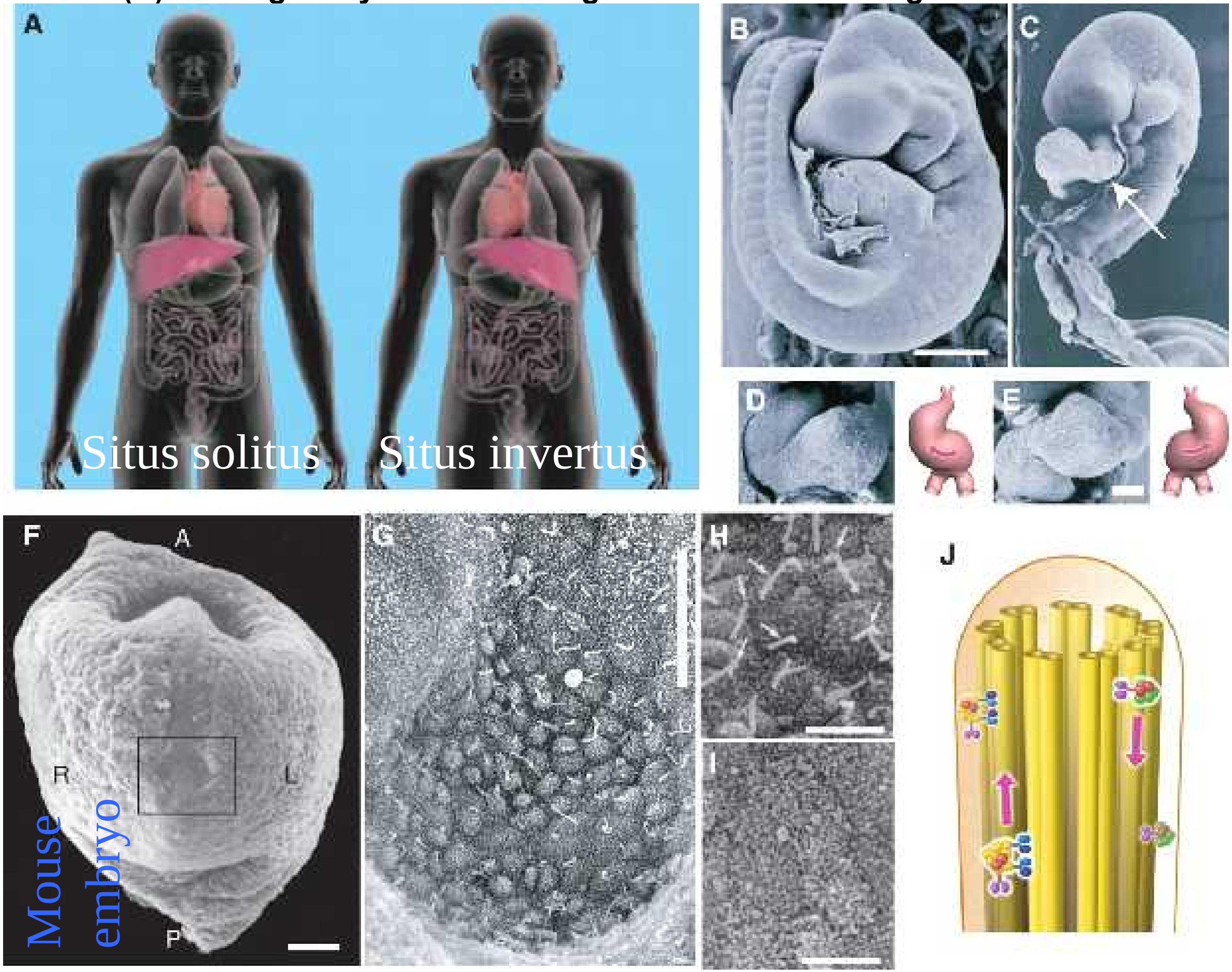
Bio435-2012

- www.iiserpune.ac.in/~cathale/blog/
- Water and crowding
- Macromolecular dyamics: Molecular motors, polymerization motors, DNA packing, protein folding
- Thermodynamics: out of equilibrium systems
- Cellular biophysics: nerves, muscles and stem cells
- Tissue dynamics and development
- Experiments: FRAP, particle tracking and crowding, bacterial patterns in colonies with substrate rigidity
- Student presentations: term paper

Water and Movement

Bio435

(A) Left–right asymmetric arrangements of internal organs in the human body.



Normal organ orientation 99%
Kartagener's syndrome 50%

Hirokawa N et al. Cold Spring Harb Perspect Biol 2009:1:a000802

Kartagener’s Syndrome

- 50% left, 50% right heart
- Bronchiectasis (breathing difficulty)
- Male sterility

- Gene expression asymmetry driven by flow
- Flow driven by Kif3B (kinesin superfamily)

Kartagener (1933), Nonaka (1998), Hirokawa (2009)

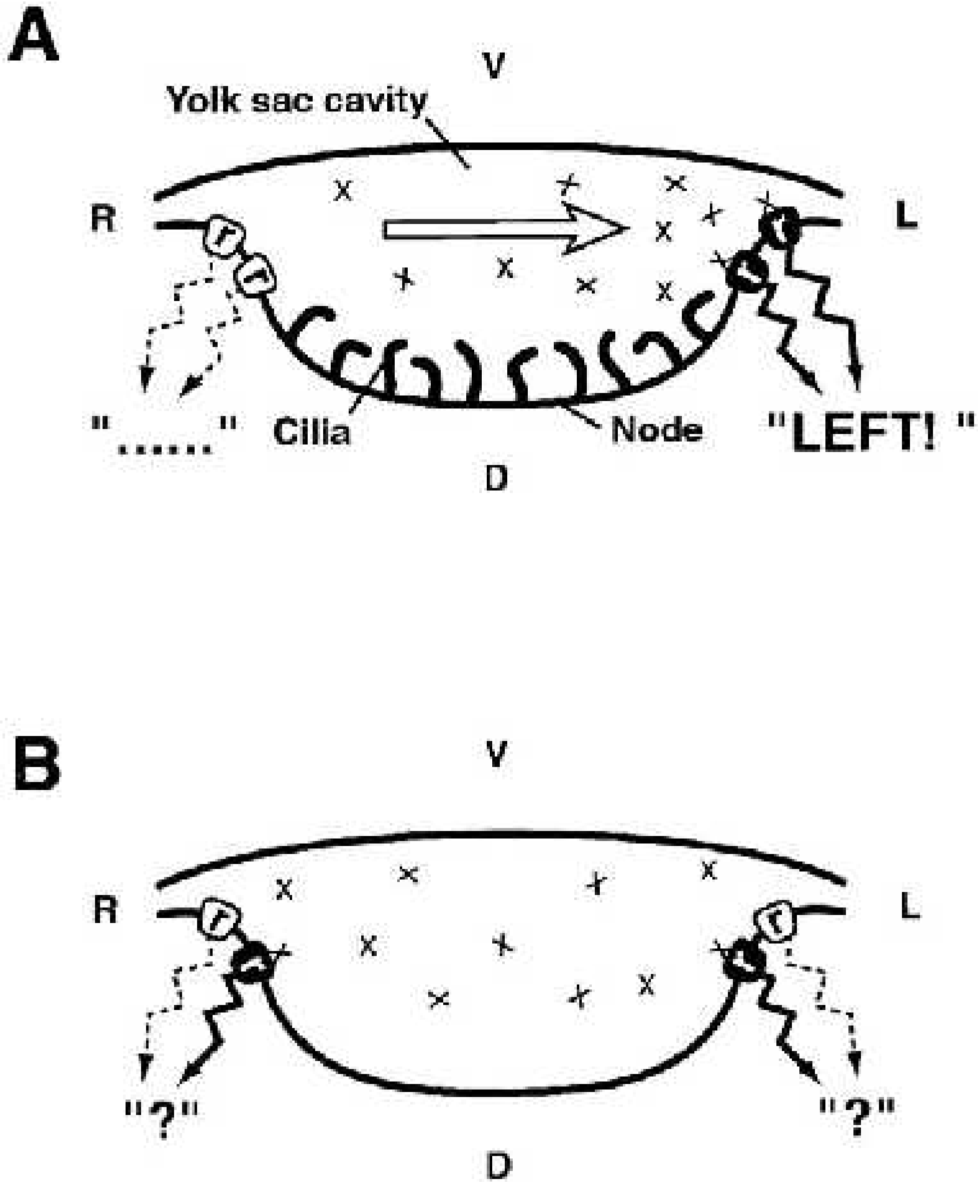
Body Axis

- Nodal Flows determine left-right asymmetry Nonaka (1998), Nonaka (2005),

  Guirao (2010)

Mammals

- DV-axis by implatantion
- AP-axis perpendicular
- Left-Right last axis to be determined



