Biological Fluid Mechanics\textsuperscript{1}

EPSRC/LMS Short Course

on

Mathematical Biology

Manchester, 9 – 14 January 2005

Matthias Heil

Department of Mathematics
University of Manchester

\href{http://www.maths.man.ac.uk/~mheil/}{http://www.maths.man.ac.uk/~mheil/}

\textsuperscript{1}Please report any typos, errors or suggestions for improvement to M.Heil@maths.man.ac.uk. Thanks!
Biological Fluid Mechanics

Biological Fluid Mechanics can be roughly sub-divided into two main areas:

- **Internal (physiological) flows**
  - Blood flow in veins and arteries
  - Respiratory flows
  - Peristaltic pumping
  - Interstitial flows
  - etc.

- **External flows**
  - Flying (‘the birds and the bees’, ...)
  - Swimming (fish, micro-organisms, man, ...)
  - etc.

This course will concentrate on **internal, physiological flows**.
Some features of physiological flows

Vast range of different flow velocities:

- High velocity (large Reynolds number), often turbulent flows, e.g. in the larger airways during forced expiration.
- Slow, viscous (small Reynolds number) flows, e.g. in the capillaries.

Newtonian and non-Newtonian behaviour:

For instance, blood is a suspension of cells in plasma. The viscosity of blood is highly shear-rate dependent.

- In the larger arteries, blood can be treated as a homogeneous, Newtonian fluid.
- In contrast, the capillaries are so narrow that the individual blood cells have to squeeze through them in single-file motion.

Strong fluid-structure interaction:

- Many fluid conveying vessels deform in response to the traction that the fluid exerts on them:
  - The fluid exerts a traction (pressure and shear stress) on the wall.
  - The wall deforms in response to the fluid traction.
  - The change to the wall geometry changes the flow field.
  - The new flow field changes the fluid traction which feeds back into the wall deformation, etc.
Course overview

In this course, we will consider:

- The pulse wave propagation in the arteries.
- Flow in collapsible tubes as a model for flow in veins and airways.
- Flow patterns in physiological vessels and their importance (for instance in atherosclerosis).
- Taylor dispersion in the lung.
- Surface tension phenomena in the lung.
I. Introduction

Characteristics of the circulatory system

- The circulatory system is a highly branched network of elastic tubes.
- Diameters range from \( \approx 30 \text{ mm (vena cava)} \) to \( \approx 8 \mu \text{m (capillaries)} \).
- Flow velocities range from 0.5 m/sec to less than 1 cm/sec in the capillaries; the associated Reynolds numbers range from \( Re \approx 4500 \) to \( Re \approx 0.001 \).
- The flow is pulsatile and hence highly unsteady.
- The vessel walls tend to deform strongly: Arteries tend to be inflated; veins can be strongly collapsed.
- The vessel walls have a very complicated structure and often include layers of active muscle fibres.
702. Diagram of the circulation
Arteries: red; veins: blue; capillaries: white.

Figure 1: Sketch of the human circulatory system; from Spalteholz (1967).
Table 1.1. Normal values for canine cardiovascular parameters. An approximate average value, and then the range, is given where possible. All values are for the dog except those for arteriole, capillary, and venule, which have only been measured in smaller mammals.

<table>
<thead>
<tr>
<th>Site</th>
<th>Ascending aorta</th>
<th>Descending aorta</th>
<th>Abdominalorta</th>
<th>Femoral artery</th>
<th>Carotid artery</th>
<th>Arteriole</th>
<th>Capillary</th>
<th>Venule</th>
<th>Inferior vena cava</th>
<th>Main pulmonary artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal diameter, $d_i$ (cm)</td>
<td>1.5</td>
<td>1.3</td>
<td>0.9</td>
<td>0.4</td>
<td>0.5</td>
<td>0.005</td>
<td>0.0006</td>
<td>0.004</td>
<td>1.0</td>
<td>1.7</td>
</tr>
<tr>
<td>Wall thickness, $h$ (cm)</td>
<td>0.065</td>
<td>0.05</td>
<td>0.04</td>
<td>0.03</td>
<td>0.02</td>
<td>0.0001</td>
<td>0.0002</td>
<td>0.015</td>
<td>0.01-0.02</td>
<td>0.01-0.03</td>
</tr>
<tr>
<td>$h/d_i$</td>
<td>0.07</td>
<td>0.06</td>
<td>0.04-0.09</td>
<td>0.055-0.11</td>
<td>0.053-0.095</td>
<td>0.17</td>
<td>0.05</td>
<td>0.015</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>In-vivo length (cm)</td>
<td>5</td>
<td>20</td>
<td>15</td>
<td>10</td>
<td>15</td>
<td>0.15</td>
<td>0.06</td>
<td>0.15</td>
<td>30</td>
<td>3.5</td>
</tr>
<tr>
<td>Approximate cross-sectional area (cm$^2$)</td>
<td>2</td>
<td>1.3</td>
<td>0.6</td>
<td>0.2</td>
<td>0.2</td>
<td>2 x 10$^{-5}$</td>
<td>3 x 10$^{-7}$</td>
<td>2 x 10$^{-5}$</td>
<td>0.8</td>
<td>2.3</td>
</tr>
<tr>
<td>Total vascular cross-sectional area at each level (cm$^2$)</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>125</td>
<td>600</td>
<td>570</td>
<td>3.0</td>
<td>2.3</td>
</tr>
<tr>
<td>Peak blood velocity (m s$^{-1}$)</td>
<td>1.2</td>
<td>1.05</td>
<td>0.55</td>
<td>1.0</td>
<td>0.75</td>
<td>0.07</td>
<td>0.35</td>
<td>0.25</td>
<td>0.15-0.4</td>
<td>0.15</td>
</tr>
<tr>
<td>Mean blood velocity (m s$^{-1}$)</td>
<td>0.2</td>
<td>0.2</td>
<td>0.15</td>
<td>0.1</td>
<td>0.005-0.01</td>
<td>0.0002-0.0017</td>
<td>0.002-0.005</td>
<td>0.06-0.28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak Reynolds number, $Re$</td>
<td>4500</td>
<td>3400</td>
<td>1250</td>
<td>1000</td>
<td>0.09</td>
<td>0.001</td>
<td>0.035</td>
<td>700</td>
<td>3000</td>
<td></td>
</tr>
<tr>
<td>Frequency parameter, $f$ (heart-rate 2 Hz)</td>
<td>13.2</td>
<td>11.5</td>
<td>8</td>
<td>3.5</td>
<td>4.4</td>
<td>0.04</td>
<td>0.005</td>
<td>0.035</td>
<td>8.8</td>
<td>15</td>
</tr>
<tr>
<td>Calculated wave speed, $c_0$ (m s$^{-1}$)</td>
<td>5.8</td>
<td>7.7</td>
<td>8.4</td>
<td>8.5</td>
<td>8.5</td>
<td>1.0</td>
<td>3.5</td>
<td></td>
<td>4.0</td>
<td>2.5</td>
</tr>
<tr>
<td>Measured wave speed, $c$ (m s$^{-1}$)</td>
<td>5.0</td>
<td>7.0</td>
<td>9.0</td>
<td>8.0</td>
<td>8.0</td>
<td>4.0</td>
<td>2.5</td>
<td></td>
<td>1.0-7.0</td>
<td>2.0-3.3</td>
</tr>
<tr>
<td>Young's modulus, $E$ (x10$^5$ kN m$^{-2}$)</td>
<td>4.8</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>9</td>
<td>0.7</td>
<td>6</td>
<td></td>
<td>0.4-1.0</td>
<td>2-10</td>
</tr>
</tbody>
</table>
Mathematical modelling of physiological flows

• Physiological fluid mechanics deals with *extremely* complicated physical systems.

• Even if we were able to (mathematically) represent all physical effects, we would still have to provide a large number of material parameters which would be very difficult to determine *in vivo*.

• Hence, we must try to include only the most important physical features into our models in order to
  
  – keep the problem manageable and
  
  – enable us to perform meaningful parameter studies.
Fluid mechanics

- For the purpose of this course, we will generally assume that the fluids are
  - incompressible
  - Newtonian (i.e. the shear stresses in the fluid are proportional to the shear rate).

- With these assumptions, the flow is governed by the Navier-Stokes equations

\[
\frac{\partial u}{\partial t} + u \frac{\partial u}{\partial x} + v \frac{\partial u}{\partial y} + w \frac{\partial u}{\partial z} = F_x - \frac{1}{\rho} \frac{\partial p}{\partial x} + \nu \nabla^2 u, \tag{1}
\]
\[
\frac{\partial v}{\partial t} + u \frac{\partial v}{\partial x} + v \frac{\partial v}{\partial y} + w \frac{\partial v}{\partial z} = F_y - \frac{1}{\rho} \frac{\partial p}{\partial y} + \nu \nabla^2 v, \tag{2}
\]
\[
\frac{\partial w}{\partial t} + u \frac{\partial w}{\partial x} + v \frac{\partial w}{\partial y} + w \frac{\partial w}{\partial z} = F_z - \frac{1}{\rho} \frac{\partial p}{\partial z} + \nu \nabla^2 w, \tag{3}
\]

where

\[ \nabla^2 \equiv \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2}, \]

and the continuity equation

\[ \text{div} \ u = \frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} + \frac{\partial w}{\partial z} = 0. \]

- \( u, v, w \) are the fluid velocities in the \( x, y, z \) directions, respectively. \( p \) is the fluid pressure and \( \rho \) and \( \nu \) are the fluid’s density and (kinematic) viscosity, respectively. \( \mathbf{F} \) is a body force per unit mass; e.g. the gravitational acceleration.

