LECTURE 1

BB 101

MODULE: *PHYSICAL BIOLOGY*

Ambarish Kunwar

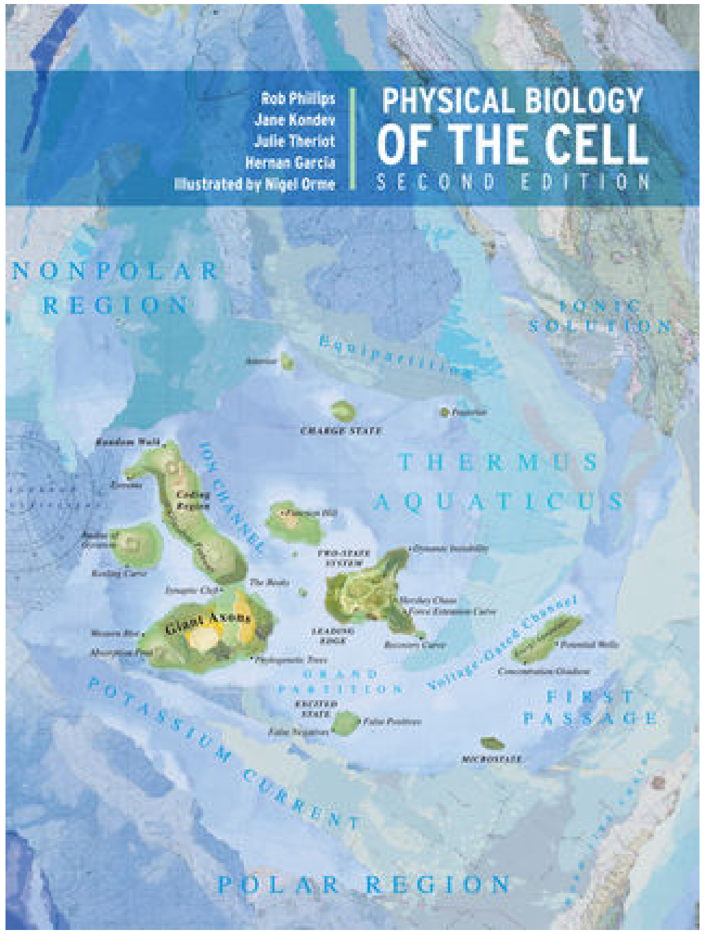
Lab No. 204
Department of Biosciences and Bioengineering
IIT Bombay

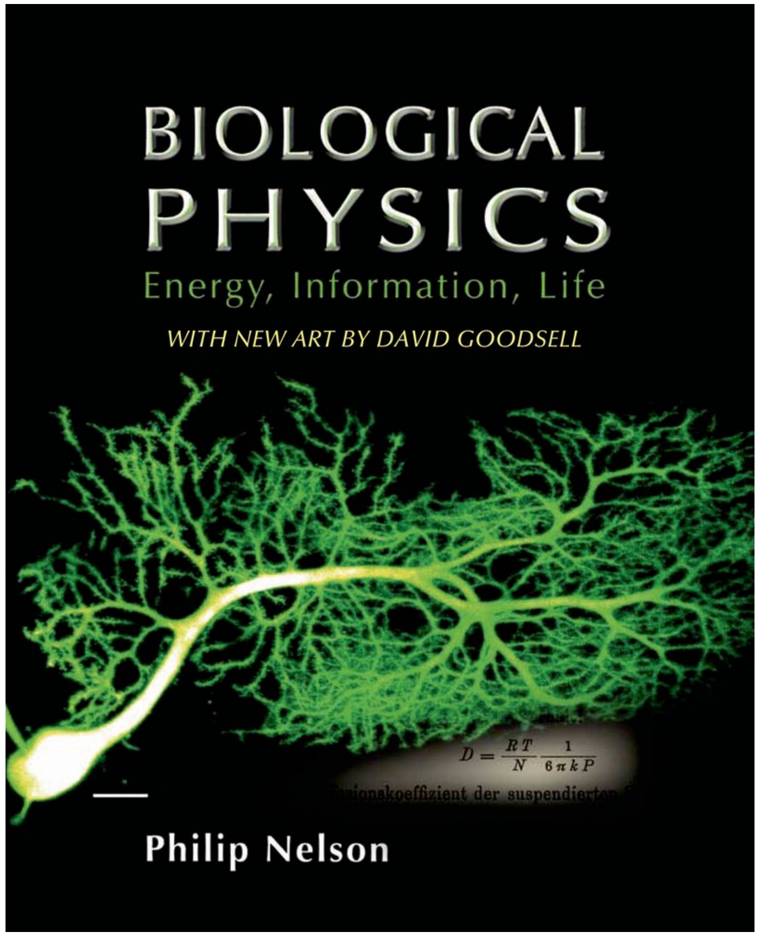
akunwar@iitb.ac.in

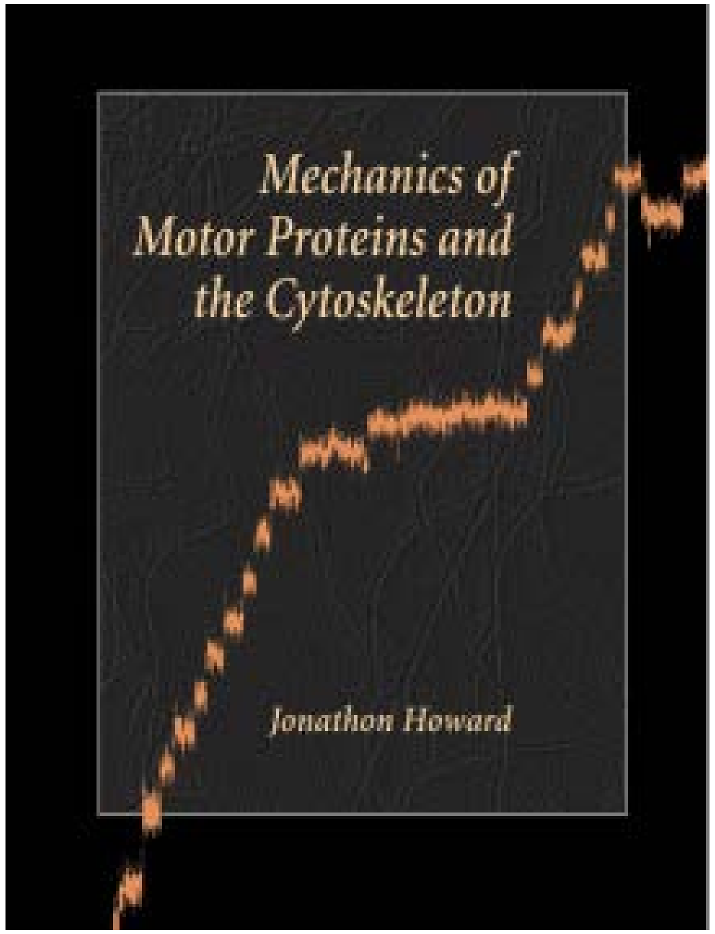
http://www.bio.iitb.ac.in/~akunwar/

Reference Books

Following books have most of the Physical Biology Module content:







1. **Physical Biology of the cell, R. Phillips, J. Kondev, J. Theriot, H. Garcia (Publisher: Garland Science)**

2. **Biological Physics, Philip Nelson (Publisher: W. H. Freeman)**

3. **Mechanics of Motor Proteins and the Cytoskeleton, Jonathan Howard (Publisher: Sinauer Associates Inc.)**

A topic guide for each lecture will be provided

LECTURES

Lecture No.	Date	Day	Batch		Venue
1	19-9-2017	TUE	D2		LA 102
1	20-9-2017	WED		D4	LA 102
2	22-9-2017	FRI	D2		LA 102
2	22-9-2017	FRI		D4	LA 102
3	26-9-2017	TUE	D2		LA 102
3	27-9-2017	WED		D4	LA 102
4	29-9-2017	FRI	D2		LA 102
4	29-9-2017	FRI		D4	LA 102
5	03-10-2017	TUE	D2		LA 102
5	04-10-2017	WED		D4	LA 102
	04-10-2017	**WED**	**QUIZ**		
6	06-10-2017	FRI	D2		LA 102
6	06-10-2017	FRI		D4	LA 102
7	10-10-2017	TUE	D2		LA 102
7	11-10-2017	WED		D4	LA 102

D2 Batch:
Tue: 03:30 PM - 05:00 PM
Fri: 03:30 PM - 05:00 PM

D4 Batch:
Wed: 11:00 AM - 12:30 PM
Fri: 11:00 AM - 12:30 PM

TUTORIALS

Tutorial No.	Date	Day	Batch		4 Venue
1	21-09-2017	THU	D2		D2-T1 (LT304), D2-T2 (LT305), D2-T3 (LT306), D2-T4 (LT205), D2-T5 (LT206)
2	28-09-2017	THU	D2		
3	05-10-2017	THU	D2		
4	12-10-2017	THU	D2		
1	21-09-2017	THU		D4	D4-T1 (LT304), D4-T2 (LT305), D4-T3 (LT306), D4-T4 (LT205), D4-T5 (LT206)
1	28-09-2017	THU		D4	
2	05-10-2017	THU		D4	
3	12-10-2017	THU		D4	

