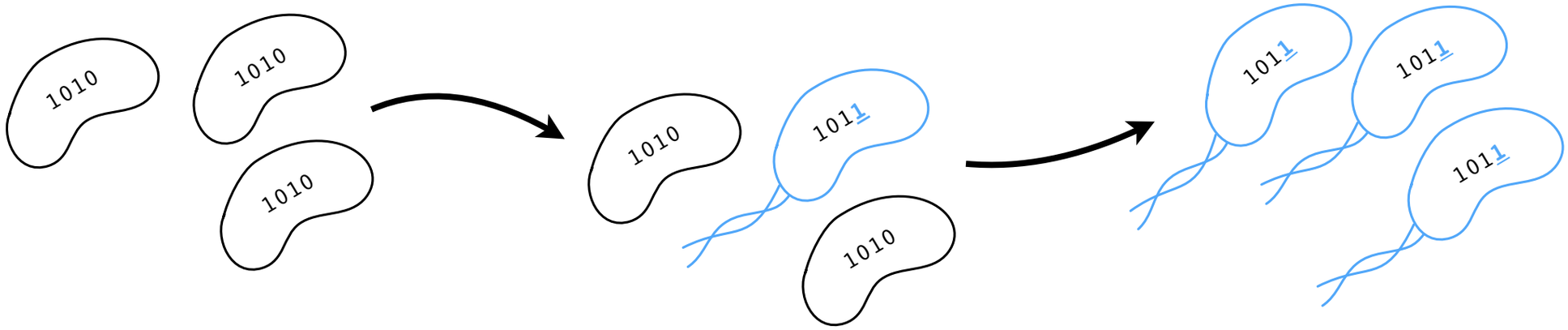
APPHYS 205 // BIO 126/226:

Introduction to Biophysics



Winter 2023

Biology generates exquisitely complex behavior from simple chemical building blocks

e.g. a human white blood cell "chasing" an S. aureus bacterium (credit: David Rogers)

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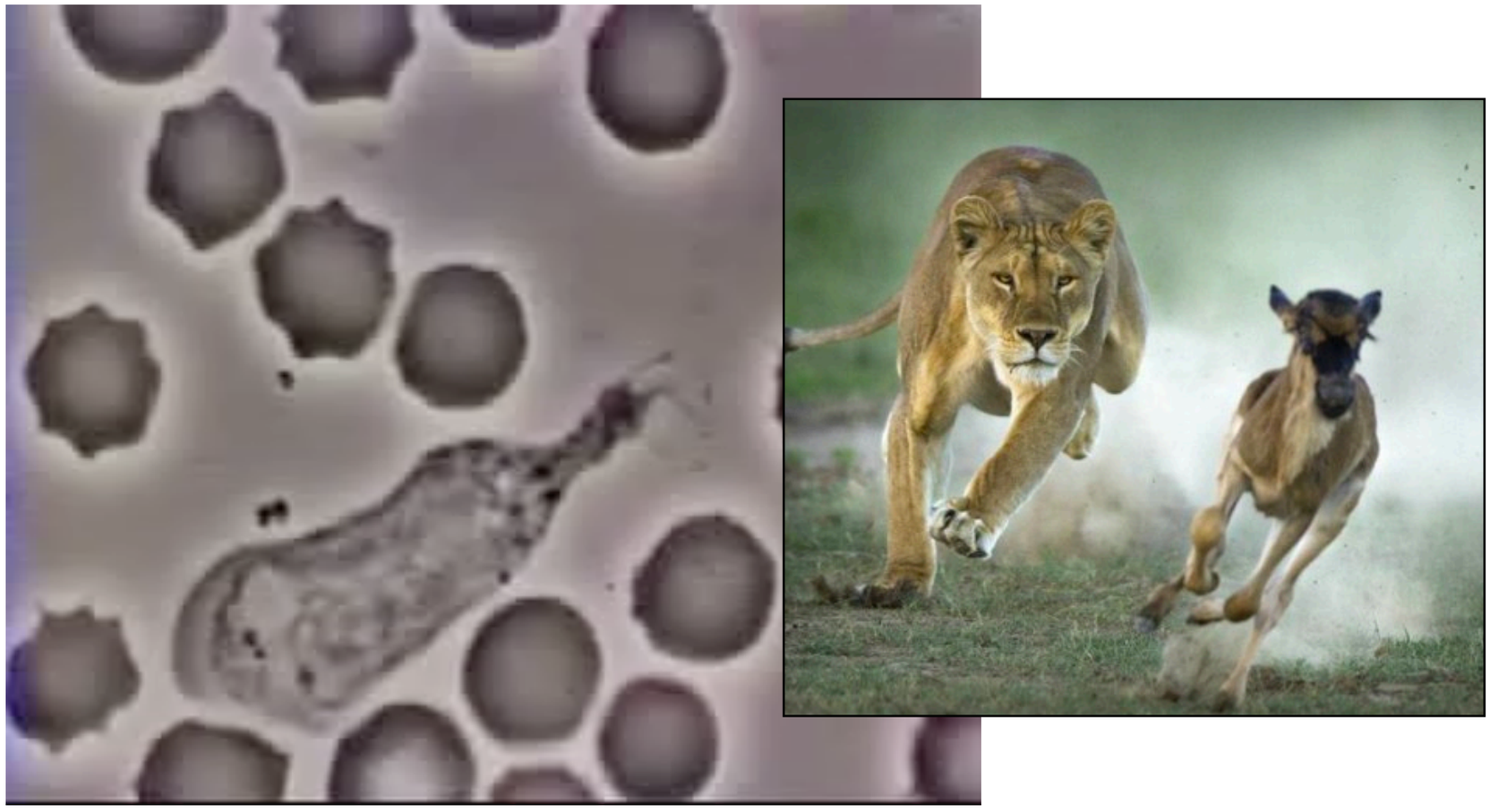

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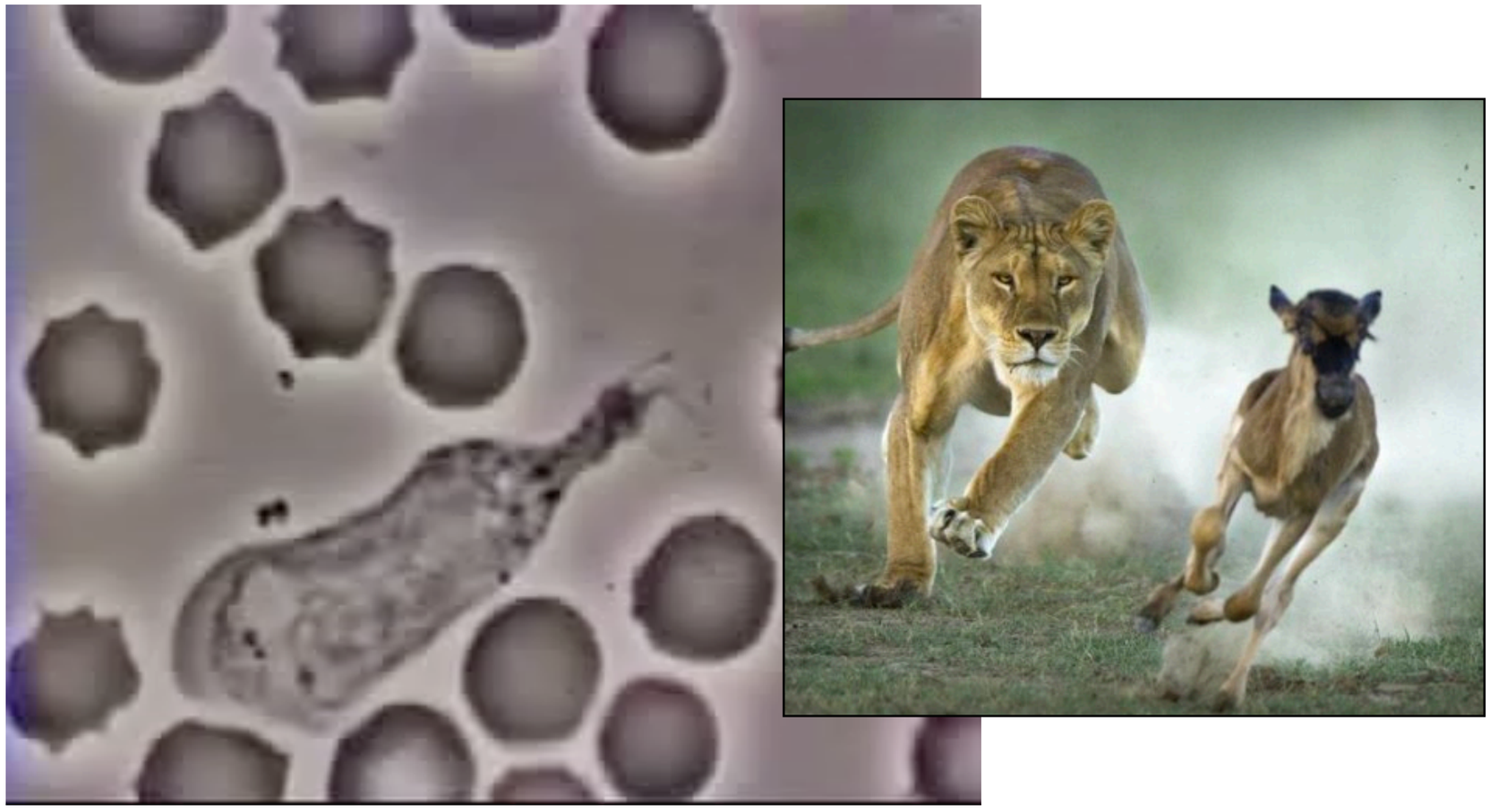

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→ **will discuss more in Lectures 7 & 8 (Chemotaxis)**

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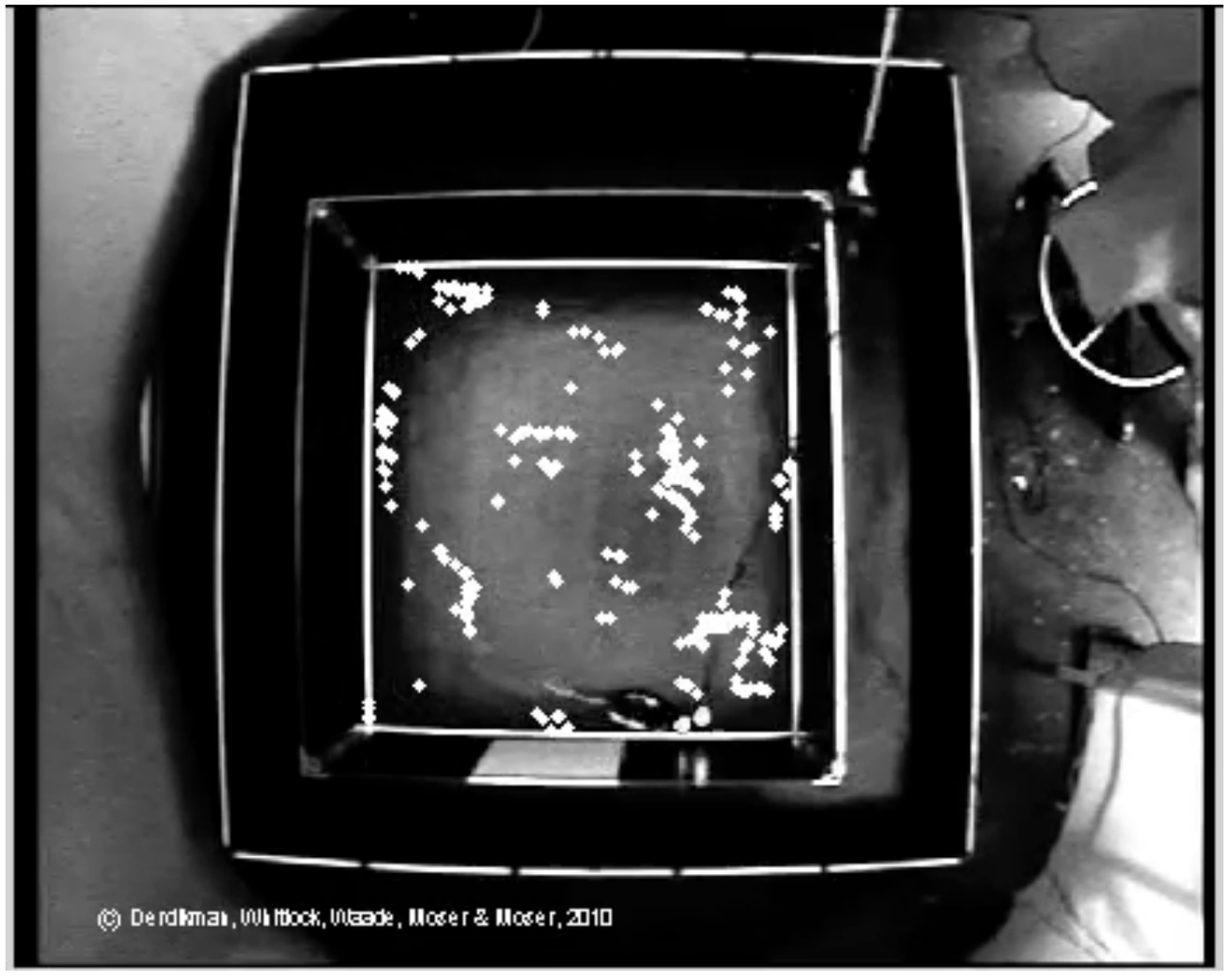

e.g. firing pattern of a single "grid neuron" in a rat moving within a box (credit: Derdikman, Whitlock, Waade, Moser & Moser)

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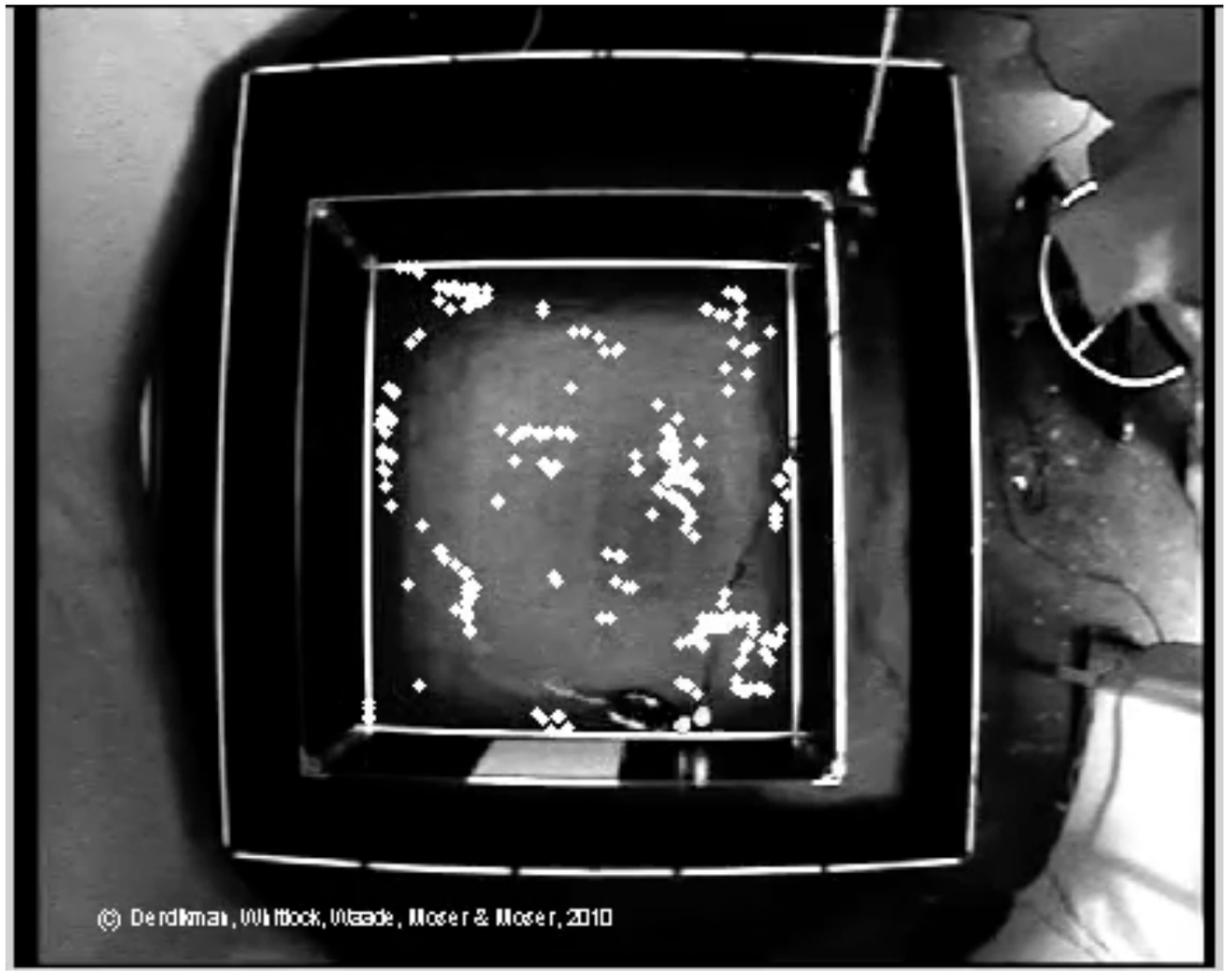

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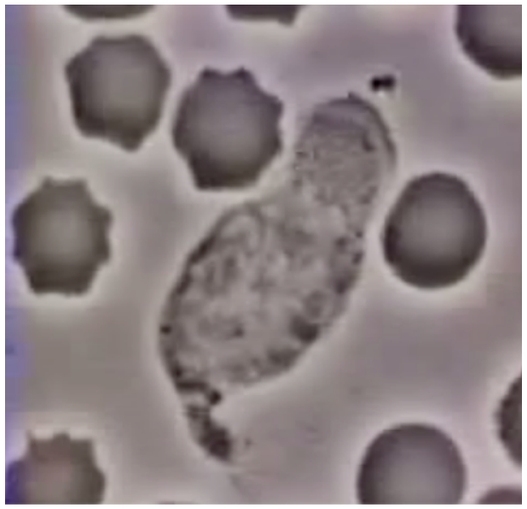
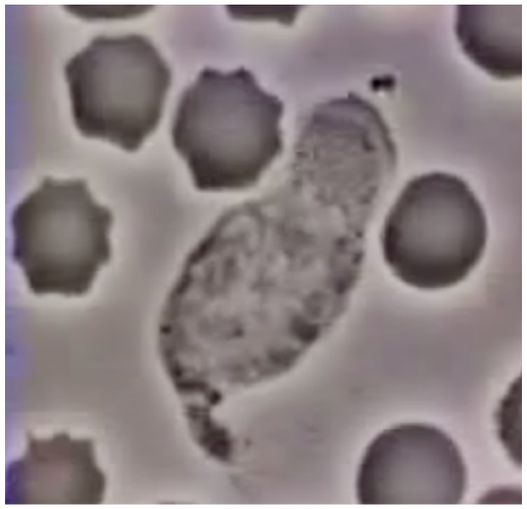


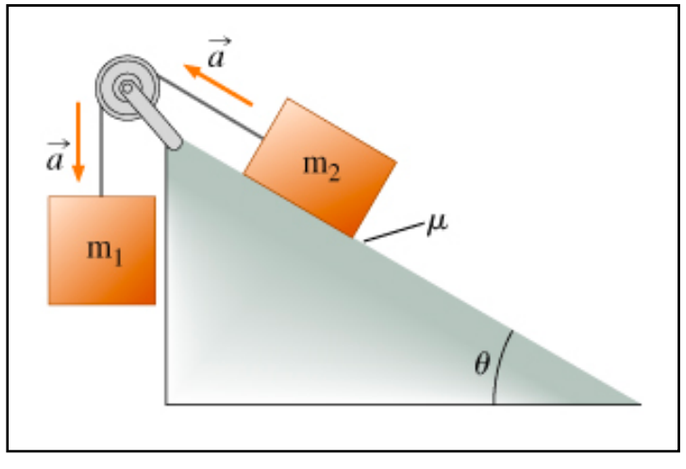
…but physics imposes strong constraints!

Biology generates exquisitely complex behavior from simple chemical building blocks

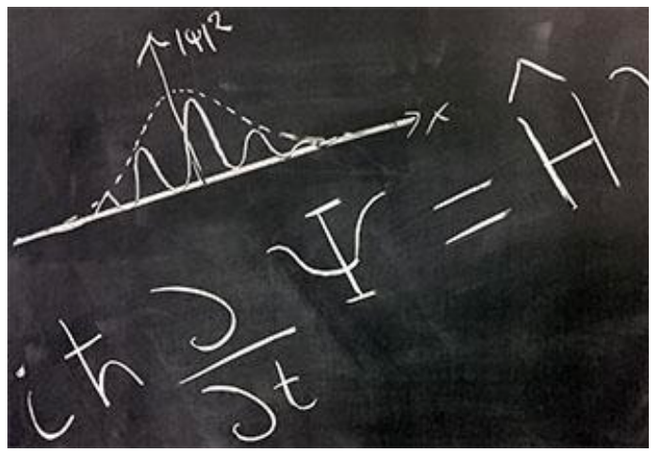


…but physics imposes strong constraints!

