Porphyrins: The Colors of Life

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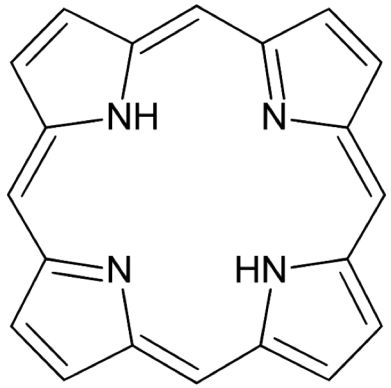
Porphyrins and Their Origins

- **What is a porphyrin?**
  - A family of vibrantly colored compounds
  - Planar structure containing alternating single and double bonds
  - Parent structure: four small rings composed of four carbons and one nitrogen, joined together by carbon linking bridges

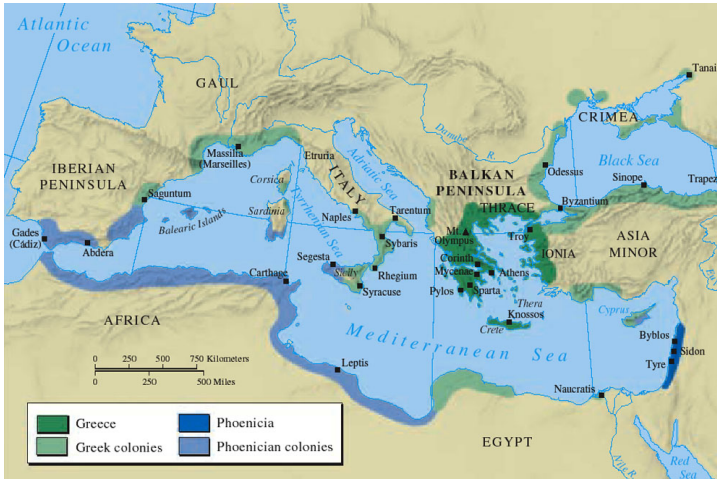


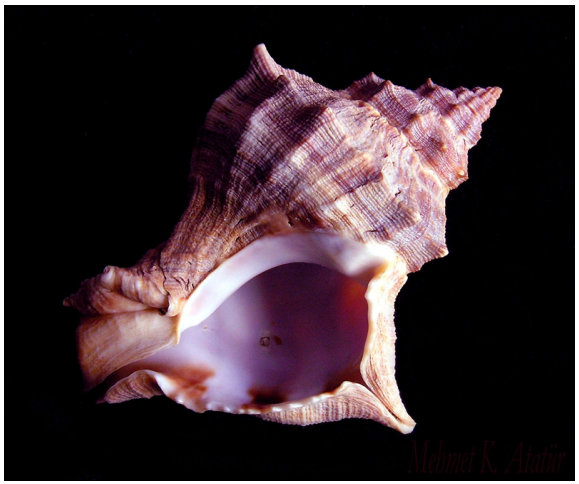
- **Nomenclature:** comes from the Greek word *porphyra* = "purple"
  - Indicates the defining characteristic of the purple nature of free base porphyrins

***Put in images of free base purple porphyrins in the lab

Porphyrins and Their Origins

- **Historical Context:**
  - Phoenicians collected mollusks containing a purple pigment known as **Tyrian Purple**
  - Pigment used to dye robes of emperors in a highly secretive process
  - Developed an association between royalty and the color purple





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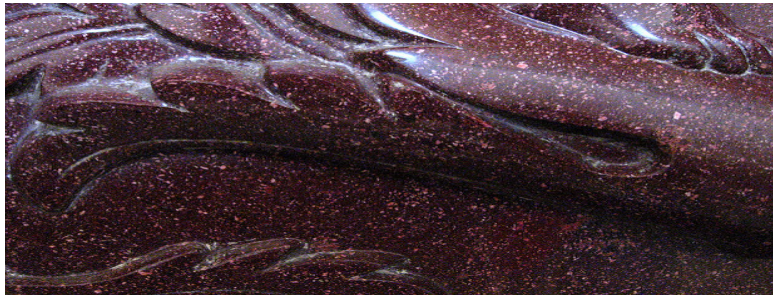
http://timetravelersguidetophoeniciadia.weebly.com/uploads/2/9/2/0/29201661/2240245_orig.jpg

Porphyrins and Their Origins

- **Historical Context:**
  - Ancient Greeks intensified the royal connection
  - Each palace contained a special room constructed entirely from a deep purple, expensive Egyptian stone known as **porphyry**
  - Sole use of the room: the birth of the heir to the throne
    - Signified the importance of the newborn