D2 (T1, T2, T3, T4, T5) Batch: THU 08:30-9:25 AM

D4 (T1, T2, T3, T4, T5) Batch: THU 02:00-2:55 AM

You learned about many interesting biological phenomena in previous module

What you are going to learn …

Physical Biology or Biophysics

A bridge between
Biology and Physics

Source: http://www.biophysics.org/Education/WhatisBiophysics/tabid/2287/Default.aspx

Biology

- Biology studies life in its variety and complexity

- Biological studies range from level of molecules and cells to organisms and ecosystems

Source: http://www.biophysics.org/Education/WhatisBiophysics/tabid/2287/Default.aspx

Physics

- On the other hand, physics looks for mathematical laws of nature

- Make detailed predictions about phenomenon that drive the systems

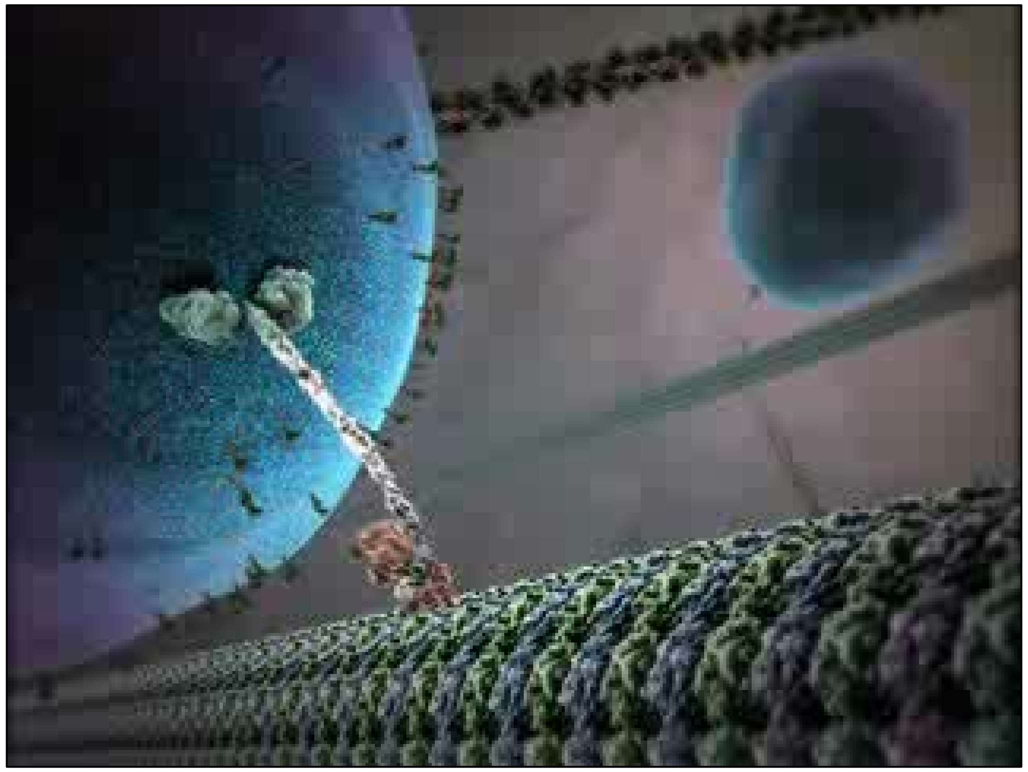
Source: http://www.biophysics.org/Education/WhatisBiophysics/tabid/2287/Default.aspx

Physical Biology or Biophysics

Look at the biological phenomena and analyze them with math and physics to gain important insights

Why our bodies need protein machines (molecular motors) for transportation?

Millions of times smaller than everyday machines, molecular machines work on the same principles. They use energy to do work.



How do these biological nano-machines work?

Insights gained may help you to design artificial nano-machines

Video Source:http://multimedia.mcb.harvard.edu/
Figure Source: http://www.wpclipart.com/working/vehicles/dump_truck/dump_truck_green.png.html

Figure Source: http://edition.cnn.com/2016/10/05/world/nobel-prize-2016-chemistry-molecular-machines/index.html

for the design and synthesis of molecular machines

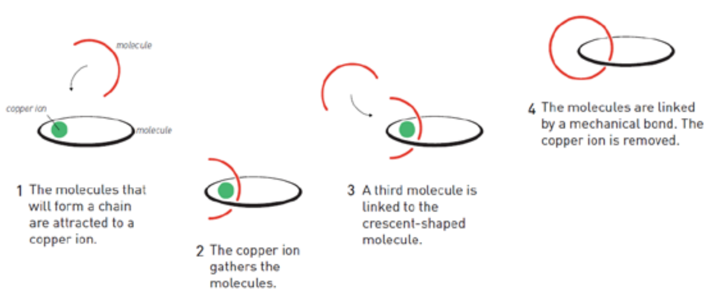


Figure 1. Jean-Pierre Sauvage used a copper ion to interlock molecules using a mechanical bond.

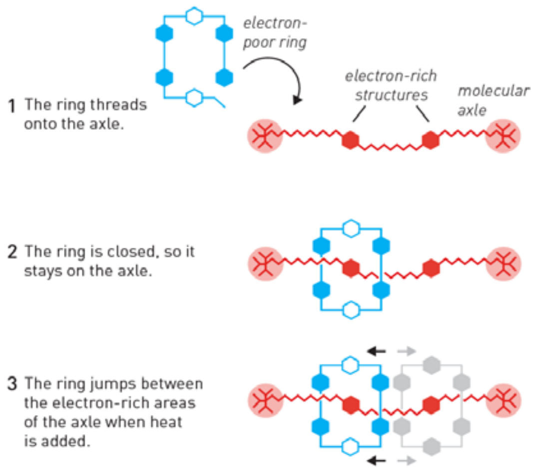


Figure 3. Fraser Stoddart created a molecular shuttle that could move along an axle in a controlled manner.

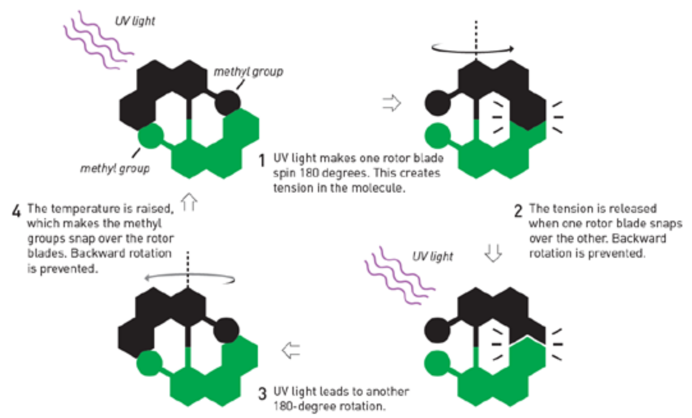


Figure 6. When Ben Feringa created the first molecular motor, it was was mechanically constructed to spin in a particular direction. His research group has optimised the motor so that it now spins at 12 million revs per second.

Figure 2a. Jean-Pierre Sauvage has created a molecular trefoil knot. This symbol is found in Celtic crosses, runestones, depictions of Thor's hammer (Mjölnir) and, in Christianity, it symbolises the Holy Trinity. b. Fraser Stoddart has produced molecular Borromean rings. The Italian Borromeo family used the symbol on their shield. It is also found on Old Norse picture stones and has symbolised the Holy Trinity. c. Stoddart and Sauvage have made a molecular version of Solomon's knot, a symbol of King Solomon's wisdom. It has been frequently used in Islam and is found in Roman mosaics.

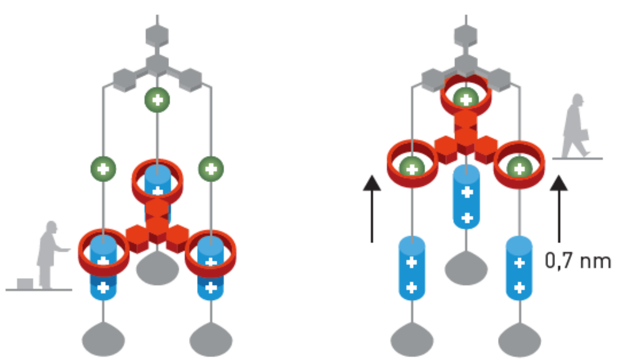


Figure 4. Fraser Stoddart's molecular lift.

