Physical Biology of the Cell

PBoC@MOLPIT

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http://molpit.com

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Robert Brooks Phillips

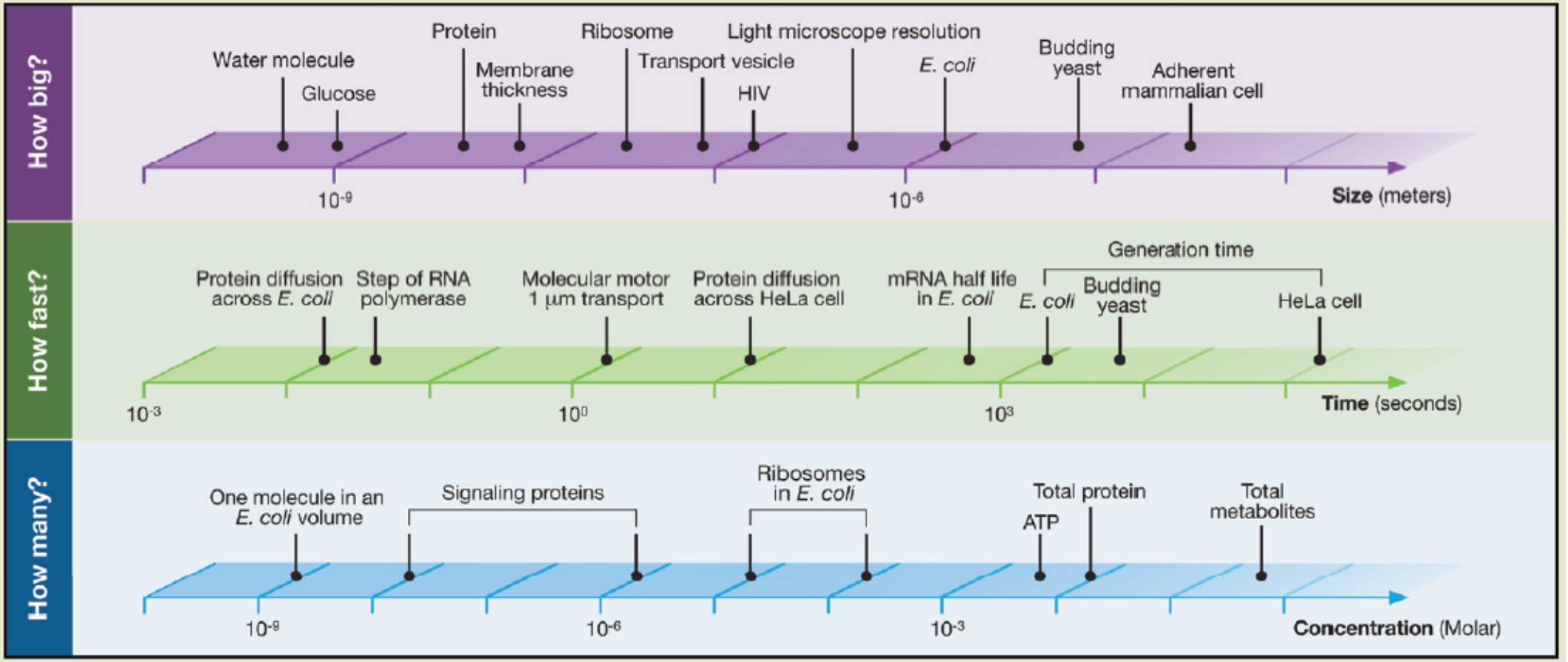
- Rob Phillips Group: **Physical Biology of the Cell**
    - http://www.rpgroup.caltech.edu/
- Rob Phillips, Jane Kondev, Julie Theriot. Physical Biology of the Cell [1 ed.] Garland Science. 2008. 826 p.
- Robert Brooks Phillips, Jane Kondev, Julie Theriot. Physical Biology of the Cell. Taylor & Francis Group, 2009, 807 p. (reprint ed.)
- Rob Phillips, Jane Kondev, Julie Theriot, Nigel Orme, Herman Garcia. Physical biology of the cell [2 nd.] Garland Science. 2013. 1040 p.

