Part III Biological Physics course - 2019

Lecturers:

Prof. Pietro Cicuta pc245

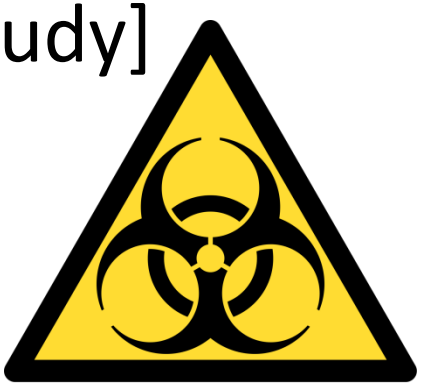
Dr Diana Fusco df390

Pre-requisites:

Part II Thermal Statistical

Part II Soft Condensed Matter [or self study]

Reading list:



Warning, this is a biology book

Phillips, Kondev, Theriot, Garcia

Physical Biology of the Cell - 2nd ed., Garland 2013

Phil Nelson

Physical Models of Living Systems - Freeman 2015

Biological Physics - : Energy, Information, Life - Freeman 2007

Uri Alon

An Introduction to Systems Biology - Chapman and Hall 2007 + 2nd ed 2020

Bruce Alberts et al.

Molecular Biology of the Cell- Garland (many editions, updated almost yearly)

Kim Sneppen and Giovanni Zocchi

Physics in Molecular Biology - CUP 2005

Kim Sneppen

Models of Life - CUP 2014 & free e-book

Useful Information:

Website, linked from TiS:
http://people.bss.phy.cam.ac.uk/courses/biolectures/

Send comments & errors to pc245 or df390. A list of known errors is maintained on the website.

Supervisions available for students in Part III and MASt
(3 supervisions, single large group, times will be communicated).

Structure of the course:

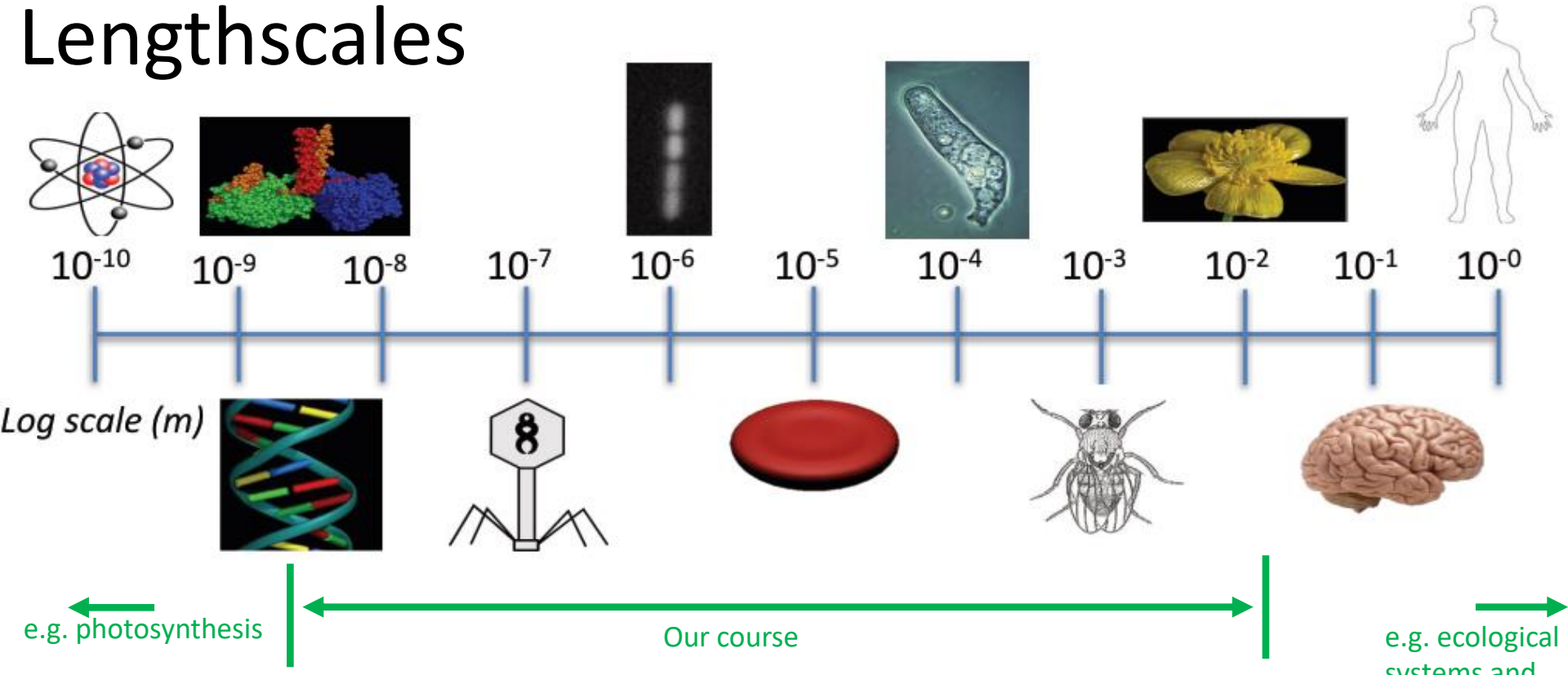
24 lectures, in 7 modules:

- A - context/overview/intro/basics, networks
- B - evolution and growth of populations
- C - dynamics in the cell
- D - elements of neuro-physics
- E - pattern formation in biology
- F - protein production and regulation of gene expression
- G - dynamical systems, switches and oscillations

Warning!
New Module
No previous exam questions

4 lectures will be given by other Cambridge colleagues active on the biology/physics interface: material closer to active research (details not examinable)

Lengthscales



e.g. photosynthesis

Our course

e.g. ecological systems and evolution

Biological systems have a hierarchical organization across many lengthscales

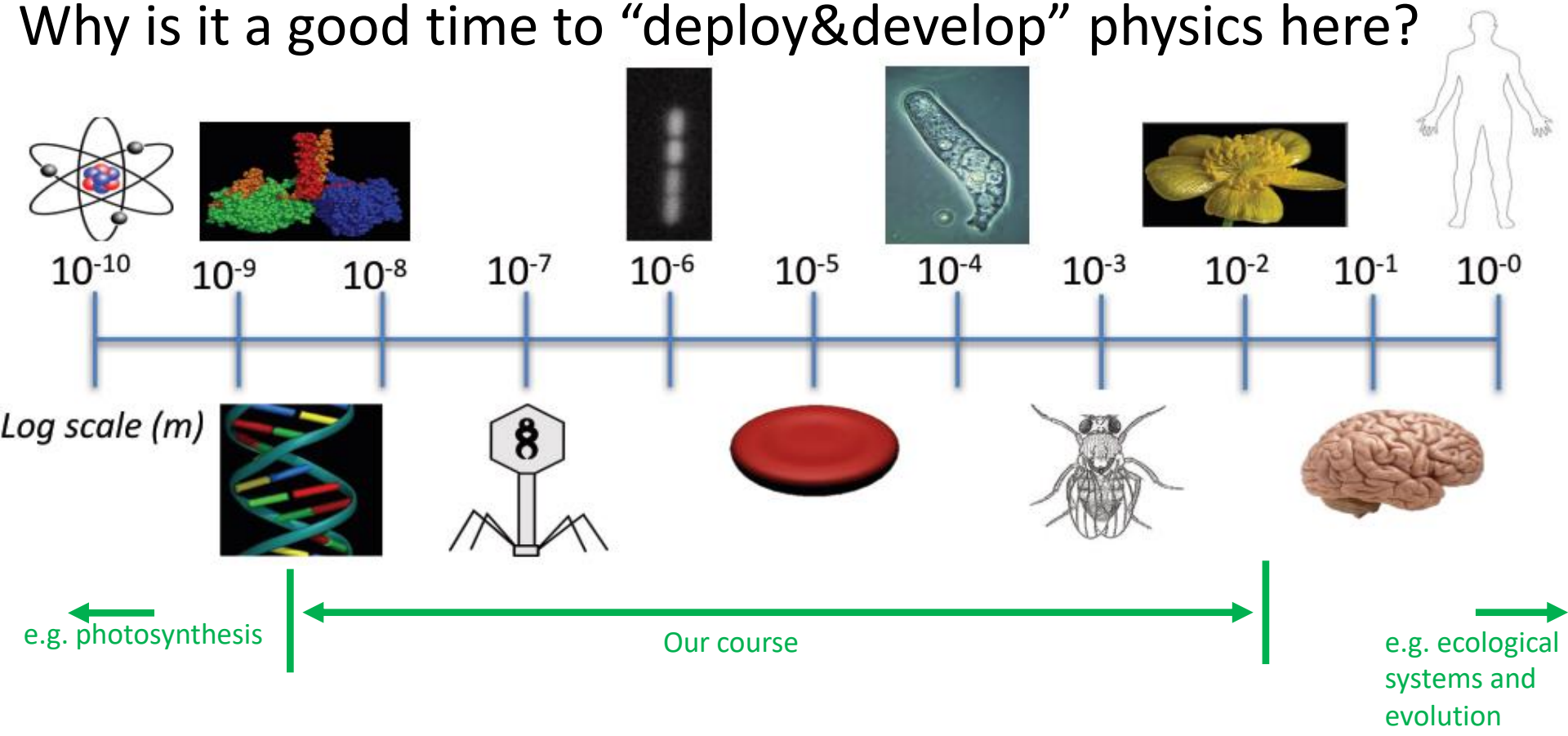
Lengthscale ← → Timescale… hence "emergence".