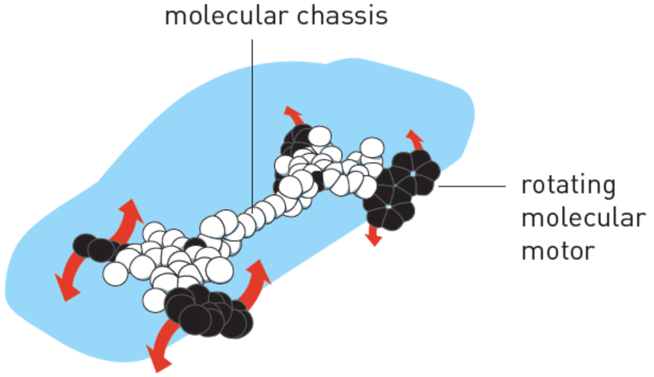
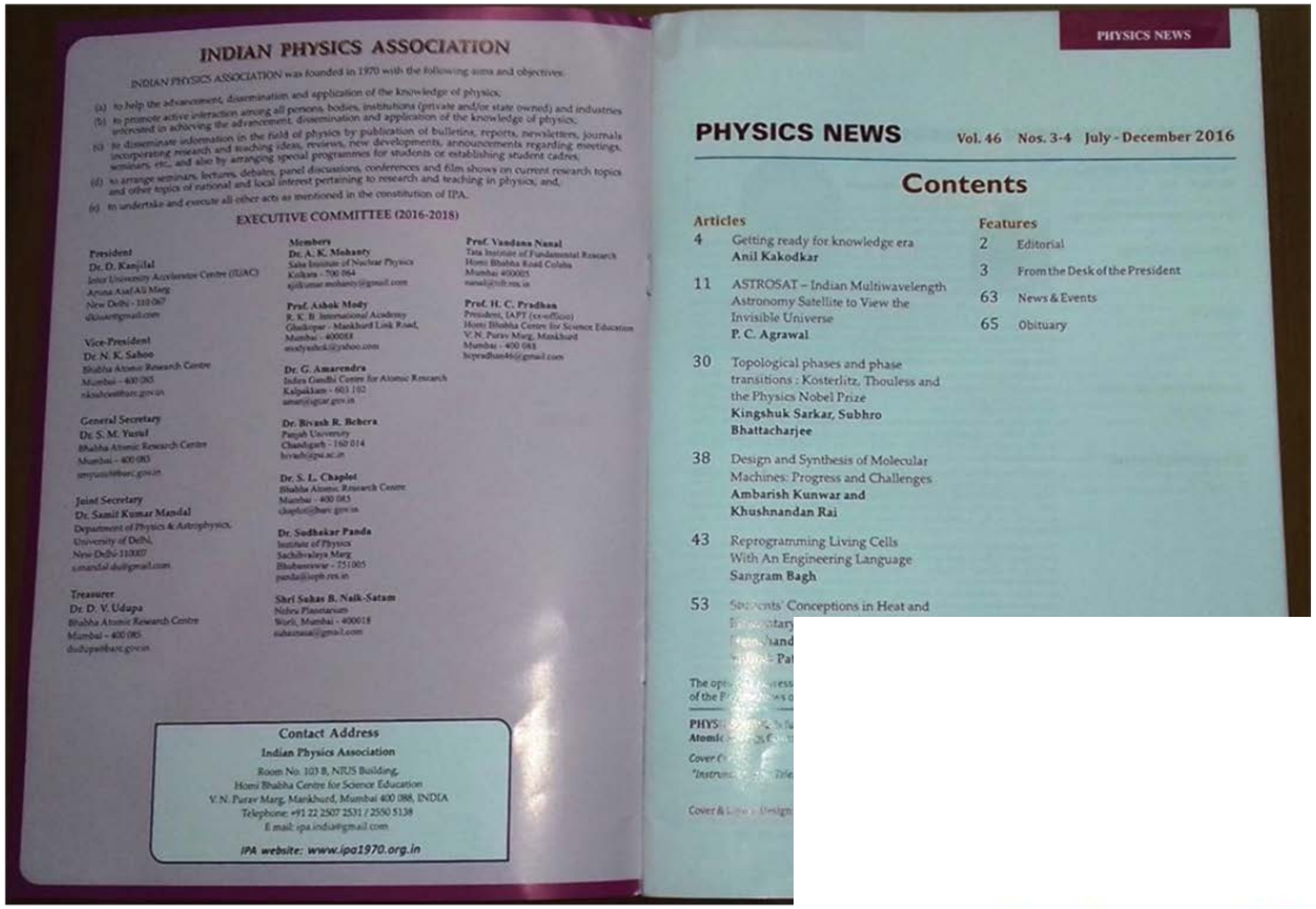


Figure 7. Ben Feringa's four-wheel drive nanocar.

Figure Source: https://www.nobelprize.org/nobel_prizes/chemistry/laureates/2016/popular-chemistryprize2016.pdf



INDIAN PHYSICS ASSOCIATION

INDIAN PHYSICS ASSOCIATION was founded in 1970 with the following aims and objectives:

(a) to help the advancement, dissemination and application of the knowledge of physics;
(b) to promote active interaction among all persons, bodies, institutions (private and/or state owned) and industries interested in achieving the advancement, dissemination and application of the knowledge of physics;
(c) to disseminate information in the field of physics by publication of bulletins, reports, newsletters, journals incorporating research and teaching ideas, reviews, new developments, announcements regarding meetings, seminars, etc., and also by arranging special programmes for students or establishing student cadres;
(d) to arrange seminars, lectures, debates, panel discussions, conferences and film shows on current research topics and other topics of national and local interest pertaining to research and teaching in physics; and,
(e) to undertake and execute all other acts as mentioned in the constitution of IPA.

EXECUTIVE COMMITTEE (2016-2018)

President
Dr. D. Kanjilal
Inter University Accelerator Centre (IUAC)
Aruna Asaf Ali Marg
New Delhi - 110 067

Vice-President
Dr. N. K. Sahoo
Bhabha Atomic Research Centre
Mumbai - 400 085

General Secretary
Dr. S. M. Yusuf
Bhabha Atomic Research Centre
Mumbai - 400 085

Joint Secretary
Dr. Samit Kumar Mandal
Department of Physics & Astrophysics,
University of Delhi,
New Delhi 110007

Treasurer
Dr. D. V. Udupa
Bhabha Atomic Research Centre
Mumbai - 400 085

Members
Dr. A. K. Mohanty
Saha Institute of Nuclear Physics
Kolkata - 700 064

Prof. Ashok Mody
R. K. B. International Academy
Ghatkopar - Mankhurd Link Road,
Mumbai - 400088

Dr. G. Amarendra
Indira Gandhi Centre for Atomic Research
Kalpakkam - 603 102

Dr. Bivash R. Behera
Panjab University
Chandigarh - 160 014

Dr. S. L. Chaplot
Bhabha Atomic Research Centre
Mumbai - 400 085

Dr. Sudhakar Panda
Institute of Physics
Sachivalaya Marg
Bhubaneswar - 751005

Shri Suhas B. Naik-Satam
Nehru Planetarium
Worli, Mumbai - 400018

Prof. Vandana Nanal
Tata Institute of Fundamental Research
Homi Bhabha Road Colaba
Mumbai 400005

Prof. H. C. Pradhan
President, IAPT (ex-officio)
Homi Bhabha Centre for Science Education
V. N. Purav Marg, Mankhurd
Mumbai - 400 088

Contact Address
Indian Physics Association
Room No. 103 B, NIUS Building,
Homi Bhabha Centre for Science Education
V. N. Purav Marg, Mankhurd, Mumbai 400 088, INDIA
Telephone: +91 22 2507 2531 / 2550 5138
E mail: ipa.india@gmail.com

IPA website: www.ipa1970.org.in

PHYSICS NEWS

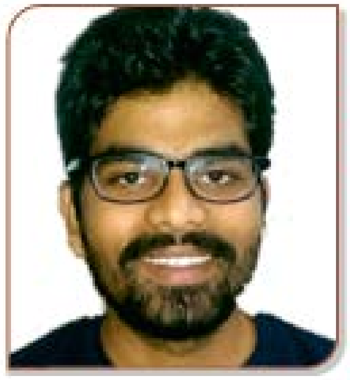
PHYSICS NEWS Vol. 46 Nos. 3-4 July - December 2016

Contents

Design and Synthesis of Molecular Machines: Progress and Challenges

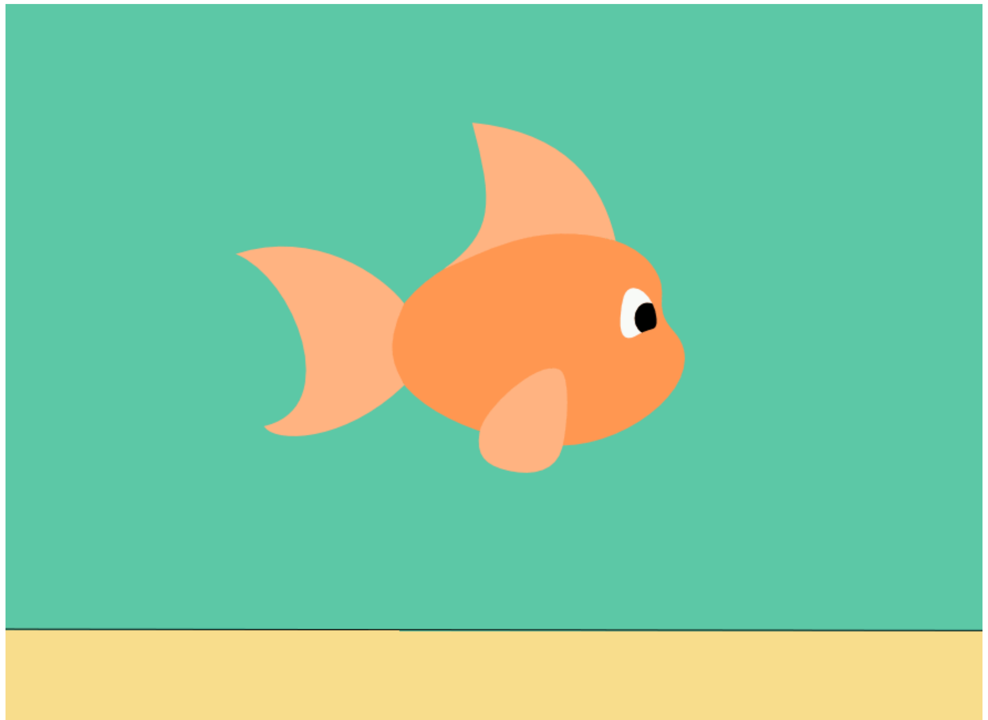
Ambarish Kunwar and Khushnandan Rai

Department of Biosciences and Bioengineering,
Indian Institute of Technology Bombay, Mumbai 400076, India
Email: akunwar@iitb.ac.in



