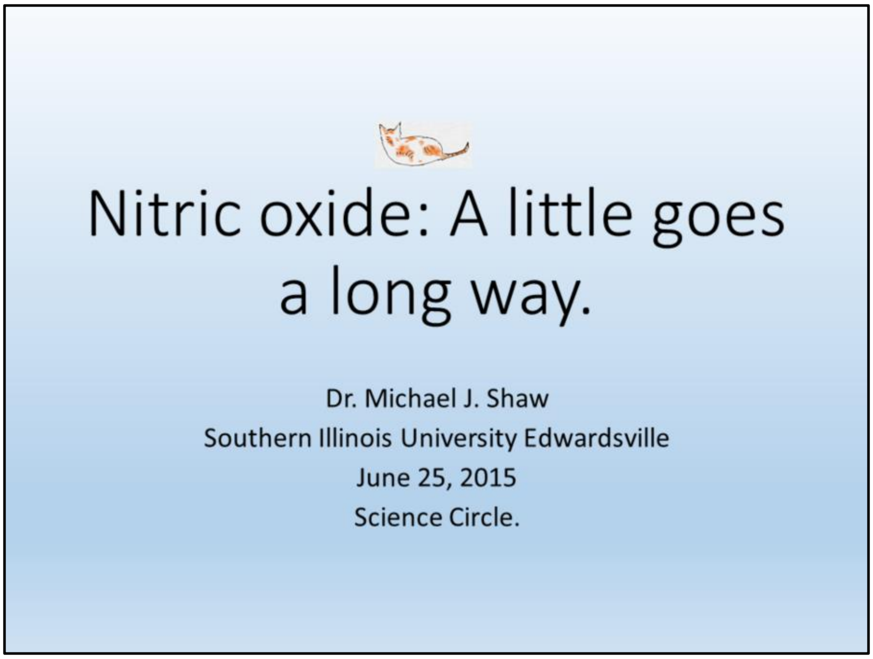


Nitric oxide: A little goes a long way.

The small diatomic molecule NO is a reactive species In the presence of air, it converts to NO2 and normally does not persist in high concentrations. It is a key player in processes that generate ground level ozone in smog, may affect the ozone layer, yet plays a vital physiological role as a neurotransmitter and in blood-pressure regulation. This talk will introduce bonding concepts in NO and in metal-NO species, will explore atmospheric chemistry, and will describe the key enzymatic players in the generation, detection and management of nitric oxide in living systems.

NO is found in a number of surprising places. It plays a role in the light-driven daily cycle of ground level ozone which contributes to the formation of smog. It is present in foodstuffs, and plays vital roles in signaling in mammalian physiology.

"What M. sez when he's asked to do a project at home"
-K.

What is NO?

Nitric Oxide
Public domain image

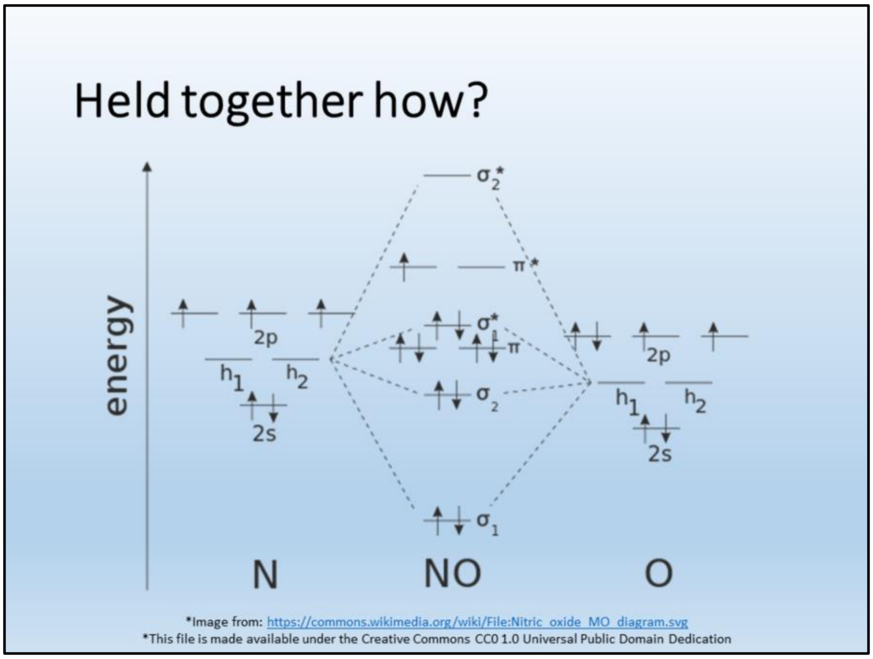
A small molecule composed of a single nitrogen atom and a single oxygen atom.

Has an unpaired electron… Makes Lewis structures annoying. Permits detection by EPR.

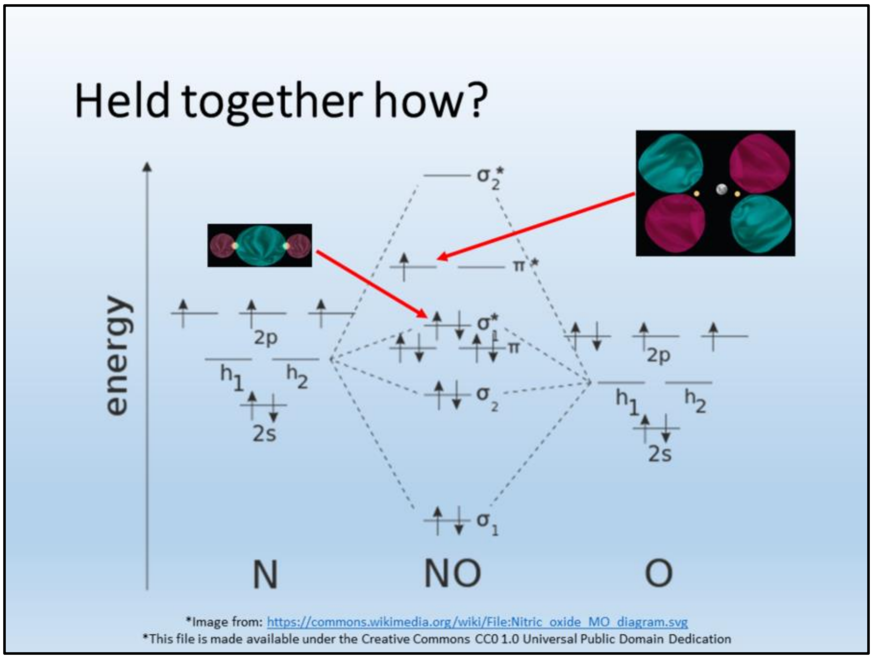
Occurs naturally, but requires energy to make it from N_2 and O_2. Can form in lightning, car engines, etc.

N_2O, NO, NO_2, N_2O_3, N_2O_4 etc are called "NO_x"

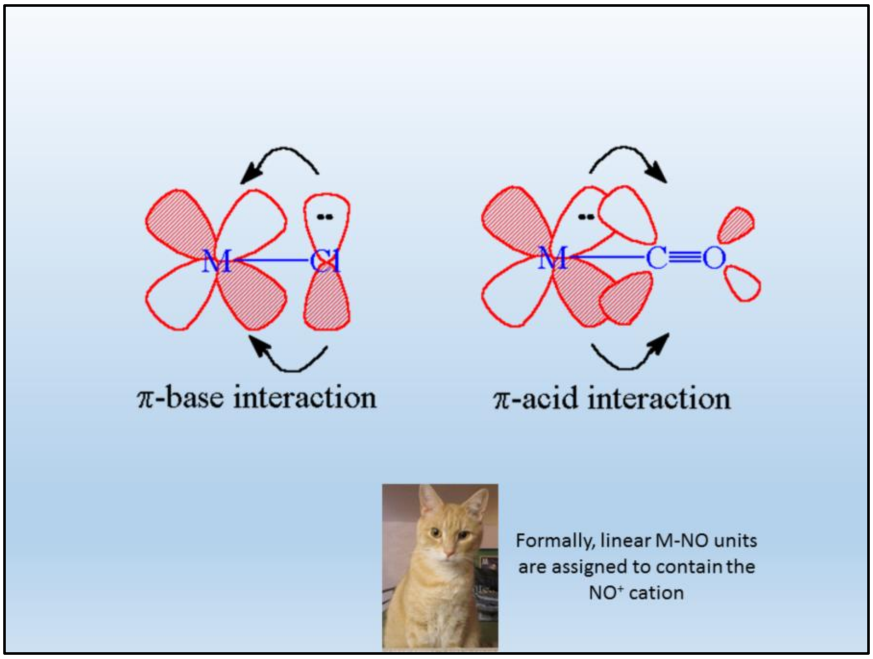
https://commons.wikimedia.org/wiki/File:Nitric-oxide-3D-vdW.png



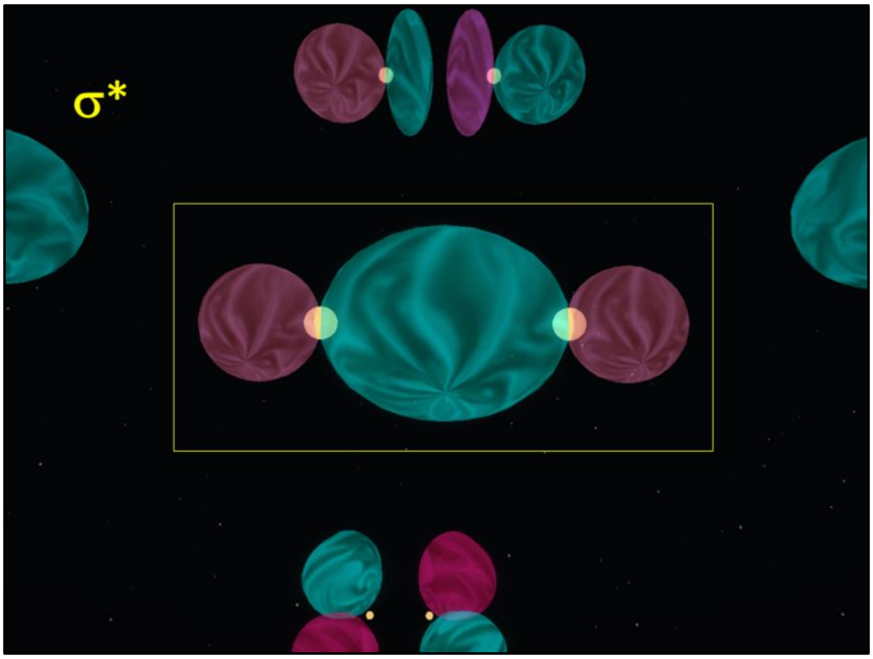
I like this MO diagram. The empty orbitals h1 and h2 are what you get when you allow the s orbital and pz orbital to interact (sp-mixing) before you make the atomic orbitals. The sp mixing makes the sigma-star-1 orbital be above the pi orbital, a feature not seen for O2, or F2. These two orbitals are the frontier orbitals and primarily govern the reactivity of NO.



