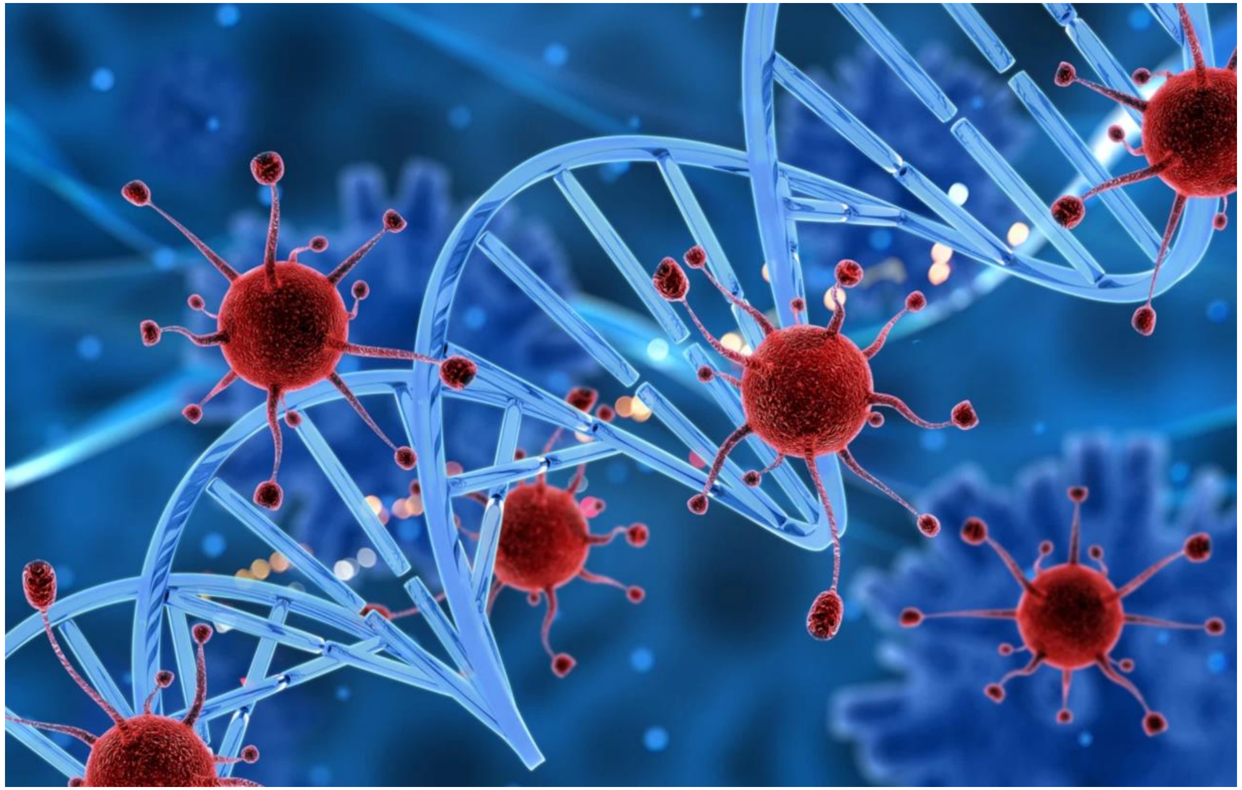
Lessons 9/10
Genes, DNA rules and DNA replication

