Introduction to BioMEMS & Medical Microdevices

Microfluidics Part 2 – Basic Fluid Mechanics

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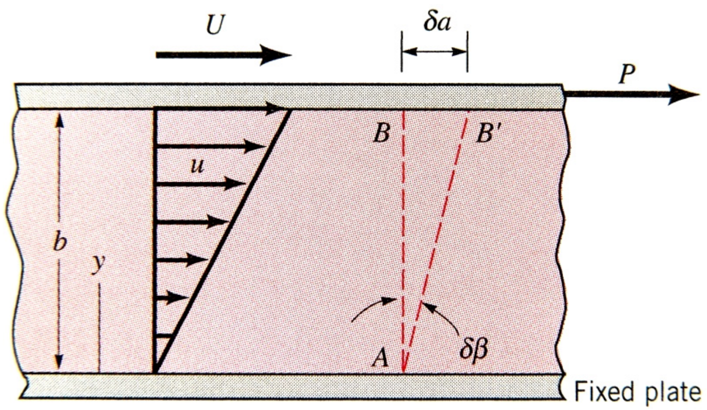
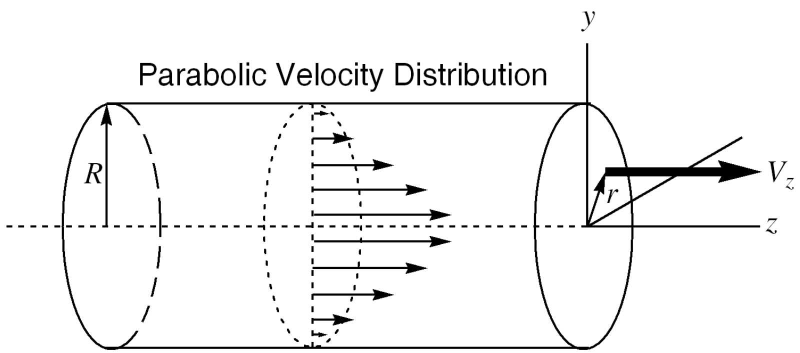
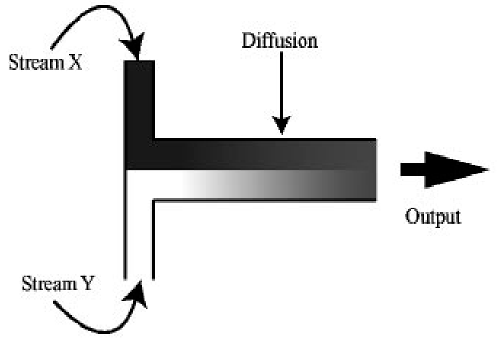


