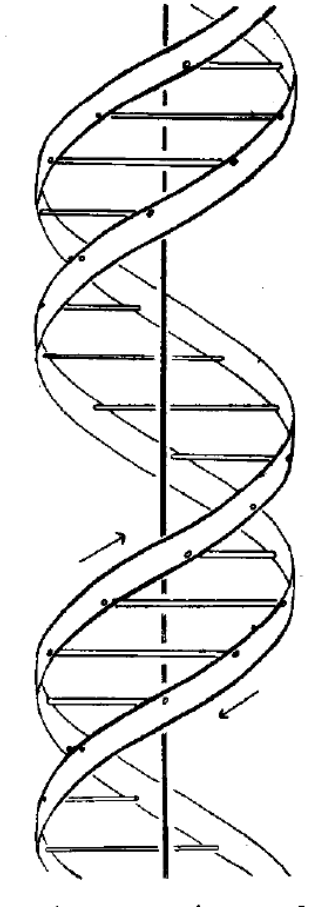


Molecular Structure of Deoxypentose Nucleic Acids

James Watson and Francis Crick, Nature 171, 737-738, 1953 (April 25)

"It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

⬇ ⬇ ⬇ ⬇

Genetical Implications of the Structure of Deoxyribonucleic Acid

James Watson and Francis Crick, Nature 171, 964-967, 1953 (May 30)

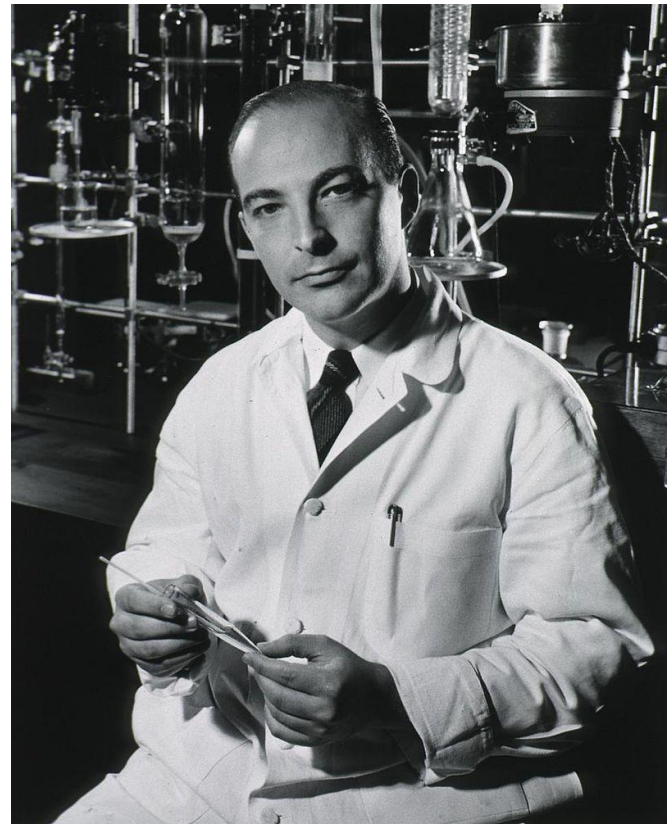
"Whether a special enzyme is required to carry out the polymerization, or whether the single helical chain already formed acts effectively as an enzyme, remains to be seen."

Arthur Kornberg…

In 1956 he isolated the first DNA polymerizing enzyme, now known as DNA polymerase I.

This won him the Nobel prize in Physiology or Medicine,…in 1959.

"for his discovery of the mechanisms in the biological synthesis of deoxyribonucleic acid."



"Half of what we know is wrong,…
the purpose of science is to determine which half."

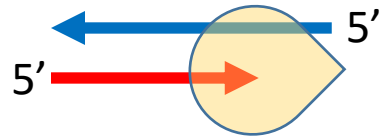
3 THINGS….

…your students need to know…
…to understand semi-discontinuous DNA replication:

1. **A DNA strand has a polarity …..i.e., a 5’ to 3’ direction.**

2. **The two strands of double-stranded DNA are antiparallel.**

3. **DNA polymerase synthesizes DNA in the 5’ to 3’ direction.**



A solid understanding of DNA replication sets your students up to understand the Sanger DNA sequencing method ……. and PCR… and ???

A couple more THINGS….

