26

Graduate seminar Report

On

Mathematical Modelling in Medical Science Through Differential Equations.

By

Eshetu Haile

Advisor

Dr. Mobin Ahmed

School of Graduate Studies
Addis Ababa University.

June 2004

Addis Ababa

Acknowledgment.

My gratitude goes to my advisor Dr. Mobin Ahmed for his valuable suggestions, comments and providing the necessary materials in the preparation of this paper.
I am also deeply indebted to my examiner Prof. Dr. rer.nat.habil.R.Deumlich for his priceless comments and advice in the general framework of the paper. My appreciation is also extended to Frehiot Tesfaye in typing part of the manuscripts of this paper. Finally, my gratitude is forwarded to my wife Assefu Anteneh for her considerate moral support.

Preface

Almost all scientists, engineers, managers and researchers in all fields of life successfully used mathematical modelling though its importance has been realized only during the last three decades. And so, the way how to prepare a mathematical model for a given real world problem is inevitable. Since mathematical modeling is not confined only in one subject, the mathematical understanding of any physical situation usually consists of the following steps:

1) Understanding the various problem parameters of the situation and then making a rough mathematical model.
2) Posing a corresponding precise mathematical problem, and analyzing it, trying to find an exact or approximate solution.
3) Comparing the result with the experimental data to check the validity of the model.

Because of the importance of this field of study in all fields of life, it is interesting to see some of its applications in biological and medical sciences. This seminar paper gives hints to interested readers how to construct models in these fields of study though we are not going to see more details.

Chapter1. Consists of introduction to mathematical modelling, its importance in our day life activities and stages of constructing the model in brief. This chapter also indicates some of the limitations of modelling.

Chapter2. Discusses ordinary differential equation models in medical and biological problems. These include brief explanations for the construction of a model detecting diabetes, cardiography and nutrient exchange in the placenta and moreover, the solution of each problem is well organized.

Chapter3. Discusses about stochastic epidemic model. Besides this, deterministic versus stochastic models are presented. Apart from these, some definitions and theorems from probability theory that are related to stochastic epidemic models are mentioned briefly with the necessary examples.

Contents Page

Chapter - one

Chapter – two

Chapter-three

Chapter-One

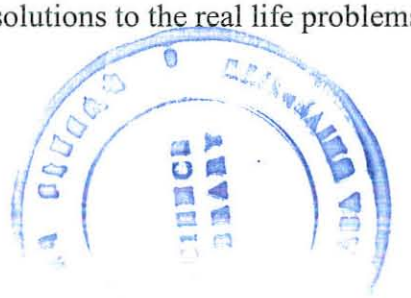
1. Introduction to Mathematical Modelling.

It is important to realize at the outset that learning to apply mathematics is a very different activity from learning mathematics. The skills needed to be successful in applying mathematics are quite different from those needed to understand concepts, to prove theorems or to solve equations. For this reason, a book of mathematical modelling is bound to appear different from a text dealing with a particular branch of mathematics.

There is no theory to learn and there are only few guiding principles. This is not to suggest, however, that mathematical modelling is an easy subject. The difficulty is not in learning and understanding the mathematics involved but in seeing where and how to apply it. There are many examples of very simple mathematics giving useful solutions to very difficult problems, although generally speaking the complexity of the problem and of the required mathematical treatment goes hand in hand.

Professional modellers have to deal with a variety of real problems, and their main task is to translate each problem into mathematical form. This is the essence of modelling, and it can involve discussions to clarify the problem, identification of the problem variables, estimation, approximation and avocation of courses of action that may cost money and time.

Mathematical modelling has been successfully used by almost all scientists, engineers, managers and researchers throughout the ages in all fields of life, but its importance has been realized only during the last three decades. Though some mathematical modelling problems acquire more than one technique for their solution, yet in practice most mathematical problems use one dominant technique. It will be accordingly useful to know as to which technique is most appropriate for a practical situation. There are growing influence of mathematical modelling on other fields. Despite nearly thirty years of effort, researchers have had but little success in developing global mathematical model for determining optimal solutions to the real life problems.



1.1 Models and Modelling

Any **model** (including a physical model) can be defined as a simplified representation of certain aspects of a real system. A mathematical model is a model created using mathematical concepts such as functions and equations. When we create mathematical models, we move from the real world into the abstract world of mathematical concepts, which is where the model is built .We then manipulate the model using mathematical techniques or computer aided numerical computation. Finally, we re-enter the real world, taking with us with the solution to the mathematical problem, which is then translated into a useful solution to the real problem. Note that the start and end of the modelling activity are the real world. It is also important to realize at the outset that mathematical modelling is carried out in order to solve problems. It must not therefore be thought that for a particular problem there is one right and proper model. We are not in the same situation as with arithmetic or algebra, where, each question, there is one correct answer. Many different models can be developed for tackling the same problem. It is also true, and a remarkable demonstration of the power of mathematics, that the same abstract model can often be used for quite different physical situations. Some models may be better than others in the sense that they are more useful or more accurate, but this is not always the case. Generally, the success of a model depend on how easily it can be used and how accurate are its predictions.

1.2 Mathematical modelling arises in simple situations in every day life

1. Estimate the population of the world in 2020. (Without waiting till then)
2. Estimate the average life span of light bulbs manufactured in a factory. (Without lighting each bulb till it gets fused)
3. Find the half-life of a radioactive carbon. (Without waiting till half of the mass of the carbon disappears)
4. Find the distance between the earth and the moon. (Without going there)
5. Estimate the temperature of the sun at its center. (Without placing a thermometer there)

6. Find the range of a projectile filed from a cannon. (Without directly measuring the distance)
7. Find the time it takes a satellite at a height h_{km} above the surface of the earth to complete one orbit. (Without sending a satellite these)
8. Estimate the number of infected persons by an epidemic disease after t days. (Without administering the disease to the society)
9. Find the width of lake Tana. (Without stretching a string)
10. Estimate time of murder. (Without knowing the exact time of death)

The notions of mathematical modelling can easily treat not only the above problems, but also millions of similar problems.

The techniques of solving the above problems are analogous to that of solving problems in algebra, arithmetic, e.t.c. To sum up the above discussions under models and modelling, the following example is inevitable.

Example. The sum of a two-digit number is 7. The new number obtained by reversing the digits is 9 more than the original number. What is the original number?

Let $xy=10x+y$ be the original number. The new number is $yx=10y+x$.

But $x+y=7$ and $10y+x-(10x+y)=9$ which is equivalent to $-x+y=1$.

Solving the two equations simultaneously gives $x=3$ and $y=4$.

The two equations $\begin{cases} x+y=7 \\ -x+y=1 \end{cases}$ give a mathematical model of the digit problem.

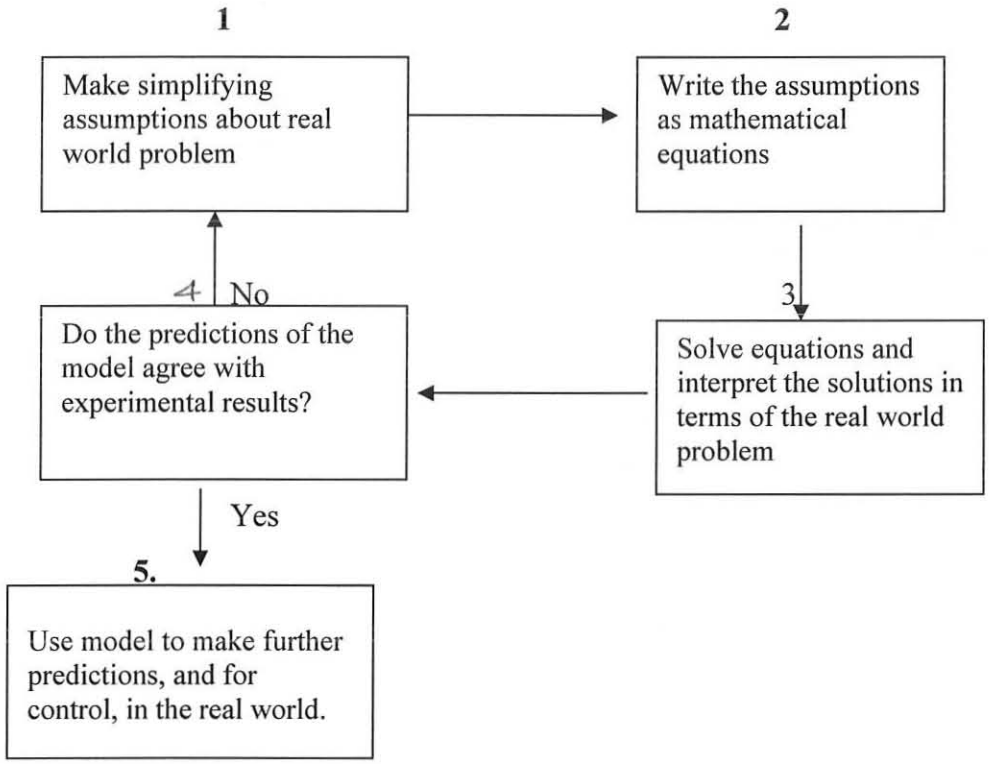
So, the digit problem is reduced to the mathematical problem of the solution of two algebraic equations.