Can be different from our "usual" physical intuition:

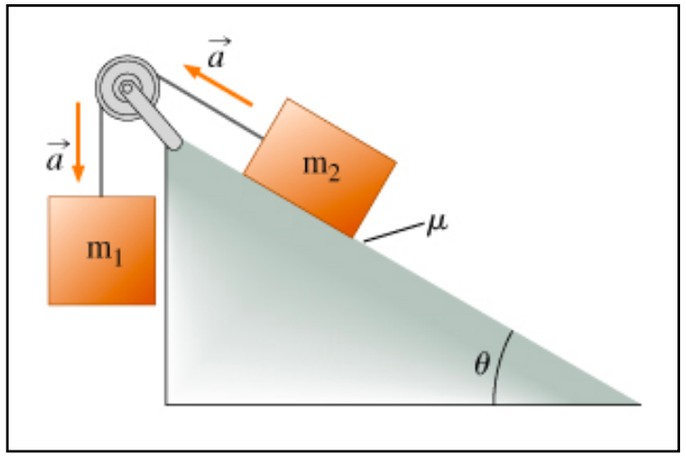


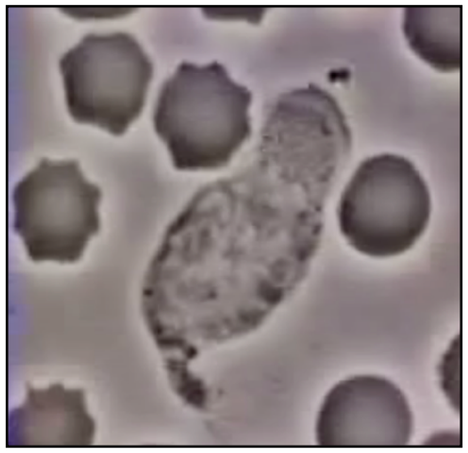
Physics of everyday objects

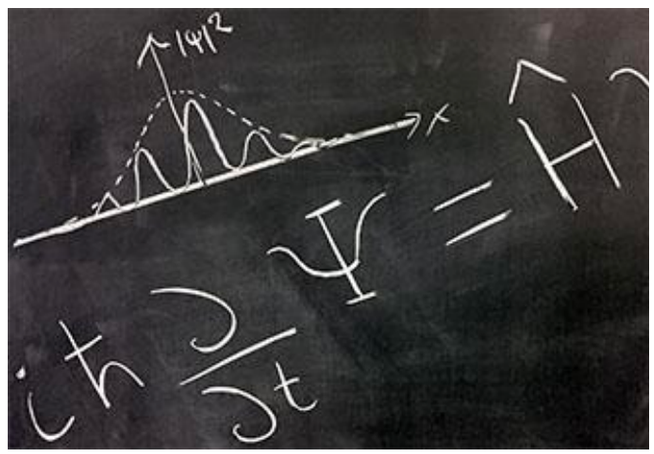


Quantum mechanics

Biology generates exquisitely complex behavior
…but physics imposes strong constraints





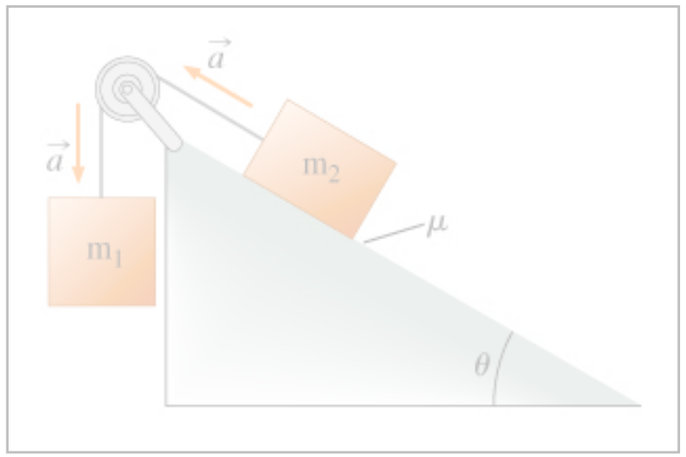


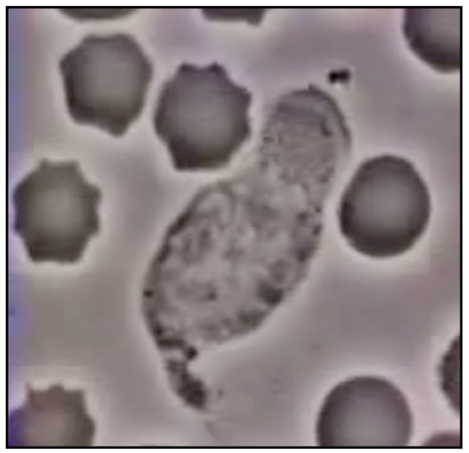
Physics of everyday objects | ***Biophysics*** | *Quantum mechanics*

↓

interesting new physics emerges at these <u>cellular</u> scales

Biology generates exquisitely complex behavior
…but physics imposes strong constraints



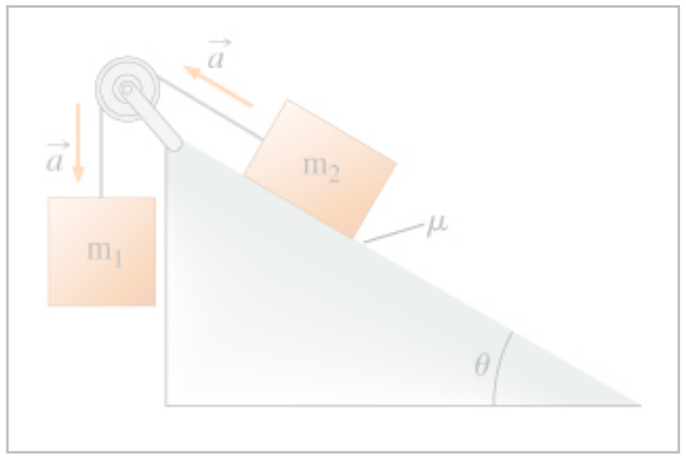


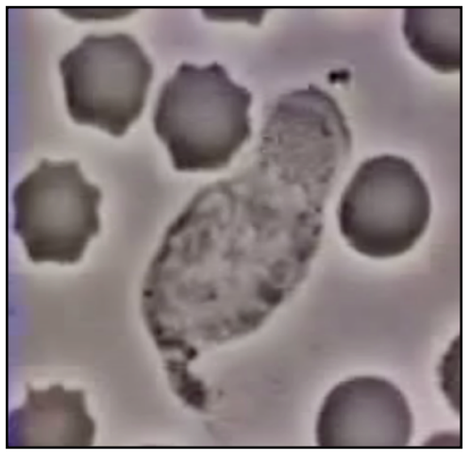
Physics of everyday objects | ***Biophysics*** | *Quantum mechanics*

Major themes:

- *Thermal fluctuations (*statistical mechanics*)*
- *Constant jostling of particles in solution (*diffusion*)*
- *Finite # molecules per cell (*counting noise*)*

Biology generates exquisitely complex behavior
…but physics imposes strong constraints



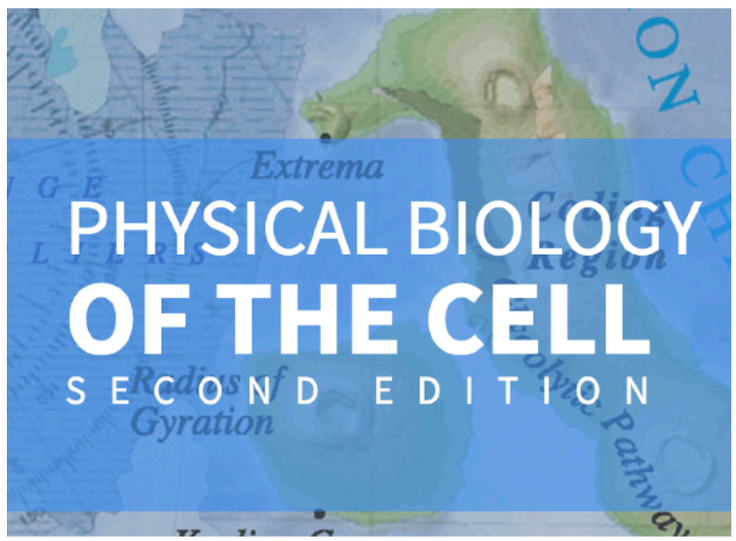


Physics of everyday objects | ***Biophysics*** | *Quantum mechanics*

Major themes:

- *Quantitative reasoning & order-of-magnitude estimation*

"biology by the numbers"



Phillips, Kondev, Theriot, & Garcia

Today:

tour of basic length, time,
& number scales in biology

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Why?

- #s impose strong constraints on what physical processes are relevant

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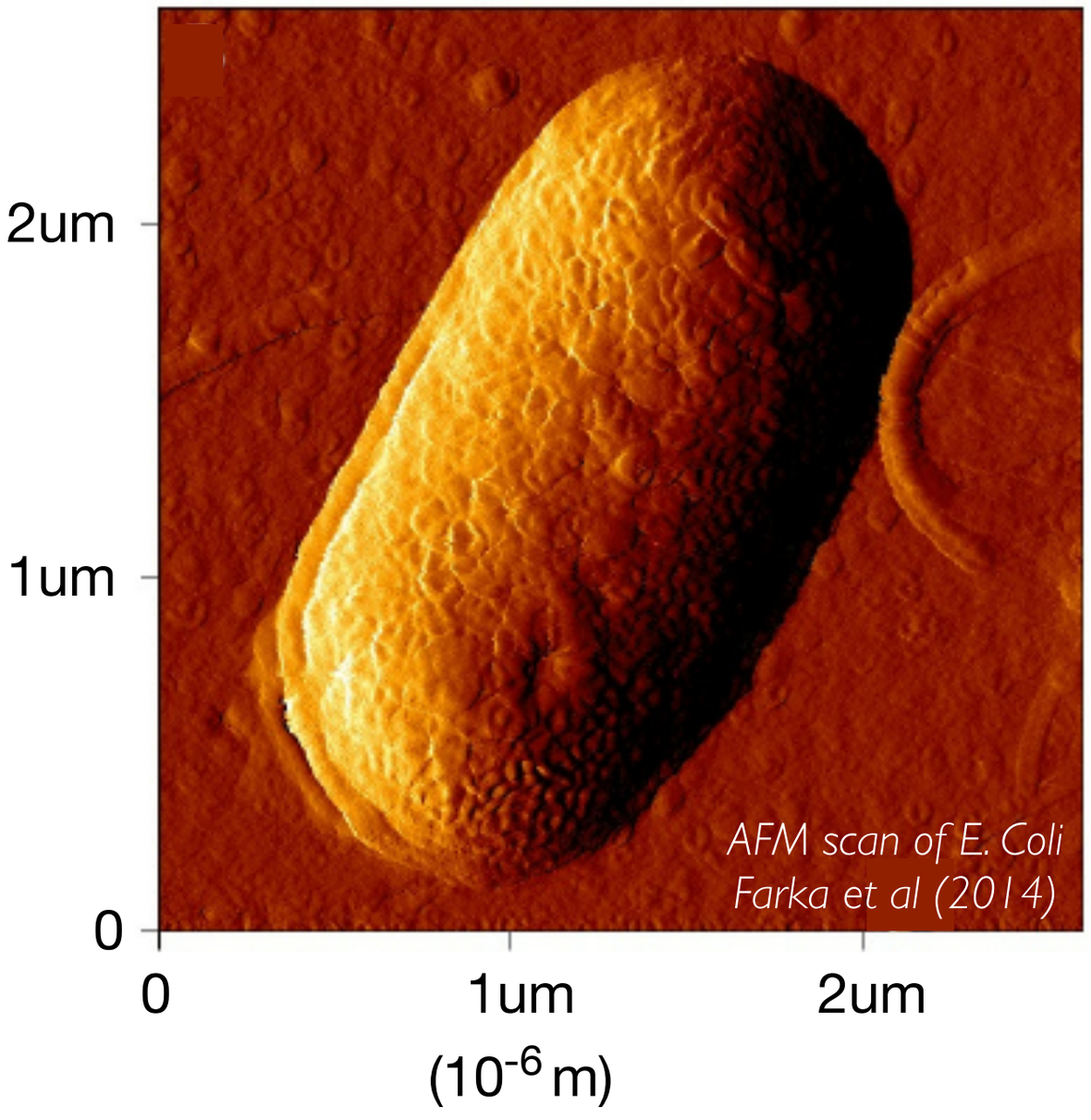
Why?

- #s impose strong constraints on what physical processes are relevant

- "trying to explain ***why*** #s have the values they do often ends up being an engine of discovery."

  — *Cell Biology by the Numbers* (Milo & Phillips) http://book.bionumbers.org/

E. Coli will be our standard ruler

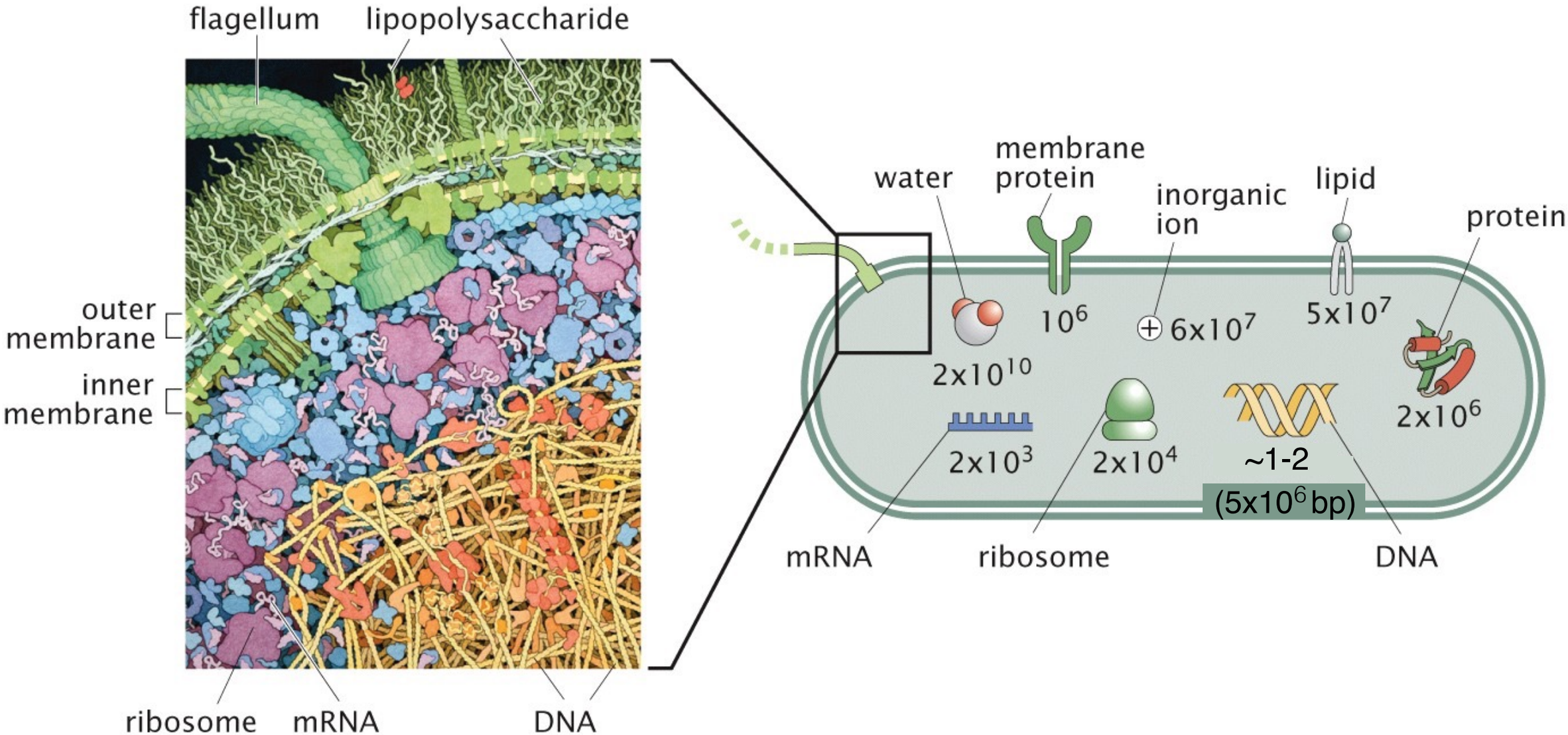


→ Volume: ~$(1um)^3 = 10^{-15}$ L

Mass ~ $(10^{-15}L)$ (1g/ml) = 10^{-12} g

(assuming density ~ water)

Taking the molecular census of an *E. Coli* cell



DNA —transcription (*RNA polymerase*)→ ***mRNA*** —translation (*ribosome*)→ ***Protein (amino acids)*** → ***Growth***

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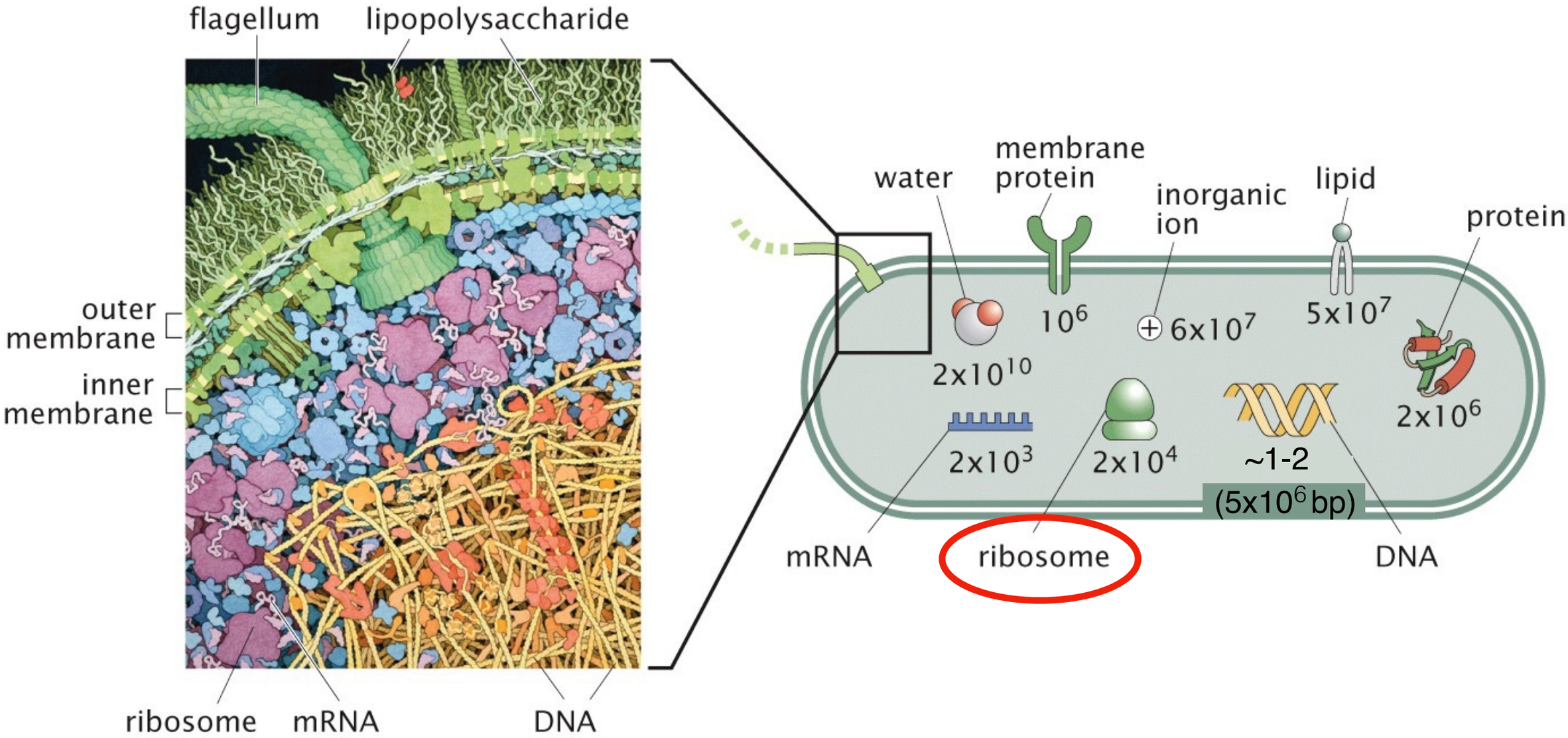

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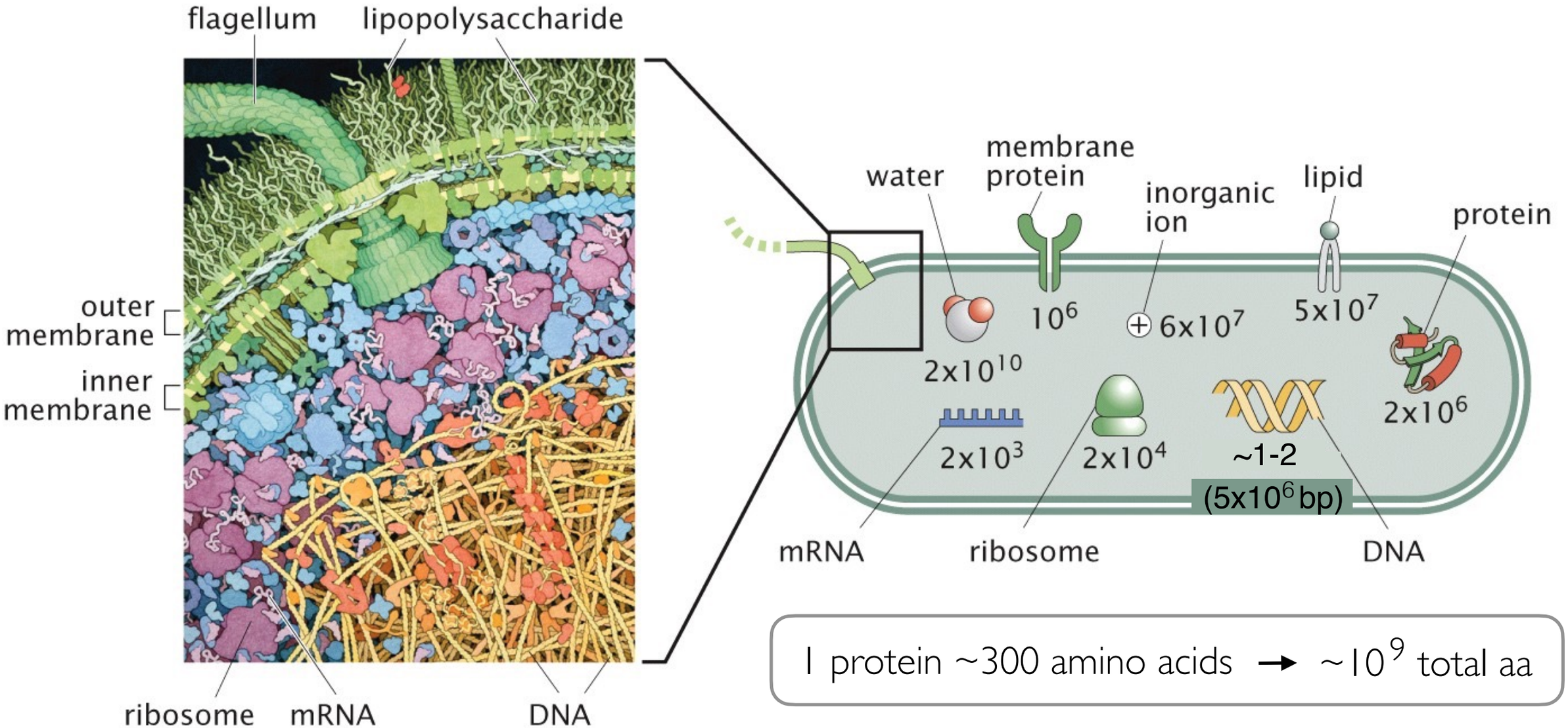


1 protein ~300 amino acids → ~10^9 total aa

DNA —transcription (*RNA polymerase*)→ ***mRNA*** —translation (*ribosome*)→ ***Protein (amino acids)*** → ***Growth***