- Occasionally, we will use the dynamic viscosity \( \mu = \nu \rho \).

\[ \text{\textsuperscript{2}}\text{See e.g. Acheson (1990) and Panton (1996) – my favourite fluids textbooks!} \]
Useful simplifications of the Navier Stokes equations

- The Navier Stokes equations form an extremely complicated system of non-linear partial differential equations.

- Luckily, we can often use simplified versions of these equations, which exploit certain features of the problem. Examples include:
  - Long wavelength approximations, e.g.
    \[ \frac{\partial}{\partial x} \ll \frac{\partial}{\partial y} \]
  - The assumption of unidirectional, uniform, one-dimensional flow,
    \[ \mathbf{u}(x, y, z, t) \approx u(x, t) \mathbf{e}_x. \]

  [This is often appropriate for high Reynolds number turbulent flows which tend to have blunt velocity profiles.]
Useful simplifications of the Navier Stokes equations (cont.)

- Large or small Reynolds numbers,

\[ Re = \frac{Ua}{\nu}, \]

where \( U \) is the typical magnitude of the flow velocity and \( a \) the length-scale over which the flow-field undergoes significant changes.

**Large** \( Re \) corresponds to (approximately) inviscid flows in which the viscous terms (such as \( \nu \nabla^2 u \) etc.) can be neglected.

**Small** \( Re \) corresponds to very viscous flows in which the (nonlinear!) inertial terms (such as \( u \frac{\partial u}{\partial x} \) etc.) can be neglected.
Solid mechanics

[...]

Dear Matthias

[...]

Best wishes
Helen

- The (possibly large) deformation of the vessel walls are governed by Cauchy’s equation

\[ \tau^{ij} \|_j + \rho \, F^i = 0, \]

where \( \tau^{ij} \) is the 2nd Piola Kirchhoff stress tensor, \( (.) \|_j \) represents the covariant derivative in the deformed configuration, \( \rho \) is the density of the wall material and the \( F^i \) are the covariant components of the body force (per unit mass) acting on the wall.

- This equilibrium equation has to be augmented by a suitable constitutive equation which relates the stress tensor to the components \( \epsilon_{ij} \) of Green’s strain tensor which is a function of the wall displacements.

- External tractions applied to the wall enter the problem via Neumann-type boundary conditions.

Sorry, Helen! This is way too complicated...

---

3See e.g. Wempner (1981) – my favourite solids textbook!
Simplified wall mechanics: The ‘tube law’.

- Consider the deformation of a straight segment of a uniform, approximately cylindrical biological vessel in response to changes of the transmural pressure $p_{tm}$ (=inside minus outside pressure):

$$p_{tm} = \frac{1}{A/A_0} p_{owc}$$

Figure 3: The ‘tube law’.

- The functional relationship between the transmural pressure and the vessel’s cross sectional area is known as the ‘tube law’:

$$p_{tm} = \mathcal{P}(A) \quad \text{or} \quad A = \mathcal{A}(p_{tm})$$

with an undeformed reference configuration such that

$$\mathcal{P}(A_0) = 0 \quad \text{or} \quad \mathcal{A}(0) = A_0.$$
Simplified wall mechanics: The ‘tube law’ (cont.).

- The tube law represents the tube’s behaviour in three distinct regimes:
  1. Pure inflation: here the vessel is very stiff, i.e.
     \[ \frac{dP}{dA} \gg 1. \]
  2. Moderate buckling: here the vessel is very floppy since it is held open only by its small bending stiffness:
     \[ \frac{dP}{dA} = O(1). \]
  3. Strong buckling/opposite wall contact: again very stiff, i.e.
     \[ \frac{dP}{dA} \gg 1. \]

- The tube law provides a good description of biological vessels provided we can sensibly
  - ignore non-uniformities of the vessel walls.
  - ignore the tethering of the vessel walls by the surrounding tissue.
  - ignore the effect of bifurcations.
  - assume that the wall deformation varies gently along the vessel [Note that the tube law is a *local* approximation!].

- If any of these effects are important, we need to develop a more complicated model.
Simplified wall mechanics: The ‘tube law’ (cont.).

- A good fit to the experimentally observed behaviour in the buckled regime is given by
  \[ P = K \left( 1 - \left( \frac{A}{A_0} \right)^{-3/2} \right) \text{ for } p_{tm} < p_b, \]  
  (4)
  where
  \[ K = \frac{Eh^3}{12(1 - \nu^2)} \]  
  (5)
is the tube’s bending stiffness in terms of the wall’s elastic modulus $E$, its thickness $h$ and its Poisson ratio $\nu$.

- In the strongly collapsed regime, the tube law given by (4) is consistent with Flaherty et al. (1972) analytical results for the collapse of thin-walled elastic rings under external pressure.
Fig. 1 Behavior of a collapsible tube. Dimensionless transmural pressure difference, $\bar{\rho}$, versus dimensionless area ratio, $\alpha$. Solid curve shows typical experimental curve for thin-walled latex tube, and adjacent to it, typical cross-sectional shapes for the different ranges of $\alpha$. Dot-dash curve represents the similarity law, $\bar{\rho} = -\alpha^{-3/2}$, and coincides with solid curve for $\alpha < \hat{\alpha}$. Dashed curve represents the modified similarity law, $\bar{\rho} = 1 - \alpha^{-3/2}$. Point contact occurs at $\alpha = \hat{\alpha}$, and line contact occurs at $\alpha = \hat{\alpha}$.

Figure 4: The tube law; from Shapiro (1977).
II. Pulse wave propagation in the arteries

Physiological observations:

- Blood is ejected from the heart during systole (the period of active contraction of the heart).
- A pressure pulse propagates along the arterial tree.
- The pulse propagation is wave-like in character.
- The shape of the pulse wave changes distinctly as it propagates through the arterial system.

Fig. 1.13. Instantaneous blood pressure records made at a series of sites along the aorta in the dog. 0 cm is at the start of the descending aorta. (After Olson, 1968.)
We observe:

- Wave propagation with a certain (average) velocity.
- Steepening of the wave front.
- Increase in the wave amplitude.

Fig. 1.13. Instantaneous blood pressure records made at a series of sites along the aorta in the dog. 0 cm is at the start of the descending aorta. (After Olson, 1968.)

Figure 6: From Pedley (1980).
A simple model:

- Consider the pulse wave propagation in a long, uniform elastic tube with tube law

\[
p = \mathcal{P}(A) \quad \text{or} \quad A = \mathcal{A}(p),
\]

with a reference cross sectional area \( A_0 \) such that \( \mathcal{P}(A_0) = 0 \).

- Use the inviscid, long wavelength approximation to the Navier-Stokes equations:

\[
\frac{\partial u}{\partial t} + u \frac{\partial u}{\partial x} = -\frac{1}{\rho} \frac{\partial p}{\partial x},
\]

with uniform pressure and velocity distributions across the cross section of the tube, i.e. \( p = p(x, t) \) and \( u = u(x, t) \ e_x \).

- The continuity equation can then be replaced by the integral relation

\[
\frac{\partial A}{\partial t} + \frac{\partial (A u)}{\partial x} = 0.
\]

- This provides three equations for \( A, u \) and \( p \).
We use the tube law to express the pressure gradient in terms of the gradient of the cross sectional area $A(x,t)$

$$\frac{\partial p}{\partial x} = \left(\frac{\partial A}{\partial p}\right)^{-1} \frac{\partial A}{\partial x}$$

or

$$\frac{\partial p}{\partial x} = \left[A \left(\frac{\partial A}{\partial p}\right)^{-1}\right] \frac{1}{A} \frac{\partial A}{\partial x}$$

where

$$D = \frac{1}{A} \left(\frac{\partial A}{\partial p}\right)$$

is the ‘distensibility’ (the inverse stiffness) of the tube.

Inserting $dp/dx$ from (9) into the momentum equation (7) yields

$$\frac{\partial u}{\partial t} + u \frac{\partial u}{\partial x} = -c^2 \frac{1}{A} \frac{\partial A}{\partial x}$$

where

$$c^2 = \frac{1}{\rho D}$$

is a quantity (of dimension velocity) which depends on the tube’s distensibility and the fluid’s density. We will soon see that $c$ represents the wave-speed.
• Note that, in general, the distensibility of the vessel varies with its state of inflation. Most biological vessels get stiffer as they get inflated:

<table>
<thead>
<tr>
<th>Vessel</th>
<th>$E$ (kN m$^{-2}$)</th>
<th>$h/d$</th>
<th>$D$ (m$^3$ kN$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$A$</td>
<td>$B$</td>
<td>$A$</td>
</tr>
<tr>
<td>Venae cavae</td>
<td>3000</td>
<td>420</td>
<td>0.006</td>
</tr>
<tr>
<td>Jugular vein</td>
<td>1000</td>
<td>110</td>
<td>0.011</td>
</tr>
<tr>
<td>Pulmonary artery</td>
<td>600</td>
<td>106</td>
<td>0.015</td>
</tr>
<tr>
<td>Aorta</td>
<td>100</td>
<td>Not</td>
<td>0.092</td>
</tr>
</tbody>
</table>

given

Figure 8: From Pedley (1980).