The solution of the equation is fairly interpreted in terms of the place values of the units and the tens digit numbers. In the same way, to solve a given physical, biological, chemical, financial or social problems, we first develop a mathematical model for it, then solve the model and finally interpret the solution in terms of the original problem. One principle of great importance to science is the following: whenever we want to find the value of an entity which can't be measured directly, we introduce symbols, x, y, z...to represent laws of Physics, Chemistry, Biology, Economics, e.t.c and use whatever

information is available to us to get relations between these variables, some of which can be measured or are known and others which can't directly measured and have to be found out. We use mathematical relations developed to solve for the entities, which can't be measures directly in terms of those entities whose values can be measured and are known. The mathematical relations we get may be in terms of algebraic, trigonometrical, differential, difference, integral equations or even in terms of inequalities.

1.3 Modelling cycles and procedures

The most important activities of modelling are the process, which involve a number of clearly identifiable stages. The most helpful way of representing these stages is by means of modelling **flow chart** as shown below. The point of the flow chart is that it gives us a framework to refer to and acts as a channel for our thoughts and ideas.



The modeling cycle

The modelling process is illustrated in the above figure, which brings out its cyclic nature. The process may fail at stage **(3)** if the equations are too complicated to be solved. One then turns to stage **(1)** of the process and tries to simplify the modelling assumptions to produce equations, which are easier to solve. At stage **(4),** moreover, there may be insufficient agreement between the actual experimental results and the results predicted from the model. If this happens, one again returns to stage **(1)** to see whether the assumptions can be made more realistic. The process of returning to **(1)** may be repeated many times until a satisfactory model is obtained although stage **(1)** of the process is in some ways the most creative; it is also the most difficult, involving the intuition and experience of specialists in the various areas.

In order to sum up the above discussions, we have to follow the following procedures in constructing mathematical models.

a) Identifying the quantities most relevant to the problem and making assumptions about the way in which the quantities are related. This usually involves simplifying the original problem.
b) Think about all the physical, chemical, biological, social, economic laws that may be relevant to the situation. If necessary collect some data and analyze it to get some initial insight in to this situation.
c) Introducing symbols to denote the various quantities, and then writing the assumptions as mathematical equations.
d) Solving the equations and interpreting their solutions as statements about the original problem.
e) Checking the results obtained to see whether they seem reasonable and, if possible, whether they are in agreement with experimental data.
f) This process continues till a satisfactory model is obtained which agrees with all earlier collected data and observations.
g) Deduce conclusions from the model and test these conclusions against earlier data, additional data that may be collected and some other extreme cases.

1.4 Advantages of a mathematical model

1. A model provides logical and systematic approach for solving or understanding a problem.
2. Models help in incorporating useful changes even without changing the system or problem under consideration.
3. Models help in finding scope of new methods for solving a problem and improvement in the system.
4. Models indicate the nature of measurable quantities in a problem.
5. Models help in the understanding and economic explanation of the operations of the system.
6. Though a model, the problem under consideration becomes controllable.

1.5 Limitations of mathematical modelling

In our models, some intangible factors may be incorporated in a realistic problem. In order to construct a mathematical model, assumptions are made about the importance and nature of some factors. Even if is possible to construct a mathematical model including all factors, it would be too complex and unwieldy for business purposes and furthermore, the manipulation needed to solve the problem would be time consuming and expensive. For these and other related reasons, mathematical modelling of large systems (in the study of global models of population environment, pollution control, economic conditions, global economy, oceanlogy, e. t. c.) possess large or even a larger number of situations which have not yet been mathematically modelled either because the situations are sufficiently complex or because mathematical models formed are numerically intractable.

Chapter-two

2. Some Mathematical Models in Medical and Biological Sciences.

Under this topic, we are going to see how mathematical models are constructed in detecting diabetes, cardiography and nutrient exchange in the placenta, which involve second order ordinary differential equations one after the other.

2.1 A Model for Detecting Diabetes

Glucose, an end product of carbohydrate digestion is converted in to energy in the cells of the body. The hormone insulin secreted by pancreas, facilities the absorption of glucose by cells other than those of the brain and nervous system.

A delicate balance is maintained between the amounts of glucose and insulin in the bloodstream. If the insulin concentration is too low, then too little glucose is absorbed from the blood stream. The unabsorbed glucose is then lost in the urine along with other nutrients. If, on the other hand, the insulin concentration is too high, then cells other than those of the brain and nervous system absorb too much glucose; lack of glucose available to the cell of the brain then impairs its function. Then end result in either case, whether too little or too much insulin, can bc coma and even death.

In the medical disorder Diabetes Mellitus, the pancreas secretes not enough insulin. People suffering from this require supplements of insulin in the form of regular injections, together with a modification of their diet to regulate glucose input. In this section a simple model of the interaction between glucose and insulin in the body is presented, we then use this model to discuss a clinical test for the detection of mild forms of diabetes.

The model

The main features that a model of a glucose insulin regulation system must take into account are as follows.

a) A rise in the concentration of glucose in the bloodstream results in the liver absorbing more of the glucose, which it converts and stores as glycogen; a drop in the concentration of glucose reverses the process.
b) A rise in the concentration of insulin in the bloodstream enables the glucose to pass more readily through the membranes of the cells in skeletal muscle, resulting in greater absorption of glucose from the bloodstream.
c) A rise in the concentration of glucose in the bloodstream stimulates the pancreas to produce insulin at a faster rate; a drop in the glucose concentration lowers the rate of insulin production.
d) Insulin produced by the pancreas is constantly being degraded by the liver.

Assumptions

1) The model omits details of the biochemistry involved and ignores the effects if other hormones.
2) It treats the bloodstream as if it were contained in a single compartment throughout which concentrations of glucose and insulin are uniform at each instant.
3) No recent digestion, glucose and insulin concentrations will be in equilibrium. It is from this equilibrium that the system responds to change.

Let x={excess glucose concentration}
y={excess insulin concentration.}, at time t.

Equilibrium occurs for x=y=0. Positive values of x and y corresponds to concentrations greater than the equilibrium values and negative values to concentrations less than the equilibrium values.

If either of x or y is given a non-zero value, then the body tries to restore the equilibrium. We assume that the rate of changes of these quantities depend only on the values of x and y so that

$$\frac{dx}{dt} = F_1(x, y)$$

$$\frac{dy}{dt} = F_2(x, y), \text{ for some functions } F_1 \text{ and } F_2.$$

The simplest way to construct a model is to assume that these differential equations are linear with constant coefficients.

Since x = y =0 are equilibrium solutions, it now follows that the linear differential equations must be homogenous. Hence, we assume them to be of the form

$$\frac{dx}{dt} = \dot{x} = \mathbf{-ax - by,} \qquad \mathbf{(1)}$$

$$\frac{dy}{dt} = \dot{y} = \mathbf{cx - dy,} \qquad \mathbf{(2)}$$

where **a, b, c** and **d** are positive constants. We are going to see that each constant is positive. What happens if initially x = 0 and y > 0 in equation **(2)?** From this we have:

$$\frac{dy}{dt} = -dy$$

at the initial instant. But the liver will immediately start to degrade the insulin, as noted in (d) above, since the concentration of the insulin has exceeded its equilibrium value. Thus its concentration starts to drop so that initially

$$\frac{\boldsymbol{dy}}{\boldsymbol{dt}} < 0$$

Hence, the previous equation shows that d must be positive.

Now, **a>0,** since $\frac{dx}{dt} < 0$ for y=0 through tissue uptake of glucose, and **b** >0, since y>0 tends to decrease blood glucose levels. It is also true that **c**>0 for x>0 causes the endocrine glands to secrete those hormones that tend to increase y.

a. Testing for diabetes (Glucose Tolerance Test)

In a glucose tolerance test a patient is asked to fast overnight and the following morning is given an injection of glucose. Blood samples are then taken at subsequent times and the concentration of glucose measured, to test the response of the glucose – insulin regulatory system. We might expect the glucose concentration to return after a time to the equilibrium level and to take longer in diabetic patients than in normal ones.

