1

**National Library
of Canada**

**Bibliothèque nationale
du Canada**

Canadian Theses Service

Service des thèses canadiennes

**Ottawa, Canada
K1A 0N4**

NOTICE

The quality of this microform is heavily dependent upon the quality of the original thesis submitted for microfilming. Every effort has been made to ensure the highest quality of reproduction possible.

If pages are missing, contact the university which granted the degree.

Some pages may have indistinct print especially if the original pages were typed with a poor typewriter ribbon or if the university sent us an inferior photocopy.

Reproduction in full or in part of this microform is governed by the Canadian Copyright Act, R.S.C. 1970, c. C-30, and subsequent amendments.

AVIS

La qualité de cette microforme dépend grandement de la qualité de la thèse soumise au microfilmage. Nous avons tout fait pour assurer une qualité supérieure de reproduction.

S'il manque des pages, veuillez communiquer avec l'université qui a conféré le grade.

La qualité d'impression de certaines pages peut laisser à désirer, surtout si les pages originales ont été dactylographiées à l'aide d'un ruban usé ou si l'université nous a fait parvenir une photocopie de qualité inférieure.

La reproduction, même partielle, de cette microforme est soumise à la Loi canadienne sur le droit d'auteur, SRC 1970, c. C-30, et ses amendements subséquents.

**SOLVING THE BIOHEAT EQUATION USING
FOURIER SERIES EXPANSIONS**

by

Wayne L. Pushka

**A thesis submitted to
the Faculty of Graduate Studies and Research
in partial fulfillment of
the requirements for the degree of
Master of Science
Department of Physics**

Carleton University

Ottawa, Ontario

December 20th, 1988

© copyright

1988 Wayne L. Pushka

Permission has been granted to the National Library of Canada to microfilm this thesis and to lend or sell copies of the film.

The author (copyright owner) has reserved other publication rights, and neither the thesis nor extensive extracts from it may be printed or otherwise reproduced without his/her written permission.

L'autorisation a été accordée à la Bibliothèque nationale du Canada de microfilmer cette thèse et de prêter ou de vendre des exemplaires du film.

L'auteur (titulaire du droit d'auteur) se réserve les autres droits de publication; ni la thèse ni de longs extraits de celle-ci ne doivent être imprimés ou autrement reproduits sans son autorisation écrite.

ISBN 0-315-51201-6

The undersigned recommend to the Faculty of Graduate Studies
and Research acceptance of the thesis

"SOLVING THE BIOHEAT EQUATION USING FOURIER SERIES EXPANSIONS"

submitted by Wayne L. Pushka, B.Sc.

in partial fulfillment of the requirements for
the degree of Master of Science

Thesis Supervisor

Chairman, Department of Physics

Carleton University

December 20th, 1988

ABSTRACT

A method for numerically evaluating the bioheat equation is developed. A computer program is then written to test the method's ability in approximating different geometries. We find that the technique adequately describes most geometries within the time frame necessary for clinical applications. The method shows enough promise to warrant further study and development.

ACKNOWLEDGMENTS

I would like to thank my supervisor Dr. P. Watson for his guidance and suggestions, and my family, friends, and fellow graduate students for their unwavering support throughout these last two years.

To my parents . . .

TABLE OF CONTENTS

1	Overview.....	1
2	Introduction to Hyperthermia and the Bioheat Equation.....	3
2.1	Hyperthermia.....	3
2.2	The Bioheat Equation.....	12
3	Numerical Methods for Solving Non-Linear Equations.....	20
3.1	Introduction.....	20
3.2	The Finite Difference Method.....	21
3.3	The Finite Element Method.....	27
4	The Fourier Method and Analysis.....	32
4.1	The Fourier Method.....	32
4.2	Analysis of the Method.....	35
5	Conclusion.....	55
	Appendix 1: A Detailed Explanation of the Fourier Method.....	56
A1.1	The Theory of Fourier Series Expansions.....	56
A1.2	The Fourier Method in Detail.....	61
	Appendix 2: A Computer Program Using the Fourier Method.....	70
	References.....	87

CHAPTER 1

Overview

Over the last twenty years interest in hyperthermia as a method of treating cancerous malignancies has increased dramatically. This has been facilitated by the rapid increase in the number of studies being done on the biological and physiological aspects of hyperthermia. With this better understanding of heat flow and its effects on a biological medium, hyperthermia, as a method for combating cancer, has begun to move out of the laboratory and into the clinic. With this increase in its clinical application, having a mathematical, and in particular a computer generated model for the purposes of thermal imaging, would be a considerable benefit. Not only would it be helpful in the study of heat flow in a biological medium, it would also aid in determining the thermal configurations of a given treatment for a patient. Unfortunately, in developing such a model with existing numerical techniques we encounter a number of problems.

This work attempts to circumvent some of those problems by developing a new method for solving the non-linear bioheat equation. This method involves separating the space dependent terms in the equation, from the time dependent terms, by applying a Fourier transformation on them. The time dependent term is then solved numerically by fitting it to

an exponential function. Whether or not this technique works is the question which will be answered here.

We begin in chapter two by introducing hyperthermia as a method for treating cancer. The biological and physiological aspects are briefly discussed, and the bioheat equation is presented and studied. Chapter three discusses other numerical methods used in solving heat transfer equations, with particular emphasis given to the two most commonly used in solving the bioheat equation; the Finite Difference, and the Finite Element methods. The benefits and drawbacks of the different numerical techniques are then discussed. In chapter four, we briefly explain the Fourier method (with a detailed explanation in Appendix 1), and analyze the results of a computer program that was developed (Appendix 2) to test the method. Finally, chapter five discusses the benefits and limitations of the method, and determines whether further development is/is not warranted.