The Nobel Prize in Chemistry 2016 was awarded jointly to Jean-Pierre Sauvage, Sir J. Fraser Stoddart and Bernard (Ben) L. Feringa for the design and synthesis of molecular machines. They have developed molecules and machines with controllable movements which can perform work when energy is supplied to them. We hope that these tiny molecular machines will most likely revolutionize the development of various new materials and technologies in the twenty first century, in a manner similar to the Industrial Revolution in the nineteenth century brought about by their macroscopic counterparts such as steam and internal combustion engines. This article summarizes the groundbreaking work done by them, as well as some challenges ahead from a physicist's perspective, and how they can be handled.

How swimming of a bacteria is different from swimming of a fish?



What type of forces play dominant role in bacterial swimming (inertial or something else)?

Insights gained may help you to design artificial micro-swimmers

Video Source:http://multimedia.mcb.harvard.edu/
Figure Source: http://cliparts.co/clipart/7800

Thermal energy can shake & bend objects a microscopic scales

How DNA is stored inside nucleus?
Can thermal energy bend DNA into loops for storage?

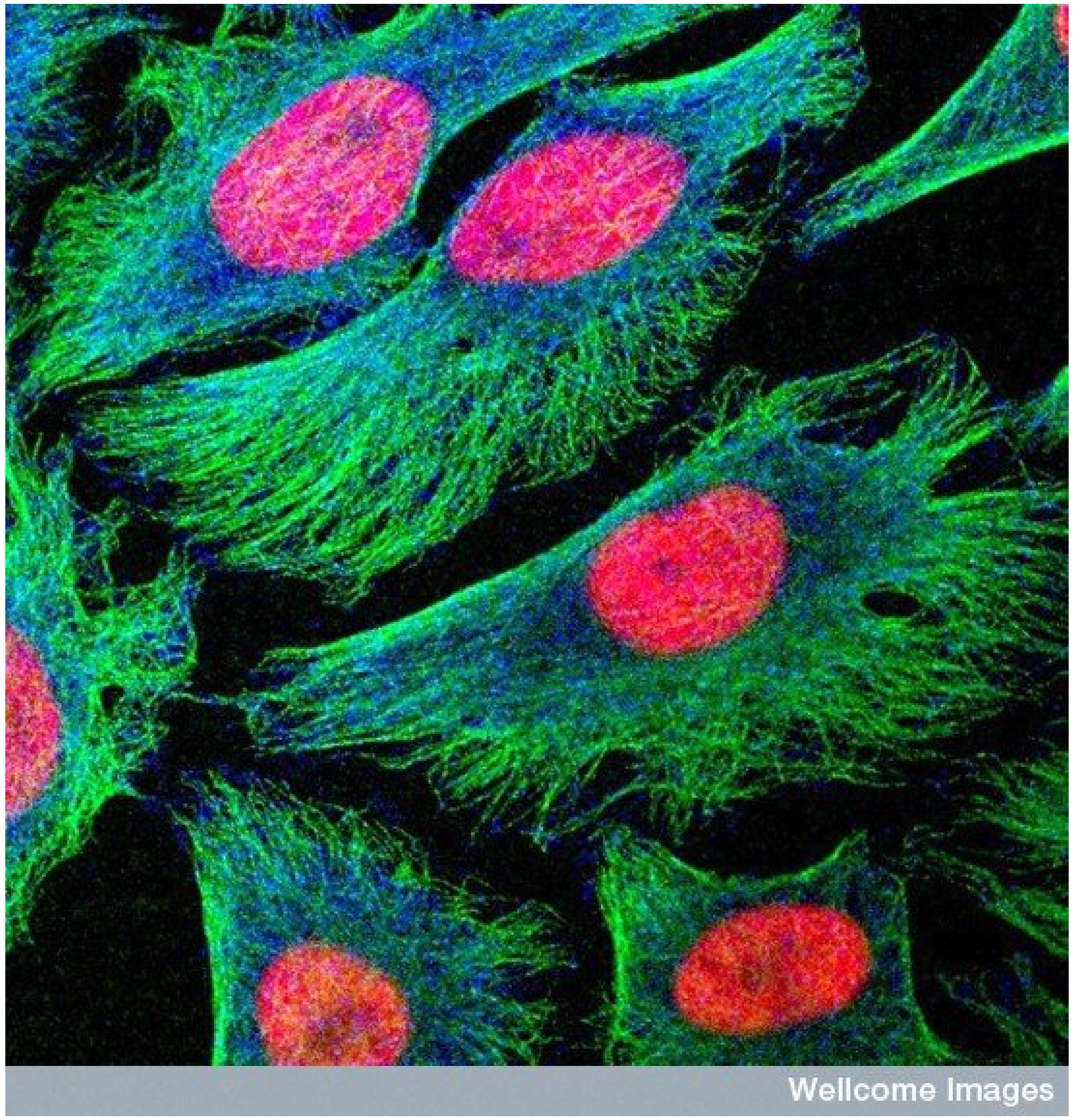
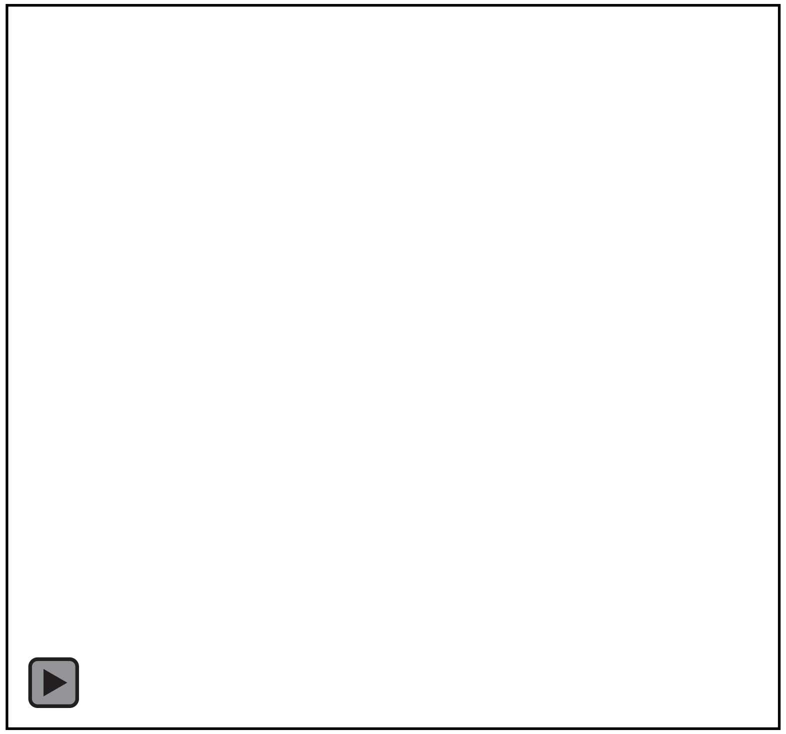
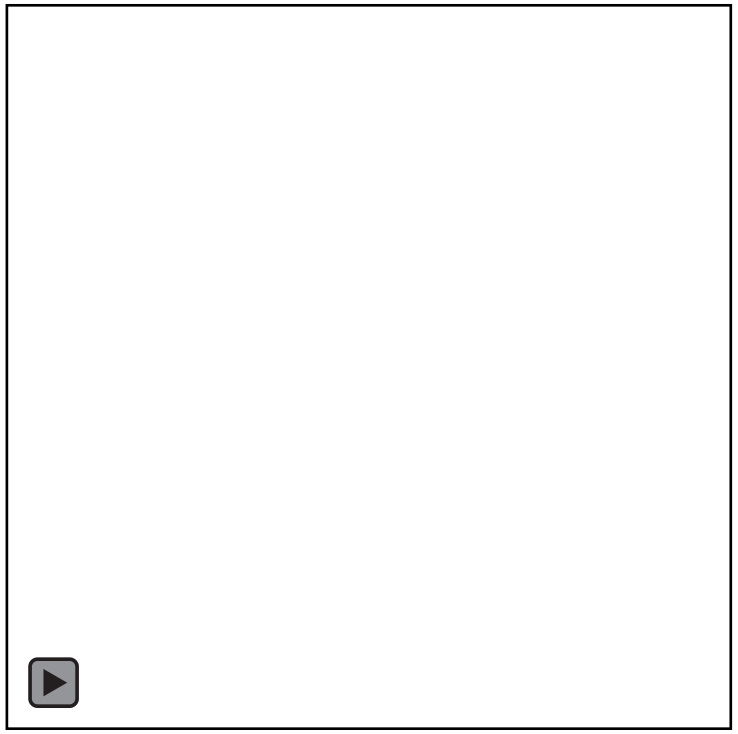