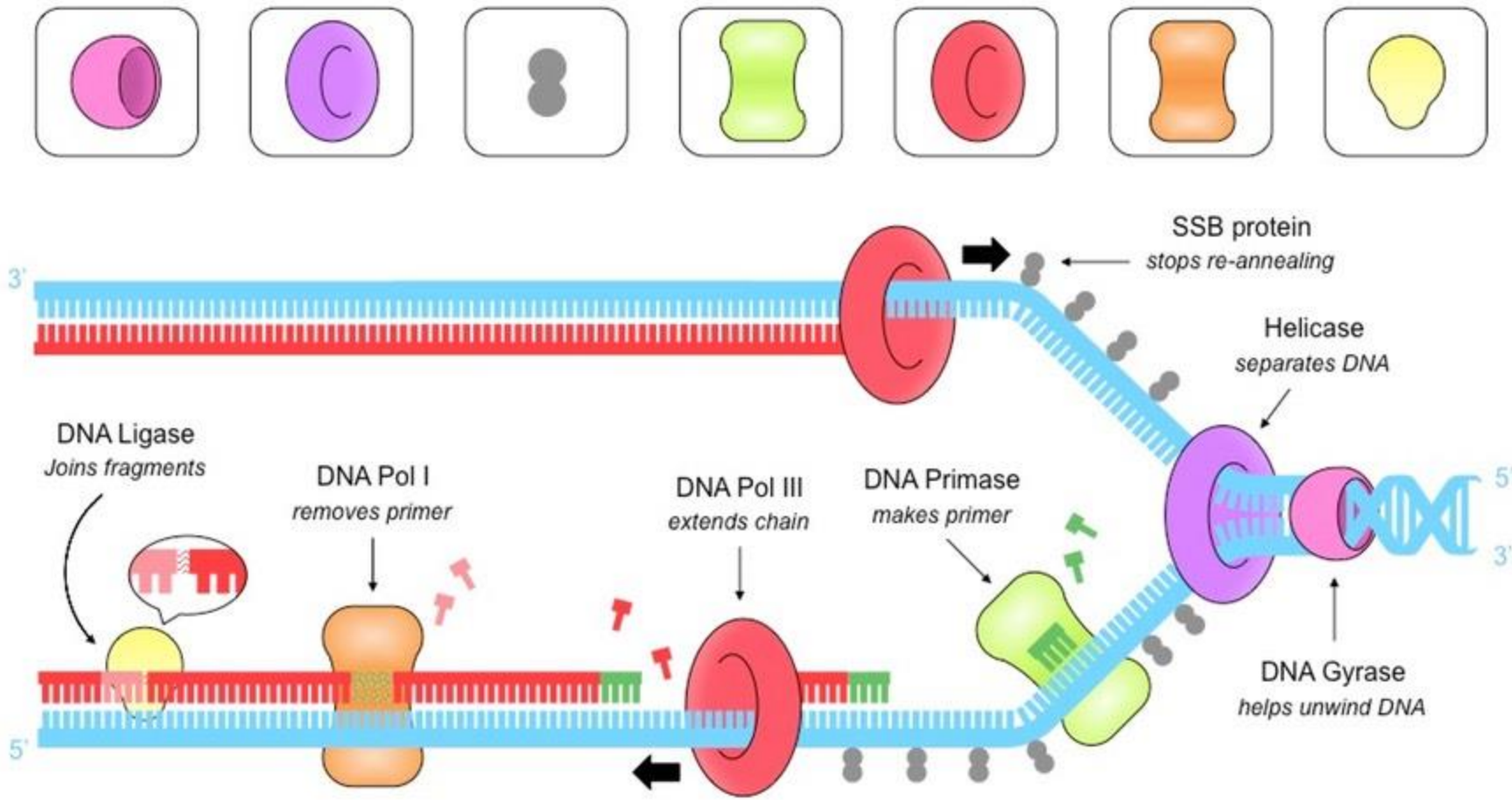
…you might need/want to know.