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https://farm4.staticflickr.com/3273/3047947149_fd23afd9e2_z.jpg

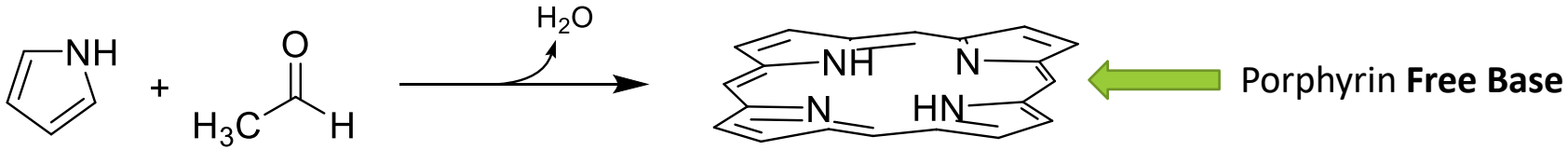
Modern Day Context

- Hans Fischer
  - The Father of modern porphyrin chemistry
  - 1929: Synthesized **heme**, the major component of blood, which binds and transports oxygen

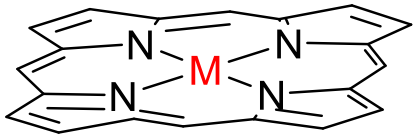
http://www.nndb.com/people/376/000100076/
http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1930/fischer-bio.html

Structure

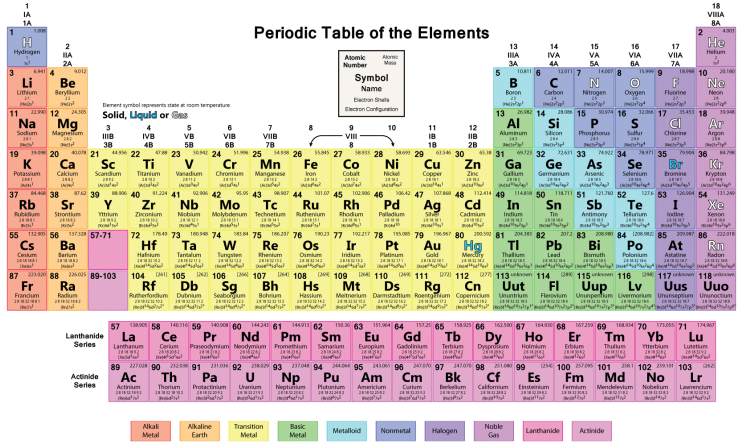
- Flat, planar structure formed through a condensation reaction
  - Condensation reaction: joining two molecules through the loss of water



- Reaction with transition metals forms a **metal complex**



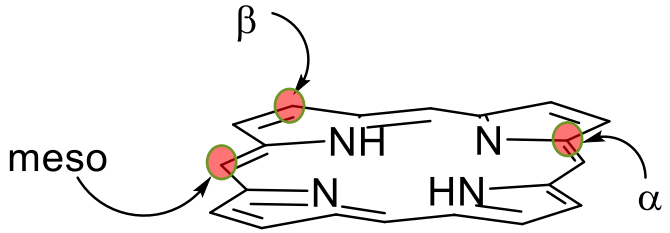
M = Transition Metal



http://sciencenotes.org/wp-content/uploads/2015/07/PeriodicTableWorks.png

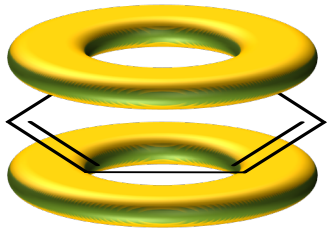
Chemical Characteristics

- Free-base porphyrin = deep purple solid; red in solution
- Addition of ligands to red reaction sites, protonation (addition of H) to single nitrogen, loss of double bonds, or complex of metal center will cause shift in color spectrum
- UV active
- Acid labile: reactive in acidic conditions
- Aromatic compounds
- Flexible: can distort and lose planarity to accommodate large metal centers

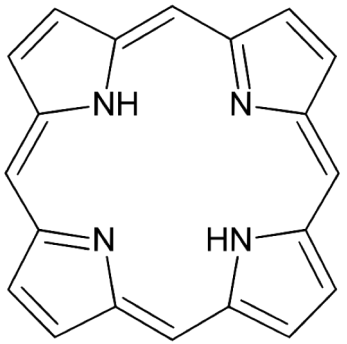


All About Aromaticity

- **What does it mean to be aromatic?**
  - A flat, ring-shaped, highly stable (unreactive) molecule containing alternating sigma and pi bonds
    - Alternating pattern is known as **conjugation**
  - Alternating bonds cause electrons in pi bonds to become delocalized → form a circulating cloud above and below the ring
  - More conjugation = higher stability