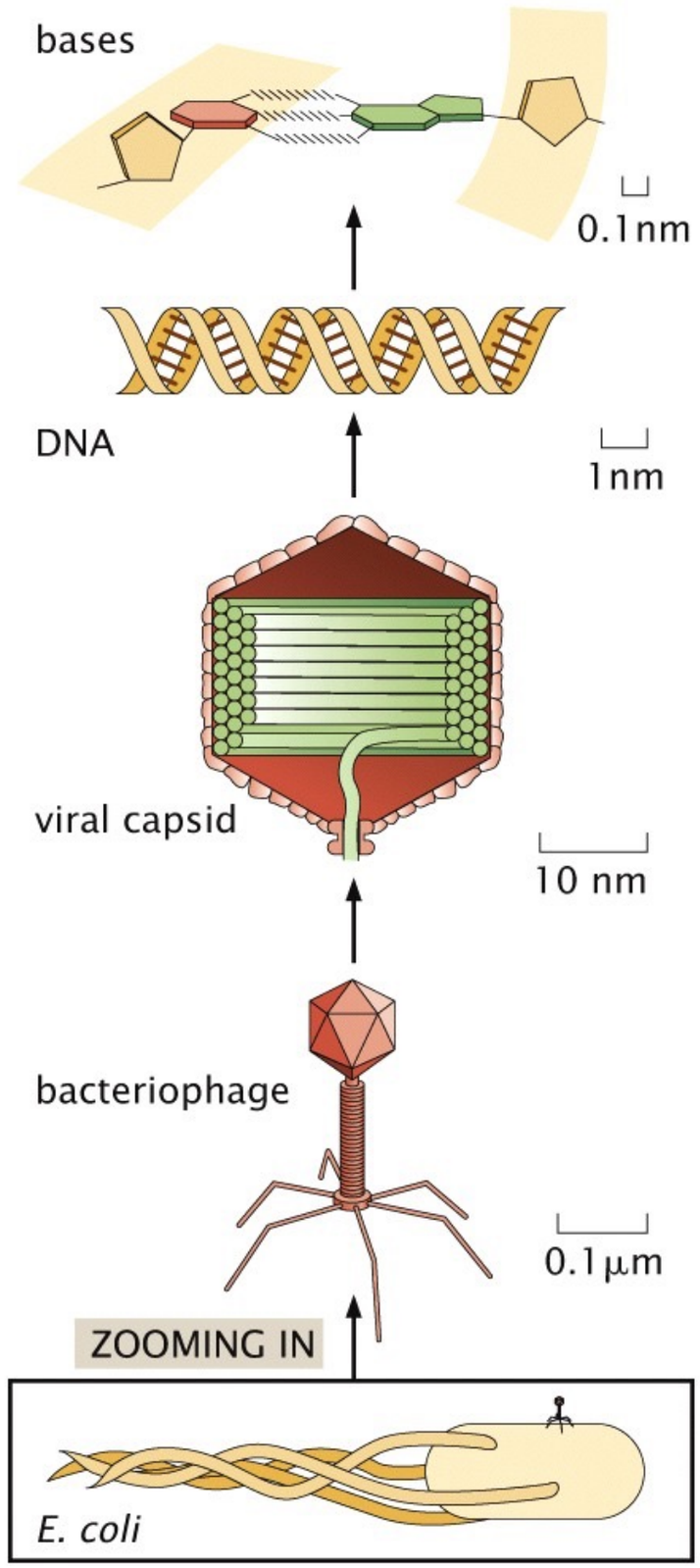
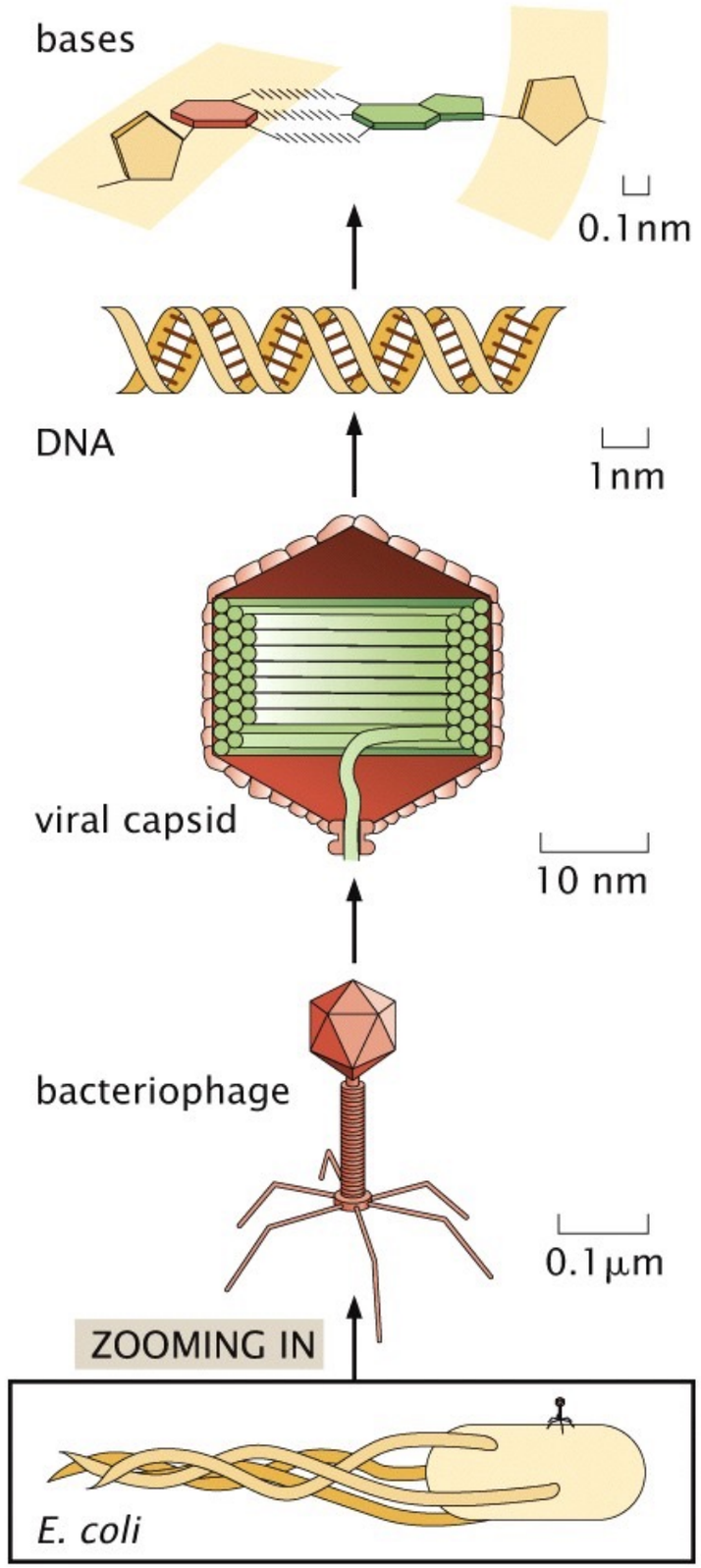


Figure 2.15 (part 1 of 2) Physical Biology of the Cell, 2ed. (© Garland Science 2013)



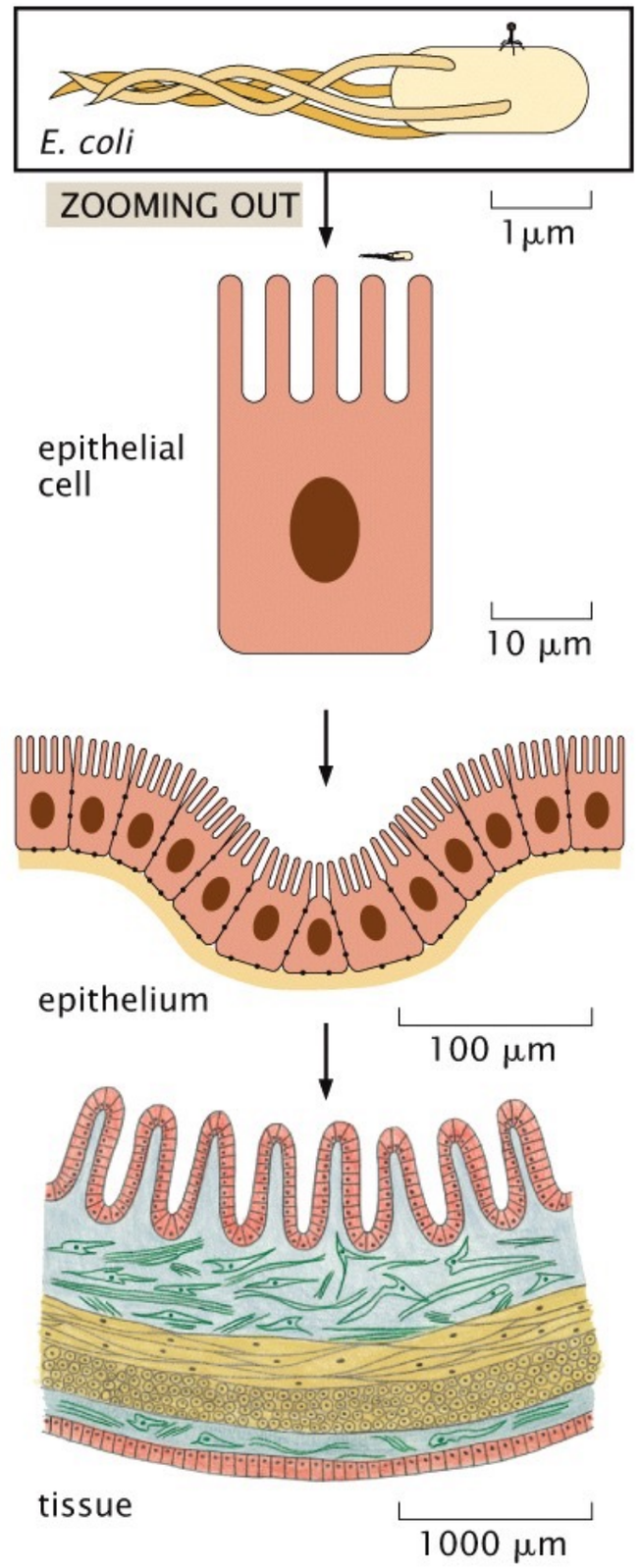
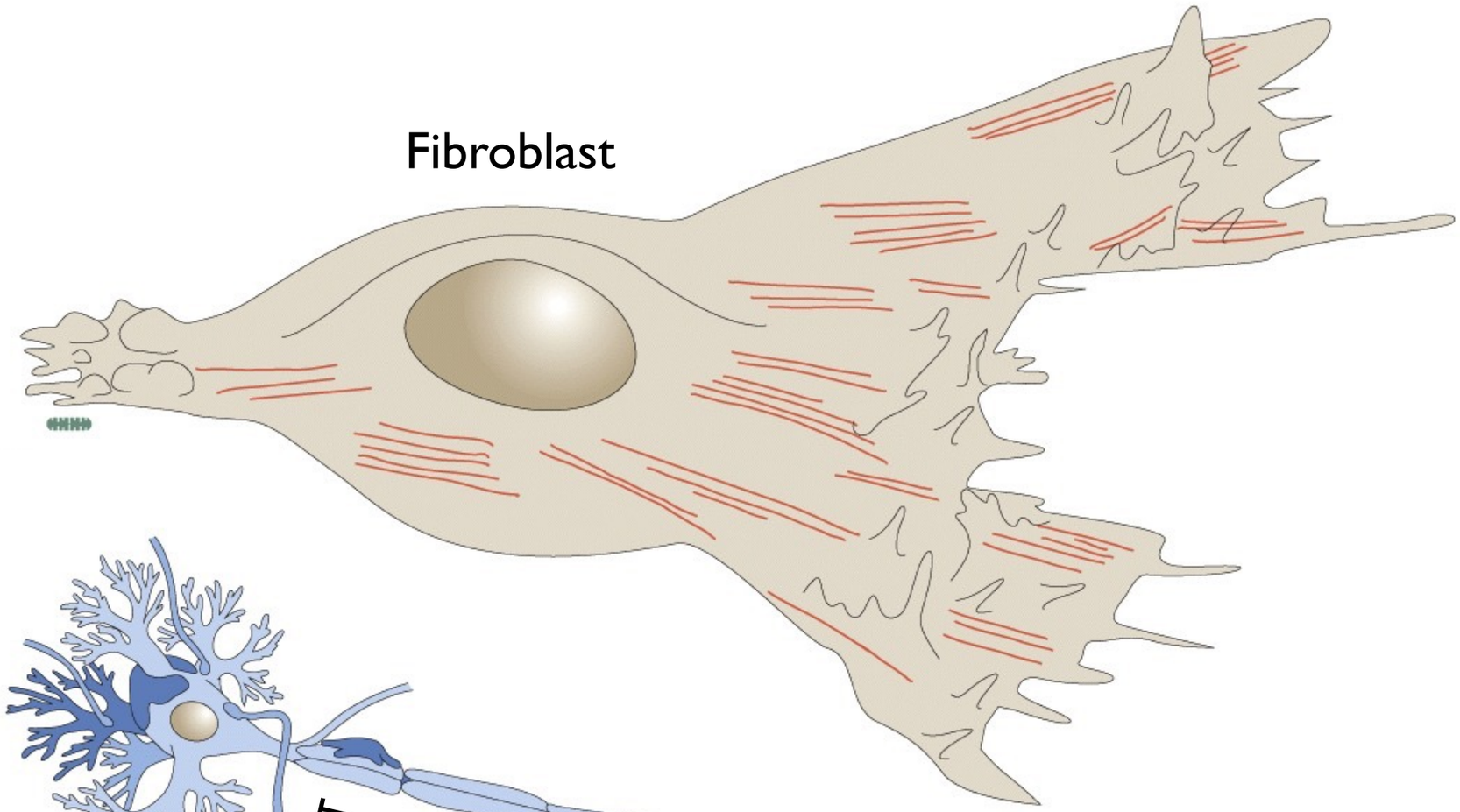


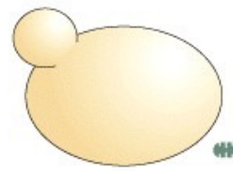
Figure 2.15 (part 1 of 2) Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Human cells have a huge diversity of structure and function

Fibroblast

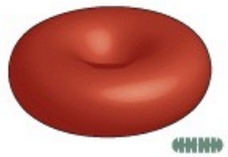


Budding yeast

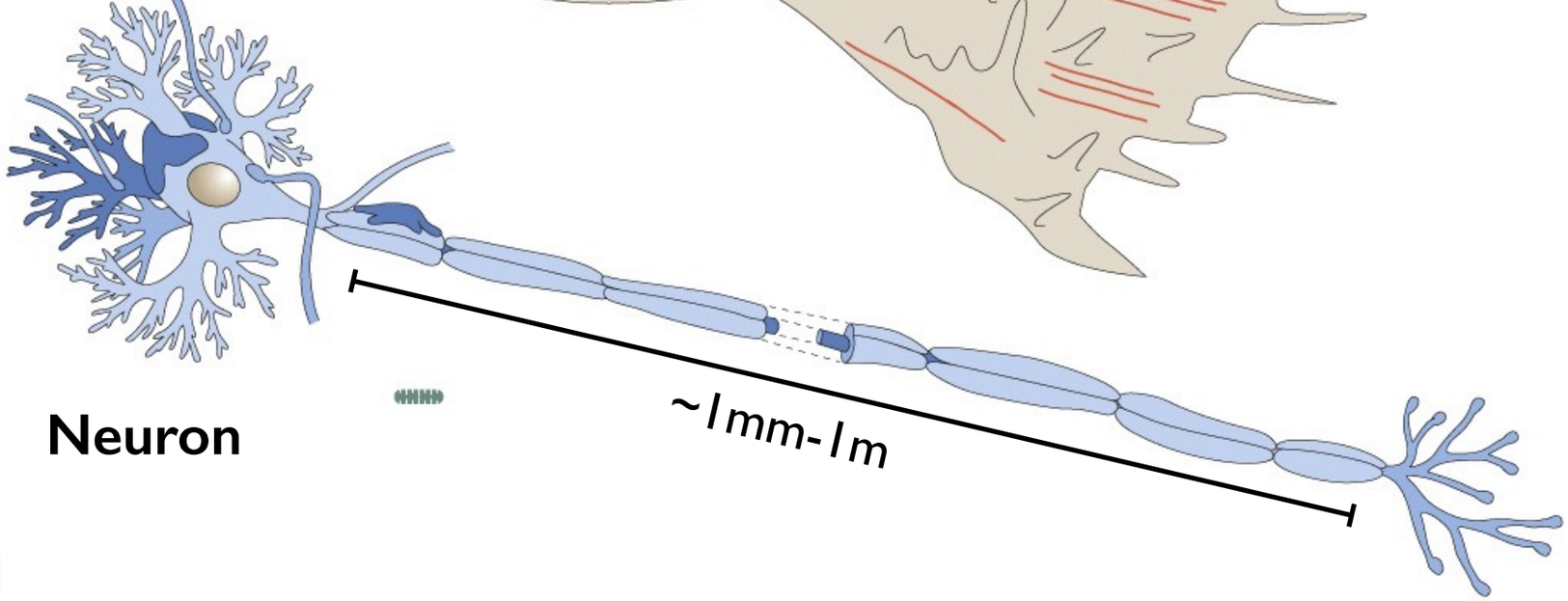


E. coli

Red blood cell



~5um

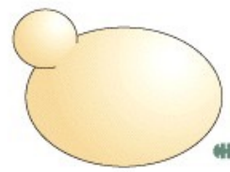


Neuron

Human cells have a huge diversity of structure and function

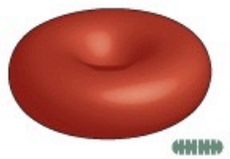
Fibroblast

Budding yeast



E. coli

Red blood cell



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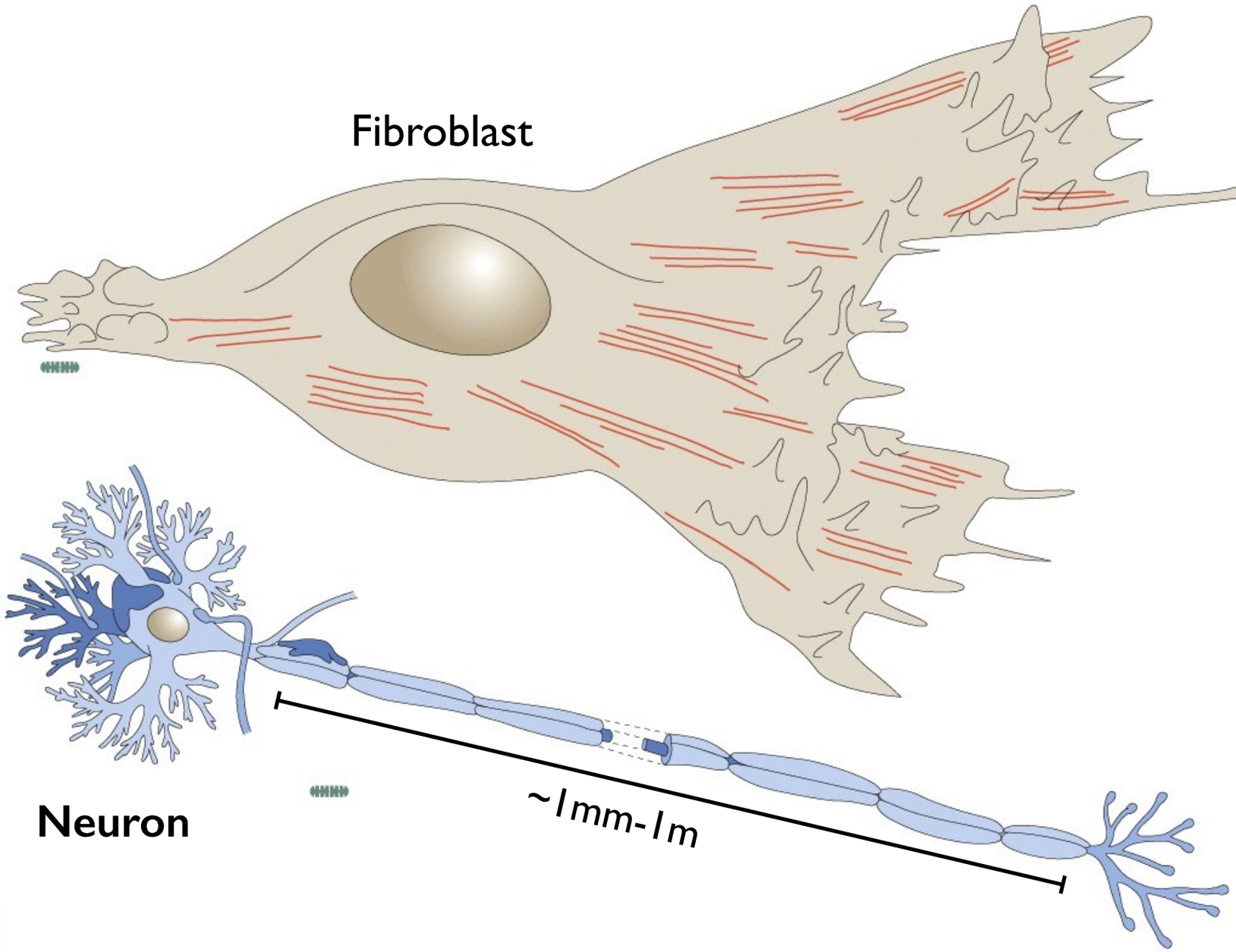

Neuron

→ **Implications for intra-cellular communication (Lectures 5 & 7)**

Biological processes occur over a huge range of timescales

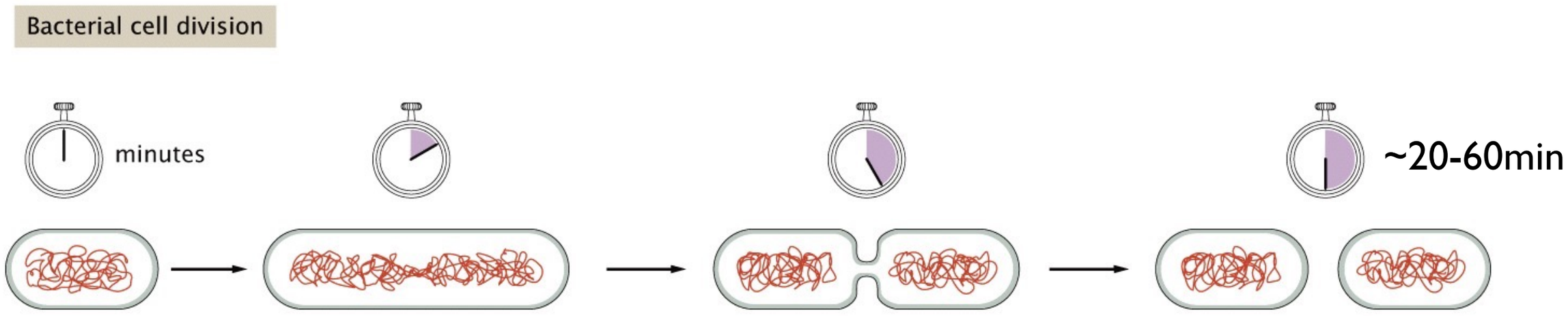

Figure 3.2c Physical Biology of the Cell, 2ed. (© Garland Science 2013)

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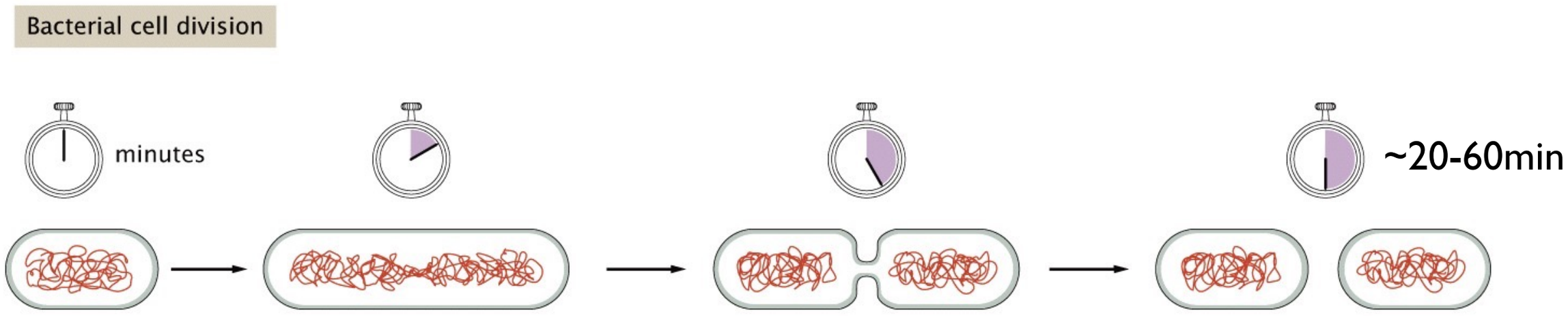

