

## **Savčí buněčná biologie v číslech**

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## Vychází z knihy:

- ▶ Ron Milo & Rob Phillips: Cell Biology by the numbers, Garland Sciences, 2016

## Matematika a chemie pro biology

### Big numbers at your disposal

- Seconds in a year  $\approx \pi \times 10^7$  (the approximate value of pi, a nice coincidence and an easy way to remember this value)
- Seconds in a day  $\approx 10^5$
- Hours in a year  $\approx 10^4$
- Avogadro's constant  $\approx 6 \times 10^{23}$
- Cells in the human body  $\approx 4 \times 10^{13}$

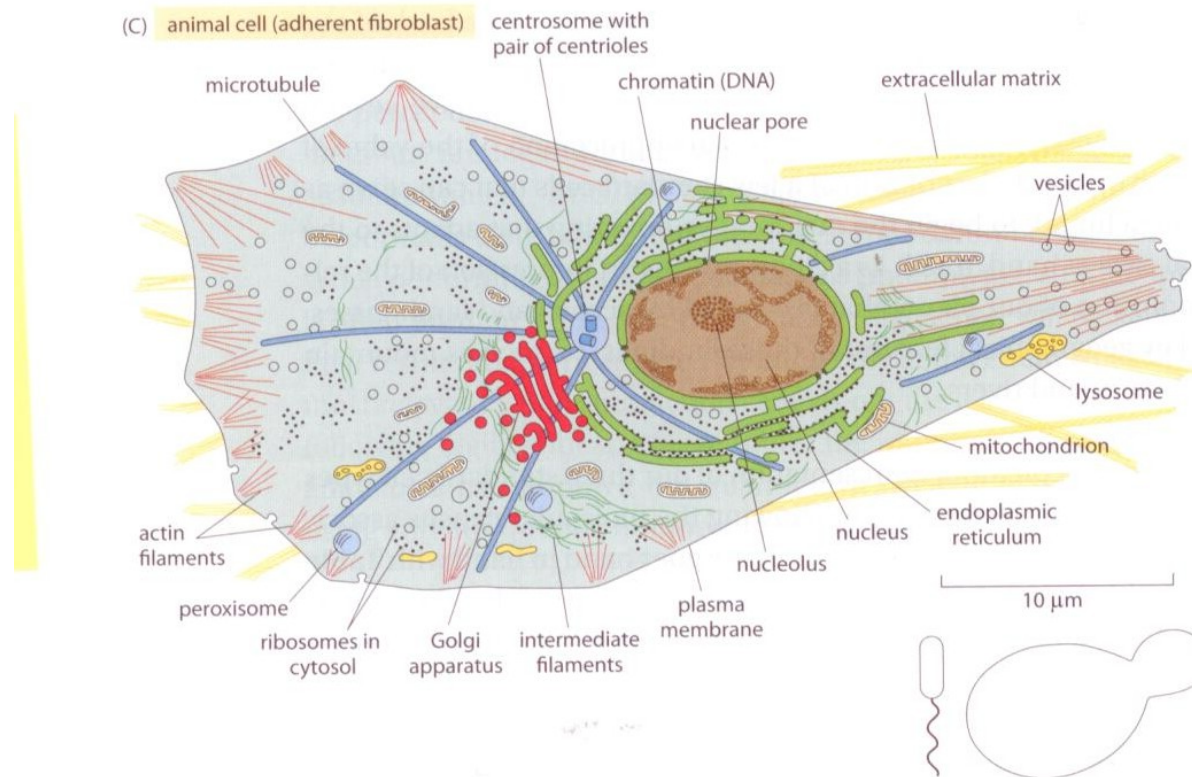
# Matematika a chemie pro biology

## Rules of thumb

Just as there are certain arithmetical rules that help us quickly get to our order-of-magnitude estimates, there are also physical rules of thumb that can similarly extend our powers of estimation. We give here some of our favorites and you are most welcome to add your own at the bottom of our list and also send them to us. Several of these estimates are represented pictorially as well. Note that here and throughout the book we try to follow the correct notation where “approximately” is indicated by the symbol  $\approx$ , and loosely means accurate to within a factor of two or so. The symbol  $\sim$  means “order of magnitude,” so only to within a factor of 10 (or in a different context it means “proportional”). We usually write approximately because we know the property value indeed roughly but to better than a factor of 10, so  $\approx$  is the correct notation and not  $\sim$ . In the cases where we only know the order of magnitude, we will write the value only as  $10^x$  without extraneous significant digits.

- 1 dalton (Da) = 1 g/mol  $\approx 1.6 \times 10^{-24}$  g (as derived in **Estimate 0-1**).
- 1 nM is about 1 molecule per bacterial volume, as derived in **Estimate 0-2**,  $10^1$ – $10^2$  per yeast cell, and  $10^3$ – $10^4$  molecules per characteristic mammalian (HeLa) cell volume. For 1  $\mu$ M, multiply by a thousand; for 1 mM, multiply by a million.
- 1 M is about one per 1 nm<sup>3</sup>.
- There are 2–4 million proteins per 1  $\mu$ m<sup>3</sup> of cell volume.

## Velikosti a počty



**Figure 0-1** The standard cells. (A) A schematic bacterium revealing the characteristic size and components of *E. coli*. (B) A budding yeast cell showing its characteristic size, its organelles, and various classes of molecules present within it. (C) An adherent human cell. We note that these are very simplified schematics. For example, only a small fraction of ribosomes are drawn. Each cell is drawn to a different scale, as indicated by the distinct scale bars in each schematic. The relative sizes of the bacterial and yeast cells at the same scale as the mammalian cell are shown in the bottom right. (A, and C, adapted from Alberts B, Johnson A, Lewis J et al. [2015] *Molecular Biology of the Cell*, 6th ed. Garland Science.)

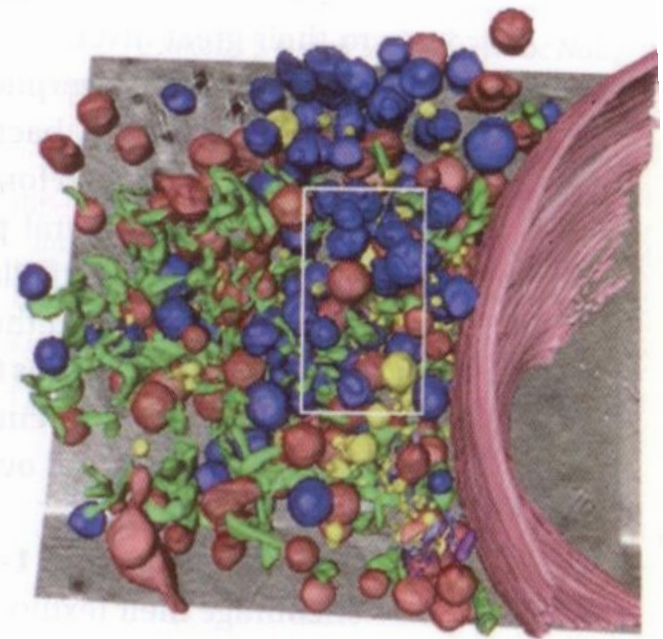
## Složení buňky

intracellular compartment	percentage of total cell volume
cytosol	50–60
mitochondria	20
rough ER cisternae	10
smooth ER cisternae plus Golgi cisternae	6
nucleus	6
peroxisomes	1
lysosomes	1
endosomes	1

**Table 1-5** The volume fraction occupied by different intracellular compartments in a liver hepatocyte cell. (Adapted from Alberts B, Johnson A, Lewis J et al. [2015] Molecular Biology of the Cell, 6th ed. Garland Science.)