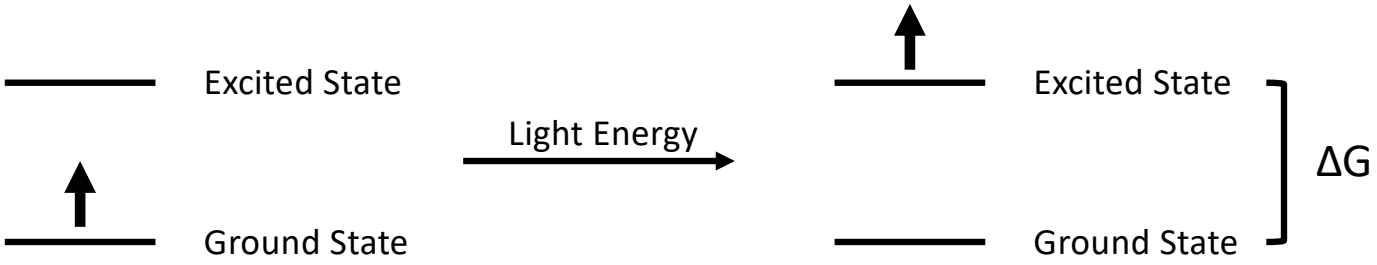


- **Huckel's Rule**: All aromatic compounds have 4n+2 pi electrons in their electron cloud
  - Free base porphyrin has 22; **Let's count them!**
    - 11 pi bonds, each containing 2 pi electrons: 2 x 11 = 22
    - 4n + 2 = 22 → n = 5



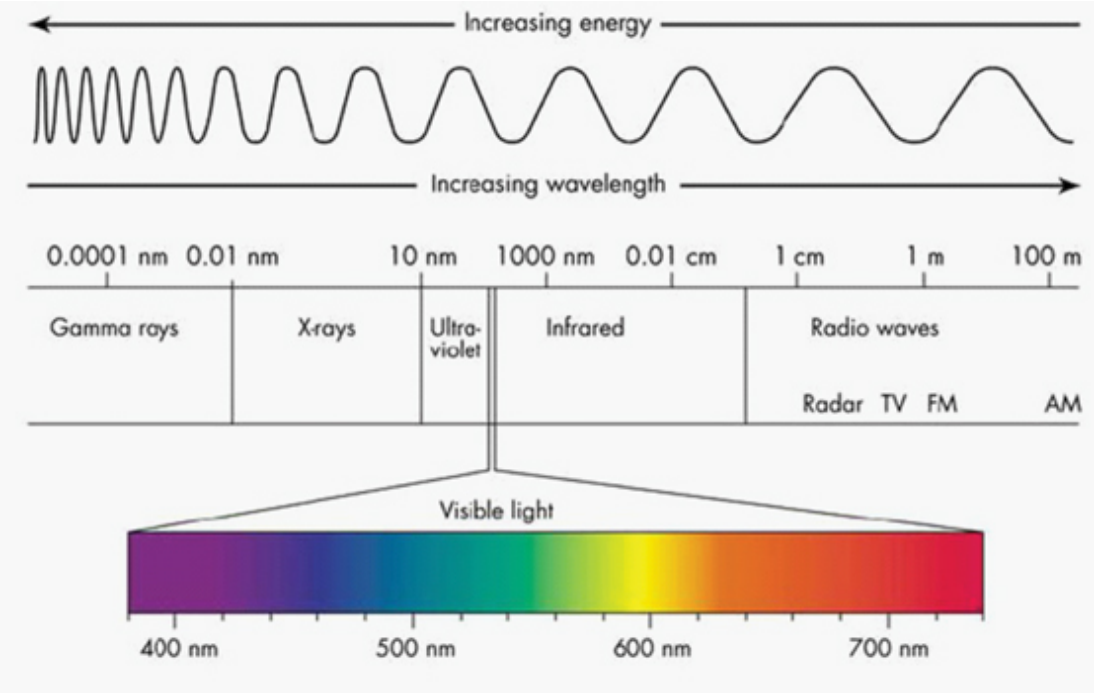
UV-Vis Spectroscopy

- UV-Visible Spectroscopy: an analytical technique used to characterize molecules
  - Compounds will absorb light at a specific frequency and reflect light at another, resulting in the colors we view
  - Involves shining light through a sample of a compound containing pi electrons
  - Electrons absorb energy and are excited to a higher energy level
  - Difference in energy level, **ΔG**, is inversely proportional to the wavelength of light it absorbs and thus, the color it reflects



