Lecture 1: Construction plans for cells and organisms

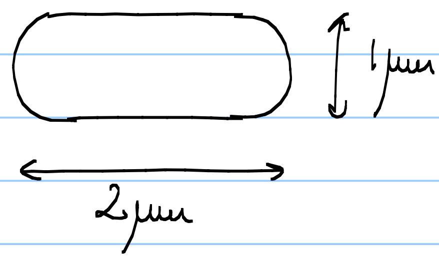
Note Title 7/1/2007

a. E. coli and yeast by the numbers

E. coli

1 kg of bacteria resides in our gut ⇒ # of E. coli cells > # of self-cells

Cell size:



$$V_{E.coli} = \frac{4\pi}{3}(0.5)^3\,\mu m^3 + \pi (0.5)^2 \cdot 1\,\mu m^3$$

$$V_{E.coli} \simeq 1.3\,\mu m^3$$

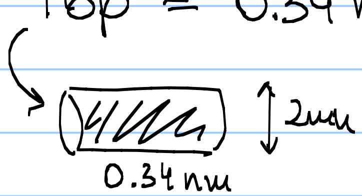
$$\frac{1}{V_{E.coli}} = \frac{1}{10^{-15}\,\ell} = \frac{10^{15}}{6 \cdot 10^{23}}\,M$$

$$= 1.3\;10^{-9}\,M = 1.3\,nM$$

1 molecule in volume of E. coli ≈ 1 nM concentration

Genome size: $N_{Genome} = 5 \cdot 10^6\,bp$

$1\,bp = 0.34\,nm \Rightarrow L_{Genome} \simeq 1.7\,mm$



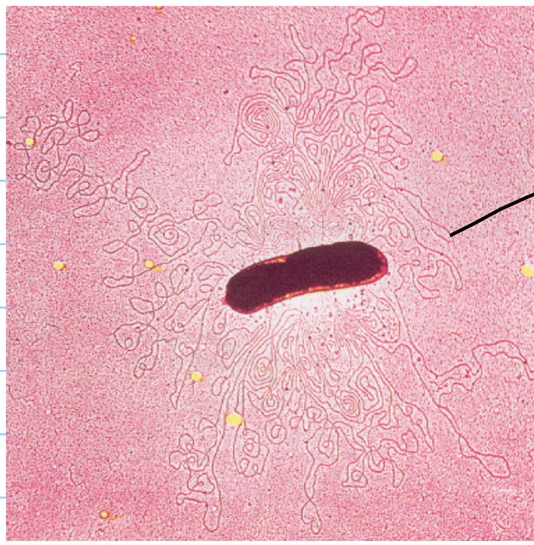
$\Rightarrow V_{bp} = 0.34 \cdot \pi \cdot 1\,nm^3 \simeq 1\,nm^3$

$$V_{Genome} \simeq 5 \cdot 10^6\,nm^3 = 5 \cdot 10^{-3}\,\mu m^3$$

N.B. $L_{genome} \gg$ linear size of bacterium

but... $V_{genome} \ll$ volume of bacterium

Which comparison paints the correct picture?



E. coli genome takes up a volume much larger than the volume of the cell.

What are the physical forces responsible for packaging the genome?

Protein content:

"typical" protein: (5 nm) $M_{protein} \simeq 30\,kDa$

(300 amino acids, each $\approx 100\,Da$)

30% of cell mass is dry, ½ of that is protein

(or volume occupied by proteins $\simeq$ 25% cell volume)

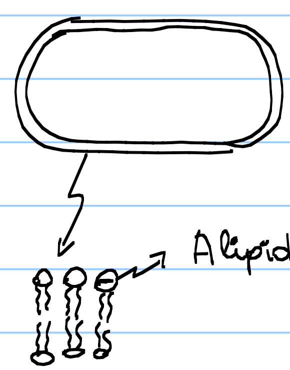
$M_{E.coli} = 1\,g/cm^3 \cdot 1\,\mu m^3 = 10^{-12}\,g = 1\,pg$

