Courant Institute of
Mathematical Sciences

Partial Differential Equations in Biology

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PARTIAL DIFFERENTIAL EQUATIONS IN BIOLOGY

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1975 - 1976

Computation for this work was supported by U.S. ERDA under Contract E(11-1)-3077 at New York University.

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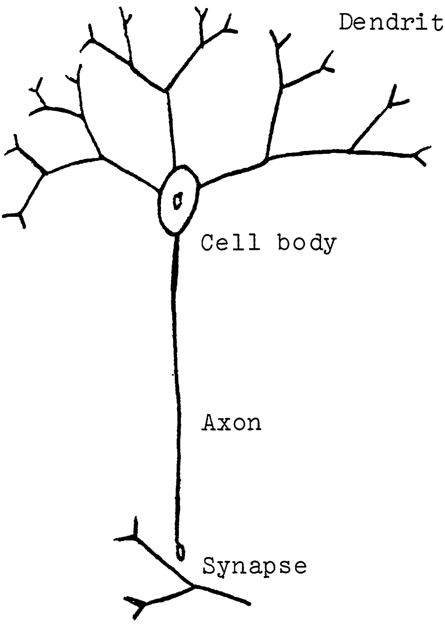
PARTIAL DIFFERENTIAL EQUATIONS IN BIOLOGY [1]

I. Introduction: The Biological Problems and their Mathematical Formulation.

1. Electrophysiology



Nerve: A neuron is a cell which is specialized to process and transmit information. Like other cells of the organism, it has a cell body with a nucleus and is surrounded by a membrane which can support a voltage difference. Unlike other cells, it has two systems of elongated extensions: the dendrites and the axon. Information is received at the dendrites in the form of packages ("quanta") of a chemical transmitter released from the terminal ends of the many axons which form synapses

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[1] In some respects these Notes constitute a sequel to: Peskin, Mathematical Aspects of Heart Physiology, C.I.M.S. Lecture Notes, 1975. In particular, the sections on Electrophysiology and Muscle in these Notes are extentions of the earlier material, and the discussions of Fluid Dynamics in the Heart notes may serve as a useful introduction to the material presented here on Arteries and the Inner Ear.

(close contacts) with the dendritic tree of the cell in question. The chemical transmitter modifies the properties of the post-synaptic membrane and a current flows into the dendritic tree at the location of the synapse. The branches of the dendritic tree are leaky transmission lines (in which inductance may be neglected). Consequently, the equation governing the spread of potential in each branch of the tree is (in appropriate units)

$$\frac{\partial V}{\partial t} = \frac{\partial^2 V}{\partial x^2} - V \tag{1.1}$$

At each junction one has the boundary conditions of continuity of voltage and conservation of current. The interesting questions are:

(i) What voltage waveform is produced at the cell body by the sudden release of transmitter at a particular synapse. How does this depend on the location of the synapse.

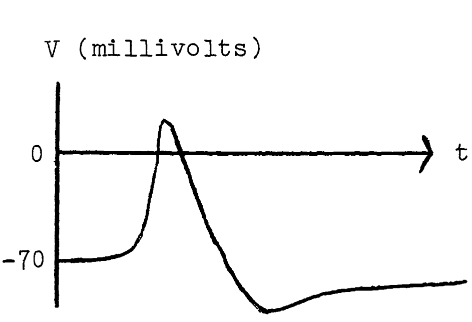
(ii) What voltage waveform is produced at synapse B by the sudden release of transmitter at A. This is important because the injected current at a synapse depends on the local membrane potential. Thus the system as a whole is non-linear, despite the linearity of (1.1), and one wants to know how the spatial organization of the inputs determines the degree of non-linear interactions between them.

At the axon, the membrane properties change, and the equations governing nerve conduction become non-linear. This appears to be because the membrane potential influences the number of aqueous channels (pores) available for the conduction of ions across the lipid membrane. There are several types of channels, specific for different ions. Moreover, the concentration of any particular ion is different on the two sides of the membrane, and these concentration differences act like batteries. (The energy for maintaining the concentration differences comes from the metabolism of the cell.) The resulting equations have the form

$$\text{(1.2)} \qquad \begin{cases} \dfrac{\partial V}{\partial t} = \dfrac{\partial^2 V}{\partial x^2} + f(V, s_1 \dots s_N) \\ \dfrac{\partial s_k}{\partial t} = \alpha_k(V)(1 - s_k) - \beta_k(V) s_k \end{cases}$$

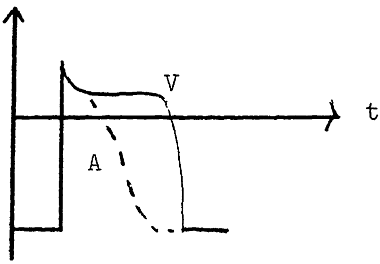
where $s_1 \dots s_N$ are membrane parameters which control the number of aqueous channels, $f(V, s_1 \dots s_N)$ is the sum of the ionic currents, and $\alpha_k(V)$, $\beta_k(V)$ are voltage dependent rate constants. (Although the general physical interpretation given here concerning voltage dependent channels is widely accepted, the physical details are unknown.)

The most striking fact about equations (1.2) is their ability (in certain cases) to support a traveling wave solution of a particular shape, the "nerve impulse".



Regardless of the pattern of input to a neuron, the output is always a train of such identical impulses. Only the timing of the impulses conveys any information, since their waveform is fixed. The fact the impulse can propagate along the axon without distortion or attenuation is a consequence of the non-linearity in the membrane behavior. This allows the impulse to tap energy from the ionic concentration differences as it moves along the axon. This mode of wave propagation is unrelated to the more familiar transmission line wave, which travels at the speed of light. Nerve impulses travel at a speed on the order of meters per second, and the resulting time delays have important biological effects.

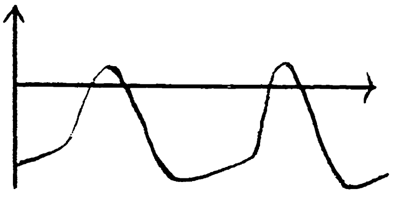
Heart: In cardiac tissue a network of specialized muscle fibers conducts the electrical signals which tigger the heartbeat in a manner which closely resembles that of the nerve axon. Equations of the form (1.2) also apply but with different functions f, α_k, β_k. The cardiac action potential is more clearly divided into



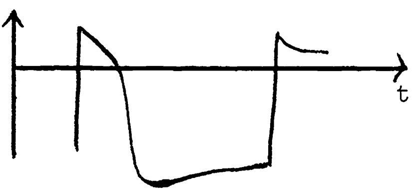
Cardiac Action Potential
A = Atrium, V = Ventricle

two states, and the temptation to refer to them as ON and OFF becomes irresistable. This is especially true in the ventricular muscle. This suggests the mathematical question of whether we can find limiting cases of equations (1.2) in which sharp front-like behavior is observed.

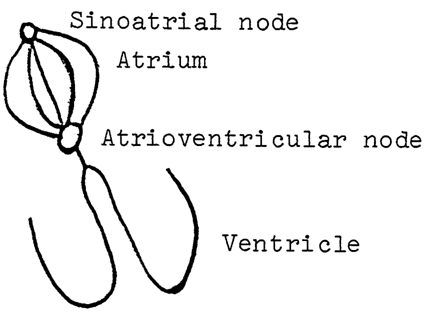
Another interesting feature of cardiac tissue is the presence of many pacemaker cells which can fire spontaneously at a frequency characteristic of the cell. Such cells lack a stable resting potential, and depolarize slowly until a threshold is reached, at which point they fire. An important property of pacemaker cells is the fact that a fast pacemaker can capture a slow one. Although pacemaker cells are distributed throughout the heart, the fastest ones are collected in a region known as the sinoatrial node. Therefore, this region initiates the heartbeat. The spatial stratification of cardiac cells according to natural frequency



Sinoatrial Pacemaker



Purkinje Fiber Pacemaker



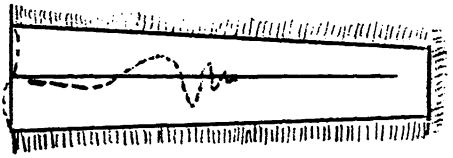
Conduction System of the Heart

is important for the stability of the cardiac rhythm. In certain cases we can introduce pacemaker activity into equations (1.2) by adding a bias current term. Spatial stratification can be included by making this term depend on x.

Abnormal rhythms of the heart are often generated when a segment of the conduction pathway becomes diseased. In such cases, the diseased segment may itself become a pacemaker, or it may conduct only a fraction of the impluses incident upon it. One can study such processes by again making equations (1.2) x-dependent.

2. The Cochlea

The inner ear ("cochlea") is a fluid-filled cavity in the skull. An elastic partition, the basilar membrane, divides the cochlea into two parts, and the fibers of the auditory nerve are distributed along this partition. The stiffness of the basilar membrane decreases exponentially with distance from the input end. When the ear is stimulated by a pure tone the vibrations of the basilar membrane-fluid system take the form of a traveling wave which peaks at a place which depends on frequency. (The location of the peak varies as the log of the frequency.)



In this way the different frequencies of a complex sound are sorted out and delivered to different fibers of the auditory nerve.

We shall study this problem both with and without viscosity. In the absence of viscosity the flow will be potential flow and the equations are:

$$(1.3)\qquad \begin{cases} \Delta\phi = 0 & -a < y < 0 \\ \dfrac{\partial\phi}{\partial y} = 0 & y = -a \\ \dfrac{\partial^2\phi}{\partial t^2} + e^{-x}\dfrac{\partial\phi}{\partial y} = 0 & y = 0 \end{cases}$$

where ϕ is the velocity potential ($\underline{u}$ = grad ϕ) and Δ is the Laplace operator $\Delta = (\partial^2/\partial x^2) + (\partial^2/\partial y^2)$.

If the factor e^{-x} were replaced by a constant this would be equivalent to the problem of waves of low amplitude in water of finite depth. In fact, the factor e^{-x} can be absorbed by a conformal mapping. The results of this analysis reveal an important fluid dynamic mechanism for concentrating the energy of the wave near the basilar membrane.

The inviscid analysis is incomplete, however, because it predicts that the amplitude and spatial frequency of the wave will increase without bound at the membrane (although at any finite depth, this difficulty does not occur.) The equations of motion with viscosity may be written as follows:

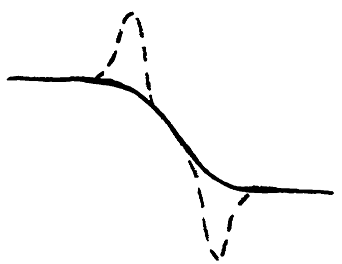
1.4)
$$\begin{cases} \dfrac{\partial u}{\partial t} + \dfrac{\partial p}{\partial x} = \nu \Delta u \\ \dfrac{\partial v}{\partial t} + \dfrac{\partial p}{\partial y} = \nu \Delta v - e^{-x} h(x,t)\delta(y) \\ \dfrac{\partial u}{\partial x} + \dfrac{\partial v}{\partial y} = 0 \\ \qquad\quad \dfrac{\partial h}{\partial t} = v(x,0,t) \end{cases}$$

where (u,v) is the velocity vector, ν is the viscosity, $h(x,t)$ is the membrane displacement.

Using Fourier transforms, this system can be reduced to an integral equation along the membrane, which can be solved numerically.

3. The Retina

The retina is essentially a two dimensional array of cells which codes a pattern of light stimulation into nerve impulses. Even at this first stage of visual processing there are interesting interactions between cells, so that the output of each cell depends not only on the light falling on that cell, but also on the surrounding cells. For example, when the objective illumination contains a ramp connecting the



__ Objective
-- Subjective

constant levels, the subjective impression is of a bright band near the corner where the graph of the illumination is concave down and a dark band at the opposite corner. These were discovered by Mach, and are called Mach bands. They can be explained by the theory that the retina computes the Laplacian of the illumination and subtracts this from the actual illumination to obtain the response. A class of models related to this idea were proposed by Hartline and Ratliff. These take the form:

$$R(x,y,t) = E(x,y,t) - \lambda\int_{-\infty}^{t} dt' \iint_{-\infty}^{\infty} dx'dy' \; K(x-x',y-y',t-t')R(x',y',t') \tag{1.5}$$

where E is the light and R is the response. Note that the response, rather than the light, appears in the integrand on the right hand side. This is because the influence of one cell of the retina on another is mediated through the response of the cell, not directly by the light.

With a particular choice of K which is not unreasonable we can reduce the equation (1.5) to a partial differential equation, which we then use to study the statics and dynamics of retinal interactions.

4. Pulse-wave Propagation in Arteries

The heart ejects blood into a branching tree of elastic tubes – the arteries. The shape of the arterial pressure pulse deforms as the wave travels toward the periphery. The changes in the shape of the pulse depend upon the properties of the artery and are therefore useful in diagnosis. In particular, atherosclerosis and diabetes result in the absence of the second wave in the peripheral pulse.

Near the Heart

In the Periphery

The one-dimensional equations governing the flow of an incompressible fluid in an elastic tube are

$$\rho\left(\frac{\partial u}{\partial t} + u\,\frac{\partial u}{\partial x}\right) + \frac{\partial p}{\partial x} = f$$

$$\frac{\partial A}{\partial t} + \frac{\partial}{\partial x}(Au) + \psi = 0 \qquad (1.6)$$

$$A = \bar{A}(p,x)$$

where ρ is the density, u is the axial velocity, p the pressure, f the frictional force, A the cross-sectional area, ψ the outflow, and $\bar{A}(p,x)$ is the relation between pressure and area at each point x as determined by the local properties of the wall.

At least two types of distortion are possible with equations (1.). To see this consider the model given by

$$(1.7)\qquad \begin{cases} f = 0 \\ \overline{A}(p,x) = A_o e^{(Kp-\lambda x)} \\ \psi = \sigma A p \end{cases}$$

In this case equations (1.6) become

$$(1.8)\qquad \begin{cases} \rho\left\{\dfrac{\partial u}{\partial t} + u\,\dfrac{\partial u}{\partial x}\right\} + \dfrac{\partial p}{\partial x} = 0 \\ K\left\{\dfrac{\partial p}{\partial t} + u\,\dfrac{\partial p}{\partial x}\right\} + \dfrac{\partial u}{\partial x} = \lambda u - \sigma p \end{cases}$$

Setting $\lambda = \sigma = 0$ we have the non-linear system

$$(1.9)\qquad \begin{cases} \rho\left(\dfrac{\partial u}{\partial t} + u\,\dfrac{\partial u}{\partial x}\right) + \dfrac{\partial p}{\partial x} = 0 \\ K\left(\dfrac{\partial p}{\partial t} + u\,\dfrac{\partial p}{\partial x}\right) + \dfrac{\partial u}{\partial x} = 0 \end{cases}$$

in which distortion is introduced by the convective terms $u\,\dfrac{\partial u}{\partial x}$ and $u\,\dfrac{\partial p}{\partial x}$.

Alternatively, one may neglect the non-linear terms but retain non-zero values for λ and σ. In that case the system becomes

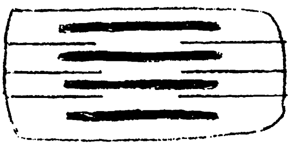
$$(1.10)\qquad \begin{cases} \rho\,\dfrac{\partial u}{\partial t} + \dfrac{\partial p}{\partial x} = 0 \\ K\,\dfrac{\partial p}{\partial t} + \dfrac{\partial u}{\partial x} = \lambda u - \sigma p \end{cases}$$

and distortion is produced by the undifferentiated terms.

Both types of distortion influence the shape of the arterial pulse.

5. Cross-Bridge Dynamics in Muscle

Skeletal and cardiac muscle contain two systems of parallel filaments (thick and thin) which slide past each other during contraction. Cross-bridges which form between the thick and thin filaments actually bring about the sliding. An attached cross-bridge may be characterized by a parameter x which measures its strain. The population of cross-bridges may be characterized by u(x) such that



$$\int_a^b u(x)dx = \text{fraction of cross-bridges with } a \leq x \leq b \tag{1.11}$$

For a given cross-bridge, x changes with time at a rate proportional to the velocity of the muscle as a whole. Moreover, the force exerted by an attached cross-bridge is proportional to x.

Assume that all cross-bridges attach in configuration $x = A$. Then with $v < 0$ (contraction) we have

$$
(1.12) \quad \begin{cases} \dfrac{\partial u}{\partial t} + v\,\dfrac{\partial u}{\partial x} = -g(x)u \\[2ex] F\left\{1 - \displaystyle\int_{-\infty}^{A} u(x)\,dx\right\} = (-v)u(A^-) \\[2ex] P = K\displaystyle\int_{-\infty}^{A} u(x)x\,dx \end{cases}
$$

The interesting problem here is an inverse problem: with measurements of $P(t)$, $v(t)$ — how can one determine $g(x)$, the rate of breakdown of cross-bridges as a function of strain? The solution of this problem yields a method by means of which macroscopic measurements on intact muscle can be used to determine the properties of a microscopic (and rather inaccessible) chemical reaction.

II. Fundamental Solutions of Some Partial Differential Equations

In this section we shall construct solutions to the following problems:

The Wave Equation:

$$(2.1)\qquad (\partial_t^2 - \Delta_n)u(t,x_1 \ldots x_n) = f(t)\delta(x_1) \ldots \delta(x_n)$$

The Klein-Gordon Equation:

$$(2.2)\qquad (\partial_t^2 - \Delta_n + k^2)u(t,x_1 \ldots x_n) = f(t)\delta(x_1) \ldots \delta(x_n)$$

(Note: when $k^2 < 0$, 2.2 is a form of the Telegrapher's equation.)

Laplace's Equation:

$$(2.3)\qquad -\Delta_n u(x_1 \ldots x_n) = \delta(x_1) \ldots \delta(x_n)$$

The Heat Equation:

$$(2.4)\qquad (\partial_t - \Delta_n)u(t,x_1 \ldots x_n) = f(t)\delta(x_1) \ldots \delta(x_n)$$

In the foregoing:

$$\Delta_n = \sum_{k=1}^{n} \partial_k^2$$

$$\partial_k = \frac{\partial}{\partial x_k} \qquad \partial_t = \frac{\partial}{\partial t}$$

Our approach will be as follows: First, solve the Wave Equation in one space dimension. Then, use the method of descent to construct solutions to the Wave Equation and the Klein-Gordon Equation in higher dimensions. A special right-hand side for the Wave Equation then yields Laplace's Equation in the limit $t \to \infty$. Setting $k^2 < 0$ in the Klein-Gordon Equation yields the Telegrapher's Equation, and a limiting case of this is the Heat Equation. In this way we exhibit the connections between the various problems, since we construct each solution from that of the Wave Equation in one space dimension. This contrasts with the usual approach in which hyperbolic (the Wave and Klein-Gordon equations), elliptic (Laplace's equation) and parabolic (the Heat equation) problems are treated separately. There are, of course, good reasons for considering these cases separately when one looks more deeply into the subject, but the connections between the different equations are also interesting and will be emphasized here. The reader who wants a thorough introduction to the partial differential equations considered in this section should consult (for example) the C.I.M.S. Lecture Notes of Fritz John (also published by Springer).

1. The Wave Equation in One Space Dimension.

The problem is:

$$(\partial_t^2 - \partial_x^2)u(t,x) = f(t)\delta(x) \tag{2.5}$$

on $-\infty < x < \infty$. We expect a solution which has $u(t,x) = u(t,-x)$, and we can state our problem as a boundary value problem on $x > 0$ by choosing $\varepsilon > 0$ and integrating (2.5) over the interval $(-\varepsilon,\varepsilon)$. We obtain

$$\lim_{\varepsilon\to 0} [-(\partial_x u)(t,\varepsilon) + (\partial_x u)(t,-\varepsilon)] = f(t)$$

or, since $(\partial_x u)$ will be an odd function:

$$\lim_{\varepsilon\to 0} (\partial_x u)(t,\varepsilon) = -\frac{1}{2} f(t) \quad . \tag{2.6}$$

On $x > 0$, (2.5) becomes

$$(\partial_t^2 - \partial_x^2)u(t,x) = 0 \tag{2.7}$$

which is easily shown to have the general solution

$$u(t,x) = g(t-x) + h(t+x) \tag{2.8}$$

that is, a sum of traveling waves of arbitrary shapes moving in opposite directions at speed 1. We are interested only in the solution which moves away from the source. Therefore set $h \equiv 0$. The boundary condition (2.6) then yields $g'(t) = \frac{1}{2} f(t)$, or $g(t) = \frac{1}{2} F(t)$ where $F'(t) = f(t)$. Therefore, on $x > 0$

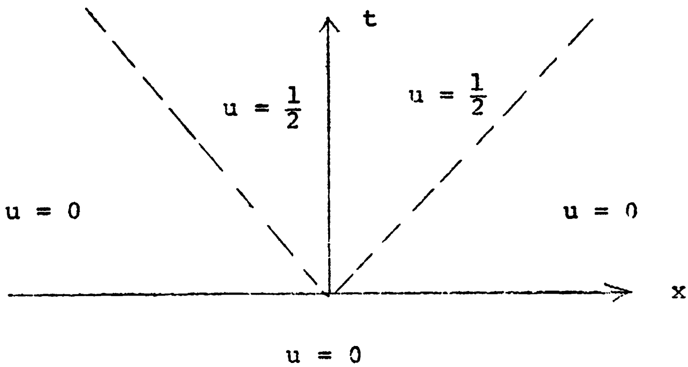
$$u(t,x) = \frac{1}{2} F(t-x)$$

and, extending this as an even function to $-\infty < x < \infty$:

(2.9) $$u(t,x) = \frac{1}{2} F(t-r) \quad , \quad r = |x|$$

It is interesting to specialize to the case where $f(t) = \delta(t)$. Then $F(t) = 1$ when $t > 0$, 0 otherwise, and we have

(2.10) $$u(t,x) = \frac{1}{2} \begin{Bmatrix} 1 & t > r \\ 0 & t < r \end{Bmatrix} \quad , \quad r = |x|$$



2. The Method of Descent.

In this section we study a family of radially symmetric functions of $x_1 \dots x_n$ which also depend upon a parameter k:

(2.11) $$\phi_n(x_1 \dots x_n ; k) = \Phi_n(r_n ; k)$$

where

$$r_n^2 = x_1^2 + \dots + x_n^2 \quad .$$

The members of this family are related to each other as follows:

$$(2.12)\qquad \phi_n(x_1 \ldots x_n;k) = \int_{-\infty}^{\infty} d\xi \cos k\xi \; \phi_{n+1}(x_1 \ldots x_n,\xi;0)$$

In the next section we will show that the solutions of the Klein-Gordon Equation form a family of functions with precisely this structure. Here, we derive formulae by means of which one can construct the entire family from the single function $\Phi_1(r;0)$.

Using the formula (2.12) twice, the second time with $k = 0$, we obtain

$$(2.13)\qquad \phi_n(x_1 \ldots x_n;k) = \int_{-\infty}^{\infty} d\xi \cos k\xi \int_{-\infty}^{\infty} d\eta \; \phi_{n+2}(x_1 \ldots x_n,\xi,\eta;0)$$

Rewrite (2.12) in polar form:

$$(2.14)\qquad \begin{aligned} \Phi_n(r;k) &= 2\int_0^{\infty} d\xi \cos k\xi \; \Phi_{n+1}(\sqrt{r^2+\xi^2};0) \\ &= 2\int_r^{\infty} \frac{RdR}{\sqrt{R^2-r^2}} \cos k\sqrt{R^2-r^2} \; \Phi_{n+1}(R;0) \end{aligned}$$

where we have used the change of variables $R^2 = r^2+\xi^2$, so that $RdR = \xi d\xi = \sqrt{R^2-r^2}\, d\xi$.

Similarly, rewrite (2.13) in polar form:

$$\Phi_n(r,k) = \int_0^{2\pi} d\theta \int_0^{\infty} \rho d\rho \cos (k\rho \sin \theta)\ \Phi_{n+2}(\sqrt{r^2+\rho^2};0)$$

(2.15)

$$= \int_r^{\infty} 2\pi R dR \Phi_{n+2}(R;0) J_o(k\sqrt{R^2-r^2})$$

where

(2.16) $$J_o(z) = \frac{1}{2\pi} \int_0^{2\pi} \cos (z \sin \theta) d\theta \quad .$$

Exercise: Show that repeated application of (2.14) yields (2.15).

In the special case k = 0, equations (2.14) and (2.15) take the form

(2.17) $$\Phi_n(r;0) = 2 \int_r^{\infty} \frac{RdR}{\sqrt{R^2-r^2}} \quad \Phi_{n+1}(r;0)$$

(2.18) $$\Phi_n(r;0) = \int_r^{\infty} 2\pi R dR \Phi_{n+2}(r,0)$$

The latter formula is easily inverted by differentiating with respect to r

$$\frac{\partial}{\partial r} \Phi_n(r;0) = -2\pi r \Phi_{n+2}(r,0)$$

(2.19) $$\Phi_{n+2}(r,0) = - \frac{1}{2\pi r} \frac{\partial}{\partial r} \Phi_n(r;0)$$

In fact, equations (2.17), (2.18) and (2.19) hold not only for $k = 0$ but for arbitrary fixed k. To see this, rewrite (2.13) as follows:

(2.20) $$\phi_n(x_1 \ldots x_n;k) = \int_{-\infty}^{\infty} d\eta \int_{-\infty}^{\infty} d\xi \cos k\xi \; \phi_{n+2}(x_1 \ldots x_n,\eta,\xi;0)$$

where ξ and η now appear in opposite order as arguments of ϕ_{n+2}. This makes no difference because of radial symmetry. But the second integral in (2.20) is equal to $\phi_{n+1}(x_1 \ldots x_n,\eta;k)$. Therefore

(2.21) $$\phi_n(x_1 \ldots x_n;k) = \int_{-\infty}^{\infty} d\eta \; \phi_{n+1}(x_1 \ldots x_n,\eta;k)$$

This is the recursive relation for fixed k. It has the same form for all k. Therefore we will have the following formulae, corresponding to (2.17), (2.18) and (2.19):

(2.22) $$\Phi_n(r;k) = 2\int_r^{\infty} \frac{RdR}{\sqrt{R^2-r^2}} \Phi_{n+1}(R;k)$$

(2.23) $$\Phi_n(r;k) = \int_r^{\infty} 2\pi RdR \; \Phi_{n+2}(R;k)$$

(2.24) $$\Phi_{n+2}(r,k) = -\frac{1}{2\pi r}\frac{\partial}{\partial r}\Phi_n(r;k)$$

(If this argument seems too indirect, one can check that these are consequences of (2.21). The manipulations will be the same as above.)

We are now in a position to construct the entire family $\{\Phi_n(r;k);\ n = 1,2,\ldots,$ and k arbitrary$\}$ from the single function $\Phi_1(r;0)$.

(2.25) $$\Phi_3(r;0) = -\frac{1}{2\pi r}\frac{\partial}{\partial r}\Phi_1(r;0)$$

(2.26) $$\Phi_2(r;k) = 2\int_r^\infty \frac{RdR}{\sqrt{R^2-r^2}}\cos k\sqrt{R^2-r^2}\ \Phi_3(R;0)$$

(2.27) $$\Phi_1(r;k) = \int_r^\infty 2\pi RdR\ J_o(k\sqrt{R^2-r^2})\ \Phi_3(R;0)$$

Finally, with $\Phi_1(r;k)$ and $\Phi_2(r;k)$ known we can construct $\Phi_n(r;k)$ by repeated application of the formula:

(2.28) $$\Phi_{n+2}(r;k) = -\frac{1}{2\pi r}\frac{\partial}{\partial r}\Phi_n(r;k)$$

3. Application of the Method of Descent to the Klein-Gordon Equation.

Consider the family of radially symmetric functions $\phi_n(t,x_1\ \ldots\ x_n;k) = \Phi_n(t,r_n;k)$ which are solutions of

(2.29) $$(\partial_t^2 - \Delta_n + k^2)\phi_n(t,x_1\ \ldots\ x_n;k) = f(t)\delta(x_1)\ \ldots\ \delta(x_n)$$

We want to show that (for each t) these functions have the same structure as the ϕ functions of the previous section.

First, we need the following identity:

$$\int_{-\infty}^{\infty} dx_{n+1}(-\Delta_{n+1}u(x_1 \ldots x_{n+1})) \cos kx_{n+1}$$

$$= \int_{-\infty}^{\infty} dx_{n+1}(-\Delta_n u(x_1 \ldots x_{n+1})) \cos kx_{n+1}$$

(2.3)

$$+ \int_{-\infty}^{\infty} dx_{n+1}(-\partial_{n+1}^2 u(x_1 \ldots x_{n+1})) \cos kx_{n+1}$$

$$= (-\Delta_n + k^2) \int_{-\infty}^{\infty} dx_{n+1} \cos kx_{n+1} u(x_1 \ldots x_{n+1})$$

Next, write (2.29) with k = 0 and n replaced by n+1:

(2.31)

$$(\partial_t^2 - \Delta_n)\phi_{n+1}(t,x_1 \ldots x_{n+1};0) = f(t)\delta(x_1) \ldots \delta(x_n)\delta(x_{n+1})$$

Multiply both sides of (2.31) by $\cos kx_{n+1}$ and integrate with respect to x_{n+1}. Using (2.30) we obtain

(2.32)

$$(\partial_t^2 - \Delta_n + k^2) \int_{-\infty}^{\infty} dx_{n+1} \cos kx_{n+1}\phi_{n+1}(t,x_1 \ldots x_{n+1};0) = f(t)\delta(x_1) \ldots \delta(x_n)$$

Comparison with (2.29) shows that

$$\phi_n(t,x_1 \ldots x_n;k) = \int_{-\infty}^{\infty} dx_{n+1} \cos kx_{n+1}\phi_{n+1}(t,x_1 \ldots x_{n+1};0) \tag{2.33}$$

which is precisely the required structure.

We are now ready to apply the method of construction outlined in the previous section. We have solved the one-dimensional wave equation in Section 1. In the present notation the result is

$$\Phi_1(t,r;0) = \frac{1}{2} F(t-r) \quad \text{where} \qquad F'(t) = f(t) \tag{2.34}$$

Therefore, applying formulae (2.25)-(2.27) we have

$$\Phi_3(t,r;0) = \frac{1}{4\pi r} f(t-r) \tag{2.35}$$

$$\Phi_2(t,r;k) = \frac{1}{2\pi} \int_r^{\infty} \frac{dR}{\sqrt{R^2-r^2}} \cos (k\sqrt{R^2-r^2}) f(t-R) \tag{2.36}$$

$$\Phi_1(t,r;k) = \frac{1}{2} \int_r^{\infty} dR J_o(k\sqrt{R^2-r^2}) f(t-R) \tag{2.37}$$

where J_o is given by (2.16). In particular, for $k = 0$ (The Wave Equation), we have:

$$\Phi_2(t,r;0) = \frac{1}{2\pi} \int_r^{\infty} \frac{dR}{\sqrt{R^2-r^2}} f(t-R) \tag{2.38}$$

$$\Phi_1(t,r;0) = \frac{1}{2}\int_r^\infty dR f(t-R) \tag{2.39}$$

This last result is equivalent to the results of Section 1, since

$$\int_r^\infty dR f(t-R) = \int_{-\infty}^{t-r} f(t')dt' = F(t-r) \tag{2.40}$$

<u>Remark</u>: Each of these problems also has a solution which represents an incoming wave. These waves do not appear here because they were excluded from the solution of the Wave Equation in Section 1.

4. Laplace's Equation.

In 3-space dimensions we can obtain the fundamental solution of Laplace's Equation from that of the Wave Equation as follows.

Let

$$(\partial_t^2 - \Delta_3)u(t,x_1,x_2,x_3) = f(t)\delta(x_1)\delta(x_2)\delta(x_3) \tag{2.41}$$

we have shown above that

$$u(t,x_1,x_2,x_3) = U(t,r) = \frac{1}{4\pi r} f(t-r) \tag{2.42}$$

where $r^2 = x_1^2 + x_2^2 + x_3^2$. Now consider the special case

(2.43) $$f(t) = \begin{cases} 1 & t > 0 \\ 0 & t < 0 \end{cases}$$

Then

(2.44) $$u(t,x_1,x_2,x_3) = \begin{cases} 1/4\pi r, & t > r \\ 0 \quad , & t < r \end{cases}$$

and

(2.45) $$\lim_{t\to\infty} u(t,x_1,x_2,x_3) = \frac{1}{4\pi r}$$

In the open spherical ball $r < t$, the result we have just found implies that

(2.46) $$-\Delta_3\left(\frac{1}{4\pi r} \right) = \delta(x_1)\delta(x_2)\delta(x_3)$$

On the other hand, we can take t as large as we like, so (2.46) must hold for all r, and

$$\frac{1}{4\pi r} = \frac{1}{4\pi} \frac{1}{\sqrt{x_1^2+x_2^2+x_3^2}}$$

is the fundamental solution of Laplace's equation in three space dimensions.

In two space dimensions we have to be more careful. Suppose we try the same method as above. From (2.38) we will have

$$U(t,r) = \frac{1}{2\pi} \int_r^\infty \frac{dR}{\sqrt{R^2-r^2}} \begin{Bmatrix} 1 & t > R \\ 0 & t < R \end{Bmatrix}$$

(2.47)
$$= \frac{1}{2\pi} \int_r^t \frac{dR}{\sqrt{R^2-r^2}}$$

$$= \frac{1}{2\pi} \int_1^{t/r} \frac{d\mu}{\sqrt{\mu^2-1}}$$

Now

(2.48)
$$\lim_{t\to\infty} U(t,r) = \frac{1}{2\pi} \int_1^\infty \frac{d\mu}{\sqrt{\mu^2-1}} = \infty$$

since $1/\sqrt{\mu^2-1} > 1/\mu$ when $\mu > 1$. On the other hand

(2.49)
$$\frac{\partial U}{\partial r}(t,r) = \frac{1}{2\pi}\left(-\frac{t}{r^2}\right) \frac{1}{\sqrt{\frac{t^2}{r^2} - 1}}$$

and

(2.50)
$$\lim_{t\to\infty} \frac{\partial U}{\partial r}(t,r) = -\frac{1}{2\pi r}$$

which suggests that

$$-\frac{1}{2\pi} \log r$$

is the fundamental solution of Laplace's Equation in two dimensions (since $\frac{\partial}{\partial r} \log r = \frac{1}{r}$).

5. The Heat Equation.

Let $v(t,x_1 \ldots x_n) = v(t,\underline{X})$ be the soultion of

(2.51) $$(\partial_t - \Delta)v(t,\underline{X}) = f(t)\delta(x_1) \ldots \delta(x_n)$$

and let $v_c(t,\underline{X})$ be the solution of

(2.52) $$(\frac{1}{c^2}\partial_t^2 + \partial_t - \Delta)v_c(t,\underline{X}) = f(t)\delta(x_1) \ldots \delta(x_n)$$

We expect that

(2.53) $$v(t,\underline{X}) = \lim_{c\to\infty} v_c(t,\underline{X})$$

Let

(2.54) $$v_c(t,\underline{X}) = u_c(t,\underline{x})e^{-\lambda t}$$

(2.55) $$\partial_t v_c = (\partial_t - \lambda)u_c e^{-\lambda t}$$

(2.56) $$\partial_t^2 v_c = (\partial_t^2 - 2\lambda\partial_t + \lambda^2)u_c e^{-\lambda t}$$

Choose $\lambda = c^2/2$. Then

(2.57) $$(\frac{1}{c^2}\partial_t^2 + \partial_t - \Delta)v_c = (\frac{1}{c^2}\partial_t^2 - \Delta - \frac{c^2}{4})u_c e^{-\lambda t}$$

And u_c satisfies

(2.58) $$\begin{aligned}(\frac{1}{c^2}\partial_t^2 - \Delta - \frac{c^2}{4})u_c(t,\underline{X}) &= f(t)e^{\lambda t}\delta(x_1) \ldots \delta(x_n) \\ &= f(t)e^{(c^2/2)t}\delta(x_1) \ldots \delta(x_n)\end{aligned}$$

Let

(2.59) $$u_c(t,\underline{X}) = \bar{u}_c(\tau,\underline{X}) \quad \text{where} \quad \tau = ct$$

Then $\bar{u}_c$ satisfies

(2.60) $$(\partial_\tau^2 - \Delta - \frac{c^2}{4})\bar{u}_c(\frac{\tau}{c})e^{c\tau/2}\delta(x_1) \ \ldots \ \delta(x_n)$$

At this point we specialize to two dimensions and use (2.36) with $k = ic/2$ and with $f(\frac{\tau}{c})e^{c\tau/2}$ instead of $f(t)$. We obtain

(2.61) $$\bar{U}_c(\tau,r) = \frac{1}{2\pi}\int_r^\infty \frac{dR}{\sqrt{R^2-r^2}} \cos\left(\frac{ic}{2}\sqrt{R^2-r^2}\right) f\left(\frac{\tau-R}{c}\right)e^{\frac{c}{2}(\tau-R)}$$

Then

(2.62) $$U_c(t,r) = \frac{1}{2\pi}\int_r^\infty \frac{dR}{\sqrt{R^2-r^2}} \cosh\left(\frac{c}{2}\sqrt{R^2-r^2}\right) f\left(t-\frac{R}{c}\right)e^{\frac{c^2}{2}(t-\frac{R}{c})}$$

$$V_c(t,r) = U_c(t,r)e^{-\frac{c^2}{2}t}$$

(2.63) $$= \frac{1}{2\pi}\int_r^\infty \frac{dR \cosh\frac{c}{2}\sqrt{R^2-r^2}}{\sqrt{R^2-r^2}} f\left(t-\frac{R}{c}\right)e^{-\frac{c^2}{2}\frac{R}{c}}$$

Let $R = ct'$. Then

(2.64) $$V_c(t,r) = \frac{1}{2\pi}\int_{r/c}^\infty \frac{c\,dt' \cosh\left(\frac{c}{2}\sqrt{c^2t'^2-r^2}\right)}{\sqrt{c^2t'^2-r^2}} f(t-t')e^{-\frac{c^2}{2}t'}$$

$$v(t,r) = \lim_{c\to\infty} v_c(t,r)$$

(2.65)

$$= \int_0^\infty dt' f(t-t') \frac{1}{2\pi t'} \lim_{c\to\infty} \left[e^{-\frac{c^2}{2}t'} \cosh \left(\frac{c^2}{2}t' \sqrt{1 - \frac{r^2}{c^2 t'^2}}\right) \right]$$

But

$$\lim_{c\to\infty} e^{-\frac{c^2}{z}t'} \cosh \frac{c^2}{z} t' \sqrt{1 - \frac{r^2}{c^2 t'^2}}$$

(2.66)

$$= \lim_{c\to\infty} \frac{1}{2} e^{-\frac{c^2}{z}t'} e^{+\frac{c^2}{z}t'\left(1 - \frac{1}{2}\frac{r^2}{c^2 t'^2}\right)}$$

$$= \frac{1}{2} e^{-r^2/4t'}$$

Therefore

(2.67) $$v(t,r) = \lim_{c\to\infty} v_c(t,r) = \int_0^\infty dt' f(t-t') \frac{1}{4\pi t'} e^{-r^2/4t'}$$

<u>Exercise</u>: We have just found the solution to the Heat Equation in two dimensions. Use this solution to construct the corresponding solution in n dimensions.