http://www.designshard.com/wp-content/uploads/2012/10/color-wheel.png

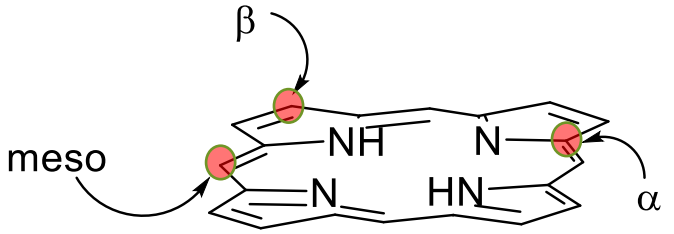
Visible Light Spectrum



https://archive-resources.coleparmer.com/TechInfo/Images/chart555.jpg

Let's Talk About Color

- Various structural changes shift the solid state color of porphyrins from deep purple to all shades of the rainbow
  - Addition of substituents to different reactive sites on the porphyrin
  - Addition of different metal centers
  - Increase or decrease in conjugation, or alteration in conjugation pattern
- Addition of Substituents:
  - Free base = wine red in solution
  - B substituted = magenta in solution
  - Meso substituted = emerald green in solution

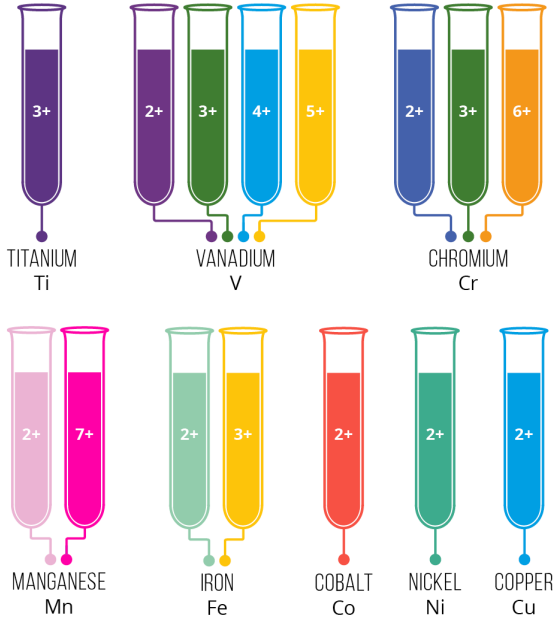


  - **Why?** Substitution at different positions leads to distortions and shape changes, creating tension which alters the energy gap between the ground and excited states
  - **Think of a spring! Tightly coiled = more likely to spring back = has more energy**

Metal Centers

- Who likes prosciutto?
  - Parma ham exhibits a red color due to a zinc center

- Blue blood vs. Red Blood
  - Ever wondered why our blood is red?
    - The iron center in the porphyrin complex called heme
  - What about lobsters?
    - Lobsters have blue blood because they have a copper atom as the center of their heme complex instead



Wakamatsu, J.; Nishimura, T. Meat Science. ***2004****, 67, 95-100.*
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http://storage.aicod.it/portale/academiabarilla/view/1200/prosciuttodiparmaDOP-34.JPG

Bird Feathers

- Found in the pigments of bird feathers such as the Turaco and Blood Pheasant
- Turacoverdin = Copper centered porphyrin
  - Blue of the copper mixes with another family of yellow compounds called carotenoids to make vivid green feathers
- Turacin
  - Also copper centered complex, but this time bright red

http://3.bp.blogspot.com/-o0QO5GtX2sU/UOhfXH6wCxI/AAAAAAAABI8/R5tntR3X0ZQ/s1600/Green_Turaco.jpg
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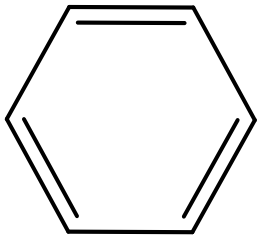
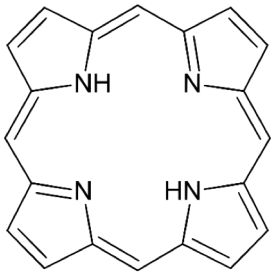
Color and Conjugation

- Increased conjugation leads to increased (longer) wavelengths of light absorption and reflection
  - Remember how aromatic compounds are more stable?
  - More stable = less energy between ground and excited state
  - Less energy = longer wavelength
- Increasing conjugation increases stability, and aromaticity increases stability even more