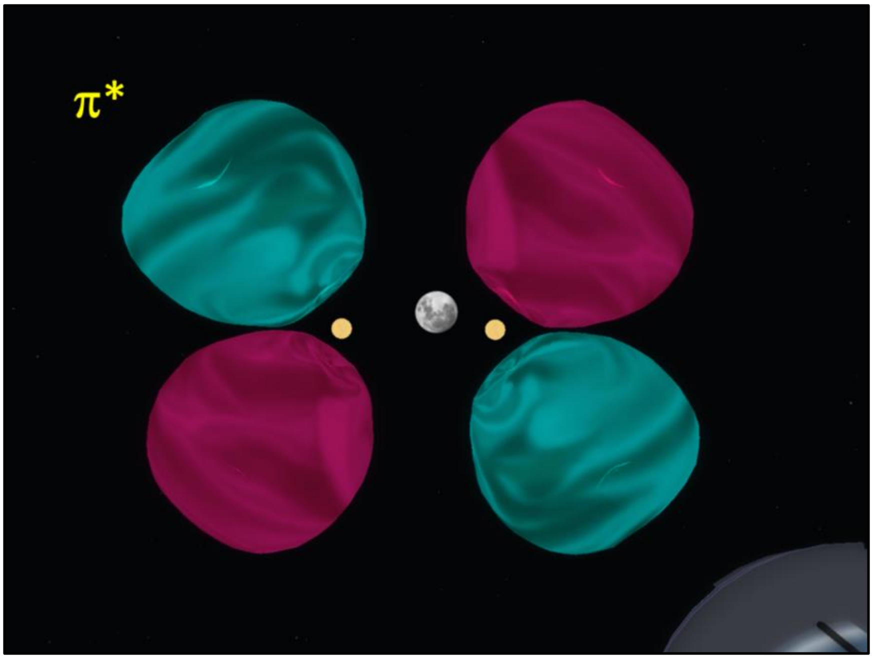
Note that NO is known in three forms: NO+ (nitrosonium), NO and NO- (nitroxyl). The different forms have zero, one, or two electrons in the pi-star orbital.



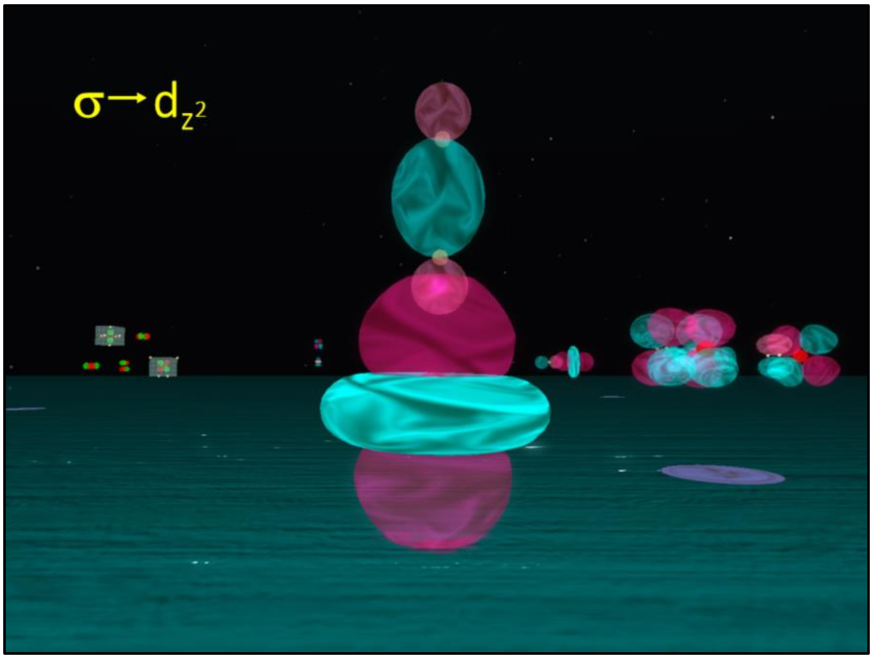
I quick word about bonding. Like CO, NO is a pi aci. That mens while it can give its sigma-star-one electrons to a metal (blue line) it can receive a pair of electrons from the metal's d-orbitals (black curved arrows). The cat is there to denote that the NO+ cation has the same electronic structure as CO, and can be described with the same bonding.



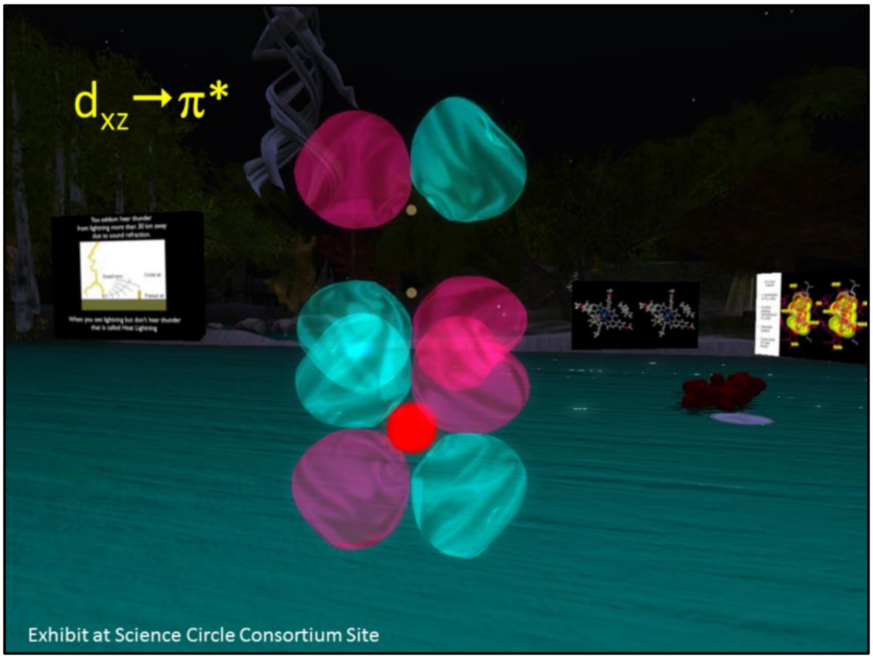
From the Science Circle Consortium display… a typical sigma-star-one orbital on a diatomic molecule.



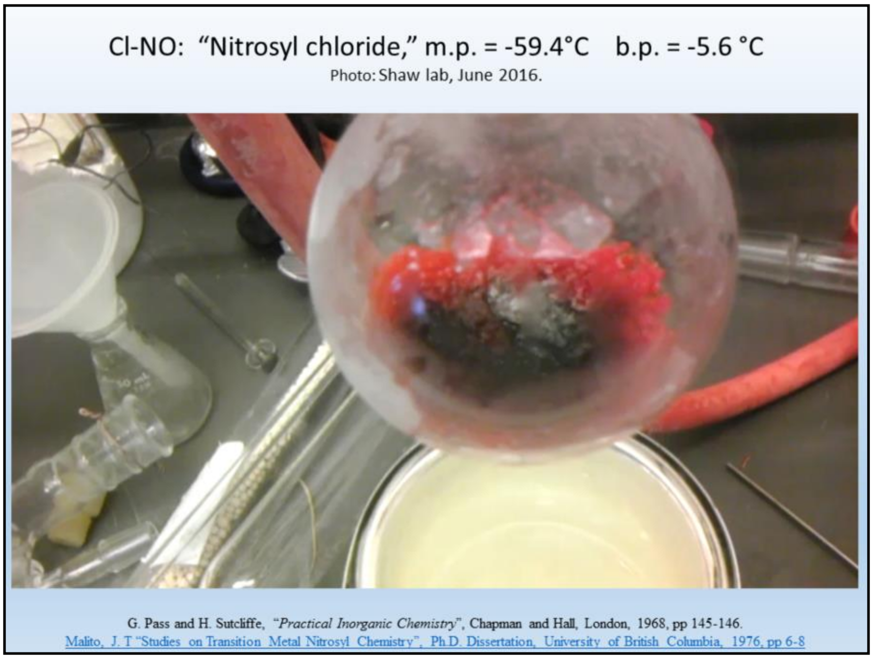
From the Science Circle Consortium display… a typical pi-star orbital on a diatomic molecule. The moon is an added bonus of seeing the display in Second Life.



From the Science Circle Consortium display… a typical sigma-star-one orbital on a diatomic molecule donating into a dz2 orbital on a metal atom.



From the Science Circle Consortium display… a typical pi-star orbital on a diatomic molecule receiving a pair of electrons from a dxz orbital on a metal atom. These two effects provide very strong bonding for NO to metals. If the metal loses an electron, the effect pictured here is weakened, and the NO is likely to fall off.



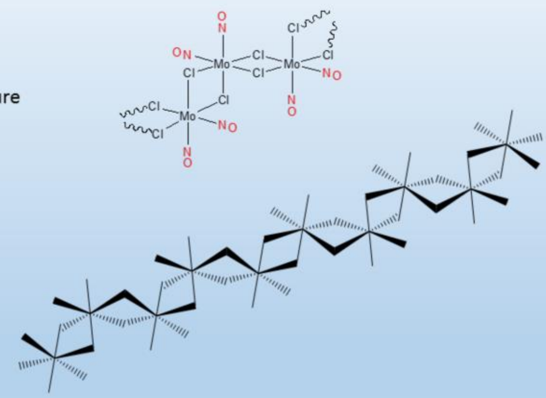
One way to introduce NO to a metal compound is by treating it with NOCl. Here is photo of some NOCl I made last year. It has a beautiful deep red color, and is very similar in chemical properties to bromine (Br2). Quite harsh! NO itself is a colorless gas.

