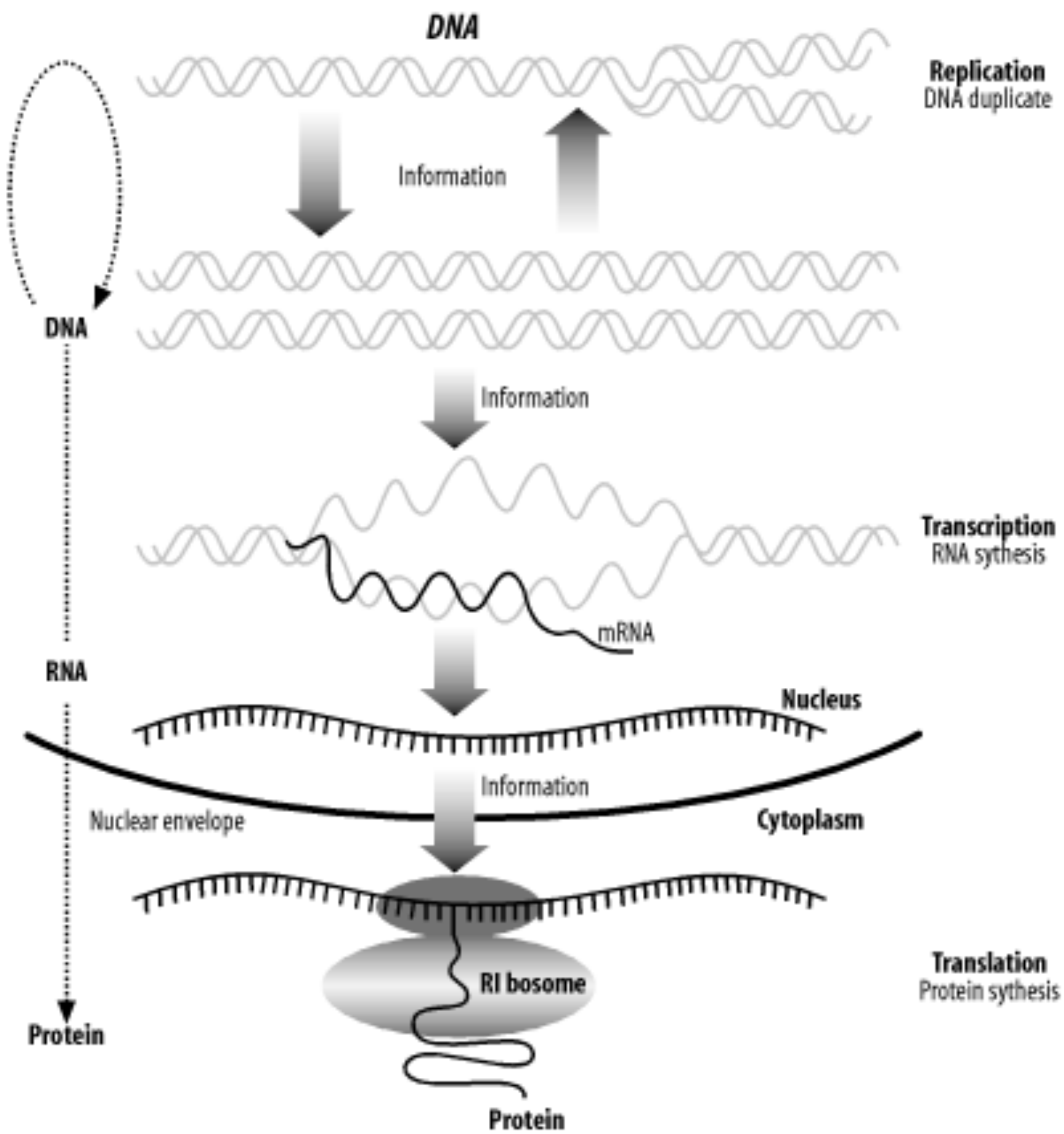
Central Dogma review and Chapter 6 (Strickberger 4th ed.)

HOW DOES EVOLUTION OCCUR?

Evolution occurs as environmental stresses drive the adaptation of organism. Mutations single-handedly change the organisms genotypically, while providing a chance for the organism to change phenotypically. But before one can understand the mechanisms driving evolution, one must be familiar with the mechanisms that underlie the structure and function of genetic materials.

THE CENTRAL DOGMA OF MOLECULAR BIOLOGY



DNA is the basic genetic material

Undergoes replication…**WHY?**

How much genetic material needs to be replicated?

How quickly is this process performed?

DNA is transcribed into RNA
m-, r-, and tRNA
Genes

RNA is translated into amino acid sequences that code for proteins
Gene expression
Functional proteins – enzymes…**WHY are enzymes important?**
Structural proteins – porins
We will review the Central Dogma in the context of three areas:
Structure of nucleic acids
Function of nucleic acids
Changes in genetic information (later)…**How are these three areas important to evolution?**

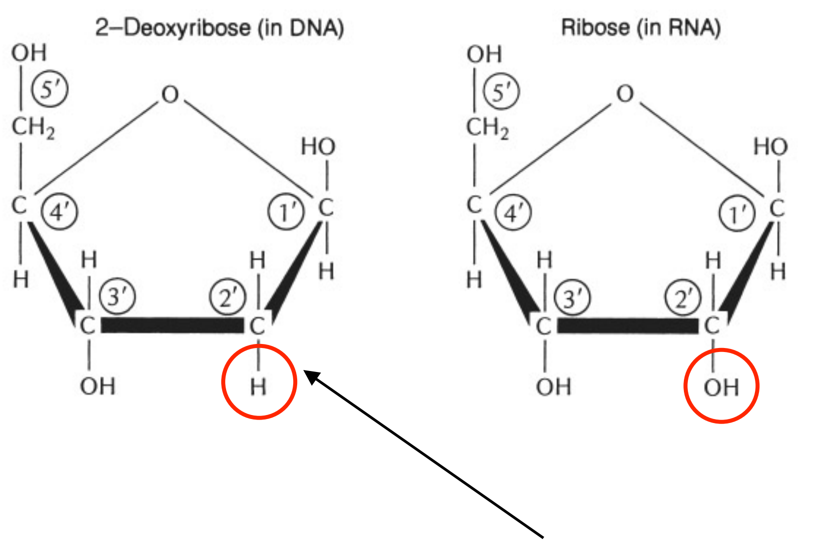
NUCLEIC ACID STRUCTURE

Primary Structure of nucleic acids (DNA for now)

Basic molecular composition is referred to as "primary structure".

DNA is a polymer of deoxyribonucleotide building blocks that consist of:

1. **Sugar** = **deoxy**ribose

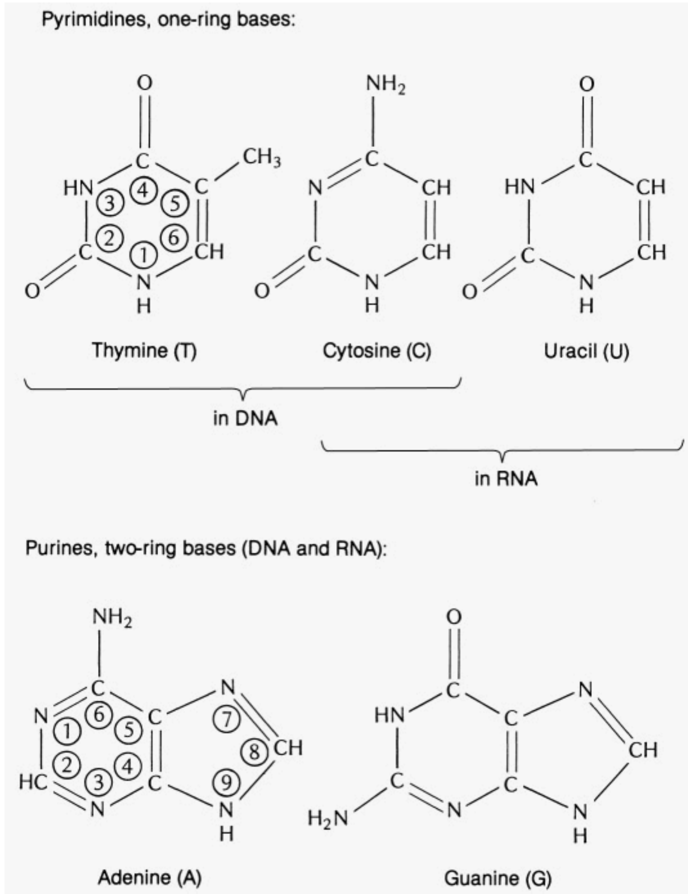


Hydroxyl is absent from the **2' C** position

2' and 3' hydroxyls are present in **ribose** (RNA)

