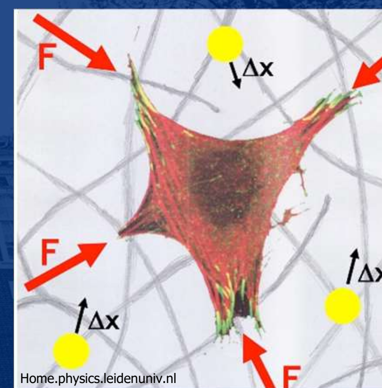
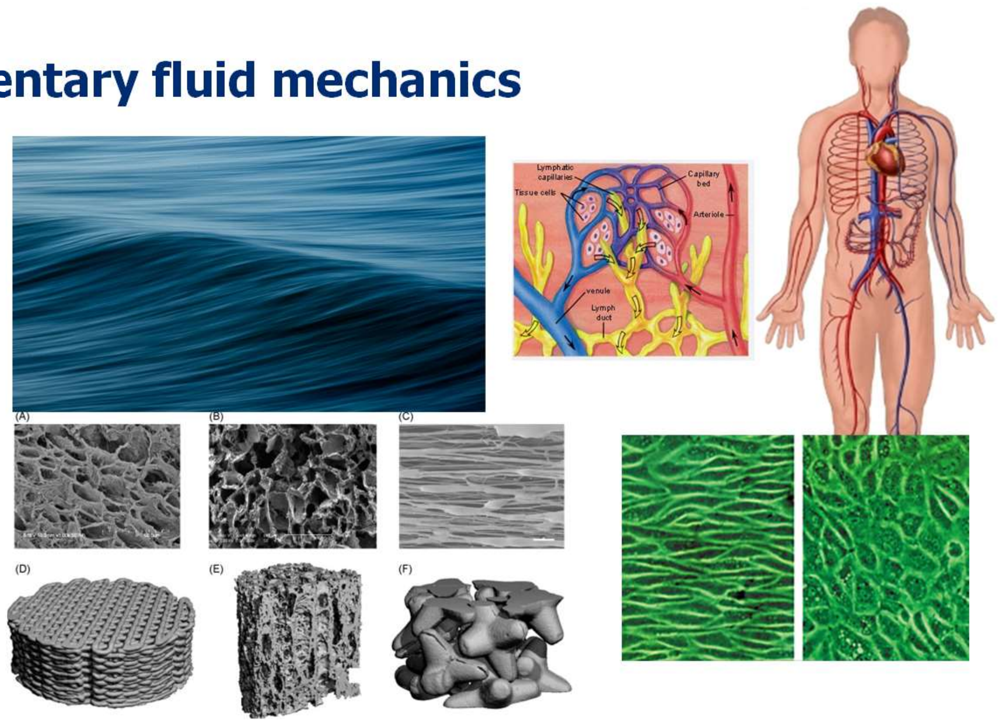
Cell and Tissue Engineering

Basic fluid mechanics



Welcome to cell and tissue engineering. In this lecture, we'll talk about fluid mechanics as they apply to biological systems.

Elementary fluid mechanics



2

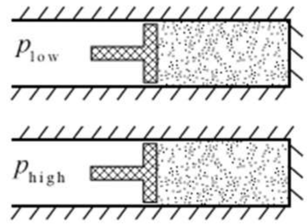
Malek et al 2009; Flickr.com; Kirbyreserach.com; Provitanutrition.com; Grayson et al 2009

Let’s talk now about basic fluid mechanics.

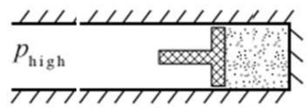
Fluid mechanics are important to **understanding** and **manipulating** flow – in the context of the human body, this can mean **blood flow** in real or engineered vessels, **interstitial flow** in our lymphatics or biomaterial constructs, or **media flow** applied in vitro for the regulation of cell phenotype.

Elementary fluid mechanics (cont.)

Incompressible – constant density, ρ



Compressible – ρ(P)



3

Flickr.com; Kirbyreserach.com; Provitanutrition.com

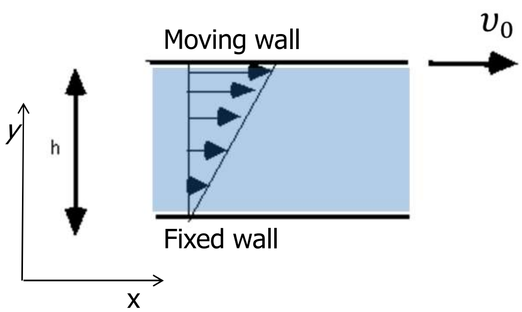
There are two classes of fluids – **incompressible fluids** where the density of the fluid is constant, and **compressible** fluids, where the density is a function of pressure.