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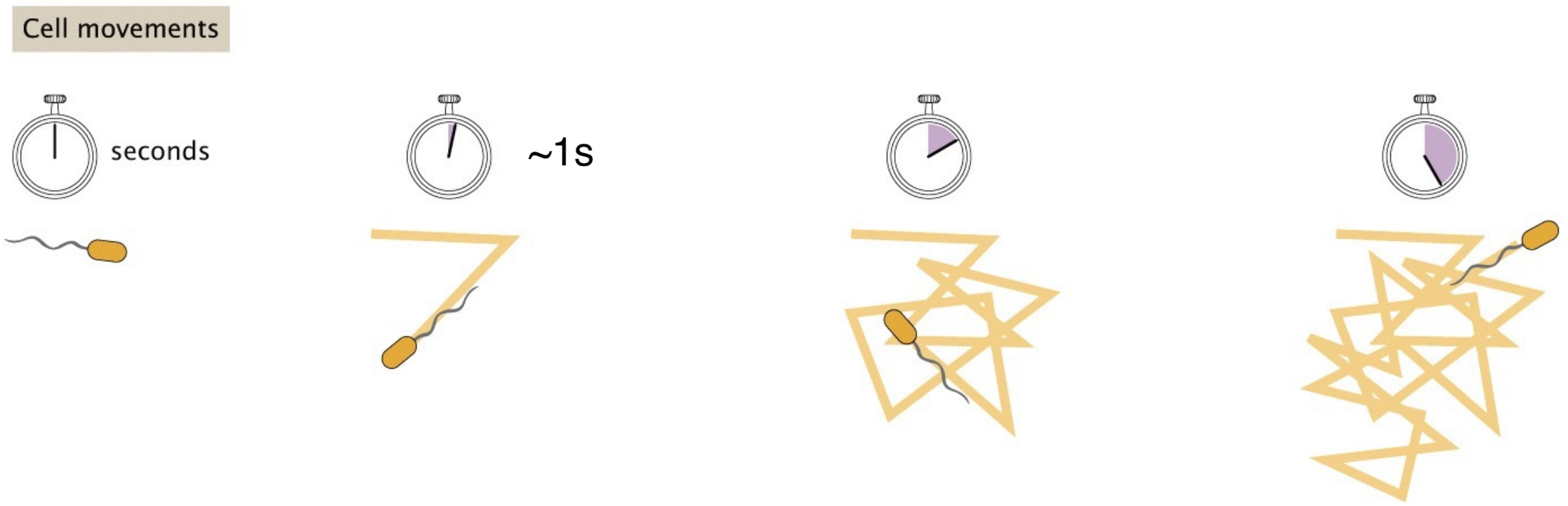

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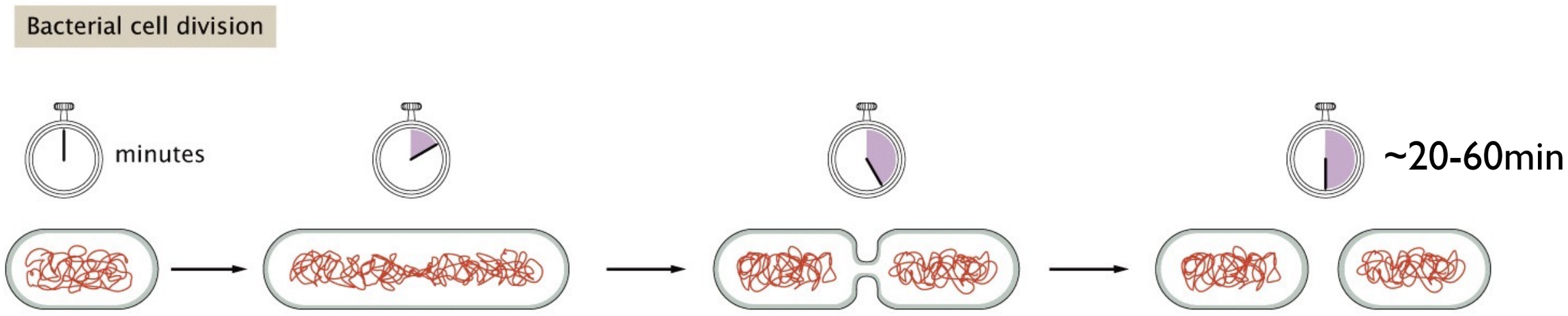

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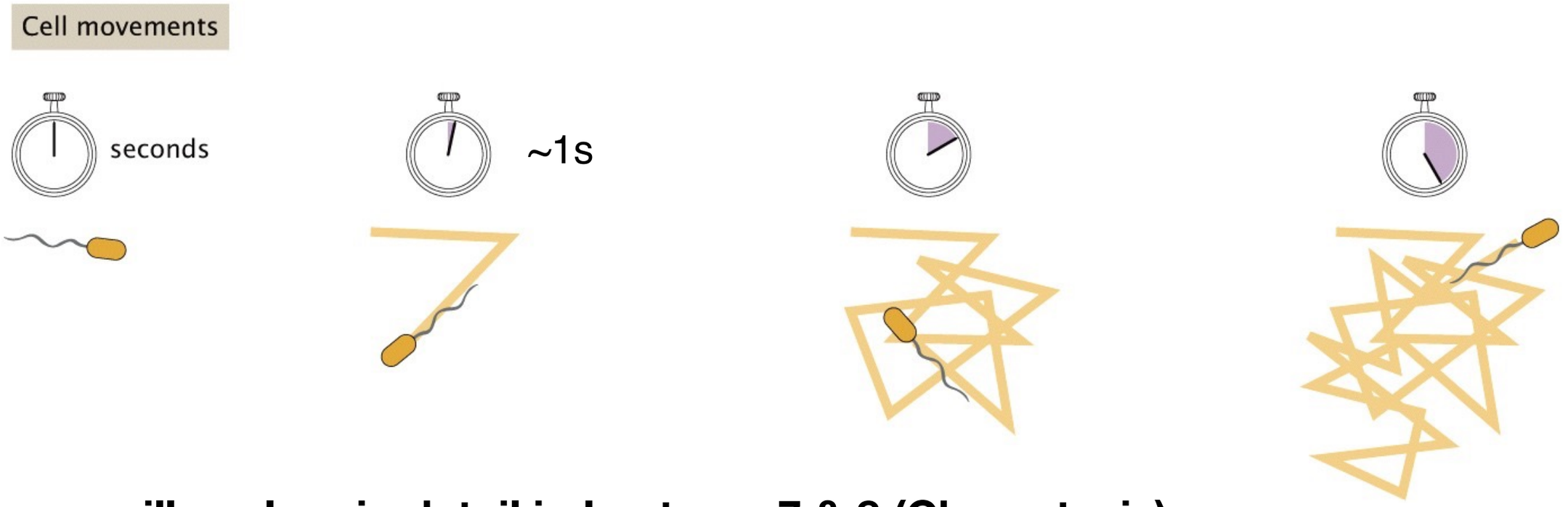
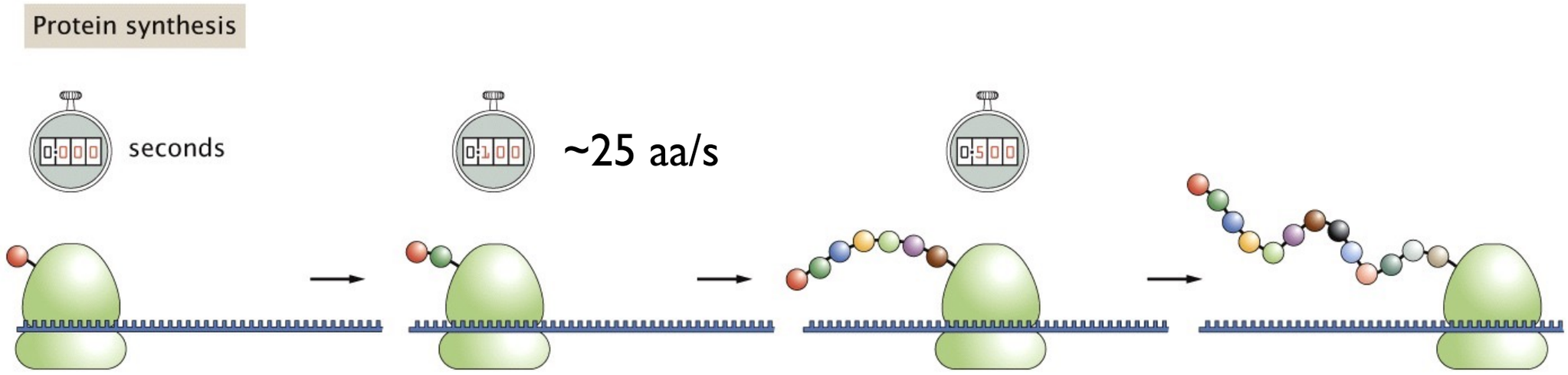
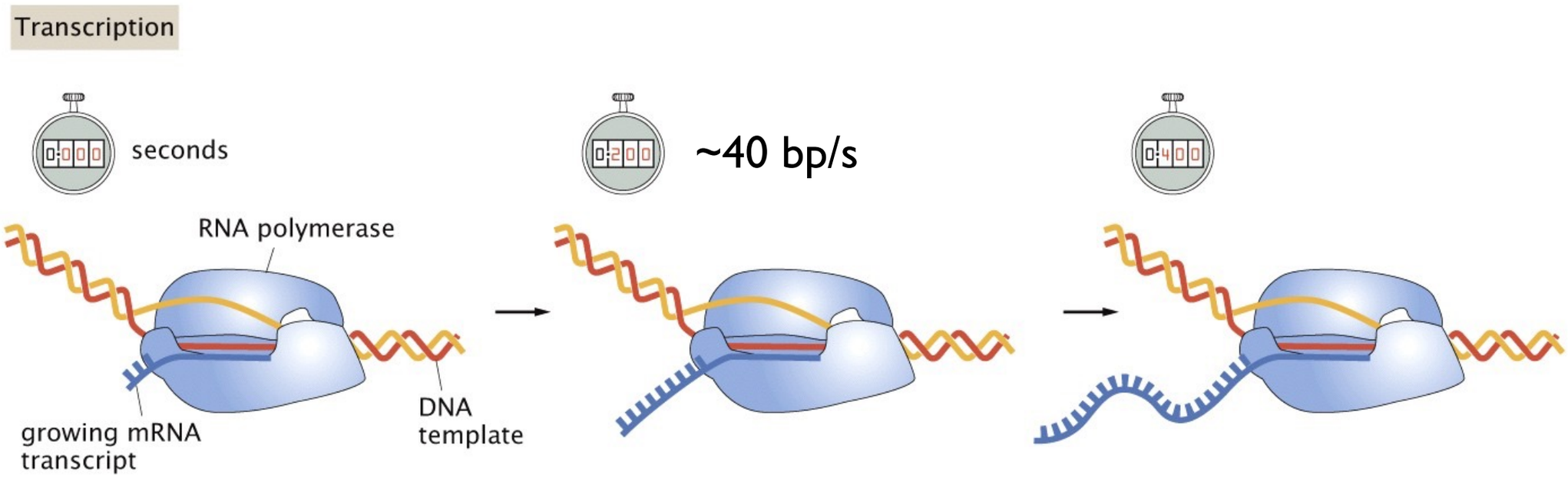


→ **will explore in detail in Lectures 7 & 8 (Chemotaxis)**

Biological processes occur over a huge range of timescales





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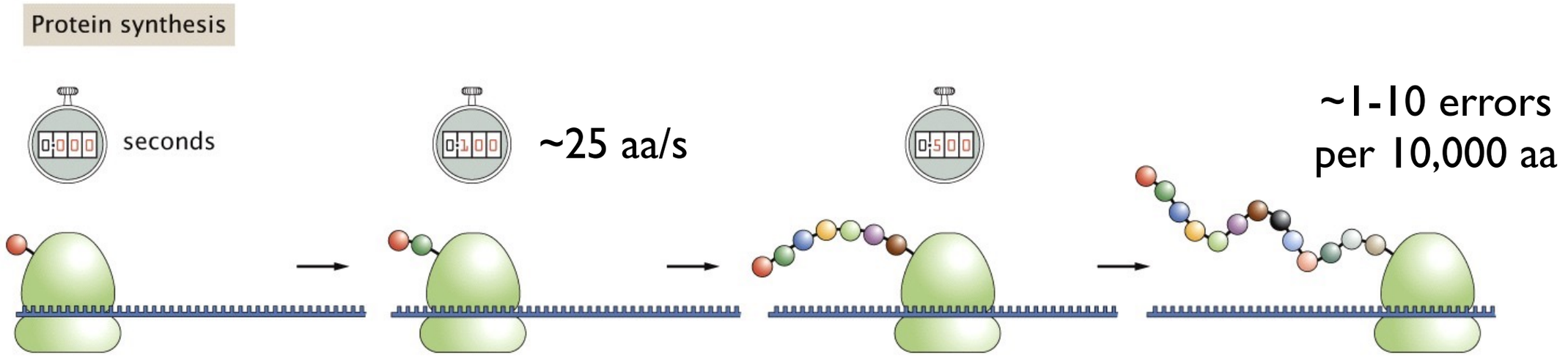

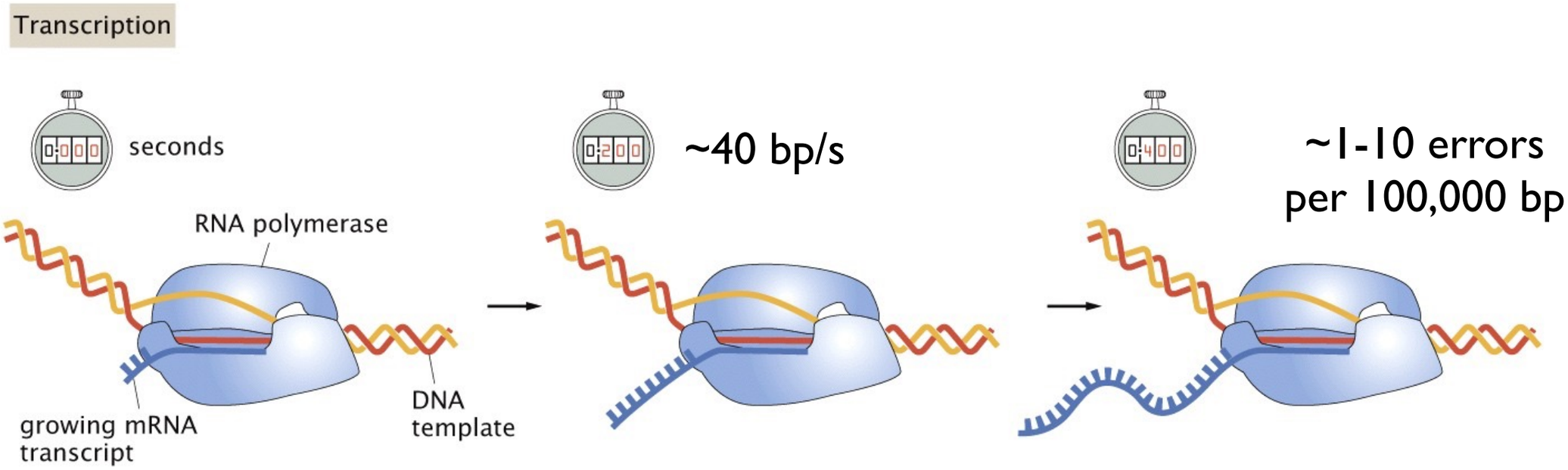

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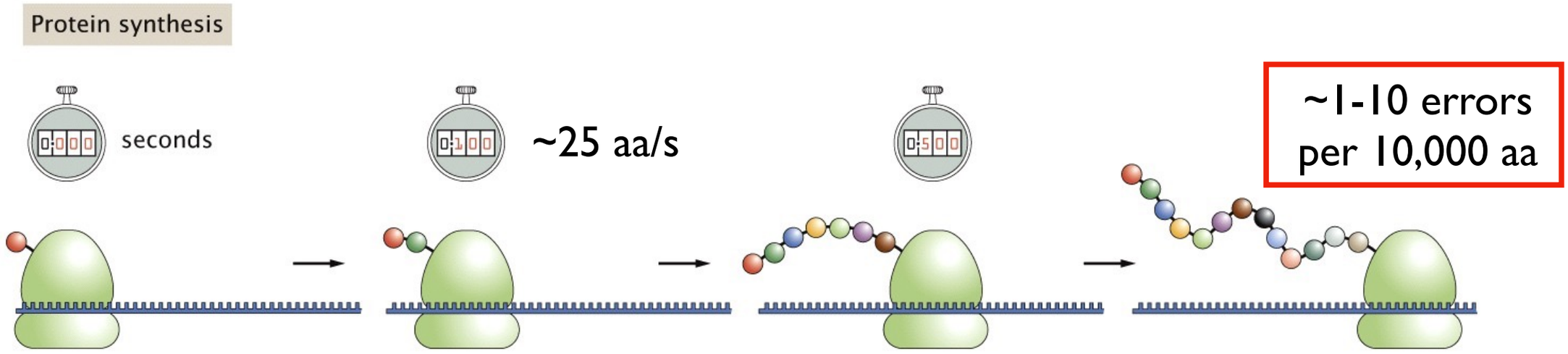
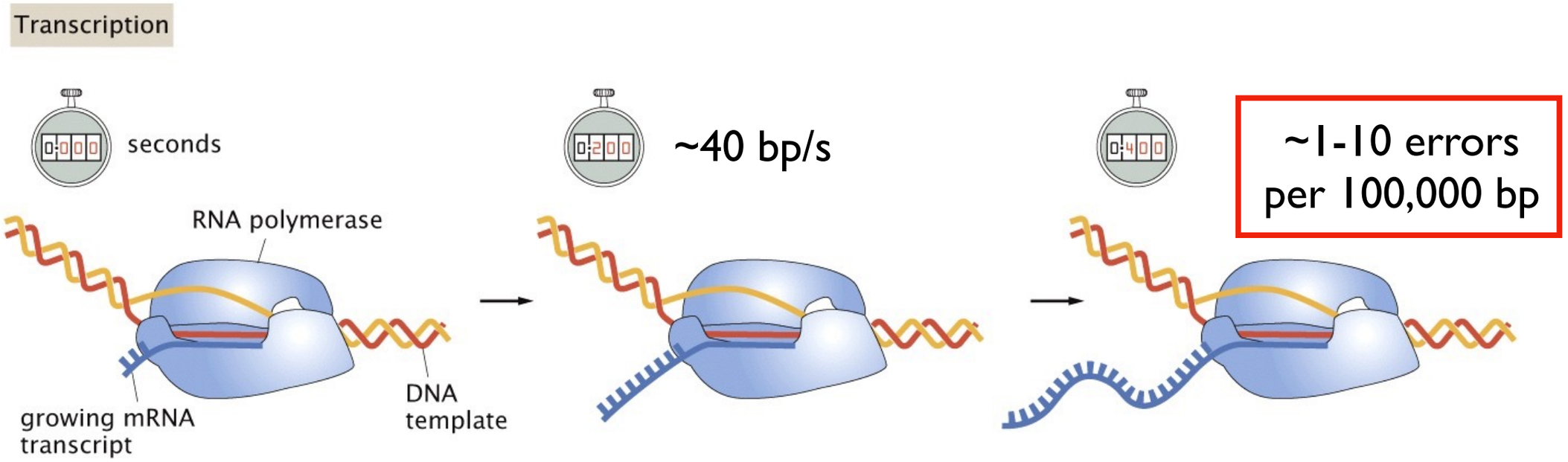
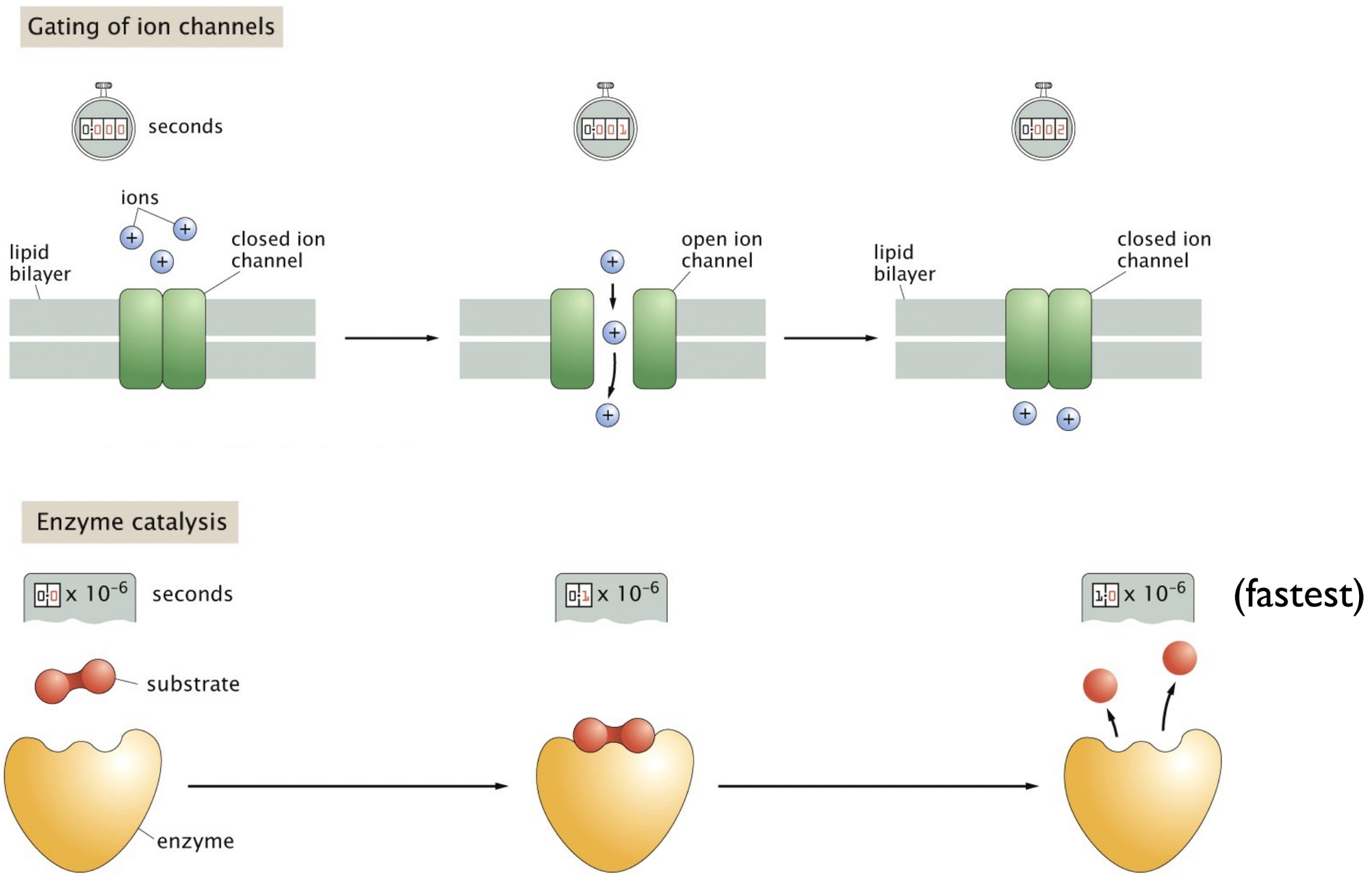