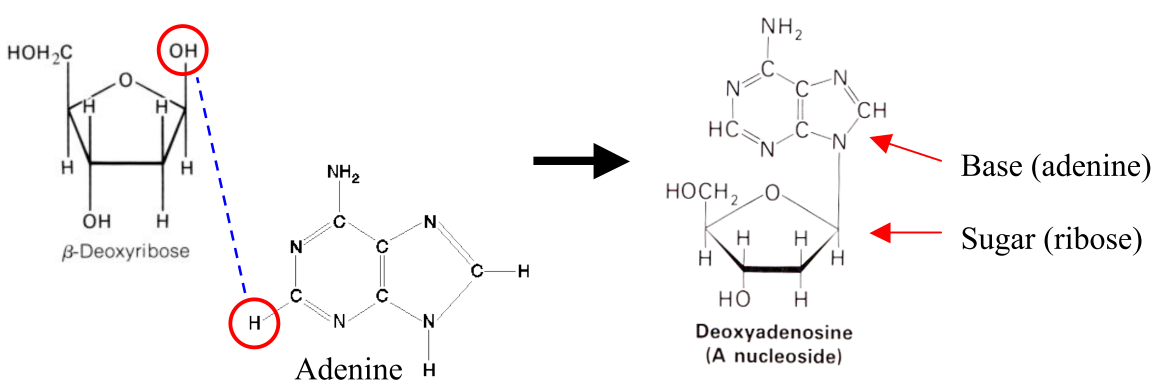
2. **Base** = **A**denine, **G**uanine (purines), **T**hymine, **C**ytosine (pyrimidines)

Thymine replaced with **U**racil in RNA.



When the sugar is bound to a base → deoxyribonucleo**side**

Four deoxyribonucleosides exist in DNA: deoxy-**adenosine** (below), -cytidine, -guanosine, -thymidine.

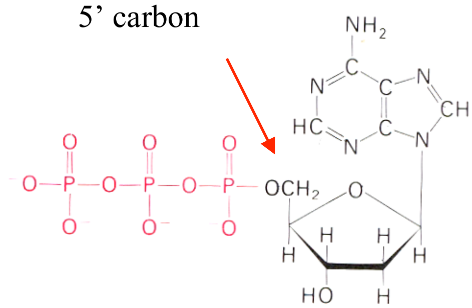


What compound is liberated when this binding occurs?

The deoxyribonucleosides polymerize to form a chain of DNA. However, before this can occur, the deoxyribonucleosides must be "charged" with energy.

Energy comes in the form of **phosphates**:

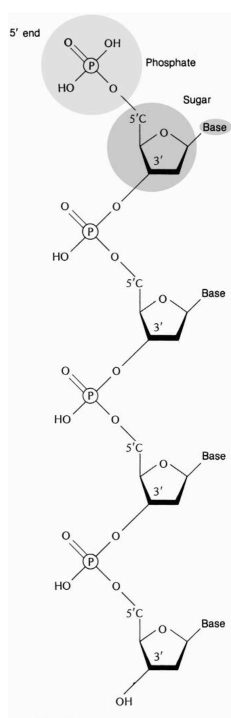
Tri-phosphate is added to the 5'-C of the nucleosides to yield a high energy **deoxynucleoside triphosphates** or "nucleotide".



Deoxyadenosine 5'-triphosphate
(dATP)
(A nucleotide)

Again, four structural possibilities exist (**A**, **C**, **G**, **T**), depending on the base.

DNA is polymerized by joining the 3'-OH of one nucleotide to the 5'-OH of another via a phosphate bridge called a **phosphodiester bond.**



Liberates di-phosphate and water

The sugar-phosphate backbone is **invariant** in every DNA molecule.

Then what makes the DNA of "different" individuals different?

A question: Are **four** bases enough to generate enough genetic diversity to facilitate all of the phenotypic diversity we have on Earth?

In other words, i*magine if we only had four letters in the English alphabet.*

Answer: for any one nucleotide position, **four** different messages are possible (A, G, C, T).

`A    C    G    T`

Therefore, for any two nucleotides in tandem, 4^2, or 16, messages are possible.

`AA, AC, AG, AT, CA, CC, CG, CT,`…etc.

Three nucleotides = 4^3, or 64, etc.

Therefore, for a typical gene @ 1500 bp, 4^{1500} permutations can result, creating considerable diversity…and lots of locations at which mutations can occur.

The double stranded nature of DNA

We often discuss DNA as a single sequence.

e.g. `AGT GTA ACC GCA CAT AGC`, i.e. one strand of a DNA molecule.

…but in 1953, Watson and Crick discovered that DNA was **double stranded**. **Why was this important?**

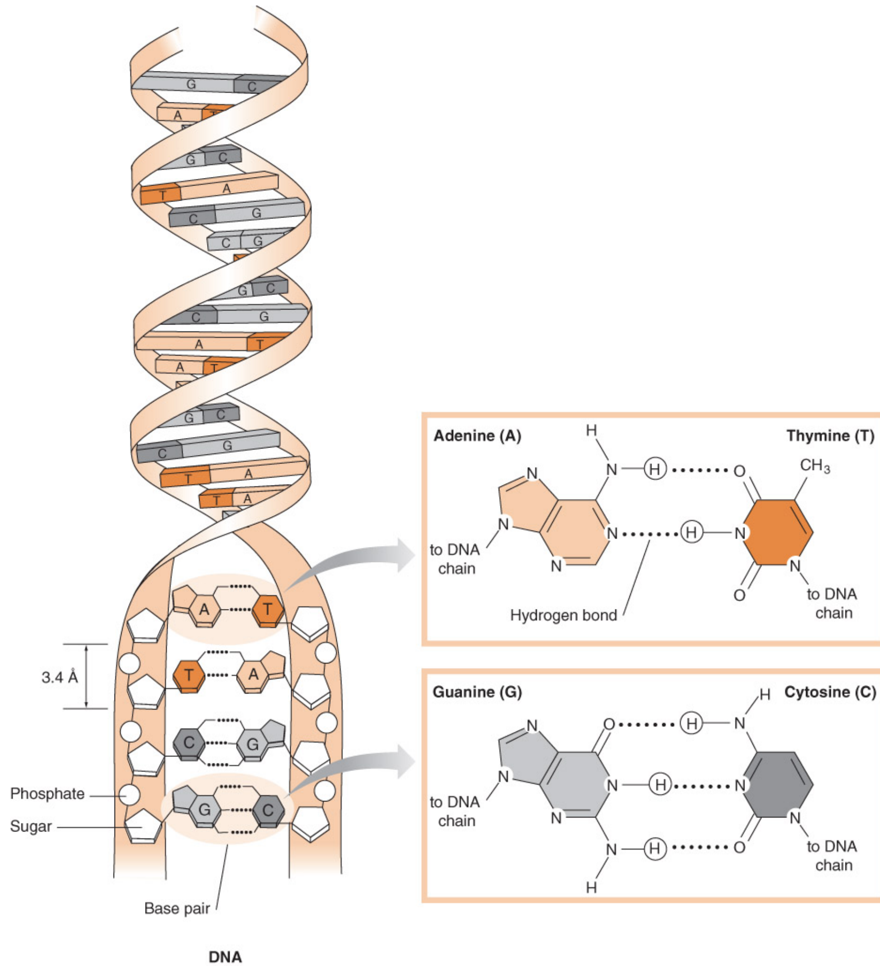
1. Each strand could serve as a **template** for a complementary, new DNA strand.

2. DNA could be more rapidly produced than with a single-strand template (i.e., two templates are present in each DNA molecule.

Something must be binding the two strands together…

Binding occurs between the **bases**.

H-bonding provides very specific associations between bases.



A – T bonds are **double** H bonds, while G – C bonds are **triple** H-bonds.

Secondary structure of nucleic acids

Double strands do not remain in a linear configuration.

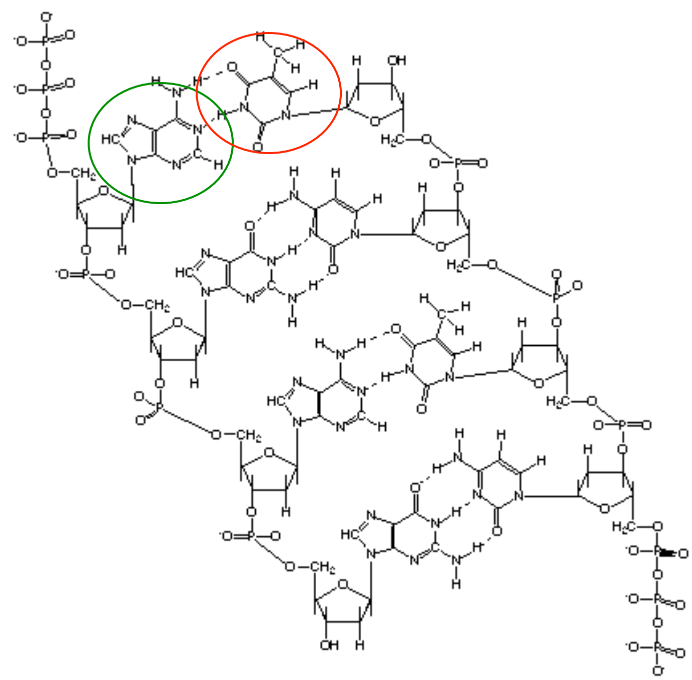
Size and charge of the sugars and bases result in steric constraints that cause the structure to coil into a helical configuration (**"double helix"**)…Think of the coil of a telephone cord.