In modelling this test we suppose that during the short time interval while the glucose is being injected, the insulin concentration stays zero. Thus, if $\mathbf{g_0}$ is the total amount of glucose injected, then

$$\mathbf{x = g_0 , y = 0 \quad at \quad t = 0} \qquad \textbf{(3)}$$

Our model for the glucose and insulin concentrations is thus the solution of the pair of differential equations **(1), (2)** with the initial conditions **(3).**

Find a second order differential equation for x alone by differentiating **(1)** to get

$$\ddot{x} = -a\dot{x} - b\dot{y}$$

$$= -a\dot{x} - b(cx - dy) \qquad \textbf{(by using equ. 2)}$$

$$= -a\dot{x} - bcx + bdy$$

$$= -a\dot{x} - bcx - bd\left(\frac{ax + \dot{x}}{b}\right) \qquad \textbf{(by using equ. 1)}$$

This implies that,

$$\ddot{x} + (a + d)\dot{x} + (ad + bc)x = 0 \qquad \textbf{(4)}$$

The solution for **x** as a function of **t** can then be substituted into

$$y = -\frac{1}{b}(\dot{x} + ax) \qquad \textbf{(5)}$$

The initial conditions for **(4)**, which can be found from **(3)** and **(5)**, are

$$x = g_0 , \quad \dot{x} = -ag_0 \quad \text{at} \quad t = 0 \qquad \textbf{(6)}$$

Let a solution to **(4)** be given by $x(t) = e^{\lambda t}$. Then the characteristic equation of **(4)** is characterized by

$$\lambda^2 + (a + d)\lambda + (ad + bc) = 0 \qquad \textbf{(7)}$$

From equation **(7),** we have three possible options:

1) Suppose **(7)** has two distinct real roots, λ_1 *and* λ_2 (say). Then the solution to equation **(4)** is given by:

$X(t) = c_1 e^{\lambda_1 t} + c_2 e^{\lambda_2 t}$ and $\dot{X}(t) = c_1\lambda_1 e^{\lambda_1 t} + c_2\lambda_2 e^{\lambda_2 t}$

But using the initial conditions in equation (6), we have:

$X(0) = c_1 + c_2 = g_0$ and $\dot{X}(0) = c_1\lambda_1 + c_2\lambda_2 = -ag_0$

$$\begin{cases} c_1 + c_2 = g_0 \\ c_1\lambda_1 + c_2\lambda_2 = -ag_0 \end{cases}$$

Solving these equations simultaneously, we have the following:

$$c_1 = \frac{g_0\ (a+\lambda_2)}{\lambda_2 - \lambda_1} \qquad \text{and} \qquad c_2 = -\frac{g_0\ (a+\lambda_1)}{\lambda_2 - \lambda_1}$$

So, the solution of equation (4) becomes:

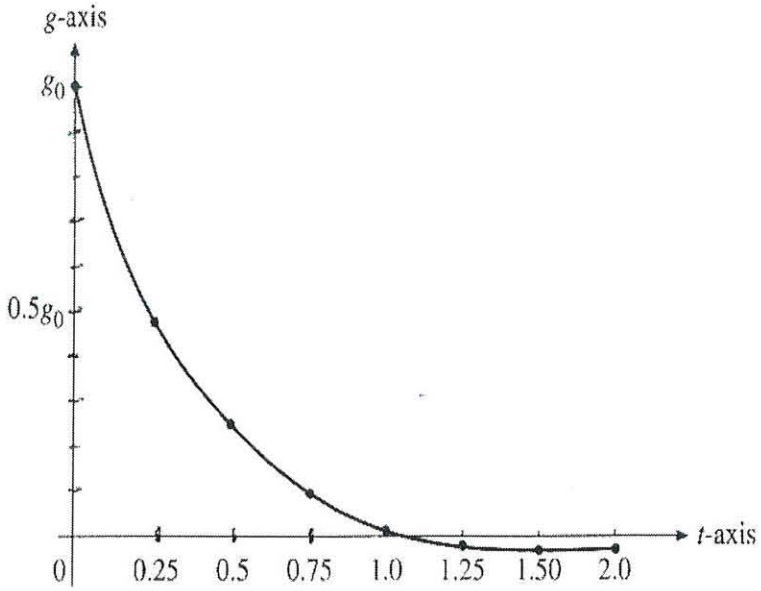
$$\text{x (t)} = g_0 \frac{\left((a+\lambda_2)e^{\lambda_1 t} - (a+\lambda_1)e^{\lambda_2 t}\right)}{\lambda_2 - \lambda_1} \qquad \textbf{(8)}$$

2). Suppose (7) has two equal roots, say λ, then the solution to this equation becomes:

$$x(t) = g_0(1-(a+\lambda)t)e^{\lambda t}$$

3). Suppose that (7) has two distinct imaginary roots, say $\lambda = -\alpha \pm i\omega$, then its solution under consideration is:

$$\text{x(t)} = g_0\left(Cos(\omega t) + \tfrac{\alpha - a}{\omega} Sin(\omega t)\right)e^{-\alpha t}$$



Glucose concentration returning to normal after glucose tolerance.

The type of solution obtained will depend on the number of real solutions of the characteristic equation

$$\lambda^2 + (a+d)\lambda + (ad+bc) = 0$$

This intern depends on the values of a, b, c and d .The solutions of x in the various cases are listed as shown above. From the fact that a, b, c and d are all positive it can be shown that the solution of (7) for λ are negative or have negative real part. Hence the factors

$e^{\lambda_1 t}, e^{\lambda_2 t}, e^{\lambda t}$ and $e^{-\alpha t}$, which occur in the previous page, must all decay exponentially with time. Thus, our model predicates that the glucose concentration will approach its original undisturbed value with sufficient lapse of time. This is just as we would expect.

In these solutions **x** is a linear function of $\mathbf{g_0}$, this is a consequence of our assumption that the differential equations are linear. It can be shown that these solutions are good approximations to those of any smooth non-linear model of the problem, if $\mathbf{g_0}$ is sufficiently small.

Experimental Results

Some experimental evidences show that the average values for normal individuals are as follows.

a= 2.92, **b**=4.34 , **c**= 0.208, **d**= 0.780

measured in units corresponding to grams for mass and hours for time. Substituting these values in to the characteristic equation **(7)** and then solving λ gives:

$$\lambda_1 = -1.36, \qquad \lambda_2 = -2.34$$

Thus the characteristic equation has two real roots. Hence substituting the numerical values to equation **(8),** we get **x** as a function of **t** and then using equation **(5)** to get **y.**

$$X(t)=g_0(-0.56e^{\lambda_1 t} + 1.56e^{\lambda_2 t})$$

$$Y(t)=0.202g_0(e^{\lambda_1 t} - e^{\lambda_2 t}) \qquad \textbf{(9)}$$

By putting x=0 we can find the time at which the glucose concentration returns to normal (and slightly undershoots before coming back up again to approach the equilibrium value exponentially)

b) Orally Administered Glucose

In an alternative version of the glucose tolerance test, the glucose is administered orally, rather than by injection. The differential equations, which model this test, are no longer homogeneous. In particular, the differential equation (4) is replaced by:

$$\ddot{x} + (a+d)\dot{x} + (ad+bc)x = S(t) \qquad (10)$$

Where **S**(t) is a "forcing" which takes account of the glucose coming in through the digestive system (the external rate at which the blood glucose concentration increased). Equation (10) can be written in the form of

$$\ddot{x} + 2\alpha\dot{x} + \omega_0{}^2 x = S(t) \qquad (11)$$

Where $2\alpha = a + d$ and $\omega_0{}^2 = ad + bc$ and where the forcing term **S** (t) is chosen on the basis of our modelling assumptions.

Let us put $\omega^2 = \omega_0{}^2 - \alpha^2$ and assume that $\omega^2 > 0$ (so that the characteristic equation has two unreal solutions) and Ackerman, Rosevar and McGuckin (1964) deduce that the solutions of **(11)** are:

$$X(t) = A\sin(\omega t)e^{-\alpha t}$$

where A is an arbitrary constant.

As experimental results show the value of the parameter ω_0 a reliable guide as to whether or not an individual is diabetic. They called the value $T_0 = \frac{2\Pi}{\omega_0}$ the "resonant period" and claimed that normal individuals have resonant period of less than 4 hrs; whereas diabetics have periods greater than 4 hrs.

2.2 Cardiography

A field of medicine that deals with the study of the heart is called **cardiology**. The nature and effects of vibrations of the heart as it pumps blood through the circulatory system of the body are a great source of mathematical applications. An important aspect involves the recording of such vibrations known as **cardiography**. The instrument that records such vibrations is called an **electrocardiograph (ECG)**. It translates the vibrations in to electrical impulses, which are then recorded.

It is interesting to translate the heart vibrations into mechanical vibrations instead of translating these vibrations into electrical impulses. This can be done in the following manner:

Suppose that a parson rests on a horizontal table, which has springs so that it can vibrate horizontally but not vertically. Then, due to the pumping of the heart, the table undergoes small vibrations, the frequency and the magnitude of which will depend on the various parameters associated with the heart. Thus, by investigating the motion of the table some important conditions about the vibrations of the heart can be drawn.

