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An Experimental Study of Dispersion in Oscillating Flows in Cylindrical Tubes

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AN EXPERIMENTAL STUDY OF DISPERSION IN OSCILLATING FLOWS IN CYLINDRICAL TUBES

by

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A Thesis Submitted in Partial Fulfillment of the Requirements for the degree of Master of Science in Mechanical Engineering.

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Date
Acknowledgments

It has been a long journey, and one of self-discovery. I have many people to thank, for being present and helping me along the way.

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Abstract

An Experimental Study of Dispersion in Oscillating Flows in Cylindrical Tubes

Siddharth Dasgupta

Supervising Professor: Dr. Steven Day

The cochlea of the inner ear has fluid filled spaces. Drugs are delivered to the cochlea via transtympanic injections to the base of the cochlea, at a membrane called the Round Window Membrane (RWM). Drugs diffuse through the RWM into the cochlear fluids. This method relies on the mechanism of pure diffusion. Hence drug delivery is slow and treatment efficacy is affected. The cochlear fluid oscillates when stimulated by sound. This thesis experimentally investigates if drug dispersion in the cochlea can be enhanced by oscillating the cochlear fluids for amplitudes as small as that of the cochlea.

To answer this question, empirical dye dispersion experiments for oscillating flows were performed in a cylindrical tube over a range of frequencies and amplitudes of oscillation. An experimental apparatus was designed and assembled to conduct experiments on the dispersion of a dye in water. Experiments were conducted for 3 sets of frequencies for amplitudes varying from 0 (pure diffusion) to 2.5 times the radius of the cylindrical tube. A time series of images of the dye were used to measure concentration and ultimately used to calculate an effective diffusion coefficient and to quantify the enhancement in diffusion.

Dispersion coefficients obtained for a constant frequency increase linearly as a function of the square of the amplitude, and for a constant amplitude dispersion coefficients increase with frequency. These trends agree with previously established results from literature. The results of the experiments, when scaled to the cochlea and feasible magnitudes of oscillation, predict that oscillation does not substantially enhance diffusion.
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TERMINOLOGY:-

Dimensional parameters

L-Characteristic Length (m)

$\omega$ -angular frequency (rad/s)

$\nu$ -kinematic viscosity (m²/s)

D- Diffusion coefficient (m²/s)

$D_{eff}$-Dispersion Coefficient (m²/s)

a- radius of cylindrical tube (m)

V-Tidal Volume (m³)

A-Amplitude of Oscillation (m)

J- Flux (kg/m².s)

C-Concentration (kg/m³)

t-time (s)

x-axial distance (m)

u-mean velocity of flow (m/s)

$\bar{C}$ -Radially averaged concentration (kg/m³)

$J_t$ - Time averaged flux (kg/m².s)
\( \overline{C} \) - Radially averaged, time averaged concentration (kg/m\(^3\))

\( A_c \) - Cross sectional area (m\(^2\))

\( M \) - Mass of dye (kg)

**Dimensionless Parameters**

\( \frac{D_{\text{eff}}}{D} \) - Effective Diffusivity

\( \alpha \) - Womersley number

\( \sigma \) - Schmidt number

\( \frac{V^2}{a^6} \) - Stroke Volume

\( \frac{A}{a} \) - Stroke Amplitude

\( \text{AP} \) - Area Parameter

\( I \) - Intensity

\( a_1 \) & \( b_1 \) - constants

\( m \) - slope
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1. INTRODUCTION:

1.1. Background and Motivation:

The cochlea of the inner ear is a coiled structure with fluid-filled spaces. Cochlear drug delivery methods rely on transtympanic injections that deliver drugs to the inner ear, and these drugs diffuse into the cochlear fluids by being absorbed through a membrane called the round window membrane at the base of the cochlea. Since this method relies on the mechanism of diffusion, significant concentration gradients occur between the base and the apex of the cochlea, which affects treatment efficacy[1]. Direct drug delivery methods to the cochlea consist of drilling holes into the cochlear walls and injecting drugs through those holes[2]. This allows good drug concentration levels in the inner ear fluids, but a hole in the cochlear wall compromises hearing function in certain cases.

It is known that a solute disperses more rapidly in an oscillating flow as compared to plain diffusion. The cochlear fluids are subjected to an oscillating flow due to the influence of sound waves. Oscillating the cochlear fluids by stimulation with sound waves may enhance drug dispersion in the cochlea. This necessitates the investigation of dispersion in cylindrical tubes in oscillating flows. This thesis experimentally investigates if drug dispersion in the cochlea can be enhanced by oscillating the flow of cochlear fluids.

1.1.1. Cochlear Anatomy:

Fig 1.1 shows the anatomy of the human auditory system. The ear consists of 3 parts

Outer ear:-The part of the ear from the outer ear up to the ear drum.
Middle ear :- The cavity behind the ear drum, comprising of bones, which aid in hearing.
Inner ear: The blue coiled structure shown in Fig is the cochlea, which makes up the inner ear.

Figure 1.1: Human Auditory System.
Reproduced from [3]
Fig 1.2 shows the geometry of the cochlea. The cochlea has fluid-filled spaces. The cochlear walls consist of bones that form cavities of gradually reducing cross section. The cochlear cavity consists of a fluid-filled membrane that runs along the center of the cavity. This fluid-filled membrane is referred to as the Scala Media, which divides the cochlea into two other chambers.

Scala Vestibuli: This chamber lies above the scala media and ends at the oval window at the base of the cochlea.

Scala Tympani: It lies below the Scala media and ends at the round window membrane at the base of the cochlea.

The Scala Tympani and Scala Vestibuli run from the base to the apex of the cochlea, where they merge at the opening called the helicotrema.

The Scala Media contains a fluid called endolymph (marked in blue), whereas The Scala Tympani and Scala Vestibuli contain a fluid called perilymph (marked in orange). The perilymph and the endolymph do not come into contact with each other.

Fig 1.3 shows the simplified model of the cochlea. External sound waves cause the tympanic membrane (ear drum) to vibrate, which causes the bones in the middle ear to vibrate and transmit the motion to the oval window. The oval window deforms and produces pressure waves in the perilymph, which are transmitted to the endolymph of the cochlear duct. The pressure waves displace the basilar membrane, which transmits the motion to the perilymph of the scala tympani and this causes a displacement of the round window membrane. The organ
of corti lies along the length of the basilar membrane. The organ of corti has hair-like cells which are displaced due to the movement of the basilar membrane. This generates electrical impulses, which are transmitted to the brain via the cochlear nerve, permitting us to hear.

![Simplified model of the cochlea](image)

**Figure 1.3: Simplified model of the cochlea. Reproduced from [4]**

1.1.2. **Cochlear Drug Delivery**

Borkholder et al. [1] conducted a cochleostomy (drilling a hole through the cochlear wall into the scala tympani) and a posterior canal canalostomy (drilling a hole through the semicircular canals) on murine cochlea. It was hypothesized that the canalostomy would induce perilymphatic flow from the apex to the base of the cochlea and aid in drug dispersion. The effects of performing just a cochleostomy for drug injection were compared to an approach which was a combination of cochleostomy with canalostomy. It was determined that a combination of both approaches reduces concentration gradients.

Chen [2] analyzed the effectiveness of a reciprocating perfusion system, where a hole is drilled into the scala tympani of the cochlea of a guinea pig, and the perilymph is drawn through a catheter and is reciprocated through a reservoir containing the desired drugs. This method delivers drugs directly to the inner ear without the need for separate holes for inlet and outlet.

Borkholder et al. [5] investigated drug delivery to murine cochlea by delivering drugs directly to the RVM and via a posterior semicircular canalostomy. It was determined that by combining both the approaches, drug efficacy increased.

Improving cochlear drug delivery methods rely on invasive procedures, which require surgical precision and may cause hearing loss. Hence an investigation of alternate methods like oscillating the flow of cochlear fluids to improve drug dispersion is required.
1.2. Dimensionless Numbers

Dimensionless numbers help in scaling experimental results. There are certain non-dimensional numbers pertinent to dispersion in oscillating flows, which are required to compare the results of this study with previous literature.