4. **DNA polymerase can only add another nucleotide to a 3’-hydroxyl primer.**

5. **In contrast, RNA polymerase can begin transcribing RNA without a primer.**

6. **Most DNA polymerases have a proofreading activity.**

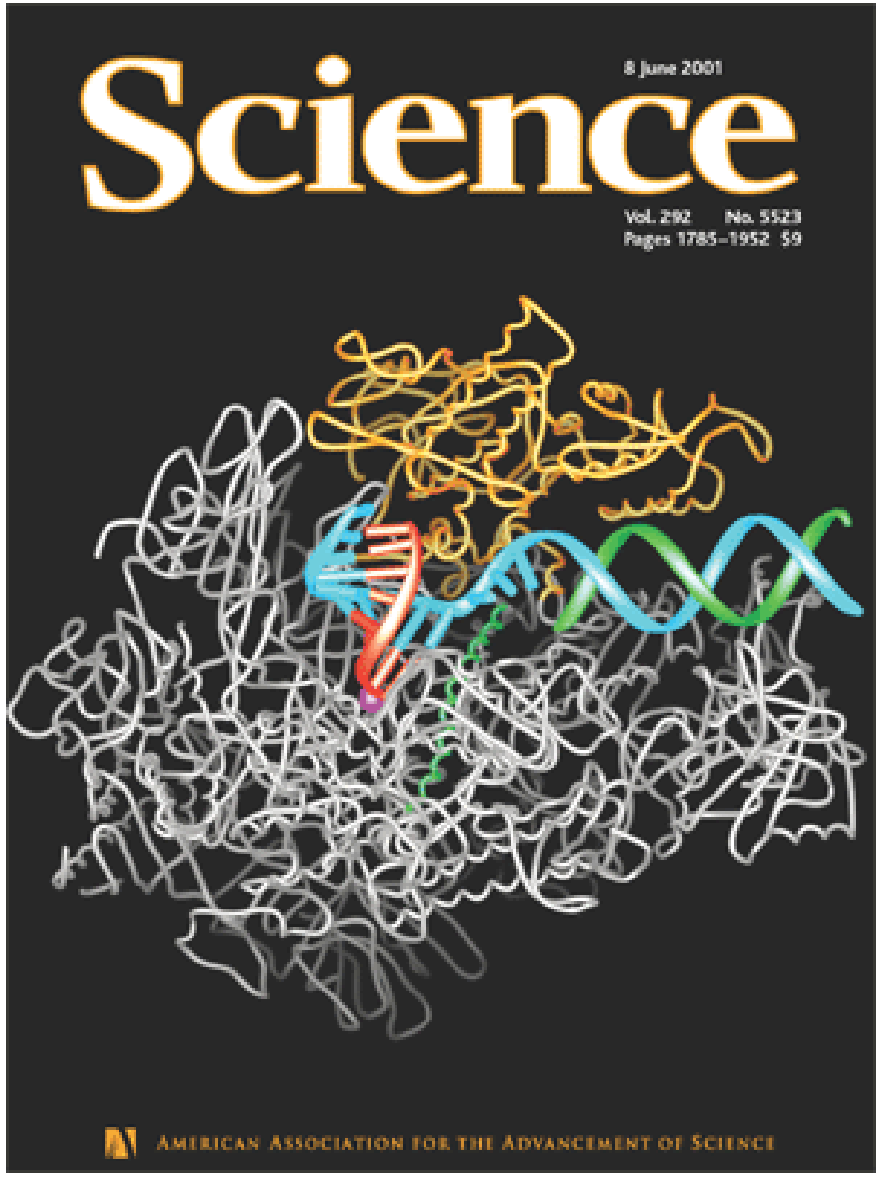
7. **Some DNA polymerases have a 5’→ 3’ exonuclease activity. This is used to remove the RNA primers from Okazaki fragments**

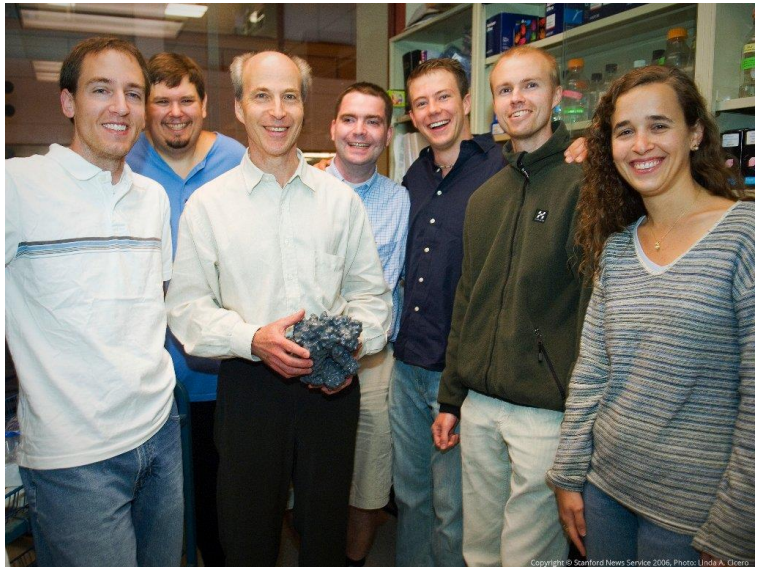

SSB protein
stops re-annealing
Helicase
separates DNA
DNA Ligase
Joins fragments
DNA Pol I
removes primer
DNA Pol III
extends chain
DNA Primase
makes primer
DNA Gyrase
helps unwind DNA
3'
5'
5'
3'