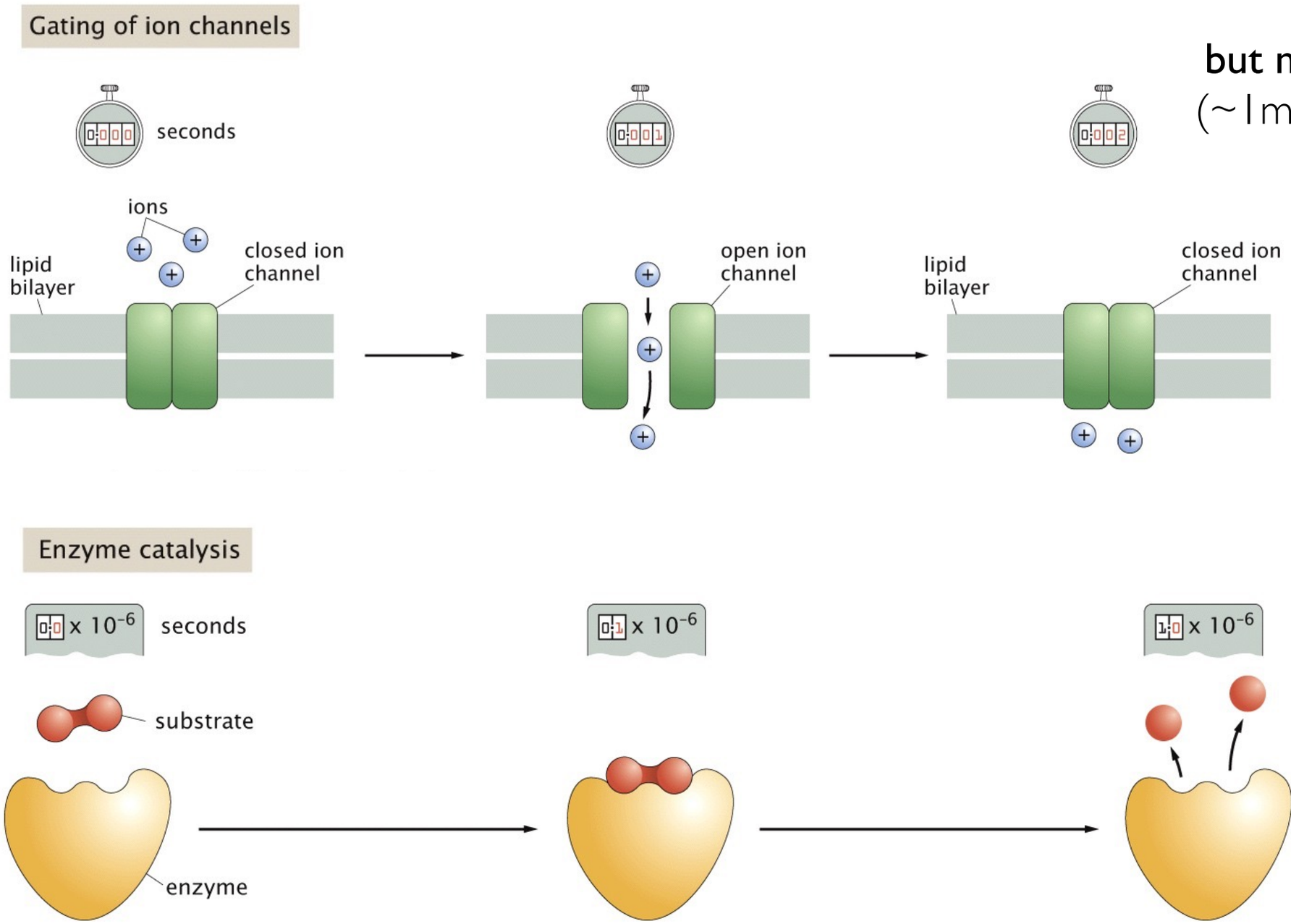
→ **Lectures 9 & 10: How do these machines achieve such low error rates?**
(& how could *evolution* make them better?)

Biological processes occur over a huge range of timescales



(Floor ~ characteristic QM timescale, h/kT ~ 10^{-12} s)

Biological processes occur over a huge range of timescales



but many still slow!
(~1ms-1s, Lecture 7)

(fastest)

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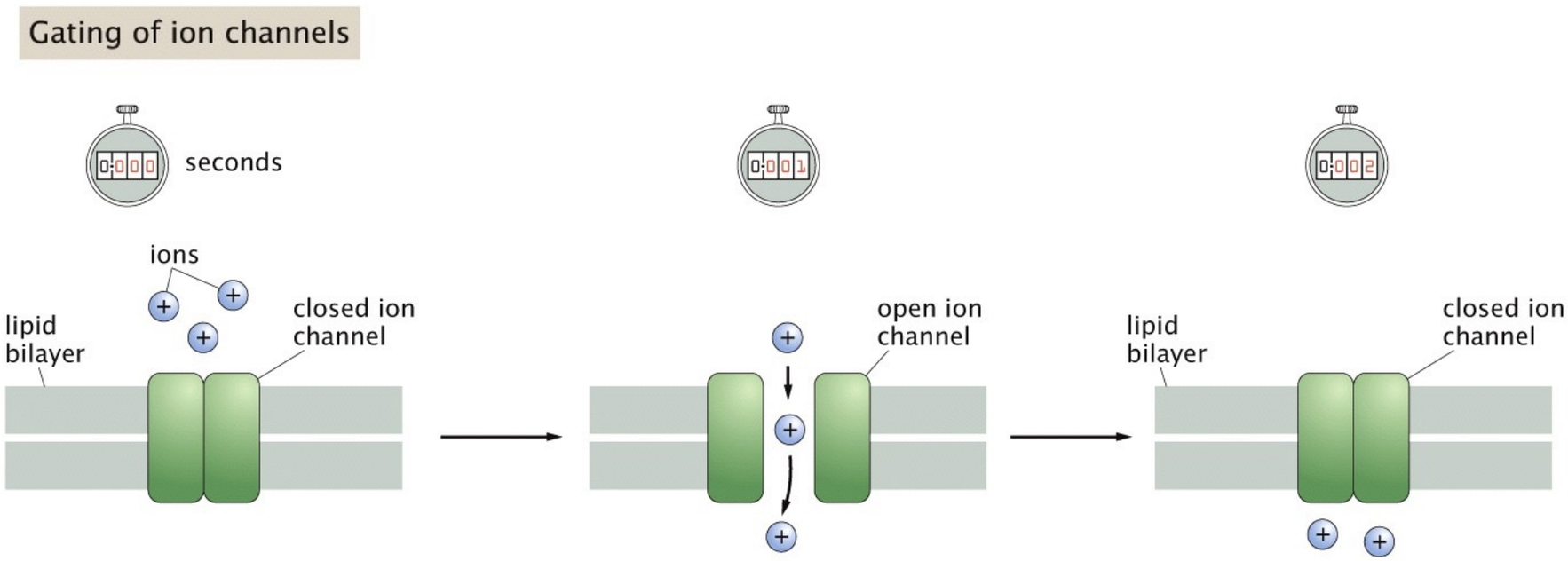
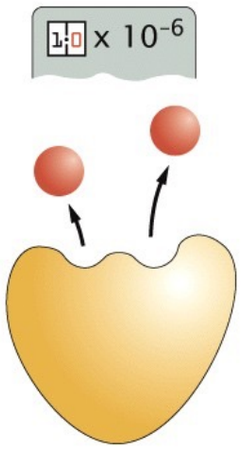
Biological processes occur over a huge range of timescales



Goal:

Understand ***physical processes*** that set timescales, & how they influence ***design*** of cells & organisms.



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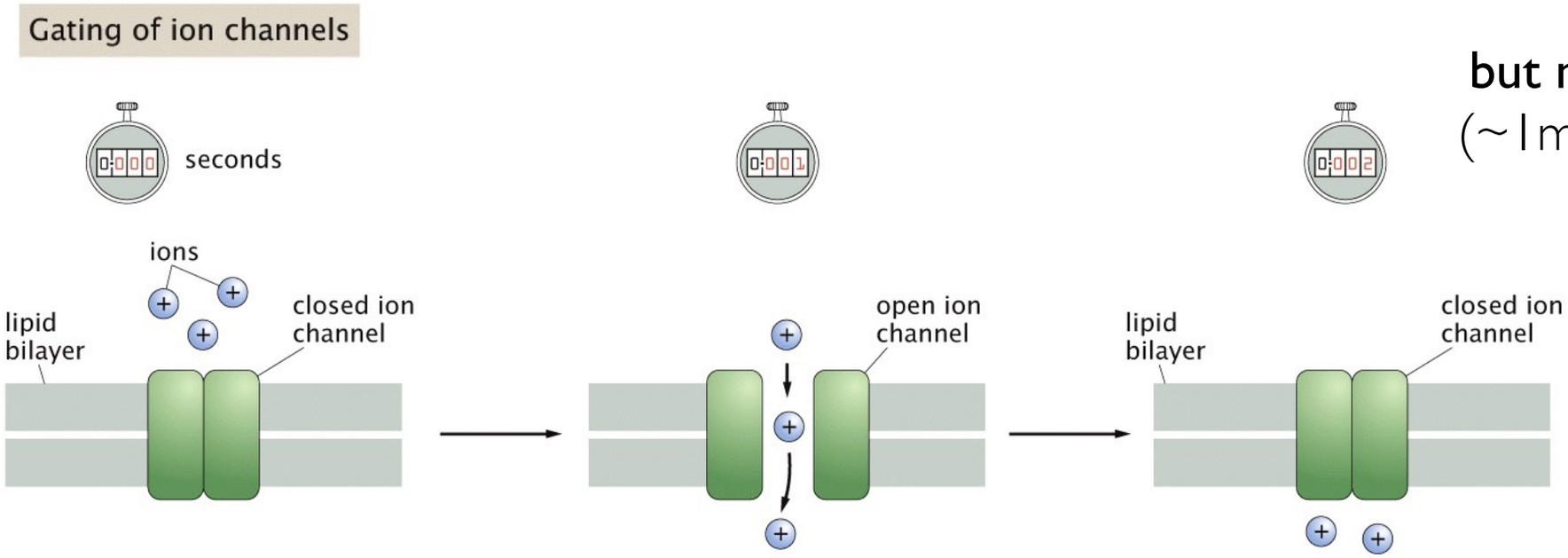

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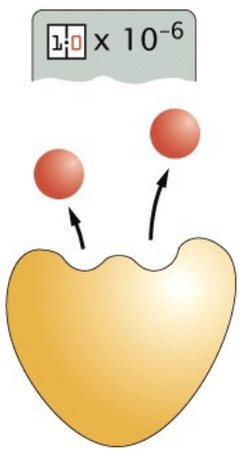
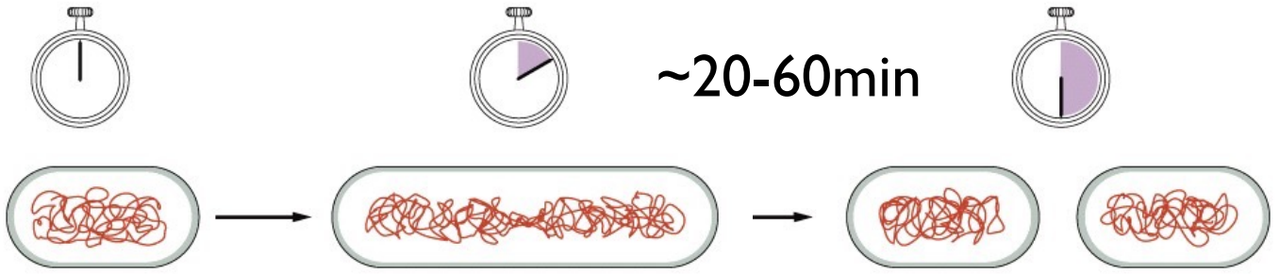
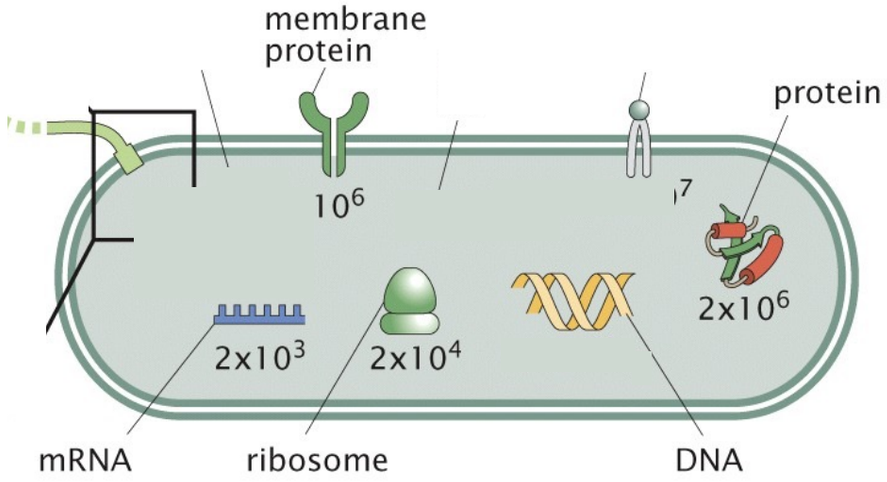


(fastest)

(Floor ~ characteristic QM timescale, h/kT ~ 10^{-12} s)

Example: what can we learn from these numbers?





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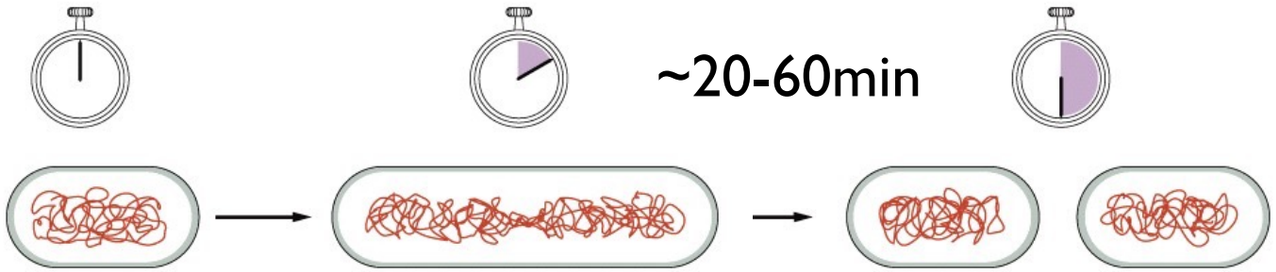

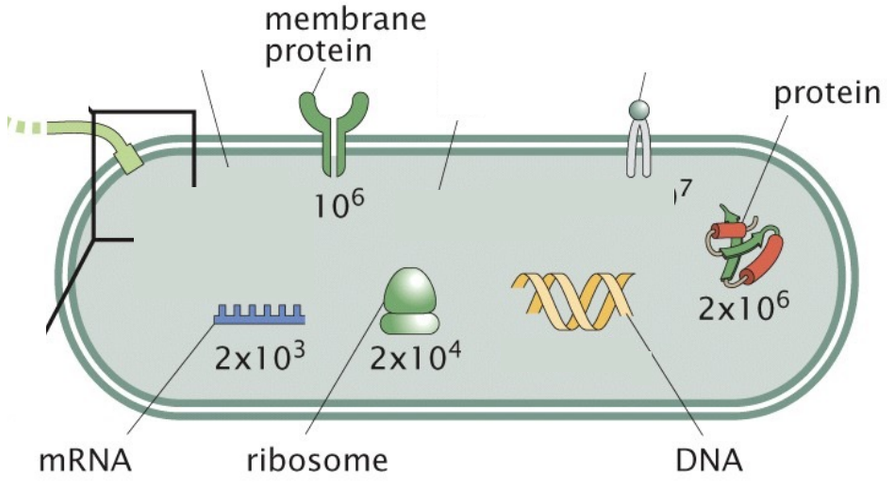

E. coli replication time $\geq$ Time required for ribosomes to synthesize all proteins for new cell

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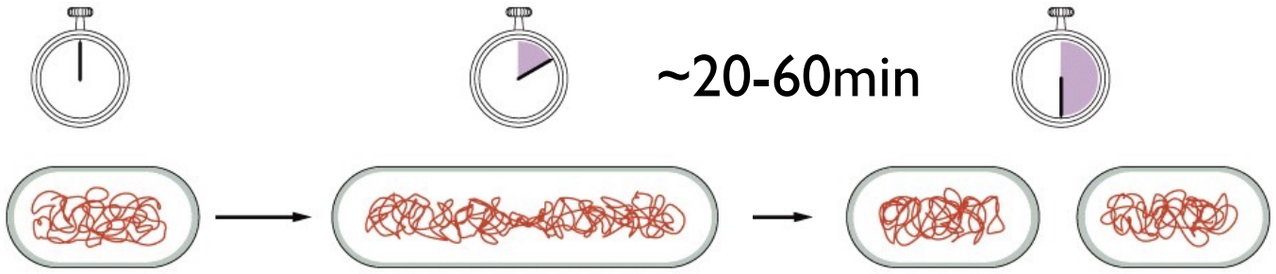

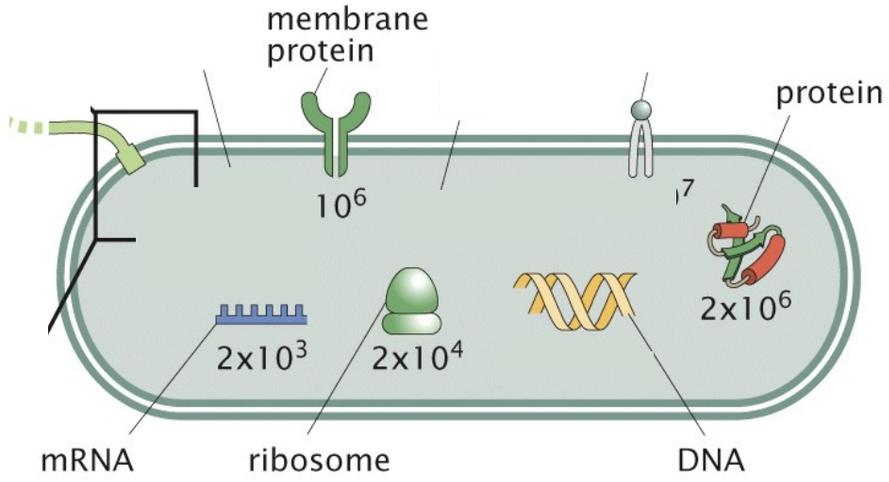

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$$\approx \frac{(\sim 3x10^6 \text{ proteins})}{}$$

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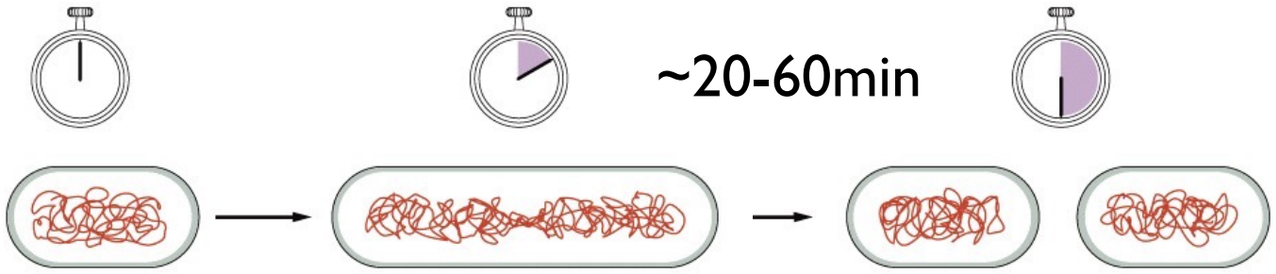

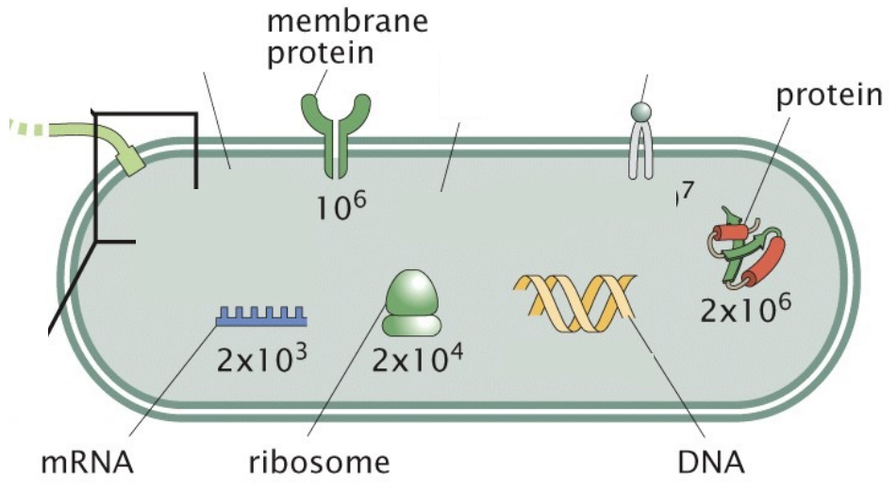

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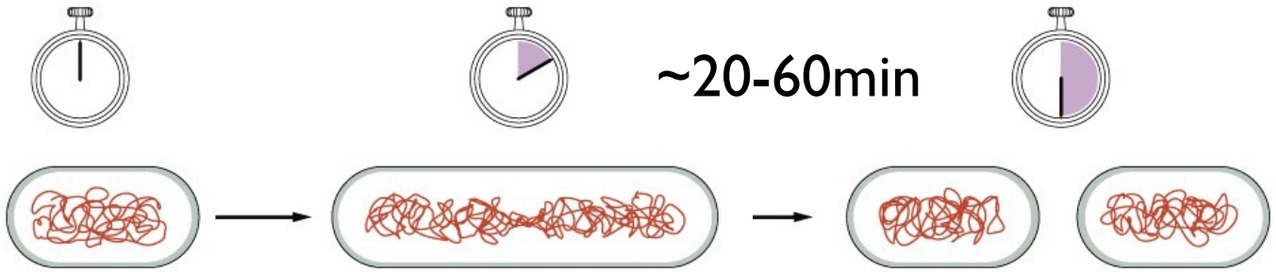

