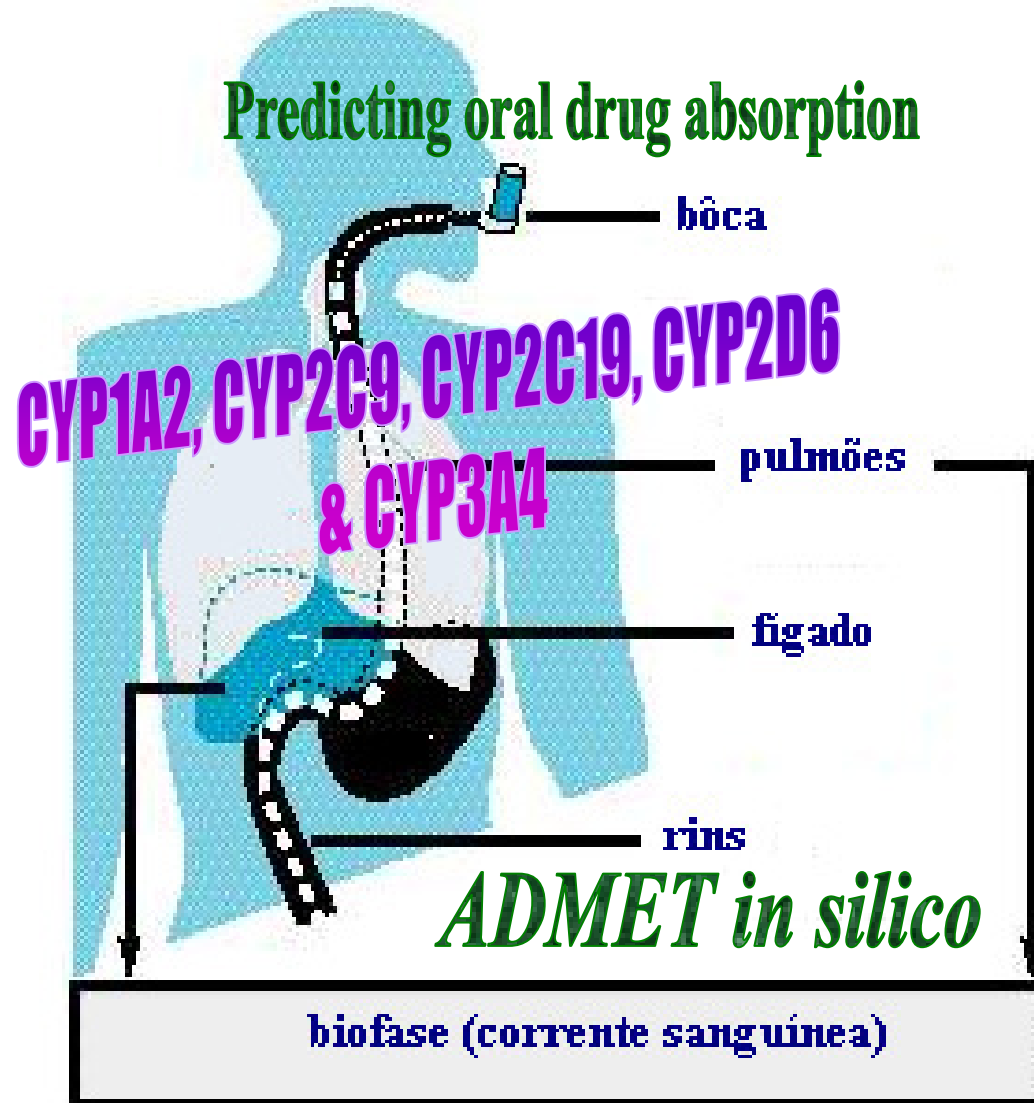


As fases da ação dos fármacos





