BME2102:
Introduction to Biomechanics

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Information

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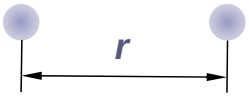
- HW6: deadline extended to **Nov. 21**
- **Tutorial 2 (Today) VI. Cellular Biomechanics** and In-class Test
- **Lecture 11 VII: Scaling Laws**
- **Lecture 12 VIII: Viscoelasticity (HW7 to be assigned) & General Review**

Van der Waals Forces

- The generalized interaction between molecules is given by the Mie pair potential

$$E(r) = -\frac{A}{r^n} + \frac{B}{r^m}$$

attractive repulsive



- A specific case of the Mie potential is the Lennard-Jones potential

$$E(r) = -\frac{A}{r^6} + \frac{B}{r^{12}}$$

where A and B are constants, e.g., for solid argon, $A = 8.0 \times 10^{-77}$ Jm^6 and $B = 1.12 \times 10^{-133}$ Jm^{12}.

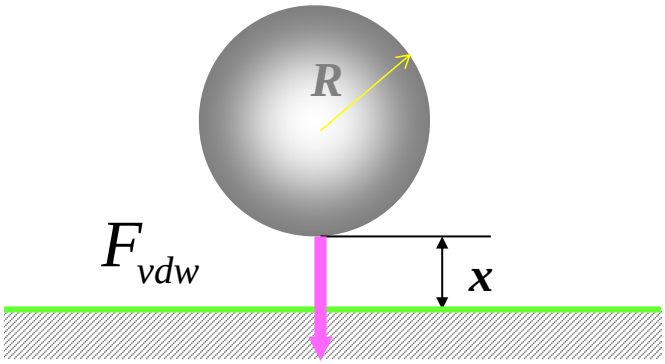
Van der Waals Forces

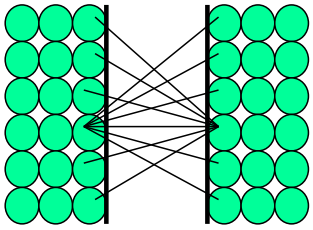
- The net van der Waals force is given by

$$F_{\mathrm{vdW}} = -\frac{dE}{dr}$$

$$= -\frac{6A}{r^7} + \frac{12B}{r^{13}}$$

Van der Waals Forces





Volume Integration

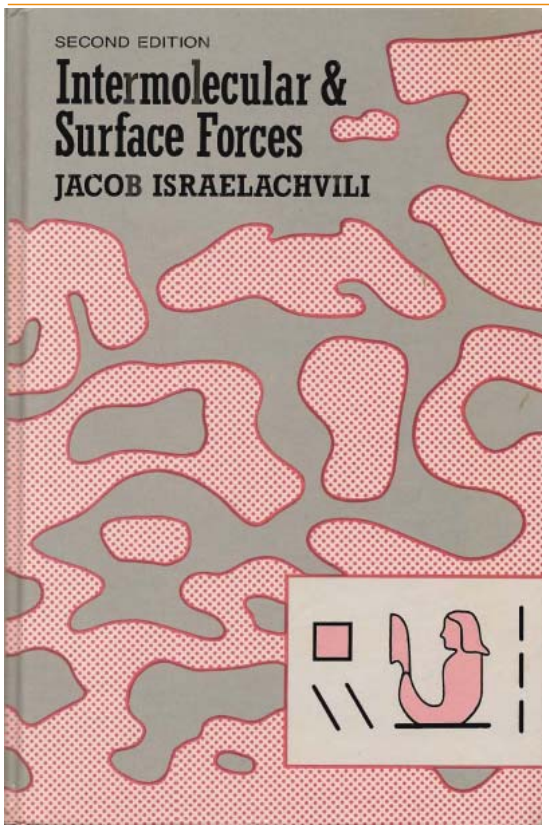
$$F_{vdw} = \frac{HR}{12x^2}$$

$F_{vdW} \sim x^{-2}$

$F_{vdW} \sim R^{1}$

H: Hamaker Constant *x*: Distance *R*: Radius of Bead

Van der Waals Forces



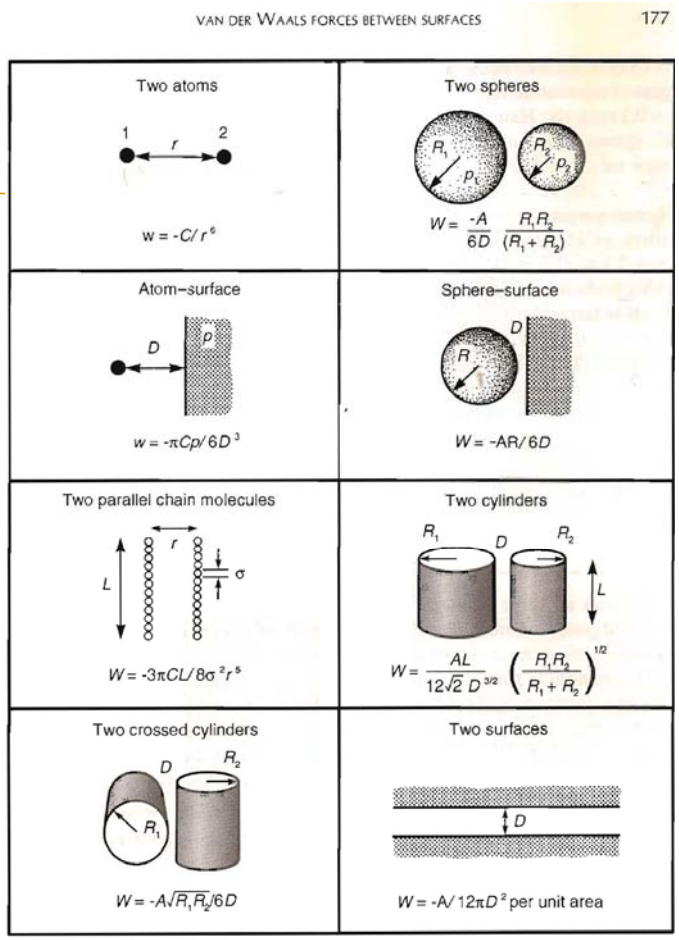
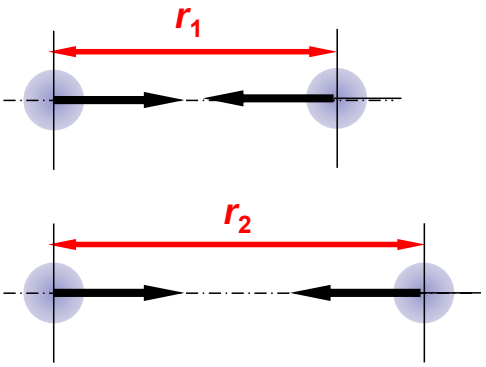


Fig. 11.1. Non-retarded van der Waals interaction free energies between bodies of different geometries calculated on the basis of pairwise additivity (Hamaker summation method). The *Hamaker constant* A is defined as $A = \pi^2 C \rho_1 \rho_2$ where ρ_1 and ρ_2 are the number of atoms per unit volume in the two bodies and C is the coefficient in the atom–atom pair potential (top left). A more rigorous method of calculating the Hamaker constant in terms of the macroscopic properties of the media is given in Section 11.3. The forces are obtained by differentiating the energies with respect to distance.

Scaling of Interatomic van der Waals Forces

- If we know the vdW force for a certain separation,
  - $F_{vdW,1} = F_{vdW,a1} - F_{vdW,r1} = -\frac{6A}{r_1^7} + \frac{12B}{r_1^{13}}$,
- how to calculate the vdW force for a different separation?
  - $r_2 = kr_1$ *or* $k = \frac{r_2}{r_1}$
  - $F_{vdW,2} = -\frac{6A}{r_2^7} + \frac{12B}{r_2^{13}} = -\frac{6A}{(kr_0)^7} + \frac{12B}{(kr_0)^{13}}$
  - $= -\frac{6A}{k^7(r_0)^7} + \frac{12B}{k^{13}(r_0)^{13}} = -k^{-7}\frac{6A}{(r_0)^7} + k^{-13}\frac{12B}{(r_0)^{13}}$
  - For argon atoms:
    - Take $r_0 = r_{max} = 0.416[nm]$
    - $F_{vdW,0} = F_{vdW,max} = -222.63[pN] + 120.28[pN] = -102.35[pN]$



e.g.
$r_1 = 10r_0 = 4.16\text{nm}$
$F_{vdW,1}$
$= -\mathbf{10}^{-7}F_{vdW,a0}$
$+ \mathbf{10}^{-13}F_{vdW,r0}$
$= -\mathbf{10}^{-7}\mathbf{222.63}[\boldsymbol{pN}]$
$+ \mathbf{10}^{-13}\mathbf{120.28}[\boldsymbol{pN}]$
$\approx -\mathbf{22.63}[\boldsymbol{aN}]$