**Womersley number:**

The Womersley number is a measure of the frequency at which the flow is oscillating. It is denoted by the symbol \( \alpha \) and is defined by the equation [6]

\[
\alpha = \frac{L}{2} \sqrt{\frac{\omega}{\nu}} \quad \text{............... (1)}
\]

Where \( L \) is characteristic length, \( \omega \) is the angular frequency in radians/sec, \( \nu \) is the kinematic viscosity of the fluid.

**Schmidt number:**

The Schmidt number is defined as the ratio of the momentum to mass diffusivity [7]. The Schmidt number is denoted by the symbol \( \sigma \). This number appears in flows when there is a diffusion of both momentum and mass.

\[
\sigma = \frac{\nu}{D} \quad \text{............... (2)}
\]

**Stroke Volume:**

This dimensionless number is expressed as \( V^2 / a^6 \), where \( V \) is the tidal volume and \( a \) is radius of the cylindrical tube.

**Stroke Amplitude:**

The *stroke amplitude* is expressed as \( A/a \), where \( A \) is the amplitude of oscillation. \( A/a \) represents the magnitude of the oscillation amplitude with respect to the radius of the cylindrical tube. The relationship between stroke volume and stroke amplitude is given by the following expression.

\[
\frac{V^2}{a^6} = \pi^2 \left( \frac{A}{a} \right)^2 \quad \text{............... (3)}
\]
1.3. Background of dispersion

When a soluble substance (solute) comes in contact with a solvent, it diffuses into the solvent due to molecular diffusion. The flux of the solute is governed by Fick’s First Law, given by equation 4.

\[ J = -D \frac{\partial C}{\partial x} \] ........................ (4)

\( J \)= flux, \( C \)= Concentration, \( x \)= axial distance, \( D \)= Diffusion coefficient. The distribution of the solute concentration is governed by Fick’s 2\textsuperscript{nd} Law of diffusion represented by Equation 5.

\[ \frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2} \] ........................ (5)

\( t \)= time. Solving Equation 5 numerically with arbitrary values yields values of concentration as a function of distance and time. Fig 1.4 shows the variation of concentration with time at a fixed axial distance from point of injection for 2 solutes/dyes with different diffusion coefficients. The initial concentration is same for both dyes. \( D \) for one dye is 0.02 and is 0.04 for the other. As time progresses, the dyes diffuse into the solvent medium at different rates. The change/drop in concentration is more rapid for the dye with a higher value of \( D \) (marked by triangles) than the other dye (marked by circles). Hence the value of \( D \) is an indicator of how fast a dye spreads.

![Figure 1.4: Variation of Concentration with time at fixed axial location. Both dyes have same initial concentration. Dye with a higher value of \( D \) diffuses faster.](image-url)
When a dye is injected into a solvent flowing steadily through a cylindrical tube, the dye mixes with the solvent due to a combined action of radial molecular diffusion and axial convective transport\cite{8}. This enhances the rate of mixing of the dye with the solvent as compared to the case when the solvent is stationary (simple diffusion). When a soluble substance mixes with a solvent due to a combination of diffusion and convection, it can be modelled using the convection diffusion equations if the velocity field is known and simple enough. However if the velocity field is complex (like the presence of secondary flows like vortices), to account for the complexity of the velocity field, the diffusion coefficient (D) is replaced with an effective diffusion coefficient (D_{eff}). This phenomenon is termed as dispersion.

Taylor\cite{8} analytically demonstrated that for a long time after a dye is injected into a solvent flowing steadily through a cylindrical tube in a laminar manner, the flux of the dye across a plane travelling with the mean velocity of the solvent is given by equation 6.

\[ J = -D_{\text{eff}} \frac{\partial \overline{C}}{\partial x} \]  \hspace{1cm} (6)

\( \overline{C} \) is the radially averaged concentration, D_{eff} is the effective longitudinal diffusion coefficient or dispersion coefficient.

Aris\cite{9} expanded upon Taylor’s theory to include the effect of molecular diffusion in the axial direction and showed that the dispersion coefficient has the following form.

\[ D_{\text{eff}} = D + \frac{u^2 a^2}{48D} \]  \hspace{1cm} (7)

u=mean velocity of flow

Taylor-Aris’s theory is valid only after the dye diffuses to a uniform concentration over the cross section of the tube. This model accounts only for the axial dispersion of the solute in the solvent. Gill et al.\cite{10} analyzed the unsteady convective diffusion problem for steady flow in a cylindrical tube and found an exact solution applicable for all times after the injection of the solute. They confirmed that Taylor’s theory is inaccurate for very small times.

Aris\cite{11}analytically investigated the effect of pressure pulsations on the dispersion of solute in a cylindrical tube and found that D_{eff} contained terms proportional to the square of the amplitude of the pressure pulsations.

Watson\cite{12} analyzed dispersion in oscillating flows. He showed that for a dye dispersing in oscillating flow, the flux across a plane is given by
\[ J_t = -D_{\text{eff}} \frac{\partial \overline{C_t}}{\partial x} \]  \hspace{1cm} (8)

\( J_t \) is the time averaged flux, \( \overline{C_t} \) is the radially averaged time averaged concentration.

Watson determined an expression for the ratio \( D_{\text{eff}}/D \) as a function of Womersley number, Schmidt number and Stroke Volume. His theory is based on the assumption that the concentration gradient in the axial direction is linear and is valid only for laminar flows in infinitely long cylindrical tubes. Joshi[13] et. al.’s experiments with methane dispersing in oscillating air, agreed with Watson’s theoretical conclusions that \( D_{\text{eff}}/D \) is proportional to the stroke volume and that increasing the frequency at constant stroke volume increases the value of \( D_{\text{eff}}/D \). However, the value of \( D_{\text{eff}}/D \) for a constant stroke volume increases with frequency up to a certain point, after which the value of \( D_{\text{eff}}/D \) decreases. Fig. 1.5 shows the variation of \( D_{\text{eff}}/D \) vs. Stroke Volume at a constant frequency for experiments conducted by Joshi et. al. For a constant frequency, \( D_{\text{eff}}/D \) varies as a linear function of the stroke volume. The linear function is of the form \( y=mx +1 \), where \( y=D_{\text{eff}}/D \) and \( x=\text{Stroke Volume} \).

![Figure 1.5: Variation of Deff/D (here K/k) with dimensionless stroke volume at constant Womersley number. The solid lines represent Watson’s[12] analytical result for variation of Deff/D with Stroke Volume. Joshi’s experimental results are denoted by dots. (Reproduced from[13])](image)

Fig 1.6 shows the variation of \( D_{\text{eff}}/D \) with Womersley number for a constant stroke volume. For a constant stroke volume, \( D_{\text{eff}}/D \) increases with Womersley number, reaches a peak value for a certain Womersley number and after that decreases from the peak value.
Comparing equations 4 & 8, dispersion can be considered to be a process of diffusion with a higher diffusion coefficient, referred to as the dispersion coefficient (D\text{eff}). D\text{eff} is a measure of how far the dye spreads axially. The ratio D\text{eff}/D can be used to interpret how fast dispersion is with respect to diffusion.

For analyzing dispersion, it is assumed that the concentration gradients in the radial direction are small compared to those in the axial direction, so the dye dispersion is considered to be 1-dimensional in the axial direction.

1.3.1. Range of parameters for conducted experiments for oscillating flows in previous literature

Harris et al. [14] developed a theory for mass transfer in pulsating flows and conducted experiments on the dispersion of Hydrochloric acid in oscillating water. The experimental results were in line with the theoretical predictions and for the range of experiments conducted, mass transfer rates obtained were 10 to 60 times greater than molecular diffusion. Jaeger et. al. [15] conducted experiments on the mixing of nitrogen in oxygen in an oscillating flow and determined that the ratio of D\text{eff}/D was proportional to the square of the amplitude of oscillation and the first power of frequency. In another paper [16], they compared the results of newly conducted experiments and their previous experiments with Watson’s [12] theory. Their experiments were in good agreement with Watson’s theory. Gaver et al. [17] conducted
experiments on the dispersion of Argon in oscillating air. They developed a new technique to experimentally determine $D_{eff}/D$, which was faster than previous methods employed to determine $D_{eff}/D$. Lee[18] conducted experiments on the mixing of smoke in air in a long cylindrical tube and found dispersion coefficients for a range of Womersley numbers and stroke volumes. Ye et. al. [19] conducted experiments on the dispersion of a dye in water in an oscillating turbulent flow in a cylindrical tube. The determined values of the dispersion coefficient were larger than those Watson predicted, owing to the turbulence.