Fig. 1.9. Dependence of effective incremental Young's modulus $E$ on transmural pressure, $p_{tm}$, for various vessels: filled circles, inferior and superior venae cavae; filled triangles, jugular vein; crosses, pulmonary artery; open circles, descending aorta; open triangles, carotid artery. The normal physiological ranges of transmural pressures for systemic arteries, pulmonary arteries and veins at the level of the heart are also indicated. (After Attinger, 1969.)

Figure 9: From Pedley (1980).
The full nonlinear wave equation:

- Add and subtract $c/A$ times the integral continuity equation (8),
  \[
  \frac{\partial A}{\partial t} + \frac{\partial (Au)}{\partial x} = 0
  \]
  to the modified 1D momentum equation (10),
  \[
  \frac{\partial u}{\partial t} + u \frac{\partial u}{\partial x} = -c^2 \frac{1}{A} \frac{\partial A}{\partial x}
  \]
  to obtain:
  \[
  \left( \frac{\partial}{\partial t} + (u \pm c) \frac{\partial}{\partial x} \right) u \pm \frac{c}{A} \left( \frac{\partial}{\partial t} + (u \pm c) \frac{\partial}{\partial x} \right) A = 0. \quad (11)
  \]

- This is beginning to look like a wave equation!
To make the wave character even more explicit, define the \textit{Riemann invariants}

\[ R_{\pm}(x, t) = u(x, t) \pm \int_{A_0(x)}^{A(x, t)} \frac{c}{A} \, dA. \]

[Remember that the wave-speed in the integrand might be a function of the cross sectional area as well!]

Then it’s easy to show\(^4\) (going backwards, at least...) that the two equations (11) can be written as:

\[ \left( \frac{\partial}{\partial t} + (u \pm c) \frac{\partial}{\partial x} \right) R_{\pm} = 0. \]  

This is a nonlinear wave equation which has a very simple interpretation: The quantities \(R_{\pm}\) remain constant along the characteristics defined by

\[ \frac{dx}{dt} = u \pm c \]

In the tutorials, we will consider a simple example which illustrates how disturbances governed by this nonlinear equation propagate along the vessel.

\(^4\)Don’t forget Leibniz’ rule for the derivative w.r.t. to the variable upper bound in the integral:

\[ \frac{\partial}{\partial x} \int_{\xi_0}^{\xi(x)} f(\eta) \, d\eta = f(\xi(x)) \frac{\partial \xi}{\partial x} \]
The linearised wave equation:

- Here we will proceed by considering the linear theory which governs small amplitude perturbations to the rest state \((u, p, A)_0 = (0, 0, A_0)\), i.e.

\[
(u, p, A) = (0, 0, A_0) + \epsilon (u_1, p_1, A_1) + \ldots
\]

with \(\epsilon \ll 1\).

- Inserting this into the momentum equation

\[
\frac{\partial u}{\partial t} + u \frac{\partial u}{\partial x} = - \frac{1}{\rho} \frac{\partial p}{\partial x}
\]

gives

\[
\epsilon \frac{\partial u_1}{\partial t} + \epsilon^2 u_1 \frac{\partial u_1}{\partial x} = -\epsilon \frac{1}{\rho} \frac{\partial p_1}{\partial x},
\]

so the leading order contribution is

\[
\frac{\partial u_1}{\partial t} = - \frac{1}{\rho} \frac{\partial p_1}{\partial x}.
\]
• Similarly we rewrite the continuity equation

\[ \frac{\partial A}{\partial t} + \frac{\partial (Au)}{\partial x} = 0 \]

\[ \frac{\partial A}{\partial p} \frac{\partial p}{\partial t} + \frac{\partial A}{\partial p} \frac{\partial p}{\partial t} = 0, \]

where

\[ D_0 = \frac{1}{A_0} \frac{\partial A}{\partial p} \bigg|_{A=A_0} \]

is the tube’s distensibility in the reference state.

• Now insert the regular perturbation expansion (13) to obtain

\[ \epsilon A_0 D_0 \frac{\partial p_1}{\partial t} + \epsilon A_0 \frac{\partial u_1}{\partial x} + \epsilon^2 \frac{\partial (A_1 u_1)}{\partial x} = 0, \]

which shows that the leading order contribution is

\[ D_0 \frac{\partial p_1}{\partial t} + \frac{\partial u_1}{\partial x} = 0. \] (15)
• Now drop the subscripts and take $\partial / \partial x$ of (14):

$$\frac{\partial^2 u}{\partial t \partial x} = -\frac{1}{\rho} \frac{\partial^2 p}{\partial x^2}$$

and add it to $\partial / \partial t$ of (15):

$$D_0 \frac{\partial^2 p}{\partial t^2} = -\frac{\partial^2 u}{\partial x \partial t}$$

• Thus we obtain the linear wave equation for the pressure

$$\frac{\partial^2 p}{\partial t^2} - c_0^2 \frac{\partial^2 p}{\partial x^2} = 0 \quad (16)$$

where

$$c_0^2 = \frac{1}{\rho D_0}$$

is the wave-speed evaluated in the reference state.

• Using the opposite differentiations, we obtain an identical equation for the velocity, namely

$$\frac{\partial^2 u}{\partial t^2} - c_0^2 \frac{\partial^2 u}{\partial x^2} = 0. \quad (17)$$
• The solutions of these wave equations are, of course, well understood: For instance, the pressure can be written as

\[ p(x, t) = f \left( t - \frac{x}{c_0} \right) + g \left( t + \frac{x}{c_0} \right) \]  

(18)

where \( f \) and \( g \) represent the profiles of waves which travel at constant speed \( c_0 \) to the right and left, respectively.

• The same argument applies to the velocity distribution \( u(x, t) \) which has its own wave profiles.

• Using (14), we see that the pressure and velocity wave profiles are related by

\[ \frac{\partial u}{\partial t} = -\frac{1}{\rho} \frac{\partial p}{\partial x} \]

so

\[ \frac{\partial u}{\partial t} = -\frac{1}{\rho} \left[ -\frac{1}{c_0} f' \left( t - \frac{x}{c_0} \right) + \frac{1}{c_0} g' \left( t + \frac{x}{c_0} \right) \right] \]

and therefore

\[ u(x, t) = \frac{1}{\rho c_0} \left[ f \left( t - \frac{x}{c_0} \right) - g \left( t + \frac{x}{c_0} \right) \right] \]  

(19)
Often we are interested in the volume flux \( q = uA \) that passes through the tube at a given location. Within the accuracy of the linear theory it is given by

\[
q(x, t) = \frac{A_0}{\rho c_0} \left( f \left( t - \frac{x}{c_0} \right) - g \left( t + \frac{x}{c_0} \right) \right).
\]  

(20)

The quantity

\[
Y = \frac{A_0}{\rho c_0} = \frac{A_0 \sqrt{\rho D}}{\rho} = A_0 \sqrt{\frac{D}{\rho}}
\]

(21)

is the ‘admittance’ (the inverse flow resistance) of the vessel.
Summary of the linearised analysis:

1. The pressure pulse consists of two travelling waves.
2. The two waves propagate upstream and downstream with constant velocity.
3. The shapes of the pressure waves remain unchanged as they propagate.
4. The fluid velocity is in phase with the pressure.

Physiological observations show that none of this is strictly true:

![Figure 10: Comparison of pressure and flow pulses; from McDonald (1960).](image)
Shortcomings of the linearised analysis:

1. The pressure amplitude increases while the velocity amplitude decreases.
2. The pressure wave steepens.
3. Velocity and pressure pulses are not in phase.

Our model needs to be improved to explain these observations. The ‘missing’ physical effects which are (mainly) responsible for these features are:

1. Wave reflections from junctions.
2. Nonlinearities in the wave propagation.
3. Viscous effects.

We will investigate these effects separately.
1. Increase in the pressure pulse amplitude: Wave reflections

- The arterial system is a highly branched network of elastic tubes.

![Diagram of the arterial system](image)

Fig. 1.3. A diagrammatic representation of the major branches of the canine arterial tree. (After McDonald, 1974.)

Figure 11: From Pedley (1980).

- Clearly, the multitude of junctions can be expected to have a pronounced effect on the pulse wave propagation.
Consider the following model of an arterial junction:

A forward travelling, incident pressure wave of amplitude $P_I$

$$p(x, t) = P_I f(t - x/c_0)$$

approaches the junction\(^5\).

The corresponding flow rate in the parent vessel is

$$q(x, t) = Y_0 P_I f(t - x/c_0),$$

where $Y_0$ and $c_0$ represent the admittance and the wave velocity in the parent vessel.

---

\(^5\)Assume that $f$ is scaled such that $\max f = 1$. 
• When the incident wave reaches the junction, it will in general:
  
  – generate a transmitted (forward travelling) wave in each of the daughter vessels \((i = 1, 2)\),
    \[ p = P_{Ti} \, g_i(t - x/c_i) \quad \text{and} \quad q = Y_i \, P_{Ti} \, g_i(t - x/c_i). \]
  
  – generate a reflected (backwards travelling) wave in the parent vessel:
    \[ p = P_R \, h(t + x/c_0) \quad \text{and} \quad q = -Y_0 \, P_R \, h(t + x/c_0). \]

• We need to determine
  
  – the functions \(g_1, g_2\) and \(h\).
  
