Reading Assignment for Lectures 5-6: Phillips, Kondev, Theriot (PKT), Chapter 3

Life is not static.
Organisms as a whole are not at "equilibrium."
As we have seen, life is in a kind of steady state, taking in high-quality energy and giving off the same energy in low-quality forms and, in the process, creating ordered structures.
The net effect is replication.

This chapter illustrates in a very general way the kinds of processes involved.
These processes take place on a huge range of timescales, ranging from chemical reactions (10 ns—10 μs) through organismal lifetimes (1 Ks—10 Ts), to evolutionary times (100 Ms—10 Ps).

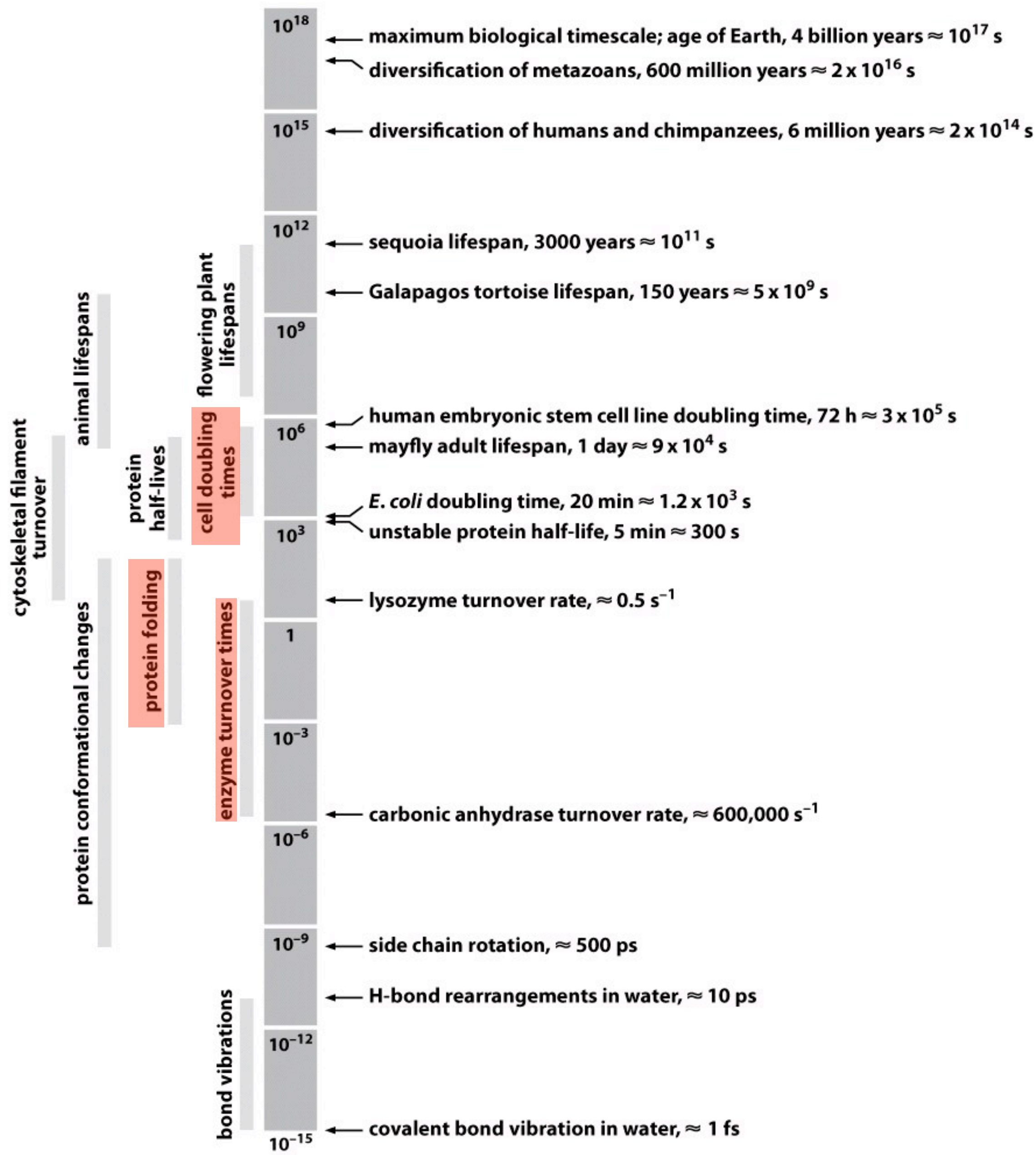


Figure 3.1 Physical Biology of the Cell (© Garland Science 2009)