Table 1.1 summarizes the range of Womersley numbers and stroke amplitudes, for which experiments have been conducted in previous literature.

<table>
<thead>
<tr>
<th>Author</th>
<th>Womersley Numbers ($\alpha$)</th>
<th>Stroke Amplitudes (A/a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joshi et. al.[13]</td>
<td>1-8</td>
<td>10.06-79.16</td>
</tr>
<tr>
<td>Jaeger et. al.[15, 16]</td>
<td>7.05-18.22</td>
<td>17.75-103.16</td>
</tr>
<tr>
<td>Gaver et. al.[17]</td>
<td>3.48-18.44</td>
<td>2.22-24.86</td>
</tr>
<tr>
<td>Lee et. al.[18]</td>
<td>9-20</td>
<td>33.08-66.17</td>
</tr>
<tr>
<td>Harris et. al.[14]</td>
<td>5.128-15.329</td>
<td>4.26-8.34</td>
</tr>
<tr>
<td>Ye et. al.[19]</td>
<td>3.52-10.87</td>
<td>7.77-377.11</td>
</tr>
</tbody>
</table>
Fig. 1.7 is a graphical representation of Table 1 and shows the Range of Womersley numbers and stroke amplitudes for previous literature. Of all the experiments performed, the experiment with the lowest stroke amplitude is 2.22 by Gaver et al.

Figure 1.7: Range of parameters for Previous Literature and current thesis. Each rectangle represents the range of parameters for experiments conducted in previous literature. Author names are included in the top left corner of each rectangle. Joshi[13] conducted experiments for dispersion of methane in oscillating air. Gaver et.al. [17] conducted experiments on the dispersion of Argon in oscillating air. Lee[18] conducted experiments on the mixing of smoke in air. Harris et al. [14] conducted experiments on the dispersion of Hydrochloric acid in oscillating water. Jaeger et. al. [15] conducted experiments on the mixing of nitrogen in oxygen. Ye et. al. [19] conducted experiments on the dispersion of a dye in water in an oscillating turbulent flow in a cylindrical tube.

The black rectangular block at the bottom of the figure indicates the range of the current experiments.

The cochlea is a small structure and the fluid displacement is small (order of $10^6 \mu m^3$) when stimulated by sound waves. The stroke amplitude, $A/a$, of the cochlea is $1.92 \times 10^{-3}$, based on the maximum fluid displacement in the cochlea possible. (Refer Appendix 6.1 for calculations of stroke amplitude in cochlea). Since available literature has not investigated dispersion for oscillatory flows with stroke amplitudes as small as that of the cochlea, this thesis shall cover the gap in the research to determine if oscillatory flows can enhance cochlear drug dispersion.
This thesis investigates the dispersion of a dye in water for stroke amplitudes ranging from 0 to 2.56 and for Womersley numbers ranging from 4.44 to 24.35.

1.4. Objectives

1) To quantify dispersion enhancement as a function of Womersley number for low stroke amplitudes.
2) To determine if drug delivery in the cochlea can be enhanced by oscillating the flow of cochlear fluids.

1.5. Analytical Solution of Fick’s 2nd law:

The rate at which the dye mixes with the water is characterized by determining a dispersion coefficient. The analytical solution for equation 5 when a pulse of mass ‘M’ is injected at x=0, the concentration distribution over a cross section of area ‘A_c’ is given by[20]

\[ C(x,t) = \frac{M}{A_c} \exp\left(-\frac{x^2}{4Dt}\right) \] ........................ (9)

Where C=Concentration (kg/m²), M=Mass of dye injected (kg), A_c=Cross sectional area of tube (m²), D=Diffusion Coefficient (m²/s), x=Axial distance (m), t=time (s). This formula characterizes the diffusion of the dye into a solvent medium. The rate at which a dye mixes with water in an oscillating flow is established by substituting the diffusion coefficient in equation 9 with a dispersion coefficient, D_{eff}.

In order to demonstrate the nature of the concentration curves, Equation 9 is evaluated by considering arbitrary values of variables M, A_c and x. The value of D_{eff} is arbitrarily considered 100, and the value of t is considered from 1 to 10 in steps of 1. The resulting concentration values are plotted vs. distance for different time steps in Fig. 1.8. Fig. 1.8 shows the decaying concentration profiles as the dye diffuses over time.
A plot of concentration vs. distance at a particular time step is a Gaussian function. The Area Parameter (AP) for a gaussian curve is the area under the curve divided by the peak concentration of the curve.

The values of AP for each concentration curve shown in Fig. 1.8 increase with time. At time t=0, Equation 9 is unsolvable because of division by zero. As time tends to zero, the AP value tends to 1. Hence the AP value at t=0 is set to 1.

If \( D_{\text{eff}} \) is kept constant, changing the values of variables \( M, A_\alpha, C \) and \( x \) have no effect on the AP value for a particular time step. However, changing the value of \( D_{\text{eff}} \) changes the AP values. Fig. 1.9 shows AP vs. Time for \( D_{\text{eff}} \) ranging from 100 to 200 in steps of 10. It is observed that a plot of AP at different time steps for a specific \( D_{\text{eff}} \) has its unique locus. The AP curve corresponding to Fig. 1.8 is represented by \( D_{\text{eff}}=100 \) in Fig.1.9. Hence the AP values over time are characteristic of \( D_{\text{eff}} \) and can be used to determine \( D_{\text{eff}} \) experimentally.
Figure 1.9: AP vs. Time for different Deff.

AP values are plotted over time for different $D_{eff}$ values. Each AP curve has a unique locus for a specific value of $D_{eff}$. These curves can be used to obtain values of $D_{eff}$ for experiments. AP values corresponding to $D_{eff}=100$, represents AP values for concentration curves shown in Fig. 1.9.

AP values obtained by solving equation 9 are hereby referred to as Analytical AP.
2. METHODS

2.1. Experimental Apparatus:
Experiments were conducted for dispersion in oscillating flows. Diffusion is considered to be a subset of dispersion with an amplitude of 0. The parameters varied were frequency and the amplitude of oscillation. A dye was injected into a cylindrical tube filled with water, after which the water was oscillated. Images of the dye were captured at fixed time steps and the concentration of the dye was determined using a relationship between image intensity and dye concentration. The concentration profiles obtained were used to plot AP values over time. AP values are compared to Analytical AP values and a value for $D_{eff}$ was determined.

2.1.1. Overview of Experimental Apparatus:
Fig. 2.1 is a schematic for the experimental apparatus used to conduct dispersion experiments. A function generator was connected to an oscillator via an amplifier. The oscillator was connected to the plunger of a syringe filled with water, and the syringe was connected to a cylindrical tube via rubber tubing. The cylindrical tube was a hole with a diameter of 0.125 inches and length of 4.7 inches drilled into a transparent acrylic rectangular block. The cylindrical tube was connected to a water filled reservoir at the other end.

A needle with an internal diameter of 0.0077 inch was used to inject the dye. The needle was glued into a hole drilled halfway across the length of the rectangular block and sat flush against the wall of the cylindrical tube.

A Microliter syringe was mounted on a syringe pump, which was programmed to inject dye into the cylindrical tube via the needle. The Microliter syringe on the syringe pump was connected to the needle on the rectangular block by a rubber tube.

A halogen light was used as the light source and a diffuser was placed in between the halogen light and the cylindrical tube to avoid light saturation. A Motion Pro X3 camera was placed opposite the cylindrical tube. Another function generator synchronized the camera to capture images at a desired frame rate. Temperatures were recorded using a thermocouple probe, which was placed at the outlet of the cylindrical tube. A signal delay generator was used to synchronize the experiment cycle.