Blood Flow

Two day

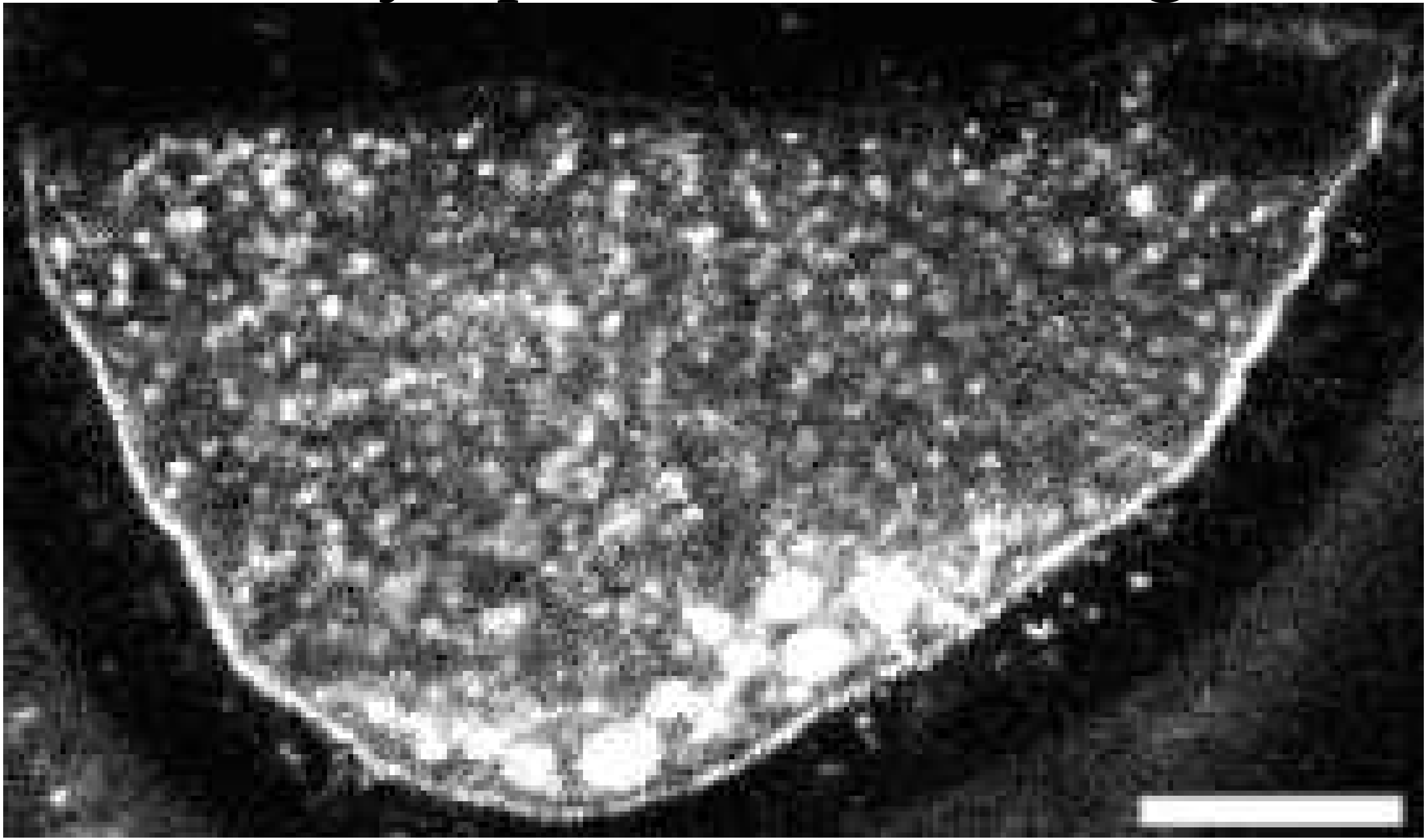
Adult

http://www.cas.vanderbilt.edu/bioimages/animals/danrer/zf sh-devel.htm

Blood Flow

Beth Roman, U. Pitt

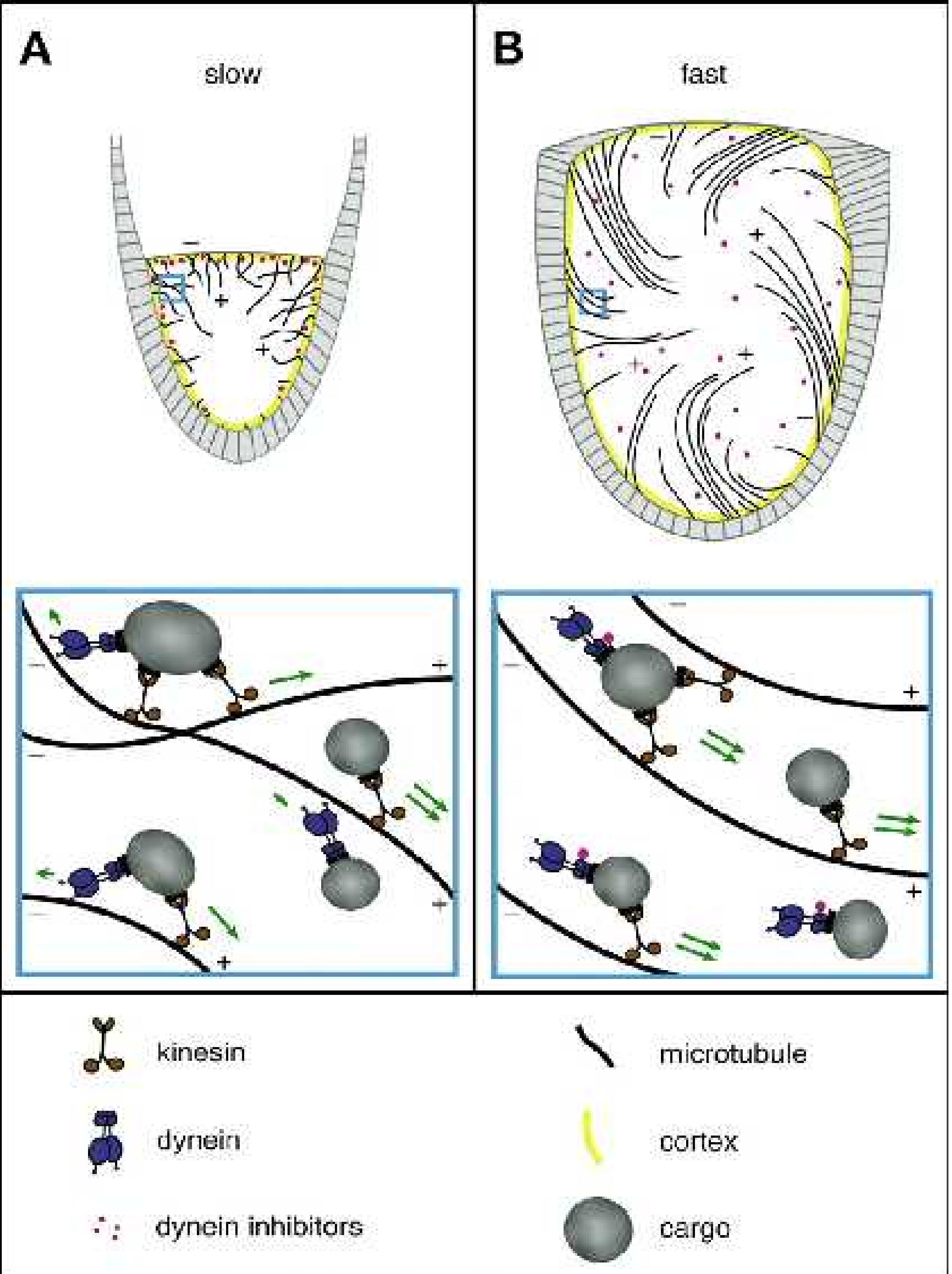
Cytoplasmic Streaming



Serbus et al (2005)

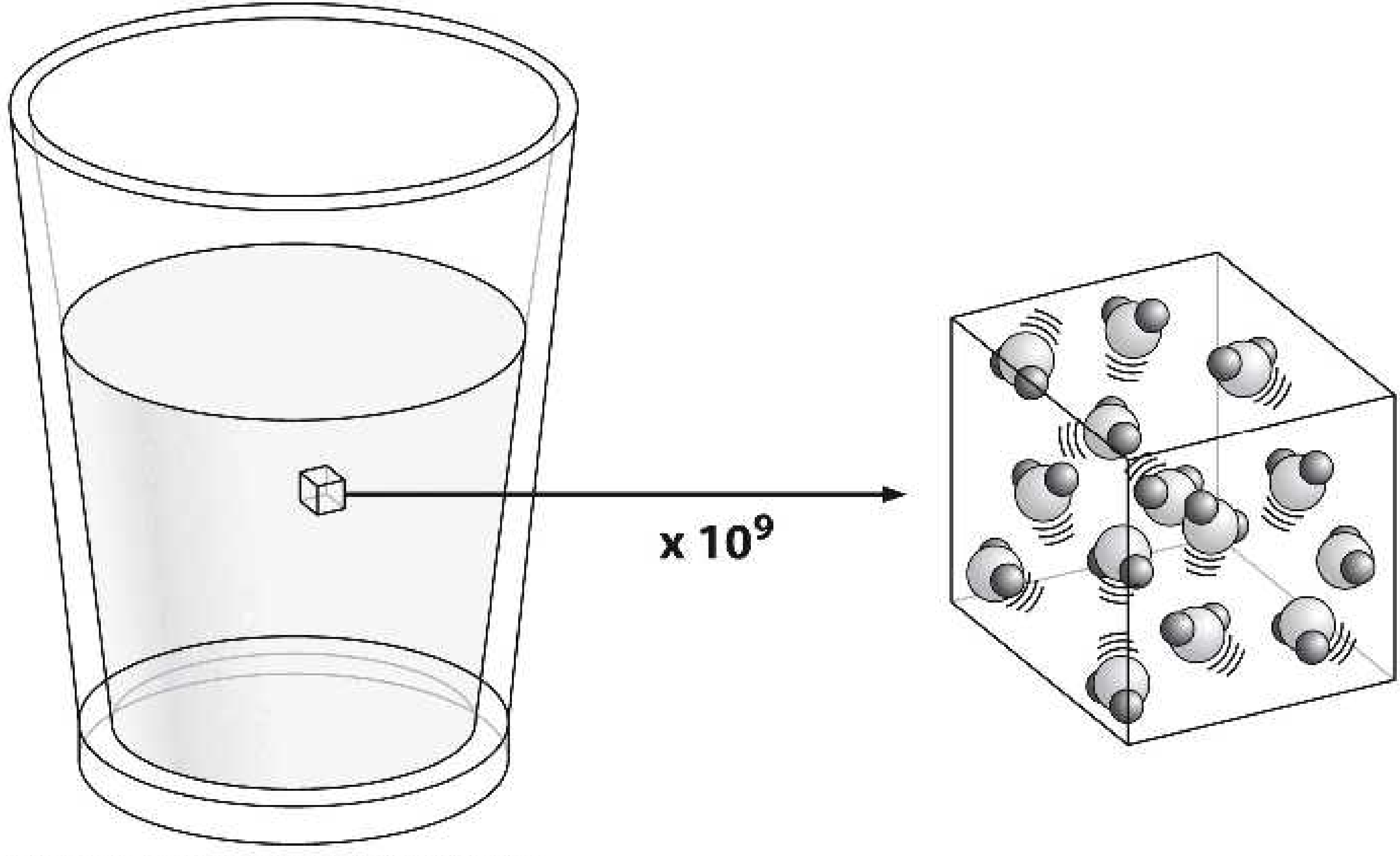
Slow cytoplasmic streaming in a Drosophila oocyte. Endosome seen in a 8 second time-lapse movie represents 30 minutes of real time. Scale bar: 25 mm.