Non-equilibrium (but considering separation of timescales, equilibrium often valid)

Self assembly and self replication

We focus in this course on scales where thermal noise and small number noise are at play - classical statistical mechanics.

Why is it a good time to “deploy&develop” physics here?



e.g. photosynthesis

Our course

e.g. ecological systems and evolution

Fantastic detailed knowledge of the molecules that make up living systems from decades of “structural biology”. Precise genetic code.

The broadly correct understanding of mechanisms of action of many of these constituents. Quantitative datasets resolved on relevant lengths & times.

Unique power of physics (stat mech, dynamical systems, soft matter) in linking up scales → models that have the “correct” mechanism, and that represent an understanding.

Physics is required.

Physics is required.
As in other fields (condensed matter, etc), what is our approach?

- Understand context - here, cell biology context.
- Make order of magnitude estimates.
- Become familiar with tools for model building.
- Critical analysis to determine limitations, and suggest refinement to models.

Crick's legacy - Polymer Languages

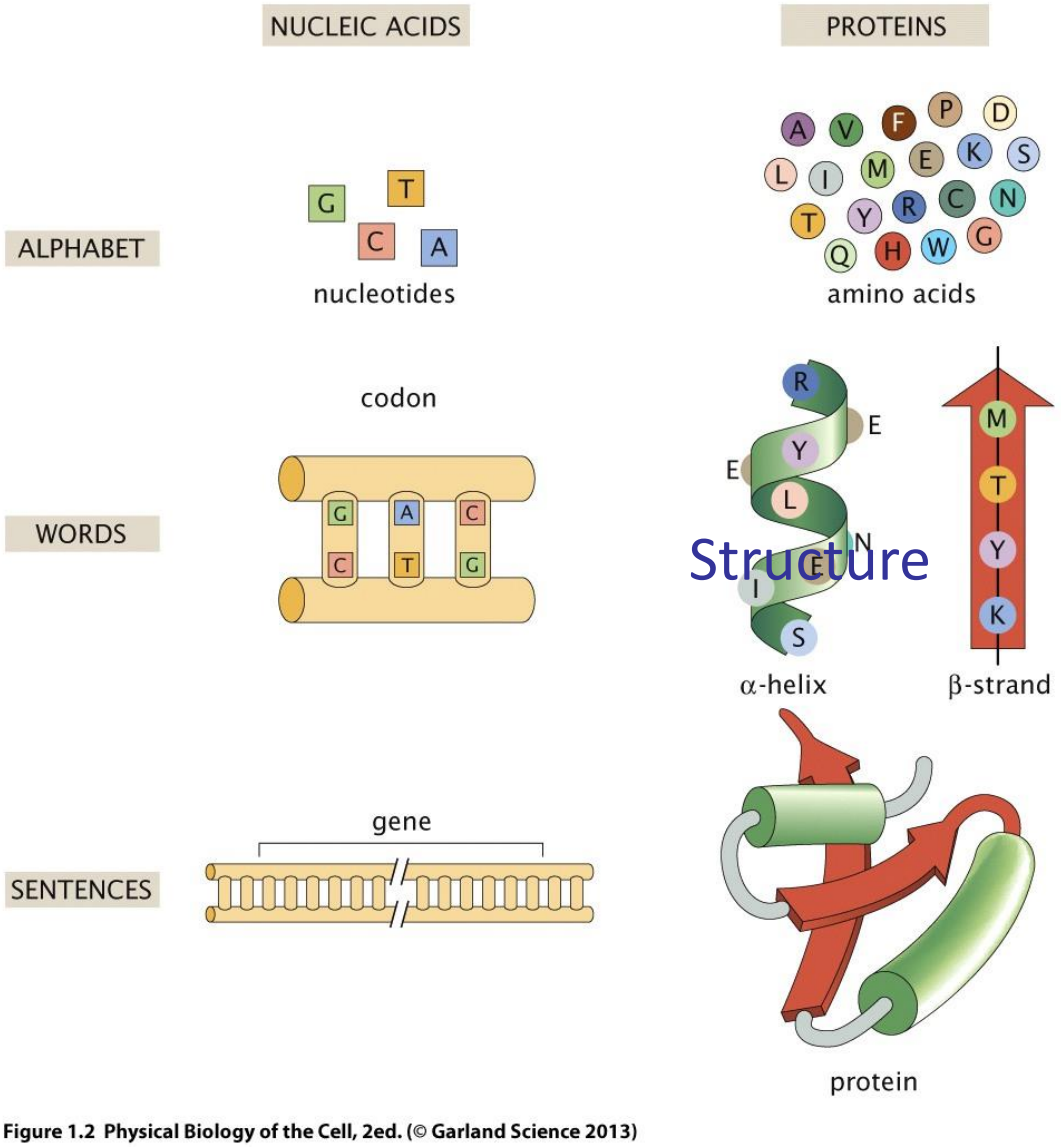


Figure 1.2 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

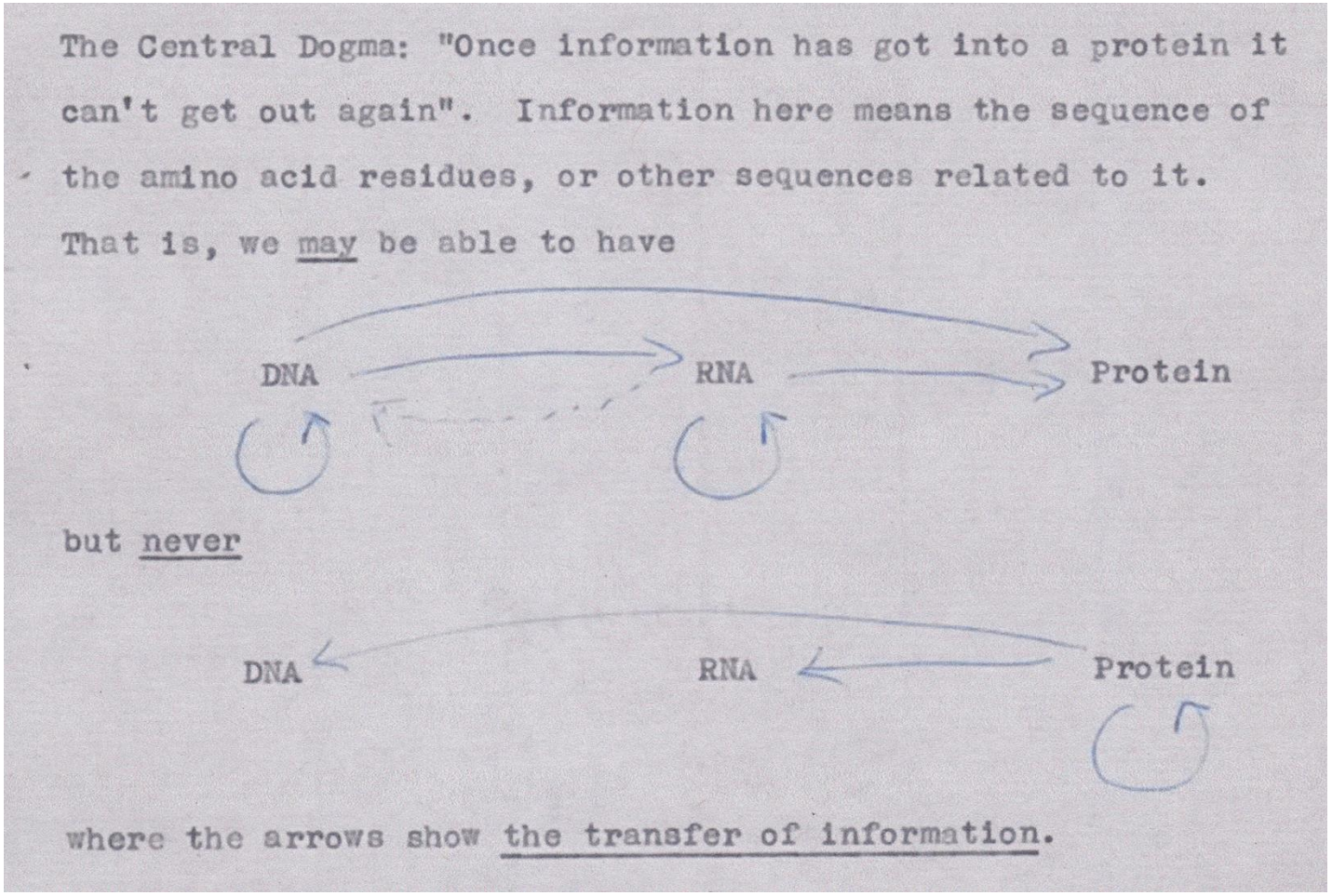
Space of "Genotypes"

Space of "Phenotypes"

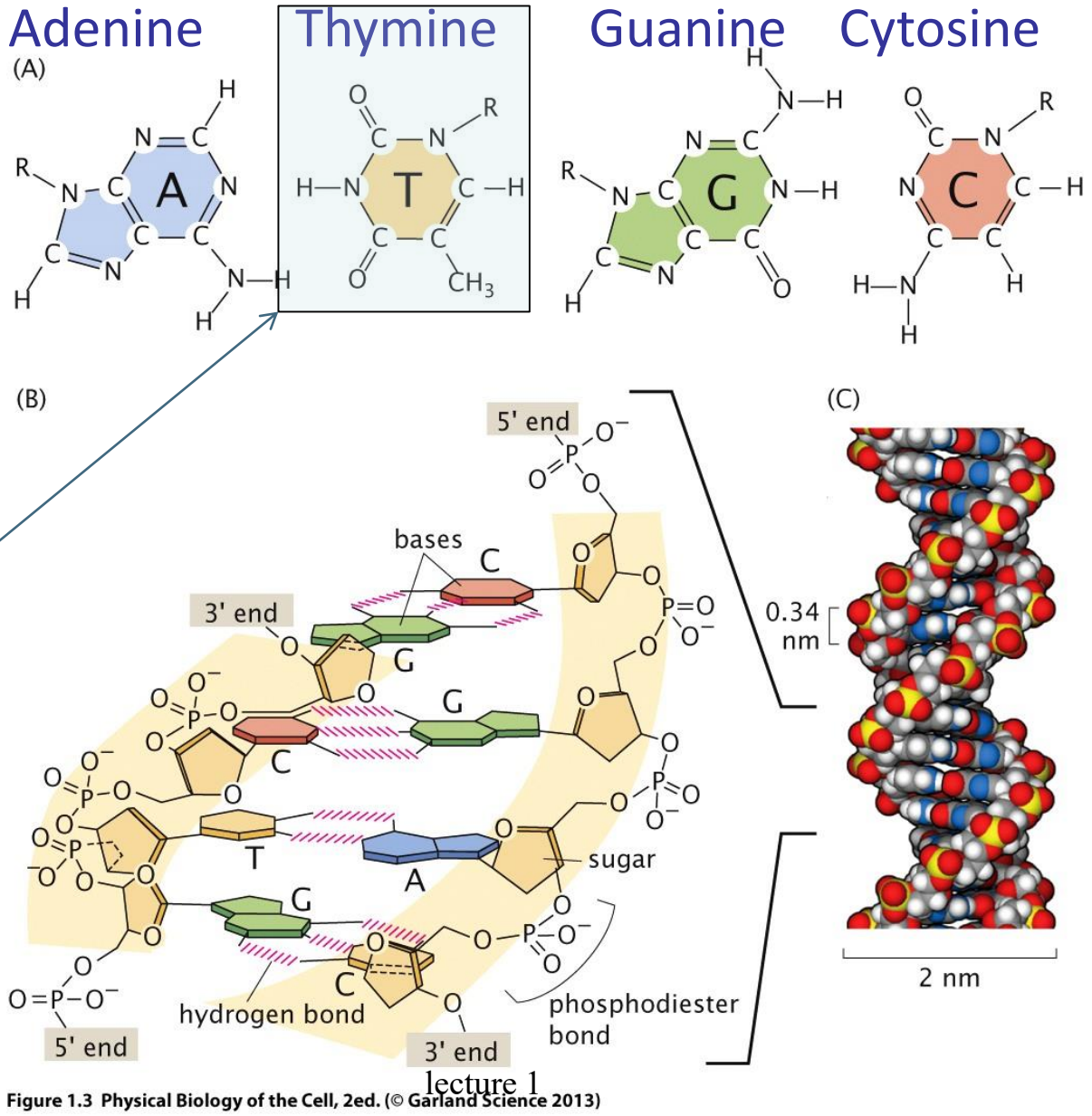
Hierarchy of scales: both Information and Structure.

Gene regulation: the “central dogma”

