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Mathematics in Bioengineering: Its Application for Today's Students

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This paper will discuss the history and development of bioengineering, the different disciplines involved in bioengineering, will compare to work of bioengineers with the other fields of engineering; the focus of bioengineers and how their work, research and inventions interface with medicine and therefore translating into the current advances that are now evident in surgery, eye care, drug delivery systems, stem cell research and gene therapy. The connections will be made between the content area of biology and models that are useful in physics. Some of the mathematical models that are employed in the field of bioengineering will be discussed. Of special interest will be the development of drug delivery systems.

The History of Bioengineering

The practice of medicine and the delivery of medication has seen many changes over the decades, but more so since the last decade. The improvements and technology in general and its application to medicine have enabled bio engineers to change the landscape of health care.

The review of the history and development of humans details the stories of how men sought to improve their existence. The journey from the cavemen, the discovery of fire and the use of wheel showed the effort men have made in seeking to improve their lives. As time progressed and as more and more studies explained the structure and the working of the human body, new and innovative tools were invented to repair the human body.

What is Bioengineering?

Traditional engineering is concerned with the application of scientific and mathematics to design and analyze, to manufacture objects and structures to improve human conditions. Bioengineers use the same concepts of science and mathematics to understand to performance of living organisms in the normal and abnormal situations then design structures and objects to enhance the performance of the human body.

Bioengineering is engineering that is applied to human health. Because human health is complex and deals with all aspects of our bodies, not just the physical aspects bio- engineers are concerned with all aspects and a wide range of problems that affect the body. The work and research of bioengineers impact all aspects of our lives, from better hospital care, diagnosis and treatment of diseases, the invention of devices to deliver better health care to the development of safer food and water sources.

Bioengineering encompasses many areas, but the common thread that runs through the various field is the application of the sciences especially biology and mathematics. The mission of all disciplines of bioengineering is to: the prevention, diagnosis, and treatment of disease, patient rehabilitation, and the improvement of health. Bioengineers are responsible for the development of artificial hips, knees, and other joints; ultra sound, MRI, and other imaging techniques; pacemakers, dialysis machines; drug delivery systems, digital hearing aids, implantable defibrillators, artificial heart valves, a laser system for eye surgery, a devise used by diabetic that delivers and regulates insulin. The findings from research in genetics are used to inform doctors to detect and treat genetic diseases, and more recently the trials in tissue growth and transplant that will be used for tissue repair and replacement.

As with the work of other engineers, the work of bioengineers is not always seen by the public. The work of the social engineer, the mechanical and structural is concerned with developing gadgets, bridges, roads, and buildings to improve the living conditions of humans. Bioengineers are also concerned in improving agricultural product, developing new and better varieties of crops, and also finding better, faster, and safer ways to get the products to market. This practice of producing genetically altered plants is not without a debate. Some critics call this redesigning nature. The claim is that these grains, fruits and vegetables that are being implanted with genes from viruses, bacteria, and animals will permanently reconfigure these original plants.

Bioengineering is a field that encompasses a number of specialties. These include biomedical engineering, biotechnology, biological engineering, bimolecular engineering, biomechanics and biochemical engineering. Each of these fields may differ slightly in their focus of interest, but they are all concerned with the improvement of human life.

Description of the field of Bioengineering

Biomedical Engineering

Is the engineering that is applicable to human health? It is concerned with what we put in our bodies and what we put on our bodies. The interest in this field spans a variety of problems.

Biomechanics

Biomechanics describes the disciplines which apply the science of mechanics to biological systems. These biological systems are not limited to the human body. Whereas mechanical systems involve the response to bodies discrete or continuous, rigid or deformable, solid, liquid or gaseous to the action of forces, biomechanics focus on kinesiology, the science of human motion and movement; the mechanical structural and geometric properties of the compartments of human body; sports mechanics, exercise and leisure activities, orthopedics, clinical, diagnostic and surgical procedures and the effects of vibration on the body.