Scaling of Interatomic van der Waals Forces

- If we know the vdW force for a certain separation,
  - $F_{vdW,1} = F_{vdW,a1} - F_{vdW,r1} = -\frac{6A}{r_1^7} + \frac{12B}{r_1^{13}}$,
- how to calculate the vdW force for a different separation?
  - $r_2 = kr_1$
  - $F_{vdW,2} = -\frac{6A}{r_2^7} + \frac{12B}{r_2^{13}} = -\frac{6A}{(kr_0)^7} + \frac{12B}{(kr_0)^{13}}$
  - $= -\frac{6A}{k^7(r_0)^7} + \frac{12B}{k^{13}(r_0)^{13}} = -k^{-7}\frac{6A}{(r_0)^7} + k^{-13}\frac{12B}{(r_0)^{13}}$
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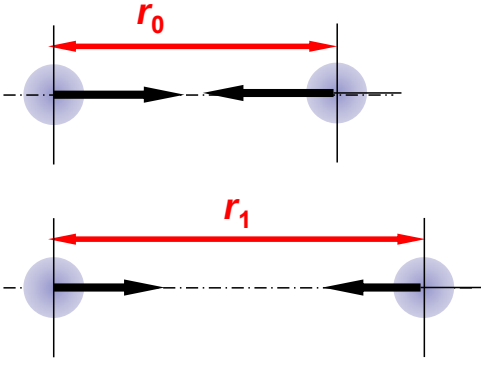
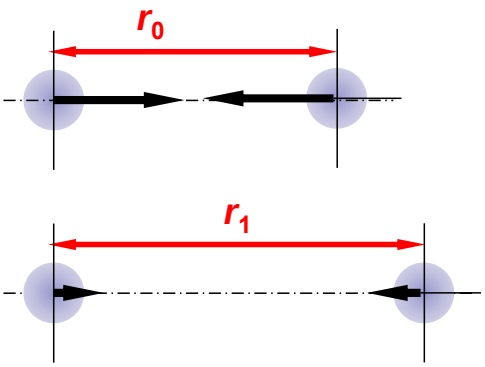


e.g.
$r_1 = 1.1r_0 = 0.4576\text{nm}$
$F_{vdW,1}$
$= -\mathbf{1.1}^{-7}F_{vdW,a0}$
$+ \mathbf{1.1}^{-13}F_{vdW,r0}$
$= -\mathbf{0.513} \times \mathbf{222.63}[\boldsymbol{pN}]$
$+ \mathbf{0.290} \times \mathbf{120.28}[\boldsymbol{pN}]$
$= -\mathbf{79.33}[\boldsymbol{pN}]$

Scaling of Interatomic van der Waals Forces

- If we know the vdW force for a certain separation,
  - $F_{vdW,1} = F_{vdW,a1} - F_{vdW,r1} = -\frac{6A}{r_1^7} + \frac{12B}{r_1^{13}}$,
- how to calculate the vdW force for a different separation?
  - $r_2 = kr_1$
  - $F_{vdW,2} = -\frac{6A}{r_2^7} + \frac{12B}{r_2^{13}} = -\frac{6A}{(kr_0)^7} + \frac{12B}{(kr_0)^{13}}$
  - $= -\frac{6A}{k^7(r_0)^7} + \frac{12B}{k^{13}(r_0)^{13}} = -k^{-7}\frac{6A}{(r_0)^7} + k^{-13}\frac{12B}{(r_0)^{13}}$
  - For argon atoms:
    - Take $r_0 = r_{max} = 0.416[nm]$
    - $F_{vdW,0} = F_{vdW,max} = -222.63[pN] + 120.28[pN] = -102.35[pN]$



e.g.

$r_1 = 1.5r_0 = 0.4576\text{nm}$

$F_{vdW,1} = -\mathbf{1.5^{-7}}F_{vdW,a0} + \mathbf{1.5^{-13}}F_{vdW,r0}$

$= -0.\mathbf{059} \times 222.\mathbf{63}[\boldsymbol{pN}] + 0.\mathbf{005} \times 120.\mathbf{28}[\boldsymbol{pN}]$

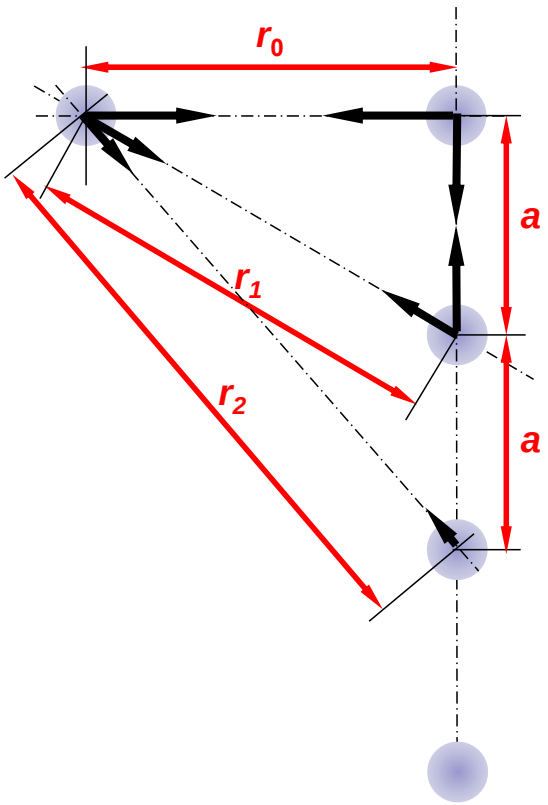
$= -\mathbf{12.53}[\boldsymbol{pN}]$

van der Waals Forces between an atom and a chain of atoms

- The net vdW force for atom A,
  - $\vec{F}_{vdW,net} = \vec{F}_{vdW,0} + \vec{F}_{vdW,1} + \vec{F}_{vdW,2} + \cdots$
  - If $a \approx r_0$,
  - $r_1 = \sqrt{2}r_0 = 1.414\ r_0$,
  - $r_2 = \sqrt{5}r_0 = 2.236\ r_0$, $\vec{F}_{vdW,2}$ *is ignorable*
  - $\vec{F}_{vdW,net} = \vec{F}_{vdW,0} + \vec{F}_{vdW,1} + \vec{F}_{vdW,2} + \cdots$

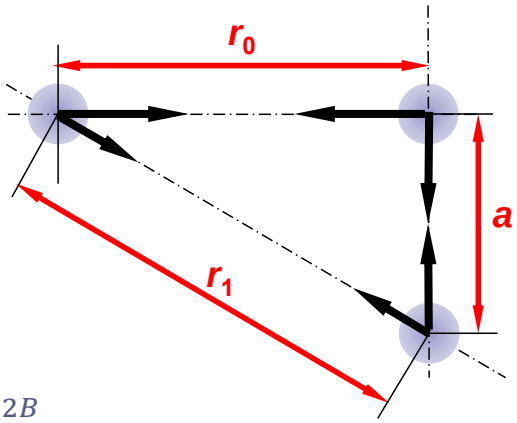
    $\approx \vec{F}_{vdW,0} + \vec{F}_{vdW,1}$ (error is acceptable)

    $\approx \vec{F}_{vdW,0}$ (error is acceptable)
  - Calculate the errors by yourself



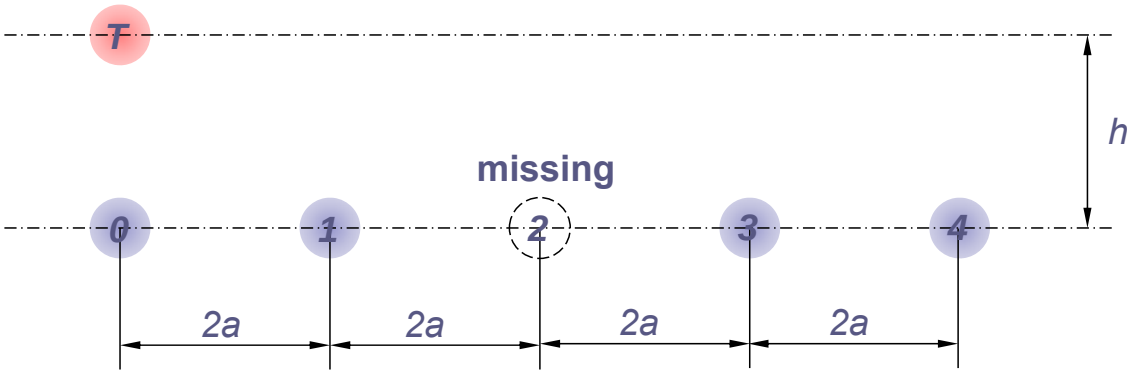
van der Waals Forces between an atom and a surface

- The net vdW force for atom A,
  - $\vec{F}_{vdW,net} = \vec{F}_{vdW,0} + \vec{F}_{vdW,1}$
  - how to calculate the vdW force for a different separation?
  - $r_1 = kr_0$
  - $F_{vdW,1} = \frac{6A}{r_1^7} - \frac{12B}{r_1^{13}} = \frac{6A}{(kr_0)^7} - \frac{12B}{(kr_0)^{13}}$
  - $= \frac{6A}{k^7(r_0)^7} - \frac{12B}{k^{13}(r_0)^{13}} = k^{-7}\ \frac{6A}{(r_0)^7} - k^{-13}\ \frac{12B}{(r_0)^{13}}$
  - For argon atoms:
    - Take $r_0 = r_{max} = 0.416[nm]$
    - $F_{vdW,0} = F_{vdW,max} = 222.63[pN] - 120.28[pN] = 102.35[pN]$



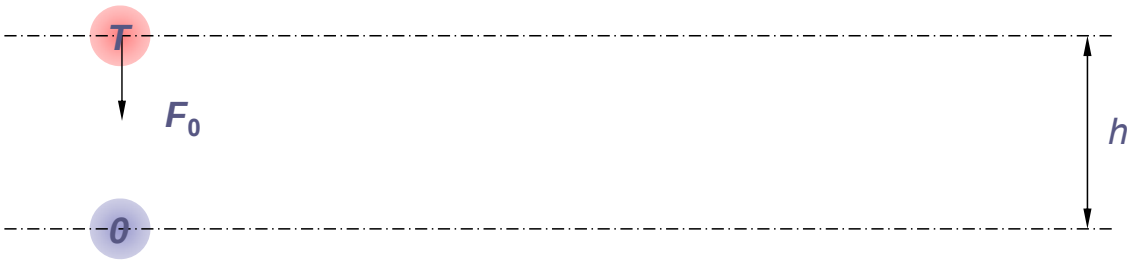
van der Waals Forces between a sliding atom and a chain of atoms

- Ignore the repulsive force, given $A = 10^{-77}$ Jm^6 and $h = 2a = 0.45$ nm, when an atom *T* slides over a chain of atoms (fixed), how the vdW force in the vertical direction on it will change?