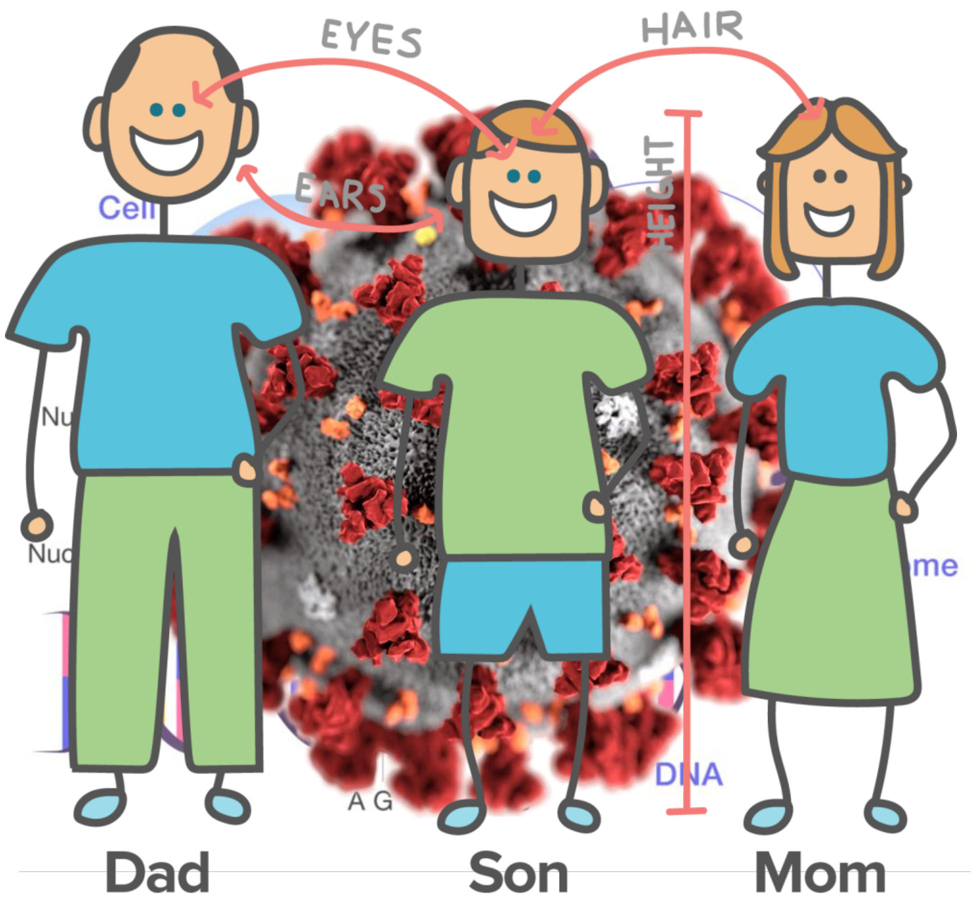


Info transfer

- Information transfer in biology
  - key, crucial aspect of modern biology
- You need to know this material in order to understand anything at a higher level in biology

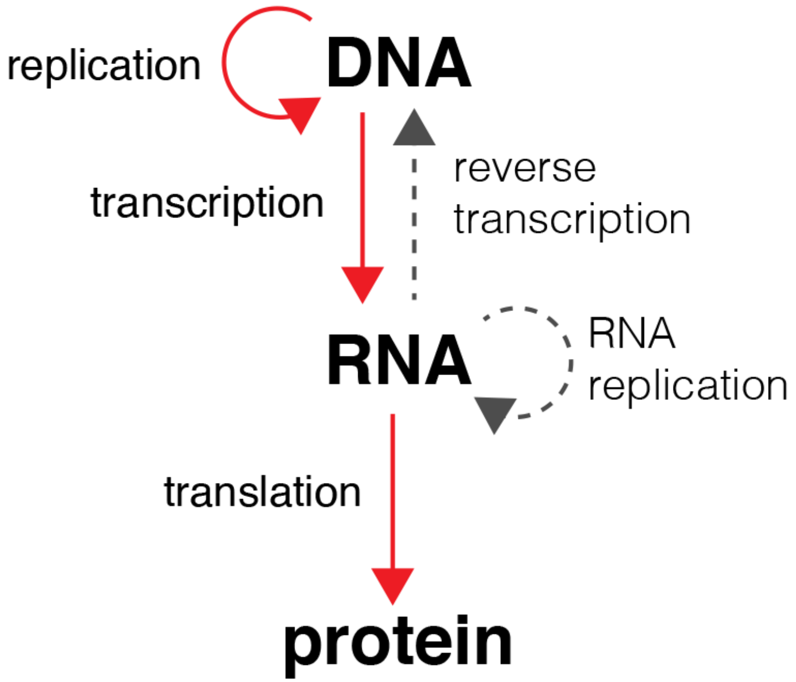
Genes

- What is a **gene**?
- A gene is a piece of nucleic acid that contains instructions to build a functional product (a protein)
- Genes are usually DNA (but sometimes RNA, e.g., in RNA viruses like SARS-CoV-2)
- Genes are the blueprints of life — they define how cells function
- They are inherited from parents and passed across generations
- 🛠 Engineering Analogy: Think of genes as software code that provides instructions to build functional molecules