http://microsite.garlandscience.com/pboc2/
Home - Physical Biology of the Cell

- http://microsite.garlandscience.com/pboc2/data.html
  - Data 164K - Physical Biology of the Cell
- http://microsite.garlandscience.com/pboc2/hints.html
  - Hints 468K - Physical Biology of the Cell
- http://microsite.garlandscience.com/pboc2/matlab.html
  - Mathematica® & Matlab® Codes 343K
- http://microsite.garlandscience.com/pboc2/powerpoints.html
  - PowerPoints® 263M - Physical Biology of the Cell
- http://microsite.garlandscience.com/pboc2/jpegs.html
  - JPEGs 204M - Physical Biology of the Cell
- http://microsite.garlandscience.com/pboc2/videos.html
  - Videos 68M - Physical Biology of the Cell **!** Nice & Useful video edu **!**

SnapShot: key numbers in biology

- Uri Moran, Rob Phillips, Ron Milo. SnapShot: key numbers in biology // *Cell*, **141** (7), 1262-1262 (2010).



Uri Moran, Rob Phillips, Ron Milo. SnapShot: key numbers in biology // *Cell*, **141** (7), 1262-1262 (2010).

Cell size

Bacteria *(E. coli):* ≈0.7-1.4 μm diameter, ≈2-4 μm length, ≈0.5-5 μm^3 in volume; 10^8-10^9 cell/ml for culture with $OD_{600} \approx 1$

Yeast *(S. cerevisiae):* ≈3-6 μm diameter ≈20-160 μm^3 in volume

Mammalian cell volume: 100-10,000 μm^3; HeLa cell: 500-5000 μm^3 (adhering to slide ≈15-30 μm diameter)

Length scales inside cells

Nucleus volume: ≈10% of cell volume

Cell membrane thickness: ≈4-10 nm

"Average" protein diameter: ≈3-6 nm

Base pair: 2 nm (D) x 0.34 nm (H)

Water molecule diameter: ≈0.3 nm

Energetics

Membrane potential ≈70-200 mV → 2-6 k_BT per electron ($k_BT \equiv$ thermal energy)

Free energy (ΔG) of ATP hydrolysis under physiological conditions
≈40-60 kJ/mol → ≈20 k_BT/molecule ATP; ATP molecules required during an *E. coli* cell cycle ≈$10-50 \times 10^9$

ΔG^0 resulting in order of magnitude ratio between product and reactant concentrations:
≈6 kJ/mol ≈60 meV ≈2 k_BT

Concentration

Concentration of 1 nM:
in *E. coli* ≈1 molecule/cell;
in HeLa cells ≈1000 molecules/cell

Characteristic concentration for a signaling protein: ≈10 nM-1 μM

Water content: ≈70% by mass; general elemental composition (dry weight) of *E. coli:* ≈$C_4H_7O_2N_1$; Yeast: ≈$C_6H_{10}O_3N_1$

Composition of *E. coli* (dry weight):
≈55% protein, 20% RNA, 10% lipid, 15% other

Protein concentration: ≈100 mg/ml = 3 mM.
10^6-10^7 per *E. coli* (depending on growth rate);
Total metabolites (MW < 1 kDa) ≈300 mM

Division, replication, transcription, translation, and degradation rates

at 37°C with a temperature dependence (Q10) of ≈2-3

Cell cycle time (exponential growth in rich media): *E. coli* ≈20-40 min;
budding yeast 70-140 min;
HeLa human cell line: 15-30 hr

Rate of replication by DNA polymerase:
E. coli ≈200-1000 bases/s;
human ≈40 bases/s. Transcription by RNA polymerase 10-100 bases/s

Translation rate by ribosome: 10-20 aa/s

Degradation rates (proliferating cells):
mRNA half life < cell cycle time;
protein half life ≳ cell cycle time

Diffusion and catalysis rate

Diffusion coefficient for an "average" protein: in cytoplasm D≈5-15 $\mu m^2/s$ → ≈10 ms to traverse an *E. coli* → ≈10 s to traverse a mammalian HeLa cell; small metabolite in water D≈500 $\mu m^2/s$

Diffusion-limited on-rate for a protein:
≈10^8-10^9 $s^{-1}M^{-1}$ → for a protein substrate of concentration ≈1 μM the diffusion-limited on-rate is ≈100-1000 s^{-1} thus limiting the catalytic rate k_{cat}

Genome sizes and error rates

Genome size:
E. coli (enterobacteria) ≈5 Mbp
S. cerevisiae (budding yeast) ≈12 Mbp
C. elegans (nematode) ≈100 Mbp
D. melanogaster (fruit fly) ≈120 Mbp
A. thaliana (plant) ≈120 Mbp
M. musculus (mouse) ≈2.5 Gbp
H. sapiens (human) ≈2.9 Gbp
T. aestivum (wheat) ≈16 Gbp