a stack of closely spaced confocal images, it is possible to gain insights into the three-dimensional structure of the organelle over time. In these images, we see that during interphase the ER is reticular (netlike). To appreciate the tangled arrangement of organellar membranes even more deeply, **Figure 1-24** provides a reconstructed image using X-ray microscopy of the ER and other ubiquitous membrane systems in the cell. In this cell type and under

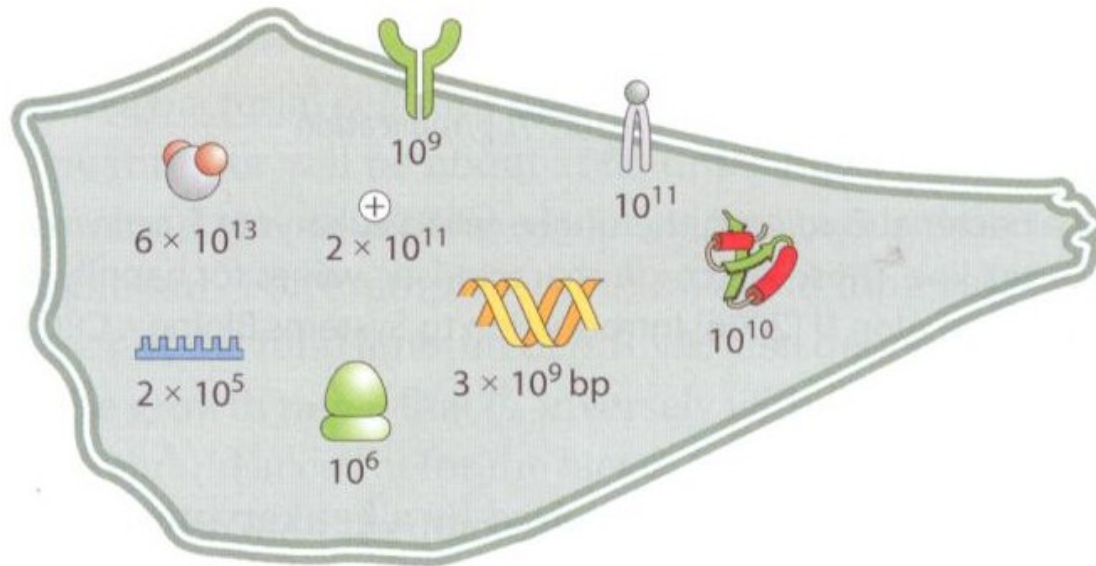
**Figure 1-24** X-ray microscopy image of cellular ultrastructure highlighting the endoplasmic reticulum. This image is a volumetric rendering of images of a mouse adenocarcinoma cell. The numbers represent percent of the volume occupied by the different compartments. (Adapted from Schneider G, Guttman P, Heim S et al. [2010] *Nature Meth* 7:985–987.)



■ lysosomes	13%
■ mitochondria	17%
■ endoplasmic reticulum	3%
■ vesicles	2%
external	65%

## Počty nejdůležitějších biomolekul

(C) mammalian cell (specifically, HeLa:  $V \approx 3000 \mu\text{m}^3$ ;  $L \approx 20 \mu\text{m}$ ;  $\tau \approx 1$  day)



**Figure 0-2** An order-of-magnitude census of the major components of the three model cells we employ often in the lab and in this book. A bacterial cell (*E. coli*), a unicellular eukaryote (the budding yeast *S. cerevisiae*), and a mammalian cell line (such as an adherent HeLa cell).

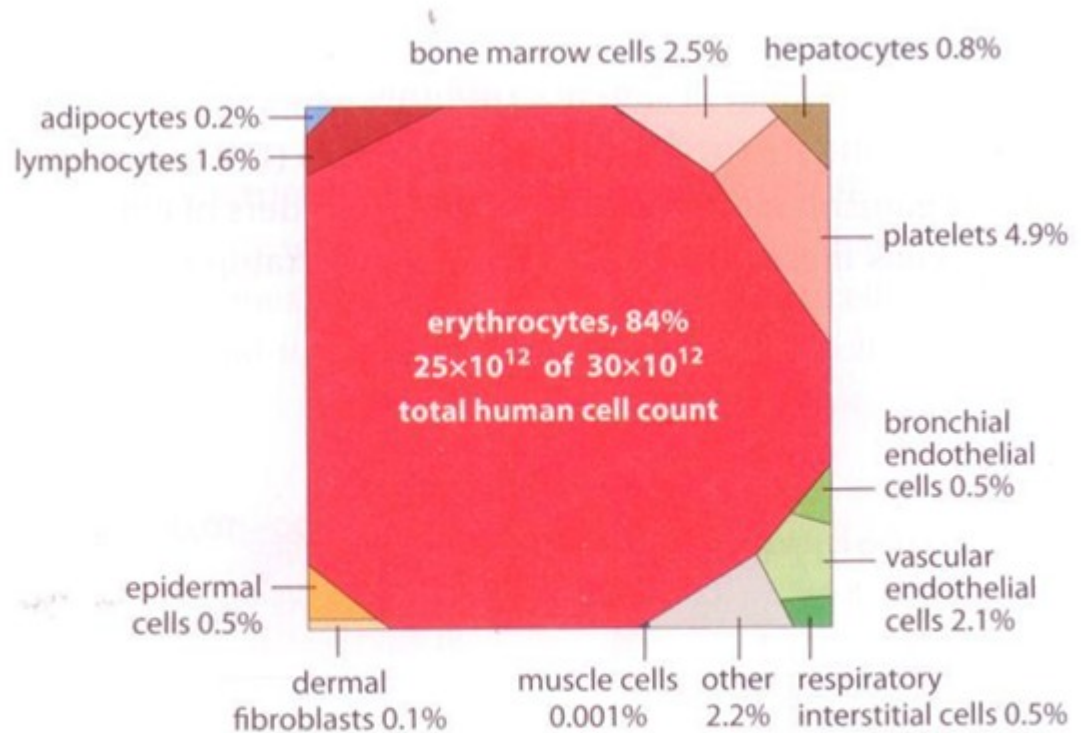


## Signální proteiny jsou relativně vzácné

organism	transcription factor	copies per cell order of magnitude	BNID
<i>E. coli</i>	LacI (carbon utilization)	$10^1$ – $10^2$	100734
<i>E. coli</i>	AraC (carbon utilization)	$10^2$	105139
<i>E. coli</i>	ArcA (general aerobic respiration control)	$10^4$	102632
<i>S. cerevisiae</i>	Gal4 (carbon utilization)	$10^2$	109208
<i>S. cerevisiae</i>	Tfb3 (general transcription initiation factor)	$10^3$	109208
<i>S. cerevisiae</i>	Pho2 (phosphate metabolism)	$10^4$	109208
<i>D. melanogaster</i> , anterior blastoderm nuclei	bicoid (development)	$10^4$	106843
<i>D. melanogaster</i> , S2 cells	GAGA zinc finger	$10^6$	106846
mouse/rat macrophage	glucocorticoid, thyroid and androgen receptors associated zinc fingers	$10^4$	106899
mouse/rat macrophage	NF-kappaB p65	$10^5$	106901
<i>H. sapiens</i> cell lines	P53 (growth and apoptosis)	$10^4$ – $10^5$	100420
<i>H. sapiens</i> cell lines	glucocorticoid, estrogen, steroid receptors associated zinc fingers	$10^4$ – $10^5$	106904, 106906, 106911
<i>H. sapiens</i> cell lines	STAT6	$10^4$ – $10^5$	106914
<i>H. sapiens</i> cell lines	NF-kappaB p65	$10^5$	106909
<i>H. sapiens</i> cell lines	Myc (global chromatin structure regulation)	$10^5$	106907