$M_{\text{total protein}} \simeq 0.15\,\text{pg} = 9.4 \times 10^{10}\,\text{Da}$

$$N_{\text{proteins}} \simeq \frac{0.15 \times 10^{-12}\,g}{30{,}000 \times \underbrace{1.6 \times 10^{-24}\,g}_{1\,\text{Da}}} \simeq \underline{\underline{3 \times 10^{6}}}$$

In a good growth medium E.coli produces at least 3×10^6 proteins every 30 minutes. This places constraints on the processes of the central dogma

Lipid content



$A_{\text{lipid}} = 0.25\,\text{nm}^2$

$$A_{E.coli} = 2\pi\,(0.5\,\mu m) \cdot 1\,\mu m + 4\pi\,(0.5\,\mu m)^2 \simeq 6\,\mu m^2$$

$$N_{\text{lipid}} \simeq \underbrace{4}_{\#\text{ of leaflets}} \times \underbrace{0.5}_{\text{fraction of area occupied by lipids}} \times \frac{6 \times 10^6\,\text{nm}^2}{0.25\,\text{nm}^2} \simeq \underline{\underline{5 \times 10^7}}$$

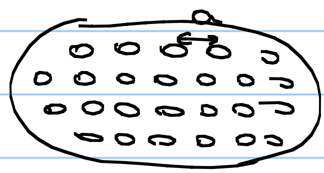
Number of ribosomes

$M_{\text{ribo}} \simeq 2.5\,\text{MDa}$ (smaller than the eukaryotic ribo)

20% of protein content = ribosomal protein

1/3 of ribosomal mass = protein

$$N_{ribo} = \frac{0.2 \times 0.15\,pg}{\frac{2.5\times 10^{6}\,Da}{3}} \simeq 20{,}000$$

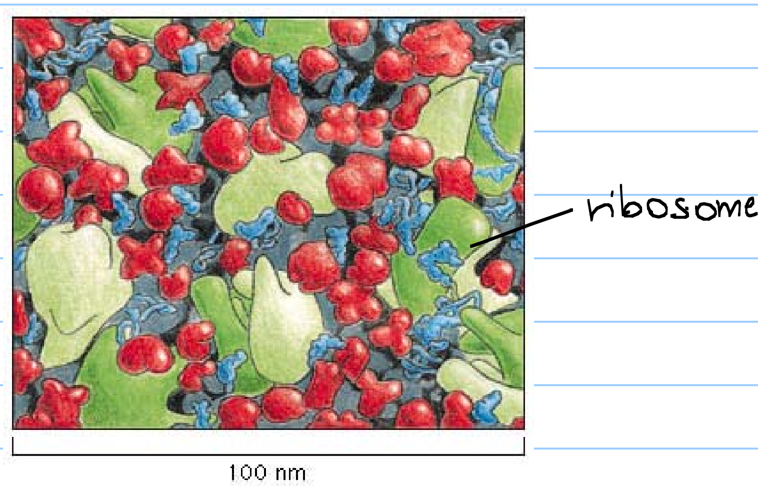


$$20{,}000 \cdot a^3 = 1\,\mu m^3$$

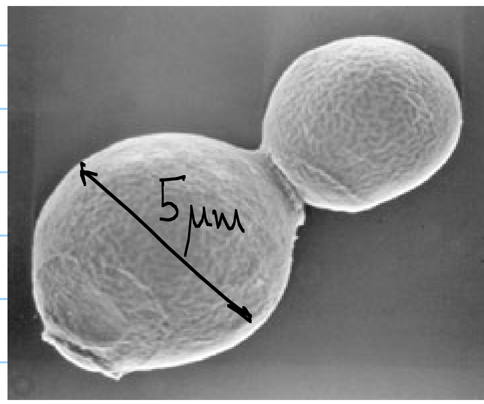
(a ↓ mean spacing)

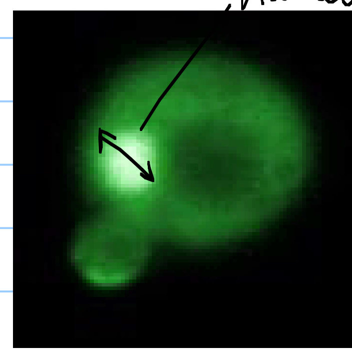
$\underline{a \simeq 40\,nm}$

The mean spacing should be compared to diameter of ribosome ≃ 20 nm. The cell is a crowded place!