Number of protein-coding genes:
E. coli ≈ 4000; *S. cerevisiae* ≈ 6000;
C. elegans, A. thaliana, M. musculus, H. sapiens ≈ 20,000

Mutation rate in DNA replication:
≈10^{-8}-10^{-10} per bp

Misincorporation rate:
transcription ≈10^{-4}-10^{-5} per nucleotide
translation ≈10^{-3}-10^{-4} per amino acid

Key Numbers for Cell Biologists

- http://www.bionumbers.org/ =>
  - http://bionumbers.hms.harvard.edu/KeyNumbers.aspx
- Cell size (1-3)
- Length Scales Inside Cells (4-8)
- Division, Replication, Transcription, Translation & Degradation Rates (9-12)
- Concentration (13-17)
- Energetics (18-20)
- Diffusion and Catalysis Rate (21, 22)
- Genome sizes & Error Rates (23-26)

Cell size

1. Bacteria *(E. coli)*: ≈0.7-1.4 μm diameter, ≈2-4 μm length, ≈0.5-5 μm^3 in volume; 10^8-10^9 cell/ml for culture with OD_{600}≈1
2. Yeast *(S. cerevisiae)*: ≈3-6 μm diameter, ≈20-160 μm^3 in volume
3. Mammalian cell volume: 100-10000 μm^3; Hela: 500-5000 μm^3 (adherent on slide ≈15-30 μm diameter)

Length Scales Inside Cells

4. Nucleus volume ≈10% of cell volume
5. Cell membrane thickness ≈4-10 nm
6. "Average" protein diameter ≈3-6 nm
7. Base pair: 2 nm (D) x 0.34 nm (H)
8. Water molecule diameter ≈0.3 nm

Division, Replication, Transcription, Translation & Degradation Rates

at 37°C with a temperature dependence Q10 of ≈2-3

9. Cell cycle time (exponential growth in rich media): *E. coli* ≈20-40 min; yeast 70-140 min; human cell line (Hela): 15-30 hours
10. Rate of replication by DNA polymerase *E. coli* ≈200-1000 bases/s; human ≈40 bases/s. Transcription by RNA polymerase 10-100 bases/s
11. Translation rate by ribosome 10-20 aa/s
12. Degradation rates (proliferating cells): mRNA half life < cell cycle time; protein half life ≳ cell cycle time

Concentration

13. Concentration of 1 nM in: *E. coli* is ≈1 molecule/cell; Hela ≈1,000 molecules/cell
14. Characteristic concentration for a signaling protein ≈10 nM-1μM
15. Water content: ≈70% by mass; General elemental composition (dry weight) of *E. coli*: $\approx C_4H_7O_2N_1$; Yeast $\approx C_6H_{10}O_3N_1$
16. Composition of *E. coli* (dry weight): ≈55% protein, 20% RNA, 10% lipids, 15% others
17. Protein conc. ≈100 mg/ml=3 mM. 10^6-10^7 per *E. coli* (depending on growth rate); Total metabolites (MW<1kD) ≈300mM

Energetics

18. Membrane potential ≈70-200 mV → 2-6 k_BT per electron (k_BT≡thermal energy)
19. Free energy (ΔG) of ATP hydrolysis under physiological conditions ≈40-60 kJ/mole → ≈20k_BT/molecule ATP; ATP molecules required to make an *E. coli* cell ≈10-50×10^9
20. ΔG^0 resulting in order of magnitude ratio between products and reactants concentrations: ≈6 kJ/mol ≈60 meV ≈2 k_BT

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 the BioNumbers website. Consult website and original references to learn about the details of the system under study including growth conditions, method of measurement, etc.

Diffusion and Catalysis Rate

21. Diffusion coefficient for an "average" protein: in cytoplasm D≈5-15 $\mu m^2/s$ → ≈10 millisec to traverse an *E. coli* →≈10 s to traverse a mammalian (Hela) cell; small metabolite in water D≈500 $\mu m^2/s$
22. Diffusion limited on-rate for characteristic protein ≈10^8-10^9 $s^{-1}M^{-1}$ → for a protein substrate of concentration ≈1μM the diffusion limited on-rate is ≈100-1000 s^{-1} thus limiting the catalytic rate k_{cat}