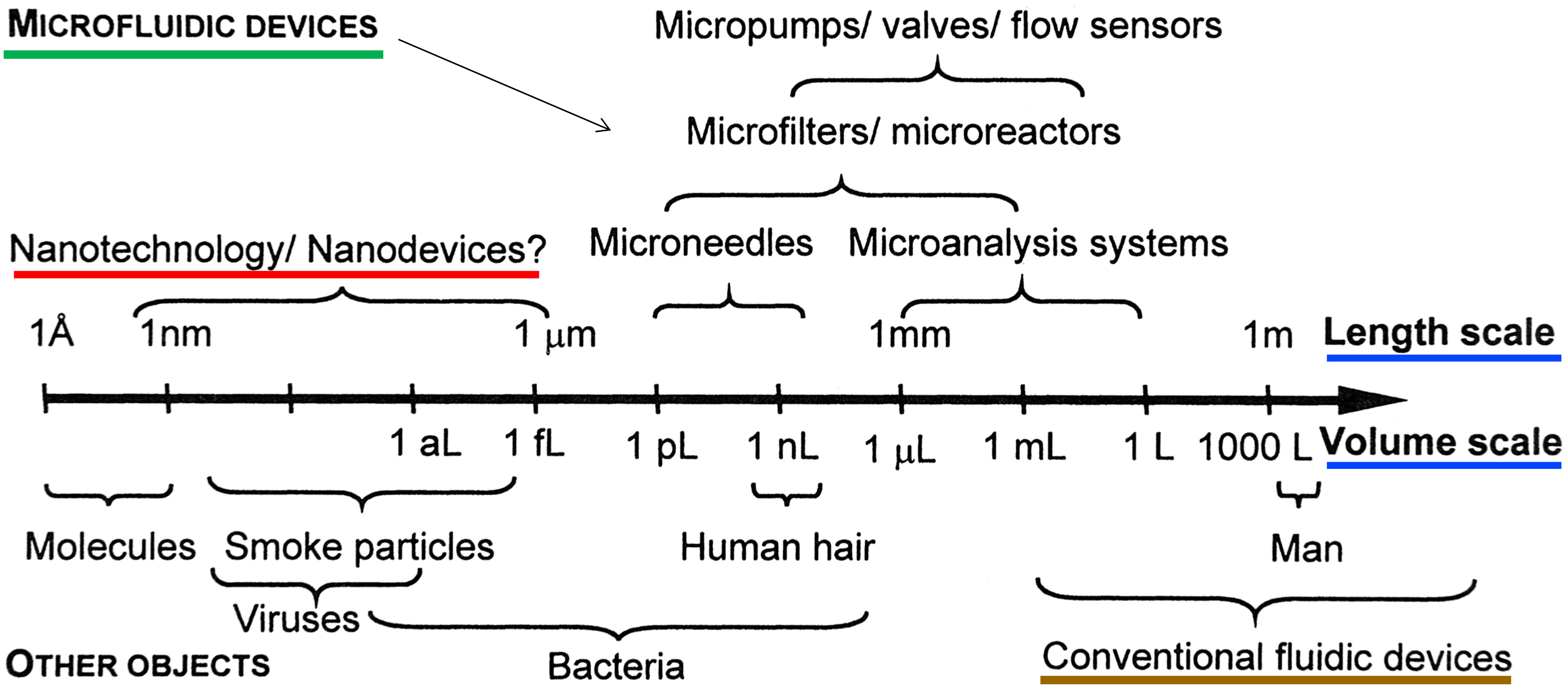




Topics

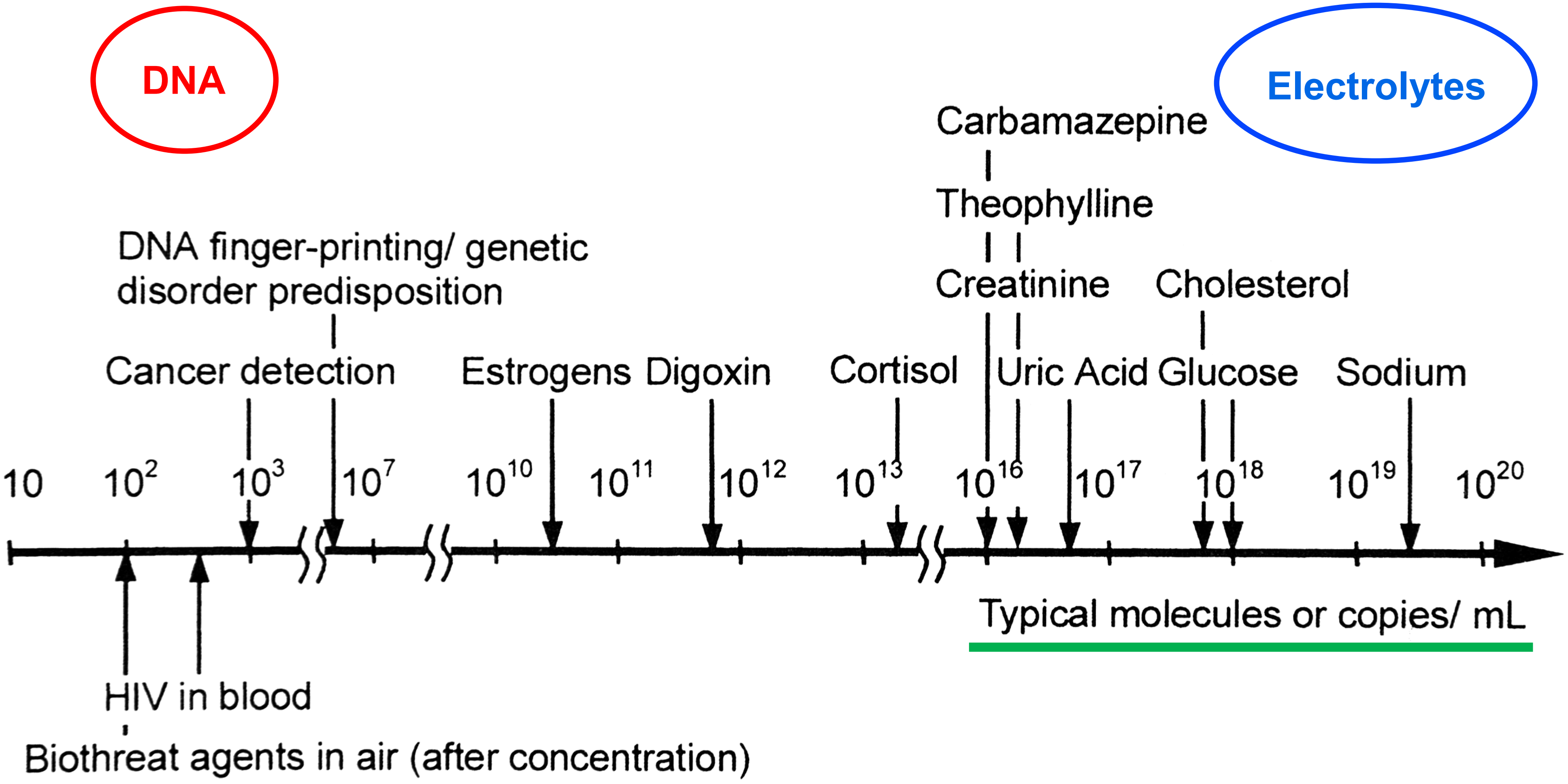
- Length & volume in the micro realm.
- Clinically relevant analyte concentrations.
- Sample volume determination.
- Fluid mechanics
- Surface area to volume
- Diffusion

Length & Volume Comparisons



Nguyen, NT and ST Wereley, *Fundamentals and Applications of Microfluidics*, Artech House, Boston, MA (2002).

Typical Serum Analyte Concentrations…



Peterson, KE et al., “Toward next generation clinical diagnosis instruments: scaling and new processing paradigms.” *Journal of Biomedical Microdevices* 2(1), pp. 71-79 (1999).

Determining Sample Volume

- The relationship between sample volume (*V*) and analyte concentration is shown here:

$$V = \frac{1}{\eta_s N_\mathrm{A} A_i},$$

Know this!

Where,

η_s (eta) is the sensor efficiency $0 \le \eta_s \le 1$,

N_A is 6.02×10^{23}, or Avogadro's number, and

A_i is the concentration of analyte, i.

- The higher the concentration of analyte and/or better the sensor, *the less the volume of sample* that is needed.

Example: K^+ (Potassium) in Serum

Potassium has a concentration of 3.5 to 5.3 mmol/liter in serum. Assume a sensor efficiency of 0.1, and concentration of 3.5 mmol/liter, approximately what is the smallest volume needed:

$$Volume = \frac{1}{.1 \times \frac{6.02 \times 10^{23}}{mole} \times \frac{3.5 \times 10^{-3} mole}{liter}}$$

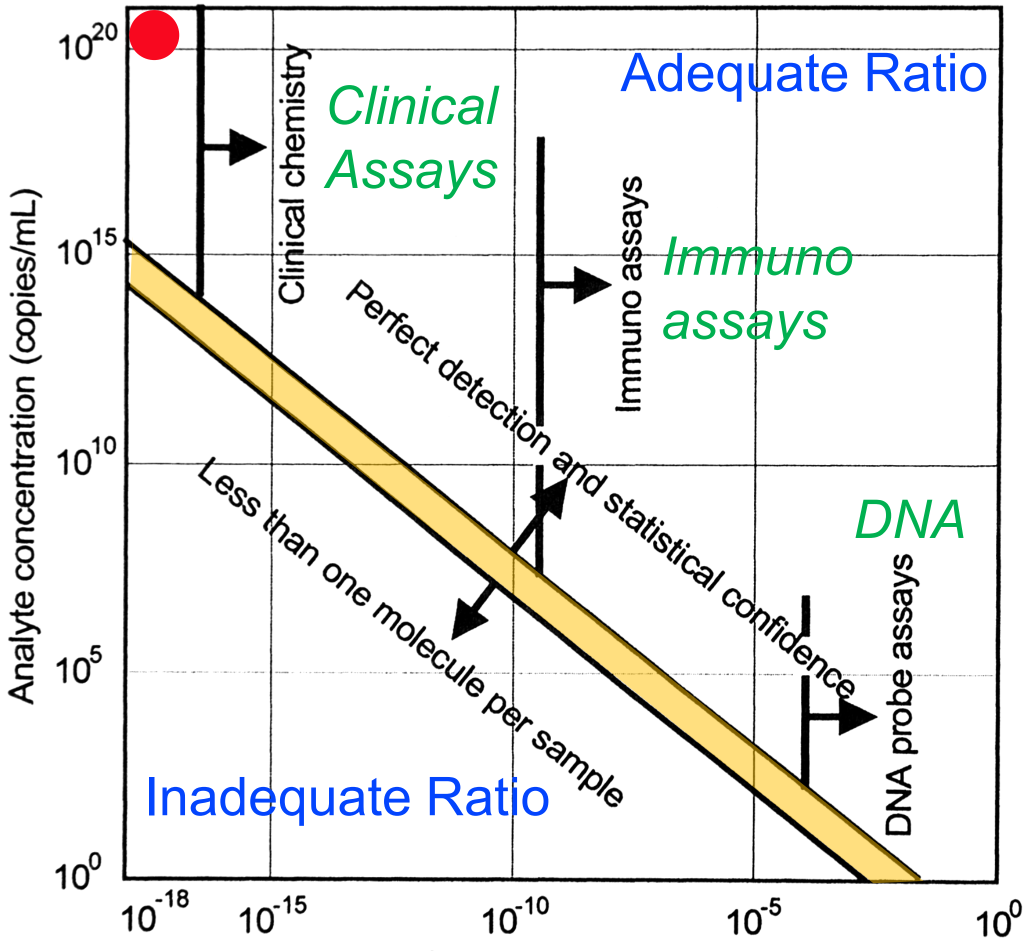
$$= \frac{1\ liter}{2.1 \times 10^{20}}$$

$$= .47 \times 10^{-20}\ liter$$

Sample Requirements for Detection…

Previous example: K⁺ →

Analyte
Concentration
(copies/ml)
to
Sample Volume (L)