Mechanism

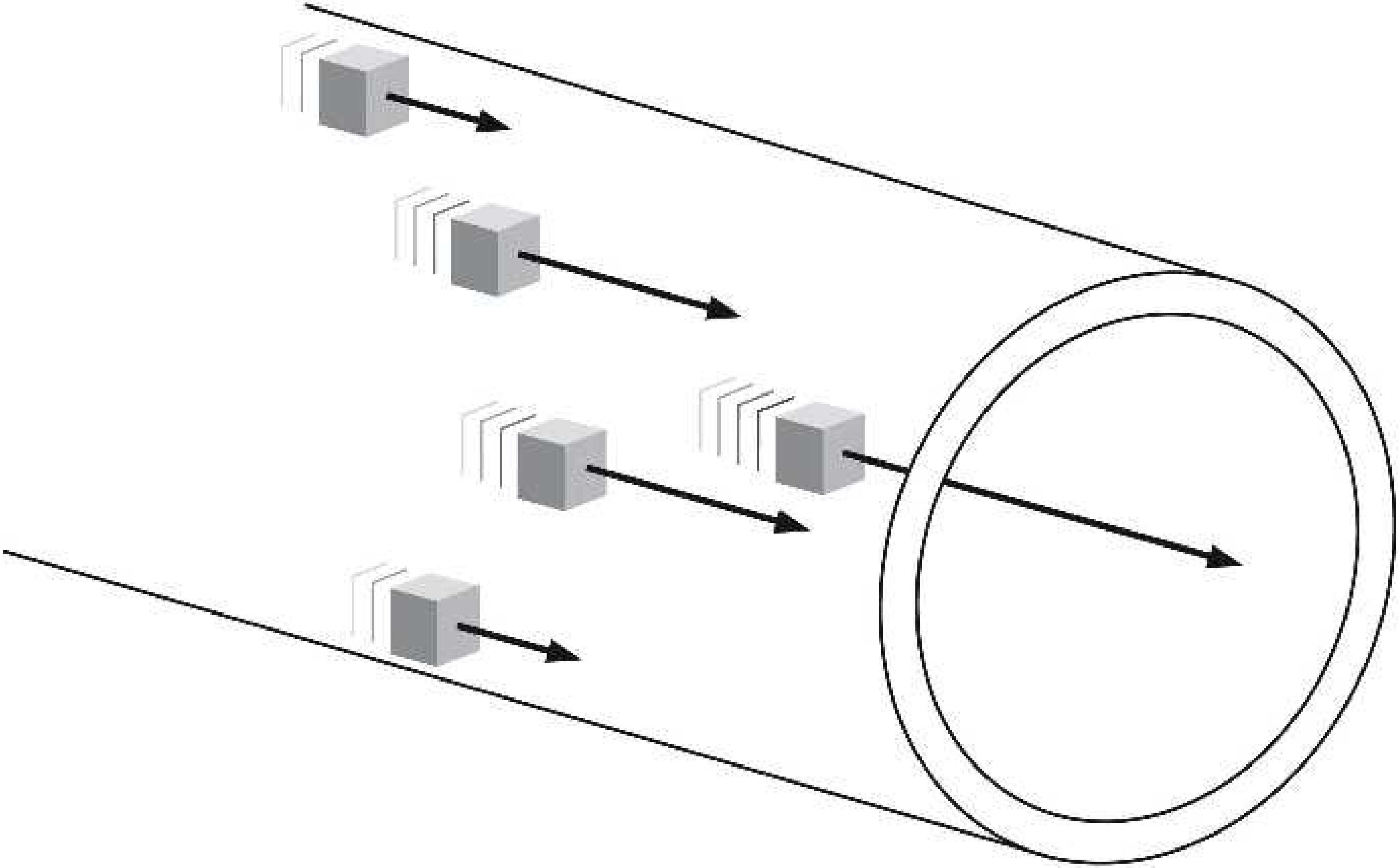


Serbus et al (2005)

