DNA NOTES: History, Structure, Replication

DNA History

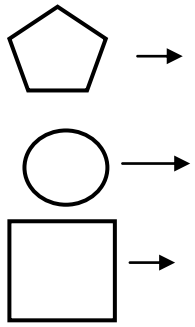
It took many years and the work of many different scientists to discover that _____ is the genetic material

Friedrich Meischer (_____)

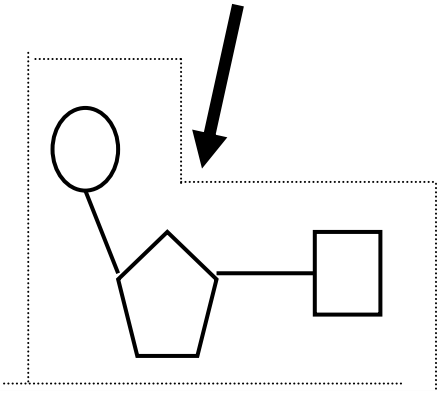
- As he studied _____ for clues to understand heredity, he was the first to isolate a material called _____ from the nucleus of the sperm.
- Chemical tests revealed that nuclein was part _____ and part _____
- Another clue that made him go "Hmmm" was when he later isolated nuclein from the nuclei of white blood cells in _____-soaked medical bandages.

P.A. Levene (_____)

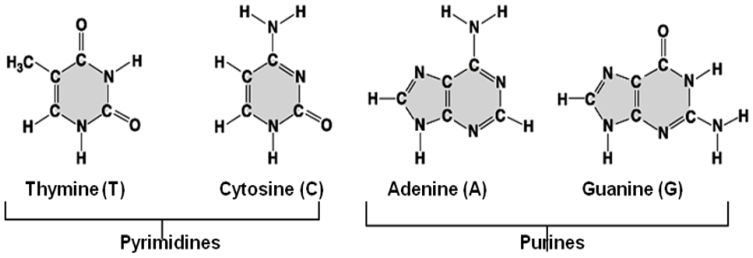
- Discovered that DNA is made from smaller ____-shaped "building blocks" called _____ that have ____ chemical parts:



1. _____
2. _____
3. _____



- DNA has four kinds of N-bases: _____



Fred Griffith (_____)

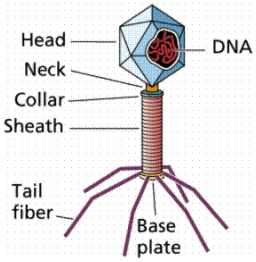
- While working on a cure for _____ with mice, he accidentally discovered the mystery of bacterial transformation

Griffith's 4-part experiments

- 1) **live <u>pathogenic (smooth = S)</u> strain of *bacteria* =** _____
- 2) **live <u>non-pathogenic (rough = R)</u> strain of *bacteria* =**_____
- 3) **heat-killed <u>pathogenic (S)</u> *bacteria* =** _____
- 4) **mix heat-killed <u>pathogenic (S)</u> & living <u>(R)</u> *bacteria*=** _____
- **<u>Explanation</u>? How could there be living _____ bacteria??**
- **2 Hypotheses:**
  - **1)** _____
  - Somehow the dead S bacteria came back to life ???
  - **2)** _____
  - Some chemical factor in the dead S bacteria was able to communicate with and transform the non-harmful R bacteria into killer S bacteria
- Fred Griffith would spend many more years in his lab trying to identify this mysterious "_____"

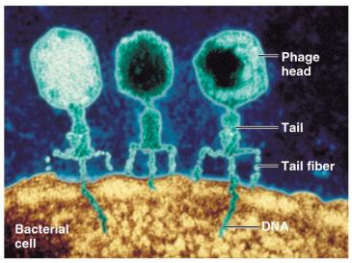
Avery, McCarty & MacLeod (_____)

- purified both DNA & proteins from *Streptococcus* pneumonia bacteria
  - which will _____ non-pathogenic bacteria?
- injected _____ into bacteria
  - _____
- injected _____ into bacteria
  - _____
- _____ is the "Transforming Factor"