Exercise: Consider the system of equations:

$$\frac{\partial u}{\partial t} + c \frac{\partial u}{\partial x} = \frac{1}{2} \nu (v-u)$$

$$\frac{\partial v}{\partial t} - c \frac{\partial v}{\partial x} = \frac{1}{2} \nu (u-v)$$

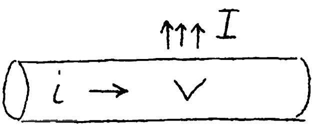
Derive a second order equation which is satisfied by $\phi = u+v$. What does this equation become in the limit $c \to \infty$, $\nu \to \infty$, $\nu = c^2$.

Give an interpretation of these results in terms of random walks.

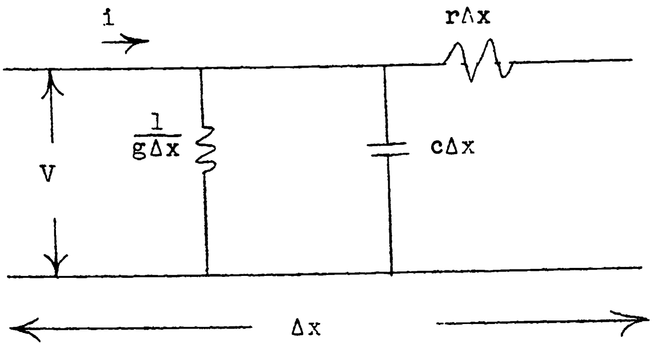
III. Input to a Neuron: The Dendritic Tree [1]

A typical neuron receives its input at selected sites (synapses) along a tree of dendrites which originates at the cell body. The input events are caused by release of a chemical transmitter at the synapse. This modifies the conductance of the post-synaptic membrane briefly, resulting in an injection of current (if the membrane potential is not at equilibrium). To a first approximation one may consider the injected current as given, but a more refined analysis shows that it depends on the local membrane potential. This makes possible non-linear interactions between nearby synaptic sites, and it means that we need to calculate the response to a synaptic event not only at the cell body, but also throughout the dendridic tree if we want to determine its interaction with subsequent synaptic events.

1. Equations of a leaky cable.



[1] This lecture is based on the following paper: Rinzel, J. and W. Rall: Transient response in a dendridic neuron model for current injected at one branch, Biophysical J., 14, 1973, pp. 759-790.



(3.1) $$ri = -\frac{\partial V}{\partial x}$$

(3.2) $$I = c\,\frac{\partial V}{\partial t} + gV$$

(3.3) $$\frac{\partial i}{\partial x} + I = 0$$

where i = axial current

I = current per unit length of membrane

V = internal voltage (external voltage = 0)

r = resistance per unit length (internal)

c = capacitance per unit length of membrane

g = conductance per unit length of membrane

When considering fibers of different radius a, it is useful to relate the quantities r, c, g to radius. Let

ρ_o = resistivity of internal medium

C_o = capacitance per unit area of membrane

G_o = conductance per unit area of membrane.

Then

$$(3.4)\qquad \begin{aligned} r &= \rho_o/\pi a^2 \\ c &= C_o 2\pi a \\ g &= G_o 2\pi a \end{aligned}$$

From equations (3.1)-(3.3) we have

$$(3.5)\qquad \frac{c}{g}\frac{\partial V}{\partial t} - \frac{1}{rg}\frac{\partial^2 V}{\partial x^2} + V = 0$$

Let

$$(3.6)\qquad T_o = \frac{c}{g} = \frac{C_o}{G_o}$$

$$(3.7)\qquad X_o^2 = \frac{1}{rg} = \frac{a}{2\rho_o G_o}$$

If we now choose T_o as our unit of time, and X_o as our unit of length (3.5) becomes

$$(3.8)\qquad \frac{\partial V}{\partial t} - \frac{\partial^2 V}{\partial x^2} + V = 0$$

2. Fundamental solution of the cable equations.

Let $\phi_n(t,r_n,k)$ be the solution of

$$(3.9)\qquad (\partial_t - \Delta_n + k^2)\phi_n(t,r_n,k) = f(t)\delta(x_1)\ \ldots\ \delta(x_n)$$

where

$$r_n^2 = x_1^2 + \ldots + x_n^2 \quad .$$

In Lecture II we showed that:

$$\phi_2(t,r,0) = \int_0^\infty dt' f(t-t') \frac{1}{4\pi t'} e^{-r^2/4t'}$$

Therefore, by the method of descent, we shall have

$$(3.10) \quad \phi_1(t,x,k) = \int_{-\infty}^\infty dy \cos ky \int_0^\infty dt' f(t-t') \frac{1}{4\pi t'} e^{-r^2/4t'}$$

where $r^2 = x^2+y^2$. Thus

$$(3.11) \quad \phi_1(t,x,k)$$
$$= \int_0^\infty dt' f(t-t') \frac{e^{-x^2/4t'}}{4\pi t'} \int_{-\infty}^\infty \cos ky \, e^{-y^2/4t'} \, dy$$

It remains to evaluate:

$$\int_{-\infty}^\infty \cos ky e^{-y^2/4t'} \, dy = \int_{-\infty}^\infty \exp(iky - \frac{y^2}{4t'}) \, dy$$

$$(3.12) \quad \begin{aligned} &= e^{-k^2t'} \int_{-\infty}^\infty \exp(k^2t' + iky - \frac{y^2}{4t'}) \, dy \\ &= e^{-k^2t'} \int_{-\infty}^\infty e^{-(y-2ikt')^2/4t'} \, dy \\ &= e^{-k^2t'} \int_{-\infty}^\infty e^{-y^2/4t'} \, dy \quad . \end{aligned}$$

But

$$(3.13) \quad \int_{-\infty}^\infty e^{-y^2/4t'} \, dy = \sqrt{4\pi t'}$$

Therefore:

(3.14)
$$\phi_1(t,x,k) = \int_0^\infty dt' f(t-t') \frac{1}{\sqrt{4\pi t'}} \exp(-(k^2 t' + \frac{x^2}{4t'}))$$

Remark: When $f(t) = \delta(t)$ we obtain the Gaussian distribution

(3.15)
$$\phi_1(t,x,k) = \frac{1}{\sqrt{4\pi t'}} \exp(-(k^2 t' + \frac{x^2}{4t'}))$$

Setting $k = 0$ we obtain the fundamental solution of the heat equation in one dimension

(3.16)
$$\phi_1(t,x,0) = \frac{1}{\sqrt{4\pi t'}} e^{-x^2/4t'}$$

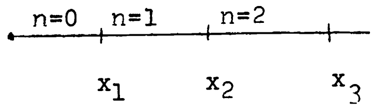
We note that $\phi_1(t,x,k) = \exp(-k^2 t)\, \phi_1(t,x,0)$. In fact the cable equation can be interpreted as a random walk in one dimension with a probability of absorbtion per unit time equal to k^2. Note that

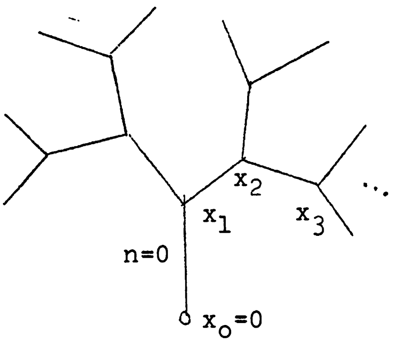
(3.17)
$$\int_{-\infty}^{\infty} \phi_1(t,x,0)\,dx = 1$$

while

(3.18)
$$\int_{-\infty}^{\infty} \phi_1(t,x,k)\,dx = e^{-k^2 t}$$

3. Equations for an infinite symmetrical tree.





Let x measure distance from the origin.

Let (n,k) be the $k^{\underline{th}}$ branch of the $n^{\underline{th}}$ generation.

$$n = 0,1,2,\ \ldots$$

$$k = 0,1,2,\ \ldots,\ (2^n-1) \quad .$$

Let V_{nk} $x_{n-1} \le x \le x_n$ be the voltage in branch (n,k).

Note that the descendents of (n,k) are:

$$(n+1,\ 2k)$$

$$(n+1,\ 2k+1)$$

The equation for the $k^{\underline{th}}$ branch in the $n^{\underline{th}}$ generation is:

$$(3.19) \qquad \left(\frac{c_n}{g_n}\,\partial_t - \frac{1}{r_n g_n}\,\partial_x^2 + 1\right)V_{nk}(t,x) = 0$$

And the boundary conditions are

(3.20) $$V_{nk}(x_{n+1}) = V_{n+1,2k}(x_{n+1}) = V_{n+1,2k+1}(x_{n+1})$$

(3.21) $$\frac{1}{r_n}\frac{\partial V_{nk}}{\partial x}(x_{n+1}) = \frac{1}{r_{n+1}}\left\{\frac{\partial V_{n+1,2k}}{\partial x}(x_{n+1}) + \frac{\partial V_{n+1,2k+1}}{\partial x}(x_{n+1})\right\}$$

Make these equations non-dimensional in space and time by choosing

(3.22) $$T_o = \frac{c_n}{g_n} = \frac{C_o}{G_o} \quad \text{independent of } n$$

(3.23) $$X_n^2 = \frac{1}{r_n g_n} = \frac{a_n}{2\rho_o G_o} \quad \text{dependent on } n \quad .$$

Then let

(3.24) $$t = T_o t'$$

(3.25) $$(x-x_n) = X_n(x'-x_n') \qquad x_n \leq x \leq x_{n+1}$$

(3.26) $$V_{nk}(t,x) = V_{nk}'(t',x')$$

With these changes of variable, but dropping the 's, the equations become:

(3.27) $$(\partial_t - \partial_x^2 + 1)V_{nk}(t,x) = 0$$

(3.28) $$V_{nk}(x_{n+1}) = V_{n+1,2k}(x_{n+1}) = V_{n+1,2k+1}(x_{n+1})$$

(3.29)
$$\frac{r_{n+1}X_{n+1}}{r_nX_n}\frac{\partial V_{nk}}{\partial x}(x_{n+1}) = \frac{\partial V_{n+1,2k}}{\partial x}(x_{n+1}) + \frac{\partial V_{n+1,2k+1}}{\partial x}(x_{n+1})$$

There is a special kind of tree which can be reduced to an equivalent cylinder. To see this, sum the equations over $k = 0,1,2,\ldots(2^n-1)$ and divide by 2^n. One obtains:

(3.30)
$$(\partial_t - \partial_x^2 + 1)\frac{1}{2^n}\sum_{k=0}^{2^n-1} V_{nk} = 0$$

(3.31)
$$\frac{1}{2^n}\sum_{k=0}^{2^n-1} V_{nk}(x_{n+1}) = \frac{1}{2^n}\sum_{k=0}^{2^n-1} V_{n+1,2k}(x_{n+1})$$
$$\frac{1}{2^n}\sum_{k=0}^{2^n-1} V_{nk}(x_{n+1}) = \frac{1}{2^n}\sum_{k=0}^{2^n-1} V_{n+1,2k+1}(x_{n+1})$$

$$\frac{1}{2^n}\sum_{k=0}^{2^n-1} V_{nk}(x_{n+1}) = \frac{1}{2^{n+1}}\sum_{k=0}^{2^{n+1}-1} V_{n+1,k}(x_{n+1})$$

(3.32)
$$\left(\frac{r_{n+1}X_{n+1}}{r_nX_n}\right)\frac{1}{2^n}\sum_{k=0}^{2^n-1}\frac{\partial V_{nk}}{\partial x}(x_{n+1}) = \frac{1}{2^n}\sum_{k=0}^{2^{n+1}-1}\frac{\partial V_{n+1,k}}{\partial x}(x_{n+1})$$
$$\left(\frac{1}{2}\frac{r_{n+1}X_{n+1}}{r_nX_n}\right)\frac{1}{2^n}\sum_{k=0}^{2^n-1}\frac{\partial V_{nk}}{\partial x}(x_{n+1}) = \frac{1}{2^{n+1}}\sum_{k=0}^{2^{n+1}-1}\frac{\partial V_{n+1,k}}{\partial x}(x_{n+1})$$

Let

$$\bar{V}_n = \frac{1}{2^n} \sum_{k=0}^{2^n-1} V_{nk} \tag{3.33}$$

Then

$$(\partial_t - \partial_x^2 + 1)\bar{V}_n = 0 \tag{3.34}$$

$$\bar{V}_n(x_{n+1}) = \bar{V}_{n+1}(x_{n+1}) \tag{3.35}$$

$$\left(\frac{1}{2} \frac{r_{n+1}X_{n+1}}{r_n X_n}\right) \frac{\partial \bar{V}_n}{\partial x} (x_{n+1}) = \frac{\partial \bar{V}_{n+1}}{\partial x} (x_{n+1}) \tag{3.36}$$

In the special case

$$\frac{1}{2} \frac{r_{n+1}X_{n+1}}{r_n X_n} = 1 \quad , \tag{3.37}$$

equations (3.35) and (3.36) merely assert the continuity of $\bar{V}$ and $\partial_x \bar{V}$ at the points x_n. This is already asserted by the differential equation if we regard these points as interior points of the domain of (3.34). Thus we have simply

$$(\partial_t - \partial_x^2 + 1)\bar{V}(t,x) = 0 \qquad \text{on} \quad x > 0 \tag{3.38}$$

with a boundary condition at $x = 0$ which remains to be imposed.

The condition (3.37) can be rewritten as follows

$$1 = \frac{1}{2}\frac{r_{n+1}X_{n+1}}{r_n X_n} = \frac{1}{2}\frac{r_{n+1}}{r_n}\sqrt{\frac{r_n g_n}{r_{n+1}g_{n+1}}} \tag{3.39}$$

$$= \frac{1}{2}\sqrt{\frac{r_{n+1}g_n}{r_n g_{n+1}}} = \frac{1}{2}\sqrt{\frac{a_n^3}{a_{n+1}^3}}$$

$$\frac{a_{n+1}}{a_n} = (\tfrac{1}{2})^{2/3} \tag{3.40}$$

where a_n is the radius of a branch of the $n^{\underline{th}}$ generation.

4. Current Injection

Pick a point x* in branch NK and inject current at rate f(t). In the dimensional form of the equations this gives rise to a boundary condition:

$$-\frac{1}{r_N}\frac{\partial V_{NK}}{\partial x}(x^*-) + f(t) = -\frac{1}{r_N}\frac{\partial V_{NK}}{\partial x}(x^*+) \tag{3.41}$$

Equivalently, one can rewrite (3.19) as follows:

$$\left(\frac{c_n}{g_n}\partial_t - \frac{1}{r_n g_n}\partial_x^2 + 1\right)V_{nk}(t,x) = \frac{1}{g_n} f(t)\delta(x-x^*)\delta_{Nn}\delta_{Kk} \tag{3.42}$$

The non-dimensional form of this (corresponding to 3.27) will be

$$(\partial_t - \partial_x^2 + 1)V_{nk}(t,x) = \frac{1}{g_n X_n} f(t)\delta(x-x^*)\delta_{Nn}\delta_{Kk} \tag{3.43}$$

The factor g_nX_n (with dimensions of conductance — only x,t have been made non-dimensional, but V is still in volts and f(t) is in amps) can be rewritten as follows:

$$g_nX_n = 2\pi a_n G_o \sqrt{\frac{a_n}{2\rho_o G_o}} = 2\pi \sqrt{\frac{G_o}{2\rho_o}}\, a_n^{3/2} \tag{3.44}$$

On the other hand, from (3.40) we have $a_n^{3/2} = a_o^{3/2}\, 2^{-n}$. Therfore,

$$g_nX_n = \frac{1}{2^n R} \quad \text{where} \quad \frac{1}{R} = 2\pi \sqrt{\frac{G_o}{2\rho_o}}\, a_o^{3/2} \tag{3.45}$$

and R has dimensions of ohms. (It is the input resistance for the tree of infinite length as seen from the cell body x = 0). Thus (3.43) becomes

$$(\partial_t - \partial_x^2 + 1)V_{nk}(t,x) = R2^n f(t)\delta(x-x^*)\delta_{Nn}\delta_{Kk} \tag{3.46}$$

As before, summing over k and dividing by 2^n we obtain

$$(\partial_t - \partial_x^2 + 1)\overline{V}(t,x) = Rf(t)\delta(x-x^*) \tag{3.47}$$

For a boundary condition at x = 0 take $\frac{\partial \overline{V}}{\partial x} = 0$ (sealed end, no current flow at x = 0). This boundary condition will be automatically satisfied if we extend the domain to $-\infty < x < \infty$ and put an image source at x = x*. Then

(3.48) $$(\partial_t - \partial_x^2 + 1)\overline{V}(t,x) = Rf(t)[\delta(x-x^*) + \delta(x+x^*)]$$

The solution is

(3.49) $$\overline{V}(t,x) = R\int_0^\infty dt' f(t-t') \frac{e^{-t'}}{\sqrt{4\pi t'}}\left[\exp\left(-\frac{(x-x^*)^2}{4t'}\right) + \exp\left(-\frac{(x+x^*)^2}{4t'}\right)\right]$$

As an important special case, consider the solution at the cell body ($x=0$) in response to a δ-function input. It is:

(3.50) $$\overline{V}_\delta(t,0) = 2R\,\frac{e^{-(t + \frac{x^*}{4t})}}{\sqrt{4\pi t}}$$

<u>Exercise</u>: Approximate $\overline{V}_\delta(t,0)$ by a function of the form

$$A\exp(-\sigma(t-t_p)^2)$$

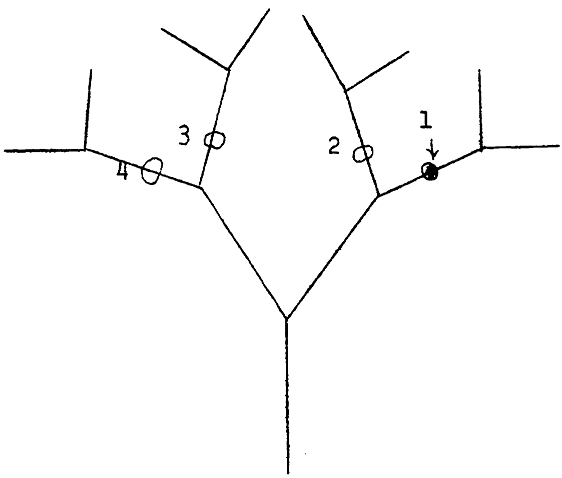
when x^* is large. To do this, take the log of $\overline{V}_\delta$ and expand it about the time t_p when $\overline{V}_\delta$ achieves its maximum. How do A, σ, t_p depend on x^* when x^* is large?

<u>Exercise</u>: Instead of the boundary condition $\frac{\partial\overline{V}}{\partial x} = 0$ at $x = 0$, consider the condition $\overline{V} = 0$ at $x = 0$. Solve this problem by a method like the one used above and find the corresponding formula for $\frac{\partial\overline{V}}{\partial x}(t,0)$. (This is the current which pours into the origin when the cell body is held at zero voltage.)

5. Unsymmetrical component of the response

We have found the symmetrical component $\bar{V}$ of the response to a single injection of current at a synapse. This depends only on the non-dimensional distance of the synapse from the cell body. At the cell body itself $\bar{V} = V$, so we have found the response. In the rest of the dendritic tree no such formula holds (except for a symmetrical distribution of inputs). Nevertheless, we can find the response by superposition of symmetrically and antisymmetrically distributed inputs.

We will illustrate this procedure for a case where the input occurs in branch n = 2, k = 1. The generalization to arbitrary n,k will be evident.



The problem we want to solve is

$$(\partial_t - \partial_x^2 + 1)V_{nk}(t,x) = R2^2 f(t)\delta(x-x^*)\delta_{1k}$$

Write δ_{1k} as a vector

$$\delta_{1k} = (1,0,0,0)$$

and note that

$$\delta_{1k} = \frac{1}{4}\left[(1,1,1,1) + (1,1,-1,-1) + 2\cdot(1,-1,0,0)\right]$$

This means that we can write

$$V_{nk} = \frac{1}{4}\left[V_{nk}^{(1,1,1,1)} + V_{nk}^{(1,1,-1,-1)} + 2V_{nk}^{(1,-1,0,0)}\right]$$

But each of these problems can be solved. $V_{n,k}^{(1,1,1,1)}$ is the solution for symmetrical imputs which has been found above. In $V_{nk}^{(1,1,-1,-1)}$ we will have $V(x_1) = 0$ by symmetry. This means that we can solve the clamped symmetrical problem (see problem, above) on the half-tree $x > x_1$, $k \leq (2^{n-1}-1)$. Similarly in $V_{nk}^{(1,-1,0,0)}$ we will have $V(x_2) = 0$ and can solve the clamped symmetrical problem on the quarter-tree $x > x_2$, $k \leq (2^{n-2}-1)$. Proceeding in this way we can find the solution for a single input.

<u>Exercise</u>: Carry out this construction and find $V_{2k}(x^*)$ for $k = 1,2,3,4$. That is, find the response at the corresponding points in other branches to an input applied at c^*. For simplicity, let $x_n = n$, so that $2 \leq x^* \leq 3$.

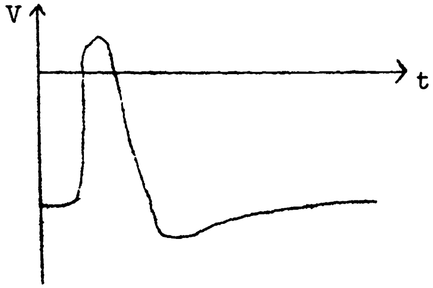
6. Random walk interpretation.

The equations for the symmetrical dendritic tree have the following interpretation. At $t = 0$ a particle is introduced somewhere along the tree. It then proceeds to do a random walk along the branches. The condition

$$\frac{a_{n+1}}{a_n} = \left(\frac{1}{2}\right)^{2/3}$$

insures that when it encounters a branch it is as likely to move toward the origin as away from the origin. If it moves away, it has equal probability of entering the two branches available to it. If we describe the particle by the trajectory $x(t)$ then the condition $a_{n+1}/a_n = (1/2)^{2/3}$ makes these trajectories uninfluenced by the branching. Also, once a particle has entered branch nk, it no longer distinguishes among the descendents of nk and is equally likely to be found in any of them which are consistent with its current value of x. Moreover, the particle has a finite probability of disappearing per unit time. If it does so, its trajectory terminates. In this interpretation, the voltage is proportional to the probability of finding the particle at a given location.

IV. Equations of the Nerve Impulse



The output of a neuron consists of a discrete sequence of pulses which propagate along the nerve axon. The waveform and amplitude of these pulses is constant, so that information can only be transmitted by means of their relative timing. In general, a stronger stimulus is coded as a higher frequency of nerve impulses.

In 1952, Hodgkin and Huxley [1] introduced a system of equations which describe the propagation of these signals along the nerve axon. Their equations can be written as follows:

$$c \frac{\partial V}{\partial t} = \frac{1}{r} \frac{\partial^2 V}{\partial x^2} + I_{ion} \tag{4.1}$$

where c = membrane capacitance per unit length

r = axial resistance per unit length

V = membrane voltage

I_{ion} = ionic current through the membrane

and where

$$I_{ion} = \bar{g}_{Na} m^3 h (V - E_{Na}) + \bar{g}_K n^4 (V - E_K) + \bar{g}_L (V - E_L) \tag{4.2}$$

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[1] Hodgkin and Huxley: A quantitive description of membrane current and its application to conduction and excitation in nerve. J. Physiol. 117, 500 (1952).

$$
(4.3) \qquad \begin{cases} \frac{\partial m}{\partial t} = \alpha_m(V)(1-m) - \beta_m(V)m \\ \frac{\partial n}{\partial t} = \alpha_n(V)(1-n) - \beta_n(V)n \\ \frac{\partial h}{\partial t} = \alpha_h(V)(1-h) - \beta_h(V)h \end{cases}
$$

In these equations the subscripts Na, K, L refer to Sodium, Potassium, and Leakage, respectively. The quantities E_{Na}, E_K, E_L give the equilibrium potential for each ion. The quantities $\bar{g}_{Na}$, $\bar{g}_K$, $\bar{g}_L$ give the conductance per unit length for a particular ion when all of the channels specific to that ion are open. The dimensionless parameters m, n, h can be thought of as controlling the instantaneous number of channels available. These quantities are confined to the interval (0,1) and obey first order equations in which the parameters α, β are functions of voltage. Qualitatively, m and n are turned on by increasing voltage, while h is turned off. The time scales are such that m changes rapidly while n, h change slowly.

The complexity of the Hodgkin-Huxley equations is such that the introduction of simpler models is advisable. A particularly attractive idea is to construct a model in which the equations are piece-wise linear. For example, the membrane potential might satisfy one set of linear equations when $V < a$, and another when $V > a$. In such a case we might hope to construct solutions by solving the two linear systems and matching the two solutions along the curve in the (x-t) plane where V = a. Such a model , introduced by H. McKean, has been extensively studied by Rinzel and Keller [2], who have determined all of its pulse shape and periodic traveling wave solutions and have also analyzed the stability of these solutions. Their model may be written as follows:

$$(4.4)\qquad \begin{cases} u_t = u_{xx} - u + m - w \\ m = \begin{cases} 1 & u > a \\ 0 & u < a \end{cases} \\ w_t = bu \end{cases}$$

In these Notes we introduce a slightly different model:

$$(4.5)\qquad \begin{cases} \varepsilon u_t = \varepsilon^2 u_{xx} - u + a_1 m(1-n) - a_2 n \\ m = \begin{cases} 1 & u > a \\ 0 & u < a \end{cases} \\ n_t = m-n \end{cases}$$

With $a_2 = 0$, this model was proposed by R. Miller [3]. The motivation for this model in terms of the Hodgkin-Huxley equations is as follows: The parameters m and n have the same meaning as in the Hodgkin-Huxley equations, while (1-n)

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2 Rinzel, J., and J.B. Keller: Traveling wave solutions of a nerve conduction equation. Biophysical J. 13, 1313 (1973).

3 Miller, R. Thesis (Dept. of Math.) University of California at Berkeley (in preparation).

corresponds to h. The term $a_1m(1-n)$ corresponds to the Na-current, $-a_2n$ corresponds to the K-current, and $-u$ corresponds to the leakage current. The parameter a is the threshhold, or the voltage at which the Na-current turns on. Once the Na-current turns on, it slowly turns itself off through the (1-n) factor while the K-current turns on because of the n factor The ε in the equations makes explicit the fact that the time constant associated with charging the membrane is much less than the time constant associated with the dynamics of n. We have chosen the latter time constant as our unit of time. The ε^2 in front of the u_{xx} term is introduced by choosing an appropriate unit of length. With these units of time and length the pulse will have finite duration and travel at a finite speed even in the limit $\varepsilon \to 0$.

Our analysis of the model (4.5) will proceed as follows. First, we find an expression for a traveling pulse solution of these equations following the methods of Rinzel and Keller (cited above). The constants in this expression can be evaluated explicitly in the limit $\varepsilon \to 0$. In this limit the front and back of the wave uncouple from each other in an interesting way, as has been shown for traveling wave solutions of a different model by Casten, Cohen and Lagerstrom [4]. In

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[4] Casten, R., H. Cohen, and P. Lagerstrom: Perturbation analysis of an approximation to Hodgkin-Huxley theory. Quart. appl. math., 32, 365 (1975).

particular, the boundary conditions at the front of the wave determine the propagation speed, while the conditions at the back (together with the propagation speed) determine the speed of the pulse.

This observation motivates the next development, in which we depart from the context of traveling waves and consider the full system of partial differential equations (4.5) in the limit $\varepsilon \to 0$. We will derive a formula for the velocity of a front in these circumstances. This formula remains valid even when the front does not have a constant velocity, that is, when the trajectory of the front is a curve in the (x,t) plane. (It also remains valid in inhomogeneous media.) We use this result to find the solution of an initial value problem in the limit $\varepsilon \to 0$ and to show how the traveling wave solution evolves out of the initial conditions. These results on the non-traveling wave case are believed to be new.

1. The Traveling pulse.

Consider the system:

$$\varepsilon u_t = \varepsilon^2 u_{xx} - u + a_1 m(1-n) - a_2 n \tag{4.6}$$

$$m = \begin{cases} 1 & u > a \\ 0 & u < a \end{cases} \tag{4.7}$$

$$n_t = m-n \tag{4.8}$$

Look for a solution of the form:

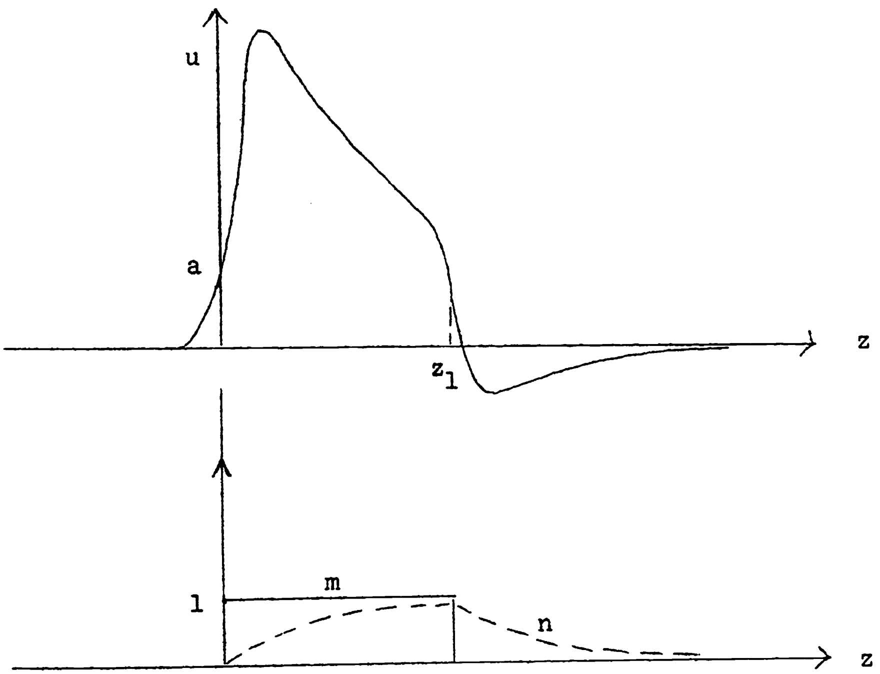
(4.9) $$u(x,t) = u_c(z)$$

(4.10) $$n(x,t) = n_c(z)$$

where

(4.11) $$z = x+ct \ , \qquad c > 0$$

Define the origin of z so that $u_c(0) = a$ and define $z_1 > 0$ by $u_c(z_1) = a$. The solution we seek is a wave traveling to the left which looks like this:



The ordinary differential equations satisfied by $u_c(z)$, $n_c(z)$ are

$$0 = \varepsilon^2 u_c'' - \varepsilon c u_c' - u + a_1 m(1-n_c) - a_2 n_c \tag{4.12}$$

$$c n_c' = m - n_c \tag{4.13}$$

$$m = \begin{cases} 1 & u_c > a \\ 0 & u_c < a \end{cases} \tag{4.14}$$

We have

$$m = \begin{cases} 0 & z < 0 \\ 1 & 0 < z < z_1 \\ 0 & z_1 < z \end{cases} \tag{4.15}$$

$$n_c = \begin{cases} 0 & z < 0 \\ 1-\exp(\lambda_c z) & 0 < z < z_1 \\ [1-\exp(\lambda_c z_1)]\exp(\lambda_c(z-z_1)) & z_1 < z \end{cases} \tag{4.16}$$

where

$$\lambda_c = -\frac{1}{c} < 0$$

$$u = \begin{cases} A_p \exp(\lambda_p z) & z < 0 \\ B_p \exp(\lambda_p z) + B_n \exp(\lambda_n z) + B_c \exp(\lambda_c z) + B_o & 0 \leq z \leq z_1 \\ C_n \exp(\lambda_n z) + C_c \exp(\lambda_c(z-z_1)) & z_1 < z \end{cases} \tag{4.17}$$

where λ_c has been given above and where λ_p, λ_n are the roots of

(4.18) $$\varepsilon^2\lambda^2 - \varepsilon c\lambda - 1 = 0$$

(4.19) $$\lambda = \frac{c}{2\varepsilon}\left(1 \pm \sqrt{1 + \frac{4}{c^2}}\right)$$

(4.20) $$\lambda_n < 0 < \lambda_p$$

The coefficients B_c, B_o, C_c are found by substitution of the formulae for u in the differential equation (4.17).

On $0 < z < z_1$

(4.21) $$a_1 m(1-n) - a_2 n = -a_2 + (a_1+a_2)\exp(\lambda_c z)$$

Therefore

(4.22) $$\left(\varepsilon^2 \frac{d^2}{dz^2} - \varepsilon c \frac{d}{dz} - 1\right)(B_c \exp(\lambda_c z) + B_o)$$

$$= a_2 - (a_1+a_2)\exp(\lambda_c z)$$

(4.23) $$(\varepsilon^2\lambda_c^2 - \varepsilon c\lambda_c - 1)B_c = -(a_1+a_2)$$

$$-B_o = a_2$$

(4.24) $$B_c = \frac{a_1 + a_2}{1 + \varepsilon c\lambda_c - \varepsilon^2\lambda_c^2}$$

(4.25) $$B_o = -a_2$$

Similarly, on $z_1 < z$

$$(4.26) \qquad a_1 m(1-n) - a_2 n = -a_2 n$$

$$= -a_2[1-\exp(\lambda_c z_1)]\exp(\lambda_c(z-z_1))$$

$$(4.27) \qquad (\varepsilon^2 \frac{d^2}{dz^2} - \varepsilon c \frac{d}{dz} - 1)C_c \exp(\lambda_c(z-z_1))$$

$$= a_2[1-\exp(\lambda_c z_1)]\exp(\lambda_c(z-z_1))$$

$$(4.28) \qquad (\varepsilon^2\lambda_c^2 - \varepsilon c\lambda_c - 1)C_c = a_2[1-\exp(\lambda_c z_1)]$$

$$(4.29) \qquad C_c = \frac{-a_2[1-\exp(\lambda_c z_1)]}{1 + \varepsilon c\lambda_c - \varepsilon^2\lambda_c^2}$$

The unknown coefficients which remain are as follows:

$$A_p,\ B_p,\ B_n,\ C_n,\ z_1,\ c$$

For these unknowns we have the 6 boundary conditions

$$(4.30) \qquad u_c(0^-) = u_c(0^+) = u_c(z_1^-) = u_c(z_1^+) = a$$

$$(4.31) \qquad u_c'(0^-) = u_c'(0^+)$$

$$(4.32) \qquad u_c'(z_1^-) = u_c'(z_1^+)$$

three of which are associated with $z = 0$ and three with $z = z_1$.

Explicitly, the boundary conditions read as follows.