Crick 1953-1957



Nucleotides and DNA



Replaced by Uracil in RNA

Figure 1.3 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

The genetic code

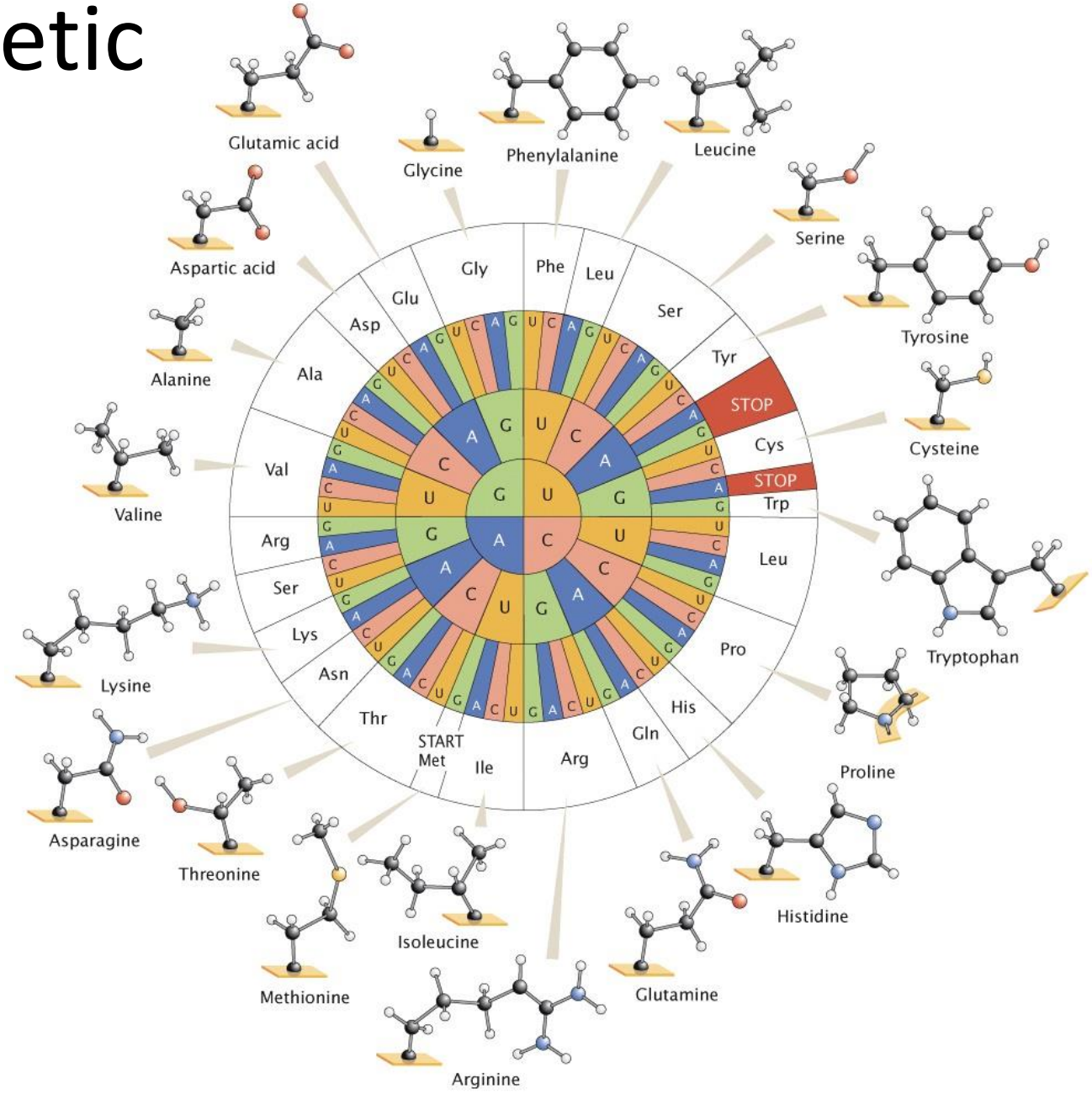


Figure 1.4 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Many ways to see a DNA double helix

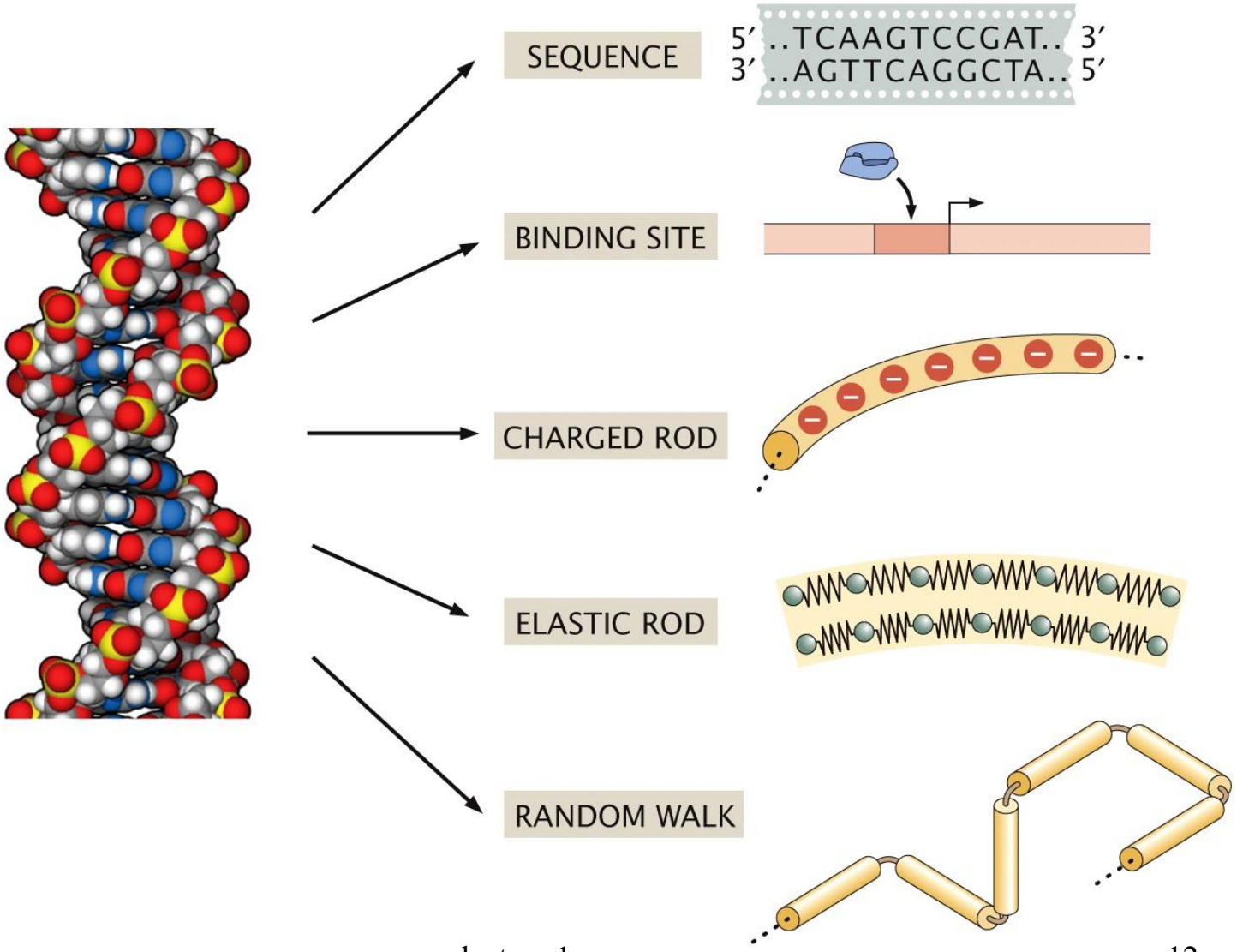


Figure 1.5 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Many ways to see a protein

