

**BE/Bi 101: Order-of-Magnitude Biology**  
**Homework 4**  
**Due date: Friday, May 6, 2016**

“Problems worthy of attack prove their worth by hitting back.”

—Piet Hein

**1. Snapshot—evolution by the numbers.**

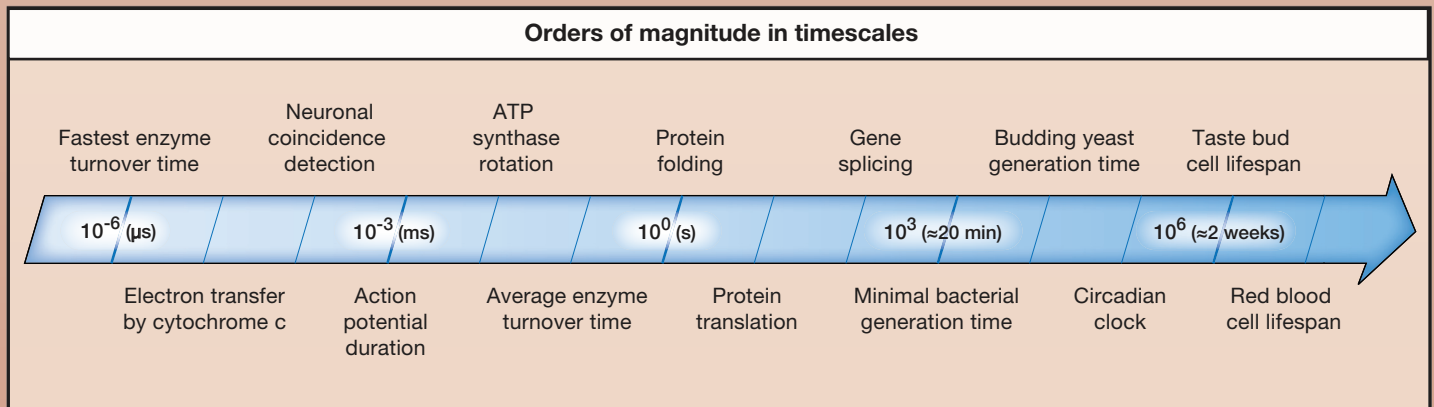
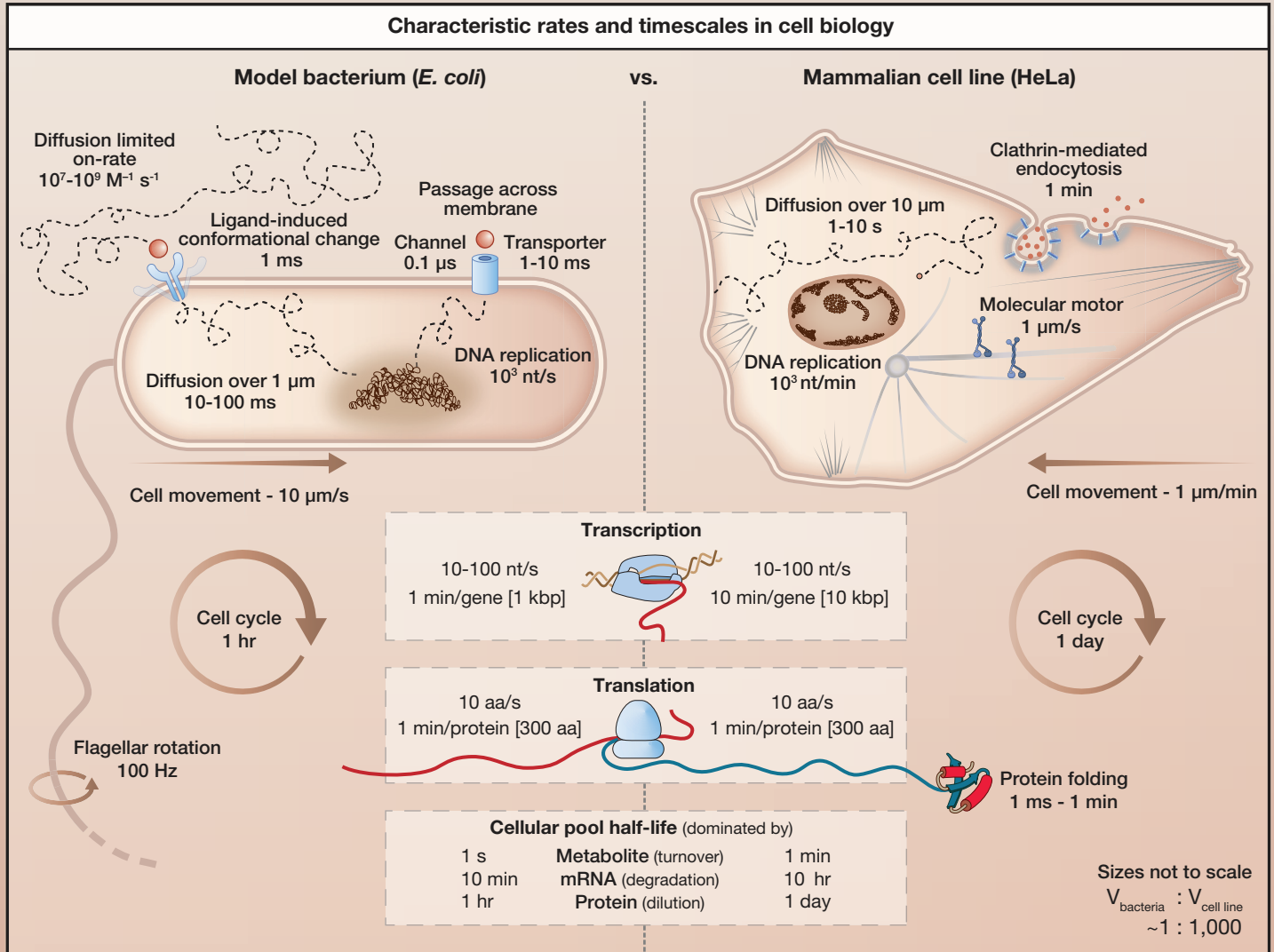
Read the two versions of snapshot that are attached with this homework. Your job in this homework is to make a version of your thinking on Evolution by the Numbers in which you have as many as 5 categories (see the Snapshot on Cell Biology where the categories are concentrations, sizes, rates, etc) and can have as many as 5 numbers per category. In addition, please also examine the supplemental material for the snapshot that gives information on the data leading to each of the different numbers. Please produce such a supplement of your own that gives the sources for your own numbers. Please submit your answer to Rob, Justin, Bill, and Manuel in PDF form by email.

# SnapShot: Timescales in Cell Biology Cell

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# 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  $\mu\text{m}$  bacterial cell and ~10 s in a 10  $\mu\text{m}$  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  $\mu\text{M}$ , and in such cases, we choose to use the geometric mean (10  $\mu\text{M}$ ). 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.

## REFERENCES

- Alon, U. (2006). An Introduction to Systems Biology: Design Principles of Biological Circuits (Chapman & Hall/CRC).
- Milo, R., and Phillips, R. (2016). Cell Biology by the Numbers (Garland Science).
- Neidhardt, F.C., Ingraham, J.L., and Schaechter, M. (1990). Physiology of the Bacterial Cell: A Molecular Approach (Sinauer Associates).
- Phillips, R., Kondev, J., Theriot, J., and Garcia, H. (2013). Physical Biology of the Cell, Second Edition (Garland Science).