At the beginning of an experiment, dye was injected into the cylindrical tube. The function generator output a sine wave at a desired frequency and amplitude, which was passed onto the oscillator via an amplifier. The sine wave sent by the function generator caused the oscillator to oscillate the plunger of the syringe, which oscillated the flow of water through the cylindrical tube. Images of the dye were captured by the camera at fixed time steps.
2.1.2. *Timing*

Fig. 2.2 shows the synchronization of all the instruments in the experiment apparatus. The Syringe Pump was connected to the Delay Generator. The Delay Generator was further connected to the function generator 1, the camera and the function generator 2. When the syringe pump was manually triggered to inject dye into the cylindrical tube, the delay generator was triggered. Upon triggering, after a certain specified time (40 seconds), the delay generator triggered the function generator 1 to start the oscillations. At the same time it triggered function generator 2 and also the camera to start recording images at a desired frame rate. The
frame rate was specified by programming function generator 2, which synchronized the camera to record at desired frame rates. Function generator 2 was programmed to switch between 2 pre-determined frequencies. As long as it received a signal from the delay generator, it recorded at one of the 2 desired frequencies. When Function Generator 2 stopped receiving a signal from the delay generator, it switched to the other desired frequency. This enabled the camera to record dye images at different frame rates for an experiment cycle.

**Figure 2.2: Timing Diagram.**
Triggering syringe pump activated delay generator, which after 40 seconds sent a signal to Function Generator 1 to start oscillations, to camera to start recording and to Function Generator 2 to synchronize camera to record at a desired frame rate.
2.2. **Experimental Procedure:**

Experiments were conducted by varying 2 parameters: Frequency of oscillation and amplitude of oscillation. The frequency was varied by changing the output frequency on the function generator connected to the oscillator, while the amplitude was varied by changing the output voltage on the function generator. For each frequency selected, experiments were conducted for a range of amplitudes while the frequency was kept constant. Experiments were conducted for 3 sets of frequencies. Experiments were repeated 5 times for each condition, i.e., at a particular frequency and stroke amplitude, each condition being referred to as a trial.

A trial began when water was injected into the cylindrical tube. The halogen light caused an increase in the water temperature. The temperature reading was observed, and when the temperature reached 27° C, the syringe pump was manually triggered, which injected dye into the cylindrical tube. The dye diffused evenly into the water after 30-40 seconds. At 40 seconds after triggering of the syringe pump, oscillations were started and the camera started recording. The oscillator oscillated for 65 seconds. Image acquisition was conducted in 2 phases.

1) The first phase of image acquisition lasted 60 seconds and images were recorded at 1 Hz. This was lower than the oscillation frequency, but recorded images at the same phase of oscillation. Each image corresponded to a time step of 1 second. These 60 images were used to determine the dispersion coefficient.

2) At the end of 60 seconds, the camera recorded images for the remaining 5 seconds at a rate of 10 times the frequency of the oscillation. These images acquired were used to determine the stroke amplitude of oscillation.

Fig 2.3 shows images from a conducted trial for both Phase 1 and 2.
<table>
<thead>
<tr>
<th>Time (seconds)</th>
<th>Phase 1</th>
<th>Image Number</th>
<th>Phase 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td><img src="image1.png" alt="Image 1" /></td>
<td>1</td>
<td><img src="image2.png" alt="Image 2" /></td>
</tr>
<tr>
<td>10</td>
<td><img src="image3.png" alt="Image 3" /></td>
<td>2</td>
<td><img src="image4.png" alt="Image 4" /></td>
</tr>
<tr>
<td>20</td>
<td><img src="image5.png" alt="Image 5" /></td>
<td>3</td>
<td><img src="image6.png" alt="Image 6" /></td>
</tr>
<tr>
<td>30</td>
<td><img src="image7.png" alt="Image 7" /></td>
<td>4</td>
<td><img src="image8.png" alt="Image 8" /></td>
</tr>
<tr>
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<td><img src="image9.png" alt="Image 9" /></td>
<td>5</td>
<td><img src="image10.png" alt="Image 10" /></td>
</tr>
<tr>
<td>50</td>
<td><img src="image11.png" alt="Image 11" /></td>
<td>6</td>
<td><img src="image12.png" alt="Image 12" /></td>
</tr>
<tr>
<td>60</td>
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<td>7</td>
<td><img src="image14.png" alt="Image 14" /></td>
</tr>
<tr>
<td>70</td>
<td><img src="image15.png" alt="Image 15" /></td>
<td>8</td>
<td><img src="image16.png" alt="Image 16" /></td>
</tr>
<tr>
<td>80</td>
<td><img src="image17.png" alt="Image 17" /></td>
<td>9</td>
<td><img src="image18.png" alt="Image 18" /></td>
</tr>
<tr>
<td>90</td>
<td><img src="image19.png" alt="Image 19" /></td>
<td>10</td>
<td><img src="image20.png" alt="Image 20" /></td>
</tr>
<tr>
<td>100</td>
<td><img src="image21.png" alt="Image 21" /></td>
<td>11</td>
<td><img src="image22.png" alt="Image 22" /></td>
</tr>
</tbody>
</table>

Figure 2.3: Sample images from a trial.
Images are captured at 1Hz in Phase 1. Phase 1 lasts 60 seconds. Images from Phase 1 are used to determine Deff. For Phase 2, images are captured at 10 times the frequency of dye oscillation to determine amplitude of oscillation. 11 images from an oscillation cycle are shown here, with the 11th image involving the beginning of a new cycle. The dye displacement with respect to the needle is seen in Phase 2. The images are processed in Matlab to determine concentration, as shown in Fig. 2.7.
2.2.1. Temperature Variation:
The Stokes-Einstein equation predicts that $D$ varies directly as a function of temperature [20]. For the oscillating case, 40 seconds after dye injection, the temperature reached 27.8 °C and at the end of 60 seconds reached a maximum of 28.6 °C. Hence the maximum variation of temperature during the course of trial is 0.8 degrees C, which corresponds to a 2.87 % change in $D_{eff}$.

In the case of trials conducted for pure diffusion (no oscillations), 60 seconds was not sufficient time to diffuse axially. Experiments for pure diffusion were conducted for 200 seconds, rather than 60 seconds for dispersion. At the end of 200 seconds after starting sampling, the average temperature increase was 2° C, which corresponds to an 8.45 % change in $D$. The table below gives a comparison of temperatures for experiments conducted for pure diffusion and dispersion.

<table>
<thead>
<tr>
<th></th>
<th>Dispersion °C</th>
<th>Pure Diffusion °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature during injection</td>
<td>27</td>
<td>26</td>
</tr>
<tr>
<td>Temperature 40 seconds after injection</td>
<td>27.8</td>
<td>27.2</td>
</tr>
<tr>
<td>Temperature at the end of experiment</td>
<td>28.6</td>
<td>29.5</td>
</tr>
<tr>
<td>Average Temperature during experiment</td>
<td>28.2</td>
<td>28.35</td>
</tr>
</tbody>
</table>

2.3. Image Processing

The images acquired by the camera were processed in Matlab to determine the percentage concentration of the dye as a function of pixel intensity. Fig. 2.4 shows the dye just after it has been injected. Region B has no dye and the mean intensity of pixels in region B ($I_{max}$) corresponds to a dye concentration of 0. Region A, on the other hand, is filled with dye, and the mean intensity of pixels in region A ($I_{min}$) corresponds to a dye concentration percentage of 100. An interpolation method was used to determine the dye concentration after dispersion as a function of pixel intensity.

![Figure 2.4](image_url)

Figure 2.4: Figure showing regions with and without dye for calculation of concentration. Mean intensities of pixels in region B correspond to a dye concentration of 0. Mean of pixel intensities in Region A correspond to a dye concentration of 1.
An experiment was carried out to determine the relation between dye concentration and pixel intensity. The cylindrical tube was filled with dye of varying concentrations, and the corresponding values of averaged pixel intensity were recorded for each concentration. Fig. 2.5 shows the variation of Concentration vs. Pixel Intensity.