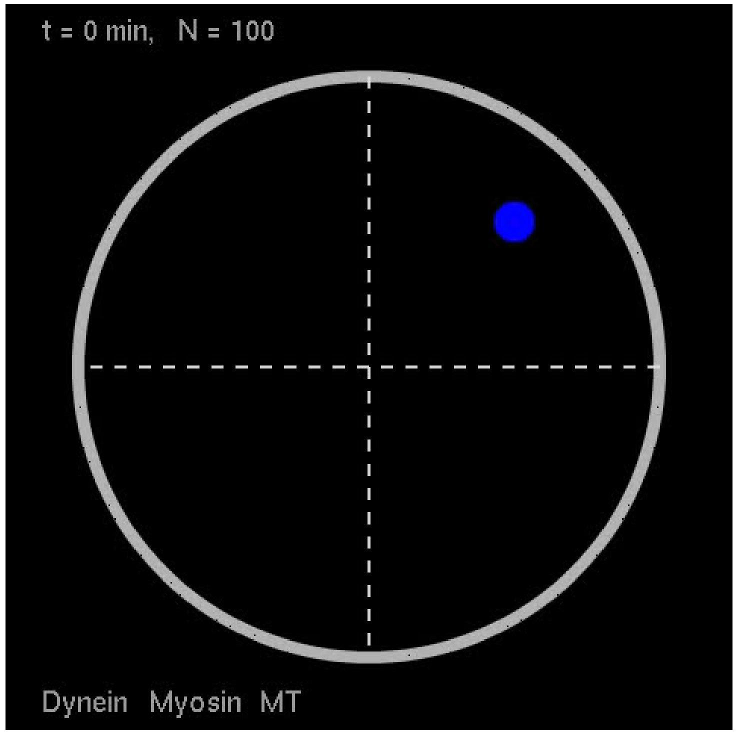
Figure Source: http://www.cellimagelibrary.org/images/38912

Biofilaments: DNA, Microtubule and Actin

Why some bio-filament can generate pushing forces







Video Sources :http://multimedia.mcb.harvard.edu/,
http://www.molbiolcell.org/content/21/24/4418.full

Protein perform their function by folding into different shapes

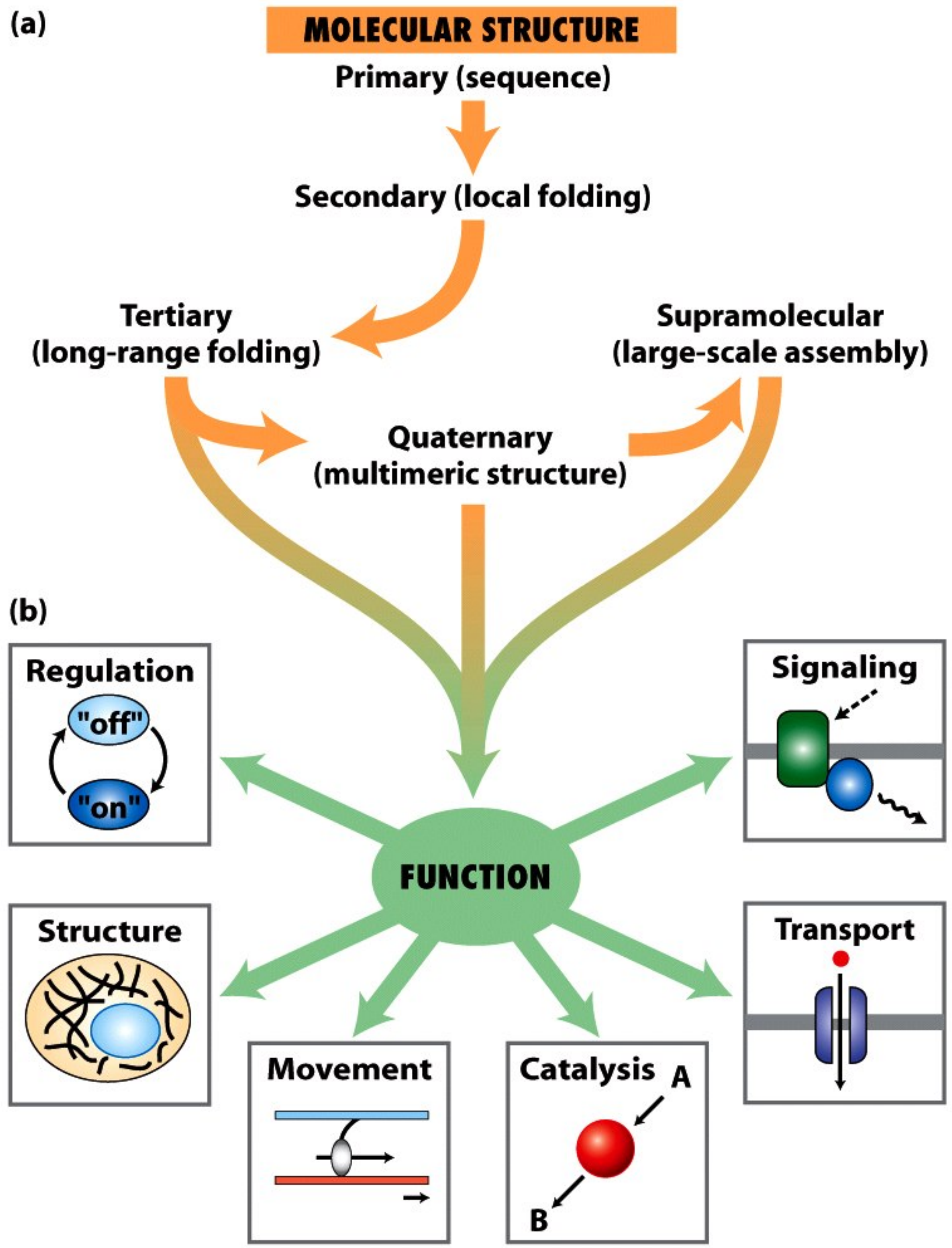


Figure 3-1
Molecular Cell Biology, Sixth Edition
© 2008 W. H. Freeman and Company

How structure of various proteins is decided?

Video Source:http://multimedia.mcb.harvard.edu/

In this part of the course…

- We will attempt to provide a quantitative description of a few biological phenomena

- Why biological problems are among the most exciting science problems and most challenging engineering problems

Let's start with proteins!!!

Physical Properties of a globular protein

Property	Value
Mass	166×10^{-24} kg
Density	1.38×10^{3} kg/m^3
Volume	120 nm^3
Radius	3 nm
Drag coefficient[a]	60 pN·s/m
Diffusion coefficient[a]	67 μm^2/s
Average speed[b]	8.6 m/s

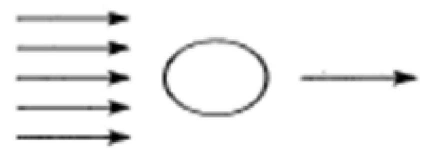
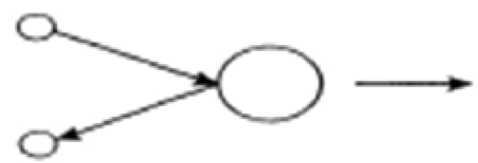
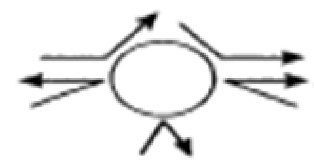
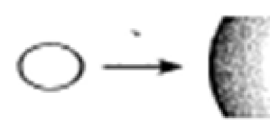
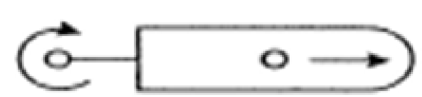
Magnitude of different forces acting on a proteins

Source: Mechanics of Motor Proteins and the Cytoskeleton, Jonathan Howard

What is force?

- Force is a push or pull
- Effect on free object (accelerate) and Effect on constrained object (deform)
- Net force is sum of all forces irrespective of their origin
- SI Unit of Force Newton
- What is 1N (weight of ___ gram object)
- Forces at single molecule level are measured in pN
- How small is 1 pN?