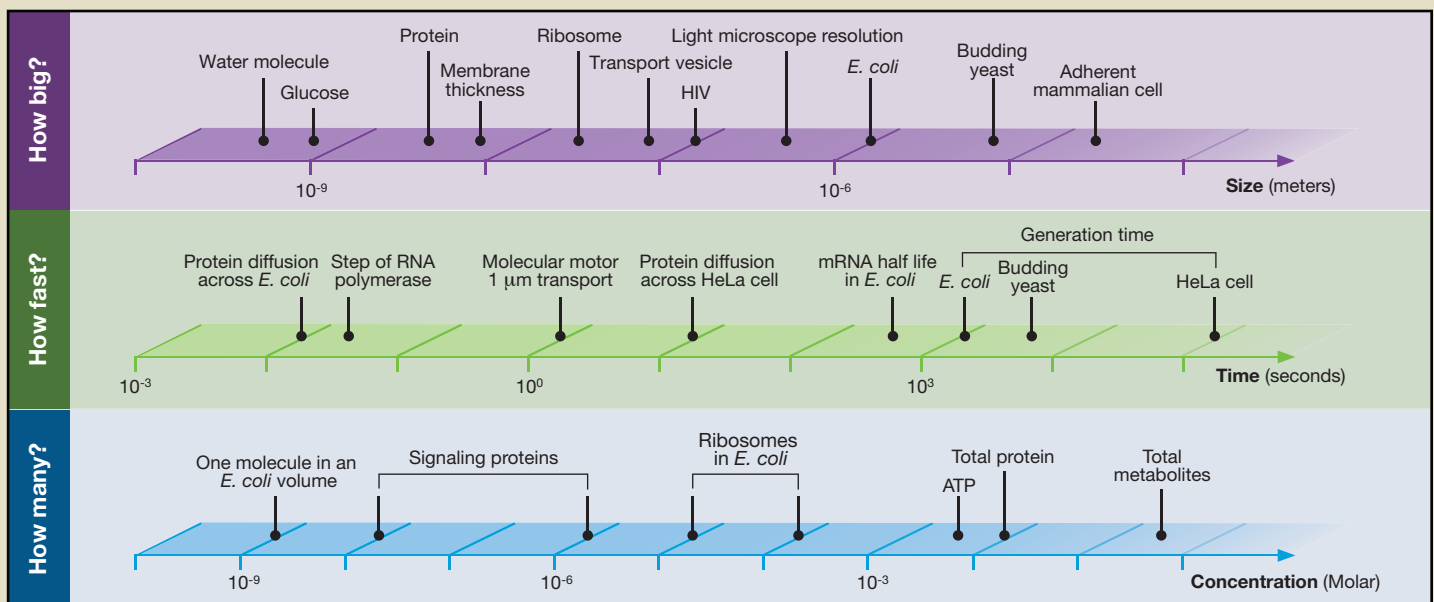
# SnapShot: Key Numbers in Biology

# Cell

Uri Moran,<sup>1</sup> Rob Phillips,<sup>2</sup> and Ron Milo<sup>1</sup>

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Cell size	Concentration	Diffusion and catalysis rate
<p><b>Bacteria (<i>E. coli</i>):</b> <math>\approx 0.7\text{-}1.4\ \mu\text{m}</math> diameter, <math>\approx 2\text{-}4\ \mu\text{m}</math> length, <math>\approx 0.5\text{-}5\ \mu\text{m}^3</math> in volume; <math>10^8\text{-}10^9</math> cell/ml for culture with <math>\text{OD}_{600} \approx 1</math></p> <p><b>Yeast (<i>S. cerevisiae</i>):</b> <math>\approx 3\text{-}6\ \mu\text{m}</math> diameter <math>\approx 20\text{-}160\ \mu\text{m}^3</math> in volume</p> <p><b>Mammalian cell volume:</b> <math>100\text{-}10,000\ \mu\text{m}^3</math>; HeLa cell: <math>500\text{-}5000\ \mu\text{m}^3</math> (adhering to slide <math>\approx 15\text{-}30\ \mu\text{m}</math> diameter)</p>	<p><b>Concentration of 1 nM:</b> in <i>E. coli</i> <math>\approx 1</math> molecule/cell; in HeLa cells <math>\approx 1000</math> molecules/cell</p> <p><b>Characteristic concentration for a signaling protein:</b> <math>\approx 10\ \text{nM}\text{-}1\ \mu\text{M}</math></p> <p><b>Water content:</b> <math>\approx 70\%</math> by mass; general elemental composition (dry weight) of <i>E. coli</i>: <math>\approx \text{C}_4\text{H}_7\text{O}_2\text{N}_1</math>; Yeast: <math>\approx \text{C}_6\text{H}_{10}\text{O}_3\text{N}_1</math></p> <p><b>Composition of <i>E. coli</i> (dry weight):</b> <math>\approx 55\%</math> protein, <math>20\%</math> RNA, <math>10\%</math> lipids, <math>15\%</math> others</p> <p><b>Protein concentration:</b> <math>\approx 100\ \text{mg/ml} = 3\ \text{mM}</math>. <math>10^6\text{-}10^7</math> per <i>E. coli</i> (depending on growth rate); Total metabolites (MW &lt; 1 kDa) <math>\approx 300\ \text{mM}</math></p>	<p><b>Diffusion coefficient for an "average" protein:</b> in cytoplasm <math>D \approx 5\text{-}15\ \mu\text{m}^2/\text{s} \rightarrow \approx 10\ \text{ms}</math> to traverse an <i>E. coli</i> <math>\rightarrow \approx 10\ \text{s}</math> to traverse a mammalian HeLa cell; small metabolite in water <math>D \approx 500\ \mu\text{m}^2/\text{s}</math></p> <p><b>Diffusion-limited on-rate for a protein:</b> <math>\approx 10^8\text{-}10^9\ \text{s}^{-1}\text{M}^{-1} \rightarrow</math> for a protein substrate of concentration <math>\approx 1\ \mu\text{M}</math> the diffusion-limited on-rate is <math>\approx 100\text{-}1000\ \text{s}^{-1}</math> thus limiting the catalytic rate <math>k_{\text{cat}}</math></p>
Length scales inside cells	Division, replication, transcription, translation, and degradation rates	Genome sizes and error rates
<p><b>Nucleus volume:</b> <math>\approx 10\%</math> of cell volume</p> <p><b>Cell membrane thickness:</b> <math>\approx 4\text{-}10\ \text{nm}</math></p> <p><b>"Average" protein diameter:</b> <math>\approx 3\text{-}6\ \text{nm}</math></p> <p><b>Base pair:</b> <math>2\ \text{nm}</math> (D) x <math>0.34\ \text{nm}</math> (H)</p> <p><b>Water molecule diameter:</b> <math>\approx 0.3\ \text{nm}</math></p>	<p><b>at <math>37^\circ\text{C}</math> with a temperature dependence (Q10) of <math>\approx 2\text{-}3</math></b></p> <p><b>Cell cycle time</b> (exponential growth in rich media): <i>E. coli</i> <math>\approx 20\text{-}40\ \text{min}</math>; budding yeast <math>70\text{-}140\ \text{min}</math>; HeLa human cell line: <math>15\text{-}30\ \text{hr}</math></p> <p><b>Rate of replication by DNA polymerase:</b> <i>E. coli</i> <math>\approx 200\text{-}1000</math> bases/s; human <math>\approx 40</math> bases/s. Transcription by RNA polymerase <math>10\text{-}100</math> bases/s</p> <p><b>Translation rate by ribosome:</b> <math>10\text{-}20\ \text{aa/s}</math></p> <p><b>Degradation rates (proliferating cells):</b> mRNA half life &lt; cell cycle time; protein half life <math>\geq</math> cell cycle time</p>	<p><b>Genome size:</b> <i>E. coli</i> <math>\approx 5\ \text{Mbp}</math> <i>S. cerevisiae</i> (yeast) <math>\approx 12\ \text{Mbp}</math> <i>C. elegans</i> (nematode) <math>\approx 100\ \text{Mbp}</math> <i>D. melanogaster</i> (fruit fly) <math>\approx 120\ \text{Mbp}</math> <i>A. thaliana</i> (plant) <math>\approx 120\ \text{Mbp}</math> <i>M. musculus</i> (mouse) <math>\approx 2.6\ \text{Gbp}</math> <i>H. sapiens</i> (human) <math>\approx 3.2\ \text{Gbp}</math> <i>T. aestivum</i> (wheat) <math>\approx 16\ \text{Gbp}</math></p> <p><b>Number of protein-coding genes:</b> <i>E. coli</i> = <math>4000</math>; <i>S. cerevisiae</i> = <math>6000</math>; <i>C. elegans</i>, <i>A. thaliana</i>, <i>M. musculus</i>, <i>H. sapiens</i> = <math>20,000</math></p> <p><b>Mutation rate in DNA replication:</b> <math>\approx 10^{-8}\text{-}10^{-10}</math> per bp</p> <p><b>Misincorporation rate:</b> transcription <math>\approx 10^{-4}\text{-}10^{-5}</math> per nucleotide translation <math>\approx 10^{-3}\text{-}10^{-4}</math> per amino acid</p>
Energetics		
<p><b>Membrane potential</b> <math>\approx 70\text{-}200\ \text{mV} \rightarrow 2\text{-}6\ k_B T</math> per electron (<math>k_B T \equiv</math> thermal energy)</p> <p><b>Free energy (<math>\Delta G</math>) of ATP hydrolysis under physiological conditions</b> <math>\approx 40\text{-}60\ \text{kJ/mol} \rightarrow \approx 20\ k_B T</math>/molecule ATP; ATP molecules required during an <i>E. coli</i> cell cycle <math>\approx 10\text{-}50 \times 10^9</math></p> <p><b><math>\Delta G^\circ</math> resulting in order of magnitude ratio between product and reactant concentrations:</b> <math>\approx 6\ \text{kJ/mol} \approx 60\ \text{meV} \approx 2\ k_B T</math></p>		



Useful biological numbers extracted from the literature. Numbers and ranges should only serve as "rule of thumb" values. References are in the online annotated version at [www.BioNumbers.org](http://www.BioNumbers.org). See the website and original references to learn about the details of the system under study including growth conditions, method of measurement, etc.