At $z = 0$:

(4.33) $$a = A_p$$

(4.34) $$a = B_p + B_n + B_c + B_o$$

(4.35) $$A_p\lambda_p = B_p\lambda_p + B_n\lambda_n + B_c\lambda_c$$

At $z = z_1$:

(4.36) $$a = B_p \exp(\lambda_p z_1) + B_n \exp(\lambda_n z_1) + B_c \exp(\lambda_c z_1) + B_o$$

(4.37) $$a = C_n \exp(\lambda_n z_1) + C_c$$

(4.38) $$B_p\lambda_p \exp(\lambda_p z_1) + B_n\lambda_n \exp(\lambda_n z_1) + B_c\lambda_c \exp(\lambda_c z_1) = C_n\lambda_n \exp(\lambda_n z_1) + C_c\lambda_c$$

Remark: If we use the equations for B_c, B_o, C_c, and regard c, z_1 as known, then these become a linear system for the 6 unknowns A_p, B_p, B_n, C_n, a_1, a_2. However, if a_1, a_2 are regarded as known, then the equations for c, z_1 are not linear.

2. The traveling pulse in the limit $\varepsilon \to 0$.

We shall look for a solution in which c, z_1 remain finite in the limit $\varepsilon \to 0$. We have $\lambda_p \to \infty$, $\lambda_n \to -\infty$. Let

(4.39) $$-R = \frac{\lambda_p}{\lambda_n} = \frac{1 + \sqrt{1 + (4/c^2)}}{1 - \sqrt{1 + (4/c^2)}}$$

which is independent of ε.

Note that

(4.40) $$B_c \to a_1 + a_2$$

(4.41) $$B_o = -a_2$$

(4.42) $$C_c \to -a_2(1-\exp(\lambda_c z_1))$$

Also let:

(4.43) $$\bar{B}_p = B_p \exp(\lambda_p z_1)$$

(4.44) $$\bar{C}_n = C_n \exp(\lambda_n z_1)$$

If $\bar{B}_p$ and $\bar{C}_n$ remain finite, then $B_p \to 0$ and $C_n \to \infty$. In the limit $\epsilon \to 0$ the boundary conditions become:

At $z = 0$:

(4.45) $$a = A_p$$

(4.46) $$a = B_p + B_n + B_c + B_o$$

(4.47) $$A_p = B_p - B_n R^{-1}$$

At $z = z_1$

(4.48) $$a = \bar{B}_p + B_c \exp(\lambda_c z_1) + B_o$$

(4.49) $$a = \bar{C}_n + C_c$$

(4.50) $$\bar{B}_p = -\bar{C}_n R^{-1}$$

Since the other terms in (4.48) are finite, $\bar{B}_p$ will also be finite. Therefore $B_p \to 0$, and the equations at $z = 0$ become

(4.51) $$A_p = a$$

(4.52) $$B_n = -(a_1 - a)$$

(4.53) $$R = -\frac{B_n}{A_p} = \frac{a_1 - a}{a}$$

This determines the propagation speed, since (4.39) can be easily solved to yield

(4.54) $$c = \frac{R-1}{R^{1/2}} = R^{1/2} - R^{-1/2}$$

The equations at $z = z_1$ become

(4.55) $$\bar{B}_p = a + a_2 - (a_1 + a_2)\exp(\lambda_c z_1)$$

(4.56) $$\bar{C}_n = a + a_2[1 - \exp(\lambda_c z_1)]$$

(4.57) $$R\bar{B}_p = -\bar{C}_n$$

Since R is known, equation (4.57) becomes an equation for z_1. After some algebra:

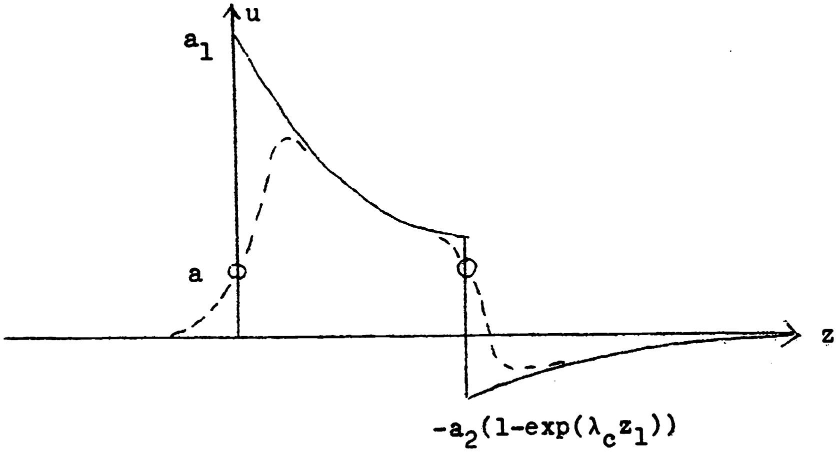
(4.58) $$\exp(\lambda_c z_1) = \frac{a + a_2}{a_1 - a + a_2}$$

Note that:

(4.59) $$\frac{a + a_2}{a_1 - a + a_2} < 1 \qquad \text{if} \quad R > 1$$

It remains to find the solution u itself. For $z \neq 0$ and $z \neq z_1$ we have in the limit $\varepsilon \to 0$

$$(4.60) \qquad u_c = \begin{cases} 0 & z < 0 \\ (a_1+a_2)\exp(\lambda_c z) - a_2 & 0 < z < z_1 \\ -a_2(1-\exp(\lambda_c z_1))\exp(\lambda_c(z-z_1)) & z_1 < z \end{cases}$$



The dotted lines give the shape of the transitions for small but non-zero ε. If we want to "capture" the form of these transitions we can introduce a scale which changes with ε. This will be done for a more general problem in the next section.

3. Propagation of Fronts.

Again consider the model:

$$\varepsilon u_t = \varepsilon^2 u_{xx} - u + a_1 m(1-n) - a_2 n \tag{4.61}$$

$$m = \begin{cases} 1 & u > a \\ 0 & u < a \end{cases} \tag{4.62}$$

$$n_t = m-n \tag{4.63}$$

We will not restrict attention to traveling waves, and the formula we derive here will remain valid if a_1, a_2, and a depend smoothly on x. Thus the results of the section will be applicable to an inhomogeneous line.

We are interested in the behavior of the solutions in the limit $\varepsilon \to 0$. Taking this limit formally we obtain the system:

$$\begin{aligned} 0 &= -u + a_1 m(1-n) - a_2 n \\ m &= \begin{cases} 1 & u > a \\ 0 & u < a \end{cases} \\ n_t &= m-n \end{aligned} \tag{4.64}$$

In the latter system different space points are uncoupled. Moreover, there is no unique solution, since it may easily happen that

(4.65) $$[a_1(1-n) - a_2n] > a > [-a_2n]$$

In such a case one can choose $m = 0$ or $m = 1$ without arriving at a contradiction. We want to find the solution of (4.64) which arises from (4.61 - 4.63) in the limit $\varepsilon \to 0$. This will be done by finding a formula for the propagation speed of the fronts. By "front" we mean the place where a transition in m from $0 \to 1$ or $1 \to 0$ occurs.

Let $x = \bar{x}(t)$ be a curve in the x,t plane along which a jump in m occurs. Introduce new variables

(4.66) $$\xi = \pm \frac{x-\bar{x}(t)}{\varepsilon}$$

(4.67) $$\tau = t$$

(4.68) $$u(x,t) = \bar{u}(\xi,\tau)$$

The ± sign in the foregoing is to be chosen so that

(4.69) $$m = \begin{cases} 1 & \xi < 0 \\ 0 & \xi > 0 \end{cases}$$

We have in the limit $\varepsilon \to 0$:

$$u_t = \bar{u}_\xi \xi_t + \bar{u}_\tau \tau_t$$

(4.70) $$= \frac{1}{\varepsilon}\, \bar{u}_\xi \left(\mp \frac{d\bar{x}}{dt}(t)\right) + \bar{u}_\tau$$

(4.71) $$\varepsilon u_t \to \bar{u}_\xi\left(\mp \frac{d\bar{x}}{dt}(t)\right)$$

(4.72) $$\varepsilon^2 u_{xx} = \bar{u}_{\xi\xi}$$

(4.74) $$n(x,t) = n(\bar{x}(t) \pm \varepsilon\xi, t) \to n(\bar{x}(t),t) = \bar{n}(t)$$

Since n is continuous through the front. Therefore in the limit $\varepsilon \to 0$

(4.74) $$0 = \bar{u}_{\xi\xi} \pm \frac{d\bar{x}}{dt}(t)\cdot\bar{u}_\xi - \bar{u} + a_1 m(1-\bar{n}(t)) - a_2\bar{n}(t)$$

where

(4.75) $$m = \begin{cases} 1 & \xi < 0 \\ 0 & \xi > 0 \end{cases}$$

In the system (4.74)- (4.75), t appears as a parameter only. (This came about because the term $\bar{u}_\tau$ was negligeable on the right hand side of (4.70).)

Let

(4.76) $$\theta = \pm \frac{d\bar{x}}{dt}$$

(4.77) $$I_A = a_1(1-n) - a_2 n$$

(4.78) $$I_B = \quad - a_2 n$$

The ordinary differential equation for the structure of the front is:

(4.79) $$0 = \bar{u}_{\xi\xi} + \theta\bar{u}_\xi - \bar{u} + \begin{cases} I_A, & \xi < 0 \\ I_B, & \xi > 0 \end{cases}$$

The solution is:

(4.80) $$\bar{u} = \begin{cases} I_A + (a-I_A)e^{\gamma_A\xi} & \xi < 0 \\ I_B + (a-I_B)e^{\gamma_B\xi} & \xi > 0 \end{cases}$$

where we have used $\bar{u}(0,t) = a$, and where $\gamma_B < 0 < \gamma_A$ are the roots of

(4.81) $$\gamma^2 + \theta\gamma - 1 = 0$$

Then

(4.82) $$\gamma_A = -\frac{\theta}{2}\left(1 - \text{sgn}(\theta)\sqrt{1 + (4/\theta^2)}\right) > 0$$

(4.83) $$\gamma_B = -\frac{\theta}{2}\left(1 + \text{sgn}(\theta)\sqrt{1 + (4/\theta^2)}\right) < 0$$

To determine θ, impose the condition

(4.84) $$\bar{u}_\xi(0^-,t) = \bar{u}_\xi(0^+,t)$$

(4.85) $$(a-I_A)\gamma_A = (a-I_B)\gamma_B$$

Let

$$R = \frac{I_A-a}{a-I_B} = -\frac{\gamma_B}{\gamma_A} = -\frac{1 + \text{sgn}(\theta)\sqrt{1 + (4/\theta^2)}}{1 - \text{sgn}(\theta)\sqrt{1 + (4/\theta^2)}}$$

Solving for θ, we find

$$\theta^2 = \frac{(R-1)^2}{R} \tag{4.87}$$

For real θ, require that $R > 0$. Since $I_A > I_B$, this implies $I_A > a > I_B$. Another consequence of $R > 0$ is $\mathrm{sgn}(\theta) = \mathrm{sgn}(R-1)$, as can be shown from (4.86). Therefore, we have, without any ambiguity of sign,

$$\theta = \frac{R-1}{R^{1/2}} = R^{1/2} - R^{-1/2} \tag{4.88}$$

where

$$R = \frac{I_A - a}{a - I_B} \tag{4.89}$$

This is the required formula for the velocity of a front. Since I_A and I_B depend on n, the velocity depends on n. The sign convention for θ is that $\theta > 0$ means the front is moving outward from the excited region, while $\theta < 0$ means the front is moving into the excited region.

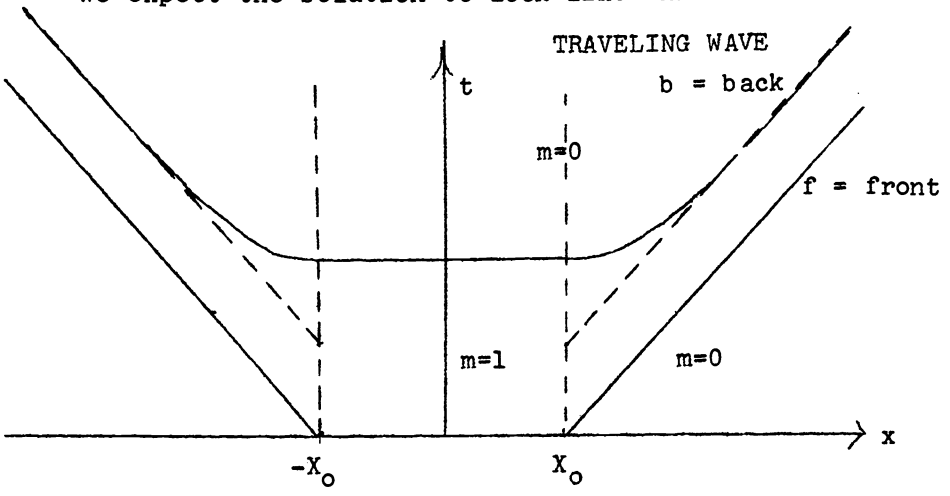
4. An initial value problem.

We shall use the results of the previous section to construct the solution of the problem (4.61 - 4.63) in the limit $\varepsilon \to 0$, with initial data

$$n(x,0) = 0 \tag{4.90}$$

$$m(x,0) = \begin{cases} 1 & |x| \le x_o \\ 0 & |x| > x_o \end{cases} \tag{4.91}$$

We expect the solution to look like this:



Because of symmetry, we can restrict our attention to $x > 0$. Let $t = t_f(x)$, $x = x_f(t)$ be the trajectory of the front and let $t = t_b(x)$, $x = x_b(t)$ be the trajectory of the back.

The front starts at $x = x_o$. Along it we have $n = 0$, and therefore

(4.92) $$R_f = R(0) = \frac{a_1 - a}{a}$$

Assume that $a_1 > 2a$. Then $R_f > 1$ and

(4.93) $$\theta_f = R_f^{1/2} - R_f^{-1/2} > 0$$

The equation for the front is

(4.94) $$x_f(t) = x_o + \theta_f t$$

Next, determine the equation of the back on $x < x_o$. This is the line along which the back of the wave arises spontaneously. Its equation will be

(4.95) $$t_b(x) = t^*$$

where t^* is the time when n becomes too large to support an excited state. To find this, note that on $x < x_o$ and $t \le t^*$ we will have

(4.96) $$n(x,t) = 1 - \exp(-t)$$

and the critical value of n is given by

(4.97) $$a = a_1(1-n^*) - a_2n^*$$

(4.98) $$n^* = \frac{a_1-a}{a_1+a_2}$$

Then

(4.99) $$\exp(-t^*) = 1-n^* = \frac{a_2+a}{a_1+a_2}$$

It remains to determine the equation of the back on $x > x_o$. The equation will be

(4.100) $$\frac{dt_b}{dx} = \frac{-1}{\theta_b}$$

where

(4.101) $$\theta_b = R_b^{1/2} - R_b^{-1/2}$$

(4.102) $$R_b = \frac{a_1 - a - (a_1+a_2)n_b}{a+a_2n_b}$$

We still need to find n_b. To do this use initial data on the front $t = t_f(x)$

(4.103) $$n(x,t_f(x)) = 0$$

and for $t_f(x) \leq t \leq t_b(x)$:

(4.104) $$\frac{\partial n}{\partial t} = 1-n$$

from which we conclude

(4.105) $$n_b = 1 - \exp[-(t_b(x) - t_f(x))]$$

Combining this with (4.100 - 4.102) we have an ordinary differential equation for $t_b(x)$. It will be convenient, however, to introduce the variable

(4.106) $$T(x) = t_b(x) - t_f(x)$$

whose equation on $x > x_o$ will be

(4.107) $$\begin{cases} \dfrac{dT}{dx} = \dfrac{dt_b}{dx} - \dfrac{dt_f}{dx} = -\left(\dfrac{1}{\theta_b} + \dfrac{1}{\theta_f}\right) \\ \theta_b = R_b^{1/2} - R_b^{-1/2} \\ \theta_f = R_f^{1/2} - R_f^{-1/2} \end{cases}$$

(4.107–cont.)

$$\begin{cases} R_b = \dfrac{a_1 - a - (a_1+a_2)n_b}{a+a_2 n_b} \\ R_f = \dfrac{a_1-a}{a} \\ n_b = 1 - \exp(-T) \end{cases}$$

The initial condition for (4.107) is $T(x_o) = t^*$.

We now show that (4.107) has an equilibrium solution $T^{(EQ)}$. To find it, set

(4.108)
$$\frac{dT}{dx} = 0$$

Then

(4.109)
$$\begin{cases} \theta_b = -\theta_f \\ R_b = \dfrac{1}{R_f} \\ \dfrac{(a_1-a) - (a_1+a_2)n_b}{(a+a_2)n_b} = \dfrac{a}{a_1-a} \end{cases}$$

Call the solution $n_b^{(EQ)}$, $T^{(EQ)}$. Then

(4.110)
$$1-\exp(-T^{(EQ)}) = n_b^{(EQ)} = \frac{(a_1-a)^2}{(a_1+a_2)(a_1-a) + a(a+a_2)}$$

Note that

(4.111)
$$n_b^{(EQ)} < \frac{(a_1-a)^2}{(a_1+a_2)(a_1-a)} = \frac{a_1-a}{a_1+a_2} = n^*$$

It follows that

$$T^{(EQ)} < t^* \tag{4.112}$$

Next we show that $T \to T^{(EQ)}$ as $x \to \infty$. Suppose $T > T^{(EQ)}$, as is the case initially. Then

$$\text{(4.113)} \quad \left\{ \begin{array}{l} n_b > n_b^{(EQ)} \\ R_b < \frac{1}{R_f} \\ \theta_b < -\theta_f < 0 \\ -\frac{1}{\theta_f} < \frac{1}{\theta_b} < 0 \\ \frac{dT}{dx} = -(\frac{1}{\theta_b} + \frac{1}{\theta_f}) < 0 \end{array} \right.$$

We have established that $(dT/dx) < 0$ when $T > T^{(EQ)}$. The inequalities can also be reversed to show that $(dT/dx) > 0$ when $T < T^{(EQ)}$. It follows that for any initial T, $T \to T^{(EQ)}$ as $x \to \infty$ (since x does not appear explicitly in the formula (4.107) for DT/dx).

Exercise: Find the equations for periodic traveling wave solutions of (4.61 - 4.63) in the limit $\varepsilon \to 0$.

V. The Inner Ear*

1. Introduction.

The cochlea (inner ear) contains an elastic structure, the basilar membrane, which is immersed in a viscous incompressible fluid. The fibers of the auditory nerve are distributed along the basilar membrane, the stiffness of which decreases exponentially with distance. A sound signal consisting of a pure tone sets up a traveling wave which propagates along the basilar membrane. This wave has a stationary envelope with a definite peak, the position of which varies systematically with the frequency of the sound stimulus. Thus, sounds of different frequencies stimulate different groups of nerve fibers. In this way the cochlea analyzes sound signals into their various frequency components. This process is fundamental to the perception of pitch and to the separation of signals from noise in hearing.

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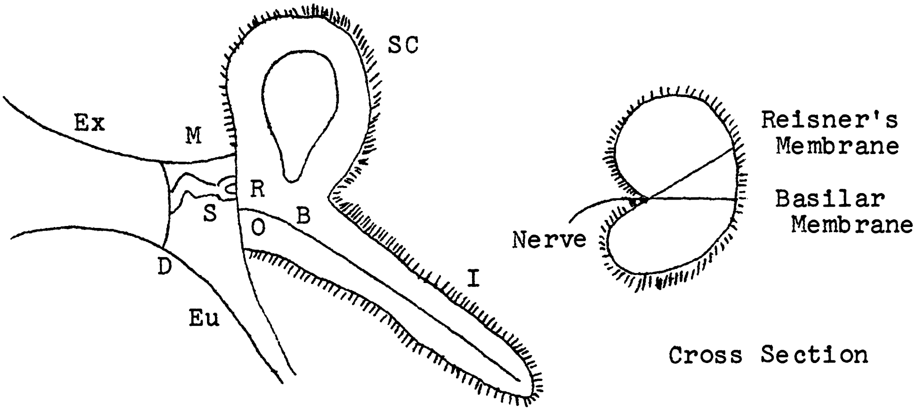
* This chapter is also a research report, and I would like to make the following acknowledgments: I have had helpful conversations regarding this work with many individuals including Olof Widlund, Alexandre Chorin, Peter Lax, Cathleen Morawetz, Eugene Isaacson, Joe Keller, Frank Hoppensteadt, Stan Osher, Ami Harten, Edward Peskin, and Michael Lacker. Much of the computer programming connected with this project was done by Antoinette Wolfe. Computation was supported by US ERDA under contract E(11-1)-3077 at New York University.

The inner ear is a spiral shaped fluid filled cavity in the temporal bone of the skull. Its relation to the other parts of the ear can be understood in terms of the following figure: *

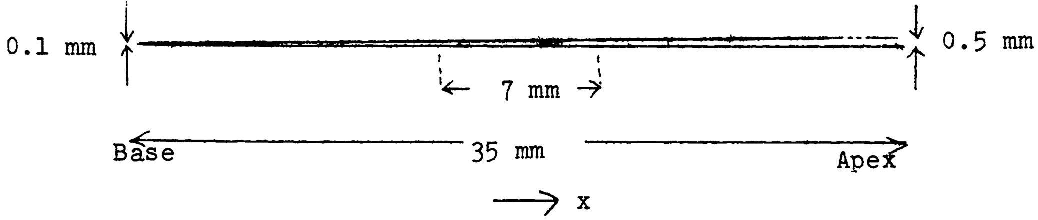


Ex. - External ear canal	S. - Stapes
M. - Middle ear	R. - Round Window
SC. - Semicircular canal	O. - Oval window
I. - Inner ear	B. - Basilar membrane
Eu. - Eustachian tube	D. - Ear drum

* redrawn after von Bekesy [1]. This is a schematic diagram in which the cochlea has been straightened out.

The mechanical events involved in the transmission of the sound wave through the ear may be described as follows. Pressure fluctuations in the external ear cause the eardrum to vibrate. This vibration is transmitted to the cochlea by a delicate chain of bones terminating in the stapes, which is attached to the round window of the cochlea. The walls of the cochlea, being made of bone (except at the round and oval windows which are covered by elastic membranes) are essentially rigid, and the cochlea is filled with an essentially incompressible fluid. Conservation of volume therefore requires that an inward motion of the round window be compensated by a simultaneous outward motion of the oval window. This reciprocal vibration sets up a wave of fluid motion which propagates along the basilar membrane, the deformations of which stimulate the fibers of the auditory nerve.

A quantitative discussion of the geometry and physical properties of the cochlea is fundamental to an analysis of its fluid dynamics. If unrolled and viewed from above the basilar membrane would look like this:



The compliance of the basilar membrane, measured as volume displaced per unit length per unit pressure difference, increases exponentially with x with a length constant of 7 mm. This is the most important single length in the cochlea for the following reason. The exponential function has the well known property that translation simply produces multiplication by a constant. A change in the frequency of the sound can therefore be compensated by a translation of the pattern of vibration along the basilar membrane to a new position at which the range of values of compliance is appropriate to the new frequency. Thus, the exponential dependence of compliance on length is fundamental to auditory frequency analysis, and the length constant of this dependence (in man, 7 mm) is the natural unit of length for cochlea physiology.

In comparison with this unit of length, the basilar membrane is obviously long and narrow. The depth of the cochlea, being about 2mm for each half cochlea above or below the basilar membrane, is moderate. It is not clear, therefore, whether one should use shallow water or deep water theory, and both approaches have been used. Experiments of von Bekesy indicate, however, that the wave on the basilar membrane is not much changed if the depth of the cochlea is increased. This appears to be an argument against the use of shallow water theory.

A very important physical quantity with dimensions of length is the boundary layer thickness, which measures the distance from the boundary within which we may expect viscosity to have a significant effect on the flow. In the present problem this is given by $(\nu/\omega)^{1/2}$, where ν is the kinematic viscosity, $\nu = 0.02\ cm^2/sec$, and where ω is the frequency of the sound, $\omega = 2\pi f$, (where f is the frequency in cycles per second). A typical value for human hearing is obtained by setting f = 1000/sec. This yields a boundary layer thickness of about 0.02 mm, which is more than 100 times smaller than the characteristic length introduced above. In Section 3 we will get an indication that the wavelength of the disturbance which propagates along the basilar membrane is of the same order of magnitude as the boundary layer thickness near the place where the amplitude of the disturbance is greatest. (The wavelength is variable because of the exponental variation in compliance.) This observation makes the use of shallow water theory even less credible and may explain von Bekesy's observation that the depth is effectively infinite. It also weakens our own claim that the basilar membrane is narrow, since its width may be small in comparison with the characteristic length associated with membrane compliance, but not always small in comparison with the wavelength of the disturbance on the basilar membrane.

The general idea that each part of the inner ear is tuned to a particular frequency was introduced by Helmholtz [2], who postualted a discrete system of resonators.

Modern theories of cochlea mechanics are founded on the following observations of G. von Bekesy [1]:

1) In response to a pure tone there is a traveling wave in the cochlea, the amplitude of wich has a peak at a position which varies linearly with the frequency of the tone.

2) The compliance of the basilar membrane increases exponentially with distance from the base of the cochlea.

3) In response to a point load, the basilar membrane deforms like a plate. (That is, the basilar membrane is not under tension, but it resists bending.)*

More recent experiments [3,4] confirm the qualitative findings of Bekesy but reveal a more localized disturbance than he originally found.

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* This means that the basilar membrane is <u>not</u> a membrane in the sense of elasticity theory. The term basilar membrane is established, however, and we continue to use it.

Both Bekesy [1] and Tonndorf [5] have constructed simplified physical models of the cochlea. These models are straight with rectangular cross sections. They contain the basilar membrane only and not Reissner's membrane. Despite these simplifications they reproduce the qualitative features of cochlea mechanics. Bekesy has constructed such models of variable depth, in order to show that the depth may be increased without changing the form of the cochlea wave. Tonndorf has given an excellent description of the motions of marker particles suspended in the fluid. These motions are not at all restricted to the longitudinal direction as in shallow water theory.

Theoretical work on the cochlea may be classified according to the equations used for the fluid and for the basilar membrane. A class of cochlea models of direct concern to the present work may be described as follows: The model is two dimensional, and the basilar membrane appears in it as a line, each point of which responds like a system with mass, damping, and elasticity to forces tending to displace it from equilibrium. The physical constants of the basilar membrane may vary with position. The fluid is assumed inviscid and the flow irrotational. The motion is of low amplitude, so that non-linear terms are neglected and the boundary conditions associated with the basilar membrane are applied to its undisturbed location. Lesser and Berkeley [6] have given a numerical method for cochlea problems of this type, and Siebert [7] has given an approximate analysis of the case of infinite depth.

Models which attempt to incorporate the properties of the basilar membrane as a plate are those of Inselberg and Chadwick [8] and Steele [9]. The model of Inselberg and Chadwick is two dimensional, so the plate is replaced by a beam. The exponential variation of compliance is omitted from the model, however, and the fluid dynamics is based on shallow water theory. Steele's model is probably the most detailed yet attempted. It is a three dimensional model in which the basilar membrane appears as a plate. Various boundary conditions for the support of the plate at its edges are considered.

The present work is organized as follows. In Section 2 we give a derivation of the equations of motion. The derivation given for the fluid is standard, but the derivation for the equations of the basilar membrane may be of some interest, since it involves the exponential variation of compliance with position. Also, we consider the case of a very narrow basilar membrane and show that in this limit the longitudinal coupling may be neglected in comparison with the coupling of a given point to the edges. It is our belief that this argument justifies the use of a point by point representation for the basilar membrane in two dimensional models as in some of the papers cited above [6,7], and that it answers the criticism of this approach which appears in [8].

In Section 3 we consider the model of Lesser and Berekely [6] and Siebert [7], described above, with the following modifications. First, we regard the cochlea as infinitely long with a source at $x = -\infty$. This point of view makes sense because the model basilar membrane becomes so rigid as $x \to -\infty$ that a source at $x = -\infty$ has nearly the same effect as a source at some finite distance. Next, we neglect the mass of the basilar membrane. As a soft biological tissue, the basilar membrane probably has nearly the same density as the fluid which surrounds it. Idealizing it as a surface, we assign it zero mass. The only inertia in the model, then, is that of the fluid. As in the papers cited, we include a dissipative force proportinal to the velocity of the basilar membrane, but we also consider the limit as the dissipative coefficent approaches zero. We assume (arbitrarily) that the dissipative force has the same exponential dependence on position as the elastic restoring force of the basilar membrane.

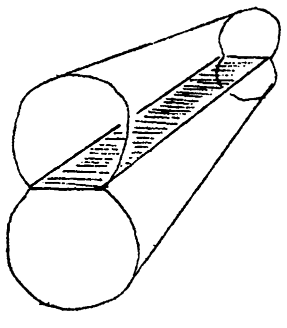
For a special finite depth, we obtain an analytic solution to the equations of motion for this model of the cochlea, and we discuss the behavior of this solution in the case of finite dissipation and in the limit of zero dissipation. This limit is very important because, to our knowledge, a special dissipative mechanism acting on the basilar membrane has not been demonstrated. Taking this limit, we find that the amplitude of the motion of the basilar membrane grows without bound as $x \to \infty$. Thus the response is no longer localized in space, even approximately, and the whole basis for auditory frequency analysis seems to be lost. This shows the fundamental role of dissipation in cochlea physiology. It would be more satisfying, however, if the dissipative mechanism in the model could be related to some known dissipative process, such as fluid viscosity.

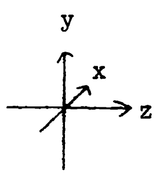
The analytic solution of the inviscid problem in Section 3 can also be used to get a rough indication of what would happen in the presence of fluid viscosity. We find that the form of the disturbance should be the same with the two types of dissipation but that the dependence of the parameters of the disturbance on the frequency of the sound should be different. These rough arguments serve as motivation for the careful treatment of fluid viscosity in the next section.

In Section 4, we formulate a two dimensional cochlea model with fluid viscosity as the dissipative mechanism. Only the case of infinite depth is considered, but the method is easily generalized to finite depth. Using spatial Fourier transforms we reduce the problem to an integral equation on the basilar membrane. (This has been done before only for the inviscid problem, see [7].) This equation has the form of an eigenproblem, which we solve numerically. The numerical method involves discretization by means of the discrete Fourier transform and solution of the discrete eigenproblem by inverse iteration. Each step of the inverse iteration involves the solution of a large linear system by the conjugate gradient method.

2. Equations of Motion.

In this discussion it may be helpful to have in mind a definite (but idealized) geometry for the cochlea. We therefore consider the following conceptual model.





The outer walls are rigid and the basilar membrane is a clamped elastic plate whose undisturbed position is the plane y = 0, which is also a plane of symmetry. The spaces above and below the basilar membrane are filled with a viscous incompressible fluid. The model cochlea is infinite in both the positive and negative x directions. The stiffness of the basilar membrane decreases exponentially with x.

a. <u>The Fluid</u>:

We begin by deriving the equations of motion of an inviscid, incompressible fluid. We use the laws of conservation of mass and momentum. Let V be an arbitrary fixed region with surface S and unit normal $\hat{\underline{n}}$ pointing outward. Let

$\underline{u} = (u_1, u_2, u_3)$ = fluid velocity

p = pressure

ρ = density (constant)

$\underline{P} = (P_1, P_2, P_3)$ = momentum contained in V

M = mass contained in V

Then

$$\frac{dP_i}{dt} = \frac{d}{dt}\int_V \rho u_i \, dV = -\int_S \{(\underline{u}\cdot\hat{\underline{n}})\rho u_i + p n_i\} \, dS \tag{5.1}$$

$$0 = \frac{dM}{dt} = \frac{d}{dt}\int_V \rho \, dV = -\int_S \rho(\underline{u}\cdot\hat{\underline{n}}) \, dS \tag{5.2}$$

Now convert the surface integrals to volume integrals, and make use of the fact that V is fixed and ρ = constant:

$$\int_V \left\{\rho\partial_t u_i + \rho\sum_{j=1}^{3} \partial_j(u_i u_j) + \partial_i p\right\} dV = 0 \tag{5.3}$$

$$\int_V \left\{ \sum_{j=1}^{3} \partial_j u_j\right\} dV = 0 \tag{5.4}$$

Finally, on account of the arbitrariness of V, we have

$$\rho\left(\partial_t u_i + \sum_{j=1}^{3} \partial_j(u_i u_j) \right) + \partial_i p = 0 \tag{5.5}$$

$$\sum_{j=1}^{3} \partial_j u_j = 0 \tag{5.6}$$

We are interested in the case of small amplitude motion, so we neglect the quadratic term. Introducing vector notation, and choosing units in which ρ = 1, the equations then become

$$\left\{ \begin{aligned} \partial_t \underline{u} + \text{grad } p &= 0 \\ \text{div } \underline{u} &= 0 \end{aligned} \right. \tag{5.7}$$

An important special case of Eqs. (5.7) occurs when $\underline{u}$ = grad ϕ. Then

$$\left\{\begin{array}{l} \partial_t\phi + p = 0 \\ \Delta\phi = 0 \end{array}\right. \qquad (5.8)$$

When fluid viscosity is considered, Eqs. (5.7) have to be modified, as follows [10,11]

$$\left\{\begin{array}{l} \partial_t \underline{u} + \text{grad } p = \nu\Delta\underline{u} \\ \text{div } \underline{u} = 0 \end{array}\right. \qquad (5.9)$$

We shall use Eqs. (5.8) in Section 3 and Eqs. (5.9) in Section 4.

b. The Basilar Membrane:

As a model of the basilar membrane, we consider a clamped elastic plate, the stiffness of which decreases exponentially with x. The undisturbed plate occupies the strip $-\infty < x < \infty$, $-b < z < b$ in the plane $y = 0$. The displacements are given by

$$y = h(x,z) \qquad (5.10)$$

We regard the displacements as small, and we therefore regard dxdz as the element of area on the plate.

Along the boundaries $z = \pm b$, we assume that

(5.11) $$h = \partial_z h = 0$$

the latter condition corresponding to the word "clamped". We also assume that h and $\partial_x h \to 0$ sufficiently rapidly as $|x| \to \pm\infty$.

Finally, we assume that the elastic energy stored in the deformed plate is given by

(5.12) $$E = \frac{1}{2} K \int_{\text{plate}} e^{-\lambda x} (\Delta h)^2 \, dxdz$$

where $\Delta = \partial_x^2 + \partial_z^2$.

We will find an equation of equilibrium for the plate in response to an imposed load. Let the force per unit area applied to the plate be given by $\ell(x,z)$, where $\ell > 0$ means a force in the negative y direction. To find the equation of equilibrium, we use the principle of virtual work, which asserts that for any small perturbation from equilibrium, the work done by the applied forces should balance the change in stored energy. That is,

(5.13) $$\delta \frac{K}{2} \int e^{-\lambda x} (\Delta h)^2 \, dxdz + \int \ell \delta h \, dxdz = 0$$

But

(5.14) $$\delta \frac{1}{2} (\Delta h)^2 = (\Delta h) \Delta (\delta h)$$

Substitute this result in the first integral, and integrate twice by parts to obtain

$$\int \left\{K\Delta(e^{-\lambda x}\Delta h) + \ell\right\}\delta h \, dxdz = 0 \tag{5.15}$$

Since δh is arbitrary

$$K\Delta(e^{-\lambda x}\Delta h) + \ell = 0 \tag{5.16}$$

We shall neglect the mass of the basilar membrane. In that case, this equation of equilibrium holds at each instant t.

In the following we will consider two dimensional models of the cochlea in which the basilar membrane necessarily appears as a line instead of a surface. We need to find an equation corresponding to (5.16).

When ℓ is a function of x alone it seems natural to look for solutions of (5.16) in which h is also a function of x and not of z. This yields the equation

$$K\partial_x^2(e^{-x}\partial_x^2 h) + \ell = 0 \tag{5.17}$$

The assumption that h is independent of z is untenable for narrow plates, however, since it violates the boundary condition along $z = \pm b$ unless $h \equiv 0$. We therefore reject (5.17), and proceed as follows.

