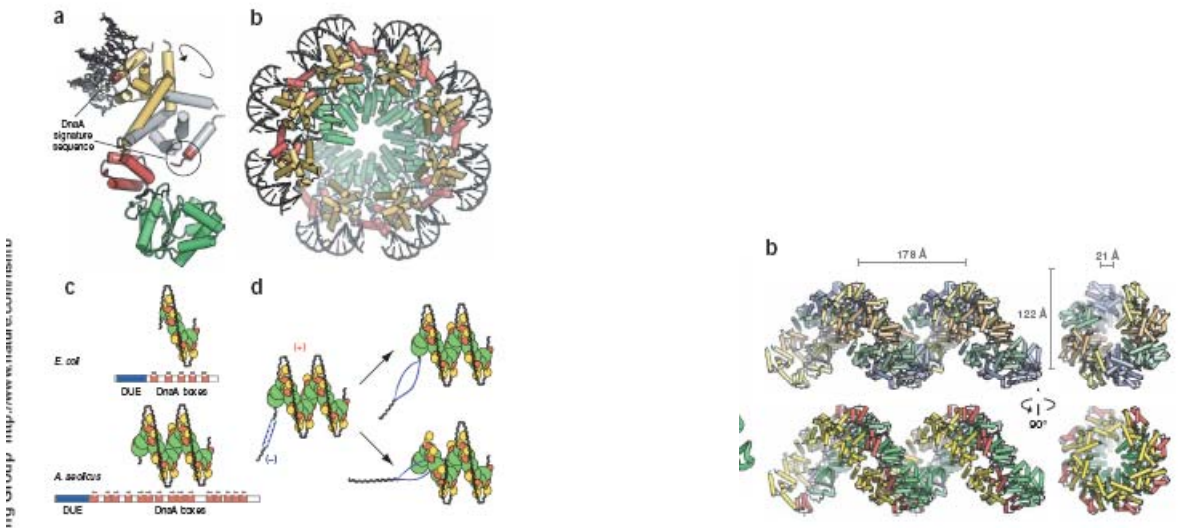
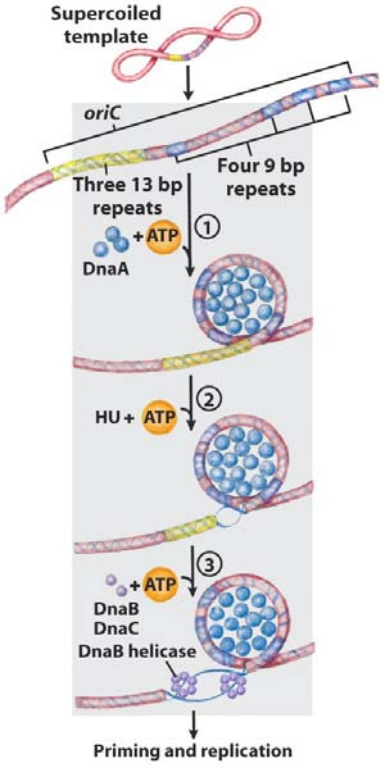


Structure of DnaA associated with its cognate binding box: An example of why Text Book diagrams are not always right

The structure of the DnaA protein (the initiator protein for DNA replication in E. coli) was solved recently by James Berger and Colleagues (shown above). The protein was associated with its binding DNA sequence in the solved complex. DnaA has ATPase activity. It hydrolyses ATP and forms a mini filament on DNA.



In text book diagrams, the DnaA filament formed on DNA is drawn as a right handed torroidal wrap (see Figure at right). [Do not worry about the terminology now. We will discuss these concepts in lectures on DNA topology.] This indicates negative supercoiling of DNA. I could not see for myself how this would help unwind the origin, if the protein soaks up some of the negative supercoils present in DNA. I argued that the DnaA should form filaments of the opposite handedness, so it introduces positive supercoils (right handed torroidal wrap). As we have already noted during discussion on replication fork progression, generation of one kind of supercoils in a closed DNA domain should introduce compensatory supercoils of the opposite sign in an adjacent domain. So if DnaA makes positive supecoils, it will help unwind DNA at the replication origin. In class I would draw the DNA bound by DnaA as a right handed (positively

supercoiled) wrap as opposed to the classic left handed wrap seen in text books.

If you look at the structure solved last year by Berger and coworkers, the filament is indeed right handed, positively supercoiled. Common sense, as it relates to DNA topology, should have told us so!

Moral: Don't believe everything the book says or I say in class. Try to think through the concepts, and satisfy yourself that they make sense.

Scientific truth is not immutable. It is more in the vein of explanations. Explanations change as new facts come to light. That is the beauty and character of science.

If you (some of you will, I hope) enter scientific research in the future, keep in mind the Karl Popper philosophy of falsification. You should always design your experiments, not to substantiate your hypothesis but to falsify it. If your experiments cannot verify predictions that contradict your hypothesis, they are not much use, as far as scientific progress is concerned. An experimental result that falsifies your hypothesis sets the stage for a modified hypothesis and a step forward in science. If multiple experiments fail to falsify your hypothesis, it must be a pretty good one, and represents 'scientific truth' at least for the time being.

By the way, Karl Popper was an Australian (later British) philosopher of the early 20^{th} century who enunciated the principle of falsification.