# SnapShot: Key Numbers in Biology

# Cell

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Biology is becoming increasingly quantitative. Taking stock of key numbers in cell and molecular biology enables back-of-the-envelope calculations that test and sharpen our understanding of cellular processes. Further, such calculations provide a quantitative context for the torrent of data from new experimental techniques. However, such useful numbers are scattered in the vast biological literature in a way that often leads to a frustrating literature-mining ordeal. Here, we have collected a set of basic numbers in biology that we find extremely useful for obtaining an order of magnitude feel for the molecular processes in cells. Several examples (see below) show how to combine these numbers to think about biological questions. The values should be considered rules of thumb rather than definitive values as variety is the spice of life and variability is ever present in biology. This compilation is based on the BioNumbers wiki project (<http://www.BioNumbers.org>) where these and the values of several thousand other biological properties are provided together with their experimental context and references to the primary literature.

## Is There Enough Time to Replicate the Genome?

The bacterium *Escherichia coli* has a genome of roughly 5 million base pairs (bp) and a replication rate in the range of 200–1000 bp/s. These numbers imply that it should take the two replisomes at least 2500 s to replicate the genome, a number that is much larger than the maximal division rate of ~20 min. How can this be? It turns out that, under ideal conditions, *E. coli* uses nested replication forks that begin to replicate the DNA for the granddaughter and great granddaughter cells before the daughter cells have even completed replication.

## How Many Mutations in a 5 ml Culture of Bacteria?

Using the  $10^{-9}$ /bp mutation rate of *E. coli* per replication and a genome size of  $\sim 10^7$  (both strands), we predict  $\sim 10^{-2}$  mutations per genome replication. In a 5 ml saturated culture (optical density  $\sim 2.0$ ) of *E. coli*, there are about  $10^9$  to  $10^{10}$  cells. The final doubling of this culture requires the replication of  $\sim 10^9$  cells, thus even this last cell division event would be responsible for  $\sim 10^7$  single base pair substitutions. If the culture started with a single bacterium, every single nonlethal base pair substitution in the *E. coli* genome is likely to be represented in the culture.

## How Long to Reach Confluence?

In a 96 multiwell plate, each well has a diameter of 5 mm (i.e., an area of  $\approx 20 \text{ mm}^2 = 2 \times 10^7 \text{ }\mu\text{m}^2$ ). Given that the diameter of a HeLa cell is  $\approx 25 \text{ }\mu\text{m}$  (i.e.,  $\approx 500 \text{ }\mu\text{m}^2$  area), it takes roughly 40,000 cells to reach confluence. Starting with a single cell (obtained by cell sorting rather than cell splitting) with a generation time of about 1 day, the time to reach confluence is about 2 weeks.

## How “Dense” Is a Saturated *E. coli* Culture?

A saturated *E. coli* culture has about  $10^9$  cells/ml. Given that each cell is about  $10^{-12}$  grams, we get a cell concentration of about 1 mg/ml or about 1 part in a thousand of the mass (or volume). The mean spacing between the cells is roughly  $10 \text{ }\mu\text{m}$  (which is not as dense as the concentration of bacteria in the gut of the termite where densities are typically a factor of ten higher).

## How Many Carbon Atoms Are in a Cell?

A cell with a volume of  $1 \text{ }\mu\text{m}^3$  and a density of about 1 g/ml has a total mass of  $10^{-12}$  grams. From the formula  $\text{C}_4\text{H}_7\text{O}_2\text{N}_1$  and the weights of the elements, we derive a carbon content of about  $12 \times 4 / (12 \times 4 + 7 \times 2 + 16 \times 2 + 14) = 48/101$  or about one half of the dry mass. With 30% dry mass (70% water), we obtain  $\sim 10^{-13}$  gm of carbon. Next we transformed the number of molecules using Avogadro's constant:  $6 \times 10^{23} \times 10^{-13} / 12 = 5 \times 10^9$  carbon atoms per cell. To verify this, we have done the calculation in a different way: assuming there are about  $3 \times 10^6$  proteins, each one consisting of about 300 amino acids, we get a total of  $\sim 10^9$  amino acids. An amino acid has about five carbon atoms, so we arrive at a similar value. Both estimates depend linearly on the cell volume, which can vary significantly based on growth conditions.

## How Far Can Macromolecules Move by Diffusion?

It takes about 10 s on average for a protein to traverse a HeLa cell. An axon 1 mm long is about 100 times longer than a HeLa cell, and as the diffusion time scales as the square of the distance it would take  $10^5$  seconds or  $\sim 2$  days for a molecule to travel this distance by diffusion. This demonstrates the necessity of mechanisms other than diffusion for moving molecules long distances. A molecular motor moving at a rate of  $\sim 1 \text{ }\mu\text{m/s}$  will take a “reasonable” time ( $\sim 15$  min) to traverse an axon 1 mm in length.

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## REFERENCES

- Alon, U. (2006). An Introduction to Systems Biology: Design Principles of Biological Circuits (New York: Chapman & Hall/CRC).
- Altman, P.L., and Katz, D.S.D. (1978). Biology Data Book (New York: John Wiley & Sons Inc.).
- Burton, R.F. (2000). Physiology by Numbers (Cambridge, UK: Cambridge University Press).
- Goldreich, P., Mahajan, S., and Phinney, S. (1999). Order-of-magnitude physics: Understanding the world with dimensional analysis, educated guesswork, and white lies (<http://www.inference.phy.cam.ac.uk/sanjoy/oom/book-a4.pdf>).
- Harte, J. (1988). Consider a Spherical Cow: A Course in Environmental Problem Solving (Mill Valley, CA: University Science Books).
- Milo, R., Jorgensen, P., Moran, U., Weber, G., and Springer, M. (2010). BioNumbers – the database of key numbers in molecular and cell biology. *Nucleic Acids Res.* 38, D750–D753.
- Neidhardt, F.C., Ingraham, J.L., and Schaechter, M. (1990). Physiology of the Bacterial Cell: A Molecular Approach (Sunderland, MA: Sinauer Associates).
- Phillips, R., and Milo, R. (2009). A feeling for the numbers in biology. *Proc. Natl. Acad. Sci. USA* 106, 21465–21471.
- Phillips, R., Kondev, J., and Theriot, J. (2008). Physical Biology of the Cell (London: Garland Science).
- Weinstein, L., and Adam, J.A. (2008). Guesstimation: Solving the World's Problems on the Back of a Cocktail Napkin (Princeton, NJ: Princeton University Press).

## **Supplementary information – SnapShot: Basic numbers for cell biology:**

### **Cell Sizes:**

- Bacteria (*E. coli*): ~1  $\mu\text{m}$  diameter (BNID 100002)  
**Ref:** Nelson DE, Young KD. Penicillin binding protein 5 affects cell diameter, contour, and morphology of *Escherichia coli*. *J Bacteriol.* 2000 PMID [10692378](#)  
**Measurement Method:** Cell measurements and analyses were performed with Image Pro. Cell diameters of individual cells were calculated by measuring the cross-sectional area and dividing that value by the cell length.  
**Comments:** The derived diameters of 92% of untreated wild-type *E. coli* CS109 cells clustered between 1.0 and 1.1  $\mu\text{m}$  (Fig. 3A)

~2.5  $\mu\text{m}$  length (BNID 103713)  
**Ref:** Grossman N, Ron EZ, Woldringh CL. Changes in cell dimensions during amino acid starvation of *Escherichia coli*. *J Bacteriol.* 1982 PMID [6749809](#)  
**Measurement Method:** Electron micrographs were projected at a final magnification of about 15,000x to 20,000x, and cell length and cell diameter were measured. At least 150 cells were measured for each sample, and dimensions were calculated according to a calibration grid which was photographed at the same magnification.  
**Comments:** Value is mean of *E. coli* *ilvA*, *thyA*, cells grown on glycerol and glucose during exponential phase, Mean doubling time 57 min.