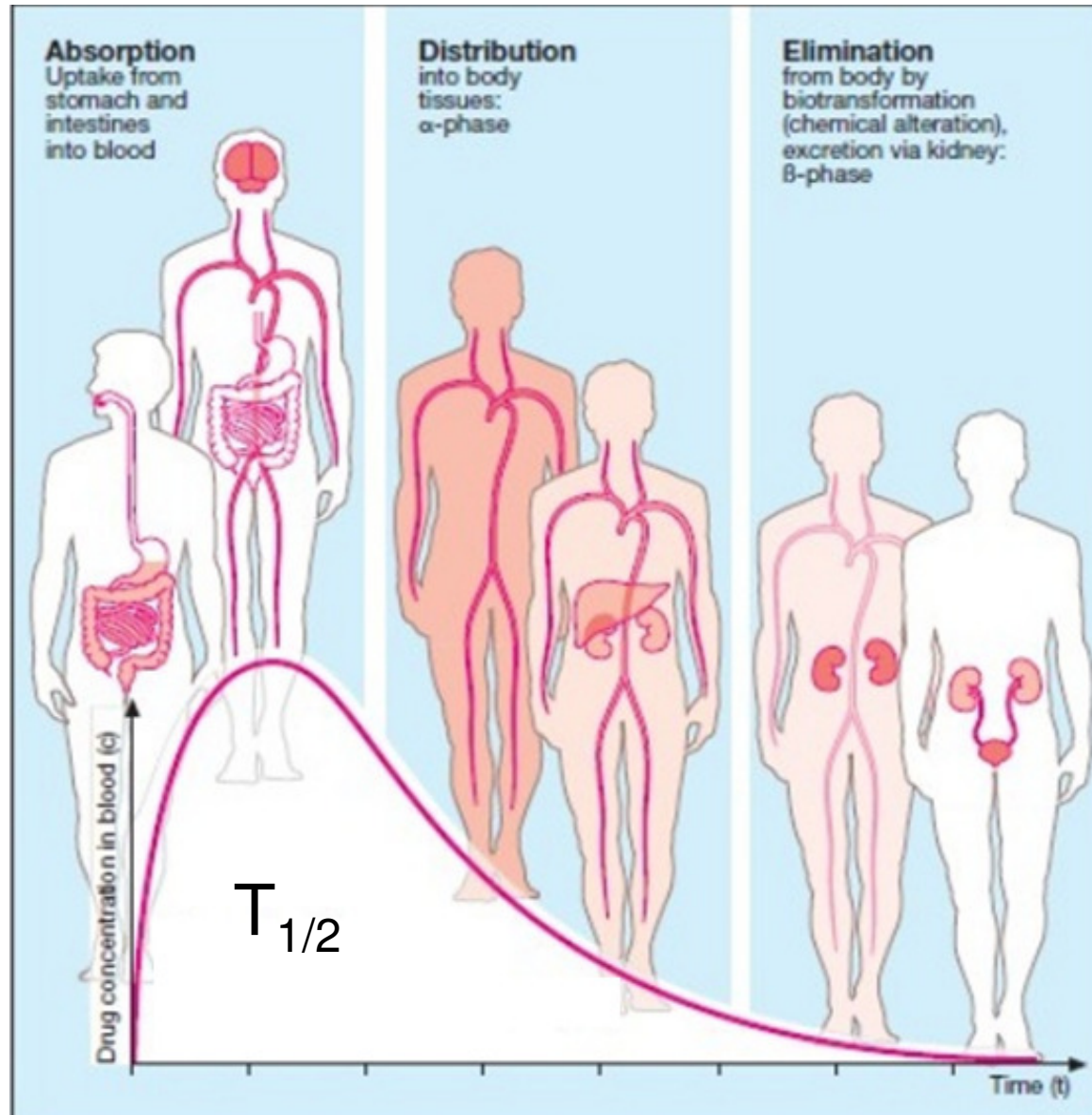
Fase Farmacocinética



- absorção, distribuição, metabolismo & eliminação