Smaller Volume Needed

Larger Volume Needed

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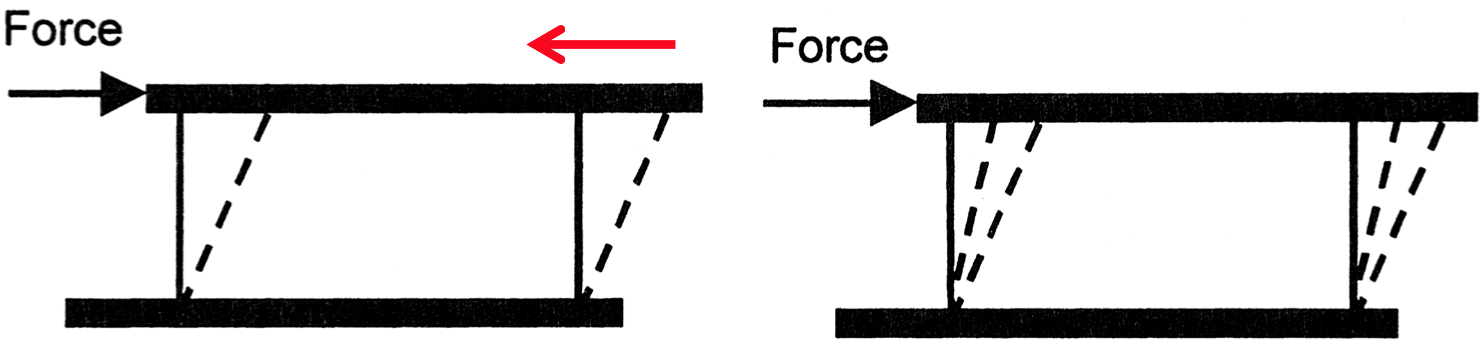
Peterson, KE et al., “Toward next generation clinical diagnosis instruments: scaling and new processing paradigms.” *Journal of Biomedical Microdevices* 2(1), pp. 71-79 (1999).

What is a Fluid?

- *A fluid is a substance that deforms continuously under the application of shear (tangential) stress of any magnitude.*
- Newtonian fluid – shear force is directly proportional to the rate of strain (shown between a fixed and moving plate).
  - This includes most fluids and gasses.



Solid - Returns **Fluid – Remains Deformed**

Adopted from Nguyen, NT and ST Wereley, *Fundamentals and Applications of Microfluidics*, Artech House, Boston, MA (2002).

Concepts in Fluid Mechanics

- Continuum assumption
  - Fluid characteristics vary continuously throughout the fluid.
  - May not be true with certain molecular content.
- Laminar vs. transitional and turbulent flow.
  - Based on Reynolds number.
- Hagen-Poiseuille flow (*pwäz-ā-ă)*
- Poiseuille’s law.
- Fluid kinematics (appendix)

Factors Influencing Flow…

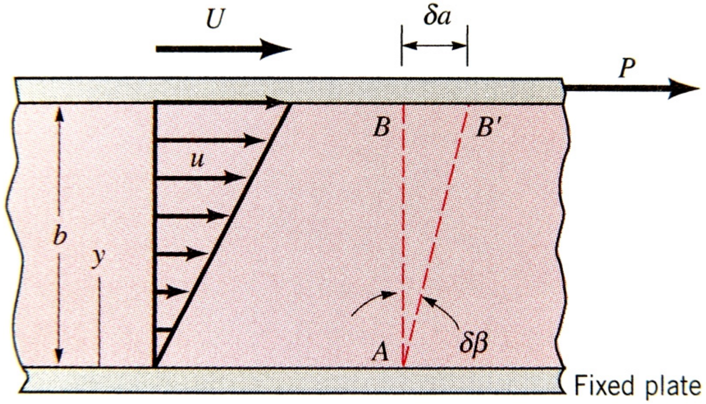
- Kinematic properties
  - Velocity, viscosity, acceleration, vorticity.
- Transport properties
  - Viscosity, thermal conductivity, diffusivity.
- Thermodynamic properties
  - Pressure, thermal conductivity, density.
- Other properties
  - Surface tension, vapor pressure, surface accommodation coefficients.