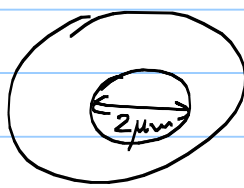


Yeast



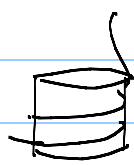


Yeast is a model eukaryotic cell (contains nucleus) and the rosette stone of molecular genetics.



$N_{Genome} = 12 \times 10^6$ bp

Genome is wrapped up into nucleosomes.



⇒ 150bp wrapped on histone | + 200bp / nucleosome
50bp linker DNA |

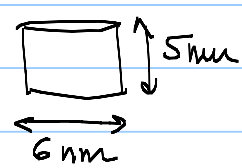
$$N_{nucleosome} \simeq \frac{12 \times 10^6 \text{ bp}}{200 \text{ bp}} = 60{,}000 \text{ nucleosomes}$$

(≈ 80,000 seems to be the actual number)

How tightly packed is the yeast genome?

Volume of nucleus $\approx \frac{4\pi}{3}(1\mu m)^3 \simeq 4\mu m^3$

Volume of histone $\approx$



$= \pi(3nm)^2\, 5nm$

$\simeq 150\, nm^3$

Total volume of all histones $\simeq 9 \cdot 10^{-3} \mu m^3$

Total volume of DNA $\simeq 12 \times 10^6\, bp \times \frac{1\, nm^3}{bp} = 12 \times 10^{-3} \mu m^3$

(N.B. The two are comparable.)

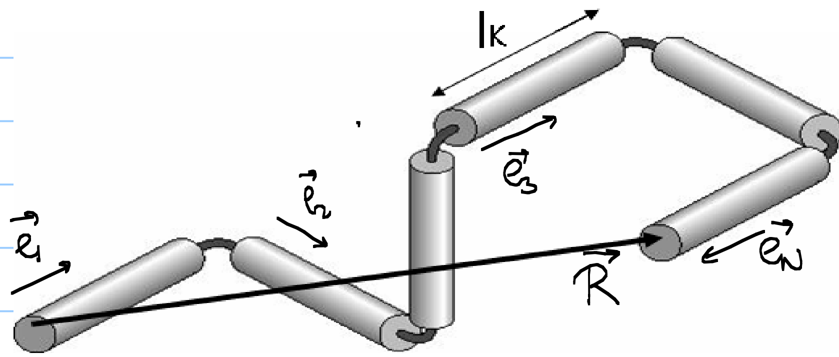
Volume fraction occupied by DNA + histones:

$$\phi \simeq \frac{20 \times 10^{-3}\, \mu m^3}{4\, \mu m^3} \simeq \underline{\underline{5 \times 10^{-3}}}$$ (same as E. coli)

What is the size of the genome?

Entropy is responsible for the volume occupied by the E. coli and yeast genomes in buffer solution, to be much larger than our estimates above.

We can estimate this effect using a random walk model of DNA (chromatin for yeast).



genome = polymer = N rigid rods connected by flexible linkers

polymer configuration = $\{\vec{e}_1, \vec{e}_2, \vec{e}_3, \ldots, \vec{e}_N\}$

$\vec{e}_i$'s are randomly oriented in space

Genome size $\simeq \sqrt{\langle \vec{R}^2 \rangle}$ where $\vec{R} = l_K(\vec{e}_1 + \vec{e}_2 + \vec{e}_3 + \ldots + \vec{e}_N)$

$$\langle R^2 \rangle = l_K^2 \langle \underbrace{\vec{e}_1^{\,2}}_{=1} + \underbrace{\vec{e}_2^{\,2}}_{=1} + \ldots + \underbrace{\vec{e}_N^{\,2}}_{=1} + \underbrace{2\vec{e}_1\cdot\vec{e}_2}_{=0} + \underbrace{2\vec{e}_1\cdot\vec{e}_3}_{=0} + \ldots + \underbrace{2\vec{e}_{N-1}\cdot\vec{e}_N}_{=0} \rangle$$