A
D
E



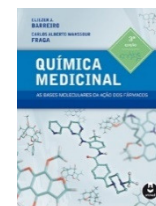
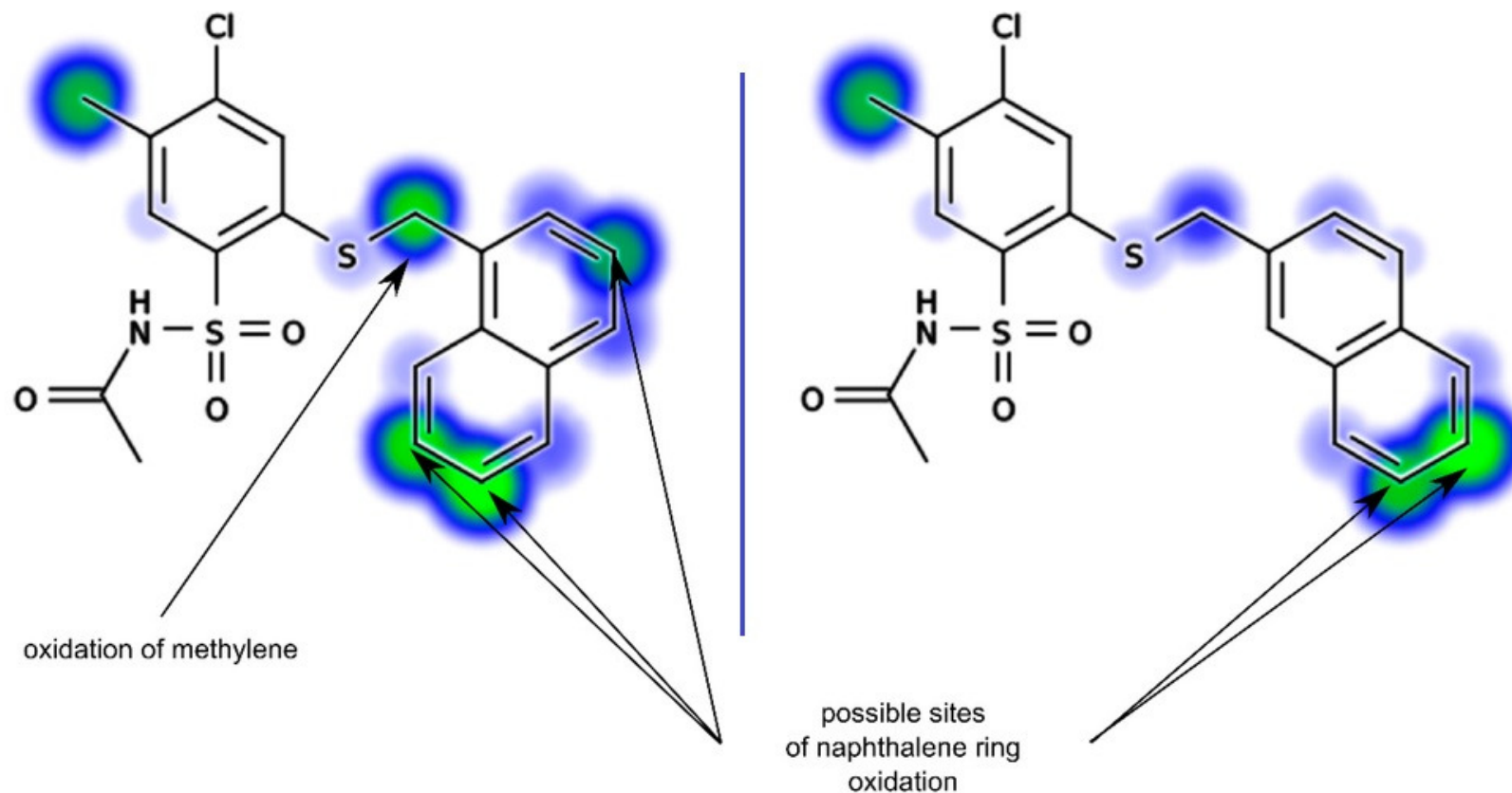
PK