Malito prep:

https://open.library.ubc.ca/cIRcle/collections/ubctheses/831/items/1.0060992

$$Mo(CO)_6 + 2\ ClNO(g) \longrightarrow [Mo(NO)_2(Cl)_2]_n + 6CO(g)$$

Presumed structure



Prep Ref: Johnson, B. F. G., Al-Obadi, K. H. and Paine, R. T. (1970) Dihalogenodinitrosylmolybdenum and Dihalogenodinitrosyltungsten, in Inorganic Syntheses, Volume 12 (ed R. W. Parry), John Wiley & Sons, Inc., Hoboken, NJ, USA. doi: 10.1002/9780470132432.ch47

A sample reaction is to treat Mo(CO)6 with NOCl to get the dichlorodinitrosylmolybdenum(0) polymer. I have drawn some views of a possible structure. The chloride bridges are weak, and can be cleaved by simple Lewis bases (water will do) to make monomeric complexes.

$$Mo(CO)_6 + 2\ ClNO(g) \longrightarrow [Mo(NO)_2(Cl)_2]_n + 6CO(g)$$

Prep Ref: Johnson, B. F. G., Al-Obadi, K. H. and Paine, R. T. (1970) Dihalogenodinitrosylmolybdenum and Dihalogenodinitrosyltungsten, in Inorganic Syntheses, Volume 12 (ed R. W. Parry), John Wiley & Sons, Inc., Hoboken, NJ, USA. doi: 10.1002/9780470132432.ch47

A photo of the polymer. I made it for my advanced inorganic class to use as a starting material. Not much chemistry has been done with this stuff, so I gave them the opportunity to make new compounds. 2 groups apparently made new compounds that had never been prepared before… they are currently under study by an undergrad researcher in my group.

Bent M-NO units

- If metal has 6 e^- already in d-orbitals, next 2 e^- localize on N atom.
- Structural consequence: M-NO bends by 30 ° per e^-
- Bent forms more related to “nitroxyl” or NO^-
- Also related to HNO, “azanone”.
  - Bio functions of HNO appear to be “orthogonal” to NO.

Some of the complicating factors for NO chemistry. Since it is a redox site itself, we have to be careful of “non-innocent redox ligands” especially when considering porphyrins, which have rich redox chemistry themselves. The 6 electrons in an octahedral metal complex fill the “t2g” orbitals (i.e. dxy, dxz, and dyz). Rather than put electrons into the dz2 or dx2-y2, the complex undergoes a structural change which puts the new electrons on the N-atom, and at a lower energy overall than if the NO remained straight.

Atmospheric chemistry

- NO is endothermic to make… needs energy to turn N_2 and O_2 into NO.
- High pressure and temperatures in internal combustion engines can make some NO and NO_2

$$N_2 + O_2 \rightarrow 2\,NO$$

- NO has a role in ground-level ozone formation

An intro to atmospheric chemistry. The atmosphere does not catch on fire because N2 is not flammable. Lucky for us. It takes energy to break the N≡N triple bond, so NOx form in lightning, engines etc.

NO_2-O_3 Cycle, Upper Atmosphere

- O_2 + UV-C light → 2 O•
- O_3 + UV-C and UV-B light → O_2 + O•
- O_2 + O• → O_3 (after energy loss through collisions)

- NOx can interfere:
  - NO + O_3 → O_2 + NO_2
  - NO_2 + O• → O_2 + NO

The normal cycle is the top set of reactions. O atoms are created when UV-C light (<280 nm) break apart oxygen molecules. These atoms have to much energy to directly recombine, so after few collisions with N2, they can either recombine, or combine with an O2 molecule to make ozone. The ozone will absorb UV-B light (280-315nm), and spit out an O-atom. After collisions allow the “hot” atom to lose energy, it can recombine with another O2 to make ozone again.

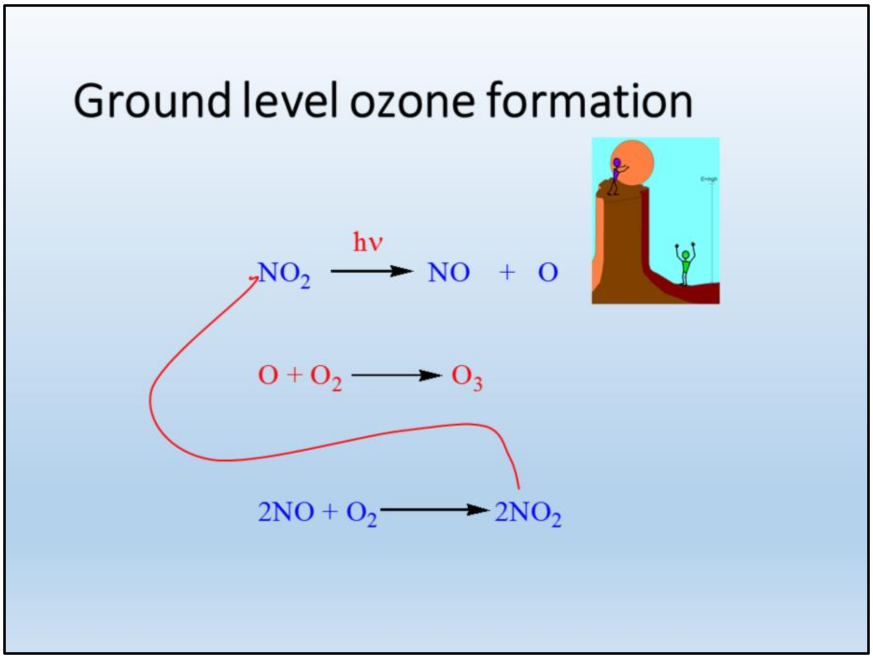
Nox may interfere by eating up ozone, and reacting with O-atoms. The impact of this chemistry is not thought to be particularly problematic, especially compared with chlorine atoms.

Ground level ozone formation

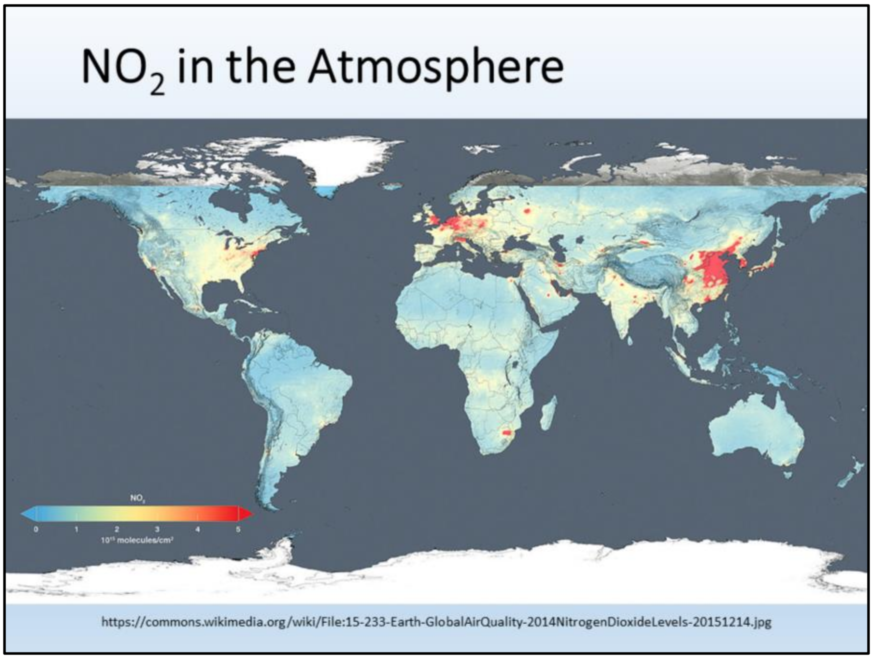
$$NO_2 \xrightarrow{h\nu} NO + O$$

$$O + O_2 \longrightarrow O_3$$

$$2NO + O_2 \longrightarrow 2NO_2$$



In the lower atmosphere, NOx converts light and O2 into ozone catalytically. Ozone contributes to the formation of aerosol particles because of reactions with VOC’s. Once the sun sets, the ozone and VOC levels go down.



Satellite data which shows NO2 levels. Particularly high over industrialized areas. This data shows decreases in U.S. since 2004 because of environmental laws.

15-233-Earth-GlobalAirQuality-2014NitrogenDioxideLevels-20151214.jpg https://commons.wikimedia.org/wiki/File:15-233-Earth-GlobalAirQuality-2014NitrogenDioxideLevels-20151214.jpg

"This file is in the public domain in the United States because it was solely created by NASA. NASA copyright policy states that "NASA material is not protected by copyright unless noted". "

English: Dec. 14, 2015 - 15-233 http://www.nasa.gov/press-release/new-nasa-satellite-maps-show-human-fingerprint-on-global-air-quality

English: Dec. 14, 2015 - 15-233 http://www.nasa.gov/press-release/new-nasa-satellite-maps-show-human-fingerprint-on-global-air-quality

New NASA Satellite Maps Show Human Fingerprint on Global Air Quality

VIDEO (01:42): Using new, high-resolution global satellite maps of air quality indicators, NASA scientists tracked air pollution trends over the last decade in various regions and 195 cities around the globe. The United States, Europe and Japan have improved air quality thanks to emission control regulations, while China, India and the Middle East, with their fast-growing economies and expanding industry, have seen more air pollution. Credits: NASA

IMAGE: The trend map of the United States shows the large decreases in nitrogen dioxide concentrations tied to environmental regulations from 2005 to 2014. Credits: NASA

IMAGE: The trend map of East Asia shows the change in nitrogen dioxide concentrations related to a mix of economic growth and environmental controls across China, South Korea and Japan from 2005 to 2014. Credits: NASA

IMAGE: The trend map of the Middle East shows the change in nitrogen dioxide concentrations from 2005 to 2014. The decreases in Syria are tied to the economic disruption caused by their civil war. Credits: NASA

IMAGE: This global map shows the concentration of nitrogen dioxide in the troposphere as detected by the Ozone Monitoring Instrument aboard the Aura satellite, averaged over 2014. Credits: NASA

DISCUSSION:

Using new, high-resolution global satellite maps of air quality indicators, NASA scientists tracked air pollution trends over the last decade in various regions and 195 cities around the globe. The findings were presented Monday at the American Geophysical Union meeting in San Francisco and published in the Journal of Geophysical Research.