The double helical structure carries an additional implication to the DNA structure.

Remember Adenine and guanine (purines) are **two-ringed** structures.
Cytosine and thymidine (pyrimidines) are **single-ringed** structures.

1. Only enough space inside the helix for **three** "rings".
   A – G binding impossible.

2. Too much distance between the sugar phosphate backbone for efficient binding of two, <u>single</u> ringed bases.
   C – T binding impossible.



Therefore, a purine must bind with a pyrimidine resulting in A – T and C – G bonds.

However mistakes will happen, leading to mutations.

NUCLEIC ACID FUNCTION

The function of nucleic acids is to **store genetic information.**

This information tells the cell when to grow, reproduce and how to maintain itself.

Information is stored on DNA segments called <u>genes</u>.

Two main products of genes.

1. Proteins (enzymes and structural components).
2. Structural RNA (e.g. 16S rRNA…more later).

To fulfill its functions, DNA must undergo two main reactions.

1. **Replication** -(potentially error prone and is ultimately a driver of evolutionary change…**WHY?**).
2. **Transcription** (DNA is used as a template to produce mRNA).

<u>**Replication**</u> – Polymerization of new DNA from an existing template using deoxyribonucleotide building blocks.

Why does a cell replicate its DNA?

Question: Does replication need to be an accurate process?

Answer: Yes and No…

In the <u>short term</u>, replication must be accurate to pass on exact information from parent to offspring.

In the long-term, inaccuracies are exactly what drives adaptation and evolution.

How does DNA replication remain accurate?

Replication is a **polymerization** reaction… reaction that creates the same products over and over.

How can this feature promote accuracy?

Remember, specific base pairing was described by Watson and Crick in 1953.

Replication combines nucleotides to form a nucleotide chain and has **two basic requirements**:

1. Requires **energy** – AT**P**

   Provided during the “charging” of deoxyribonucleosides.

2. Requires a **catalyst** – DNA polymerase enzyme.

   Responsible for joining nucleotides together

TRANSCRIPTION AND TRANSLATION

Transcription and translation create proteins using DNA as a template (discussed in-brief here)

While DNA replication provides the means to duplicate genetic material, processes that allow organisms to grow, reproduce and metabolize are dependent on expression of the **genes** (proteins) encoded by DNA.

The DNA sequence is used as the **template** that provides the "instructions" from which proteins are created.

Problem: proteins cannot be generated **directly** from a DNA template.

Transcription – information in the DNA sequence is copied to one of three types of RNA:

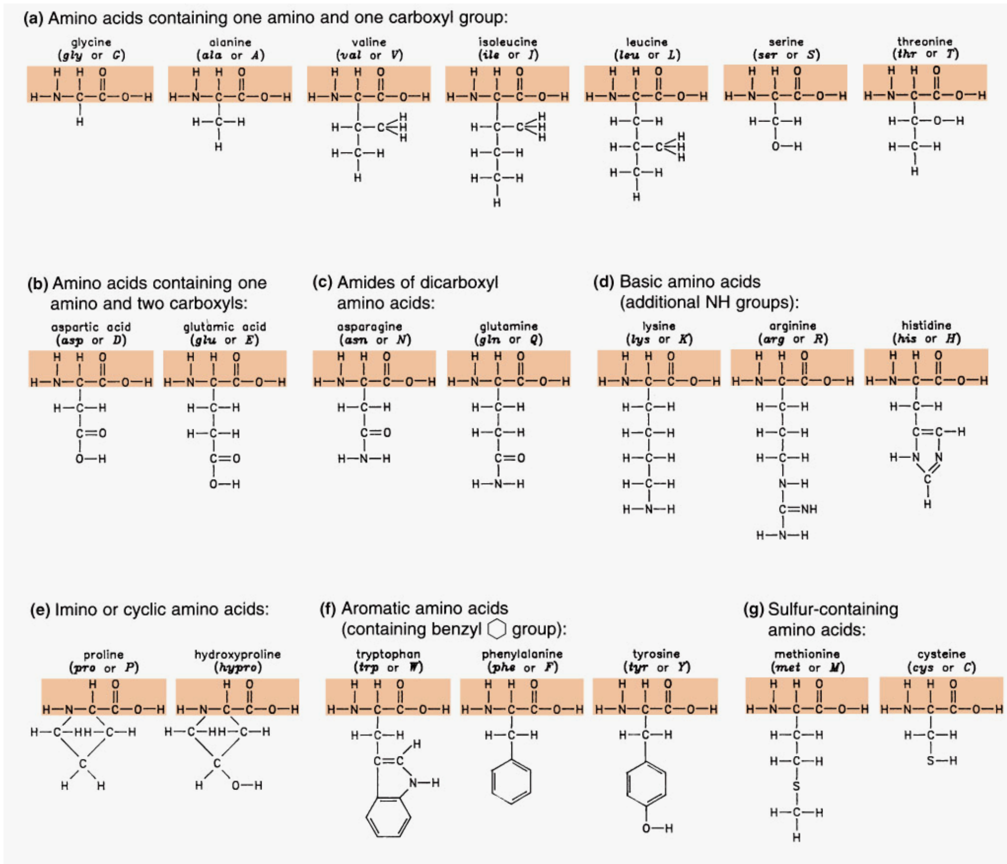
1. mRNA messenger RNA
2. tRNA transfer RNA
3. rRNA ribosomal RNA

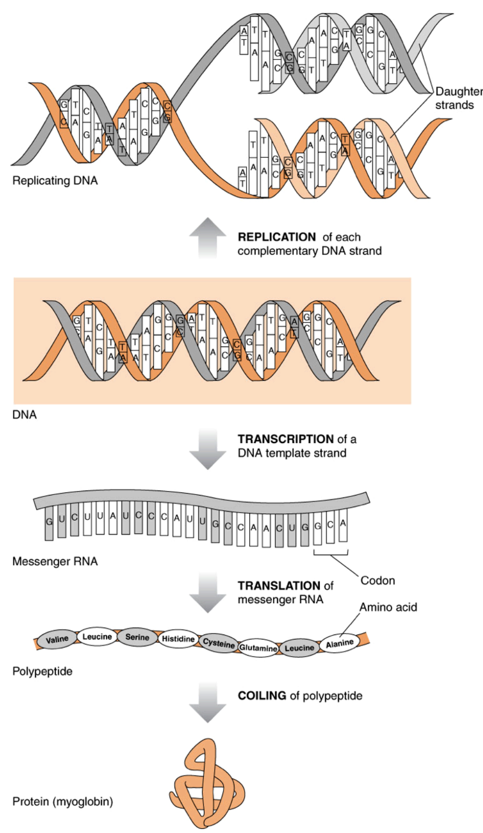
We will focus on the mRNA as the main information intermediate.

mRNA is polymerized as a complement to one strand of DNA (remember the Central Dogma figure).

This is accomplished by an enzyme called **RNA polymerase**.

A ribosome attaches to the strand of mRNA (remember, a complement to one DNA strand) and adds **amino acids** to a growing polypeptide chain according to the mRNA sequence.


(a) Amino acids containing one amino and one carboxyl group:
glycine (gly or G)
alanine (ala or A)
valine (val or V)
isoleucine (ile or I)
leucine (leu or L)
serine (ser or S)
threonine (thr or T)
(b) Amino acids containing one amino and two carboxyls:
aspartic acid (asp or D)
glutamic acid (glu or E)
(c) Amides of dicarboxyl amino acids:
asparagine (asn or N)
glutamine (gln or Q)
(d) Basic amino acids (additional NH groups):
lysine (lys or K)
arginine (arg or R)
histidine (his or H)
(e) Imino or cyclic amino acids:
proline (pro or P)
hydroxyproline (hypro)
(f) Aromatic amino acids (containing benzyl group):
tryptophan (trp or W)
phenylalanine (phe or F)
tyrosine (tyr or Y)
(g) Sulfur-containing amino acids:
methionine (met or M)
cysteine (cys or C)


Daughter strands
Replicating DNA
REPLICATION of each complementary DNA strand
DNA
TRANSCRIPTION of a DNA template strand
Messenger RNA
Codon
TRANSLATION of messenger RNA
Amino acid
Valine
Leucine
Serine
Histidine
Cysteine
Glutamine
Leucine
Alanine
Polypeptide
COILING of polypeptide
Protein (myoglobin)

THE TERRESTRIAL ORIGIN OF LIFE…EARLY CHAOS

How could a highly complex life form like humans have arisen from the molecular chaos assumed to have existed on early Earth?

Did this just occur randomly? Probably not.