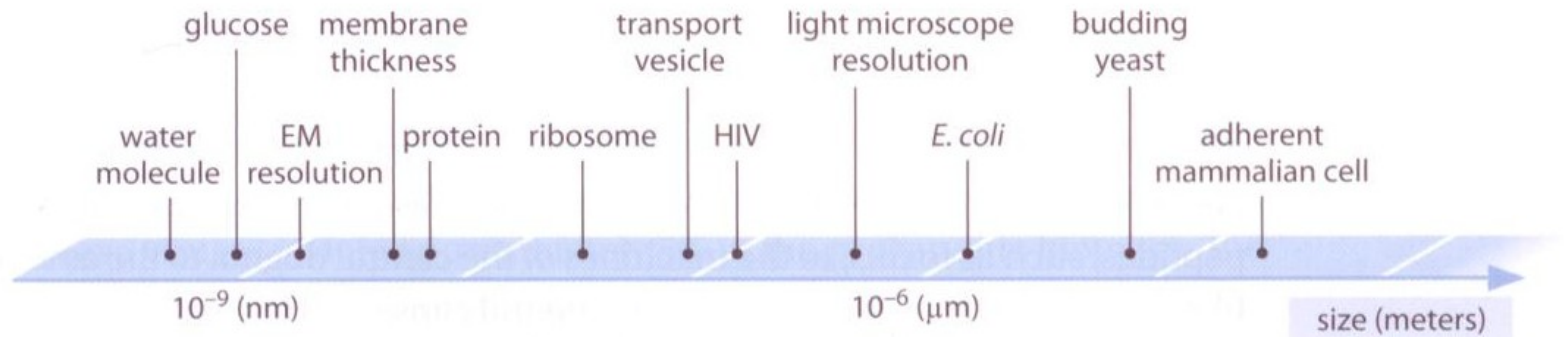
**Table 2-8** Absolute copy numbers from a number of different organisms. Values are rounded to closest order or magnitude. For more values, see Biggin MD [2011] *Dev Cell* 21:611–626; BNID 106842).

## Počty buněk v těle



**Figure 6-1** Estimate of the number of cells in an adult human partitioned according to cell type. Each cell type in the human body is represented as a polygon with an area proportional to the number of cells. The dominant component is red blood cells. (Based on data from Sender R et al. [2015] in preparation.)

## Velikosti



**Figure 1-1** Range of characteristic sizes of the main biological entities relevant to cells. On a logarithmic scale we depict the range from single molecules, serving as the nuts and bolts of biochemistry, through molecular machines, to the ensembles that are cells.

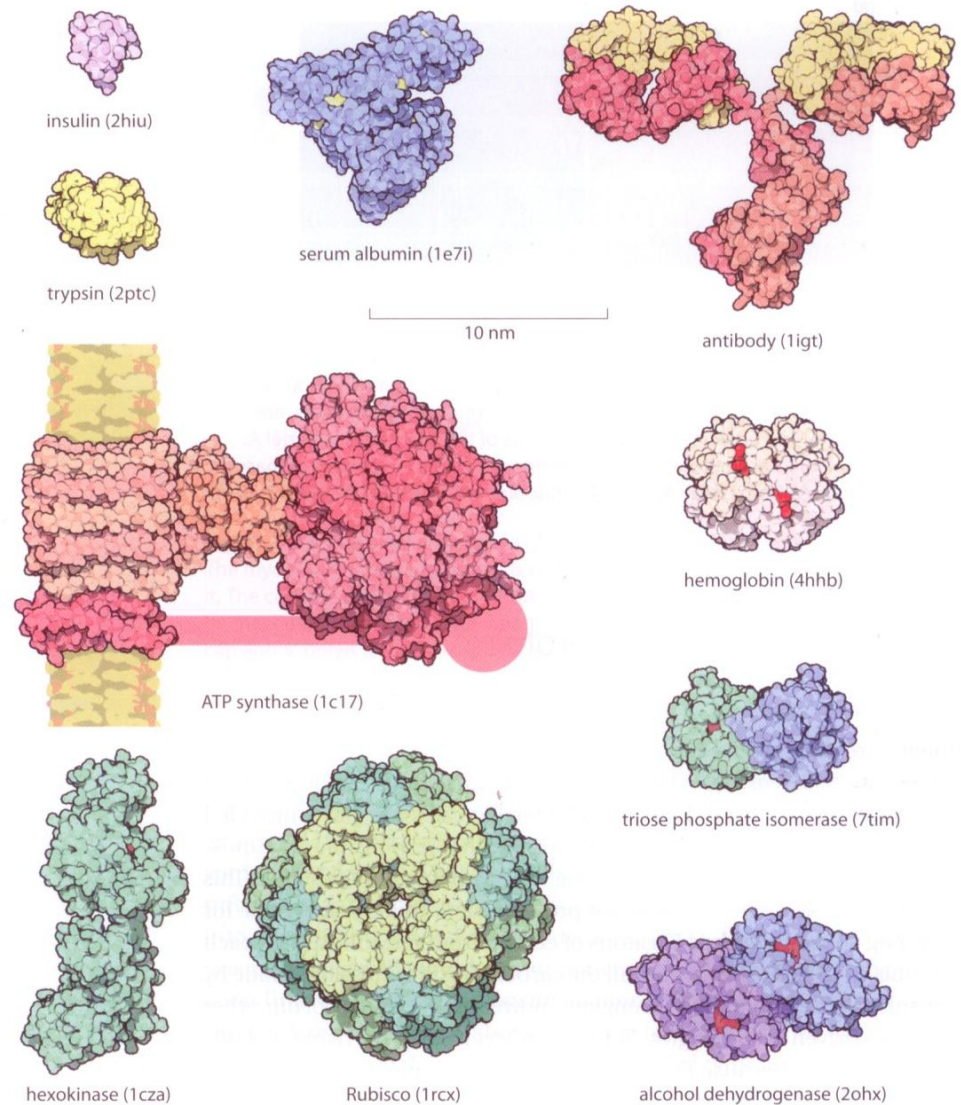
## Velikosti buněk

cell type	average volume ( $\mu\text{m}^3$ )	BNID
sperm cell	30	109891, 109892
red blood cell	100	107600
lymphocyte	200	111788
neutrophil	300	108241
beta cell	1000	109227
enterocyte	1400	111216
fibroblast	2000	108244
HeLa, cervix	3000	103725, 105879
hair cell (ear)	4000	108242
osteoblast	4000	108088
alveolar macrophage	5000	103566
cardiomyocyte	15,000	108243
megakaryocyte	30,000	110129
fat cell	600,000	107668
oocyte	4,000,000	101664

**Table 1-3** Characteristic average volumes of human cells of different types. Large cell-cell variation of up to an order of magnitude or more can exist for some cell types, such as neurons or fat cells, whereas for others the volume varies by much less (for example, red blood cells). The value for a beta cell comes from a rat, but we still present it because average cell sizes usually change relatively little among mammals.

## Velikosti a tvary proteinů

? Nejpočetnější živočišný protein na Zemi?



