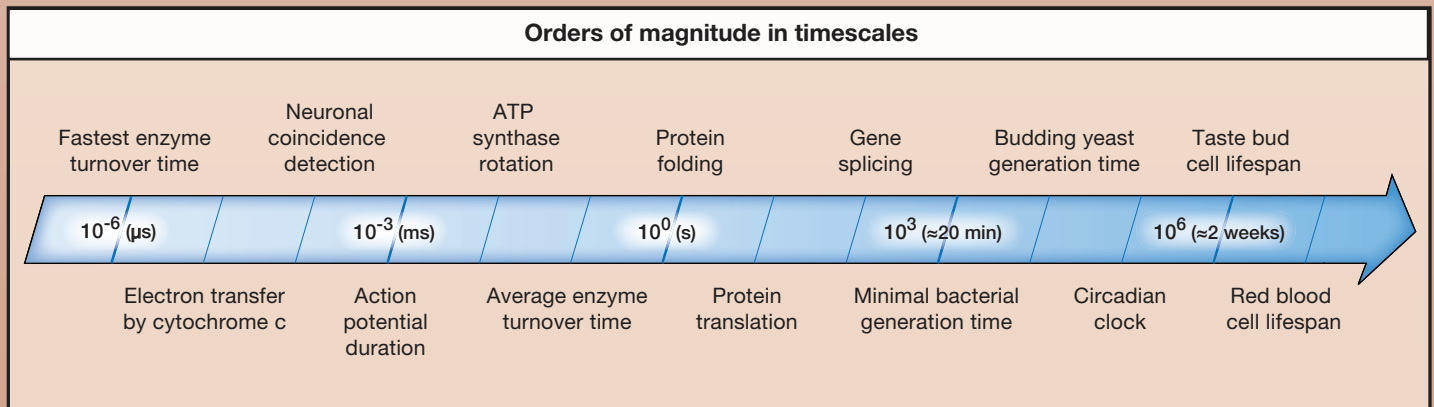
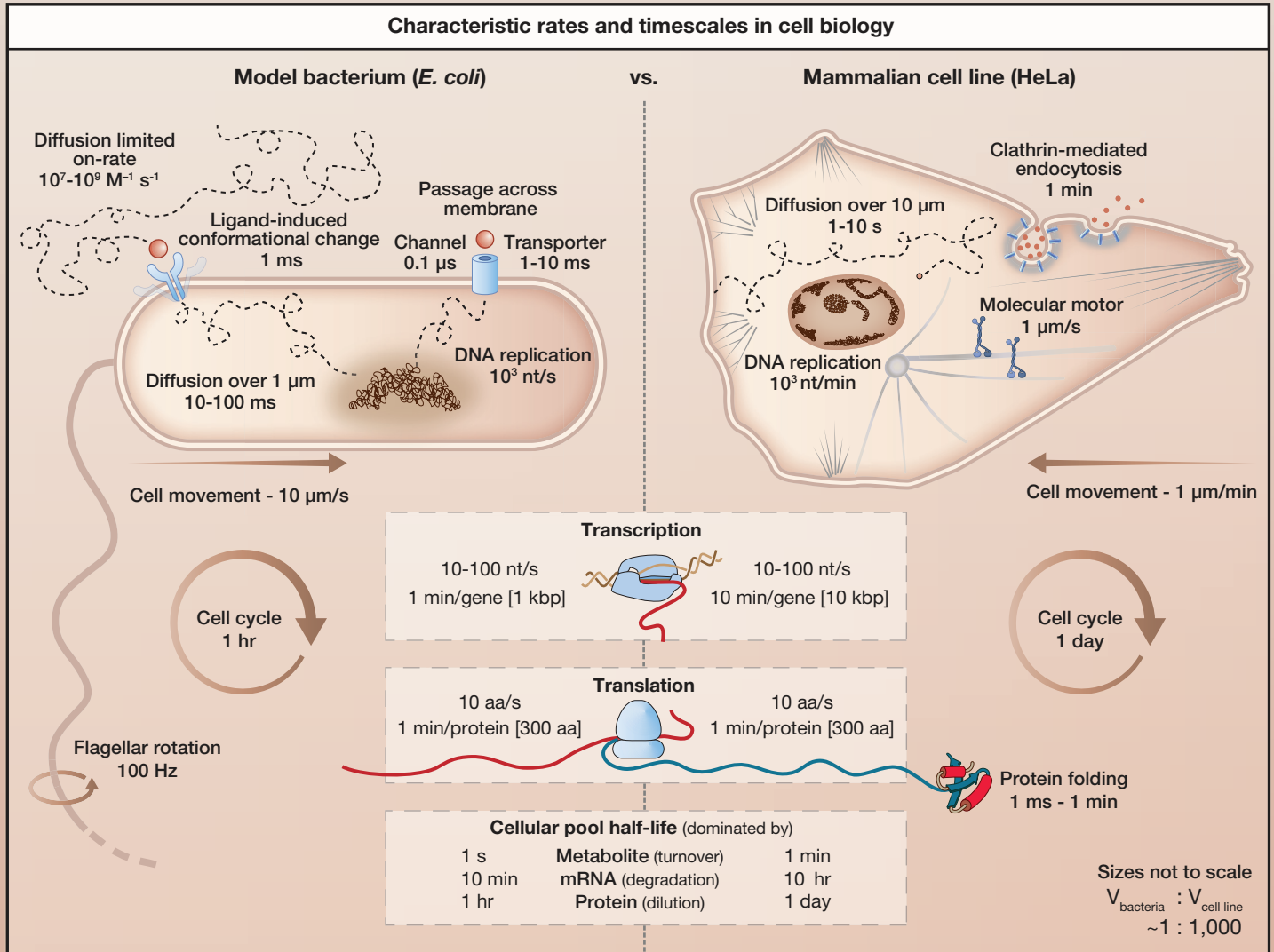