Here you can see that under high pressure the incompressible fluid **doesn't change volume**, while the compressible fluid does. Most liquids including blood are **incompressible** at atmospheric pressures.

However many gases are compressible.

Instead of the instantaneous deformation that we see with an elastic solid, a fluid deforms **constantly** under a shearing stress.

Shear stress is proportional to viscosity



Tangential shear stress

$$\tau = \frac{F}{A} \qquad \tau \propto \frac{v_0}{h}$$

4

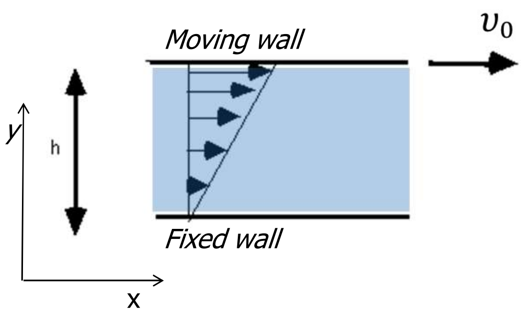
Wikipedia.org

Let’s take the example of a fluid between two parallel plates – where the bottom plate is stationary and the top plate/wall is moving.

The tangential shear stress is applied to the entire area of the top plate or moving wall that is in contact with the fluid.

The shear stress is **proportional** to the **velocity** of this moving wall, and **inversely proportional** to the **distance** between plates (the gap distance0.

Shear stress is proportional to viscosity



Tangential shear stress

$$\tau = \frac{F}{A} \qquad \tau \propto \frac{v_0}{h}$$

$$\tau_{xhy} = -\eta \frac{dv_x}{dy}$$

η, viscosity

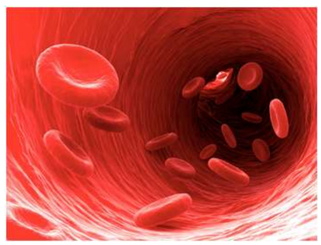
5

Wikipedia.org

If you want to calculate shear stress, you need to know the **velocity gradient** or **shear rate** (that is the change in velocity in the x direction with respect to y) and the viscosity of the fluid in the system

NOTE the negative sign is because this is a drag force – the force exerted by the fluid on the moving plate – it opposes the direction of flow

The viscosity of Newtonian fluids is not a function of shear rate



Tangential shear stress

$$\tau = \frac{F}{A} \qquad \tau \propto \frac{v_0}{h}$$

$$\tau_{xhy} = -\eta \frac{dv_x}{dy}$$

η, viscosity

6

Holisticprimarycare.net; Gravensen.info

Non-Newtonian fluids have viscosity that changes with shear rate… Some examples include quick sand, gravy, quicksand, and yogurt.

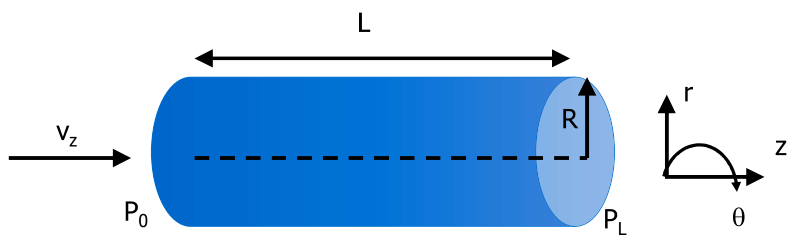
When you struggle in quicksand the viscosity of the sand trap changes – it becomes more fluid, causing you to sink faster. – this is why its recommended to remain still when trapped.

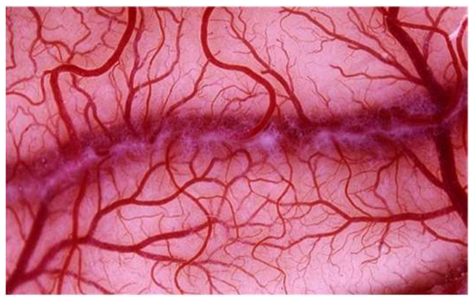
Similarly, when you stir gravy it will get thicker, an increase in viscosity.