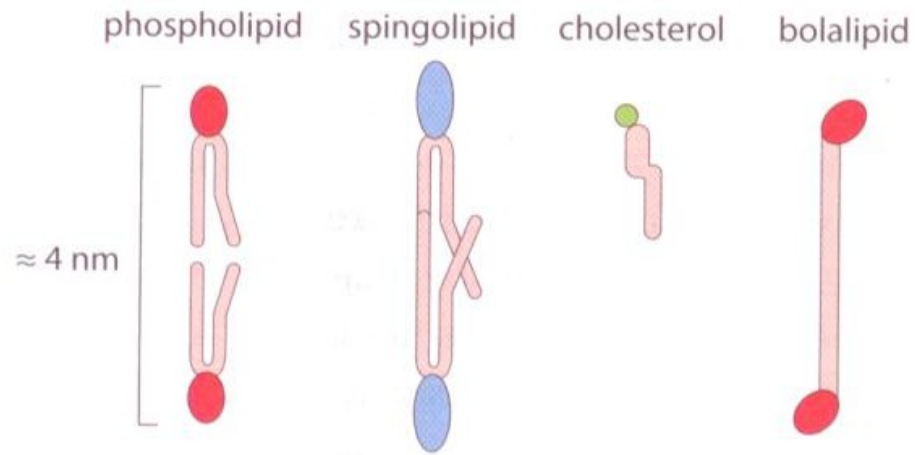
**Figure 1-35** Gallery of proteins. Representative examples of protein size are shown with examples drawn from across biology to illustrate some of their key functional roles. Examples range from the antibodies so important to the immune system to Rubisco and photosynthesis. All the proteins in the figure are shown on the same scale to give an impression of their relative sizes. The small red objects shown on some of the molecules are the substrates for the protein of interest. For example, in hexokinase, the substrate is glucose. The handle in ATP synthase is known to exist, but the exact structure was unavailable and thus only schematically drawn. Names in parentheses are the PDB database identifiers. (Courtesy of David Goodsell.)

## Velikosti složek cytoskeletu

	actin	microtubules
functions	cell motility, cytokinesis, muscle contraction, hearing	cell division, intracellular transport
subunit	actin monomer	$\alpha$ -tubulin + $\beta$ -tubulin
subunit weight	$\approx 40$ kDa	$\approx 50$ kDa
subunit size	5 nm	4 nm (dimer)
protofilaments number	2	13 (variable)
cross section area	20 nm <sup>2</sup>	200 nm <sup>2</sup>
filament diameter	6 nm	25 nm
helical repeat period	36 nm	8 nm
persistence length	10 $\mu$ m	1–10 mm
filament length	from 35 nm in erythrocyte cortex to 10–100 $\mu$ m in ear hair cells	from <1 $\mu$ m in <i>S. pombe</i> through 100 $\mu$ m in rat neurons to >1 mm in insect sperm

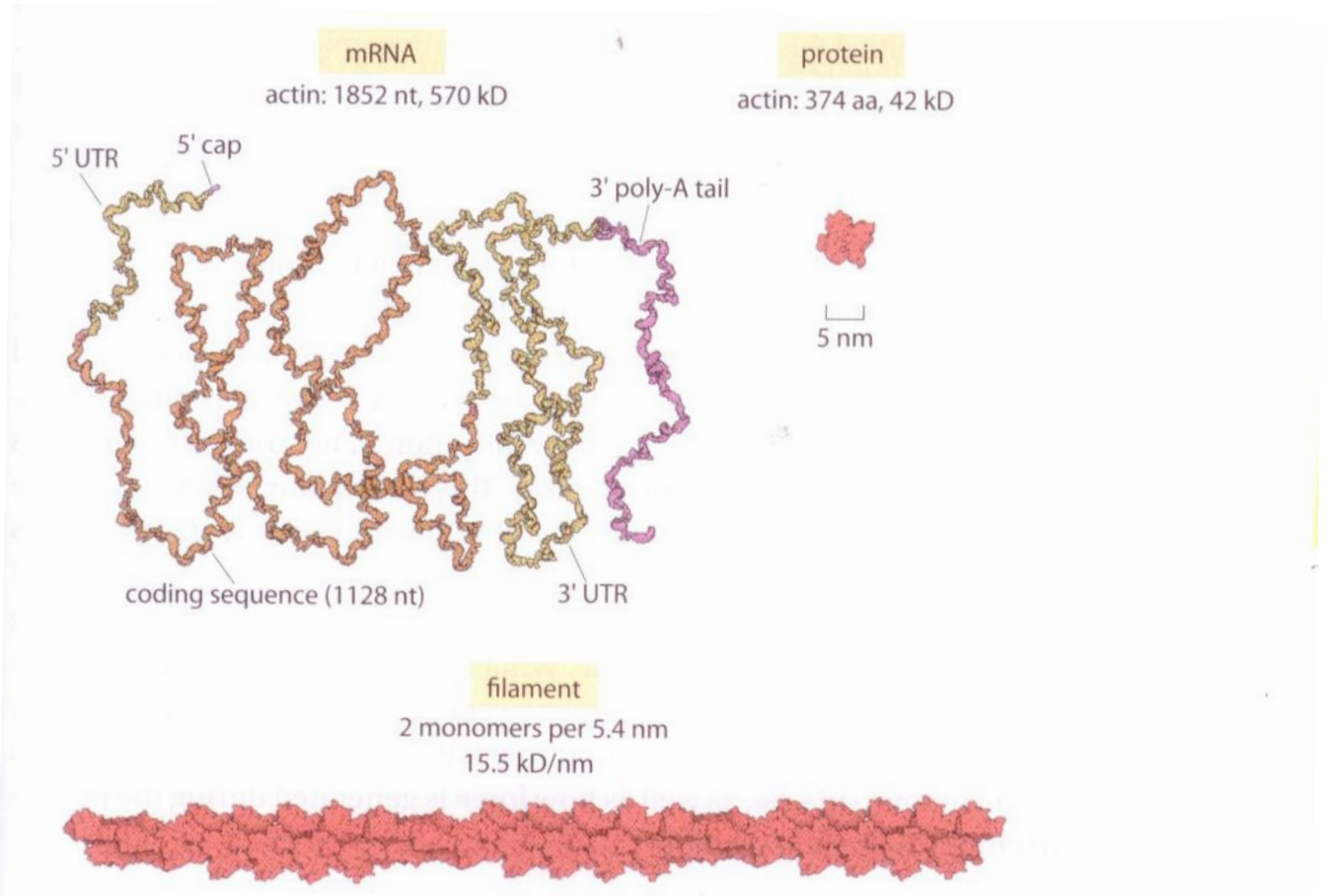
**Table 1-7** Properties of the main cytoskeleton components: actin and microtubules (BNID 107897).

## Velikosti a tvary lipidů



**Figure 1-42** Characteristic relative sizes and shapes of the lipid molecules making up biological membranes.

## Velikost RNA a proteinu



**Figure 1-45** Sizes of actin mRNA, protein, and filament. The mRNA molecule is shown next to the corresponding protein monomer that it codes for (based on human actin A). The monomers assemble into actin filaments such as the one indicated schematically at the bottom. For reference, this filament fragment is only 1% of the measured persistence length of these structures. (Courtesy of David Goodsell.)



## DNA

- Lidská DNA – 3 mld párů bazí (haploidní) – 1 m
- Buněk –  $3 \times 10^{13}$
- Buněk s DNA: 5-10 %
- DNA v těle:  $2 \times 1.5 \times 10^{12}$  m
- Vzdálenost Země-Slunce: 150 milionů kilometrů =  $1,5 \times 10^{11}$