Of major interest is the development of biocompatible implantable materials. Developments have been made in the area of organ replacement, advanced surgical procedures such as arthroscopy, microsurgery, breathing machines that can communicate with the wheelchairs.(this has aided rehabilitation in cases of spine and neck injuries). Biomechanics employs mathematical models and experimental tests to analyze biological systems and their responses to stress. Although much has been done biomechanics still seek to understand better the performance of the human body.

Section I: Drug Delivery System

The History of Drug Delivery Systems

Traditionally the drug delivery systems that existed consisted of simple chemical compounds that were dispensed orally either as a liquid, or as pills and in some cases given as injections. Recently with the development and more knowledge of how the body works and the understanding of chemical compounds, drug formulations that control the rate and period (time released drug) of its delivery and application to targeted areas of the body have become popular.

The improvements in the delivery of drugs followed the research findings that resulted in the advances in the understanding of the human body and how it works. The physician of the earliest civilizations dispensed drugs in the form of pills ointments, and liquids. The literature in early African cultures speaks to the witch doctors whose responsibility was to dispense drugs made from the local herbs. It was not until 1665 after the circulatory system was understood that intravenous injections were used in the medical practice.

Before 1850 evidence has been found where materials such as wood and ivory were used with metals such as iron, gold, silver and copper to make various prosthetic devices such as teeth and noses and to fix fractured bones. The problems faced in those early years were that the patient could not endure the long surgeries to enable the doctors to perform the procedure because there was no anesthesia. Between 1850 and 1925 the discovery of anesthesia and X -- Rays coupled with the introduction of aseptic surgical procedures enabled the doctors to performance procedures without the risk of post surgical infections.

From 1925 to the present advances were made in the use of different biomaterials. The development of cobalt chrome and stainless steel alloys in the industrial sector contributed to the use of these materials in surgery. The advancements in chemistry in the 1940's and the1950's, produced polymers and plastics that found their way in the medical field. Coupled with the production of penicillin and other antibodies that reduced the risk of infection these materials have been improved and are now used extensively in the medical field.

Present Developments

The present drug delivery systems (time released medication for example) have specific problems that bioengineers are attempting to provide answers for. These questions include the fact that the effectiveness of many drugs are reduced because of the degradation that occurs before the administered drug reaches the targeted areas. Once taken and digested, time released medication administer the treatment continuously, and not providing relief only when necessary and in some cases can cause adverse effects to non-infected areas. Medications given in the form of injections could be made more cheaply, and could be administered with less pain and suffering to the patient if they were given orally.

The investigations into new materials for drug delivery systems that will delivery medication intact to the targeted area have been ongoing. The research and use of polymeric, microsphers, polymers micelles, and hydrogel type materials have proven to be very effective. These materials have perfected drug targeting specificity, lowering the of drug toxicity, improving the absorption rates, and providing protection of pharmaceuticals against biochemical degradation.

It has been found that cells will do their structural work with two primary man made materials. These are non metallic minerals and polymers. Polymers can be classified as elastomers and plastics. Elastomers is more rubbery and have fewer cross links while plastics are more crystalline.

Silicone rubber is made from sand and was first used for shunts in 1955. It is biological compatible. Its compatibility has been justified from a variety of clinical trials using a number of different grades and used in a variety of applications. It is has shown to have superior biocompatibility and mechanical properties. It can be sterilized by steam, radiation or ethylene oxide. Silicone rubber is commonly used for catheters, the gel for breast transplants. It is also used as a functional membrane in kidney dialysis and blood oxygenation machines. In orthopedics it is used to support arthritic fingers and wrists.

Dacron is another material used . It is used for blood vessel prostheses. The pores in the fabric can be filled with coagulated blood, which is the replaced by tissue called neointima. This serves as a biological wall between the dacron and the blood. Dacron is also used in the prosthetic heart valve.

The product polytelraflaoroethylene is used to produce small blood vessels, prostheses and is also used to make heart valves, ligaments and artificial ossicles for the ear.