To put it in perspective, ask yourself: Can a monkey on a typewriter produce the works of Shakespeare?

26 typewriter keys and 10^6 words: chance is $(1/26)^{10}$.
If the monkey types 1 million words per second, it would take $7 \times 10^{1,414,965}$ years.

So, yes, *but it is highly unlikely*.

Another example in biological terms: one protein sequence of 100 AA would have only one chance in 20^{100} (10^{130}) of arising randomly (we have 20 AA to choose from).

If a random 100 AA sequence was generated every second, it would take 4×10^{122} years to generate the correct sequence.

So, life most certainly *did not* arise as a result of *random* reactions.

The probability is slight that all of the necessary components of life were in the right place at the right time, so it makes sense that some organization and helpful factors must have existed.

1. Early organisms were **simple**.

Basic qualities: growth and replication
Absence of competition **(why no competition?)**

2. The formation of organic molecules and structures was **not completely random**. It did follow natural laws that were already in place (and still are today).

3. By using available **energy** and **raw materials**, early biomolecules could be synthesized.

Characteristics of the early solar system supported the development of biomolecules:

1. The Sun provided adequate energy.
Which forms?

TABLE 6-2 Present energy sources that probably were available for organic synthesis early in Earth's history

Source	Energy (calories/cm^2/year)
Total solar radiation (all wavelengths)	260,000
Ultraviolet light wavelengths (in angstroms)	
Below 3,000	3,400
Below 2,500	563
Below 2,000	41
Below 1,500	1.7
Electrical discharges (lightning, corona discharges)	4
Shock waves (meteorite impacts, lightning bolt pressure waves)	1.1
Radioactivity (to depth of 1 km)	0.8
Volcanoes (heat)[a]	0.13
Cosmic rays	0.0015

[a] Not all volcanic eruptions release the same amount of energy. Of the four categories, *Hawaiian volcanoes* such as Mauna Loa release lava but are not explosive and do not expel fragments of rock. *Stumbling eruptions,* such as Mt. Storable, expel lava in frequent explosions accompanied by incandescent, luminous vapor. *Vulcan Ian eruptions,* the second most violent, erupt violently after the build up of gases that release the magma plug blocking the vent. Finally, *Paleyan eruptions* (named after Mt. Pelé in Martinique) expel rock, ash, lava and superheated gas high in the air (See *TIME Magazine,* 2006. Nature's Extremes. Inside the Great Natural Disasters that Shape Life on Earth. Time, Inc., New York).

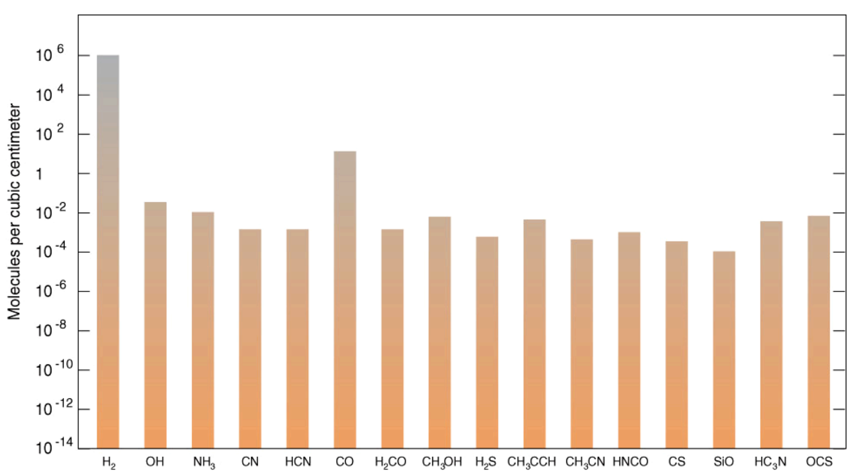
Source: Reprinted by permission from Miller, S. L. and L. E. Orgel, 1974. *The Origins of Life on the Earth.* Prentice Hall, Englewood Cliffs, NJ.

2. Several essential elements to sustain reactions and form organic molecules existed: **H, O, C, N**, S, **P**, and Ca.

C, in particular was very important. **Why?**

.

Think about its bonding properties.



Densities of various molecules observed in molecular clouds within our galaxy.

3. Earth's orbital distance from the sun was consistent. **(Why important?)**

4. Water was plentiful once Earth cooled.

Excellent solvent
Liquid over a wide range of temperatures
Will transport other molecules **(Why important?)**

5. Hydrogen gas was plentiful.

Binds with C to generate hydrocarbon compounds.

Precursors for AA, fatty acids, nucleic acid bases.

The stage was certainly set to support the rudimentary precursors of life. **How were the first biomolecules formed?**

ORIGIN OF BASIC BIOMOLECULES – The Oparin-Haldane hypothesis

In the 1920s, Aleksandr Oparin and John Haldane hypothesized that organic molecules could be formed in Earth's early **reducing** atmosphere.

The hypothesis wasn't tested until 30 years later by Harold Urey and his student, Stanley Miller (1953)

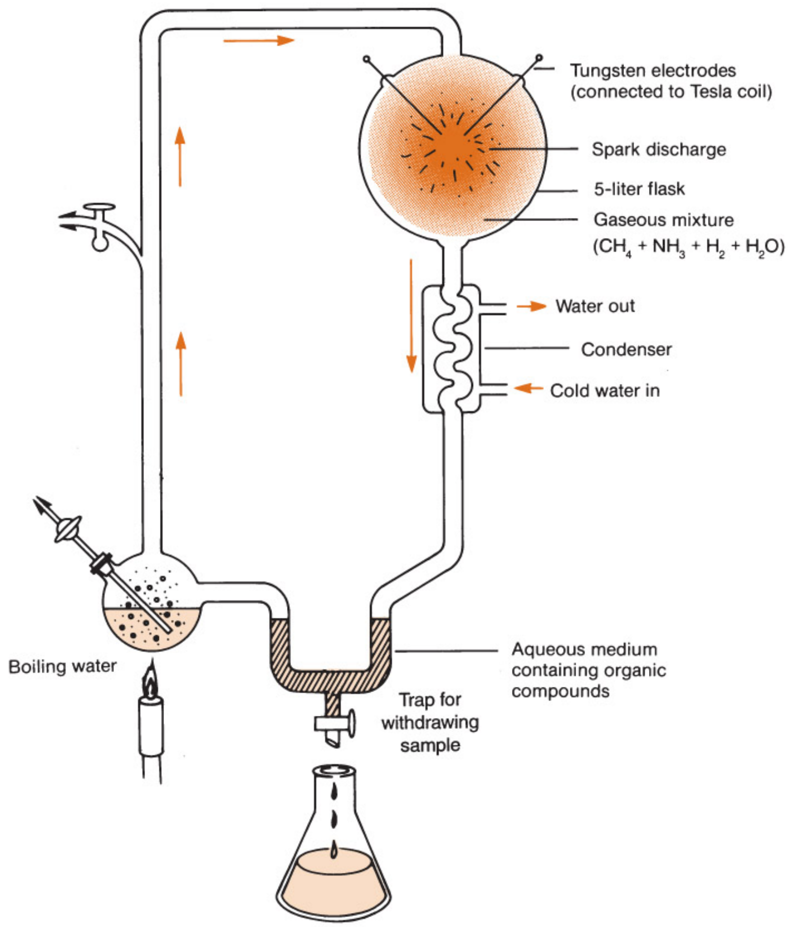
Miller-Urey experiment:

1. Combined methane, ammonia, and hydrogen gas in a glass, 5 L flask.

2. Boiled water in an attached flask to produce water vapor and circulate gasses.

3. Introduced a continuous spark.

Explain why these conditions were relevant.



Compounds produced from this reaction were collected after one week.

Result: Several organic compounds essential for life were produced.

TABLE 6-3 Yields of various organic compounds obtained from a mixture of water, hydrogen, methane, and ammonia exposed to electrical sparking[a]

Compound	Yield (%)[b]
Glycine	2.1
Glycolic acid	1.9
Sarcosine	0.25
Alanine	1.7
Lactic acid	1.6
N-methylalanine	0.07
α-amino-n-butyric acid	0.34
α-aminoisobutyric acid	0.007
α-hydroxybutyric acid	0.34
β-alanine	0.76
Succinic acid	0.27
Aspartic acid	0.024
Glutamic acid	0.051
Iminodiacetic acid	0.37
Iminoaceticpropionic acid	0.13
Formic acid	4.0
Acetic acid	0.51
Propionic acid	0.66
Urea	0.034
N-methyl urea	0.051
TOTAL	15.2

[a] These products represented only about 15% of the carbon that had been added to the apparatus. The remaining carbon products, mostly in the form of polymerized tar-like substances, were not analyzed.

[b] The percent yields are based on the amount of carbon that was added to the mixture as methane.

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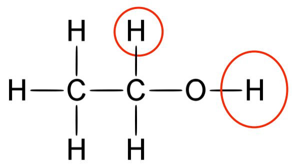
Supported the notion that the early atmospheric composition could support molecules necessary for life.