Viscosity

12 m, https://youtu.be/VvDJyhYSJv8

Some Definitions: *Viscosity…*

- *Viscosity*



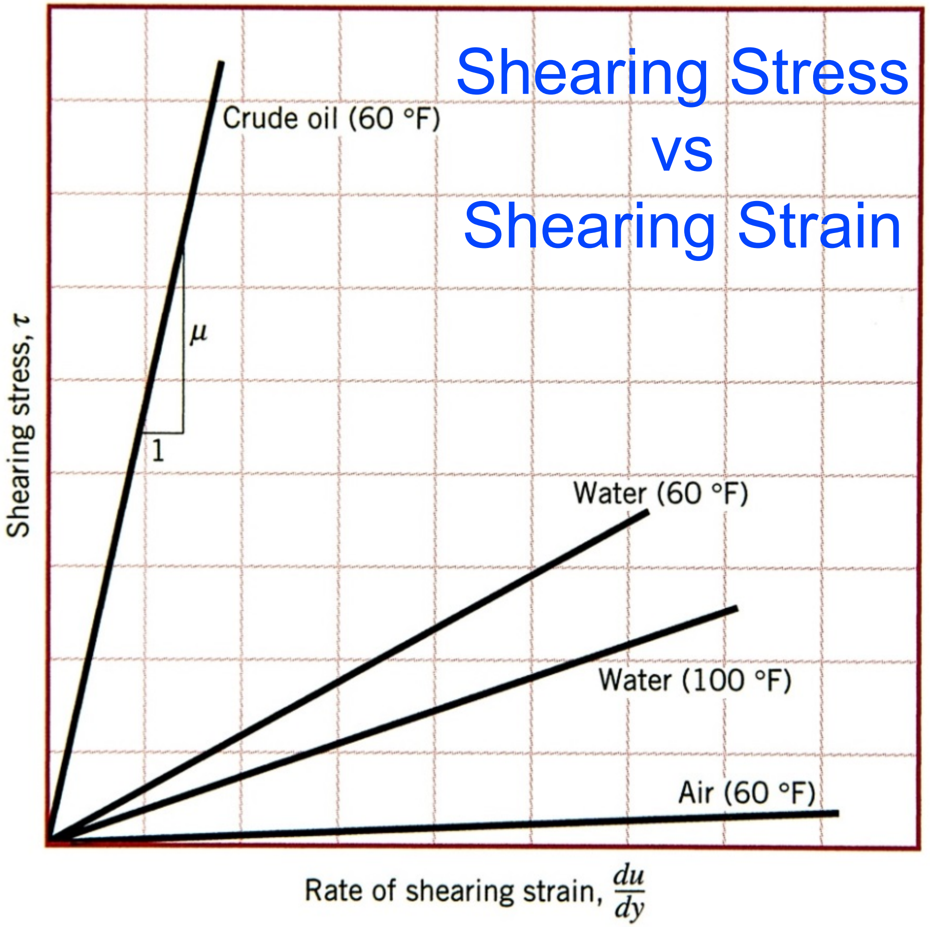
$$\tau = \mu \frac{du}{dy},$$

where

τ (tau) is the shearing stress,

μ (mu) is the absolute or dynamic viscosity, and

$\frac{du}{dy}$ is the velocity gradient.



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Young, DF, et al, *A Brief Introduction to Fluid Mechanics, 2nd ed.*, Wiley, New York (2001).

Kinematic Viscosity…

- *Kinematic viscosity* of a fluid relates the absolute viscosity to density:

$$\nu = \frac{\mu}{\rho},$$

where
ν (nu) is the kinematic velocity (m^2/s),
μ (mu) is the absolute viscosity, and
ρ (rho) is the density or mass per unit volume;

Specific Weight & Specific Gravity…

- The *specific weight* of a fluid is defined as the weight per unit volume:

$$\gamma = \rho g,$$

where
γ (gamma) is specific weight,
ρ (rho) is the density or mass per unit volume,
g is the local acceleration due to gravity;

- The *specific gravity* (SG) of a fluid is the ratio of the density of the fluid to the density of water at some specified temperature:

$$\mathrm{SG} = \frac{\rho}{\rho_{H_2O@4^\circ\mathrm{C}}}$$

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Reynolds Number

- In circular tube flows without obstruction, conventional fluid mechanics would dictate that Reynolds numbers smaller than about 2100 typically indicate *laminar flow*, while values greater than 4000 are *turbulent*. In between is *transitional*.
- Ratio between inertial and viscous forces:

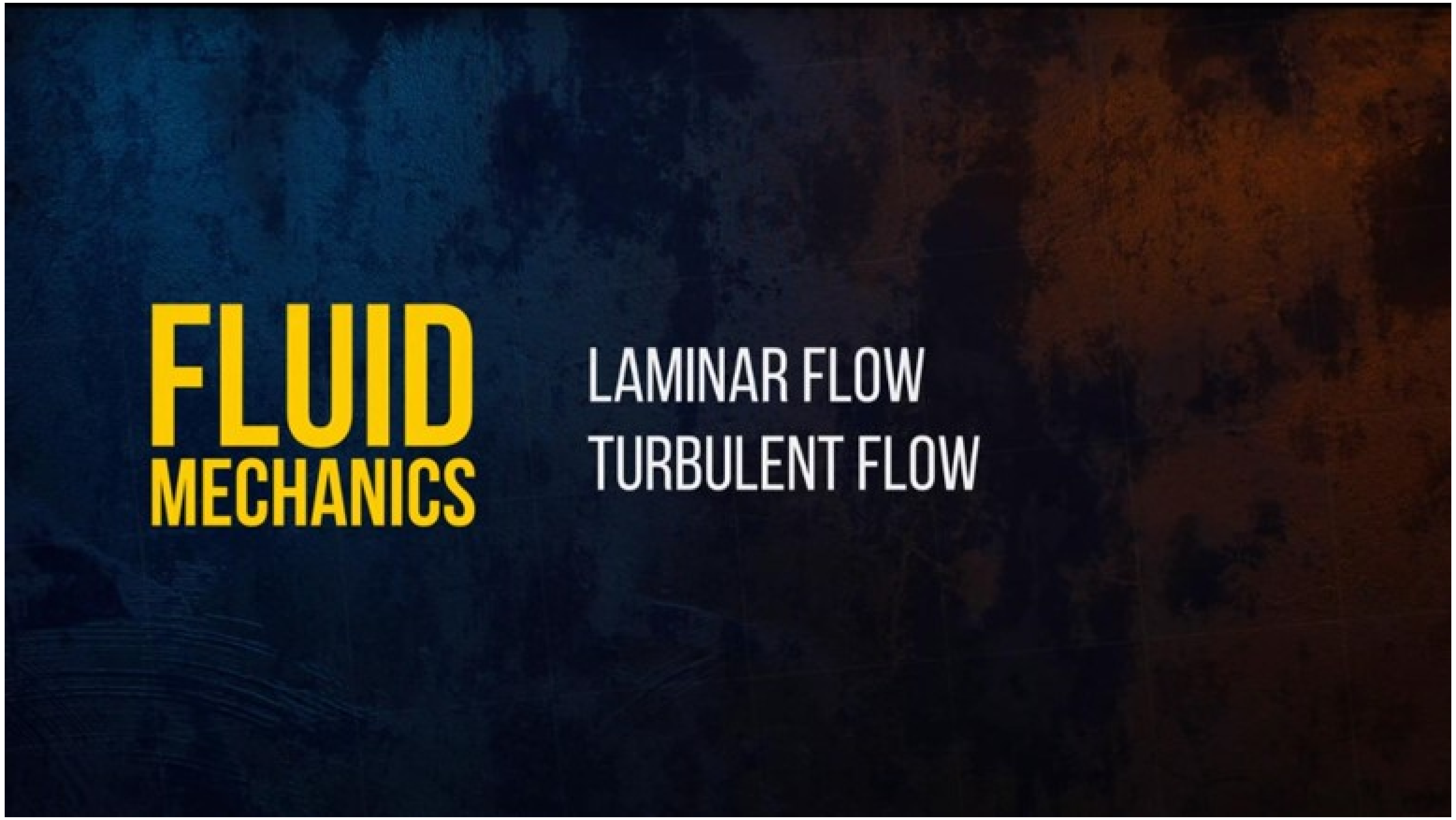
$$\mathrm{Re} = \frac{\rho V D}{\mu}$$

Know this!

Where,
ρ (rho) is the fluid density,
V is the mean fluid velocity (or u)
D is the pipe diameter(or L, the characteristic lenght)
μ (mu) is the fluid viscosity.

Osborne Reynolds lived from 1842 to 1912 and was an Irish fluid dynamics engineer.