SnapShot: Timescales in Cell Biology Cell

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Knowing key timescales enables us to quickly gain intuition, perform sanity checks and serves as a sixth sense in understanding how cells grow and communicate. This SnapShot briefly communicates some of the insights we collected about rates and durations of these processes from thinking about cell biology by the numbers.

Can Metabolism Wait for Gene Expression?

Metabolic networks and gene regulatory networks, the epicenters of biological regulation, exert their control on distinct timescales. The characteristic concentration of a metabolite in central metabolism is on the order of 1 mM, while the flux in the cellular metabolic highway of glycolysis is usually on the order of 1 mM/s in bacteria and 0.1–0.01 mM/s in mammalian cell lines. Thus, the turnover time is on the order of a second for bacteria and a minute for mammalian cell lines. If the production and consumption reactions are not in balance, the metabolite pool will be consumed (or compounded) rapidly, before gene expression of metabolic enzymes—which takes minutes—can do anything about it. Instead, allosteric regulation and post-translational modification are used to control metabolic flux.

How Long Does It Take to Get a Functional GFP?

Induction of GFP expression begins with the addition of an inducer to the medium. The inducer diffuses into the cell or binds to a receptor to activate transcription within seconds. Transcription and translation in bacteria take on the order of a minute, with protein folding occurring concurrently. However, a maturation process, which involves cyclization and oxidation of the GFP chromophore, takes tens of minutes. Evolved versions reduce the maturation time so that the whole process, from induction to fluorescence, is achieved within minutes.

Which Processes Govern the Half-Life of Cellular Components?

Cellular components, such as metabolites, mRNA, and proteins, have different timescales for turnover. The cellular pool half-life of a metabolite results from the ratio between the metabolite pool size and the flux through it. For mRNA, the half-life is dictated by nuclease degradation. Proteins are much more stable and are usually degraded at timescales longer than the fast doubling time achieved in the lab, which makes dilution by cellular division the predominant process controlling their turnover. These are, of course, broad generalizations and biology thrives on bending them; for example, rapid regulated proteolysis leads to much faster protein turnover.