A
D
M
E

Posologia



Metabolismo de fármacos

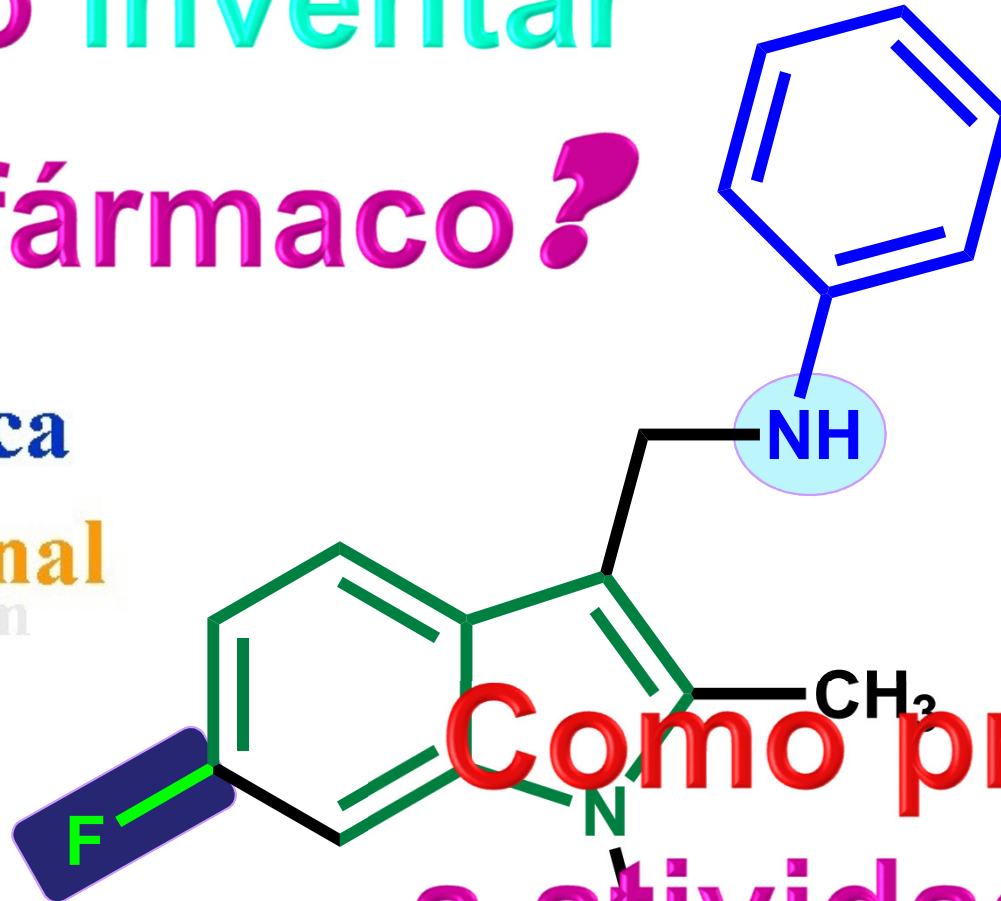




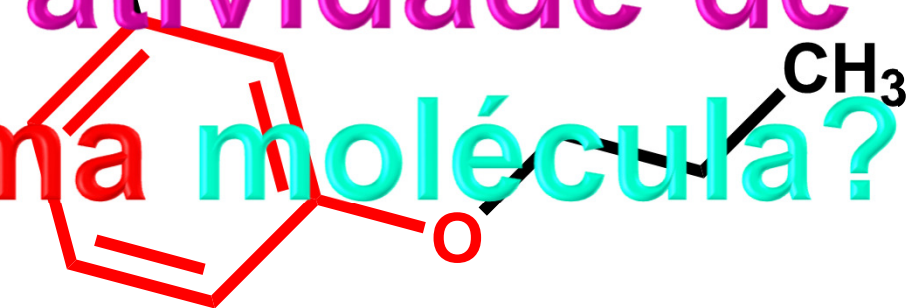
Como inventar *um* fármaco?

Química
med
Medicinal
chem

C O
S
F N
H Cl



Como prever
a atividade de
uma molécula?





Physiologic
A abordagem
approach
fisiológica

**A eleição do
alvo-terapêutico**



**Conhecimento
da fisiopatologia**

Doenças multifatoriais

**Quimioterapia
SNC**

Doença crônica



Physiologic approach
A abordagem fisiológica





O processo da descoberta de fármacos