2006 Nobel Prize in Chemistry

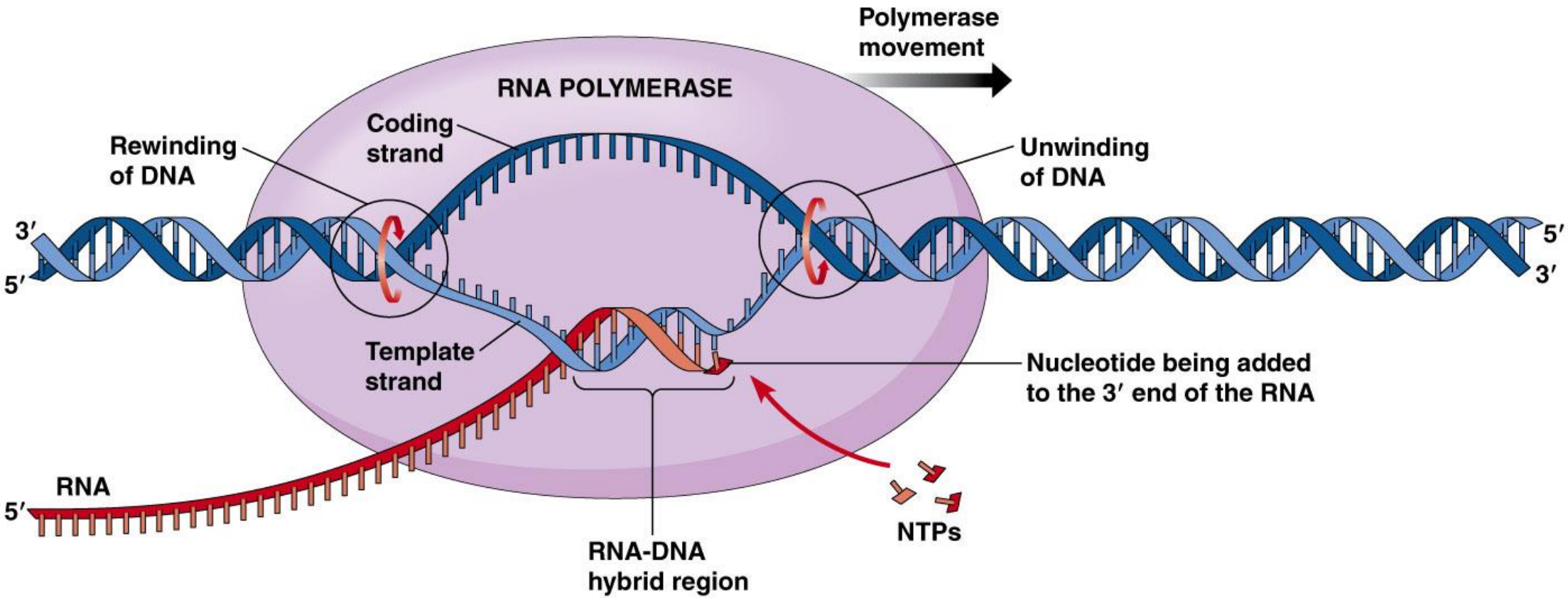
…to Roger Kornberg….

“for his studies of the molecular basis of eukaryotic transcription”

