Biological Activity

Molecular Structures Continued

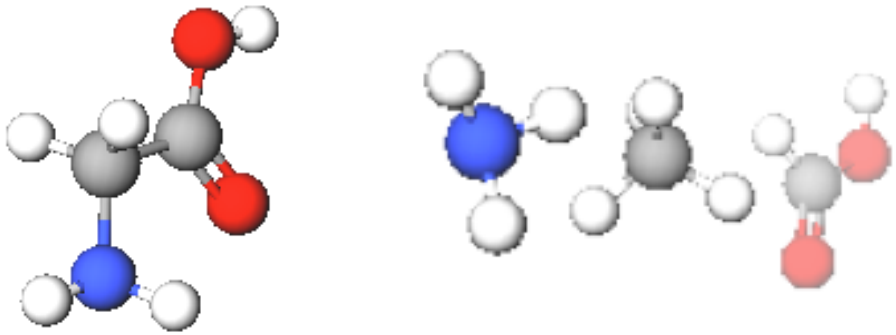
Stereospecific interactions of

Amino acids / Proteins / Enzymes

Dr. Ron Rusay

Amino Acids
Legos of Chemical Biology

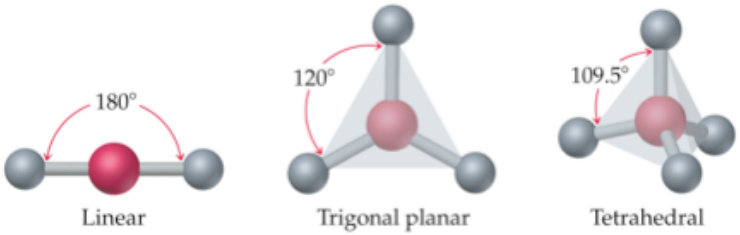
Amino acids contain carbon, hydrogen, oxygen, and nitrogen, which resemble the following shapes & structural components



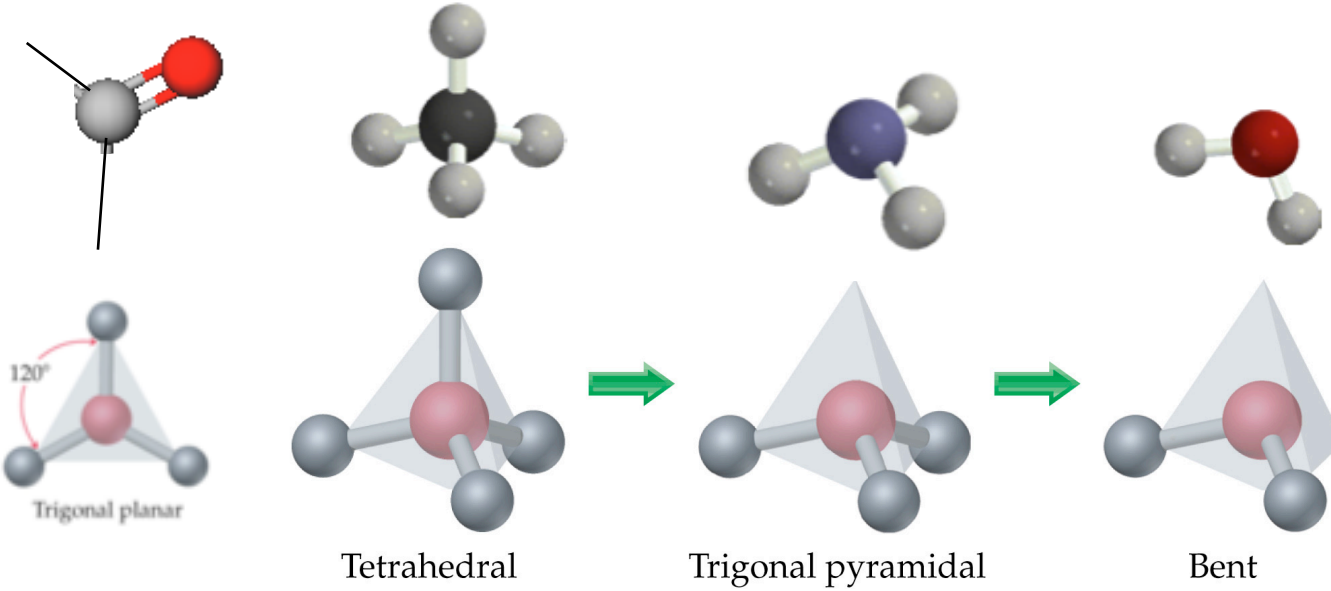
- *20 different amino acids are encoded by the genetic code, which is archived in DNA.*
- *Hundreds of amino acids link together to form proteins, which provide the physical structure and chemical machinery for life.*
- *There are less than 20,000 total proteins produced from humans' entire DNA genome, each coded by a specific gene in DNA's ~3 billion genetic bases.*

