7.2: Semi-Conservative DNA Replication

DNA replication is similar to transcription in its most general idea: a polymerase enzyme reads a strand of DNA one nucleotide at a time, it takes a random nucleotide from the nucleoplasm, and if it is complementary to the nucleotide in the DNA, the polymerase adds it to the new strand it is creating. Of course, there are significant differences between replication and transcription too, not the least of which is that both strands of DNA are being read simultaneously in order to create two new complementary strands that will eventually result in a complete and nearly perfect copy of an entire organismal genome.

Figure 7. DNA replication. Prior to the discovery of the enzymes involved in replication, three general mechanisms were proposed. In conservative replication, the original DNA strands stay associated with each other, while the newly made DNA forms its own double-helix. Semi-conservative replication posits the creation of hybrid old-new...
One of the most important concepts of DNA replication is that it is a semi-conservative process (Figure \(\PageIndex{7}\)). This means that every double helix in the new generation of an organism consists of one complete “old” strand and one complete “new” strand wrapped around each other. This is in contrast to the two other possible models of DNA replication, the conservative model, and the dispersive model. A conservative mechanism of replication proposes that the old DNA is used as a template only and is not incorporated into the new double-helix. Thus the new cell has one completely new double-helix and one completely old double-helix. The dispersive model of replication posits a final product in which each double helix of DNA is a mixture of fragments of old and new DNA. In light of current knowledge, it is difficult to imagine a dispersive mechanism, but at the time, there were no mechanistic models at all. The Meselson-Stahl experiments (1958) clearly demonstrated that the mechanism must be semi-conservative, and this was confirmed once the key enzymes were discovered and their mechanisms elucidated.

In the Meselson-Stahl experiments, E. coli were first incubated with \(^{15}\text{N}\), a heavy isotope of nitrogen. Although it is only a difference in mass of one neutron per atom, there is a great enough difference in mass between heavy nitrogen-containing DNA (in the purine and pyrimidine bases) and light/normal nitrogen-containing DNA that they can be separated from one another by ultracentrifugation through a CsCl concentration gradient (Figure \(\PageIndex{7}\)).

Over 14 generations, this led to a population of \(E.\ coli\) that had heavy nitrogen incorporated into all of the DNA (shown in blue). Then, the bacteria are grown for one or two divisions in “light” nitrogen, \(^{14}\text{N}\). When the DNA from the bacterial populations was examined by centrifugation, it was found that instead of light DNA and heavy DNA, as would be expected if DNA replications was conservative, there was a single band in an intermediate position on the gradient. This supports a semi-conservative model in which each strand of original DNA not only acts as a template for making new DNA, it is itself incorporated into the new double-helix.