  – the pressure wave amplitudes \(P_{T1}, P_{T2}\) and \(P_{R}\).
Matching conditions at the junction:

- We have to ensure continuity of pressure and flux at $x = 0$ for all $t$.
- This can only be achieved if
  
  $$g_1(t) = g_2(t) = h(t) = f(t),$$
  
i.e. all wave profiles have the same form as the incoming wave.

- The amplitudes are determined from
  
  - the continuity of pressure:
    
    $$P_I + P_R = P_{T_i}$$
    
    Pressure in the parent branch: Superposition of incident and reflected waves.
    Pressure in each of the two daughter vessels due to the transmitted waves.

  - the continuity of volume flux:
    
    $$q_I + q_R = q_{T_1} + q_{T_2}$$
    
    Volume flux in the parent branch: Superposition of the fluxes due to the incident and reflected waves.
    Sum of volume fluxes into the two daughter vessels due to the transmitted waves.

  which implies

  $$Y_0(P_I - P_R) = Y_1 P_{T_1} + Y_2 P_{T_2}.$$
Solving these three equations for $P_{T_1}, P_{T_2}$ and $P_R$ yields

$$P_R = P_I \frac{Y_0 - \sum Y_i}{Y_0 + \sum Y_i}$$

and

$$P_{T_i} = P_I \frac{2Y_0}{Y_0 + \sum Y_i} \quad \text{for } i = 1, 2.$$

Now, for most arteries, the cross sectional area and distensibility decrease with the distance from the heart.

Therefore, the admittance

$$Y = A \sqrt{\frac{D}{\rho}}.$$

decreases with the distance from the heart.

A sufficiently rapid reduction of the admittance at junctions such that

$$Y_0 > \sum Y_i$$

causes an increase in pressure amplitude as the pressure wave propagates forward through the arterial tree.

Furthermore, since

$$q \sim Y \ p$$

the decrease in admittance $Y$ explains why the amplitude of the volume flux is reduced (relative to the pressure amplitude).
Further remarks

• Taper of the vessels (i.e. the continuous reduction of their cross sectional area in the direction of flow) can be shown to have similar effects to that of wave reflections at junctions; see e.g. Taylor (1965).

• Note that wave reflections also lead to changes in the velocity and pressure profiles since measurements at a fixed location record the superposition of incident and (possibly multiply) reflected waves.
2. Wave steepening: Nonlinear effects

- The steepening of the pressure wave can be explained by nonlinear effects. We will study this in detail in the tutorial.

- An excellent reference for wave phenomena in fluids is Lighthill (1980). His discussion of nonlinear wave steepening (p. 137 ff) is directly applicable to the present problem.
3. Differences between pressure and velocity waves: Viscous effects (in a linear theory)

- So far we have assumed that the velocity profile is approximately uniform over the vessel’s cross section.

- However, viscous effects will reduce the fluid velocity to zero on the walls and this might have an effect on the system’s behaviour.

- To study the effect of fluid viscosity, we will use the long wavelength assumption and assume that the wall deformation is small, i.e.

$$\frac{\partial}{\partial x} \ll \frac{\partial}{\partial r} \quad \text{and} \quad |a(x, t) - a_0| \ll 1.$$  

where $a(x, t)$ is the slowly varying radius of the axisymmetric vessel whose average radius is $a_0$. 
• With these assumptions, the leading order contribution to the momentum equations is the $x$-component of the Navier Stokes equations (in cylindrical polars):

$$\frac{\partial u}{\partial t} = -\frac{1}{\rho} \frac{\partial p}{\partial x} + \nu \left( \frac{\partial^2 u}{\partial r^2} + \frac{1}{r} \frac{\partial u}{\partial r} \right). \tag{22}$$

• The fluid fulfills the no-slip boundary conditions on the tube wall:

$$u(x, r = \pm a(x, t)) = 0.$$  

• Linearisation gives the leading order contribution:

$$u(x, r = \pm a_0) = 0. \tag{23}$$

• Now assume that the flow is driven by a time-periodic pressure gradient

$$\frac{\partial p}{\partial x} = \sum_{n=0}^{\infty} G_n e^{i\omega nt}, \tag{24}$$

where

$$\omega = \frac{2\pi}{T}$$

is the fundamental frequency of the pressure pulse (of period $T \approx 0.5$ sec).

• The coefficients $G_n$ can be assumed to be known from a Fourier analysis of the observed (or calculated) pressure pulse.

• Note that the problem defined by equations (22) to (24) contains $x$ only as a parameter in $\partial p/\partial x$. 
• We expand the local velocity in a corresponding Fourier series

\[ u(r, t) = \sum_{n=0}^{\infty} U_n e^{i\omega nt}. \]

• Term by term solution of the linear equation (22) subject to the boundary condition (23) gives

\[ U_0 = -\frac{G_0 a_0^2}{4\mu} \left( 1 - \left( \frac{r}{a_0} \right)^2 \right) \quad \text{(Poiseuille flow)} \]

and

\[ U_n = \frac{i a_0^2 G_n}{\mu \alpha_n^2} \left[ 1 - \frac{J_0(i^{3/2}) \alpha_n r/a_0}{J_0(i^{3/2}) \alpha_n} \right] \quad \text{for } n = 1, 2, \ldots \]

• Here

\[ \alpha_n = \alpha \sqrt{n}, \]

where

\[ \alpha^2 = \frac{\omega a_0^2}{\nu} = \frac{\omega U a_0 \rho}{U \mu/a_0} = \frac{\text{‘inertia’}}{\text{‘viscosity’}} \]

is the Womersley parameter.

• \( \alpha \approx O(15) \) in the large arteries.

• Note that the (complex!) velocity amplitudes have a radius dependent phase angle.
Figure 13: Velocity profiles, $Re(U_n e^{im\omega t})$, for different values of $\alpha_n = \alpha\sqrt{n}$.

- Note that the blunt velocity profile is consistent with our earlier assumptions about the velocity distribution!
Here’s a comparison between the calculated and measured velocity profiles:

Figure 14: Calculated and experimentally observed velocity profiles; from Lighthill (1975).
• The Fourier components of the volume flux

\[ \dot{V} = \int u(r, t) \, dA = 2\pi \int_0^{a_0} u(r, t) \, r \, dr = \sum_{n=0}^{\infty} \dot{V}_n e^{i\omega t} \]

are given by

\[ \dot{V}_n = \frac{i\pi G_n a_0^4}{\mu \alpha_n^2} (1 - F(\alpha_n)), \]

where

\[ F(\alpha_n) = \frac{2J_1(i^{3/2}\alpha_n)}{\alpha_n J_0(i^{3/2}\alpha_n)}. \]

• Note that the \( \dot{V}_n \) are generally complex

\[ \dot{V}_n = |\dot{V}_n| e^{i\Phi} \]

• This introduces a phase difference \( \Phi \) between the pressure gradient and the volume flux (i.e. the average velocity):

![Graph](Image)

Figure 15: Phase angle between pressure gradient and volume flux versus \( \alpha_n = \alpha \sqrt{n} \).
• Note that at

small $\alpha_n$: The volume flux is $180^\circ$ out of phase with the pressure gradient: In the viscous regime, the flow is against the pressure gradient.

large $\alpha_n$: The volume flux is $90^\circ$ out of phase with the pressure gradient: The balance of forces is between the acceleration and the pressure gradient.

• Here’s a comparison between the observed and calculated volume flux. The calculation was based on the given (Fourier decomposed) pressure signal.

![Graph showing waveforms](image-url)

*Fig. 2.5. Waveforms of average velocity (upper traces) in a dog’s femoral artery; continuous curve, measured with an electromagnetic cuff flowmeter; broken curve, calculated from the measured pressure gradient (lower trace) according to Womersley’s rigid-tube theory. (After McDonald, 1974.)*

Figure 16: From Pedley (1980).
III. Flow in collapsible tubes: Veins & the airways

Motivation:

- The arteries tend to be subject to a positive transmural pressure. The pressure pulse inflates them further.

- Many fluid conveying vessels are (or can become) subject to negative transmural pressures:
  - The veins (e.g. above the level of the heart – try it!).
  - The arteries (e.g. during sphygmomanometry).
  - The coronary arteries during systole.
  - The lung airways during forced expiration.
  - The ureter during peristaltic pumping.
  - ...

- If compressed, the vessels collapse (buckle) strongly.

- In a buckled state, the vessels’ stiffness is small, therefore only small changes in fluid pressure are required to lead to large changes in cross sectional area.

- This tends to result in strong fluid structure interaction, which can give rise to phenomena like:
  - Flow limitation (viscous and inviscid; e.g. during forced expiration).
  - Self-excited oscillations (e.g. wheezing and the Korotkoff sounds during sphygmomanometry).
Laboratory experiments: The Starling resistor

![Diagram of a collapsible tube with labeled pressures and volumetric flow rate](image)

Figure 17: A collapsible tube.