![Graph showing Concentration vs. Pixel Intensity](image)

Figure 2.5: Relation between concentration and pixel intensity

According to Beer’s Law, the relationship between concentration and intensity is logarithmic. Hence the following equation is used to fit the experimental values of concentration (C) and intensity (I).

\[ I = a_1 \exp(b_1 C) \] \hspace{1cm} (10)

\( a_1 \) & \( b_1 \) are constants with values 91.17 and -0.02271 respectively obtained by fitting equation 10 to the experimental values. The equation used to determine the concentration of the dye at a particular pixel is given by:

\[ C = \frac{1}{b_1} \ln \left( \frac{I}{a_1} \right) \] \hspace{1cm} (11)

Values of \( I_{\text{min}} \) and \( I_{\text{max}} \) depend on the lighting used and the exposure of the lens, both of which remain unchanged during all experiments. Hence values of \( I_{\text{min}} \) and \( I_{\text{max}} \) stay constant for all experiments. Values of \( I_{\text{max}} \) and \( I_{\text{min}} \) were recorded once, and the same values were used for all trials.

For each trial, in the first image, an interrogation region was selected as shown in Fig.2.6 (marked in white). The region was selected so that it was centered about the axis of the cylindrical tube. The concentration of the dye was determined at every pixel as a function of
intensity within this region, for every image. For each image in a trial, the obtained dye concentrations were averaged radially within this region.

![Figure 2.6: Selection of interrogation region for dye concentration determination. A region is selected where the concentration of the dye is determined as a function of pixel intensity.](image)

The dye concentrations recorded for each image in a trial were recorded in Matlab in a matrix with dimensions H x W,

Where H=Height of region in number of pixels, W= Width of region in number of pixels

When the dye concentrations were radially averaged for each image, it generated a row vector of length W. Each row vector corresponding to each image was concatenated to form a matrix of dimensions T x W, where T is the total time in seconds the experiment was conducted/Number of images being analyzed. Therefore, each row of the resulting matrix corresponded to a time step and each column represented the axial distance from the left edge of the region in pixels.

Hence the radially averaged normalized dye concentration was recorded as a function of distance for each time step of 1 second for the entire duration a trial was conducted in the form C(T,W), where C is the normalized concentration, T is the time and W is the axial location.
2.4. **Determination of $D_{eff}$:**

For each trial conducted, a dispersion coefficient was determined. The concentration profiles obtained after processing the images were used to determine the AP values. For a trial, AP values were determined for each concentration profile at each time step. Fig. 2.7 shows the radially averaged concentration plotted against distance for different time steps during the course of a typical trial. Fig. 2.8 shows the corresponding AP values over time for the same trial.

![Concentration vs. Distance for different times](image)

*Figure 2.7: Normalized Concentration vs. Distance in pixels for different time steps. Images shown in Fig. 2.3 are processed in Matlab to obtain the concentration curves.*
Figure 2.8: Experimental AP vs. time.

AP values were numerically calculated from concentration curves at each time step of 1 second. The concentration profiles shown in Fig. 2.7 and the corresponding AP values in Fig. 2.8 follow a similar trend as compared to the concentration profiles and their AP values obtained by solving equation 9 respectively. By comparing the AP values obtained by solving equation 6 (hereby referred to as Analytical AP) with experimentally determined AP values (hereby referred to as Experimental AP), a dispersion coefficient was determined.

Since the Analytical AP at t=0 equals 1, to compare Analytical AP with Experimental AP, for each trial the Experimental AP value at t=0 was set to 1. The subsequent AP values were offset by the difference between the original AP value at t=0 and 1.

Analytical AP’s were calculated for a range of $D_{eff}$, which encompassed all the trials conducted. The Experimental AP curves were fit to an Analytical AP curve by regression using least squares of residuals. The $D_{eff}$ of the Analytical AP curve with the best fit was considered to be the $D_{eff}$ for the trial. Fig. 2.9 shows an Experimental AP for a conducted trial, overlaid on Analytical AP for $D_{eff}$ ranging from 2.5 to 12.5 in steps of 0.1. The Analytical AP curve with a Deff of 7.4 is the best fit for the Experimental AP curve.
Figure 2.9: Experimental AP and Analytical AP with best fit. Experimental AP curves were overlaid on Analytical AP curves. By regression using least squares of residuals, Analytical AP curve with best fit was used to determine $D_{\text{eff}}$. $D_{\text{eff}}$ of the experimental trial shown here is 7.4.
2.5. **Determination of Stroke Amplitude:**

For each trial the sequence of images which record dye displacement were opened in an image editor, and the image numbers which record the dye displacement at 0 and 180 degrees of the oscillation cycles were noted manually. Concentration profiles corresponding to 0 and 180 degrees of the oscillation cycle were plotted against distance. Fig. 2.10 shows the concentration profiles plotted at 0 and 180 degrees of the oscillation cycle. Interrogating the data points marked in the figure in Matlab, the axial displacement of the dye was determined. Subtracting the distances between the points gave the amplitude of displacement in pixels. Dividing the amplitude of displacement by the radius of the cylindrical tube gave the Stroke Amplitude. The radius of the cylindrical tube was 18 pixels for the field of view of the camera.

![Figure 2.10: Determination of Stroke Amplitude. Concentration profiles corresponding to oscillation cycles at 0 and 180 degrees of phase were plotted and the dye displacement amplitude in pixels was recorded for each trial. Stroke amplitude was determined by dividing the amplitude by the radius of the cylindrical tube.](image)

\[ X_2 - X_1 = 236 - 194 = 42 \]
3. RESULTS:
Experiments are conducted at 3 frequencies (1Hz, 20Hz and 30Hz) corresponding to Womersley numbers of 4.446, 19.88 and 24.35 respectively. For each frequency, 6 stroke amplitudes, ranging from 0 (diffusion) to at least 2.2 are reported. For each set of conditions (a constant frequency and average A/a), trials are repeated 5 times for the oscillating case and 4 times for the diffusion case. The amplitude of oscillation is varied by changing the voltage output on the Function Generator. Despite feeding the oscillator the same voltage, amplitudes of oscillation vary by a small margin for some trials. Since experiments are performed for small amplitudes, the amplitude of oscillation is recorded for each trial and an average A/a is reported, which corresponds to trials conducted for the same voltage of the Function generator.

Table 3.1 shows the $D_{\text{eff}}$ obtained from each trial. Each row of Table 3.1 represents a set of conditions and the columns represent $D_{\text{eff}}$ and corresponding A/a for each trial.

4 trials are conducted for diffusion. The mean D is 0.1375. To compare the dispersion with diffusion, effective diffusivities ($D_{\text{eff}}/D$) are obtained by dividing $D_{\text{eff}}$ by D.

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Average A/a</th>
<th>Trial 1</th>
<th>Trial 2</th>
<th>Trial 3</th>
<th>Trial 4</th>
<th>Trial 5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$D_{\text{eff}}$</td>
<td>$A/a$</td>
<td>$D_{\text{eff}}$</td>
<td>$A/a$</td>
<td>$D_{\text{eff}}$</td>
<td>$A/a$</td>
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<td></td>
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<td></td>
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<td>2.39</td>
<td>52</td>
<td>2.28</td>
<td>53.5</td>
</tr>
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</table>
Values of $D_{\text{eff}}/D$ and $A/a$ from Table 3.1 are plotted in Fig 3.1 for each frequency.

Watson’s [12] analytical equation predicts that $D_{\text{eff}}/D$ is a linear function of the Stroke Volume $\frac{V^2}{a^6} \cdot \frac{V^2}{a^6}$ for a cylindrical tube translates to $\pi^2 \left( \frac{A}{a} \right)^2$. For each frequency, the data points are fit using an equation of the form $y=mx+1$,

Where $y=D_{\text{eff}}/D$, $x=\pi^2 \left( \frac{A}{a} \right)^2$, $m$=slope of the line. Figure 3.1 shows the variation of $D_{\text{eff}}/D$ against the Stroke Volume for all 3 frequencies at which experiments are conducted.

![Effective Diffusivity vs. Stroke Volume](image)

**Figure 3.1: Variation of Deff/D against Stroke Volume**

Deff/D is plotted for all trials conducted vs. Stroke Volume. Data set for each frequency is fit with data of the form $y=mx+1$. 

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Experimental data points are shown by markers, namely diamonds, squares and circles respectively for 1Hz, 20Hz and 30Hz respectively. The fit lines for each frequency are shown in Fig. 3.1. The slopes of the lines for 1Hz, 20Hz and 30Hz are 0.04, 1.99 and 6.55 respectively. Since both the x and the y axes are non-dimensional numbers, the values of slope have no units.

