

Randomness and information in biological data

BIO-369

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EPFL

Lecture 4

Outline of the course

I Randomness in biological processes and biological data

1 Randomness and random variables

1.1 Coins and dice: discrete random variables

1.2 Medical testing and conditional probabilities

1.3 Luria-Delbrück experiment: Poisson distribution vs. jackpot distribution

2 Importance of thermal fluctuations at the cellular scale

2.1 Thermal fluctuations and associated energy scale

2.2 Strength of various chemical bonds

2.3 Flexibility of biopolymers and biomembranes

3 Random walks

3.1 Population genetics

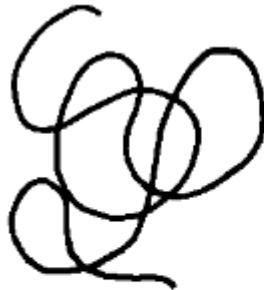
3.2 Protein abundances in single cells

3.3 Importance of random walks in biological systems

Reminder: flexibility of biopolymers

■ Persistence length

(a): total length \gg persistence length



(a)

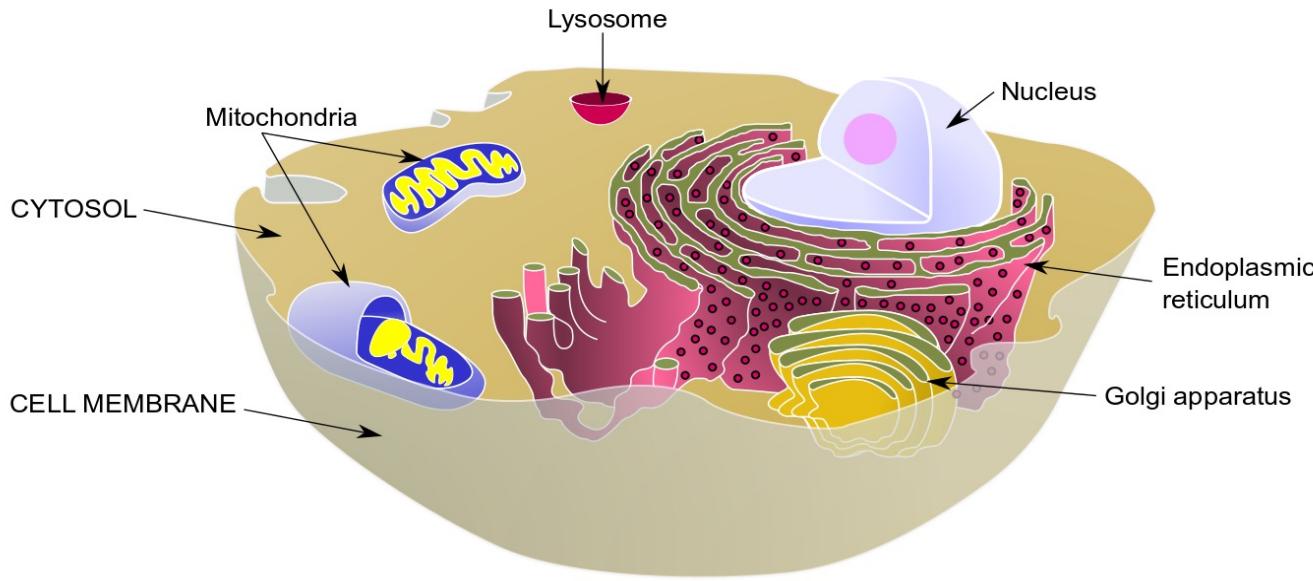
(b) total length \ll persistence length



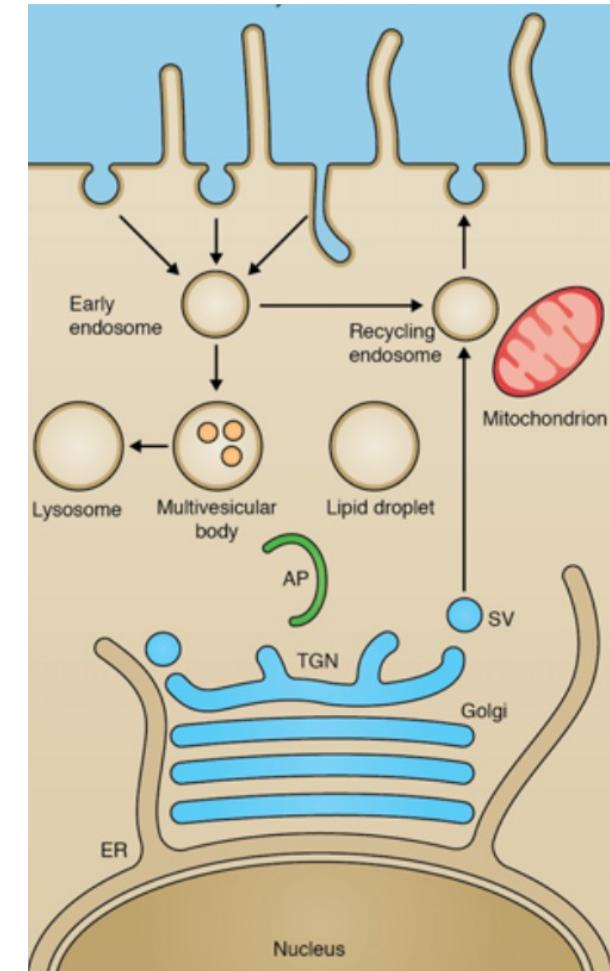
(b)

