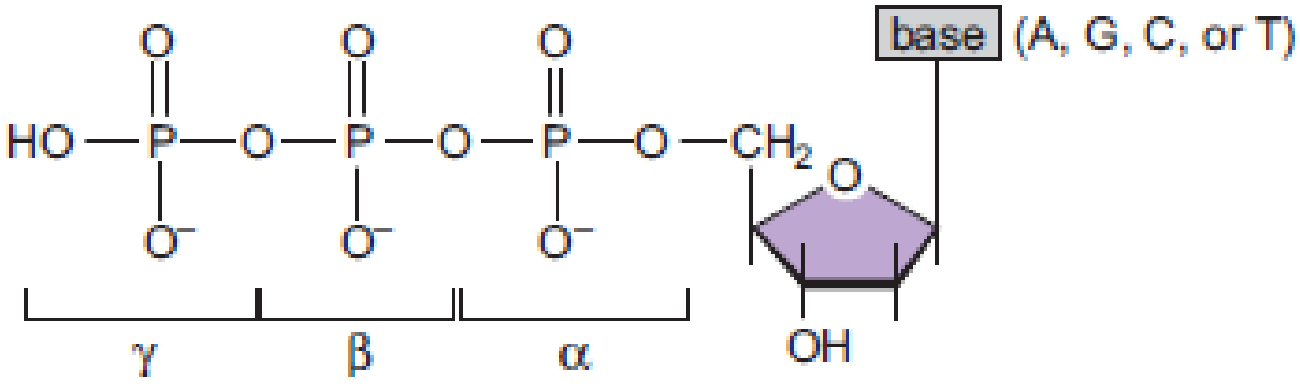
Notes

- Nucleoside triphosphates have three phosphoryl groups that are attached via the 5`-hydroxyl of the 2`-deoxyribose. The phosphoryl group proximal to the deoxyribose is called the α-phosphate, whereas the middle and distal groups are called the β-phosphate and the γ-phosphate, respectively.

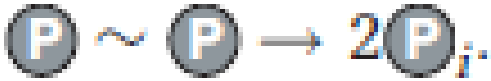


- **DNA Is Synthesized by Extending the 3` End of the Primer**: the hydroxyl group at the 3` end of the primer strand attacks the α-phosphoryl group of the incoming nucleoside triphosphate. The leaving group for the reaction is pyrophosphate, which is composed of the β-phosphate and γ-phosphate of the nucleotide substrate.

Hydrolysis of Pyrophosphate Is the Driving Force for DNA Synthesis

- The addition of a nucleotide to a growing polynucleotide chain of length n is indicated by the following reaction:

- But the free energy for this reaction is rather small. What, then, is the driving force for the polymerization of nucleotides into DNA? Additional free energy is provided by the rapid hydrolysis of the pyrophosphate into two phosphate groups by an enzyme known as **<u>pyrophosphatase</u>**.



- All DNA polymerases require a primer with a free 3`-OH. **They cannot initiate a new DNA strand de novo**. **How, then, are new strands of DNA synthes is started?** To accomplish this, the cell takes advantage of the ability of RNA polymerases to do what DNA polymerases cannot: start new RNA chains de novo.

- Although the leading-strand DNA polymerase can replicate its template as soon as it is exposed, synthesis of the lagging strand must wait for movement of the replication fork to expose a substantial length of template before it can be replicated. Each time a substantial length of new lagging-strand template is exposed, DNA synthesis is initiated and continues until it reaches the 5` end of the previous newly synthesized stretch of lagging –strand DNA.

- **Eukaryotic cells** also have multiple DNA polymerases. Of these, three are essential to duplicate the genome: **DNA Pol δ, DNA Pol ε, and DNA Pol α/primase.**
- Each of these eukaryotic DNA polymerases is composed of multiple subunits. DNA Pol α/primase is specifically involved in initiating new DNA strands. This four-subunit protein complex consists of a two-subunit DNA Pol α and a two-subunit primase.
- After the primase synthesizes an RNA primer, the resulting RNA primer:template junction is immediately handed off to the associated DNA Pol α to initiate DNA synthesis. **Because of its relatively low processivity, DNA Pol α/primase is rapidly replaced by the highly processive DNA Pol δ and Pol ε.** The process of replacing DNA Pol a/primase with DNA Pol δ or Pol ε is called **polymerase switching** and results in three different DNA polymerases functioning at the eukaryotic replication fork.
- DNA Pol δ and ε are specialized to synthesize different strands at the replication fork, with **DNA Pol ε synthesizing the leading strand** and **DNA Pol δ the lagging strand.**
- *Processivity, the average number of bases a pol will extend before falling off a template.*