Lewis Structures → Molecular Shapes
Molecular Models for C, H, N, O

- *Fundamental repeating shapes found in every biological molecule*



C =black
H = gray
N = blue
O = oxygen

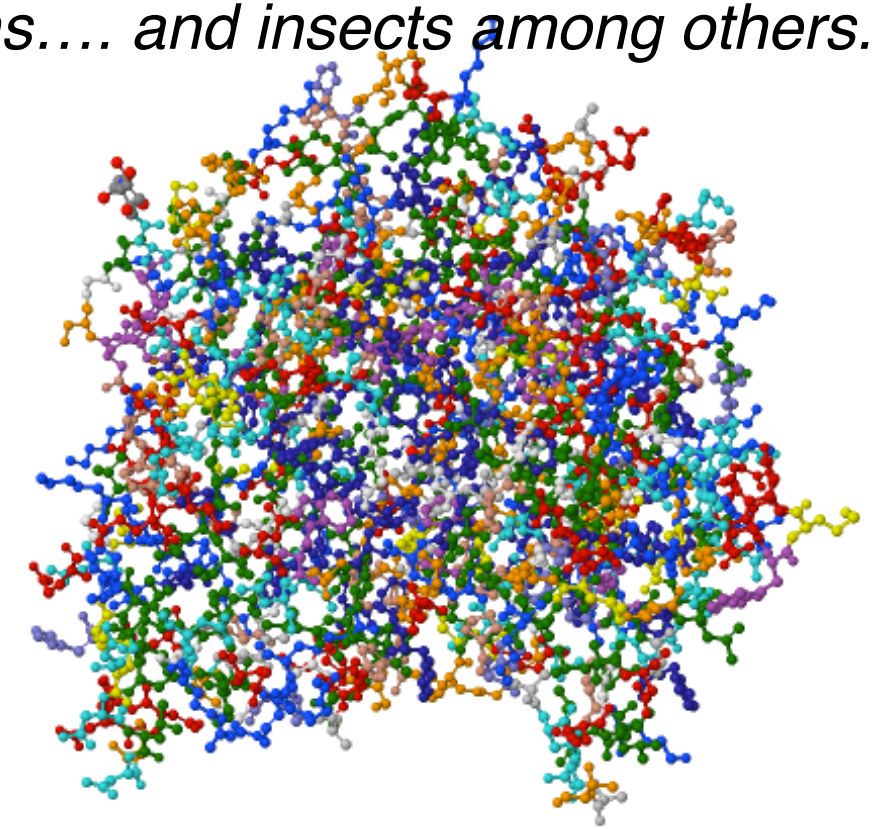


pink = generic atom

Proteins: Indispensible Biopolymers

Acetylcholinesterase (ACE)

ACE, an enzyme, which catalyzes a key reaction in a repetitive biochemical cycle that is crucial to neurological and physiological functions in humans…. and insects among others.