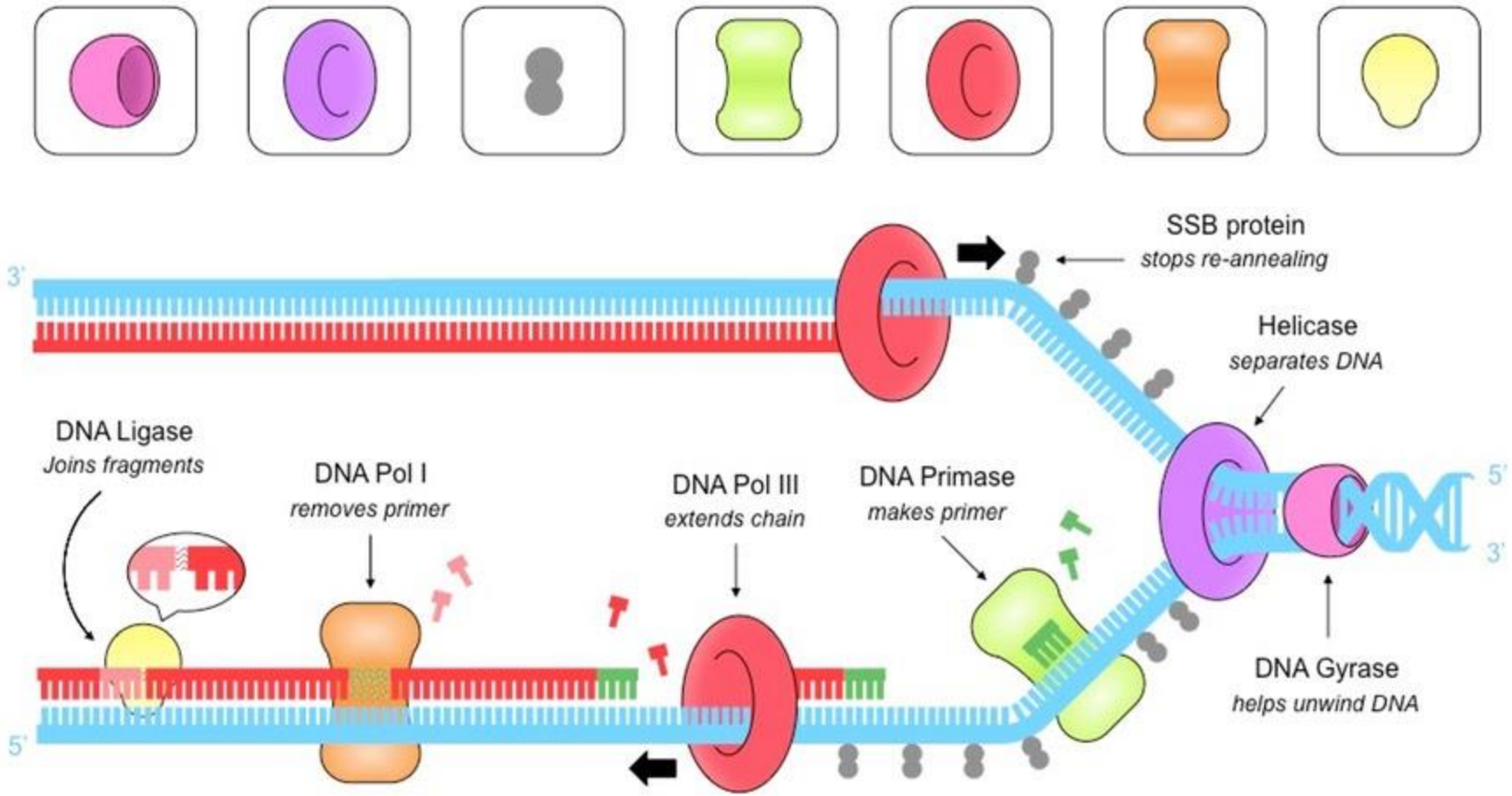




RNA Transcription

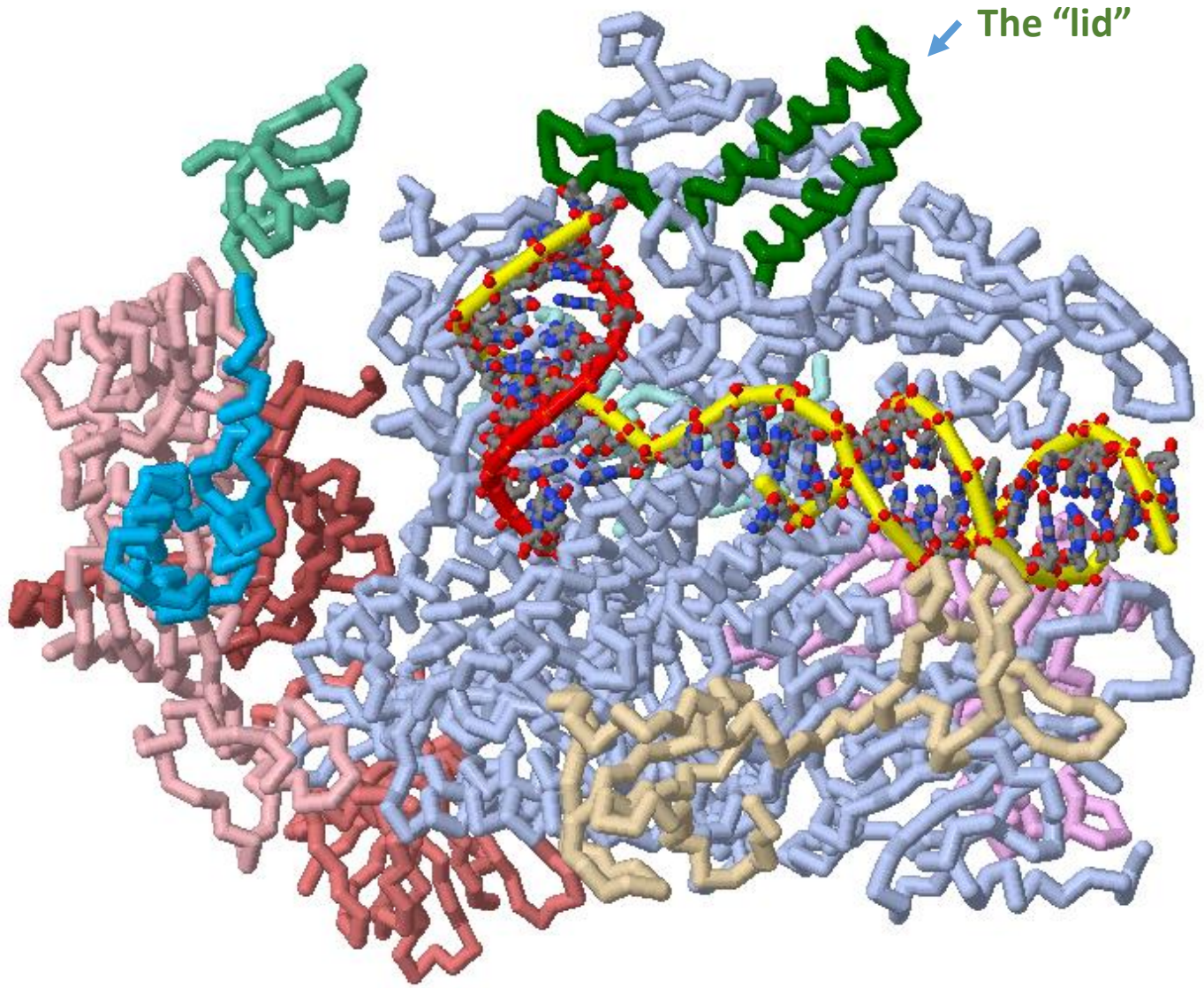


DNA Replication



Structural conservation across two domains of life…..

A 2-stranded **beta sheet (the lid) followed by a helix-turn helix motif**…..wedges the newly transcribed mRNA (red) off of its DNA template (yellow).



There is no discernable amino acid sequence homology between bacterial RNAPs and eukaryotic RNPs….and yet ***this structural feature of RNA polymerases is conserved across the evolutionary time separating prokaryotes and eukaryotes.***

Regulation of Gene Expression….