Laminar vs Turbulent Flow…



https://youtu.be/9A-uUG0WR0w

Example: Reynolds Number

- In a channel carrying water (viscosity of 10^{-3} kg/(s m), density of 10^3 kg/m^3), in a channel with diameter of 10 µm, at a velocity of 1 mm/s, the Reynolds number is 10^{-2}:

$$Re = \frac{10^3 \frac{kg}{m^3}\, x\ 10^{-3} \frac{m}{s} x\ 10^{-5} m}{10^{-3} \frac{kg}{s\ m}} = .01$$

- Contrast this to a channel with diameter of 100 µm and fluid velocity of 10 m/s, where the Reynolds number is a 1000:

$$\boldsymbol{Re} = \frac{10^3 \frac{kg}{m^3} \times 10 \frac{m}{s} \times 10^{-4} m}{10^{-3} \frac{kg}{s \cdot m}} = 1000$$

- With channels < 1 mm in width and height, and velocities not greater than cm/s range, the Reynolds number for flow will be so low that all flow will be laminar.
  - In laminar flow, velocity of a particle is not a random function of time.
  - Useful for assays and sorting by particle size, and allows for creation of discrete packets of fluid that can be moved around in a controlled manner.

Microfluidic Flow Challenges

- Flows at low *Reynolds numbers* pose a challenge for mixing. Two or more streams flowing in contact with each other will mix only by *diffusion*.
- As *surface area to volume* increases, *surface tension* forces become significant, leading to nonlinear free-boundary problems.
- As suspended *particle sizes* approach the size of the channel, there is a breakdown of the traditional constitutive equations.

Hagen-Poiseuille Flow *(French - pwäz-ā-ă)*

- *Hagen-Poiseuille flow* or *Poiseuille flow* is the steady, incompressible, laminar flow through a circular tube of constant cross section. The velocity distribution is expressed as :

$$v_z = \frac{1}{4\mu}\left(\frac{\partial p}{\partial z}\right)(r^2 - R^2),$$

Where,

v_z is the longitudinal velocity,

μ (mu) is the fluid viscosity,

$\partial p/\partial z$ is the z component of the pressure gradient,

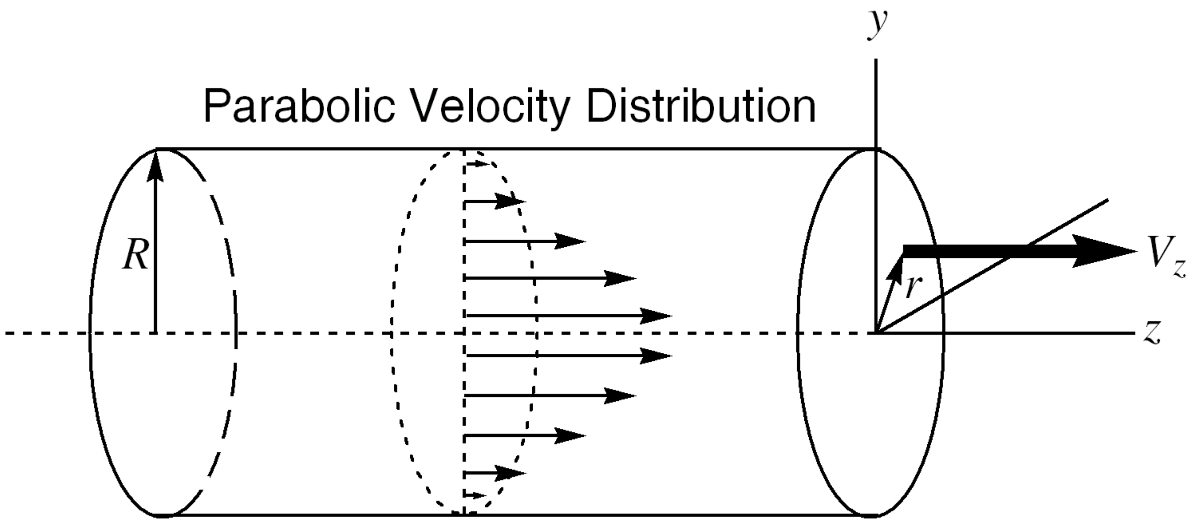
r is the distance from the center of the tube, and

R is the radius of the tube.

Young, DF, et al, *A Brief Introduction to Fluid Mechanics, 2nd ed.*, Wiley, New York (2001).

Velocity Distribution…

- The velocity distribution is parabolic at any cross-sectional view:



- Each part of the fluid can be visualized as moving along its own path line.
- The *maximum velocity* is at the pipe center.
- *The minimum velocity* (zero) is at the pipe wall.
- Shear stress is the consequence of the velocity variation and fluid viscosity.

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Adopted from Young, DF, et al, *A Brief Introduction to Fluid Mechanics, 2nd ed.*, Wiley, New York (2001).

Poiseuille's Law (pwäz-ā-ă)…

- *Poiseuille's law* describes the relationship between the *volume rate of flow*, Q, passing through the tube and the pressure gradient (from the Navier-Stokes equations):

$$Q = \frac{\pi D^4 \Delta p}{128 \mu \ell} = \frac{\pi R^4 \Delta p}{8 \mu \ell},$$

Know this!

where

Q is the volume rate of flow,

D is the diameter of the tube,

Δp is pressure drop over length, ℓ along the tube,

μ (mu) is the fluid viscosity, and

R is the radius of the tube.

Poiseuille's Law…

- For a given pressure drop per unit length, the volume flow rate is inversely proportional to the viscosity and proportional to the tube radius to the fourth power.
- Doubling of the tube radius produces a 16-fold increase in flow.
  - Conversely, decreasing the radius by half (such as in an atherosclerotic coronary artery), decreases flow by 16-fold.

- The *mean velocity* is:

$$V = \frac{Q}{\pi R^2} = \frac{R^2 \Delta p}{8 \mu \ell}$$

and the *maximum velocity* occurring at the center of the tube is:

$$v_{\mathrm{max}}$$

Surface Area to Volume

- Surface area to volume (SAV) increases significantly as dimensions are reduced for microfluidic channels.
  - For example, for a circular microchannel 100 µm in diameter, the SAV ratio is:

$$\mathrm{SAV} = \frac{2\pi r L}{\pi r^2 L} = \frac{2}{r} = 4 \times 10^4 \mathrm{m}^{-1},$$

Where,

r is the radius, and

L is the length.

Know this!

Diffusion

- In laminar flow, two or more streams flowing in contact with each other mix only by *diffusion*.

$$\bar{x}^2 = 2Dt,$$

Where,

x is the distance a particle moves,

t is the amount of time, and

D is the diffusion coefficient.

$$D = \frac{RT}{6\pi r\eta N_\mathrm{A}}\left[1 + C\left(\frac{\partial \ln y}{\partial C}\right)_{T,P}\right],$$

Where,

R is the gas constant, T is temperature,

r is particle radius,

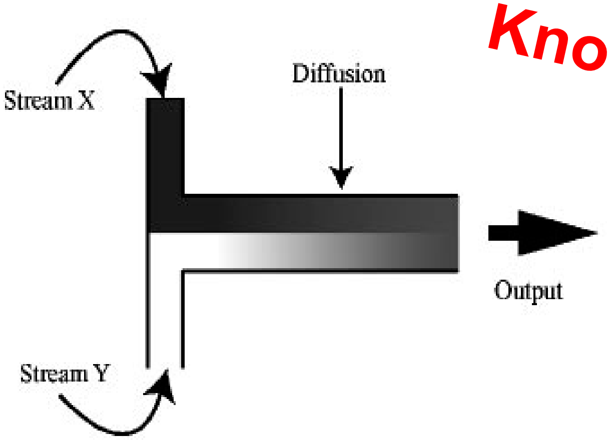
N_A is Avogadro's number,

C is concentration in moles/liter,

η (eta) is the solution viscosity, and

y is the activity coefficient in moles/liter.