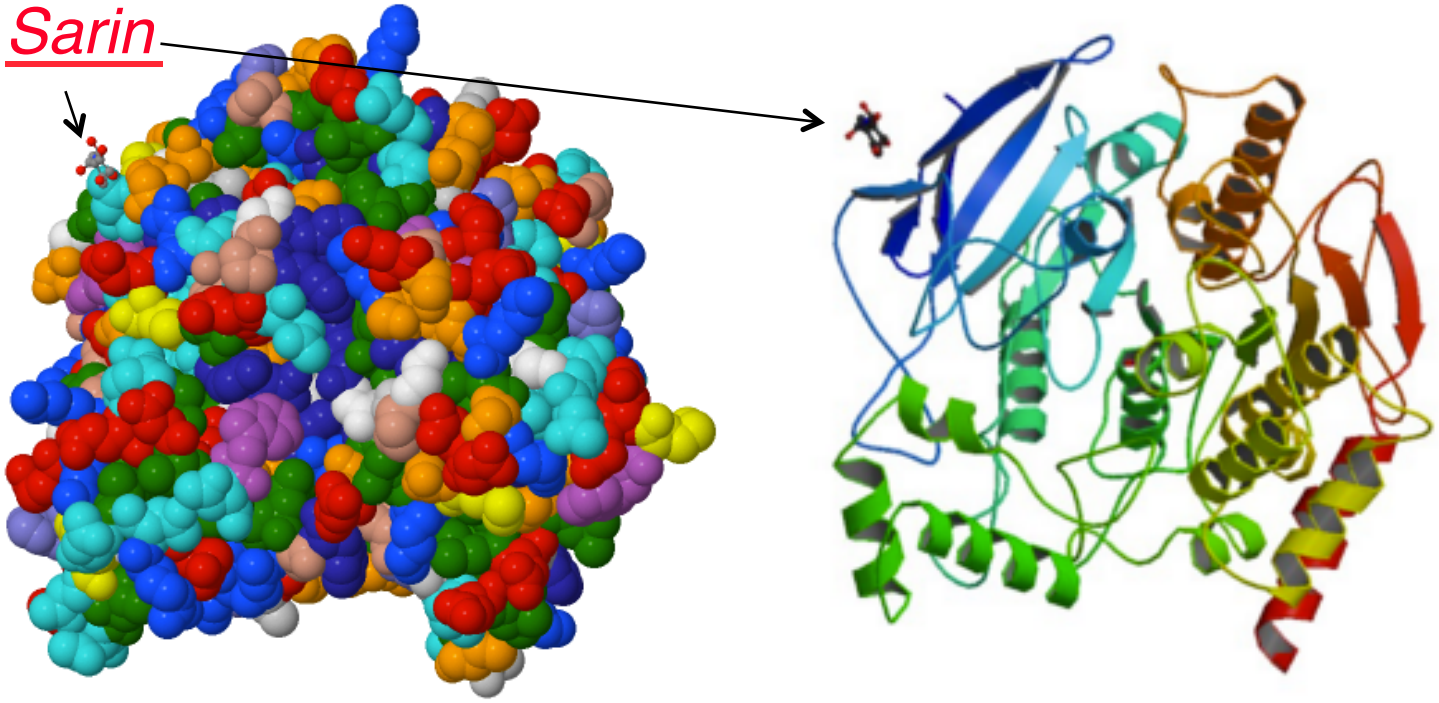
4,496 atoms; 4,404 bonds

574 amino acid residues

Proteins & Small Molecules

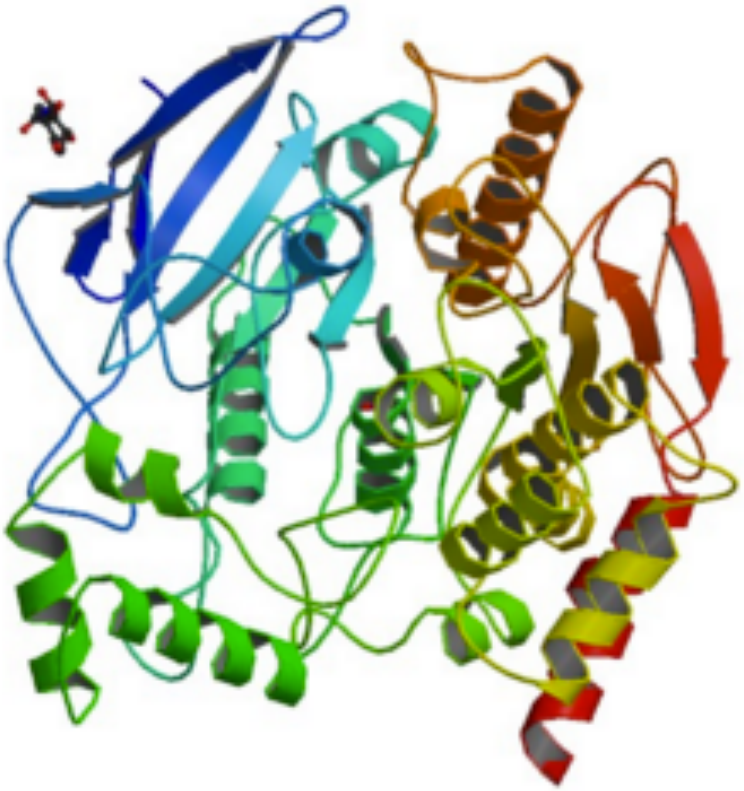
Acetylcholinesterase

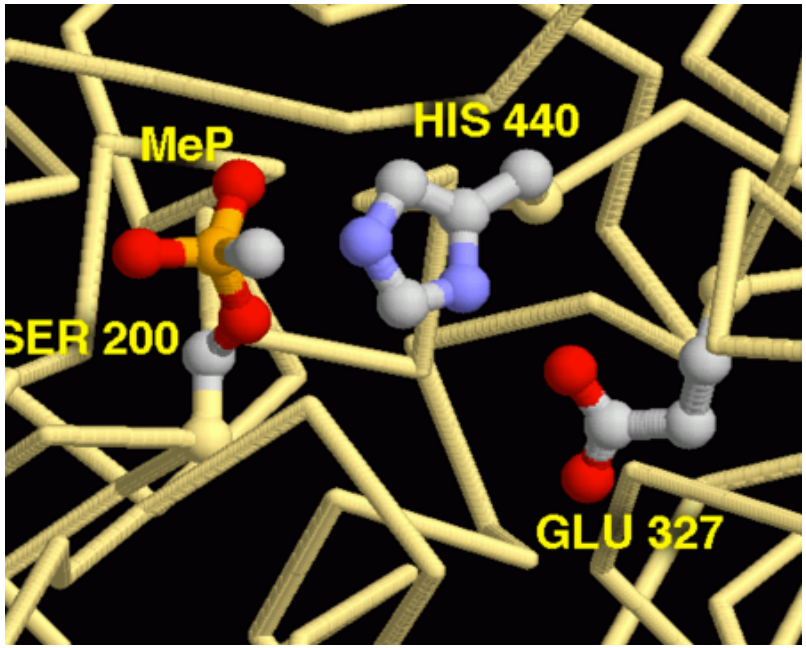
Two images with Sarin, a potent nerve agent, which inhibits acetylcholinesterase, and causes convulsions and death if not antidoted with atropine.



