C1. It is a double-stranded structure that follows the AT/GC rule.

C2. Bidirectionality refers to the idea that two replication forks emanate from one origin of replication. There are four DNA strands being made in two directions radiating outward from the origin.

C3. Statement C is not true. A new strand is always made from a preexisting template strand. Therefore, a double helix always contains one strand that is older than the other.

C4. A.

TTGGHTGUTGG
HHUUTHUGHUU

B.

TTGGHTGUTGG
HHUUTHUGHUU
↓
TTGGHTGUTGG CCAAACACCAA
AACCCACAACC HHUUTHUGHUU
↓
TTGGHTGUTGG TTGGGTGTTGG CCAAACACCAA CCAAACACCAA
AACCCACAACC AACCCACAACC GGTTTGTGGTT HHUUTHUGHUU

C5. No. In a conservative mechanism, one double helix would always be fully methylated so the cell would not have any way to delay the next round of DNA replication via a methylation mechanism.

C6. If we assume there are 4,600,000 bp of DNA, and that DNA replication is bidirectional at a rate of 750 nucleotides per second:

If there were just a single replication fork:

4,600,000/750 = 6,133 seconds, or 102.2 minutes

Because replication is bidirectional: 102.2/2 = 51.1 minutes

Actually, this is an average value based on a variety of growth conditions. Under optimal growth conditions, replication can occur substantially faster.

With regard to errors, if we assume an error rate of one mistake per 100,000,000 nucleotides:

4,600,000 × 1,000 bacteria = 4,600,000,000 nucleotides of replicated DNA

4,600,000,000/100,000,000 = 46 mistakes

When you think about it, this is pretty amazing. In this population, DNA polymerase would cause only 46 single mistakes in a total of 1,000 bacteria, each containing 4.6 million bp of DNA.

C7.

5′————————DNA POLYMERASE——>3′
3′————————————————————————————5′

Template strand

C8. DNA polymerase would slide from right to left. The new strand would be

3′–CTAGGGCTAGGCGTATGTAAATGGTCTAGTGGTGG–5′

C9. 1. DnaA boxes—binding sites for the DnaA protein

2. Methylation sites—sites of adenine methylation that are important for regulating DNA replication

3. AT-rich region—site where the DNA initially denatures to form a replication bubble

C10. A. When looking at Figure 11.5, the first and third DnaA boxes are running in the same direction and the second and fourth DnaA boxes are running in the opposite direction. Once you realize that, you can see that the sequences are very similar to each other.

B. According to the direction of the first DnaA box, the consensus sequence is

TGTGGATAA
ACACCTATT

C. This sequence is nine nucleotides long. Because there are four kinds of nucleotides (i.e., A, T, G, and C), the chance of this sequence occurring by random chance is 4^{-9}, which equals once every 262,144 nucleotides. Because the *E. coli* chromosome is more than 10 times longer than this, it is fairly likely that this consensus sequence occurs elsewhere. The reason why there are not multiple origins, however, is because the origin has four copies of the consensus sequence very close together. The chances of having four copies of this consensus sequence occurring close together (as a matter of random chance) are very small.

C11. A. Your hand should be sliding along the white string. The free end of the white string is the 5′ end, and DNA helicase travels in the 5′ to 3′ direction.

B. The white string should be looped by your right hand. The black string is the template strand for the synthesis of the leading strand. DNA polymerase moves directly toward the replication fork to synthesize the leading strand. The white string is the template for the lagging strand. The template DNA for the lagging strand must be looped around DNA polymerase III so it can move toward the replication fork.

C12. First, according to the AT/GC rule, a pyrimidine always hydrogen bonds with a purine. A transition still involves a pyrimidine hydrogen bonding to a purine, but a transversion causes a purine to hydrogen bond with a purine or a pyrimidine to hydrogen bond with a pyrimidine. The structure of the double helix makes it much more difficult for this later type of hydrogen bonding to occur. Second, the induced-fit phenomenon of the catalytic site of DNA polymerase makes it unlikely for DNA polymerase to catalyze covalent bond formation if the wrong nucleotide is bound to the template strand. A transition mutation creates a somewhat bad interaction between the bases in opposite strands, but it is not as bad as the fit caused by a transversion mutation. In a transversion, a purine is opposite another purine or a pyrimidine is opposite a pyrimidine. This is a very bad fit. And finally, the proofreading function of DNA polymerase is able to detect and remove an incorrect nucleotide that has been incorporated into the growing strand. A transversion is going to cause a larger distortion in the structure of the double helix and make it more likely to be detected by the proofreading function of DNA polymerase.

C13. A primer is needed to make each Okazaki fragment. The average length of an Okazaki fragment is 1,000 to 2,000 bp. If we use an average value of 1,500 bp for each Okazaki fragment, then there needs to be approximately

$$\frac{4,600,000}{1,500} = 3,067 \text{ copies}$$

C14. Primase and DNA polymerase are able to knock the single-strand binding proteins off the template DNA.

C15. A. The removal of RNA primers occurs in the 5′ to 3′ direction, while the proofreading function occurs in the 3′ to 5′ direction.

B. No. The removal of RNA primers occurs from the 5′ end of the strand.

C16. A. The right Okazaki fragment was made first. It is farthest away from the replication fork. The fork (not seen in this diagram) would be to the left of the three Okazaki fragments, and moving from right to left.