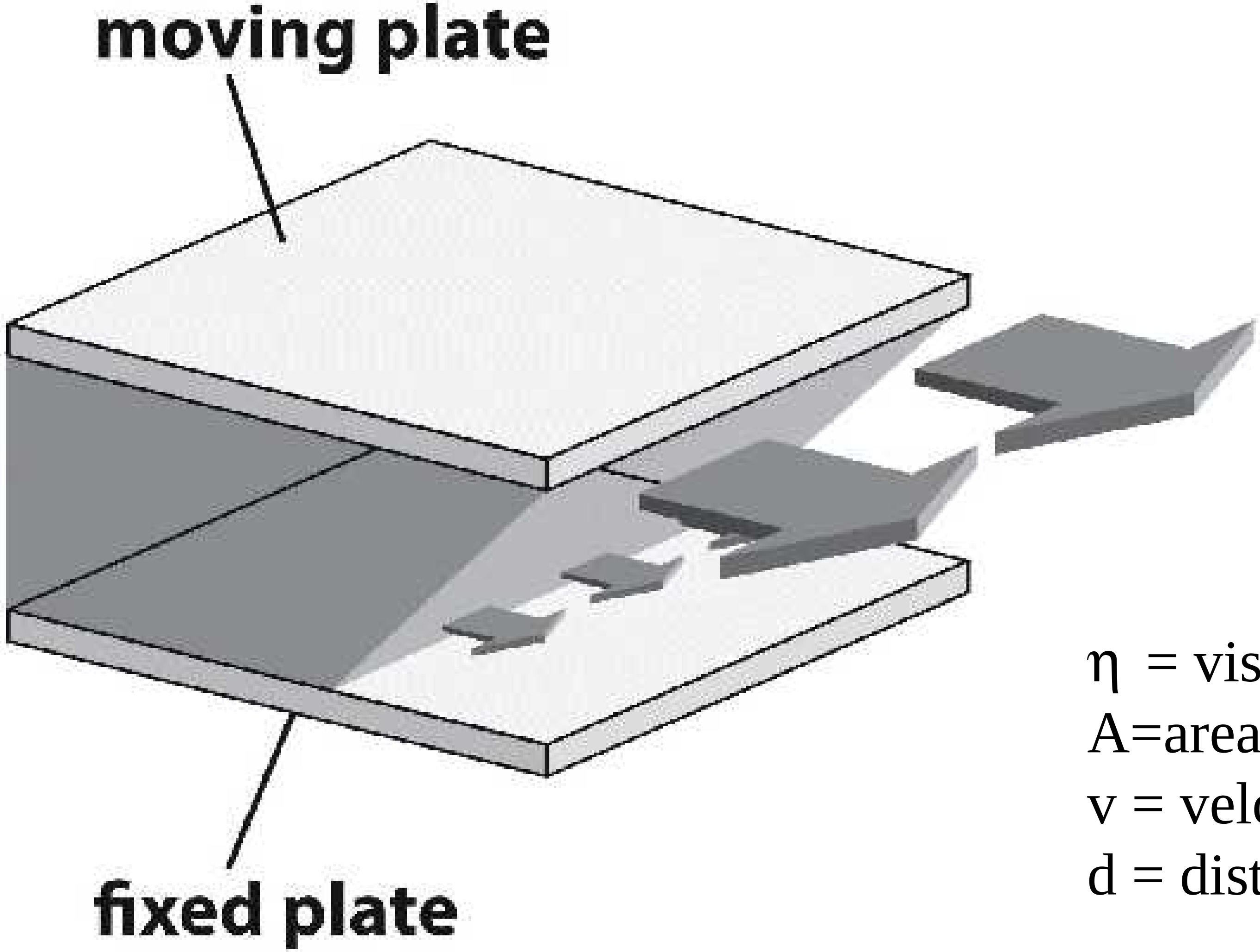
Molecular Description of Water



Velocity Field Formalism



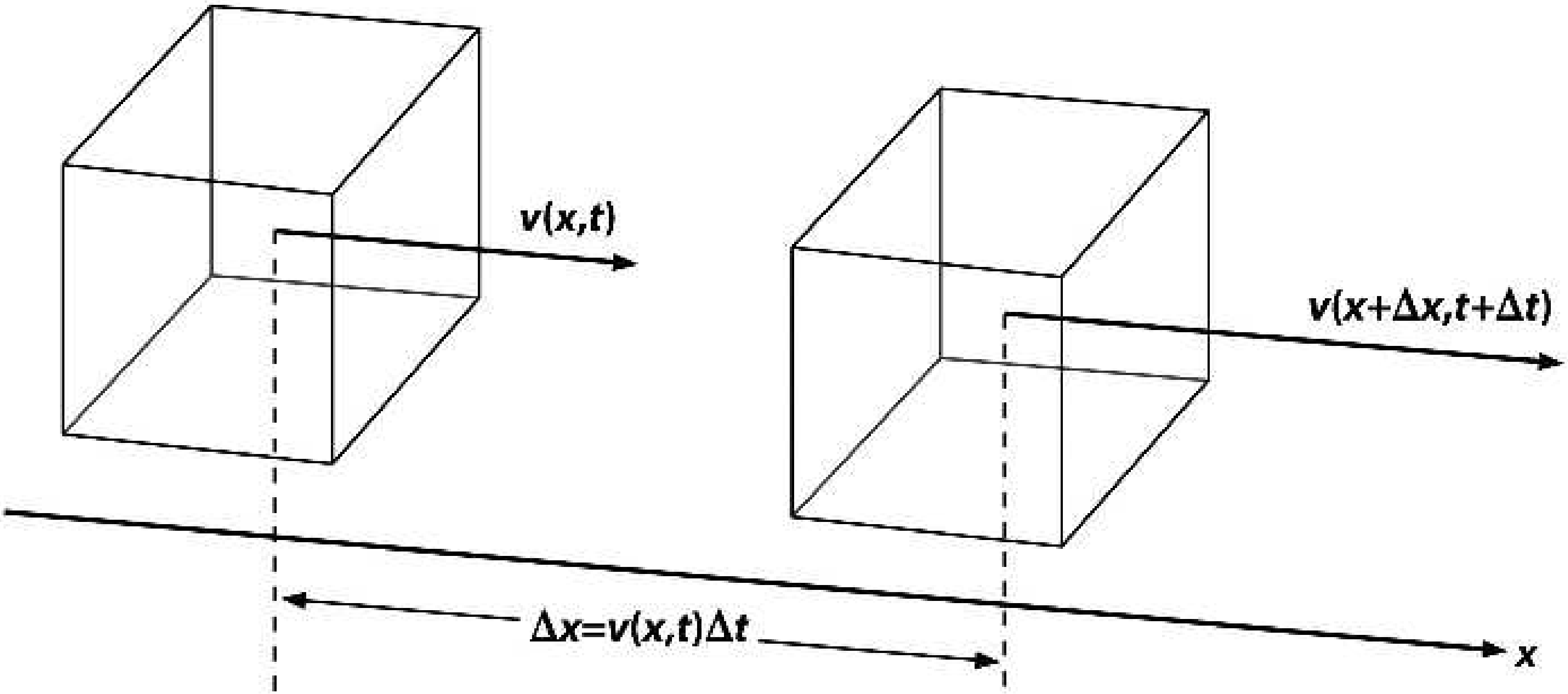
Fluid Viscosity Measurement



$$\frac{F}{A} = \eta \frac{v}{d}$$

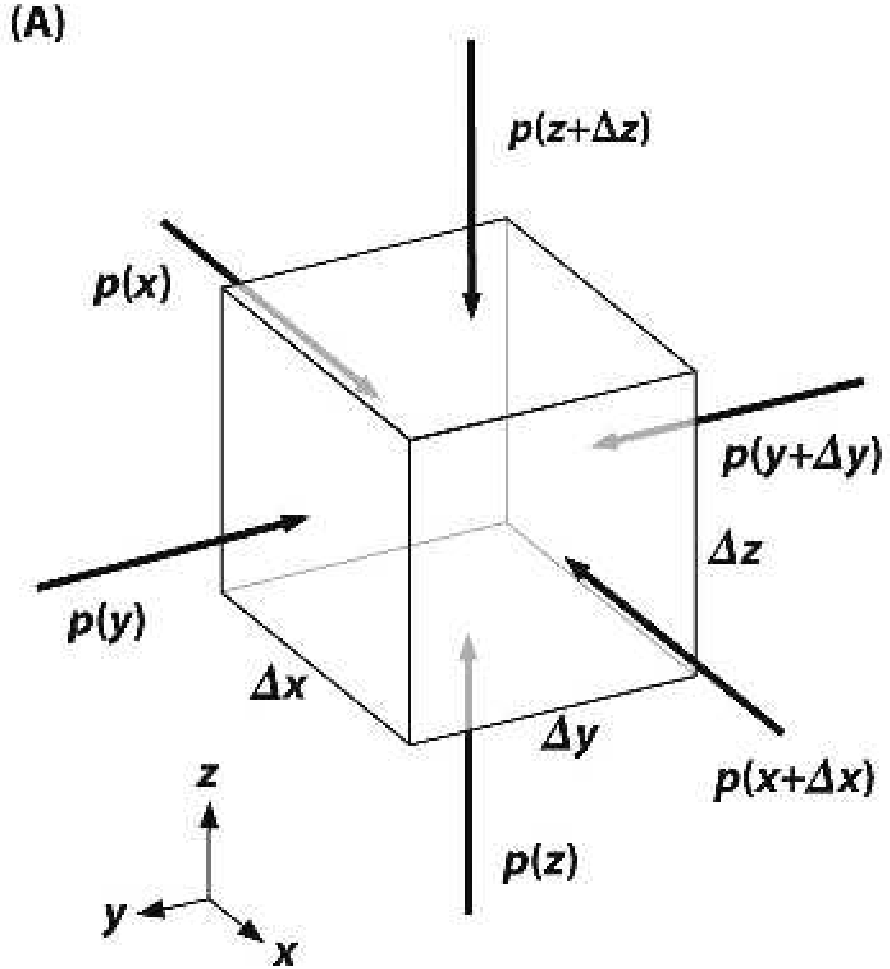
η = viscosity of fluid
A=area of plate
v = velocity
d = distance between plates