Forces acting on a protein molecule

Type of force	Diagram	Approximate magnitude
Elastic		1–100 pN
Viscous		1–1000 pN
Collisional		10^{-12} to 10^{-9} pN for 1 collision/s
Thermal		100–1000 pN
Gravity		10^{-9} pN
Centrifugal		$< 10^{-3}$ pN
Magnetic		$<< 10^{-6}$ pN

Source: Mechanics of Motor Proteins and the Cytoskeleton, Jonathan Howard

Protein and other biomolecules

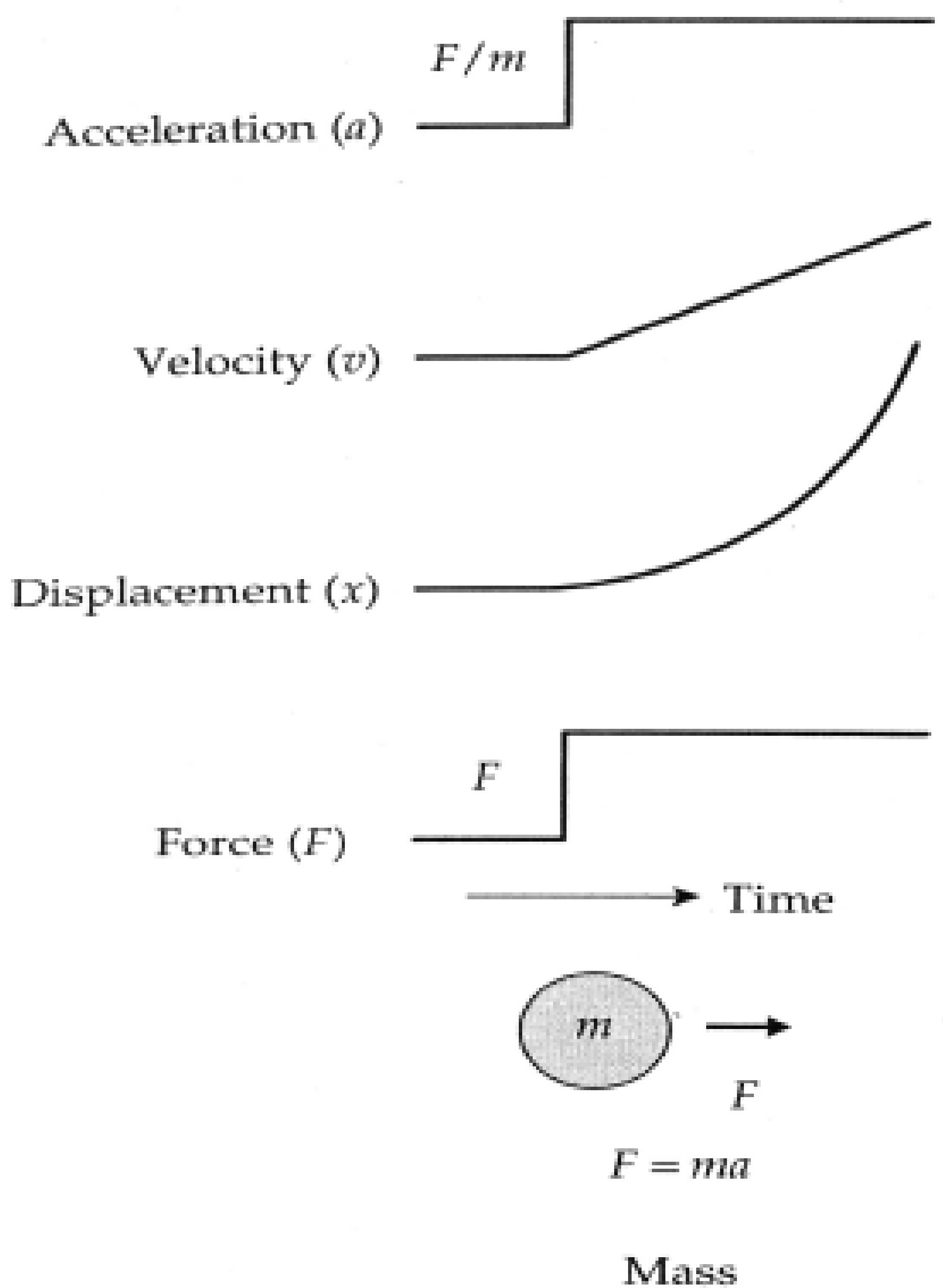
- Protein and other biomolecules are so tiny that inertial forces are very small in comparison to viscous forces due to surrounding medium

- Most of the mechanics discussed in standard school Physics text books is irrelevant at molecular and cellular levels as inertial forces are small

- Since effect of gravity can be ignored
- Oscillatory motions such as of pendulum and planets, which occupy so much of mechanics textbooks, simply do not occur at level of single molecule

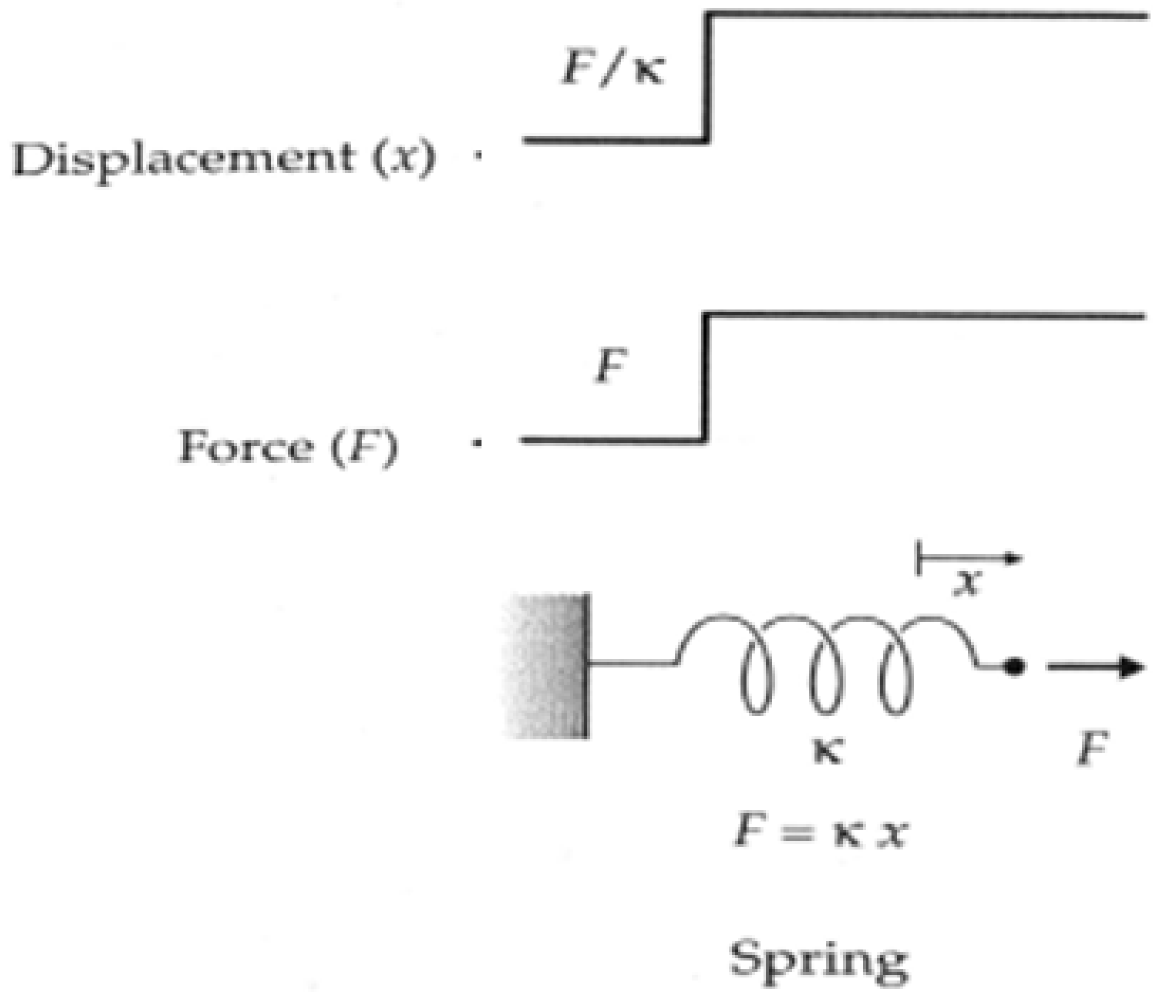
- However, we can still use mechanics to understand biological systems
- Some biological systems can be modelled as combinations of three fundamental mechanical elements mass, springs and <u>dashpots</u>
- Let’s review their properties