Various types of polymers and elastomers have been developed and used as biodegradable implants, but there is still the problem that living organisms have one motivation, that is to seek out foreign agents that enter the body and either destroy them or encapsulate them. Biomaterials should therefore be able to avoid the body's natural behavior to either encapsulate or destroy. It is therefore necessary to find materials for implantation that will become invisible to the cells chemical reaction or that has the same chemical composition as the cells. These materials should have molecules which look life biological materials, so that they will not be attacked by cells.

Polymers that are used to encapsulate drugs for delivery and implantation must have the same basic qualities of any biomaterials that are used for implantation of other devices. It should be geometrically compatible with the body, it must not poison the body' it must not corrode in the presence of body fluids' it must be free of toxic substances, and it should be easily sterilized. In must cases the drug delivery system should not need replacement, but should disintegrate in the body.

Two types of polymer system are in use. They are both microspheres, because of their size and shape. The reservoir device enables the pharmaceutical product (the drug) to be enclosed or wrapped in the interior of the polymer shell, while the matrix device has the drug trapped within a polymer network. The release of the drug from both these two systems follow the fundamental molecular transport processes that of diffusion and convection. The newer replication of these systems is being investigated. These will be designed using biodegradable polymer systems that will break down into lactic and glycolic acids, and is then reduced to carbon dioxide and water, the medication is then released and the waste expelled from the body.

Future Development

There is always the quest to not only to find new drugs but also to find or develop new ways of administering the medication. The goal of all drug delivery system is to place medication intact and to the specific part of the body through a device that can control the amount administered either by a physiological or by a chemical trigger. To make this realistic bio- engineers are working with micro- and nanotechnology.

Drug delivery systems that include biodegradable polymers, dendrimers, electroactive polymers are being studied. The results have yielded a fast degrading matrix that consists of a hydrophilic, amorphous, low-molecular- weight polymer that contain heteroatoms in its make up. This gives the researcher the ability to adjust the rate of its degradation, and therefore control the rate of drug delivery. Some of these have spokes coming out of the central core to which the biomolecules are attached and have the ability to hide the molecule from the immune system.

Bioengineers are exploring new strategies to find other innovative drug delivery systems. One new technology involve the use of dendrimers, these are highly branched, globular, synthetic macromolecules and buckyballs that will be used to deploy medications and is capable of moving drugs to targeted areas. The dendritic macromolecules make suitable carriers because their structure and sizes they can be controlled by synthetic means, they can also be processed and made biodegradable. The advantages of these are that they can hold small drug molecules, and can serve as recipients for large numbers high densities of drug molecules that can be transported to the affected areas. Researchers are also exploring ways to construct polymers that the body will not recognize as foreign. The polymer mielles is very tiny. It is only a tens of nanometers in diameter. Their size is ideal for enclosing individual drug molecules. Their outer shell of hydrophilic protect the contents of their inner core from the chemical reaction while they travel in the blood or plasma.. They finally release the drug after the degradation of the outer core.

It is not only in the area of drug delivery systems that that this new research is evident, but progress need to be made in areas such as: forced inhalation devices, transdermal methodologies, forced- pressure injectables, and biodegradable polymer networks that are designed specifically to transport new gene therapies; replacement parts for tissues and bones; artificial kidneys for patients with severe kidney diseases. Researchers also need to investigate the safety and efficacy of the current treatments, finding ways to administer injectable only medications orally, and making multiple dosage life long drug therapies in expensive, also needed are potent, time releasing or self triggering drug formulations. These new developments need to be cost effective and user friendly so that patients will be able to treat themselves.

Section II: The Mathematical Models: Pharmacokinetics

Pharmacodynamics and Pharmacokinetics are both concerned with the response of drugs on the body. Pharmacodynamics is concerned with the effect of a drug on the body. It has to do with the relationship between the dosage and the molecular mechanisms of the drug activity. Pharmacokinetics is concerned with the effect of the body on the drugs. It has to do with drug metabolism, transport, absorption and elimination.