Acceleration of Small Fluid Parcel

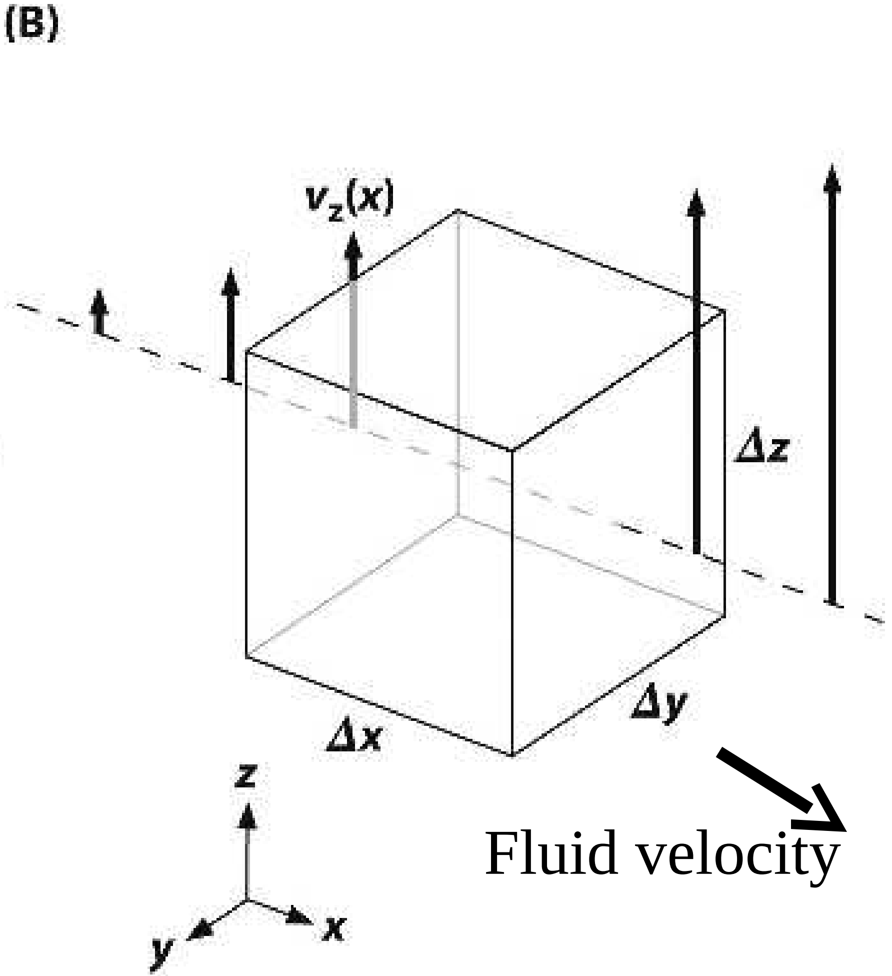


Forces Acting on Fluid Element

Pressure



Viscous

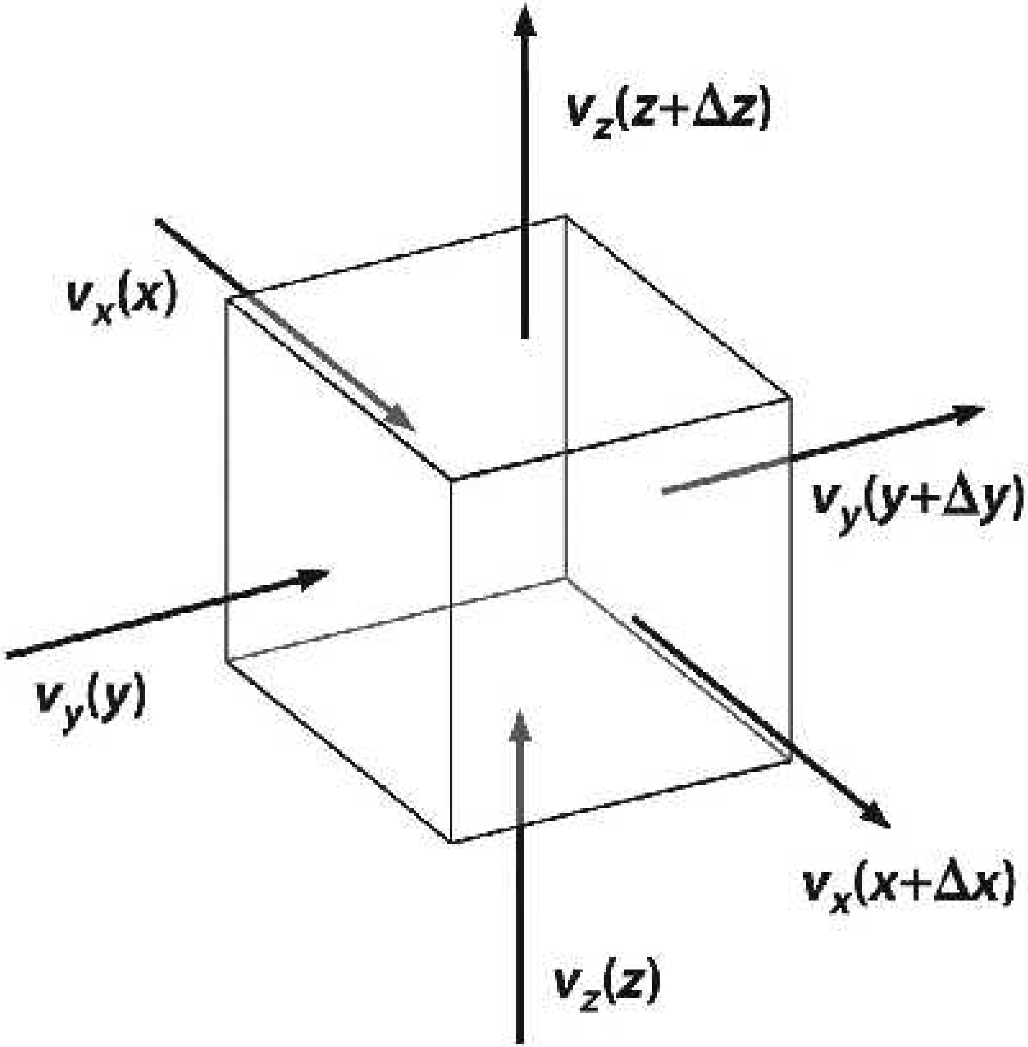


Fluid velocity

Forces

- Pressure Forces (F_P)
- Viscous stress forces

Incompressible Flow- Newtonian Fluid



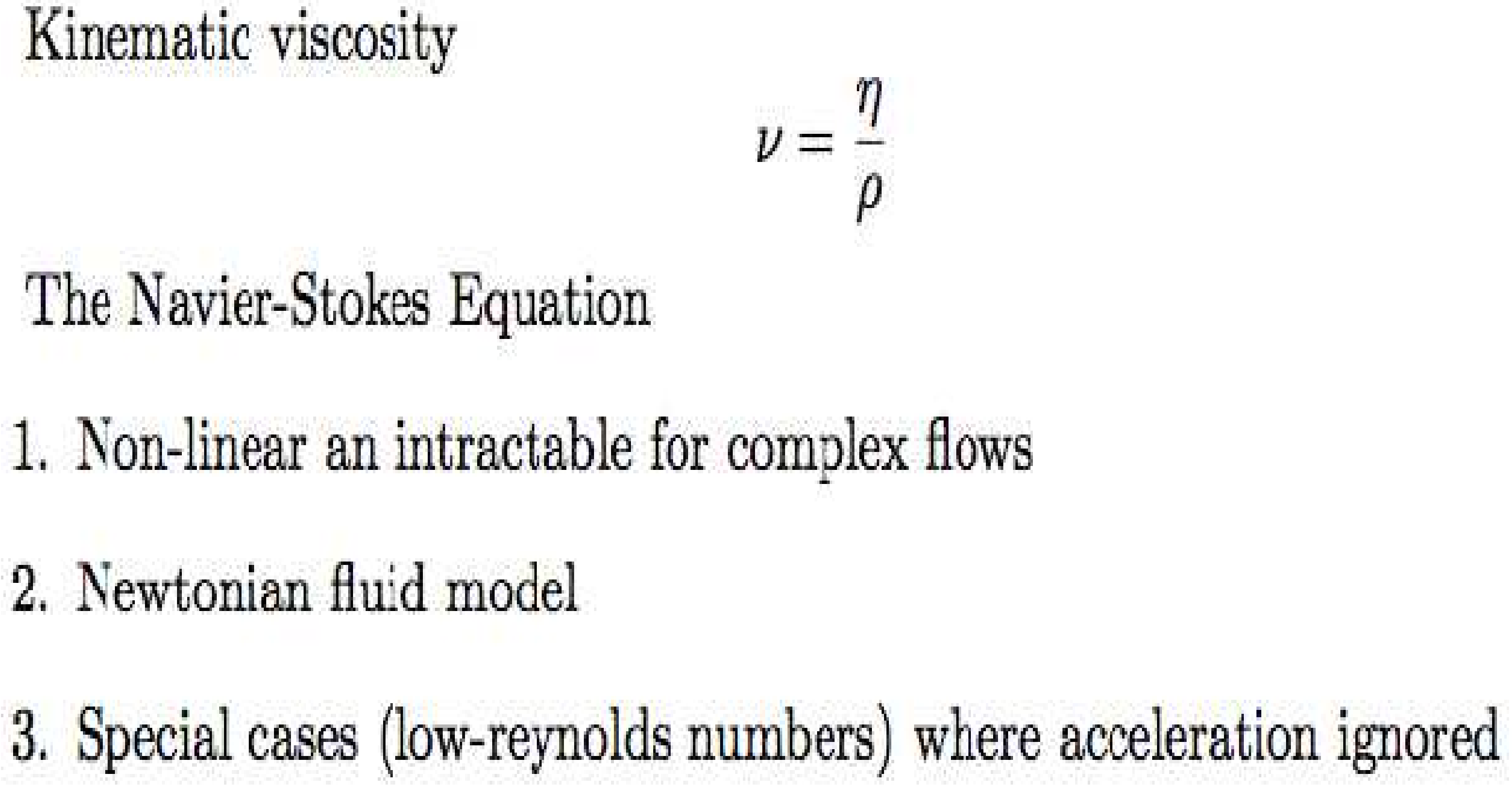
Newtonian Fluids

$$\Delta m\mathbf{a} = \delta F_p + \delta F_v$$

The Navier-Stokes Equation

$$\frac{\delta \mathbf{v}}{\delta t} + (\mathbf{v} \cdot \nabla)\mathbf{v} = -\frac{1}{\rho}\nabla p + \nu \nabla^2 \mathbf{v}$$

Navier-Stokes Equation



Kinematic viscosity

$$\nu = \frac{\eta}{\rho}$$

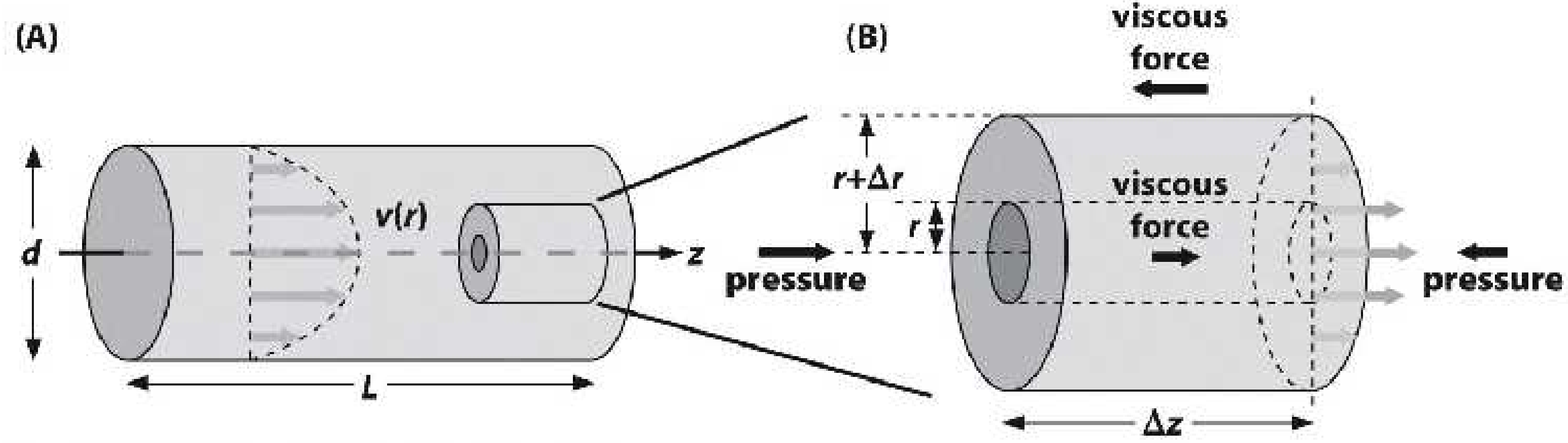
The Navier-Stokes Equation

1. Non-linear an intractable for complex flows
2. Newtonian fluid model
3. Special cases (low-reynolds numbers) where acceleration ignored

Blood Circulation

- Blood vessel sizes: 1 cm to 2 μm
- RBCs: 5 μm (human)

Fluid Dynamics of Pipe Flow



Flow through a pipe of diameter d and Length L

Cylindrical fluid element

Viscous forces balanced
by
pressure forces

Velocity profile varies along radius

Velocity of Flow

- Pressure and viscous forces balanced
- Derive Fp and Fv in z-direction
- Get expression for v(r) velocity
- Volume flux rate

- What is the expression for maximal velocity?

Speed of Blood

Different animal capillaries

d=5 μm

Δp 20 mm Hg 3000 Pa

Length of capillary l 1 cm

Avg. flow velocity?

η = ?

Hagen-Poisuelle's Equation

Q= volumetric flow rate (dV/dt)

p= pressure difference across the pipe

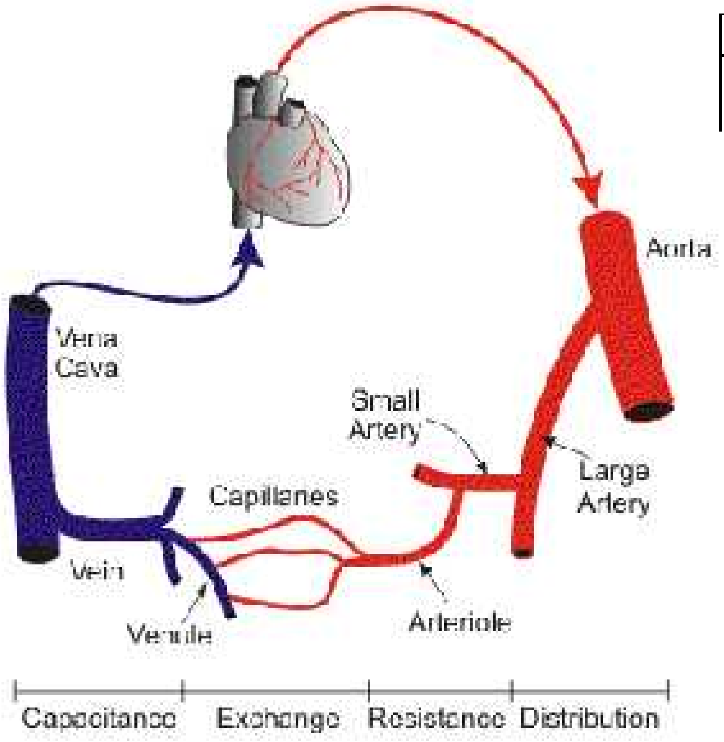
d= diameter of the pipe

= kinematic viscosity

l = length of the vessel

$$Q = \frac{\pi \Delta p d^4}{128 \eta l}$$

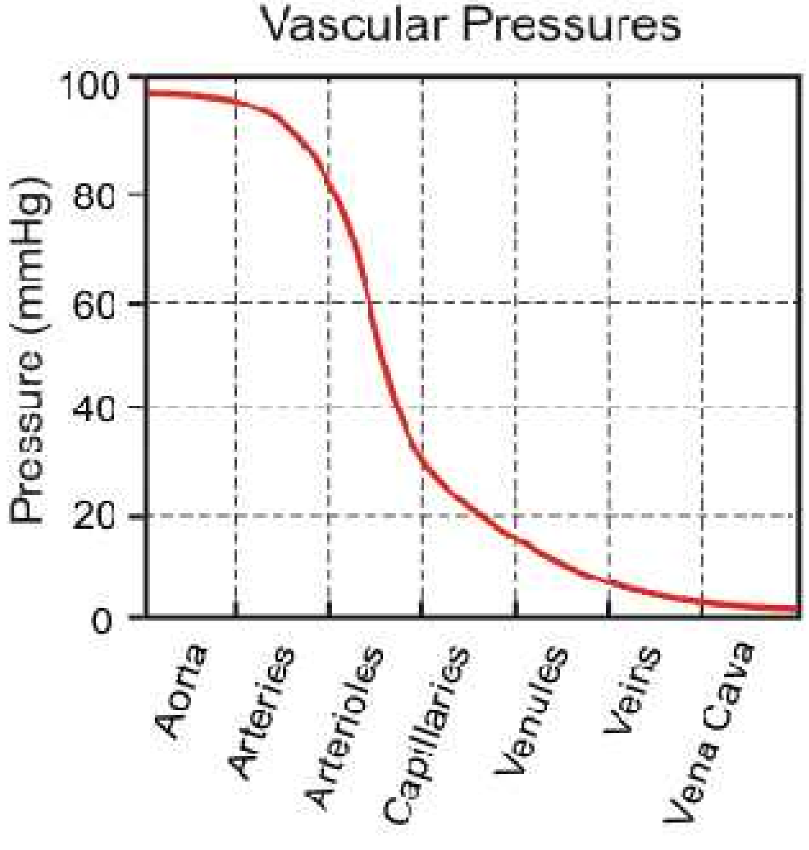
Hemodynamics



VESSEL TYPE	DIAMETER (mm)	FUNCTION
Aorta	25	Pulse dampening and distribution
Large Arteries	1.0 - 4.0	

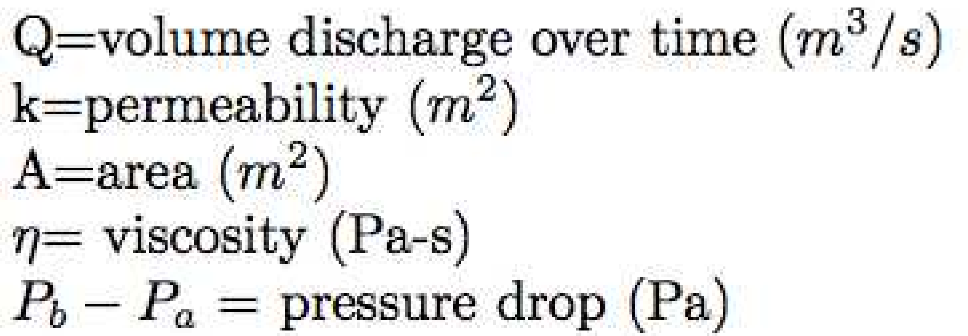
Distribution of Pressure

Pressure vs vessel diameter?