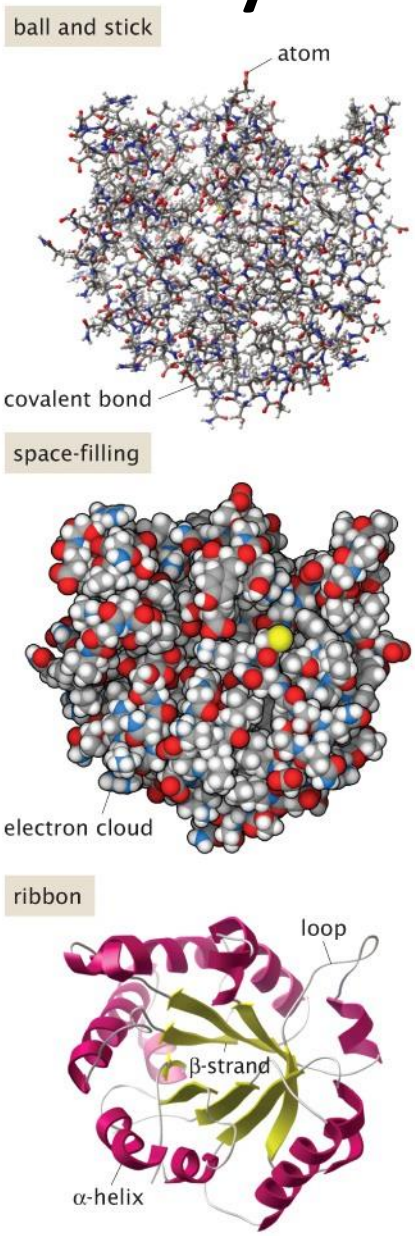


Figure 2.32 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

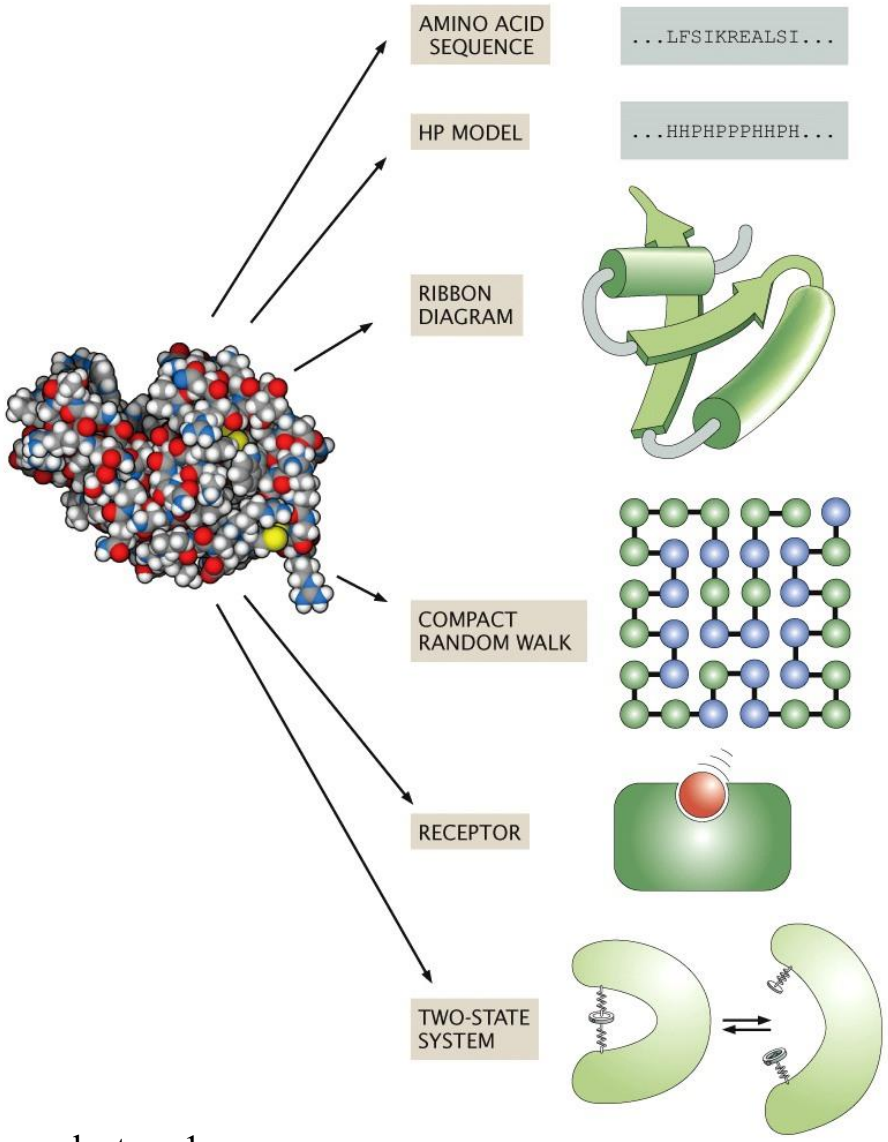


Figure 1.6 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Many ways to see a lipid membrane

