Replication in Bacteria

Cellular control of replication in bacteria

We have seen that the initiator protein DnaA and the replicator element oriC are needed for the initiation of replication, and that the slow rate of methylation at GATC motifs prevents re-initiation for some time. The bacterial cell can sense when the nutritional conditions, levels of nucleotide pools, and protein concentrations are adequate to support a round of replication. The details of this monitoring are beyond the scope of this presentation, and can be explored in references such as Niedhart et al. In general, initiation is triggered by the increase in cell mass. Initiation occurs at a constant ratio of cell mass to the number of origins. This suggests that a mechanism exists to titrate out some regulatory molecule as the cell mass increases, but the molecule and mechanism have not been elucidated.

The result of this monitoring and signalling is the formation of an active DnaA complex at oriC, followed by unwinding the DNA and the other events discussed above.

Depending on the growth conditions, bacteria can divide rapidly or slowly. In rich media, the cell number can double every 18 min, whereas when nutrients are scare, the doubling time can be long as 180 min. The bacterial cells accomplish this by varying the rate of re-initiation of replication. Re-initiation has to occur at the same frequency as the cell doubling time.

Although the frequency of re-initiation can be varied 10-fold, the time required for the replication cycle is constant. This cycle consists of two periods called C and D. The elongation time, or C period, is the time required to replicate the bacterial chromosome. From initiation to termination, this is about 40 min. The division time, or D period, is the time that elapses between completion of a round of DNA replication and completion of cell division. This is about 20 min. Hence the time for the replication cycle (C period plus D period) is essentially constant in bacterial cultures with doubling...
times shorter than 60 min.

In order to accommodate the variation in cell doubling time within the constraints of the constant time for replication (C+D), rapidly growing bacteria have chromosomes with multiple replication forks. The constant replication cycle time means that a round of replication must be initiated 60 min (i.e. C+D) before cell division. However, re-initiation can occur before 60 min has past. This is illustrated in Figure 6.16 for cells in a culture dividing every 30 min. When the cell doubling time is less than 60 min, a cycle of replication must initiate before the end of the preceding cycle. This results in chromosomes with more than one replication fork.

**Figure 6.16.** Multiple replication forks per chromosome allow bacteria to divide more rapidly than the replication cycle time. This diagram illustrates a bacterial cell dividing every 30 min, and hence initiating a new cycle of replication every 30 min.

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If the time required for two replication forks traveling in opposite directions to traverse the entire *E. coli* chromosome at 37°C is about 40 min, regardless of the culture conditions and the time required for cell division (D period) is 20 min, how many replication forks will be present on each DNA molecule in the culture?

**Answer**

TBA
Contributors

- Ross C. Hardison, T. Ming Chu Professor of Biochemistry and Molecular Biology (The Pennsylvania State University)