# Je lidský genom velký nebo malý?

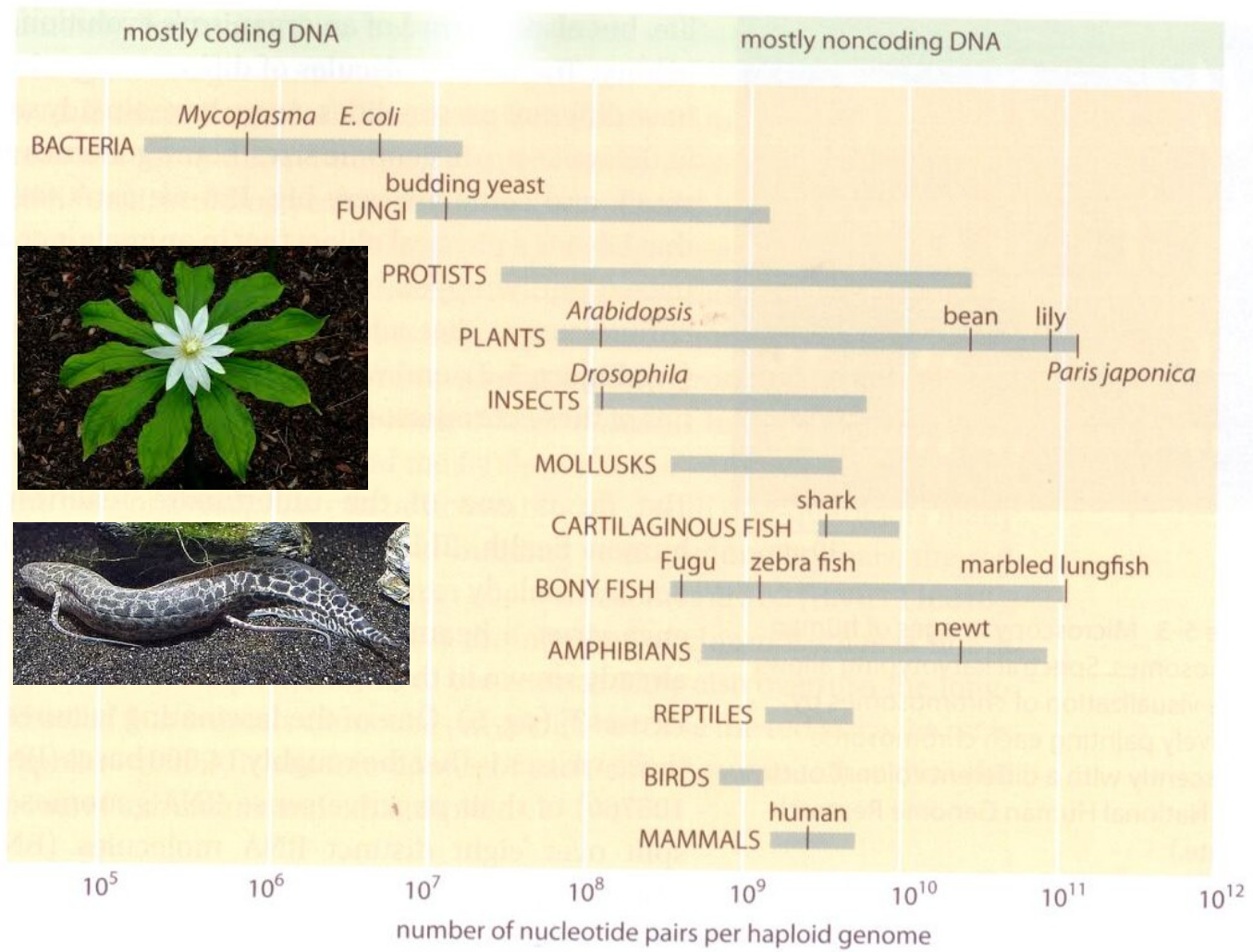


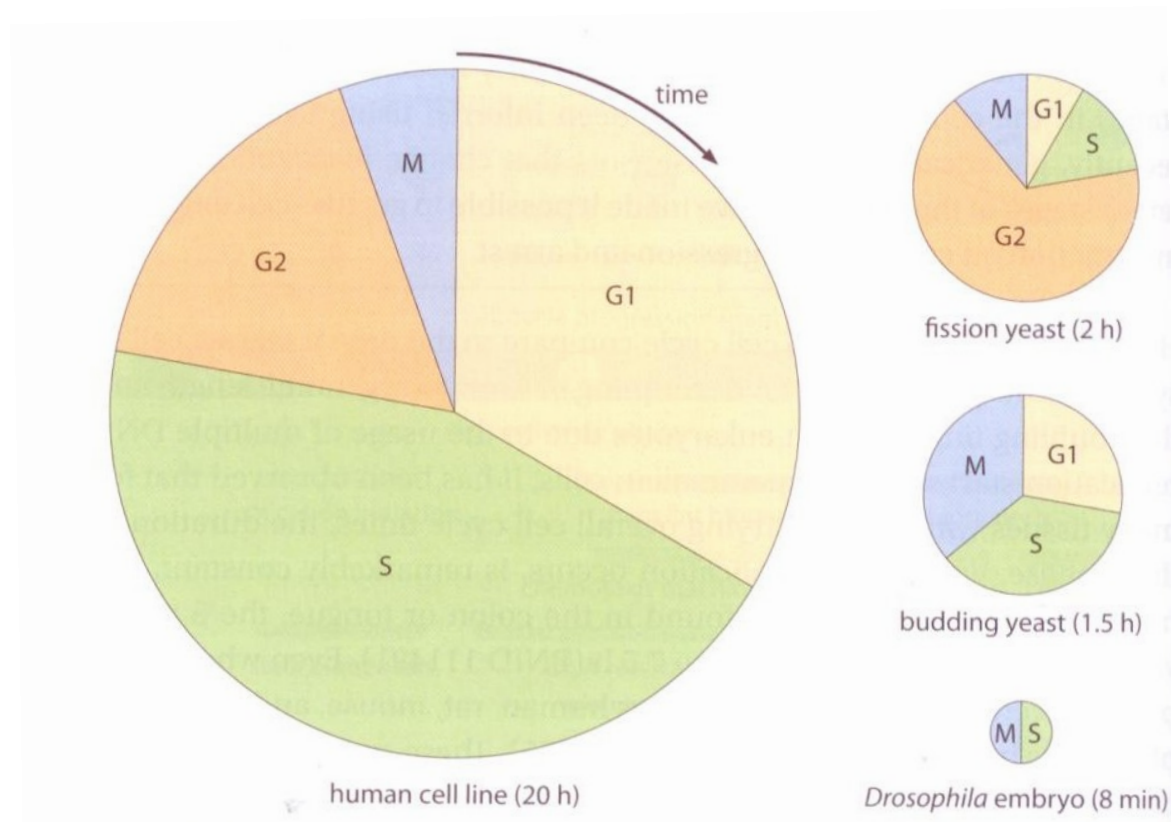
Figure 5-2 Genome sizes of different organisms.

## Je lidský genom velký nebo malý?

	organism	# of protein-coding genes	# of genes naïve estimate: (genome size / 1000)	BNID
viruses	HIV 1	9	10	105769
	Influenza A virus	10–11	14	105767
	Bacteriophage $\lambda$	66	49	105770
	Epstein-Barr virus	80	170	103246
prokaryotes	<i>Buchnera sp.</i>	610	640	105757
	<i>T. maritima</i>	1900	1900	105766
	<i>S. aureus</i>	2700	2900	105500
	<i>V. cholerae</i>	3900	4000	105760
	<i>B. subtilis</i>	4400	4200	111448
	<i>E. coli</i>	4300	4600	105443
eukaryotes	<i>S. cerevisiae</i>	6600	12,000	105444
	<i>C. elegans</i>	20,000	100,000	101364
	<i>A. thaliana</i>	27,000	140,000	111380
	<i>D. melanogaster</i>	14,000	140,000	111379
	<i>F. rubripes</i>	19,000	400,000	111375
	<i>Z. mays</i>	33,000	2,300,000	110565
	<i>M. musculus</i>	20,000	2,800,000	100308
	<i>H. sapiens</i>	21,000	3,200,000	100399, 111378
<i>T. aestivum</i> (hexaploid)	95,000	16,800,000	105448, 102713	

**Table 5-2** A comparison between the number of genes in an organism and a naïve estimate based on the genome size divided by a constant factor of 1000 bp/gene—that is, predicted number of genes = genome size/1000. This crude rule of thumb works surprisingly well for many bacteria and archaea, but fails miserably for multicellular organisms.