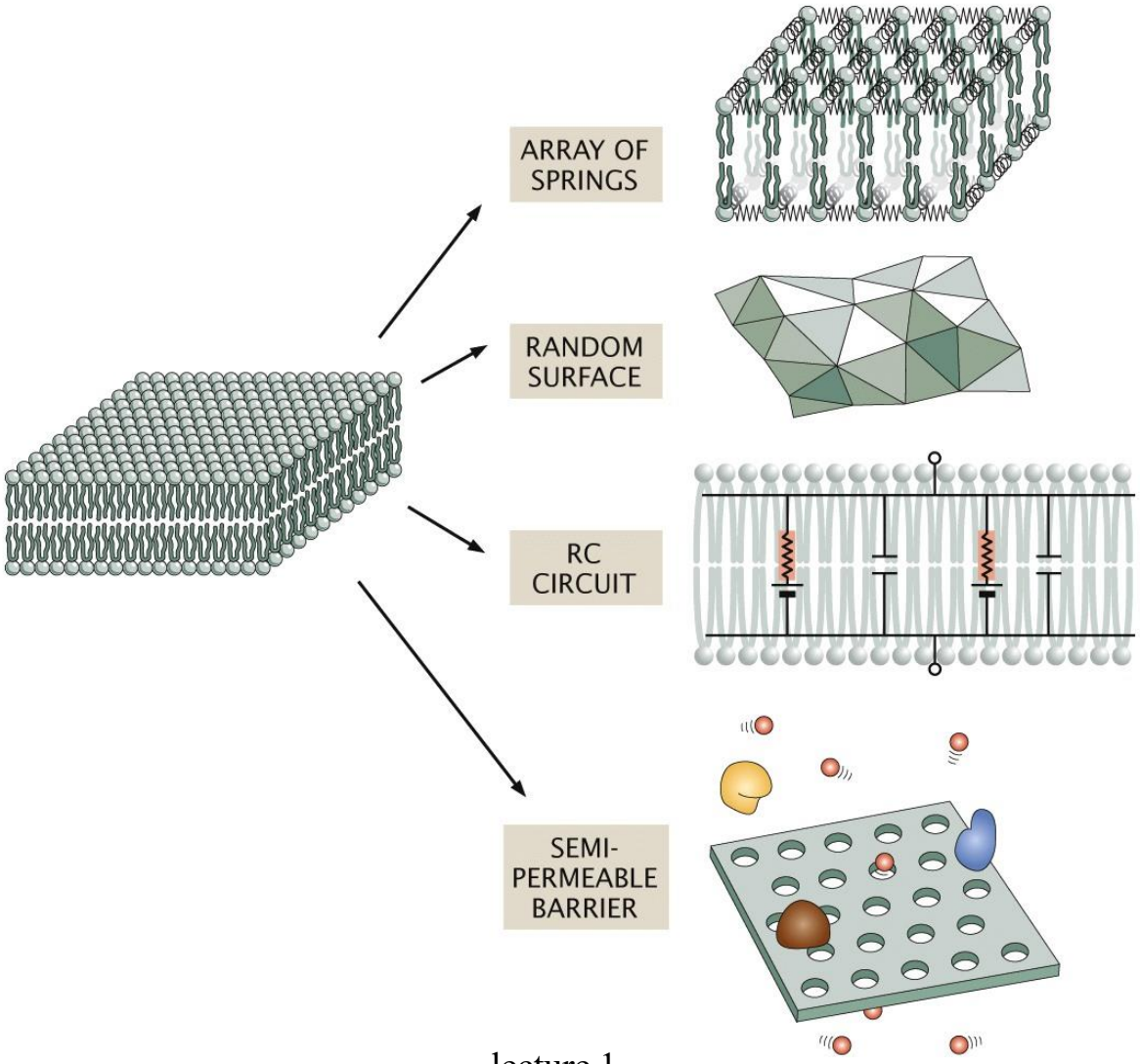


Figure 1.7 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

To cells: Many ways to see a bacterium

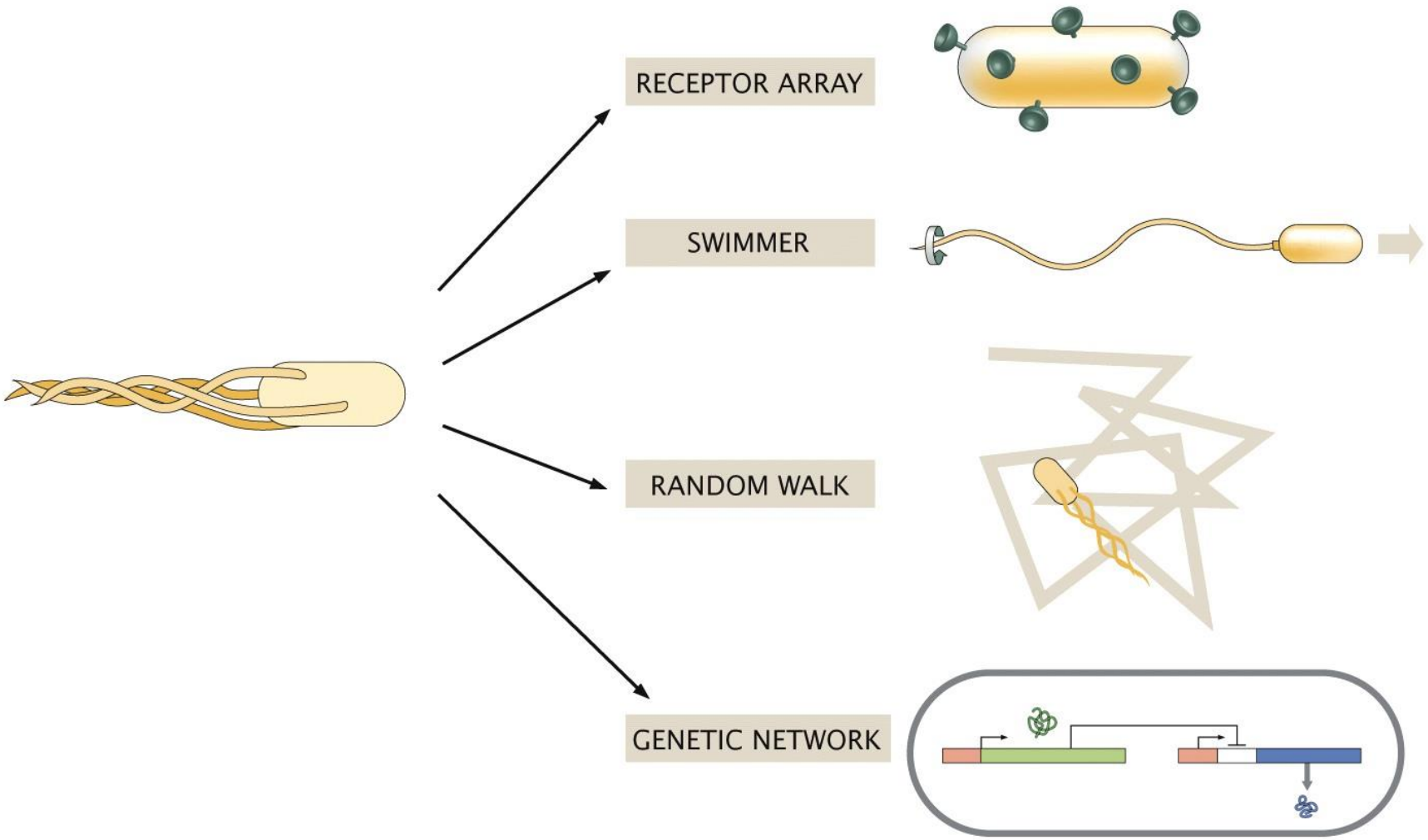