Hershey & Chase (_____)

- classic "blender" experiment
- worked with _____ viruses that infect bacteria
- grew phage viruses in 2 media, radioactively labeled with either
  - ^{35}_____in their proteins
  - ^{32}_____ in their DNA
- infected bacteria with labeled phages



Draw a diagram below to summarize the famous "blender" experiment

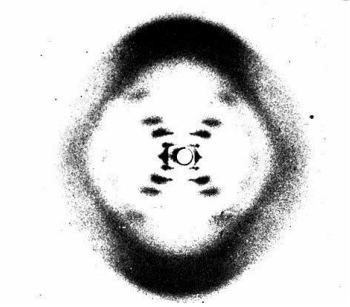
Blender experiment conclusions

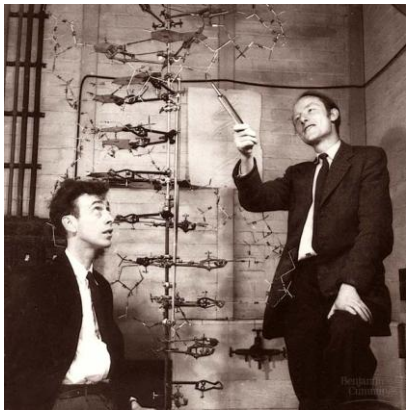
- Radioactive phage & bacteria in blender
  - ^{35}S phage = indicates protein
- radioactive proteins stayed in _____ ….. therefore protein _____ enter bacteria
  - ^{32}P phage = indicates DNA
- radioactive DNA found in _____ ….. therefore DNA _____ enter bacteria
- Confirmed _____ is "transforming factor"

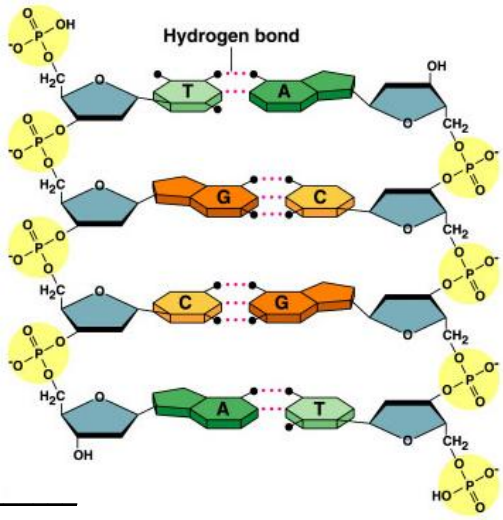
Chargaff (_____) Chargaff's big clue: Base Pair RATIOS in DNA A = _____ C = _____

Another clue: Franklin & Wilkins (_____)

- _____ pictures of DNA suggest that it consists of 2 chains twisted in **a helix**



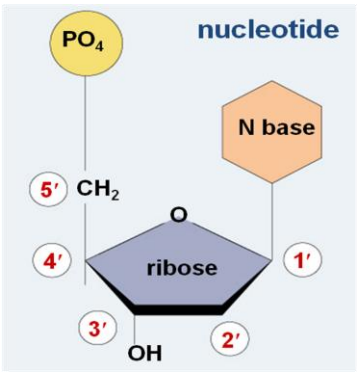


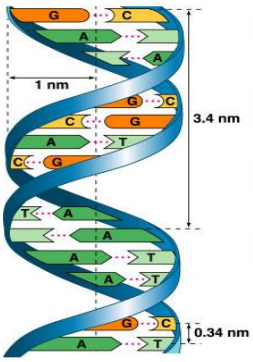


Watson and Crick (_____)