Proteins & Small Molecules

Acetylcholinesterase





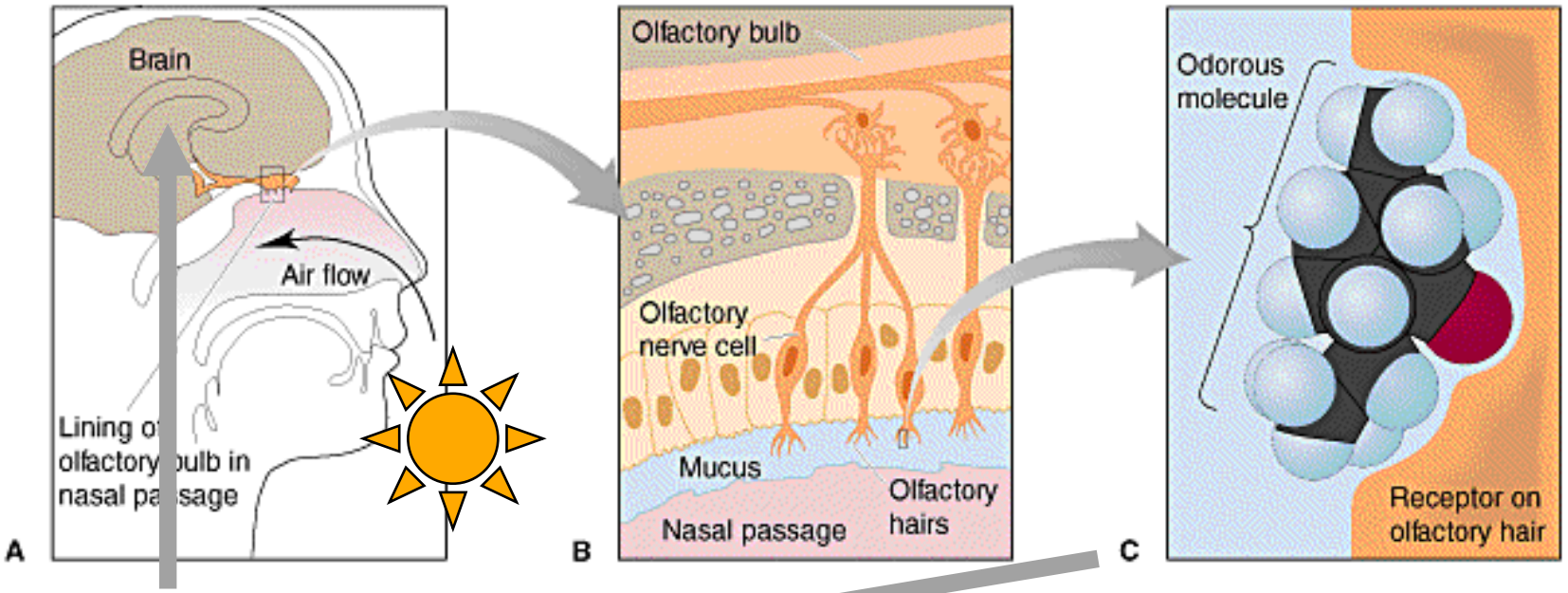
The ACE enzyme has a receptor, a site in the molecule defined by the 3 amino acids in the image on the right. It binds acetylcholine, which then hydrolyzes. Sarin out competes acetylcholine, binds, and the enzyme cannot work.

Proteins & Small Molecules

Acetylcholinesterase

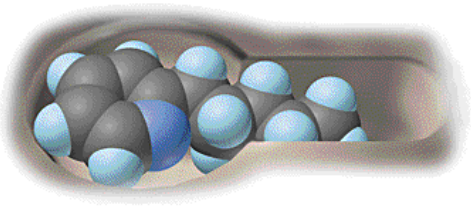
Detecting molecules we cannot see: the Sense of Smell Models & Interactions

http://ep.llnl.gov/msds/orgchem/Chem226/smell-links.html

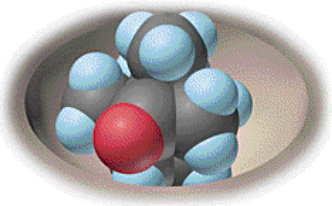


Structure-Odor Relationships
Karen J. Rossiter, *Chem. Rev.*, 1996, *96*, 3201-3240

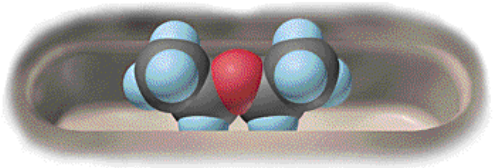
Historical view of a few smell receptors.



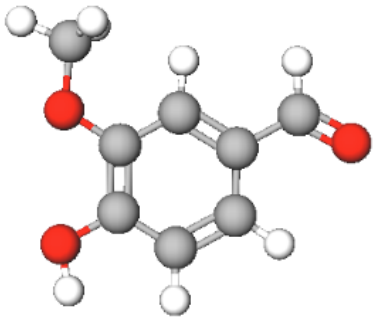
Floral



Camphor-like



Ethereal



Vanillin (Smell)
Sensitivity ~ 1 x 10^{-5}
mol / L_{air}

4 October 2004

The Nobel Assembly at Karolinska Institutet has today decided to award

The Nobel Prize in Physiology or Medicine for 2004

jointly to

Richard Axel and **Linda B. Buck**

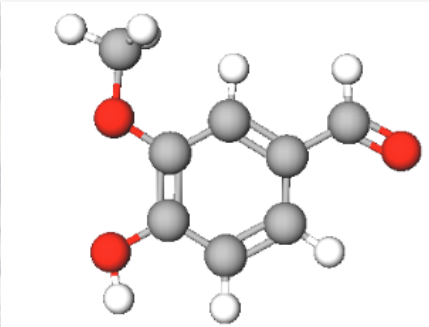
for their discoveries of

"odorant receptors and the organization of the olfactory system"

QUESTION

Receptor Sensitivity

If 1.0 gram of vanillin was placed in an open container at center court in the Oakland Coliseum and dispersed, it might be possible to detect it sitting in a seat in the top row.