The body influences how the drug is distributed within the body, and this influence is due to the rates of drug intake in the body's tissues; and the rate of which the drug is eliminated from the body. Pharmacokinetics,

then is devoted to the development of mathematical models, that are designed to study the three activities of drug intake and its relationship with the body. These models are then used to predict the outcomes of different dosages of drug concentrations in the body with respect to time. These models are difficult to construct for any specific drugs because of the complications that can be introduced through the interactions of the compound, (the drug make up) the organism and the presence of the disease.

The underline concept of pharmacokinetics is to consider the simple situation of the introduction of the drug in the body, and the elimination of this drug from the body over time. The three processes involved are biotransformation, absorption or bioavailability, distribution, and excretion. The biotransformation and excretion of drugs are concerned with the passing of medication across cell membranes. For the process to be effective we have to be concerned with the properties of molecules and membranes that influences this process.

In biotransformation two products are of importance, the composition of the drug and the structure of the cells.

(table available in print form)

Drug Absorption and Bio-Availability

The rate at which a drug leaves the site where it enters the body is called absorption. Bio- availability is concerned with the availability of the administered drug at the needed site. Many factors affect the bioavailability and absorption of drugs in the body.

Site of Absorption

If the drug enters the body through the mouth and is absorbed in the stomach and the intestines, then the drug is metabolized in the liver, and excreted in the bile. In this situation some of the drug will be diverted before it reaches the circulatory system and can be distributed to the needed site.

Drug Solubility

Drugs given in a water solution are more easily absorbed than drugs in oily solution, suspension or solid form. Drugs that are water soluble mixes readily at the site of absorption than those that are given in solid form. The absorption of drugs given in solid form will depend on the rate at which it dissolves. The local conditions at the site of absorption also alter solubility, some drugs are insoluble in acidic conditions.

The concentration of drugs also influences its rate of absorption. Drugs that are delivered in solution of high concentration are absorbed more rapidly than the drugs that are administered in solution of low concentration.

The circulation at site of administration

The circulation at the site of administration also affects the absorption of drugs. Increased blood flow enhances the chance of greater absorption rates are compared to areas of decreased blood flow. Increased blood flow can be brought about by the application of heat or by massaging the site.

The surface area

The area of the site at which the drug is given affects the rate of absorption. Drugs will be absorbed more rapidly from large surface areas. The absorbing surface is also determined by the route of administration.

The Route of Administration

Oral administration

Oral administration is the most common choice, and is considered the safest and most convenient. There are disadvantages to this route of administration. These include:

- The incapability to absorb some drugs because of their physical characteristics
- Irritation to the mucosa membrane of the mouth
- Destruction of some drugs by the digestive system
- The irregularities in absorption or propulsion when food is present
- Metabolization by the enzymes of the intestines or the liver before they reach the circulation system.
- Cooperation on the part of the patient

Parenteral Injections

This form of administration is vital to drugs that need to be absorbed in active form. Bio-availability is usually more rapid, and the dosage can therefore is more suitable if the patient is uncooperative, or if treatment is needed in an emergency situation. The disadvantages are that pain may accompany the injection, the injection may be given in a vascular, or the injection may be given when it is not necessary. It is also difficult to self medicate.

Sublingual Administration

Absorption from the oral mucosa has special significance for certain drugs. Drugs such as nitroglycerin is absorbed quite rapidly. Only a few molecules need to be absorbed for the drug to be effective. The drainage from the mouth goes to the superior vena cava, therefore the drug is protected from metabolism by the liver.

Rectal Administration

The rectal route is preferred if the oral ingestion causes vomiting or if the patient is unconscious. Most of the drug that is absorbed from the rectum will bypass the liver. The disadvantage of the rectal absorption is that absorption of the drug is often irregular and incomplete, and some drugs can cause irritation of the rectal mucosa.

Drug Distribution

After the drug is absorbed, or injected in the body it needs to be distributed into the interstitical and cellular fluids. Drug distribution consist of physiological factors and physiochemical properties. The heart, liver, kidney, brain, and fused organs receive most of the drug during the first minutes after absorption. The muscles, the skin, and fat have a slower rate of absorption.