These observations showed that laboratory experiments could reflect actual chemical processes that occurred in the synthesis of Earth's first biomolecules.

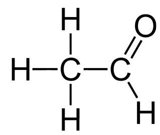
POTENTIAL SCENARIOS FOR BIOMOLECULE GENERATION ON EARLY EARTH

Amino acids

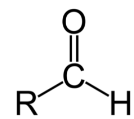
Arose from the formation of aldehydes (**al**cholols **dehy**drogenated):



Ethanol

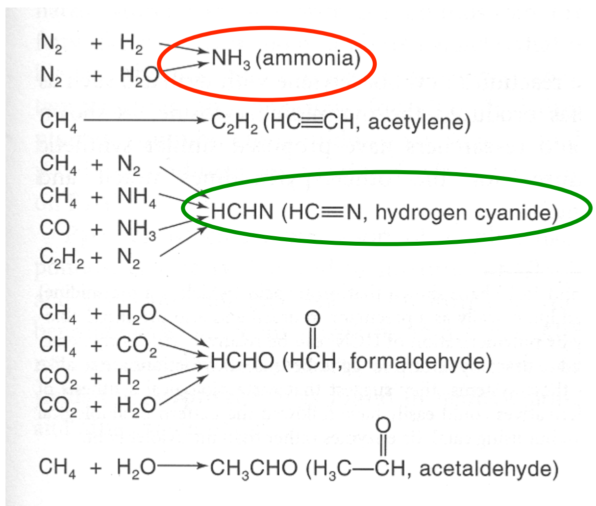


Acetaldehyde

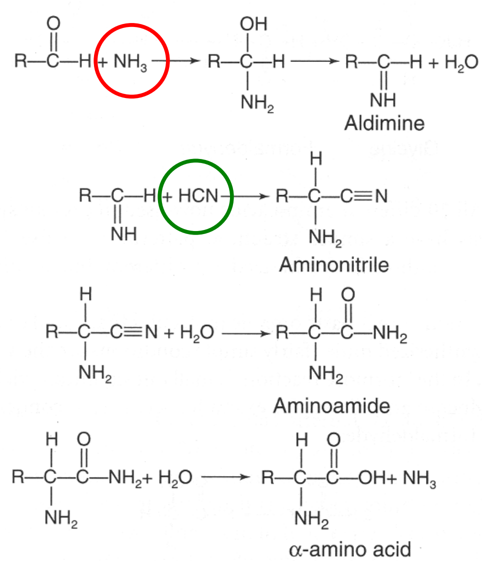


Generic aldehyde

Aldehydes interacted with ammonia and cyanide (both ubiquitous, arising from a variety of reactions).



…to produce a generic **amino acid**.



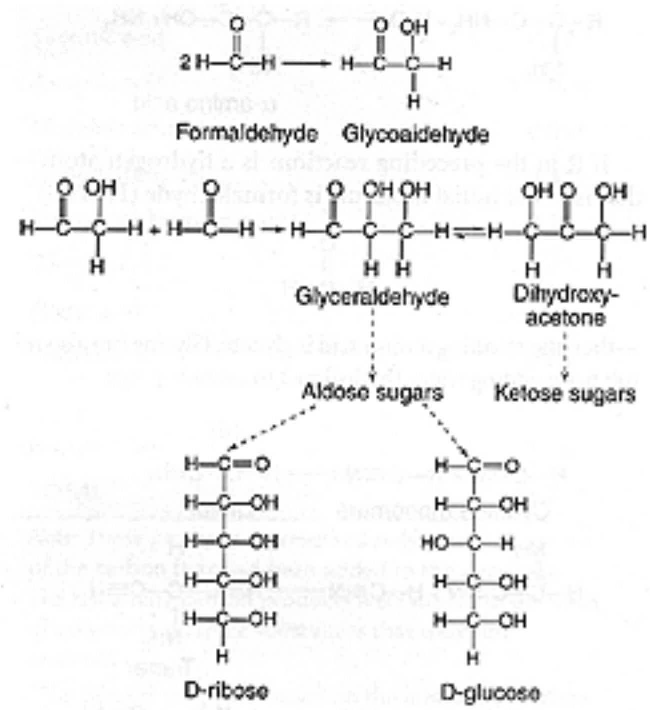
Note the role of water…

All 20 amino acids used in protein synthesis today have the same general structure. Why might this structural similarity be important for an early organism?

Sugars

The **formose** reaction yielded glucose and ribose.

Begins with the condensation of formaldehyde…

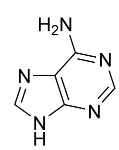


Where have we seen ribose before?

Glucose is quite stable and could have accumulated. **Important?**

Purine and Pyrimidine bases (nucleic acids)

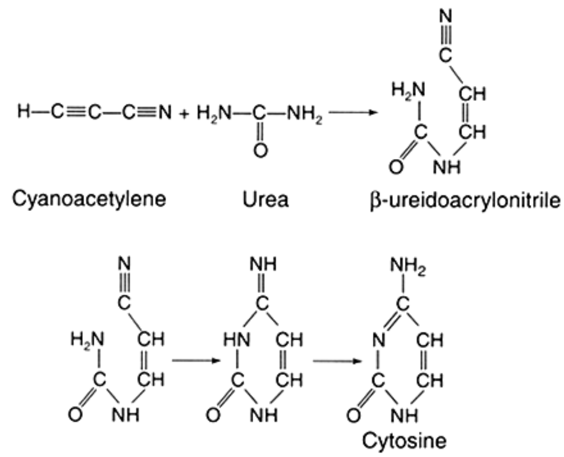
Heating solutions of ammonium cyanide produces a 0.5% yield of adenine.

$HCN + NH_3(aq) \rightarrow NH_4CN(aq) \rightarrow \rightarrow$ 

UV light causes hydrogen cyanide solution to produce adenine and guanine.

Cytosine could be produced from a reaction involving urea and cyanoacetylene.

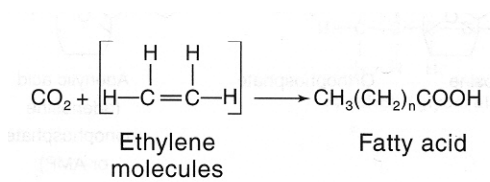
Example:



Similar reactions exist for thymine and uracil. **What are the implications of having a common reaction pathway to make three (of five total) bases?**

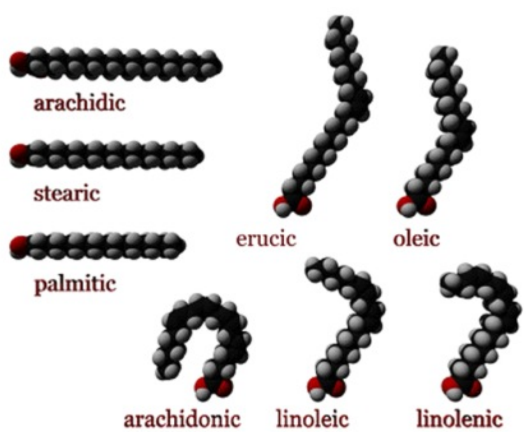
Fatty acids

Can be synthesized under high pressure and energy (radiation).



Interior portions of meteorite samples have contained fatty acids up to eight carbons long.

Examples:



All of these reactions take ENERGY, so, could enough energy be produced and harnessed to generate these biomolecules?

Example:

Given: 1 photon of UV radiation produces a **quantum yield** of $10^{-5} – 10^{-6}$ of a simple organic molecule. **What fraction is that?**

If the average mass of a simple organic molecule is 10^{-22} g, then the quantum yield per photon is $10^{-5} \times 10^{-22} = 10^{-27}$ g.

The photon density at the top of Earth's early atmosphere was 3×10^{14} photons cm^2 sec^{-1}.

Therefore the quantum yield cm^{-2} $sec^{-1} = 10^{-27}$g x $(3 \times 10^{14}) = 3 \times 10^{-13}$ g.

If the reducing atmosphere lasted for 500 million years (1.5×10^{16} sec), almost 5000 g of organic matter could have been produced per cm^2 of Earth's surface.

BIOMOLECULE-GENERATING PROCESSES
(Condensation and polymerization)

Amino acids and sugars must each combine to form functional molecules such as polypeptides and polysaccharides.

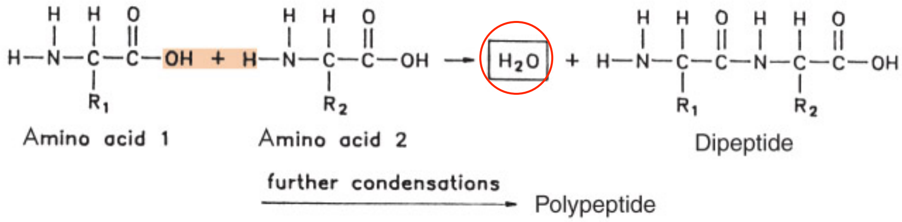
Single molecules usually don't provide for necessary biochemical functions.