Figure 1.8 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

What is “right” level of description ?

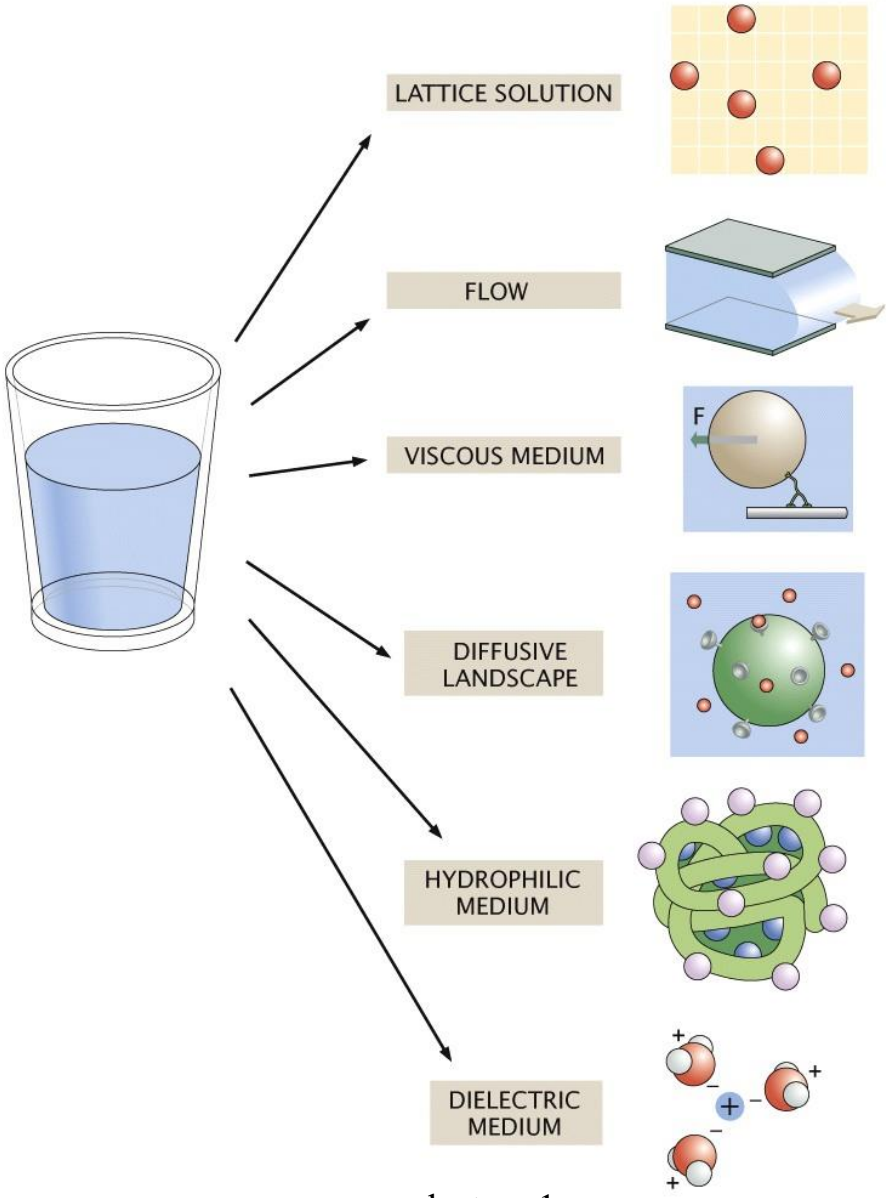
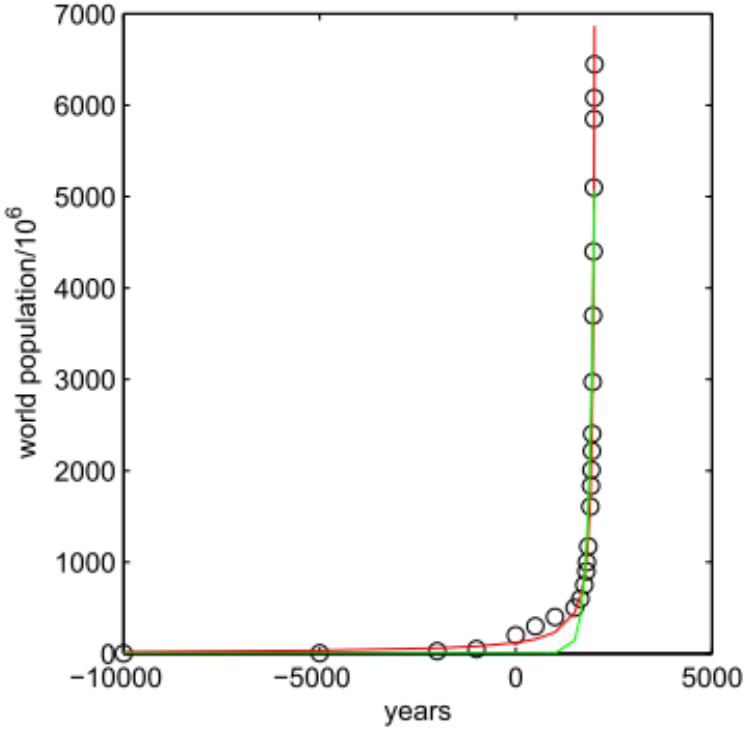