van der Waals Forces between a sliding atom and a chain of atoms

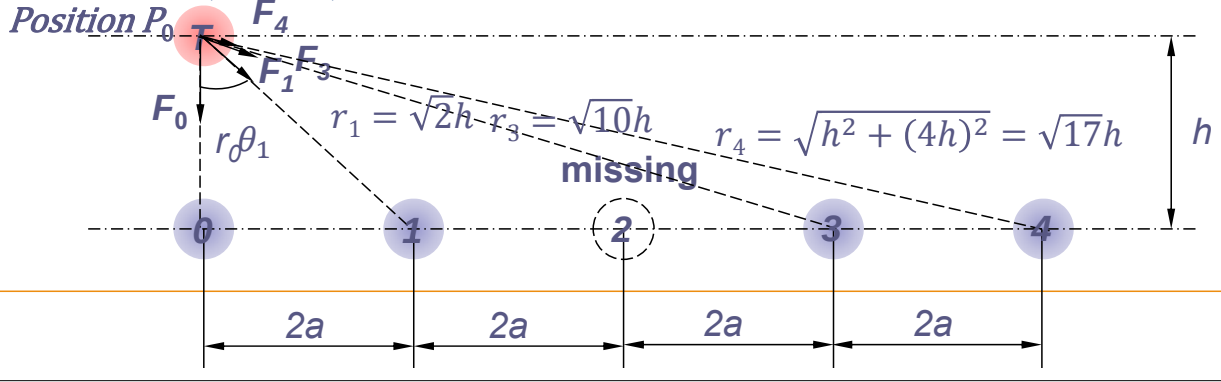
- Calculate the vdW force for a simple case like



$$F_0 = -\frac{6A}{h^7} = -\frac{6 \times 10^{-77}}{(0.45 \times 10^{-9})^7} = -16.06[pN]$$

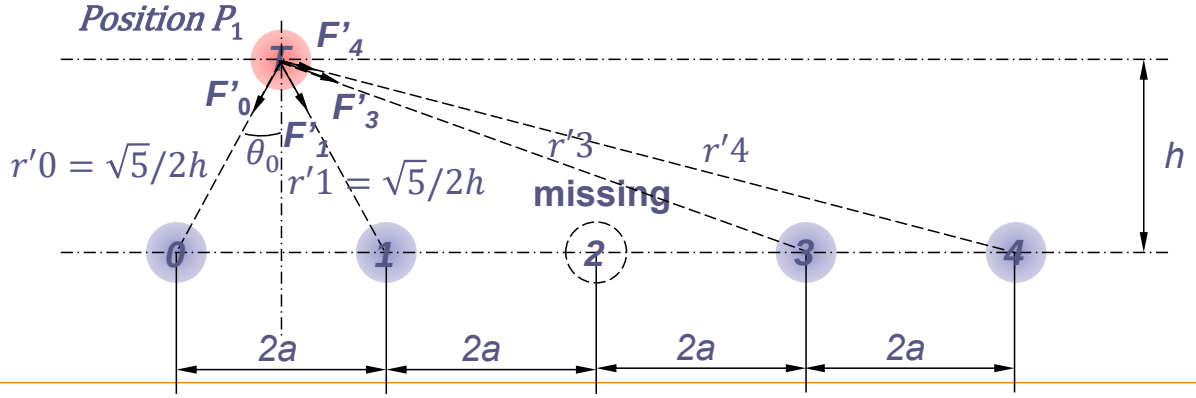
van der Waals Forces between a sliding atom and a chain of atoms

- $F_0 = -16.06[pN]$
- $F_1 = k^{-7} \times F_0 = (\frac{r_1}{r_0})^{-7} \times F_0 = (\sqrt{2})^{-7} \times F_0 = 0.088 \times (-16.06)[pN] = -1.42[pN]$
  - $F_{1,v} = F_1 cos\theta_1 = -1.42 cos45° = -1.00[pN]$ (ignore this will cause 6% error)
- $F_3 = (\sqrt{10})^{-7} \times F_0 = 0.00032F_0$ (negligible)
- $F_4 = (\sqrt{17})^{-7} \times F_0 = 0.000049F_0$ (negligible)
- $F_{P0} = F_{0,v} + F_{1,v} = -17.06[pN]$



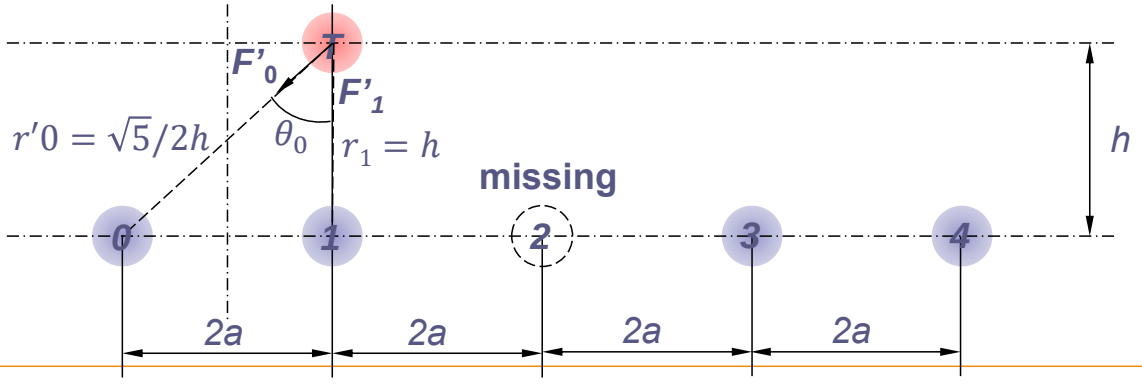
van der Waals Forces between a sliding atom and a chain of atoms

- $r'_0 = r'_1 = \sqrt{h^2 + (h/2)^2} = \sqrt{5}/2h$
- $F'_0 = F'_1 = (\frac{r'_0}{r_0})^{-7} \times F_0 = (\sqrt{5}/2)^{-7} \times F_0 = 0.4579 \times (-16.06)[pN] = -7.35[pN]$
  - $F'_{0,v} = F'_{1,v} = F_0 cos\theta_0 = -7.35 \times 2/\sqrt{5} = -6.58[pN]$
- F'_3, F'_4 (negligible)
- $F_{P1} = F'_{0,v} + F'_{1,v} = -13.16[pN]$



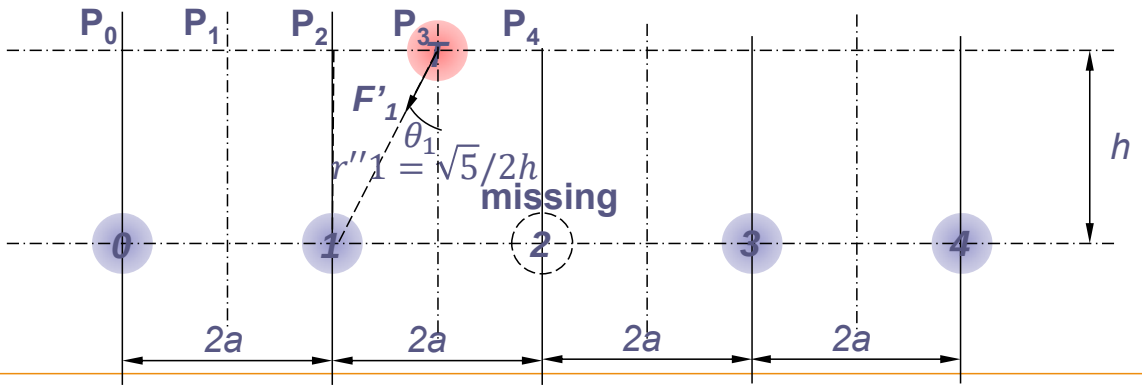
van der Waals Forces between a sliding atom and a chain of atoms

- Position P_2 –The same as P_1
- $F_{P2} = -17.06[pN]$



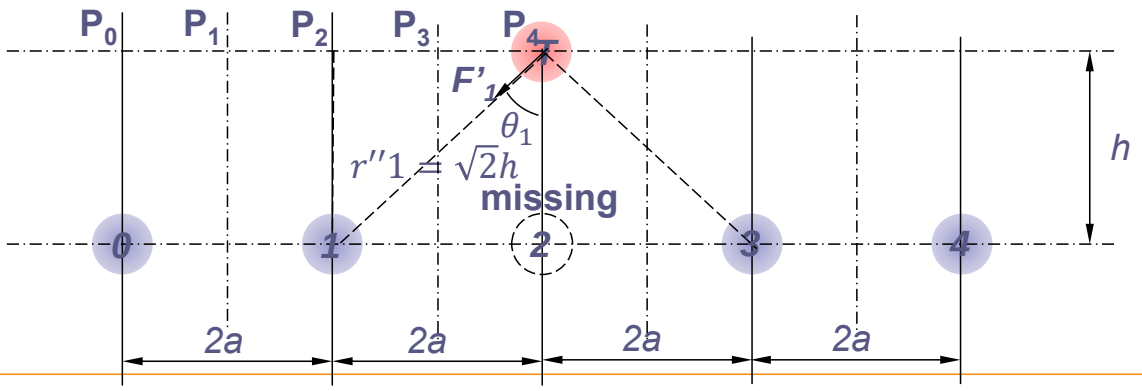
van der Waals Forces between a sliding atom and a chain of atoms

- Position P_3 –Similar to P_1 but the value is a half of that
- $F_{P3} = -6.58[pN]$