There is a substantial change in the slope of the line from 20 Hz to 30Hz. The change in slope from 1Hz to 20Hz is smaller than the change from 20 to 30Hz. The values of $D_{eff}/D$ for a constant Stroke Volume for the 30 Hz line show huge variation.

The general trend observed is that for a constant frequency, an increase in the stroke volume causes an increase in the value of $D_{eff}/D$. The fact that the slopes of the lines increase as the frequency increases, is indicative of the fact that for a constant Stroke Volume, the dispersion rate increases with frequency. These trends are consistent with Watson’s[12] theory and Joshi et al.'s [11] experimental findings.
4. DISCUSSION

4.1. Comparison to Previous Literature

Fig 4.1 shows the variation of $D_{\text{eff}}/D$ against Stroke Volume for experiments conducted at the 3 frequencies 1Hz, 20Hz and 30Hz corresponding to Womersley numbers of 4.446, 19.88 and 24.35 respectively. The lines plotted are the regression lines obtained from Fig 3.1. Fig. 4.2 shows the analytical variation of $D_{\text{eff}}/D$ vs. Stroke Volume for the same set of conditions as the experiment. The values of $D_{\text{eff}}/D$ obtained experimentally are much higher than those predicted by the theory.

![Figure 4.1: Experimental Variation of $D_{\text{eff}}/D$ against stroke Volume. Each line corresponds to experiments conducted for a particular frequency.](image)

![Figure 4.2: Variation of $D_{\text{eff}}/D$ against Stroke Volume using Watson’s [10] Analytical equation. Each line corresponds to experiments conducted for a particular frequency. The input variables to the equation are Womersley Number, Stroke Amplitude and Schmidt Number=3200 [21] for dye FD&C Blue # 1.](image)

The experimental and the analytical data for a constant frequency, predict an increase in $D_{\text{eff}}/D$ for an increase in stroke volume. Also the slope of the line increases with frequency, indicating that for a constant Stroke Volume an increase in frequency increases $D_{\text{eff}}/D$.

Fig 4.3 shows the variation of $D_{\text{eff}}/D$ with Womersley Number for lines of constant Stroke Volume obtained by solving the analytical equation by Watson[12] and also the experimental data obtained by regression. The analytical equation is shown by solid lines and the experimental data is shown by markers.

The analytical trend shown in Fig 4.3 is that for a constant Stroke Volume, $D_{\text{eff}}/D$ increases from a Womersley number of 0 to 27. This trend is consistent with that seen in the
experimental data, where $\text{Deff}/D$ increases from a Womersley number of 4.446 to 24.35. However the analytical data predicts saturation in the values for $\text{Deff}/D$ with Womersley number, whereas the experimental data does not predict this saturation. To get a better understanding of the effect of increasing the frequency on the values of $\text{Deff}/D$, experiments have to be conducted at higher frequencies. With the current experimental apparatus, conducting experiments at higher Womersley Numbers were not possible. At frequencies of around 40Hz and above, the syringe plunger head after certain use got stuck to the syringe walls owing to friction. Hence the maximum frequencies for the experiments were kept limited to 30Hz. So for the current experimental apparatus, the value of the Womersley number where $\text{Deff}/D$ reaches its peak is unknown. Even though the theory predicts that the threshold Womersley number is 27, there is no way to say with certainty what the threshold Womersley Number is for the current experimental apparatus.

![Analytical and Experimental results of Deff/D vs. Womersley Number for Different Stroke Volumes ($V^2/a^5$)](image)

**Figure 4.3:** Experimental and Analytical Variation of Deff/D with Womersley Number for lines of constant Stroke Volume. Analytical solution is shown by solid lines. Experimental data is shown by markers. Each line/marker represents a constant stroke volume. Stroke Volume varies from 0 to 70 in steps of 10, which encompass range of amplitudes for conducted experiments. Womersley number varies from 0 to 50 for the analytical solution (solid lines).

The values of $\text{Deff}/D$ predicted by Gaver[17] and by Harris[14] for similar Womersley Numbers and stroke amplitudes are higher for Harris than Gaver. Harris conducted experiments of HCl in
water which has a Schmidt number of 238. Gaver conducted experiments on dispersion of Argon in air with a Schmidt number of 0.815. The stroke amplitudes for this thesis are smaller than those conducted by Harris and Gaver. For the highest stroke amplitudes conducted in the current experiments, at similar Womersley numbers, the values of $D_{\text{eff}}/D$ for the current thesis are higher than that of Gaver and Harris. The Schmidt number of FD&C Blue#1 and water is 3200[21]. It is probable that the high values of Schmidt number are as reason for reporting higher values of $D_{\text{eff}}/D$. This is consistent with theory that a higher Schmidt number causes higher values of $D_{\text{eff}}/D$.

### 4.1.1. Probable Reasons for Mismatch of $D_{\text{eff}}/D$

The theory given by Watson[12] is valid for infinitely long cylindrical tubes for long times after injection when the concentration gradient in the axial direction is linear. For some of the experiments conducted by Joshi[13], 20 hours were needed to conduct experiments, in order to achieve a steady state of axial transport i.e. a linear concentration gradient in the axial direction. The concentration gradient in the current set of experiments is not linear. It is possible that the reservoir filled with water attached to one end of the cylindrical tube affects the velocity field in the cylindrical tube to increase dispersion. There are secondary flows like vortices, which may be the cause of disagreement in the values of $D_{\text{eff}}/D$ between the experiments and the theory. The conditions of these experiments resemble the conditions of the cochlea more closely than those in previous literature.

### 4.2. Experimental Uncertainties

#### 4.2.1. Variation in Stroke Amplitude:

The stroke amplitude varies over the duration of an experiment after the oscillator starts. The amplitude starts off at a specific displacement and gradually tapers down to a constant value after roughly 10 seconds. The amplitude after 10 seconds is fairly constant. 4 trials are conducted- 2 each for an oscillating case of 20Hz and 30Hz. Hence amplitude of dye displacement is calculated at the end of a trial. The value of the displacement amplitude at the end of a trial is considered to be the amplitude of the entire trial. Fig 4.4 shows the amplitude of dye displacement over a period of 60 seconds.
Figure 4.4: Variation in amplitude with time.

Amplitude reduces from a higher value at the beginning of oscillations and stabilizes at a constant value after 10 seconds. 2 Trials are conducted for dye dispersion at 20Hz and 30Hz each.

4.3. Diffusion Enhancement in Cochlea

The experiments conducted at 1Hz, 20Hz and 30Hz, when scaled to the cochlea; correspond to 8.33Hz, 167.16Hz and 250.78Hz respectively (Refer appendix 6.3 for calculations). The range of human hearing being 20Hz-20kHz, the frequencies of 167.16 and 250.78Hz lie within the range of human hearing. The experiments conducted predict an increase in dispersion with an increase in frequency. Increasing the frequency beyond the current range would increase the dispersion. However Watson’s analytical theory predicts a saturation frequency beyond which values of $\text{Deff}/D$ reduce. Experiments conducted at higher frequencies will confirm if values of $\text{Deff}/D$ scaled to the cochlea will increase or reduce.

The standard pain level for the cochlea is 120dB. When stimulated by sound at 80dB, the maximum volumetric displacement of the cochlear fluid (perilymph) is of the order of $10^4 \mu m^3$ [22]. The pressure at 120dB is 100 times more than that at 80dB. Assuming that the Round Window Membrane is elastic, the volumetric displacement of the perilymph at 120dB would be
$10^6 \mu m^3$. The corresponding stroke amplitude ($A/a$), is $1.92 \times 10^{-3}$, which lies within the range of 0 to 2.2 in the experiments conducted.

To scale the results of the experiments to that of the cochlea, a linear relationship is assumed between $D_{eff}/D$ and the Stroke Volume.

From the results section, we know that the variation of stroke amplitude as a function of effective diffusivity is of the form

$$\frac{D_{eff}}{D} = m \left( \frac{\pi \times A}{a} \right)^2 + 1 \ldots \ldots (12)$$

where $m$ is the slope of the line and is a function of the Womersley number. To apply the results of the experiments performed to the cochlea, the values of $D_{eff}/D$ in the cochlea were calculated in 2 ways:

1) The value of the stroke amplitude of $1.92 \times 10^{-3}$ is substituted in Equation 12 for each Womersley number at which experiments have been performed. The corresponding values of $D_{eff}/D$, when scaled to the cochlea are summarized in the Table 4.1.