Let **x** denote the horizontal displacement of some specified point of the table (as, for example, one end) from some fixed location (such as a wall). Let **M** be the combined mass of the person and that portion of the table, which is set into motion. If we assume that there is a damping force proportional to the instantaneous velocity and a restoring force proportional to the instantaneous displacement, then the differential equation describing the motion of the table is:

$$M\frac{d^2x}{dt^2}+\beta\frac{dx}{dt}+\alpha x = F \qquad (1)$$

Where β and α are constants of proportionality and **F** is the force on the system due to the pumping action of the heart. Suppose that **m** is the mass of the blood pumped out of the heart during each vibration and **y** is the instantaneous center of mass of this quantity of blood. Then by **Newton's law**, we have

$$F = m\frac{d^2y}{dt^2} \qquad (2)$$

As a first approximation it may be assumed that **y** can be expressed as a simple sinusoidal function of t given by

$$y = aSin(\omega t) \qquad (3)$$

Where **a** and ω are constants. Equation **(3)** suggests that there is only one frequency associated with the vibrations of the heart, where as evidences show that there are many frequencies. This leads us to replace equation **(3)** by

$$y = a_1Sin(\omega t) + a_2Sin(2\omega t) + a_3Sin(3\omega t) + \ldots \qquad (4)$$

The series of the terms on the right is called a **Fourier Series**. The first term on the right of equation **(4)** represents a first approximation to the function, the sum of the first two terms a better approximation, and so on. Using only the first two terms of the series **(4)** in **(2),** and then putting the result into equation 1, we obtain:

$$M\frac{d^2x}{dt^2} + \beta\frac{dx}{dt} + \alpha x = -m\omega^2\left(a_1Sin(\omega t) + a_2Sin(2\omega t)\right) \qquad (5)$$

Which can be solved subject to various possible conditions. The general solution of equation **(5)** consists of two parts:

1) the general solution of the equation with the right side replaced by zero.
2) a particular solution

The first part is the **transient solution** and will disappear rapidly provided β >0.The second part will be the **steady state solution** in which we are interested. This steady state solution can be easily obtained as

$$X(t) = \frac{m\omega^2 a_1\left[(M\omega^2 - \alpha)Sin(\omega t) + \beta\omega Cos(\omega t)\right]}{\left(M\omega^2 - \alpha\right)^2 + \beta^2\omega^2}$$

$$+\frac{4m\omega^2 a_2\left[(4M\omega^2 - \alpha)Sin(2\omega t) + 2\beta\omega Cos(2\omega t)\right]}{\left(4M\omega^2 - \alpha\right)^2 + 4\omega^2\beta^2}$$

The corresponding solution can be found assuming any number of terms in equation **(4).**

2.3. Nutrient exchange in the placenta

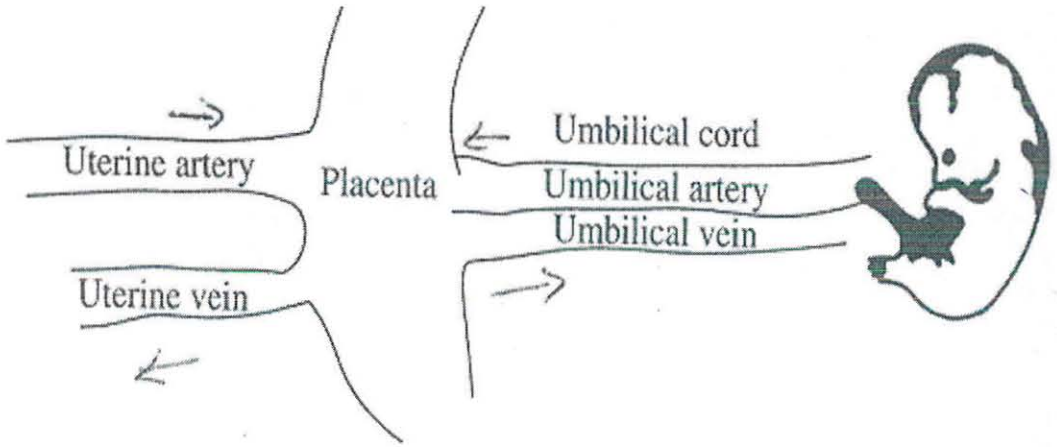
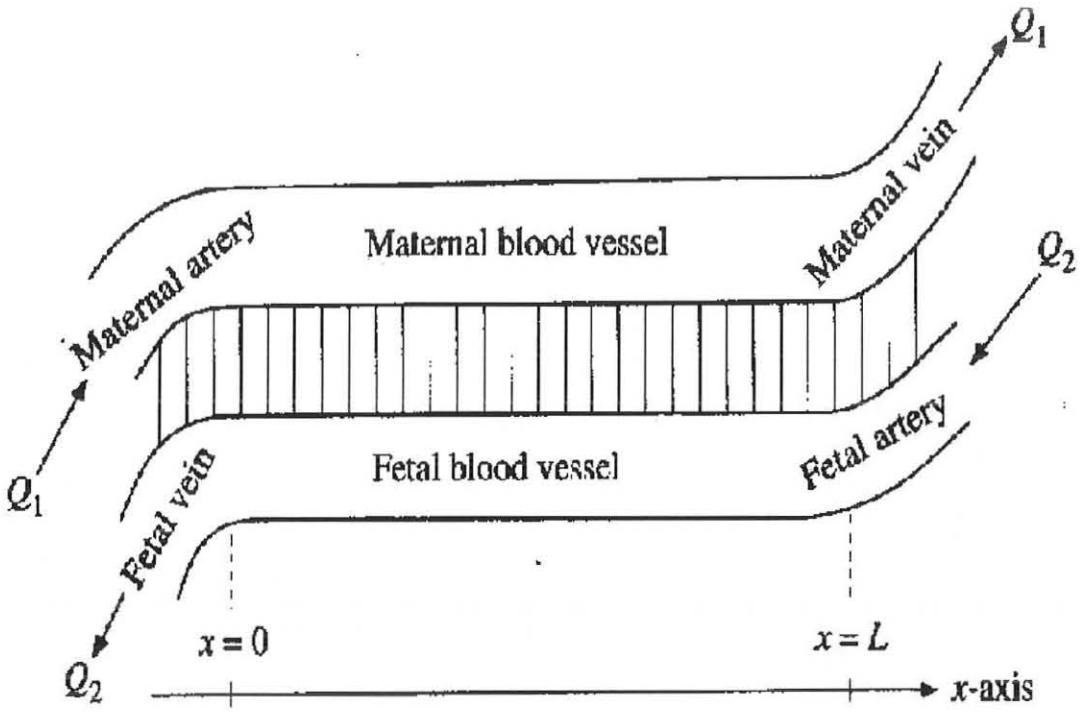


Fig.1 Placenta provides interface between the bloodstream of the mother and fetus.

.

In the placenta nutrients pass from mothers to fetus, while waste products from the fetus go the other way. During this exchange the blood of the mother and the fetus don't mix but are separated by a membrane across which nutrients and waste must pass. The nutrients flow from a high concentration in the mother blood to a lower concentration in the fetal blood. For both mother and fetus, blood flows to the placenta along an artery and returns via a vein, as shown in **figure 1**.



Fig,2 schematic view of countercurrent blood flow in neighbouring blood vessels in a rabbit or sheep placenta.

There is some variation among species in the arrangement of blood vessels within the placenta. In humans, fetal blood vessels are bathed in maternal blood. In rabbit and sheep,on the other hand,there is a system of maternal blood vessel adjacent to the fetal ones. The blood which they contain is believed to flow in opposite directions as shown in **fig.2 above**.

Simple mathematical models can be used to compare the advantages and disadvantages of the different types of arrangements of blood vessels with in the placenta. The model to be described here is for the type of placenta shown in **fig. 2.**

The nutrient concentrations in both maternal and fetal blood vessels can be expected to vary with the distance along fetal blood vessels since, as nutrients are transferred, the concentrations change. It will be assumed that the concentrations have reached a steady state, so that they depend only on the distance along the blood vessels.