Let $\varepsilon = \lambda b << 1$, and suppose that $\ell = \ell(x)$. Introduce new variables

(5.18)
$$\begin{cases} x_1 = \lambda x \\ z_1 = z/b \end{cases}$$

and functions h_1 and ℓ_1 defined so that $h_1(x_1,z_1) = h(x,z)$ and $\ell_1(x_1) = \ell(x)$ at corresponding points. Equation (5.16) becomes

(5.19)
$$K\left(\lambda^2\partial_{x_1}^2 + \frac{1}{b^2}\,\partial_{z_1}^2\right)e^{-x_1}\left(\lambda^2\partial_{x_1}^2 + \frac{1}{b^2}\,\partial_{z_1}^2\right)h_1 + \ell_1 = 0$$

or

(5.20)
$$\frac{K}{b^4}\left(\varepsilon^2\partial_{x_1}^2 + \partial_{z_1}^2\right)e^{-x_1}\left(\varepsilon^2\partial_{x_1}^2 + \partial_{z_1}^2\right)h_1 + \ell_1 = 0$$

Now let $K/b^4 = K_o$ and take the limit $\varepsilon \to 0$ with K_o fixed. We obtain

(5.21)
$$K_o e^{-x_1}\,\partial_{z_1}^4\,h_1 + \ell_1 = 0$$

In this equation x_1 appears as a parameter only. The solution of (5.21) subject to the boundary conditions

(5.22)
$$h_1(x_1, \pm 1) = \partial_{z_1} h_1(x_1, \pm 1) = 0$$

is given by

$$h_1 = -\frac{\ell_1 e^{x_1}}{K_o} \frac{1}{4!} (z_1-1)^2(z_1+1)^2 \tag{5.23}$$

Therefore the displacement of the middle of the basilar membrane is given by

$$h(x,0) = h_1(\lambda x,0) = -\frac{\ell(x)e^{\lambda x}}{K_o(4!)} \tag{5.24}$$

It will be convenient to set $2s_o = K_o(4!)$. Then

$$\ell(x) = -2s_o \exp(-\lambda x)h(x,0) \tag{5.25}$$

In the two dimensional models which are discussed below, we shall use this equation with $h(x,0)$ replaced by $h(x)$. In (5.25) each point in the middle of the basilar membrane seems to be attracted to the equilibrium position $h = 0$ and seems to be uncoupled from points with different values of x. This uncoupling, which in reality is only approximate, comes about because we have taken the limit $\varepsilon \to 0$ in (5.20). The physical meaning of this result is that in the case of a narrow plate the coupling of points to the edges is more important than the coupling in the direction parallel to the edges.

A generalization of (5.25) which also will be considered in Section 3 is obtained by assuming that the basilar membrane is visco-elastic instead of purely elastic. In that case, we might have, for example

$$\ell = -2s_0 \exp(-\lambda x)(h + \beta \frac{\partial h}{\partial t}) \tag{5.26}$$

We will not give a detailed justification of this formula since we know of no evidence that there is any special dissipative mechanism residing in the basilar membrane. Instead, we regard the term $\beta \frac{\partial h}{\partial t}$ as a mathematical device designed to include some dissipation in the model while avoiding the mathematical difficulties associated with fluid viscosity. In Section 4 we abandon this approach, set $\beta = 0$, and let fluid viscosity supply the necessary dissipation.

c. <u>Coupling of the Fluid and Basilar Membrane</u>:

We assume that the displacements of the basilar membrane are small. We will therefore write the boundary conditions which hold along the basilar membrane as if they applied to the plane $y = 0$. A careful justification for this procedure is given in Stoker [12]. Note that this approximation is essentially the same as neglecting the non-linear terms in the equations of motion of the fluid, since these terms arise from the distinction between the derivative with respect to time at a point and the derivative with respect to time following the motions of a fluid particle.

Since the fluid is incompressible, the vertical component of velocity is continuous across the basilar membrane and we have

$$\frac{\partial h}{\partial t}(x,z,t) = v(x,0,z,t) = \frac{\partial \phi}{\partial y}(x,0,z,t) \tag{5.27}$$

where the last equality holds only in the case of potential flow.

It remains to consider the formula for the load on the basilar membrane ℓ. In the inviscid case this is simply given by the pressure difference

$$\ell = p_2 - p_1 = [p] \tag{5.28}$$

where the subscripts refer to the two sides of the basilar membrane (1 = below, 2 = above), and where [p] means the jump in p.

In a viscous fluid, we have, in addition to the pressure difference, a load due to the vertical component of the viscous stress. This is given by $\nu \frac{\partial v}{\partial y}$ where ν is the viscosity and therefore

(5.29) $$\ell = [p] - \nu\left[\frac{\partial v}{\partial y}\right]$$

We can express this result in another way by considering the force per unit volume exerted by the basilar membrane on the fluid. This force density is singular and is given by

(5.30) $$\underline{F} = \ell\ \delta(y)\ \hat{\underline{y}}$$

in terms of $\underline{F}$ the equation of motion of the fluid may be written

(5.31) $$\frac{\partial \underline{u}}{\partial t} + \text{grad } p = \nu\Delta\underline{u} + \underline{F}$$

which has the y-component

(5.32) $$\frac{\partial v}{\partial t} + \frac{\partial p}{\partial y} = \nu\Delta v + \ell\ \delta(y)$$

integrating over the interval $-\varepsilon < y < \varepsilon$ and taking the limit $\varepsilon \to 0$ we recover (5.29), as required.

d. Symmetry:

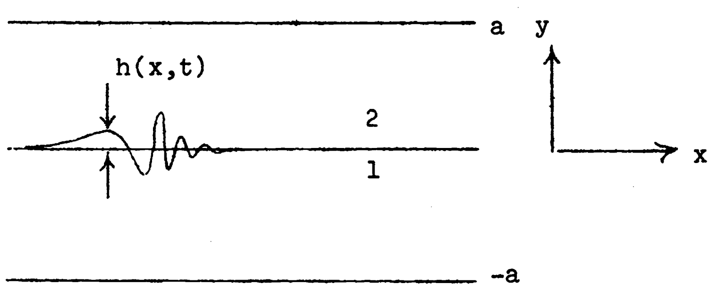
We shall look for solutions of the cochlea problem with the following symmetry

$$p(x,y,z,t) = -p(x,-y,z,t) \tag{5.33}$$ *

(from which it follows that $\frac{\partial v}{\partial y}$ has the same symmetry). To justify this one could appeal to the manner in which the cochlea is driven. It is simpler, however, to remark that the problem is linear and that a general solution can be split into solutions with even and odd symmetry. The solutions with even symmetry are trivial however, since $\ell = 0$, and they fail to deform the basilar membrane.

3. The Two Dimensional Cochlea of Finite Depth. Analytic Results for the Case of Potential Flow.

In this section we consider the cochlea model shown in the figure:



* The quantity p here is the pressure measured with respect to some standard pressure, such as the atmosphere. Thus $p < 0$ does not mean negative total pressure.

We neglect fluid viscosity in the interior of the cochlea and look for potential flow solutions of small amplitude. The interior equations therefore have the form:

$$\frac{\partial\phi}{\partial t} + p = 0 \tag{5.34}$$

$$\Delta\phi = 0 \tag{5.35}$$

We assume that the outer walls are rigid, and that the basilar membrane is visco-elastic but massless. Moreover, we assume that the coefficients of stiffness and viscosity for the basilar membrane both depend on x like exp $(-\lambda x)$. These assumptions lead to the boundary conditions

$$y = \pm a : \qquad \frac{\partial\phi}{\partial y} = 0 \tag{5.36}$$

$$y = 0 : \qquad p_1 - p_2 = 2s_o \exp(-\lambda x)\left\{h + \beta \frac{\partial h}{\partial t}\right\} \tag{5.37}$$

$$\frac{\partial h}{\partial t} = \left.\frac{\partial\phi}{\partial y}\right|_1 = \left.\frac{\partial\phi}{\partial y}\right|_2$$

For a special depth, we shall give the analytic solution to this problem corresponding to a source at $x = -\infty$ whose time-dependence is $\exp(i\omega t)$. For $\beta > 0$, we shall be interested in evaluating $\left\{\frac{\partial h}{\partial t}\right\}$ along $y = 0$. If we attempt to take the limit $\beta \to 0$, we will find that both the amplitude and the spatial frequency of the solution grow without bound as $x \to \infty$. This shows the crucial role of dissipation in chochlea physiology. On the other hand, there is no evidence for a special dissipative mechanism in the basilar membrane, and we ought therefore consider the case $\beta = 0$. This paradox is resolved by considering fluid viscosity, which is not explicit in the model. At high enough frequencies, the effects of fluid viscosity will be confined to a thin layer around $y = 0$, and the inviscid solution will be valid outside of this layer. On the other hand, the normal components of velocity should be nearly constant across this boundary layer, which suggests that we can get at least a rough indication of the behavior of the basilar membrane by examining the inviscid solution at the edge of the boundary layer.

As a first step, we eliminate p and h from our system of equations. We are interested in solutions which satisfy the symmetry condition

$$p(x,y,t) + p(x,-y,t) = 0 \tag{5.38}$$

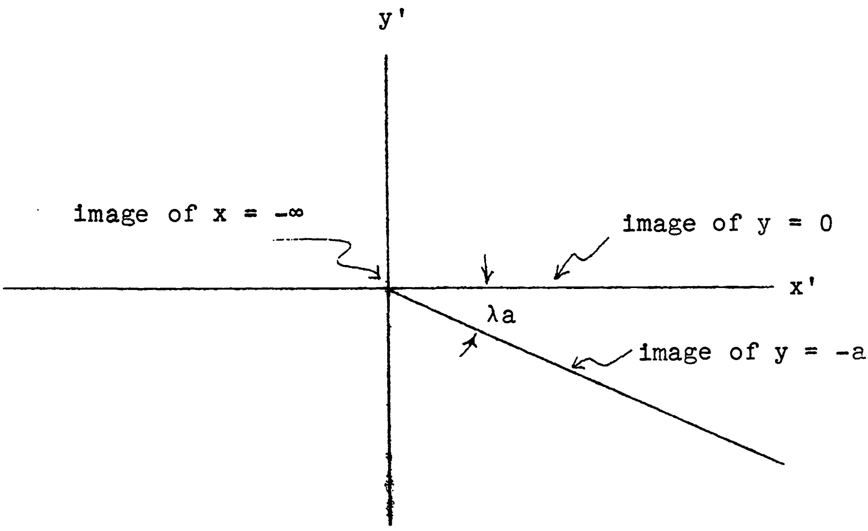
Along $y = 0$, this becomes $p_1+p_2 = 0$, and therefore

$$p_1 = s_o \exp(-\lambda x)\left(h + \beta \frac{\partial h}{\partial t}\right) \tag{5.39}$$

Differentiating with respect to t, and expressing everything in terms of ϕ we obtain

$$(5.40)\quad \begin{cases} \dfrac{\partial^2\phi}{\partial t^2} + s_o \exp(-\lambda x)\left(\dfrac{\partial\phi}{\partial y} + \beta \dfrac{\partial^2\phi}{\partial y\partial t}\right) = 0 & y = 0 \\ \Delta\phi = 0 & -a < y < 0 \\ \dfrac{\partial\phi}{\partial y} = 0 & y = -a \end{cases}$$

The factor $\exp(-\lambda x)$ can be absorbed by a conformal mapping which converts the strip $-a < y < 0$ into the wedge $-\lambda a < \theta < 0$.



The required conformal mapping is

$$(5.41)\qquad \begin{cases} x'+iy' = \exp\left[\lambda(x+iy)\right] \\ \text{or} \qquad x' = \exp(\lambda x)\cos(\lambda y) \\ \qquad\quad y' = \exp(\lambda x)\sin(\lambda y) \end{cases}$$

Also let

$$(5.42)\qquad \phi'(x',y') = \phi(x,y)$$

at corresponding points, and let

$$\Delta' = \left(\frac{\partial}{\partial x'}\right)^2 + \left(\frac{\partial}{\partial y'}\right)^2$$

Of course, conformal mappings take Laplace's equation into Laplace's equation and normal derivatives into normal derivatives. However, we need to change variables in the boundary condition along $y = 0$.

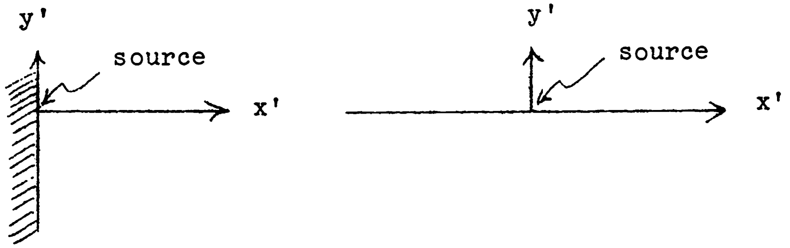
$$(5.43)\qquad \frac{\partial\phi}{\partial y} = \frac{\partial\phi'}{\partial y'}\frac{\partial y'}{\partial y} + \frac{\partial\phi'}{\partial x'}\frac{\partial x'}{\partial y} = \lambda\exp(\lambda x)\frac{\partial\phi'}{\partial y'}$$

The factor $\exp(\lambda x)$ cancels the factor $\exp(-\lambda x)$ which appears in the boundary condition, and we have the following problem on the wedge $-\lambda a < \theta < 0$:

$$
(5.44)\quad \begin{cases} y' = 0 : & \dfrac{\partial^2\phi'}{\partial t^2} + \lambda s_o \left(\dfrac{\partial\phi'}{\partial y'} + \beta\,\dfrac{\partial^2\phi'}{\partial y'\partial t}\right) = 0 \\ \text{interior} : & \Delta'\phi' = 0 \\ \dfrac{y'}{x'} = -\tan\lambda a : & \dfrac{\partial\phi'}{\partial n'} = 0 \end{cases}
$$

where $\left(\frac{\partial\phi'}{\partial n'}\right)$ stands for the normal derivative.

When $\beta = 0$, the boundary condition along $y' = 0$ is the same as that on a free surface, and the problem is equivalent to the problem of waves on a sloping beach, see [12]. (In the present case, however, we are interested in a source at the shoreline, $x' = 0$, $y' = 0$, which is the image of $x = -\infty$.) We shall be interested in the special depth $\lambda a = \frac{\pi}{2}$, which is simplest to consider because it maps into the problem of waves generated at a vertical cliff.



Evidently, the latter problem is equivalent to the corresponding problem with the cliff removed, with fluid filling up the lower half plane $y' < 0$, and with a source at the origin. The symmetry of the problem then guarantees that there will be no flow across $x' = 0$, so that these two problems are equivalent.

We are therefore led to consider the following problem on the lower half plane:

$$(5.45)\quad \begin{cases} \dfrac{\partial^2 \phi'}{\partial t^2} + \lambda s_o \left(\dfrac{\partial \phi'}{\partial y'} + \beta\, \dfrac{\partial^2 \phi'}{\partial t \partial y'}\right) = e^{i\omega t}\delta(x')\ , & y' = 0 \\ \Delta' \phi' = 0\ , & y' < 0 \\ \phi' \to 0 & y' \to -\infty \end{cases}$$

A problem nearly idential to this was solved by Lamb [13], who introduced into his water wave equations a frictional force acting in the interior proportional to fluid velocity. This frictional force was a fictitious device, introduced by Lamb in order to secure the uniqueness of the solution (that is, to rule out waves coming in from $\pm\infty$). At a certain stage of the calculation, the frictional forces were reduced to zero. In the present problem, the dissipative forces act on the surface only. This introduces a slight change in the equations. A more important difference is that we shall be interested in the form of the solution for finite β, as well as in the limit $\beta \to 0$. Lamb's method of solution, applied to the present problem, is as follows: Let

$$\phi'(x',y',t) = \Phi'(x',y')e^{i\omega t} \tag{5.46}$$

Then Φ' satisfies

$$\begin{cases} -\omega^2\Phi' + \lambda s_o(1+i\omega\beta)\dfrac{\partial\Phi'}{\partial y'} = \delta(x') & y' = 0 \\ \Delta'\Phi' = 0 & y' < 0 \\ \Phi' \to 0 & y' \to -\infty \end{cases} \tag{5.47}$$

The general solution of the last pair of equations can be written

$$\Phi'(x',y') = \frac{1}{2\pi}\int_{-\infty}^{\infty} d\xi\ f(\xi)\ \exp(i\xi x'+|\xi|y') \tag{5.48}$$

Note that

$$\Phi'(x',0) = \frac{1}{2\pi}\int_{-\infty}^{\infty} d\xi\ f(\xi)\ \exp(i\xi x') \tag{5.49}$$

$$\frac{\partial\Phi'}{\partial y'}(x',0) = \frac{1}{2\pi}\int_{-\infty}^{\infty} d\xi\ f(\xi)|\xi|\ \exp(i\xi x') \tag{5.50}$$

$$\delta(x') = \frac{1}{2\pi}\int_{-\infty}^{\infty} d\xi \, \exp(i\xi x') \tag{5.51}$$

Substituting in the boundary condition which holds along $y' = 0$, we obtain

$$\left\{-\omega^2 + \lambda s_o(1+i\omega\beta)|\xi|\right\} f(\xi) = 1 \tag{5.52}$$

Therefore

$$\Phi'(x',y') = \frac{1}{2\pi}\int_{-\infty}^{\infty} \frac{d\xi \, \exp(i\xi x' + |\xi| y')}{-\omega^2 + \lambda s_o(1+i\omega\beta)|\xi|} \tag{5.53}$$

We can split up this integral into two parts and write $\Phi'(x',y') = I_+ + I_-$, where

$$\begin{cases} I_+ = \dfrac{1}{2\pi}\displaystyle\int_0^{\infty} \dfrac{d\xi \, \exp(+i\xi x' + \xi y')}{-\omega^2 + \lambda s_o(1+i\omega\beta)\xi} \\ \\ I_- = \dfrac{1}{2\pi}\displaystyle\int_0^{\infty} \dfrac{d\xi \, \exp(-i\xi x' + \xi y')}{-\omega^2 + \lambda s_o(1+i\omega\beta)\xi} \end{cases} \tag{5.54}$$

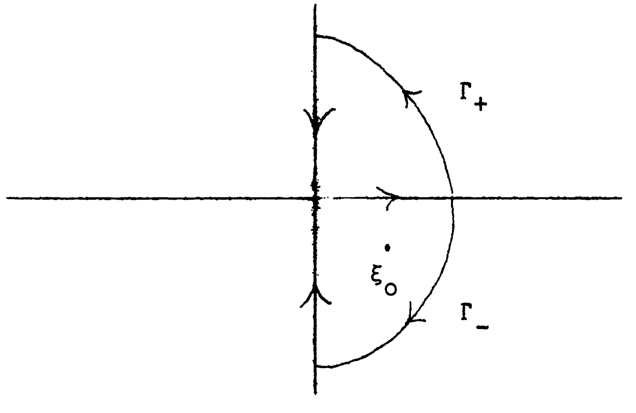
It is convenient to introduce the notation $z' = x' + iy'$, $\overline{z'} = x' - iy'$, in terms of which we have

$$
(5.55) \quad \begin{cases} I_+ = \dfrac{1}{2\pi} \displaystyle\int_0^\infty \dfrac{d\xi \, \exp(i\xi \bar{z}')}{-\omega^2 + \lambda s_o (1+i\omega\beta)\xi} \\[2ex] I_- = \dfrac{1}{2\pi} \displaystyle\int_0^\infty \dfrac{d\xi \, \exp(-i\xi z')}{-\omega^2 + \lambda s_o (1+i\omega\beta)\xi} \end{cases}
$$

Each of the integrands has a pole at

$$
(5.56) \qquad \xi_o = \frac{(\omega^2/\lambda s_o)}{1+i\omega\beta}
$$

The constants λ, s_o, β are positive. In the following we will assume that $\omega > 0$. Then Re $(\xi_o) > 0$, Im $(\xi_o) < 0$. Also, we restrict consideration to $x' = \text{Re}\,(z') = \text{Re}\,(\bar{z}') > 0$.



Using the contours indicated in the figure, we can therefore show that

(5.57)
$$\begin{cases} I_+ = \dfrac{1}{\lambda s_o(1+i\omega\beta)} \dfrac{i}{2\pi} \displaystyle\int_0^\infty \dfrac{d\eta \, \exp(-\eta\bar{z}')}{-\xi_o+i\eta} \\ \\ I_- = \dfrac{1}{\lambda s_o(1+i\omega\beta)} \dfrac{i}{2\pi} \displaystyle\int_0^\infty \dfrac{d\eta \, \exp(-\eta z')}{\xi_o+i\eta} + \end{cases}$$

$$\frac{-1}{\lambda s_o(1+i\omega\beta)} \, i \, \exp(-i\xi_o z')$$

Therefore $\Phi(x,y) = \Phi_1(x,y) + \Phi_2(x,y)$, where

(5.58)
$$\begin{cases} -\lambda s_o(1+i\omega\beta)\Phi_1(x,y) = i \exp(-i\xi_o z') \\ \\ \lambda s_o(1+i\omega\beta)\Phi_2(x,y) = \dfrac{i}{2\pi} \displaystyle\int_0^\infty d\eta \left\{ \dfrac{\exp(-\eta\bar{z}')}{-\xi_o+i\eta} + \dfrac{\exp(-\eta z')}{\xi_o+i\eta} \right\} \\ \\ z' = \exp(\lambda z) = \exp\left[\lambda(x+iy)\right] \end{cases}$$

The interesting part of the motion is associated with Φ_1 (Φ_2 will be considered below). Substituting for z' and differentiating with respect to y:

$$(5.59)\quad \begin{cases} -\lambda s_o(1+i\omega\beta)\Phi_1(x,y) = i\exp(-i\xi_o\exp(\lambda z)) \\ -\lambda s_o(1+i\omega\beta)\dfrac{\partial\Phi_1}{\partial y}(x,y) = \lambda i\xi_o\exp(\lambda z)\exp(-i\xi_o\exp(\lambda z)) \end{cases}$$

where we have used $\frac{\partial z}{\partial y} = i$.

Note that

$$(5.60)\qquad |\xi_o\exp(\lambda z)| = |\xi_o|\exp(\lambda x)$$

Therefore

$$(5.61)\qquad \xi_o\exp(\lambda z) = |\xi_o|\exp(\lambda x)\exp(-i\delta)$$

where δ is a real function of y and ξ_o. With this notation we have

$$-\lambda s_o(1+i\omega\beta)\frac{\partial\Phi_1}{\partial y}$$

$$= \lambda i|\xi_o|\exp\left\{\lambda x - i\delta - i|\xi_o|\exp(\lambda x - i\delta)\right\}$$

$$(5.62)\qquad = \lambda i|\xi_o|\exp\left\{\lambda x - |\xi_o|\sin\delta\exp(\lambda x)\right\}\cdot\exp\left\{-i\delta - i|\xi_o|\cos\delta\exp(\lambda x)\right\}$$

Provided that $\sin\delta > 0$, $|\partial\Phi_1/\partial y|$ therefore has a peak at $x = x_p$ given by

$$1 - |\xi_0| \sin\delta \exp(\lambda x_P) = 0$$

(5.63)

$$\lambda x_P = \log\left(\frac{1}{|\xi_0| \sin\delta}\right)$$

Let $x = x_P + \tilde{x}$. Then

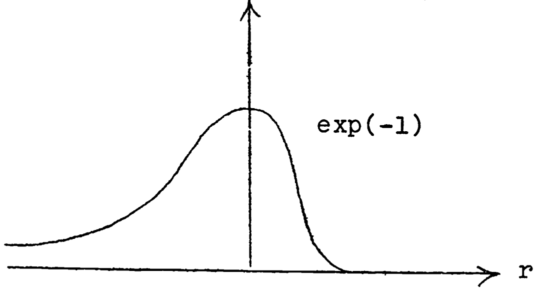
$$-\lambda s_o(1+i\omega\beta)\frac{\partial\Phi_1}{\partial y}$$

$$= \lambda i|\xi_o| \exp(\lambda x_P - i\delta) \circ \exp\left[\lambda\tilde{x} - \exp(\lambda\tilde{x})\right] \exp\left[-i\frac{\exp(\lambda\tilde{x})}{\tan\delta}\right]$$

(5.64) $$= \frac{\lambda i \exp(-i\delta)}{\sin\delta} \exp\left[\lambda\tilde{x} - \exp(\lambda\tilde{x})\right] \circ \exp\left[-i\frac{\exp(\lambda\tilde{x})}{\tan\delta}\right]$$

It is useful to introduce the real function A defined as follows

(5.65) $$A(r) = \exp\left[r - \exp(r)\right]$$



The function A has a peak at the origin given by $A(0) = \exp(-1)$. For $r \ll 0$, $A(r) \sim \exp(r)$. For $r \gg 0$, $A(r) \sim \exp(-\exp(r))$. In terms of A

$$-\lambda s_o(1+i\omega\beta)\frac{\partial\Phi_1}{\partial y}$$

$$= \frac{\lambda i\ \exp(-i\delta)}{\sin\delta} A(\lambda(x-x_P)) \circ \exp\left\{-i\frac{\exp(\lambda(x-x_P))}{\tan\delta}\right\} \tag{5.66}$$

There are two special cases which we shall consider.

I. Suppose $\beta > 0$, and examine the solution along $y = 0$. We have

$$\xi_o = \frac{\omega^2/\lambda s_o}{1+i\omega\beta} = |\xi_o| \exp(-i\delta_I) \tag{5.67}$$

where

$$\begin{cases} \tan\delta_I = \omega\beta \\ \sin\delta_I = \dfrac{\omega\beta}{\sqrt{1+\omega^2\beta^2}} > 0 \end{cases} \tag{5.68}$$

and $0 < \delta_I < \frac{\pi}{2}$. Since $y = 0$, $z = x$, and

$$\xi_o \exp(\lambda z) = |\xi_o| \exp(\lambda x) \exp(-i\delta_I) \tag{5.69}$$

We can therefore identify δ_I with the quantity δ which appears in the foregoing.

II. On the other hand, suppose $\beta = 0$, and examine the solution along $\lambda y = -\delta_{II}$. When $\beta = 0$, $\xi_o = \omega^2$, and we have

$$\xi_o \exp(\lambda z) = |\xi_o| \exp(\lambda x - i\delta_{II})$$

$$= |\xi_o| \exp(\lambda x) \exp(-i\delta_{II}) \tag{5.70}$$

Since $0 < \lambda y < -\frac{\pi}{2}$, $0 < \delta_{II} < \frac{\pi}{2}$, and $\sin \delta_{II} > 0$, as required for the existence of a peak in the amplitude of the solution. Again, we can identify δ_{II} with the quantity δ which appears above.

An important difference between the two cases is the following. The quantity δ_I is a definite function of ω, but δ_{II} is an arbitrarily chosen constant which determines a certain non-zero depth through $\lambda y = -\delta_{II}$. It seems natural to let $\delta_{II} \to 0$ in order to study the motion of the basilar membrane when $\beta = 0$ (no dissipation). When this is attempted, serious difficulties arise immediately. For example $x_p \to \infty$. In fact, if we consider $\beta = 0$, fix x, and let $y \to 0$, we obtain

$$\lim_{y \to 0} \frac{\partial \Phi_1}{\partial y}(x,y) = \frac{i\xi_o \exp(\lambda x)}{s_o} \exp\left[-i\xi_o \exp(\lambda x)\right] \tag{5.71}$$

which grows without bound as $x \to \infty$. Of course, no such phenomenon is observed in the cochlea. Note that, in this limiting solution, not only the magnitude but also the spatial frequency of $(\partial\Phi_1/\partial y)$ grows without bounds. This suggests that ultimately the viscosity of the fluid, which is not included in the model, must limit the growth of the solution when membrane viscosity is absent. It is well known that the effects of fluid viscosity are often confined to a thin layer near the boundary, the remainder of the flow being essentially inviscid. Moreover, the component of velocity normal to the boundary should be nearly constant across the boundary layer, since the layer is thin and the fluid is incompressible. This suggests that we can get a rough indication of the motion of the basilar membrane in the presence of fluid viscosity by inspecting the inviscid solution at the edge of the boundary layer. This suggests that we identify (δ_{II}/λ) with the boundary layer thickness, which at frequency ω is given roughly by $\sqrt{\nu/\omega}$, where ν is the kinematic viscosity of the fluid. Thus set

$$\delta_{II} = \lambda\left(\frac{\nu}{\omega}\right)^{\frac{1}{2}} \tag{5.72}$$

In the human cochlea, $\lambda^{-1} = 0.7$ cm, $\nu = 0.02$ cm^2/sec, and a typical value of ω would be $2\pi \times 10^3$/sec. This gives as a typical value

$$\delta_{II} = 2.5 \times 10^{-3} \tag{5.73}$$

Since δ_{II} is proportional to $\omega^{-1/2}$, the frequency of the sound could change by a factor of up to 16 (that is, by 4 octaves) in either direction (covering much of the range of human hearing) without changing δ_{II} by a factor of more than 4.

This identification of δ_{II}/λ with the boundary layer thickness puts our two cases on the same footing in the sense that δ_I and δ_{II} are now definite functions of ω. Note, however, that $(\partial\delta_I/\partial\omega) > 0$, while $(\partial\delta_{II}/\partial\omega) < 0$.

We would like assert that the expression derived above for $\partial\Phi_1/\partial y$ describes the motion of the basilar membrane. Before this claim can be made, however, we have to show that $\partial\Phi_2/\partial y$ can be neglected in comparison with $\partial\Phi_1/\partial y$. In fact we will not be able to prove this in general because of the decay of $\partial\Phi_1/\partial y$ away from $x = x_P$ which is especially rapid when $x > x_P$. But we will be able to show, for sufficiently small δ, that $|\partial\Phi_2/\partial y| << |\partial\Phi_1/\partial y|$ near $x = x_P$.

We begin by deriving a bound on $|\partial\Phi_2/\partial y|$. We have

$$(5.74) \qquad \lambda s_o(1+i\omega\beta)\Phi_2 = \frac{i}{2\pi}\int_0^\infty d\eta \left\{\frac{\exp(-\eta\bar{z}')}{-\xi_o+i\eta} + \frac{\exp(-\eta z')}{\xi_o+i\eta}\right\}$$

where

$$(5.75) \qquad \begin{cases} z' = \exp(\lambda z) = \exp(\lambda(x+iy)) \\ \bar{z}' = \exp(\lambda\bar{z}) = \exp(\lambda(x-iy)) \end{cases}$$

Therefore

$$\left\{\begin{aligned} \frac{\partial z'}{\partial y} &= \lambda i z' \\ \frac{\partial \bar{z}'}{\partial y} &= -\lambda i \bar{z}' \end{aligned}\right. \tag{5.76}$$

and

$$\lambda s_o(1+i\omega\beta)\ \frac{\partial \Phi_2}{\partial y}$$

$$= \frac{\lambda}{2\pi}\int_0^\infty d\eta\ \frac{\eta\bar{z}'\ \exp(-\eta\bar{z}')}{\xi_o - i\eta} + \frac{\eta z'\ \exp(-\eta z')}{\xi_o + i\eta} \tag{5.77}$$

$$\lambda s_o|1+i\omega\beta|\ \left|\frac{\partial \Phi_2}{\partial y}\right| \le \lambda\ \frac{|z'|}{2\pi}\ 2\int_0^\infty d\eta\ \frac{\eta\ \exp(-\eta x')}{\text{Re}\ (\xi_o)} \tag{5.78}$$

But

$$\int_0^\infty d\eta\ \eta\ \exp(-\eta x') = \frac{1}{(x')^2} = \frac{1}{\exp(2\lambda x)\ \cos^2\lambda y} \tag{5.79}$$

$$|z'| = \exp(\lambda x) \tag{5.80}$$

Therefore

$$\lambda s_o|1+i\omega\beta|\ \left|\frac{\partial \Phi_2}{\partial y}\right| \le \lambda\ \frac{1}{\pi \text{Re}\ (\xi_o)}\ \frac{1}{\exp(\lambda x)\ \cos^2\lambda y} \tag{5.81}$$

Now write $x = (x-x_P)+x_P$, and use

$$\exp(\lambda x_p) = \frac{1}{|\xi_o| \sin \delta} \tag{5.82}$$

to obtain

$$\lambda s_o |1+i\omega\beta| \left|\frac{\partial \Phi_1}{\partial y}\right| \le \frac{\lambda |\xi_o| \sin \delta}{\pi \operatorname{Re}(\xi_o)} \frac{\exp(-\lambda(x-x_P))}{\cos^2 \lambda y} \tag{5.83}$$

But

$$\lambda s_o |1+i\omega\beta| \left|\frac{\partial \Phi_2}{\partial y}\right| = \lambda \frac{A(\lambda(x-x_P))}{\sin \delta} \tag{5.84}$$

Therefore

$$\frac{|\partial \Phi_2/\partial y|}{|\partial \Phi_1/\partial y|} \le \frac{1}{\pi} \frac{|\xi_o|}{\operatorname{Re}(\xi_o)} \frac{\sin^2 \delta}{\cos^2 \lambda y} \frac{\exp(-\lambda(x-x_P))}{A(\lambda(x-x_P))} \tag{5.85}$$

Let

$$\alpha = \frac{1}{\pi} \frac{|\xi_o|}{\operatorname{Re}(\xi_o)} \frac{\sin^2 \delta}{\cos^2 \lambda y} \tag{5.86}$$

$$B(r) = \frac{\exp(-r)}{A(r)} = \frac{1}{\exp(2r-\exp(r))} \tag{5.87}$$

Let $I(C)$ be the interval of values of r such that $B(r) \le C$. For $C > \exp(1)$, this interval includes $r = 0$, and the interval can be extended as much as as we like in both directions by choosing C sufficiently large. Then for $\lambda(x-x_p) \in I(C)$ we have

(5.88) $$\frac{|\partial\Phi_2/\partial y|}{|\partial\Phi_1/\partial y|} \leq \alpha C$$

We now show that by choosing the appropriate range of frequencies, α can be made arbitrarily small. In Case I, $y = 0$, and $\xi_o = |\xi_o| \exp(-i\delta_I)$. Therefore $\text{Re}(\xi_o) = |\xi_o| \cos \delta_I$. Thus

$$\alpha_I = \frac{1}{\pi} \frac{\sin^2\delta_I}{\cos \delta_I} = \frac{1}{\pi} \tan \delta_I \sin \delta_I$$

(5.89) $$= \frac{1}{\pi} \frac{\omega^2\beta^2}{\sqrt{1+\omega^2\beta^2}} < \frac{1}{\pi} \omega^2\beta^2$$

In Case II, ξ_o is real and positive. Thus $|\xi_o| = \text{Re}(\xi_o)$. Also $-y = (\delta_{II}/\lambda) = (\nu/\omega)^{1/2}$. Therefore

(5.90) $$\alpha_{II} = \frac{1}{\pi} \tan^2 \left\{\lambda\left(\frac{\nu}{\omega}\right)^{\frac{1}{2}}\right\} = O\left(\frac{1}{\pi} \lambda^2 \frac{\nu}{\omega}\right)$$

To make α as small as we like, we need only choose ω sufficiently small in Case I and sufficiently large in Case II.

Suppose, then, that we are given a bounded interval of values of $\lambda(x-x_p)$, on which we want to impose the requirement

(5.91) $$\frac{|\partial\Phi_2/\partial y|}{|\partial\Phi_1/\partial y|} < \varepsilon$$

We can always do this by choosing C so large that the given interval is a subset of I(C) and then by restricting ω so that $\alpha < \frac{\varepsilon}{C}$.

In the following we assume that ω has been thus restricted, and we interpret $\partial\Phi_1/\partial y$ as the complex amplitude of the velocity of the basilar membrane. Putting in the time dependence, we have

$$\frac{\partial h}{\partial t} = \frac{1}{s_o(1+i\omega\beta)} \frac{i\,\exp(-i\delta)}{\sin\delta} A(\lambda(x-x_P)) \cdot \exp\left\{ i\left(\omega t - \frac{\exp(\lambda(x-x_P))}{\tan\delta}\right)\right\} \tag{5.92}$$

where

$$\lambda x_P = \log \frac{1}{|\xi_o| \sin\delta} \tag{5.93}$$

$$\xi_o = \frac{\omega^2/\lambda s_o}{1+i\omega\beta} \tag{5.94}$$

$$A(r) = \exp(r-\exp(r)) \tag{5.95}$$

and where, in Case I

$$\delta = \delta_I = \text{arc tan } \omega\beta \tag{5.96}$$

while in Case II, $\beta = 0$, and

(5.97) $$\delta = \delta_{II} = \lambda\left(\frac{\nu}{\omega}\right)^{\frac{1}{2}}$$

This solution is a traveling wave with a stationary envelope. The envelope has the shape of the function A, independent of ω. It has a peak at $x = x_P$, which depends on ω. To the left of the peak the envelope decays exponentially, while to the right of the peak it decays like an exponential of an exponential. The phases of the wave travel to the right, and the spatial frequency increases exponentially with increasing x.

To conclude this section we examine the dependence on ω of the position of the peak and of the spatial frequency at the peak. In Case I,

(5.98) $$|\xi_o| = \frac{\omega^2}{\lambda s_o} \frac{1}{\sqrt{1+\omega^2\beta^2}}$$

(5.99) $$\sin \delta_I = \frac{\omega\beta}{\sqrt{1+\omega^2\beta^2}}$$

(5.100) $$(\lambda x_P)_I = \log \frac{1}{|\xi_o| \sin \delta_I} = \log \frac{1+\omega^2\beta^2}{\left(\frac{\omega^2}{\lambda s_o}\right) \omega\beta}$$

For $\omega\beta << 1$, which is the situation of interest in Case I, we have approximately

(5.101) $$(\lambda x_P)_I = \log \frac{1}{\left(\frac{\omega^2}{s_o}\right) \omega\beta} = -3 \log \frac{\omega}{\omega_o}$$

where $\omega_o^3 = \lambda s_o/\beta$. In Case II,

(5.102) $$|\xi_o| = \frac{\omega^2}{\lambda s_o}$$

(5.103) $$\sin \delta_{II} = \sin \lambda\left(\frac{\nu}{\omega}\right)^{\frac{1}{2}}$$

(5.104) $$(\lambda x_P)_{II} = \log \frac{1}{\frac{\omega^2}{\lambda s_o} \sin \lambda\left(\frac{\nu}{\omega}\right)^{1/2}}$$

For $\lambda\left(\frac{\nu}{\omega}\right)^{1/2} << 1$, which is the situation of interest in Case II, we have approximately

(5.105) $$(\lambda x_P)_{II} = \log \frac{1}{\frac{\omega^2}{s_o}\left(\frac{\nu}{\omega}\right)^{1/2}} = -\frac{3}{2} \log \frac{\omega}{\omega_o}$$

where ω_o is now given by $\omega_o^{3/2} = s_o/\nu^{1/2}$.