Flow and Resistivity

- Ohm’s law V=IR, V=potential difference, I=current, R=resistance
- D’arcy’s law ∆P=QR (for low reynold’s numbers) where ∆P is the pressure difference, Q is flow rate and R is resistivity



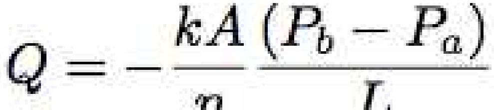
Q=volume discharge over time (m^3/s)

k=permeability (m^2)

A=area (m^2)

η= viscosity (Pa-s)

$P_b - P_a$ = pressure drop (Pa)



$$Q = -\frac{kA}{\eta}\frac{(P_b - P_a)}{L}$$

Leukocyte Invasion into a Tissue

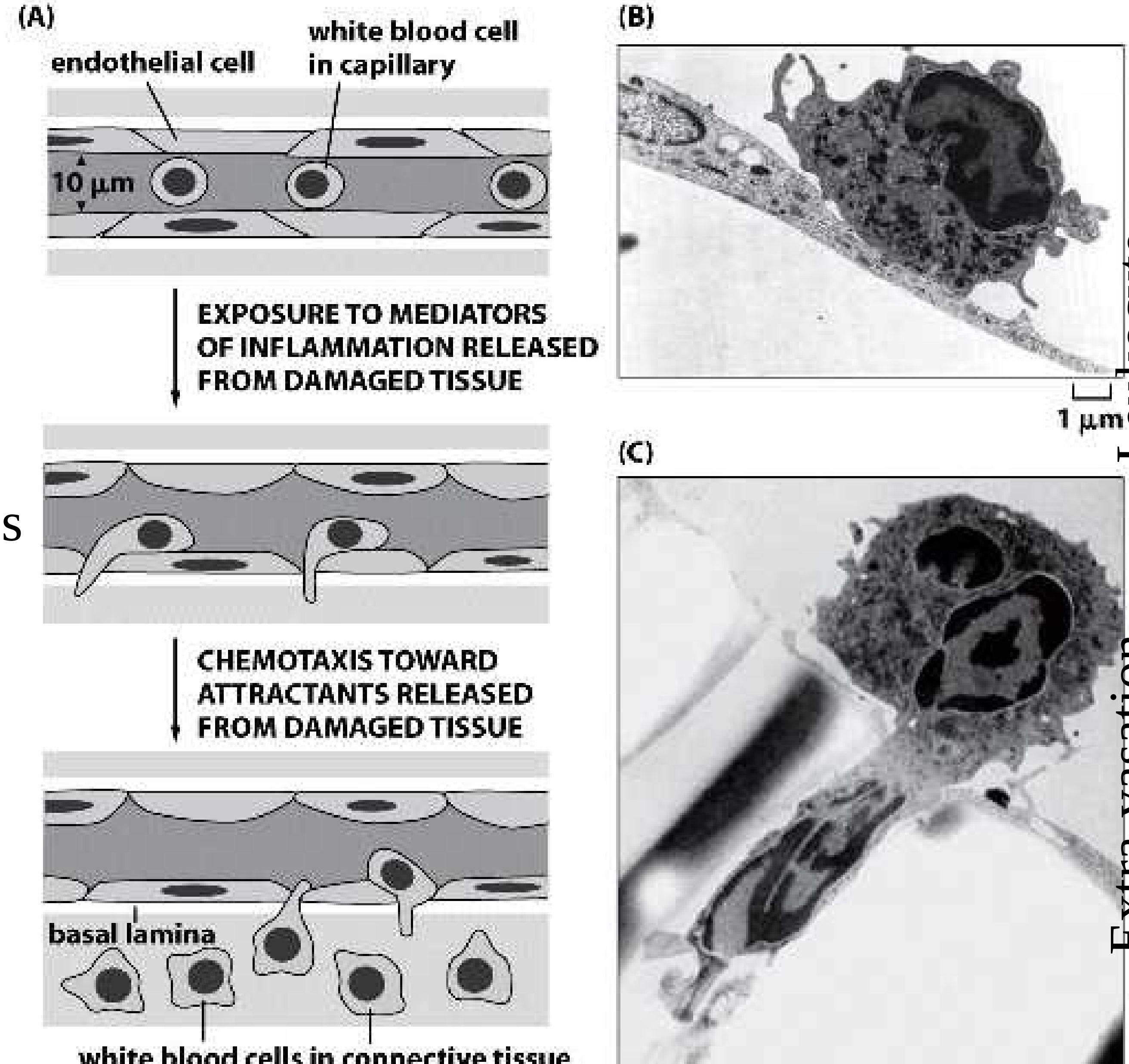
Leukocytes:

Flow

Infection

Adhesive forces

Rolling



Leukocyte adherent to an endothelial cell

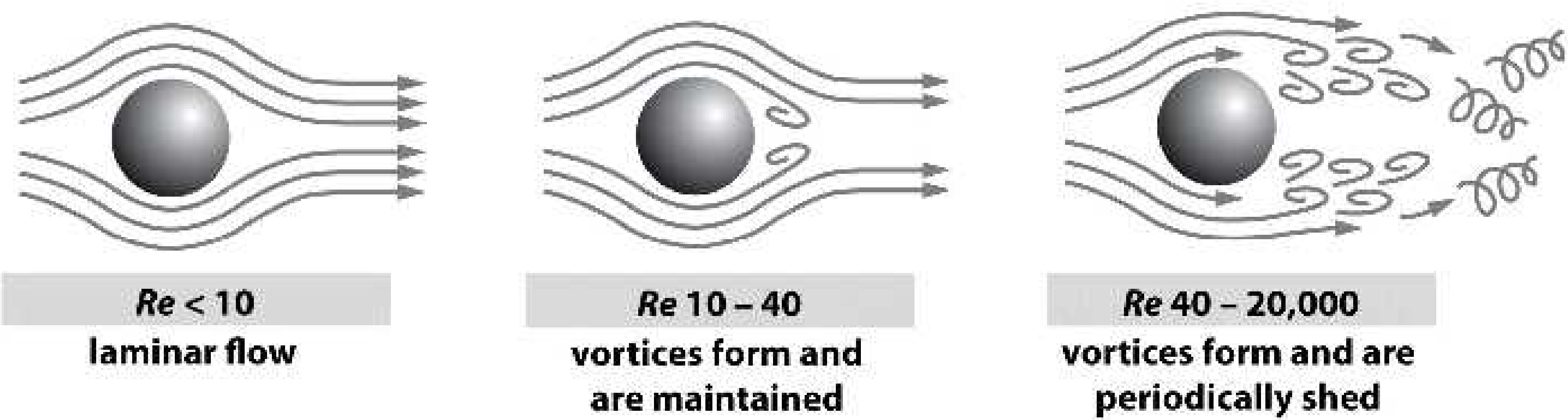
Extra-vasation across endothelial cell barrier

The 100-year Experiment

- 1927 Australia
- Flow under gravity
- 8 drops

Edgeworth, Dalton, Parnell (1927) The Pitch Drop Experiment http://www.physics.uq.edu.au/physics_museum/pitchdrop.shtml

Stoke’s Formula for Drag Force on a Sphere



Re < 10
laminar flow

Re 10 – 40
vortices form and are maintained

Re 40 – 20,000
vortices form and are periodically shed

Figure 12.10 Physical Biology of the Cell (© Garland Science 2009)

Flow types away from the wall at constant velocity **v**

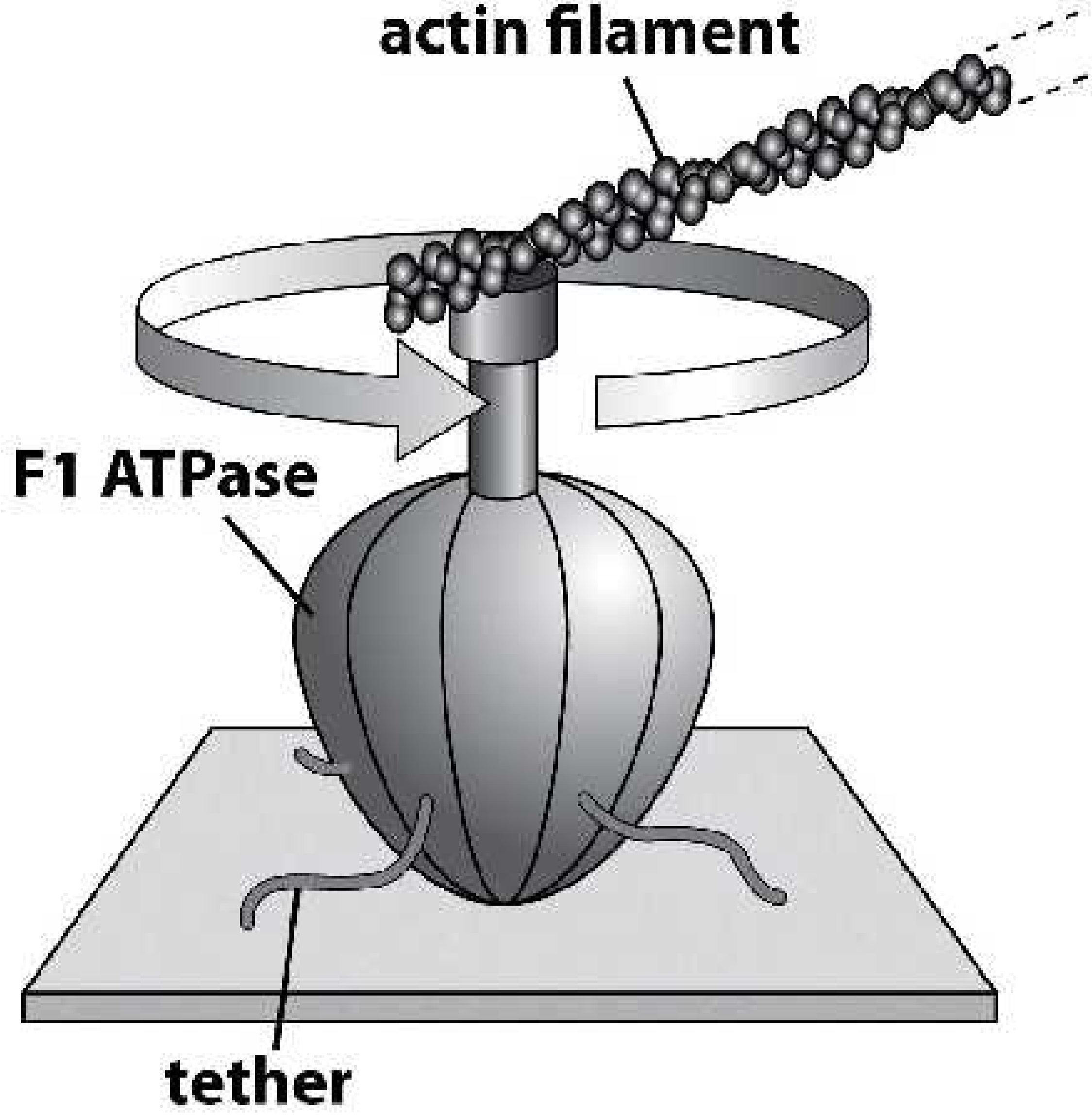
Fundamental solution for sphere in a flow-