CHAPTER 2

Introduction to Hyperthermia and the Bioheat Equation

2.1 Hyperthermia

The word "hyperthermia" originates from the Greek words "hyper" meaning excessive, and "therme" meaning heat. It has been used in medicine as a treatment since the ancient Greeks induced fevers in patients to facilitate a cure. Not only can hyperthermia be used as a treatment for viral and bacterial related illnesses, but there is evidence that elevated temperatures may give rise to tumor regressions.

It was in the late nineteenth century that hyperthermia as a method of treating malignant tumors was first documented [1]. The results were sporadic however, and although some progress was made throughout the first half of the twentieth century [2-5], it was not until the 1960s [6-8], and especially the early 1970s that a systematic study of hyperthermia's effects on malignant tumors was first carried out. The results obtained in these studies proved encouraging enough to warrant an increase in the amount of research done on hyperthermic effects in cancer - as can be seen by the abundance of published material in the 1980s [9-13].

Hyperthermia can be applied in two different ways, either over a patient's entire body, or as a local dose to treat an isolated problem. In the case of full body heating, techniques have shown the feasibility of producing core temperatures of 42 celsius. The temperature must be kept below 41.5 - 42.0 celsius, since at these temperatures damage to the central nervous system begins, for up to several hours [10,14,15]. The benefits of full body heating have been documented [16,17], but for clinical applications the method still has a number of drawbacks, including toxicity, physiological stress, cumbersomeness and cost of equipment, temperature monitoring, and the requirement for general anesthesia [18,19]. Hence, full body treatment remains therapeutically experimental, and for modelling purposes will not be discussed here. Instead, attention will be focused on local hyperthermic effects.

In order for local heat to be most effective in combating cancer, the cytotoxicity of hyperthermia (its ability to kill cells) must be clearly understood. Unfortunately, this is not a trivial problem, for hyperthermia cytotoxicity is dependent upon the temperature of the tissue, the length of time over which it is applied, the cell biology, the environment in which the cell is located and whether heat is being applied in conjunction with other cancer treatment methods [10]. All these factors must be taken into consideration if an accurate model is to be constructed.

Two of these factors, tissue temperature and the length of time over which it is applied, have a non-linear relationship with the cell survival rates (see figure #1) [20-21]. This non-linear relationship means there is no single variable, or linear combination of variables that can be used to define heat dose, where the definition is based on cell damage or death. Therefore, analytical solutions are in most cases impractical, due to the difficulty in solving non-linear equations with non-homogeneous geometries. To make matters worse, it was found that most cells behave differently at temperatures above 43 degrees celsius than at lower temperatures (see figures #1 & #2) [20-22].

Figure # 1: Chinese hamster cells were exposed to various temperatures for the times indicated, and the ability of individual cells to multiply indefinitely was determined. The values for the slopes of the exponential portions of the survival curves are indicated as D37 in minutes of heat treatment [14].

Figure # 2: Survival curves for Chinese hamster cells exposed to temperatures below 43 degrees celsius [16].

By defining heat dose as a measure of cell damage or death one must understand the non-linear relationship between temperature and cell survival. Tissue damage by hyperthermia is dependent upon temperature, duration of heating and tissue environmental factors. The temperature of the tissue is dependent upon heat dissipation by blood perfusion and, to a lesser extent, conduction, whose properties vary from one tissue to the next. Also, the decreases in pH, and the depletion of nutrients and oxygen, which greatly enhance heat damage, are the result of a complex cellular biology. Hence, using cell damage as a means of defining thermal dose, although more accurate, is rather difficult, so instead it will simply refer to the combination of temperature and duration of heating at the point of application.

Different behaviour at different temperatures is not the only unusual property of cells undergoing hyperthermic treatment. When a local heat treatment is given in a clinical situation, it does not take the form of a single thermal deposition but rather a series of separate heatings, with each lasting for as long as a few hours. In this situation of multiple heat treatments, two interesting phenomena may occur. The first is called step-down heating [23,24] and is found when cells are treated at temperatures of 43 degrees celsius or higher, for short periods of time. For a few hours after the treatment, the surviving cells are much more susceptible to subsequent heatings, even when they are applied at lower temperatures. The second effect is called thermotolerance [24, 25]. In this situation, the initial treatment is below 43 degrees celsius, and results in cells being more resistant to subsequent heatings, above and below 43 degrees celsius. This resistance may last for as long as one hundred hours (see figure #3). In the last few years it has become evident that thermotolerance is the result of the production of a small set of polypeptides called heat shock proteins, which are generated after mild heat shocks to maintain the homeostasis of the cells [26]. These two phenomena should be taken into consideration during clinical treatments, mathematical modelling, and the designing of equipment for use in the clinic.

Figure # 3: Survival curves for Chinese hamster ovary cells, after inducing thermotolerance [10].

Hyperthermia is only useful for treatment purposes if there is preferential damage to cancerous tissue over normal tissue. Preferential damage to cancerous tissue is derived from many factors including the inability of malignant cells to repair damage and the differences in certain physiological parameters such as pH, nutrition and oxygen tension. As well, there is usually a compromised vasculature associated with bulky tumor and a complex synergism exists between hyperthermia and other cytotoxic agents such as chemotherapy or radiation [27]. To ensure that the heat from the local application does not seriously damage the surrounding normal tissue, the body's methods of temperature control must be clearly understood. This control is achieved by the metabolic generation of heat, absorption of thermal energy, thermal conduction, and dissipation of heat through blood flow. So, if there is localized heating of a tumor, the maximum damage will generally occur at the point where the heat is applied. In the case of hyperthermia, dissipation of heat through blood flow and thermal conductivity are the dominant methods for thermoregulation. For most large tumors, the center tends to have lower blood flow rates than normal tissue resulting in a poor oxygen (hypoxia) and nutrient supply for the cells and a low pH in the region. This combination of nutritional deprivation, hypoxia, acidity and poor blood flow all contribute to making tumor cells more sensitive to heat [9].