Are Mammalian Cells Slow-Motion Versions of Bacterial Cells?

Bacteria and mammalian cells work under similar physical and chemical constraints. For example, the diffusion coefficients and the rates of the RNA polymerase and ribosomes are similar. Yet, with a larger cell size and gene length, the functional timescales in a mammalian cell are extended. For example, diffusion of a protein across a cell will take ~0.1 s in a 1 μm bacterial cell and ~10 s in a 10 μm mammalian cell. Similarly, an average bacterial gene is 1 kbp long and thus will take about a minute to transcribe, while introns cause the average mammalian gene to be 10 kbp long and thus will take about 10 min. Similar timescale differences occur in additional cellular processes, such as the turnover of metabolites. For such key processes, what is true for a bacterium on a 1 second timescale is true for a mammalian cell in about 1 min.

How to Get a Protein across a Neuron on Time?

For a protein to get from the tip of the axon to the soma in a 1 cm long neuron, two main mechanisms are possible. Diffusion ($D \approx 10 \mu\text{m}^2/\text{s}$) would take over a month (scaling like R^2/D). Alternatively, a molecular motor with a speed of 1 $\mu\text{m}/\text{s}$ can transport the protein within a few hours. In neurons over a meter long—in humans or giraffes for example—even with molecular motors, the journey should take several days.

A Speed Limit on Crawling Cells?

Cellular motility is powered by actin polymerization at the lamellipodium leading edge. The speed limit for a growing actin network is the growth rate of a single filament oriented perpendicular to the leading edge. The on-rate for the addition of an actin monomer to the growing tip is $10^7\text{--}10^8 \text{ M}^{-1} \text{ s}^{-1}$. The reported cellular concentration of polymerizable actin monomers ranges between 1 and 100 μM , and in such cases, we choose to use the geometric mean (10 μM). Each polymerized actin monomer adds 3 nm to the filament, and we thus get a velocity on the order of 1 $\mu\text{m}/\text{s}$ ($3 \times 10^7 \text{ M}^{-1} \text{ s}^{-1} \times 10 \mu\text{M} \times 3 \text{ nm}$), which is observed, for example, for *Listeria*. The observed crawling speeds of fish keratocytes and mammalian fibroblasts are one and two orders of magnitude slower, respectively. The counteracting membrane tension, cell adhesion, and the fact that a lamellipodium is an ensemble of filaments reduce the speed of cells below the polymerization-based speed limit.

What Is the Lifespan of Different Cells in Our Body?

The intestine epithelium turns over in less than a week, our skin epidermis in a week to a month, and if you burn your tongue, taste buds return in about 2 weeks. Red blood cells have a lifespan of 4 months, such that donating 0.5 L from our 5 L of blood every few months does not deplete them. A striking difference in lifespan exists between sperm cells (~50 days) and oocytes (~50 years). Fat cells and skeleton replace themselves in about 10 years, while most of the neurons in the central nervous system and our eye lens cells are not replaced at all throughout our life.

How Fast Can Olympic Athletes Respond to the Starter's Pistol?

Upon hearing the shot, athletes process and propagate an electric impulse from the brain all the way to their feet (~1 m). Considering the speed of the action potential (10–100 m/s), this implies a latency of 10–100 ms regardless of other processes, such as the speed of sound and signal processing in the brain. The best athletes respond after ~120 ms, and a reaction time below 100 ms is immediately disqualified as a false start.

ACKNOWLEDGMENTS

We thank O. Avinoam, A. Bar-Even, D. Ben-Zvi, A. Bershadsky, E. Bibi, E. Bouchbinder, D. Davidi, A. de Graff, A. Erez, M. Heinemann, U. Moran, N. Orme, M. Piel, J. Rabinowitz, U. Schwarz, A. Sigal, R. Sorek, D. Tawfik, T. Wiesel, Y. Yovel, and the Weizmann students of “Cell Biology by the Numbers” course 2015–16 for help in preparing this SnapShot.

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