Solve Stokes Equation

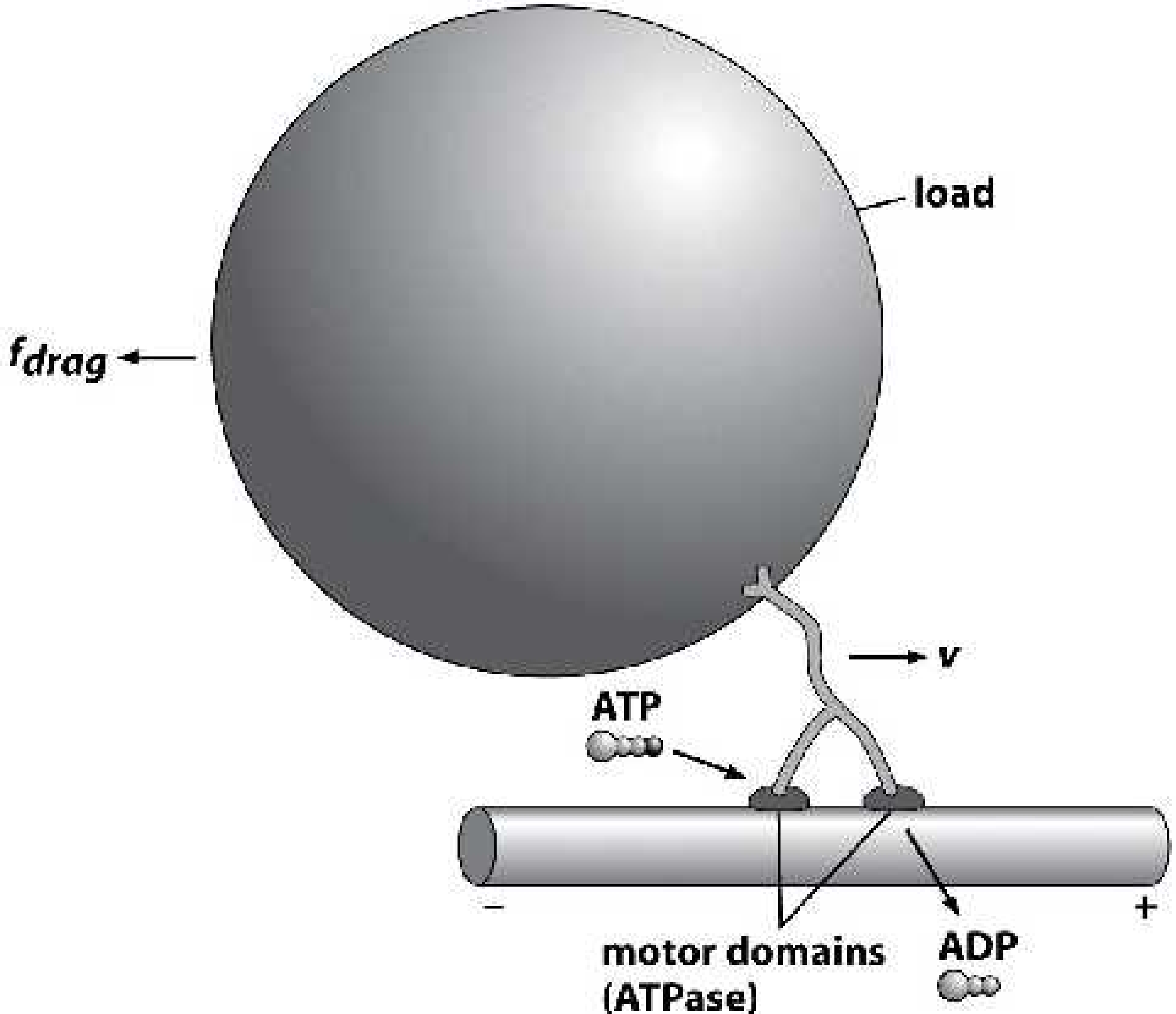
Stokes Drag

- Cylinder
- Arbitrary shapes
- Movement of Bacteria in Re<<

Stokes Drag in Single Molecule Experiments

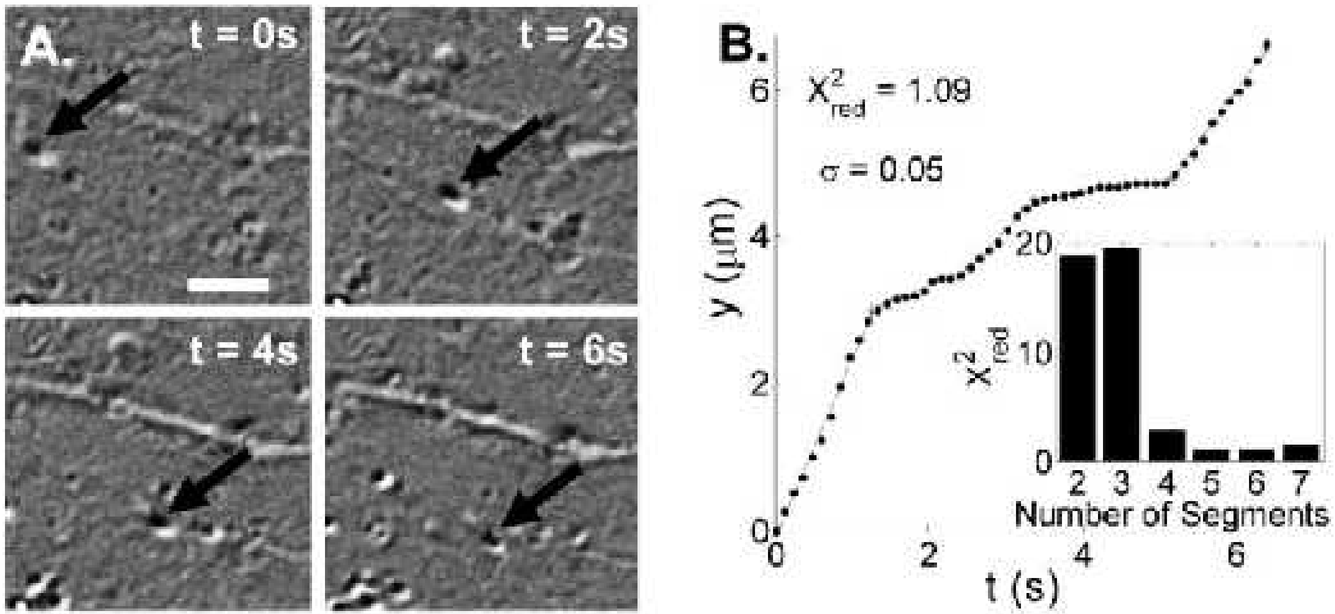


Viscous Forces In Optical Tweezer Experiments



- Bead diameter ~500 nm
- Motor speed 1 micron/s

Vesicle Transport



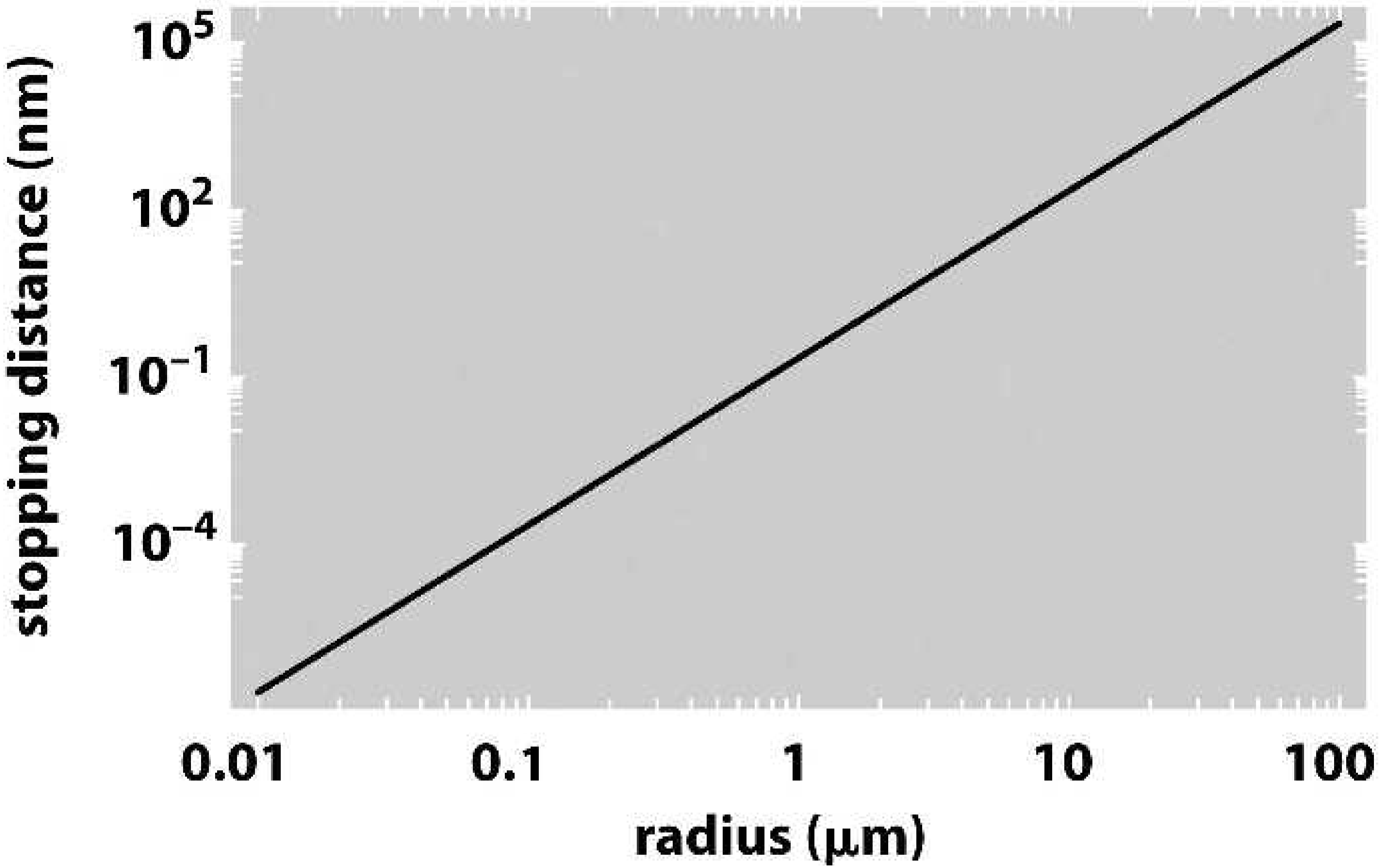
-DIC

Motion enhanced differential interference contrast (MEDIC) movies of living NT2 (neuron-committed teratocarcinoma) velocity (v), radius (a), and effective cytoplasmic viscosity (')