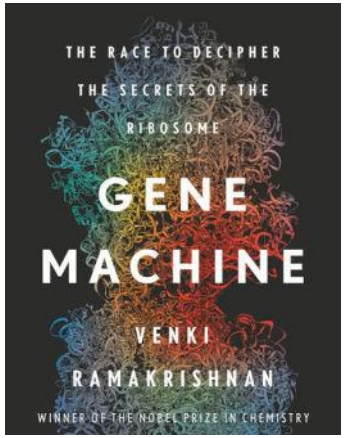
ONLY 1.5 % of genome encodes proteins

(…does that means that 98.5% of our genome is "junk DNA"?)

The 70S bacterial ribosome…. an amazing achievement of modern structural biology.

Atomic structure solved by x-ray diffraction.

Nobel Prize in 2009
to Venki Ramakrishnan,
Tom Steitz and Ada Yonath.



Small subunit: ~21 proteins and 16S rRNA…
…composed of 1542 nucleotides

Large subunit: ~31 proteins and 23 S rRNA…
…composed of 2904 nucleotides

The ribosome is a ribozyme!

Venki Ramakrishnan

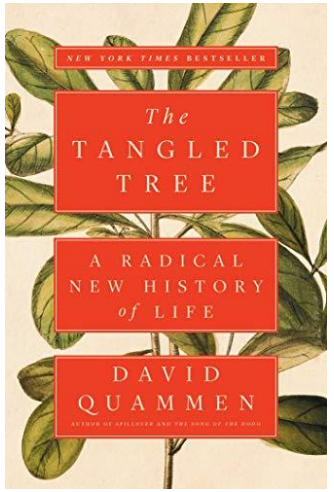
Mark Hoelzer

John Atkins

a reMARKable model

In the beginning,…i.e., in the years following the 1953 discovery of the structure of DNA….

…. But copying that material, for hereditary continuity, was one thing. Translating it into living organisms was another. Translated how? **By what steps does the information in DNA become physically animate?**



This fundamental matter— **how do bases designate aminos**?—became known as "the coding problem," to which **Francis Crick** addressed himself in the late 1950s.

Now he was sharing his office, his pub lunches, his fevered conversations, and his blackboard with another scientist, **Sydney Brenner**, rather than with Watson. One colleague at the Cavendish, upon early acquaintance with Crick, concluded that "his method of working was to talk loudly all the time."