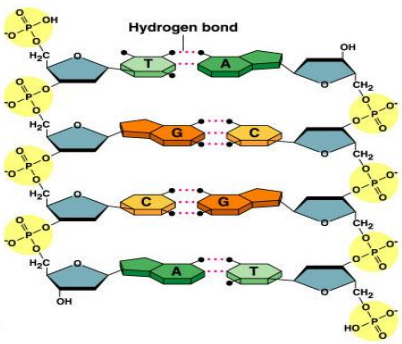
- Win the "race" to build the _____
- _____Model = 2 DNA chains that spiral like a "twisted rope ladder"
- ladder sides formed by alternating 5-C sugars & phosphates = _____
- ladder rungs formed by nitrogen base pairs held together by _____ bonds
  - A – T (____ H bonds)
  - C – G (____ H bonds)

Double helix structure of DNA : the structure of DNA suggested a mechanism for _____ by the cell

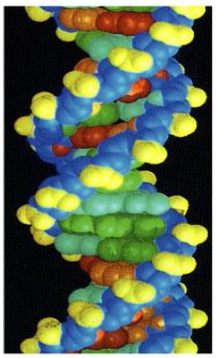




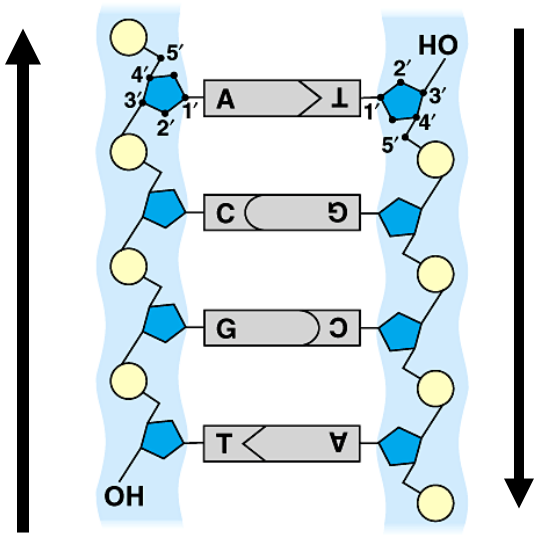
(a) Key features of DNA structure



(b) Partial chemical structure


(c) Space-filling model

- Each strand of the double helix is oriented in the opposite direction = _____



DNA REPLICATION

- WHAT ? →a process that produces two DNA molecules _____ to the original.
- WHY? → so when cells _____ they can give each daughter cell its own identical copy of the DNA blueprint
- WHEN? → right _____ cell division as new body cells are made:
  - _____
  - _____
  - _____

→Producing _____ or _____ (gametes)

- **HOW?**

1)DNA Helicase enzymes bind to the DNA at different locations and then _____ and _____ the 2 strands

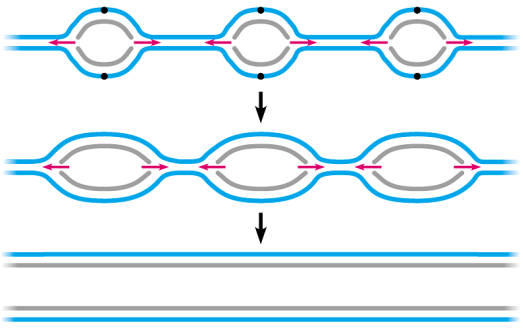
2)DNA Polymerase enzymes use each old strand as a _____ to assemble the new strand

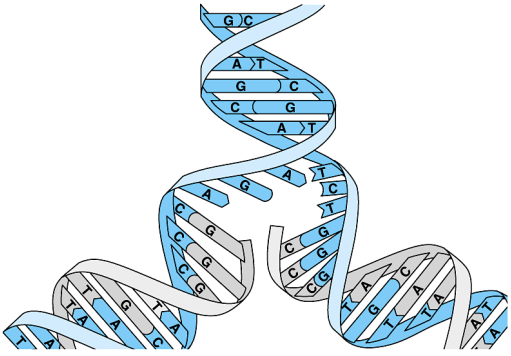
3)DNA Ligase enzymes _____ together DNA _____ until long, continuous strands are formed