<table>
<thead>
<tr>
<th>Womersley Number</th>
<th>4.44</th>
<th>19.88</th>
<th>24.35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slope (m)</td>
<td>0.04</td>
<td>1.99</td>
<td>6.55</td>
</tr>
<tr>
<td>$D_{eff}/D$</td>
<td>1.000001455</td>
<td>1.0000724</td>
<td>1.0002383</td>
</tr>
<tr>
<td>Percentage Increase of D</td>
<td>$1.5 \times 10^{-4}$</td>
<td>$7.24 \times 10^{-3}$</td>
<td>$2.383 \times 10^{-2}$</td>
</tr>
</tbody>
</table>

It is seen that the highest predicted percentage increase in D is of the order of $10^{-2}$. Hence oscillating the flow of fluid in the cochlea, via sound stimulation will not increase the rate of drug dispersion by a significant amount to consider the method viable. Hence by virtue of the small fluid volumetric displacements in the cochlea, the predicted increase in diffusion is not substantial.

2) Substituting the value of $A/a$, for resulting fluid displacements in the cochlea, when the Round Window Membrane is mechanically deformed.

Takahashi[23] conducted experiments on 4 cadavers of the human Round Window Membrane (RWM). The RWM’s were clamped and were deformed by applying a known force using a cylindrical pin. The maximum deformation of the membrane before it broke was recorded.
It is assumed that when the membrane deforms, the volumetric displacement is the frustum of a cone. The minimum and the maximum displacements for the RWM specimens before breaking are 122 µm and 270 µm respectively. The stroke amplitude considering that the Max displacement is 122 µm is $7.31 \times 10^{-3}$ (Refer Appendix 5.1.2 for calculations of Stroke Amplitude). The stroke amplitude considering that the Max displacement is 270 µm is 0.079 (Refer Appendix 5.1.2 for calculations of Stroke Amplitude). Table 4.2 summarizes the experimental results scaled to the cochlea, when the RWM is mechanically displaced.

<table>
<thead>
<tr>
<th>Womersley Number</th>
<th>Slope (m)</th>
<th>D_{eff}/D</th>
<th>Percentage Increase of D</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0.04</td>
<td>1.0008</td>
</tr>
<tr>
<td>270 µm</td>
<td></td>
<td>1.99</td>
<td>1.0399</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6.55</td>
<td>1.1317</td>
</tr>
<tr>
<td>122 µm</td>
<td></td>
<td>1.0000</td>
<td>1.00015</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.05</td>
<td>1.0017</td>
</tr>
</tbody>
</table>

Hence a percentage increase of 13.17% is seen considering the maximum displacement of the membrane for a Womersley number of 24.35. Even though an increase of 13.17% is seen for the maximum RWM displacement, this is the breaking point of the RWM. For a membrane which displaces by 122 µm, the increase in $D$ for the same Womersley number is 0.17%.

The breaking strength of the RWM varies from person to person. Hence the process of trying to increase the dispersion of drug in the cochlea, by displacing the RWM mechanically can’t be standardized. Also The RWM is a critical component of the cochlea which aids in hearing. It is not possible to displace the RWM up to breaking point for drug dispersion. Another component which has to be taken into consideration is that if the cochlea can sustain hearing function by increased volumetric displacements. Hence on the basis of this study, it is improbable that oscillating the flow of fluids in the cochlea can enhance drug dispersion.

### 4.4. Summary

The objectives in Section 1.3 of conducting experiments for dispersion and determining if drug dispersion in the cochlea can be enhanced have been achieved. Even though the experimental results are not in line with the values of $D_{eff}/D$ predicted by previous theory, they do show general trends consistent with previous studies. It is evident that dispersion enhancement in oscillating flows is largely dependent on the amplitude of oscillation. Hence for very small amplitudes as that in the cochlea, mixing by dispersion in oscillating flows is limited.
4.4.1. **Suggested Improvements**

The cochlea is a coiled structure. The perilymph of the cochlea which undergoes oscillation is bounded by 2 deformable membranes with a rigid wall below and an elastic wall above. Additionally, the cross sectional area of the cochlea gradually tapers off. The geometry which has been analyzed for this thesis is a cylindrical tube with a constant cross section with rigid walls. For a better understanding of the dispersion process in the cochlea, further experiments can be performed on a conical geometry and subsequently on a model of the cochlea itself.

The diffusion coefficient is a function of temperature. In the experiments conducted for this thesis, the temperature is not constant but varies as shown in Table 2.1. The apparatus can be further improved by using a precise temperature control mechanism.

The apparatus can be modified to operate at higher frequencies by replacing the syringe with a diaphragm pump.
5. REFERENCES:-


6. APPENDIX:-

6.1. **Stroke Amplitudes in the cochlea**

The average cross sectional area of the scala tympani is $1.13 \text{mm}^2$ and of that of the scala vestibuli is $0.77 \text{mm}^2$. Average of the areas is $0.95 \text{mm}^2$. Assuming a cylindrical tube of average cross sectional area of $0.95 \text{mm}^2$, the radius is $0.549 \text{mm}$. Volumetric displacement in the cochlea:

The maximum volumetric displacement in the cochlea is $10^5 \mu \text{m}^3$. Hence the dimensionless stroke volume is $0.365 \times 10^{-6}$. The maximum displacement of the round window is $200 \text{nm}$ for stimulation by bone conduction and the average cross sectional area is $0.95 \text{mm}^2$.

6.1.1. **Sound Stimulation**

\[
V = 10^6 \mu \text{m}^3 = 10^{-3} \text{mm}^3
\]

\[
V = \pi a^2 \times A
\]

\[
a = 0.549 \text{mm}
\]

\[
A = \frac{V}{a^3 \pi} = \frac{10^{-3}}{0.549^3 \times \pi} = 1.92 \times 10^{-3}
\]
6.1.2. Mechanical Membrane displacement

\[ h = 122 \mu m, R = 100 \mu m, r = 65 \mu m \]

\[ V = \frac{\pi h}{3} \left( R^2 + Rr + r^2 \right) = \frac{\pi \times 122}{3} \left( 100^2 + 100 \times 65 + 65^2 \right) = 2.6478 \times 10^6 \mu m^3 \]

\[ V = \pi a^2 \times A \]

\[ a = 0.549 \text{mm} \]

\[ \frac{A}{a} = \frac{V}{a^3 \pi} = \frac{2.6478 \times 10^{-3}}{0.549^3 \times \pi} = 0.0051 \]

\[ h = 270 \mu m, R = 250 \mu m, r = 65 \mu m \]

\[ V = \frac{\pi h}{3} \left( R^2 + Rr + r^2 \right) = \frac{\pi \times 270}{3} \left( 250^2 + 250 \times 65 + 65^2 \right) = 2.3461 \times 10^7 \mu m^3 \]

\[ V = \pi a^2 \times A \]

\[ a = 0.549 \text{mm} \]

\[ \frac{A}{a} = \frac{V}{a^3 \pi} = \frac{2.3461 \times 10^{-2}}{0.549^3 \times \pi} = 0.0451 \]
6.2. Calculation of Womersley Numbers for Range of experiments performed

\[ \alpha = a \sqrt{\frac{\omega}{\nu}} \]

\[ a = 0.15875\text{ cm} \]

\[ \nu = 0.801 \times 10^{-2} \text{ cm}^2 / \text{s} \]

1 Hz

\[ \alpha = a \sqrt{\frac{2\pi f}{\nu}} = 0.15875 \left( \frac{2\pi \times 1}{0.801 \times 10^{-2}} \right) = 4.44 \]

20 Hz

\[ \alpha = a \sqrt{\frac{2\pi f}{\nu}} = 0.15875 \left( \frac{2\pi \times 20}{0.801 \times 10^{-2}} \right) = 19.88 \]