# Časy – buněčný cyklus

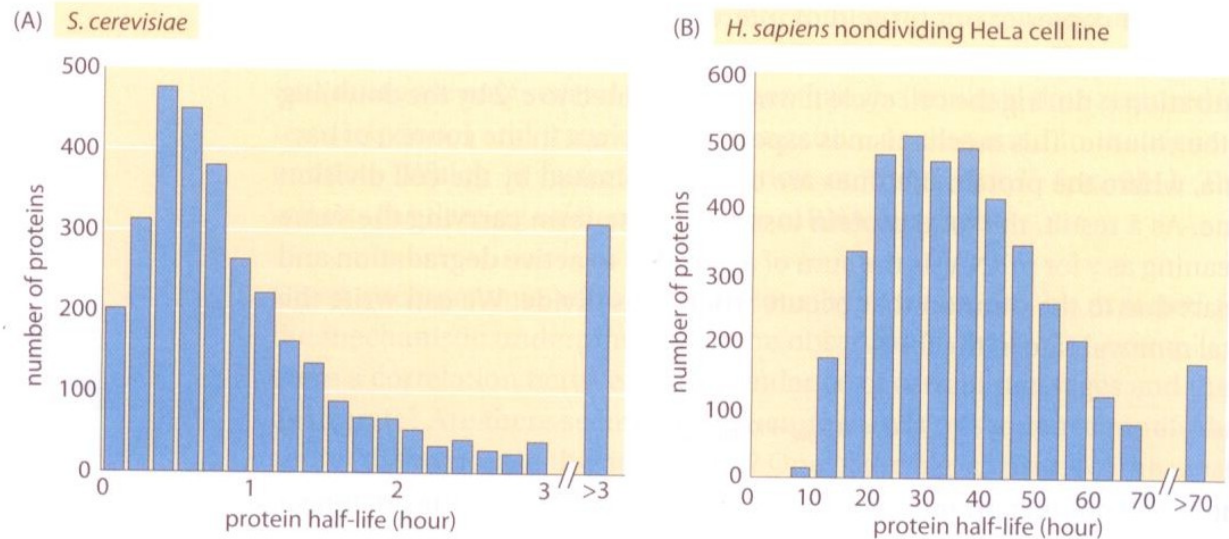


**Figure 4-45** Cell cycle times for different cell types. Each pie chart shows the fraction of the cell cycle devoted to each of the primary stages of the cell cycle. The area of each chart is proportional to the overall cell cycle duration. Cell cycle durations reflect minimal doubling times under ideal conditions. (Adapted from Morgan D [2007] *The Cell Cycle: Principles of Control*. Sinauer Associates.)

## Časy – délka „života“ buněk

cell type	turnover time	BNID
small intestine epithelium	2–4 days	107812, 109231
stomach	2–9 days	101940
blood neutrophils	1–5 days	101940
white blood cells eosinophils	2–5 days	109901, 109902
gastrointestinal colon crypt cells	3–4 days	107812
cervix	6 days	110321
lungs alveoli	8 days	101940
tongue taste buds (rat)	10 days	111427
platelets	10 days	111407, 111408
bone osteoclasts	2 weeks	109906
intestine paneth cells	20 days	107812
skin epidermis cells	10–30 days	109214, 109215
pancreas beta cells (rat)	20–50 days	109228
blood B cells	1 month	111516
trachea	1–2 months	101940
hematopoietic stem cells	2 months	109232
sperm (male gametes)	2 months	110319, 110320
bone osteoblasts	3 months	109907
red blood cells	4 months	101706, 107875
liver hepatocyte cells	0.5–1 year	109233
fat cells	8 years	103455
cardiomyocytes	0.5–10% per year	107076, 107077, 107078
central nervous system	life-time	101940
skeleton	10% per year	109908
lens cells	life-time	109840
oocytes (female gametes)	life-time	111451

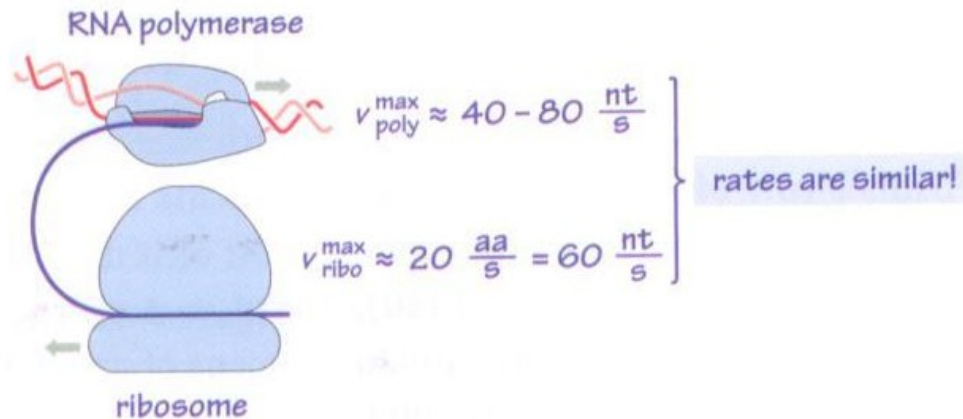
## Časy – délka života proteinů



**Figure 4-22** Measured half-lives of proteins in budding yeast and a HeLa human cancer cell line. The yeast experiment used the translation inhibitor cycloheximide, which disrupts normal cell physiology. The median half-life of the 4100 proteins measured in the nondividing HeLa cell is 36 h. (A, adapted from Belle A, Tanay A, Bitincka L et al. [2006] *Proc Natl Acad Sci USA* 103:13004–13009. B, adapted from Cambridge S, Gnad F, Nguyen C et al. [2011] *J Proteome Res* 10:5275–5284.)

# Rychlosti transkripce a translace

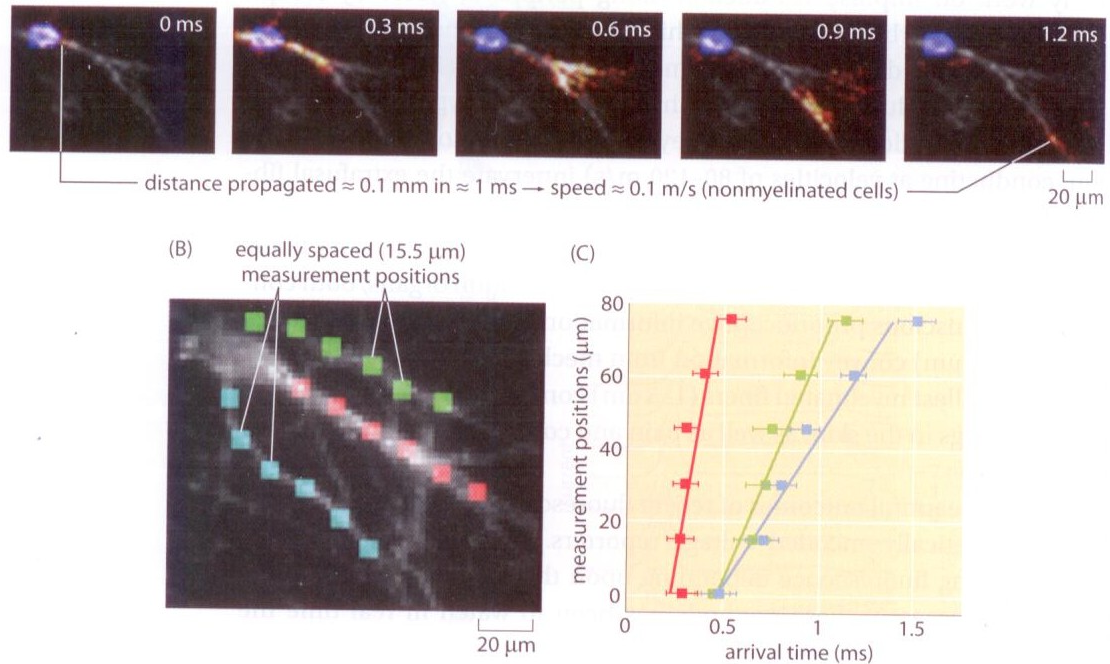
Which is faster: transcription or translation?



