Nucleotides and Nucleic Acids

Brief History…[1]

1869 - Miescher – Isolated nuclein from soiled bandages

1902 - Garrod – Studied rare genetic disorder: Alkaptonuria; concluded that specific gene is associated with absence of a specific enzyme.

1903 - Sutton – Chromosome structure

1913 - Morgan – Gene mapping

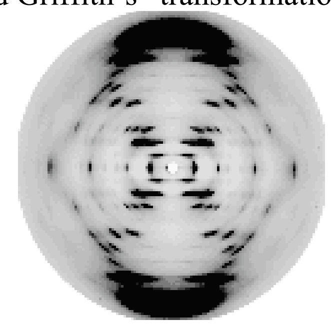
1926 - Sumner – Purified Urease; identified enzyme to be proteins

1928 - Griffith – Transforming Principle – a chemical transferred from dead bacteria to living cells caused genetically converted strains ("transformation")

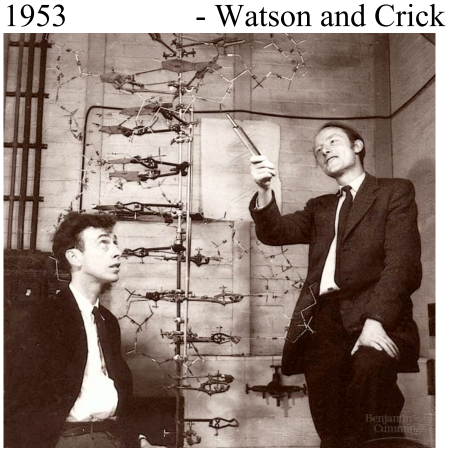
1944 - Avery, McCarty, and Macleod – Identified Griffith's "transformation principle" as DNA

1947 - Chargaff – Base pairing

1950's - Franklin – X-ray of DNA

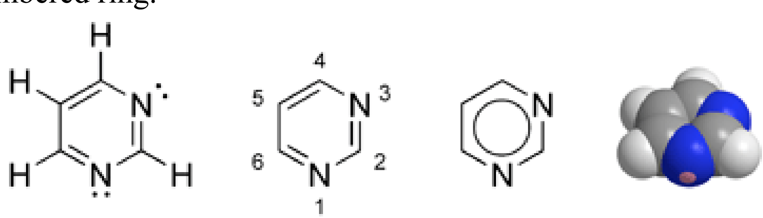


1953 - Watson and Crick – DNA double helix



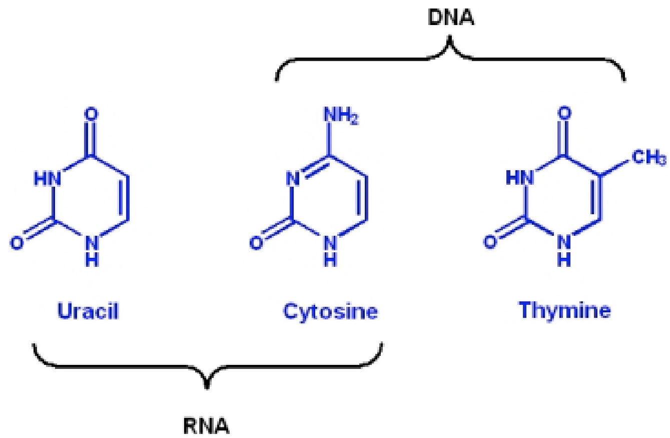
Three components make up a nucleotide:

1. **Heterocyclic base** – either a pyrimidine or a purine
   - *Heterocyclic* – "molecule with at least one ring containing an atom other than carbon"[2]
   - ***Pyrimidine*** – aromatic organic compound with 2 nitrogens at C1 & C3 of a six-membered ring.

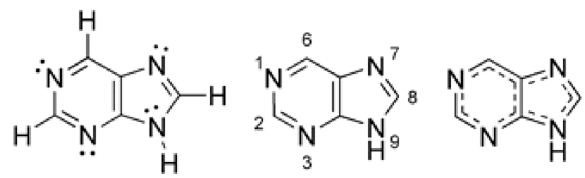


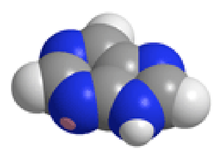
[1] http://kirkpatrick.troyhigh.com/page2.html
[2] Hardinger. *Chem14C Thinkbook*. p. 101.