$$= N l_K^2$$

$\Rightarrow$ **Genome size $\simeq \sqrt{N}\, l_K$**

$$L_{genome} = \underbrace{N_{genome}}_{\#\text{ of base pairs}} \cdot \underbrace{\nu}_{nm/bp}$$

$$= N\, l_K$$

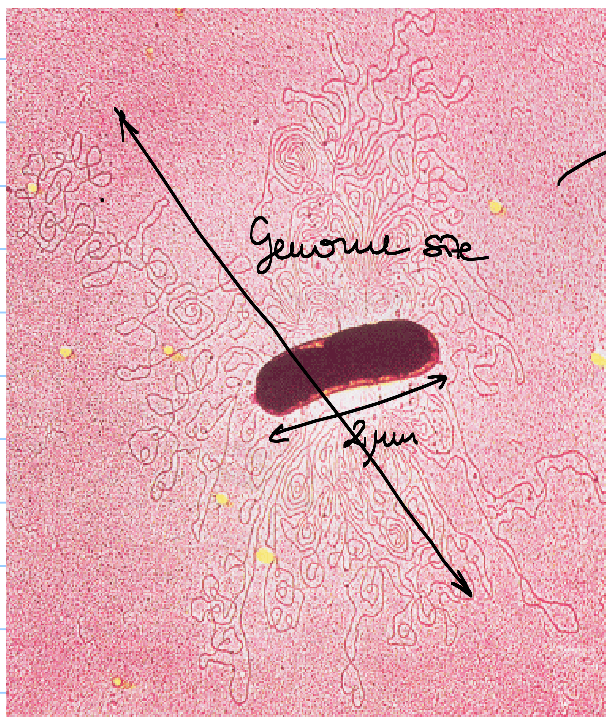
$\nu_{DNA} = 0.34 \frac{nm}{bp}$

$\nu_{chromatin} = ?$

$$\text{Genome size} = \sqrt{\frac{N_{genome}}{l_k}\nu}\; l_k$$

$$\boxed{\text{Genome size} = \sqrt{N_{genome}}\,\sqrt{\nu\, l_k}}$$

For E. coli:



$\text{Genome size} \simeq 10\,\mu m$

$10\,\mu m \simeq \sqrt{N_{genome}}\,\sqrt{0.34 \cdot 100\,nm}$

$N_{genome} \simeq 3 \cdot 10^6$ bp

(actual size $= 5 \times 10^6$ bp!)

b. Cellular part list : organelles and "somes"

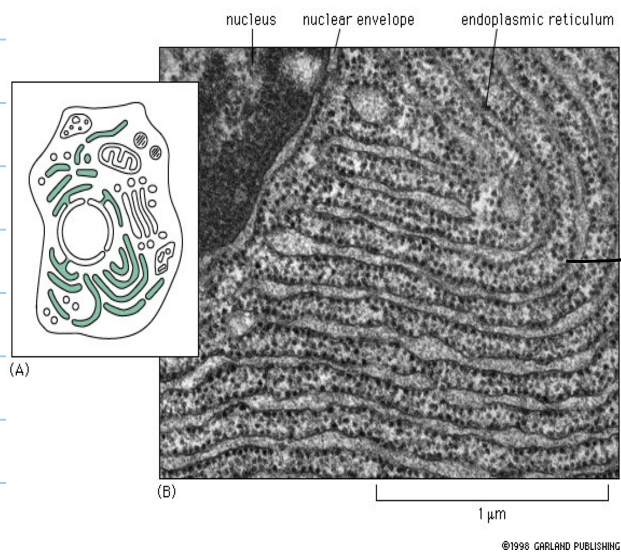
Nucleus : information storage and processing
↳ nucleosomes