from,…. **The Tangled Tree: A Radical New History of Life** by David Quammen

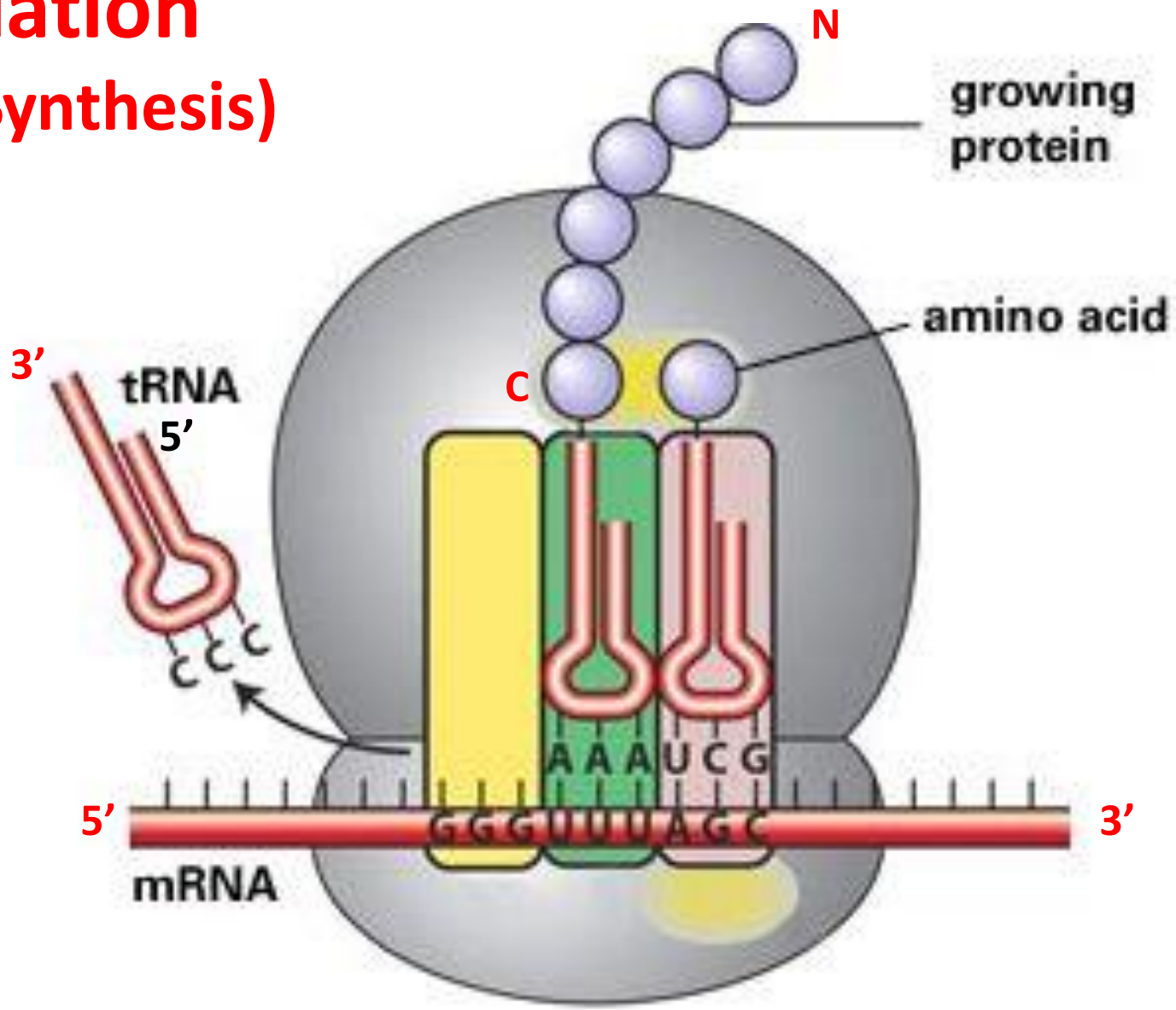
Ribosomes as assembly machines…

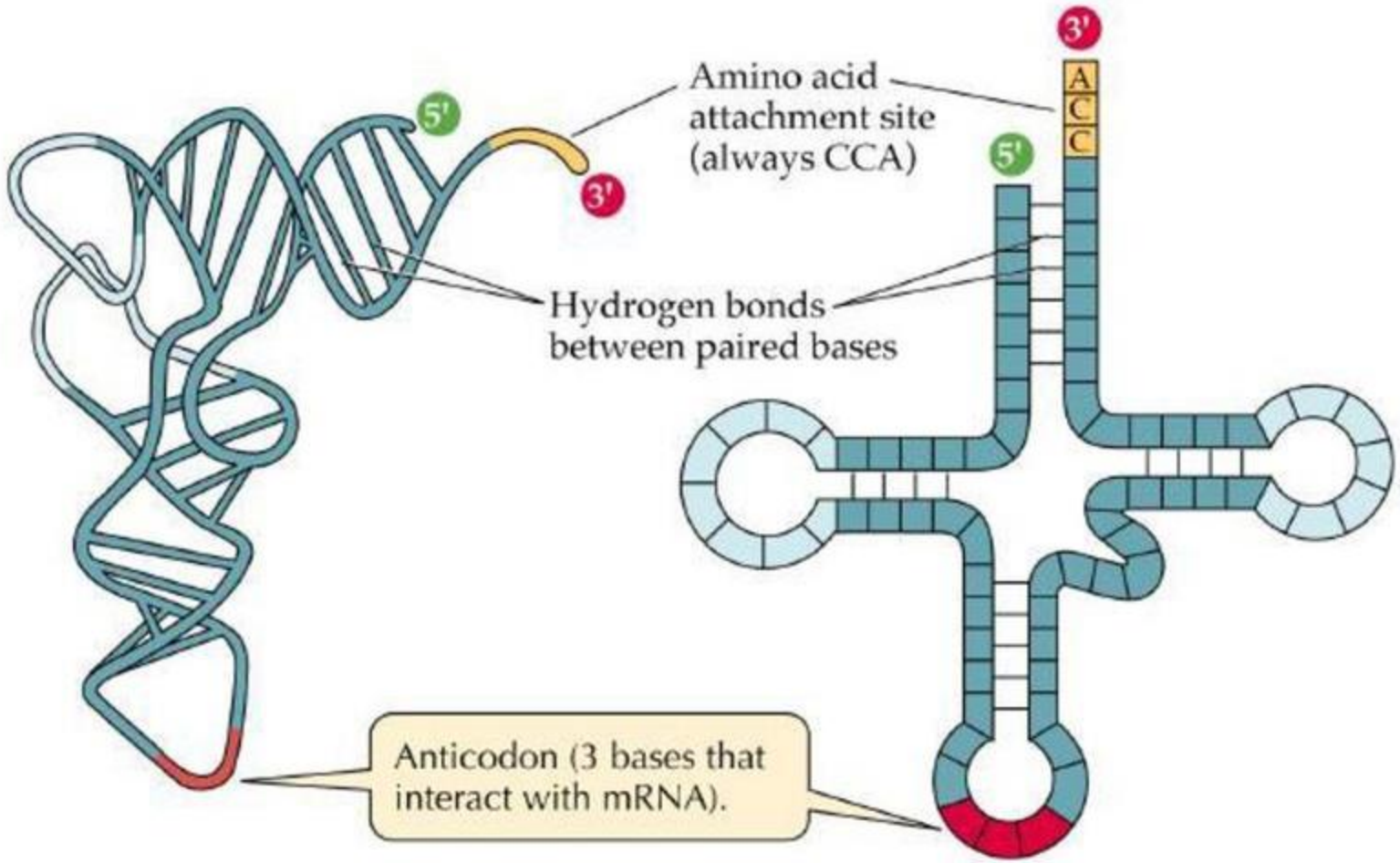
Then suddenly Brenner let out a “yelp.” He began talking fast. Crick began talking back just as fast. Everybody else in the room watched in amazement. ***Brenner had seen the answer, and Crick had seen him see it.*** The ribosome did not contain the recipe for the protein; it was a tape reader. It could make any protein so long as it was fed the right tape of “messenger” RNA.