- Pyrimidines in DNA & RNA:

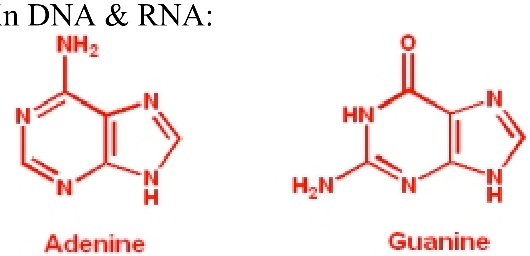


- ***Purine*** – aromatic organic compound that consists of a pyrimidine ring and an *imadazole* ring ($C_3H_4N_2$).

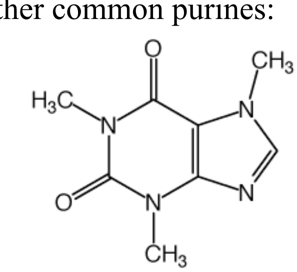


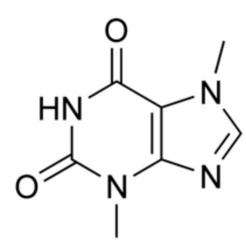


- Purines in DNA & RNA:



- Other common purines:





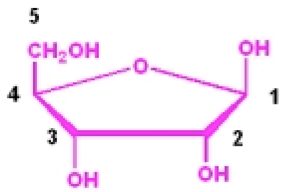
Caffeine Theobromine (found in chocolate)

- ***Properties of pyrimidines & purines***
  - Pyrimidine conformations are planar; purines are somewhat puckered
  - Plain pyrimidines and purines have low solubility (not many polar bonds)

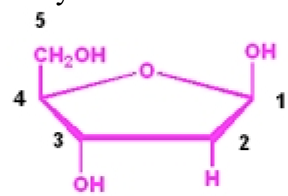
- Cytosine, Thymine, Uracil, Guanine, and Adenine are more soluble because they have many polar groups that are available for hydrogen bonding.

- Because they are aromatic, pyrimidines and purines can all absorb UV light.
    - DNA & RNA concentration in a sample can be found by measuring UV absorbance[3].

2. **Carbohydrate** – The carbohydrate component consists of a sugar, which is usually a pentose. Each nucleic acid has a different carbohydrate.



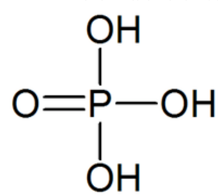
D-Ribose (furanose form)
RNA



D-2-deoxyribose (furanose form)
DNA

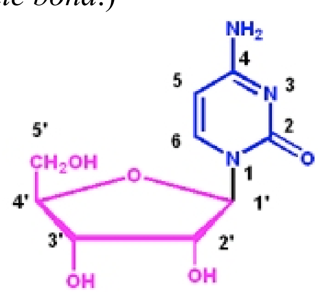
Note: *Superscript prime* is used to number the carbons when a heterocyclic base is attached to the carbohydrate (i.e. 1', 2' instead of 1, 2).

3. **Phosphoric acid –** forms *phosphodiester* bonds between nucleotides



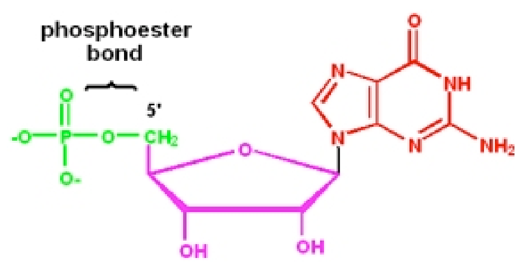
Phosphoric acid

Nucleosides
- formed by covalently joining the sugar to a heterocyclic base (bond formed is called a *glycosidic bond*.)



A nucleoside:
β-glycosidic bond between D-ribose and cytosine nitrogenouos base

Nucleotides
- formed by joining phosphoric acid to a *nucleoside* at the C5' or the C3'.



Guanosine 5' monophosphate
(5'-GMP)
(Guanylic acid)
a "nucleotide"

Helpful mnemonic (maybe):
Nucleotides = has two groups joined to the sugar.
Nucleoside = has only a nitrogenous base joined to *one* side.