Time Scales of Movement

- Viscous time scale $\tau_v = \rho a^2 / \eta$
- Inertial time scale $\tau_i = a / u$

- u=velocity, a=characteristic length



Viscous time

Inertial time

Viscosity

= **dynamic viscosity** (Pa-s = N-s/m^2), **absolute viscosity**

1 Poise = 0.1 Pa-s

For water η = from 0.1 to 0.01 Pa-s

At 293K, =1 mPa-s = 1×10^{-3} Pa-s

At 300K, η=0.798 mPa-s = 0.798×10^{-3} Pa-s

= **kinematic viscosity =** ρ/η

(1 Stokes = 10^{-4} m^2/s)

For water at 293K, =10^{-6} m^2/s

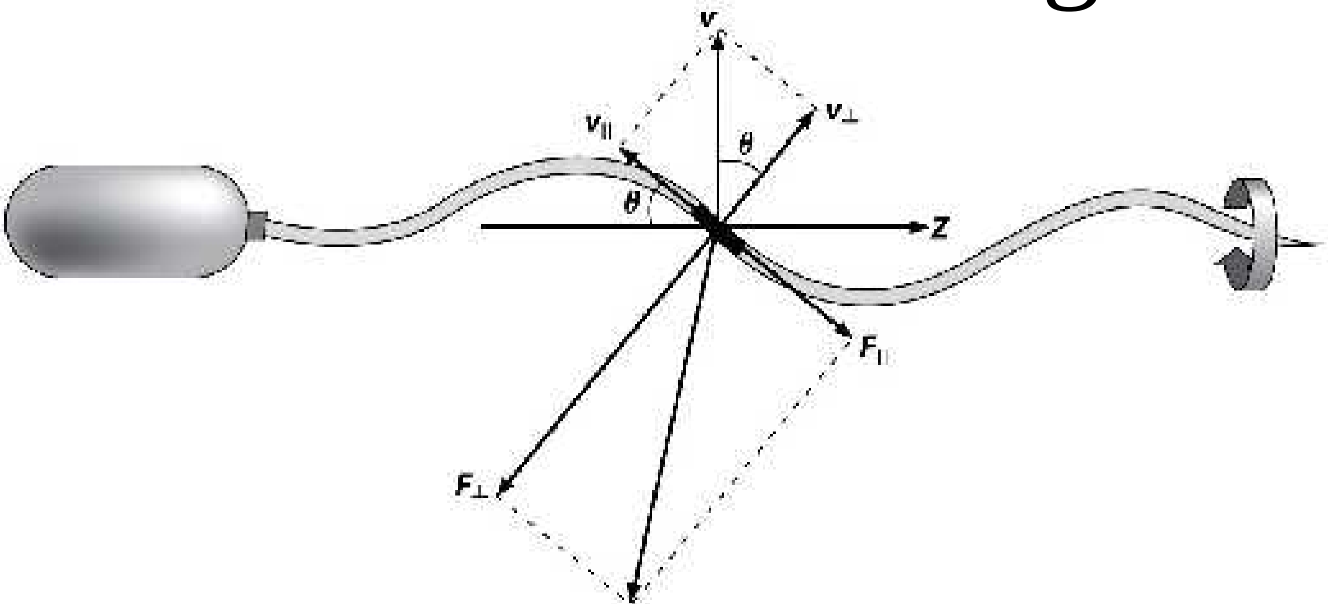
ρ= density (kg/m^3)

Swimming E. coli

Fuorescently-labeled cells with strobed laser illumination, using an ordinary CCD camera at These cells where grown on T-broth. They are about 1 µm in diameter by 2 µm long and swim at about 30 µm/s

Turner et al. (2000) J. Bacteriol. 182(10) 2793-2801

Velocity Components of E. coli Swimming



Rotation of E. coli flagellum: Length L=10 m

Frequency f=100Hz

Pitch P=2 m

Diameter D=0.5 m

Drag Coefficients

- Small segment of length *l*
- Angle with z-direction
- Linear velocity v= Df
- Angle tan = D/P
- Forces- viscous drag and propulsive
- Propulsive force components: perpendicular, parallel

Velocity of Swimming

$$V = v \cos\theta \sin\theta = \pi D f \sin\theta \cos\theta$$

Since $v = \pi D f$

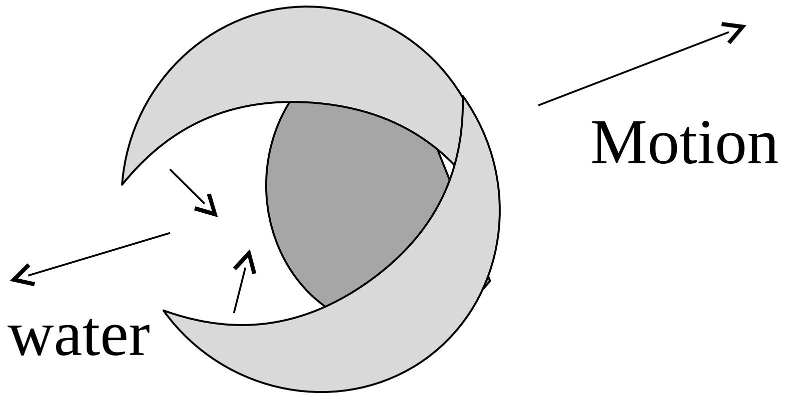
Where v = linear velocity along z-direction

D = diameter, f = frequency of rotation

Estimate V ~?

Reciprocal Deformation

Scallop
swimming

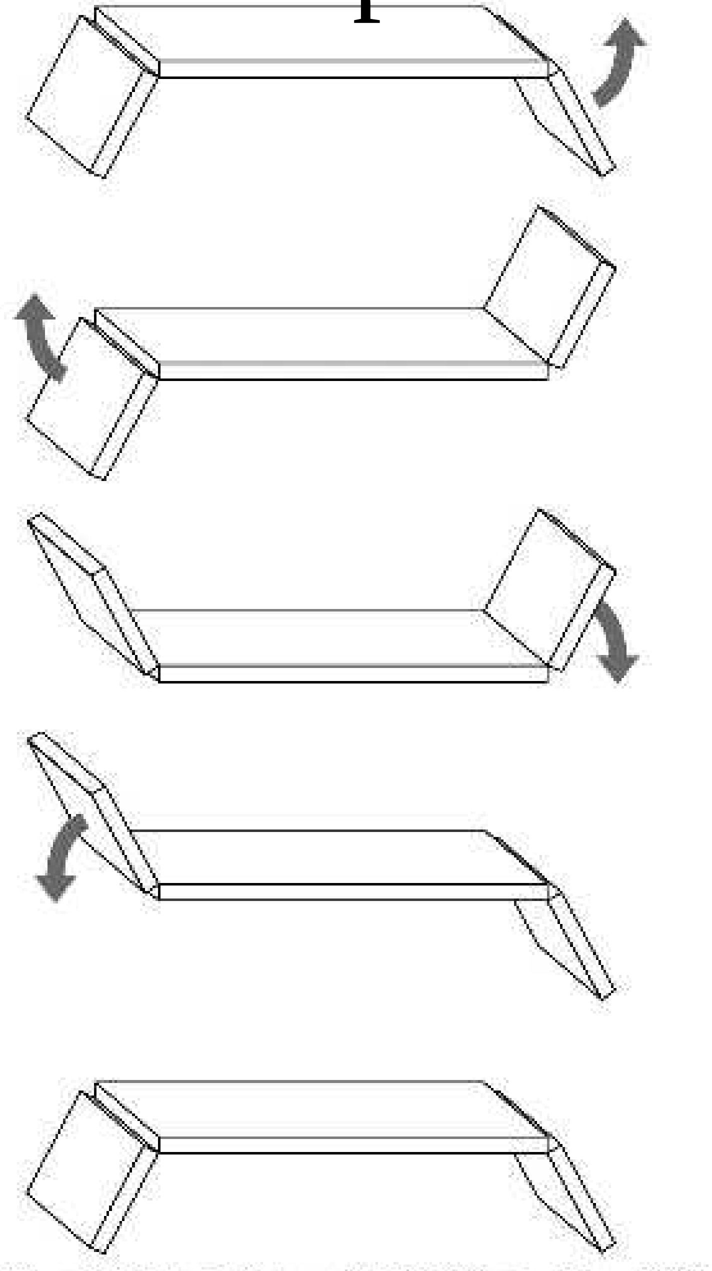


Fast closing, slow opening
Single hinge

At low Re a bacterium-sized clam-like mechanisms will go nowhere!

E.M. Purcell (1977) Life at Low Reynolds Numbers. Am. J. Phys. Vol 45, No. 1

Purcell’s Simple Swimmer



3 plates, 2 hinges can avoid reciprocal motion- so long as order of folding up and opening (LR) is the same

Oars In a Submarine in Molasses

Rigid Oars: reciprocal motion

Flexible oars: Propulsion

Application

Centrifugation and separation

- Fractionation (cells, organelles, chromatin)
- Separation of proteins
- Purification

Centrifugation

Centrifugal force on each molecule ~ $m\omega^2r$

If particle size << distance from axis,
Force per unit mass approx. constant

$$v_{drift} = mg_c/\gamma$$

Frictional force drift velocity

g_c = centrifugal force/mass, = friction coeff.

Size Depedent Separation

- Spherical particle frictional coeff $\gamma = 6\pi\eta R$
- Svedberg (const) $S = m/\gamma$

1S = 10^{-13} s for globular protein 1nm radius

Dependent on particle and nature of medium

Paper Reading

- E. M. Purcell (1977) Life at Low Reynolds Numbers. Am. J. Phys.
- Chen and Springer (1999) An Automatic Braking System That Stabilizes Leukocyte Rolling by an Increase in Selectin Bond Number with Shear. J.Cell.Biol.