Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Übung 8

Vorlesung Bio-Engineering

Frühlingssemester 2021

Part 1. Biopolymers, motility, and migration

Biological Relevance: Cellular microtubule networks are known to play an important role in cellular transport, as well as in providing the propulsive force behind cell division. The role of the microtubule network in driving cell motility remains heavily debated.

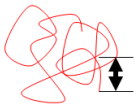
Biotechnological Background: Predicting how biopolymers behave (mechanically) is often critical to predicting protein function.

An important empirical descriptor of biopolymer mechanical behavior is called the "persistence length". This quantity can be measured by visual observation, for instance in electron microscopy experiments.

The **persistence length** is a basic mechanical property quantifying the stiffness of a long polymer.

Informally, for pieces of the polymer that are **shorter** than the persistence length, the molecule behaves rather like a **flexible elastic rod**

while for pieces of the polymer that are much **longer** than the persistence length, the properties **can only be described using statistical mechanics**.



The persistence length of a piece of cooked spaghetti is approximately 5 cm, the persistence length of a DNA molecule is approximately 50 nm.

The persistence length (ξ_p) is directly proportional to the flexural rigidity kf (stiffer filaments are straighter) and inversely proportional to temperature k_BT (colder filaments are straighter). Mechanical analysis shows that the combination κf / kBT is in fact the persistence length ξ_p of the filament:

$$\xi_p = \kappa_f / k_B T$$

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Assignment: Find the maximum pressure exerted on the boundary of a spherical (3D) eukaryotic cell of radius 3 μm by a collection of (for instance, 50) microtubules growing in random directions from the cell's center. Treat the growth mechanism to be a thermal ratchet and assume that the free tubulin dimer concentration in the cell is 100 μM.

- What is the buckling force of a single microtubule?
  - 0.014 pN
  - 1.1 pN
  - 0.37 pN
  - 0.0075 pN
- What is the maximum force that a single microtubule can achieve (assuming the polymer ratchet model) at the stated tubulin dimer concentration?
  - 220 pN
  - 13 pN
  - 5.8 pN
  - 1.6 pN
  - 0.03 pN
- Assuming the stated tubulin concentration, what number of microtubules would be required to balance an extracellular hydrostatic pressure of 0.1Pa?
  - 30
  - 100
  - 800
  - 12'000
- What is the consequence if the persistence length of the MT is doubled to 6 micrometers?
  - Approximately four times the number of MT are needed to generate a similar pressure against the cell wall
  - Approximately twice the number of MT are needed to generate a similar pressure against the cell wall
  - Approximately half the number of MT are needed to generate a similar pressure against the cell wall
  - Approximately one quarter the number of MT are needed to generate a similar pressure against the cell wall
  - It doesn't make a difference, because the maximum pressure on the cell wall depends much more heavily on tubulin concentration

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Important/ Helpful Information:

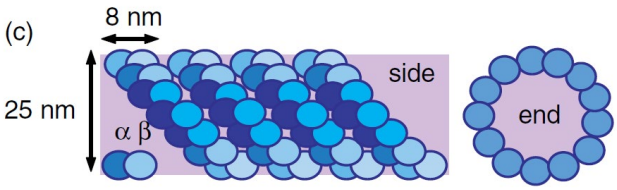

Figure 1. Dimensions of a microtubule assembled from tubulin dimers.

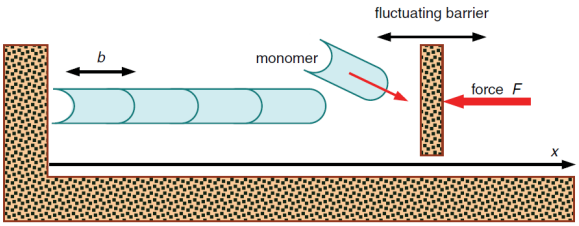

Fig. 11.25 Thermal ratchet model for a filament growing against a fluctuating barrier subject to a force *F*. When added to the filament, each monomer of length *b* does work *Fb* on the barrier.