Know this!



Example: Diffusion of Hemoglobin

- How long does it take hemoglobin to diffuse 1 cm in water ($D=10^{-7}cm^2s^{-1}$)?

$$t_s = \frac{(1cm)^2}{2 \times \frac{cm^2}{10^7 s}} = 5 \times 10^6 \text{ s}$$

(58 days!)

- How long to diffuse 10 µm (.001 cm)?

$$t_s = \frac{(10^{-3} cm)^2}{2 \times \frac{cm^2}{10^7 s}} = 5 \text{ s}$$

Design Considerations…

- The optimal size domain for microfluidic channel cross sections is somewhere between 10 -100 μm.
- At smaller dimensions detection is too difficult and at greater dimensions unaided mixing is too slow.
- Therefore, the cross sectional area for a square channel with width of 50 μm will be ~2.5 x 10^{-3} mm^2. The flow range will be 1 to 20 nL/sec.
- *When diluting an assay component, the two flows must be controlled within ~1%, or pL/sec range.*

Key Points

- Micro- & nanoscales create unique design solutions and challenges.
- The relationship between sample volume and analyte concentration is important, and the higher the concentration of analyte and/or better the sensor, the less the volume of sample that is needed.
- Depending on the analyte to be measured, there is a minimal sample volume to analyte concentration necessary to assure detection and statistical confidence in the measurement.
- Microfluidic flow is typically laminar, and a continuum assumption is made in our calculations.
- Factors influencing flow include kinematic, transport, thermodynamic and other properties.

Key Points…

- Reynolds number is the ratio between inertial and viscous forces, and numbers smaller than 2100 typically indicate laminar flow, and above 4000 turbulent flows.
- Hagen-Poiseuille flow or Poiseuille flow is the steady, incompressible, laminar flow through a circular tube of constant cross section. The velocity distribution is parabolic at any cross-sectional view of a pipe.
- Surface area to volume (SAV) increases significantly as dimensions are reduced for microfluidic channels.
- In laminar flow, two or more streams flowing in contact with each other mix only by diffusion.

Addendum

- COMSOL in Bioengineering: https://youtu.be/TyLcN_N60gw.
- Modeling diffusion in a model biosensor using COMSOL Multiphysics:
  - Part 1: https://youtu.be/s8cfMxd_FYE.
  - Part 2: https://youtu.be/GT8LWS71d1A.
  - Part 3: https://youtu.be/ZrEO5E8JK2g.
- COMSOL demo of laminar flow through branch pipes: https://youtu.be/ZZbe5DBvRf0.
- More on fluid kinematics.

Fluid Kinematics

- A field representation of flow is the representation of fluid parameters as functions of spacial coordinates and time.
- The velocity field is defined as:

$$\mathbf{V} = u(x, y, z, t)\hat{\mathbf{i}} + v(x, y, z, t)\hat{\mathbf{j}} + w(x, y, z, t)\hat{\mathbf{k}},$$

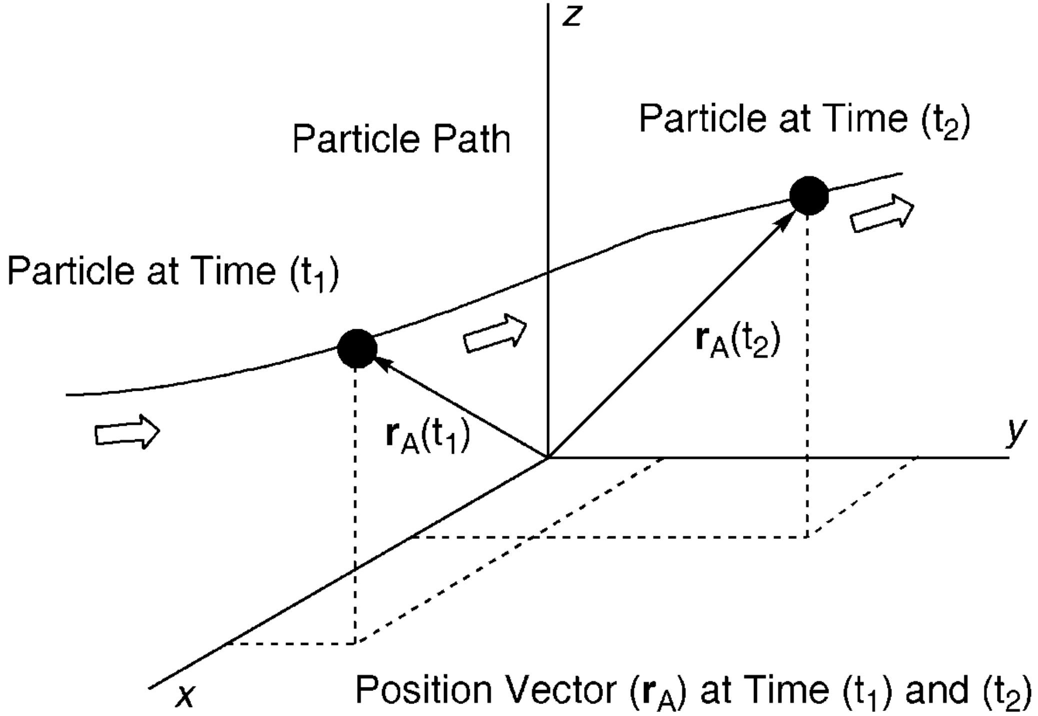
where

u, v, w are the $x, y,$ and z components of the velocity vector, and t is time.

- For problems related to flow in most microchannels, we can consider that one or two of the velocity components will be small relative to the others, and reduce the problem to 1D or 2D flow.

Position Vector…

- Particle *location* is in terms of its position vector r_A:



Position Vector ($\mathbf{r}_A$) at Time (t_1) and (t_2)

The velocity of a particle is the time rate of change of the position vector for that particle.

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Adopted from Young, DF, et al, *A Brief Introduction to Fluid Mechanics, 2nd ed.*, Wiley, New York (2001).

- The *velocity* of a particle is the time rate of change of the position vector r_A for that particle:

$$d\mathbf{r}_A/dt = \mathbf{V}_A$$

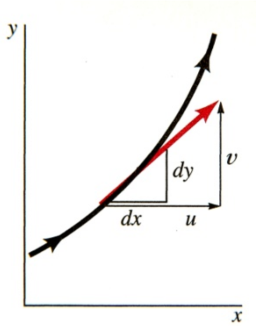
- The *direction* of the fluid velocity relative to the *x* axis is given by:

$$\tan\theta = \frac{v}{u}$$

Young, DF, et al, *A Brief Introduction to Fluid Mechanics, 2nd ed.*, Wiley, New York (2001).