Vanillin ($C_8H_8O_3$)

Smell detection limit

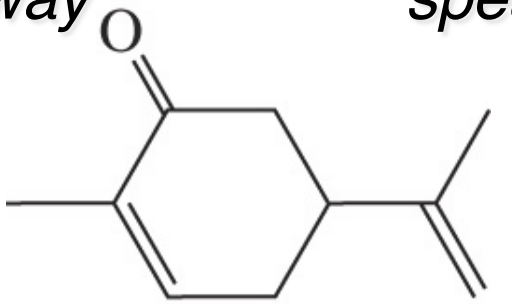
~ 1.0 x 10^{-5} mol / Liter$_{air}$

How many grams of vanillin would there be per Liter$_{air}$ assuming that vanillin's concentration was at its detection limit?

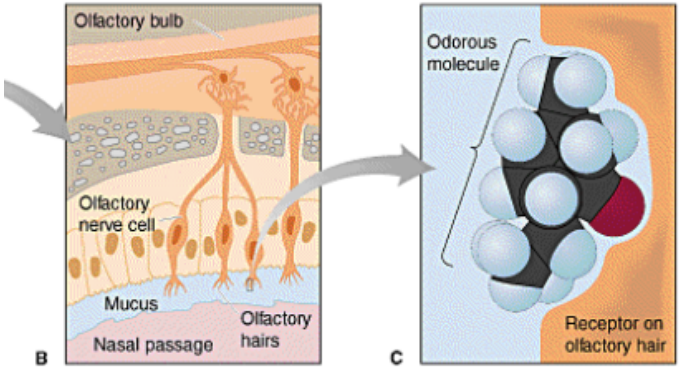
A) 0.015 g
B) 1.5 mg
C) 3.0 mg
D) 0.030 mg