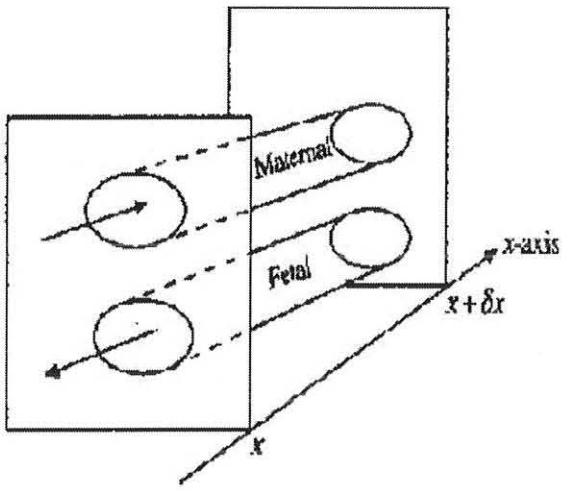
The model

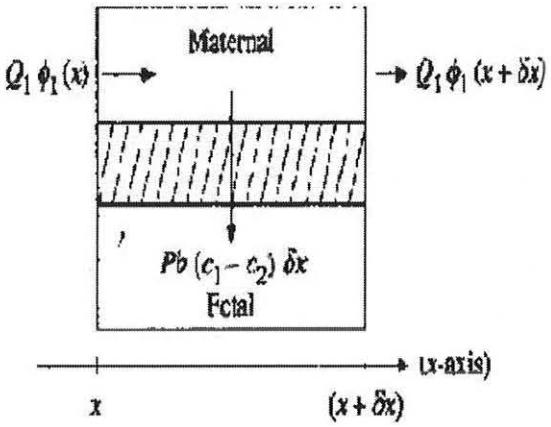
The model of the placenta we will describe is illustrated above, our notation being as follows. We use $\mathbf{Q_1}$ and $\mathbf{Q_2}$ to denote the **rates of flow** of the maternal and fetal blood respectively. We suppose that the blood vessels of the mother and fetus stay in contact with the membrane along a total length **L**.We choose as coordinate the distance **x** of a typical point along the blood vessels from the point where they first make contact with the membrane. The concentration of nutrient in each blood vessel is then a function of **x** and we put

$$\mathbf{C_1}= \begin{pmatrix} \textit{nutrient} & \textit{concentration} \\ \textit{in} \quad \textit{the} & \textit{maternal} \quad \textit{blood} \\ \textit{at} \quad \textit{a} & \textit{distance} \quad \textit{x} \end{pmatrix} = \Phi_1(x) \tag{1}$$

$$\mathbf{C_2}= \begin{pmatrix} \textit{nutrient} & \textit{concentration} \\ \textit{in} \quad \textit{the} & \textit{fetal} \quad \textit{blood} \\ \textit{at} \quad \textit{a} & \textit{distance} \quad \textit{x} \end{pmatrix} = \Phi_2(x)$$

Thus,$\mathbf{C_1}$ and $\mathbf{C_2}$ are functions of **x** while **L**,$\mathbf{Q_1}$ and $\mathbf{Q_2}$ are constants independent of **x**. we now consider the amount of nutrient contained within two planes, perpendicular to the blood vessels, which pass through the points with coordinates **x** and **x**+ δx respectively. See the planes as follows:





In the maternal bloodstream, nutrient enters at the first plane and leaves at the second. It also leaves, to enter the fetal bloodstream, via the membrane. Thus, as the mass of nutrient is conserved,

$$\begin{pmatrix} mass\ \text{int}ering \\ through\ plane \\ at\ x \end{pmatrix} = \begin{pmatrix} mass\ leaving \\ through\ plane \\ at\ x+\delta x \end{pmatrix} + \begin{pmatrix} mass\ leaving \\ across \\ membrane \end{pmatrix} \qquad \textbf{(2)}$$

Now in any time interval of length δt ;

$$\begin{pmatrix} mass\ entering \\ through\ plane \\ at\ x \end{pmatrix} = \begin{pmatrix} rate\ of\ flow \\ of\ blood \end{pmatrix} \text{ x } \begin{pmatrix} concentration \\ of\ nutrient \end{pmatrix} \text{ x } (time)$$

$$= \quad Q_1 \Phi_1(x)\delta t \qquad \textbf{(3)}$$

and similarly ,

$$\begin{pmatrix} mass\ leaving \\ through\ plane \\ at\ x+\delta x \end{pmatrix} = Q_1 \Phi_1(x+\delta x)\delta t \qquad \textbf{(4)}$$

The princeple which enables us to estimate the amount of nutrient transported across the membrane, known as **Fick's law,** states that if the concentrations on either side of the membrane were homogeneous, then

$$\begin{pmatrix} Rate\ of\ transport \\ through\ the \\ membrane \end{pmatrix} = \text{p x } \begin{pmatrix} area\ of \\ membrane \end{pmatrix} \text{ x } \begin{pmatrix} difference\ between \\ concentrations \\ of\ either\ side \end{pmatrix}$$

where **p** is called the **permeability** of the membrane and is a constant.

In our problem, we wish to apply **Fick's law** across the portion of memberane cut off by the two planes, which has area $b\delta x$ where b is the width of the membrane, assumed constant.The difference in concentration across this portion of membrane is approximately $\Phi_1(x) - \Phi_2(x) = c_1 - c_2$, with an error which approaches 0 as δx approaches 0.

Thus, Fick's law gives:

$$\begin{pmatrix} Rate\,of\ flow \\ through\,membrane \end{pmatrix} \cong pb\delta x(c_1 - c_2)$$

and hence

$$\begin{pmatrix} mass\,of\ nutrient \\ leaving\,across \\ membrane \end{pmatrix} \cong pb\delta x(c_1 - c_2)\delta t \qquad \textbf{(5)}$$

Now substitute **(3),(4)** and **(5)** into **(2)** and then divide by δt and rearrange to get

$$Q_1\left(\Phi_1(x+\delta x) - \Phi_1(x)\right) + pb(c_1 - c_2)\delta x \cong 0,$$

the error involved in the approximation being small compared with δx.Hence, dividing by δx and then letting δx approach 0 gives:

$$\frac{d\Phi_1(x)}{dx} = \frac{dc_1}{dx} = -\alpha_1(c_1 - c_2) \qquad \textbf{(6)}$$

where $\alpha_1 = pb/Q_1$

A similar derivation for the fetal bloodstreem gives:

$$\frac{d\Phi_2(x)}{dx} = \frac{dc_2}{dx} = -\alpha_2(c_1 - c_2) \qquad \textbf{(7)}$$

where $\alpha_2 = pb/Q_2$

Let us use the notations

$$\dot{\Phi}_1(x) = \frac{d\Phi_1}{dx}, \quad \ddot{\Phi}_1(x) = \frac{d^2\Phi_1}{dx^2}, \quad \dot{\Phi}_2(x) = \frac{d\Phi_2}{dx} \quad \text{and} \quad \ddot{\Phi}_2(x) = \frac{d^2\Phi_2}{dx^2}$$

Solving the differential equations

The pair of differential equations **(6),(7)** are linear with constant coefficients and their solutions are as follows:

From equation **(6),** we have:

$$\ddot{\Phi}_1 = -\alpha_1(\dot{\Phi}_1 - \dot{\Phi}_2) \quad \text{as} \quad \Phi_1 = c_1 \quad \text{and} \quad \Phi_2 = c_2 \quad \text{noticed above.}$$

$$= -\alpha_1[\dot{\Phi}_1 + \alpha_2(\Phi_1 - \Phi_2)] \qquad \text{using equ.(7)}$$

$$= -\alpha_1\dot{\Phi}_1 - \alpha_1\alpha_2\Phi_1 + \alpha_1\alpha_2\Phi_2$$

Equation (6) is equivalent to:

$$\Phi_2 = \Phi_1 + \dot{\Phi}_1 / \alpha_1 \qquad \textbf{(8)}$$

Substituting **(8)** in the equation previous to it yields:

$$\ddot{\Phi}_1 = (-\alpha_1 + \alpha_2)\dot{\Phi}_1 \qquad \textbf{(9)}$$

The auxilary equation of **(9)** is given by:

$r^2 + (\alpha_1 - \alpha_2)r = 0$, its roots are r=0,and r=$\alpha_2 - \alpha_1$

Hence, the solution of equation **(9)** is:

$$\Phi_1(x) = \beta_1 + \beta_2 e^{(\alpha_2 - \alpha_1)x} \qquad \textbf{(10)}$$

where β_1 *and* β_2 are arbitrary constants whose values are going to be determined.

From equ.**(10)** , $\Phi_1(0) = \beta_1 + \beta_2$

But $\dot{\Phi}_1(x) = \beta_2(\alpha_2 - \alpha_1)e^{(\alpha_2 - \alpha_1)x}$ **(11)**

Substituting equ.**(10)** and equ.**(11)** in equ.**(8),** we can get the following derivations:

$$\begin{aligned} \Phi_2(x) &= \Phi_1(x) + \dot{\Phi}_1 / \alpha_1 \\ &= \frac{(\alpha_2 - \alpha_1)\beta_2 e^{(\alpha_2 - \alpha_1)x} + \alpha_1\beta_1 + \alpha_1\beta_2 e^{(\alpha_2 - \alpha_1)x}}{\alpha_1} \qquad \textbf{(12)} \\ \Phi_2(0) &= \frac{\alpha_1\beta_1 + \alpha_2\beta_2}{\alpha_1} \end{aligned}$$

By solving the pair of equations

$$\begin{cases} \Phi_1(0) = \beta_1 + \beta_2 \\ \Phi_2(0) = \dfrac{\alpha_1\beta_1 + \alpha_2\beta_2}{\alpha_1} \end{cases}$$

simultaneously for β_1 *and* β_2 ,we can get:

$$\beta_1 = \Phi_1(0) + \frac{\alpha_1(\Phi_1(0) - \Phi_2(0))}{\alpha_2 - \alpha_1} \qquad \textit{and}$$

$$\beta_2 = -\frac{\alpha_1(\Phi_1(0) - \Phi_2(0))}{\alpha_2 - \alpha_1}$$

By substituting these values in equations **(10)** and **(12)** ,the solutions respectively are:

$$\Phi_1(x) = \Phi_1(0) - \frac{\alpha_1(\Phi_1(0) - \Phi_2(0))}{\alpha_2 - \alpha_1}\left(e^{(\alpha_2 - \alpha_1)x} - 1\right) \qquad \text{and} \qquad \textbf{(13)}$$

$$\Phi_2(x) = \Phi_2(0) - \frac{\alpha_2(\Phi_1(0) - \Phi_2(0))}{\alpha_2 - \alpha_1}\left(e^{(\alpha_2 - \alpha_1)x} - 1\right) \qquad \textbf{(14)}$$

Comparisons

The placenta modelled above is called a **countercurrent** type of placenta because the two bloodstreams flow in opposite directions. Middleman (1972) gives further details, and he modelled other types of placenta, obtained solutions analogous to equ.**(13)** and equ.**(14)** for the concentrations of the nutrients. On the basis of solutions, he is able to make some comparisons between the efficiency of the various types of placenta in exchanging nutrients. Models analogous to that of the countercurrent nutrient exchange system also occur in othe applications. These include simple models of an artificial kidney machine and oxygen exchange in the swim bladders of deep sea fish.