"These changes in air quality patterns aren't random," said Bryan Duncan, an atmospheric scientist at NASA's Goddard Space Flight Center in Greenbelt, Maryland, who led the research. "When governments step in and say we're going to build something here or we're going to regulate this pollutant, you see the impact in the data."

Duncan and his team examined observations made from 2005 to 2014 by the Dutch-Finnish Ozone Monitoring Instrument aboard NASA's Aura satellite. One of the atmospheric gases the instrument detects is nitrogen dioxide, a yellow-brown gas that is a common emission from cars, power plants and industrial activity. Nitrogen dioxide can quickly transform into ground-level ozone, a major respiratory pollutant in urban smog. Nitrogen dioxide hotspots, used as an indicator of general air quality, occur over most major cities in developed and developing nations.

The science team analyzed year-to-year trends in nitrogen dioxide levels around the world. To look for possible explanations for the trends, the researchers compared the satellite record to information about emission controls regulations, national gross domestic product and urban growth.

"With the new high-resolution data, we are now able to zoom down to study pollution changes within cities, including from some individual sources, like large power plants," said Duncan.

Previous work using satellites at lower resolution missed variations over short distances. This new space-based view offers consistent information on pollution for cities or countries that may have limited ground-based air monitoring stations. The resulting trend maps tell a unique story for each region.

The United States and Europe are among the largest emitters of nitrogen dioxide. Both regions also showed the most dramatic reductions between 2005 and 2014. Nitrogen dioxide has decreased from 20 to 50 percent in the United States, and by as much as 50 percent in Western Europe. Researchers concluded that the reductions are largely due to the effects of environmental regulations that require technological improvements to reduce pollution emissions from cars and power plants.

China, the world's growing manufacturing hub, saw an increase of 20 to 50 percent in nitrogen dioxide, much of it occurring over the North China Plain. Three major Chinese metropolitan areas -- Beijing, Shanghai, and the Pearl River Delta -- saw nitrogen dioxide reductions of as much as 40 percent.

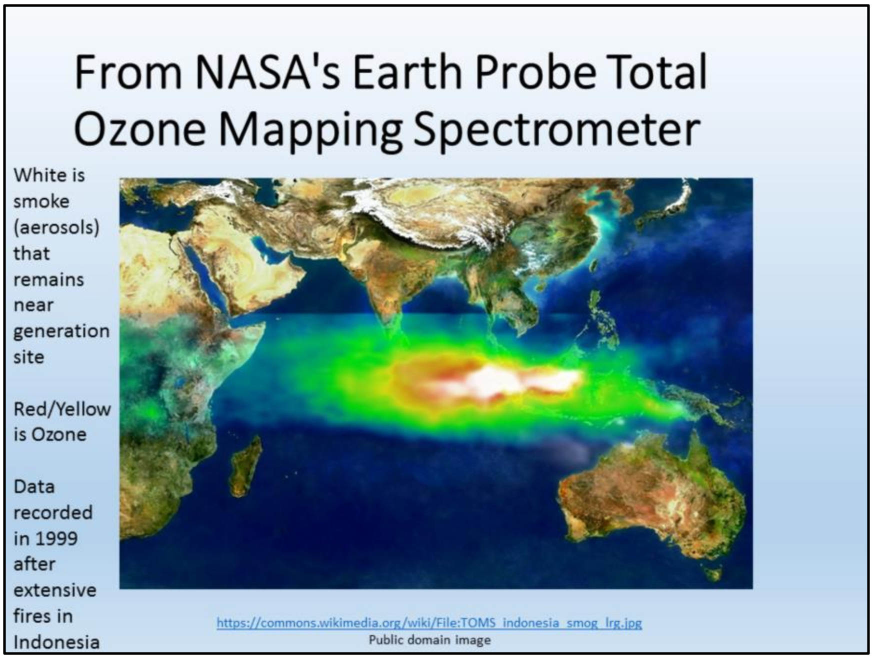
The South African region encompassing Johannesburg and Pretoria has the highest nitrogen dioxide levels in the Southern Hemisphere, but the high-resolution trend map shows a complex situation playing out between the two cities and neighboring power plants and industrial areas.

"We had seen seemingly contradictory trends over this area of industrial South Africa in previous studies," said Anne Thompson, co-author and chief scientist for atmospheric chemistry at Goddard. "Until we had this new space view, it was a mystery."

The Johannesburg-Pretoria metro area saw decreases after new cars were required in 2008 to have better emissions controls. The heavily industrialized area just east of the cities, however, shows both decreases and increases. The decreases may be associated with fewer emissions from eight large power plants east of the cities since the decrease occurs over their locations. However, emissions increases occur from various other mining and industrial activities to the south and further east.

In the Middle East, increased nitrogen dioxide levels since 2005 in Iraq, Kuwait and Iran likely correspond to economic growth in those countries. However, in Syria, nitrogen dioxide levels decreased since 2011, most likely because of the civil war, which has interrupted economic activity and displaced millions of people.

To view and download high-resolution air quality maps, go to:
http://svs.gsfc.nasa.gov/12094
For more on NASA's research into nitrogen dioxide, and air quality data for 195 cities, visit:
https://airquality.gsfc.nasa.gov/



Ozone, rather than NO… from forest fires in Indonesia. But the ozone would be exacerbated by NOx.
From summary:
This image shows the pollution over Indonesia and the Indian Ocean on October 22, 1997. White represents the aerosols (smoke) that remained in the vicinity of the fires. Green, yellow, and red pixels represent increasing amounts of tropospheric ozone (smog) being carried to the west by high-altitude winds.

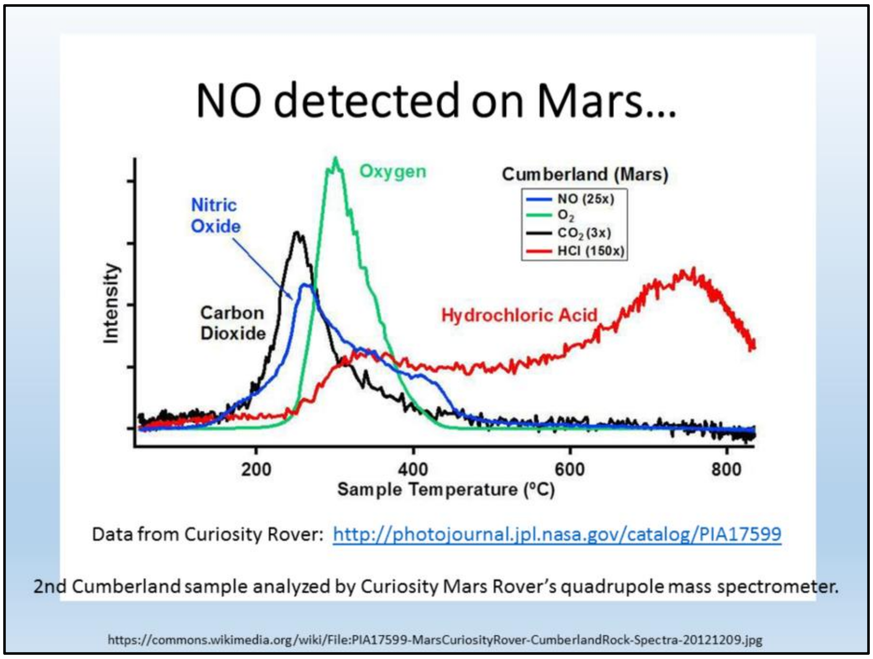
Researchers have discovered that smoke and smog move in different ways through the atmosphere. A series of unusual events several years ago created a blanket of pollution over the Indian Ocean.

In the second half of 1997, smoke from Indonesian fires remained stagnant over Southeast Asia while smog, which is tropospheric, low-level ozone, spread more rapidly across the Indian Ocean toward India.

Researchers tracked the pollution using data from NASA's Earth Probe Total Ozone Mapping Spectrometer (TOMS) satellite instrument. "TOMS is the only satellite instrument that follows both smoke and smog, globally," said Anne Thompson, NASA

Earth Scientist at Goddard Space Flight Center, Greenbelt, MD. "The extreme pollution generated during the Indonesian fires was the first time we saw smoke move more slowly and in different directions from where smog moved."

http://visibleearth.nasa.gov/view_rec.php?id=1651



NO has been detected on other planets!. Presumably the perchlorates at >200 °C oxidize nitrogen compounds in the rock to form NO. The mass-spec data can easily discriminate between the various gases. Note that no that much NO is made relative to the O2 detected. Maybe 1/30th? Would have to integrate area under the curve then worry about the 25x magnification for NO).

English: PIA17599: Volatiles Released by Heating Sample Powder from Martian Rock 'Cumberland' http://photojournal.jpl.nasa.gov/catalog/PIA17599
This image graphs four gases released ("evolved") when powdered rock from the target rock "Cumberland" was heated inside the Sample Analysis at Mars (SAM) instrument suite on NASA's Curiosity Mars rover. The data come from the second Cumberland sample analyzed by SAM. The released gases were detected by SAM's quadrupole mass spectrometer.
The graphic shows four gases (oxygen, hydrochloric acid, carbon dioxide, and nitric oxide) evolved.
The mass spectrometer signal for each gas is scaled separately so that the same graph can illustrate the temperatures that caused the gas to be released (for example, nitric oxide, NO, has been scaled up 25 times). These evolved gases and the temperatures at which they evolved suggest the presence of oxychlorine compounds,

such as perchlorates, and of carbon- and nitrogen-bearing components in the rock-powder sample.
20 December 2013, 16:35:21
The Cumberland target rock is in the "Yellowknife Bay" area of Mars' Gale Crater.
NASA's Jet Propulsion Laboratory, Pasadena, Calif., manages the Mars Science Laboratory Project and the mission's Curiosity rover for NASA's Science Mission Directorate in Washington. The rover was designed and assembled at JPL, a division of the California Institute of Technology in Pasadena.
More information about Curiosity is online at http://www.nasa.gov/msl and http://mars.jpl.nasa.gov/msl/

Tory and Syn a few years ago. Note the giant paws on the polydactile kitty.