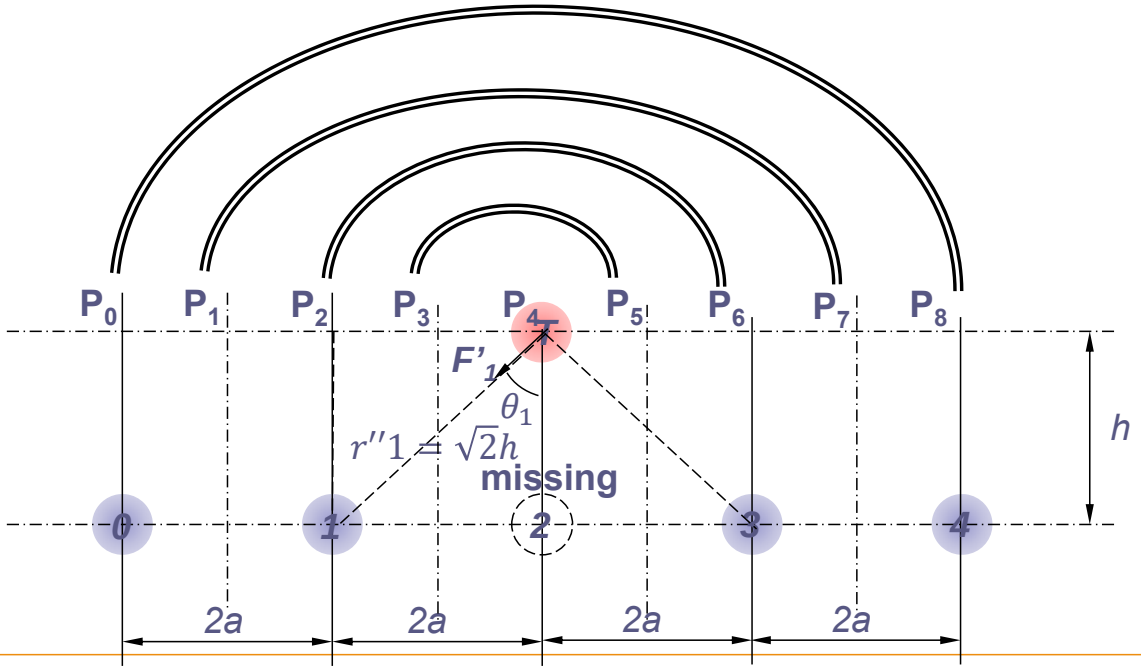
van der Waals Forces between a sliding atom and a chain of atoms

- Position P_4
- $F_{P4} = -2.00[pN]$

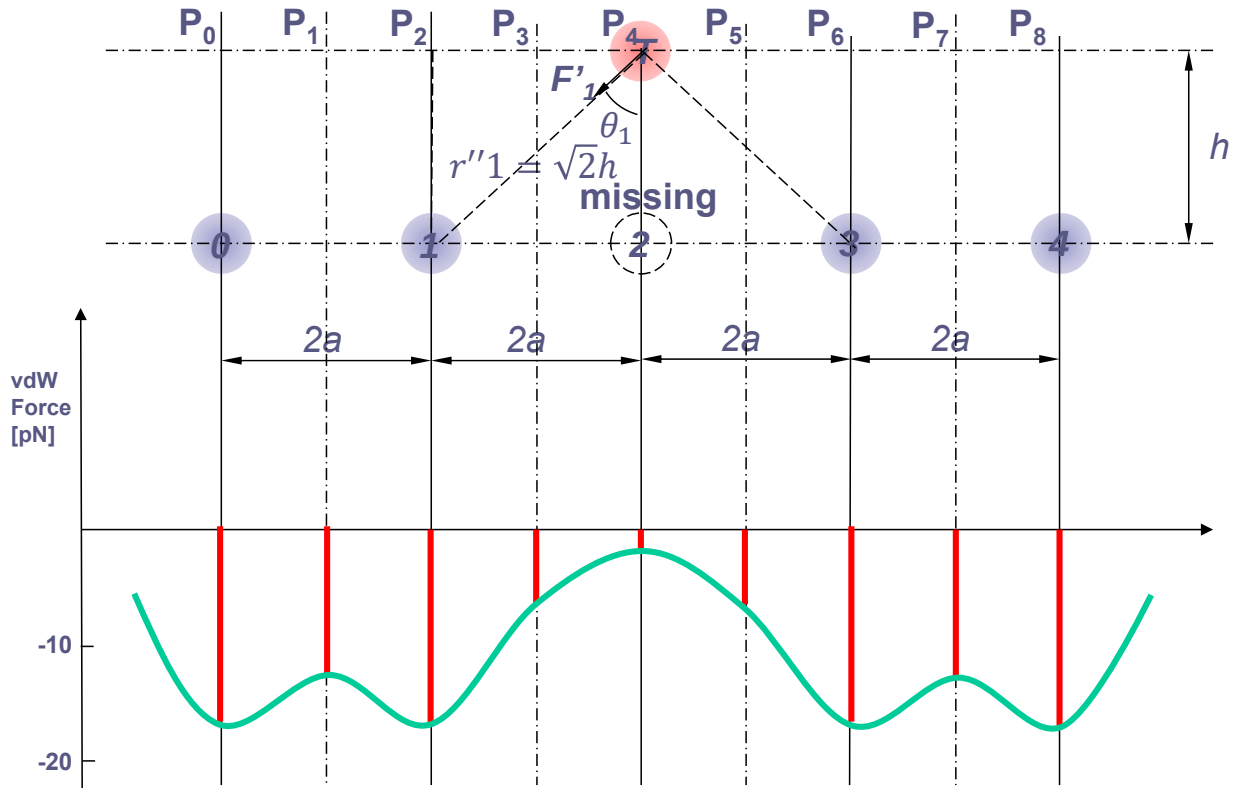


van der Waals Forces between a sliding atom and a chain of atoms

- Position P_4 –Similar to P_1 but the value is a half of that
- $F_{P3} = -2.00[pN]$

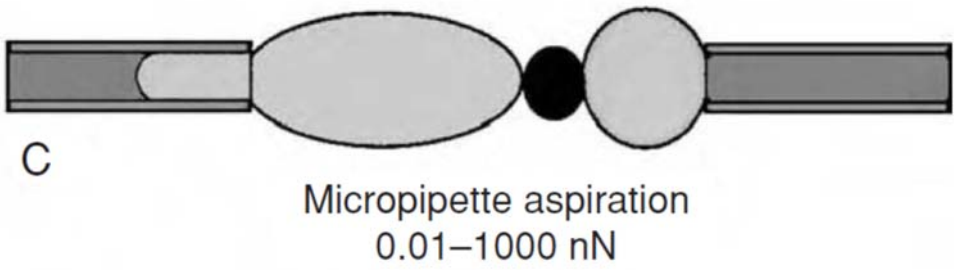


van der Waals Forces between a sliding atom and a chain of atoms



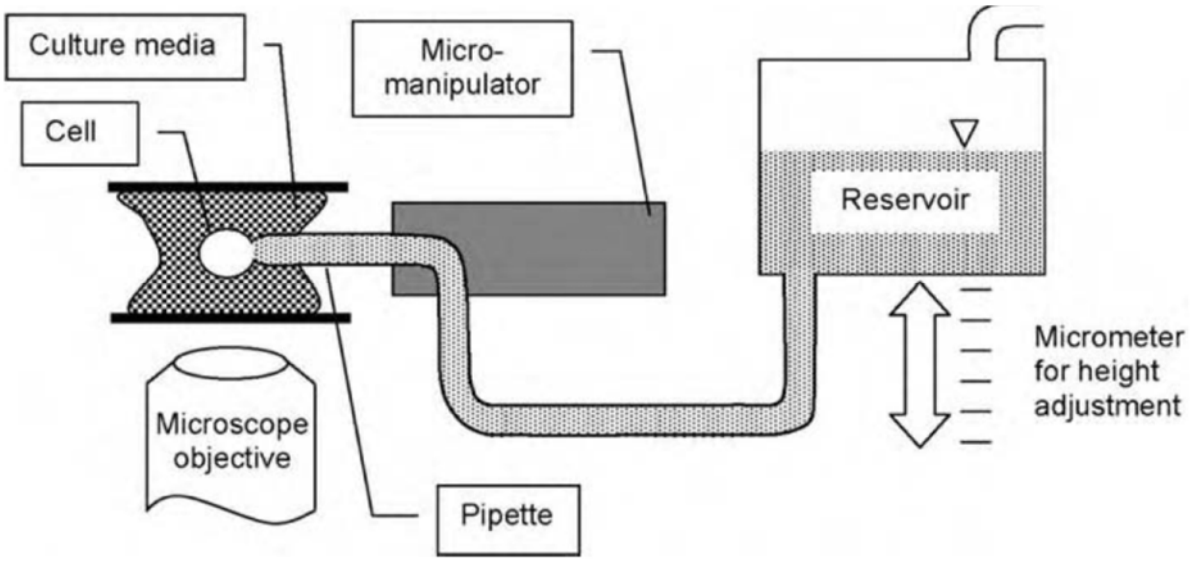
Micropipette aspiration

- The third methodology is micropipette aspiration. This is one of the oldest techniques for measuring cellular (and subcellular) biomechanical properties, dating back to the middle of the twentieth century. There are different ways in which micropipette aspiration can be used, but all approaches employ a very fine glass micropipette, typically having internal diameter of 1–10 μm and with a tip that can be moved about by a micromanipulator.



Micropipette aspiration
0.01–1000 nN

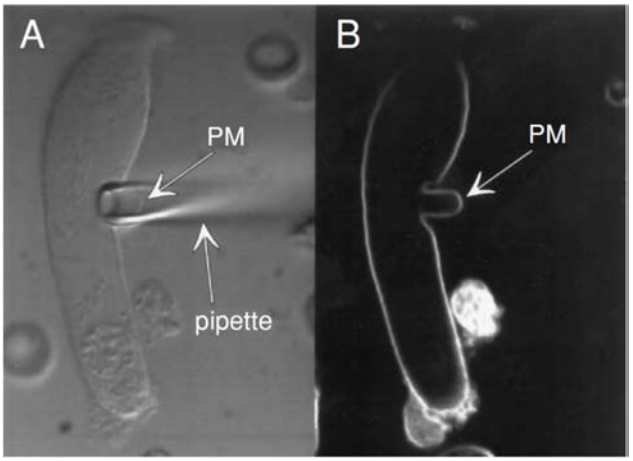
Micropipette aspiration



- Schematic overview of apparatus used for micropipette aspiration of a living cell (not to scale). Adapted from Shao and Hochmuth with kind permission of the authors and the Biophysical Society.

Micropipette aspiration

- In the simplest form of micropipette aspiration, the pipette tip is brought into contact with a cell and a small suction (aspiration) pressure is generated by the reservoir. Direct microscopic observation reveals the cell's deformation and motion in real-time as it is acted upon by the micropipette. From knowledge of the reservoir height and the pipette tip cross-sectional area, the force applied to the cell can be determined.