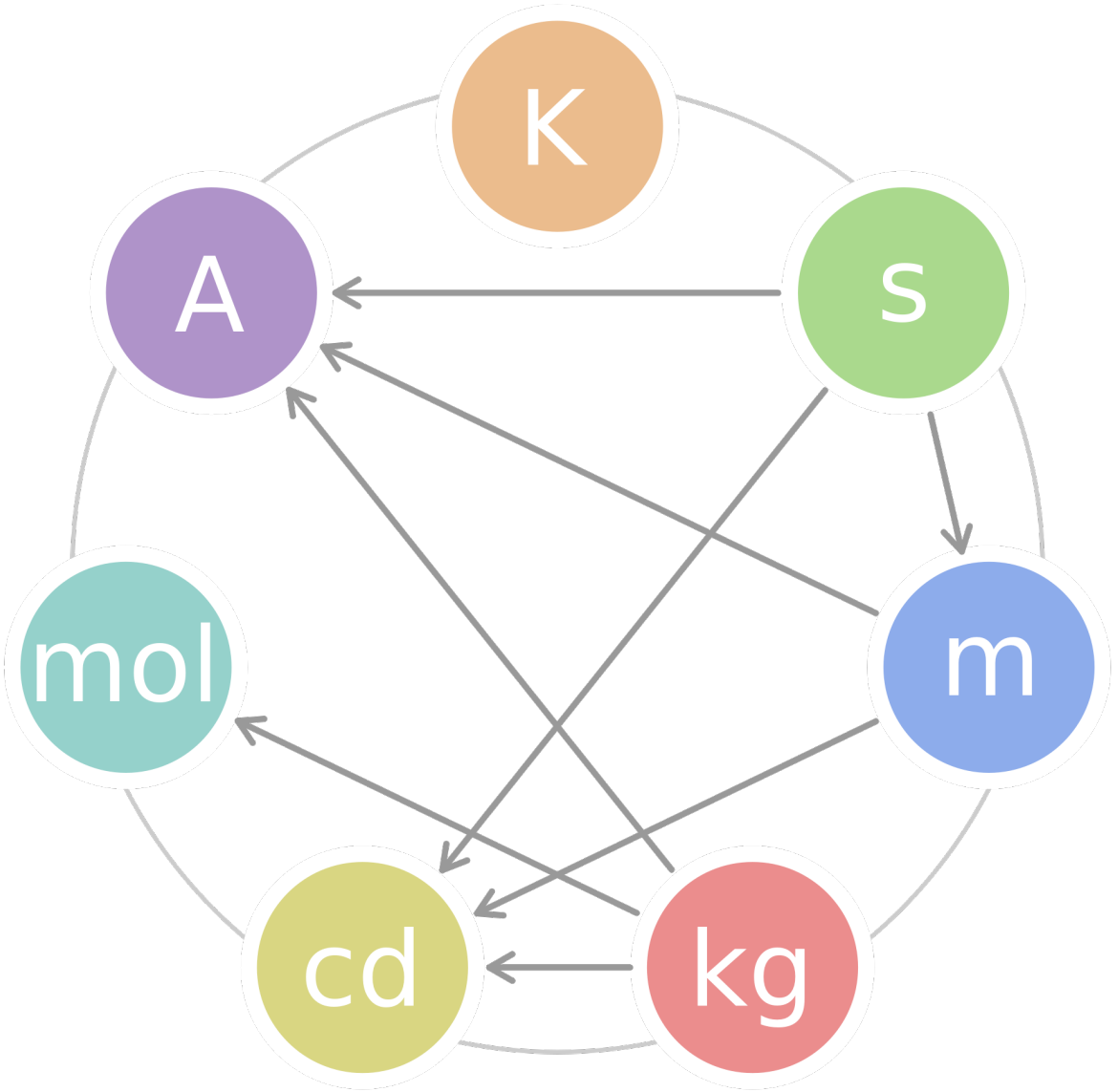
Genome sizes & Error Rates

23. Genome size: *E. coli* ≈5 Mbp; *S. cerevisiae* (yeast) ≈12 Mbp; *C. elegans* (nematode) ≈100 Mbp; *D. melanogaster* (fruit fly) ≈120 Mbp; *A. thaliana* (arabidopsis) ≈120 Mbp; *M. musculus* (mouse) ≈2.5 Gbp; *H. sapiens* (human) ≈2.9 Gbp; *T. aestivum* (wheat) ≈16 Gbp
24. Number of protein-coding genes: E. coli ≈4,000; S. cerevisiae ≈6,000; C. elegans, A. thaliana, M. musculus, H. sapiens ≈20,000
25. Mutation rate in DNA replication ≈10^{-8}-10^{-10} per bp
26. Misincorporation rate: transcription ≈10^{-4} per nucleotide; translation ≈10^{-3}-10^{-4} per amino-acid