Hyperthermia is even more effective when used in combination with radiotherapy and certain chemotherapeutic drugs (see figure #4) [20, 28-31]. The cytotoxicity of X-rays is enhanced if the cells are exposed to elevated temperatures either before or after irradiation. This is the result of a complex synergism between hyperthermia and other cytotoxic agents such as radiation. Part of this synergism comes about because most human tumors contain hypoxic cells which have a high resistance to radiotherapy on their own. These same cells however, tend to be more susceptible to heat than oxygenated cells. As well as cell environment, different phases of the cell cycle are not equally sensitive to treatment, either by irradiation or heat. In fact, a number of studies have indicated that there is a synergism between radiation and hyperthermia [10, 27, 32]. Hence, this synergism is more than just

Figure # 4(a): Survival curves of Chinese hamster ovary cells after being X irradiated at a low dose rate at various temperatures [10].

Figure # 4(b): Survival curves of Chinese hamster ovary cells at low and high LET irradiations at 37 and 43 degrees celsius [10].

the sum of the two parts. Thus, the combination of radiation and hyperthermia appears very attractive for clinical cancer treatments.

There is also evidence showing the benefits in combining hyperthermia with drug treatments (see figure #5). As in the case of radiation, a synergism exists between hyperthermia and chemotherapy such that the net biological effect is greater than the sum of the two individual effects. This synergism varies with different drugs, and may be related to increased membrane transport of drugs, increased thermal activation of the cytotoxic process, or other undefined mechanisms.

There are several methods used in applying heat to tissue. The non-invasive methods include microwave radiation, radio frequency (RF) waves, ultrasound, and conductive - convective methods which include warm water baths, infrared lamps, warm air, etc. The invasive methods involve inserting microwave and RF applicators, and in the case of systemic heating, saline and blood injections are used. Each of these methods has benefits and liabilities, but they will not be discussed here. Further information on applicability, thermal distribution patterns, and equipment design can be found elsewhere [33].

The prime concern of cancer therapy is the elimination of cancerous tissue while at the same time minimizing the damage to normal tissue. In the case of hyperthermic treatment there is the problem of cold spots developing in different regions of the tumor. Even one inadequately heated region increases the probability that cancerous cells will survive, leading to possible tumor regrowth and treatment failure. These cold spots do not have to have a large temperature difference with the surrounding tissue. As can be seen in figures #1 and #2, a temperature difference of only one degree celsius can lead to a considerable difference in the cell survival curves.

Cold spots can arise from a number of biological and physiological effects. If a tumor is located near a large blood vessel, cooling develops in the vicinity of the vessel due to its high blood flow rate. In the case of ultrasound heating, if the tumor is near a bone there is a non-uniformity in the thermal distribution because bone reflects ultrasound. In addition,

Figure # 5: Dose response curves of Chinese hamster cells exposed to nitrosoureas or to cis-platinum at various temperatures [10].

bones are also reasonably good at conducting heat, thus creating non-uniformities in the temperature of the tissue which surrounds a bone. Other effects can be found depending upon the heating modality being used and the biological environment in which the heating takes place. When one combines all of these effects, one finds that to theoretically determine thermal distributions for a given treatment becomes a complex task.

Why bother then?

The prime beneficiaries of an accurate prediction of the temperature field from a given heat source would be found in the clinic. With a mathematical prediction available, the efficiency of the treatment could be maximized by adjusting the field to suit the different thermal properties of the tissue. Likewise, a mathematical model would help in comparing different heating modalities before treatment takes place. Post-treatment evaluation of the therapy, as well as a feedback control for the treatment, are additional benefits of thermal modelling. The ideal objective would be to image, heat, and control the temperature field of a tumor in three-dimensions without having to insert probes into the patient. However, for the foreseeable future, most modelling will be aided by real time thermometry.

2.2 The Bioheat Equation

The first step in building a thermal model of tissue is to construct a mathematical equation which accurately predicts heat flow in a given tissue geometry. Since tissue is a very complex medium, only the most important parameters should be included in any mathematical model. There are a number of mathematical models that can be used to model heat flow [34-36], however, we will use the most common model, that being the Bioheat Equation [35,36]. Its most general form is:

$$\frac{\partial}{\partial t} \int_V c_t T dV = - \int_S k_{ij} \frac{\partial T}{\partial x_j} n_i dS + \int_V \dot{q}_m dV + \int_V \dot{q}_a dV + \int_S c_b T_b \dot{f}_i n_i dS \quad (1)$$

where

T = the local temperature of the tissue.

c_t = specific heat of the tissue.

k_{ij} = thermal conductivity.

n_i = unit outward normal vector

c_b = specific heat of blood.

T_b = temperature of blood.

$\dot{f}_i$ = blood perfusion rate vector.

$\dot{q}_m$ = power generated by tissue.

$\dot{q}_a$ = power absorbed by tissue.