Motion of Mechanical element: Mass



Source: Mechanics of Motor Proteins and the Cytoskeleton, Jonathan Howard

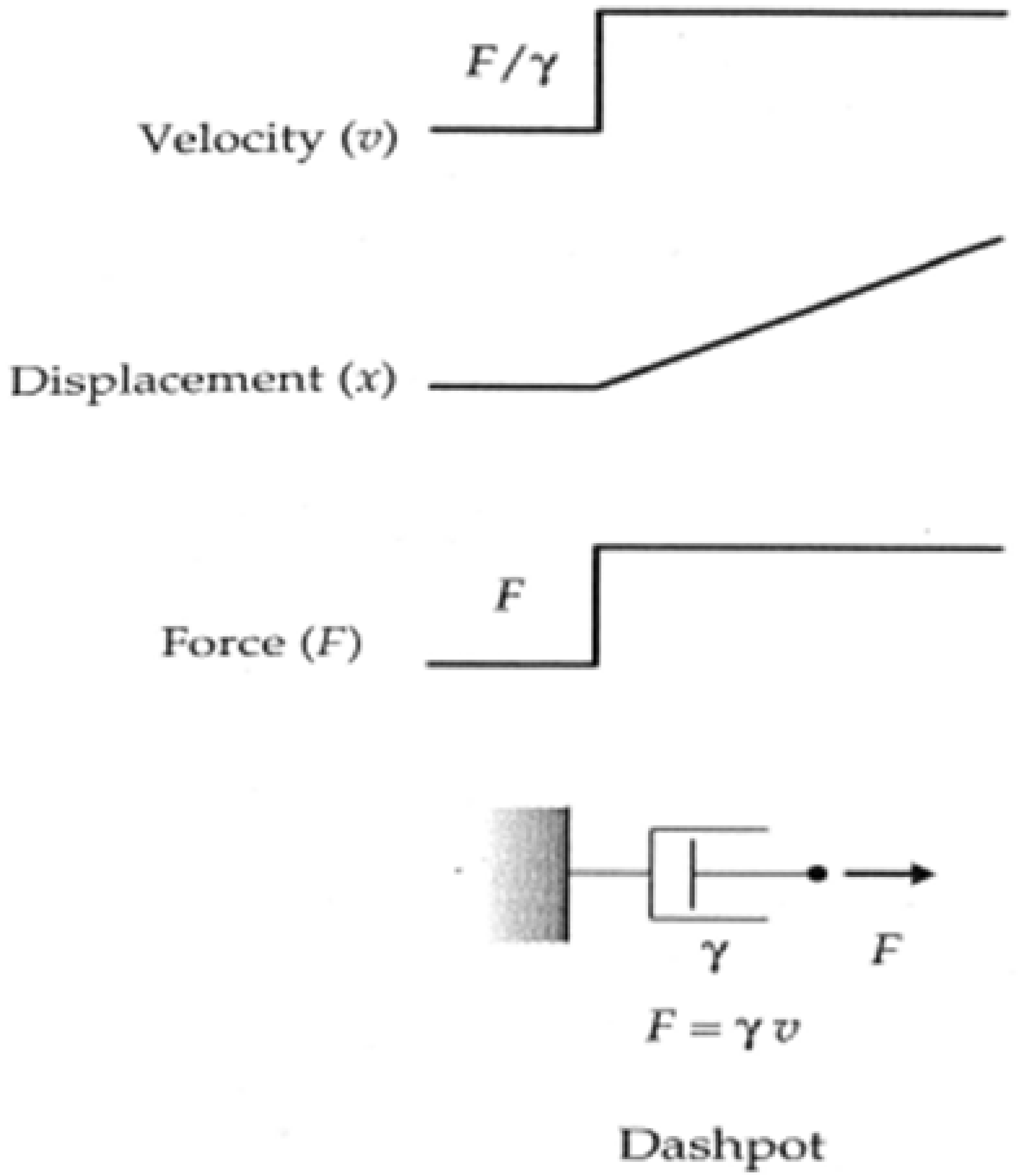
Motion of Mechanical element: Spring



Source: Mechanics of Motor Proteins and the Cytoskeleton, Jonathan Howard

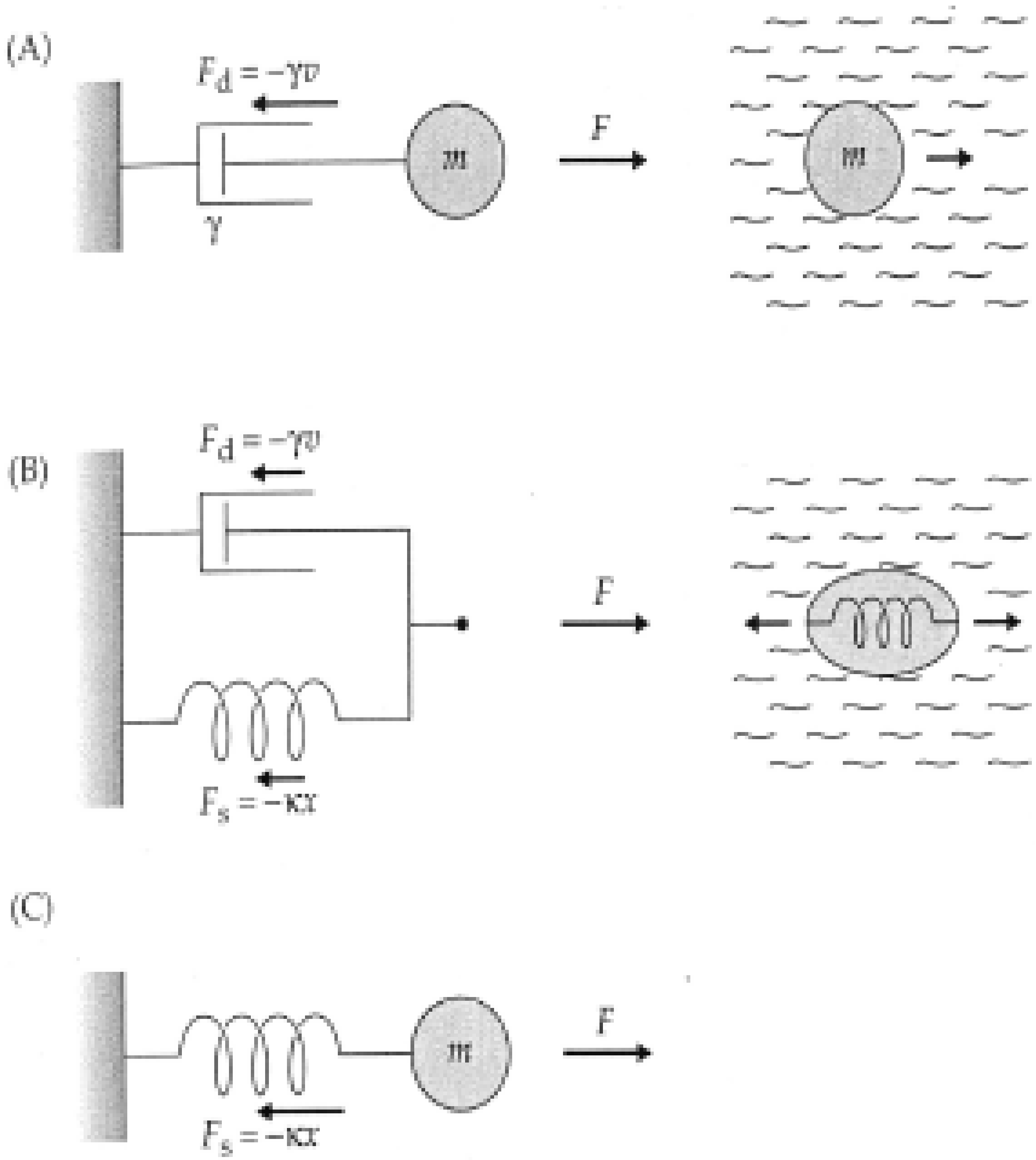
Motion of Mechanical element: Dashpot

- Responds to force by elongating at constant velocity
- No net force, external force is balanced by drag force
- Dashpot model is used to describe how an object move in fluid
- Strategy: model submerged object connected to dashpot)



Source: Mechanics of Motor Proteins and the Cytoskeleton, Jonathan Howard

Motion of combination of mechanical elements



Object damped by viscous fluid

Low mass object deformed in viscous fluid

Undamped objects

Source: Mechanics of Motor Proteins and the Cytoskeleton, Jonathan Howard

Motion of combination of mechanical elements

(A) Mass & Dashpot

$$m\frac{dv}{dt} + \gamma v = F$$

$$v(t) = \frac{F}{\gamma}[1 - exp(-\frac{t}{\tau})]$$

(B) Spring & Dashpot

$$\gamma\frac{dx}{dt} + \kappa x = F$$

$$x(t) = \frac{F}{\kappa}[1 - exp(-\frac{t}{\tau})]$$

(c) Mass & Spring

$$m\frac{d^2x}{dt^2} + \kappa x = F$$

$$x(t) = \frac{F}{\kappa}[1 - cos(\omega t)]$$

Source: Mechanics of Motor Proteins and the Cytoskeleton, Jonathan Howard

Inertia of moving bacterium

Consider a bacterium swimming through water at a speed of 10 micron/s. How long bacterium will continue to move after its flagellar motors stop working? Assume bacteria to be a sphere of radius 0.5 micron with density 5 times that of water (5×1000 kg/m^3).

Time constant $\tau \sim 0.28 \times 10^{-6}$s $\sim 0.28\mu$s
Distance travelled $\sim 0.028 \times 10^{-10}$ m ~ 0.028 Angstrom

Video Source: https://www.youtube.com/watch?v=6bEacq-ow50

Sedimentation of a 100 kDa globular protein

Consider the sedimentation of a globular protein of radius 3nm and mass 100 KDa, initially right below the surface, in an Eppendorf tube filled with water upto 1cm height. How much time it would take for this protein to sediment under the effect of gravity?