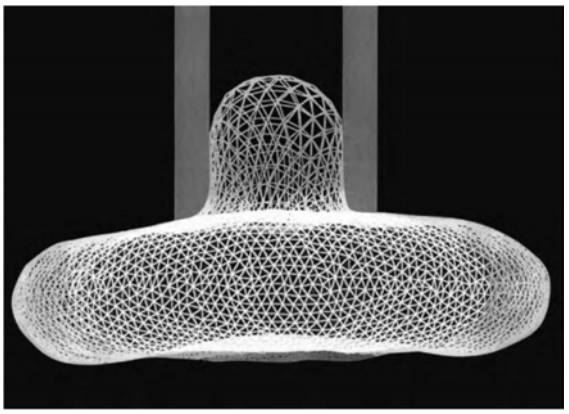


Micropipette aspiration

- This apparatus can generate forces ranging from 10 pN to about 10^4 nN, which is sufficient to cause appreciable cellular deformation. The smallest resolvable force in this technique depends on the precision with which the reservoir can be positioned; typical vertical positioning accuracy is several μm, which translates into a force of order 1–10 pN for a 10 μm diameter pipette.

Micropipette aspiration

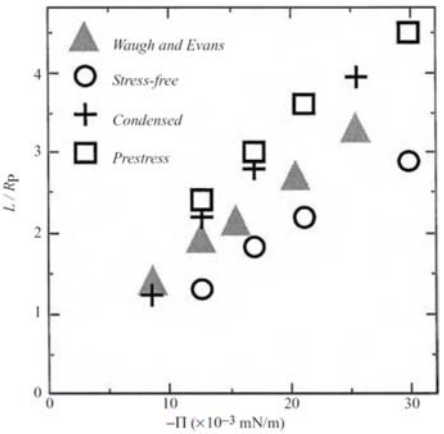
- When red cells are aspirated by a micropipette, a portion of the red cell is drawn inside the lumen of the pipette and is elongated.
- Simulation of a flaccid red cell being aspirated by a micropipette. The spectrin network within the cell is modeled as a network of non-Hookean springs, shown in this image as white segments. There are 6110 vertex nodes, each of which is connected to six neighbors by spectrin strands. From Discher *et al.* with kind permission of the authors and the Biophysical Society.



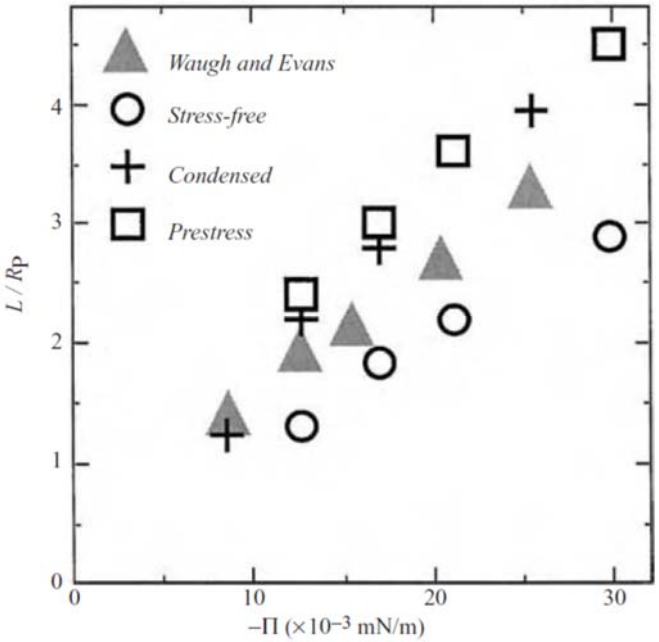
D. E. Discher, D. H. Boal and S. K. Boey. Simulations of the erythrocyte cytoskeleton at large deformation. II. Micropipette aspiration. *Biophysical Journal*, **75** (1998), 1584–1597.

Micropipette aspiration

- If the applied suction pressure is low enough to avoid red cell rupture, an equilibrium is established in which the applied suction pressure is balanced by mechanical stresses within the cortical cytoskeleton of the red cell. One measure of the cell's elastic properties is the distance that this aspirated segment extends into the pipette, *L*. Experimental measurements of this distance as a function of the applied pressure are shown in the figure, where we see that there is an approximately linear relationship between *L* and applied pressure, at least over the range of pressures plotted.



Micropipette aspiration



R. Waugh and E. A. Evans. Thermoelasticity of red blood cell membrane. *Biophysical Journal*, **26** (1979), 115–131.

- Length of the aspirated segment, *L*, as a function of aspiration pressure for micropipette aspiration of a flaccid human red cell. The aspirated segment length has been non-dimensionalized by inner pipette radius *R*p. The quantity Π is defined to be *2PR*p, where *P* is the aspiration pressure (taken to be <0 for suction). This implies that Π values < 0 correspond to tension in the cortical cytoskeleton/membrane. The grey triangles are experimental data from Waugh and Evans.

Electrostatic Forces

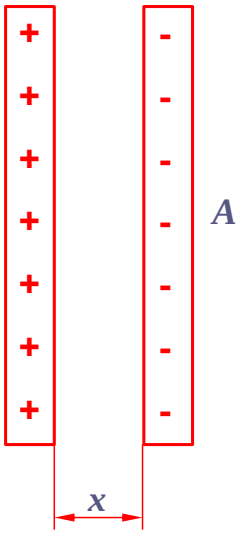
- Let us consider the electrostatic force between two parallel plates and examine how that force is affected by scaling. Let *A* denote the surface area of the plates, and let *x* be the separation distance. Assume *x* is small relative to the dimensions of the plates. The capacitance is given by

$$C = \varepsilon \frac{A}{x}$$

where *ε* is the permittivity of the dielectric material separating the plates. The capacitance relates a voltage *U* that is applied to the plates to the charge Q that is accumulated on each plate: *Q* = *CU*. The electrostatic co-energy stored in the capacitor can be expressed by

$$W = \frac{1}{2} C U^2$$

and the attractive force between the plates is computed as *F* = −*dW*/*dx*.



Electrostatic Forces

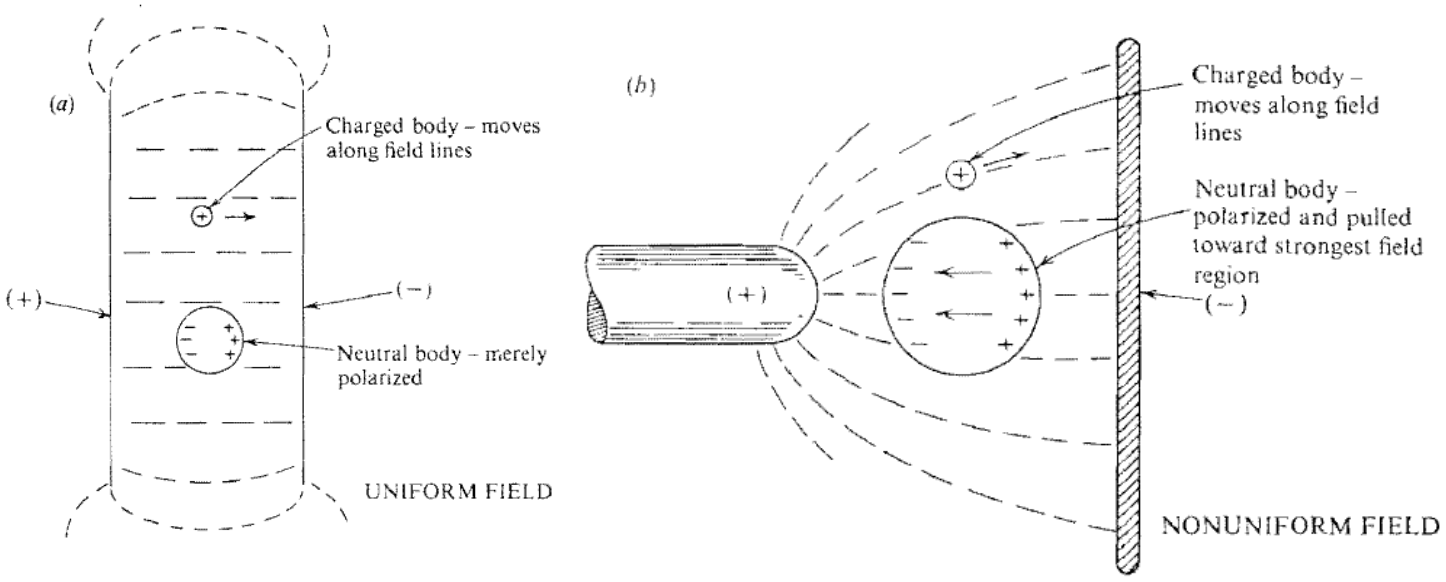
- In the case of constant voltage

$$W = \frac{\varepsilon A}{2x} U^2 \qquad F = -\frac{dW}{dx} \qquad F_U = \frac{\varepsilon A U^2}{2x^2}$$

- In the case of constant charge:

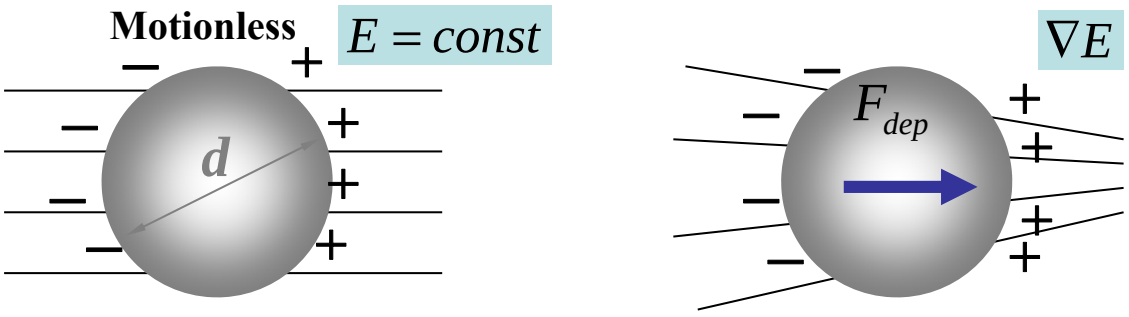
$$W = \frac{1}{2}\frac{Q^2}{C} = \frac{1}{2}\frac{Q^2 x}{\varepsilon A} \qquad F = -\frac{dW}{dx} \qquad F_Q = \frac{Q^2}{2\varepsilon A}$$