The term on the left is the rate at which energy is accumulated per unit volume. When the total energy entering a control volume is greater than the energy leaving that volume, the difference takes the form of heat. The change in the energy difference over time is subsequently the change in temperature, and is given by the time derivative of the integral of the product $c_t T$ over the control volume V .

$$\frac{\partial}{\partial t} \int_V c_t T \, dV$$

The first term on the right is the rate at which energy is transferred per unit surface via Fourier conduction. This is founded on what is called Fourier's Law, which in an isotropic, homogeneous medium is described by:

$$\vec{q}(r,t) = -k \vec{\nabla} T(r,t) \quad \text{W/m}^2$$

Where $\vec{q}(r,t)$ is the conduction heat flux vector in heat flow per unit time, per unit area, k is the thermal conductivity, and $\vec{\nabla} T$ the temperature gradient. It states that there is a net

transport of heat in the form of heat conduction from a region of higher to lower temperature. This conduction travels in the direction normal to the isotherm surface, and thus in the same direction as the decreasing temperature. In order to make the heat flow a positive quantity, a negative sign is included. For anisotropic media, such as tissue, the heat flow vector is not always normal to the isotherm surface. In order to generalize Fourier's Law in such media, the isotherm surface is divided into segments, and at each of these points the heat flux vector is assumed to be normal to the surface. Consequently, the thermal conductivity must be segmented as well. The total heat conduction is then found by integrating the conduction heat flux vector over the entire surface S , so that:

$$q_c = - \int_s k_{ij} \frac{\partial T}{\partial x_j} n_i dS$$

The second term on the right of the bioheat equation is the rate at which energy is being generated via aerobic (oxygenated) and anaerobic (non-oxygenated) metabolic processes, as well as the rate at which energy is being absorbed from external sources. In hyperthermia, the metabolic heat generation term q_m is quite small in comparison with the energy absorption q_a , conduction, and convection terms. Therefore, in most modelling situations the heat generation term can be ignored. The energy absorption term q_a , is a result of energy absorbed from external sources. The form of this term is dependent upon the modality being used, whether it be ultrasound, microwaves, etc. and can thus have a host of shapes and sizes [37]. The total energy generation and absorption rate, Q , is found by integrating over the total volume V of the energy generation rate $\dot{q}_m$ and the energy absorption rate $\dot{q}_a$:

$$Q = \int_V (\dot{q}_m + \dot{q}_a) dV$$

The final term in the bioheat equation is the rate at which energy is transported via the circulatory system. This term involves the specific heat c_b , and temperature T_b of the blood, as well as the blood perfusion rate vector $\dot{f}_i$. This vector equals zero everywhere on the control surface, except where a blood vessel is found. A different vector $\dot{f}_i$ must be assigned to each blood vessel that penetrates the control surface. By determining all the blood flow rates of every capillary entering the control volume, and integrating over the entire surface, we find the total energy transported by the vascular network:

$$Q_b = \int_s c_b T_b \dot{f}_i n_i dS \quad (2)$$

To determine the blood flow rates of every vessel is impractical, so a blood perfusion term W_b is used instead. This term represents the average amount of blood that flows in a given volume per unit time. Equation (2) is then rewritten in the form:

$$Q_b = W_b c_b (T_a - T)$$

where T_a is the arterial blood flow temperature, and T the tissue temperature. For most calculations, it is assumed that the arterial blood temperature is unaffected by the temperature of the surrounding tissue. Although this is necessary to simplify the mathematics, this assumption may be responsible for a major source of error in the final solution. Even with these simplifications, Q_b is the term which causes the most difficulty in applying the bioheat equation. These difficulties are a result of two major problems with modelling blood perfusion in tissue. First, the blood flow rate changes non-linearly as a function of temperature, and the other stems from the fact that there are markedly different

blood flow rates across most large tumors. These two problems must first be understood and solved before a reasonable model of the blood perfusion rate can be used.

When heat is applied to tissue there is a swelling of the blood vessels which service that region. This swelling causes an increase in blood flow, thereby increasing the blood perfusion rate. A blood vessel's response to temperature change is dependent upon the size of the temperature differential, the absolute temperature of the tissue, the type of tissue being heated, and the length of time heating has taken place (see figures #6(a & b)). All these factors combine to make the blood perfusion rate as a function of temperature a non-linear relationship. There have been a number of studies done describing this relationship for various tissue types [38-41]. As of yet there is a great deal unknown about how perfusion rates change with time and temperature in various tissues in human systems, and therefore, caution should be taken when constructing the blood perfusion rate term.

The second difficulty with calculating blood perfusion rates is with the tumor itself. Different ages of a tumor result in different blood perfusion configurations. These are not just dependent upon a tumor's age however, they also depend upon the shape and type of tumor involved. Fortunately, the very nature of cancerous cells helps make tumor shape not as serious a problem as it could be. Since cells in a solid tumor grow in densely packed populations that develop into ellipsoid or spheroid aggregates, the vascularization of some tumors tends to be symmetric in two or even three dimensions.

Originally, the cells obtain oxygen and nutrients from the host via diffusion. This is called the avascular stage. In order to effectively maintain the cells in the center of the tumor, there comes a time (tumor approximately 2 mm in diameter) when the neoplasm must generate a capillary bed of its own, and connect it with the main vascular network. This is done by releasing a tumor angiogenesis factor (TAF) which stimulates the growth of new capillaries from the host vascular system. Once this is done, the tumor is said to be in the vascular stage. The extent of this vascularization, and subsequently the blood

Figure # 6(a): The blood flow rates of rat leg skin and muscle heated at 43 degrees celsius for one hour [9].

Figure # 6(b): The blood volume changes in rat leg skin and muscle heated at 43 degrees celsius for one hour [9].

perfusion rate, is dependent upon the type of tumor involved, with some brain tumors being the most vascularized, followed by carcinomas and the sarcomas.

When the tumor reaches approximately 1 cm in diameter, its growth begins to slow. This is due to the deterioration of the vascular network in the center of the tumor, causing those cells to eventually become necrotic. Some mature tumors (gliomas, some kidney and liver tumors) can be divided into five zones (see figure #7)

- (1) Necrotic area with no vascularization.
- (2) Semi-Necrotic area with long capillaries and little branching.
- (3) Stabilized micro-circulation on the inside edge of the tumor.
- (4) Advancing tumor front with high blood flow.
- (5) Normal tissue.