Figure 1.9 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

What do we want to avoid?

Example of population growth data



f(t) = a1/[a2 – (t/1yr)] a1=10000, a2=2050 works very well

or

f(t) = a1 exp (a2 t)

Physical Models need to reflect a mechanism, and can point us to further key insights.

A success in quantitative biology (and still ongoing): The Lac repressor

Where Stat mech and Polymer physics meet the biology of gene regulation

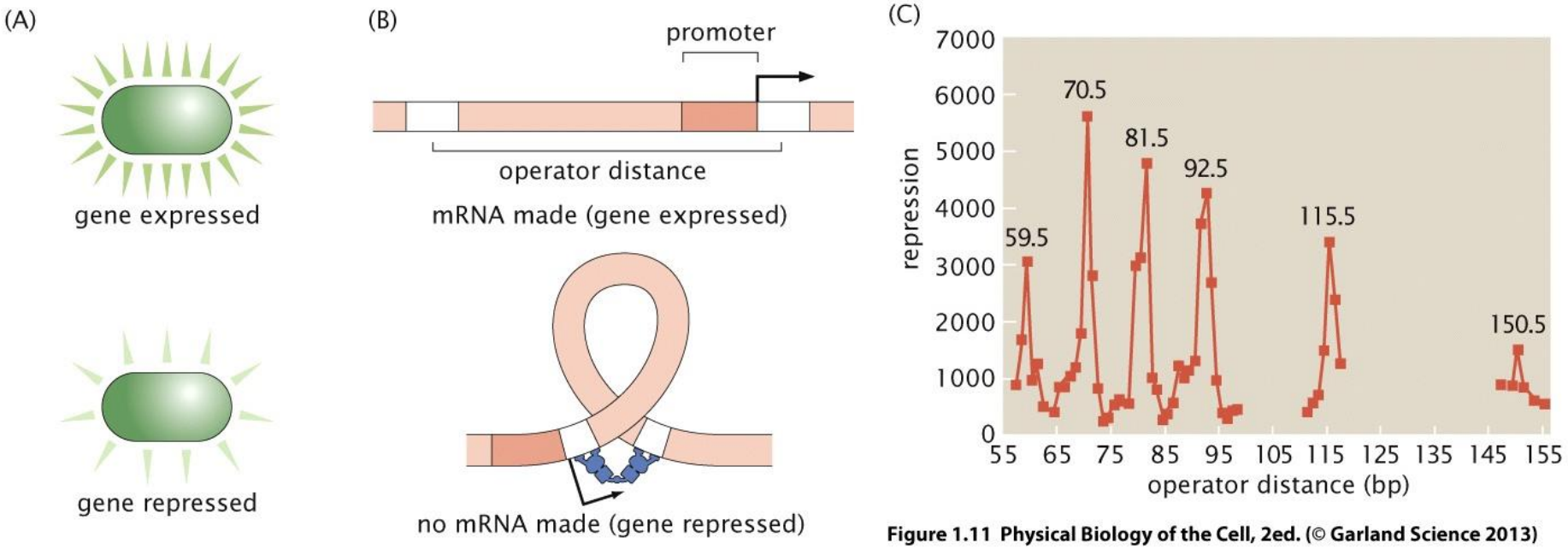


Figure 1.11 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Table 1.1: Rules of thumb for biological estimates.

	Quantity of interest	Symbol	Rule of thumb
E. coli			
	Cell volume	$V_{E.\,coli}$	$\approx 1\,\mu m^3$
	Cell mass	$m_{E.\,coli}$	≈ 1 pg
	Cell cycle time	$t_{E.\,coli}$	≈ 3000 s
	Cell surface area	$A_{E.\,coli}$	$\approx 6\,\mu m^2$
	Macromolecule concentration in cytoplasm	$c_{E.\,coli}^{macromol}$	≈ 300 mg/mL
	Genome length	$N_{bp}^{E.\,coli}$	$\approx 5 \times 10^6$ bp
	Swimming speed	$v_{E.\,coli}$	$\approx 20\,\mu m/s$
Yeast			
	Volume of cell	V_{yeast}	$\approx 60\,\mu m^3$
	Mass of cell	m_{yeast}	≈ 60 pg
	Diameter of cell	d_{yeast}	$\approx 5\,\mu m$
	Cell cycle time	t_{yeast}	≈ 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	$d_{vesicle}$	≈ 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	≈ 1 centipoise (10^{-2} g/(cm s))
	Hydrophobic embedding energy	$\approx E_{hydr}$	2500 cal/(mol nm^2)

Table 1.1 (part 1 of 2) Physical Biology of the Cell, 2ed. (© Garland Science 2013)

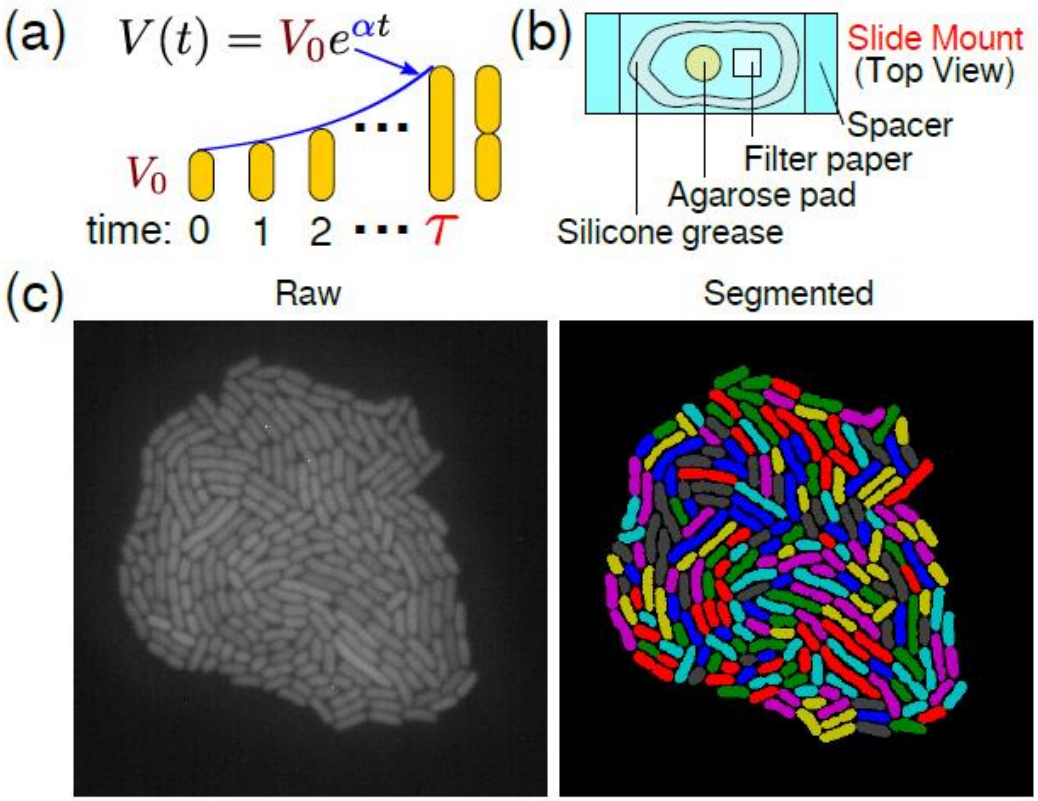
Table 1.1: Rules of thumb for biological estimates.