Dielectrophoretic (DEP) Forces



Dielectrophoretic (DEP) Forces

Forces subjected on neutral objects inside a nonuniform electric field



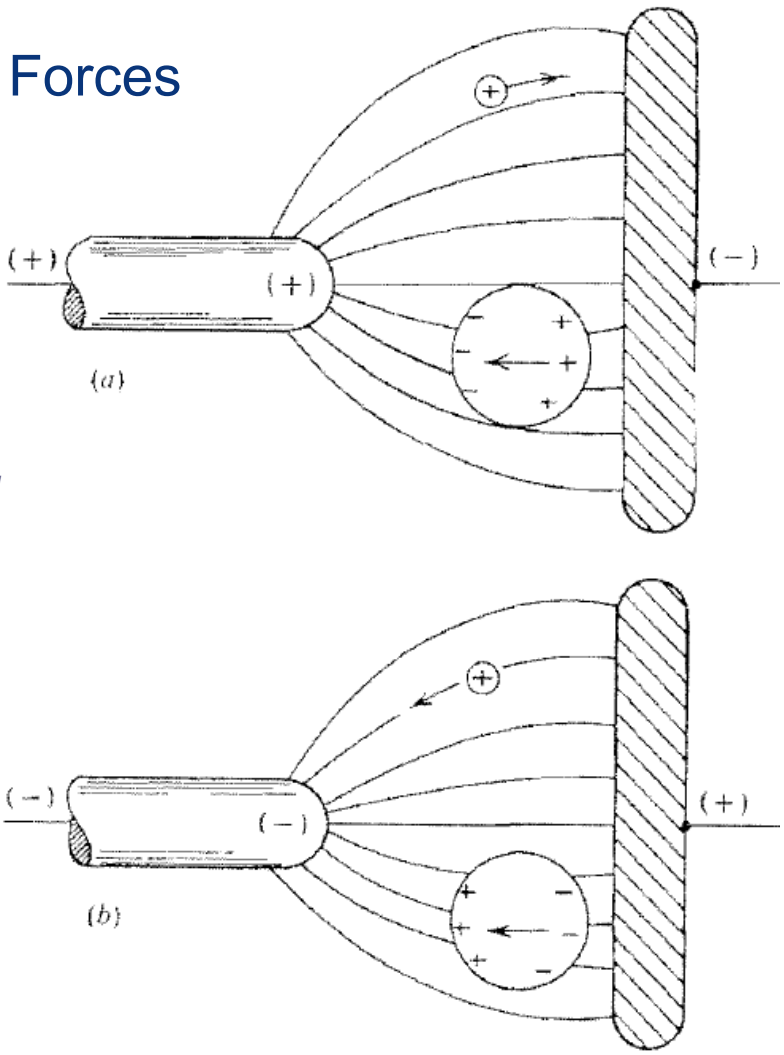
$$F_{dep} = \frac{1}{4}\pi d^3 \frac{\varepsilon_0(\varepsilon - \varepsilon_0)}{\varepsilon + 2\varepsilon_0}\nabla|\mathbf{E}|^2$$

E: Electric field intensity

ε : Dielectric coefficient of object

ε_0 : Dielectric coefficient of medium

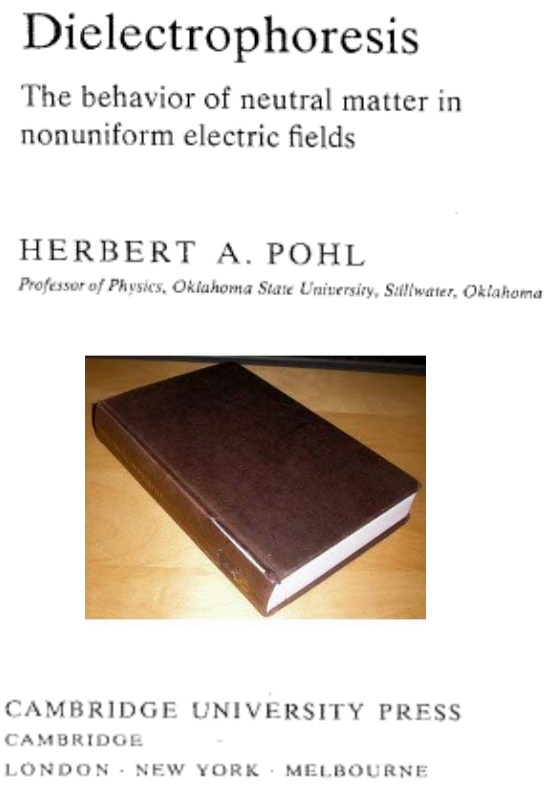
Dielectrophoretic (DEP) Forces



(a) Positively charged body moves towards negative electrode. Neutral body is polarized, then is attracted towards point where field is strongest. Since the two charge regions on the neutral body are equal in amount of charge, but the force is proportional to the local field, a net force towards the region of more intense field results.

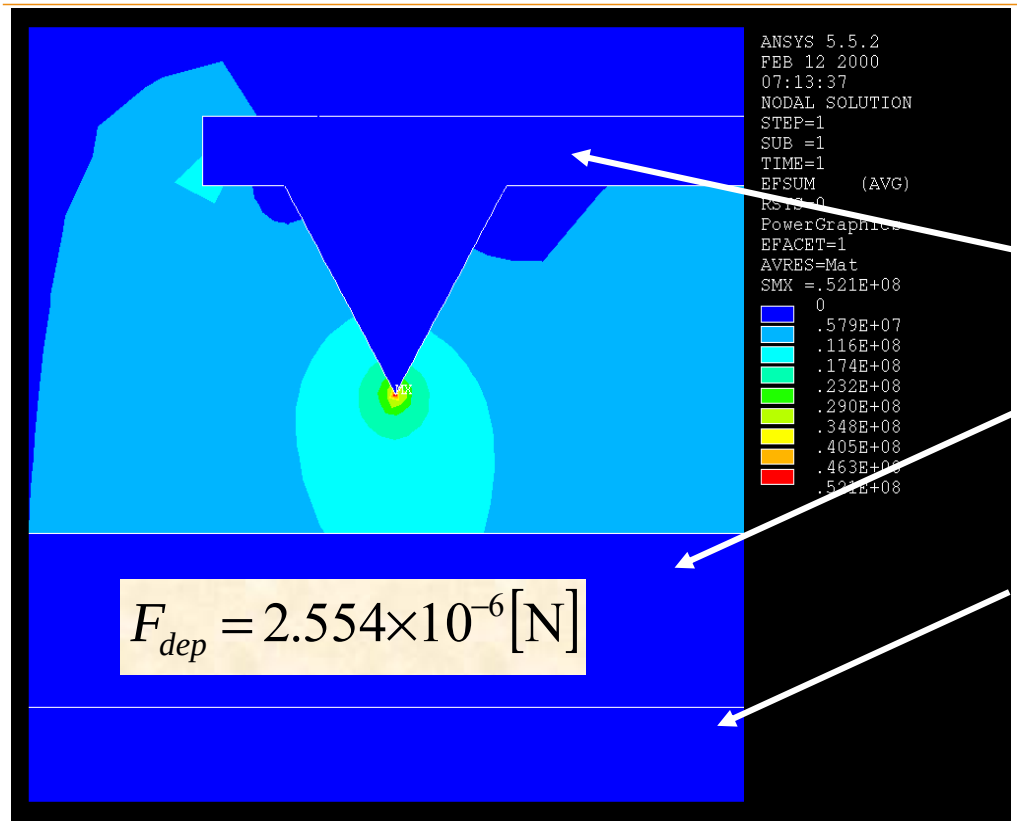
(b) Positively charged body moves towards the negative electrode. Again, the neutral body is polarized, but does not reverse direction although the field is reversed. It still moves towards the region of **higbest field intensity.**

Dielectrophoresis (DEP)



- The behavior of matter in electrical fields, especially nonuniform fields, is of interest to scientists of various branches: physics, chemistry, engineering, or life science.
- To chemists and physicists it is a science of many and varied phenomena.
- To engineers it is a source of new and useful techniques for separating materials or improving materials behavior.
- To ecologists it provides a major means of minimizing pollution.
- To life scientists it offers new ways to study and manipulate cells and their sub-particles, and to help unravel the nature of living systems. It constitutes a novel method of separating and distinguishing cells that differ in kind or physiological state.

Electric Field Analysis with FEM



Analytic Conditions

Vacuum
Permittivity:
8.85×10^{-12}[F/m]

Cantilever
Material: gold
Relative Permittivity:
∞

Insulate Film
Material:
Polyimide
Relative
Permittivity:2.2

Coating Film
Material: Al
Relative Permittivity: ∞

Voltage Applied
200 [V]

Magnetic Forces

- Consider the force between two identical magnets with magnetization *M and volume v,* aligned along their dipole axes, and separated by a distance *x. The field created by one magnet* along its axis is expressed using the point dipole model as

$$H(x) = \frac{M v}{2\pi x^3}$$

- The magnitude of the attractive/repulsive force on the other magnet is then given by