Molecular biology and information transfer

- Molecular biology relies on information transfer
- The MB notion of information transfer:
- **REPLICATION**: DNA (gene) replicates
- **TRANSCRIPTION**: DNA is copied into RNA
- **TRANSLATION:** RNA is translated into a protein
- This constitutes the **CENTRAL DOGMA OF MB** (already mentioned in Lesson 3)



DNA rules

- DNA base pairing rule
  - A makes **2 hydrogen bonds** with T
  - G makes **3 hydrogen bonds** with C
- Base pairing is associated with **complementary DNA strands**

5’A A T C 3’
3’T T A G 5’

DNA replication

- **DNA replication** is the mechanism by which genes (DNA) make more of themselves before they undergo cell division (mitosis or meiosis)
- Takes place in the cell nucleus
- DNA replication occurs before cell division to pass genetic information to new cells
- Because of strict base pairing rules, each strand of DNA serves as a template to make an exact copy

DNA replication – the semiconservative model

- Accordingly, each new DNA molecule resulting from replication contains **one original (old) strand and one newly synthesized strand**
  - ✅ This is called **semiconservative replication**
- Semiconservative replication:
  - Ensures **genetic continuity** across generation
  - **Minimizes errors** during DNA replication

🛠 Engineering Analogy: Imagine a cloud-based backup system

✅ Each new DNA molecule keeps one original strand (like mirrored storage) while generating a new copy

DNA replication main stages

1. DNA strands separate

5’ – – – – – 3’

3’ + + + + + 5’

→

5’ – – – – – 3’

+

3’ + + + + + 5’

DNA replication - **a semiconservative process**

2. Both strands are used as templates and copied

5’ – – – – – 3’

+

3’ + + + + + 5’

5’ – – – – – 3’

3’ + + + + + 5’

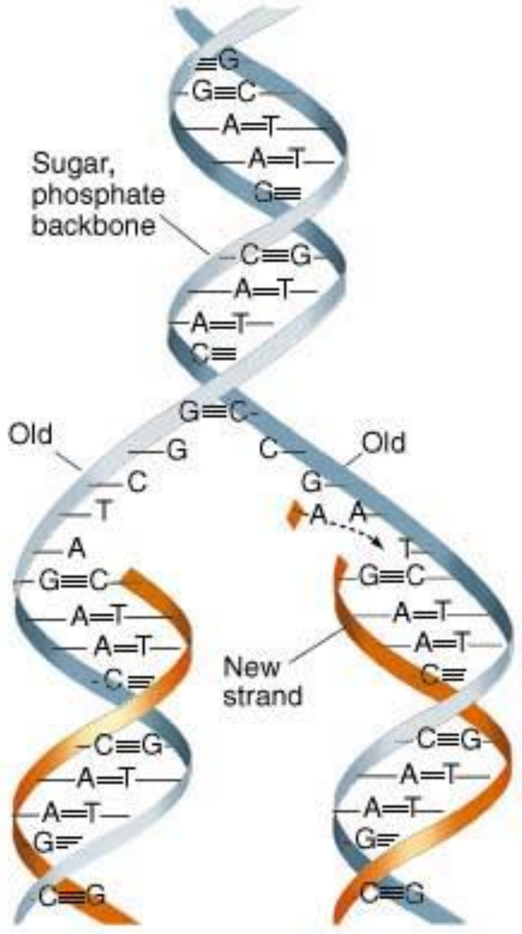
+

5’ – – – – – 3’

3’ + + + + + 5’

DNA replication

- The process is absolutely dependent on the major DNA rule: BASE PAIRING (BP)
  - Only because of BP (complementarity) you can:
    - Take the two DNA strands apart
    - Fill them in
    - Come up with two new DNA molecules identical to the parent DNA
- **<u>DNA replication occurs from each 3' end of each strand</u>**
- **DNA replication requires a highly specialized and efficient crew**