"Streamlines"…

- A *streamline* is a line that is everywhere tangent to the velocity field. In steady flows, the streamline is the same as the *path line*, the line traced out by a given particle as it flows from one point to another.



$$\tan\theta = \frac{v}{u}$$

- For a 2D flow the slope of the streamline must be equal to the tangent of the angle that the velocity vector makes with the x axis:

$$\frac{dy}{dx} = \frac{v}{u}$$

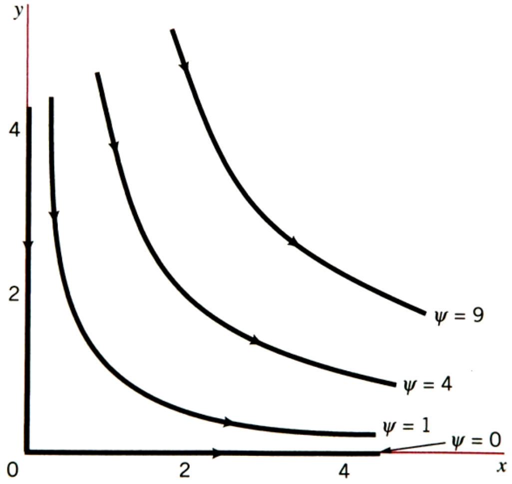
Young, DF, et al, *A Brief Introduction to Fluid Mechanics, 2nd ed.*, Wiley, New York (2001).

- If the velocity field is known as a function of x and y, this equation can be integrated to the give the equation of the streamlines.
- The notation for a streamline is:

$$\psi\ (\text{psi}) = \ \text{constant on a streamline}$$

- The *stream function* is:

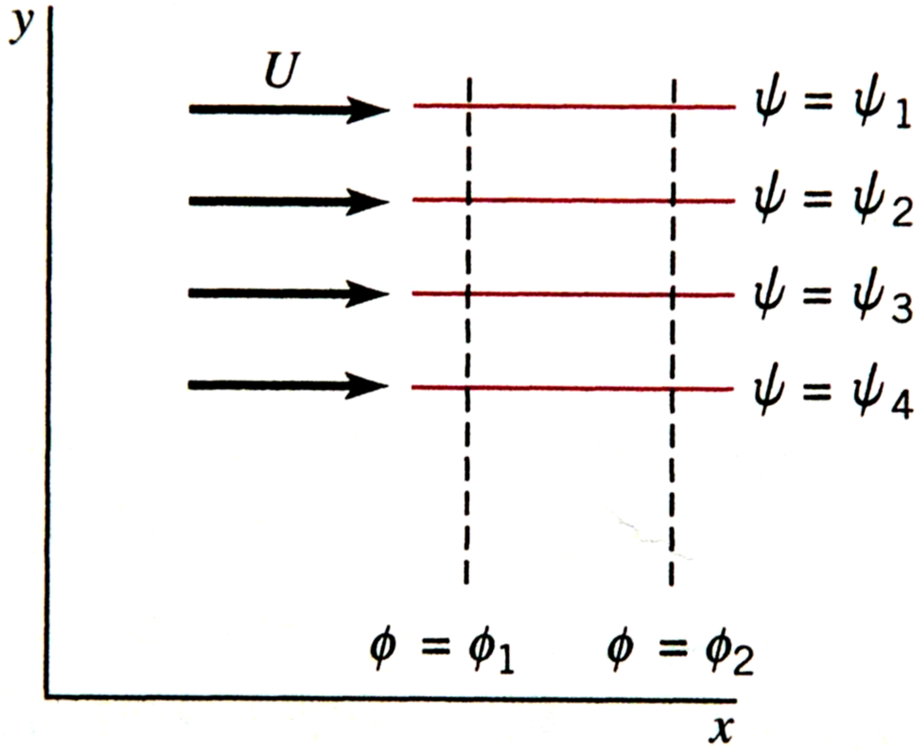
$$\psi = \psi(x, y)$$



- Various lines can be plotted in the x-y plane for different values of the constant. For steady flow, the resulting streamlines are lines parallel to the velocity field.

Young, DF, et al, *A Brief Introduction to Fluid Mechanics, 2nd ed.*, Wiley, New York (2001).

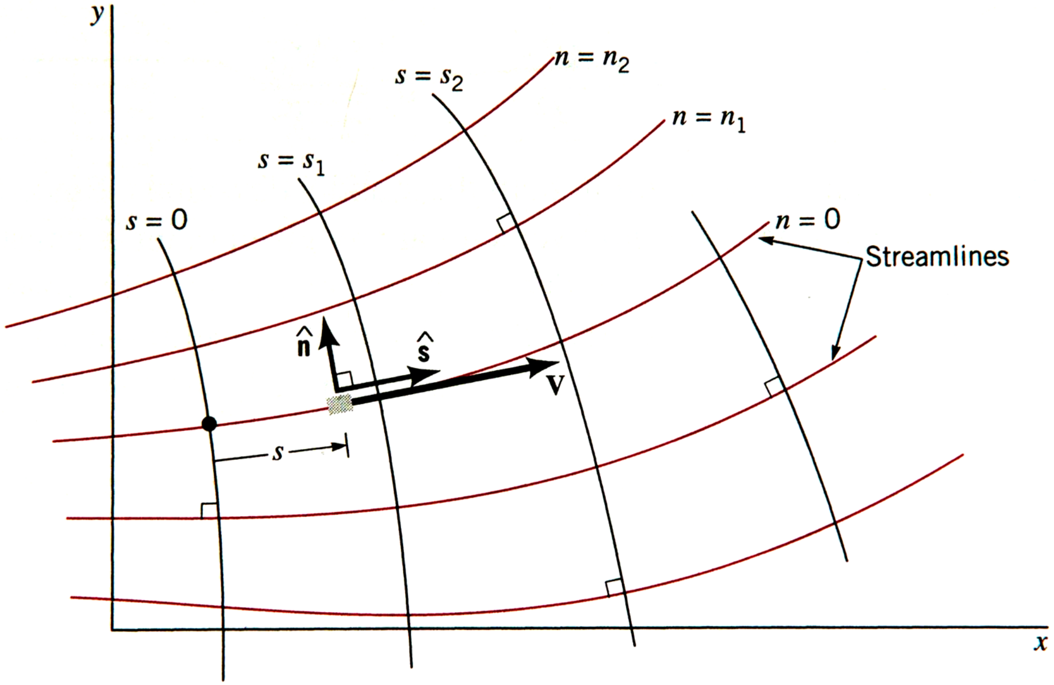
Uniform Flow…



The streamlines are all straight and parallel, and the magnitude of the velocity is constant.

Young, DF, et al, *A Brief Introduction to Fluid Mechanics, 2^{nd} ed.*, Wiley, New York (2001).