1998 Nobel Prize in Physiology or Medicine:

For “the nitric oxide as a signaling molecule in the cardiovascular system”

Robert F Furchgott

Louis J Ignarro

Ferid Murad

http://www.nobelprize.org/nobel_prizes/medicine/laureates/1998/illpres/

NO is recognized as an important component of our physiology.
http://www.nobelprize.org/nobel_prizes/medicine/laureates/1998/illpres/

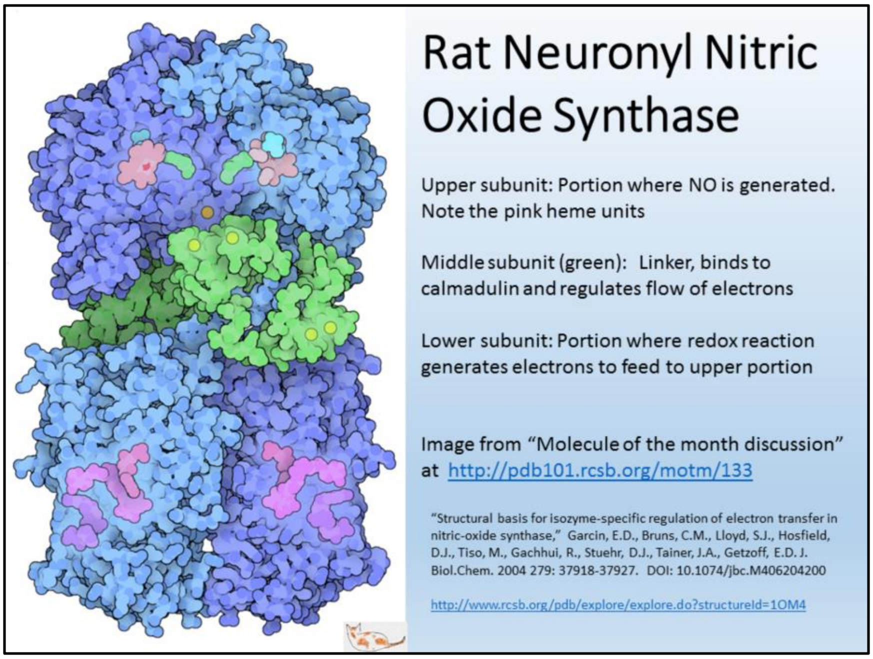
Other Recognition for NO's Biochemical Roles

Science 1992: Molecule of the Year

RCSB Molecule of the Month, January 2011

Vasodilator
Neurotransmitter
Immune response

[The roles NO plays in the human body….](http://pdb101.rcsb.org/motm/133)
http://pdb101.rcsb.org/motm/133

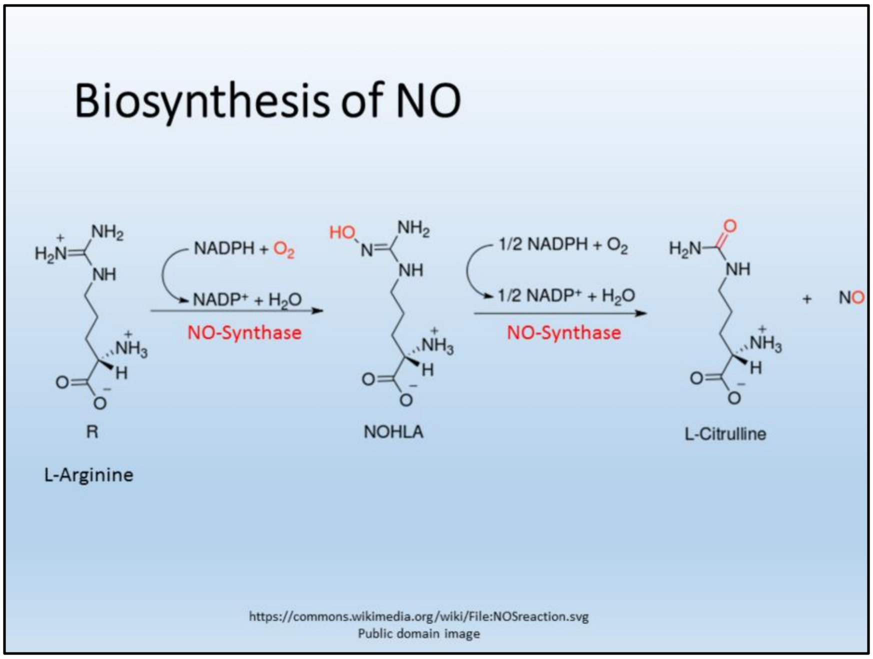


So here is a picture of a dimer of three enzymes which fit together to make larger machine, which produces electrons, manages their flow, and effects the transformation of l-arginine into citrulline and NO. This enzyme is found in rat neurons, and is presumably similar to the human variant.

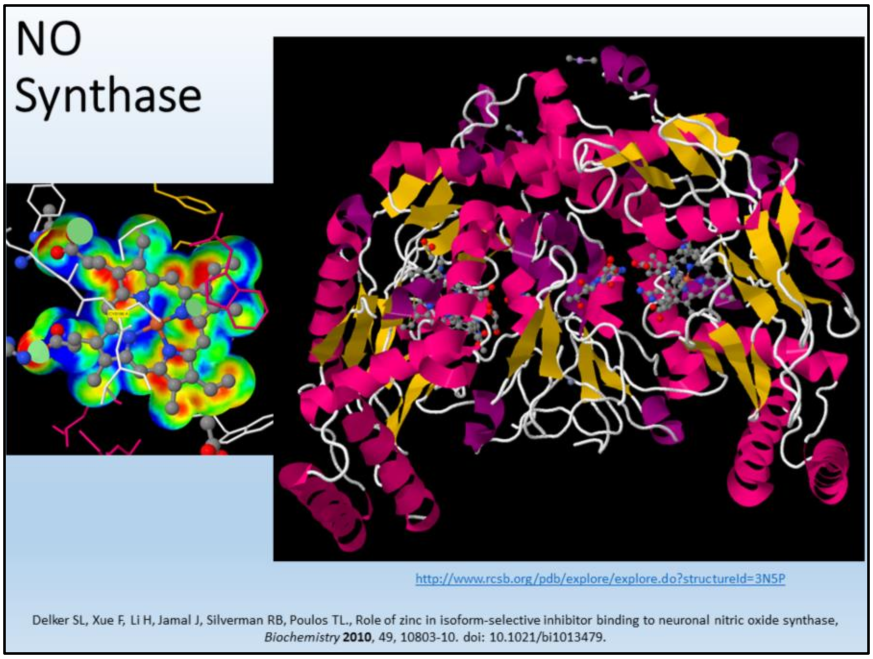
http://pdb101.rcsb.org/motm/133

NOS

Animal cells make three similar types of nitric oxide synthase (NOS), to produce NO for these different functions. Neuronal NOS (shown here) and endothelial NOS continually produce low levels of NO used for signaling. Inducible NOS, on the other hand, makes large toxic bursts of NO to fight pathogens. All are complex enzymes with many functional parts, and researchers have determined their structures by breaking them into manageable pieces. The portion shown at the top creates NO by adding oxygen to the amino acid arginine, using a heme group to assist with the reaction. It was the first portion to be studied by crystallography, first for inducible NOS (PDB entry 1nod) then for the neuronal version shown here (PDB entry 1om4). The portion at the bottom (PDB entry 1tll) feeds electrons to the upper portion. The short segment connecting the two halves binds to calmodulin (shown here in green, PDB entry 2o60), which helps to control the flow of electrons.

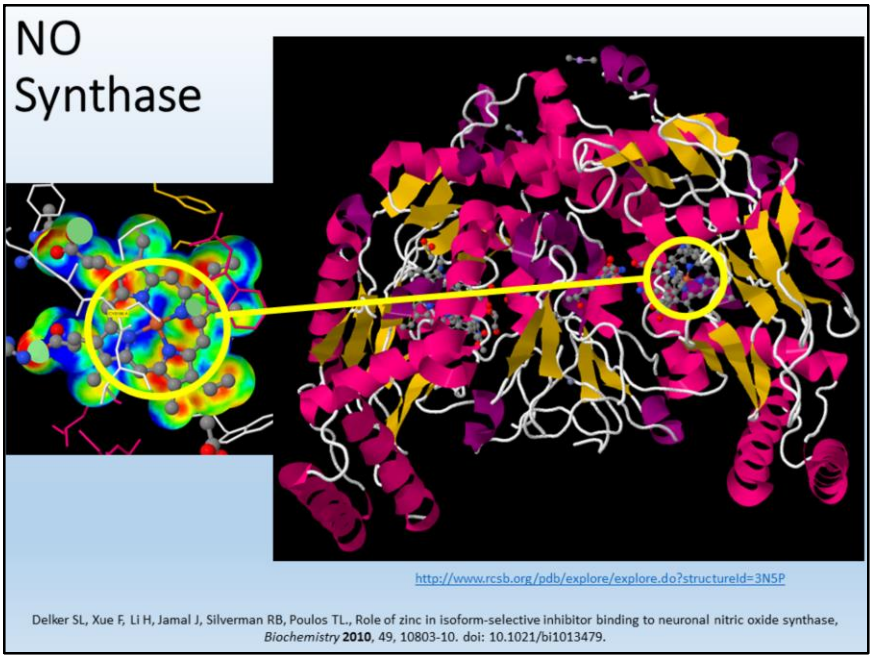


The molecule L-arginine is transformed stepwise into citrulline and NO by the heme-based NOS enzyme. The oxygen comes from O2. These transformations are very difficult for synthetic chemists to accomplish, even after years of study of the enzyme. The citrulline can be converted back into l-arginine. I was surprised to see many l-arginine supplements sold “to improve NO levels in the body as we age.” Sadly, these supplements are probably useless, since NOS makes NO, and having more starting materials around is not going to make more NO. Think of Lucy and Ethyl (hah!) packing chocolates at the chocolate factory.