30 Hz

\[ \alpha = a \sqrt{\frac{2\pi f}{\nu}} = 0.15875 \left( \frac{2\pi \times 20}{0.801 \times 10^{-2}} \right) = 24.35 \]
6.3. Calculation of frequencies in Cochlea scaled to Womersley numbers for experiments

\[ \alpha = a \sqrt{\frac{\omega}{v}} \]
\[ \alpha = 0.549 \text{mm} \]
\[ v = 0.801 \times 10^{-2} \text{cm}^2 / s \]

\[ \alpha = 4.44 \text{Hz} \]
\[ \alpha = a \sqrt{\frac{2\pi f}{v}} = 4.44 = 0.549 \sqrt{\frac{2\pi \times f}{0.801}} \therefore f = 8.338 \text{Hz} \]

\[ \alpha = 19.88 \]
\[ 19.88 = 0.549 \sqrt{\frac{2\pi \times f}{0.801}} \therefore f = 167.16 \text{Hz} \]

\[ \alpha = 24.35 \]
\[ 24.35 = 0.549 \sqrt{\frac{2\pi \times f}{0.801}} \therefore f = 250.78 \text{Hz} \]

6.4. Matlab code for Concentration Determination

```matlab
clc
clear all
% a1=514.1;
% b1=-0.07615;
a2=91.17
b2=-0.02271
% S=[143.5 29.5 428 17]; %OSR Final
S=[80.5 17.5 146 34]; %Diffusion
% S=[216.5 19.5 281 33]; %Area Corrections for thesis 20Hz and 30Hz
% S=[325 15.0000000000001 180 30]; %Area Corrections for thesis 1Hz
x=ceil(S(1));
y=ceil(S(2));
W=ceil(S(3));
H=ceil(S(4));

% Cmax=112.2456;
% Cmin=27.3750;

D=dir;
D1=D(3:length(D));
```
% img=zeros(68,708);
% Davg=zeros(1,length(D1));
% for i=1:length(D1)
% for i=1:1055
% str=D1(i).name;
% img=imread(str);
% I=img(y:(y+H),x:(x+W));
% Id=double(I);
% for j=1:H
% for k=1:W
% C(j,k)=inv(Cmax-Cmin)*(Cmax-Id(j,k));    %Linear
% Ce(j,k)=al*exp(b1*Id(j,k));    %Exponential
% Cb(j,k)=a2*exp(b2*Id(j,k))    %Beers Law
% Cb(j,k)=inv(b2)*log((Id(j,k)-11)/a2);
% end
% end
% Y=mean(C);
% Z(i,:)=% Y;
% Ye=mean(Ce);
% Ze(i,:)=% Ye;
% Yb=mean(Cb);
% Zb(i,:)=% Yb;
% end
%
% flag=2;
% for i=200:200:1000
% Zlinear(flag,:)=Z(i,:);    %Storage Linear 20Hz
% flag=flag+1;
% end
% Zlinear(1,:)=% Z(1,:);
% Zlinear(flag:61,:)=% Z(1001:1055,:)
%
% flag=2;
% for i=200:200:1000
% Zexp(flag,:)=% Ze(i,:);    %Storage Exponential 20Hz
% flag=flag+1;
% end
% Zexp(1,:)=% Ze(1,:);
% Zexp(flag:61,:)=% Ze(1001:1055,:)
%
% flag=2;
% for i=200:200:1000
% Zbeers(flag,:)=% Zb(i,:);    %Storage Beers 20Hz
% flag=flag+1;
% end
% Zbeers(1,:)=% Zb(1,:);
% Zbeers(flag:61,:)=% Zb(1001:1055,:)
%
% flag=2;
% for i=300:300:1500
% Zlinear(flag,:)=% Z(i,:);    %Storage Linear 30Hz
% flag=flag+1;
% end
% Zlinear(1,:) = Z(1,:);
% Zlinear(flag:61,:) = Z(1501:1555,:)

% flag=2;
% for i=300:300:1500
% Zexp(flag,:) = Zc(i,:); %Storage Exponential 30Hz
% flag=flag+1;
% end
% Zexp(1,:) = Zc(1,:);
% Zexp(flag:61,:) = Zc(1501:1555,:)

% flag=2;
% for i=300:300:1500
% Zbeers(flag,:) = Zb(i,:); %Storage Beers 30Hz
% flag=flag+1;
% end
% Zbeers(1,:) = Zb(1,:);
% Zbeers(flag:61,:) = Zb(1501:1555,:)

% Zlinear = Z(1:60,:); %Storage Linear 1Hz
% Zexp = Zc(1:60,:); %Storage Exponential 1Hz
% Zbeers = Zb(1:60,:); %Storage Beers 1Hz

% Linear
% [m,n] = size(Zlinear)
% for i=1:m
% width(i) = fwhm(1:W,Zlinear(i,:)); %FWHM
% end
% width = width - width(1);
% width = width + 1;
% figure(1)
% plot(width,'o')
% title('FWHM Linear')
%
% [m,n] = size(Zlinear);
% for i=1:m
% area(i) = trapz(1:W,Zlinear(i,:));
% newwidth(i) = area(i) / max(Zlinear(i,:)); %Area Width
% end
% newwidth = newwidth - newwidth(1);
% newwidth = newwidth + 1;
% figure(2)
% plot(newwidth,'o')
% title('Area Linear')

% Exponential
% [m,n] = size(Zexp)
% for i=1:m
% widthexp(i) = fwhm(1:W,Zexp(i,:)); %FWHM
% end
% widthexp = widthexp - widthexp(1);
% widthexp = widthexp + 1;
% figure(3)
% plot(widthexp,'o')
% title('FWHM exp')
```matlab
% [m,n]=size(Zexp);
% for i=1:m
%     area(i)=trapz(1:W,Zexp(i,:));
% end
% newwidthexp(i)=area(i)/max(Zexp(i,:)); %Area Width
% newwidthexp=newwidthexp
% figure(4)
% plot(newwidthexp,'o')
% title('Area Curve exp')

% Beers
% [m,n] = size(Zbeers)
% for i=1:m
%     widthbeers(i) = fwhm(1:W,Zbeers(i,:)); %FWHM
% end
% widthbeers=widthbeers
% % figure(5)
% % plot(widthbeers,'o')
% % title('FWHM beers')

% Diffusion

[m,n] = size(Zb)
for i=1:m
    widthbeers(i) = fwhm(1:W,Zb(i,:)); %FWHM
end
widthbeers=widthbeers
% figure(5)
% plot(widthbeers,'o')
% title('FWHM beers')
```
newwidthbeers=newwidthbeers+1;
figure(6)
plot(newwidthbeers,'o')
title('Area Curve Beers')

figure(5)
plot(0:199, widthbeers, 'o',
    'LineWidth',3,...
    'MarkerSize',10)
set(gca,'FontSize',22)
xlabel('Time (seconds)','FontSize',22)
ylabel('FWHM (pixels)','FontSize',22)
title('FWHM vs. Time','FontSize',22)

figure(6)
plot(0:199, newwidthbeers, 'o',
    'LineWidth',3,...
    'MarkerSize',10)
set(gca,'FontSize',22)
xlabel('Time (seconds)','FontSize',22)
ylabel('Area Parameter','FontSize',22)
title('Area Parameter vs. Time','FontSize',22)
## 6.5. Dispersion Curve Fitting

Dispersion Curve Fitting

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<tr>
<th>Diffusion</th>
<th>Deff</th>
<th>A/a</th>
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<td>Frequency -1Hz</td>
<td>Deff</td>
<td>A/a</td>
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<tr>
<td>Value 1</td>
<td>Value 2</td>
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<td>0.09</td>
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Experimental AP with Best Analytical AP fit

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<th>Time (seconds)</th>
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<th>Time (seconds)</th>
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Experimental AP with Best Analytical AP fit

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Experimental AP with Best Analytical AP fit

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<tr>
<td>1.5</td>
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<td>1.06</td>
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**Graphical Representation:**

- **Experimental AP**
- **Analytical AP**

**Legend:**
- **Experimental AP** (circles)
- **Analytical AP** (solid line)
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**Experimental AP with Best Analytical AP fit**

- **Experimental AP**
- **Analytical AP**

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![Experimental AP with Best Analytical AP fit](image)
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60   2.17

85.7 2.39