In both cases, the position of the peak varies linearly with the log of the frequency of the sound. The slopes are different, however, being -3 in the case of membrane viscosity, and -3/2 in the case of fluid viscosity.

A more dramatic difference between the two cases appears when we consider the spatial frequency of the waves as a function of ω. By spatial frequency we mean the derivative of the phase with respect to x. Evaluating this quantity at $x = x_p$ we get $\frac{\lambda}{\tan \delta} \approx \frac{\lambda}{\delta}$. Thus in Case I we get $\frac{\lambda}{\omega\beta}$. In Case II we get approximately $(\omega/\nu)^{1/2}$, which is just the reciprocal of the boundary layer thickness. Thus the theory based on membrane viscosity predicts that the principal spatial frequency will vary *inversely* with the temporal frequency of the sound, while the theory based on fluid viscosity predicts that it will vary *directly* with the square root of the frequency of the sound.

4. The Two Dimensional Cochlea with Fluid Viscosity.

a. Formulation:

Here we generalize the model of the previous section by including fluid viscosity. At the same time we set $\beta = 0$ and let the depth $a \to \infty$. These simplifications are not essential, and could be removed without substantial changes in method.

The appropriate equations for this case were derived in Section 2, and we state them together as follows:

(5.106)
$$\begin{cases} \dfrac{\partial u}{\partial t} + \dfrac{\partial p}{\partial x} = \nu\Delta u \\[2ex] \dfrac{\partial v}{\partial t} + \dfrac{\partial p}{\partial y} = \nu\Delta v + \ell\delta(y) \\[2ex] \dfrac{\partial u}{\partial x} + \dfrac{\partial v}{\partial y} = 0 \\[2ex] \dfrac{\partial h}{\partial t}(x,t) = v(x,0,t) \\[2ex] \ell(x,t) = -e^{-x}h(x,t) \end{cases}$$

where (u,v) = velocity field of the fluid

p = pressure

ν = viscosity

h = displacement of the basilar membrane

ℓ = force per unit length exerted by the basilar membrane on the fluid.

$\Delta = \partial_x^2 + \partial_y^2$

and where we have chosen our unit of length as the length constant of the basilar membrane and our unit of mass in such a way that $\rho = 1$.

b. Reduction to a Problem on the Basilar Membrane:

First, look for a solution in which all quantities depend on time like $\exp(i\omega t)$. Thus let $h(x,t) = \text{Re}\,\{H(x)\exp(i\omega t)\}$, etc. The quantities H, etc., are complex. Their magnitudes give the amplitudes and their angles give the phases of the corresponding physical variables. The equations relating the quantities H, etc., can be found by replacing ∂_t by $i\omega$ in Eqs.(5.106):

(5.107) $$i\omega U + \frac{\partial P}{\partial x} = \nu \Delta U$$

(5.108) $$i\omega V + \frac{\partial P}{\partial y} = \nu \Delta V + L\delta(y)$$

(5.109) $$\frac{\partial U}{\partial x} + \frac{\partial V}{\partial y} = 0$$

(5.110) $$i\omega H(x) = V(x,0)$$

(5.111) $$L(x) = -e^{-x}H(x)$$

This problem is not translation invariant because of the factor $\exp(-x)$ which appears in the boundary condition along $y = 0$. But the partial problem consisting of Eqs.(5.107-5.110) is translation invariant and can be solved through the use of Fourier transforms. We want to express $H(x)$ in terms of $L(x)$. This will achieve the desired reduction to a problem along $y = 0$.

Let

$$(5.112)\qquad \begin{cases} \hat{L}(\xi) = \int_{-\infty}^{\infty} e^{-i\xi x}\, L(x)\, dx \\ L(x) = \frac{1}{2\pi}\int_{-\infty}^{\infty} e^{i\xi x}\, \hat{L}(\xi)\, d\xi \end{cases}$$

and similarly for other quantities. Then for each ξ we have the system of ordinary differential equations

$$(5.113)\qquad \begin{cases} i\omega\hat{U} + i\xi\hat{P} = \nu\left(-\xi^2 + \frac{d^2}{dy^2}\right)\hat{U} \\ i\omega\hat{V} + \frac{d\hat{P}}{dy} = \nu\left(-\xi^2 + \frac{d^2}{dy^2}\right)\hat{V} + \hat{L}\delta(y) \\ i\xi\hat{U} + \frac{d\hat{V}}{dy} = 0 \end{cases}$$

A convenient way to solve this system is to begin by solving for $\hat{P}$. Multiply the first equation by $i\xi$ and apply $\frac{d}{dy}$ to the second. Adding, and using the third equation, we obtain

$$(5.114)\qquad \left(-\xi^2 + \frac{d^2}{dy^2}\right)\hat{P} = \hat{L}\delta'(y)$$

Incidently, this shows that for given $L(x)$, the distribution of pressure in the fluid is independent of viscosity. The solution is

$$\hat{P} = \frac{1}{2} e^{-|\xi||y|} \operatorname{sgn}(y) \hat{L} \tag{5.115}$$

which has

$$\frac{d\hat{P}}{dy} = \left\{ -\frac{|\xi|}{2} e^{-|\xi||y|} + \delta(y) \right\} \hat{L} \tag{5.116}$$

Substituting this in (5.113) we find

$$\left(\frac{i\omega}{\nu} + \xi^2 - \frac{d^2}{dy^2} \right) \hat{V} = \frac{|\xi|}{2\nu} e^{-|\xi||y|} \hat{L} \tag{5.117}$$

There is a solution of the following form

$$\hat{V} = C_1 \frac{|\xi|}{2\nu} \left\{ e^{-|\xi||y|} + C_2 e^{-\sqrt{\xi^2 + \frac{i\omega}{\nu}}\, |y|} \right\} \hat{L} \tag{5.118}$$

The constant C_1 is to be chosen so that (5.118) is a solution of (5.117) on $y > 0$ and $y < 0$. The constant C_2 is to be chosen so that $\partial\hat{V}/\partial y$ is continuous at $y = 0$. Since $\hat{V}$ is an even function, this is equivalent to $\partial\hat{V}/\partial y = 0$ at $y = 0$. We find

$$\frac{i\omega}{\nu} C_1 = 1 \tag{5.119}$$

$$|\xi| + \sqrt{\xi^2 + \frac{i\omega}{\nu}}\, C_2 = 0 \tag{5.120}$$

Therefore

$$\hat{V}(\xi,0) = \frac{|\xi|}{2i\omega}\left[1 - \frac{1}{\sqrt{1 + \frac{i\omega}{\nu\xi^2}}}\right]\hat{L}(\xi) \tag{5.121}$$

In terms of the displacements of the basilar membrane we have

$$i\omega\hat{H}(\xi) = \hat{V}(\xi,0) \tag{5.122}$$

and hence

$$\hat{H}(\xi) = -\hat{K}(\xi)\hat{L}(\xi) \tag{5.123}$$

where

$$\hat{K}(\xi) = \frac{|\xi|}{2\omega^2}\left[1 - \frac{1}{\sqrt{1 + \frac{i\omega}{\nu\xi^2}}}\right] \tag{5.124}$$

Note that for small values of ξ^2,

$$\hat{K}(\xi) \cong \frac{|\xi|}{2\omega^2} \tag{5.125}$$

and that the viscosity ν does not appear in this approximate formula. Thus the viscosity does not influence the low spatial frequencies. For large values of ξ^2, on the other hand

$$\hat{K}(\xi) \cong \frac{|\xi|}{2\omega^2}\left[1 - (1 - \frac{1}{2}\frac{i\omega}{\nu\xi^2})\right] = \frac{i}{4\omega\nu|\xi|} \tag{5.126}$$

Thus $\hat{K}(\xi)$ behaves like $|\xi|^{-1}$ for large values of ξ^2 because of the non-zero viscosity. The spatial frequency at which the viscosity begins to play an important role is given by

$$\frac{1}{\xi} = \sqrt{\frac{\nu}{\omega}} \tag{5.127}$$

In the previous section this quantity was used as an estimate of the boundary layer thickness.

Let F denote the Fourier transform and F* its inverse. Let $\hat{K}$ stand for multiplication by $\hat{K}(\xi)$ and let E stand for multiplication by e^{-x}. We then have the following equation for H:

$$H = - F^*\hat{K}FL \tag{5.128}$$

but

$$L = -EH \tag{5.129}$$

Therefore:

$$H = F^*\hat{K}FEH \tag{5.130}$$

This completes the reduction of our equations to a problem on the basilar membrane.

Remark: Eq.(5.130) is an eigenproblem for the operator $F^*\hat{K}FE$. We seek the eigenvector corresponding to eigenvalue 1. If this problem has a solution, say $H_0(x)$, then the spectrum of $F^*\hat{K}FE$ is continuous and includes at least the positive real axis. Moreover, the eigenvectors are simply all the possible translates of $H_o(x)$. To see this, let $K = F^*\hat{K}F$ and note that K is a convolution operator. In particular it commutes with translation. Let

$$(5.131)\qquad (T_aH)(x) = H(x-a)$$

Then $T_aK = KT_a$, but

$$(5.132)\qquad \begin{aligned}(T_aEH)(x) &= (EH)(x-a) = e^{-(x-a)}H(x-a)\\ &= e^a(ET_aH)(x)\end{aligned}$$

Thus $T_aE = e^aET_a$. Now, by hypothesis

$$(5.133)\qquad H_o = KEH_o$$

$$(5.134)\qquad (T_aH_o) = T_aKEH_o = e^aKE(T_aH_o)$$

Therefore T_aH_o is an eigenvector of $KE = F^*\hat{K}FE$ with eigenvalue e^a. Since a may be any real number, and since the function e^a maps the real line onto the positive real line, this confirms the statement made above.

The problem $H = F^*\hat{K}FEH$ can also be stated in variational form. This will be important in the next section. The least-squares form of this problem is as follows. Minimize:

$$(5.135)\qquad \int_{-\infty}^{\infty} |(I-F^*\hat{K}FE)H|^2\,dx$$

Subject to the constraint

$$\int_{-\infty}^{\infty} |H(x)|^2 \, dx = 1 \tag{5.136}$$

In the continuous context we expect the minimum to be zero, but in the discrete context we expect some finite minimum which $\to 0$ as $N \to \infty$.

c. Discretization:

The discrete Fourier transform [14] $F_N: C^N \to C^N$ is given by the matrix

$$(F_N)_{kj} = \frac{1}{\sqrt{N}} e^{-i\frac{2\pi}{N} jk} \qquad j,k = 1,2,\ldots,N \tag{5.137}$$

Its Hermitian conjugate is given by

$$(F_N^*)_{jk} = \frac{1}{\sqrt{N}} e^{+i\frac{2\pi}{N} jk} \tag{5.138}$$

and we have

$$(F_N^* F_N)_{jj'} = \frac{1}{N} \sum_{k=1}^{N} e^{i \frac{2\pi}{N}(j-j')k} = \delta_{jj'} \tag{5.139}$$

so that $F_N^* F_N = I_N$, the identity in C^N, and F_N is unitary.

Note that the matrix elements of F_N are periodic in j and k with period N. This makes the choice $j,k = 1,\ldots,N$ arbitrary. In the following we shall set $N = 2m$, m an integer, and use

$j,k = -m,\dots,m-1$.

The correspondance between F_N and the continuous Fourier transform can be brought out in the following way. Given a vector ϕ^N in C^N with components $\{\phi_j^N,\ j = -m,\dots,m-1\}$ and its discrete Fourier transform $\hat{\phi}^N = F_N\phi^N$, we construct two complex-valued functions $\phi^N(x)$ and $\hat{\phi}^N(\xi)$ as follows

(5.140) $$\hat{\phi}^N(\xi) = \sum_{j=-m}^{m-1} (\Delta x)_N\, e^{-i\xi x_j^N}\, \phi_j^N$$

(5.141) $$\phi^N(x) = \frac{1}{2\pi} \sum_{k=-m}^{m-1} (\Delta\xi)_N\, e^{i\xi_k^N x}\, \hat{\phi}_k^N$$

where

(5.142) $$N = 2m, \quad m \text{ an integer}$$

(5.143) $$x_j^N = jN^{-1/2} \qquad (\Delta x)_N = N^{-1/2}$$

(5.144) $$\xi_k^N = 2\pi kN^{-1/2} \qquad (\Delta\xi)_N = 2\pi N^{-1/2}$$

so that

(5.145) $$(\Delta x)_N(\Delta\xi)_N = \frac{2\pi}{N}$$

(5.146) $$\xi_k^N x_j^N = \frac{2\pi}{N}\, jk$$

Note that when $j,k = -m,\dots,m-1$

(5.147) $$\hat{\phi}^N(\xi_k^N) = \hat{\phi}_k^N$$

(5.148) $$\phi^N(x_j^N) = \phi_j^N$$

which justifies the use of the name ϕ^N for both the vector in C^N and the corresponding complex-valued function.

The trigonometric polynomials $\phi^N(x)$ and $\hat{\phi}^N(\xi)$ are periodic functions with period $N^{1/2}$ and $2\pi N^{1/2}$, respectively. Using this fact and the periodicity of the matrix elements of F_N, we may write

(5.149) $$\hat{\phi}^N(\xi) = \sum_{j=-m}^{m}{}^{T} (\Delta x)_N \, e^{-i\xi x_j^N} \phi^N(x_j^N)$$

(5.150) $$\phi^N(x) = \frac{1}{2\pi} \sum_{k=-m}^{m}{}^{T} (\Delta\xi)_N \, e^{i\xi_j^N x} \hat{\phi}^N(\xi_k^N)$$

where $\sum^T$ means the following

(5.151) $$\sum_{j=a}^{b}{}^{T} c_j = \frac{1}{2} c_a + c_{a+1} + \ldots + c_{b-1} + \frac{1}{2} c_b$$

Formulae (5.149-5.150) are therefore discretizations of the integrals in the Fourier transform and its inverse according to the trapezoidal rule.

Using the correspondance established above between vectors in C^N and trigonometric polynomials, we can easily introduce diagonal matrices corresponding to the muliplication operators

E and $\hat{K}$. The off-diagonal elements will be zero, and the diagonal elements will be given by

$$(5.152) \qquad (E_N)_{jj} = \begin{cases} e^{-x_j^N} , & j = -(m-1),\ldots,(m-1) \\ \dfrac{e^{-x_m^N} + e^{-x_{-m}^N}}{2} , & j = -m \end{cases}$$

$$(5.153) \qquad (\hat{K}_N)_{kk} = \hat{K}(\xi_k^N)$$

The norm that we should use in C^N is the Euclidian norm, except for a factor $N^{-1/4}$. This can be seen as follows. Let

$$||\phi^N||^2 = \int_{-x_m^N}^{x_m^N} |\phi^N(x)|^2 \, dx = \frac{1}{N} N^{\frac{1}{2}} \sum_{k=-m}^{m-1} |\hat{\phi}_k^N|^2$$

$$(5.154) \qquad = N^{-\frac{1}{2}} \sum_{j=-m}^{m-1} |\phi_j^N|^2$$

At the end of the previous section we gave our continuous problem the following variational form: Minimize

$$(5.155) \qquad \int_{-\infty}^{\infty} |(I-F^*\hat{K}FE)H|^2 \, dx$$

subject to the constraint

$$(5.156) \qquad \int_{-\infty}^{\infty} |H|^2 \, dx = 1$$

The corresponding discrete problem is as follows: Find a vector H^N in C^N which minimizes

(5.157) $$||(I-F_N^*\hat{K}_N F_N E_N)H^N||$$

subject to the constraint

(5.158) $$||H^N|| = 1$$

This is equivalent to finding the eigenvector corresponding to the smallest eigenvalue of the non-negative Hermitian matrix $A_N^*A_N$ where

(5.159) $$A_N = I - F_N^*\hat{K}_N F_N E_N$$

(5.160) $$A_N^* = I - E_N F_N^* \hat{K}_N^* F_N$$

d. Solution of the discrete problem:

Given an Hermitian matrix $M > 0$ with a unique smallest eigenvalue, one can find the corresponding eigenvector by the method of inverse iteration [15]. That is, let

(5.161) $$MX^{n+1} = \frac{X^n}{||X^n||}$$

If $X^n \to X$, then $MX = \lambda X$, where $\lambda = \frac{1}{||X||}$. It remains to show that convergence occurs and that λ is the smallest eigenvalue. Let the eigenvalues be given by $0 < \lambda_1 < \lambda_2 \leq \lambda_3 \leq \cdots \leq \lambda_N$.

and let an orthonormal choice of the corresponding eigenvalues be $\{V_1,\ldots,V_N\}$. Let

(5.162) $$X^{o} = \sum_{j=1}^{N} c_j V_j$$

and assume $c_1 \neq 0$. Then

(5.163) $$X^{n} = \alpha_n \sum_{j=1}^{N} \lambda_j^{-n} c_j V_j$$

where α_n is real. After some algebra

(5.164) $$\frac{X^n}{||X^n||} = \frac{\beta V_1 + e^n}{\sqrt{1 + ||e^n||^2}}$$

where $\beta = c_1/|c_1|$ and

(5.165) $$e^n = \sum_{j=2}^{N} \left(\frac{\lambda_1}{\lambda_j}\right)^n \frac{c_j}{|c_1|} V_j$$

But

(5.166) $$||e^n||^2 = \sum_{j=2}^{N} \left(\frac{\lambda_1}{\lambda_2}\right)^{2n} \frac{|c_j|^2}{|c_1|^2} \leq \left(\frac{\lambda_1}{\lambda_2}\right)^{2n} C$$

where

(5.167) $$C = \sum_{j=2}^{N} \frac{|c_j|^2}{|c_1|^2}$$

Since $\lambda_1 < \lambda_2$, $||e^n||^2 \to 0$, and

$$\frac{X^n}{||X^n||} \to \beta V_1 \tag{5.168}$$

as required.

In the present problem it is very convenient to take the limit $N \to \infty$ during the process of inverse iteration. At each step of the inverse iteration we multiply N by 4. Because of the formula $x_j^N = jN^{-1/2}$, $j = -m,\ldots,m$ where $m = \frac{N}{2}$, this makes the computational mech twice as fine and twice as long. Thus we organize the computation as follows

$$A_N^* A_N H^N = \text{inter}\left\{ \frac{H^{N/4}}{||H^{N/4}||} \right\} \tag{5.169}$$

where inter is the interpolation - embedding process which takes us from $(\frac{N}{4}) \to N$. This process may be described as follows. First, the interior points are filled in by fitting a trigonometric polynomial to the mesh function $H^{N/4}$. Then, the resulting function is extended by zero on exterior mesh points. Because of the factor $N^{-1/2}$ which occurs in our definition of $||\ \ ||^2$, the operation inter is norm-preserving.

At each step of the iteration, we have to solve a linear system of the form $A_N^* A_N H^N = B^N$. Written out in terms of real and imaginary parts, this is a system of 2N equations in 2N unknowns with a real symmetric matrix.

A linear system with a real symmetric matrix can be solved by the iterative algorithm SYMMLQ [16] which is a form of the conjugate gradient method [17]. This algorithm does not require that the matrix be stored, but it does require a subroutine ATIMES which will multiply the matrix by an arbitrary vector.

In the present problem ATIMES can be very efficient. Recalling the definition of A_N, Eq.(5.159) we see that the operation to be performed by ATIMES can be broken down into simple steps which consist of multiplications by diagonal matrices or discrete Fourier transforms. The latter can be executed by means of the Fast Fourier Transform [14] which has an operation count proportional to N log N. The operation count for ATIMES will also have this form, since the rest of the operations grow linearly with N. The amount of storage required will grow only linearly with N.

In principle, the conjugate gradient method converges to the exact solution in N steps, and in practice with the proper scaling (see below) we have achieved accuracy limited by the machine precision in less than N steps. Thus the number of operations required to solve each linear system will be at worst proportional to $N^2 \log N$.

Numerical difficulties can be expected in the present problem because of the continuous spectrum of the operator $F^*\hat{K}FE$. Presumably the corresponding discrete operator has eigenvalues which are close together. In practice we found extremely slow convergence of the conjugate gradient method when we attempted to solve $A_N^* A_N H^N = B^N$. With N = 256 as many as 40 N iterations were required to get an accurate solution, and with N = 512 we could not achieve an accurate solution within reasonable limits of machine time. Since an accurate solution had been achieved in N steps with N = 64, the impression was that the performance was falling apart rapidly with increasing N. These difficulties were completely removed by the method of symmetric diagonal scaling. Such scaling is introduced as follows. Let D_N be a diagonal matrix with real elements to be determined below. Let $H^N = D_N G^N$. Multiplying through by D_N our system becomes

$$D_N A_N^* A_N D_N G^N = D_N B^N \tag{5.170}$$

Let the elements of A_N be a_{ij} and let the real diagonal elements of D_N be d_i. Then the elements of $D_N A_N^* A_N D_N$ are

$$\sum_{k=1}^{N} d_i \bar{a}_{ki} a_{kj} d_j = d_i d_j \quad (\underline{a}_i, \underline{a}_j) \tag{5.171}$$

where $\underline{a}_i$ = $i^{\underline{th}}$ column of A_N, and where $(\circ,\circ)$ is the usual inner product. Now set

$$d_i = \frac{1}{\sqrt{(\underline{a}_i, \underline{a}_i)}} \tag{5.172}$$

This choice gives the elements of $D_N A_N^* A_N D_N$ the form

$$(5.173) \qquad \frac{(\underline{a}_i, \underline{a}_j)}{\sqrt{(\underline{a}_i, \underline{a}_i)(\underline{a}_j, \underline{a}_j)}}$$

Thus the diagonal elements are all equal to 1, and the off-diagonal elements have magnitudes which are less than 1 (Schwarz inequality). In practice, this procedure completely removes the numerical difficulties mentioned above.

e. Results:

In the cochlea problem as formulated here, there is essentially only one parameter. This can be seen by writing $\hat{K}(\xi)$ as follows

$$(5.174) \qquad \hat{K}(\xi) = C_o|\xi| \left\{1 - \frac{1}{\sqrt{1 + \frac{1}{\delta^2 \xi^2}}}\right\}$$

where

$$(5.175) \qquad C_o = \frac{1}{2\omega^2}$$

$$(5.176) \qquad \delta^2 = \left(\frac{\nu}{\omega}\right)\lambda^2$$

(In the system of units of this section, $\lambda = 1$, but we insert the factor λ^2 so that the expression for δ will be correct in any system of units.)

As remarked above, changes in the parameter C_o merely produce a translation of the solution along the x axis. This can be used to put the peak of the solution near the center of the computational mesh. Otherwise the parameter C_o is inessential.

In the computational experiments to be discussed below we used the value $\delta = 10^{-2}$ which is 4 times the typical value of δ_{II} cited in Section 3. Our results therefore correspond to a low frequency tone applied to the human cochlea (62.5 cycles/sec).

With this choice of δ we performed the iteration

$$A_N^* A_N H^N = \text{inter} \frac{H^{N/4}}{||H^{N/4}||} \tag{5.177}$$

with $\log_2 N = 6,8,10$ and with $\log_2 N = 7,9,11$. The initial guess was a constant. As a test of convergence we used the parameter θ defined as follows

$$\cos\theta = \frac{|(H^N, H^{N/4})|}{||H^N||\ ||H^{N/4}||} \tag{5.178}$$

Thus, θ measures the angle between solutions at successive stages of the iteration.

The quantity $||H^N||$ is also of interest, because $||H^N||^{-1}$ measures, in a sense to be made precise below, the distance between the matrix $A_N^* A_N$ and a nearby singular matrix.

Let $Y = H^N$, $X = \text{inter } (H^{N/4})$, $M = A_N^* A_N$. We have

$$MY = \frac{X}{||X||} \tag{5.179}$$

Now construct the matrix

$$\delta M = \frac{1}{||Y||} \frac{XY^T}{||X|| \; ||Y||} \tag{5.180}$$

Note that

$$(\delta M)Y = \frac{X}{||X||} = MY \tag{5.181}$$

Thus, $M-\delta M$ is singular, since Y lies in its null space. On the other hand, the norm of the operator δM is $||Y||^{-1} = ||H^N||^{-1}$. Thus the computed value of $||H^N||^{-1}$ is an a posteriori bound on the norm of the smallest perturbation which makes M singular *.

The computational results are as follows:

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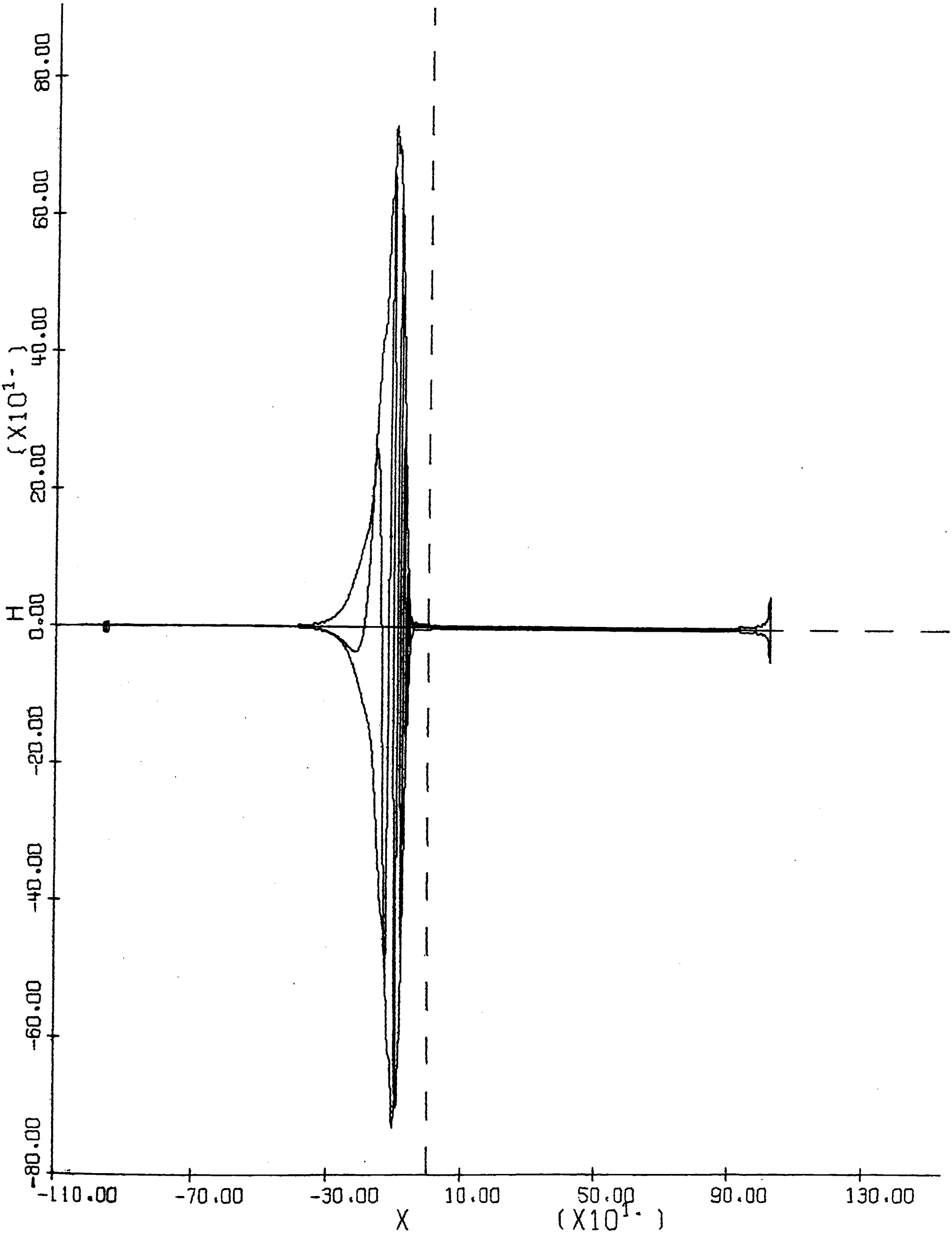
* I would like to thank Olof Widlund for pointing this out to me.

$\log_2 N$	$\|\|H^N\|\|$	$\theta(H^N, H^{N/4})$
6	2.45	1.32
8	473.	0.472
10	712.	0.057
7	4.89	1.36
9	615.	0.227
11	782.	0.035

In the figure which follows we plot Re $(H^N(x))$ together with $\pm |H^N(X)|$ for the case $\log_2 N = 11$, $N = 2048$. Note that the general features of the solution are as predicted in Section 3. It is a wave, the spatial frequency of which increases with x. Its evelope has a prominent peak and the decay to the left of the peak is much more gradual than to the right. Next, we give a similar plot of the Fourier transform of H. The predominance of negative spatial frequencies shows that the direction of wave propagation is to the right (consider $\exp(i(\omega t-\xi_0 x))$ where $\xi_0 > 0$).

We close this discussion with the following remark. Nowhere in the formulation of the problem in this section do we explicitly include a source of any kind. Nevertheless, we find a solution corresponding to a wave moving from left $\rightarrow$ right as though we had introduced a source at $x = -\infty$. Thus the form of the solution and even the direction of wave propagation must be properties of cochlea, rather than of the manner in which it is excited. This corresponds to von Bekesy's observation of paradoxical waves traveling toward the source which can be elicited by a vibrating stimulus at the apex of the cochlea.



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H
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X
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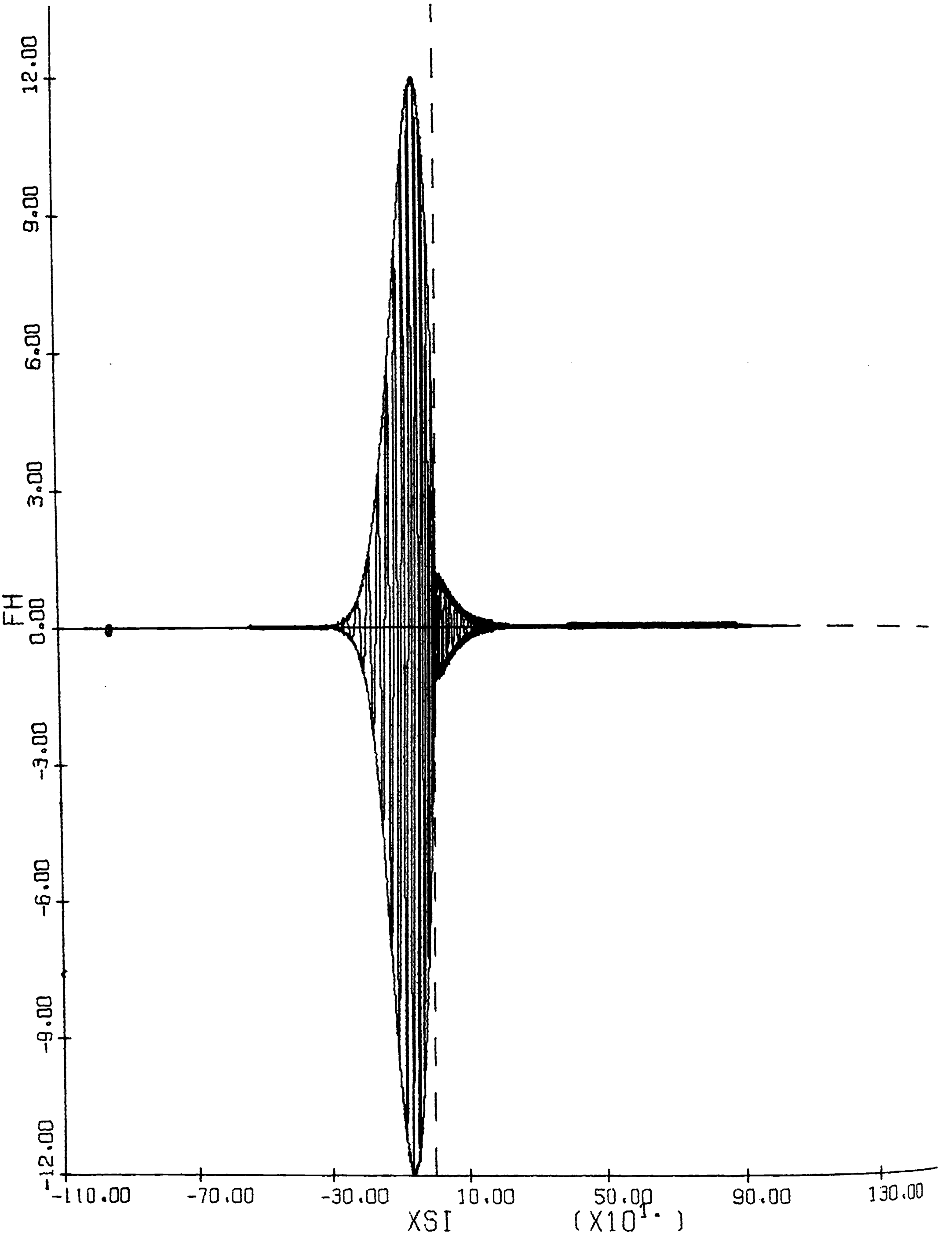
FH
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-12.00
-110.00
-70.00
-30.00
10.00
50.00
90.00
130.00
XSI
(X10^{1})

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VI. The Retina

The pattern of light shining on the retina is coded into a pattern of nerve impulses in the optic nerve. This code exhibits interesting spatial and temporal interactions which explain why certain patterns are easier to perceive than others. These interactions have been extensively studied in the compound eye of the horseshoe crab (Limulus), and a mathematical model, closely correlated with experiments, has been formulated by Bruce Knight [1].

This model assumes that the light shining on a receptor cell is coded into a generator potential, which in turn is coded into nerve impulses. The generator potential is influenced not only by the light, however, but also by the firing rate (frequency of nerve impulses) of the cell in question and also of other nearby cells. These feedback, or "recurrent" influences are inhibitory. That is, they oppose the action of light on the generator potential and they tend to reduce the firing rate of the cell.

The retina behaves approximately like a linear system when the light signal consists of small deviations superimposed on a constant background and when the response is measured in

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1 Knight, B.W., The Horseshoe Crab Eye: A little nervous system that is solvable; in Some mathematical questions in Biology 4. American Mathematical Society (1973). pp.113-144.

in terms of the changes in impulse frequency in the fibers of the optic nerve. Under these conditions, a general formulation of recurrent inhibition has been given as follows:

(6.1) $R(x,y,t)$

$$= E(x,y,t) - \lambda \int_{-\infty}^{\infty} dt' \iint_{-\infty}^{\infty} dx'dy'K(x-x',y-y',t-t')R(x',y',t')$$

where

$E(x,y,t)$ = Excitation. In the simplest case this would be proportional to the light intensity, but more generally it will be linearly related to the light intensity, e.g., through some ordinary differential equation at each point.

$R(x,y,t)$ = Response. This is the change in frequency of nerve impulses on an optic nerve fiber originating at point (x,y).

$\lambda K(x-x',y-y',t-t')$ = Inhibitory potential generated at (x,y,t) by an impulse of activity on the optic nerve at $x'y't'$. By writing the arguments of K as $x-x'$, $y-y'$, $t-t'$ we are assuming that the system is translation invariant in space and time. Since the system is also causal, $K(x,y,t) = 0$ for $t < 0$.

Equation (6.1) has the discrete counterpart:

$$R_j(t) = E_j(t) - \lambda \int_{-\infty}^{\infty} dt' \sum_{k=1}^{N} K_{jk}(t-t')R_k(t') \qquad (6.2)$$

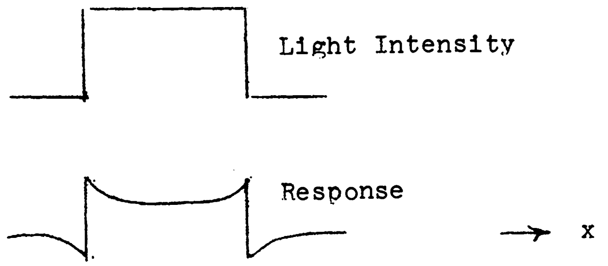
which is useful when the fact that the retina consists of discrete cells is of interest. Equations (6.1) or (6.2) are referred to as the Hartline-Ratliff equations.