Achieved through condensation and polymerization reactions.

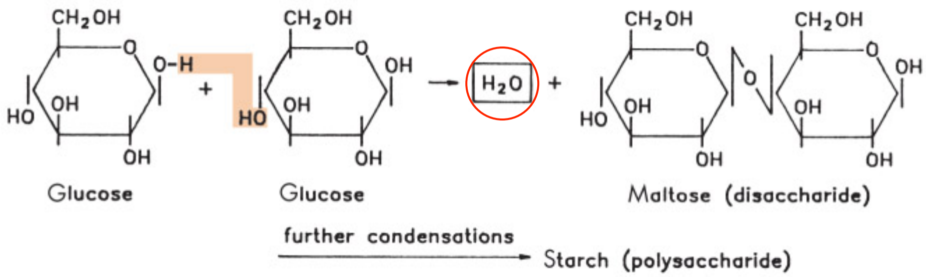
Not a spontaneous event.

Depends on the removal of water.

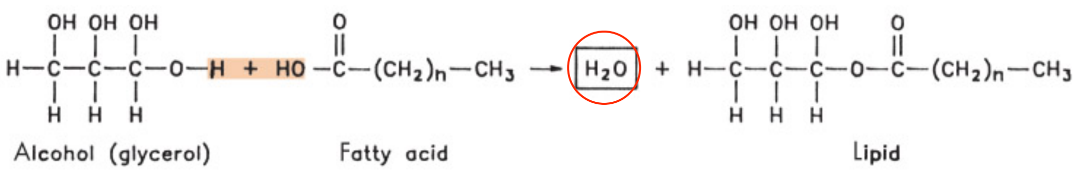
Proteins



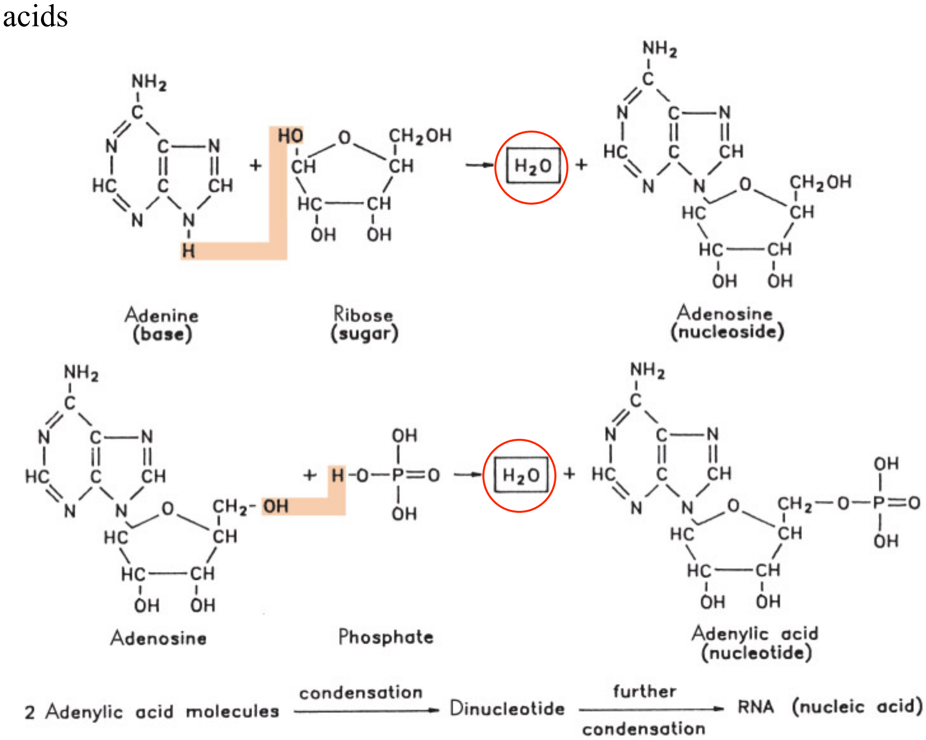
Sugars



Fats/Lipids

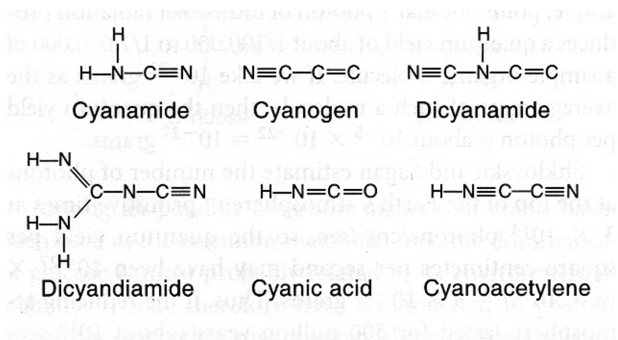


Nucleic acids



How was this water removed?

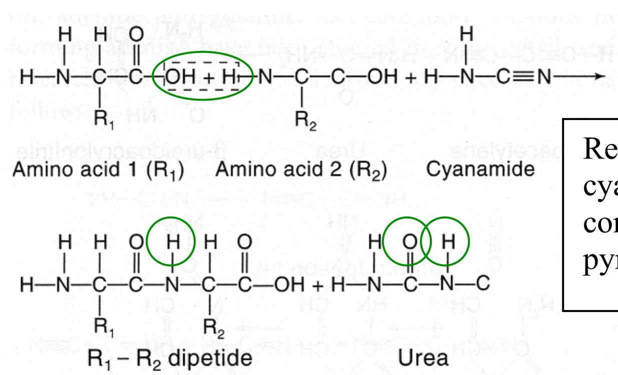
Several compounds that existed in Earth's early atmosphere were **condensing agents**. These compounds are high-energy chemicals that remove water.



Cyano (carbon-nitrogen) bonds allow the compound to combine with water.

The condensing agent gets hydrolyzed (hydrated, or split by the water).

Example: condensation of two amino acids coupled with the hydration of cyanamide to produce urea.



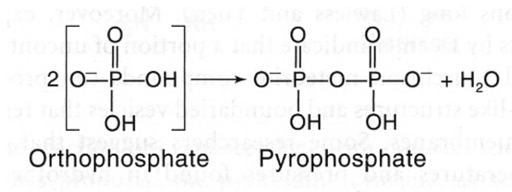
Remember, urea and cyanoacetylene can be combined to help form pyrimidine bases

What other form of energy could have been used to drive condensation reactions (removal of water)?

Heat works to remove water molecules. For example, the conversion of orthophosphate (one phosphate) to pyrophosphate (di-phosphate, or pyrophosphate).

Why are phosphates important?

Orthophosphate is a natural form of phosphorous.



Pyrophosphates **and heat** can be used to form AMP, ADP and ATP, which can eventually yield cellular energy under the correct conditions.

ATP + H2O >> ADP + orthophosphate (7.3 kcal per mole)

ADP + H2O >> AMP + orthophosphate (7.3 kcal per mole)

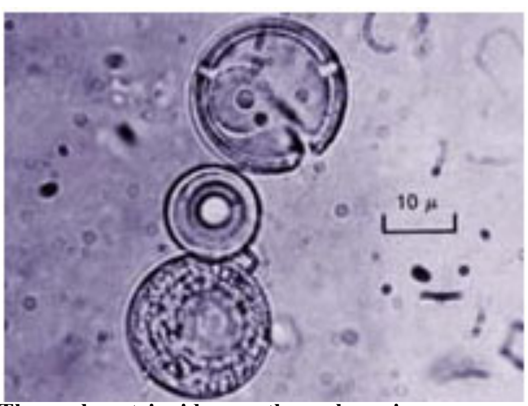
AMP + H2O >> adenosine + orthophosphate (3.4 kcal per mole)

This sequence provides a source of energy (ATP) as well as condensing agents (ATP, ADP, and AMP) to promote further condensation reactions.

EARLY FUNCTIONAL BIOMOLECULES

Thermal Proteinoids (primitive proteins)

Experiments in the 1950s showed that heating dry amino acid mixtures resulted in the formation of polypeptides that in many ways resemble proteins of today.



Thermal proteinoids seen through a microscope.

Two important aspects of the resulting proteinoids:

1. Proteinoids possessed a **non-random** proportion of amino acids.

The resulting polypeptide composition in the proteinoid did not always match the amino acid composition in the initial mixture.

Some ordered, non-random use of amino acids was taking place…it was not simply a function of the initial proportions.