Drug distribution is affected by:

a) Blood flow
b) The rate at which drug diffuse into the issue
c) Drug binding to plasma protein
d) The accumulation of drugs in tissues in high concentration.
e) The function of the patient's age, gender, and body composition.

The volume of drug distribution relates the amount of drug in the body to the concentration of drug in the blood plasma based on the type of fluid measured.

Volume = Amount of drug in the body / Concentration. To calculate the distribution of drugs, the body is considered as a one compartment model (like a box). All drugs is administered into the central compartment and the distribution of the drug is instantaneous throughout the volume. Simplified the amount of drug eliminated per unit of time depends on the amount of drug in the body's compartment. The equation C= (d/V) - exp(kt) is used to calculate the decline of a drug introduced in the body (compartment). K is the rate of constant elimination.

The half life of the drug is the time it takes for the drug's concentration in the body to be reduced by 50%. This half life can be used to determine how to administer successive dosages of the drug. It has been shown that half life of a drug is the function of both clearance, and volume of distribution. Therefore a formula for half life can be adjusted to t1/2 = 0.693. (v/cl).

Biotransformation of Drugs

This is the process that permits rapid passage of the drugs across cellular membranes. The enzyme systems that are responsible for the biotransformation of many drugs are located in the liver. Fewer are also present in other organs such as the kidney, lungs, and gastrointestinal lining.

There two phases involved in biotransformation.

Phase 1: The drug is converted to a more polar metabolite by oxidation, reduction or hydrolysis. Phase II: The drug is coupled with metabolites, with sulfate acetate or with an amino acid. These actions occur concurrently or consecutively so that the original drug is converted to several metabolites. These actions usually take place

in the liver.

Excretion of Drugs

The excretion of drugs has to do with how drugs are eliminated from the body either unchanged or as metabolites. The excretory organs eliminate polar compounds more efficiently than substances with high lipid solubility. Drugs that are not lipid soluble are not eliminated unless they are metabolized to polar compounds. The kidney is the organ the is responsible for the elimination of drugs, however some drugs are eliminated through the feces, the breast milk, the lungs, through the sweat glands, saliva and the tears.

Renal Excretion

This excretion of drugs in the urine involve three processes

a) Glomerular filtration

b) Active tubular secretion

c) Passive tubular re- absorption

Biliary and Fecal Excretion

The metabolites of drugs formed in the liver are excreted into the intestinal tract in the bile. Some of the metabolites may be reabsorbed into the blood and then is excreted in the urine.

Pulmonary Excretion

Pulmonary excretion is responsible for the elimination of anesthetic gases and vapors, and small quantities of some other drugs.

Excretion from Other Routes

Drug is also excreted from the sweat glands and the tears in small amounts. Drugs is excreted from the mouth through the saliva where it is swallowed. The saliva provides another place where drug concentration can be obtained.. Drug is also excreted in the breast milk. Milk is more acidic than plasma therefore certain drugs will enter the breast milk in small amounts. Certain drugs are also excreted through the skin and hair follicles.

Clearance

Clearance of drug is the rate of elimination by all routes of the concentration of drug in a biological fluid. Clearance is of great concern when considering the administration of a drug over time. Clearance does not refer to how much drug is being removed from the body but means the volume of fluid for example blood that would have to be completely free of drug to account for elimination. It is imperative to maintain steady state concentrations of drugs within a given range. Clearance is expressed as a volume per unit of time and is given by the equation CL = Rate of elimination / C(the concentration). It is assumed that for complete bioavailability the rate of drug elimination must equal the rate of drug administration, this can be represented by: Dosing =

CL (Css) where CL is clearance and Css is steady state.

Clearance of drugs by different organs is summative and is given by the equation

CL(renal) + CL(Liver) + CL(other organs) = CL(systemic). The absolute clearance of drug is considered as a linear function of its concentration in plasma. In respect the elimination of drugs follows a first order kinetics that is a constant fraction of drug is eliminated per unit of time. For a single dose of with complete bioavailability and first order kinetics of elimination, the total systemic clearance is determined by CL = Dose / total concentration of drug in circulation.