Colorless (Absorbs in the UV range)

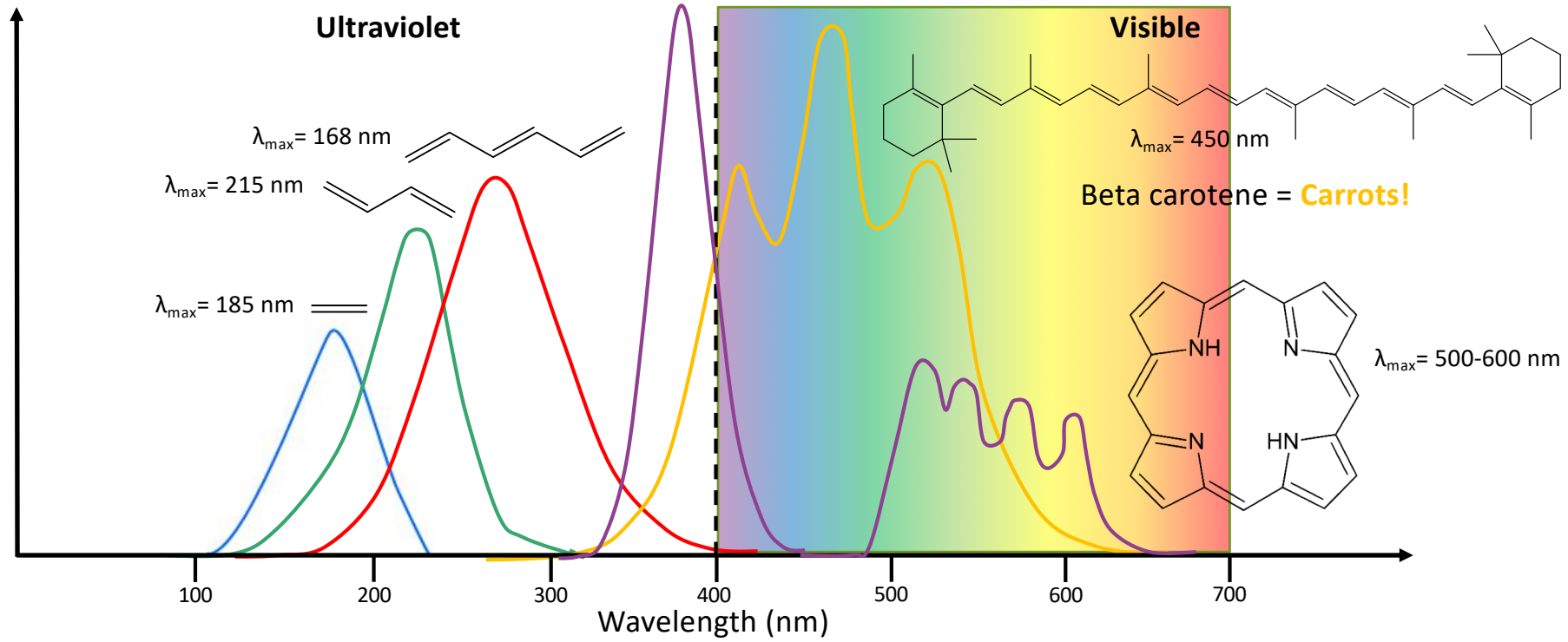
Benzene, a simple aromatic compound



Colored (Absorbs in the Visible range)