TABLE 6-5 Amino acid compositions in molar percentages of two polymers compared to the initial reaction mixtures

	2:2:1 Polymer		2:2:3 Polymer	
Amino Acid	Initial Polymer Mixture	Polymer Product	Initial Polymer Mixture	Polymer Product
Aspartic acid	42.0	66.0	30.0	51.1
Glutamic acid	38.0	15.8	27.0	12.0
Alanine	1.25	2.36	2.72	5.46
Lysine	1.25	1.64	2.72	5.38
Semicystine	1.25	0.94	2.72	3.37
Glycine	1.25	1.32	2.72	2.79
Arginine	1.25	1.32	2.72	2.44
Histidine	1.25	0.95	2.72	2.03
Methionine	1.25	0.94	2.72	1.73
Tyrosine	1.25	0.94	2.72	1.66
Phenylalanine	1.25	1.84	2.72	1.48
Valine	1.25	0.85	2.72	1.16
Leucine	1.25	0.88	2.72	1.06
Isoleucine	1.25	0.86	2.72	0.90
Proline	1.25	0.28	2.72	0.59
Serine[a]	1.25	0.6	0.0	0.0
Threonine[a]	1.25	0.1	0.0	0.0

[a]Serine and threonine were omitted from the 2:2:3 polymer. Tryptophan was present in the 2:2:1 polymer.

Source: Reprinted by permission from S. W. Fox, K. Harada, K. R. Woods, C. R. Windsor, 1963. Amino acid compositions in proteinoids. *Arch. Biochem. Biophys.*, **102**, 439–445.

2. The position of certain amino acids in the polypeptide chain was invariant.

Possibly some order based on chemistry was present.

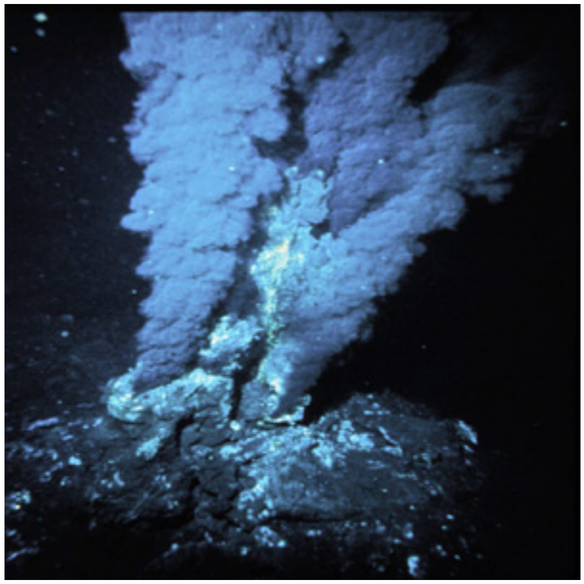
Today we know that some amino acids have very important, invariant positions in all proteins.

It follows that some proteinoid reactions, when combined in sequence with other types of reactions, could have been precursors of the first metabolic systems.

SO…under what conditions on early Earth were proteinoids made?

Thermal proteinoids could have been produced near surfaces of volcanic regions or marine hydrothermal plumes.

High temperature was maintained here.

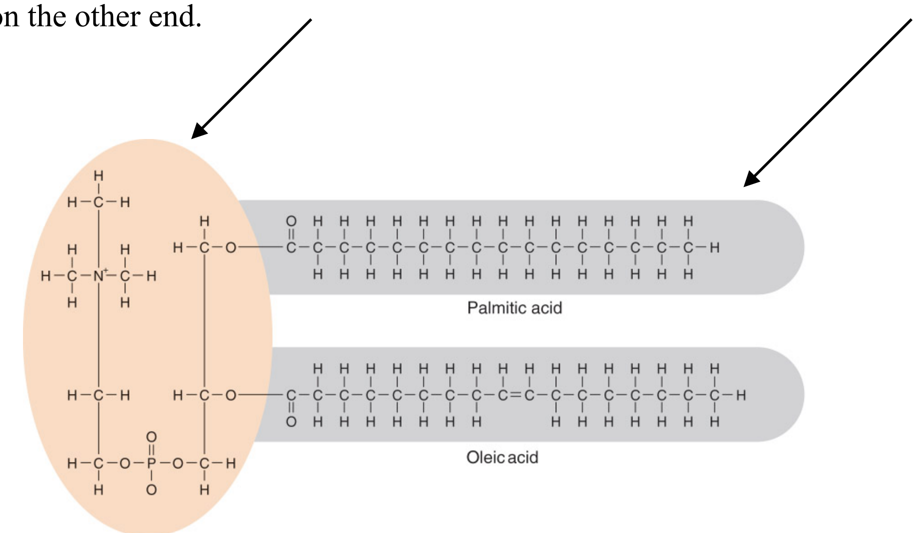


Rains or ocean waters cooled the proteinoid products and dispersed them to locations where further condensation reactions might have taken place.

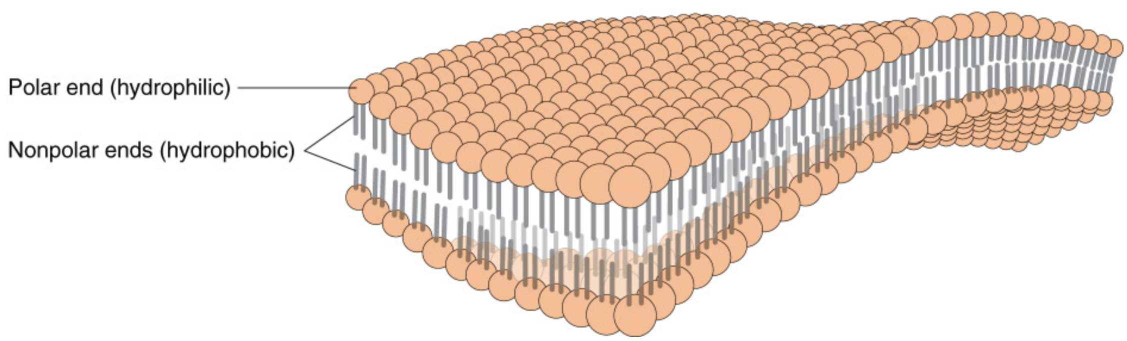
Membranes – why important for living cells?

Dependent on the structure and charge of **phospholipids.**

Phosphorous-containing group (polar) on one end, and fatty acid groups (lipids, non-polar) on the other end.

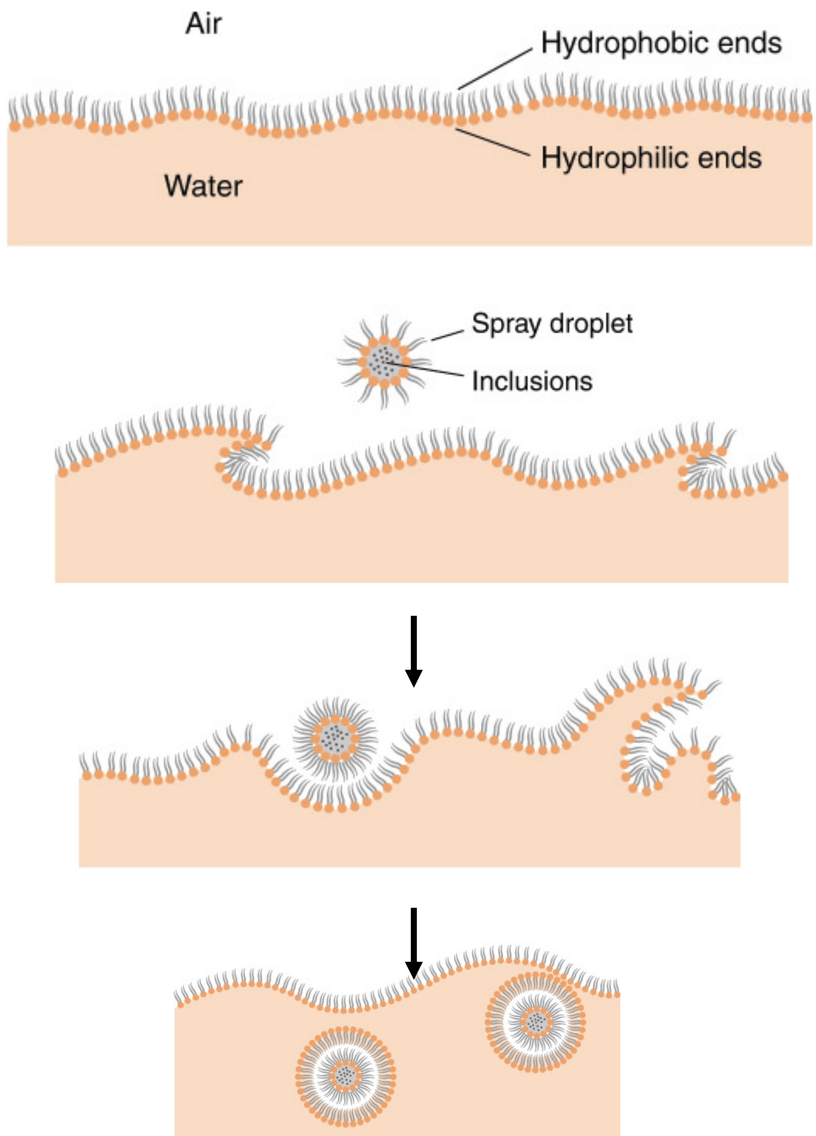


Together, phospholipds can form membranous structures in aqueous environment.