~1.1  $\mu\text{m}^3$  in volume 0.44-1.79  $\text{mm}^3$  (BNID 100004)  
**Ref:** Kubitschek HE, Friske JA. Determination of bacterial cell volume with the Coulter Counter. *J Bacteriol.* 1986 Dec 168(3):1466-7. Table link-<http://tinyurl.com/cphmpq> PMID [3536882](#)  
**Measurement Method:** Coulter Counter analyzer system  
**Comments:** value is average of 10 measurements in table 1

$2 \times 10^7$  cell concentration for culture with OD600 of 0.1 (BNID 103625)  
**Ref:** Sezonov G, Joseleau-Petit D, D'Ari R. *Escherichia coli* physiology in Luria-Bertani broth. *J Bacteriol.* 2007 Fig. 1a PMID [17905994](#)  
**Measurement Method:** The widely used wild-type *E. coli* K-12 strain MG1655 was chosen for this study. An overnight culture in Luria-Bertani broth was diluted 5,000-fold in 250 ml fresh medium in a 1-liter Erlenmeyer flask and cultivated in a shaking water bath (180 rpm) at 37°C. The OD600 and number of cells per milliliter were monitored.  
**Comments:** Note that cell concentration of a different strain with OD600 of 0.1 is  $10^8$  cells/ml, greater by a factor of 5 (see BNID 100985). The optical density of yeast and bacterial cultures is due to light scattering, not absorption. Therefore it is sensitive to the geometry of the detector relative to the cuvette, as well as the size and shape of the cells.
- Yeast (*Saccharomyces cerevisiae*): ~5  $\mu\text{m}$  diameter (BNID 103896)  
**Ref:** Teerapatr Srinorakutara, Determination of yeast cell wall thickness and cell diameter using new methods, *Journal of Fermentation and Bioengineering Volume 86, Issue 3, 1998, Pages 253-260*  
**Measurement Method:** The cell diameters were measured using a Coulter counter and an image analyser. Micromanipulation was used for measuring the bursting strength of individual yeast cells. The basic principle of this technique is the capture and squeezing of a single cell between parallel surfaces.  
**Comments:** *S. cerevisiae* Yg grown in YEPG medium at 60%  $\text{DO}_2$ .

~70  $\text{mm}^3$  in volume (BNID 100452)  
**Ref:** Roskams and Rodgers, *LabRef*
- Volume of mammalian (HELA) cell 4400-5000  $\mu\text{m}^3$  (BNID 103719)  
**Ref:** Cohen LS, Studzinski GP. Correlation between cell enlargement and nucleic acid and protein content of HeLa cells in unbalanced growth produced by inhibitors of DNA synthesis. *J Cell Physiol.* 1967 Jun 6 9(3):331-9. PMID [4230858](#)  
**Measurement Method:** Cells allowed to enter logarithmic phase. Cell number was obtained with a Coulter counter, while cell sizing was performed with the automatic particle size distribution analyser Model J Electronic Co., Hialeah, Fla.  
**Comments:** Please note-BNID 103725 gives HeLa cell volume range of 760-2730  $\mu\text{m}^3$



Human erythrocyte 97  $\mu\text{m}^3$  in volume (BNID 101711)

**Ref:** Frank, A. O., C. J. Chuong, et al. (1997). "A finite-element model of oxygen diffusion in the pulmonary capillaries." *J. Appl. Physiol* 82(6): 2036-2044. PMID [9173974](#)

COS-7 cell 2016+-209  $\text{mm}^3$  (BNID 101666)

**Ref:** Bohil et al. Myosin-X is a molecular motor that functions in filopodia formation. *PNAS* 2006. 103(33): pp.12411-12416 PMID [16894163](#)

**Comments:** value is found in supplemental figure 7. The COS cell line was obtained by immortalizing a CV-1[1] cell line derived from kidney cells of the African green monkey.

Human alveolar macrophage cell 4990+-174  $\mu\text{m}^3$  (BNID 103566)

**Ref:** Krombach F, Münzing S, Allmeling AM, Gerlach JT, Behr J, Dörger M. Cell size of alveolar macrophages: an interspecies comparison. *Environ Health Perspect.* 1997 Sep 105 Suppl 5:1261-3. Table 2 PMID [9400735](#)

**Measurement Method:** Morphometric analysis of AM was performed using a flow cytometer that generates volume signals based on the Coulter-type measurement of electrical resistance.

Perikaryon of purkinje cell in human cerebellum 13700  $\text{mm}^3$  (BNID 103180)

**Ref:** Andersen BB, Gundersen HJ, Pakkenberg B. Aging of the human cerebellum: a stereological study. *J Comp Neurol.* 2003 Nov 17466(3):356-65. PMID [14556293](#)

**Measurement Method:** stereological tools designed for estimating mean particle volume: The nucleator and the rotator.

**Comments:** Cerebella from 19 normal Caucasian males, ages 19-84 years, were studied. The perikaryon is also known as the cell body.

#### Organelles and cell constituents:

4. Fraction of Budding yeast nucleus volume out of total cell volume ~7% (BNID 104708)

**Ref:** Jorgensen P, Edgington NP, Schneider BL, Rupes I, Tyers M, Fitcher B. The size of the nucleus increases as yeast cells grow. *Mol Biol Cell.* 2007 Sep 18(9):3523-32. Table link - <http://tinyurl.com/ncgbno> PMID [17596521](#)

**Measurement Method:** Morphometry

**Comments:** Analysis of mutant yeast strains spanning a range of cell sizes revealed that the ratio of average nuclear volume to average cell volume was quite consistent, with nuclear volume being approximately 7% that of cell volume. See Nuclear volume of 2.9  $\mu\text{m}^3$  BNID 100447

HeLa cell nucleus in cervix tissue ~400  $\mu\text{m}^3$  in volume (BNID 101402)

**Ref:** Maul GG, Deaven L. Quantitative determination of nuclear pore complexes in cycling cells with differing DNA content. *J Cell Biol.* 1977 Jun 73(3):748-60.3. Table 1 Table link - <http://tinyurl.com/58x8ay> PMID [406262](#)

**Measurement Method:** HeLa, mouse L, and CHO cells were grown in suspension culture. Their nuclei appeared mostly round. The long and short axes of these nuclei were averaged, and the surface and volume were calculated as if the nuclei were spheres.

5. Cell membrane thickness ~4-10 nm

(BNID 103944) 5-10 nm for *E. coli*

**Ref:** EL-Hag, A. Jayaram, S.H. Effect of biological cell size and shape on killing efficiency of pulsed electric field, *Dielectric Liquids*, 2008. ICDL 2008. IEEE International Conference on Volume, Issue, June 30 2008-July 3 2008 Page(s):1 - 4 Table 2

(BNID 101276) 4.1 nm for spinach

**Ref:** Proton-powered turbine of a plant motor. Seelert H et al. *Nature.* 2000 May 25;405(6785):418-9 PMID [10839529](#)

**Primary Source:** Hine, Robert. "Membrane." *The Facts on File Dictionary of Biology.* 3rd ed. New York: Checkmark, 1999: 198.

**Measurement Method:** atomic force microscopy

(BNID 103948) 7.5 nm for vertebrate erythrocyte

**Ref:** Jaspard F, Nadi M, Rouane A. Dielectric properties of blood: an investigation of haematocrit dependence. *Physiol Meas.* 2003 Feb 24(1):137-47. PMID [12636192](#)

**Primary Source:** *Aim'e-Genty N 1999 Le sang Dictionnaire Encyclop'edique (Paris: Vuibert)*

6. "Average" protein diameter ~4 nm (BNID 101827)  
**Ref:** *"Physical Biology of the Cell", Rob Phillips, Jane Kondev and Julie Theriot (2009). Page 26*  
**Comments:** See Stokes radius of Casein 2.9-3.7 nm (BNID 103862), Radius of gyration of myoglobin 1.52 nm (BNID 103782), Radius of gyration of ribonuclease 1.43 nm (BNID 103781), Radius of gyration of conalbumin 2.95 nm (BNID 103737), albumin diameter 3 nm (BNID 103736), insulin receptor diameter 6.5 nm (BNID 103212), Diameter of the LacY transporter ~6 nm (BNID 102929)  
  
Properties of casein, BSA, and lysozyme Table link - <http://tinyurl.com/cu28na> (BNID 103880)  
**Ref:** *Pim van Hee, Selective recovery of micrometer bioparticles using aggregation and air flotation, thesis, 2006, Department of Biotechnology, Delft University of Technology The Netherlands*  
**Comments:** Radii of casein, BSA, and lysozyme 2.9-3.7, 3.48, and 1.8 nm, respectively  
  
Radius of gyration of ribonuclease 1.43 nm (BNID 103781)  
**Ref:** *Yaoqi Zhou, Salt Effects on Protein Titration and Binding, J. Phys. Chem. B, 1998, 102 (51), pp 10615-10621 table 1*  
**Measurement Method:** X ray crystallography  
**Comments:** Estimated hydrated protein radius is 1.71 nm  
  
Radius of gyration of myoglobin 1.52 nm (BNID 103782)  
**Ref:** *Yaoqi Zhou, Salt Effects on Protein Titration and Binding, J. Phys. Chem. B, 1998, 102 (51), pp 10615-10621 table 1*  
**Measurement Method:** X ray crystallography  
**Comments:** Estimated hydrated protein radius is 1.84 nm
7. Water molecule diameter ~0.28 nm (BNID 103723)  
**Ref:** *D'Arrigo JS. Screening of membrane surface charges by divalent cations: an atomic representation. Am J Physiol. 1978 Sep 235(3):C109-17 PMID 696813*  
**Comments:** Other sources give value of 2.63 Angstrom

#### **Concentrations:**

8. Concentration of 1 nM in a cell the volume of *E. coli* is ~ 1 molecule/cell (BNID 102068)  
**Ref:** Calculated according to cell volume in Primary Source, please see Measurement Method  
**Primary Source:** *Kubitschek HE, Friske JA. Determination of bacterial cell volume with the Coulter Counter. J Bacteriol. 1986 Dec 168(3):1466-7. Table link-http://tinyurl.com/cphmpq PMID 3536882*  
**Measurement Method:** Calculated using Avogadro's constant according to one cell volume=1E-12 cm<sup>3</sup>=1E-15 liter (Average of 10 measurements in table from Primary source, BNID 100004). Calculated using Avogadro's constant according to one cell volume=1E-12 cm<sup>3</sup>=1E-15 liter. 1 particle/1E-15 liter=X particles/liter>>X=1E15 particles/liter 1E15(particles/liter)/6E23(particles/mole)=1.666E-9M=~1 nM.  
  