Mitochondria : energy production
↳ ATP synthase

Endoplasmatic reticulum : protein production
↳ ribosomes

Golgi apparatus : protein packaging and distribution

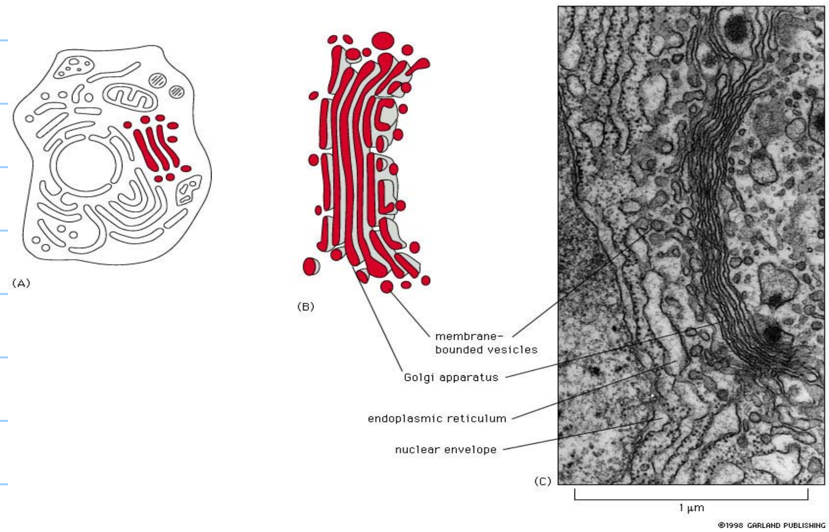
Internal membrane systems



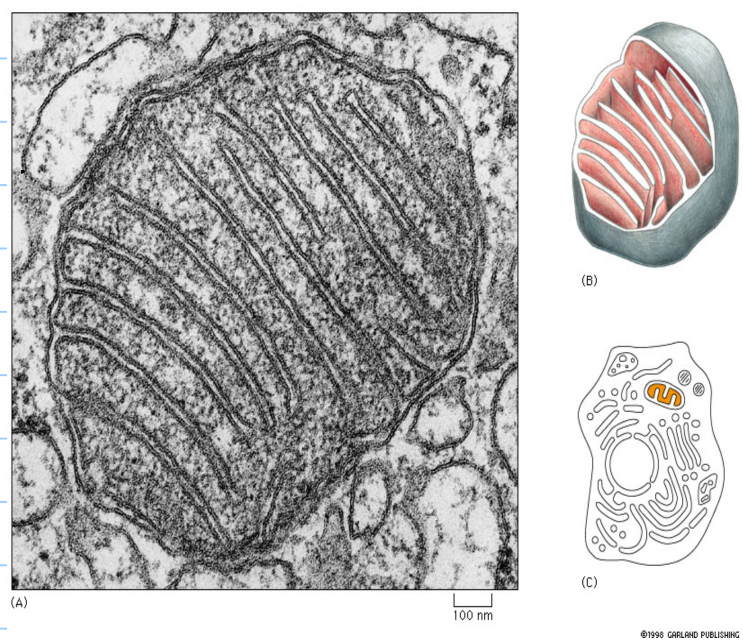
Endoplasmatic reticulum

ribosomes

Golgii apparatus

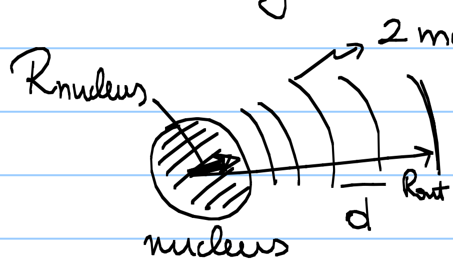


Mitochondria



Is there a common mechanism responsible for the membrane shapes of these organelles?

Estimate of membrane area within ER



$$\frac{4\pi}{3} R_{out}^3 - \frac{4\pi}{3} R_{nucleus}^3 = \sum_i A_i d$$

$$A_{membrane} = 2 \sum A_i$$

$R_{nucleus} = 5 \mu m$
$R_{out} = 10 \mu m$
$d \simeq 0.1 \mu m$

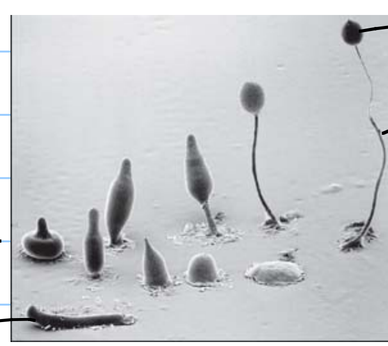
$$\simeq \frac{2}{d} \frac{4\pi}{3} (R_{out}^3 - R_{nucleus}^3)$$