DNA replication – Unwinding the duplex

- The first step in DNA replication is DH unwinding
    - This action is performed by enzymes called **helicases**
        - Unzip all H bonds leading to strand separation
- The second step is stabilizing the two single strands to prevent rejoining
    - This action is performed by a group of proteins called single-strand DNA binding proteins (**SSBPs**)

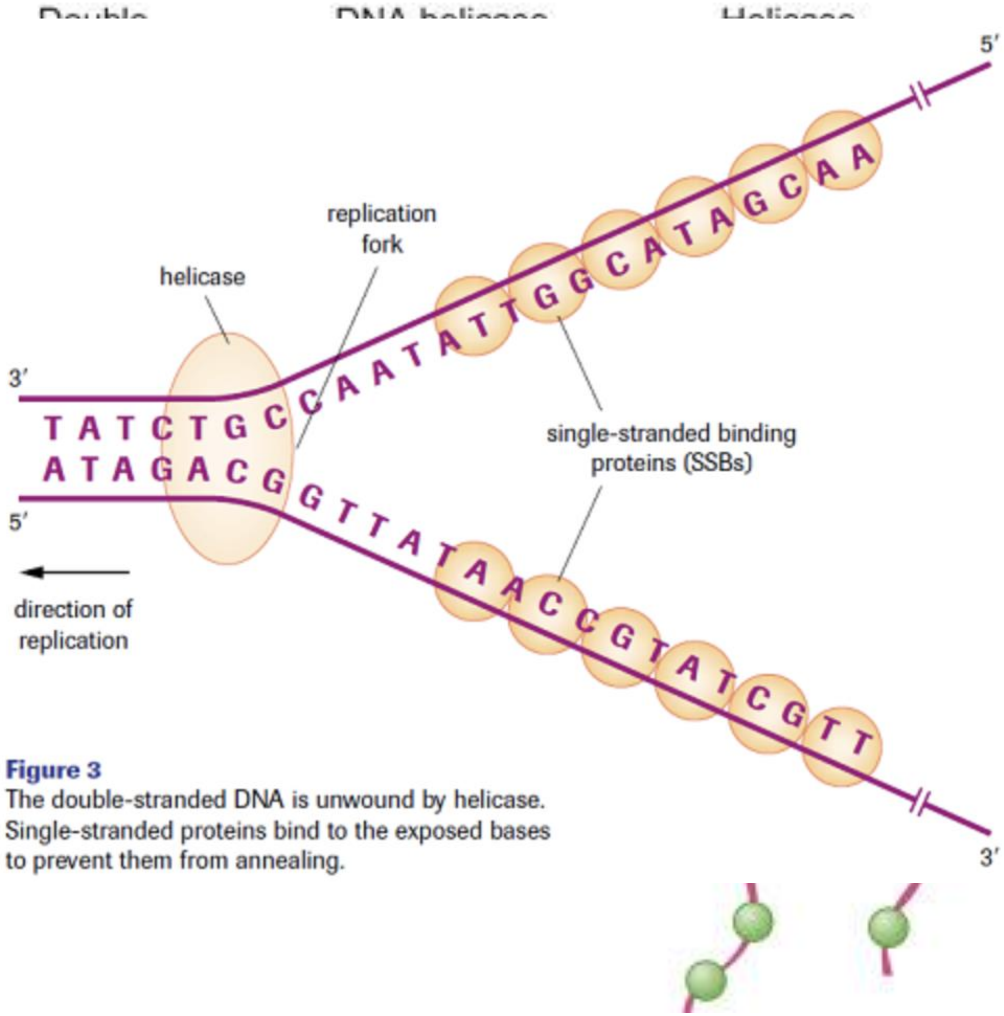
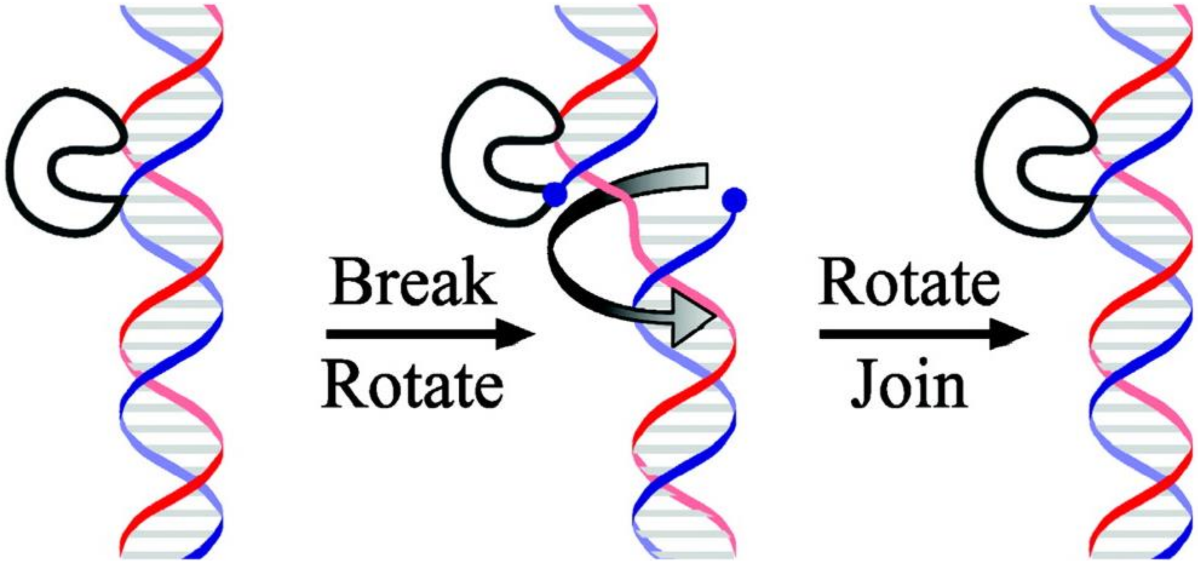