B. The RNA primer in the right Okazaki fragment would be removed first. DNA polymerase would begin by elongating the DNA strand of the middle Okazaki fragment and remove the right RNA primer with its 5′ to 3′ exonuclease activity. DNA polymerase I would use the 3′ end of the DNA of the middle Okazaki fragment as a primer to synthesize DNA in the region where the right RNA primer is removed. If the middle fragment was not present, DNA polymerase could not fill in this DNA (because it needs a primer).

C. You only need DNA ligase at the right arrow. DNA polymerase I begins at the end of the left Okazaki fragment and synthesizes DNA to fill in the region as it removes the middle RNA primer. At the left arrow, DNA polymerase I is simply extending the length of the left Okazaki fragment. No ligase is needed here. When DNA polymerase I has extended the left Okazaki fragment through the entire region where the RNA primer has been removed, it hits the DNA of the middle Okazaki fragment. This occurs at the right arrow. At this point, the DNA of the middle Okazaki fragment has a 5′ end that is a monophosphate. DNA ligase is needed to connect this monophosphate with the 3′ end of the region where the middle RNA primer has been removed.

D. As mentioned in the answer to part C, the 5 end of the DNA in the middle Okazaki fragment is a monophosphate. It is a monophosphate because it was previously connected to the RNA primer by a phosphoester bond. At the location of the right arrow, there was only one phosphate connecting this deoxyribonucleotide to the last ribonucleotide in the RNA primer. For DNA polymerase to function, the energy to connect two nucleotides comes from the hydrolysis of the incoming triphosphate. In this location shown at the right arrow, however, the nucleotide is already present at the 5 end of the DNA, and it is a monophosphate. DNA ligase needs energy to connect this nucleotide with the left Okazaki fragment. It obtains energy from the hydrolysis of ATP. C17. DNA methylation is the covalent attachment of methyl groups to bases in the DNA. Immediately after replication, there has not been sufficient time to attach methyl groups to the bases in the newly made daughter strand. The time delay of DNA methylation helps to prevent premature DNA replication immediately after cell division.

C18. 1. It recognizes the origin of replication.

2. It initiates the formation of a replication bubble.

3. It recruits helicase to the region.

C19. It would be difficult to delay DNA replication after cell division because the dilution of the DnaA protein is one mechanism that regulates replication. One might expect that such a strain would have more copies of the bacterial chromosome per cell compared to a normal strain.

C20. The picture would depict a ring of helicase proteins traveling along a DNA strand and breaking the hydrogen bonding between the two helices, as shown in Figure 11.6.

C21. An Okazaki fragment is a short segment of newly made DNA in the lagging strand. It is necessary to make short fragments because the fork is exposing the lagging strand in a 5′ to 3′ direction but DNA polymerase can slide along a template strand in a 3′ to 5′ direction. Therefore, the newly made lagging strand is synthesized in short pieces in the direction away from the replication fork.

C22. The leading strand is primed once, at the origin, and then DNA polymerase III makes it continuously in the direction of the replication fork. In the lagging strand, many short pieces of DNA are made. This requires many RNA primers and DNA polIII. The primers are removed by polI, which then fills in the gaps with DNA. DNA ligase then covalently connects the Okazaki fragments together. Having the enzymes within a complex provides coordination among the different steps in the replication process and thereby allows it to proceed more efficiently and faster.

C23. The active site of DNA polymerase has the ability to recognize a distortion in the newly made strand and remove it. This occurs by a 3′ to 5′ exonuclease activity. After the mistake is removed, DNA polymerase resumes DNA synthesis.

C24. A processive enzyme is one that remains clamped to one of its substrates. In the case of DNA polymerase, it remains clamped to the template strand as it makes a new daughter strand. This is important to ensure a fast rate of DNA synthesis.

C25. Nucleosomes are made during the S phase. The original histones become bound to each of the two DNA double helices in a random manner. The newly made histones then bind to regions where histones are missing. Following DNA replication, the nucleosomes in both double helices are a random mixture of newly made histone octamers and original histone octamers.

C26. It is necessary to have the correct number of chromosomes per cell. If DNA replication is too slow, daughter cells may not receive any chromosomes. If it is too fast, they may receive too many chromosomes.

C27. The inability to synthesize DNA in the 3′ to 5′ direction and the need for a primer necessitate the action of telomerase. Telomerase is different in that it uses a short RNA sequence, which is part of its structure, as a template for DNA synthesis. Since it uses this sequence many times in row, it produces a tandemly repeated sequence in the telomere.

C28. The opposite strand is made in the conventional way by DNA polymerase using the “telomerase added strand” as a template.

C29. Fifty, because two replication forks emanate from each origin of replication. DNA replication is bidirectional.

C30. The ends labeled *B* and *C* could not be replicated by DNA polymerase. DNA polymerase makes a strand in the 5′ to 3′ direction using a template strand that is running in the 3′ to 5′ direction. Also, DNA polymerase requires a primer. At the ends labeled *B* and *C*, there is no place (upstream) for a primer to be made.

C31. A. Both reverse transcriptase and telomerase use an RNA template to make a complementary strand of DNA.

B. Since reverse transcriptase does not have a proofreading function, it makes it more likely for mistakes to occur. This creates many mutant strains of the virus. Some mutations might prevent the virus from proliferating. However, other mutations might prevent the immune system from battling the virus. These kinds of mutations would enhance the proliferation of the virus.

C32. As shown in Figure 11.23, the first step involves a binding of telomerase to the telomere. The 3′ overhang binds to the complementary RNA in telomerase. For this reason, a 3′ overhang is necessary for telomerase to replicate the telomere.