Concentration of ~0.1 pM in a mammalian (HeLa) cell is ~ 1 molecule/cell (BNID 104519)  
**Ref:** *Calculated according to cell volume, please see Measurement Method*  
**Measurement Method:** Calculated using Avogadro's constant according to one cell volume=5000 um<sup>3</sup>=5E-12 liter (BNID 103719). 1 particle / 5E-12 liter = X particles/liter >> X = 2E11 particles/liter 2E11 (particles/liter)/6E23 (particles/mole) = ~3E-13 M=~0.1 pM. Thus 1 mM=~10<sup>10</sup> molecules per cell. Note: 3E-13 M and 1E-13 M are on same order of magnitude, allowing approximation.
9. Characteristic concentration for a signaling protein ~10 nM-1 mM (BNID 103954)  
**Ref:** *S Legewie, H Herzel, H Westerhoff, and N Bluthgen. Recurrent design patterns in the feedback regulation of the mammalian signalling network. Molecular Systems Biology. 2008.*



4:190 Table link - <http://tinyurl.com/5sm66v> PMID [18463614](https://pubmed.ncbi.nlm.nih.gov/18463614/)

**Primary Source:** See table for primary sources

**Measurement Method:** The Table gives a characteristic range of signaling proteins 10000-1000000 molecules per cell. Calculated using Avogadro's constant according to one cell volume (mammalian cell culture volume BNID 100434)  $\sim 2E-15 \text{ cm}^3 = 2E-12 \text{ liter}$ .  $2E-12 \times 6E23 = \sim 1E12$  particles per cell with concentration of 1 Molar. Concentration of 0.1-1  $\mu\text{M}$  would give  $1e4-1e6$  molecules per cell.

**Comments:** Table gives Number of various signaling protein molecules in one cell. This table can be found in the supplementary information section of the above-mentioned reference.

0.4 mM concentration of Ras in HeLa cells (BNID 100853)

**Ref:** Fujioka et al., Dynamics of the Ras/ERK MAPK cascade as monitored by fluorescent probes. *J Biol Chem.* 2006 Mar 31;281(13):8917-26 PMID [16418172](https://pubmed.ncbi.nlm.nih.gov/16418172/)

**Measurement Method:** FRET (Fluorescence Resonance Energy Transfer) probe

10. Water content:  $\sim 70\%$  of cell

*E. coli* 74%, (BNID 100044)

**Ref:** Jerry W. King, Gary R, *Supercritical fluid technology in oil and lipid chemistry*, 1996, American Oil Chemists' Society, pp. 303

Yeast, 68% (BNID 103689)

**Ref:** Jerry W. King, Gary R, *Supercritical fluid technology in oil and lipid chemistry*, 1996, American Oil Chemists' Society, pp. 303

Rat Alveolar macrophage 67% (BNID 103960)

**Ref:** Banks MA, Porter DW, Pailes WH, Schwegler-Berry D, Martin WG, Castranova V. Taurine content of isolated rat alveolar type I cells. *Comp Biochem Physiol B.* 1991 100(4):795-9. Table link - <http://tinyurl.com/cybwjc> PMID [1782762](https://pubmed.ncbi.nlm.nih.gov/1782762/)

**Measurement Method:** Rat alveolar type I cells were isolated by enzymatic digestion and purified by centrifugal elutriation and specific surface adsorption. The identity of the harvested cells was confirmed using electronic cell sizing and transmission electron microscopy. Calculated according to cell volume of  $1456 \mu\text{m}^3 = 1.456e-12$  liter and water content of  $0.97 \text{ ul}/10^6 \text{ cells} = 0.97 \times 10^{-12}$  Liter per cell

Empirical elemental formula for biomass of *E. coli*  $\text{C}_{1.77}\text{H}_{1.77}\text{O}_{0.49}\text{N}_{0.24}$  (BNID 101800)

**Ref:** von Stockar, U. Liu, J. Does microbial life always feed on negative entropy?

*Thermodynamic analysis of microbial growth.* 1999. *Biochim Biophys Acta.* 1412(3) p.198 PMID [10482783](https://pubmed.ncbi.nlm.nih.gov/10482783/)

**Comments:** This means that for every mole of carbon, there is 1.77 moles of hydrogen, 0.49 moles of oxygen and 0.24 moles of nitrogen. From this the carbon content of a cell is about 48% of the dry weight

11. Composition of dry weight of an *E. coli*:  $\sim 55\%$  protein, 20% RNA, 10% Lipids, 15% others (BNID 101436)

**Ref:** Neidhardt F.C. *Escherichia coli and Salmonella: Cellular and Molecular Biology. Vol 1.* pp. 14, ASM Press 1996. Table I Table Link - <http://tinyurl.com/cr3y57>

**Comments:** General information on quantities of macromolecules per cell

Composition of dry weight of an *S. cerevisiae*: protein 40% fiber 30% RNA 10% ashes 4% lipids 1% others 15% (BNID 104157)

**Ref:** Yamada EA, Sgarbieri VC. Yeast (*Saccharomyces cerevisiae*) protein concentrate: preparation, chemical composition, and nutritional and functional properties. *J Agric Food Chem.* 2005 May 18;53(10):3931-6 Table link - <http://tinyurl.com/nl8z68> PMID [15884819](https://pubmed.ncbi.nlm.nih.gov/15884819/)

**Measurement Method:** Water content, ashes, and crude protein (N X5.8) were determined according to the AOAC (ref 15) procedures. Total lipids were determined according to the Bligh and Dyer method (16). Soluble and insoluble fibers were quantified by treating the sample first with proteolytic enzymes (pepsin/pancreatin) to digest sample protein, followed by filtration to retain the insoluble fiber and precipitation of the soluble fiber from the filtrate with ethanol.

12. Number of proteins in an *E. coli* cell  $2.35 \times 10^6$  (depending on growth rate) (BNID 102990)

**Ref:** Neidhardt F.C. *Escherichia coli and Salmonella: Cellular and Molecular Biology. Vol 1.* ASM Press 1996. table link- <http://tinyurl.com/cr3y57>

**Measurement Method:** Calculated for an average cell of *E. coli* B/r in balanced growth at 37 degrees celsius in aerobic glucose minimal medium with a 40 minute mass doubling time. This cell is 44% through its division cycle.

Calculated concentration of total protein in *E. coli* cell ~4 mM (BNID 104726)

**Ref:** Calculated according to Primary Source. Please see Measurement Method Neidhardt F.C. *Escherichia coli and Salmonella: Cellular and Molecular Biology. Vol 1.* ASM Press 1996. table link- <http://tinyurl.com/cr3y57>

**Measurement Method:** Calculated for an average cell of *E. coli* B/r in balanced growth at 37 degrees celsius in aerobic glucose minimal medium with a 40 minute mass doubling time. This cell is 44% through its division cycle. Calculated from Protein number of 2.35e6 (See BNID 102990 and table link in Primary Source) and assuming cell volume of  $\sim 1 \mu\text{m}^3 = 1 \text{e-15 liter}$  (BNID 10004) and avogadro's constant =  $6 \text{e}23$  particles/mole (BNID 101907).  $(2.35 \text{e}6 \text{ proteins/cell}) / [(6 \text{e}23 \text{ proteins/mole}) * (1 \text{e-15 liter/cell})] = \sim 4 \text{e-3 M}$

Total observed intracellular metabolite pool in *E. coli* 300 mM (BNID 104678)

**Ref:** Bennett BD, Kimball EH, Gao M, Osterhout R, Van Dien SJ, Rabinowitz JD. *Absolute metabolite concentrations and implied enzyme active site occupancy in Escherichia coli.* *Nat Chem Biol.* 2009 Aug 5(8):593-9 Table link - <http://tinyurl.com/m8rymt> PMID 19561621

**Measurement Method:** Researchers quantified metabolites by Liquid chromatography-mass spectrometry (LC-MS/MS) using an isotope ratio-based approach (8). As isotope-labeled standards for many metabolites are not available, they used uniformly  $^{13}\text{C}$ -labeled glucose medium to label the intracellular metabolome of *E. coli* (25). This enabled the use of commercially available unlabeled compounds as internal standards.