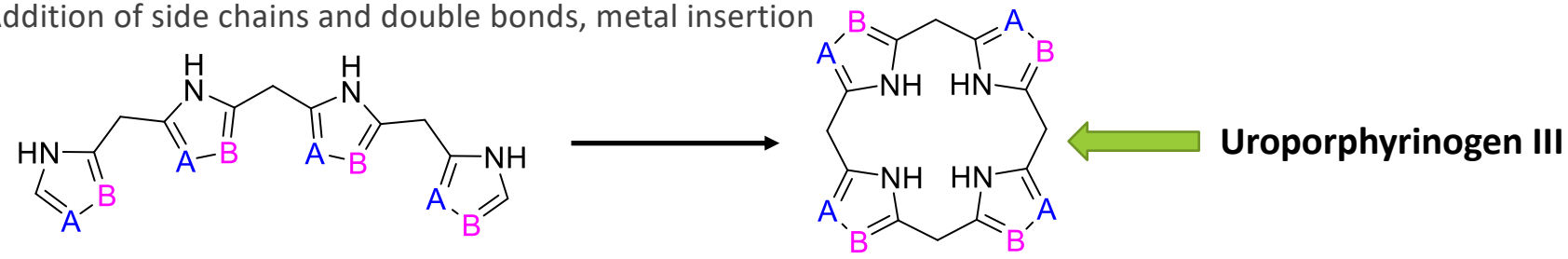
Porphyrins, with much more conjugation

Comparison Study



Biosynthesis

- Synthesized in a series of **enzyme catalyzed** steps
- Occurs in the **mitochondria** and **cytosol** of the cell
- Join together four rings in a head to tail fashion to form a linear molecule
  - **Uroporphyrinogen III** = the parent molecule for all biosynthesized porphyrins
  - Why III? There are four different ways to arrange atoms A and B. These are called **isomers**
    - The third arrangement is the most **thermodynamically favorable**
    - During the cyclization step, enzymes instinctively flip the last ring subunit…notice the pattern of A and B changes!
- Following steps diverge to form specific biological molecule
  - Addition of side chains and double bonds, metal insertion



Vampires vs. Werewolves

Where did the myths come from?

- Porphyrias = a class of diseases occurring due to malfunctions during biosynthesis
- Symptoms:
  - Extreme sensitivity to light, implications in psychiatric disorders, other genetic abnormalities
- This led to the creation of myths about vampires and werewolves
  - Light sensitive skin = won't go outside during the day, but will at night when it's dark
  - Psychiatric disorders = can lead to sleep abnormalities, such as being nocturnal
  - Porphyrins are red = when deposited in the teeth, would stain teeth red
  - Causes gums to tighten and shrink = teeth appear elongated
  - Minimized levels of correctly synthesized heme (major component of blood) = would drink blood to increase heme levels
  - Garlic breaks down red blood cells = Inflicted would avoid eating garlic

Heme

- Iron-centered porphyrin complex
- Plays a variety of roles during cellular respiration
- Different substituents attached to central porphyrin ring determine its function
  - Oxygen storage
  - Oxygen transport
  - Electron transport
- Iron cycles between 2+ and 3+ oxidation states
- Cyanide poisoning = When cyanide binds to iron instead of oxygen, causing it to remain stuck in the 3+ state
- Anti-aging = Defends against oxygen radicals

http://1.bp.blogspot.com/-z_aid0ORaZY/Uud-SjiBI7I/AAAAAAAAAJo/kVIc4bFHrKE/s1600/red-blood-cells.jpg

Hemoglobin

- Binds oxygen in the blood and transports it around the cell
- Iron-centered heme complex is deeply buried inside protein chains
  - Hydrophobic = water fearing
  - Proteins form hydrophobic compartment around heme complex ,repelling polar molecules
  - Extremely protected from interactions with any small molecules in exterior environment
- Iron is too big to fit inside porphyrin cavity, until it binds to oxygen
- Iron shrinks to fit within porphyrin ring

Cytochrome C

- Binds oxygen as an electron supplier to power energy synthesis
- Heme unit close to the surface of the protein unit, unlike hemoglobin
- Quick biology lesson!
  - During cellular respiration, a molecule of O_2 splits, transferring electrons
  - Electrons are used in the synthesis of ATP (energy!)
- Iron center in cytochrome C picks up electrons and transfers them to the following enzyme
- Picking up electrons = reduction to Fe^{2+}
- Transferring them = oxidation back to Fe^{3+}

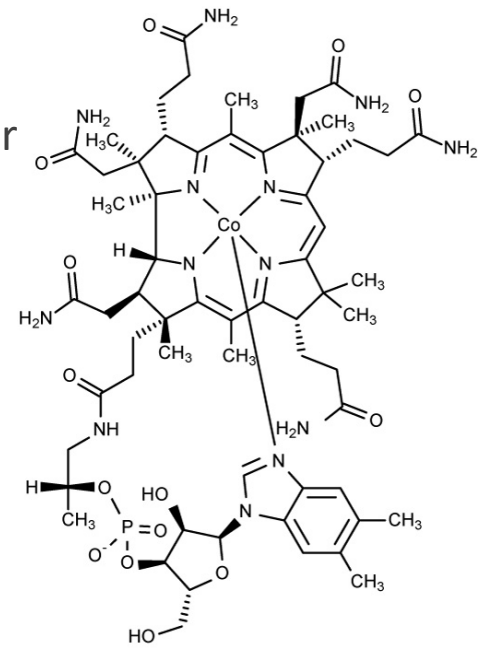
Chlorophyll

- Light absorbing pigment contained in photosynthetic organisms
- Magnesium centered porphyrin analogue
  - Chlorin = contains fewer double bonds than original parent porphyrin
- Contains a magnesium center
  - Metal center binds to water (source of electrons) and oxidizes it and produce oxygen
- Molecule absorbs strongly in the visible light range due to conjugation
  - Photons of light are used as reactants in photosynthesis

http://3.bp.blogspot.com/-1IuLh95NyM/TVlDysc6hI/AAAAAAAAAy8/3QrkvVkJT_0/s1600/Green%2BMaple%2BLeaves%2BRain%2BDrops%2Blong%2Bgoodbye.png