S-(+)-d-carvone
caraway

R-(-)-l-carvone
spearmint

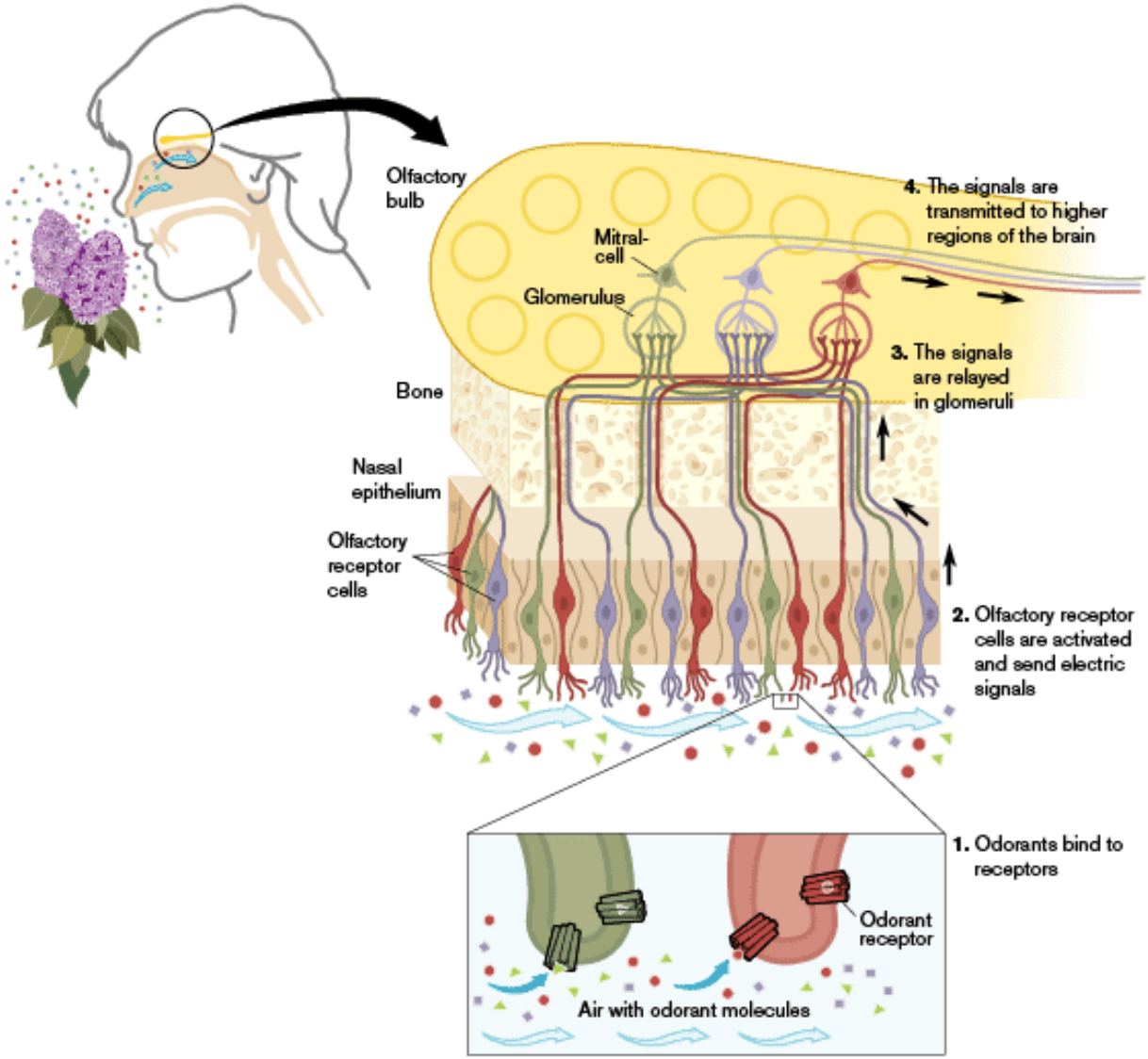


Carvone
($C_{10}H_{14}O$)



They discovered a large gene family, comprised of some 1,000 different genes (three per cent of our genes) that give rise to an equivalent number of olfactory receptor types. These receptors are located on the olfactory receptor cells, which occupy a small area in the upper part of the nasal epithelium and detect the inhaled odorant molecules.

Odorant Receptors and the Organization of the Olfactory System

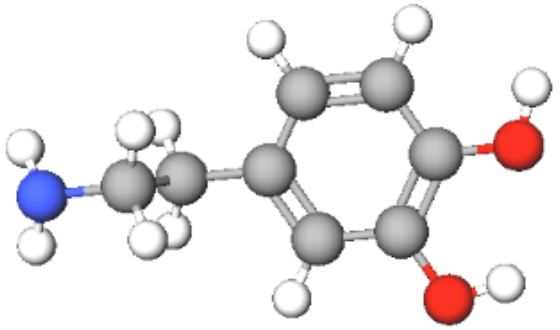


Opioid Addiction

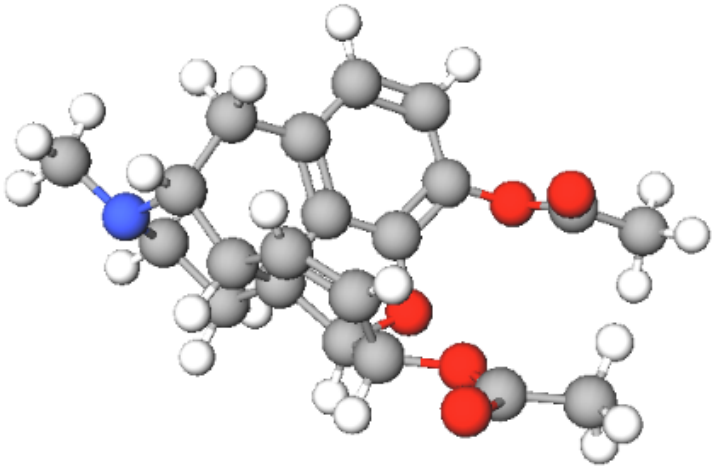
Neurologically active drugs like opioids mimic neurotransmitters that are naturally produced in the body, such as endorphins, which slow breathing, block pain and produce a calming, pleasant, anti-depressing sensation.

However, opiates bind to receptors and flood the nervous system with dopamine, which regulates pleasure among other emotions & functions, producing a level of euphoria that stimulates a craving for more and more, ***which can never be satisfied!!!!***