	Quantity of interest	Symbol	Rule of thumb
DNA			
	Length per base pair	l_{bp}	$\approx 1/3$ nm
	Volume per base pair	V_{bp}	≈ 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	$r_{protein}$	≈ 2 nm
	Volume of "average" protein	$V_{protein}$	≈ 25 nm^3
	Mass of "average" amino acid	M_{aa}	≈ 100 Da
	Mass of "average" protein	$M_{protein}$	$\approx 30{,}000$ Da
	Protein concentration in cytoplasm	$c_{protein}$	≈ 150 mg/mL
	Characteristic force of protein motor	F_{motor}	≈ 5 pN
	Characteristic speed of protein motor	v_{motor}	≈ 200 nm/s
	Diffusion constant of "average" protein in cytoplasm	$D_{protein}$	$\approx 10\,\mu$m^2/s
Lipid bilayers			
	Thickness of lipid bilayer	d	≈ 5 nm
	Area per molecule	A_{lipid}	$\approx \frac{1}{2}$ nm^2
	Mass of lipid molecule	m_{lipid}	≈ 800 Da

Table 1.1 (part 2 of 2) Physical Biology of the Cell, 2ed. (© Garland Science 2013)

An example of “important question” that can be addressed in very different ways:

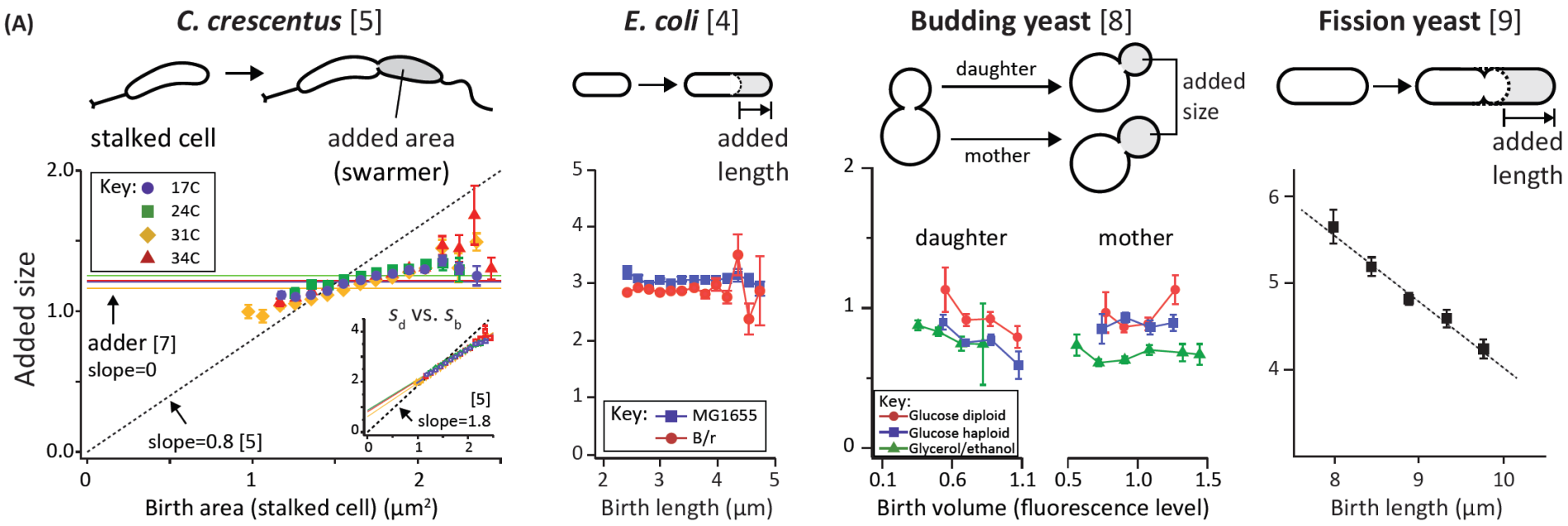
How do cells regulate division to have a mean size?



E.coli bacteria Imaged in fluorescence microscopy.

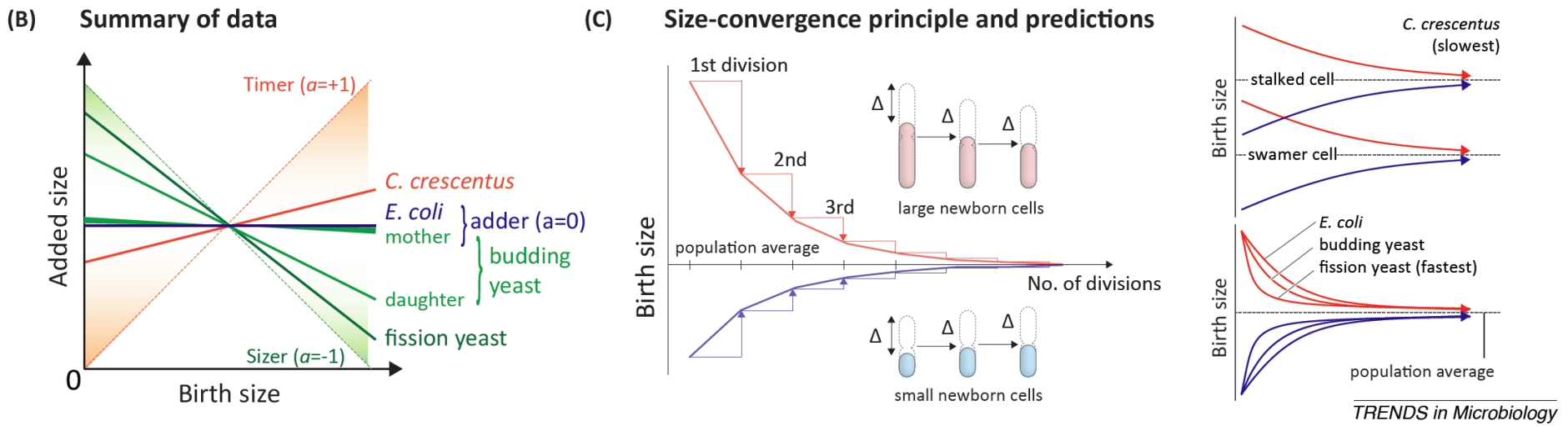
In principle, control could be through “sizer”, “timer” or some combination.

Data on regulation of division



From S.Jun, S.Taheri-Araghi, Trends in Microbiology 4, 23 (2015)

How do cells regulate division to have a mean size?
One can also try to establish the general control theory, looking at the data.



One can search for the molecular mechanism, but certainly more complex than "the gene"!

Not so simple to come up with sizer mechanisms: plausible scenario put forward in yeast might involve sensing size through the balance between a species that has constant concentration in the cell volume as monomers, an adsorption equilibrium with the membrane (hence # prop to area), and a polymerisation "sink". Concentration at the sink is then a membrane area sensor, triggering division.

Recap:

- Spirit and remit of this course.
- How physics contributes to this area of science.
- A first overview of cell machinery.
- Confidence in developing models and determining the right level of description.
- Next two lectures are “intro” to networks.