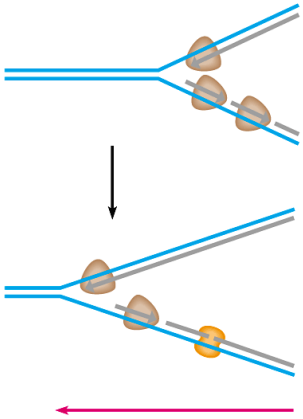
- DNA replication is a semi-conservative process = 1 strand is _____ and 1 strand is _____

10.5 DNA replication: A closer look

- DNA replication begins at many different sites, so… the whole molecule can be copied _____







- Because DNA is Antiparallel and Polymerase only builds new DNA in _____ direction (5' → 3'), this affects how DNA daughter strands are synthesized:
  1 side _____ & 1 side in _____

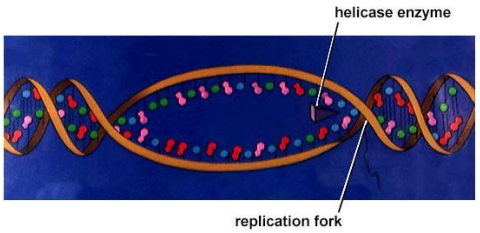
- The fragments on one side are linked together by _____ enzymes

Replication Details:

Step 1: Open a Replication Bubble

- Helicase _____ & _____ the 2 strands
  - stabilized by _____

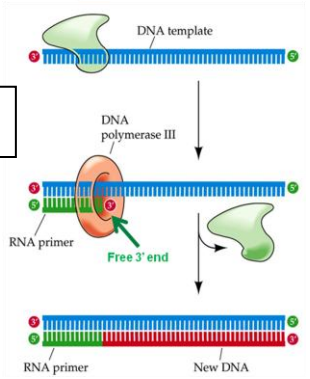
1



Step 2: Priming DNA synthesis

- DNA polymerase I can only attach a new DNA nucleotide on a _____
  - cannot start building a new DNA strand without a free 3' end
  - short _____ with a free 3' end is built first by _____

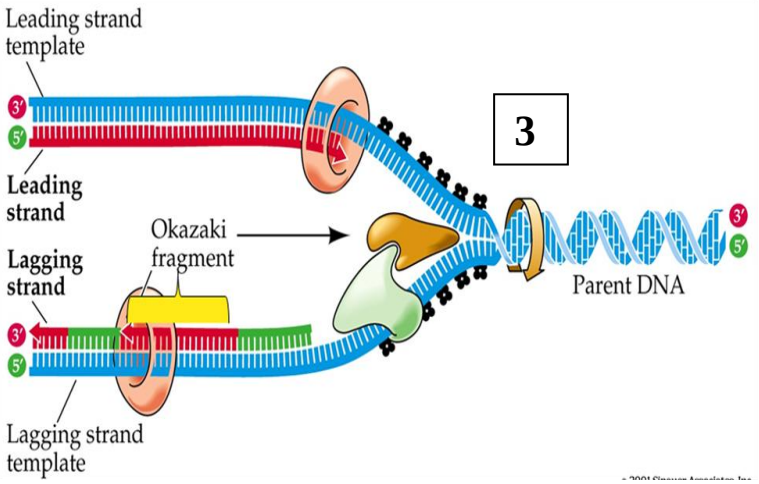
2



Step 3: Polymerase I builds Leading & Lagging strands

- Leading strand- _____ synthesis
- Lagging strand- _____ fragments- joined by _____