In the case of blood, high shear rates can results in the aggregation of blood cells, RBCs becoming stuck together, which changes the apparent viscosity.

Depending on the situation, it may be ok to assume that you have **Newtonian fluid behavior** – this assumption is commonly used for blood when there is a low shear rate and no cell aggregation.

Consider flow in a cylindrical tube





7
Telegraph.co.uk

We've discussed the importance of blood vessel growth in tissue engineering before – almost all tissues are vascularized, so if you want to make a tissue that is **larger** than the oxygen-diffusion limit, you **must** think about engineering a blood supply.

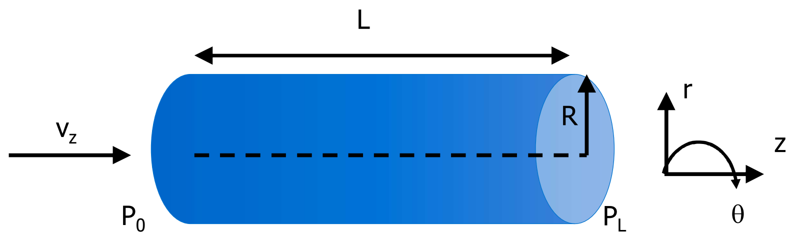
For this reason it is critical that we think about **how blood flows** through blood vessels. To discuss the basics of this let's go through an example of fluid flow through a cylinder.

The driving force for flow through our blood vessel segment or cylinder is **the pressure drop** from P_0 to P_L at the entrance and exit of the vessel.

In our example flow is only going in **this axial direction** – here denoted as the z direction.

We are now going to derive an equation for flow in the vessel as it relates to the driving pressure, geometry and viscosity. Flow after all is what we **want** to measure – it is what we **need** to perfuse our tissues.

Consider flow in a cylindrical tube (cont.)



Navier-Stokes Equation

$$\rho(\frac{\delta v_z}{\delta t} + v_r \frac{\delta v_z}{\delta r} + \frac{v_\theta}{r}\frac{\delta v_z}{\delta \theta} + v_z \frac{\delta v_z}{\delta z}) = -\frac{\delta p}{\delta z} + \eta\left[\frac{1}{r}\frac{\delta}{\delta r}\left(r\frac{\delta v_z}{\delta r}\right) + \frac{1}{r^2}\frac{\delta^2 v_z}{\delta^2 r} + \frac{\delta^2 v_z}{\delta^2 z}\right] + \rho g_z$$

Transient inertia + Convective inertia = Body force + Pressure force + Viscous force

A continuum version of $F = ma$

ρ – *density*
υ – *velocity*
t – *time*
η – *viscosity*
g – *gravitational forces*

8

Using **conservation of momentum principles** you can derive what is called the Navier Stokes equation. This equation describes the **motion** of fluid and here I've written it in **cylindrical** coordinates. Our vessel (our pipe) is cylindrical, so this is the appropriate representation.

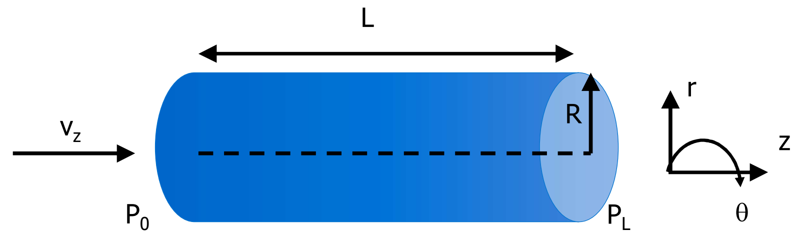
This equation represents the balance of four kinds of forces that move flow through our vessel:
Transient and **convective** Inertia,
body forces (rho*g),
pressure forces (dP/dz),
and **viscous** forces (mew and radius term).

This is the equation only represents the z-component of flow – that is flow in the axial, z-direction – v_z. This equation relates density here to the pressure drop and viscosity

(There are separate equations for flow in the other directions – r and theta.)

To get here it was assumed that our fluid (blood) is an **incompressible**, **Newtonian** fluid – that density is not a **function of time** or position. And that the **flow is laminar**.

Consider flow in a cylindrical tube (cont.)