**Comments:** The total observed intracellular metabolite pool was approximately 300 mM. A small number of metabolites dominate the metabolome on a molar basis, with glutamate being the most abundant.

### Energetics:

13. DG needed to achieve order of magnitude ratio of concentrations:  $\sim 6$  kJ/mole  
 $-5.7$  kJ/mole (BNID 103912)  
**Ref:** Nelson & Cox, *Lehninger's Principles of Biochemistry 4th Edition, 2004, WH Freeman Table 6-4 pp.195*  
**Measurement Method:**  $\Delta G = -RT \ln(K_{eq})$ . Calculating for  $R = 8.315$ ,  $T = 298$ ,  $K_{eq} = 10$ ,  $\Delta G = 5705.5$  J/mole  
**Comments:** Approximately  $2kT =$  Approximately  $60 \text{meV}$ . Calculating  $RT = kT / (\text{Avogadro's number})$
14. Energetic contribution of a hydrogen bond:  $\sim 6-20$  kJ/mole (BNID 103914, 103913, 101067, 101069, 101068, 101070)  
 $9$  kJ/mole Strength of hydrogen bond in water (BNID 103914)  
**Ref:** van der Spoel D, van Maaren PJ, Larsson P, Timneanu N. *Thermodynamics of hydrogen bonding in hydrophilic and hydrophobic media.* *J Phys Chem B.* 2006 Mar 9 110(9):4393-8. PMID 16509740  
**Measurement Method:** An extensive series of over 400 molecular dynamics simulations with an aggregate length of over 900 ns was analyzed using an analysis technique in which hydrogen bond (HB) breaking is interpreted as an Eyring process, for which the Gibbs energy of activation  $\Delta G$  can be determined from the HB lifetime.
15. DG of ATP hydrolysis under physiological conditions in *E. coli*  $\sim 50$  kJ/mole (BNID 101701)  
**Ref:** Quang Hon Tran, Gottfried Uden. *Changes in the proton potential and the cellular energetics of Escherichia coli during growth by aerobic and anaerobic respiration or by fermentation.* *European Journal of Biochemistry.* 1998. 251(1-2) pp. 538-543  
PMID 949233  
**Measurement Method:** calculated from the equation:  $\Delta G(\text{Phos}) = \Delta G(\text{at standard conditions}) + RT \ln([ATP]/[ADP][\text{Pi}])$ , where  $R$  is the gas constant,  $T$  = temperature, and  $-30.5$  kJ/mol was used for  $\Delta G$  at standard conditions.

**Comments:** The number has been converted from positive to negative so that it describes the Gibbs free energy of hydrolysis as opposed to the phosphorylation potential. The *E. coli* was growing in the presence of oxygen. See reference for more details.

16. Number of ATP molecules required to make an *E. coli* cell on minimal medium and glucose under Aerobic conditions  $\sim 10^{10}$  ATP (BNID 101981)

**Ref:** Farmer, I.S. and Jones, C.W. *The energetics of Escherichia coli during aerobic growth in continuous culture.* (1976) *Eur. J. Biochem.* 67(1):115-22. PMID [786616](#)

**Measurement Method:** YATP(max) was determined by measuring the rate of oxygen consumption(QO<sub>2</sub>) and growth rate(D), and calculating the value of mol ATP formed per mol oxygen (N) and the energetic maintenance cost (M). The equation  $QO_2 = D/YATP(max)*N + M/N$  was used.

**Comments:** This number is calculated from the value for YATP(max) of 13.9 in the reference. YATP(max) is the number of grams of cells (dry weight) produced per mol of ATP corrected for cellular maintenance energy costs. 1/13.9 gives 0.0719 mol of ATP per gram of cells. One *E. coli* cell weighs 0.28pg (dry wt), so there are 3.57 trillion cells/gram.  $0.0719*6.02E23/(3.57E12 \text{ cells/g (dry wt)})$  gives 12.1 billion ATP/cell.

Number of ATP molecules to make an *E. coli* cell on minimal media and glucose under anaerobic conditions  $1.64 \times 10^{10}$  ATP (BNID 101983)

**Ref:** Hempling, W. and Mainzer, S. *Effects of Varying the Carbon Source Limiting Growth on Yield and Maintenance Characteristics of Escherichia coli in Continuous Culture.* (1975) *J. Bacteriol.* 123(3): 1076-1087. PMID [169226](#)

**Comments:** This number is calculated from the value for YATP(max) of 10.3 in the reference. YATP(max) is the number of grams of cells (dry weight) produced per mol of ATP corrected for cellular maintenance energy costs. 1/10.3 gives 0.0971 mol of ATP per gram of cells. One *E. coli* cell weighs 0.28pg (dry wt), so there are 3.57 trillion cells/gram.  $0.0971*6.02E23/(3.57E12 \text{ cells/g (dry wt)})$  gives 16.4 billion ATP/cell.

ATP requirement for growth on acetate and minimal media under aerobic conditions  $2.48 \times 10^{10}$  ATP (BNID 101982)

**Ref:** Farmer, I.S. and Jones, C.W. *The energetics of Escherichia coli during aerobic growth in continuous culture.* (1976) *Eur. J. Biochem.* 67(1):115-22. PMID [786616](#)

**Measurement Method:** YATP(max) was determined by measuring the rate of oxygen consumption(QO<sub>2</sub>) and growth rate(D), and calculating the value of mol ATP formed per mol oxygen (N) and the energetic maintenance cost (M). The equation  $QO_2 = D/YATP(max)*N + M/N$  was used.

**Comments:** This number is calculated from the value for YATP(max) of 7.1 in the reference. YATP(max) is the number of grams of cells (dry weight) produced per mole of ATP corrected for cellular maintenance energy costs. 1/7.1 gives 0.1408 mol of ATP per gram of cells. One *E. coli* cell weighs 0.28pg (dry wt), so there are 3.57 trillion cells/gram.  $0.1408*6.02E23/(3.57E12 \text{ cells/g (dry wt)})$  gives 24.8 billion ATP/cell.

ATP requirement for growth and Yatp under different nutritional conditions Table Link - <http://tinyurl.com/qjojft> (BNID 101637)

**Ref:** Byung Hong Kim, Geoffrey Michael Gadd. *Bacterial Physiology and Metabolism.* Cambridge University Press.

**Primary Source:** Dawes, Edwin A. *Microbial Energetics.* Chapman and Hall: New York, NY. 1986. It appears to be based on a table from a chapter of *Microbial Biochemistry* - see Stouthamer, A.H. *The search for correlation between theoretical and experimental growth yields.* (1979) *Int. Rev. Biochem. Microb. Biochem.* 21:1-47 ed. J.R. Quayle. University Park Press.

**Comments:** After consulting primary sources, it appears that for columns E and F, and possibly G, the energy requirement for mRNA turnover was already included in the RNA cost, and so has been counted twice in this table. This would reduce the "Total" by 1.39 mmol of ATP for these columns, which would cause a very slight change in Yatp.

### Diffusion and catalysis rate

17. Diffusion coefficient of dextran (40kDa) in *Drosophila* cytoplasm  $17.6 \pm 1.8 \mu\text{m}^2/\text{sec}$  (BNID 100198)

**Ref:** Gregor T, Bialek W, de Ruyter van Steveninck RR, Tank DW, Wieschaus EF. Diffusion and scaling during early embryonic pattern formation. *Proc Natl Acad Sci U S A*. 2005 Dec 20;102(51):18403-7. PMID [16352710](#)

**Measurement Method:** Fluorescent dextran injected into Drosophila embryo, confocal imaging, and fitting with 3D diffusion model

7.7+-2.5  $\mu\text{m}^2/\text{sec}$  GFP Diffusion coefficient in *E. coli* cytoplasm (BNID 100193)

**Ref:** Elowitz MB, Surette MG, Wolf PE, Stock JB, Leibler S. Protein mobility in the cytoplasm of *Escherichia coli*. *J Bacteriol*. 1999 Jan;181(1):197-203. PMID [9864330](#)

**Measurement Method:** FRAP and photoactivation

Time for protein to diffuse across *E. coli* cell ~0.1 sec (BNID 104667)

**Ref:** Calculated manually. Please see measurement method.

**Measurement Method:** According to equation:  $t_{\text{diffusion}} \sim X^2/2D$ . Taking X, distance to be traveled, as 1  $\mu\text{m}$  and D, diffusion coefficient, as 100  $\mu\text{m}^2/\text{sec}$ . D calculated from  $D = KBT/6\pi\eta R$  where  $R = 2.5 \text{ nm}$ , typical protein diameter.  $K_B$  = Boltzmann's constant,  $\eta$  (eta) = viscosity of the medium, taken as 0.001 Pa\*sec for water at ~300 Kelvin,