Thus, the different vascularization throughout the tumor results in a non-homogeneous blood perfusion rate across its interior. Since the curve in figure #7 is only qualitative, there are different perfusion values for different tumor ages, types, and locations. But, there are enough data available that a reasonable model of most tumors can be generated [42-48].

Hyperthermia has shown signs of becoming an effective method in treating malignant tumors, on its own or in conjunction with other modalities. Whether it will become a major cancer fighting tool in the future, remains to be seen. Before this can be determined however, the thermal response properties of tissue must be better understood. Additional studies are needed to investigate thermotolerance, the micro-biology of heat in tissue, macro effects, and a variety of other problems. Mathematical modelling is a useful tool in understanding these effects, as well as being potentially helpful in predicting thermal distributions of tumors in the clinical environment. Hopefully, with further studies these models can be improved to become more accurate and efficient.

Figure # 7: Distribution of perfusion in the tumor volume [27].

CHAPTER 3

Numerical Methods for Solving Non-linear Equations

3.1 Introduction

In the previous chapter we discussed what hyperthermia is, the mathematical modelling involved, and the difficulties in implementing such models. In particular, we focused on the classical bioheat equation. The other aspect of such models is finding a solution for them, whether it be through analytical or numerical means.

There is a variety of methods which can be used in solving these partial differential equations, ranging from purely analytical to numerical solutions. In the case of the bioheat equation, emphasis is placed on numerical solutions due to the impracticalities of solving a non-linear, non-homogeneous equation using analytical techniques. In addition, the incredible increase in speed and power of the micro computer over the last ten years, coupled with the steady drop in price has increased the popularity of using these numerical methods to solve partial differential equations. In the following chapter, we will discuss the methods available to us and their usefulness in solving the bioheat equation.

The five most common numerical techniques for solving heat transfer problems are the finite difference [49, 53-56], finite element [49, 50, 53-56], boundary element (boundary integral) [49, 51, 52, 54], perturbation [54], and Monte Carlo methods [54]. The two most

commonly used are the finite difference and finite element methods, which involve dividing the physical continuum into discrete spatial and temporal points called nodes. This enables these methods to solve an extensive number of different shaped geometries, thus giving them a wide range of applications. The boundary element method involves dividing the boundary elements into discrete elements and then solving for each of these elements using Green's functions. Although this method has shown a high degree of efficiency and speed, its main drawback is its limited range of application with non-uniform physical geometries. This means that for any change in geometry, new boundary conditions and subsequently a new Green's function must be determined. For complex geometries this can be a difficult task. The perturbation method combines analysis with numerical computation, making it impractical for use in a purely computer medium. Finally, there is the Monte Carlo method, which is based on a random walk principle. It is quite effective in solving problems based solely on radiation and conduction. But in biological media, macro heat transfer is dominated by convection through blood flow, making the Monte Carlo method impractical for this environment.

It is the Finite Difference and Finite Element methods which provide the greatest versatility in solving heat transfer problems, and are the two methods most widely used for finding solutions to the bioheat equation. To better understand their advantages and limitations, we will now describe them in detail.

3.2 Finite Difference Method

The Finite Difference method is a straightforward technique for finding the numerical solution of a partial differential equation. The method involves expanding the partial derivatives into Taylor series. A set of linear equations is then obtained, and evaluated.

We begin by dividing the physical continuum into a series of discrete points called nodes. In a time-independent two dimensional space this would appear as in figure #8. The points (i,j) , $(i,j+1)$ etc. are the nodes, and it is at these nodes the heat equation is evaluated. The

Figure # 8: Grid System used for the finite difference method in two dimensions.

Figure # 9: Nomenclature used for the finite difference representation of $f(x)$.

added dimension is not necessary in understanding the technique, so we will deal only in one-dimensional space.

In one dimension the function $f(x)$ over the interval $[a,b]$, is divided into N equal parts, each with a width h . We now perform a Taylor series expansion on the functions:

$$f(x+h) = f(x) + h f'(x) + \frac{h^2}{2!} f''(x) + \frac{h^3}{3!} f'''(x) + \dots \quad (3)$$

$$f(x-h) = f(x) - h f'(x) + \frac{h^2}{2!} f''(x) - \frac{h^3}{3!} f'''(x) + \dots \quad (4)$$

To generalize, the notation is converted into the form $x=ih$, $f(x)=f_i$, $f(x+h)=f_{i+1}$ (see figure #9), and we find the first derivatives by rearranging (3) and (4) respectively:

$$f'_i = \frac{f_{i+1} - f_i}{h} - \frac{h}{2} f''_i - \frac{h^2}{6} f'''_i \dots \quad (5)$$

$$f'_i = \frac{f_i - f_{i-1}}{h} + \frac{h}{2} f''_i - \frac{h^2}{6} f'''_i \dots \quad (6)$$

Combining (5) and (6) we find the first derivative can be written as:

$$f'_i = \frac{f_{i+1} - f_i}{h} + O(h) \quad \text{forward difference}$$

$$f'_i = \frac{f_i - f_{i-1}}{h} + O(h) \quad \text{backward difference}$$

$$f'_i = \frac{f_{i+1} - f_{i-1}}{2h} + O(h^2) \quad \text{central difference}$$

where $O(h)$ is the error (of order h) due to truncating the Taylor series.

The same technique is used in determining the second derivatives, where we find:

$$f''_i = \frac{f_i - 2f_{i+1} + 2f_{i+2}}{h^2} + O(h) \quad \text{forward difference}$$

$$f''_i = \frac{f_{i-2} - 2f_{i-1} + f_i}{h^2} + O(h) \quad \text{backward difference}$$

$$f''_i = \frac{f_{i-1} - 2f_i + f_{i+1}}{h^2} + O(h^2) \quad \text{central difference}$$

It is possible to increase the accuracy of these differences, by nesting the second order derivative expansion back into equations (5) and (6), and solving. This can be done to whatever order of accuracy desired.