Navier-Stokes Equation

$$\rho\left(\frac{\delta v_z}{\delta t} + v_r \frac{\delta v_z}{\delta r} + \frac{v_\theta}{r}\frac{\delta v_z}{\delta \theta} + v_z \frac{\delta v_z}{\delta z}\right) = -\frac{\delta p}{\delta z} + \eta\left[\frac{1}{r}\frac{\delta}{\delta r}\left(r\frac{\delta v_z}{\delta r}\right) + \frac{1}{r^2}\frac{\delta^2 v_z}{\delta^2 r} + \frac{\delta^2 v_z}{\delta^2 z}\right] + \rho g_z$$

1. Stead flow, no transient inertia
2. Flow is axial, neglect convective inertia
3. Gravity is negligible

ρ – *density*
υ – *velocity*
t – *time*
η – *viscosity*
g – *gravitational forces*

9

Next, We will simplify this equation with the following assumptions, that

1. the flow is **steady with time** (dvz/dt = 0)
2. flow is only **axial** – no flow in the r or theta directions (vr and vtheta = 0)
3. **Gravity** is negligible. Gz = 0

Reynold's number tells us about the type of flow

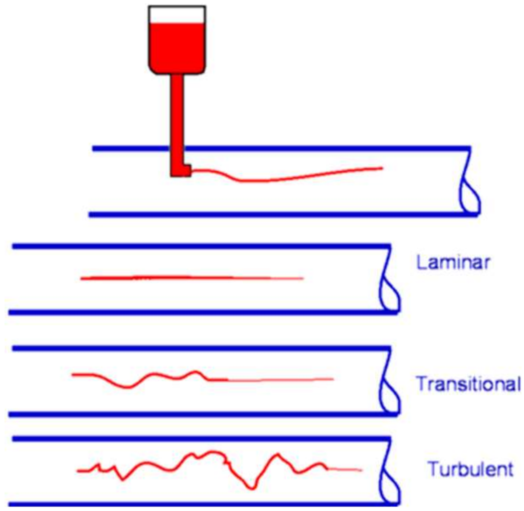
$$\mathrm{Re} = \frac{\rho v^2 / L}{\mu v / L^2} = \frac{\rho v L}{\mu}$$

$$\frac{\text{inertial force}}{\text{viscous force}}$$

Non-dimensional number

If Re << 1, we can neglect inertial forces

If Re >> 1, inertial forces dominate



10
Mdp.eng-cam.ac.uk

Let's talk a little more about our **second** assumption, that **flow is steady and axial** and we can **ignore** convective inertia. We can do this because we are assuming a **Reynolds number** in our system.

Reynolds number is a non dimensional number that describes the flow. It is the **balance between inertial forces** and **viscous** forces.

If Reynolds number is **less than one** we can **neglect** inertial forces, and for those **greater** than one the **inertial forces dominate**.

We typically think of **viscous** forces as **normal** and **organizing**, and **inertial** forces as **turbulent** and **chaotic**.

We should also know the terms **laminar**, **turbulent**, and **transitional**:
Laminar flow is when Re # is less than 2300
Turbulent flows have Reynolds number over 4000
And then in the middle, we have the **transient** region between 2300-4000

Reynold's number tells us about the type of flow

$$\mathrm{Re} = \frac{\rho v L}{\mu} = \frac{(1g/cm^3)\times(100cm/\sec)\times 30cm}{0.01dyn-\sec/\,cm^2} = 300,000$$

11

Desktopwallpaperhd.net

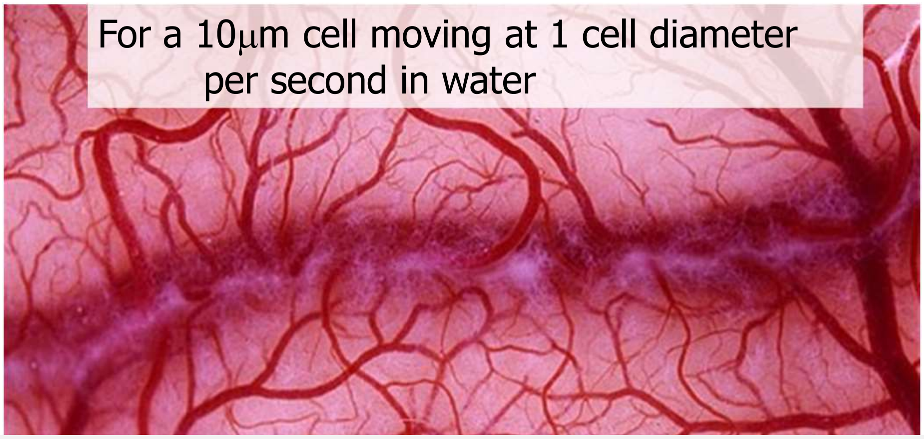
Let's take a moment to calculate Reynolds numbers. The first example is this surfer, in Hawaii, riding this giant wave. Let's talk about the flow around that surfboard.