Evidently, equations (6.1) or (6.2) define a broad class of models, depending on the choice of K and on he relation between E and the light. In the paper by Knight, referrred to above, the different transfer functions of the model are measured using sinusoidally varying stimuli of three types:

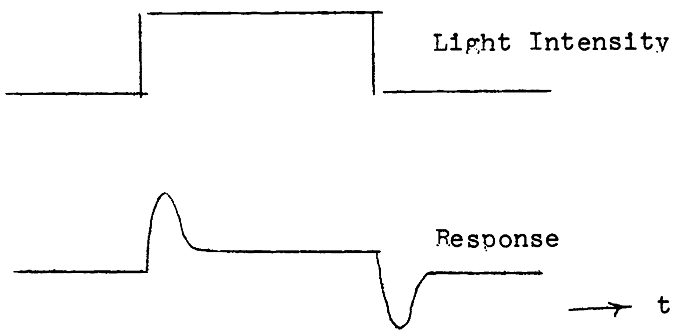
1) light
2) electric current injected at the sight of of the generator potential
3) electrical stimulation of the optic nerve (to control R directly).

In these notes, we shall study a similar model with properties which resemble those of the horseshoe crab retina. The model has the great advantage that it can be solved exactly for many light patterns of interest. Our purpose is not to give a detailed model of the horseshoe crab retina, but rather to give a simple analytic model based on recurrent inhibition which can explain the following phenomena:

1) When a time-independent strip of light is shined on the retina the response exhibits Mach Bands, as follows:



2) When a space-independent pulse of light is shined on the entire eye, the retina responds mainly to the transient:



3) When a sinusoidally varying spot of light is shined on the retina, the frequency response has a peak at a certain frequency, and this phenomenon is more pronounced for large spots than for small spots.

The model we shall use is a special case of (6.1) defined as follows. Let L be the light intensity, and let I be the second term on the right hand side of (6.1). That is, let I be the inhibition. Then our model will be given by the following equations:

$$(\tau\partial_t + 1)E = L \tag{6.3}$$

$$(\partial_t - \Delta + 1)I = \lambda R \tag{6.4}$$

$$R = E - I \tag{6.5}$$

where Δ is the Laplace operator, $\Delta = \partial_y^2 + \partial_y^2$.

To make the identification of (6.4)-(6.5) with (6.1), let K be the fundamental solution of (6.4). That is, let:

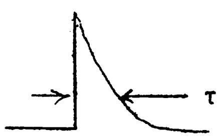
$$(\partial_t - \Delta + 1)K = \delta(t)\delta(x)\delta(y) \tag{6.6}$$

Then

$$K = \begin{cases} 0 & t < 0 \\ \frac{1}{4\pi t} \exp(- \frac{x^2+y^2}{4t} - t) & t > 0 \end{cases} \tag{6.7}$$

See Chapter III of these Notes for a derivation of the corresponding fundamental solution in the one-dimensional case.

A "physiological" picture corresponding to equations (6.3)-(6.5) can be given. Eq.(6.3) asserts that the response of the photoreceptor to a flash of light is a generator potential which is a step followed by an exponential decay. The actual generator potential is less sharp, corresponding to several steps of



integration. Eq.(6.4) asserts that the inhibitory potential diffuses latterally in all directions, according to the same equation that governs the spread of electrical charge in dendrites, that is, the diffusion equation with leakage. The source for the inhibitory potential is the local response R multiplied by a constant λ which measures the strength of the inhibitory coupling. Although it is not at all clear that such diffusion of the inhibitory interaction actually occurs, the anatomical substrate for it is present in the horseshoe crab retina in the form of a plexus of interconnecting fibers. Finally, equation (6.5) asserts that the excitatory part of the generator potential and the inhibitory part are summed (with the appropriate sign) and the result is converted into nerve impulses.

1. The Steady State.

In the steady state the model reduces to:

$$E = L \tag{6.8}$$

$$(-\Delta + 1)I = \lambda R = \lambda(E - I) = \lambda(L - I) \tag{6.9}$$

Therefore

$$(-\Delta + (\lambda+1))I = \lambda L \tag{6.10}$$

Suppose that

$$(6.11) \qquad L(x,y) = \begin{cases} 1 & x > 0 \\ 0 & x < 0 \end{cases}$$

Then I will be a function of x only and we expect a solution of the form:

$$(6.12) \qquad I = \begin{cases} \frac{\lambda}{\lambda+1} + Ae^{-(\lambda+1)^{1/2}x} & x > 0 \\ Be^{(\lambda+1)^{1/2}x} & x < 0 \end{cases}$$

Continuity of I and its derivative at x = 0 yield the equations

$$(6.13) \qquad \frac{\lambda}{\lambda+1} + A = B$$

$$(6.14) \qquad - A = B$$

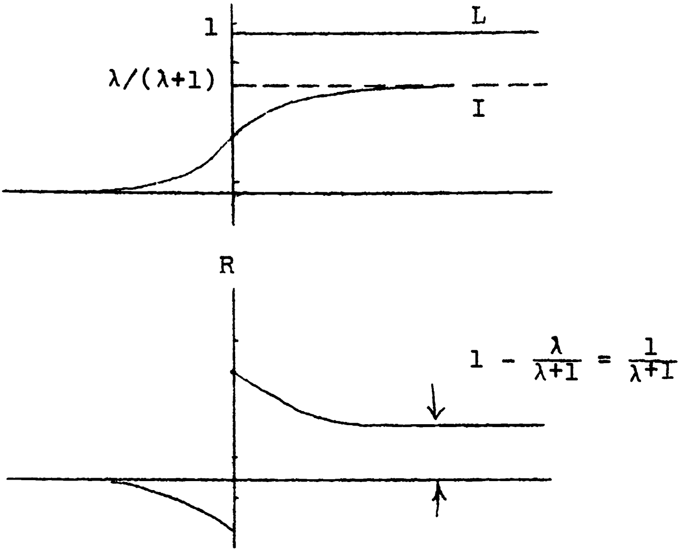
Therefore

$$(6.15) \qquad B = \frac{1}{2}\,\frac{\lambda}{\lambda+1} = - A$$

and

$$(6.16) \qquad I = \begin{cases} \frac{\lambda}{\lambda+1}\,(1 - \frac{1}{2}\,e^{-(\lambda+1)^{1/2}x}) & x > 0 \\ \frac{\lambda}{\lambda+1} \circ \frac{1}{2}\,e^{(\lambda+1)^{1/2}x} & x < 0 \end{cases}$$

This gives the following pictures for L, I, and R = L-I:



Note that the steady part of the response is reduced by the factor $(\lambda+1)^{-1}$, while the jump is unchanged.

2. Space-independent Dynamics.

For space-independent dynamics, the model reduces to

(6.17) $$(\tau\partial_t + 1)E = L$$

(6.18) $$(\partial_t + 1)I = \lambda R = \lambda(E-I)$$

or

(6.19) $$(\partial_t + (\lambda+1))I = \lambda E$$

If L is a unit step, then

(6.20) $$E = 1 - e^{-kt}, \qquad k = \tau^{-1}$$

(6.21) $$I = \frac{\lambda}{\lambda+1} - \frac{\lambda}{-k+\lambda+1}\, e^{-kt} + Ae^{-(\lambda+1)t}$$

where A is determined from

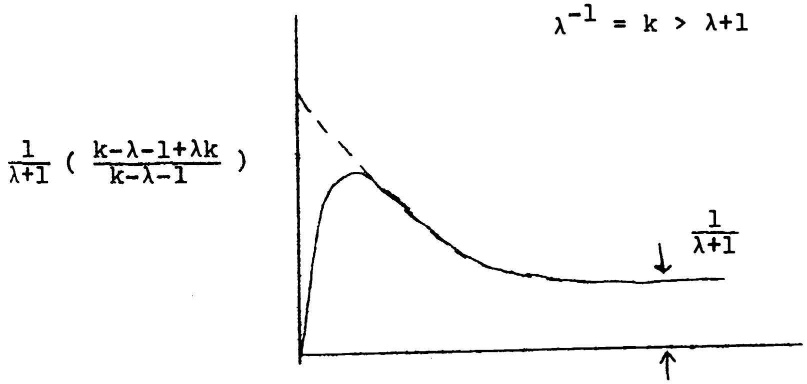
(6.22) $$0 = I(0) = \frac{\lambda}{\lambda+1} + \frac{\lambda}{k-\lambda-1} + A$$

Thus

(6.23) $$I = \frac{\lambda}{\lambda+1} + \frac{\lambda}{k-\lambda-1}\, e^{-kt} - \left(\frac{\lambda}{\lambda+1} + \frac{\lambda}{k-\lambda-1} \right) e^{-(\lambda+1)t}$$

(6.24) $$R = E - I$$

$$= \frac{1}{\lambda+1} - \left(\frac{k-1}{k-\lambda-1} \right) e^{-kt} + \frac{\lambda k}{(\lambda+1)(k-\lambda-1)}\, e^{-(\lambda+1)t}$$



3. Sinusoidal Steady State

Let

$$(6.25)\qquad \begin{cases} L = L_\omega(x,y)e^{i\omega t} \\ E = E_\omega(x,y)e^{i\omega t} \\ I = I_\omega(x,y)e^{i\omega t} \\ R = R_\omega(x,y)e^{i\omega t} \end{cases}$$

Then equations (6.3)-(6.5) become

$$(6.26)\qquad (i\omega\tau + 1)E_\omega = L_\omega$$

$$(6.27)\qquad [-\Delta + (i\omega+1)]I_\omega = \lambda R_\omega$$

$$(6.28)\qquad R_\omega = E_\omega - I_\omega$$

Eliminating R_ω and E_ω, we get the following equation for I_ω:

$$(6.29)\qquad [-\Delta + (i\omega+1+\lambda)]I_\omega = \frac{\lambda L_\omega}{i\omega\tau + 1}$$

Now consider the case where the spatial pattern is a bar. That is, let

$$(6.30)\qquad L_\omega = \begin{cases} 1 & |x| < a \\ 0 & |x| > a \end{cases}$$

Then we expect a solution I_ω with the form

$$(6.31)\quad I_\omega = \begin{cases} \dfrac{\lambda L_\omega}{(i\omega\tau+1)(i\omega+1+\lambda)}\{1 + A\cosh(\lambda+1+i\omega)^{1/2}x\} & |x| < a \\ Be^{-(\lambda+1+i\omega)^{/2}|x|} & |x| > a \end{cases}$$

In the quantity $(\lambda+1+i\omega)^{1/2}$, the square root with positive real part is to be taken. Matching I_ω and its derivative at $x = a$ yields

$$(6.32)\qquad 1 + A\cosh(\lambda+1+i\omega)^{1/2}a = Be^{-(\lambda+1+i\omega)^{1/2}a}$$

$$(6.33)\qquad A + \sinh(\lambda+1+i\omega)^{1/2}a = -Be^{-(\lambda+1+i\omega)^{1/2}a}$$

Adding these two equations yields

$$(6.34)\qquad A = -e^{-(\lambda+1+i\omega)^{1/2}a}$$

where we have used $\cosh\theta + \sinh\theta = e^\theta$. Therefore

$$(6.35)\qquad I_\omega(0,y) = \frac{\lambda L_\omega}{(i\omega\tau+1)(i\omega+1+\lambda)}\{1 - e^{-(\lambda+1+i\omega)^{1/2}a}\}$$

$$(6.36)\qquad E_\omega(0,y) = \frac{L_\omega}{i\omega\tau+1}$$

$$(6.37)\qquad G(\omega) = \frac{R_\omega(0,y)}{L_\omega(0,y)}$$

$$= \frac{1}{i\omega\tau+1}\{1 - \frac{\lambda\{1 - e^{-(\lambda+1+i\omega)^{1/2}a}\}}{i\omega + 1 + \lambda}\}$$

When a = 0:

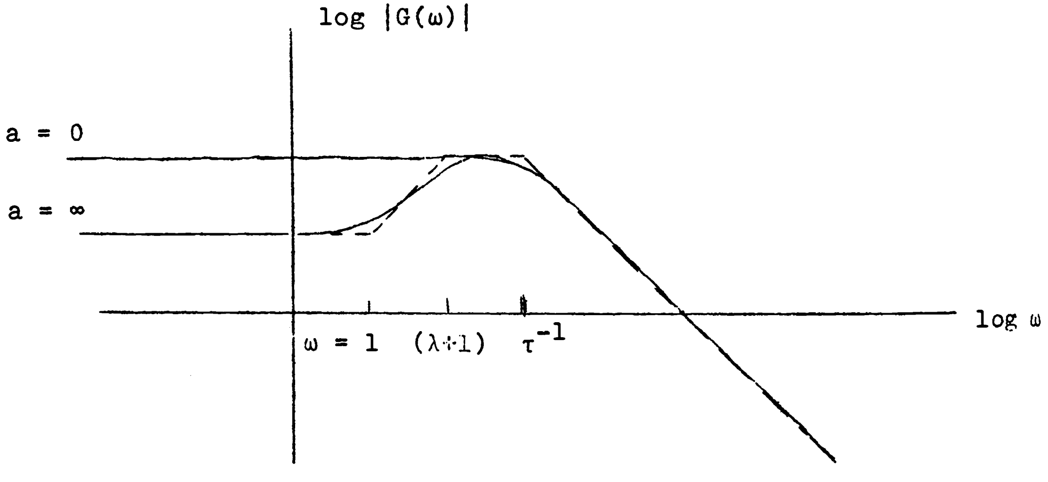
$$G(\omega) = \frac{1}{i\omega\tau+1} \tag{6.38}$$

When a = ∞:

$$G(\omega) = \frac{1}{i\omega\tau+1}\{1 - \frac{\lambda}{i\omega+1+\lambda}\} \tag{6.39}$$

$$= \frac{1}{i\omega\tau+1}\,\frac{i\omega+1}{i\omega+1+\lambda} = \frac{1}{\lambda+1}\,\frac{1 + i\omega}{(1+i\omega\tau)(1 + \frac{i\omega}{\lambda+1})}$$

If we plot log |G(ω)| against log ω in the two cases we get graphs which look like this:



Exercises:

1. Consider the response of the model to a circular flash of light with radius r

$$L(x,y,t) = \delta(t) \begin{cases} 1, & x^2 + y^2 \leq r^2 \\ 0, & x^2 + y^2 > r^2 \end{cases} \tag{6.40}$$

Show that

$$R(0,0,t) = ke^{-kt}\{1 - \lambda \int_0^t e^{(k-\lambda+1)t'}(1 - e^{-r^2/4t'})dt'\} \tag{6.41}$$

Sketch this solution for large and small r, and check that in the limit $r \to \infty$ this result is the time derivative of Eq. (6.24).

2. Consider the case where one has a traveling step of light. That is

$$L(x,y,t) = \begin{cases} 1 & x + ct > 0 \\ 0 & x + ct < 0 \end{cases} \tag{6.42}$$

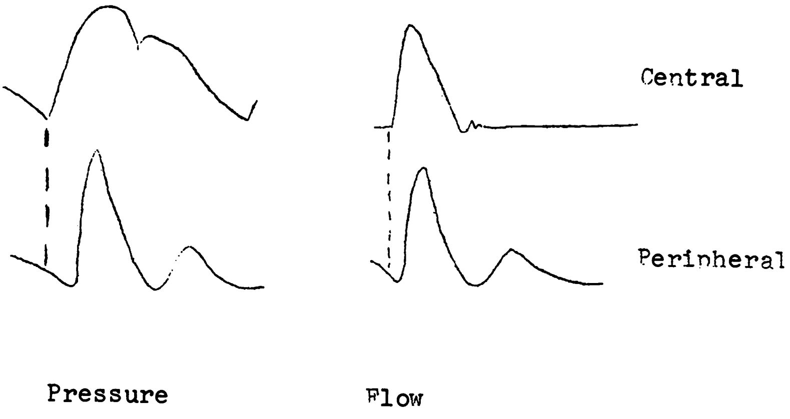
Find the response R, and show that in the limit $c \to 0$ it looks like the response to a steady step, while in the limit $c \to \infty$ it looks like the response to a temporal step of light presented simultaneously to he entire retina.

To exhibit the space-like limit one should write R as a function of x + ct, while to exhibit the time-like limit one should write R as a function of $t + \frac{x}{c}$.

(This problem was suggested by the corresponding observation for the Horseshoe crab retina as described in the article by B.W. Knight, cited above.)

VII. Pulse-Wave Propagation in Arteries

The arterial pulse is distorted in an interesting way as it propagates through the arterial tree from the heart toward the tissues of the body.



The features to be noted are:

1) Increased amplitude and steepness of the leading edge of the pressure pulse.
2) The formation of a second wave.
3) The delay associated with wave propagation.
4) The approximate proportionality of pressure and flow far from the heart, and the absence of such proportionality near the heart.

The shape of the arterial pulse is of great importance because it can measured non-invasively and because it changes in various disease states. In particular it has been found that the second wave is missing in diabetes and atherossclerosis [1*]. In both cases the changes in the arterial pulse occur early and therefore have predictive value [1,2]. Comparison of pulses at different sites has also been used to asses the state of partially blocked arteries before, after and during surgery. [3] The temporary effect of exercise on the arterial pulse is marked (it can abolish the second wave) and has diagnostic significance [3].

The non-invasive method which is used to record the arterial pulse was first developed by H. Lax and A. Feinberg [1], and later independently developed by J.K. Raines [3]. Raines' machine is more suitable for routine clinical use and is commercially available. The principle of operation of both machines will be briefly described here: An air cuff with a fairly rigid outer backing is placed around the arm, leg, finger, or toe where the measurement is to be made, and is inflated to some standard pressure. This pressure should be high enough to occlude the veins, but it should be below the lowest pressure which occurs in the artery. The fluctuations in pressure in the cuff are then recorded. The relationship of the changes in cuff pressure to the changes in the arterial

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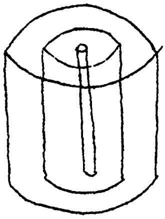
* References at the end of the section.

blood pressure can be estimated in the following way. (This analysis follows that of Raines [3], except that we include a term omitted by him). Treat the artery, arm, and cuff as a system of concentric cylinders. The outer wall is rigid, so the total volume of the system is constant. Therefore (since the volume of the non-blood part of the arm does not change):



$$\Delta V_a + \Delta V_c = 0 \tag{7.1}$$

where

ΔV_a = change in arterial volume

ΔV_c = change in cuff volume .

For the artery we shall assume that:

$$\Delta V_a = C_a \, \Delta(P_a - P_c) \tag{7.2}$$

where

C_a = compliance of the arterial segment under the cuff

ΔP_a = change in arterial pressure

ΔP_c = change in cuff pressure .

Following Raines, we assume that the changes in the cuff are adiabatic, so that the cuff pressure and volume are related by

(7.3) $$P_c V_c^{\gamma} = \text{constant}$$

or, to first order

(7.4) $$\Delta P_c \; V_c^{\gamma} + \gamma P_c \; V_c^{\gamma-1} \; \Delta V_c = 0$$

which gives

(7.5) $$\Delta V_c = - \frac{V_c}{\gamma P_c} \Delta P_c = - C_c \; \Delta P_c$$

where

(7.6) $$C_c = \frac{V_c}{\gamma P_c}$$

= compliance of the air in the cuff.

Combining these equations we find,

(7.7) $$C_a(\Delta P_a - \Delta P_c) - C_c \; \Delta P_c = 0$$

or

(7.8) $$\Delta P_c = \frac{C_a}{C_a + C_c} \Delta P_a$$

There are two interesting limits of this equation, since we can make C_c either large or small by constructing a large or small cuff (see Eq. 7.6). If $C_c << C_a$, then

(7.9) $$\Delta P_c \approx \Delta P_a$$

In this limit, which appears to have been achieved by the Lax-Feinberg machine, the device essentially measures arterial pressure and is insensitive to changes in arterial compliance. In this limit the arterial wall is essentially unloaded and changes in pressure inside are reflected at once outside the artery. (The changes in volume which would normally occur are thus prevented by the device, as can be seen from Eq. 7.2.)

In the opposite limit, when $C_a << C_c$, we have

(7.10) $$\Delta P_c \approx \frac{C_a}{C_c} \Delta P_a \approx \frac{\Delta V_a}{C_c}$$

This limit describes the usual operating condition of the Raines machine, which is therefore appropriately called a "Pulse Volume Recorder".

In fact, the pressure-volume curve of an aterial segment is nearly linear over the physiologic range of pressures. Therefore the two methods yield very similar looking records. It appears not to have been noticed, however, that a combination of the two methods would make it possible to record the pressure-volume curve of the arterial segment under the cuff. From experimental records of P(t), V(t), one can easily eliminate t and construct a relation between P and V. As will appear below, this relation, differentiated with respect to length to yield a relation between pressure and cross-section, is fundamental to the theory of pulse wave propagation in arteries.

The rest of this chapter is concerned with mathematical mehtods for predicting the shape of the arterial pulse. We begin with a derivation of the one-dimensional theory of blood flow in arteries. Viscosity will be ignored, and a detailed treatment of branching will be circumvented by considering a single artery with outflow all along its length. These omissions are related, since viscosity plays a fundamental role in determining the distribution of flow over a cross-section of the artery, and since this distribution is especially complicated near points where the arteries give off branches. It is not clear how to include these effects within the context of the one-dimensional theory. The equations we derive, however, will include the influence of taper, outflow, non-linear (convection) terms in the fluid equations, and non-linear wall properties. We will discuss several different methods for solving these equations, in order of increasing generality. In outline, then, we will proceed as follows:

1) Derivation of the one-dimensional theory.
2) The limit of infinite wave speed.
3) The fundamental solution.
4) The sinusoidal steady state.
5) The methods of characteristics:
    a) Analytic
    b) Numerical
6) The Lax-Wendroff method.

Sections 3 and 4 are restricted to the linear case, but the outflow and taper terms in the equations are retained. In Section 5a, taper and outflow are neglected but the non-linear terms are retained. Section 5b deals with the general case except that the solution is required to be free of shocks (discontinuities), while Section 6 gives a method for the general case which works even in the presence of shocks.

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1. Derivation of the one-dimensional, inviscid theory [1].

Consider an arbitrary surface S moving at velocity $\underline{v}$ and enclosing a volume V. The volume enclosed by S is filled with an incompressible fluid with velocity field $\underline{u}$, density ρ, and pressure p. The surface does not necessarily move with the fluid so that $\underline{u}$ and $\underline{v}$, may be different. We will now write down the laws of conservation of volume and of conservation of x-momentum for the volume V enclosed by S. These laws do not assert that the conserved quantities are independent of time, but rather that their changes are explained by a flux of the conserved quantity across the surface S. Thus we have

conservation of volume:

$$\partial_t V + \iint_S (\underline{u}-\underline{v})\cdot\underline{\hat{n}}\, dS = 0 \qquad , \tag{7.11}$$

conservation of x-momentum:

$$\partial_t \iiint_V (\rho u) dV + \iint_S \rho(\underline{u}-\underline{v})\cdot\underline{\hat{n}}\, dS + \iint_S p(\underline{\hat{n}}\cdot\hat{x}) dS = 0 \tag{7.12}$$

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[1] Most of this section is based on: Hughes, T.J.R.: A study of the one-dimensional theory of arterial pulse propagation. Report #UC SESM 74-13, Structural Engineering Laboratory, University of California at Berkeley, December 1974. The notational devices beginning with Eq.(7.23) which result in the form (7.30) are believed to be new, however.

where:

$\hat{n}$ = unit normal (outward) to the surface S

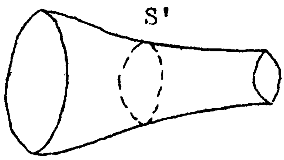
$\underline{u}-\underline{v}$ = velocity of the fluid relative to that of the surface.

$\underline{\hat{x}}$ = unit vector in the x-direction.

u = x-component of velocity = $\underline{u}\cdot\underline{\hat{x}}$

ρu = density of x-momentum.

We now specialize a little by assuming that S is a tubular surface with ends which are portions of the planes $x = 0$ and $x = L$. Let the rest of the surface be designated by the symbol S'. Note that $\underline{v} = 0$ along S-S'. Let $A(x_o)$ denote the cross-section of the tube which is cut by the plane $x = x_o$ and also let the same symbol stand for the area of this cross-section. Then we have



$$(7.13) \qquad \partial_t \int_0^L dx \iint_{A(x)} dA + \left[\iint_{A(x)} u dA \right]_0^L + \iint_{S'} (\underline{u}-\underline{v})\cdot\underline{\hat{n}}\, dS = 0$$

$$(7.14) \qquad \partial_t \int_0^L dx \iint_{A(x)} \rho u dA + \left[\iint_{A(x)} \rho u^2 dA \right]_0^L$$

$$+ \iint_{S'} \rho u(\underline{u}-\underline{v})\cdot\underline{\hat{n}}\, dS + \int_0^L dX \iint_{A(x)} (\partial_x p) dA = 0$$

Introduce functions ψ and ψ_p such that

$$\int_0^L \psi(x)dx = \iint_{S'} (\underline{u}-\underline{v})\cdot\underline{\hat{n}}\ dS \tag{7.15}$$

$$\int_0^L \psi_p(x)dx = \iint_{S'} (\underline{u}-\underline{v})\cdot\underline{\hat{n}}\ \rho u\ dS \tag{7.16}$$

We require these equations to hold for arbitrary L. They therefore define the functions ψ and ψ_p, which have the interpretation of being outflow (per unit length) of volume and momentum, respectively. (Note that ψ and ψ_p both vanish when the normal component of the surface velocity equals that of the fluid).

Now, differentiate (7.13) and (7.14) with respect to L, and then replace the symbol L by x throughout. We obtain

$$\partial_t A + \partial_x \iint_{A(x)} u dA + \psi = 0 \tag{7.17}$$

$$\partial_t \iint_{A(x)} \rho u dA + \partial_x \iint_{A(x)} \rho u^2 dA + \psi_p + \iint_{A(x)} (\partial_x p) dA = 0 \tag{7.18}$$

These equations are exact, but do not constitute a one-dimensional theory since the distribution of velocity over a cross-section still enters. Without knowing this distribution there is no way of relating $\iint udA$ to $\iint u^2 dA$. Nevertheless, these equations serve as a good starting point for the introduction of approximations. The simplest of these is obtained by assuming that u and p depend only on (x,t). In that case we have

(7.19) $$\psi_p = \rho u \psi$$

and

(7.20) $$\partial_t A + \partial_x (Au) + \psi = 0$$

(7.21) $$\rho[\partial_t (Au) + \partial_x (Au^2)] + \psi_p + A\partial_x p = 0$$

Using (7.19), Eq.(7.21) can be rewritten as follows:

$$\rho u[\partial_t A + \partial_x (Au) + \psi] + A[\rho(\partial_t u + u\partial_x u) + \partial_x p] = 0$$

But (7.20) asserts that the first bracket is equal to zero. Therefore:

(7.22) $$\rho(\partial_t u + u\partial_x u) + \partial_x p = 0 \quad .$$

The pair (7.20)-(7.22) can therefore be taken as the basis for a one-dimensional theory of arterial pulse propagation. To complete the theory we need to supply relations which define A and ψ as functions of x and p. Without loss of generality we may write

(7.23) $$A = A_o \exp g(p,x)$$

(7.24) $$\psi = A\sigma(p,x)p$$

Introduce the notation

(7.25) $$K = \frac{\partial g}{\partial p}$$

(7.26) $$\lambda = -\frac{\partial g}{\partial x}$$

In some sense, K measures the elasticity of the artery while λ measures its rate of taper. Then

(7.27) $$\partial_t A = AK\partial_t p$$

(7.28) $$\partial_x A = -A\lambda + AK\partial_x p$$

Equation (7.20) then reduces to

(7.29) $$K(\partial_t p + u\partial_x p) + \partial_x u = \lambda u - \sigma p$$

where we have divided through by the common factor A.

Finally, we take as our one-dimensional equations the pair:

(7.30) $$\begin{cases} \rho(u_t + uu_x) + p_x = 0 \\ K(p_t + up_x) + u_x = \lambda u - \sigma p \end{cases}$$

with unknowns

u = axial velocity

p = pressure

and coefficients

ρ = density

K = elastic coefficient

λ = taper coefficient

σ = outflow coefficient .

The coefficients K, λ, σ may depend on x and p.

2. The limit of infinite wave speed.

An instructive limit of the equations of motion (7.30) is achieved by setting $\rho = 0$. In that case $p_x = 0$ which implies $p = p(t)$. We will find an ordinary differential equation for p(t). Rearranging the second equation of the pair (7.30) and multiplying through by exp(g(p,x)) we find:

(7.31) $$(u_x - \lambda u)\exp(g(p,x)) = -(Kp_t + \sigma p)\exp(g(p,x))$$

(7.32) $$\partial_x(u\exp(g(p,x))) = -(Kp_t + \sigma p)\exp(g(p,x))$$

(7.33) $$-u\exp(g(p,x'))\Big|_0^x$$

$$= p_t\int_0^x K(p,x')e^{g(p,x')}dx' + p\int_0^x \sigma(p,x')e^{g(p,x')}dx'$$

Take the limit as $x \to \infty$, and assume that

(7.34) $$u\exp(g(p,x)) \to 0$$

and that the quantities

(7.35) $$K_*(p) = \int_0^\infty K(p,x) \exp(g(p,x))dx$$

(7.36) $$\sigma_*(p) = \int_0^\infty \sigma(p,x) \exp(g(p,x))\, dx$$

are finite. Then

(7.37) $$u(0,t) \exp(g(p,0)) = K_*(p)p_t + \sigma_*(p)p$$

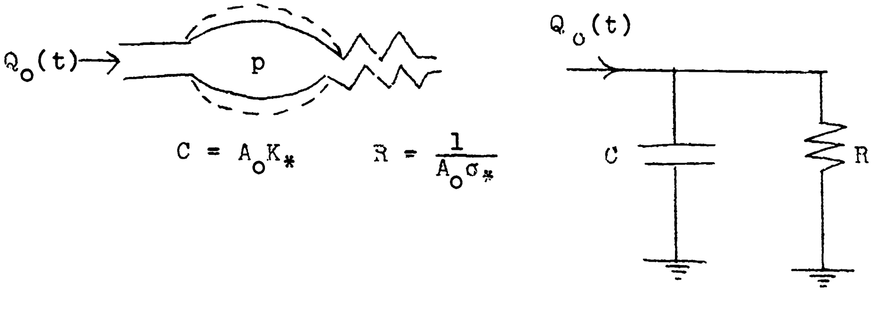
Multiply through by A_o, and let

(7.38) $$Q_o(t) = A_o u(0,t) \exp(g(p,0))$$

Then

(7.39) $$Q_o(t) = A_o K_*(p)p_t + A_o\sigma_*(p)p$$

This is the "Windkessel" model which is often used by physiologists to explain the qualitative features of the arterial pulse. The quantity A_oK_* is the total arterial compliance, $A_o\sigma_*$ is the reciprocal of the peripheral resistance, and Q_o is the outflow from the heart.



We conclude this section by specializing to the case where λ, K, σ are constant. Then $g = -\lambda x + Kp$, and

(7.40) $$K_* = \frac{K}{\lambda} e^{Kp}$$

(7.41) $$\sigma_* = \frac{\sigma}{\lambda} e^{Kp}$$

(7.42) $$Q_o(t) = A_o e^{Kp} u(0,t)$$

In this special case, then (7.39) can be rewritten

(7.43) $$u(0,t) = \frac{K}{\lambda} p_t + \frac{\sigma}{\lambda} p$$

Moreover (7.33) becomes

(7.44) $$\begin{aligned} &- u \exp(Kp-\lambda x')\Big|_0^x \\ &= - p_t \frac{K}{\lambda} \exp(Kp-\lambda x')\Big|_0^x - p \frac{\sigma}{\lambda} \exp(Kp-\lambda x')\Big|_0^x \end{aligned}$$

which, using (7.43) becomes

(7.45) $$u(x,t) = \frac{K}{\lambda} p_t + \frac{\sigma}{\lambda} p = u(0,t)$$

In this special case, then, the velocity like the pressure becomes independent of x. (This implies that the flow decreases exponentially with x.)

The "Windkessel" model explains in a qualitative way the shape of the arterial pulse near the heart. Thus, according to Eq. (7.39), a sudden ejection of blood from the heart will elicit a sudden rise in pressure followed by a roughly exponential runoff-period during which $Q_o(t) = 0$. This model certainly does not explain the distortions in the arterial pulse as it propagates toward the periphery. To investigate these phenomena we need to look at Eqs. (7.30) with non-zero ρ and consequently with a finite speed of wave propagation.

3. The fundamental solution.

In this section we consider the problem

$$\begin{cases} \rho u_t + p_x = 0 \\ K p_t + u_x = \lambda u - \sigma p \end{cases} \tag{7.46}$$

with ρ, K, λ, σ constants. We are interested in the domain $x > 0$ and the boundary data are $u(0,t) = u_o(t)$ and the absence of any waves coming in from ∞.

Let

$$\begin{cases} u = \phi_x \\ p = -\rho\phi_t \end{cases} \tag{7.47}$$

With these substitutes $\rho u_t + p_x$ is identically zero, and the second equation becomes

$$\frac{1}{c^2}\left(\phi_{tt} + \frac{\sigma}{K}\phi_t\right) = \phi_{xx} - \lambda\phi_x \tag{7.48}$$

where

$$c^2 = \frac{1}{\rho K} \tag{7.49}$$

Applying ∂_t or ∂_x to both sides of (7.48), we see that u and p satisfy the same equation as ϕ. In particular

(7.50) $$\frac{1}{c^2}\left(u_{tt} + \frac{\sigma}{K} u_t\right) = u_{xx} - \lambda u_x$$

The following change of variables absorbs the first derivative terms but introduces an undifferentiated term. Let

(7.51) $$u = vE \ , \quad \text{where} \quad E = \exp \frac{1}{2}\left(\lambda x - \frac{\sigma}{K} t\right)$$

Then

(7.52) $$\begin{cases} u_t = \left(v_t - \frac{1}{2}\frac{\sigma}{K} v\right)E \\ u_{tt} = \left(v_{tt} - \frac{\sigma}{K} v_t + \frac{1}{4}\frac{\sigma^2}{K^2} v\right)E \\ u_x = \left(v_x + \frac{1}{2}\lambda v\right)E \\ u_{xx} = \left(v_{xx} + \lambda v_x + \frac{1}{4}\lambda^2 v\right)E \end{cases}$$

Then

(7.53) $$\frac{1}{c^2} = \left(v_{tt} - \frac{1}{4}\frac{\sigma^2}{K^2} v\right) = v_{xx} - \frac{1}{4}\lambda^2 v$$

(7.54) $$\frac{1}{c^2} v_{tt} - v_{xx} + a^2 v = 0$$

where

(7.55) $$a^2 = \frac{1}{4}\left(\lambda^2 - \frac{\sigma^2}{c^2K^2}\right) = \frac{1}{4}\left(\lambda^2 - \frac{\sigma^2\rho}{K}\right)$$

Depending on the sign of a^2, Eq.(7.54) is the Klein-Gordon equation ($a^2 > 0$), the wave equation $a^2 = 0$, or a form of the Telegrapher's equation ($a^2 < 0$). In Chapter II we showed that the solution of

(7.56) $$\bar{w}_{\tau\tau} - \bar{w}_{xx} + a^2\bar{w} = \bar{f}(\tau)\delta(x)$$

is

(7.57) $$\bar{w}(x,\tau) = \frac{1}{2}\int_{|x|}^{\infty} dRJ_o(a\sqrt{R^2-x^2})\bar{f}(\tau-R)$$

where

(7.58) $$J_o(z) = \frac{1}{2\pi}\int_0^{2\pi} \cos(z \sin\theta)d\theta$$

To introduce the factor c, let $\bar{w}(x,\tau) = \bar{w}(x,ct) = w(x,t)$, and let $\bar{f}(\tau) = \bar{f}(ct) = f(t)$. Then (7.56) becomes

(7.59) $$\frac{1}{c^2} w_{tt} - w_{xx} + a^2 w = f(t)\delta(\chi)$$

and (7.57) becomes

(7.60) $$w(x,t) = \frac{1}{2}\int_{|x|}^{\infty} dRJ_o(a\sqrt{R^2-x^2})f(t - \frac{R}{c})$$

Note that

(7.61) $$w_x(0^+,t) = -\frac{1}{2} f(t)$$

This can be demonstrated by integrating (7.59) over the x interval $(-\varepsilon,\varepsilon)$, and then letting $\varepsilon \to 0$ and using the fact that w is an even function of x. Alternatively, one can use the formula (7.60), keeping in mind that $J_o(0) = 1$ and noting that the term which comes from differentiating the integrand with respect to x is zero at x = 0.

We can therefore solve our problem by letting $v = w_x$ and choosing f(t) so that the boundary condition is satisfied. That is, let

$$f(t) = -2v(0^+,t) \tag{7.62}$$

$$= -2u_o(t)\exp\left(\frac{1}{2}\frac{\sigma}{K}t\right)$$

$$v(x,t) = \partial_x \frac{1}{2}\int_{|x|}^{\infty} dR J_o(a\sqrt{R^2-x^2})f(t-\frac{R}{c}) \tag{7.63}$$

$$u(x,t) = v(x,t)\exp\frac{1}{2}(\lambda x - \frac{\sigma}{K}t) \tag{7.64}$$

Once u is known, p can be found using either equation of the pair (7.46).