Answer: ~1.2 x 10^9 seconds ~ 38.05 years

Figure Source: http://www.nature.com/scitable/content/eppendorf-tube-6488888

Why biologists need ultra-centrifuges

Optima™ XPN

Up to 100,000 RPM
Up to 802,000 x *g*
Floor Preparative

Optima™ XE

Up to 100,000 RPM
Up to 802,000 x *g*
Floor Preparative

Optima™ MAX-XP

150,000 RPM
1,019,000 x *g*
Tabletop

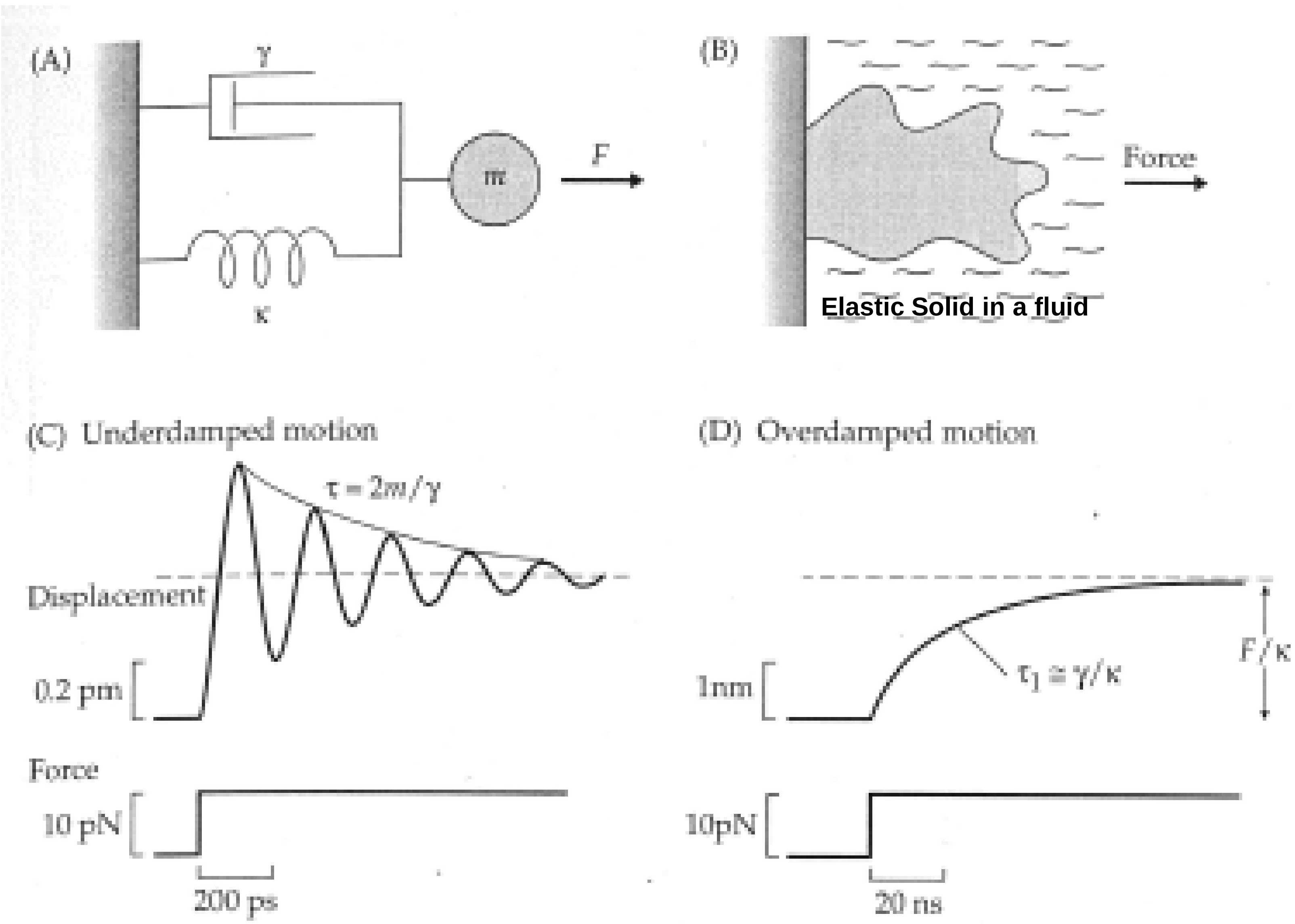
Optima™ MAX-TL

120,000 RPM
627,000 x *g*
Tabletop

Ultracentrifuges are very expensive. Typical prices $150000

https://www.beckmancoulter.com/wsrportal/wsr/research-and-discovery/products-and-services/centrifugation/index.htm

Motion of combination of mechanical elements: Mass and Spring with Damping



Inertial forces
(tend to produce oscillations)

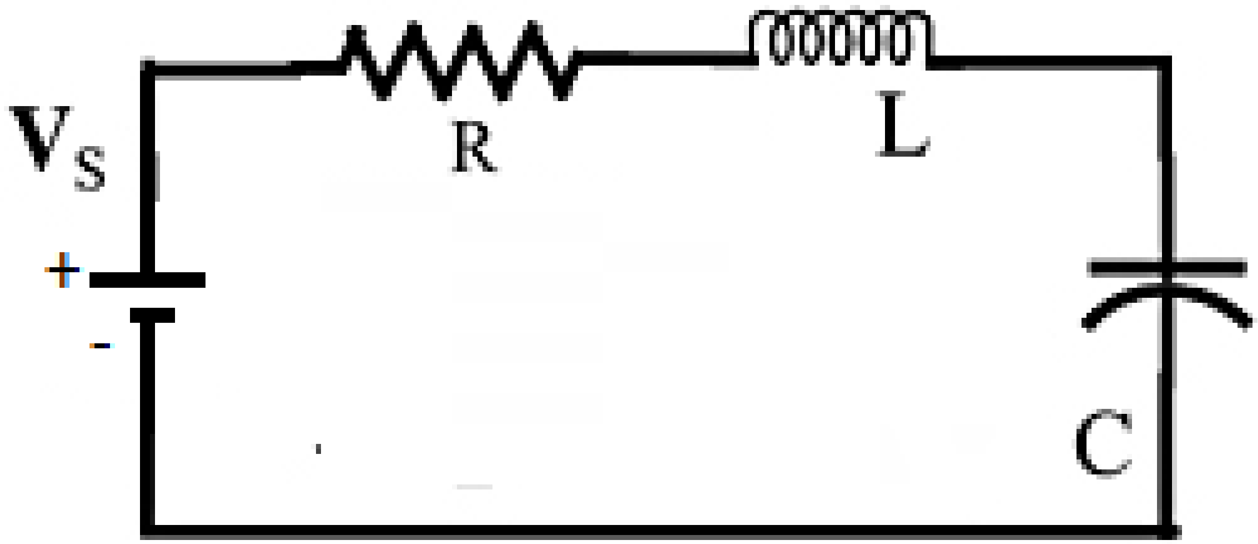
viscous forces
(tend to damp the oscillations out)

Underdamped: $\gamma^2 < 4m\kappa$

Overdamped: $\gamma^2 > 4m\kappa$

Source: Mechanics of Motor Proteins and the Cytoskeleton, Jonathan Howard

Similarity with series LCR circuit



Homework

Derive expression for x(t) for overdamped, underdamped and critically damped motion

The equation of motion:

$$m\frac{d^2x}{dt^2} + \gamma\frac{dx}{dt} + \kappa x = F$$

Underdamped Motion ($\gamma^2 < 4m\kappa$)

$$x(t) = \frac{F}{\kappa}\left[1 - \exp\left(-\frac{t}{\tau}\right)\frac{\sin(\omega t + \phi)}{\sin\phi}\right]$$

where $\tau = \frac{2m}{\gamma}$, $\omega^2 = \omega_0^2 - \frac{1}{\tau^2}$, $\omega_0^2 = \frac{\kappa}{m}$, $\tan\phi = \omega\tau$

Overdamped Motion ($\gamma^2 > 4m\kappa$)

$$x(t) = \frac{F}{\kappa}\left[1 - \frac{\tau_1}{\tau_1 - \tau_2}\exp\left(-\frac{t}{\tau_1}\right) + \frac{\tau_2}{\tau_1 - \tau_2}\exp\left(-\frac{t}{\tau_2}\right)\right]$$

where $\tau_1 = \frac{\gamma + \sqrt{\gamma^2 - 4m\kappa}}{2\kappa}$ and $\tau_2 = \frac{\gamma - \sqrt{\gamma^2 - 4m\kappa}}{2\kappa}$

Critically Damped Motion ($\gamma^2 = 4m\kappa$)

$$x(t) = \frac{F}{\kappa}\left[1 - \left(1 + \frac{t}{\tau}\right)\exp\left(-\frac{t}{\tau}\right)\right]$$

where $\tau = \frac{2m}{\gamma} = \frac{\gamma}{2\kappa} = \sqrt{\frac{m}{\kappa}}$

Source: Mechanics of Motor Proteins and the Cytoskeleton, Jonathan Howard

Hint

1. Write down equation of motion in terms of variable p (=kx-F), 2b(=γ/m) and $w_0^2 = \frac{k}{m}$

2. Assume a general solution either of the form $P = Ae^{-\frac{t}{\tau}}(easy) \quad or \quad P = Ae^{\alpha t}(hard)$

Summary

- *What is Physical Biology/Biophysics?*
- *Proteins molecules and forces acting on protein molecules*
- *Inertial forces are negligible and effect of gravity can be ignored*
- *Many biological systems can be modeled as combination of three fundamental mechanical elements-mass, spring and dashpot. Similarity with LCR circuit*