https://www.sciencedaily.com/releases/2007/10/071014163647.htm



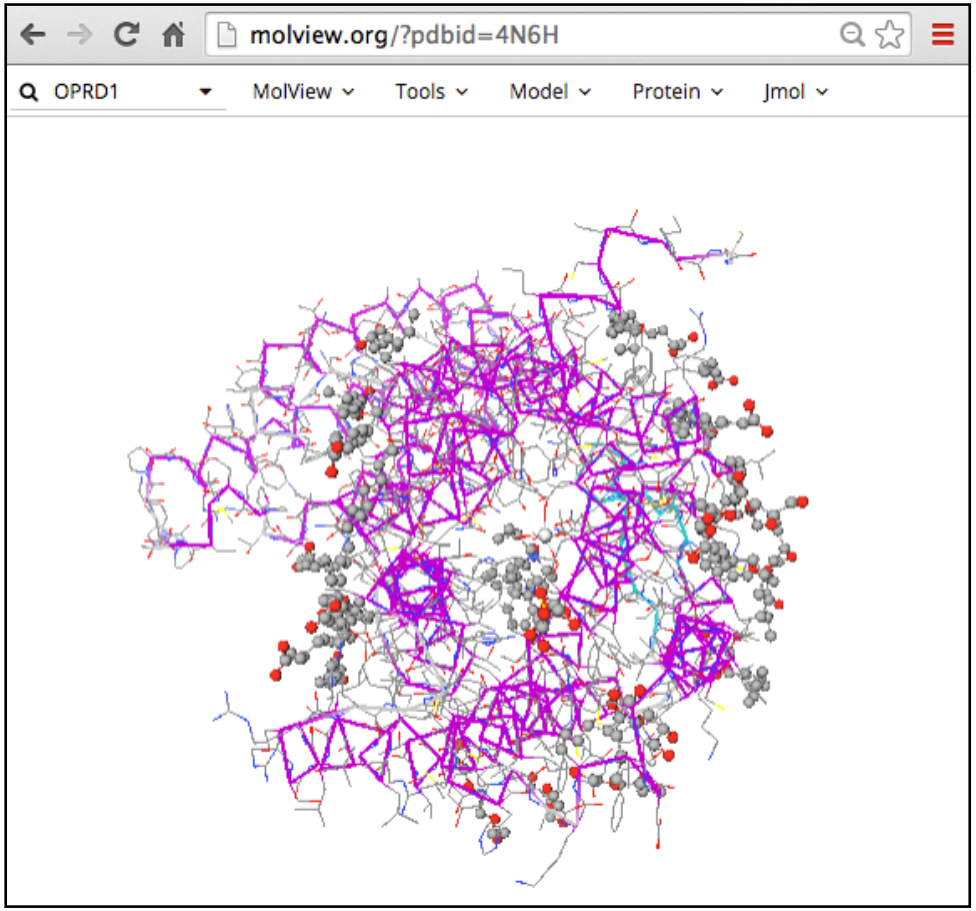
Dopamine

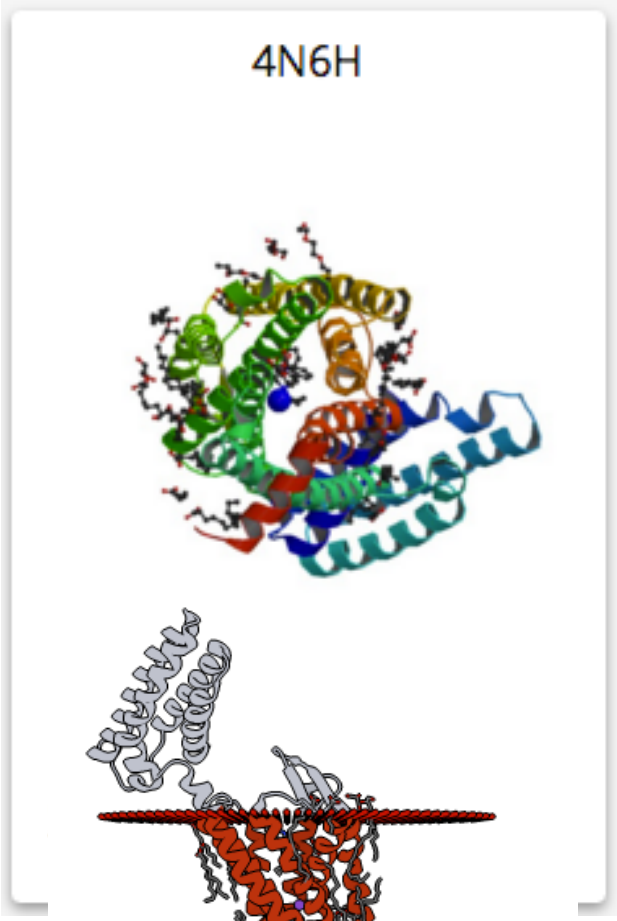


Heroin

4N6H: Structure of human delta opioid receptor

Molar Mass: 52,088.38 g/mol;
Atoms: 3,481;
Amino Acid Residues: 414





DOI: 10.2210/pdb4N6H/pdb
Classification: SIGNALING PROTEIN
Organism(s): Escherichia coli, Homo sapiens

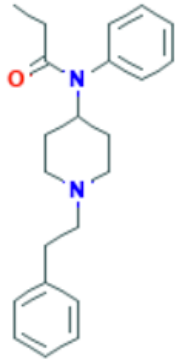
Trans-membrane

molview.org/?cid=3345

Fentanyl | MolView | Tools | Model | Protein | Jmol

Return

Opioid receptor agonist



Fentanyl

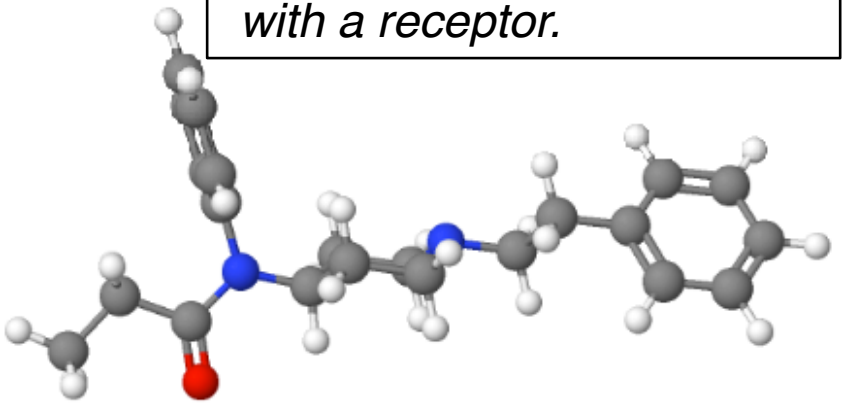
A potent narcotic analgesic, abuse of which leads to habituation or addiction. It is primarily a mu-opioid agonist. Fentanyl is also used as an adjunct to general anesthetics, and as an anesthetic for induction and maintenance. (From Martindale, The Extra Pharmacopoeia, 30th ed, p1078)