Total clearance of drugs can be determined using the equation CL = Dose / AUC where AUC is the total area under the curve that describes the concentration of drug in the systemic circulation as a function of time.

Bioavailability

Bioavailability means the amount of drug that reaches the systemic circulation. This amount can be a fraction of the drug that entered the body initially. There many reasons for the reduction in the bioavailability of the drug. For example the drug may be metabolized by the liver or excreted by the bile; some drugs are absorbed from the gastrointestinal tract and will be inactivated by the liver before it reaches the general circulation for distribution to the needed site.

Section III: Lesson Plans: Connecting the Unit to the Curriculum

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The NTCM standards in mathematics suggest that students should be given real world mathematics problems instead of contrived problems that have no relationship to real world situation. The lessons in this unit will attempt to provide students with problem situations that are rooted in real life phenomena in the area of bio-engineering, so that students can use mathematics to make connections to the issues that are confronted in this field of science.

This unit's lessons will seek to adhere to selected standards detailed both in the NTCM standards and the Connecticut Core Curriculum. Standard 9 (NTCM Connection) states that:

> a) Students should be given the opportunity to recognize and use connections among mathematical ideas connection.
> b) Understand how mathematical ideas interconnect and build on one another to produce a coherent whole
> c) Recognize and apply mathematics in contexts out side of mathematics.

The unit will use scenarios from the content of the seminar to provide the mathematical connections to bio-engineering. Students will be able to see the connection between mathematics and real-life, and mathematics

and other disciplines. They will also be able to see mathematical concepts as the thread that runs through scientific innovations.

Standard 8 Communication states that Students should be given the opportunity to:

a) Organize and consolidate their mathematical thinking through communication
b) Communicate their mathematical thinking coherently and clearly
c) Analyze and evaluate the mathematical thinking and strategies to others
d) Use the language of mathematics to express mathematical ideas.

Students will be required to communicate their problem solving strategies, or to write responses to scenarios in which they will be able to explain their findings and communicate their opinions.

The integration of the Big Content Ideas

The scenarios will present students with background information from the concepts of bioengineering (ex. drug delivery, the growth of cancer cells, artificial implantation). They will use mathematical models to provide solutions to the problem situations.

Lesson Plan I

Purpose

To investigate the rapid growth of cancer cells

To generate a model from a problem situation

To communicate the rapid spread of a disease in an organism

Materials

Graph paper, graphing calculator, (Math)

Petri dish, organism (science)

Scenario I: Cancer Cells too Aggressive to be contained

The evidence of certain cancer has been found to be prevalent the population of mice. Researchers have found that the tumor is growing at a rapid rate when the growth rate is compared with the cells of the organ in which it is located. You have been asked to do a research on the growth of this cancer cell and compare it with

the growth of other cells.

For your research you found the following description of cancer cell growth.

Cancer cells can arise in almost any location in the body or tumors or collection of cancer cells can be vastly different from organ to organ and person to person. A cell forming a tumor is different from normal cells within the organ; it has undergone a malignant transformation. The molecular event that occurs during this transformation are not completely understood, and there is more than one set of molecular changes that will cause a malignant transformation. All cancer cells share a number of characteristics. They proliferate or divide rapidly compared to normal signals. They generally do not respond normally to signals that are provided by neighboring cells. They do not differentiate normally, but tend to remain as immature dedifferentiated cells. They do not become specialized or die, even when they are moved to a part of the body that is different from their normal environment.

From your research project you are required to examine the growth of these cells in the lab.