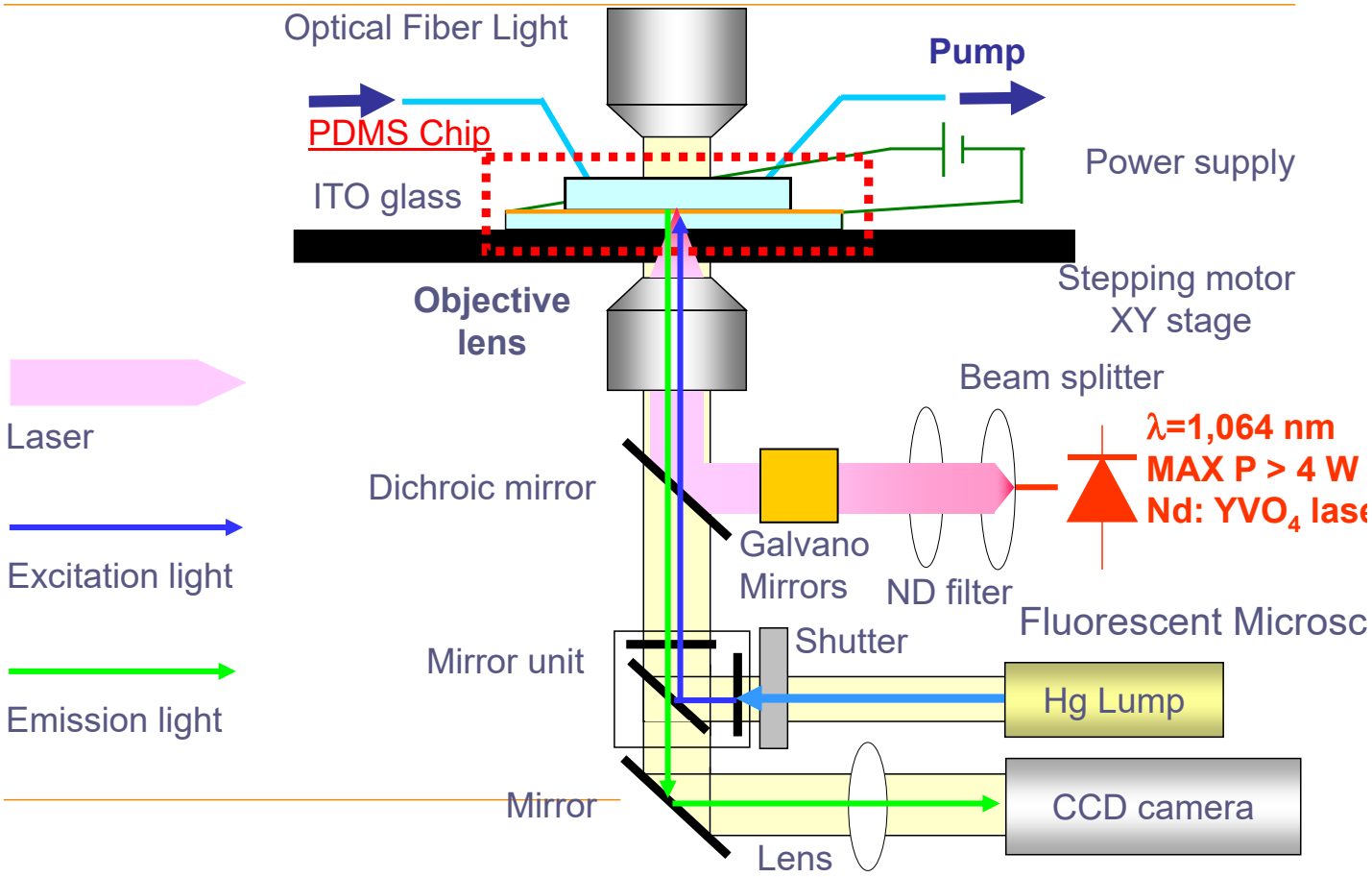
$$F_m = \mu_0 M v \left|\frac{\partial H}{\partial x}\right| = \frac{3\mu_0 M^2 v^2}{2\pi x^4}$$

where μ_0 is the permeability of free space. Note that the magnetization *M* remains constant for scaling as it is an intrinsic physical property of the magnets.

Optical trapping ("optical tweezers")

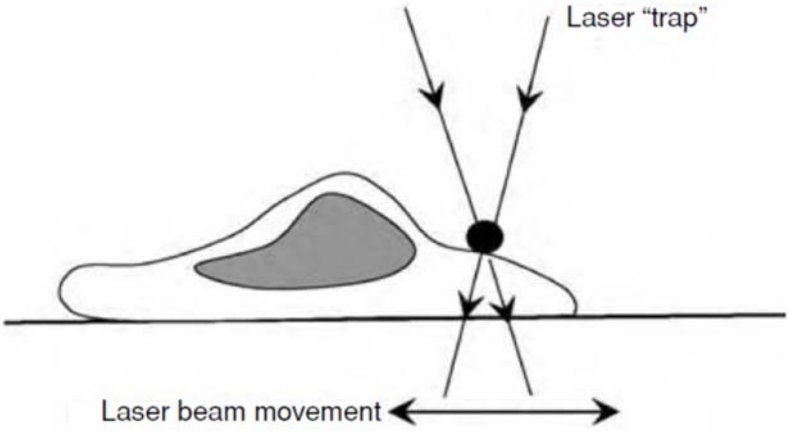
- Photons carry momentum; consequently when light shines on a surface there is an effective force exerted on that surface.
- Usually this effect is very small and can be neglected.
- However, for intense light shining on a small particle, forces in the range of 1 to 200 pN can be generated. An extension of this concept is to create a specially focused light beam that creates a potential "well" that traps a bead or small particle, typically 1–2 μm in diameter.

Configuration of System



Optical tweezers for biological measurements

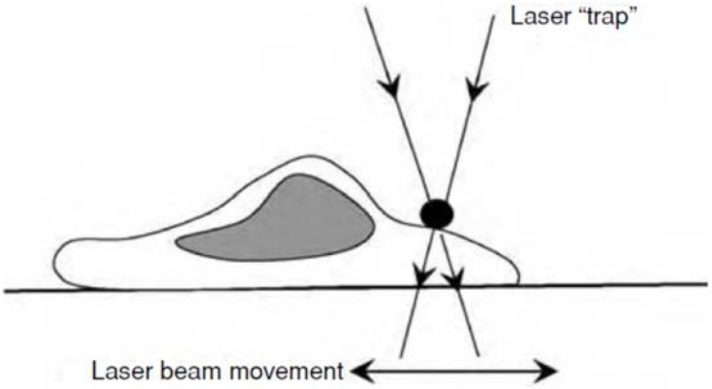
- This principle can be used for biological measurements by coating the bead with fibronectin (or some other molecule that will bind to receptors on the cell surface) so that the bead adheres to a given location on the cell. The beam is then moved laterally, and the motion of the bead is observed microscopically.



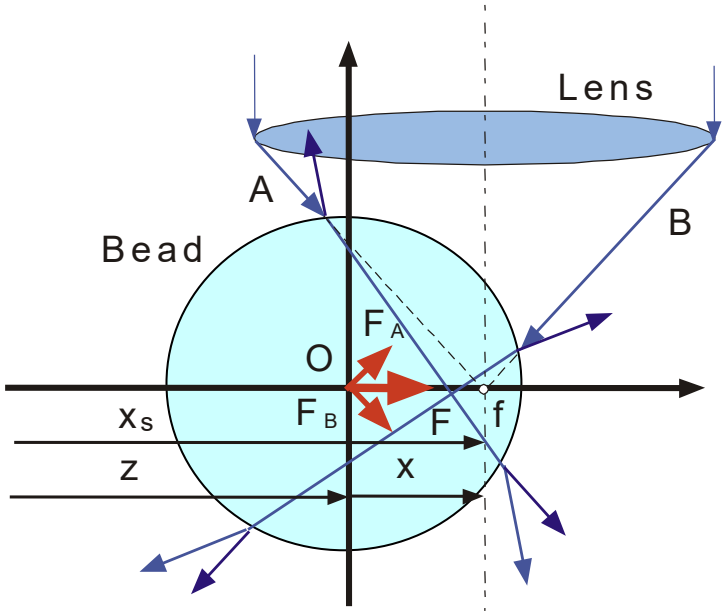
Optical tweezers for biological measurements

- From knowledge about the characteristics of the light trap, the force exerted on the bead by the moving light beam can be determined from the bead position relative to the center of the optical trap. Since the displacement of the bead is simultaneously monitored, this information can be used to determine the local stiffness of the cell. Essentially the same technique can be used to measure the force exerted by individual molecules.

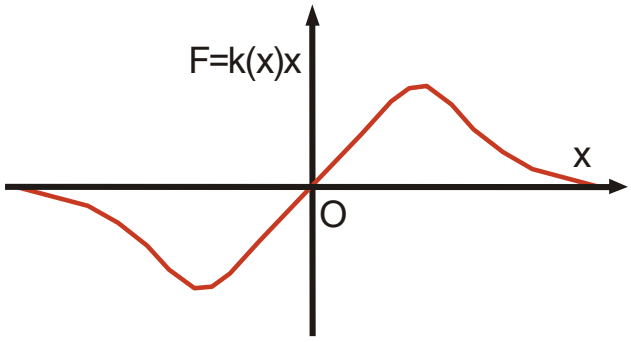
Schematic description of the "optical tweezers" manipulating a bead that is attached to a cultured cell. Bead position is monitored by microscopy and so the relative position of the bead and the optical trap center are known.



Laser Trap Model in Ray Optics Regime



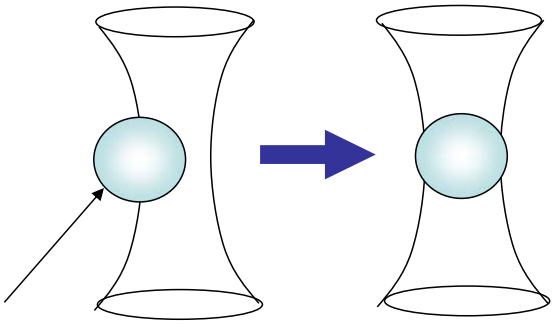
Coordinate system

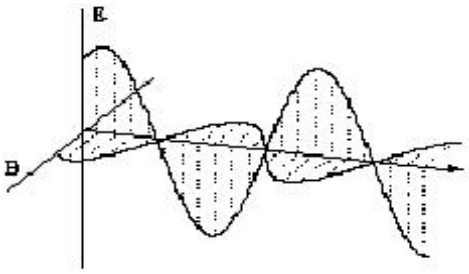


Optical trapping force image

Laser Traps for High Dielectric Objects

Focused Laser





Rayleigh particle

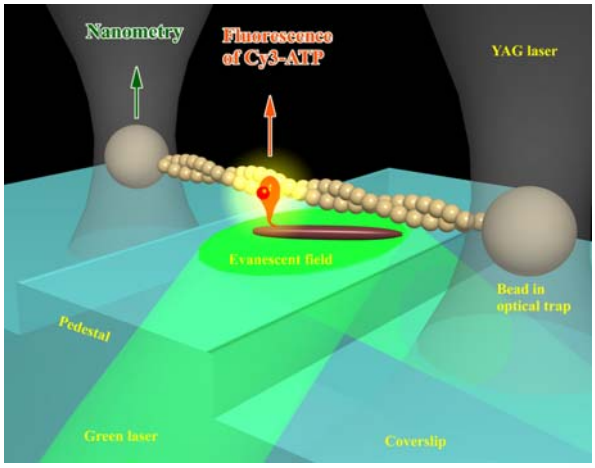
$$F = \alpha\left\{\frac{\nabla E^2}{2} + \frac{d(E\times B)}{dt}\right\}$$