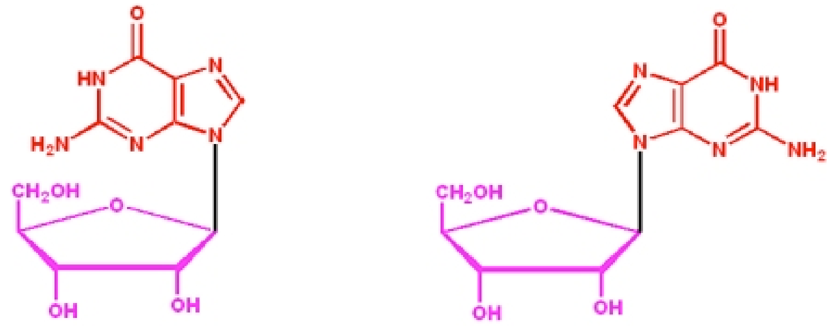
3 http://wine1.sb.fsu.edu/BCH4053/Lecture18/Lecture18.htm

Nucleoside Nomenclature[4]

- add suffix '-idine' to pyrimidine; add "-osine" to purine.
- Pyrimidine nucleosides: Cytidine, Thymidine, Uridine
- Purine nucleosides: Adenosine, Guanosine

Conformations of bases in Nucleosides[5]

- *syn* and *anti* orientations

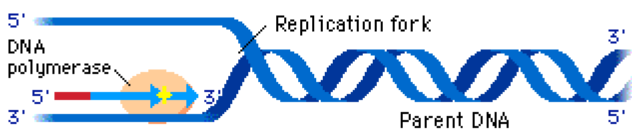


syn Guanosine   *anti* Guanosine

- Rotation around glycosidic bond has a slight barrier because of the H on the C2' of the ribose.

DNA

- **D**eoxyribo**n**ucleic **A**cid – polymer of nucleic acids (*polynucleotide*)
- Functions as storage for genetic information.
- DNA polymerase is used to catalyze the synthesis of DNA. Synthesis occurs in the 5'→ 3' direction.



http://www.phschool.com/science/biology_place/biocoach/dnarep/biosynth.html

- Each strand of the double helix is orientated in the opposite direction.
- DNA is acidic due to the phosphate groups between each 2'deoxyribose.
- Contains Adenine, Guanine, Cytosine, and *Thymine*
- *Primary* structure: nucleic acid sequence; *Secondary* structure: double helix; *Tertiary* structure: nucleic acids supercoil and wrap around histones (proteins)
- In eukaryotic cells (plants, animals, fungi, & protists), DNA is located in the cell nucleus.
- In prokaryotic cells (eubacteria & archaea), DNA is located in the nucleoid; there is no nuclear envelope to separate DNA from the cytoplasm.

RNA

- **R**ibo**n**ucleic **A**cid – polymer of nucleic acids (polynucleotide)
- Functions as template for translating genes into proteins, transfers amino acids to the ribosome site on a growing polypeptide chain, etc.
- Unlike DNA, RNA is single-stranded and consists of a shorter nucleotide chain.

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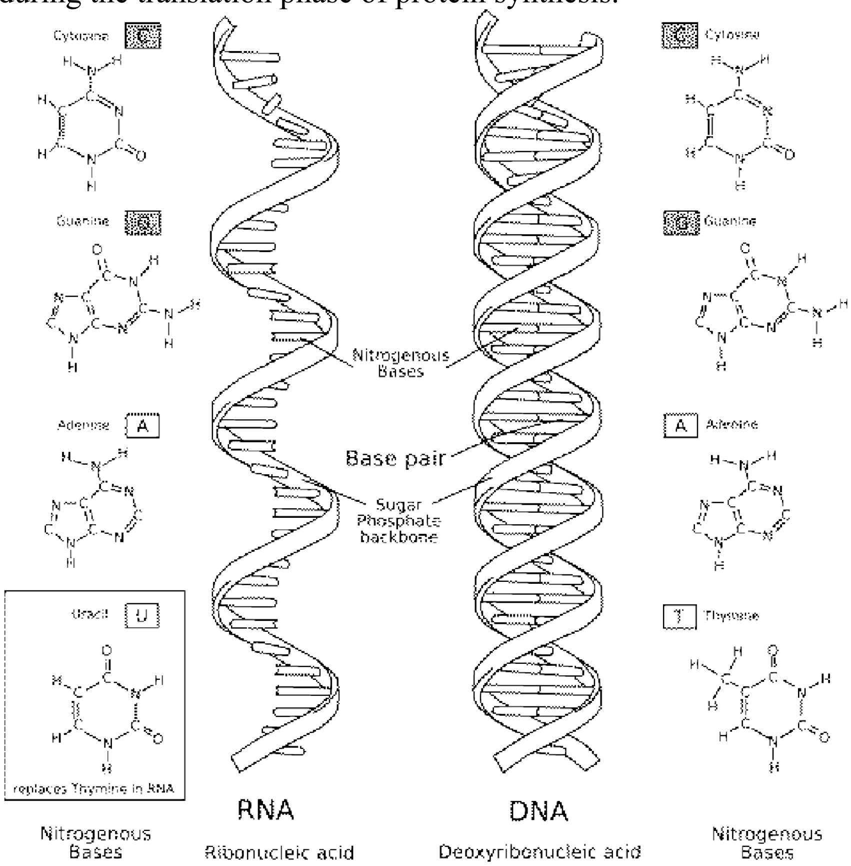
[4] http://wine1.sb.fsu.edu/BCH4053/Lecture18/Lecture18.htm
[5] http://wine1.sb.fsu.edu/BCH4053/Lecture18/Lecture18.htm