Phillips, Kondev, Theriot, Fig. 3.2

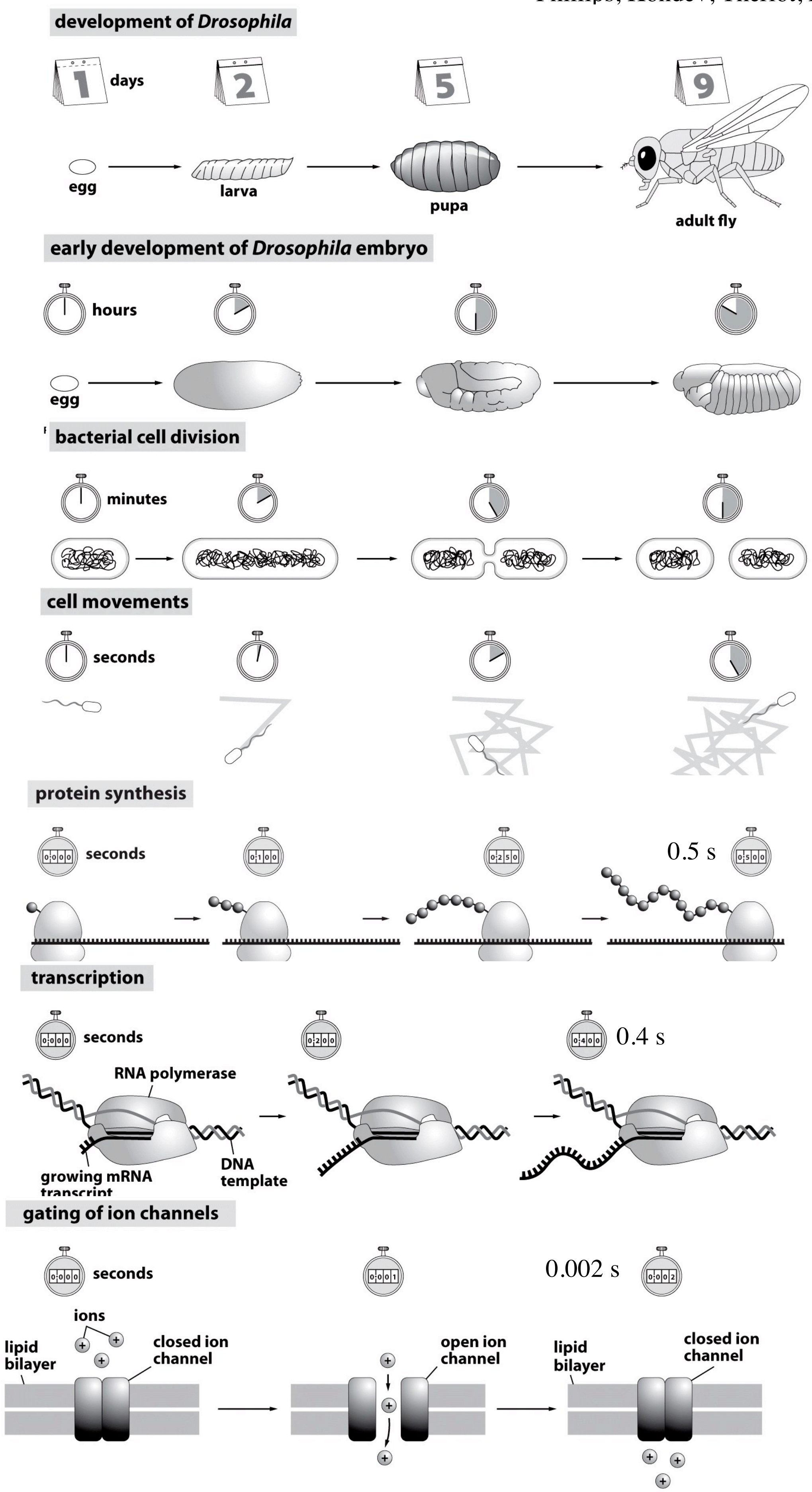


Figure 3.2g Physical Biology of the Cell (© Garland Science 2009)