Using Reynolds number equation, we can plug in the **density** of water, the **velocity**, the **length** or diameter of the surfboard, and **divide** by the **viscosity** of water. This results in a Reynolds number of **three hundred thousand**.

This is **Turbulent, because it is** over 4,000

This number make sense, because we can see the turbulence behind the surfer in the water. But this example doesn't help with our flow in a tube, because we assume laminar flow.

Reynold’s number tells us about the type of flow



$$\mathrm{Re} = \frac{\rho v L}{\mu} = \frac{(1g/cm^3)\times(0.001cm/\sec)\times 0.001cm}{0.01dyn-\sec/\,cm^2} = 10^{-4}$$

12

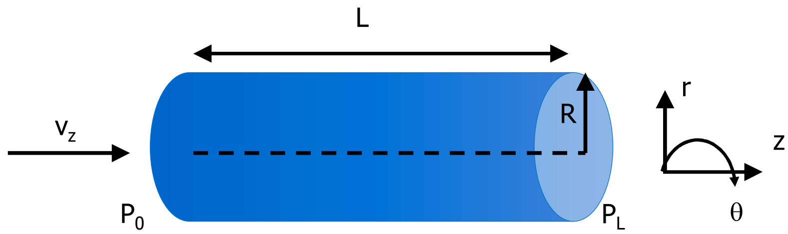
Desktopwallpaperhd.net

Instead, let’s consider a capillary, similar to our example vessel. Let’s talk about a RBC, which is about 10 micrometers in diameter, moving at about one cell diameter per second, in a water-like fluid.

We use the density of water, the speed of the cell, the dimension of the capillary, and the viscosity of water.

This Reynolds number is far less than one, so our assumption of **neglecting inertial forces** holds in this case.

Consider flow in a cylindrical tube



Navier-Stokes Equation

$$\rho(\frac{\delta v_z}{\delta t} + v_r \frac{\delta v_z}{\delta r} + \frac{v_\theta}{r}\frac{\delta v_z}{\delta \theta} + v_z \frac{\delta v_z}{\delta z}) = -\frac{\delta p}{\delta z} + \eta\left[\frac{1}{r}\frac{\delta}{\delta r}\left(r\frac{\delta v_z}{\delta r}\right) + \frac{1}{r^2}\frac{\delta^2 v_z}{\delta^2 r} + \frac{\delta^2 v_z}{\delta^2 z}\right] + \rho g_z$$

1. Stead flow, no transient inertia
2. Flow is axial, neglect convective inertia
3. Gravity is negligible

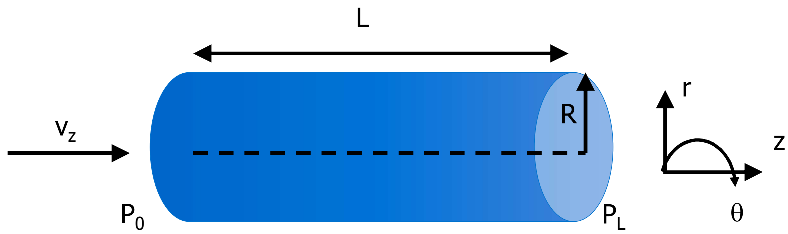
$$\frac{\delta p}{\delta z} = +\frac{\eta}{r}\frac{\delta}{\delta r}\left[r\frac{\delta v_z}{\delta r}\right]$$

13

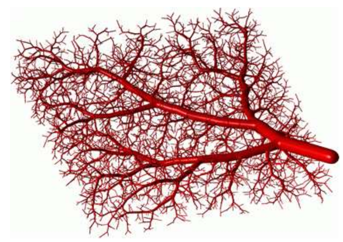
We’ve made the three assumptions. What does that mean? We can simplify this large equation.