$= \underline{7 \times 10^4 \mu m^2}$ which is an order of magnitude larger than the surface area of the plasma membrane

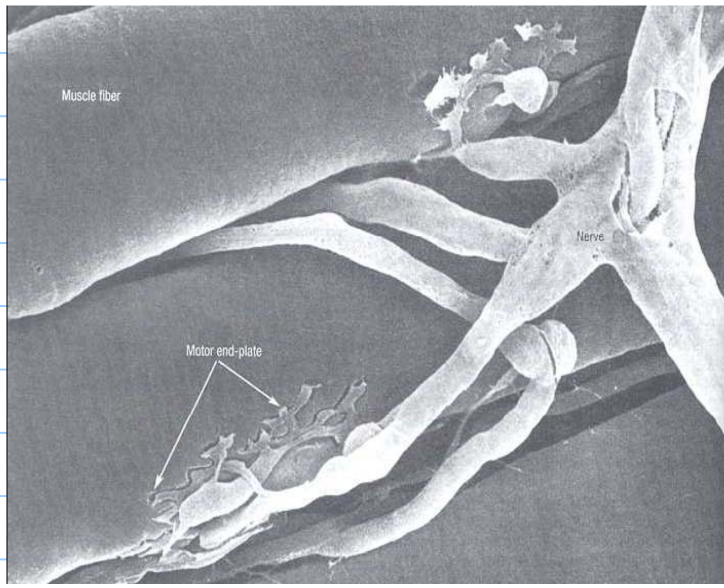
c. Assemblies of cells

Multicelularity is one of evolutions great inventions.

Lifestyle of a social amobea Dictyostelium discoideum



Cell-cell contacts



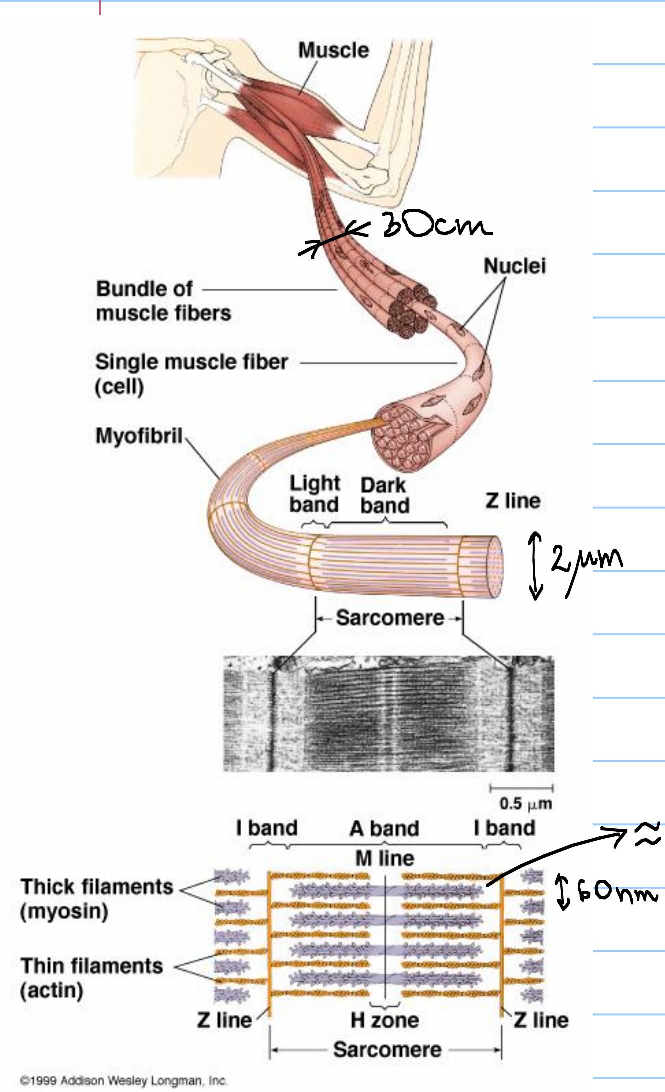
The neuromuscular junction is a microcosm of biology:

- ion channels
- membrane depolarization and action potential
- acto-myosin / molecular motors
- chemical signaling / membrane transport

Sequence of events leading to muscle contraction:

- action potential arrives at junction via motor neuron
- ACh (acetylcholine) release via vesicle fusion in the presynaptic neuron

- Opening of nicotinic-ACh receptors on post-synaptic muscle cell
- Depolarization of membrane of the muscle cell
- opening of Ca channels in membrane of muscle
- Ca binds to troponin allowing myosin to bind to actin → muscle contracts



Estimate of force exerted by 1 myosin

30cm : muscle fiber

In a cross section of a muscle cell there are:

$$N_{myosin} = \frac{(30\,cm)^2}{(60\,nm)^2} \times 300 \simeq 10^{14}$$

myosin motors.

If the myosins support a weight of 10 kg · g ≃ 100 N

then each myosin exerts

$$F_{myosin} \approx \frac{10^2}{10^{14}} N \simeq \underline{1\,pN}$$

Appendix A

Biology by the numbers:

Quantity of interest	Symbol	Rule of thumb
	E. coli	
Cell volume	$V_{E.coli}$	$\approx 1\ \mu m^3$
Cell mass	$m_{E.coli}$	$\approx$ 1pg
Cell cycle	$t_{E.coli}$	$\approx$ 3000 sec
Cell area	$A_{E.coli}$	$\approx 5\ \mu m^2$
Genome Length	$N_{bp}^{E.coli}$	$\approx 5 \times 10^6$ bp
Swimming speed	$v_{E.coli}$	$\approx 20\ \mu m/sec$
	Yeast	
volume of cell	V_{yeast}	$\approx 60\mu m^3$
Mass of cell	m_{yeast}	$\approx$ 60 pg
diameter of cell	d_{yeast}	$\approx 5\ \mu m$
Cell cycle time	t_{yeast}	$\approx$ 200 min
Genome Length	N_{bp}^{yeast}	$\approx 10^7$ bp
	Organelles	
Diameter of nucleus	$d_{nucleus}$	$\approx 5\ \mu m$
Length of mitochondrion	l_{mito}	$\approx 2\ \mu m$
Diameter of transport vesicles	$d_{vesicle}$	$\approx$ 50 nm
	Water	
Volume of molecule	V_{H_2O}	$\approx 10^{-2}\ nm^3$
Density of water	ρ	$1\ g/cm^3$
Viscosity of water	η	$\approx$ 1 centipoise (10^{-2} g/cm sec
Hydrophobic embedding energy	$\approx E_{hydr}$	25 cal/mol A^2
	DNA	
Length per base pair	l_{bp}	$\approx 1/3$ nm
Volume per base pair	V_{bp}	$\approx 1\ nm^3$
charge density	λ_{DNA}	2 e/0.34 nm
Persistence length	ξ_P	50 nm
	Amino acids and Proteins	
Radius of "Average" Protein	$r_{protein}$	$\approx$ 2 nm
Volume of "Average" Protein	$V_{protein}$	$\approx 25\ nm^3$
Mass of "Average" Amino Acid	M_{aa}	$\approx$ 100 Da
Mass of "Average" Protein	$M_{protein}$	$\approx$ 30,000 Da
Protein concentration in cytoplasm	$c_{protein}$	$\approx$ 200 mg/ml
Characteristic force of protein motor	F_{motor}	$\approx$ 5 pN
Characteristic speed of protein motor	v_{motor}	$\approx$ 200 nm / sec
Diffusion constant of "Average" Protein	$D_{protein}$	$\approx 100\ \mu m^2/sec$
	Lipid Bilayers	
Thickness of lipid bilayer	d	$\approx$ 5 nm
Area per molecule	A_{lipid}	$\approx \frac{1}{2}\ nm^2$
Mass of lipid molecule	m_{lipid}	$\approx$ 800 Da