They function as assembly mechanisms, taking in genetic information, plus raw material in the form of amino acids, and producing those larger physical products: proteins. ***In plainer words: ribosomes turn genes into living bodies***. Because the proteins they produce become three-dimensional molecules, a better metaphor than Brenner’s tape-reader, for our own day, might be this: ***the ribosome is a 3-D printer***.

That a string of nucleotides could make a human being,…. that just blows my mind.

Translation
(Protein Synthesis)




3'
A
C
C
5'
Amino acid
attachment site
(always CCA)
5'
3'
Hydrogen bonds
between paired bases
Anticodon (3 bases that
interact with mRNA).

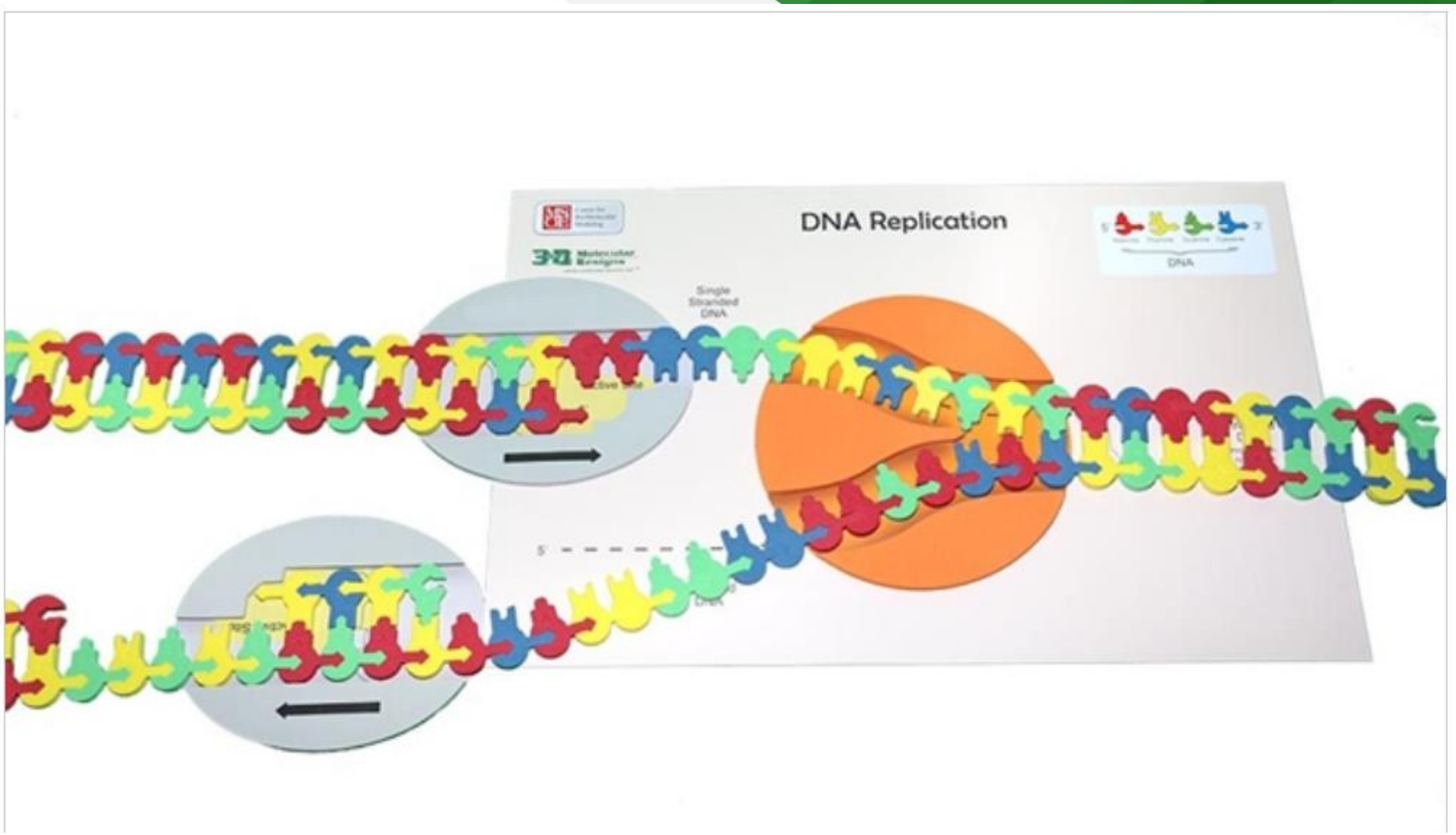

Amino acid
attachment site
A
A
G
3′
5′
Anticodon

Symbol used

Other topics….related to protein synthesis….

- **Initiation….how does the ribosome know where to start?**
- **Peptidyl transferase….** “the ribosome is a ribozyme”.
- **The translocation mechanism….**
- **Rough and smooth endoplasmic reticulum….**
- **The ribosomal “decoding center”….** A1492, A1493,G530 and C1054

https://pdb101.rcsb.org/motm/121


DNA Replication
DNA
Single Stranded DNA