Vitamin B_{12}

- Important in the metabolism of amino acids
- More reduced structure = contains less double bonds within ring
  - Allows for increased flexibility
  - Tends to adopt buckled configurations rather than standard planar formation
  - Lack of double bonds leads to conjugation on only a portion of the ring
- Contains a cobalt atom in its center
- Only known stable biomolecule containing a metal-carbon bond
- Microorganisms are the only producers of Vitamin B_{12}
- Higher organisms obtain vitamin through metabolism



http://www.chm.bris.ac.uk/motm/vitb12/b12.htm
Krautler, B. Biochemical Society Transactions. ***2005,*** *33, 806-810.*
http://f.tqn.com/y/chemistry/1/S/U/R/1/cobalamin.jpg

Dinosaur Porphryins

- Petroporphyrins (geoporphryins) = Extinct class of exotic porphyrins no longer found in living organisms
- Molecular fossils of heme, chlorophyll
  - Formed through their degradation
- Found in coal, petroleum and shale deposits
- Used to determine the relative age of rock and fossils
- First petroporphyrin discovered contained a vanadium center and was known as VODPEP
- Nickel or vanadium centered complexes
- Extreme environment leads to all types of interesting chemistry
- Abelsonite = the only known geoporphyrin with a crystalline structure, containing a nickel center

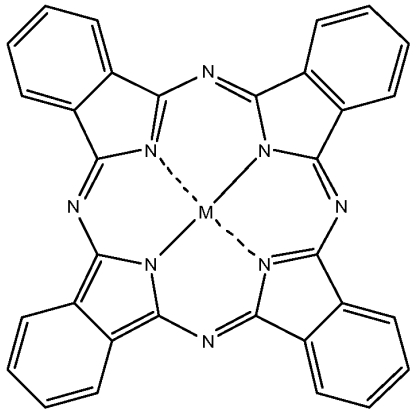
Abelsonite

https://upload.wikimedia.org/wikipedia/commons/6/66/Getchellite.jpg

Huseby, B.; Barth, T.; O'Campo, R. *Org. Geochem.* **1997,** *25*, 273-294.

Phthalocyanines

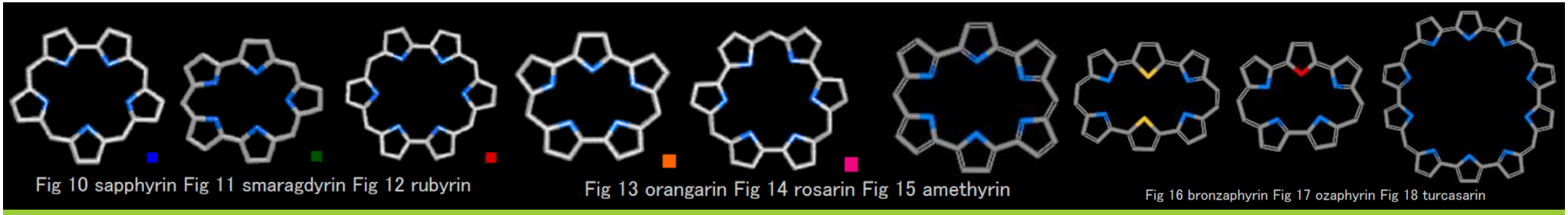
- Chemically synthesized porphyrin derivative
- Contains an iron or copper metal center
- Highly stable, even in acidic or high temperature conditions
- Deep blue crystalline solid
  - More electronegative nitrogens in porphyrin ring attract electrons, increasing pi density and stabilizing (lowering) energy levels
  - Benzene rings increase conjugation, shifting light reflection from purple visible light to blue visible light
- Intense color makes it highly useful in dyes and pigments
- Chemists attach chlorine to rings to shift the color towards more green hues



https://upload.wikimedia.org/wikipedia/commons/4/45/Phthalocyanine_blue.jpg
http://patentimages.storage.googleapis.com/WO2013020067A1/imgf000002_0001.png