$T$  = temperature in degrees Kelvin,  $\pi \sim 3.14$ .  $(1.3806504(24) \times 10^{-23} \text{ Kgm}^2 \text{ sec}^{-2} \text{ K}^{-1} \times 300 \text{ K}) / (6 \times 3.14 \times 0.001 \text{ Kgm}^{-1} \text{ sec}^{-1} \times 2.5 \times 10^{-9} \text{ m}) = 8.8 \times 10^{-11} \text{ m}^2/\text{sec} = 88 \mu\text{m}^2/\text{sec} \sim 100 \mu\text{m}^2/\text{sec}$

**Comments:** Diffusion coefficient of 100  $\mu\text{m}^2/\text{sec}$  refers to water. In cytoplasm D is smaller than 100  $\mu\text{m}^2/\text{sec}$  as there are solutes, in the range of 5-15  $\mu\text{m}^2/\text{sec}$  (BNIDs 100193, 100198). Taking D as 10  $\mu\text{m}^2/\text{sec}$ , actual time of diffusion would be  $(1 \mu\text{m})^2 / (2 \times 10 \mu\text{m}^2/\text{sec}) \sim 0.1 \text{ sec}$

~5 sec for hemoglobin to traverse erythrocyte (BNID 104677)

**Ref:** Calculated according to erythrocyte diameter. Please see Measurement Method

**Measurement Method:** Calculated with equation  $d^2 = 2Dt$  where  $d$  = distance to pass, length of erythrocyte, 10  $\mu\text{m}$ . D of hemoglobin in erythrocyte cytoplasm is lower than in water due to presence of solutes, in the range of 5-15  $\mu\text{m}^2/\text{sec}$  (BNIDs 100193, 100198). Taking D as 10  $\mu\text{m}^2/\text{sec}$ , actual time of diffusion would be  $(10 \mu\text{m})^2 / (2 \times 10 \mu\text{m}^2/\text{sec}) \sim 5 \text{ sec}$  BNID 104106 for diffusion time in water medium

D (metabolite) ~500  $\text{mm}^2/\text{sec}$

Diffusion coefficient of sucrose in water 520  $\mu\text{m}^2/\text{sec}$  (BNID 100614)

**Ref:** S. Vogel Life's Devices (1988)

Diffusion coefficient of glucose in water 600  $\mu\text{m}^2/\text{sec}$  (BNID 104089)

**Ref:** Stein, Wilfred D., *Channels, carriers and pumps An introduction to Membrane Transport*, 1990 Academic press inc. Harcourt Brace Jovanovich, Publishers pp.32 Table link - <http://tinyurl.com/prfosd>

**Primary Source:** R. Hober (1967) "Physical Chemistry of cells and tissues" Churchill, London AND Daniels and Alberty (1961) "Physical Chemistry" Wiley, New York

**Comments:** Table gives Molecular/Ionic weight and Diffusion coefficients of various substances in specified temperatures

18. Diffusion limited on-rate for a characteristic protein  $\sim 10^8$ - $10^9$  1/sec/Molar (BNID 103916)

**Ref:** Nelson & Cox, *Lehninger's Principles of Biochemistry 4th Edition*, 2004, WH Freeman & Co, pp.207 Table link - <http://tinyurl.com/cgoqnu>

**Comments:** There is an upper limit to  $K_{\text{cat}}/K_{\text{m}}$ , imposed by the rate at which E and S can diffuse together in an aqueous solution. This diffusion controlled limit is  $10^8$  to  $10^9 \text{ M}^{-1} \times \text{s}^{-1}$ , and many enzymes have a  $k_{\text{cat}}/K_{\text{m}}$  near this range

#### Division, Replication, transcription, translation rates

19. Exponential cell cycle time:

*E. coli* ~30 minutes (BNID 103890)

**Ref:** Bremer, H., Dennis, P. P. (1987) *Modulation of chemical composition and other parameters of the cell by growth rate*. Neidhardt, et al. eds. *Escherichia coli and Salmonella typhimurium: Cellular and Molecular Biology*, 1st ed. chapter 96, Table 2 pp.1530-1

**Comments:** Table gives Protein/mass, RNA/mass, DNA/mass, cell no./mass, protein/genome, RNA/genome, origins/genome, protein/origin and more parameters at 5 different doubling times

Yeast: ~100 minutes (BNID 100270)

**Ref:** JR Warner; *The economics of ribosome biosynthesis in yeast*, *Trends Biochem Sci.* 1999 Nov24(11):437-40. PMID [10542411](#)

**Comments:** Can reach ~70 minutes under ideal conditions (see BNID 101747)

Population doubling time, percent budded cells, and mean cell volume for different batch culture media 71-477 min (BNID 101747)

**Ref:** Tyson CB, Lord PG, Wheals AE. *Dependency of size of Saccharomyces cerevisiae cells on growth rate.* *J Bacteriol.* 1979 Apr138(1):92-8. PMID [374379](#)

**Measurement Method:** The mean size and percentage of budded cells of a wild-type haploid strain of *Saccharomyces cerevisiae* grown in batch culture over a wide range of doubling times ( $\tau$ ) have been measured using microscopic measurements and a particle size analyzer.

**Comments:** Shortest generation time 71 min on YEP+fructose medium Longest generation time 477 min on EMM+acetate+phthalate

Human cell line (Hela): 16.2 h (BNID 103804)**Ref:** Kumei Y, Nakajima T, Sato A, Kamata N, Enomoto S. *Reduction of G1 phase duration and enhancement of c-myc gene expression in HeLa cells at hypergravity.* *J Cell Sci.* 1989 Jun93 (Pt 2):221-6. PMID [2693468](#)

**Measurement Method:** Hypergravity cell culture, [<sup>3</sup>H] thymidine incorporation, Cell cycle analysis, RNA blot hybridization (Northern analysis)

**Comments:** Research checked difference between HeLa cells in hypergravity conditions and control.

Doubling time of cancerous cell lines 17-80 hours (BNID 100685)

**Ref:** [http://dtp.nci.nih.gov/docs/misc/common\\_files/cell\\_list.html](http://dtp.nci.nih.gov/docs/misc/common_files/cell_list.html)

**Measurement Method:** In vitro

**Comments:** Information on generation time, in hours, of the NCI set of 60 cancerous cell lines. Range 17-80 hours

Doubling time of human cancerous cell lines 13-80 hours (BNID 103994) *Table link - <http://tinyurl.com/clejlo>*

**Ref:** Patent - JOINT USE OF SULFONAMIDE BASED COMPOUND WITH ANGIOGENESIS INHIBITOR-OWA, OZAWA, and SEMBA 20.06.2007 link - <http://tinyurl.com/cd9eko> page 38 table 1

**Measurement Method:** Cells of these cell lines were seeded in 96-well microplates (flat-bottomed) (50 Pl/well) at the cell numbers indicated in Table 1. After 24 hours, a 3-fold dilution series of each compound was added (50 Pl/well). After 72 hours, WST-8 (10 Pl/well) was further added and the absorbance at 450 nm was measured. Additional information under table.

**Comments:** Information on generation time, in hours, of 36 cancerous cell lines. Range 13-80 hours.

20. Average replication rate of T7 bacteriophage DNA in *E. coli* 220+ -80 nucleotides/sec (BNID 103995)

**Ref:** Lee JB, Hite RK, Hamdan SM, Xie XS, Richardson CC, van Oijen AM. *DNA primase acts as a molecular brake in DNA replication.* *Nature.* 2006 Feb 2439(7076):621-4. *Supplementary information.* PMID [16452983](#)

**Measurement Method:** in vitro, single molecule measurements. The 5' end of one strand of a 48.5 kilobase (kb)-long duplex lambda phage DNA molecule is attached to the bottom surface of a glass flow cell using a biotin-streptavidin linker. The opposite 3' end bears a digoxigenin moiety and is linked to a bead that is 2.8 microm in diameter and coated with anti-digoxigenin antibody

**Comments:** These values are in agreement with those observed in a previously published single-molecule experiment: Wuite, G. J. L., Smith, S. B., Young, M., Keller, D. & Bustamante, C. Single-molecule studies of the effect of template tension on T7 DNA



polymerase activity. Nature (London) 404, 103-6 (2000). PubMed ID 10716452, that give polymerization rates of over 100 bases/sec for T7 DNA

DNA synthesis rate of *E. coli* DNA polymerase III holoenzyme ~750nts/sec (BNID 104120)

**Ref:** Kelman Z, O'Donnell M. DNA polymerase III holoenzyme: structure and function of a chromosomal replicating machine. *Annu Rev Biochem.* 1995 64:171-200 PMID [7574479](#)

**Primary Source:** Studwell PS, O'Donnell M. Processive replication is contingent on the exonuclease subunit of DNA polymerase III holoenzyme. *J Biol Chem.* 1990 Jan 15265(2): 1171-8 PMID [2153103](#)

**Measurement Method:** In vitro. The reconstitution approach was taken to study which subunits of the heterotrimer core polymerase (alpha, epsilon, theta) participate in the highly processive replication of long DNA templates by DNA polymerase III holoenzyme (holoenzyme).