Biomembranes: motivation

- Biomembranes are curved and constantly change shape



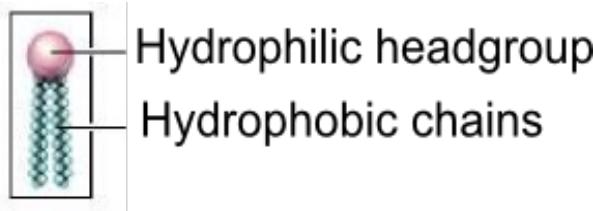
Membrane thickness: a few nm
Cell size: 1 – 100 μm



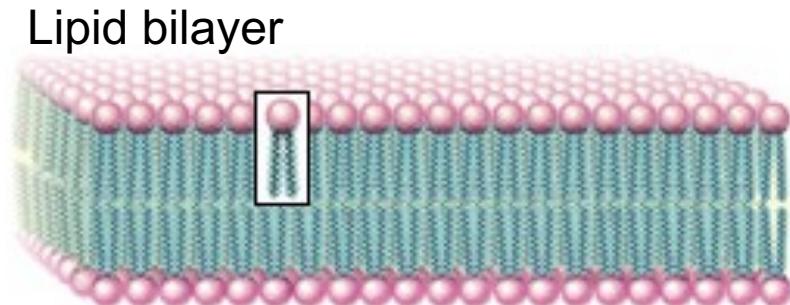
Biomembrane properties

■ Basic structure

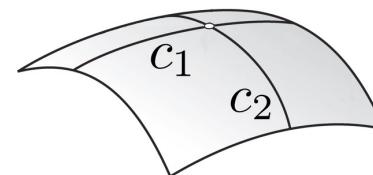
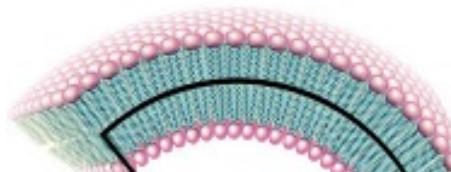
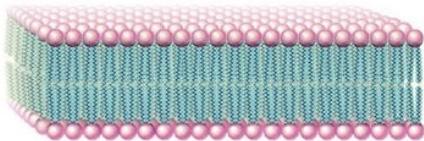
Lipid molecule: amphiphilic



Self-assembly
in water



■ Elasticity: bending



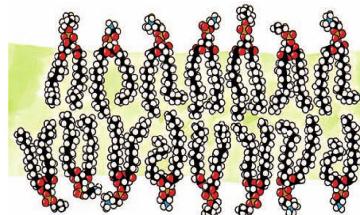
$$R_1 \rightarrow c_1 = \frac{1}{R_1}$$

Curvature energy:

$$H = \int_A dA \frac{\kappa}{2} (c_1 + c_2)^2$$

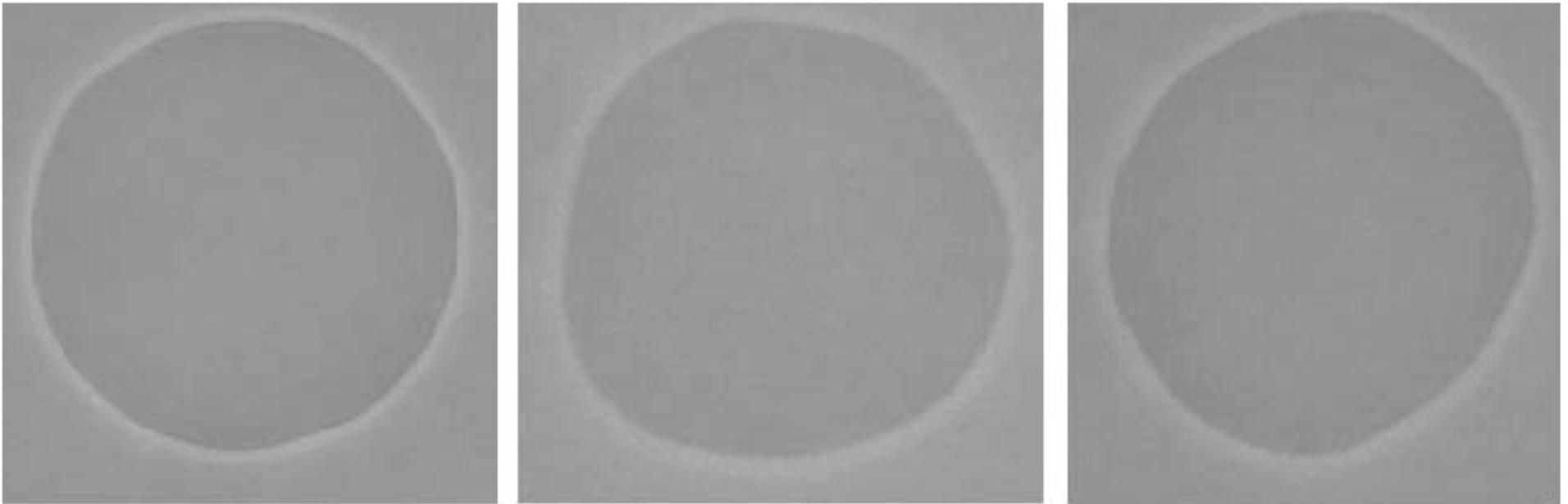
Helfrich (1973)