Figure 3
The double-stranded DNA is unwound by helicase. Single-stranded proteins bind to the exposed bases to prevent them from annealing.

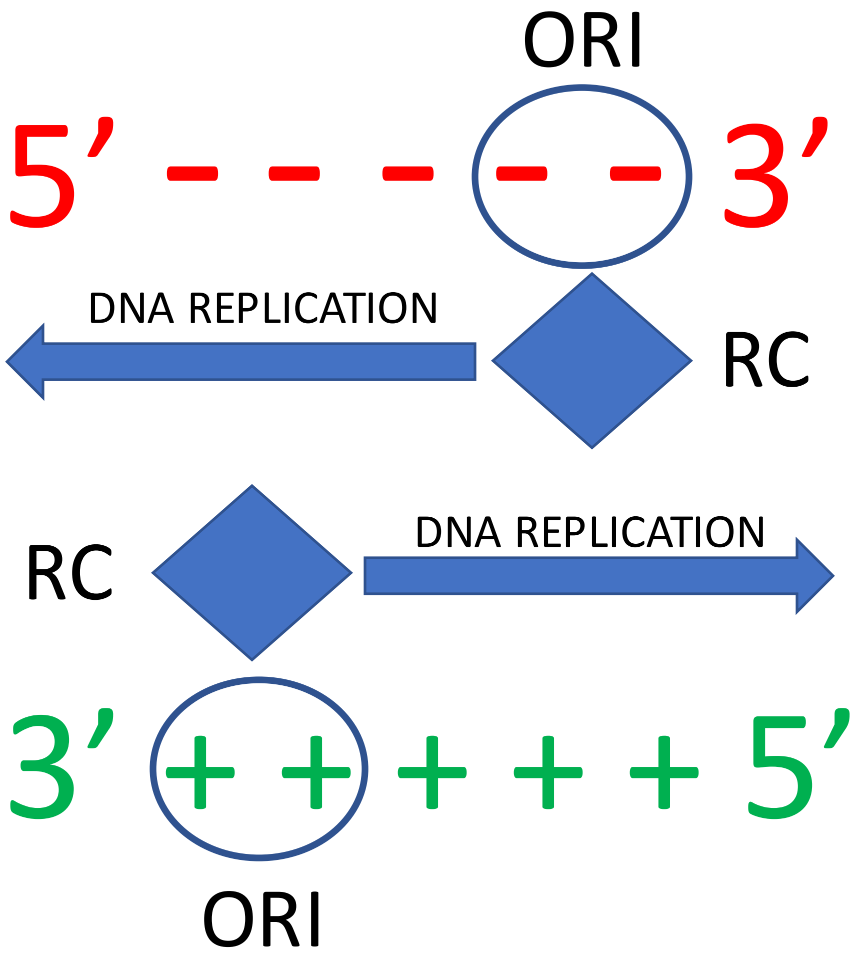
DNA replication – Unwinding the duplex

- DH unwinding is more complex
  - The DNA DH is twisted
  - As it gets unzipped, these twists get pushed together, creating tension along the backbone
  - If not relaxed, the DNA backbone would become kinked preventing helicase from continuing its job
- Another enzyme, called **topoisomerase**, prevents this by:
  - Breaking backbone covalent bonds
  - Allowing for tension release
  - Resealing the DNA backbone



DNA replication – it takes a lot more than two to tango

- DNA replication requires a ”running start”
  - Specific nucleotide sequences within the chromosome called **origins of replication (ORI) (or DNA Primers)** where replication begins
    - There will be one ORI on each DNA strand
    - These are AT-rich sequences
  - A specific set of proteins recognizes the ORI and recruits other enzymes (replication complex - RC) to do the job