- E.g. prescribe \( \dot{V} \) (volumetric pump) and \( p_{\text{down}} \) (exit into atmosphere) and vary \( p_{\text{ext}} \) to control the degree of collapse.
1. A simple model for viscous flow limitation:

- Consider a 2D channel in which part of one wall has been replaced by an elastic membrane under tension $T$:

![Figure 18: Flow in a collapsible channel.](image)

- Use the low Reynolds number, long wavelength approximation to the Navier-Stokes equations (‘lubrication theory’):

$$\frac{\partial p}{\partial x} = \mu \frac{\partial^2 u}{\partial y^2} \quad (25)$$

with uniform pressure $p = p(x)$.

- Velocity boundary conditions:

$$u(y = 0) = 0 \quad \text{and} \quad u(y = h(x)) = 0 \quad (26)$$

- Equation (25) can immediately be integrated to give

$$u(x, y) = -\frac{1}{2\mu} \frac{\partial p}{\partial x} y (h(x) - y)$$

- I.e., in every cross section, the flow is the same as that in a uniform, infinitely long channel whose width is the same as the local width $h(x)$.
• The (local) volume flux is given by

\[ \dot{V} = \int_0^{h(x)} u(x, y) \, dy = -\frac{1}{12\mu} h(x)^3 \frac{\partial p}{\partial x}. \]  

(27)

Wall mechanics: ‘String under tension’

• Use a simple wall model to relate the transmural pressure to the wall deformation:

\[ T \frac{\partial^2 h}{\partial x^2} = -p(x) \]  

(28)

• This describes the deformation of a string under constant tension \( T \) subject to the fluid pressure \( p(x) \).

• Wall boundary conditions:

\[ h(x = 0) = h(x = L) = H_0. \]  

(29)
The coupled equation:

- For steady problems, the volume flux has to be the same in every cross section, i.e.

\[ \dot{V} = \frac{1}{12\mu} h^3 \frac{\partial}{\partial x} \left( T \frac{\partial^2 h}{\partial x^2} \right) \]  

(30)

- In addition to the two wall boundary conditions (29) we also have to prescribe the fluid pressure at one point in the channel, e.g.

\[ p(x = 0) = p_{up} \quad \text{or} \quad p(x = L) = p_{down} \]

i.e.

\[ \left. \frac{\partial^2 h}{\partial x^2} \right|_{x=0} = -\frac{p_{up}}{T} \quad \text{or} \quad \left. \frac{\partial^2 h}{\partial x^2} \right|_{x=L} = -\frac{p_{down}}{T} \]  

(31)
• A suitable non-dimensionalisation (Exercise!) of all variables transforms this problem into a 3rd order ODE with only two control parameters:

\[ q = h^3 h'' \]

subject to the boundary conditions

\[ h(0) = 1 \quad \text{and} \quad h(1) = 1 \]

and either

\[ h''(0) = -p_{up} \quad \text{or} \quad h''(1) = -p_{down} \]

• All quantities are now non-dimensional (but I didn’t introduce any tildes etc.)
Parameter variations:
   a) Constant downstream transmural pressure

Figure 20: Wall shape and pressure distribution for various values of the volume flux $q$ and for $p_{\text{down}} = -5 = \text{const.}$
• An increase in the upstream pressure increases the flow rate and inflates the channel.

• The channel’s inflation reduces its flow resistance:

\[ \frac{\partial^2 q}{\partial (\Delta p)^2} > 0. \]

• This is known as ‘pressure drop limitation’:

![Figure 21: Volume flux \( q \) versus the driving pressure drop \( \Delta p \) for \( p_{\text{down}} = -5 = \text{const.} \)](image)

• Unfortunately (?), there is no direct physiological application for this scenario.
b) Constant upstream transmural pressure

Figure 22: Wall shape and pressure distribution for various values of the volume flux $q$ and for $p_{up} = 5 = \text{const.}$
An decrease in the downstream pressure increases the flow rate and collapses the channel.

The channel’s collapse increases its flow resistance:

\[
\frac{\partial^2 q}{\partial (\Delta p)^2} < 0.
\]

This is known as ‘flow limitation’:

Figure 23: Driving pressure drop versus volume flux \( q \) for \( p_{up} = 5 = \text{const} \).

What happens if we increase \( \Delta p \) even further?
The flow rate cannot be increased beyond $q_{max}$.

After the maximum, a further increase in the driving pressure difference reduces the flux through the tube!

This is known as ‘negative effort dependence’ and is observed, e.g., during forced expiration.

Negative effort dependence can also be caused by an inviscid mechanism (via the Bernoulli effect).
Here’s a (very!) simple model of flow limitation during forced expiration:

Figure 25: A simple model for flow limitation during forced expiration.

- Flow is driven by the active compression of the chest cavity.
- The alveoli (and very small airways) are very thin walled and offer little structural resistance. Therefore the transmural pressure differences in this part of the lung are small.
- The viscous and/or inertial pressure drop in the larger airways can lead to large transmural pressure differences which can cause them to collapse strongly.
- Once initiated, airway collapse leads to a strong increase in the fluid pressure drop which enhances the airways’ collapse even further.
How good is our simple (viscous) model?

- The changes to the flow geometry in a collapsing 3D vessel are far more pronounced than in a 2D channel:

![Figure 26: Collapse of a tube conveying viscous fluid; from Heil (1997).](image)

![Figure 27: Viscous flow in a strongly collapsed tube; from Heil (1997).](image)
Behaviour for constant upstream transmural pressure

Figure 28: Negative effort dependence in a 3D tube. $p_{up} = \text{const.}$ along the various curves. The arrow indicates the direction of an increase in $p_{up}$; from Heil (1997).

- Negative effort dependence occurs for large upstream transmural pressures on the post-buckling branch.
- The details of the system’s behaviour are somewhat different from what was predicted by the simple 2D model.
- Nevertheless, some of the important physical mechanisms are clearly captured by the much simpler model.
2. ‘Choking’ and the onset of self-excited oscillations

- Questions:
  1. How does vessel collapse manifest itself in the tube law model of flow in elastic tubes?
  2. What is the mechanism behind the self-excited oscillations frequently observed at large Reynolds number?

- Consider steady flow in an elastic tube.

- Use the long wavelength approximation to the steady Navier-Stokes equations with body force and ‘lumped’ viscous effects:

\[
\frac{\partial u}{\partial x} = -\frac{1}{\rho} \frac{\partial p}{\partial x} + g_x - \mathcal{R} u. \tag{32}
\]

- Here:
  - \( u = u(x) \) is the average velocity through the tube,
  - \( \mathcal{R} > 0 \) is a friction factor whose value depends on \( A \) (e.g. \( \mathcal{R} = \frac{8\nu}{a^2} \) for Poiseuille flow in a tube of radius \( a \)),
  - \( g_x \) is the \( x \)-component of the gravitational acceleration.

- We also have the steady integral continuity equation

\[
\frac{\partial (uA)}{\partial x} = 0, \tag{33}
\]

and the tube law

\[
p = \mathcal{P}(A). \tag{34}
\]
• Solve the continuity equation, (33), \( u \frac{\partial A}{\partial x} + A \frac{\partial u}{\partial x} = 0 \) for

\[
\frac{\partial u}{\partial x} = -\frac{u}{A} \frac{\partial A}{\partial x}
\]

and insert into the momentum equation (32),

\[
-u \frac{\partial u}{\partial x} = -\frac{1}{\rho} \frac{\partial p}{\partial x} + g_x - \mathcal{R}u.
\]

• This yields

\[
\frac{1}{A} \frac{\partial A}{\partial x} \left( \frac{1}{\rho} \frac{A \frac{\partial p}{\partial A}}{1/D} - u^2 \right) = g_x - \mathcal{R}u,
\]

and so

\[
\frac{1}{A} \frac{\partial A}{\partial x} (c^2 - u^2) = g_x - \mathcal{R}u,
\]

where we have used the familiar wave velocity

\[ c^2 = \frac{1}{\rho D}. \]

• The system’s behaviour is easiest to analyse if we transform equation (35) into an equation for the ‘wall slope’,

\[
\frac{1}{A} \frac{\partial A}{\partial x} = \frac{g_x - \mathcal{R}u}{c^2 - u^2}.
\]

• We will study this equation for two different cases.
A. No gravity

\[ \frac{1}{A} \frac{\partial A}{\partial x} = \frac{-\mathcal{R}u}{c^2 - u^2}. \] (37)

- Assume that \( u < c \) at some point in the tube.
- Eqn. (37) implies that \( \partial A / \partial x < 0 \).
- Continuity implies that \( \partial u / \partial x > 0 \), i.e. the flow is accelerated in the stream-wise direction.
- At some finite point, we will reach a situation where \( u \to c \) and hence \( \partial A / \partial x \to -\infty \).
- If the vessel is long enough for this to occur, then no steady flow is possible\(^6\). The situation is completely analogous to the phenomenon of ‘choking’ in gas dynamics.
- In many physical systems, the disappearance of steady solutions indicates the onset of unsteady phenomena.
- For this reason, choking has frequently been associated with the onset of self-excited oscillations.
- Note that ‘choking’ tends to manifest itself in collapsible vessels rather than distended ones since the wave-speed \( c \) is much smaller in a buckled tube.