Activities

1. Make a table and generate a graph showing the number of cells created during a 3 hour period if there was 100 cancer cells present initially C = 10t
2. Generate a table to show the rate of growth of the normal tissue cells assume that the initial population was 1,000 and these cells reproduce at
N(t) = 2t.
3. Compare the graph of both cell growths. Write a paragraph describing the behavior of the graph.
4. a) If the cancer cells grow at the rate of Pn = Po ekt estimate the number of cells when t = 5 with the initial population of 1,000 cells and k = 0.05.
b) If there were also 1000 normal cells in the tissue sample and the normal cells reproduce at Pn = Po ekt with k = 0.02. Graph the cancer cells and the normal cells on the same axis use (0 =t=20). Determine when the cancer cells will out number the normal cells.
5. a) A group of cancer cells starts with 400 and grows at a constant rate The Amount after t hours is given by A(t) = (450.268)e1.125 t cells per day. How many cells will there be in 3 days
b) Graph the growth of the cells from 0 =t=10 days.

For Calculus Students: Rate of change Application problem

6. A spherical cell is growing at a constant rate of 4000 um3 / day (1um = 10 - 6). At what rate is its radius increasing when the radius is 10um?
7. When the growth of a spherical cell depends on the flow of nutrients through the surface, the growth rate dv/dt is proportional to its surface area, s. Assume that for a particular cell dv/dt = 1/3 s. At what rate is its radius r increasing.
8. The rate of growth of a tumor is proportional to the size of the tumor.
a) Write a differential equation for S the size of the tumor, in mm, as a function of time.
b) Find the general solution to the differential equation.
c) If the tumor is 5 mm across at time t = 0 what does that mean?
d) If the tumor is 8 mm across at t =3 what does the solution mean?

Lesson Plan II

Purpose

To investigate the concentration of medication in the blood

To calculate the re-medication times for a given medication

To graph the concentration of medication with respect to time

Materials

Graph paper

Calculator

Background

All drugs have a serum half life, or the time it takes for excretion processes to lower the serum concentration by half. To maintain the effect of the drug the patient must receive regular fixed doses, this enables the drug to maintain its concentration. Pharmacokinetic models can be used to regulate the administration of drugs for the patient so that the concentration of drugs can remain at a certain peek. The half life t1/2 of a drug is the time for the plasma concentration or the amount of the drug in the body to be reduced by 50%> In some cases the disease may affect the half life of the drug, therefore the formula t1/2 = 0.693 (V/CL) gives the relationship between the half life, clearance and the volume of distribution.

Steady State

Steady state concentration will be reached when the drug is administered at a constant rate.

Drug Elimination: CL = (Rateofconcentration/ concentration) or Drug Elimination = Clearance x concentration.

During each dosage of a drug the concentration of the drug rises and falls, therefore steady state rises and falls and is identical in each interval.

Activities

1. After an 8 mg injection of a drug, the readings of the drug concentration after 2 seconds intervals are given in the table.

(table available in print form)

Graph the concentration of this drug over time. Then use the graph to respond to the following questions;

a) What was the concentration of the drug at t(2)
b) When was the concentration at its peak?
c) At what times if any was the concentration the same?
d) At what time was the concentration at its lowest?
e) To be effective the concentration of the drug should be between 7.00 and 5.00 what times should the drug be re-administered?

2. The half- life of a certain cancer drug is 4 hours. Suppose a patient is given 10mg of this drug.

a) Find an equation that can be used to model the amount remaining after t hours
b) When will there be 8 mg of drugs remaining?
c) After how long will there be only 2 mg?

3. A patient is given a drug intravenously at a rate of 43.2 mg/ hr to relieve her headache. If the drug is entering a component of volume 35,000 ml (this is the volume of the part of the body through which the drug circulates). The rate at which the drug leaves the patient is proportional to the quantity entered, with the proportionality constant 0.080.

a) Make a table and graph the concentration of the drug in the patient for 5 hours.
b) Write a differential equation that can be used to satisfy the concentration of the drug.

Lesson Plan III

Purpose

To calculate using rate of change the amount of drug eliminated from the body over time.

Materials

Calculator

Background: The Elimination of Drugs from the Body

Pharmacokinetics provides a functional (mathematical) relationship between the dose of drugs, its effect and way with which to interpret the concentration of drugs in the blood stream. This important issue in pharmacokinetics in most important in patient care, because it can dictate the intervals when the drug doses will be repeated.