  - Replication occurs in both directions away from the ORI
    - Conducted by two enzyme complexes that move away from each other along the DNA



DNA replication – Houston, we have a problem here….

- Within the RC, **DNA polymerase** is the enzyme that reads the code in the 3’-5’ direction and build the new DNA strands
- But DNA POL cannot start replication on its own ❌
  - It can only extend an existing strand, NOT create one from scratch
  - It needs a helper enzyme to get the new strand started

🛠 Engineering Analogy: Think of it like a 3D printer - it can build layers but needs a base to start

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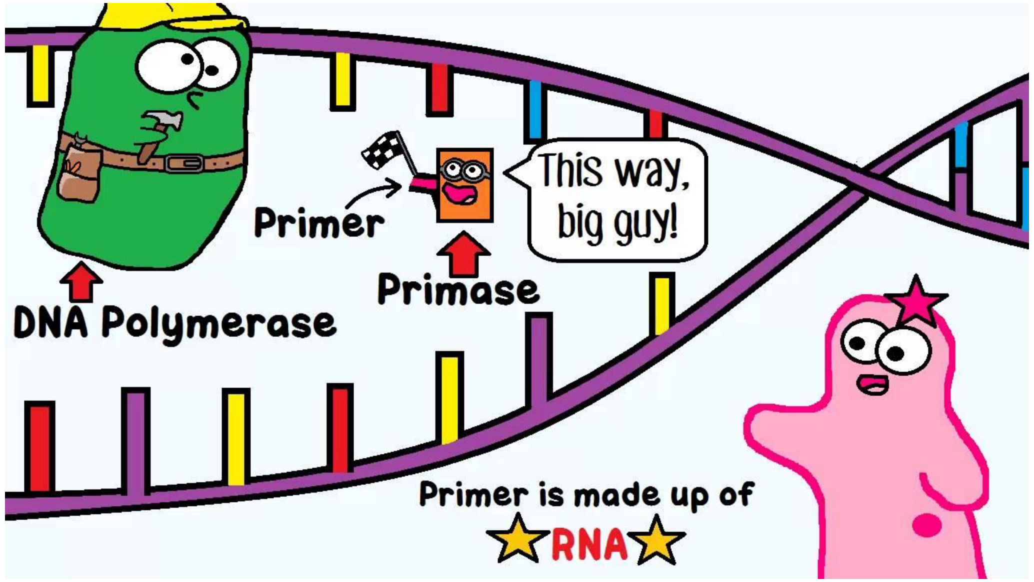
Engineering Analogy: Think of it like a 3D printer - it can build layers but needs a base to start

- This helper enzyme is the **DNA primase**
  - An **RNA polymerase** that builds RNA strands and that can start a strand *per se*



DNA replication – DNA Primase to the rescue!