\(^6\)Of course, the situation where \( \partial A / \partial x \to -\infty \) is really outside the limits of applicability of our long wavelength theory!
B. Effect of gravity

- Note that in the presence of gravity, the governing equation

\[
\frac{1}{A} \frac{\partial A}{\partial x} = \frac{g_x - \mathcal{R}u}{c^2 - u^2}
\]  

(38)

allows a smooth transition through the critical state where

\( u = c \) iff

\[ g_x - \mathcal{R}u = 0 \]

in that cross section.

- This is similar to the behaviour of 1D compressible flow in a ‘Laval nozzle’ which accelerates the fluid from sub- to super-sonic velocities.

- Physiological applications exist in venous return flow since the flow from the legs to the heart has to overcome a significant gravitational pressure difference.

- Gravitational effects are particularly important in giraffes (!): see e.g. Pedley et al. (1996).

- Other mechanisms by which continuous transitions from sub- to supercritical flows are possible include

  - stream-wise variations in the tube’s stiffness
  - stream-wise variations in the external pressure

- Such variations are the collapsible tube equivalent of area variations in a (rigid) Laval nozzle.
Further analogies with gas dynamics:

- Shapiro (1977) comments on the striking similarities between the 1D collapsible tube equations and the equations of gas dynamics (and the shallow water equations!).

- By analogy we might therefore expect to see the occurrence of shock like structures in collapsible tube flow....

- ...and we’re not disappointed:

Figure 29: An ‘elastic jump’ in the collapsible tube experiment by Kececioglu et al. (1989).
How good is our simple (inviscid) model?

- Here are some numerical results which show self-excited oscillations in a 2D channel with an elastic wall (similar to the one we considered earlier but here we have finite Reynolds number flow):

![Figure 30: Self-excited oscillations in a 2D channel. The elastic part of the wall is in the range $x \in [0, 5]$. The thin solid lines show the instantaneous streamlines; from Luo & Pedley (1998).](image)

- The oscillations appear to be closely related to the interaction between the wall deformation and the vorticity waves generated behind the most strongly collapsed cross section.

- Is this related to ‘choking’ or is this due to a different (two-dimensional!) instability?
Further remarks:

- Shapiro (1977) provides a complete overview of steady flows in collapsible tubes based on the simple 1D model described here.

- Kamm & Pedley’s (1989) review paper gives a good overview of the physiological background and theoretical and experimental work on collapsible tube flow.

- Pedley & Luo (1998) review more recent work which includes improvements to the 1D model (attempting to incorporate the effects of flow separation and finite tube length) as well as numerical work.

- (Un?)fortunately, it is probably fair to say that to date we do not have a complete understanding of the mechanisms leading to the large amplitude self-excited oscillations observed experimentally and physiologically.
Further remarks (cont.):

- The ‘Starling resistor’ used in laboratory experiments (and in many theoretical studies) has occasionally been criticized as being of little relevance to physiological flows because the rigid tubes at either end of the collapsible segment provide rather artificial end conditions.

- The experiments of Bertram et al. (1989) have shown that many of the system’s key features can be reproduced without the presence of rigid tubes.

![Diagram of modified Starling resistor](image)

**Fig. 1** The diagram shows only the central part of the collapsible tube which was compressed by the external sleeve, which was mounted as the inner surface of an annular pressure chamber. Pressure in the chamber caused the tube and the sleeve to collapse together. Oversize sleeve mountings allowed the tube to continue collapsed through the ends of the chamber.

Figure 31: The modified Starling resistor used by Bertram *et al.* (1989) to eliminate the effect of the rigid upstream and downstream tubes.
IV. Physiological flow patterns and their significance

• So far we have mainly considered one-dimensionally averaged forms of the Navier-Stokes equations in long straight tubes.

• These equations describe the macroscopic behaviour of the flow but they can neither reveal its fine details nor do they allow an analysis of the effects of vessel curvature and bifurcations.

• A detailed (mathematical) analysis of these flow patterns is beyond the scope of this lecture course because they require either
  
  – heavy computations

  or

  – sophisticated asymptotic techniques,

  neither of which can sensibly be presented in the limited time available here.
However, details of the flow field are potentially important because it is found that the sites at which various diseases develop are closely correlated with the characteristics of the local flow field.

For instance, atherosclerosis (the #1 killer in the Western world!) tends to develop in regions where the fluid shear stress is low and oscillatory; see e.g. Caro et al. (1971) or Ku et al. (1985).

This could be due to:

– wall remodelling in response to the flow conditions

and/or

– the effect that the fluid flow has on the mass transport from the blood into the artery walls.
Curvature effects

- Flow in curved tubes generates centrifugal pressure gradients which can drive secondary flows:

![Diagram showing secondary flows in curved tube flow](image)

Figure 32: Secondary flows in curved tube flow.

- The secondary flow creates azimuthal wall shear stresses and shifts the maximum of the stream-wise velocities towards the outside walls.

- The axial shear stress is reduced on the inside wall and increased on the outside wall.
Figure 33: Flow-fields in uniformly curved tubes; from Pedley (1980).

- For a uniform, weakly curved tube, the flow can be shown to be governed by a single non-dimensional parameter, the *Dean number*

\[ D = 4Re \left(2\delta\right)^{1/2} \]

where

\[ \delta = \frac{a}{R} \]

is the curvature ratio; see Dean (1928).
Further complications arise from:

- the unsteadiness of the flow in the curved vessels; e.g. Lyne (1971).
- entrance effects arising when (fully developed) flow in a relatively straight tube enters a strongly curved section:

![Figure 34: Entrance flow in a 180° bend; from Pedley (1980).](image)

Fig. 4.14. Measured velocity patterns in a curved tube, with $D^* = 258$, $\delta = 0.4$, and 180° of bend (after Olson, 1971). (a) Axial velocity profiles in the plane of the bend; parabolic entry profile. (b) Axial velocity profiles in the plane of the bend; flat entry profile.
the time-dependent curvature of the vessels, e.g. in the coronary arteries; see e.g. Lynch et al. (1996) or Waters & Pedley (1999).

Figure 35: The coronary blood vessels; from Spalteholz (1967).

Figure 36: The coronary arteries; from Lynch et al. (1996).
Figure 37: The coordinate system adopted to describe oscillatory flow in a tube of time-dependent curvature; from Waters & Pedley (1999).

\[
\frac{x^2}{Re} u_r + u_w + \frac{1}{r} v_{r0} + \frac{1}{h} w u_r - \frac{1}{r} v_w^2 \\
+ \frac{x^2}{Re} \cos \theta \left( \frac{\partial}{\partial \hat{s}} + \frac{2 \delta^2}{\partial \hat{s}^2} \right) (1 - \cos \theta \delta) - \frac{x^2}{Re} \delta \cos \theta \left( \frac{2w + \frac{x^2}{Re} \delta h}{\delta} \right) - \frac{\delta \cos \theta}{h} w^2 \\
= -p_r - \frac{1}{Re h} \left\{ \frac{\partial}{\partial \hat{\theta}} \left[ h \left( v + ru_v - u_w \right) \right] - \frac{\partial}{\partial \hat{s}} \left[ r \left( -\delta \cos \theta w - hw_r - u_r \right) \right] \right\} \\
- \frac{2x^2}{Re} \frac{\delta \cos \theta}{h}, \quad (2.3b)
\]

Figure 38: The momentum equations for oscillatory flow in a tube of time-dependent curvature; from Waters & Pedley (1999).

\[
\frac{x^2}{Re} v_r + u_r + \frac{1}{r} v_{r0} + \frac{1}{h} w v_r + \frac{1}{r} w v_w \\
- \frac{x^2}{Re} \sin \theta \left( \frac{\partial}{\partial \hat{s}} + \frac{2 \delta^2}{\partial \hat{s}^2} \right) (1 - \cos \theta \delta) + \frac{x^2}{Re} \delta \sin \theta \left( \frac{2w + \frac{x^2}{Re} \delta h}{\delta} \right) + \frac{\delta \sin \theta}{h} w^2 \\
= -\frac{1}{r} p_0 + \frac{1}{Re h} \left\{ \frac{\partial}{\partial \hat{r}} \left[ h \left( v + ru - u_w \right) \right] - \frac{\partial}{\partial \hat{s}} \left[ \frac{1}{r h} \left( -\delta \sin \theta w + hw_r - v_{r0} \right) \right] \right\} \\
+ \frac{2x^2}{Re} \frac{\delta \sin \theta}{h} \quad (2.3c)
\]

\[
\frac{x^2}{Re} w_r + u_r + \frac{1}{r} v_{r0} + \frac{1}{h} w w_r + \frac{x^2}{Re} \left( \frac{\partial}{\partial \hat{s}} + \frac{2 \delta^2}{\partial \hat{s}^2} \right) \sin \theta \delta + 2 \frac{x^2}{Re} \sin \theta \cos \theta u \\
- \frac{2x^2}{Re} \frac{\delta \sin \theta}{h} w - 2 \frac{x^2}{Re} \frac{\delta}{\partial \hat{s}} \left( \frac{2w + \frac{x^2}{Re} \delta h}{\delta} \right) + \frac{\delta \cos \theta}{h} w_w - \frac{\delta \sin \theta}{h} v_{r0} + \frac{x^2}{Re} \frac{\delta \cos \theta}{h} w \\
= -\frac{1}{r} p_0 + \frac{1}{Re h} \left\{ \frac{\partial}{\partial \hat{r}} \left[ \frac{1}{r h} \left( hw_r - \delta \sin \theta w - v_{r0} \right) \right] \\
- \frac{\partial}{\partial \hat{s}} \left[ \frac{r}{h} \left( -hw_r - \delta \cos \theta w + u_r \right) \right] \right\} \quad (2.3d)
\]
The effect of bifurcations

- The flow fields in bifurcations contain some element of flow in curved tubes as the daughter tubes are bent away from the flow divider.