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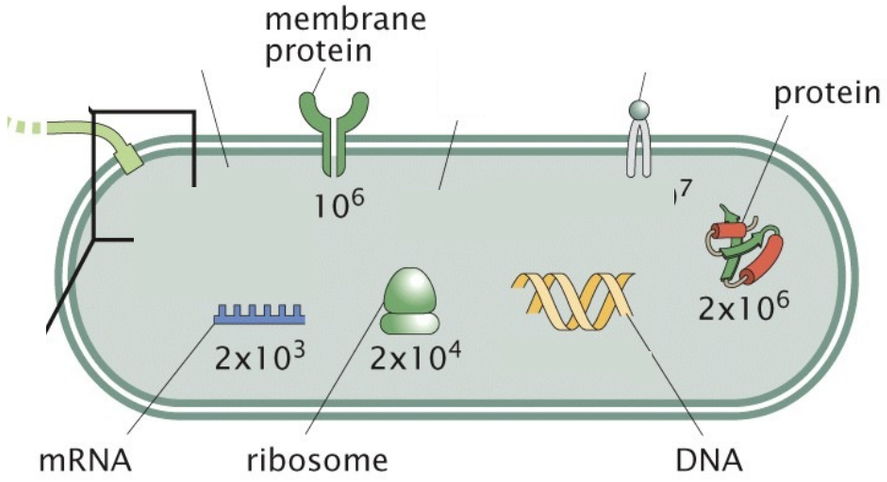
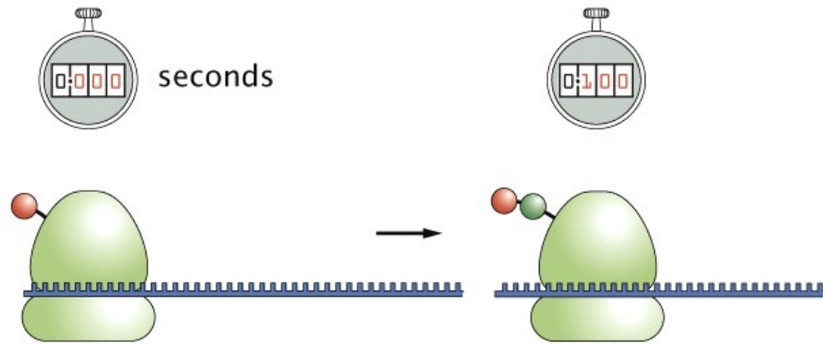


Protein synthesis ~25 aa/s



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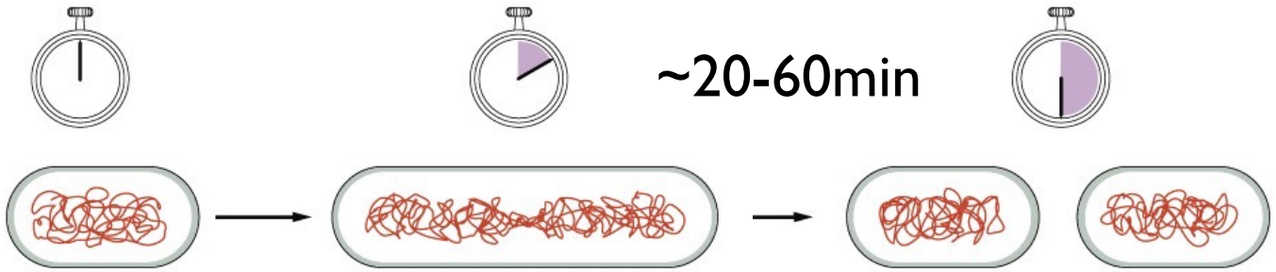

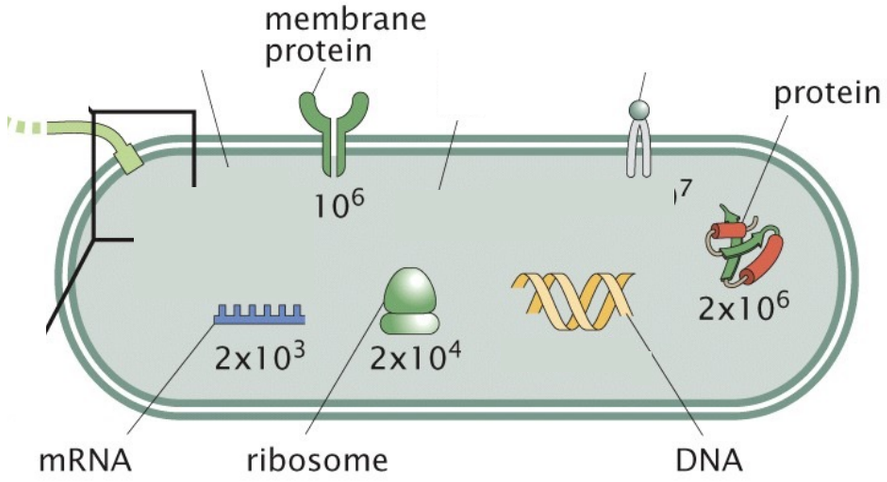

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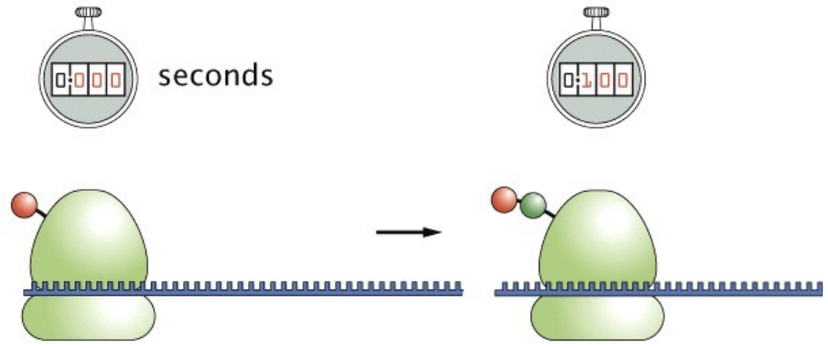

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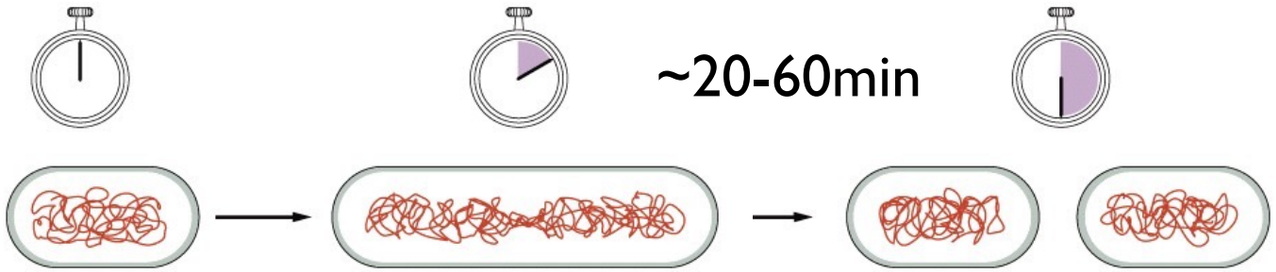

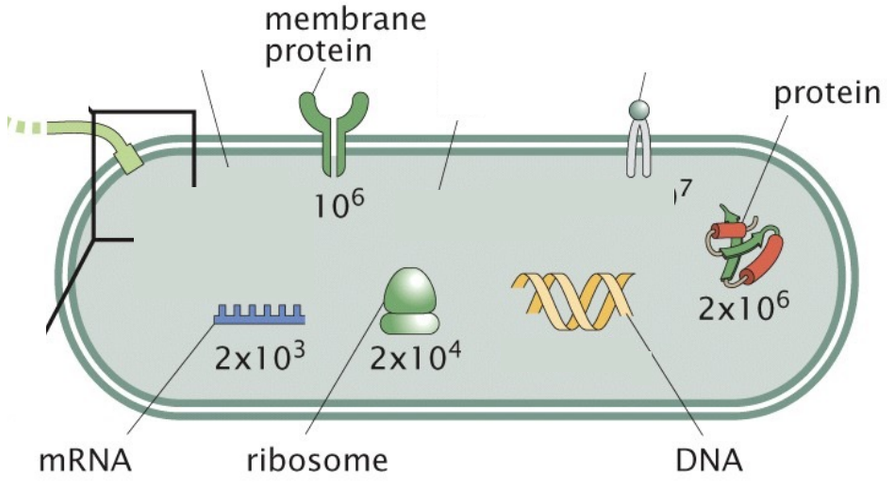

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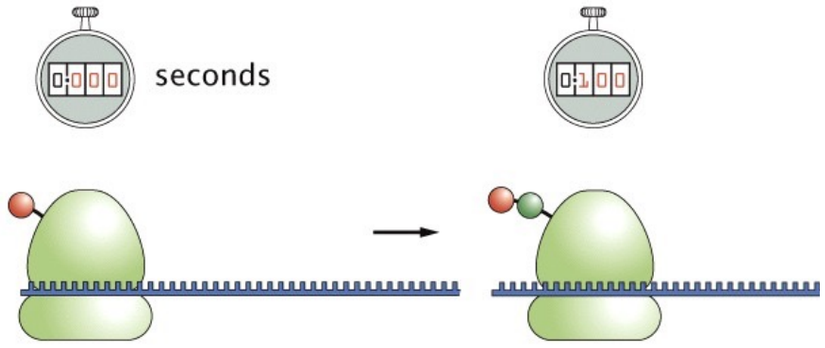

$\approx$ 30 mins!

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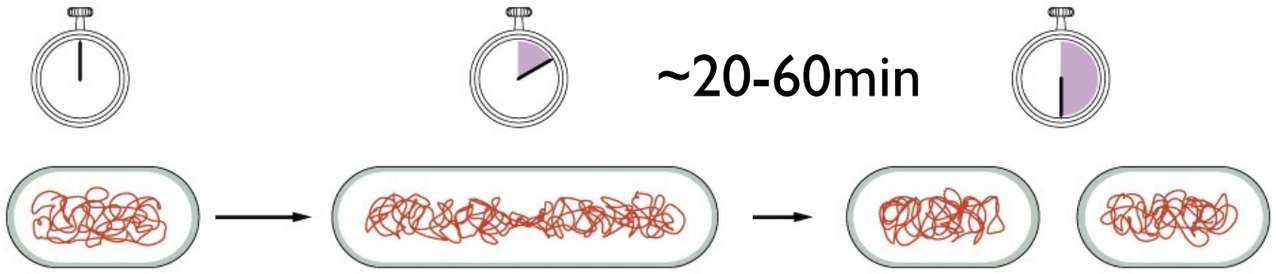

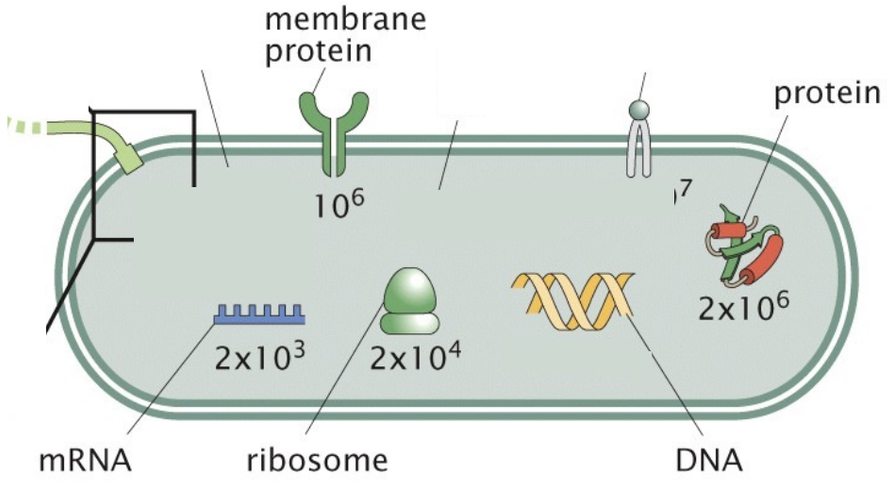

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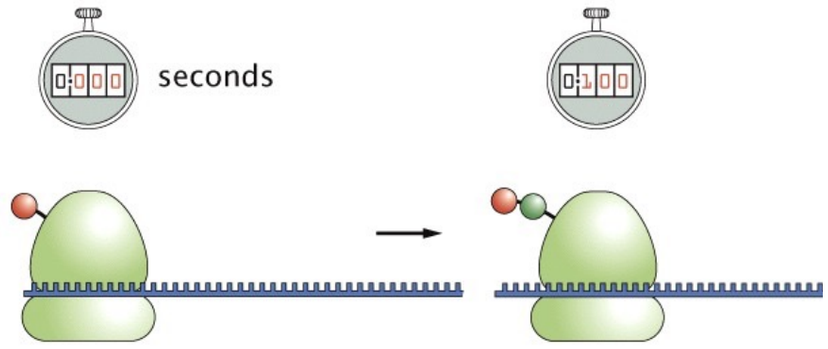

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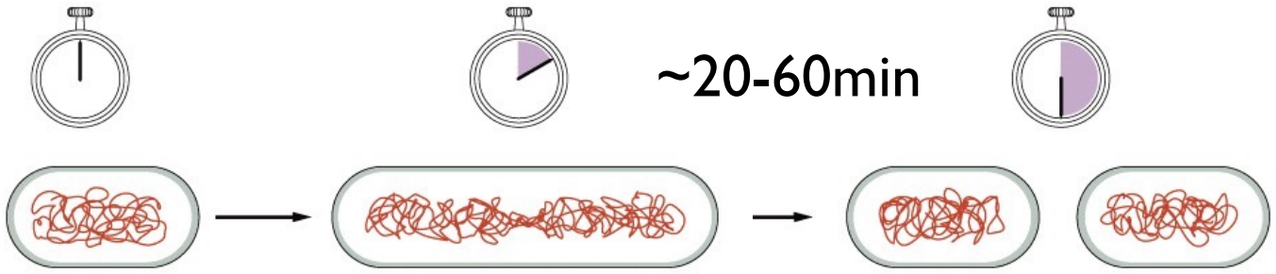

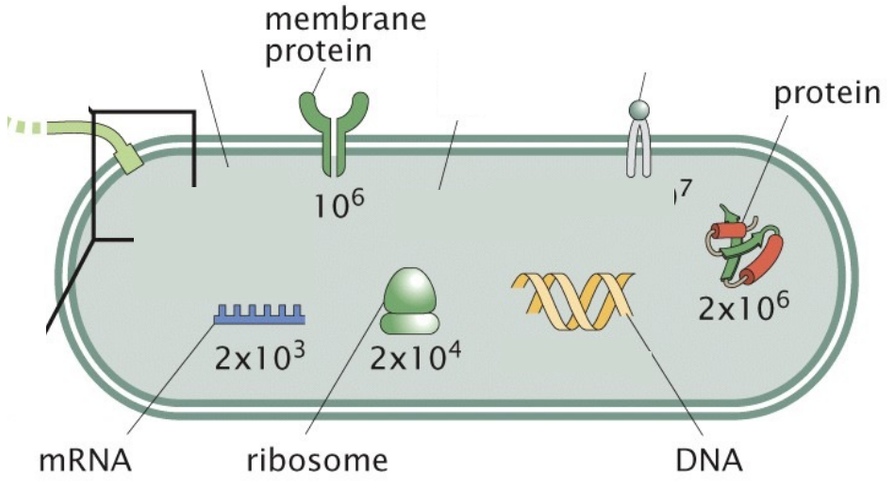

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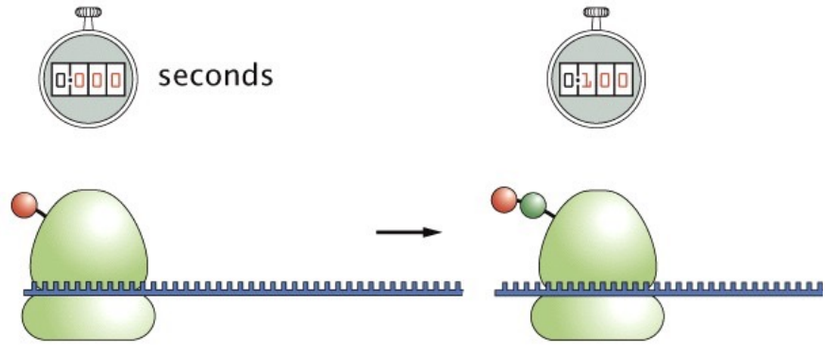

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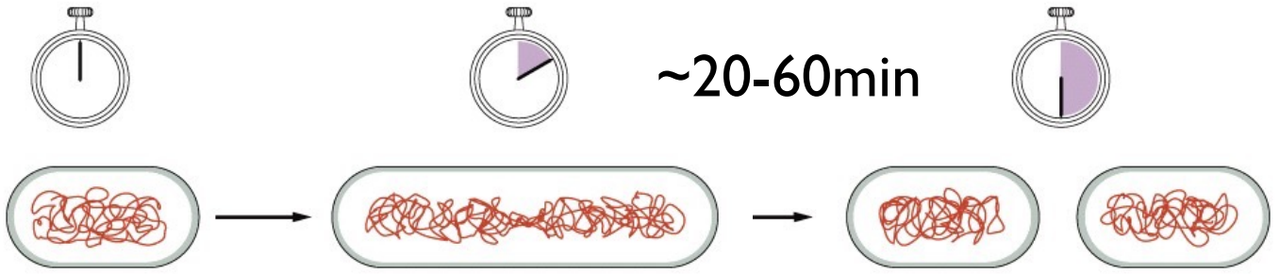

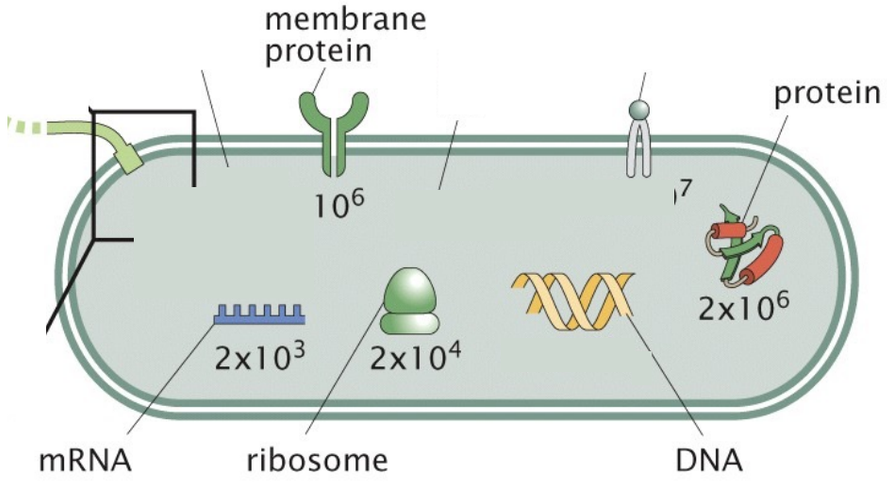

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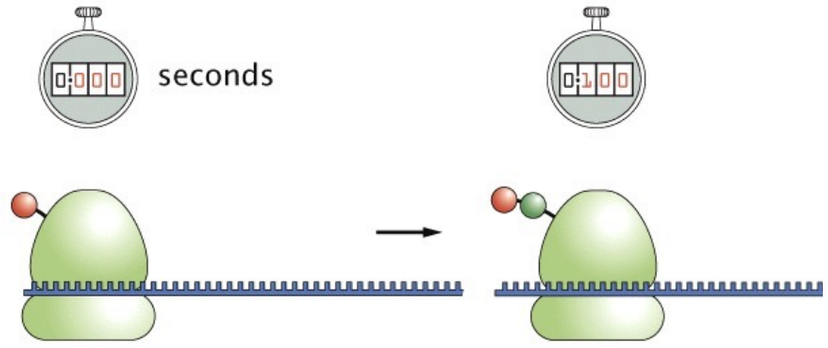

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E. coli replication time $\geq$ Time required for DNAp to copy entire genome $\approx \frac{1 \times (\sim 4x10^6 \text{ bp})}{(\sim 1000 \text{ bp/s}) \times 1}$

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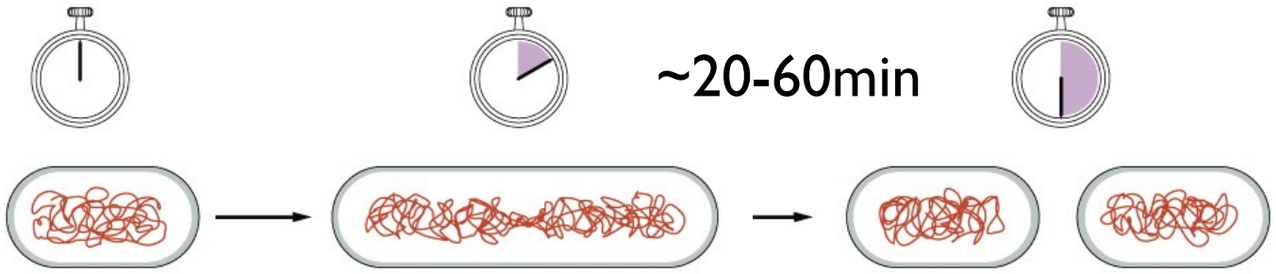

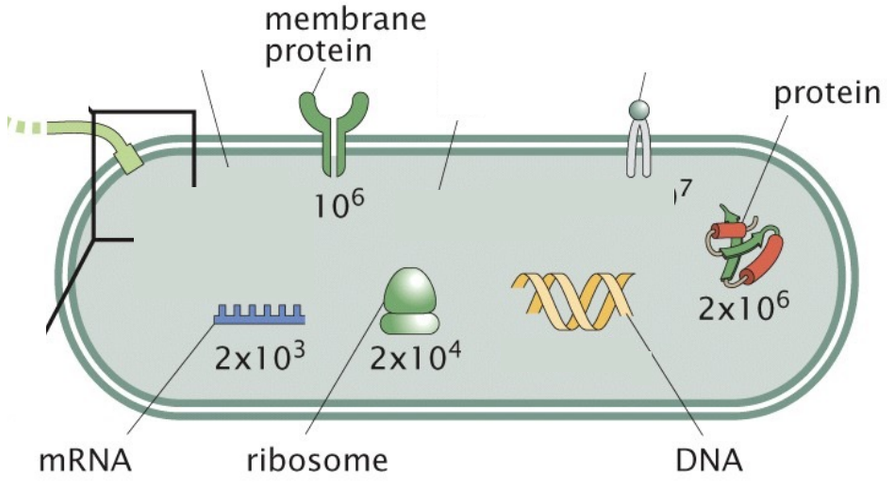

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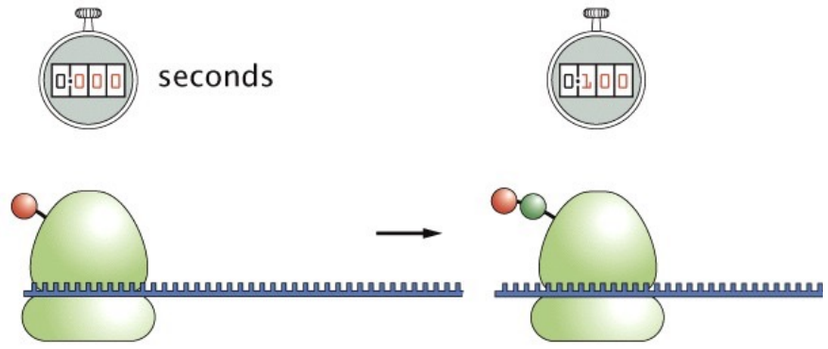

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E. coli replication time $\geq$ **Time required for DNAp to copy entire genome** $\approx \frac{1 \times (\sim 4x10^6 \text{ bp})}{(\sim 1000 \text{ bp/s}) \times 1} \approx$ 1 hr (too long!)