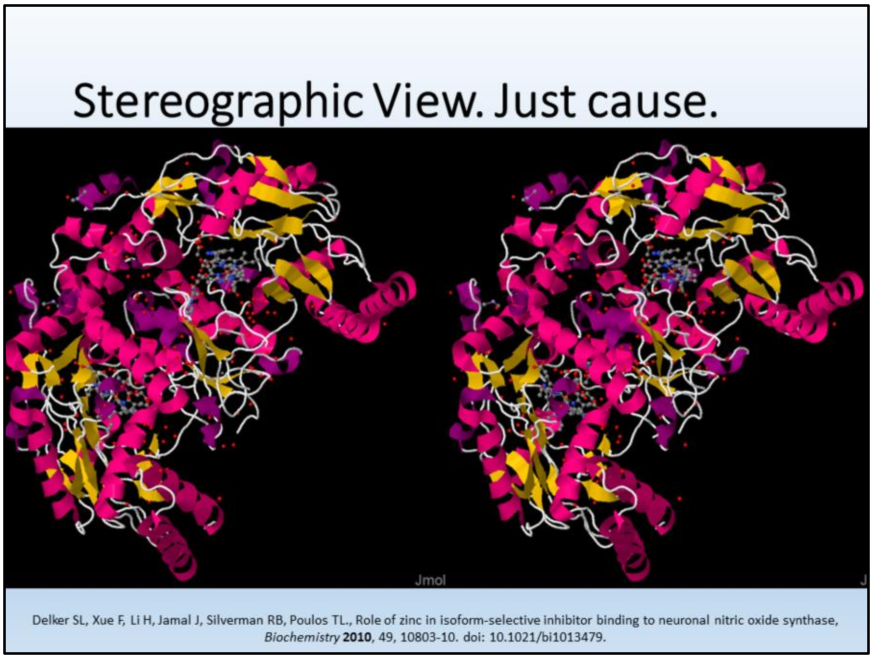


This is the top part of the enzyme showed a couple of sides ago. This particular subunit has had an inhibitor attached to it so it will not produce NO. Such inhibitors, and how they occupy the active sites, can yield information which can be used for drug design. For example, if NO is a neurotransmitter for pain signals, a neuronal-NO-inhibitor may reduce pain. The enzyme has two identical subunits, and the heme unit, and a pterin unit (electron source) are visible. On h left is a close up of the heme group from the side that has an S-atom from cysteine attached.

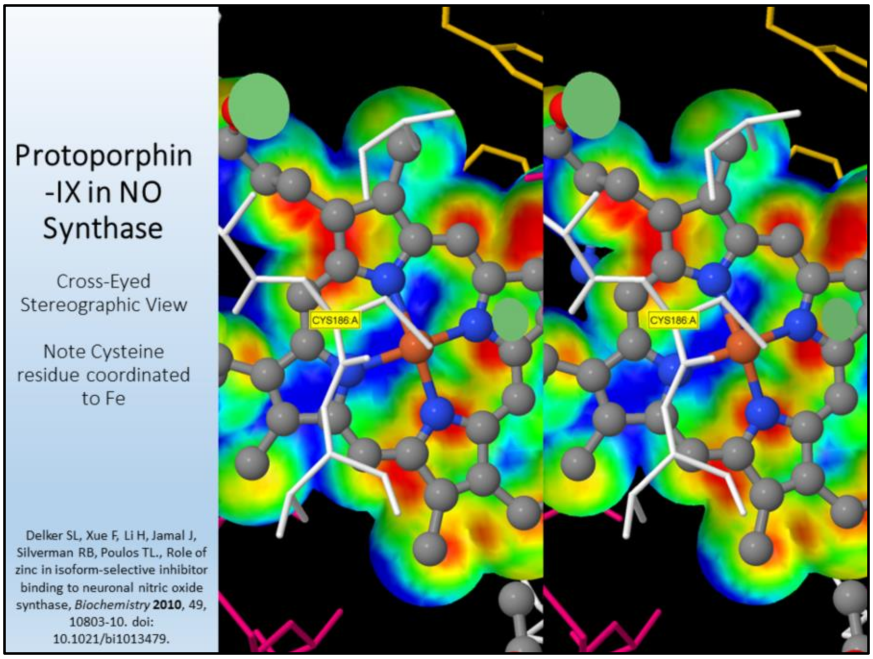
http://www.rcsb.org/pdb/explore/explore.do?structureId=3N5P



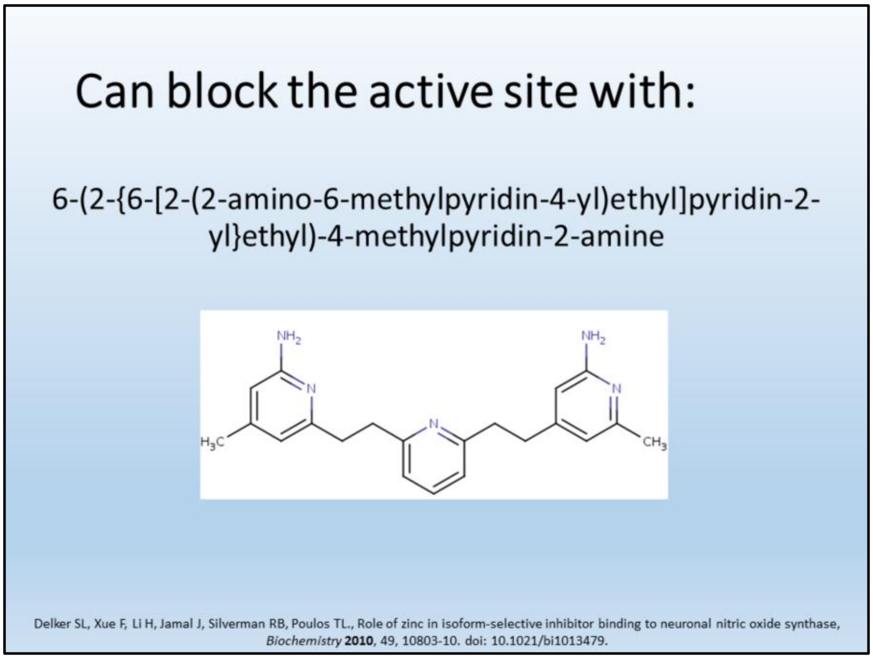
http://www.rcsb.org/pdb/explore/explore.do?structureId=3N5P
This slide shows where the heme group sits in the enzyme.



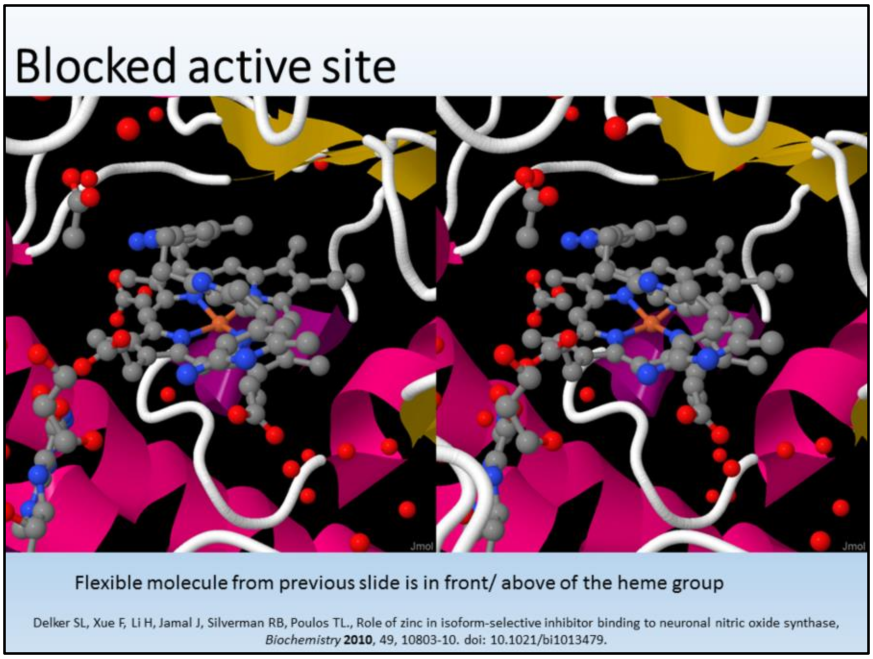
Same enzyme, but a stereograph view. Little red dots are water molecules. The alpha helices (pink) and beta sheets (yellow) are repeating domains of amino acids that help are part of the secondary structure of the enzyme. Primary structure is th einear sequence of amino acids. Tertiary structure is the 3-D arrangement. Quaternary structure is how these 3D arrangements nestle against each other.



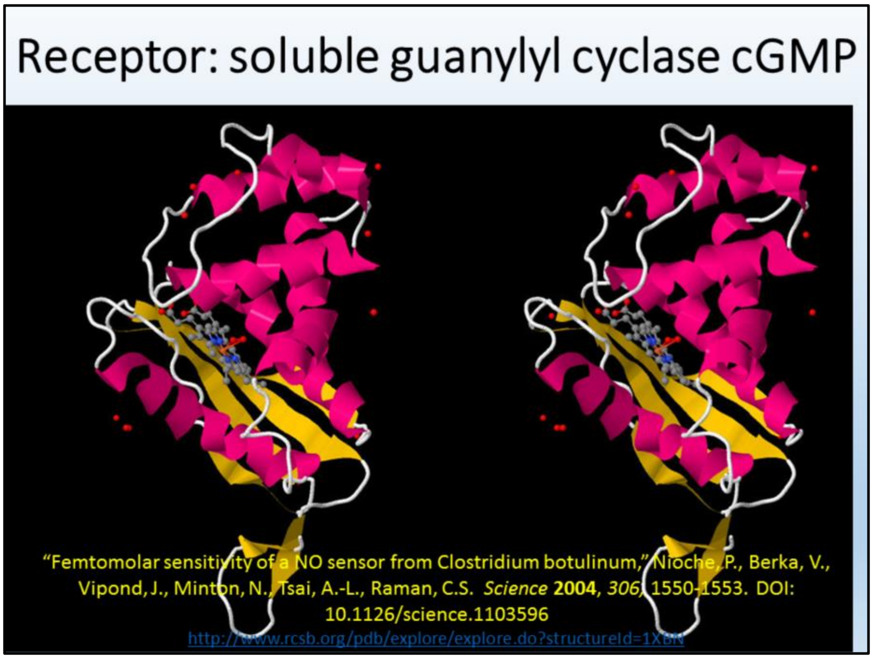
The other side is blocked. This is the cross-eyed stereo view of the heme group shown from a couple of slides ago. The cysteine reside can be seen close to the iron atom.