We can get some qualitative insight into the shape of the arterial pulse by considering the case $u_o(t) = \delta(t)$, which represents a sudden ejection of blood from the heart. Then $f(t) = -2\delta(t)$, since the exponential factor is equal to one at t = 0 which is the only place that matters. Thus we have for the impulse response on x > 0:

$$v(x,t) = -\partial_x \int_x^{\infty} dR J_o(a\sqrt{R^2-x^2})\delta(t-\frac{R}{c}) \tag{7.65}$$

Let R = ct' to obtain

$$v(x,t) = -\partial_x c \int_{\frac{x}{c}}^{\infty} dt' J_o(a\sqrt{c^2t'^2-x^2})\delta(t-t')$$

$$= -\partial_x \begin{cases} c\ J_o(z), & x < ct \\ 0 \quad , & x > ct \end{cases}$$

where

(7.67) $$z = a\sqrt{c^2t^2-x^2}$$

Note that

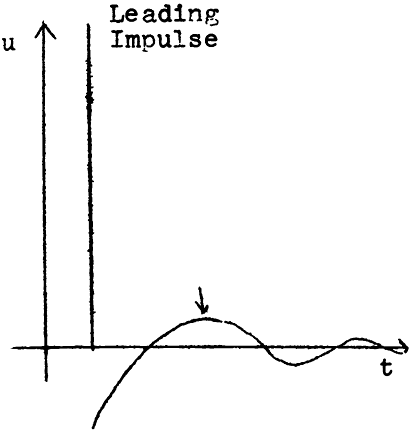
(7.68) $$\frac{\partial z}{\partial x} = \frac{-ax}{\sqrt{c^2t^2-x^2}} = -\frac{a^2x}{z}$$

Therefore

(7.69) $$v(x,t) = c\delta(x-ct) + a^2cx \begin{cases} \frac{J_o'(z)}{z}, & x < ct \\ 0 \quad , & x > ct \end{cases}$$

(7.70) $u(x,t)$

$$= \exp\left(\tfrac{1}{2}\left(\lambda x - \tfrac{\sigma}{K}\,t\right)\right)\left[\delta\left(t - \tfrac{x}{c}\right) + \begin{cases} a^2cx\,\frac{J_o'(z)}{z} & , \quad t > \frac{x}{c} \\ 0 & , \quad t < \frac{x}{c} \end{cases}\right]$$



The impluse response consists of a traveling impulse followed by a smooth wave. Because of the factor x, which multiplies the smooth part of the solution, the smooth wave becomes increasingly prominent as x increases. The smooth wave is oscillatory when $a^2 > 0$, which is case we have sketched here. Is is non-oscillatory when $a^2 < 0$, and absent when $a^2 = 0$. It seems reasonable to postulate that the first positive peak of the smooth part of the solution can be identified with the second wave which is seen in the arterial pulse, especially since the amplitude of this wave is observed to grow with increasing distance from the heart.

We need to determine whether a^2 is positive, negative, or zero. For this purpose, rewrite a^2 as follows (cf. Eq. 7.55)

(7.71) $$a^2 = \frac{1}{4} \lambda^2 (1 - \alpha^2)$$

where

(7.72) $$\alpha = \frac{\sigma}{\lambda c K} = \frac{\sigma}{\lambda} \sqrt{\frac{\rho}{K}}$$

Next, we solve our equations for the special case of steady flow, and identify the results with the mean values of the corresponding quantities which occur in life. The steady solution required has u and p independent of both x and t, and therefore has

$$\lambda u = \sigma p \tag{7.73}$$

Therefore we write

$$\frac{\sigma}{\lambda} = \frac{u}{p} = \frac{\bar{Q}}{A_o \bar{p}} \tag{7.74}$$

Since the wave speed has been measured in arteries, and the density is known, it will be convenient to write

$$K = \frac{1}{\rho c^2} \tag{7.75}$$

Then

$$\alpha = \frac{\bar{Q}}{A_o \bar{p}} \rho c \tag{7.76}$$

As an illustrative case we will evaluate α for dogs, since the relevant constants are available in a paper of Anliker and Rockwell [1]

$$\left\{\begin{array}{l} \rho = 1 \text{ gm/cm}^3 \\ c = 5 \times 10^2 \text{ cm/sec} \\ \bar{Q} = 60 \text{ cm}^3\text{/sec} \\ A_o = 4.9 \text{ cm}^2 \\ \bar{p} = 1.33 \times 10^5 \quad \text{dynes/cm}^2 \quad (= 100 \text{ mm Hg}) \end{array}\right. \tag{7.77}$$

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1 Anliker, M., and Rockwell, R.: Nonlinear analysis of flow pulses and shock waves in arteries. ZAMP 22, 217-246, 563-581 (1971).

Therefore

$$\alpha \gtrsim 5 \times 10^{-2} \tag{7.78}$$

The assumption that $a^2 > 0$ therefore seems well justified, since a^2 is proportional to $1-\alpha^2$.

The changes which will reduce the amplitude of the second wave may now be listed. They are changes which increase α and hence reduce a. From (7.76) we see that two such changes are an increase in wave speed (such as would occur with stiffening of the artery in atherosclerosis), and an increase in the ratio $\overline{Q}/\overline{p}$ as in exercise. Whether these qualitative predictions can be made quantitative remains to be seen.

We conclude this section by demonstrating that in the limit $c \to \infty$, our solution reduces to that of the Windkessel model of the previous section. What has to be shown is that $u(x,t) \to u(0,t)$ in the limit $c \to \infty$.

Returning to Eq. (7.60), we have as $c \to \infty$

$$w(x,t) \to W(x)f(t) \tag{7.79}$$

where

$$W(x) = \frac{1}{2} \int_{|x|}^{\infty} dR J_0(a\sqrt{R^2-x^2}) \tag{7.80}$$

Returning again to Eqs. (7.59) and (7.60), however, we see that W(x) is also the steady solution of (7.59), that is, the solution which results by setting $f(t) \equiv 1$. Thus W(x) satisfies

$$(-\partial_x^2 + a^2)W(x) = \delta(x) \tag{7.81}$$

It follows that:

$$W(x) = \frac{1}{2a} \exp(-a|x|) \tag{7.82}$$

We can also show without appealing to any time-dependent problem that W(x) satisfies (7.81) and therefore is given by (7.82). First rewrite W(x) as follows:

$$W(x) = \frac{1}{2} \int_{|x|}^{\infty} dR \, \frac{1}{2\pi} \int_0^{2\pi} \cos\left((a\sqrt{R^2-x^2}) \sin\theta\right) d\theta \tag{7.83}$$

Let $\rho^2 = R^2-x^2$, so that $\rho d\rho = RdR$. Then

$$W(x) = \frac{1}{4\pi} \int_0^{\infty} \frac{\rho d\rho}{\sqrt{\rho^2+x^2}} \int_0^{2\pi} \cos(a\rho \sin\theta) d\theta \tag{7.84}$$

Regard ρ, θ as polar coordinates in the y, z plane. Then

$$W(x) = \frac{1}{4\pi} \iint_{-\infty}^{\infty} dydz \, \frac{\cos ay}{\sqrt{x^2+y^2+z^2}} \tag{7.85}$$

Now exploit the fact that $1/4\pi r$ is the fundamental solution of Laplace's equation in three dimensions. That is,

$$-(\partial_x^2 + \partial_y^2 + \partial_z^2) \frac{1}{4\pi\sqrt{x^2+y^2+z^2}} = \delta(x)\delta(y)\delta(z) \tag{7.86}$$

Multiply both sides of (7.86) by cos ay, and integrate over the y,z plane. The term involving ∂_x^2 yields $-\partial_x^2 W$. The term involving ∂_y^2 gives (after integration by parts) $+a^2W$. The term involving ∂_z^2 gives zero. The right hand side becomes $\delta(x)$. Thus W satisfies (7.81), as claimed.

Therefore, as $c \to \infty$,

$$w(x,t) \to \frac{1}{2a} \exp(-a|x|)f(t) \tag{7.87}$$

But we also have $a \to \frac{\lambda}{2}$. It then follows from equations (7.62)-(7.64) that $u(x,t) \to u_o(t)$ as required. What is interesting (and perhaps surprising) here is the absence of any space dependence in the limit. One might have expected $u(x,t) \to u_o(t)\psi(x)$, but in fact ψ turns out to be 1.

4. The sinusoidal steady state.

In this section we consider again the linear system (7.46) but we look for solutions of the form

$$\begin{cases} u = u_o e^{\mu x + i\omega t} \\ p = p_o e^{\mu x + i\omega t} \end{cases} \tag{7.88}$$

This leads to the linear equations

$$\begin{pmatrix} i\omega\rho & \mu \\ \mu-\lambda & i\omega K+\sigma \end{pmatrix} \begin{pmatrix} u_o \\ p_o \end{pmatrix} = 0 \tag{7.89}$$

To permit non-trivial solutions, set the determinant equal to zero. This gives

$$
(7.90) \quad \begin{cases} \mu^2 - \lambda\mu - i\omega\rho(i\omega K+\sigma) = 0 \\ \mu = \frac{\lambda}{2}\left[1 \pm \sqrt{1 + \frac{4i\omega\rho(i\omega K+\sigma)}{\lambda^2}}\right] \end{cases}
$$

Note that

$$
(7.91) \quad \frac{4i\omega\rho(i\omega K+\rho)}{\lambda^2} = \frac{-4\omega^2\rho K}{\lambda^2} + \frac{4i\omega\rho\sigma}{\lambda^2}
$$

Let

$$
(7.92) \quad \begin{cases} \frac{\lambda^2}{4\rho K} = \omega_0^2 \\ \frac{\lambda^2}{2\rho\sigma} = \omega_1 \end{cases}
$$

Then

$$
(7.93) \quad \mu = \frac{\lambda}{2}\left[1 \pm \sqrt{1 - \frac{\omega^2}{\omega_0^2} + 2i\,\frac{\omega}{\omega_1}}\right]
$$

Let μ_1 and μ_2 be the two solutions given by (7.93), with $Re(\mu_1) < Re(\mu_2)$. We will show that only μ_1 is of physical interest. Our method will be to impose a boundary condition $u = 0$ at $x = L$, and then take the limit as $L \to \infty$. Perhaps, surprisingly, the result will hold even for cases in which $Re(\mu_1) > 0$, so that the limiting solution is growing and does not tend to zero as $x \to \infty$.

Suppose then, that the boundary conditions are $u = u_o e^{i\omega t}$ at $x = 0$, and $u = 0$ at $x = L$. The solution will have the form

$$(7.94)\qquad \begin{cases} u = u_1 e^{\mu_1 x + i\omega t} + u_2 e^{\mu_2 x + i\omega t} \\ p = p_1 e^{\mu_1 x + i\omega t} + p_2 e^{\mu_2 x + i\omega t} \end{cases}$$

where (u_1, p_1) and (u_2, p_2) satisfy (7.89) with $\mu = \mu_1$ and $\mu = \mu_2$ respectively. Thus p_1 and p_2 can be expressed in terms of u_1 and u_2 and we need only satisfy the boundary conditions on u. These become:

$$(7.95)\qquad \begin{cases} u_1 + u_2 = u_o \\ u_1 e^{\mu_1 L} + u_2 e^{\mu_2 L} = 0 \end{cases}$$

Solving for (u_1, u_2) yields

$$(7.96)\qquad \begin{cases} u_1 = u_o \dfrac{1}{1 - \exp(\mu_1 - \mu_2)L} \\ u_2 = u_o \dfrac{1}{1 - \exp(\mu_2 - \mu_1)L} \end{cases}$$

As $L \to \infty$, since $\mathrm{Re}(\mu_1) < \mathrm{Re}(\mu_2)$, $u_1 \to u_o$ and $u_2 \to 0$. Therefore the limiting solution is

$$(7.97)\qquad \begin{cases} u = u_o e^{\mu_1 x + i\omega t} \\ p = p_o e^{\mu_1 x + i\omega t} \end{cases}$$

Returning to the formula (7.93) and adopting the convention that $\text{Re}\sqrt{z} > 0$ for any z, we have

$$\mu = \mu_1 = \frac{\lambda}{2}\left[1 - \sqrt{1 - \frac{\omega^2}{\omega_0^2} + 2i\frac{\omega}{\omega_1}}\right] \tag{7.98}$$

To complete the solution, we need only express p_o in terms of u_o. This can be done from either of the two equations of the pair (7.89). The two equivalent expressions are:

$$\begin{cases} p_o = \dfrac{-i\omega\rho}{\mu} u_o \\ p_o = \dfrac{\lambda-\mu}{i\omega K+\sigma} u_o \end{cases} \tag{7.99}$$

<u>Exercise</u>: When $\omega_0 = \omega_1$, show that the solution looks like a traveling wave with speed $c = (\rho K)^{-1/2}$, independent of ω.

<u>Exercise</u>: Show that $\text{Re}(\mu)$ is a monotonic function of ω on $0 < \omega < \infty$. Find $\text{Re}\,\mu(0)$ and $\text{Re}\,\mu(\infty)$, and give a condition which determines whether $\text{Re}\,(\mu)$ is increasing or decreasing.

<u>Exercise</u>: Let the wave speed become infinite by letting $\rho \to 0$. Find the limiting relation between u_o and p_o and check that this agrees with the "Windkessel" soultion of Section 2.

We will now find approximate solutions for low and high frequencies. In the low frequency case:

(7.100) $$\mu \approx -\frac{\lambda}{2}\frac{i\omega}{\omega_1} = -i\omega\frac{\rho\sigma}{\lambda} = -\frac{i\omega}{c_1}$$

where

(7.101) $$c_1 = \frac{\lambda}{\rho\sigma} = \frac{\lambda}{\sigma}\sqrt{\frac{K}{\rho}}\frac{1}{\sqrt{\rho K}} = \frac{1}{\alpha}c$$

where α is the dimensionless constant defined by (7.72). In the previous section we found that $\alpha < 1$. Therefore $c_1 > c$. Using this expression for μ we find that, to 1^{st} order in ω

(7.102) $$\begin{cases} u = u_o e^{i\omega(t - \frac{x}{c_1})} \\ p = p_o e^{i\omega(t - \frac{x}{c_1})} \\ p_o = \frac{\lambda}{\sigma}\left(1 - i\omega\left\{\frac{K}{\sigma} - \frac{1}{2\omega_1}\right\}\right)u_o \end{cases}$$

The high frequency behavior will be considered next. For large ω,

(7.103) $$\mu \approx \frac{\lambda}{2}\left[1 - \frac{i\omega}{\omega_o}\right]$$

(Remark: To verify the negative sign in 7.103, one has to look at terms which have been neglected in the end. The $\sqrt{\;}$ which appears in μ has the form $\sqrt{-1+\varepsilon}$ for large ω, after a positive factor has been removed.. The root with positive real part lies near the positive imaginary axis. Then we subtract this root from 1.)

Note that

$$\frac{2\omega_o}{\lambda} = \sqrt{\frac{1}{\rho K}} = c \tag{7.104}$$

Therefore, with this expression for μ we have

$$\left\{\begin{aligned} u &= u_o e^{i\omega(t - \frac{x}{c}) + \frac{\lambda}{2}x} \\ p &= p_o e^{i\omega(t - \frac{x}{c}) + \frac{\lambda}{2}x} \\ p_o &= \rho c u_o = \sqrt{\frac{\rho}{K}}\, u_o \end{aligned}\right. \tag{7.105}$$

(In the last expression we have let $\omega \to \infty$.)

Comparison of the low frequency and high frequency behavior yields the following points of interest:

1) The low frequencies have a very high phase velocity $c_1 = \frac{c}{\alpha} > c$. Of course, this is not a signal velocity; we have seen in the previous section that signals propagate at speed c. It will take several cycles to build up the low frequency response given by (7.102). The high frequencies, on the other hand, propagate at the signal velocity c.

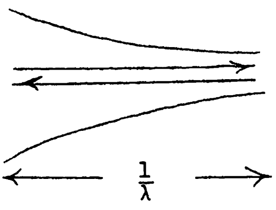
2) To 1st order in ω, the low frequencies are not amplified with distance. The high frequencies are amplified by the factor exp $\frac{\lambda}{2}x$.

3) As $\omega \to \infty$, the ratio of pressure to flow becomes independent of ω and equal to $\sqrt{\rho/K}$, in agreement with the result for an untapered line with no outflow. In the low frequency case, the first order expression for the ratio of pressure to flow is like that of the "Windkessel" model, except that the term K/σ is replaced by $(K/\sigma) - (1/2\omega_1)$.

The following interpretation of these results may be given. The frequency ω_o, can be written as follows

(7.106) $$\frac{1}{\omega_o} = 2(\frac{1}{\lambda})\ \sqrt{\rho K} = 2(\frac{1}{\lambda})\ \frac{1}{c}$$

Since $(1/\lambda)$ is the distance in which the area decreases by the factor exp (-1), it follows that $(1/\omega_o)$ is the round trip time for the wave "bouncing off the taper". If the frequency is much higher that this, the wave length becmoes much less than $1/\lambda$ and the taper can be regarded as gradual. For much lower frequencies, on the other hand, the wave length is much longer than the taper. In the latter circumstances, the taper fails to amplify the wave and the phase velocity becomes very large.



5. The method of characteristics

This method has been used successfully by M. Anliker and R.L. Rockwell [1] to construct numerical solutions for the one-dimensional arterial pulse problem. The reader is refered to their work for a comprehensive discussion of the results of such calculations.

Here, we will confine our discussion to methods rather than results. We will develop the method of characteristics for the equations

$$(7.107)\quad \begin{cases} \rho(u_t + uu_x) + p_x = 0 \\ K(p_t + up_x) + u_x = \lambda u - \sigma p \end{cases}$$

where K, λ, σ may depend on p and x. The method will then be applied in analytic form to the simpler problem, $\lambda = \sigma = 0$, $K = K(p)$, which corresponds to a uniform artery without outflow. Following this, we will state a numerical method for the general case.

A characteristic is a curve in the (x,t) plane along which there is a restriction, in the form of an ordinary differential equation, which relates the values of u and p along the curve. For non-characteristic curves, u and p can be specified arbitrarily without ariving at a contradiction

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1 cited above.

of the partial differential equation (7.107). The characteristics are the exceptional curves where an arbitrary choice of u and p may lead to such a contradiction. The characteristics are not determined by the partial differential equation alone (except in the linear case), but depend on the solution. In particular, the slopes (that is, the speeds) of the characteristics are determined by the values of u and p at each point.

Dividing through by ρ and K, and using matrix and vector notation, we find that 7.107 has the form

(7.108) $$w_t + Aw_x = Bw$$

where

(7.109) $$w = \begin{pmatrix} u \\ p \end{pmatrix}$$

(7.110) $$A = \begin{pmatrix} u & \rho^{-1} \\ K^{-1} & u \end{pmatrix}$$

(7.111) $$B = \begin{pmatrix} 0 & 0 \\ \frac{\lambda}{K} & -\frac{\sigma}{K} \end{pmatrix}$$

Now consider a curve $x = \bar{x}(s)$, $t = s$ in the (x,t) plane. Let

(7.112) $$c = \frac{d\bar{x}}{ds}$$

Along such a curve we have (for any differentiable function w) the identity

$$w_t + cw_x = w_s \tag{7.113}$$

Combining this with (7.108) yields the system

$$\begin{pmatrix} I & A \\ I & cI \end{pmatrix} \begin{pmatrix} w_t \\ w_x \end{pmatrix} = \begin{pmatrix} Bw \\ w_s \end{pmatrix} \tag{7.114}$$

which has 4 equations and 4 unknowns u_t, p_t, u_x, p_x. The right hand side is known if u, p are given along the curve.

Recalling the definition of a charactersitic curve, we want to find those speeds c for which (7.114) is solvable only for certain right hand sides but not for all. Subtracting the first equation from the second yields the system

$$\begin{pmatrix} I & A \\ 0 & cI-A \end{pmatrix} \begin{pmatrix} w_t \\ w_x \end{pmatrix} = \begin{pmatrix} Bw \\ w_s - Bw \end{pmatrix} \tag{7.115}$$

which is solvable if and only if the 2×2 problem

$$(cI - A)w_x = w_s - Bw \tag{7.116}$$

is solvable.

The characteristic speeds c can therefore be found by setting

$$\det (cI - A) = 0 \tag{7.117}$$

which yields

$$c = u \pm \sqrt{\frac{1}{\rho K}} \tag{7.118}$$

We want to find the restriction on the right hand side which allows (7.116) to have solutions. This can be found as follows. Multiply by the arbitrary 2-vector $\gamma^T = (\gamma_1, \gamma_2)$ to obtain

$$(7.119) \qquad \gamma^T(cI - A)w_x = \gamma^T(w_s - Bw)$$

Now choose γ^T so that

$$(7.120) \qquad \gamma^T(cI - A) = 0$$

which is possible since $(cI - A)$ is singular. Then (7.119) becomes

$$(7.121) \qquad 0 = \gamma^T(w_s - Bw)$$

which is therefore a necessary condition for the existence of a solution.

We now determine γ^T explicitly. Let

$$(7.122) \qquad c_o = \sqrt{\frac{1}{\rho K}}$$

Then γ^T satisfies

$$(7.123) \qquad (\gamma_1, \gamma_2)\begin{pmatrix} \pm c_o & -\rho^{-1} \\ -K^{-1} & \pm c_o \end{pmatrix} = 0$$

Let $\gamma_1 = 1$. Then

$$(7.124) \qquad \gamma_2 = \pm Kc_o = \pm\sqrt{\frac{K}{\rho}}$$

The vector

$$w_s - Bw = \begin{pmatrix} u_s \\ p_s - \frac{\lambda u - \sigma p}{K} \end{pmatrix} \tag{7.125}$$

Therefore our restrictions on (u,p) along the charactersitic becomes

$$u_s \pm \sqrt{\frac{K}{\rho}} \left[p_s - \frac{\lambda u - \sigma p}{K} \right] = 0 \tag{7.126}$$

or

$$\left[u \pm \sqrt{\frac{K}{\rho}}\, p \right]_s = \pm c_o [\lambda u - \sigma p] \tag{7.127}$$

where the ± signs holds along the characteristic given by

$$\frac{dx}{ds} = u \pm c_o \ , \quad \frac{dt}{ds} = 1 \tag{7.128}$$

which we shall refer to below as $C_\pm$.

The quantities

$$J_\pm = u \pm \sqrt{\frac{K}{\rho}}\, p \tag{7.129}$$

are therefore conserved along their own charactersitcs in the special case $\lambda = \sigma = 0$. In the general case, however, they change according to the differential equation (7.127). The quantities $J_\pm$ can be interpreted as the amplitude of the forward and backward waves, respectively, and the changes in $J_\pm$ which are prescribed by (7.127) can be regarded as continuous refelctions generated by the taper and outflow.

5a. Uniform artery with no outflow.

Here we consider the case $\lambda = \sigma = 0$, $K = K(p)$. Thus the artery is uniform, but the problem is still non-linear, and the charactersitics speed depends on the solution, being given by

$$c = u \pm c_o \tag{7.130}$$

where c_o is a function of p.

To make the problem as simple as possible, choose a finite spatial domain $0 < x < L$, and impose the boundary conditions

$$\begin{cases} u(0,t) = u_o(t) \\ u(L,t) = \sqrt{\frac{K}{\rho}}\; p(L,t) \end{cases} \tag{7.131}$$

The latter boundary condition is chosen to make $J_- = 0$ at $x = L$ (no reflected wave). Therefore, since $(J_-)_s = 0$ along C_-, we shall have $J_- \equiv 0$ throughtout the domain. It follows that

$$u = \sqrt{\frac{K}{\rho}}\; p \tag{7.132}$$

everywhere, not just at $x = L$, and that

$$J_+ = 2u = 2\sqrt{\frac{K}{\rho}}\; p \tag{7.133}$$

Since J_+ is constant along each of the C_+ charactersitics, it follows that u,p are also constant, and therefore, that the charactersitic itself is a straight line, with a speed determined by the value of $u_o(t)$ at the moment of origin of the characteristic. The equations of the C_+ characteristics are found as follows: Let

$$p_o(t) = \sqrt{\frac{\rho}{K}}\; u_o(t) \tag{7.134}$$

$$\theta(t) = u_o(t) + c_o(p_o(t)) \tag{7.135}$$

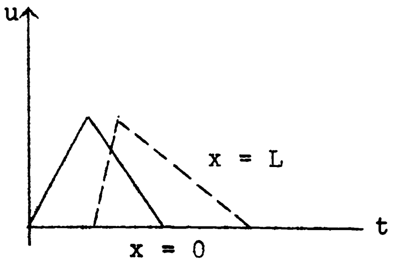
Then the equation of the characteristic which is created at the time t_* is simply

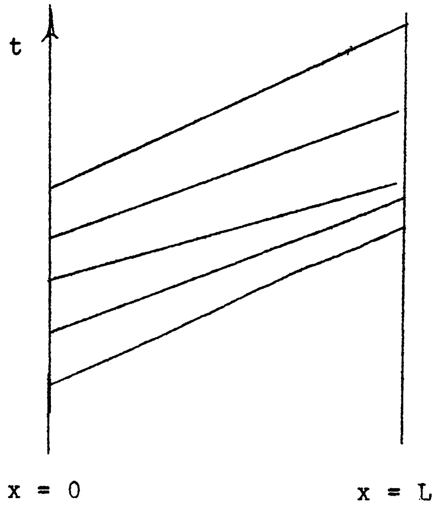
$$x = \theta(t_*)(t - t_*) \tag{7.136}$$

Since, in this case, the C_+ characteristics carry constant values of u an p, the solution is given implicitly by (7.136) and

$$\begin{cases} u(x,t) = u_o(t_*) \\ p(x,t) = p_o(t_*) \end{cases} \tag{7.137}$$

In arteries, c_o is an increasing function of p. From (7.134) and (7.135) it follows that θ is an increasing function of u. Therefore, the high amplitude parts of the solution are carried along at a greater velocity than the low amplitude parts.





Thus wave fronts become steeper, and backs become less steep as the wave propagates. The characteristics are converging where u is increasing and diverging where u is decreasing.

An important question which now arises is whether the C_+ characteristics intersect with each other anywhere on the interval $0 < x < L$. If they do, a shock (discontinuity) forms and the solution constructed above becomes double-valued, while the physically relevant solution of the problem becomes discontinuous. A numerical method which succeeds in constructing the solution even in the presence of shocks (the Lax-Wendroff method) will discussed in Section 6. Here, we shall derive a restriction on the boundary data which will guarantee that. the interval $0 < x < L$ is free of shocks.

According to (7.136), two C_+ charactersitics which originate at times t_1 and t_2 will intersect at (x,L) given by

(7.138) $$x = \theta(t_1)(t - t_1) = \theta(t_2)(t - t_2)$$

That is

(7.139) $$\begin{cases} t = \dfrac{\theta(t_2)t_2 - \theta(t_1)t_1}{\theta(t_2) - \theta(t_1)} \\ \\ x = \dfrac{\theta(t_1)\theta(t_2)(t_2-t_1)}{\theta(t_2) - \theta(t_1)} \end{cases}$$

Intersections on $0 < x < L$ will be avoided if $x > L$ or $x < 0$. Both possibilities are contained in $x^{-1} < L^{-1}$, which reads:

(7.140) $$-\frac{\theta^{-1}(t_2) - \theta^{-1}(t_1)}{t_2 - t_1} < \frac{1}{L}$$

Shocks will be avoided if and only if (7.140) holds for all t_1, t_2. This condition is equivalent to

(7.141) $$-\frac{d}{dt}\frac{1}{\theta} < \frac{1}{L}$$

or

(7.142) $$\frac{1}{\theta^2}\frac{d\theta}{dt} < \frac{1}{L}$$

Note that this condition restricts the rate of rise of θ, but not its rate of decrease. If this condition is satisfied by the boundary data, then the solution we have constructed is valid. If not, shocks will form and further considerations are necessary to construct the solution.

5b. The numerical method of characteristics.

We now drop the restriction $\lambda = \sigma = 0$ and construct a numerical method for the problem (7.107) in the general case. The domain will be $x > 0$, $t > 0$, with $u(0,t) = u_o(t)$ and $u(x,0) = p(x,0) = 0$.

Recall that the equations which define the characteristics are

$$\left\{ \begin{aligned} \frac{dx}{ds} &= u \pm c_o \\ \frac{dt}{ds} &= 1 \end{aligned} \right. \tag{7.143}$$

while the equations which hold along the charactersitics are

$$\frac{d}{ds} (J_{\pm}) = \pm \Delta \tag{7.144}$$

where

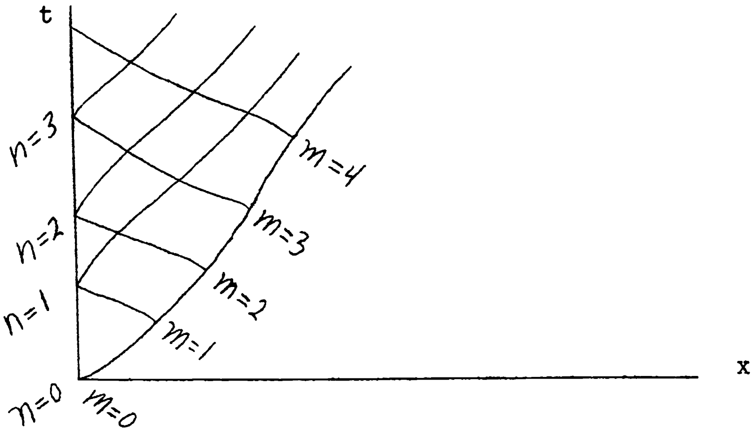
$$\Delta = c_o(\lambda u - \sigma p) \tag{7.145}$$

$$J_{\pm} = u \pm \sqrt{\frac{K}{\rho}}\, p \tag{7.146}$$

$$c_o = \sqrt{\frac{1}{\rho K}} \tag{7.147}$$

Note that Eqs. (7.146) are easily inverted to yield u, p as functions of $J_{\pm}$.

The discretization of these equations proceeds as follows:



Introduce a mesh made up of characteristic lines. The point $P_m^n = \left(x_m^n, t_m^n\right)$ lies at the intersection of the $n^{\underline{th}}$ discrete C_+ characteristic and the $m^{\underline{th}}$ discrete C_- characteristic. The notation ϕ_m^n will mean $\phi\left(x_m^n, t_m^n\right)$.

First consider interior points of the mesh. Suppose that all quantities have been determined on the mesh points P_{m-1}^n and P_m^{n-1}. Then we determine the location of the point P_m^n by solving the following pair of equations:

(7.148) $$x_m^n - x_{m-1}^n = \left(t_m^n - t_{m-1}^n\right)\left(u + c_o\right)_{m-1}^n$$

(7.149) $$x_m^n - x_m^{n-1} = \left(t_m^n - t_m^{n-1}\right)\left(u - c_o\right)_m^{n-1}$$

Next, we determine $(J_\pm)_m^n$ as follows:

(7.150) $$(J_+)_m^n = (J_+)_{m-1}^n + (t_m^n - t_{m-1}^n)\Delta_{m-1}^n$$

$$(7.151) \qquad (J_-)_m^n = (J_-)_m^{n-1} - (t_m^n - t_m^{n-1})\Delta_m^{n-1}$$

The region of interest has two boundaries which require special treatment. First, consider the boundary $n = 0$, which corresponds to the leading C_+ characteristic. Just to the right of this boundary the system is at rest. But J_- is continuous accross this boundary (J_+ is not). Therefore $J_- = 0$ along $n = 0$. This condition replaces Eq. (7.151). Another modification along this boundary is that we drop Eq. (7.149), which refers to the mesh point P_m^{-1}. This allows us to choose $(t_m^o - t_{m-1}^o)$ arbitrarily in (7.148). For example, we could set this quantity equal to a constant, and this constant will then determine the resolution of the mesh.

Next, consider the boundary $n = m$, which corresponds to $x = 0$. Along this boundary we have to drop the two equations which refer to the C_+ characteristic. That is, we drop (7.148) and (7.150). In their place, we have the two conditions $x_n^n = 0$ and $u_n^n = u_o(t_n^n)$.

The equations we have outlined suffice to determine the quantities x_m^n, t_m^n, y_m^n, p_m^n on the entire mesh $0 \leq n \leq m < \infty$. These quantitites can be determined in any order having the property that all four quantities are determined at P_m^{n-1} and P_{m-1}^n before they are determined at P_m^n.

In this way, an approximate solution can be constructed. Here, as before, there is nothing to prevent the computed C_+ characteristics from intersecting with each other. If such an intersection occurs it can be interpreted as the formation of a shock, but some modification of the stated method is required to continue the solution further. Such modifications will not be discussed here, however, because a numerical method is available which handles shocks automatically. This method is the subject of the next section.

6. The Lax-Wendroff method *

In this section we consider systems of equations of the form

(7.152) $$u_t + f_x = g$$

where u is a vector, and where f and g are vector-valued functions of u. Such a system has a simple interpretation which can be found by integrating with respect to x over some interval (a,b). One obtains

(7.153) $$\frac{d}{dt}\int_a^b u\,dx + f\Big|_a^b = \int_a^b g\,dx$$

Eq. (7.153) asserts that u is the space-density of some quantity which has flux f and which is created at the rate g.

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* References at end of section.

When $g = 0$, this amounts to a conservation law.

In this section we will begin by deriving a system of difference equations which is satisfied by smooth solutions of (7.152) up to terms of second order in Δx and Δt. These difference equations constiute Richtmeyer's two-step version of the Lax-Wendroff method. The stability of these difference equations will then be investigated in the linear, constant coefficient case. Finally, we will discuss the question of how to put the equations of the arterial pulse in the form (7.152).

The following notation will be used. Let $h = \Delta x$, $k = \Delta t$, and, for any function $\phi(x,t)$, let $\phi_j^n = \phi(jh,nk)$. We will need certain formulae relating divided differences of smooth functions to the corresponding derivatives. These can be derived using the Taylor series. For example, consider a smooth function $\phi(x)$:

$$(7.154)\quad \begin{cases} \phi_{j+1} = \phi_j + h(\phi_x)_j + \frac{1}{2} h^2(\phi_{xx})_j + \frac{1}{6} h^3(\phi_{xxx})_j + O(h^4) \\ \phi_{j-1} = \phi_j - h(\phi_x)_j + \frac{1}{2} h^2(\phi_{xx})_j - \frac{1}{6} h^3(\phi_{xxx})_j + O(h^4) \end{cases}$$

Adding and subtracting we obtain:

$$(7.155)\quad \phi_{j+1} + \phi_{j-1} - 2\phi_j = h^2(\phi_{xx})_j + O(h^4)$$

$$(7.156)\quad \phi_{j+1} - \phi_{j-1} = 2h(\phi_x)_j + O(h^3)$$

Dividing through by h^2 and by 2h, respectively, we obtain:

$$\frac{\phi_{j+1} + \phi_{j-1} - 2\phi_j}{h^2} = (\phi_{xx})_j + O(h^2) \tag{7.157}$$

$$\frac{\phi_{j+1} - \phi_{j-1}}{2h} = (\phi_x)_j + O(h^2) \tag{7.158}$$

A further consequence of (7.155) is

$$\tfrac{1}{2}(\phi_{j+1} + \phi_{j-1}) = \phi_j + O(h^2) \tag{7.159}$$

In all three formulae (7.157)-(7.159), the second order accuracy is a consequence of the symmetry. Corresponding formulae hold in the t-direction, and also with space steps of other sizes such as h/2. We will use these formulae freely in the following.