Chapter-three.

3. Stochastic Epidemic Model

3.1 Nature and Spread of Epidemic Diseases.

An important problem in biology and medicine deal with the occurrence , spread and control of a contagious disease, that is one which can transmitted from one individual to another. The science that deals with this study is called *epidemiology*, and if a large number of population gets the disease, we say that there is an epidemic.

In nature, populations of different species interact with each other. Forexample, one species may be the food for another species or two species may be in direct competition for the same food supply.Even populations of a single species may be divided into several groups which interact with each other. An example of this is the study of infectious diseases where the population can be divided into several groups: those who have *recovered* and those who are *susceptible* to catching the disease.Problems involving the spread of disease can be very complicated. Forexample, it is known that some individuals may not actually get a disease even when exposed for long periods of time to others having the disease. In such case, we say that the individual has an *immunity* to the disease either because having had the disease before he has built up resistance to recurrence or by having initial resistance (natural immunity) he is not able to contract the disease. In some cases, individuals are immune to a disease but are capable of transmitting into others; such individuals are called *carriers.*An example to this effect is the cause of typhoid fever.

We are going to see how mathematical models on epidemic diseases are classified based on the *latent period* (the period between catching the disease and becoming contagious), size of the popullation and other parameters.

a) when sufficient latent period is registered

A typical example to this class of diseases is measles epidemic. Measles is a highly contagious disease, caused by virus and spread by effective contact between individuals. It tends to affect mainly children. Immediately after a child fist catches the disease, there is a latent period where the child is not contagious and does't exhibit any syptoms of the

disease. This is because the virus has not yet multiplied sufficiently. The latent period lasts, on average, 5 to 7 days. After this the child enters the contagious period. The child is now called an infective since it is possible for another child who comes in contact with the infective to catch the disease. This period lasts approximately one week. After this time red spots appear on the skin of the child for a few days after which the child recovers. During this period, and subsequently, the child is immune to the disease and cannot be reinfected.Due to the sufficient latent period and other assumptions mentioned above, leads to a *coupled difference equationes* which have as their solution a pair of infinite sequences.

b) when latent period is not noticeable

The reason for the applicability of difference equations mentioned above was the significant latent period between catching the disease and becoming contagious. If this latent period is small (ideally zero) a model of an epidemic involving coupled differential equations can be formulated.

For this purpose of formulating our model for the spread of a disease, the popullation will be divided into three groups: *susceptibles, infectives and removed*(who hove previously had the disease and may not be reinfected because they are immune, have been quarantined or have died from the disease.)

The following modelling assumptions will be made:

1. The disease is transmitted by close proximity or contact between an infective and susceptible.
2. A susceptible becomes an infective immediately after transmission.
3. Infectives eventually become removed.
4. The popullation of susceptibles is not altered by immigration, emigration, births and deaths.
5. Each infective infects a constant fraction β of the susceptible popullation per unit time.
6. The number of infectives removed is proportional to the number of infectives present.

As mentioned above it is assumption**(2)** which makes a formulation involving differential equations rather than difference equations.

Diseases for which this assumption is applicable include diphtheria, scarlet fever and herpers. The mathematical model of a pair of differential equations based on the above assumptions is formulated in the book"Australian Mathematical Society Lecture Series 10."

Alternative versions of the model can be formulated by altering some of the assumptions **(1)** to **(6).** These include allowance for births, diseases where immunity is not conferred on sufferers with the disease, and diseases with carriers. These models are prototypes for much more complicated **Stochastic Models**.Which allows for randem variation in infectivity and are not restricted to large popullations.

3.2 Deterministic Versus Stochastic Models.

A debate that has involved philosophers for many years is whether the world is basically deterministic or whether there are elements of chance in the unfolding of natural processes. Whether to look at the world as deterministic or stochastic is a fundamental decision, which faces the mathematical modeller. He is not necessarily making a philosophical decision by making this choice. We may be able to understand a fundamentally stochastic world by looking at it deterministically, or a fundamentally deterministic world by looking at it stochastically.

Deterministic models of popullation growth are derived under the assumptions that popullation growth is such that the future development of the popullation can be predicted exactly once its state at some initial time is specified. These models donnot permit many random fluctuations; that is, a particular event such as a birth must occur with absolute certainty. In deterministic models, the popullation is assumed large enough and the factors determining individual bith and death rates are constant enough that the consequence of random fluctuations can be ignored. This would probabily be true only for a very large popullation under highly idealized conditions, where we can ignore the choice or random aspects.

Stochastic models of popullation growth are derived under the basic assumption that popullation growth is a random event; that is, an organism(cell or parasite) may reproduce during a given time period with a certain probability p , where $0 \leq p \leq 1$.

No events occur with absolute certainty. We can build these ideas into the model by allowing chance or random fluctuations in the process. Some popullations are small enough or variable enough that random fluctuations can be appreciable.For a given problem, stochastic solution gives us, in a sense, more information than the deterministic solution; may modellers therefore consider it to be the better approach, regardless of one's philosophy of the world. Some people feel, on the other hand, that one goes to stochastic models only because one doesn't realy understand the correct deterministic process. What we are going to see in this seminar paper is a stochastic epidemic model which is mentioned under section **(3.4)**

A stochastic process is much more complicated in that it is connected with the dynamics of a system, the process of which is determined by elementary random variables. It has nice applications in the growth of populations, the theory of nuclear reactors, and the dynamics of a service system with variable times of arrival of users and/or variable times involved in service, a field known as Queueing Theory.

3.3 Basic Definitions and Theorems

Definition1: Two events $\mathbf{A_1}$ and $\mathbf{A_2}$ are said to be **mutually exclusive** if they have no outcome in common.

This condition can be written as $A_1 \cap A_2 = \phi$, the empty set.

Theorem: If **n** events $A_1, A_2, \ldots, A_n$ are mutually exclusive, then

$$p(A_1 \cup A_2 \cup \ldots\ldots \cup A_n) = p(A_1) + p(A_2) + \ldots + p(A_n).$$

Definition 2: A number of events $A_1, A_2, \ldots, A_n$ are said to be **exhaustive** if their union is the possibility space S, hence we have $p(A_1 \cup A_2 \cup \ldots \cup A_n) = 1$.

$p(A_1 | A_2)$ is a probability that $\mathbf{A_1}$ occurs, given that A_2 has occurred. The probability space is no longer S, but $\mathbf{A_2}$. The event set is no longer $\mathbf{A_1}$, but that part of $\mathbf{A_1}$, which lies inside $\mathbf{A_2}$, namely $A_1 \cap A_2$.

Therefore, $p(A_1 \mid A_2) = \dfrac{n(A_1 \cap A_2)}{n(A_2)} = \dfrac{p(A_1 \cap A_2)}{p(A_2)}$

And $p(A_2 \mid A_1) = \dfrac{n(A_1 \cap A_2)}{n(A_1)} = \dfrac{p(A_1 \cap A_2)}{p(A_1)}$.

In general, the two conditional probabilities are not equal. If we cross-multiply, we have

$p(A_1 \cap A_2) = p(A_1)p(A_2 \mid A_1) = p(A_2)p(A_1 \mid A_2)$.

This relationship is known as the *multiplicative law* (the *compound probability* property) for probabilities and it is this aspect of conditional probability, which we deal with first.