- DNA Primase is an enzyme that creates **RNA primers** (short starter sequences)
- These primers give DNA Polymerase a starting point
- Once primers are placed, DNA Polymerase can begin DNA replication

🛠 Engineering Analogy: Think of Primase as a bootloader - it initiates the startup process before the operating system (DNA Polymerase) takes over

DNA replication – DNA Primase to the rescue!

- The DNA primase
  - Synthesizes two short pieces of RNA (5-to-10 bp long) called **RNA primers**
    - These RNA primers are complementary to the ORIs (DNA primers) located on the two DNA strands
  - Attaches (**hybridizes**) the DNA and RNA primers via BP (complementarity)

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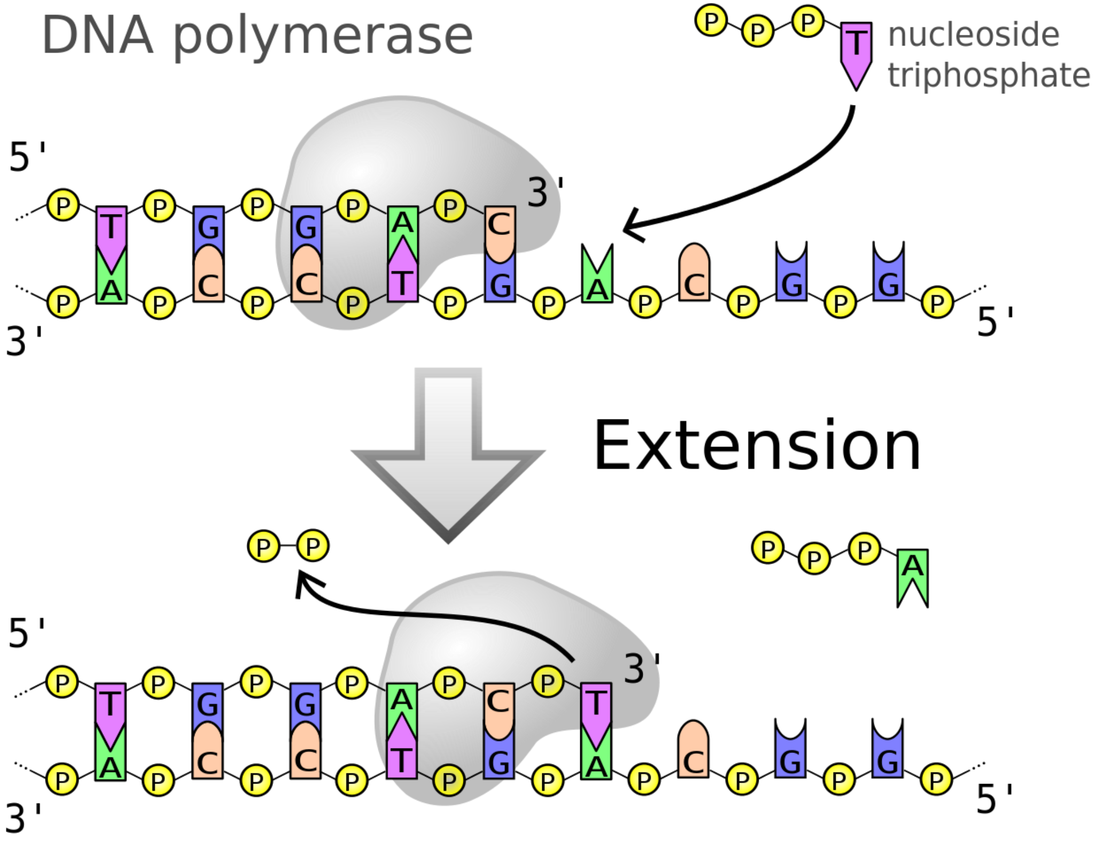
- Once RNA primers are in place, DNA POL can start synthesizing DNA by attaching the correct nucleotides to the 3' ends of the primers (again via BP complementarity)