With a little rearranging this brings us to this simplified equation.

Consider flow in a cylindrical tube (cont.)



$$\frac{\delta p}{\delta z} = +\frac{\eta}{r}\frac{\delta}{\delta r}\left[r\frac{\delta v_z}{\delta r}\right]$$



Apply two boundary conditions:

1. No-slip $v_z = 0$ when r = R And $\frac{\delta v_z}{\delta r} = 0$ when r = 0
2. Known pressures at the inlet and outlet

$p = P_0$ when z = 0 And $p = P_L$ when z = L

14 ljbem.org

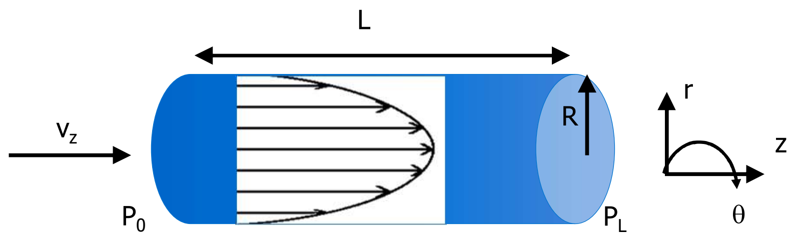
If we solve this equation for flow, for vz, we'll be able to relate **fluid velocity** to system parameters like **pressure drop, fluid viscosity, and** radius and length of the tube.

So let's do that now.

To solve we need to apply two boundary conditions . The first is called the **no-slip boundary condition**. This is the condition that there is no fluid flow at the wall. That Vz=0 at r=R. This is along the top, bottom, and walls of the vessels. Additionally, that there is no change in velocity at the center of the pipe.

The second set of boundary conditions are **the known or measured pressures at either end** of our blood vessel. In the lab you may measure the pressure drop across a particular part of the vascular tree – for example you may be interested in what's happening in the **feed** artery to this capillary bed or one of these **lower order** arterioles. *Draw on the schematic.*

Consider flow in a cylindrical tube (cont.)



$$\frac{\delta p}{\delta z} = +\frac{\eta}{r}\frac{\delta}{\delta r}\left[r\frac{\delta v_z}{\delta r}\right]$$

ρ – density
υ – velocity
t – time
η – viscosity

Hagen-Poiseuille flow

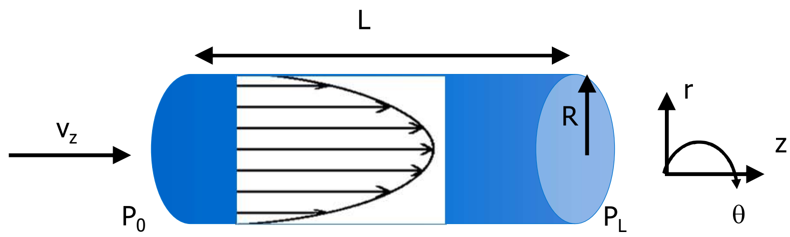
$$v_z = \frac{(P_0 - P_L)R^2}{4\eta L}\left(1 - \frac{r^2}{R^2}\right)$$

15 ljbem.org

Notes on applying these conditions are in your text. You may want to pause this video and read that section now – on page 131.

What you get out is this equation which describes **Hagen-Poiseuille flow.** This equation shows you that the velocity profile through the blood vessel or tube is **parabolic** with the **fastest flow at the center** - you can see the boundary conditions **physically** in this image. There is **no flow** at the top and bottom edges.

Consider flow in a cylindrical tube (cont.)



ρ – density
υ – velocity
t – time
η – viscosity

$$\frac{\delta p}{\delta z} = +\frac{\eta}{r}\frac{\delta}{\delta r}\left[r\frac{\delta v_z}{\delta r}\right]$$

Hagen-Poiseuille flow

$$v_z = \frac{(P_0 - P_L)R^2}{4\eta L}\left(1 - \frac{r^2}{R^2}\right) \longrightarrow Q = \int_0^{2\pi}\int_0^{R} v_z(r)\,r\,dr\,d\theta = \frac{(P_0 - P_L)\pi R^4}{8\eta L}$$

Alright we know something about velocity – but what we really want to know about is flow.

We care about **volumetric** flow rate – what's needed to **perfuse** our tissue or biomaterial construct.