Figure 2. Schematic of a thermal ratchet.

$$F_{\max} = (k_B T/b) \ln([M] / [M]_c), \qquad (11.28)$$

Figure 3. Equation for maximum force that can be generated at the end of thermal ratchet. The values depend on monomer concentration.

Experimental observations of persistence length for microtubules is on the order of 3µm
Boltzman's constant: (1.381×10^{-23} m^2 kg s^{-2} K^{-1})

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Table 11.1 Samples of measured values for rate constants of actin filaments (Pollard, 1986) and microtubules (Walker *et al.*, 1988); units of $(\mu M \cdot s)^{-1}$ for k_{on}, s^{-1} for k_{off}, and μM for $[M]_c$

Monomer in solution	k_{on}+ (plus end)	k_{off}+ (plus end)	k_{on}^- (minus end)	k_{off}^- (minus end)	$[M]_c$+	$[M]_c^-$
Actin						
ATP-actin	11.6±1.2	1.4±0.8	1.3±0.2	0.8±0.3	0.12±0.07	0.6±0.17
ADP-actin	3.8	7.2	0.16	0.27	1.9	1.7
Microtubules						
growing (GTP)	8.9±0.3	44±14	4.3±0.3	23±9	4.9±1.6	5.3±2.1
rapid disassembly	0	733±23	0	915±72	not applicable	

Notes. The actin measurements vary by a factor of two or more with the solute concentration (for a more complete compilation, see Sheterline *et al.*, 1998). The growth mode of microtubules is measured with GTP-tubulin, while rapidly retreating microtubules are presumably GDP-tubulin.

The buckling force of a polymeric segment (length L_C) can be described using the following relationship:

$$F_{buckle} = \pi^2 \kappa_f / L_c^2$$

Part 2: Additional Questions on the Cytoskeleton

2.1 **Which of the following cytoskeletal elements is directly involved in active protein transport?**

a) Integrins.
b) Microtubules emanating from the centrosome.
c) Actin filaments at the cell leading edge
d) Focal adhesion anchored myosin II.
e) All of the above.

2.2 **Protrusive forces enabling advance of the cell leading edge is mostly generated by**

a) Polymerization of actin biopolymer chains.
b) Actomyosin motors anchored at focal adhesions.
c) Dynamic regulation of the cell membrane stiffness.
d) All of the above
e) None of the above

2.3 **Which of the following molecular motor / function pairs are/is correct?**

a) Myosin / directional transport on the microtubule network
b) Kinesin / tension applied to the actin network
c) Dynesin / directional transport on the microtubule network
d) All of the above motor/function pairs are correct
e) None of the above motor/function pairs are correct

Part 3. Cell cycle & Mitosis

3.1 **The goal of the mitosis (cell division) is to produce daughter cells, which ….**

a) are genetic identical with their mother cell.
b) have the same number of chromosomes as the mother cell, but different genetic dispositions.
c) have half of the chromosomes as their mother cell.
d) No answer is correct.
d) All answers are correct.

3.2 **Sister chromatids …..**

a) are produced by the DNA replication.
b) are connected via the Centromere before cell division.
c) are separated during Mitosis.
d) are identical copies of DNA.
e) None of the above
e) All of the above

3.3 **How many Chromosomes does a human cell have during the G1 phase?**

a) 23
b) 46
c) 92
d) 184

3.4 **«Cytokinesis» is …**

a) The division of nucleus.

b) The division of the cytoplasm.
c) the replication of chromosomes.
d) None of the above.
e) All of the above.

3.5 **Which one of the following statements is <u>not</u> correct?**
a) In the Prophase the chromosomes condense.
b) The chromosomes align at the equator of the cell during the Metaphase.
c) During the Telophase the Chromosomes decondense.
d) The nuclear envelope decays during the Metaphase.

Part 4. Stem cells

4.1 **Which one of the following statements is <u>not</u> correct about embryonic stem cells?**
a) Embryonic stem cells are totipotent.
b) Embryonic stem cells can differentiate into all cell types.
c) Embryonic stem cells are cells derived from the early embryo
d) Adult stem cells are better suited to develop basic mechanisms of organ and tissue development as embryonic stem cells.