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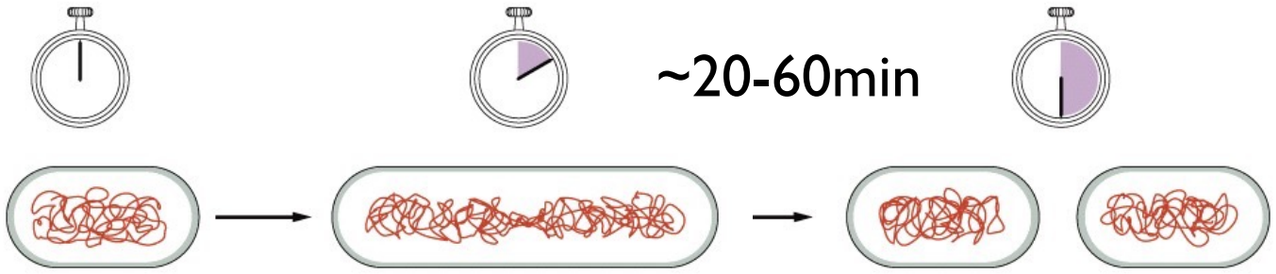

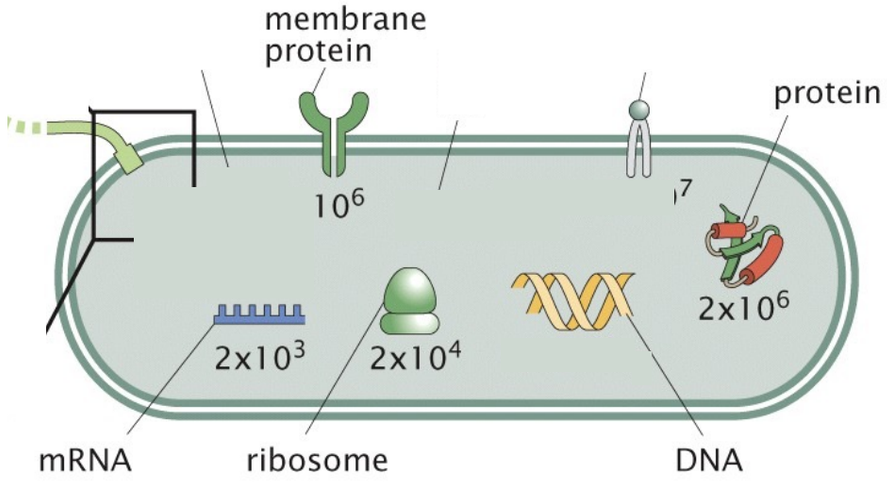

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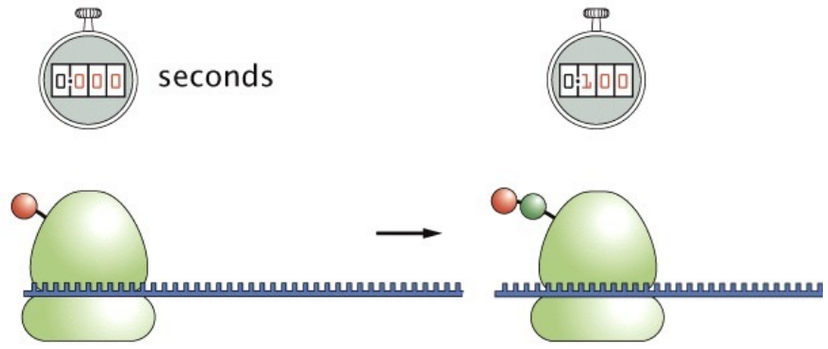

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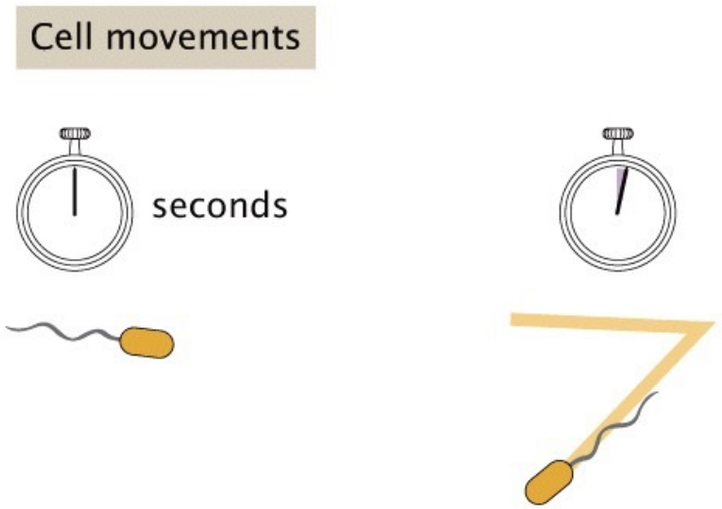
Solution: E. Coli starts copying *next* genome before first one finishes!

Challenge Question:

How long does it take a cell to transcribe and translate a single protein?



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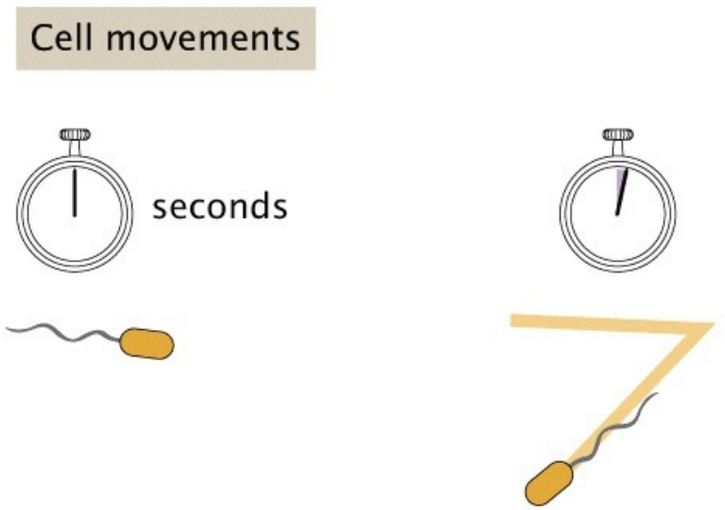

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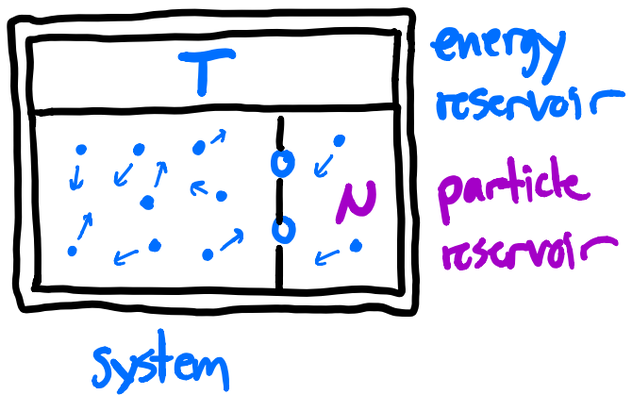
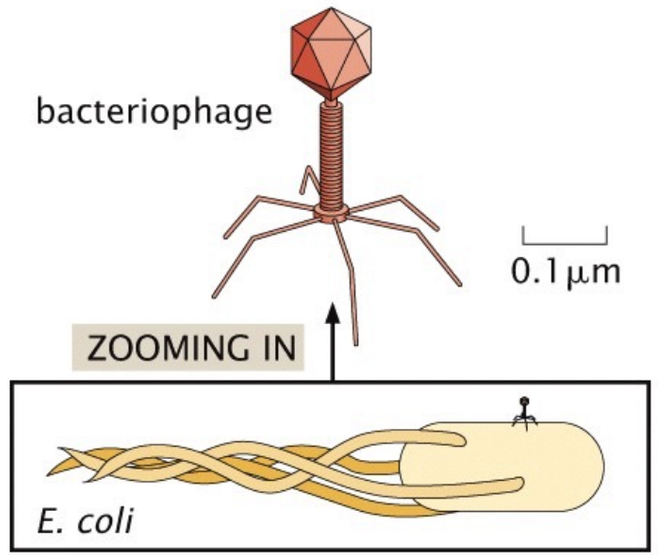
Next time:

Introduction to

Statistical Mechanics





How can we count absolute # of molecules per cell?

One way: *fluctuations during division*

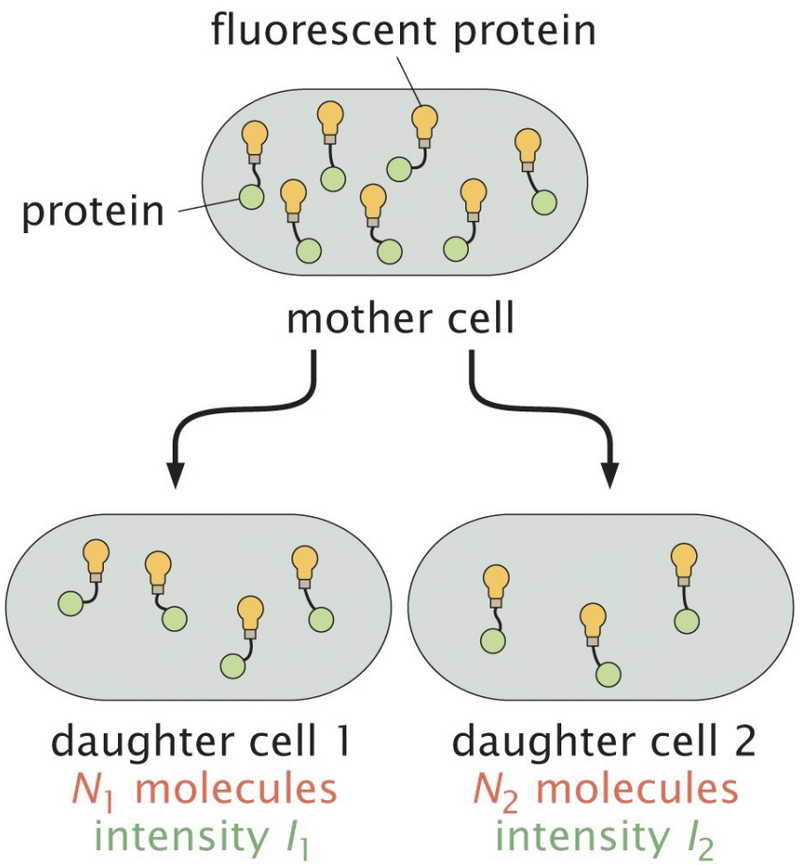


Figure 2.10a Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Each molecule flips a coin:

$$\Pr[N_1 = k] = \binom{N}{k} \left(\frac{1}{2}\right)^k \left(1 - \frac{1}{2}\right)^{N-k}$$

"binomial distribution"

Rosenfeld et al, Science 2005

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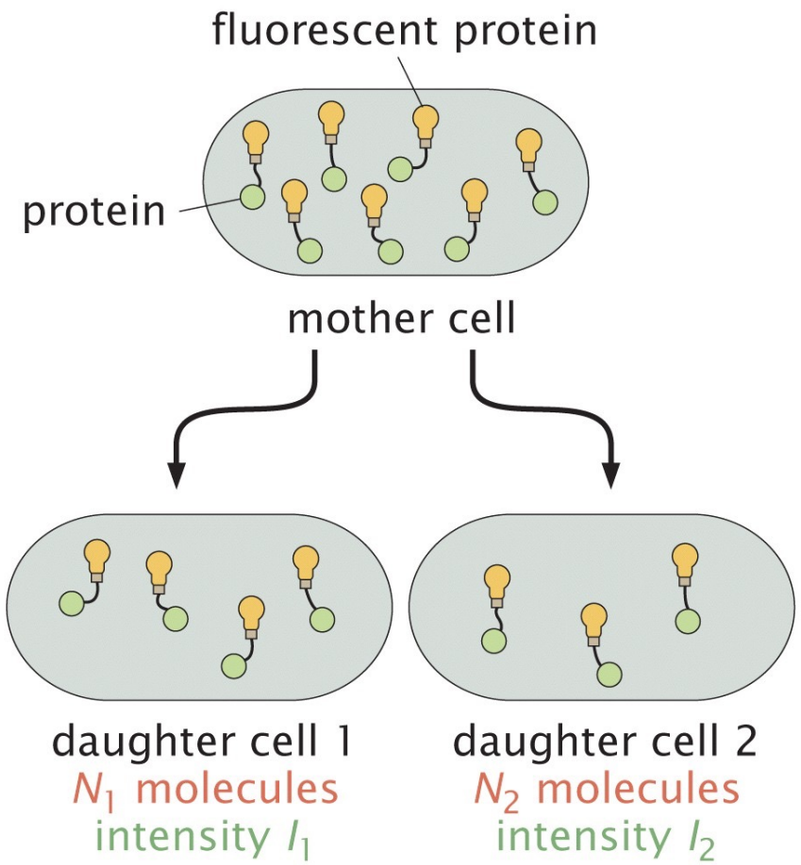

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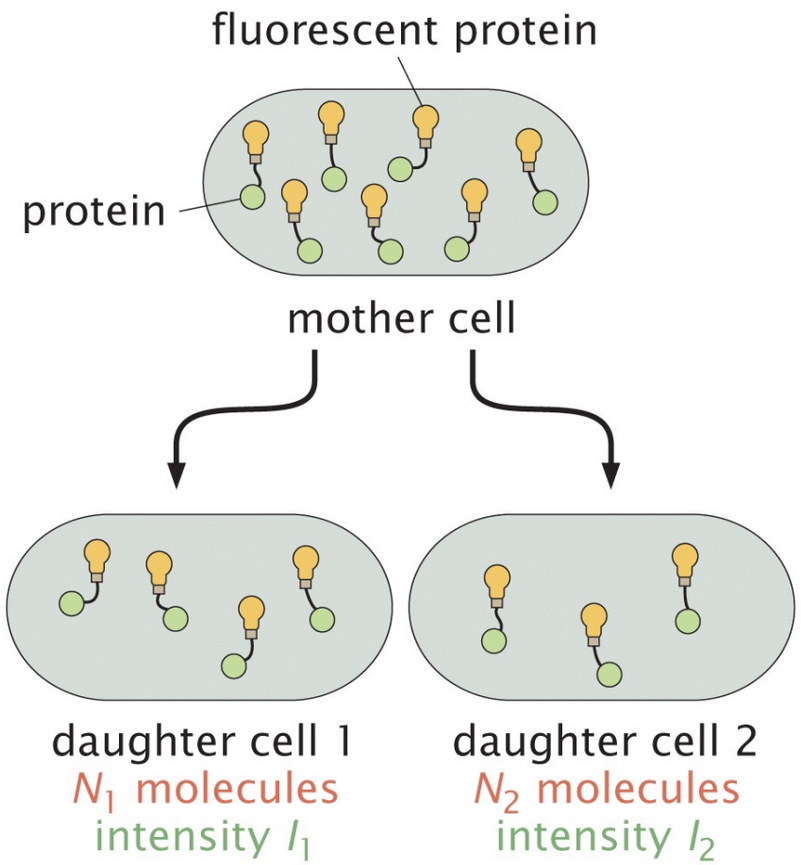

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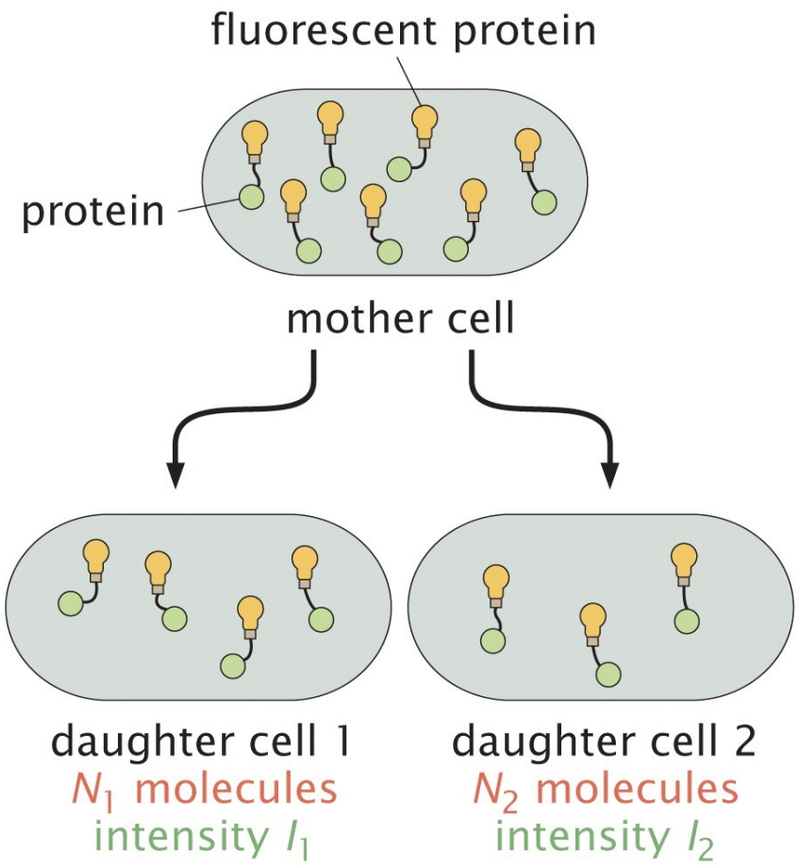

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Fluorescence differences between daughters:

$$\left\langle \left(\frac{\delta I}{I}\right)^2 \right\rangle = \left\langle \left(\frac{\delta N}{N}\right)^2 \right\rangle = \frac{1}{N}$$

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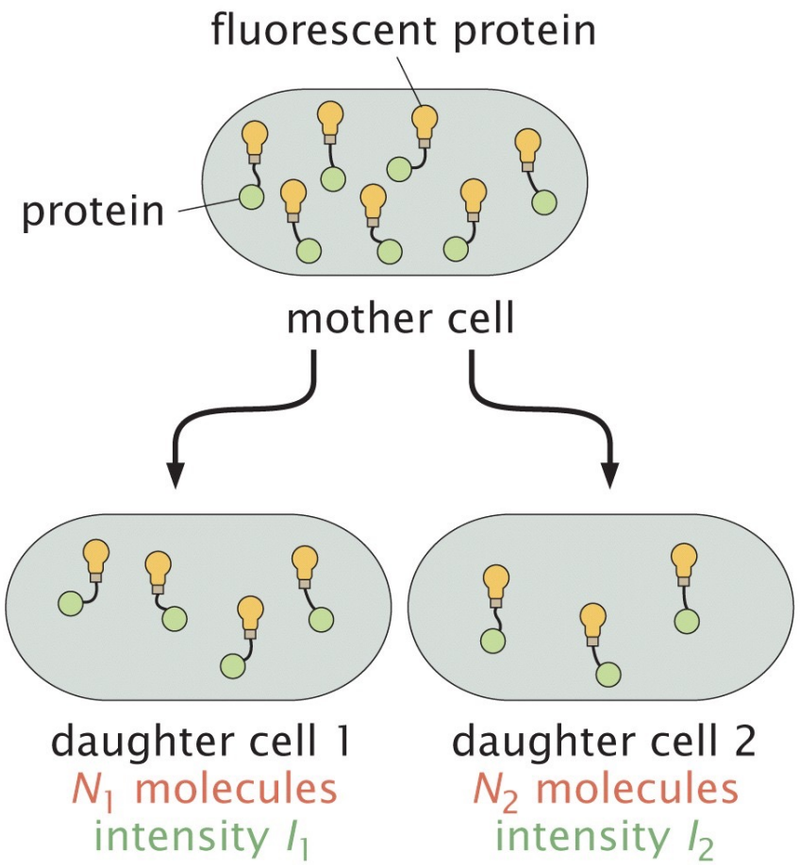

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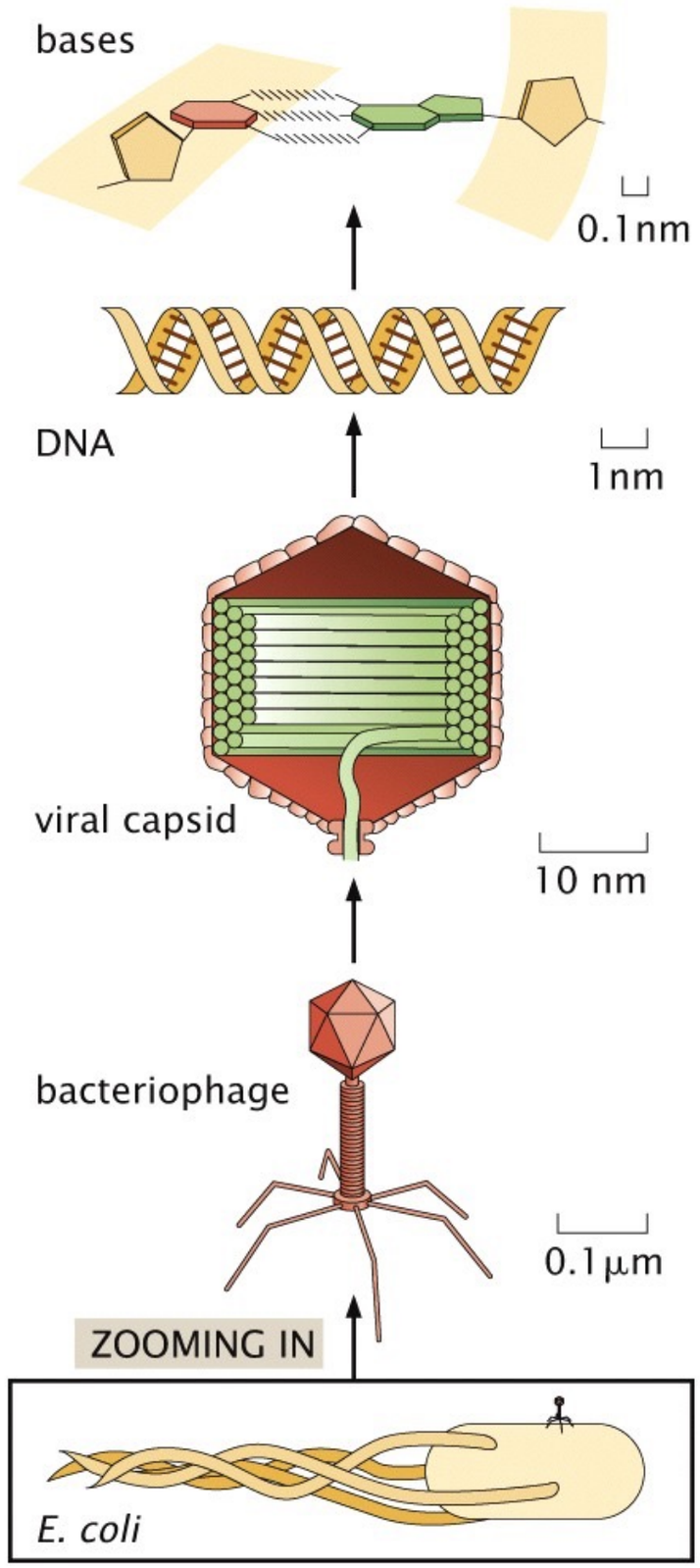

Figure 2.15 (part 1 of 2) Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Next time:

Introduction to

Statistical Mechanics

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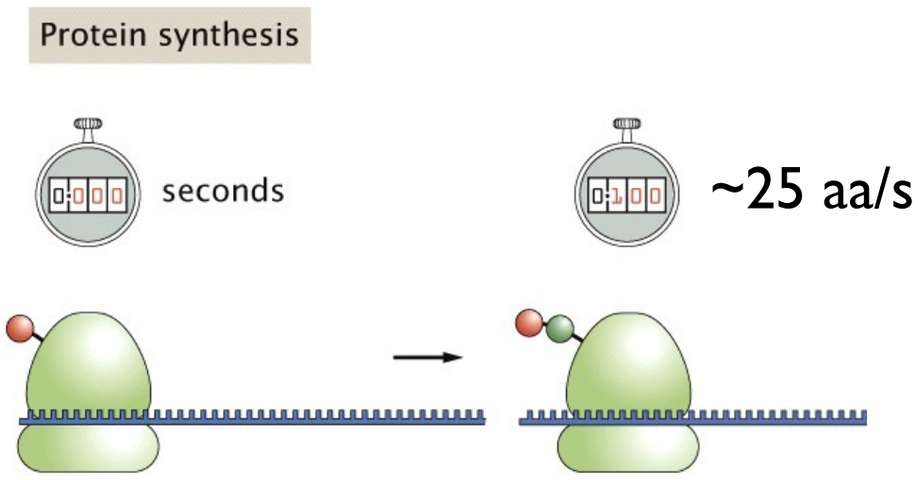