There is a variety of methods for finite differencing the time-dependent heat equation [58], ranging from the explicit, to the implicit forms. In the explicit case, we approximate the time derivative using the forward difference approximation, whereas the implicit case uses the backward difference approximation.

To understand the method, consider the very simple one-dimensional, time-dependent, heat-conduction equation:

$$\frac{\partial T}{\partial t} = \frac{\partial^2 T}{\partial x^2} \quad \text{where } 0 < x < L \quad (7)$$

$$t > 0$$

Divide the one-dimensional space into N nodes with width Δx , and the time nodes an interval Δt .

$$x = j\Delta x \quad j=0,1,2,3,\dots,N$$

$$t = n\Delta t \quad n=0,1,2,3,\dots$$

Let the temperature $T(x,t)$ be represented by:

$$T(x,t) = T(j\Delta x, n\Delta t) \approx T_j^n$$

Using the central difference approximation for the space derivative, and the forward difference approximation for the time derivative, and substituting them both into the heat conduction equation (7) we find:

$$\frac{T_j^{n+1} - T_j^n}{\Delta t} = \frac{T_{j-1}^n - 2T_j^n + T_{j+1}^n}{\Delta x^2}$$

where we have truncated $O(\Delta t) + O(\Delta x)^2$.

Solving for T_j^{n+1} we have:

$$T_j^{n+1} = \mu T_{j-1}^n + (1 - 2\mu) T_j^n + \mu T_{j+1}^n \quad (8)$$

$$\text{where } \mu = \frac{\Delta t}{(\Delta x)^2}$$

This is the gist of the explicit method. As seen in (8) we determine the node temperature T_j at the new time $(n+1)$ from the temperatures at the nodes $j, j-1, j+1$ at time n (see figure #10).

Figure # 10: Explicit finite difference spatial and temporal discretization.

Figure # 11: Implicit finite difference spatial and temporal discretization.

A major limitation of the explicit method is that once Δx has been fixed, there is a maximum value for Δt , after which instabilities set in. For (7) this restriction is [58]:

$$0 < \mu < 1/2$$

The implicit method differs from the explicit, in that it uses the backward difference approximation, rather than the forward (see figure #11). It has the advantage over its explicit counterpart, in that it is stable for all sizes of μ , thus eliminating the size restriction on Δt .

To determine the solution of T_j^{n+1} , we use equation (8), and require (at least) the boundary condition:

$$T(x,0) = f(x) \quad \text{where } j = 0,1,2,\dots,N$$

(ie: the initial temperature of the system).

This can be substituted into (8) to determine T_j^1 for every value of j , and repeated n times to obtain the values for T_j^n .

3.3 Finite Element Method

As with the Finite Element method, the Finite Difference methods divides the physical continuum divided into a series of discrete points. But, while FD methods provide approximations at the node points, the FE methods provide regional approximations about the node points. This means that for irregular boundary conditions, the Finite Element method is more accurate. This arises because the elements do not have to be identical. Different element shapes can be chosen to suit the geometry. As seen in figure #12 the triangular shaped elements conform more closely to an irregular geometry than a rectangular grid. In this example the nodal points are at the corners of each triangle, and the triangle itself is the finite element.

The Finite Element method calculates the partial differential equation over every finite element region, rather than just at node points. In order to do this, we must construct an

Figure # 12: Finite element spatial discretization in two dimensions using triangles.

Figure # 13: One-dimensional linear basis functions.

integral representation of the partial differential equation. There are several different methods used in constructing these integrals, the three most common are the methods of variational calculus, weighted residuals, and moments of energy balances. For the method of convective heat transfer, it is the weighted residual method which is the most efficient [57].

In constructing the integral representation of the partial differential equation, consider the equation

$$L(\phi) - f = 0 \quad (9)$$

where L is the differential operator defined over a region A , and f is a known function or constant.

The variable ϕ (in the bioheat equation this would be temperature) is then approximated as a finite series expansion:

$$\tilde{\phi}_i(\tilde{x}, t) = \sum_{i=1}^N N_i(\tilde{x}) \tilde{\phi}_i(t) \quad (10)$$

where $N_i(\tilde{x})$ are finite, linearly independent, trial basis functions. These basis functions are finite in number, and local. For the Finite Difference method the basis functions can be seen in the Taylor series expansion, where they are global, and infinite in number.

If we insert (10) into (9) then we find the difference between the exact solution, and the approximate one:

$$L\tilde{\phi}_i(\tilde{x}, t) - f = R(\tilde{x}, t) \quad (11)$$

This difference $R(\tilde{x}, t)$, is the error, or residual.

The method of weighted residuals is now applied [57]. This involves choosing N linearly independent weighting functions W_i . If we have an error β in a region R , and we wish for the average error to be zero over the entire region, then we choose W_i such that:

$$\int_R W_i \delta \, dR = 0 \quad \text{where } i=1,2,\dots,N \quad (12)$$

What this means is that the weighted average of our error is zero.

Inserting (11) into (12), where the residual $R(\tilde{x}, t)$ is the error, we obtain:

$$\int_A (L \tilde{\phi}_i(\tilde{x}, t) - f) W_i \, dA = 0 \quad \text{where } i=1,2,\dots,N \quad (13)$$

There is a variety of weighting functions W_i which could be inserted here. An interesting method however, is to set the weighting functions W_i , and the basis functions N_i , to be the same. This is known as Galerkin's Method. Hence, we have for (13):

$$\int_A \left[\left(L \left(\sum_{i=1}^N N_i(\tilde{x}) \tilde{\phi}_i(t) \right) - f \right) N_i(\tilde{x}) \, dA = 0 \quad (14)$$

which is the basic Galerkin expression.