## Estimate 4-9

” Bakshi S, Siryaporn A, Goulian M et al. (2012) Superresolution imaging of ribosomes and RNA polymerase in live *Escherichia coli* cells. *Mol Microbiol* 85:21–38.

## Rychlosti – šíření vzruchu

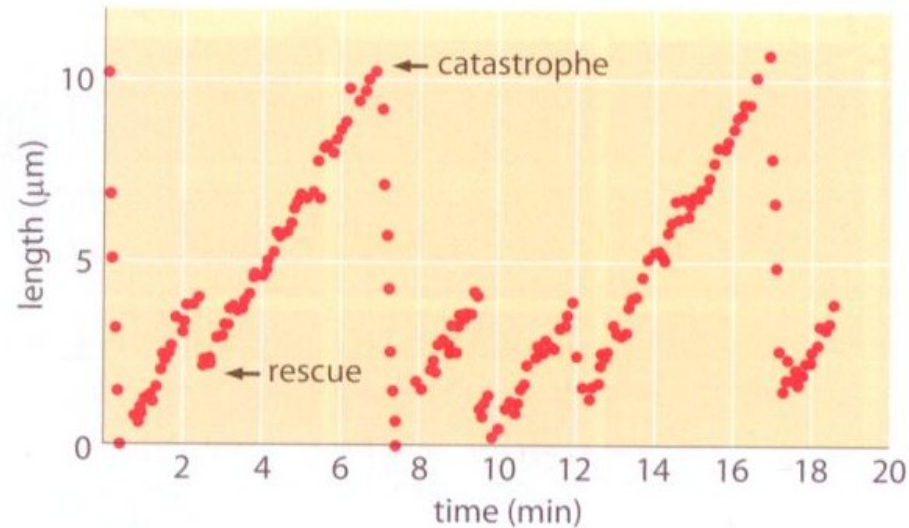


**Figure 4-28** Optical measurement of action potential speed. (A) Series of images of the fluorescence in the cell as a function of time. (B) A series of equally spaced (15 μm) measurement points along three different processes are used to measure the arrival time of a propagating action potential. (C) Arrival times for the three processes shown in (B). For example, for the action potential propagating along the fiber labeled with red boxes, the signal arrives with a time delay of roughly 0.05 ms from one measurement point to the next. The action potential speed can be read off of the graph in the usual way by dividing distance traveled by time elapsed. Due to technical limitations, these are unmyelinated neuronal cells, and thus the propagation speed is much slower than *in vivo*. (Courtesy of Daniel Hochbaum and Adam Cohen.)

Myelinizované vlákno – 100 m/s tj. až 1000x rychlejší



## Rychlosti – růstu mikrotubulů



**Figure 4-33** Microtubule length vs. time. The length of microtubules as a function of time reveals periods of growth punctuated by catastrophes in which the filaments rapidly depolymerize. (Adapted from Fygenson DK, Braun E & Libchaber A [1994] *Phys Rev E* 50:1579–1588.)

# Rychlosti – pohybu motorů po cytoskeletu

motor	function	speed <i>in vivo</i> (nm/s)	rate (ATPase, s <sup>-1</sup> , <i>in vitro</i> )	mode of action
<b>myosins</b>				
myosin XI	cytoplasmic streaming in algae	60,000	not determined	unknown
myosin II	fast skeletal muscle	6000	20	large arrays (10 <sup>4</sup> –10 <sup>9</sup> )
myosin IB	amoeboid motility, hair cell adaptation	200 ( <i>in vitro</i> )	6	small arrays (10–10 <sup>3</sup> )
myosin II	smooth muscle contraction	200	1.2	large arrays (10 <sup>4</sup> –10 <sup>9</sup> )
myosin V	vesicle transport	200	5	alone or in small numbers (<10)
myosin VI	vesicle transport?	-60 ( <i>in vitro</i> )	0.8	unknown
<b>dyeins</b>				
axonemal	sperm and ciliary motility	-7000	10	large arrays (10 <sup>4</sup> –10 <sup>9</sup> )
cytoplasmic	retrograde axonal transport, mitosis, transport in flagella	-1000	2	alone or in small numbers (<10)
<b>kinesins</b>				
			<b>1 μm/s</b>	
Fia10/Kinii	transport in flagella, axons, melanocytes	2000	not determined	small arrays (10–10 <sup>3</sup> )
conventional	anterograde axonal transport	1800	40	alone or in small numbers (<10)
Nkin	secretory vesicle transport	800	80	alone or in small numbers (<10)
Unc104/KIF	transport of synaptic vesicle precursors and mitochondria	700	110	alone or in small numbers (<10)
Bimc/Eg5	mitosis and meiosis	18	2	small arrays (10–10 <sup>3</sup> )
Ncd	mitosis and meiosis	-90 ( <i>in vitro</i> )	1	small arrays (10–10 <sup>3</sup> )

**Table 4-7** Summary of experimental data on the dynamics of translational molecular motors. Based on BNID 106501, 101506. Values were rounded to one significant digit. Negative speeds indicate movement towards the minus end of the filament.

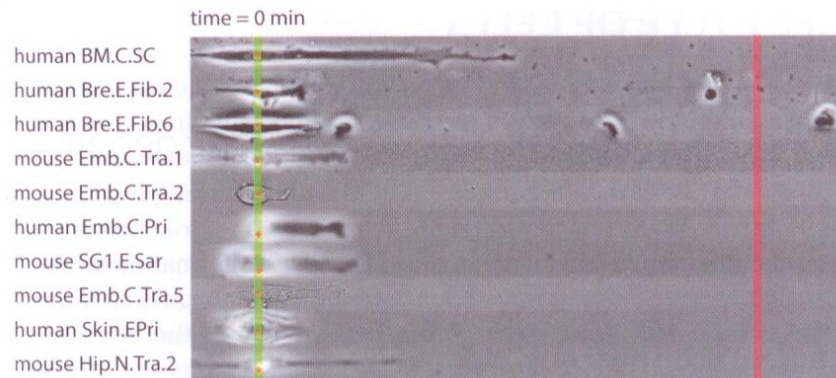
## Rychlosti – pohybu buněk

organism	speed	speed in body lengths (bl) per time	BNID and comments
eukaryotes			
Ciliate <i>Paramecium tetraurelia</i>	100–1000 $\mu\text{m/s}$	1–5 bl/s	108087, ciliated, assuming 200 $\mu\text{m}$ cell length
<i>Tetrahymena thermophila</i>	200–400 $\mu\text{m/s}$	4–8 bl/s	111429, 111435, 111436, ciliated
<i>Gyrodinium dorsum</i>	300 $\mu\text{m/s}$	10 bl/s	111432, flagellated
green algae <i>Chlamydomonas Reinhardtii</i>	50–150 $\mu\text{m/s}$	5–15 bl/s	108086, 111430
fish keratocytes - wound healing fibroblasts of the cornea	10–50 $\mu\text{m/min}$	0.7–3 bl/min	106807, 106817
<i>Amoeba Dictyostelium discoideum</i>	10 $\mu\text{m/min}$	$\approx 1$ bl/min	106825
human neutrophil	9 $\mu\text{m/min}$	$\approx 1$ bl/min	106809
glioma cells	50 $\mu\text{m/h}$	4 bl/h	106810
mouse fibroblastoid L929 cells	30 $\mu\text{m/h}$	2 bl/h	106808
human H69 small cell lung cancer cell	16 $\mu\text{m/h}$	1 bl/h	106815