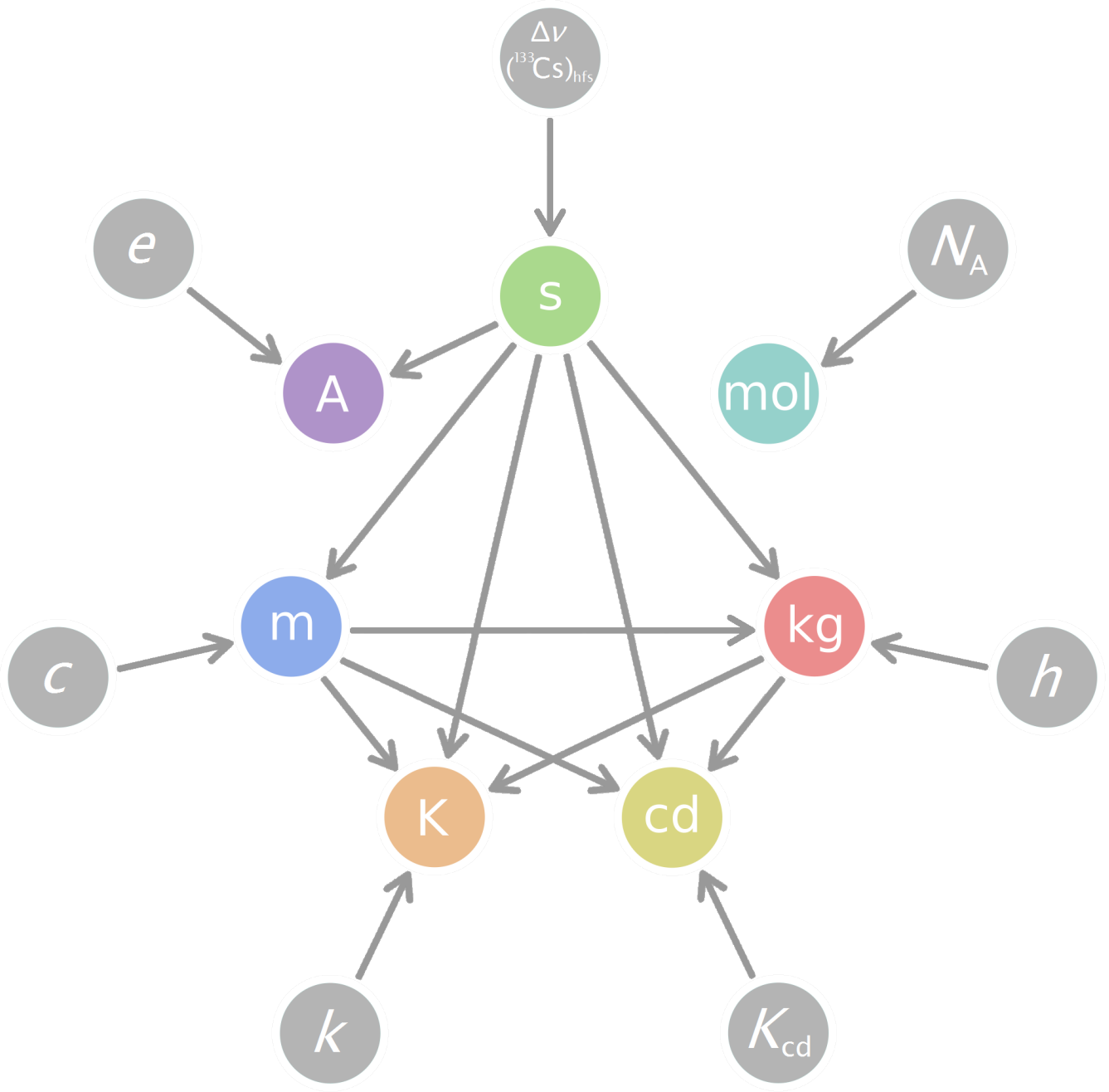
Click on a number to see full description and reference
www.BioNumbers.org

Current (2013) SI System:

Dependence of base unit definitions on other base units



Proposed «Quantum SI» System (2014)



Biological measures & gauges

- From Key Numbers for Cell Biologists
- Towards BioMeasures & BioGauges
- ? who, where, when
- To make «Biological SI» System
- With Fundamental Biological Constant
- Based on «Quantum SI» System

- Let's act together