E. coli:

Translation:
15 amino acids per sec per ribosome

Transcription:
40 bases per sec per transcription complex

Replication:
1000 base pairs per sec per replication complex

Q: How can we deal with this vast range of processes?
A: Different questions at different timescales.
When we choose a timescale of interest:
Processes much slower than this set the parameters but are otherwise irrelevant.
Example: In studying human physiology today, you don't need to know what happened over evolutionary timescales.
Processes much faster than this are largely in "equilibrium" and can be treated on the average.
Example: In studying the overall human energy balance, we didn't need to know what was going on with the detailed metabolic processes.

It is natural to start with looking at processes on the scale of organismal lifetimes.
Key processes on this timescale are those involved in growth and replication.

"The Central Dogma"
1. Replication:
(DNA helicase splits/unwinds double stranded DNA)
DNA polymerase copies each strand to its complement. ("Replication complex")

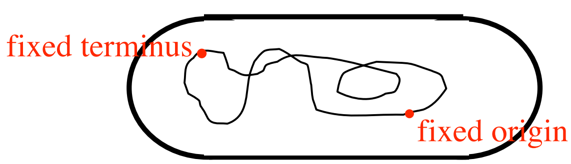
2. Transcription:
RNA polymerase reads segment of DNA strand, creating an mRNA.

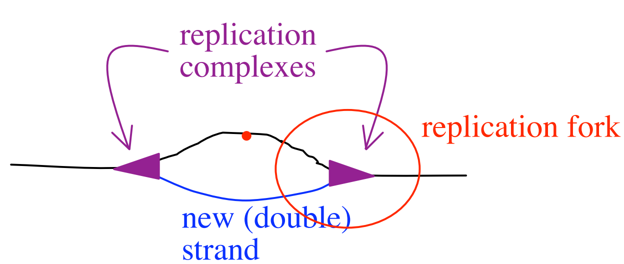
3. Translation:
Ribosome uses 3-letter codons in mRNA template to construct protein amino-acid sequence, using tRNA's linked to amino acids.

Each of these processes involves lovely pieces of molecular machinery. The rate at which the machinery works determines organism lifetimes.

For prokaryotes, the genome is relatively short, so replication is carried out relatively simply in the cytosol.

Replication timescales: Example E. coli
How fast does the replication machinery work? We start with E. coli.





The replication complex includes:
Helicase to unwind double strand (+primase=primosome) plus two DNA polymerase complexes.

Example: E. coli
E. coli genome consists of 5×10^6 base pairs (bp). Lifetime is 3000 s (50 min, about an hour).
DNA (double strand) replicates starting at a given origin and processing with two replication complexes operating in opposite directions. When they meet, replication is complete and the cell can begin the division process, which involves separating the DNA to the ends of the cell and laying down proteins at the center of the cell, which will eventually pinch off the cell into two daughters.

Thus, rate of processing by each (single replication complex) must be *at least* $\frac{5\times10^6}{2(3000)} \approx 10^3\ bp/s$, which turns out to be a reasonable estimate.

Q: How long is the genome?

A: 1/3 nm/bp means ~2x10^6 nm or about 2 mm. How does this fit into cell?!
(note defects in above picture! How does it pack?)

So, the rate at which each replication fork moves is 10^3 bp/s × 1/3 nm/bp ≈ 300 nm/s.