Definition 3:Two events $\mathbf{A_1}$ and $\mathbf{A_2}$ are said to be **independent** if and only if

$$p(A_1 \cap A_2) = p(A_1)p(A_2).$$

This is the special simplified form of the multiplicative law for independent events. It may be extended to any number of independent events, so that

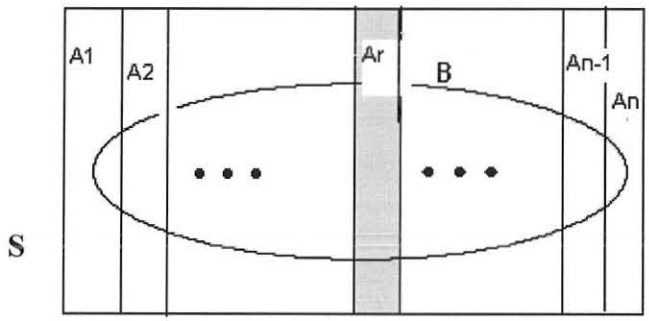
$p(A_1 \cap A_2 \cap \ldots\ldots \cap A_n) = p(A_1)p(A_2)\ldots\ldots p(A_n)$ if and only if $A_1, A_2, \ldots, A_n$ are independent events. We can say intuitively that events are independent if knowledge of the occurrence or non-occurrence of one of them doesn't alter the probabilities of the others occurring.

Total probability and Bayes' Theorem.

Let us consider a possibility space **S** with two events **A** and **B**. We have

$p(B) = p(A \cap B) + p(A' \cap B)$. Therefore, $p(B) = p(A)p(B \mid A) + p(A')\ p(B \mid A')$.

This idea can be extended to situations where the probability space is divided into more mutually exclusive parts as shown below.



Suppose the probability space **S** is divided into *n* mutually exclusive and exhaustive events $A_1, A_2, \ldots, A_n$. Then:

$$P(B) = p(A_1 \cap B) + p(A_2 \cap B) + \ldots\ldots + p(A_n \cap B)$$

$$= p(B \mid A_1)p(A_1) + p(B \mid A_2)p(A_2) + \ldots\ldots + p(B \mid A_n)p(A_n)$$

$$= \sum_{r=1}^{n} p(B \mid A_r)p(A_r)$$. This is known as the **Total Probability** expression for p(B).

Bayes' Theorem

But B can be written in the probability form. Therefore,

$$p(A_r \mid B) = \frac{p(B \mid A_r)p(A_r)}{\sum_{r=1}^{n} p(B \mid A_r)p(A_r)}$$. In general if the possibility space **S** in the above figure can be divided into mutually exclusive and exhaustive events $A_1, A_2, \ldots\ldots, A_n$ and B is some other event. Then

$$p(A_r \mid B) = \frac{p(B \mid A_r)p(A_r)}{p(B)}$$

which is what we call **Bayes' Theorem.**

Definition 4: Let $a_0, a_1, a_2, \ldots\ldots$ be a sequence of real numbers. If

$A(s) = a_0 + a_1 s + a_2 s^2 + a_3 s^3 + \ldots\ldots$ converges in some interval $-s_0 < s < s_0$, then A(s) is called the **Generating Function** of the sequence $\{a_i\}$.

Two points must be noticed are:

1) **s** is just a dummy, in effect a place holder
2) if the sequence $\{a_i\}$ is bounded, then A(s) will converge for at least $|s| < 1$.

Example. Let $a_0=1$, $a_1=1/1!$, $a_2=1/2!$, $a_3=1/3!, \ldots, a_k=1/k!, \ldots$

Then $A(s)=1+1/1!s+1/2!s^2+1/3!s^3+\ldots=e^s$. The generating function for the sequence $1, 1/1!, 1/2!, 1/3!, \ldots, 1/k!, \ldots$ is e^s.

A very interesting special case occurs where the elements of the sequence $\{a_i\}$ are probabilities. All such sequences are bounded. Suppose X is a discrete random variable which takes on the values 0, 1, 2, 3, 4, ... with certain probabilities $p_i=p_r[X=i]$. Then the generating function $p(s) = \sum_{all\ values} p_i s^i$ is called the **probability generating function.**

3.4. Partial Differential Equation Model For a Stochastic Epidemic Process With No Removal.

Let X(t) be the size of susceptibles at time t. The value of X(t) will be governed by probabilistic laws. Technically, X(t) is a random variable and $\{X(t) : t \geq 0\}$ defines a stochastic process .The parameter t, which we interpret as time, is real and continuous, but the random variable X(t) will have a discrete set of possible values, the non-negative integers, corresponding to population sizes of susceptibles. Our aim is to determine the probability distribution $p_n(t) = p_r[X(t) = n]$, $n = 0,1,2,\ldots$.

We will use the following notation in our development.

1) $o(\Delta t)$ is a quantity such that $\lim_{\Delta t \to 0} \frac{o(\Delta t)}{\Delta t} = 0$ .That is $o(\Delta t) -> 0$ more quickly than $\Delta t -> 0$.
2) E_n is the set of the system at some point in time t, where $t > 0$, if exactly n individuals are present at the end of the interval 0 to t. Therefore, we can say that $p_n(t)$ is the probability of being in state E_n at time t.

Our stochastic model will be derived by using the following postulates.

1) If, at time t, the system is in state E_n, the probability of an increase or decrease of one in the population of susceptibles in the ensuing short interval of time, t to $t + \Delta t$, is assumed to be $f_j(n)\Delta t + o(\Delta t)$. Here $f_j(n)$ is the infectivity rate of susceptibles when the system is in state E_n.
2) If we assume that at time t, the system is in state E_n, then the probability of an increase or decrease greater than or less than one organism in the ensuing short interval of time, t to $t + \Delta t$, is assumed negligible, i.e., $o(\Delta t)$.
3) We assume that events in non-overlapping time intervals are independent.

These assumptions will be used to determine $p_n(t)$, the probability that at time t, the susceptible size will be n, with $n>0$.The whole process is easy to conceptualize by consider two adjacent (non-overlapping) intervals of time $(0,t)$ and $(t,t+\Delta t)$. Schematically, we represent these two intervals by.

Specially, we will start by considering the possible ways we can have a population of susceptibles of size n at time $t+\Delta t$, by considering what can happen in the intervals $(0,t)$ and $(t,t+\Delta t)$. Schematically, we find the following ways to attain a population of susceptibles of size n, where Δt is small.

	Number of susceptibles in each interval	Total
Case1.	$0 \_\_\_\_\_ n \_\_\_\_\_ t \underbrace{\_\_0\_\_}_{\Delta t} t+\Delta t$	n
Case2.	$0 \_\_\_\_\_ n-j \_\_\_\_\_ t \underbrace{\_\_j\_\_}_{\Delta t} t+\Delta t$, $j \neq 0$	n

The following factors enable us to use this formulation.

1) The events in the non-overlapping intervals are independent.
2) The process has a lack of memory. That is, the only thing of interest in case1 is that at time t the population size of susceptibles is n, not what happened before; in case2, the population size of susceptibles is n-j at time t, not what happened before time t.
3) We have a time homogeneous process. That is the probability of getting an infective in short interval of time depends only on the length of the interval and not on when it occurs. We are assuming that all factors governing the process remain constant so that the probability of an increment or decrease is the same for all short time intervals and is independent of the past development of the process.

For each of the two cases, we can determine the probability that there will be n susceptibles at time $t+\Delta t$ by using our assumptions.

Case1: Exactly n events occur in (0,t) and none in $(t,t+\Delta t)$. This happens with probability $p_n(t)\left(1-\sum_{j\neq 0} f_j(n)\Delta t\right)$.

Case2: Exactly n-j events occur in (0,t) and j in $(t,t+\Delta t)$, $j \neq 0$.Since these events are mutually exclusive for each value of j, the probability that one of these events occurs is

$$\sum_{j\neq 0} p_{n-j}(n) f_j(n-j)\Delta t + o(\Delta t)$$

Since all these events are mutually exclusive, it follows that

$$p_n(t+\Delta t) = p_n(t)\left(1 - \sum_{j\neq 0} f_j(n)\Delta t\right) + \sum_{j\neq 0} p_{n-j}(t) f_j(n-j)\Delta t + o(\Delta t)$$

All the above details are summarized as follows:

Let $p_n(t)$ be the probability that there are *n susceptible* persons in a system and let $f_j(n)\,\Delta t + o(\Delta t)$ give the probability that the number will change to *n-j* in the time interval $(t, t+\Delta t)$. Here *j* is any positive or negative integer and $o(\Delta t)$ is an infinitesimal which is such that $\lim_{\Delta t \mapsto 0} \frac{o(\Delta t)}{\Delta t} = 0$. The probability that there is no change in the time interval $(t, t+\Delta t)$ is given by $p_n(\Delta t) = 1 - \sum_{j\neq 0} f_j(n)\Delta t + o(\Delta t)$.