We now have N equations for the N unknown basis function values $N_i(\tilde{x})$. The next step is to choose the form of these local basis functions. For one-dimensional problems, the most commonly used local basis function is linear:

$$\psi(x) = a + bx$$

(Other basis functions can be found in one and higher dimensions [59].)

We approximate the function $\psi(x)$ on the interval $[x_{i-1}, x]$ such that

$$\psi(x) = N_{i-1} \psi_{i-1} + N_i \psi_i$$

and obtain:

$$N_{i-1} = \frac{x_i - x}{\Delta x} \quad \text{and} \quad N_i = \frac{x - x_{i-1}}{\Delta x} \quad (15)$$

where Δx is the mesh size ($\Delta x = x_i - x_{i-1}$). These basis functions in (15) are piecewise linear functions, also called pyramid, or roof functions (see figure #13). Using these basis functions, we insert the boundary conditions and solve for the N equations in the Galerkin expression. This method can be expanded into two and three dimensions, but the expression is more difficult to calculate and construct than in the Finite Difference case [54].

Careful consideration must be used in deciding which method to be implemented. In some situations, the Finite Difference method has advantages over the Finite Element method, and vice versa. The Finite Difference method is easily mastered and implemented, and provides good results for simple geometries. Due to its relative simplicity, it is easily extended to two or three dimensions, but that same simplicity contains drawbacks as well. In some flow situations, lower-order boundary approximations must be included in order to achieve stable solutions, and since these boundary conditions are determined after solving the domain interior, they usually give an accuracy of low-order. The major drawback of the Finite Difference method however, is that it does not describe complex geometries very well.

The Finite Element method can easily handle irregular geometries, and higher-order approximations can be easily generated without requiring special treatment of the boundaries. In addition, the mesh size can be altered, allowing small mesh sizes in regions where the solution changes significantly, and large ones in regions with little change. The main drawbacks to the Finite Element method is that it is storage intensive, and slower - especially in three dimensions. It is also more difficult to learn, extend into two and three dimensions, and because the method is convergent in the mean, local oscillations can occur where the initial temperature is discontinuous. Hence, the type of method to be used, whether it be the Finite Element or the Finite Difference, is dependent upon the type of geometry involved, and what properties the researcher deems most important.

CHAPTER #4

The Fourier Method and Analysis

4.1 The Fourier Method

It may be beneficial to investigate other numerical methods to find a more effective means in solving the bioheat equation. The method to be explored in this chapter involves using Fourier Series expansions to extract the space components from the bioheat equation. Once in Fourier space, the function is then evaluated and an inverse Fourier transform is performed on it to convert it back to real space for the final solution. In this chapter the method is presented and tested using a computer program. The results are then presented and discussed.

The impetus for using a Fourier series expansion can be found in some simple heat conduction problems which use Fourier series expansions in determining analytical solutions. In addition, Fourier series have a number of properties which make them particularly well suited for evaluating the bioheat equation. One, is that the sine and cosine functions are global basis functions, so theoretically they can model nearly any physical geometry. Second, the series converges for any function with a finite maxima, minima and discontinuities in a given interval. This means that for any real life biological situation the

series will converge. These properties and other behaviour associated with Fourier series expansions are discussed in detail in Appendix 1.

In order to evaluate the bioheat equation using Fourier series expansions, we must first convert it into a form which can be solved numerically. This form is:

$$\rho_t c_t \frac{\partial T(r,t)}{\partial t} = \nabla (K \nabla T) - W_b c_b (T - T_b) + q'_m(r,t) + q'_a(r,t) \quad (16)$$

where $T(r,t)$ = the temperature of the tissue ($^{\circ}\text{C}$)

r = spatial co-ordinate (m)

t = time (sec)

ρ_t = density of tissue (kg/m^3)

c_t = specific heat of tissue ($\text{J/kg } ^{\circ}\text{C}$)

K = thermal conductivity of tissue ($\text{W/m } ^{\circ}\text{C}$)

W_b = mass flow rate of blood per unit volume of tissue ($\text{kg/m}^3 \text{ sec}$)

c_b = specific heat of blood ($\text{J/kg } ^{\circ}\text{C}$)

T_b = temperature of arterial blood entering volume V ($^{\circ}\text{C}$)

q'_m = power generated per unit volume of tissue (W/m^3)

q'_a = power absorbed per unit volume of tissue (W/m^3)

Since the power generated and absorbed per unit volume of tissue is extremely small in comparison to the other terms, they will be ignored. Instead, a power deposition term $Q(r,t)$ will be included. This term represents the modality used in applying power to the system, whether it be a point source applicator, or ultrasound waves, etc. The q'_m and q'_a

terms can be easily incorporated into $Q(r,t)$ if so desired.

The thermal conductivity term K , is separated into a constant and a spatial dependent component:

$$K = K_N + K_a(r)$$

The temperature dependent aspect of the system is found in the blood flow rate term $W_b c_b (T - T_b)$. It is assumed that the application of heat to the system does not affect the temperature of the blood anywhere, so the blood temperature T_b is assumed to be uniform throughout and is considered a constant. This results in the blood flow term acting as a heat sink.

Since T_b remains a constant, we set:

$$\bar{T}(r,t) = T(r,t) - T_b$$

and we rewrite equation (16) as

$$\rho_t c_t \frac{\partial \bar{T}(r,t)}{\partial t} = \nabla [(K_N + K_a(r)) \nabla \bar{T}(r,t)] - W_b c_b \bar{T}(r,t) + Q(r,t) \quad (17)$$

The spatial component is separated from time via Fourier series expansions of the form:

$$\bar{T}(r,t) = \sum_{mn=-\infty}^{+\infty} \bar{T}_{mn}(t) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}}$$

(see Appendix 1 for the detailed calculation).