Streamline Coordinates…



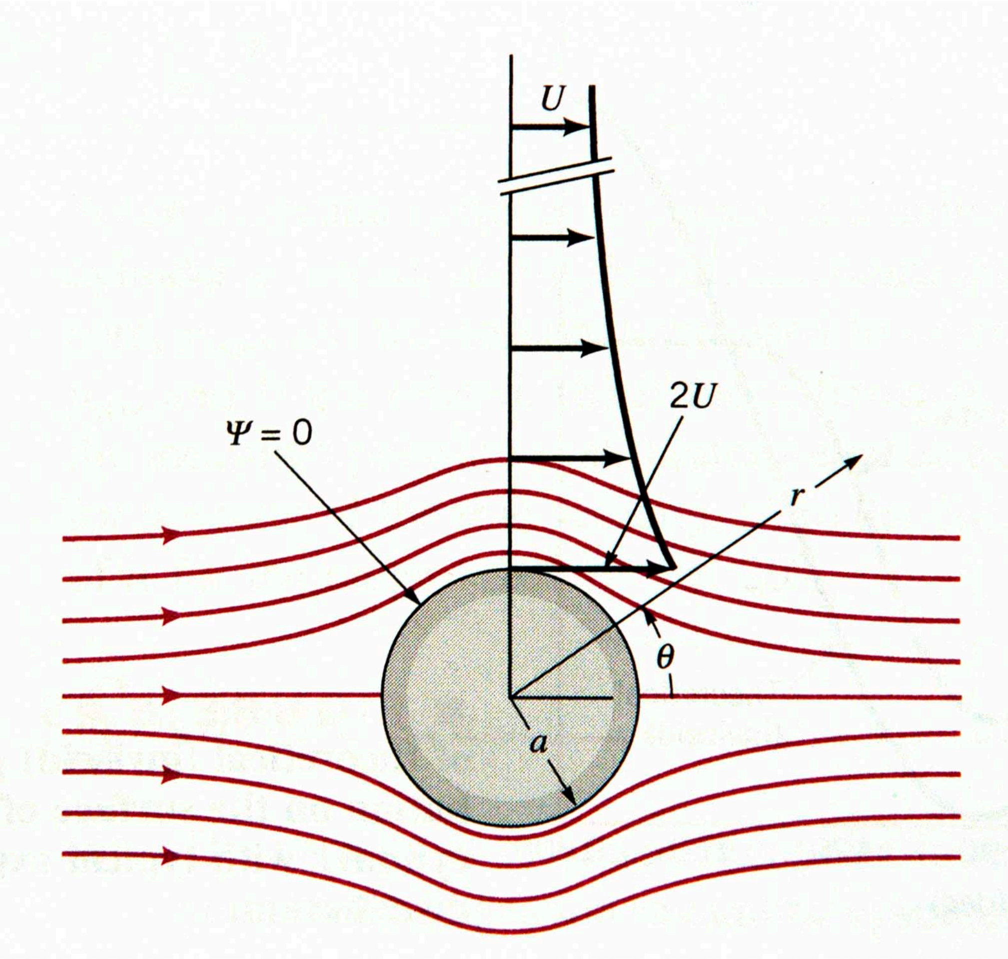
$$\mathbf{V} = V\hat{s}$$

Velocity is always tangent to the s direction.

- Example of a steady 2D flow.
- “s” is a unit vector along the streamline.
- “n” is normal to the streamline.
- Velocity is always tangent to the “s” direction.

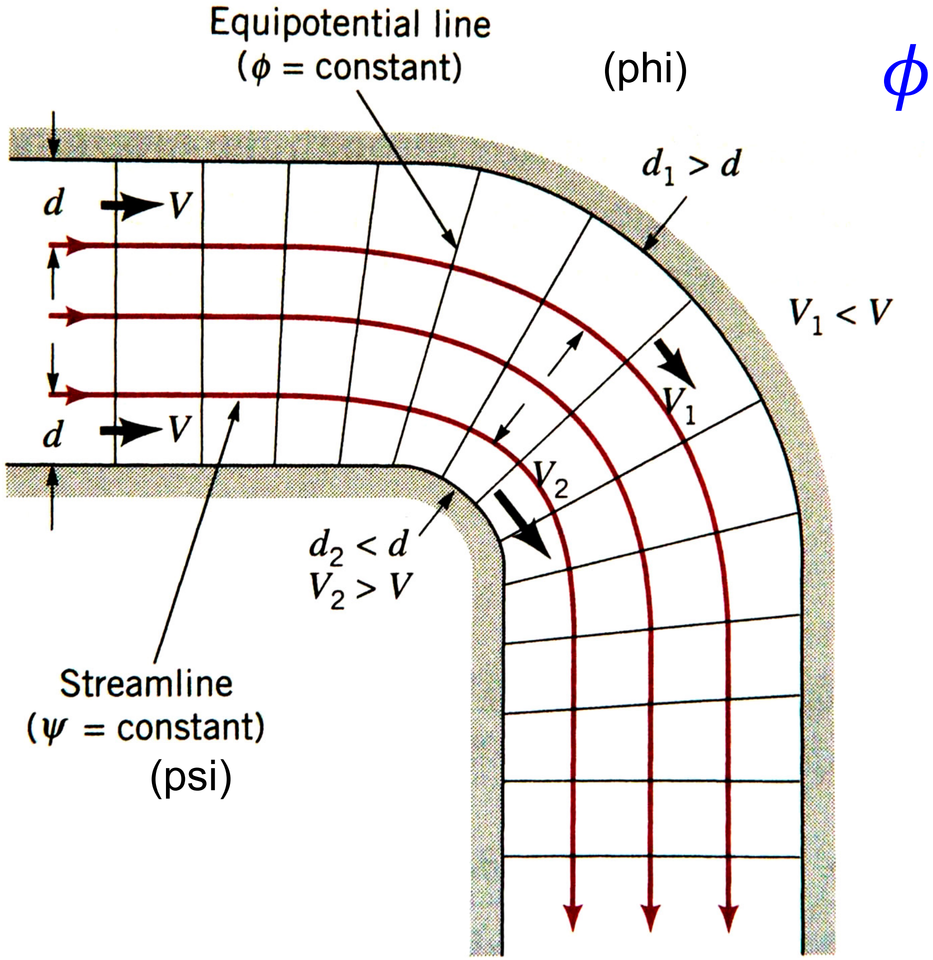
Young, DF, et al, *A Brief Introduction to Fluid Mechanics, 2nd ed.*, Wiley, New York (2001).

Flow Around a Circular Cylinder…



Young, DF, et al, *A Brief Introduction to Fluid Mechanics, 2nd ed.*, Wiley, New York (2001).

"Flow Net" and the Velocity Potential Phi…



$$\phi(x, y, z, t) \qquad u = \frac{\partial\phi}{\partial x} \quad v = \frac{\partial\phi}{\partial y} \quad w = \frac{\partial\phi}{\partial z}$$

- A flow net consists of a family of streamlines and equipotential lines.
- Velocities can be estimated from the flow net, as the velocity is inversely proportional to the streamline spacing.
- At the 90^{o} bend, velocity is higher near the inside corner.

Young, DF, et al, *A Brief Introduction to Fluid Mechanics, 2nd ed.*, Wiley, New York (2001).