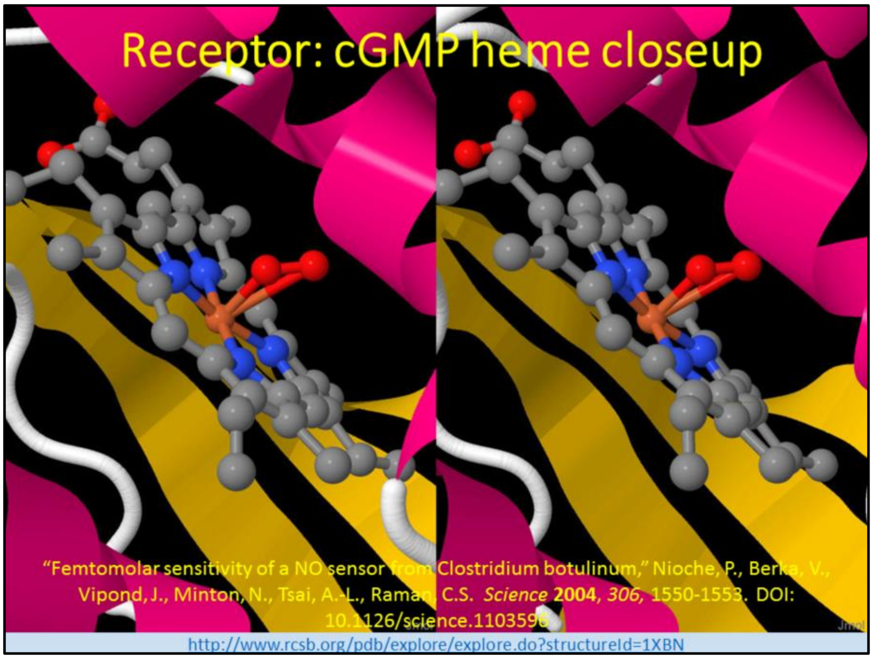
This molecule mimics the l-arginine well enough ot get into the active site. But it is like a bill in a china shop, and can't really get out again. It also is not able to be transformed into NO, so I shuts down the machinery.



The other side has the cysteine residue on it. The inhibitor is shown occupying the active site, in front of and above the heme group.
How does NO get around? Hemoglobin can transport it in 2 ways. It can bind to the Fe, as we have seen and will see here. It can also bind to a sulfur atom on the outside of the hemoglobin molecule (i.e. a cysteine residue) and hitch a ride without getting into the active site.



The previous slides show the enzyme responsible for making NO, and also show that we can inhibit that enzyme. NO would not work as a signaling molecule if there were not a "receiver." In us, the cGMP is the NO receptor for a lot of things. This one is from a bacterium, but humans have a version, too. The NO binds to the Fe and activates it to perform the next step in the signaling pathway. In this structure an O2 molecule occupies the active site.
http://www.rcsb.org/pdb/explore/explore.do?structureId=1XBN



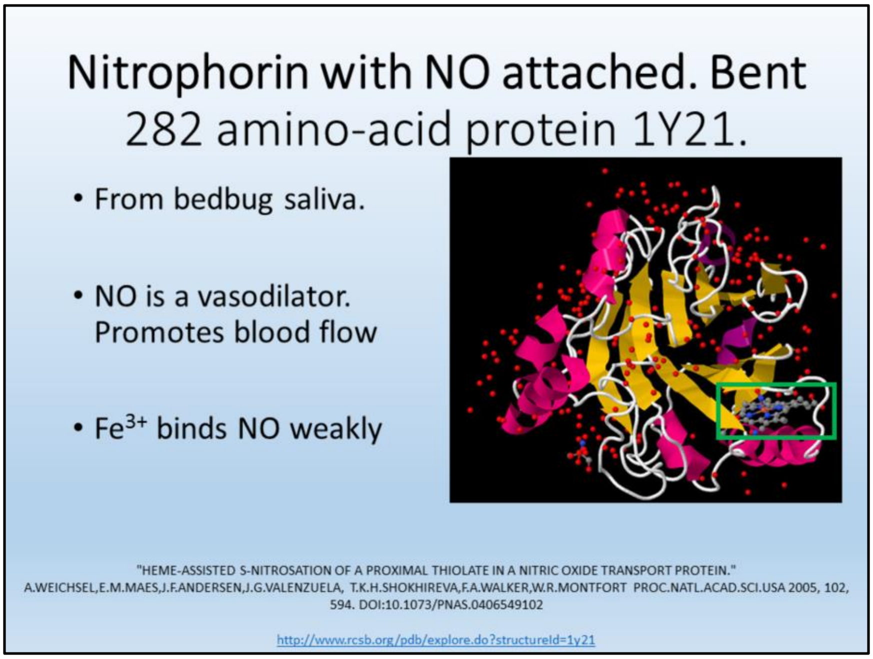
This one is from a bacterium, but humans have this too. The NO binds to the Fe and activates it to perform the next step in the signaling pathway. In this structure an O2 molecule occupies the active site.
http://www.rcsb.org/pdb/explore/explore.do?structureId=1XBN

The Kissing bug…

- A variety of "nitrophorins" are known in the saliva of biting pests.
- "Saliva of the blood-sucking bug *Rhodnius prolixus* contains at least seven homologous nitrophorins, designated NP1 to NP7 in order of their relative abundance in the glands."*
- Unrelated species (bedbugs) have apparently independently evolved functionally similar proteins.
- Chagas disease (protozoan), gets in bites from kissing bugs' poop.

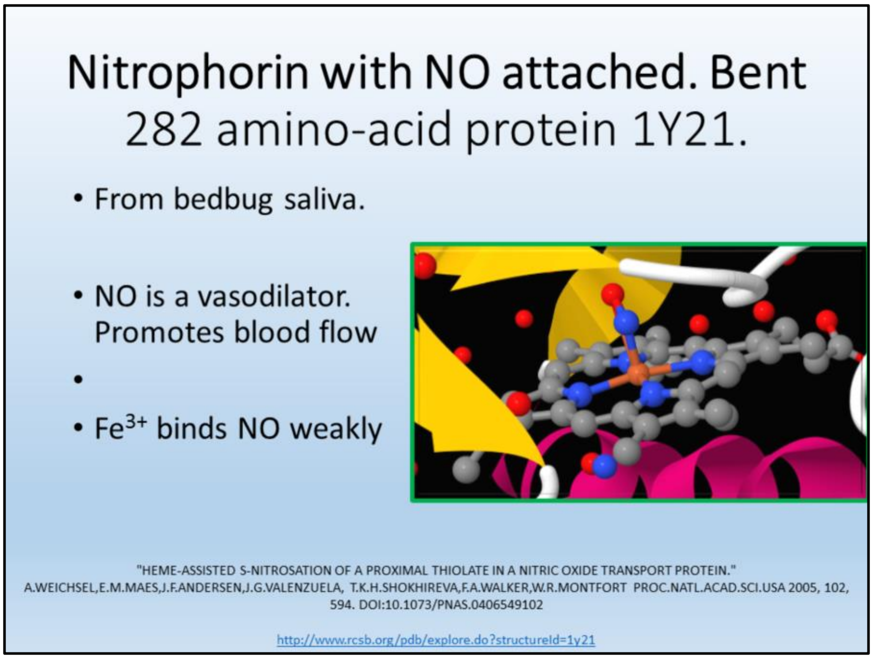
- A Wikipedia ref! https://en.wikipedia.org/wiki/Nitrophorin
- Public domain image from https://commons.wikimedia.org/wiki/File:Rhodnius_prolixus.jpg

We use NO, but it can be used against us.



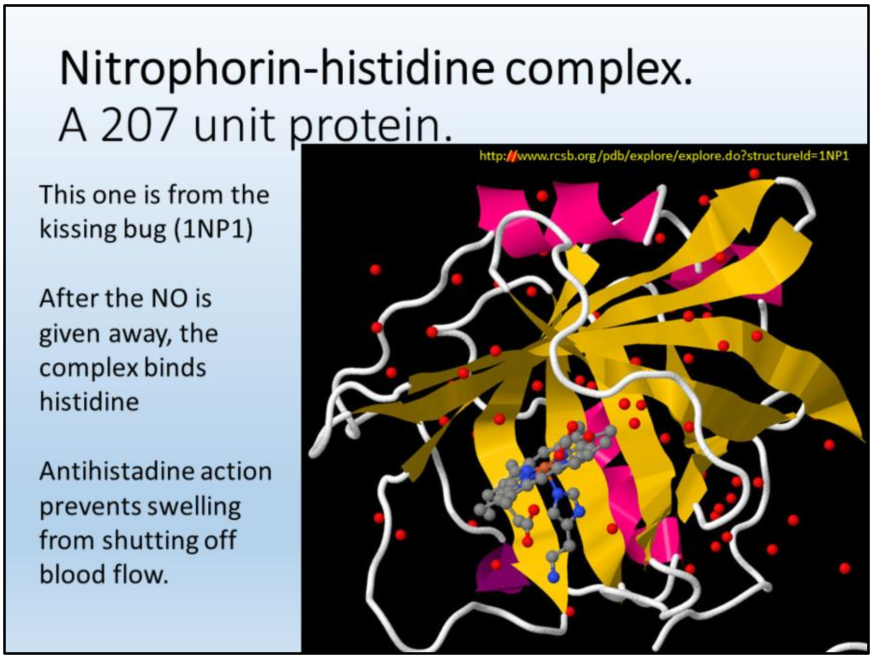
Bedbugs do this too! It makes sense that the blood flow increases with NO vasodilation, and it kept going by suppressing the immune response signaled by histamine. Note that the saliva of these bugs may contain over 40 different enzymes which can serve as anesthetic, anti-coagulant, etc. The green box is the heme unit, magnified next slide.