- Hydroxyl group on the ribose causes RNA to be less stable than DNA because it is easier to undergo hydrolysis.
- Contains Adenine, Guanine, Cytosine, and *Uracil*
- Many types of RNA[6]

Examples:

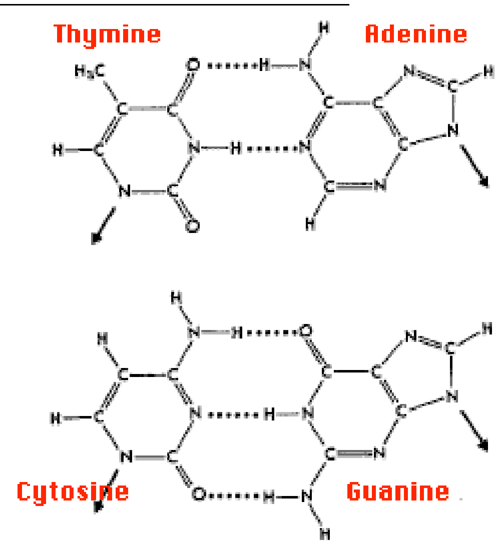
- mRNA – Messenger RNA; brings information from DNA to ribosome sites for protein synthesis.
- tRNA – Transfer RNA; transfers a specific amino acid to a polypeptide chain during the translation phase of protein synthesis.



Chargaff's Rules

- A pairs with T (ratio 1:1); G pairs with C (ratio 1:1)

Note: Ratios are random in RNA



http://fig.cox.miami.edu/~cmallery/150/gene/chargaff.htm

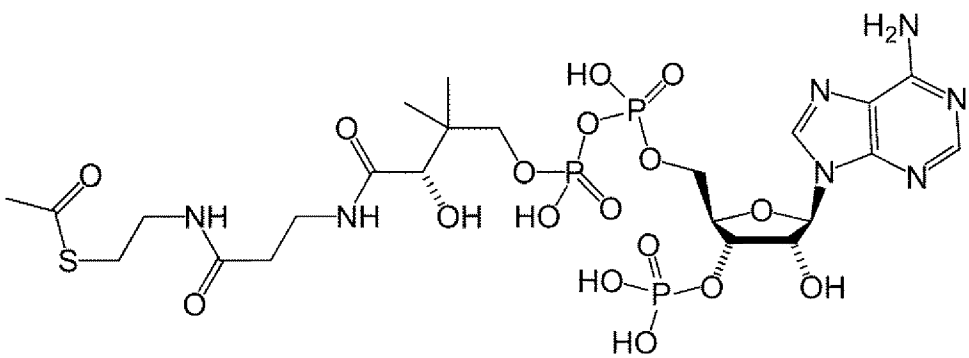
[6] http://en.wikipedia.org/wiki/RNA

Stability of DNA

- DNA must be stable in order to store genetic information. What accounts for DNA's stability?

- ***Aromatic Stacking***
  - Weak noncovalent force caused by overlapping of p-orbitals; also called *pi stacking*. In DNA, aromatic stacking between the nucleotides contributes to its stability. The pyrimidine and purine bases, which are parallel to each other in DNA, participate in aromatic stacking due to the overlap of their p-orbitals.
- ***Hydrogen Bonding***
  - Millions of hydrogen bonds in DNA is the main structural feature that explains why DNA is stable. Hydrogen bonding is strong, but can easily be broken for DNA replication.

Practice problem:



Coenzyme A (acetyl CoA) is important in the oxidation of fatty acids and lipid biosynthesis (ie. from acetyl CoA to cholesterol).[7] Its structure is shown above.

1. Which heterocyclic base is a part of acetyl CoA?
2. Which carbohydrate is a part of acetyl CoA?

Answers:
1. Adenine   2. Ribose

* Pictures taken from http://en.wikipedia.org/wiki/Main_Page or http://wine1.sb.fsu.edu/BCH4053/Lecture18/Lecture18.htm unless otherwise stated.

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[7] http://www.medterms.com/script/main/art.asp?articlekey=32063