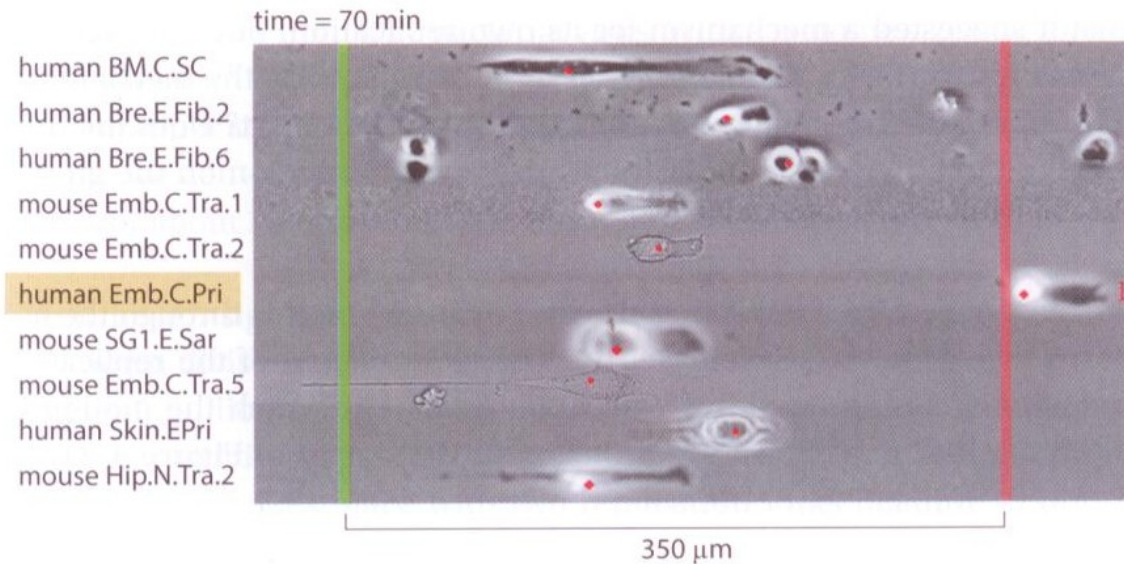
**Table 4-8** Cell speeds of different cells given in  $\mu\text{m}$  per time unit and as body lengths per time unit. Assume a bacterial length of  $\approx 2 \mu\text{m}$  and a eukaryotic cell length of  $\approx 15 \mu\text{m}$  unless otherwise stated. Speeds depend on temperature, experimental conditions, etc. Values given here are those reported in the literature. Most measurements are based on time-lapse microscopy.

## Rychlosti – pohybu buněk

# World Cell Race 2011



## Rychlosti – pohybu buněk



**Figure 4-40** Finals of the World Cell Race. The 10 fastest cell lines are displayed competing over a 350  $\mu$ m micro-fabricated sprinting lane. Each of the cells was found to be the fastest among its cell type. Each cell type was recorded in a separate well, and movies were combined to show one lane per cell type. The time difference between the two images is about an hour. The winner is highlighted in brown. (Courtesy of Matthieu Piel.)

## Malé shrnutí

property	<i>E. coli</i>	budding yeast	mammalian (HeLa line)
cell volume	0.3–3 $\mu\text{m}^3$	30–100 $\mu\text{m}^3$	1000–10,000 $\mu\text{m}^3$
proteins per $\mu\text{m}^3$ cell volume	2–4 $\times 10^6$		
mRNA per cell	$10^3$ – $10^4$	$10^4$ – $10^5$	$10^5$ – $10^6$
proteins per cell	$\sim 10^6$	$\sim 10^8$	$\sim 10^{10}$
mean diameter of protein	4–5 nm		
genome size	4.6 Mbp	12 Mbp	3.2 Gbp
number protein coding genes	4300	6600	21,000
regulator binding site length	10–20 bp	5–10 bp	
promoter length	$\sim 100$ bp	$\sim 1000$ bp	$\sim 10^4$ – $10^5$ bp
gene length	$\sim 1000$ bp	$\sim 1000$ bp	$\sim 10^4$ – $10^6$ bp (with introns)
concentration of one protein per cell	$\sim 1$ nM	$\sim 10$ pM	$\sim 0.1$ – $1$ pM
diffusion time of protein across cell ( $D \approx 10 \mu\text{m}^2/\text{s}$ )	$\sim 0.01$ s	$\sim 0.2$ s	$\sim 1$ – $10$ s
diffusion time of small molecule across cell ( $D \approx 100 \mu\text{m}^2/\text{s}$ )	$\sim 0.001$ s	$\sim 0.03$ s	$\sim 0.1$ – $1$ s
time to transcribe a gene	<1 min (80 nts/s)	$\sim 1$ min	$\sim 30$ min (incl. mRNA processing)
time to translate a protein	<1 min (20 aa/s)	$\sim 1$ min	$\sim 30$ min (incl. mRNA export)
typical mRNA lifetime	3 min	30 min	10 h
typical protein lifetime	1 h	0.3–3 h	10–100 h
minimal doubling time	20 min	1 h	20 h
ribosomes/cell	$\sim 10^4$	$\sim 10^5$	$\sim 10^6$
transitions between protein states (active/inactive)	1–100 $\mu\text{s}$		
time scale for equilibrium binding of small molecule to protein (diffusion limited)	1–1000 ms (1 $\mu\text{M}$ –1 nM affinity)		
time scale of transcription factor binding to DNA site	$\sim 1$ s		
mutation rate	$10^{-8}$ – $10^{-10}$ /bp/replication		

**Table 0-1** Typical parameter values for a bacterial *E. coli* cell, the single-celled eukaryote *S. cerevisiae* (budding yeast), and a mammalian HeLa cell line. These are crude characteristic values for happily dividing cells of the common lab strains. (Adapted from Alon U [2006] Introduction to Systems Biology. CRC Press. See full references at BNID 111494.)

# Matematika a chemie pro biology

- Concentration of 1 ppm (part per million) of the cell proteome is  $\approx 5$  nM.
- 1 mg of DNA fragments 1 kb long is  $\approx 1$  pmol or  $\approx 10^{12}$  molecules.
- Under standard conditions, particles at a concentration of 1 M are  $\approx 1$  nm apart.
- Mass of typical amino acid  $\approx 100$  Da.
- Protein mass [Da]  $\approx 100 \times$  Number of amino acids.
- Density of air  $\approx 1$  kg/m<sup>3</sup>.
- Water density  $\approx 55$  M  $\approx \times 1000$  that of air  $\approx 1000$  kg/m<sup>3</sup>.
- 50 mM osmolites  $\approx 1$  atm osmotic pressure (as shown in **Estimate 0-3**).
- Water molecule volume  $\approx 0.03$  nm<sup>3</sup>, ( $\approx 0.3$  nm)<sup>3</sup>.
- A base pair has a volume of  $\approx 1$  nm<sup>3</sup>.
- A base pair has a mass of  $\approx 600$  Da.
- Lipid molecules have a mass of  $\approx 500$ – $1000$  Da.
- $1 k_B T \approx 2.5$  kJ/mol  $\approx 0.6$  kcal/mol  $\approx 25$  meV  $\approx 4$  pN nm  $\approx 4 \times 10^{-21}$  J.
- $\approx 6$  kJ/mol sustains one order of magnitude concentration difference [ $= k_B T \ln(10) \approx 1.4$  kcal/mol].

**Děkuji za pozornost!**