"HEME-ASSISTED S-NITROSATION OF A PROXIMAL THIOLATE IN A NITRIC OXIDE TRANSPORT PROTEIN." A.WEICHSEL,E.M.MAES,J.F.ANDERSEN,J.G.VALENZUELA, T.K.H.SHOKHIREVA,F.A.WALKER,W.R.MONTFORT PROC.NATL.ACAD.SCI.USA 2005, 102, 594. DOI:10.1073/PNAS.0406549102
http://www.rcsb.org/pdb/explore.do?structureId=1y21

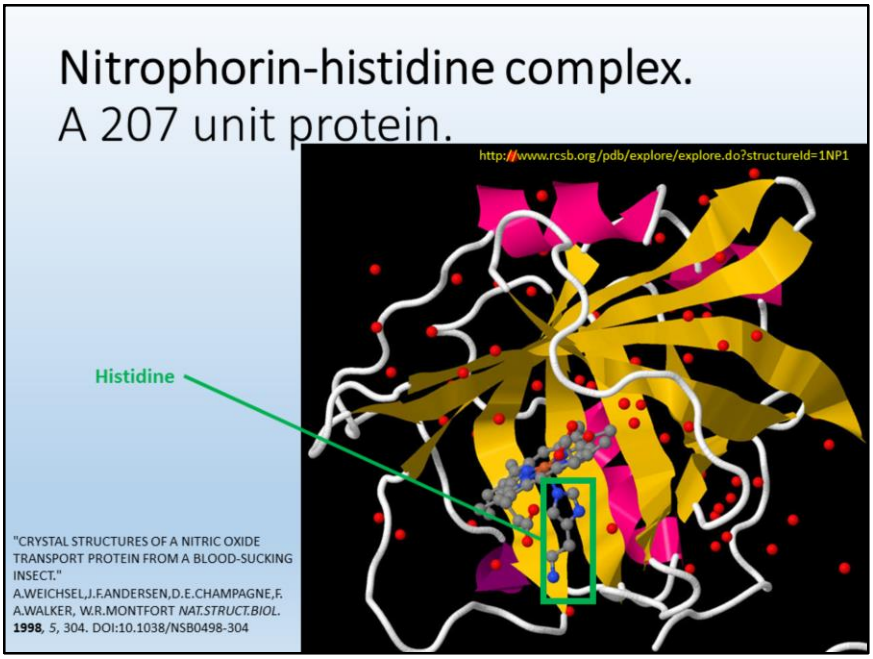


And here is the heme unit. 5-coordinate with a bent Fe-NO unit, as expected. Note that a protein can influence the magnitude of the bending. My collaborator (GRA) has shown that for myoglobin, the Fe-NO angle can be reproducibly influenced by how the NO got there, i.e. from NO diffusion vs reduction of NO2- "on-site."

"HEME-ASSISTED S-NITROSATION OF A PROXIMAL THIOLATE IN A NITRIC OXIDE TRANSPORT PROTEIN." A.WEICHSEL,E.M.MAES,J.F.ANDERSEN,J.G.VALENZUELA, T.K.H.SHOKHIREVA,F.A.WALKER,W.R.MONTFORT PROC.NATL.ACAD.SCI.USA 2005, 102, 594. DOI:10.1073/PNAS.0406549102
http://www.rcsb.org/pdb/explore.do?structureId=1y21

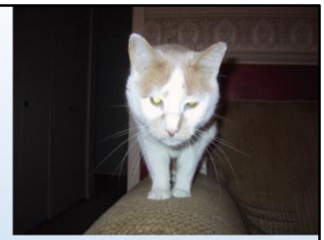


After NO is released, the nitrophorin soaks up histidine.
http://www.rcsb.org/pdb/explore/explore.do?structureId=1NP1
"CRYSTAL STRUCTURES OF A NITRIC OXIDE TRANSPORT PROTEIN FROM A BLOOD-SUCKING INSECT." A.WEICHSEL,J.F.ANDERSEN,D.E.CHAMPAGNE,F.A.WALKER, W.R.MONTFORT NAT.STRUCT.BIOL. 1998, 5, 304. DOI:10.1038/NSB0498-304



Green box shows the histidine molecule.
http://www.rcsb.org/pdb/explore/explore.do?structureId=1NP1
"CRYSTAL STRUCTURES OF A NITRIC OXIDE TRANSPORT PROTEIN FROM A BLOOD-SUCKING INSECT." A.WEICHSEL,J.F.ANDERSEN,D.E.CHAMPAGNE,F.A.WALKER, W.R.MONTFORT NAT.STRUCT.BIOL. 1998, 5, 304. DOI:10.1038/NSB0498-304

The Story So far…



Burt wants to know what's going on.

- Biological Systems Can:
  - Can make NO
  - Can sense NO
  - Bugs take advantage of how we use NO

  - NO is toxic… Any way to get rid of it?

A brief interlude to catch one's breath with a cat pic.

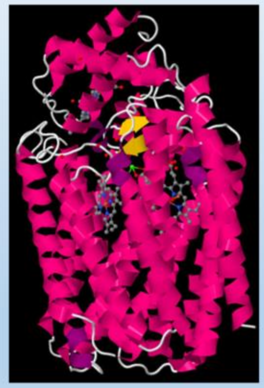
Nitric oxide reductase from Roseobacter denitrificans (RdNOR)

Transmembrane protein… straddles cell membranes

Lots of alpha helices arranged "parallel", helps to orient and anchor in membrane

3 porphyrin units

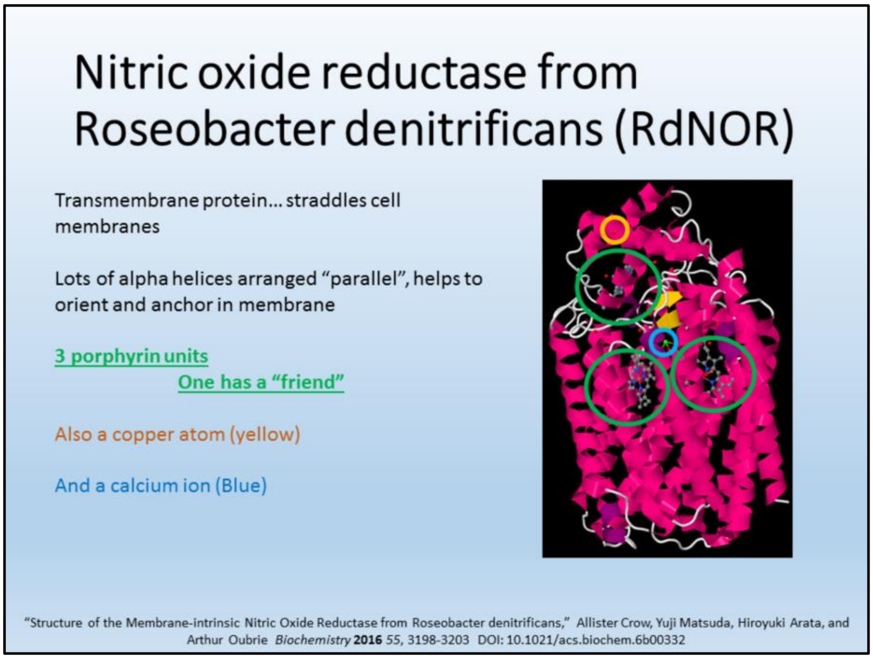
Gets rid of NO… back to water and N_2O



"Structure of the Membrane-intrinsic Nitric Oxide Reductase from Roseobacter denitrificans," Allister Crow, Yuji Matsuda, Hiroyuki Arata, and Arthur Oubrie *Biochemistry* **2016** *55*, 3198-3203 DOI: 10.1021/acs.biochem.6b00332

The signaling function of NO requires that it be made and then detected. But white blood cells secrete NO as a defense against bacteria. NO is toxic to bacteria… but many have found ways to tolerate NO. This recent example is an enzyme that sites straddling a cell membrane. It has a lot of functionality, and is the third example structurally characterized of an NO reductase. There are some interesting features.

http://www.rcsb.org/pdb/explore/explore.do?structureId=4XYD



This enzyme is metal-rich. The Ca atom may be structural, or it may serve some "gating" function. It is not clear what the Cu atom does. The active site appears to have a heme group which is attached by an O-atom to a non-heme iron group. The other Fe is complexes by atoms from the protein, but the bonds are not explicitly shown.

http://www.rcsb.org/pdb/explore/explore.do?structureId=4XYD

A close-up cross-eyed stereogram of the active site. Heme connected to a non-heme Fe by an O-atom. Non heme iron atoms are important too! Not all bonds to the 2nd Fe atom are shown, but it has a normal set of ligands.

What was with that first slide?

- Meat: nice red color due to Myoglobin-NO complex… would otherwise be grayish. Yum!
- Nitrites in curing meat give rise to same substance, nice red colors!
- ED Drugs?
  - NO regulates blood pressure by vasodilation
  - NO-reuptake inhibitor can make the NO last longer in specific body parts. Means more blood in the tissues that use hydraulic pressure to function.
  - Early ED drugs had to be injected.
  - https://en.wikipedia.org/wiki/Giles_Brindley

Bawdy parts. So we've talked about a number of heme-NO proteins, but the most common in the world is likely the red color of myoglobin-NO that packaged meat has. Maybe from a small addition of nitrite (as in cured meats) from "curing salt", maybe from additives to the plastic wrap.
Also ED drugs work by increasing the lifetime of NO by suppressing the mechanism by which NO is deliberately destroyed. Note that NO lasts a few seconds at most in oxygenated aqueous environments, so the receptors are very sensitive. The inhibitory effect does not have to be extremely strong to show a noticeable change in the balance.

Acknowledgements

- Students (as always) since 1998.

- George Richter-Addo, University of Oklahoma

- SIUE Department of Chemistry,
- College of Arts and Sciences,
- Graduate School

- NSF Award NSF - CHE 1213680

A Redbud tree, native to Illinois

As always, my friend George, and the NSF for continued support.

Images

Unacknowledged pics were taken or drawn by me.

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- "JMOL: an open-source Java viewer for chemical structures in 3D"
  - http://jmol.sourceforge.net/
- Data repositories:
  - Crystallography Open Database
  - Research Collaboratory for Structural Bioinformatics

Here is where some of the resources used to make this talk were obtained.