**Comments:** This value is consistent with the rate of fork movement in *E. coli*. This rapid rate results from the high processivity of holoenzyme, which extends a chain for several thousand nucleotides without dissociating from the template even once

DNA replication rate in human 33 nts/sec (BNID 104136)

**Ref:** Fangman WL, Brewer BJ. A question of time: replication origins of eukaryotic chromosomes. *Cell.* 1992 Oct 3071(3):363-6 PMID [1423601](#)

**Measurement Method:** Replication fork speed of ~ 2000 base pairs/min=2000/60base pairs/sec=33 base pairs/sec

**Comments:** Article also gives info on distance between origins of replication: For a human cell, the approximately 3,000,000 kb genome is replicated in about 8 h. Since the rate at which replication forks plow through chromatin is no greater than~ 2 kb/min, bidirectional origins would need to be spaced at roughly 2000 kb intervals to finish replication in the allotted time.

21. Rate of transcription by RNA polymerase ~70 bp/sec

70 nt/sec for *E. coli* (BNID 100060)

**Ref:** (1) Dennis, P. P., and H. Bremer. 1974. Differential rate of ribosomal protein synthesis in *Escherichia coli* B/r. *J. Mol. Biol.* 84:407-422.

PMID 4618855 (2) [Dennis PP, Nomura M. Stringent control of ribosomal protein gene expression in coli B/r Proc Natl Acad Sci U.S.A. 1974 Oct;71\(10\):3819-23. PMID 4610562](#)

**Comments:** ~80 nt/sec according to Benno Muller-hill, 1996, The Lac Operon:

A Short History Of A Genetic Paradigm, Publisher: Walter de Gruyter. Berlin. New York. Part 3.2 pp.134

~71.6 nt/sec mammalian tissue culture cell (BNID 100662)

**Ref:** Darzacq X. et al, In vivo dynamics of RNA polymerase II transcription, *Nature Structural & Molecular Biology* - 14, 796 - 806 (2007) PMID [17676063](#)

**Measurement Method:** parameter optimization of FRAP and photoactivation data in U2OS 200 copy gene array. LacI gene integrated into Human U2OS osteosarcoma cells

**Comments:** See also average polymerase velocity and pause residence time. YFP-Pol II is amanitin resistant allele.

22. Rate of translation by the ribosome ~20 aa/sec

12-21 aa/sec for *E. coli* (BNID 100059)

**Ref:** Bremer, H., Dennis, P. P. (1996) Modulation of chemical composition and other parameters of the cell by growth rate. Neidhardt, et al. eds. *Escherichia coli and Salmonella typhimurium: Cellular and Molecular Biology*, 2nd ed. chapter 97, pp. 1559, Table 3

**Primary Source:** (1) Young, R. and H. Bremer (1976). "Polypeptide-chain-elongation rate in *Escherichia coli* B/r as a function of growth rate." *Biochem J* 160 PMID [795428](#) (2): 185-94

Dennis, P. P., and H. Bremer. Differential rate of ribosomal protein synthesis in *Escherichia coli* B/r. *J Mol Biol.* 1974 Apr 1584 PMID [4618855](#) (3):407-22..Dennis, P. P., and M. Nomura.

1974. Stringent control of ribosomal protein gene expression in *e.coli*, *PNAS* 1974 Oct71(10): 3819-23 PMID [4610562](#)

**Comments:** lower value is for slow division rate (100 minutes) and higher value is for fast division rate (24 minutes)

**Genomes, Mutation and error rates**

23. Genome size:

*E. coli* ~4×10<sup>6</sup> bp (BNID 100269)



**Ref:** Blattner FR et al, *The complete genome sequence of Escherichia coli K-12*, *Science*. 1997 Sep 5277(5331):1453-74. PMID [9278503](#)

**Comments:** The 4,639,221-base pair sequence of Escherichia coli K-12 is presented.

*S. cerevisiae* ~12×10<sup>6</sup> bp (BNID 100459)

**Ref:** <http://www.yeastgenome.org/cache/genomeSnapshot.html>

**Comments:** The Budding yeast genome size is 12,156,676 base Pairs as of May 6th 2009

*C. elegans* ~100×10<sup>6</sup> bp (BNID 101363)

**Ref:** Hillier LW, Coulson A, Murray JI, Bao Z, Sulston JE, Waterston RH. *Genomics in C. elegans: so many genes, such a little worm*. *Genome Res*. 2005 Dec 15(12):1651-60 PMID [16339362](#)

**Comments:** The complete Caenorhabditis elegans genome sequence, fully contiguous telomere to telomere totals 100,291,840 bp.

*D. melanogaster* ~120×10<sup>6</sup> bp (BNID 100199)

**Ref:** Adams MD et al, *The genome sequence of Drosophila melanogaster*. *Science*. 2000 Mar 24287(5461):2185-95. PMID [10731132](#)

*Arabidopsis* ~157×10<sup>6</sup> bp (BNID 104000)

**Ref:** Bennett MD, Leitch IJ, Price HJ, Johnston JS. *Comparisons with Caenorhabditis (approximately 100 Mb) and Drosophila (approximately 175 Mb) using flow cytometry show genome size in Arabidopsis to be approximately 157 Mb and thus approximately 25% larger than the Arabidopsis genome initiative estimate of approximately 125 Mb* *Ann Bot (Lond)*. 2003 Apr 91(5):547-57. PMID [12646499](#)

Mouse ~3×10<sup>9</sup> bp (BNID 100305)

**Ref:** <http://wormlab.caltech.edu/briggsae/genomeSize.html>

Human ~3×10<sup>9</sup> bp (BNID 100396)

**Ref:** International Human Genome Sequencing Consortium. *Finishing the euchromatic sequence of the human genome*. *Nature*. 2004 Oct 21431(7011):931-45. PMID [15496913](#)

**Comments:** Value refers to Euchromatic genome. For heterochromatic genome see BNID 101484

24. Mutation rate in DNA replication ~10<sup>-9</sup> per bp in *E. coli*

5.4E-10 mutation/bp/replication (BNID 100263)

**Ref:** Drake JW, *A constant rate of spontaneous mutation in DNA-based microbes*. *Proc Natl Acad Sci U S A*. 1991 Aug 1588(16):7160-4 Table 1 PMID [1831267](#)

**Measurement Method:** Value is mean of two strains-hisGDCBHAFE (one measurement) and LacI (2 measurements)

Mutation rate in DNA replication 5×10<sup>-11</sup> per base pair per replication in human (BNID 100414)

**Ref:** Drake JW, Charlesworth B, Charlesworth D, Crow JF. *Rates of spontaneous mutation*. *Genetics*. 1998 Apr 148(4):1667-86 PMID [9560386](#)

25. Error rate in transcription ~10<sup>-4</sup> per nucleotide (BNID 103453)

**Ref:** Hani S. Zaher and Rachel Green, *Fidelity at the Molecular Level: Lessons from Protein Synthesis*. *Cell Volume 136, Issue 4, 20 February 2009, Pages 746-76* PMID [19239893](#)

**Primary Source:** Bouadloun F, Donner D, Kurland CG., *Codon-specific missense errors in vivo*, *EMBO J*. 2 (1983), pp.1351-1356. PMID [10872330](#) AND Rosenberger RF, Foskett G. *An estimate of the frequency of in vivo transcriptional errors at a nonsense codon in Escherichia coli*. *Mol Gen Genet*. 1981 183(3):561-3 PMID [7038382](#)

**Comments:** This level of accuracy is lower than that of DNA replication and similar to that of translation.

Error rate in translation ~10<sup>-3</sup>-10<sup>-4</sup> per amino-acid (BNID 103454)

**Ref:** Hani S. Zaher and Rachel Green, *Fidelity at the Molecular Level: Lessons from Protein Synthesis*. *Cell Volume 136, Issue 4, 20 February 2009, Pages 746-76* PMID [19239893](#)

**Primary Source:** (1) Bouadloun, D. Donner and C.G.

Kurland, *Codon-specific missense errors in vivo*, *EMBO J*. 2 (1983), pp. 1351-1356. PMID [10872330](#) AND (2) P. Edelman and J. Gallant, *Mistranslation in E. coli*, *Cell* 10

(1977), pp. 131–137. PMID [138485](#)

**Comments:** This level of accuracy is lower than that of DNA replication and similar to that of transcription