■ Fluidity



Each monolayer is a 2D fluid

Flexibility of biomembranes



Snapshots of a giant unilamellar vesicle (i.e., a closed bilayer of lipids in water) of diameter 50 μm observed under the microscope at different times

Conclusion

- Thermal fluctuations have a strong impact at the microscopic scale, esp. at the cellular scale
- Importance of comparing the energy scales involved in important cell biology processes to the energy scale $k_B T$ of thermal fluctuations (Boltzmann distribution)
- Many cell biology processes, including DNA base pairing, protein-protein interactions, biopolymer and biomembrane deformations, involve energies larger than $k_B T$, but not by a lot, typically of order 10 to 20 $k_B T$ → stable to thermal fluctuations but readily deformable
- In particular, can be deformed by active processes involving ATP consumption:
Hydrolysis of ATP to ADP releases an energy of 30 kJ/mol, thus for the hydrolysis of one molecule of ATP:

$$\Delta E_{\text{ATP}} \approx 12 k_B T$$

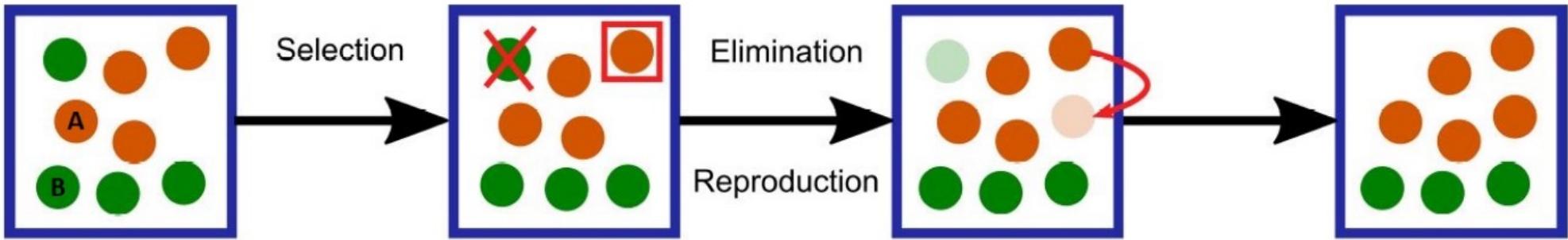
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 - 3.3 Importance of random walks in biological systems

Random walks

- The Moran model in population genetics



Schematic of one step of the Moran process

The population comprises two types of individuals, type A (orange) and type B (green)

Upon one step of the Moran process, involving one birth and one death, how can the number i of mutants possibly vary?

- A. It depends on fitnesses: if the mutant is fitter than the wild-type, i will increase
- B. It can increase or decrease by up to N , or stay constant
- C. It can increase or decrease by up to N , but not stay constant
- D. It can increase or decrease by 1, or stay constant
- E. It can increase or decrease by 1, but not stay constant

To answer, please:

- Connect to <http://tppoll.eu>
- Enter the session ID **bio369**
- Select your answer

Assuming that we start from one mutant ($i=1$) among N individuals, and that there are no new mutations, what are the possible states of the population after a very large number of steps of the Moran process?

- A. The wild type will take over and the mutant will disappear
- B. The mutant will take over and the wild type will disappear
- C. Answer A if the wild type is fitter, answer B if the mutant is fitter
- D. The two types will coexist forever
- E. It depends – A, B and D can all happen
- F. It depends – A and B can happen, but D cannot happen

To answer, please:

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- Enter the session ID **bio369**
- Select your answer

Assuming that we start from no mutant ($i=0$) among N individuals, and that there are no new mutations, what is the probability of fixation of the mutant type?

- A. 0
- B. 1
- C. $1/N$
- D. It depends on fitnesses and on N

To answer, please:

- Connect to <http://tppoll.eu>
- Enter the session ID **bio369**
- Select your answer

Assuming that we start from one **neutral** mutant ($i=1$) among N individuals, what is the probability of fixation of the mutant type in the population?

- A. 0
- B. 1
- C. $1/N$
- D. It depends

To answer, please:

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- Select your answer