3



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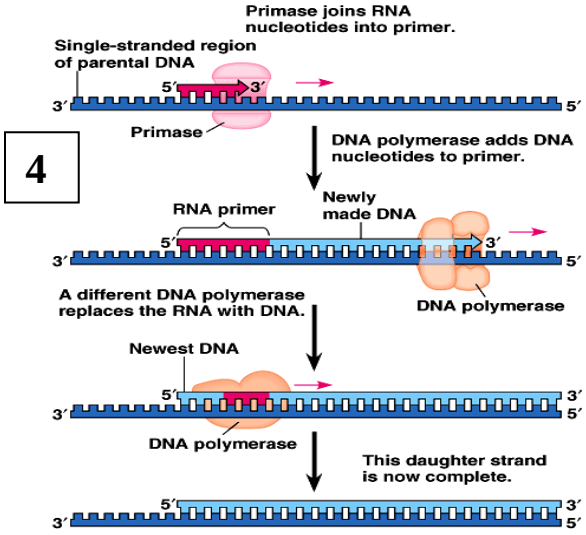
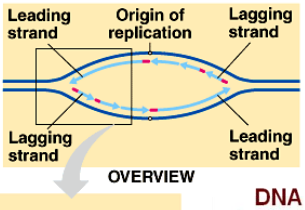


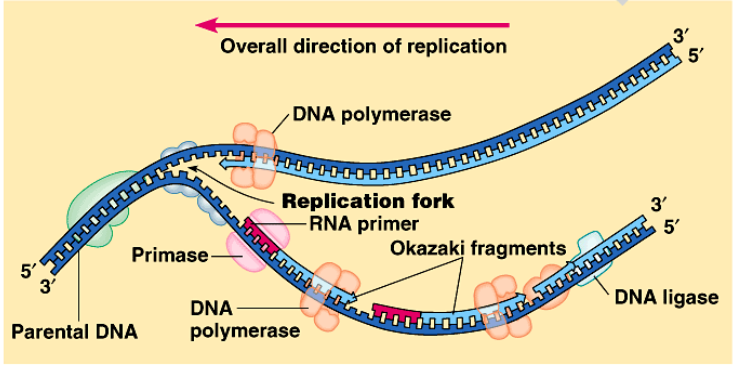
Step 4: Polymerase II cleans up primers

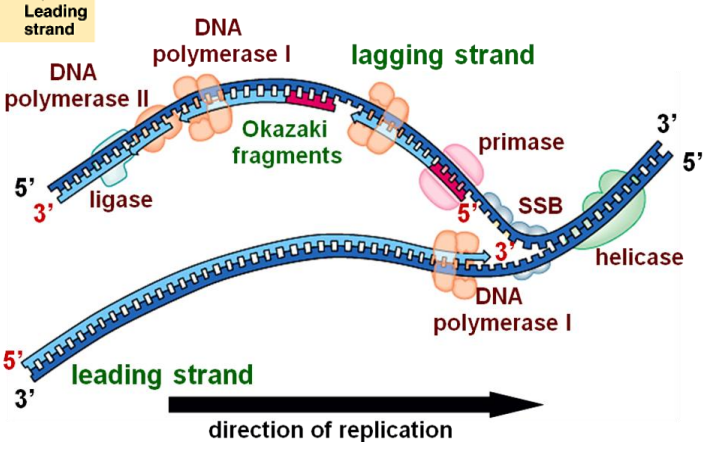
- DNA polymerase II removes sections of _____ primer and replaces with _____ nucleotides

Step 5: Ligase <u>links</u> all DNA fragments

5







Replication Speed & Accuracy

- Because the DNA molecule is copied so _____ (~50 new letters per second in mammals), occasionally the _____ letters are paired together
  - Most of these mismatch errors are fixed by the Polymerase enzyme as it backs up and inserts the correct matching base.
  - However, 1 mistake or mismatch every 1 _____ letters does not get fixed and remains to be copied
- An army of **repair enzymes** constantly _____ the new DNA strands and _____ most (99.9%) mistakes.
- Any unfixed DNA mistake = _____

Replication enzymes

- helicase
- DNA polymerase I
- primase
- DNA polymerase II
- ligase
- Repair Enzymes

And in the end…

- Ends of chromosomes are _____ with each replication
  - an issue in aging?
  - ends of chromosomes are protected by _____

Telomeres

- Expendable,_____ sequences at ends of DNA
  - short sequence of bases repeated 1000s times
  - TTAGGG in humans
- _____ enzyme is active in certain cells
  - enzyme extends telomeres allowing for more cell divisions
  - prevalent in cancers
    - Why**?**