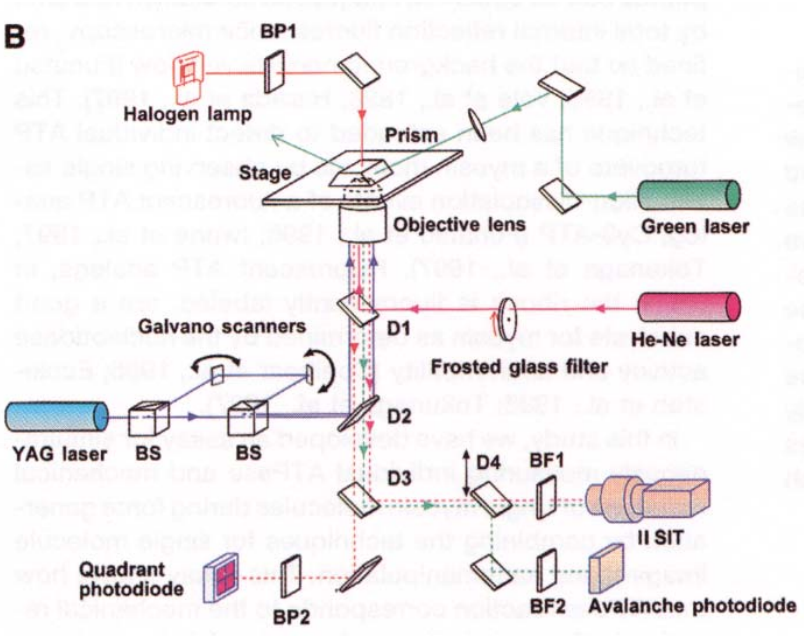
Gradient force **Scattering force**

Any object which has a higher dielectric constant than the surrounding material, which enters the optical trap, will become trapped.

Simultaneous Observation of Individual ATPase and Mechanical Events by a Single Myosin Molecule during Interaction with Actin

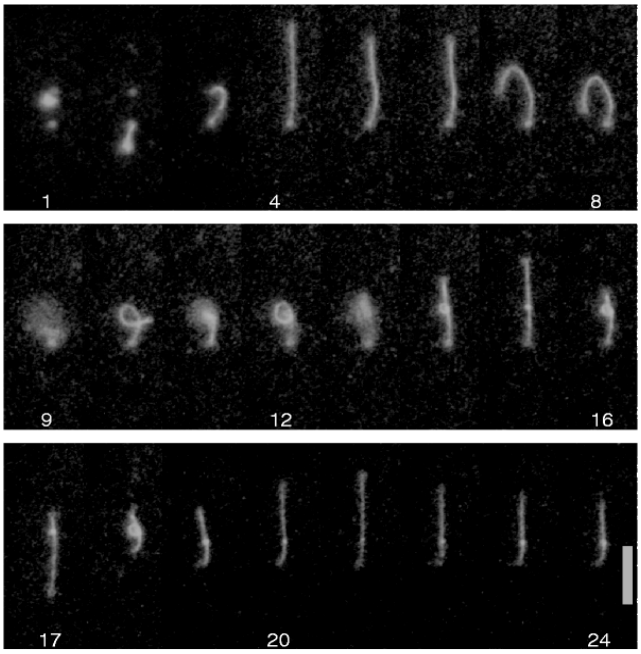
Akihiko Ishijima,*† Hiroaki Kojima,* Takashi Funatsu,* Makio Tokunaga,* Hideo Higuchi,* Hiroto Tanaka,‡ and Toshio Yanagida*‡§





A. Ishijima, Nagoya Univ.

Knotting a single DNA molecule

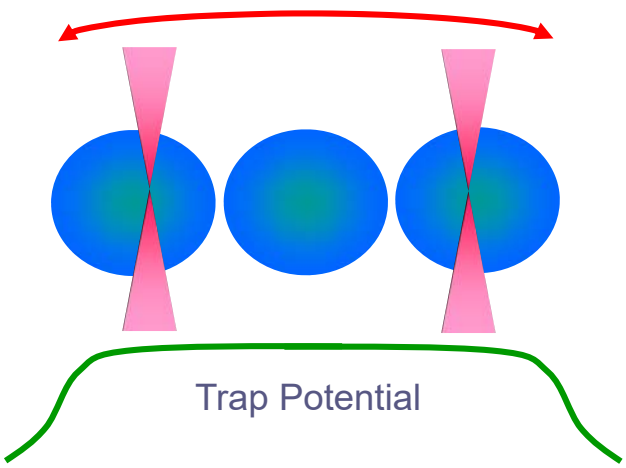


Knotting a single DNA molecule. Two beads were held with optical tweezers, and a DNA molecule stained with POPO-3 was attached to the lower bead by moving the microscope stage (images 1 and 2). The knot diameter in image 21 is estimated as <0.2 μm from its intensity. Scale bar, 10 μm

Nature 1999, Kinoshita et al.

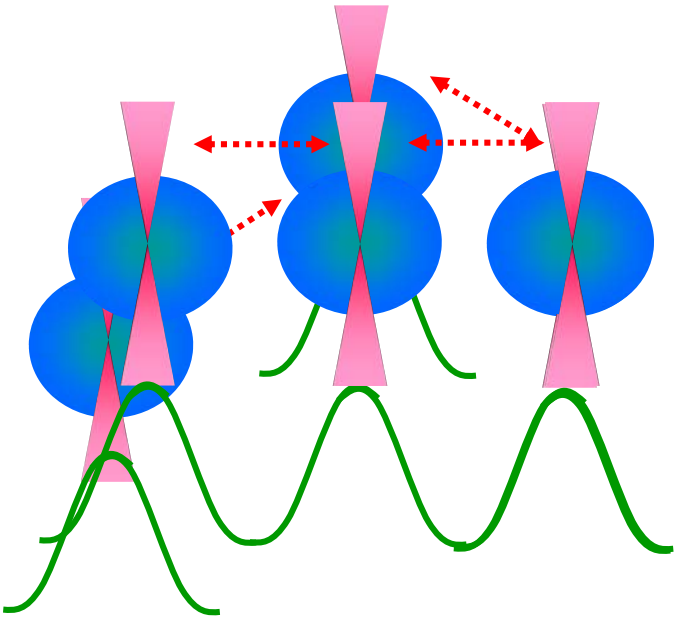
SLM for Trajectory Control of Multiple Objects

Laser Scanning Micromanipulation



Scanning Laser Micromanipulation
Masuhara et al., 1991

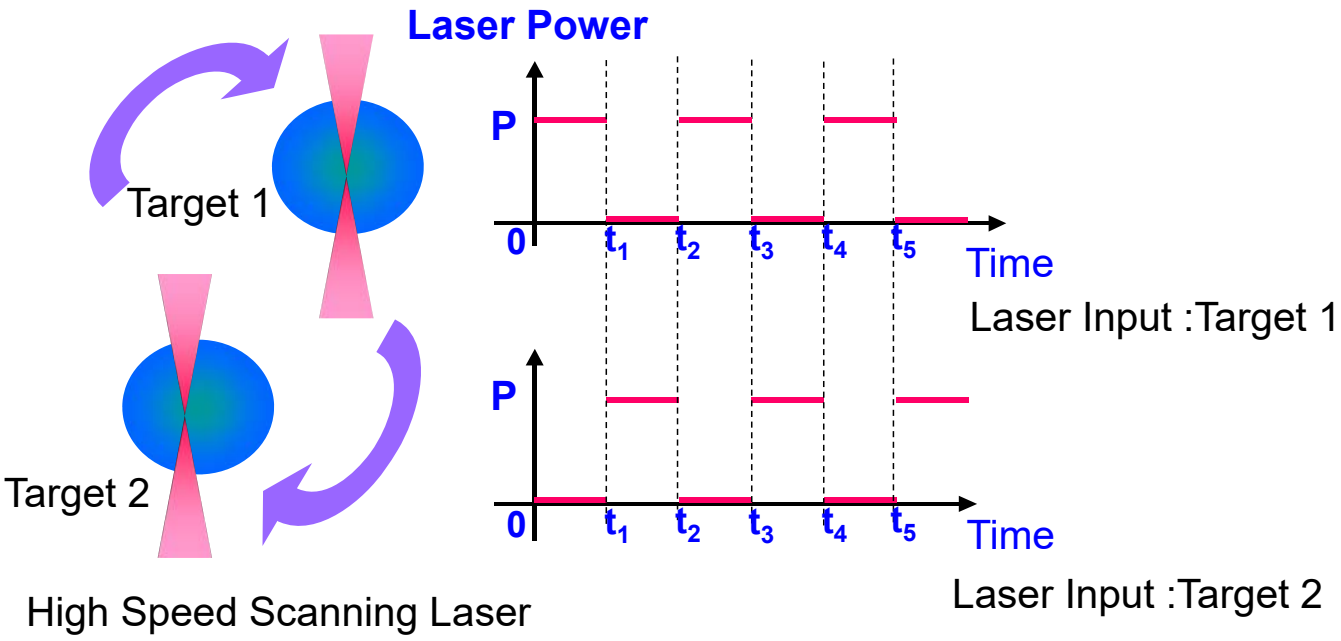
Synchronized Laser Micromanipulation



A single laser scanned in high speed

Synchronized Laser Micromanipulation: SLM

Trajectory control of multiple targets by a single laser



Discontinuous laser trap pattern

Dancing with Cells

- Robot hand
  - Laser
- Cells
  - 5μm

ICRA2003 Video Proceedings
6 Dancing Yeast Cells