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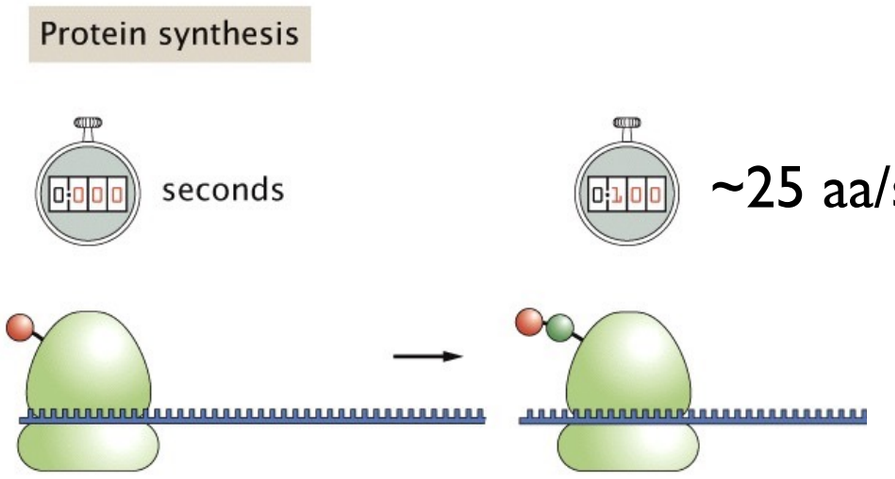

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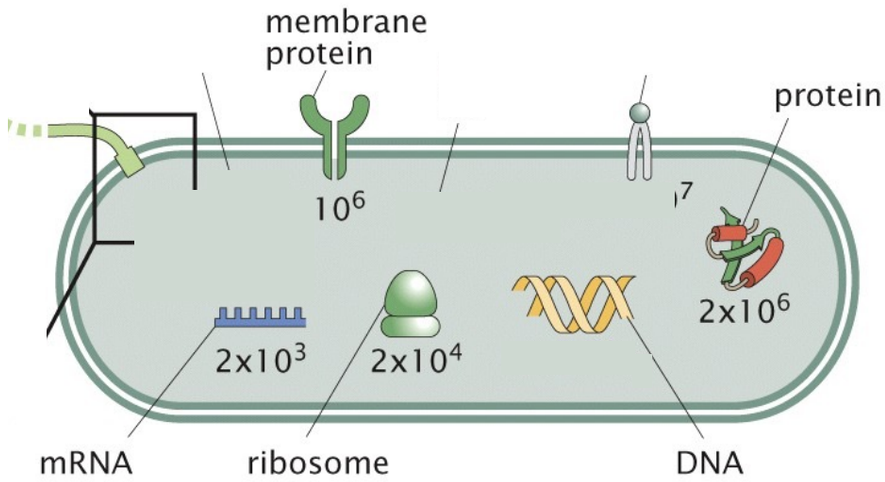

~300 aa / protein → ~10^9 aa / cell

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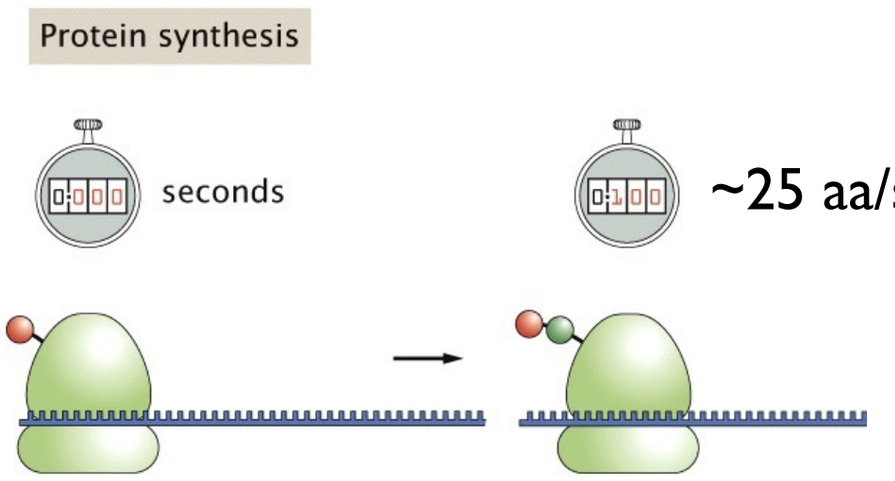

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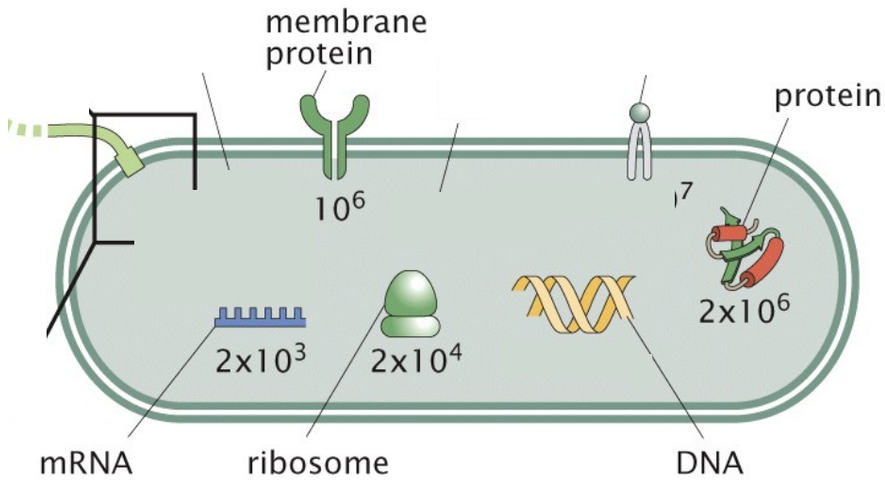

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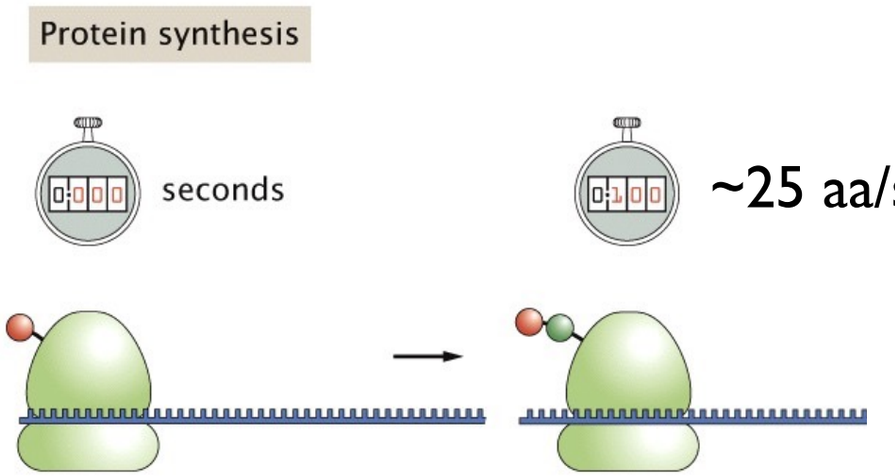
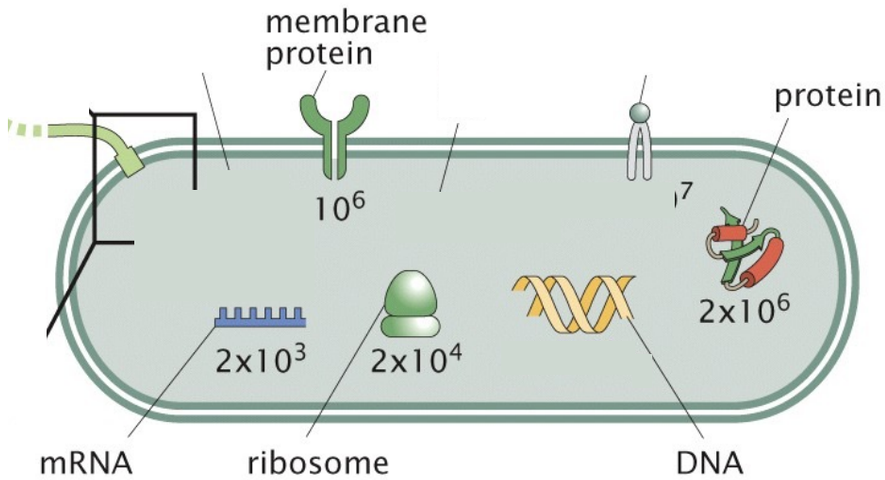
Minimum replication time = ~10^9 aa

What can we learn from these numbers?



~25 aa/s

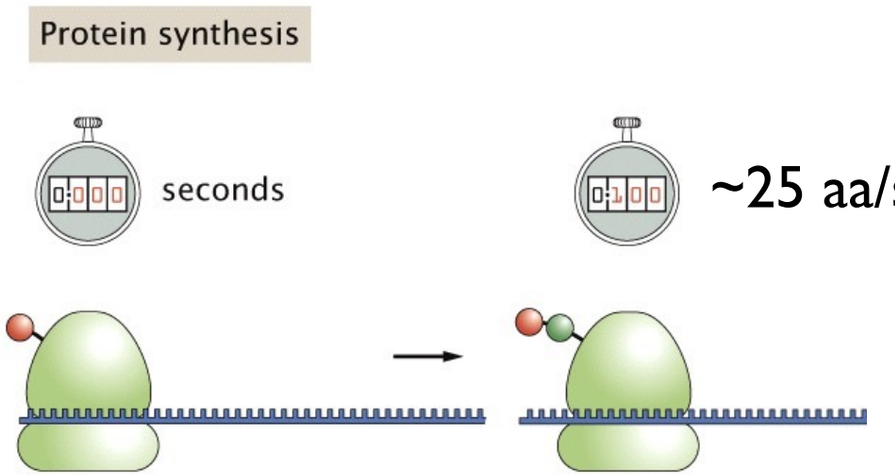
+



~300 aa / protein → ~10^9 aa / cell

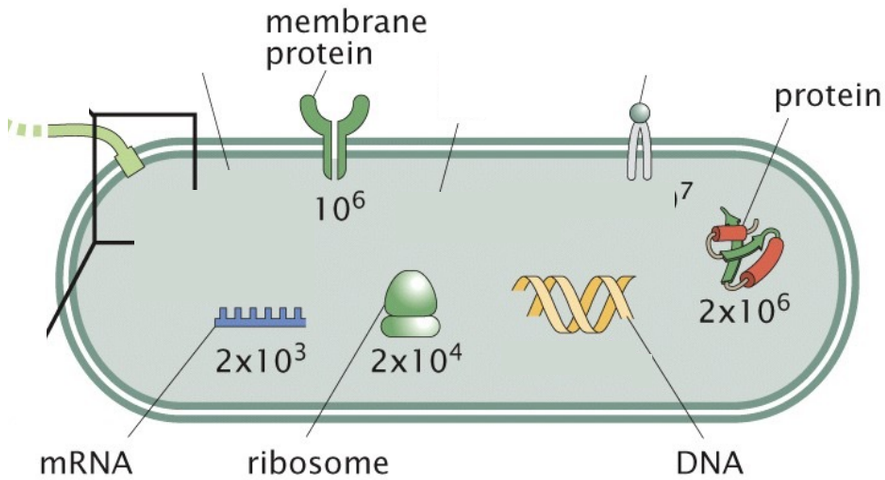
Minimum replication time = ~10^9 aa / ~25 aa / s **x** ~2×10^4 ribosomes

What can we learn from these numbers?



~25 aa/s

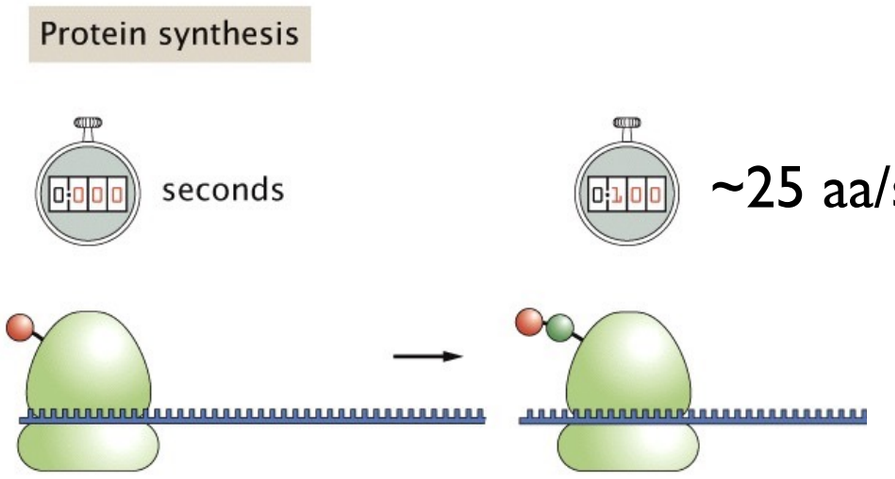
+



~300 aa / protein → ~10^9 aa / cell

Minimum replication time = ~10^9 aa / ~25 aa / s **x** ~2×10^4 ribosomes = ~30 mins!

What can we learn from these numbers?



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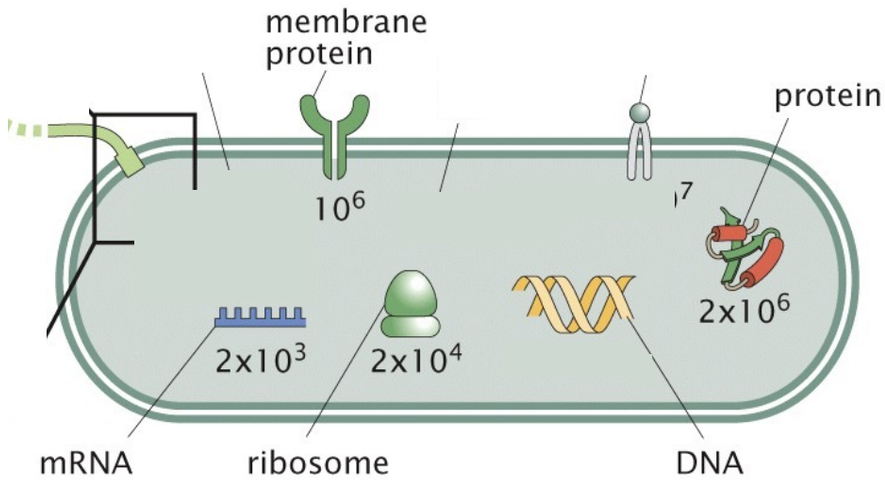

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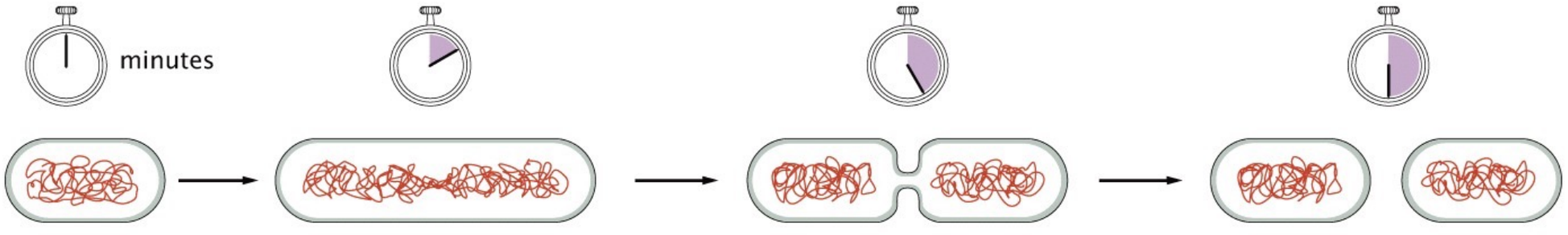
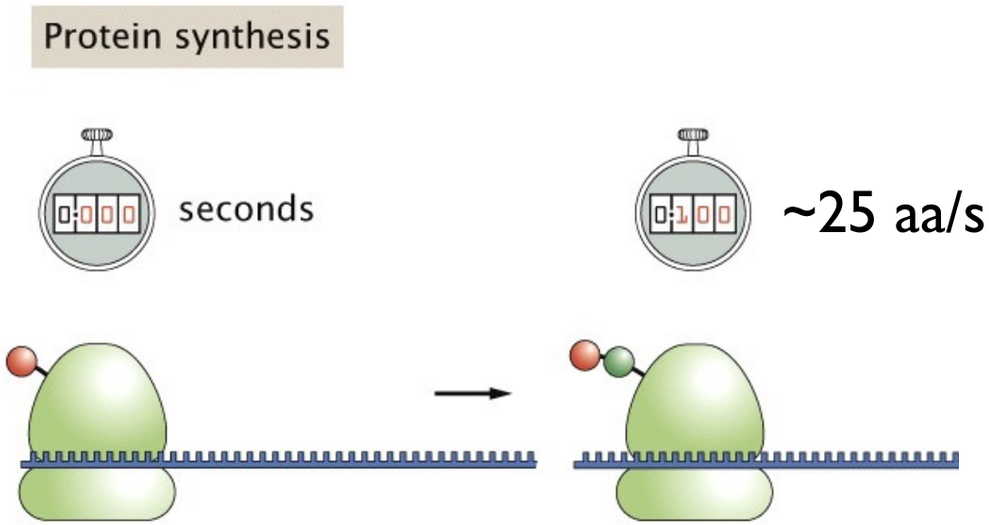


What can we learn from these numbers?



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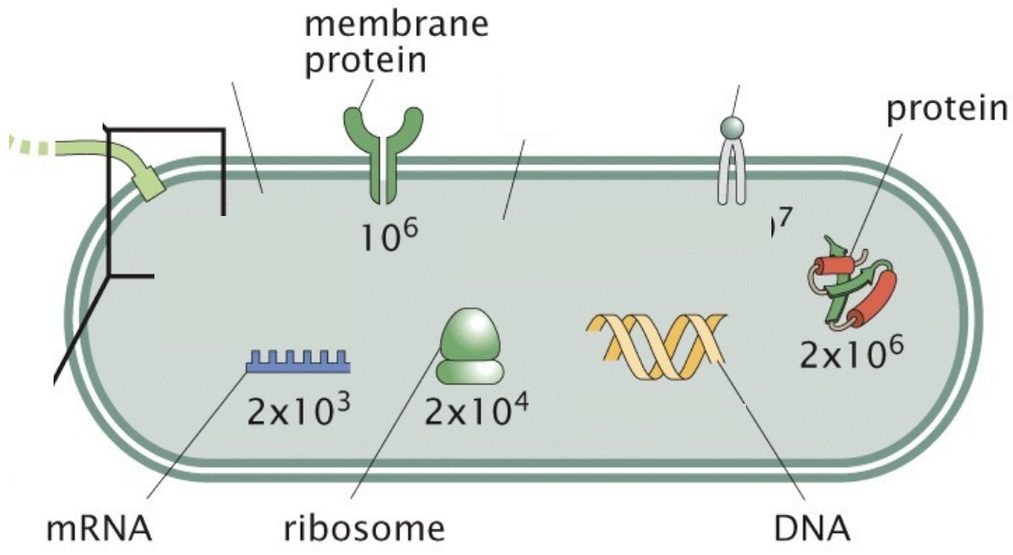

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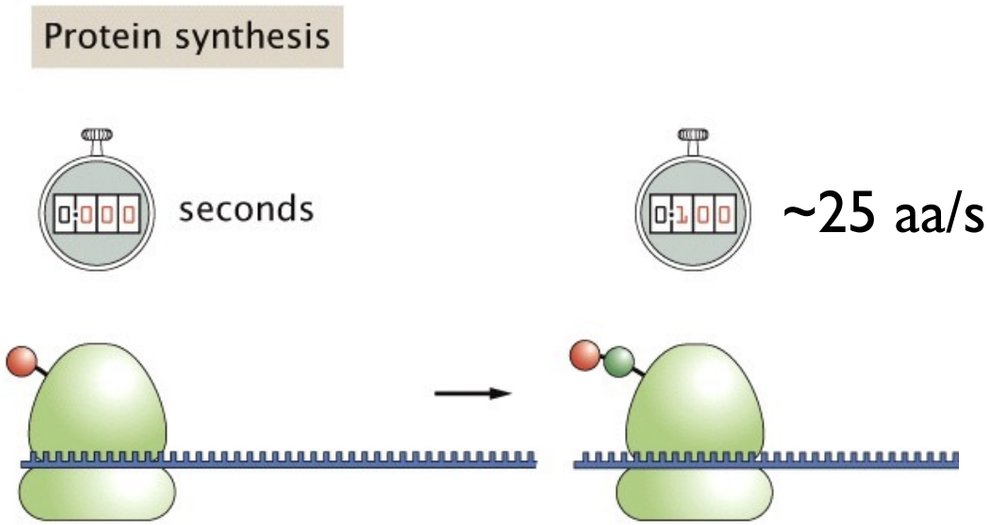
→ ~10s per protein

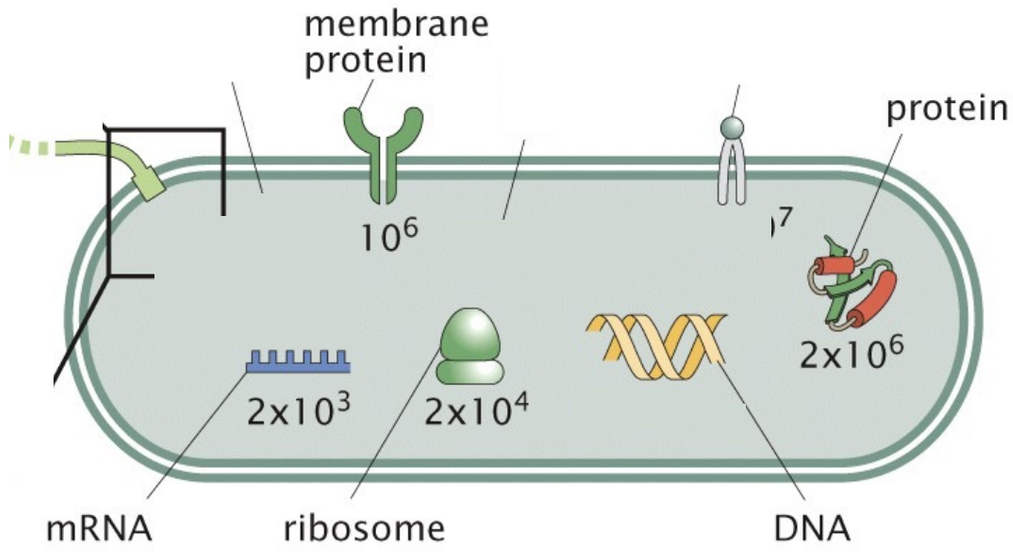
(~20s / mRNA)

What can we learn from these numbers?



~25 aa/s

+



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