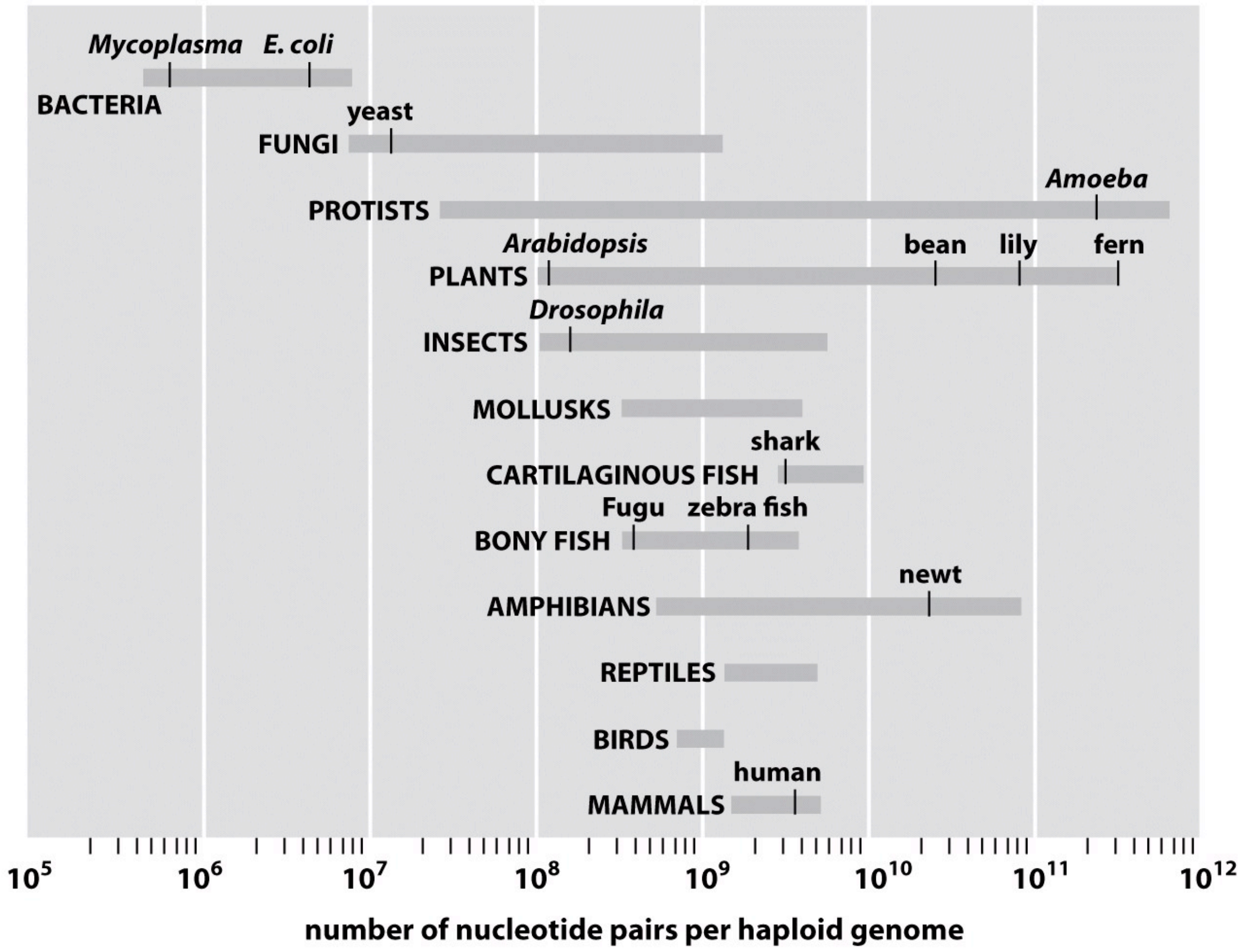


Figure 18.1 Physical Biology of the Cell (© Garland Science 2009)

Note: The human genome is much larger (~3x10^9 bp~10^9 nm~1 m!). If replication of the human genome occurred by the same simple mechanism, then it would take about 10x longer than E. coli, i.e., cells would take a minimum of about $\frac{3\times10^9}{2(10^3)} = 17\ days$ to divide only once. This is much too slow, so we know that there is a significant difference in the mechanism of cell division in E. coli and humans.

Comment:

Human embryonic cells divide 1—2 times/day for the first several days.

Q: How many divisions required to reach 1 kg total mass?