Protocells

Mechanical agitation of membranes on the surfaces of liquids likely formed numerous **protocells** – self-assembled membrane-bound system containing molecules.



The membranes/vesicles were important to the origin of life for several reasons.

1. They were **selectively permeable**

Enabled concentration differences across the membrane.

Facilitated biochemical reactions by creating appropriate conditions. **How?**

2. **Proteins** (remember thermal proteinoids) **could enter** the vesicles and cause increased entrapment of biomolcules (nucleic acids).

Facilitated protein-nucleic acid interactions (early protein synthesis?).

3. Some proteins could have **spanned the membranes** to form channels.

Lead to the evolution of proton pumps that established H^+ gradients, early energy generation (Chapter 9) and mechanisms for nutrient and waste transport.

Some forms of vesicles generated in the lab under controlled conditions have been show to exhibit characteristics consistent with "life".

Increase in size (growth)
Divide
Maintain individuality following division

Early types of membranes

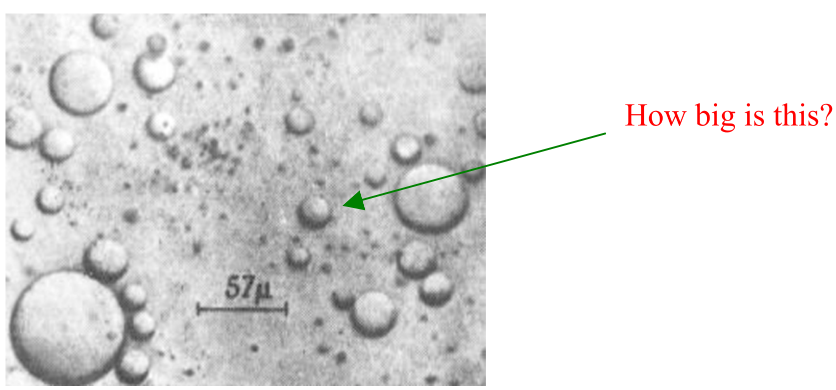
Coacervates - from the Latin *coacervare*, meaning "to assemble together or cluster".

Experimentally-produced membranes based on the aqueous aggregation of gum Arabic (simulated lipids) and histones (simulated proteins).

These can be spontaneously-produced. **Why is this important?**

Behaved much like natural cellular membranes although the structure was likely more simple than what we see in today's membranes.

Contain a colloid, rich in organic compounds, surrounded by a tight skin of water molecules.



From: http://www.daviddarling.info/encyclopedia/C/coacervate.html

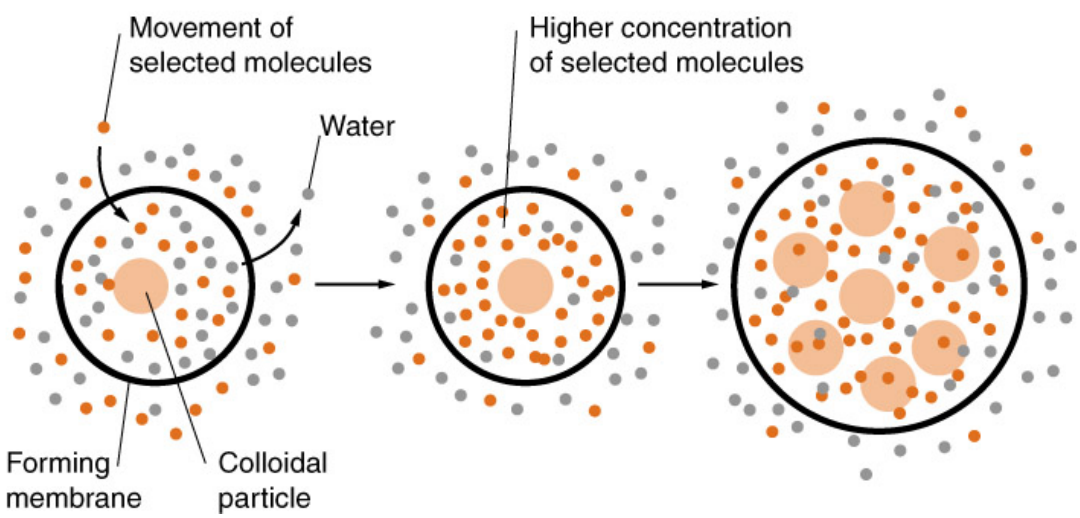
Capable of **selective uptake** of substances from the environment.

In Oparin's view this amounted to an elementary form of metabolism.

What compounds were around to "take-up"?

Primitive enzymes, RNA, e' carriers, photosynthetic pigments.

These substances could be trapped as well (coacervate serves as an early vacuole).



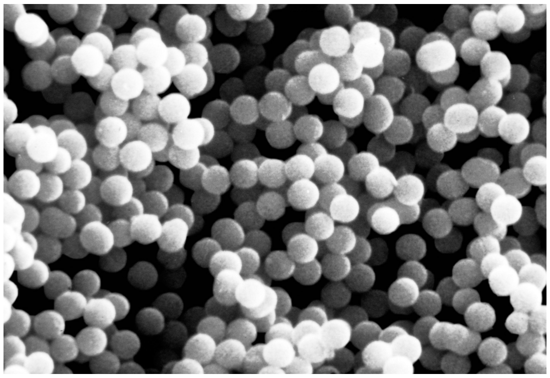
Research showed that cocervates could incorporate enzymes that perform vital cellular functions such as degradation and synthesis reactions.

Coacervate growth was possible, but they maintained limited **division capabilities**.

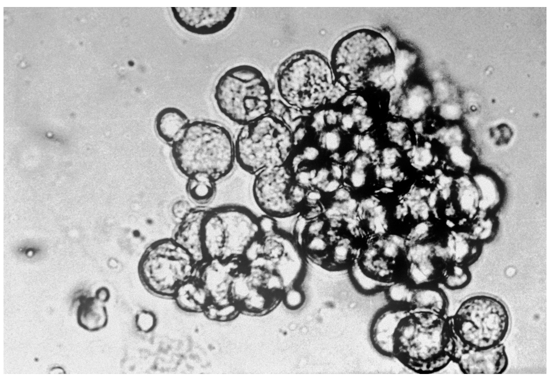
Why is this a limitation for life?

Microspheres

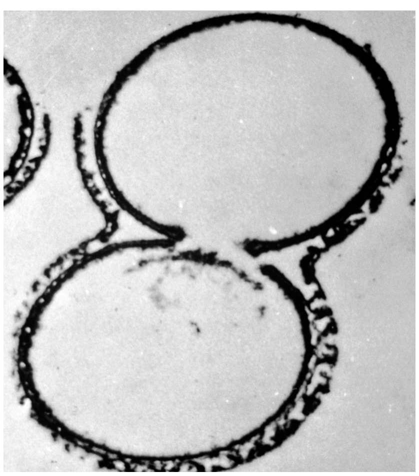
Small spheres formed when thermal proteinoids were heated in water, and then allowed to cool.



Proteinoid microshperes



Microshperes showing evidence of outgrowth and budding.



Microshperes showing evidence of double membrane and budding.

While not true, functioning cells, microspheres possess several characteristics that justify them as a concept cell (protocell).

1. Inner and outer boundaries resemble lipid bilayer of today's membranes.

2. They can self-assemble.

3. Grow by a process similar to **fission and budding** in today's cells.

4. Capable of selective uptake of substances from the environment.

5. Capable of **information transfer**.

   Proteinoid particles can move through junctions between microspheres.

Thus far, we have described several potential structures, reactions, and bioprocesses that could have occurred on early Earth to facilitate the beginnings of life.

How could organization of biochemical reactions and macromolecule self-assembly have occurred amidst all of the chaos that characterized the conditions of early Earth?…**Selection**.

THE ORIGIN OF SELECTION

What are the requirements of "selection"?

Cell-like structures (protocells) represented the first multi-chemical individuals interacting in their environment.

The group of individuals likely formed a population on which selection could act.

Protocells that exhibited the organizational and metabolic features that would **best ensure successful/efficient growth and division** would increase in relative frequency or area occupied.

Overall, selection occurs when several conditions are reached:

1. A population of individuals exists.

2. Individuals are dependent on the absorption and transformation of environmental materials into their own material.

3. Individuals differ in metabolic efficiency.

4. Availability of materials and energy is limited.

All this boils down to the fact that not all individuals will survive.

Selection bridged the gap between chemical evolution (non-reproductive molecules, coacervates, microspheres) and biological evolution (inherited differences among efficiently reproducing organisms).

Early selection was most likely confined to individual protocells that could obtain and transform the most resources from the environment with the least energy expenditure…and sustain this activity.

Survival of a group would have involved the most efficient transfer of whatever molecular "stuff" that allowed a competitive advantage to the offspring.

Selection allows for a succession of accumulated adaptations.

Funnel-down process whereby the most adaptive traits are concentrated in each successive generation.