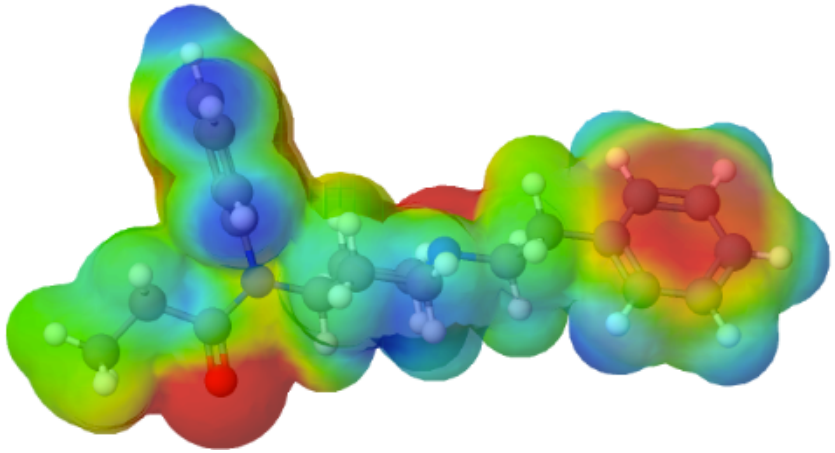
Formula	$C_{22}H_{28}N_2O$
Molecular weight	336.479 u
Hydrogen bond donors	0
Hydrogen bond acceptors	2

Percent composition

C	12.0107 u × 22	78.532 %
H	1.00794 u × 28	8.3878 %
N	14.0067 u × 2	8.3257 %
O	15.9994 u × 1	4.7551 %

Agonist: A substance that initiates a physiological response when combined with a receptor.



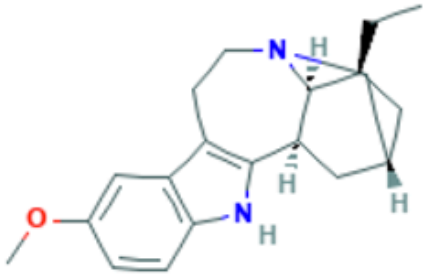


molview.org/?cid=197060

Ibogaine | MolView | Tools | Model | Protein | Jmol

Return

Opioid receptor inhibitor (antagonist)



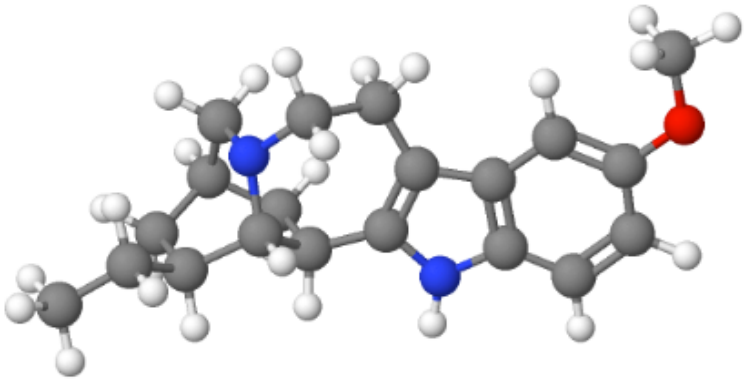
Ibogaine

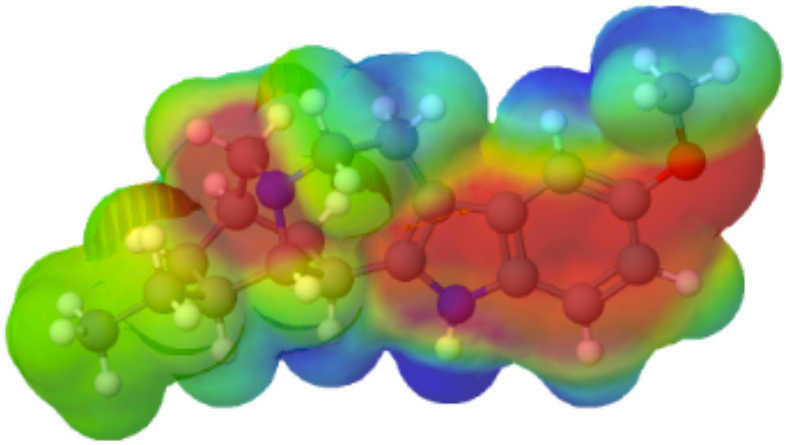
One of several indole alkaloids extracted from Tabernanthe iboga, Baill. It has a complex pharmacological profile, and interacts with multiple systems of neurotransmission. Ibogaine has psychoactive properties and appears to modulate tolerance to opiates.

Formula	$C_{20}H_{26}N_2O$
Molecular weight	310.441 u
Hydrogen bond donors	1
Hydrogen bond acceptors	2

Percent composition

C	12.0107 u × 20	77.380 %
H	1.00794 u × 26	8.4419 %
N	14.0067 u × 2	9.0240 %
O	15.9994 u × 1	5.1539 %





http://chemconnections.org/general/movies/106-nicotine-smoking.mov