A: Cell mass~

$$V_{cell}\rho_{water} \sim \left(10^{-6}\right)^3 \cdot 10^3 = 10^{-15}\ kg = 1\ pg$$, so $\begin{cases} 2^n = 10^{15} \\ n = \dfrac{15 \ln 10}{\ln 2} \sim 50 \end{cases}$, i.e.,

roughly 50 cellular generations. Generation time slows down in later development.
Replication process is more complicated for eukarylotes:

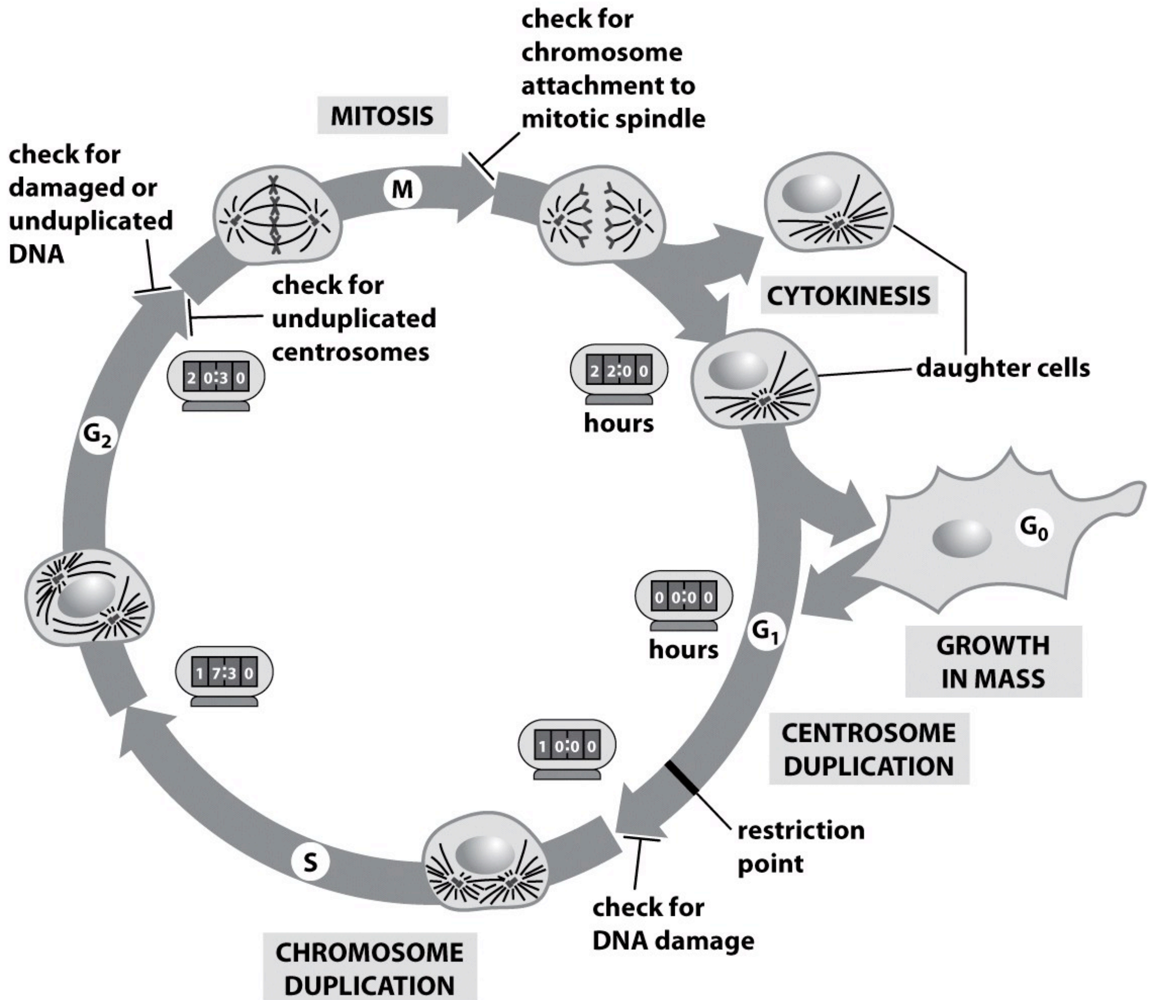


Figure 3.15a Physical Biology of the Cell (© Garland Science 2009)

mitotic spindle
microtubule organizing centre