To get to flow rate, we rearrange this equation and integrate over the cross section of the vessel – so integrate from 0 to R and then around from 0 to 2pi. We will end up with the volumetric flow rate Q. So we are going from distance/time to distance cubed per time or volume per time.

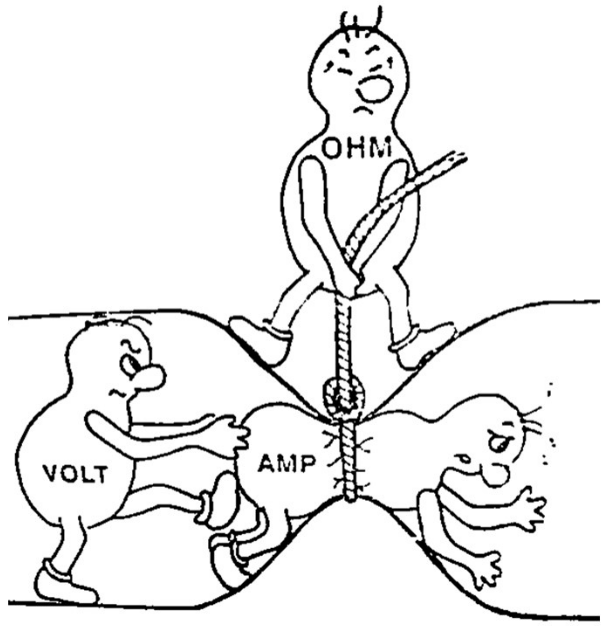
Consider flow in a cylindrical tube (cont.)

$$Q = \frac{(P_0 - P_L)\pi R^4}{8\eta L}$$

$$P_0 - P_L = \Delta P$$

$$\Omega = \frac{\Delta P}{Q} = \frac{8\eta L}{\pi R^4}$$

$$\text{Resistance} = \frac{\text{voltage}}{\text{current}}$$



17

Finally, here is our equation for **volumetric flow rate** as relates to known pressure drop, vessel geometry, and fluid viscosity.

We can re-arrange this a little bit to examine the relationship between pressure and flow rate. Let's **divide** the pressure drop by flow rate.

This gives us the **driving force** – or you can think of this as **the resistance to flow.**

Recall back to your physics days - remember Ohm's law? It told us that Resistance = voltage over current. This is the analogous equation for fluid flow.

The pressure is pushing the fluid through the vessel, and the resistance is holding it back.

Why do we want to know about resistance?

$$\Omega = \frac{\Delta P}{Q} = \frac{8\eta L}{\pi R^4}$$

18

Abacon.com

We've made it though the math – now we're here and now you are asking me why we care to know about resistance.

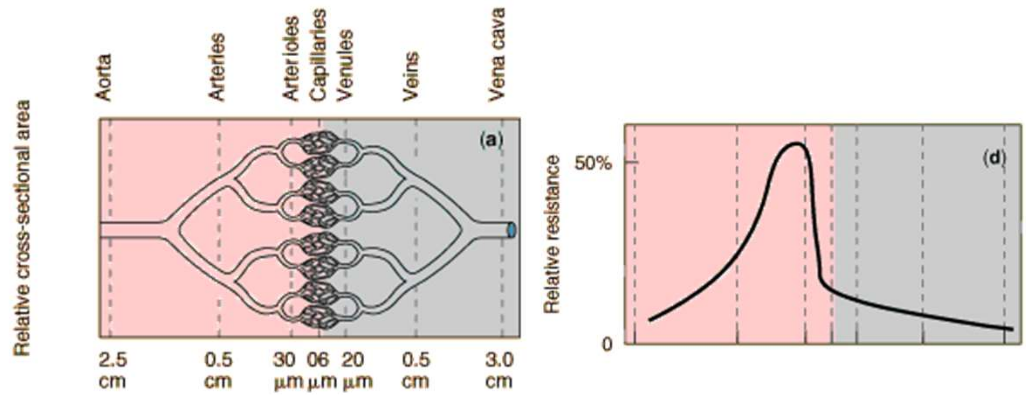
Resistance tells us about how structure governs function.

Let's look at this equation again.

It says that resistance varies with the **inverse radius to the fourth power**. So as the **radius increases** the resistance will **drop dramatically**. And conversely when the radius gets small the resistance will increase dramatically.

