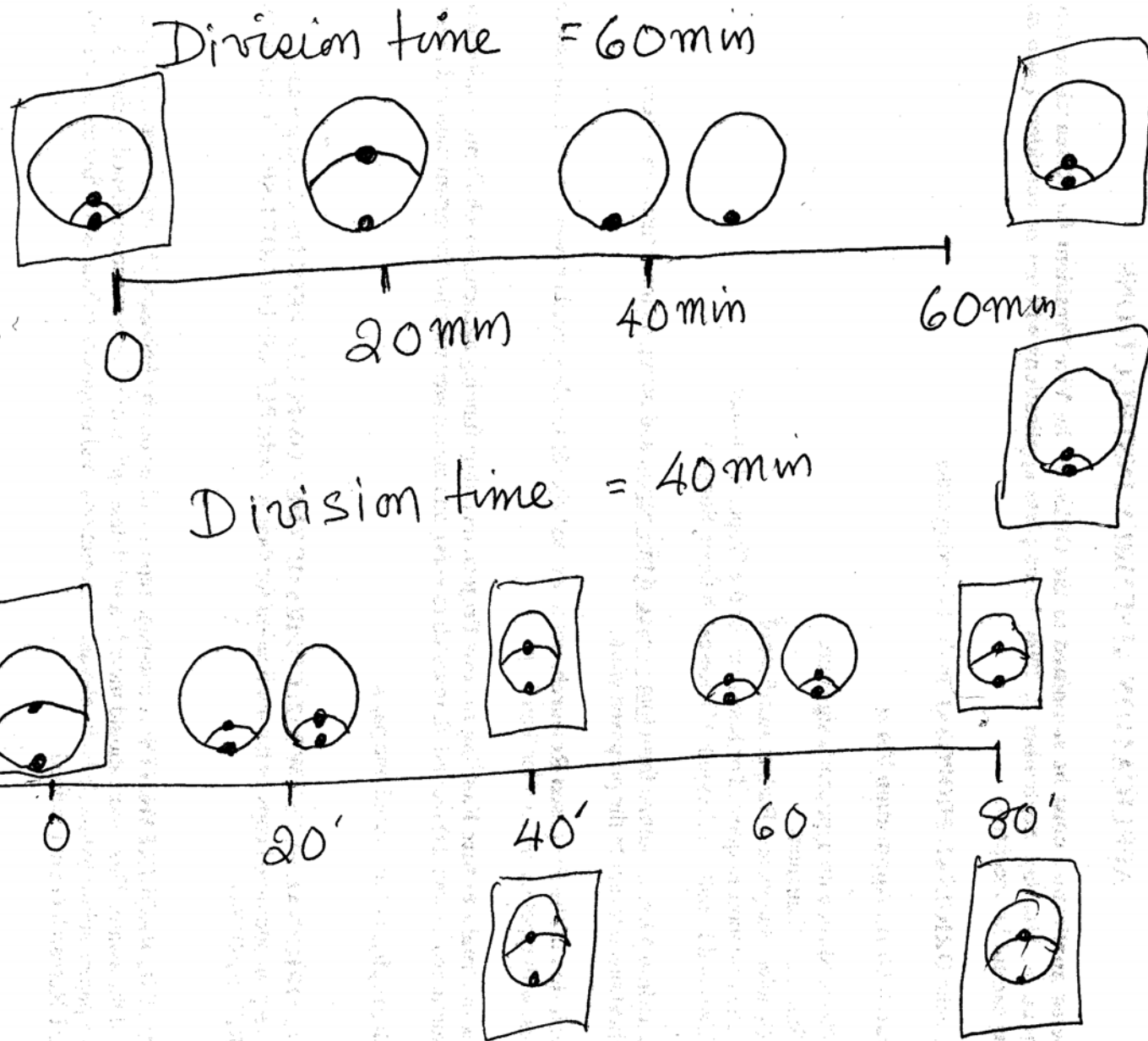


Adjusting replication to match cell division (generation) time in bacteria



As I explained in class, there is an internal cell clock in the bacterium that determines the time of cell division following the firing of the replication origin (initiation of DNA synthesis). In *E. coli*, this happens to be 60 min. Out of this time period, DNA replication takes 40 minutes. The gap of 20 minutes gives time to remove RNA primers, correct mismatches, separate the linked daughter DNA molecules etc.). This internal clock does not change even when the generation time changes because of the nutrient conditions in the medium. In rich medium, the generation

time becomes shorter than 60 min, say 40 min or even 20 min depending on how good the nutrient source is. The DNA replication time is invariant, always 40 min or so, as long as the nucleotide pools in the cell are normal. It cannot go any faster because the synthesis rate by the polymerase enzyme has been evolutionarily optimized to be this value.

As illustrated in the figures above, when the generation time is 60 min, each new born cell contains one copy of the genome. The origin fires every 60 minutes, that is, as soon as a baby cell is formed, it initiates replication as part of the next cell cycle. A division event follows 60 min later to form two cells containing one copy of the genome. Each of the two new cells initiates replication, and after 60 minutes gives rise to two cells, again each with one copy of the chromosome. In other words, in this state of growth, the genome content in each newborn cell is one.

When the generation time is reduced to 40 min, the situation changes. The paradox is that the cell has to divide in 40 minutes, but it takes 60 minutes from the firing of the replication origin to cell division. So the division at 40 min corresponds to an initiation event (origin firing) that occurred 60 min before or at -20 min. So at time 0, replication has continued for 20 minutes, or the genome is half duplicated. In another 20 minutes, the genome is fully duplicated, you have two copies of it. But now, it is already time to fire the origin again to meet the 60 min. requirement of the next cell division event, which must occur at 80 min (division 1 at 40 min; division 2 at 80 min and so on). So at the 40 min point (or time for the first division), each DNA molecule has been half replicated. The newborn cells contain not just one equivalent of the genome but one and one half equivalents.