- On the inside of the curved wall, flow often separates while boundary layers develop on the outside wall downstream of the flow divider.

- Centrifugal pressure gradients lead to the development of secondary vortices in the daughter tubes.

Fig. 3.2. Qualitative picture of flow downstream of a single junction with Poiseuille flow in the parent tube. Direction of secondary motions, new boundary layer and separation region are indicated in the lower branch; velocity profiles in the plane of the junction (continuous curve) and the normal plane (broken curve) are indicated in the upper branch.

Figure 39: Flow patterns in a bifurcation; from Pedley (1980).
- If flow through the bifurcation is reversed (e.g. during expiration in the lung) the secondary vortices persist for some distance into the parent branch, leading to the development of four (!) vortices.

*Figure 4* Wall-bounded secondary flows in a model bifurcation (from Jan et al 1989).

Figure 40: Forward and reverse flow through a bifurcation; from Grotberg (1994).
Flow patterns through bifurcations are also strongly affected by the pulsatility of the flow:

![Flow field in a 3D model of the carotid artery bifurcation](image)

*Figure 41: Flow field in a 3D model of the carotid artery bifurcation; from Perktold et al. (1994).*

- Note how a large recirculation area develops in the carotid sinus during flow deceleration.

- Wall elasticity can also be seen to be playing a role in the problem.
Further remarks:

- Pedley (1995a) gives a good overview of the effects of the vessel geometry on the flow field and the associated shear stress distribution in representative geometries.

- Clearly, if all the fine flow details are relevant, then the value of any theoretical or even computational analysis will be limited as it will never be possible (or even sensible!) to try to incorporate all such features into a mathematical model.

- Consider the effects of patient specific vessel geometries, changes in posture, changes in the flow condition during exercise and rest, ...
V. Taylor dispersion and gas mixing in the lung

- The primary function of the lung is the gas exchange, i.e. the simultaneous oxygenation and removal of $CO_2$ from the blood.
- The gas exchange takes place in the alveoli which form the terminal sacs of the highly branched network of airways which consists of 24 generations (starting from the trachea).

Figure 42: Cast of the bronchial tree; from West (1985).
Is there a problem?

- An interesting observation is that even during normal breathing, a considerable residual volume of fluid remains in the lung after expiration.

![Figure 2.2. Lung volumes. Note that the functional residual capacity and residual volume cannot be measured with the spirometer.](image)

Figure 43: Lung volumes during normal and deep breathing. Note the large residual volumes; from West (1985).

- High frequency ventilation (a novel technique for mechanical ventilation) uses very small tidal volumes (approximately 35-150 ml compared to > 500 ml during normal breathing) at very high frequencies (60 - 1800 breaths/min compared to ≈ 15 breaths/min during normal breathing).
**Question**: How does the ‘fresh’ air ever get near the gas-exchanging alveoli?

- Pure advection of ‘fresh’ air is obviously not sufficient.
- Molecular diffusion, driven by the concentration gradients of $CO_2$ and $O_2$ helps in the mixing process but can also be shown to be insufficient to explain the observed high efficiency of the gas exchange.

- The explanation is ‘Taylor dispersion’ which produces highly effective gas mixing by a *combination* of advection and diffusion.
Taylor dispersion.

Consider the transport of a solute (e.g. oxygen) of concentration \( c(x,y,t) \) in a steady 2D unidirectional flow field \( u = u(y) \, e_x \), e.g.

\[
u(y) = \frac{6U}{a^2} \, y \,(a - y),
\]

where \( U \) is the average velocity in the channel.

![Figure 44: Sketch illustrating the geometry for the Taylor dispersion problem in a 2D channel.](image)

- The evolution of the solute concentration is governed by the advection-diffusion equation

\[
\frac{\partial c}{\partial t} + u \frac{\partial c}{\partial x} = D \left( \frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2} \right) = D \nabla^2 c ,
\]  

(39)

where \( D \) is the molecular diffusivity.

- The boundary conditions for the solute concentration are

\[
\frac{\partial c}{\partial y} = 0 \quad \text{at } y = 0 \text{ and } y = a
\]

(40)

i.e. there is no flux into the wall.
• Now decompose the concentration into a cross sectional average

\[ \bar{c}(x, t) = \frac{1}{a} \int_0^a c(x, y, t) \, dy \]

and the local deviation from the average

\[ c'(x, y, t) = c(x, y, t) - \bar{c}(x, t). \]

• Note that the definitions of \( \bar{c} \) and \( c' \) imply that

\[ \bar{c}' = 0, \quad \bar{c} = \bar{c}, \quad \left( \frac{\partial c}{\partial x} \right)' = \frac{\partial c'}{\partial x} \quad \text{and} \quad \frac{\partial \bar{c}}{\partial x} = \frac{\partial \bar{c}}{\partial x}. \] (41)

• Equivalent decompositions can be applied to all other quantities in the problem.

• We’re interested in an evolution equation for the average concentration \( \bar{c}(x, t) \).
Inserting the decomposition into the governing advection diffusion equation (39) yields

\[
\frac{\partial \bar{c}}{\partial t} + \frac{\partial c'}{\partial t} + u \frac{\partial \bar{c}}{\partial x} + u \frac{\partial c'}{\partial x} = D \left(\nabla^2 \bar{c} + \nabla^2 c'\right)
\]

or

\[
\frac{\partial \bar{c}}{\partial t} + \frac{\partial c'}{\partial t} + u \frac{\partial \bar{c}}{\partial x} + u \frac{\partial c'}{\partial x} = D \left(\frac{\partial^2 \bar{c}}{\partial x^2} + \frac{\partial^2 c'}{\partial x^2} + \frac{\partial^2 c'}{\partial y^2}\right)
\] (42)

since the \(\bar{c} = \bar{c}(x, t)\).

Now we take the average of this equation while observing the rules (41) to obtain:

\[
\frac{\partial \bar{c}}{\partial t} + U \frac{\partial \bar{c}}{\partial x} + u \frac{\partial \bar{c}}{\partial x} = D \frac{\partial^2 \bar{c}}{\partial x^2}.
\] (43)

To make any further progress, we need a closure condition which expresses the average of the fluctuations \(u \frac{\partial c'}{\partial x}\) in terms of the average quantities.

To that end, we subtract (43) from (42) which yields:

\[
\frac{\partial c'}{\partial t} + (u - U) \frac{\partial \bar{c}}{\partial x} + u \frac{\partial c'}{\partial x} - u \frac{\partial c'}{\partial x} = D \left(\frac{\partial^2 c'}{\partial x^2} + \frac{\partial^2 c'}{\partial y^2}\right).
\] (44)

This is still exact!
Let us now consider the long wavelength limit
\[ \partial / \partial x \ll \partial / \partial y, \]
i.e. we assume cross-stream gradients to be much larger than those in the stream-wise direction.

Formally, we will assume that the axial length-scale is \( O(\epsilon^{-1}) \gg 1 \) larger than the transverse length-scale, i.e.
\[ \frac{\partial / \partial x}{\partial / \partial y} = O(\epsilon) \ll 1. \]

Furthermore, note that at large times, i.e. for
\[ t \gg a^2 / D, \]
cross-stream diffusion will have nearly averaged out the cross-stream variations which implies that
\[ |c'| \ll \bar{c}. \]

A balance of terms in (44) is possible if
\[ \frac{|c'|}{\bar{c}} = O(\epsilon) \]
and the corresponding leading order equation is given by
\[ (u - U) \frac{\partial \bar{c}}{\partial x} = D \frac{\partial^2 c'}{\partial y^2}. \]

Note that the \( y \)-dependence of the LHS is known therefore we can integrate twice w.r.t. to \( y \).

The constants of integration come from the boundary conditions (40) and the condition that \( \bar{c}' = 0 \).
The result provides the concentration fluctuations \( c' \) in terms of the average quantities

\[
c'(x, y, t) = \frac{U a^2}{D} \frac{\partial \bar{c}}{\partial x} \left[ \frac{1}{60} - \frac{1}{2} \left( \frac{y}{a} \right)^2 + \left( \frac{y}{a} \right)^3 - \frac{1}{2} \left( \frac{y}{a} \right)^4 \right]
\]

This allows us to evaluate

\[
u \frac{\partial c'}{\partial x} = -\frac{1}{210} \frac{U^2 a^2}{D} \frac{\partial^2 \bar{c}}{\partial x^2},
\]

which provides the closure condition.

Inserting this back into (43) yields the desired evolution equation for the average concentration:

\[
\frac{\partial \bar{c}}{\partial t} + U \frac{\partial \bar{c}}{\partial x} = D_{\text{eff}} \frac{\partial^2 \bar{c}}{\partial x^2}, \tag{45}
\]

where

\[
D_{\text{eff}} = D + \frac{1}{210} \frac{U^2 a^2}{D}
\]

is the effective diffusivity.