Using the theorems of total and compound probabilities, we get:

$$p_n(t+\Delta t) = p_n(t)\left(1 - \sum_{j\neq 0} f_j(n)\Delta t\right) + \sum_{j\neq 0} p_{n-j}(t) f_j(n-j)\Delta t + o(\Delta t) \qquad \textbf{(1)}$$

Transferring $p_n(t)$ to the left hand side, dividing by Δt and taking the limit as $\Delta t \mapsto 0$, we get $\frac{dp_n}{dt} = -p_n(t)\sum_{j\neq 0} f_j(n) + \sum_{j\neq 0} p_{n-j}(t) f_j(n-j)$ **(2)**

Multiplying (2) by s^n, summing for all *n* and using the definition of the probability generating function $\Phi(s,t) = \sum_{n=0}^{\infty} p_n(t) s^n$, we get

$$\frac{\partial \Phi}{\partial t} = -\sum_{j\neq 0}\sum_{n} p_n(t) f_j(n) s^n + \sum_{j\neq 0}\sum_{n} s^j p_{n-j}(t) f_j(n-j) s^{n-j} \qquad \textbf{(3)}$$

giving the basic partial differential equation,

$$\frac{\partial \Phi}{\partial t} = \sum_{j\neq 0}\left(s^j - 1\right) f_j\left(s\frac{\partial}{\partial s}\right)\Phi(s,t) \qquad \textbf{(4)}$$

For a two dimensional stochastic epidemic process, the corresponding partial differential equation obtained in the same manner is

$$\frac{\partial \Phi}{\partial t} = \sum_{j\neq 0}\sum_{k\neq 0}\left(u^j v^k - 1\right) f_{j,k}\left(u\frac{\partial}{\partial x}, v\frac{\partial}{\partial y}\right)\Phi(u,v,t) \qquad \textbf{(5)}$$

where $\Phi(u,v,t)=\sum_m\sum_n p(m,n,t)u^m v^n$ (6)

p(m,n,t) is the probability of there being m individuals of the first kind and n individuals of the second kind and $f_{j,k}(m,n)\Delta t+o(\Delta t)$ is the probability of the number of the two kinds changing from m to $m+j$ and n to $n+k$ in the time interval $(t,t+\Delta t)$.

Example: (Showing Stochastic Epidemic Model with No Removal)

Let there be initially at $t=0$, n susceptibles and one infective in the system. Also let the probability of there being r susceptible persons at time t be $p_r(t)$. We assume that the probability of one more person becoming infected in time Δt is

$p_r(\Delta t)=\beta r(n+1-r)\Delta t+o(\Delta t)$, so that

$$f_j(r)=\begin{cases}\beta r(n+1-r) & when\ j=-1\\ 0 & when\ j\neq -1\end{cases} \quad (7)$$

Construct the model to this problem and find its solution.

Construction of the model

Substituting equ.(7) in equ.(4), we get

$$\frac{\partial\Phi}{\partial t}=\beta\left(s^{-1}-1\right)\left[s\frac{\partial}{\partial s}\left(n+1-s\frac{\partial}{\partial s}\right)\Phi\right]$$

$$=\beta(1-s)\left[(n+1)\frac{\partial\Phi}{\partial s}-\frac{\partial\Phi}{\partial s}-s\frac{\partial^2\Phi}{\partial s^2}\right]$$

or $$\frac{\partial\Phi}{\partial t}=\beta(1-s)\left(n\frac{\partial\Phi}{\partial s}-s\frac{\partial^2\Phi}{\partial s^2}\right) \quad (8)$$

This is the required partial differential equation model. We find the solution of this equation. The initial conditions are as follows:

$p_n(0)=1$ by the given assumption. Since $\sum_{r=0}^{n}p_r(0)=p_n(0)+\sum_{r=0}^{n-1}p_r(0)\leq 1$

(by the laws of probability), then we can draw the conclusion that $p_r(0)=0$ for each $r \in \{0,1,2,...,n-1\}$.

The probability generating function $\Phi(s,t)=\sum_{r=0}^{n} p_r(t)s^r$ has the following partial derivatives:

$$\frac{\partial\Phi}{\partial t}=\sum_{r=0}^{n}\frac{dp_r}{dt}s^r \quad , \quad \frac{\partial\Phi}{\partial s}=\sum_{r=1}^{n} rp_r s^{r-1} \quad \text{and} \quad \frac{\partial^2\Phi}{\partial s^2}=\sum_{r=2}^{n} r(r-1)p_r s^{r-2}$$

Substituting the probability generating function and its derivatives in equ.**(8),** and equating coefficients of various powers of **s** , we have the following:

$$\sum_{r=0}^{n}\frac{dp_r}{dt}s^r=\beta(1-s)\left(n\sum_{r=1}^{n} rp_r s^{r-1}-s\sum_{r=2}^{n} r(r-1)p_r s^{r-2}\right)$$

$$=\beta\left\{\sum_{r=1}^{n} nrp_r s^{r-1}-\sum_{r=2}^{n} r(r-1)p_r s^{r-1}-\sum_{r=1}^{n} nrp_r s^r+\sum_{r=2}^{n} r(r-1)p_r s^r\right\}$$

$$=\beta\left\{np_1-np_1 s+\sum_{r=2}^{n} r(n+1-r)p_r s^{r-1}-\sum_{r=2}^{n} r(n+1-r)p_r s^r\right\}$$

From the final result, we can conclude that:

i) $\frac{dp_r}{dt}=\beta(r+1)(n-r)p_{r+1}-\beta r(n+1-r)p_r$; for $r \in \{0,1,2,3,.....,n-1\}$ and;

ii) $\frac{dp_n}{dt}=-\beta np_n$ for r=n.

From (ii), $\frac{dp_n(t)}{dt}+\beta np_n(t)=0$. We have the integrating factor $\mu(t)=e^{\int \beta n dt}=e^{\beta nt}$.

And so, $\left(e^{\beta nt}p_n\right)'=0$. This implies that $p_n(t)=c_1 e^{-\beta nt}$ for an arbitrary constant c_1.

But from the initial condition $p_n(0)=1$, $c_1=1$ and hence,

$$p_n(t)=e^{-\beta nt} \qquad \textbf{(9)}$$

Substituting equ.**(9)** into **(i)** and letting r=n-1, we have:

$\frac{dp_{n-1}(t)}{dt}=\beta np_n(t)-2\beta(n-1)p_{n-1}(t)$. From this follows,

$\frac{dp_{n-1}(t)}{dt}+2\beta(n-1)p_{n-1}(t)=\beta ne^{-\beta nt}$. The integrating factor is $\mu(t)=e^{2\beta(n-1)t}$.

And so, $\left(e^{2\beta(n-1)t}\, p_{n-1}(t)\right)' = \beta n e^{-\beta nt + 2\beta(n-1)t}$

$$p_{n-1}(t) = \beta n e^{-2\beta(n-1)t} \int e^{\beta(n-2)t}\, dt + c_2 e^{-2\beta(n-1)t}$$

$$= \frac{n}{n-2} e^{-\beta nt} + c_2 e^{-2\beta(n-1)t} \text{ where } c_2 \text{ is an arbitrary constant to be determined.}$$

But from the initial condition $p_r(0) = 0$ for each $r \in \{0,1,2,3,...,n-1\}$, we have

$p_{n-1}(0) = \frac{n}{n-2} + c_2 = 0$. This implies that $c_2 = -\frac{n}{n-2}$. And therefore,

$$p_{n-1}(t) = \frac{n}{n-2}\left(e^{-\beta nt} - e^{-2\beta(n-1)t}\right) \qquad \textbf{(10)}$$

Following the same procedure what we did above, we can get the following:

$$p_{n-2}(t) = n(n-1)\left\{\frac{e^{-\beta nt}}{(n-2)(n-3)} - \frac{2e^{-2\beta(n-1)t}}{(n-2)(n-4)} + \frac{e^{-3\beta(n-2)t}}{(n-3)(n-4)}\right\}$$

$$p_{n-3}(t) = \frac{n(n-1)(n-2)}{(n-4)}\left\{\frac{e-\beta nt}{(n-2)(n-3)} - \frac{3e^{-2\beta(n-1)t}}{(n-2)(n-5)} + \frac{3e^{-3\beta(n-2)t}}{(n-3)(n-6)} - \frac{e^{-4\beta(n-3)t}}{(n-5)(n-6)}\right\}$$

As it is expected from our solutions, the initial conditions are satisfied, that is

$p_n(0) = e^{-\beta n(0)} = 1$; $p_{n-1}(0) = \frac{n}{n-2}(1-1) = 0$; and so on.

This shows the validity of our solution to the initial value problem. For any positive constant β and a positive integer n , $0 \le e^{-\beta nt} \le 1$, for all $t \ge 0$.

References

1. Glenn Fulford, Modelling with Differential Equations, Aus. Math. Soc. Lecture Series.10 (1997).
2. Zafar Ahsan, Differential Equations and their Applications, New Delhi (2001).
3. Helen Marcus-Roberts and Maynard Thompson, Modules in Applied Mathematics, Berlin, Vol.4 (1983).
4. J.N. Kapur, Mathematical Modelling, New Delhi (1994).
5. G.W. Jenkins and J.L. Slack, Statistics and Probability, London,(1985)
6. Oscar Kempthorne and Leroy Folks, Probability, Statistics and Data Analysis, U.S.A. (1971).
7. J.G. Andrews and R.R. McLone, Mathematical Modelling, London (1976).