Why do we want to know about resistance? (cont.)

$$\Omega = \frac{\Delta P}{Q} = \frac{8\eta L}{\pi R^4}$$



19

Abacon.com

The bottom left shows the cross sectional area of blood vessels as we move through the vascular tree. We can see that the radius varies throughout the vascular tree, **large** in the aorta and vena cava and **very low** in the capillaries.

On the right, the same graph is presented but for relative **resistance**.

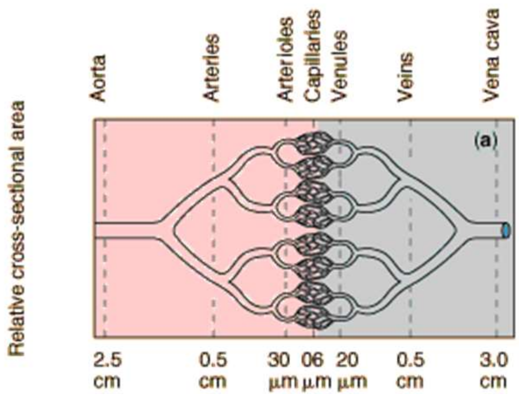
So in the large conduit vessels like the **aorta**, arteries and veins, the resistance is **low** – so flow is easy.

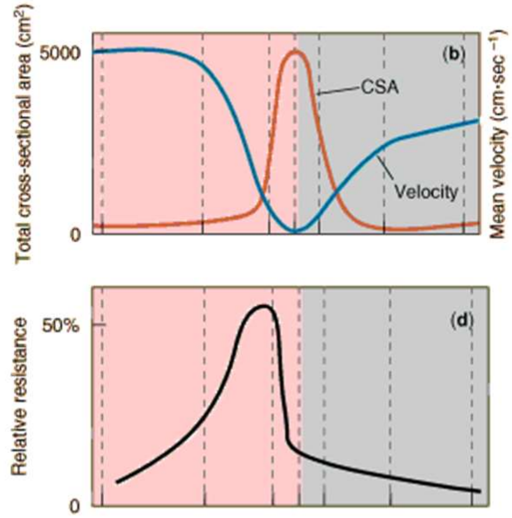
But in small arterioles and capillaries there is **high resistance** to flow, because of the small diameters of those vessels.

So if the resistance is so high, how are we getting adequate **perfusion** of our tissues in these capillaries bed?

Why do we want to know about resistance? (cont.)

$$\Omega = \frac{\Delta P}{Q} = \frac{8\eta L}{\pi R^4}$$





20

Well it works out because we have a **LOT** of capillaries.

This graph shows you the **total cross sectional area** of vessels in red trace and the mean velocity in blue. You can see we have a very large cross sectional area in capillaries, really maximizing surface area.

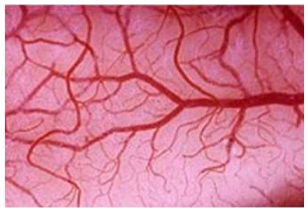
You can see that we have a drop in velocity at that same point, which is because of the spike in resistance just before the capillary beds in the upstream arterioles.

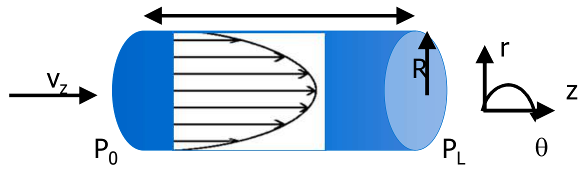
So we have the **lowest** velocity in the capillaries – plus the **greatest** cross sectional area – this makes for maximization of gas and nutrient exchange.

You want **slow flow** to **allow** for **diffusion**, and for that diffusion to occur over **the greatest possible cross sectional area**.

Review and rewind

Fluid mechanics in a cylindrical pipe





$$\mathrm{Re} = \frac{\rho v L}{\mu} \qquad Q = \frac{(P_0 - P_L)\pi R^4}{8\eta L} \qquad \Omega = \frac{\Delta P}{Q} = \frac{8\eta L}{\pi R^4}$$

21

In this lecture we talked about the basics of fluid mechanics.

We worked through the derivation of equations describing flow through a cylinder-like blood vessel, arrived at Poiseuille’s law, fluid resistance, and discussed Reynold’s numbers.

Next up, we will use the basic concepts we've already covered to cover complex materials in the human body, that are a mixture of solid and fluid mechanical behaviors.