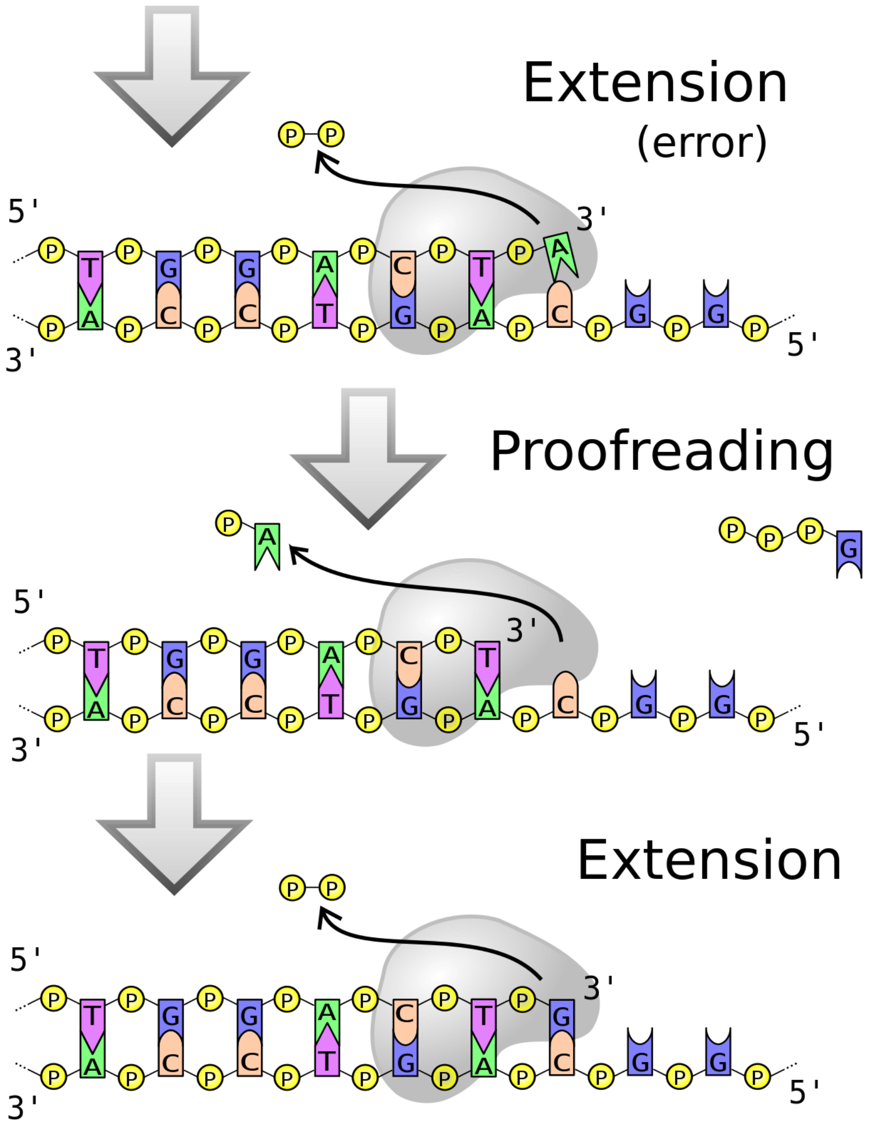
DNA POL Proofreading

- During the DNA synthesis, DNA POL moves from 3’ to 5’
  - The 5’ end of the new nucleotide will be added to the 3’ end of the growing chain
  - The new DNA strands grows in the 5’ to 3’ direction :)



DNA POL Proofreading

- DNA POL do make mistakes at a rate of about 1 per every 100,000 nucleotides
- That might not seem like much but
  - We humans have 6 billion base pairs in each diploid cell
    - that would amount to about 120,000 mistakes every time a cell divides
- DNA POL work is supervised by a proofreading mechanism
- 🛠 Engineering Analogy: Think of this as a real-time spell checker that fixes errors as you type



DNA SEMICONSERVATIVE REPLICATION