The three most important parameters are clearance (the body's ability to eliminate drugs), volume distribution (a measure of the space in which the patient's body to contain the drug), bioavailability (the fraction of the drug that is absorbed in the body).

Clearance of drug is usually constant over the range of concentrations, and can be determined by a linear function. A constant fraction of the drug is eliminated per unit of time.

Clearance (CL) = Rate of elimination / concentration

Since clearance can take place in different organs of the body, the elimination of drugs can be considered as a summative relationship and systemic clearance given by

CL systemic = CL renal + CL liver + CL other

Drugs are eliminated from the body either unchanged or as metabolites. Each excretory organ plays its role in the elimination process. The kidney is the organ that has the responsibility of excreting most of the waste from the body.

Problem: Let C(t) be the concentration of a drug in the blood stream. As the body eliminates the drug C(t) decreases at a rate that is proportional to the amount of the drug that is present at the time. C (t) = - k c(t) where k is a positive number called the elimination constant of the drug.

a) If c is the concentration at t = 0 find the concentration at time t

b) If the body eliminates half the drug in 30 hrs, how long does it take to eliminate 90 % of the drug?

Lesson Plan IV

Purpose

To engage students in Invention

To have students research the types of systems that can be used for the delivery of drugs

Activities: Interdisciplinary

From the readings in the unit your task is to do research on, and then design (invent) an instrument that could be used in the field of medicine. This instrument or device could be used either in research, for clinical use by the doctors or by the patients at home.

Explain your project then describe what it is and how it should be used.

Draw a design of your instrument or device and explain how it will impact health care.

Lesson Plan V

Purpose

To calculate the rate of change in the size of a devise.

Material

Calculator and graph paper

Paper

Background

You are studying devices for drug delivery. From the readings you found that the administration of medication to a specific part of the body can be done in many ways, but the most efficient way would be to get the drug to the site where it is needed. You found that if the drug is taken orally its passage through the digestive system to the circulatory system is not efficient because

a) the required amount of drug does not reach the targeted area
b) the drug could cause undesired effects in different areas of the body.

You realized that a local delivery system would be best but realized that there are constraints on the system;

a) time
b) constant drug concentration vs time variation
c) Number of application (one time or repeated administration).

You also found that there exist the following types of devices

1. Membrane device: a polymeric membrane encapsulates the drug, which is then carried in the form of a saturated aqueous solution that consists of undissolved particle of the drug. The membranes are usually spherical in shape, and consist of an outer membrane and an inner reservoir that holds the drugs.
2. The Matrix device: This can be compared to a sponge that is loaded with drugs. When the matrix is implanted the drug molecules in the solution diffuse across the body surface of the matrix.

Activities

1. Under certain conditions, the movement of a diffused substance across a cell's membrane is given by the equation $dy/dt = k(A/V)(c-y)$. In the equation y is the concentration of the substance inside the cell, and dy/dt is the rate with which y changes over time. The letters k, A, V and c are constants. K is the permeability coefficient of the membrane and A is the surface area of the membrane, v is the cell's volume and c is the concentration of the substance outside the cell. The equation says that the rate at which the concentration changes within the cell is proportional to the difference between it and the outside concentration.
a) Solve the equation for $y(t)$ using $y0 = y(0)$
b) find the steady state concentration, $\lim t \to \infty y(t)$.
2. You designed a spherical drug delivery system that has an inner and outer shell. The radius of the outer shell is 4 nanometer and the radius of the inner shell is 1.5 nanometer. Find the volume of this device.
3. Suppose a membrane type device containing drug was implanted. The membrane will dissolve at a rate $y = y0\ e^{-0.18t}$ with t in days.

a) About how long will it take for the membrane to dissolve?
b) How long before it is 90% of its original size?
4. If you design a rectangular wafer with dimension l = b = 5 mm and h = 0.5 mm, and it dissolve at the given rate. Graph the remaining size of the wafer for ten days.
5. You designed a spherical matrix devise with radius r = 2mm. The dissipation rate is given by y = y0 e - 0. 005 t
a) Find the half life of the device.
b) After how many days will the devise disintegrate?

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