Now, consider a smooth function u which satisfies (7.152). Then

$$\frac{u_j^{n+1} - u_j^n}{k} = (-f_x + g)_j^{n+\frac{1}{2}} + O(k^2) \tag{7.160}$$

We need to construct a second order accurate difference approximation to the quantity $(-f_x + g)_j^{n+1/2}$. For the resulting difference equations to be useful as a numerical method, the required approximation should be constructed from the values of u at the time level n. We can do this as follows. Note that

$$u_{j+\frac{1}{2}}^{n+\frac{1}{2}} = u_{j+\frac{1}{2}}^n + \frac{k}{2}(u_t)_{j+\frac{1}{2}}^n + O(k^2) \tag{7.161}$$

and

$$u^n_{j+\frac{1}{2}} = \frac{1}{2}(u^n_{j+\frac{1}{2}} + u^n_j) + O(h^2) \tag{7.162}$$

$$\begin{aligned}(u_t)^n_{j+\frac{1}{2}} &= (-f_x + g)^n_{j+\frac{1}{2}} \\ &= -\left(\frac{f^n_{j+1} - f^n_j}{h}\right) + \left(\frac{g^n_{j+1} + g^n_j}{2}\right) + O(h^2)\end{aligned} \tag{7.163}$$

Substituting the last two formulae in (7.161), we obtain

$$\begin{aligned}u^{n+\frac{1}{2}}_{j+\frac{1}{2}} &= \frac{1}{2}(u^n_{j+1} + u^n_j) \\ &+ \frac{k}{2}\left[-\left(\frac{f^n_{j+1}-f^n_j}{h}\right) + \left(\frac{g^n_{j+1}+g^n_j}{2}\right)\right] + O(h^2 + k^2)\end{aligned} \tag{7.164}$$

Therefore, let

$$\tilde{u}^{n+\frac{1}{2}}_{j+\frac{1}{2}} = \frac{1}{2}(u^n_{j+1}+u^n_j) + \frac{k}{2}\left[-\frac{f^n_{j+1}-f^n_j}{h} + \frac{g^n_{j+1}+g^n_j}{2}\right] \tag{7.165}$$

For theoretical purposes, we require this formula, which defines $\tilde{u}$, to hold for all (n,j), not just for integral values of n and j. It therefore defines a smooth function $\tilde{u}$ over the whole x,t plane, which, according to (7.164) is related to u as follows:

$$\tilde{u} = u + O(h^2 + k^2) \tag{7.166}$$

We will now show that a corresponding relation holds between $\tilde{u}_x$ and u_x. This can be established by computing the quantity

$$\tilde{u}_{j+\frac{1}{2}}^{n+\frac{1}{2}} - \tilde{u}_{j-\frac{1}{2}}^{n+\frac{1}{2}} = \frac{1}{2}(u_{j+1}^n - u_{j-1}^n) + \frac{k}{2}\left[-\frac{f_{j+1}^n+f_{j-1}^n-2f_j^n}{h} + \frac{g_{j+1}^n-g_{j-1}^n}{2}\right] \tag{7.167}$$

Dividing through by h yields

$$(\tilde{u}_x)_j^{n+\frac{1}{2}} + O(h^2) = (u_x)_j^n + \frac{k}{2}\left[-f_{xx}+g_x\right]_j^n + O(h^2) \tag{7.168}$$

But:

$$\left(-f_{xx} + g_x\right)_j^n = \left(u_{xt}\right)_j^n \tag{7.169}$$

$$\left(u_x\right)_j^n + \frac{k}{2}\left(u_{xt}\right)_j^n = \left(u_x\right)_j^{n+\frac{1}{2}} + O(h^2) \tag{7.170}$$

Therefore:

$$\tilde{u}_x = u_x + O(h^2+k^2) \tag{7.171}$$

Now let $\tilde{f} = f(\tilde{u})$, $\tilde{g} = g(\tilde{u})$. If f and g are smooth functions, we can write as a consequence of (7.166) and (7.171):

$$(-f_x+g) = (-\tilde{f}_x+\tilde{g}) + O(h^2+k^2) \tag{7.172}$$

$$(7.173)\qquad (-\tilde{f}_x+\tilde{g})_j = -\frac{\tilde{f}_{j+\frac{1}{2}}-\tilde{f}_{j-\frac{1}{2}}}{h} + \frac{\tilde{g}_{j+\frac{1}{2}}+\tilde{g}_{j-\frac{1}{2}}}{2} + O(h^2)$$

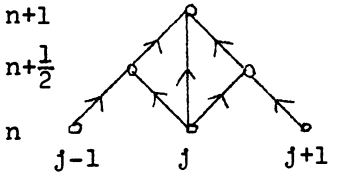
Substituting (7.172) and (7.173) in (7.160), we get the required formulae:

$$(7.174)\qquad \frac{u_j^{n+1} - u_j^n}{k} = -\frac{\tilde{f}_{j+\frac{1}{2}}^{n+\frac{1}{2}} - \tilde{f}_{j-\frac{1}{2}}^{n+\frac{1}{2}}}{h} + \frac{\tilde{g}_{j+\frac{1}{2}}^{n+\frac{1}{2}} + \tilde{g}_{j-\frac{1}{2}}^{n+\frac{1}{2}}}{2} + O(k^2+h^2)$$

where, as before, $\tilde{f} = f(\tilde{u})$, $\tilde{g} = g(\tilde{u})$, and:

$$(7.175)\qquad \tilde{u}_{j+\frac{1}{2}}^{n+\frac{1}{2}} = \tfrac{1}{2}(u_{j+1}^n + u_j^n) + \frac{k}{2}\left[-\frac{f_{j+1}^n-f_j^n}{h} + \frac{g_{j+1}^n+g_j^n}{2}\right]$$

The Lax-Wendroff method (Richtmeyer's two-step version) is now obtained by dropping the terms symbolized by $O(k^2+h^2)$. (Once this is done the quantity u no longer represents the exact solution of the partial differential equation, but we will retain the notation u nonetheless.) The resulting formulae give u_j^{n+1} in terms of u_{j-1}^n, u_j^n, u_{j+1}^n. They are therefore sutiable for constructing the approximate solution u recursively from initial data.



We now examine the stability of the Lax-Wendroff method in the special case $f = Au$, $g = Bu$, where A and B are constant matrices. There will be no further restrictions on B, but we require that A have real eigenvalues and N linearly independent eigenvectors, where N is the order of the matrix A. The latter condition will be satisfied if the eigenvalues of A are distinct, and it will also be satisfied if A is a symmetric matrix. Recall that the eigenvalues of A are the characteristic speeds. In the present problem N = 2 and the characteristic speeds are given by $u \pm c_o$, which are certainly real and distinct.

When A and B are constant matrices, the difference equations are linear with constant coefficients, and it is useful to look for solutions of the form

$$u_j^n = U^n e^{i\alpha jh}$$
(7.176)
$$\tilde{u}_j^n = \tilde{U}^n e^{i\alpha jh}$$

With these substitutions, the difference equation becomes:

(7.177)
$$\begin{cases} U^{n+1} = U^n + \frac{k}{h} D \tilde{U}^{n+\frac{1}{2}} \\ \tilde{U}^{n+\frac{1}{2}} = \left[\cos \frac{\alpha h}{2} + \frac{k}{2h} D\right] U^n \end{cases}$$

where

(7.178) $$D = -2iA \sin \frac{\alpha h}{2} + hB \cos \frac{\alpha h}{2}$$

Let $\lambda = \frac{k}{h}$, $\theta = \frac{\alpha h}{2}$, and eliminate $\tilde{U}^{n+\frac{1}{2}}$:

$$(7.179) \qquad U^{n+1} = \left\{ I + \lambda D\left[\cos\theta + \frac{\lambda}{2} D\right]\right\} U^n$$

<u>Regard λ as fixed</u>, and let

$$(7.180) \qquad M(\theta,h) = I + \lambda D\left[\cos\theta + \frac{\lambda}{2} D\right]$$

$$(7.181) \qquad D(\theta,h) = -2iA \sin\theta + hB\cos\theta$$

The the difference equations become:

$$(7.182) \qquad U^{n+1} = M(\theta,h)U^n$$

Let $T = nk = n\lambda h$. Then

$$(7.183) \qquad U(T) = [M(\theta,h)]^n U(0)$$

Note that $M(\theta,h)$ can be written

$$(7.184) \qquad M(\theta,h) = M_o(\theta) + hM_1(\theta) + h^2 M_2(\theta)$$

where

$$(7.185) \qquad M_o(\theta) = I - 2i\sin\theta\cos\theta\,\lambda A - 2\lambda^2 A^2 \sin^2\theta$$

We will not need explicit formulae for M_1 and M_2. Note, however, that they, like M_o, have elements which are bounded independent of θ, since $\sin\theta$ and $\cos\theta$ always stay on the interval [-1,1].

We assumed that the matrix A has real eigenvalues and a linearly independent set of eigenvectors. Let the eigenvalues, which are also the characteristic speeds, be written c_j and the corresponding eigenvectors be written ϕ_j, $j = 1,2,\ldots,N$. The ϕ_j are also eigenvectors of the matrix $M_0(\theta)$ with eigenvalues

(7.186) $$\mu_j(\theta) = 1 - 2i \sin\theta \cos\theta\, \lambda c_j - 2\lambda^2 c_j^2 \sin^2\theta$$

Note that

$$|\mu_j|^2 = 1 - 4\lambda^2 c_j^2 \sin^2\theta + 4\lambda^4 c_j^4 \sin^4\theta + 4 \sin^2\theta \cos^2\theta\, \lambda^2 c_j^2$$

$$= 1 - 4\lambda^2 c_j^2 \sin^2\theta(1 - \cos^2\theta) + 4\lambda^4 c_j^4 \sin^4\theta$$

$$= 1 - 4 \sin^4\theta(1 - \lambda^2 c_j^2)\lambda^2 c_j^2$$

(This cannot give a negative result because $(1-\chi)\chi \leq \frac{1}{4}$). It follows that $\lambda^2 c_j^2 \leq 1$ implies $|\mu_j(\theta)|^2 \leq 1$. Also, when $\lambda^2 c_j^2 > 1$, then $|\mu_j(\theta)|^2 > 1$ except when θ is such that $\sin\theta = 0$. Incidently, where $\lambda^2 c_j^2 > 1$, the largest value of $|\mu_j|^2$ occurs when $\theta = \frac{\pi}{2}$.

When λ is such that $\lambda^2 c_j^2 \leq 1$ for all j, the difference equations are said to be stable for the following reason. Let $||U||$ be the norm of the vector U which is defined by expanding U in terms of the eigenvectors of A and then taking the ℓ_2 norm of the vector of coefficients. Thus when $U = \sum_{j=1}^{N} b_j\phi_j$,

(7.188) $$||U||^2 = \sum_{j=1}^{N} |b_j|^2$$

Also, let $||M||$ be the norm of the matrix M which is defined as follows

(7.189) $$||M|| = \max_{||U||=1} ||MU||$$

Then

(7.190) $$||M(\theta,h)|| \leq ||M_o(\theta)|| + h||M_1(\theta)|| + h^2||M_2(\theta)||$$

Now M_1 and M_2 have elements which are bounded independent of θ, and, in the case under consideration $||M_o(\theta)|| \leq 1$. The latter statement is proved by considering the arbitrary vector

(7.191) $$\begin{cases} U = \sum_{j=1}^{N} b_j \phi_j \\ M_o(\theta)U = \sum_{j=1}^{N} b_j \mu_j(\theta)\phi_j \\ ||M_o(\theta)U||^2 = \sum_{j=1}^{N} |b_j|^2 |\mu_j(\theta)|^2 \leq ||U||^2 \end{cases}$$

since $|\mu_j(\theta)|^2 \leq 1$.

Therefore, for h sufficiently small, there is some constant C, independent of θ and h, such that

(7.192) $$||M(\theta,h)|| < 1 + Ck$$

(Recall that $k = \lambda h$).

Then

(7.193) $$||U^n|| < (1 + Ck)^n ||U(0)|| < e^{Ckn} ||U(0)||$$

Letting $T = nk$

$$\|U(T)\| < e^{CT} \|U(0)\| \tag{7.194}$$

Thus the growth of U is controlled independent of h, θ, a property which is called stability.

In the opposite case, when λ is such that $\lambda^2 c_j^2 > 1$ for some j, the difference equations are said to be unstable because one can find initial conditions, depending on h but satisfying $\|U(0)\| = 1$, such that $\|U(T)\| \to \infty$ as $h \to 0$.

To do this, pick θ and j so that $|\mu_j| > 1$. Pick $\varepsilon > 0$ so that $|\mu_j| - \varepsilon > 1$. Now the eigenvalues of a matrix are continuous functions of the matrix elements. Therefore, there is some eigenvalue $\tilde{\mu}_j(\theta,h)$ of $M(\theta,h)$ which approaches $\mu_j(\theta)$ as $h \to 0$. Therefore, for h sufficiently small, $|\tilde{\mu}_j - \mu_j| < \varepsilon$ and

$$|\tilde{\mu}_j| > |\mu_j| - \varepsilon > 1 \tag{7.195}$$

If we choose as our initial condition U^o an eigenvalue of M corresponding to eigenvalue $\tilde{\mu}_j$ then

$$\|U^n\| > (|\mu_j| - \varepsilon)^n \|U^o\| \tag{7.196}$$

$$\|U(T)\| > (|\mu_j| - \varepsilon)^{\frac{T}{\lambda h}} \|U(0)\| \tag{7.197}$$

Pick $\|U(0)\| = 1$. Then $\|U(T)\| \to \infty$ as $h \to 0$, since $|\mu_j| - \varepsilon$ is independent of h and greater than 1. This situation is called instability.

In summary, the difference equations are stable if $\lambda = \frac{k}{h}$ is chosen so that $(\lambda c_j)^2 \leq 1$ for all of the characteristic speeds c_j. Otherwise they are unstable. Stability depends only on the matrix A, whose eigenvalues are the characteristic speeds, and not on the matrix B.

We have yet to consider the problem of putting the equations of the arterial pulse in the form (7.152). In fact, this can be done in several ways, all of which are equivalent for smooth solutions but which yield different formulae for the speed of propagation of a shock [1]. In problems of gas dynamics, the choice of the appropriate form of the equations is dictated by the physical conservation laws. In arteries, the situation is less clear-cut because the physical conservation laws do not by themselves determine a one-dimensional theory. An extra assumption has to be brought in, that the velocity and pressure depend only on x and t. This assumption cannot be accurate when the cross-section of the artery changes. It will be especially bad when the change occurs abruptly, as a shock.

This problem has been carefully considered by Hughes [2], who recommends that the following form of the equations be used:

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1 For a discussion of the circumstances in which shock waves might occur in arteries, see Anliker and Rockwell cited above.

2 Hughes, T., cited above.

$$(7.198)\qquad \begin{pmatrix} u \\ A \end{pmatrix}_t + \begin{pmatrix} \frac{1}{2}u^2 + \frac{1}{\rho}p(A,x) \\ Au \end{pmatrix}_x = \begin{pmatrix} 0 \\ -\psi(A,x) \end{pmatrix}$$

where u is the velocity, A is the cross-sectional area, $p(A,x)$ is the pressure, and $\psi(A,x)$ is the outflow. For smooth solutions, these equations are equivalent to the equations that we have been using throughout this chapter. Moreover, they are in conservation form, as required by the Lax-Wendroff method.

References

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3 Kreiss, H., and Oliger, J.: Methods for the approximate solutions of time dependent problems, in: Global Atmospheric Research Program Publication #10, World Meteorological Organization (1973).

4 Thomee, V.: Topics in Stability Theory for Partial Differential Operators, in: Symposium on the Theory of Numerical Analysis (Dundee, Scotland, 1970) Berlin, Springer, 1971. pp.41-91.

5 Widlund, O.: Introduction to finite difference approximations to initial value problems for partial differential equations, in: Symposium on the Theory of Numerical Analysis (cited above). pp.111-152.

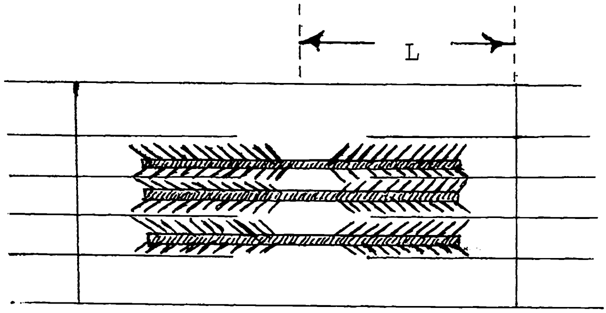
VIII. An Inverse Problem in Muscle Mechanics *.

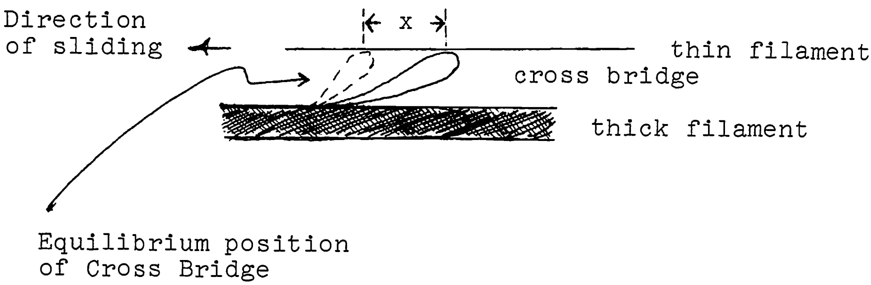
The shortening which occurs in muscle is brought about through the sliding of one system of filaments past another. The filaments involved do not change length. Originating from the thick filaments is a system of projections, called cross-bridges. These projections can attach to the thin filaments, pull them in the direction which shortens the muscle, and then let go. Immediately after the cross-bridge has attached to the thin filament, it is in a state of tension. This tension arises from a chemical reaction which forces the cross-bridge into a strained configuration and which thereby supplies the energy which makes it possible for the muscle to shorten against a load.

The shortening which occurs in one cross-bridge cycle is much less than the maximum shortening of which the muscle is capable. During a single contraction, a given cross-bridge may go through its cycle many times. The different cross-bridges function independently and asynchronously; the smooth behavior of the muscle as a whole is a consequence of the average behavior of the whole population of cross-bridges [2].

* This lecture is based on the Ph.D. thesis of H.M. Lacker [1].

Sarcomere





The dynamics of the cross-bridge population may be studied as follows. Let x be the displacement of the cross-bridge from its equilibrium position, and let the population density function u(x) be defined so that

$$\int_a^b u(x)dx = \text{fraction of cross-bridges with } x \in (a,b).$$

We take the point of view that x is undefined for cross-bridges which are not attached to the thin filament. Thus

$$1 > \int_{\infty}^{\infty} u(x)dx = \text{fraction of cross-brdiges which are attached.}$$

We assume that all cross-bridges attach in the same configuration $x = A$. Following attachment they are constrained to move according to

$$\frac{dx}{dt} = \frac{dL}{dt}$$

where L is the length of a half-sarcomere. Note that L is proportional to the length of the muscle as a whole.

We assume that each cross-bridge acts like a linear spring. Thus the total force measured at the ends of the muscle is proportional to

$$P = \int_{-\infty}^{\infty} u(x)x\,dx$$

Let F be the rate constant for attachment of an unattached cross-bridge, and let g(x) be the rate constant for detachment of a cross-bridge in configuration x. This means that the rate of formation of cross-bridges at any instant will be:

$$\left(1 - \int_{-\infty}^{\infty} u(x)\,dx\right)F$$

while the rate of breakdown will be:

$$\int_{-\infty}^{\infty} g(x)u(x)\,dx \quad .$$

We are now ready to derive an equation for the dynamics of the cross-bridge population density $u(x,t)$. In the following, let $v = \frac{dL}{dt} = \frac{dx}{dt}$, and restrict consideration to $v < 0$ (shortening). Consider any interval (a,b) such that $a < b < A$, where $x = A$ is the configuration in which attachment occurs. We have

$$\int_a^b \frac{\partial u}{\partial t}\, dx = \frac{d}{dt}\int_a^b u\,dx = v[u(a) - u(b)] - \int_a^b gu\,dx \tag{8.1}$$

where the term $v[u(a) - u(b)]$ arises from convection of cross-bridges across the boundaries of the interval and the term $-\int_a^b gu\,dx$ arises from the breakdown of cross-bridges. Differentiating with respect to b and setting $b = x$, we obtain the partial differential equation

$$\frac{\partial u}{\partial t} + v\,\frac{\partial u}{\partial x} + g(x)u = 0 \quad , \quad x < A \quad . \tag{8.2}$$

We shall use this equation only for the case $v(t) < 0$, which corresponds to shortening. The boundary condition at $x = A$ is obtained by equating the rate of formation of new cross-bridges with the flux of bridges away from $x = A$. Thus

$$(-v)u(A) = \left(1 - \int_{-\infty}^{A} u\,dx\right) F \tag{8.3}$$

1. The Steady State.

The steady state solution of (8.2) is

$$u(x) = u(A)\exp\left\{\frac{1}{v}\int_x^A g(x')dx'\right\} \tag{8.4}$$

The constant u(A) can be determined from the boundary condition (8.3). First let

$$N = \int_{-\infty}^{A} u dx = \text{fraction of cross-bridges attached.}$$

Then from (8.3) and (8.4) we have

$$N = \frac{(1-N)F}{-v}\int_{-\infty}^{A} dx\ \exp\left\{\frac{1}{v}\int_x^A g(x')dx'\right\} \tag{8.5}$$

This equation can be solved for N, and u(A) can be evaluated from

$$u(A) = \frac{(1-N)F}{-v} \tag{8.6}$$

Instead of doing this in general, consider the limit of low activation, $F \to 0$. In that case

$$\lim_{F\to 0}\frac{N}{F} = \frac{1}{-v}\int_{-\infty}^{A} dx\ \exp\left\{\frac{1}{v}\int_x^A g(x')dx'\right\} \tag{8.7}$$

$$\lim_{F\to 0}\frac{u(A)}{F} = \frac{1}{-v} \tag{8.8}$$

Next we evaluate the quantity P which is proportional to the force measured at the ends of the muscle. We have, if each cross-bridge acts like a linear spring,

(8.9) $$P = \int_{-\infty}^{A} uxdx$$

and therefore

(8.10) $$\lim_{F\to 0} \frac{P}{F} = \frac{1}{-v} \int_{-\infty}^{A} x \exp\left(\frac{1}{v} \int_{x}^{A} g(x')dx'\right) dx$$

It will be very convenient to rewrite this expression in terms of new variables. Let

(8.11) $$y(x) = \int_{x}^{A} g(x')dx'$$

Since $g > 0$, there is an inverse function $\bar{x}(y)$, such that

(8.12) $$\bar{x}(y(x)) = x$$

Note that $y(A) = 0$; and $y(-\infty) = \infty$, provided that $g > \delta > 0$. Also let

(8.13) $$s = \frac{-1}{v}$$

Then

(8.14) $$\lim_{F\to 0} \frac{P}{F} = s \int_{0}^{\infty} dy \, \frac{d\bar{x}}{dy} \cdot \bar{x} \cdot \exp(-sy)$$

Let

$$Q(y) = \frac{1}{2}\frac{d}{dy}\overline{x}^2 \tag{8.15}$$

Then

$$\lim_{F\to 0}\frac{P}{F} = s\int_0^\infty dyQ(y)e^{-sy} = \int_0^\infty dy'Q\left(\frac{y'}{s}\right)e^{-y'} \tag{8.16}$$

The latter form of this integral is especially convenient for considering the limit $v \to 0$, $s \to \infty$ which corresponds to a muscle held at constant length (isometric). Let $P_o = P|_{v=0} = P|_{s=\infty}$. Then

$$\lim_{F\to 0}\frac{P_o}{F} = Q(0)\int_0^\infty e^{-y'}dy' = Q(0) \tag{8.17}$$

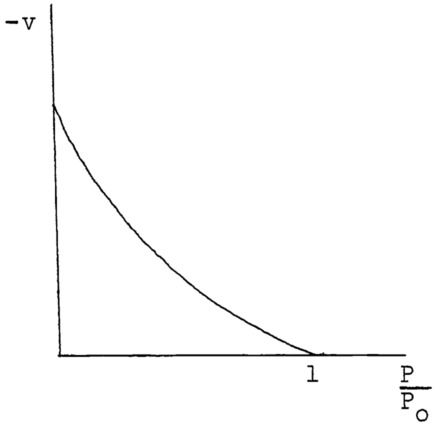
Therefore the ratio of force to isometric force in the limit of low activation is given by

$$\overline{P} = \lim_{F\to 0}\frac{P}{P_o} = s\int_0^\infty dy\,\frac{Q(y)}{Q(0)}\,e^{-sy} \tag{8.18}$$

These results are of interest because they can be used in conjunction with experimental data to determine the shape of the function g(x) which appears in the cross-bridge model. In particular, steady state force velocity curves have been determined experimentally, and an excellent fit has been obtained to the equation [3]

$$(8.19) \qquad \left(\frac{P}{P_o} + a\right)\left(-v + b\right) = (1 + a)b$$

where a, b, P_o are constants (P_o has the interpretation of being the isometric force). It has also been found [4] that when $-v$ is plotted against P/P_o, the resulting curve is nearly independent of activation. Thus Eq. (8.19) holds as written even in the limit of low activation. This fact turns out to be enough to determine the shape of the function g(x).



Once g(x) has been determined in this way, one can go back and check whether the model predicts that (8.19) should also be satisfied for finite activations. In fact, it is not exactly satisfied, but it is satisfied to within experimental error over the range of activations which are likely to occur in muscle.

In order to solve for g, Lacker proceeds as follows. First, rewrite (8.19) in terms of $\overline{p}$ and $s = -1/v$

$$(8.20) \qquad \overline{P} = -a + \frac{(1 + a)b}{\frac{1}{s} + b} = \frac{s - (\frac{a}{b})}{s + (\frac{1}{b})}$$

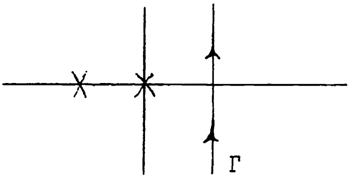
Next, equate the experimental result (8.20) with the theoretical result (8.18). Dividing through by s, one obtains

(8.21) $$\int_0^\infty dy \, \frac{Q(y)}{Q(0)} \, e^{-sy} = \frac{s - (\frac{a}{b})}{s(s + (\frac{1}{b}))}$$

This has the form of the Laplace Transform. Using the inversion integral along the path Γ in the complex s-plane, and noting that there are poles at s = 0 and s = -1/b we have:

(8.22) $$\frac{Q(y)}{Q(0)} = \frac{1}{2\pi i} \int_\Gamma \frac{s - (\frac{a}{b})}{s(s + \frac{1}{b})} \, e^{sy} ds$$

$$= -a + (1 + a)e^{-y/b}$$



s-plane

(The reader who is unfamiliar with Laplace Transforms can at least verify that the expression for $\frac{Q(y)}{Q(0)}$ obtained in (8.22) satisfies (8.21).)

Recalling the definition of Q(y) we have

(8.22) $$\frac{1}{2} \frac{d}{dy} \overline{x}^2 = \left[\frac{1}{2} \frac{d}{dy} \overline{x}^2\right]_{y=0} \left[-a + (1+a)e^{-y/b}\right]$$

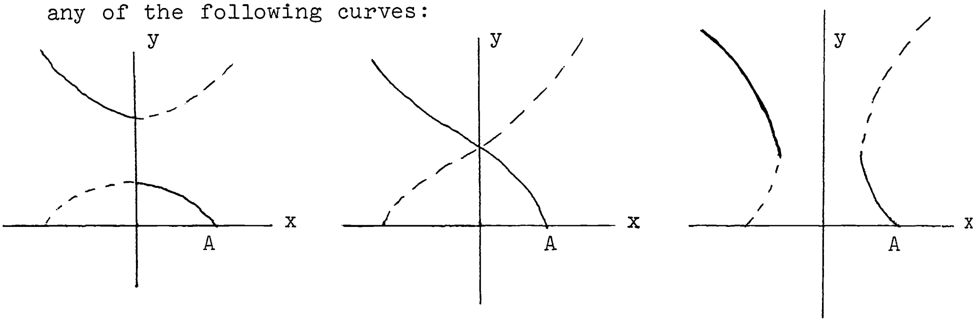
The constant in (8.22) can be evaluated:

$$\left[\frac{1}{2}\frac{d}{dy}\bar{x}^2\right]_{y=0} = \bar{x}(0)\frac{d\bar{x}}{dy}(0) = -\frac{A}{g(A)} \tag{8.23}$$

Integrating from 0 to y and writing x for $\bar{x}(y)$ we obtain the following relation between x and y

$$\frac{1}{2}(x^2 - A^2) = \frac{A}{g(A)}\left[ay - (1+a)b(1 - \exp(-\frac{y}{b}))\right] \tag{8.24}$$

Depending on the parameters, this relation may look like any of the following curves:



For a typical point x there are two values of y, but one may choose which branch is physically relevant by noting that $-\frac{dy}{dx} = g > 0$. Therefore we should choose the branch with negative slope. Considerations of continuity then require that we choose the middle situation sketched above. Analytically this means that $\frac{dx}{dy}$ is finite at $x = 0$ and therefore $x(\frac{dx}{dy}) = 0$. Using (8.22) we can then determine $y(0)$, and, substituting this in (8.24) we can find a restriction on the parameters. The critical value of y is given by

$$\exp(-\frac{y_o}{b}) = \frac{a}{1+a} \tag{8.25}$$

and the restriction on the parameter is

$$g(A) = \frac{2b}{A}\left[1 - \log\left(\frac{1+a}{a}\right)^a\right] \tag{8.26}$$

Note that $g(A) > 0$, since

$$\left(\frac{1+a}{a}\right)^a = \left(1 + \frac{1}{a}\right)^a < e \quad .$$

Using this restriction we can rewrite (8.24) as follows:

$$1 - (\frac{x}{A})^2 = \frac{1}{1-\log\left(\frac{1+a}{a}\right)^a}\left[(1+a)(1 - \exp(-\frac{y}{b})) - a\frac{y}{b}\right] \tag{8.27}$$

With this curve given, the function g can be derived from $g = -\frac{dy}{dx}$. Note that the parameters a and b are available from experiments. Although A is unknown, changing it merely causes a scale change on the x axis. Consequently the shape of the function g can be determined.

2. Transients.

One may conjecture that the steady force-velocity curve of muscle is not too sensitive to the shape of the function $g(x)$. In that case, the method outlined above could be subject to significant errors. Also, the method assumes that the cross bridge acts like a linear spring, and it seems likely that a choice of a different cross-bridge force-extension curve would lead to a different choice of $g(x)$. Finally, the method does not give any independent check on the model.

To overcome these difficulties, Lacker has proposed a transient experiment called a "velocity clamp" in which a muscle is first put in a state of isometric contraction and then allowed to shorten at a controlled velocity. The force on the ends of the muscle is measured as a function of time. If this experiment is performed at low activation for several different velocities, Lacker has shown how the data could be used to determine not only the function $g(x)$, but also the force-extension curve of the cross-bridges. Moreover, the method is self-checking, since it can be carried out with data from any pair of velocities and the results from different pairs can be compared.

The equations of the model with an arbitrary force-extension curve $p(x)$, with constant velocity of shortening $v < 0$, and in the limit of low activation $N \ll 1$ are as follows:

$$u_t + vu_x + g(x)u = 0 \qquad x < A, \quad t > 0 \tag{8.28}$$

$$u(A) = \frac{F}{-v} \tag{8.29}$$

$$P(t) = \int_{-\infty}^{A} u(x,t)p(x)dx \tag{8.30}$$

The advantage of regarding v rather than P as given is that the pair (8.28)-(8.29) can be solved without considering (8.30). (When P is given and v is unknown, (8.28)-(8.30) has to be regarded as a non-linear system.)

We shall consider two different initial conditions for Eqs. (8.28)-(8.29), as follows

$$u_I(x,0) = 0 \tag{8.31}$$

$$u_{II}(x,0) = \frac{\delta(x-A)F}{g_A} \tag{8.32}$$

where $g_A = g(A)$. The initial conditions $u_I(x,0) = 0$ correspond to a muscle which was first stimulated at time zero but which switches on instantaneously. This experiment cannot be performed in practice because it takes a finite amount time to activate the muscle. The function $u_{II}(x,0)$ corresponds to a muscle in a steady isometric contraction at low activation, since all of the attached cross-bridges have the configuration $x = A$. This is the initial condition which may be realized in an experiment.

One can construct both solutions u_I and u_{II} from the steady solution $u_o(x)$. Restricting attention to $x < A$ we may write

$$u_o(x) = \frac{F}{-v} \exp\left\{ - \int_0^{\frac{A-x}{-v}} g(A+v\tau)d\tau \right\} \tag{8.33}$$

$$u_I(x,t) = \begin{Bmatrix} u_o(x) & x > A+vt \\ 0 & x < A+vt \end{Bmatrix} \tag{8.34}$$

$$= u_o(x)H(x - (A+vt))$$

$$u_{II}(x,t) = u_I(x,t) + \frac{1}{g_A} \frac{\partial}{\partial t} u_I(x,t) \tag{8.35}$$

Exercise: Verfiy that u_o, u_I, u_{II} satisfy Eqs. (8.28)-(8.29) and that u_I and u_{II} satisfy the initial conditions (8.31) and (8.32), respectively. (Recall that $\frac{d}{dx} H(x) = \delta(x)$).

It now follows from (8.30) and (8.35) that the forces $P_{II}(t)$ and $P_I(t)$ corresponding to $u_{II}(x,t)$ and $u_I(x,t)$ are related as follows

(8.36) $$P_{II}(t) = P_I(t) + \frac{1}{g_A}\frac{d}{dt}P_I(t)$$

If $P_{II}(t)$ has been measured, and if a value for g_A has been determined (this point will be discussed below), then we can solve (8.36) for $P_I(t)$ using the initial condition $P_I(0) = 0$. In the following we assume that $P_I(t)$ has been determined. The next step is to derive equations for g(x) and p(x) in terms of $P_I(t)$.

The first observation is that $P_I(t)$ may be written

(8.37) $$P_I(t) = \int_{A+vt}^{A} p(x)u_o(x)dx$$

on account of the cut-off in the formula for $u_I(x,t)$. Taking derivatives with respect to time:

(8.38) $$P_I'(t) = -vp(A+vt)u_o(A+vt)$$

(8.39) $$P_I''(t) = -v^2[p'(A+vt)u_o(A+vt) + p(A+vt)u_o'(A+vt)]$$

Before proceeding further, we note that the constant A can be determined from a single record of $P_I(t)$. By definition, x = 0 is the equilibrium point of the cross-bridge. Therefore p(0) = 0. Assume that p(x) > 0 for x > 0, and p(x) < 0 for x < 0. Physically this means that all cross-bridges with x > 0 are in a configuration favorable for shortening, while all cross-bridges with $x < 0$ are in a configuration which opposes shortening. Let

$$t^* = \frac{A}{-v} \tag{8.40}$$

(Recall that $v < 0$). Then from (8.38), since $u_o > 0$ we have

$$\begin{cases} P_I'(t) > 0 , & t < t^* \\ P_I'(t) = 0 , & t = t^* \\ P_I'(t) < 0 , & t < t^* \end{cases} \tag{8.41}$$

In other words, $P_I(t)$ has a single maximum at $t = t^*$. (The presence of several extrema would indicate multiple equilibria for the cross-bridge: maxima will indicate stable equilibria while minima will indicate unstable equilibria). If t^* is measured and v is known, then A can be determined from (8.40).

At this point it is important to recall that $P_I(t)$ is not to be directly measured, but to be determined from measurements of $P_{II}(t)$ by solving Eqn. (8.36). Before this can be done, a value of g_A must be determined. If the wrong g_A is chosen, this will shift the position of the peak in the calculated curve $P_I(t)$ and hence lead to an incorrect determination of A. Lacker has conjectured that there is precisely one value of g_A which will lead to the same value of A being derived from two or more experiments at different velocities. (This conjecture was confirmed analytically for the case g(x) = constant.) If this conjecture is correct, then g_A can be determined from two or more experiments by imposing the requirement that the values of A computed from the different experiments are mutually consistent.

Assuming, then, that g_A and A have been determined, and that $P_I(t)$ has been computed from the measured curve $P_{II}(t)$, we may proceed as follows:

From Eqs. (8.38)-(8.39) we have

$$\frac{P_I''(t)}{P_I'(t)} = v\left[\frac{p'(A+vt)}{p(A+vt)} + \frac{u_o'(A+vt)}{u_o(A+vt)}\right] \tag{8.42}$$

On the other hand, from the steady differential equation satisfied by u_o, we have

$$\frac{vu_o'}{u_o}(x) = -g(x) \tag{8.43}$$

Therefore:

$$\frac{P_I''(t)}{P_I'(t)} = v\,\frac{p'(A+vt)}{p(A+vt)} - g(A+vt) \tag{8.44}$$

In is convenient to rewrite (8.44) in terms of x = A+vt

$$\frac{P_I''}{P_I'}\left(\frac{x-A}{v}\right) = v\,\frac{p'(x)}{p(x)} - g(x) \tag{8.45}$$

Now suppose that $P_I(t)$ has been determined for two different values of v. Then we have equations of the form

$$\begin{cases} f_a(x) = v_a\,\dfrac{p'(x)}{p(x)} - g(x) \\ \\ f_b(x) = v_b\,\dfrac{p'(x)}{p(x)} - g(x) \end{cases} \tag{8.46}$$

where $f_a(x)$ and $f_b(x)$ are known. For each c, this is a linear system in the unknowns $\frac{p'(x)}{p(x)}$ and g(x). The determinant is

$$\Delta = \begin{vmatrix} v_a & -1 \\ \\ v_b & -1 \end{vmatrix} = v_b - v_a$$

which is different from zero if two different velocities are used. Therefore, for each x we can determine the two unknowns $\frac{p'(x)}{p(x)}$ and g(x). The function p(x) can then be determined by integration. (There will be numerical difficulties near $x = 0$ where the functions $f_a(x)$ and $f_b(x)$ are expected to become infinite. However, the functions p(x) and g(x) are expected to go smoothly through $x = 0$, so they can be determined near $x = 0$ by continuity.)

It is important to note that the foregoing method can be used to construct g(x) and p(x), from a single pair of experiments at two arbitrarily chosen velocities. Other pairs of velocities can also be chosen, and g(x) and p(x) can computed independently from the resulting experimental records. The results for different pairs of velocities should be consistent. This provides a rigorous test of the model.

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