Other Synthetic Porphyrins

- Synthetic porphyrins open up a realm of colorful possibilities
- Scientists synthesized a series of porphyrins named after gemstones
  - Even one named after the Wizard of Oz, called **ozaphyrin**
- Sapphyrin = First "jewel" molecule; accidentally synthesized during attempts to synthesize Vitamin B_{12}
- Modification to the number of double bonds, the number of bridging carbons, and the bridging pattern between rings drastically alters the color spectrum
- Changing the nitrogens within the porphyrin ring to other electronegative atoms (sulfer, oxygen) also lead to color changes



http://www.org-chem.org/yuuki/porphyrin/porphyrin.html

A Renewable Energy Source

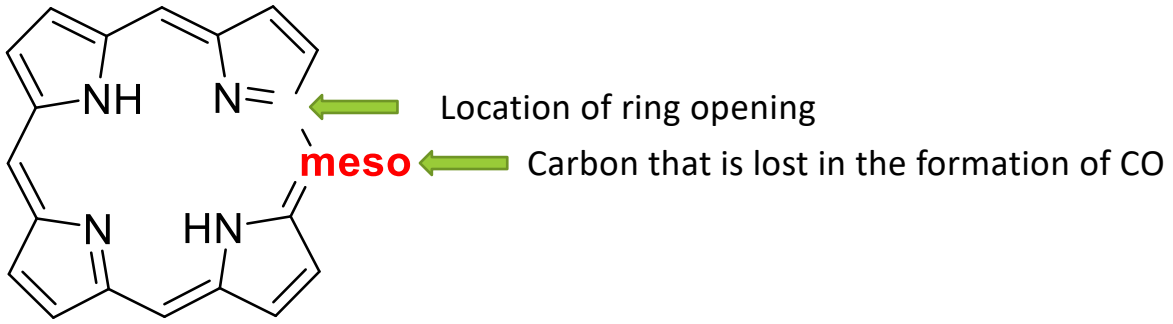
- Hydrogen is a solution to the search for renewable energy…but how to produce it?
- Photochemical water splitting = mimics photosynthesis by using sunlight to split water molecules and generate hydrogen gas
- Makes use of rechargeable photoelectrochemical cells
  - Semiconductor absorbs light energy and generates electrons, which pass into solution to split water molecules and produce H_2
- Zinc centered porphyrins are highly successful semiconductors in photoelectrochemical cells
  - Porphyrins absorb large amounts of visible light, conduct a small current when exposed to sunlight, and have favorable redox potentials
  - Zinc's electrons remain excited for long periods of time, extending the lifetime of the cell
- Lord Porter, at the Royal Institute of Great Britain, developed one of the most successful photochemical water splitting systems known

Treating Cancer

- Photodynamic Therapy (PDT) = using light sensitive compounds to trigger cell death
- Inject patients with a mixture of porphyrins called HpD
  - Some of these are photoactive
- Porphyrins attracted to and accumulate in the tumor
- When exposed to light rays, produce oxygen to trigger cell death
- Problems:
  - Not all porphyrins in HpD are photoactive
  - HpD also travels to healthy cells
  - HpD absorbs in the wrong region of the electromagnetic spectrum
- Scientists working to develop porphyrins which will absorb light that is able to pass through human tissues

Biodegradation

- Heme and chlorophyll are broken down into linear molecules called **bile pigments**
- Chemical term = bilin
  - We saw this as an intermediate during the biosynthesis!
- Formed through a ring opening at the alpha carbon and a loss of the adjacent meso carbon to produce carbon monoxide as a byproduct
- **Biliverdin** and **bilirubin** = important bile pigments at various stages during breakdown



Biliverdin and Bilirubin

- Biliverdin = a green pigment
  - Responsible for the green color in bruises
  - Found in green skin pigment of animals and reptiles
  - Gives eggshells a green tint
  - Highly useful in helping organisms camouflage within the environment
  - Water soluble and easily excreted = gives bird, reptile and amphibian droppings their green color
  - Further reduced to form bilirubin
- Bilirubin = a yellow pigment
  - Gives bruises their yellow color
  - Further breakdown of biliverdin to produce bilirubin is the reason why bruises fade from green to yellow

Jaundice

- Bilirubin is not water soluble
- Processing occurs in the liver, where structural changes are made to allow the body to excrete the compound
- If processing does not occur, compound is insoluble
  → **build up** of bilirubin
- Bilirubin is **lipid-soluble** → it is capable of passing back through the cell membrane
- Build-up of bilirubin leads to **Jaundice**
  - Symptoms of jaundice include yellowing skin, caused by the yellow color of excess bilirubin

http://www.searchhomeremedy.com/wp-content/uploads/2013/04/Jaundice.jpg

Acknowledgements

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