\( D_{\text{eff}} \) represents the long-time limit of the diffusivity for the average concentration under the combined effects of advection and diffusion.
• Equation (45) shows that (at large times) the solute is advected by the average velocity $U$ and diffuses with a diffusivity which is different from the molecular diffusivity $D$.

• For instance, a unit amount of solute which is localised at $x = 0$ when $t = 0$ spreads according to

$$\bar{c}(x, t) = (4\pi D_{eff} t)^{-1/2} \exp\left(\frac{-(x - Ut)^2}{4 D_{eff} t}\right).$$

• It is instructive to rewrite the expression for $D_{eff}$ as

$$D_{eff} = D \left(1 + \gamma Pe^2\right),$$

where

$$Pe = \frac{Ua}{D}$$

is the Peclet number which describes the ratio of advection and diffusion.
Analysis of $D_{eff}$:

\[
D_{eff} = D + \frac{1}{210} \frac{U^2 a^2}{D}
\]

(i) No advection (zero $Pe$)

- For $U = 0$ (no flow) we have $D_{eff} = D$, i.e. axial spreading by pure diffusion.

\[c(x,t)\]

\[\bar{c}(x,t_0)\]

\[\bar{c}(x,t_1)\]

\[\bar{c}(x,t_2)\]

Figure 45: Purely diffusive spreading of a blob of solute.
(ii) Small diffusivity (large $Pe$):

- The blob of solute is spread out primarily by the distortion of the volume of fluid it is contained in.

![Diagram showing purely advective spreading of a blob of solute.](image)

Thus the ‘effective’ (axial!) spreading is much larger than would be suggested by the small value of the molecular diffusivity.
• Furthermore, the axial spreading of the fluid sets up very large cross-stream concentration gradients.

![Combination of advective and diffusive spreading of a blob of solute.](image)

• Thus, despite the small value of the molecular diffusivity, effective cross-stream diffusion becomes possible, leading to effective overall mixing.

(iii) Large diffusivity (small $Pe$):

• Finally, if the diffusion becomes very large, the cross-stream diffusion immediately smoothes out any cross-stream concentration gradients.

• This keeps the concentration profile uniform across the cross section (as in the case of $U = 0$) and results in

$$\lim_{D \to \infty} D_{eff} = D.$$
Further remarks:

- The classical references for Taylor dispersion are Taylor (1953) and Aris (1956).

- Note that Taylor dispersion only ‘works’ if the velocity profile contains an element of shear.

- The analysis can be carried out for any velocity profile in any given geometry. The functional form of the effective diffusivity always has the form

\[ D_{eff} = D + \gamma \frac{U^2 a^2}{D}, \]

where the parameter \( \gamma \) depends on the flow profile and the tube shape (\( \gamma = 1/210 \) for 2D channel flow; \( \gamma = 1/48 \) for Poiseuille flow).

- Harris & Goren (1967) analyse the case where an oscillatory pressure gradient (leading to a flow of Womersley type, as considered in the section on pulse wave propagation) enhances mixing in a tube with an underlying linear concentration gradient. This is important in the context of High Frequency Ventilation as the analysis shows that \( D_{eff} \) increases with the frequency of the oscillation.
VI. Airway closure and reopening

- The airways of the lung are lined with a thin liquid film.
- The small airway radius leads to large interface curvatures and strong surface tension effects since the pressure jump over the air-liquid interface is given by
  \[ \Delta p = \sigma \kappa, \]
  \hspace*{1cm} (46)
  where \( \sigma \) is the surface tension and \( \kappa \) the mean curvature of the air-liquid interface.
- The liquid film can undergo a surface-tension-driven instability, leading to the formation of occluding liquid bridges which block the airway.
- This is known as ‘airway closure’ which occurs (e.g.)
  - in oedema, a condition in which the lung contains too much fluid.
  - in patients suffering from the Respiratory Distress Syndrome which is caused by an abnormally high surface tension of the liquid lining, e.g. in prematurely born babies.
  - at the end of expiration during normal breathing (crackling noises at the beginning of inspiration indicate the ‘popping’ of the liquid bridges when the airways re-expand).
Airway closure in a rigid tube: The Rayleigh instability

- What is the mechanism behind this instability?
- What is the minimum volume of fluid required to form an occluding liquid bridge?
A simple axisymmetric lubrication theory model:

\[ \frac{\partial p}{\partial z} = \mu \frac{\partial^2 u}{\partial r^2} \]  (47)

and we have

\[ p = p(z). \]

• Over length-scales comparable to the (small!) film thickness \( H_0 \ll R_0 \), the curved airway wall appears to be flat.

• Then, using the ‘usual’ scaling arguments, we can show that the axial flow \( u(r, z, t) \) is governed by lubrication theory:

- no slip on the wall:
  \[ u = 0 \quad \text{at } r = R_0 \]

- no tangential shear on the free surface:
  \[ \mu \frac{\partial u}{\partial r} = 0 \quad \text{at } r = R_0 - h(z, t). \]
We integrate (47) twice and use the boundary conditions to obtain the velocity distribution:

\[ u(r, z, t) = \frac{1}{2\mu} \frac{\partial p}{\partial z} (R_0 - r)(R_0 - 2h - r) \]

and the local volume flux

\[ Q(z, t) = \int_{R_0-h}^{R_0} u(r, z, t) \, dr = -\frac{1}{3\mu} h^3 \frac{\partial p}{\partial z}. \quad (48) \]

Conservation of mass implies that

\[ \frac{\partial h}{\partial t} + \frac{\partial Q}{\partial z} = 0. \quad (49) \]

The fluid pressure is determined by the condition (46) for the pressure jump relative to the air pressure, \( p_{\text{air}} = 0 \), i.e.

\[ p(z, t) = -\sigma \kappa, \quad (50) \]

where

\[ \kappa = \frac{1}{R_0 - h} + \frac{\partial^2 h}{\partial z^2} \left( 1 + \left( \frac{\partial h}{\partial z} \right)^2 \right)^{-3/2} \]

is the mean curvature of the air-liquid interface.

Inserting (50) and (48) into (49) then provides an evolution equation for \( h(z, t) \):

\[ \frac{\partial h}{\partial t} + \frac{\sigma}{3\mu} \frac{\partial}{\partial z} \left( h^3 \frac{\partial \kappa}{\partial z} \right) = 0. \quad (51) \]
Stability analysis:

- The state $h(z, t) = H_0$ is obviously an equilibrium state.
- To investigate its stability we consider the evolution of axisymmetric small amplitude perturbations

$$h(z, t) = H_0 + H_1 \exp(ikz + \omega t)$$

where $|H_1| \ll 1$.
- Linearisation of (51) then yields the dispersion relation

$$\omega = \frac{\sigma}{3\mu} H_0^3 k^2 \left( \frac{1}{R_{int}^2} - k^2 \right)$$

where

$$R_{int} = R_0 - H_0$$

is the initial radius of the air-liquid interface.
- This shows that perturbations with wave-numbers

$$k < \frac{1}{R_{int}}$$

are unstable and grow exponentially in time.
- Translating this into wavelengths via

$$k = \frac{2\pi}{\lambda}$$

shows that the instability affects all waves of length

$$\lambda > 2\pi R_{int}.$$
Implications for airway closure:

- Provided the airway is long enough, the liquid film will be unstable to the Rayleigh instability regardless of its thickness!

- However, airway closure via the formation of an occluding liquid bridge can only occur if there is enough fluid available!

- The minimum volume of fluid required to form an axisymmetric liquid bridge in a circular cylindrical tube is:

\[
\nu_{(ax.)_{\text{min}}} = \frac{2\pi R_0^3}{3} \frac{2 \sin^3 \gamma + 3 \cos^2 \gamma - 2}{\cos^3 \gamma},
\]

where \( \gamma \) is the contact angle that the liquid bridge forms with the dry (!?) airway wall:

- If there is less fluid in the initial liquid lining, the instability results in the formation of an unduloid shaped interface which leaves the airway open:
The role of wall elasticity:

- Halpern & Grotberg (1992) showed that wall elasticity helps the formation of occluding liquid bridges since the fluid mechanical Rayleigh instability is accompanied by significant wall deformations:
• Thus wall elasticity reduces the minimum volume of fluid required to occlude the airway (compared to the rigid tube Rayleigh instability).
The role of non-axisymmetric instabilities

- Axisymmetric, occluded tubes are statically unstable to non-axisymmetric instabilities [Heil (1999b)]:
  
  - I.e. this (axisymmetric) configuration is unstable...

- ...and buckles non-axisymmetrically; see Heil (1999a):

- Note: These are static equilibrium configurations!
The role of non-axisymmetric instabilities

- Non-axisymmetric airway collapse allows airway occlusion at much smaller liquid volumes; see Heil (1999b).

- This non-axisymmetrically buckled tube is occluded by a liquid volume of about 10% of the volume required to occlude an axisymmetric tube.
VII. References and further reading

- Pedley (1995b) provides a good review of the entire field of biological fluid mechanics (internal and external flows).
- The standard reference on mathematical modelling of flow in the large blood vessels is still Pedley (1980).
- Grotberg (1994) provides the most recent review of pulmonary fluid mechanics. An earlier (but still relevant) review can be found in Pedley (1977).

References