The final solution is constructed so as to satisfy:

$$\bar{T}_{mn}(t) = [\bar{T}_{mn}(\infty) - \bar{T}_{mn}(t_0)] [1 - e^{-\Omega_{mn}t}] + \bar{T}_{mn}(t_0) \quad (18)$$

(See Appendix 1 for calculating the Ω_{mn} and $\bar{T}_{mn}(\infty)$ values.)

This is done, because heat conduction tends to behave exponentially. By forcing the solution to take the above form we hope to avoid any divergences which may be associated

with rapid heat changes. In addition to avoiding divergent terms, by using (18) we might also be able to have larger time steps "t" between calculations than if linear fitting were used. In order to test this hypothesis a linear fit is also constructed by truncating a Taylor series expansion to first order (see Appendix 1):

$$\bar{T}_{mn}(t) = \bar{T}_{mn}(t_0) + t \bar{T}'_{mn}(t_0) \quad (19)$$

In order to test the method, we construct a computer program (Appendix 2) which evaluates the bioheat equation for different two-dimensional geometries. Although three dimensions would be optimal, this was deemed impractical due to the enormous number of iterations required to solve even the simplest three-dimensional problem.

4.2 Analysis of the Method

The analysis begins by first evaluating the Fourier series ability to simulate a given geometry. Due to the nature of Fourier series expansions - a summation of smooth, continuous sine and cosine waves - sharp discontinuities are particularly difficult to approximate. Because of this, the step function, and in two dimensions the square function, is a good geometry to use to study the limitations of a Fourier series approximation.

In evaluating the one-dimensional step function, a computer program similar to the one found in Appendix 2 is used. The real space field is composed of a line divided into 40 identical pixels. In turn, the Fourier space field is also a line divided into identical pixels, the number of which depends on the desired level of precision. A precision of $PREC=10$ represents a range of pixels from $m=-10$ to $m=10$ in Fourier space giving a total of 21 pixels. Likewise, $PREC=20$ has a range of $m=-20$ to $m=20$ for a total of 41 pixels, and so on. In order to model a function of a given width, the Nyquist sampling rate must also be taken into consideration. What this says is that for the highest frequency component present Ω , we must have a sampling rate of at least $\Delta x = 1/2\Omega$ in order to recover the original

function. For the case of the step function, if the real field has a width of 40 and the step width is 4 then the Fourier series cannot have a width less than 20.

In determining the Fourier series ability to simulate a one-dimensional step function, we set the PREC levels at 10, 20, 30, 40, and 100 (see figures #14(a-e)). The Lanczos convergence factor [63,64] was applied to all of these cases. Although it succeeded in eliminating the Gibbs phenomenon, the lower PREC levels still have poor resolution at the discontinuous edges of the step. Even at a high precision level there is still difficulty with the edges. This can best be seen for PREC=100 case and is explained by the second Dirichlet condition (see Appendix 1), that of averaging the arithmetic mean, which causes the step function sides to be averaged over the discontinuity. Hence, any benefits in increasing the PREC level above 40 will be diminished due to the effects of averaging the arithmetic mean.

The Fourier series' difficulties in simulating discontinuities is intensified when extended to two dimensions. Not only is there smearing at a discontinuity, but in the case of a square, the corners have half the accuracy again (see figures #15 & #16).

Fourier series are much better in simulating functions without discontinuities. Comparing a Gaussian and a step function of equal size (see figures #17 & 14(b)) at PREC=20, we see that the Fourier series simulation of the Gaussian has excellent agreement with the analytical solution, whereas the step function has no edges.

If this method is to be used in a clinical situation, it must be able to accurately model heat flow in a biological medium in a reasonable amount of time. As with all numerical methods, there is a trade-off between accuracy and time. This trade-off becomes important when the problem is extended to two dimensions. The real space field is now a 40x40 or 1600 pixel grid, and a PREC=10 level represents a $m=-10$ to 10 and $n=-10$ to 10, or 441 element field in Fourier space. In order to determine the trade-off between accuracy and time for a two-dimensional problem, four computer runs were made on a VAX 8250, each with 5 time steps. The runs were at PREC levels of 10, 20, 30, and 40, and the amount of

A TEMPERATURE HISTOGRAM IN ONE DIMENSION

KM2=5.0.....KM1=0.0.....LEN=40
 LAMC008 FACTOR INCLUDED.....PRSC=10

```

-3.0030031E-04-
1.6202182E-03--
2.0622141E-03--
2.3999279E-03--
2.0963660E-04--
-2.8006339E-03-
-4.1967163E-03-
-3.2101010E-03-
4.1067132E-04--
4.0009150E-03--
7.1033304E-03--
4.3764350E-03--
-3.8041234E-03-
-1.2891997E-02-
-1.4491981E-02-
1.9011983E-03--
4.6959108E-02--
0.1261273  -----
0.2368013  -----
0.3686194  -----
0.4932427  -----
0.5966252  -----
0.6333000  -----
0.6833000  -----
0.6962232  -----
0.4932427  -----
0.3686194  -----
0.2368013  -----
0.1261273  -----
4.6959108E-02--
1.9011983E-03--
-1.4491981E-02-
-1.2891997E-02-
-3.8041234E-03-
4.3764350E-03--
7.1033304E-03--
4.0009150E-03--
4.1067132E-04--
-3.2101010E-03-
-4.1967163E-03-
-2.8006339E-03-

```

THE AREA ABOVE THE
ZERO AXIS IS 5.161759

T
S
M
P
A
A
T
U
R
E
(C)

Figure #14(a)

One-dimensional step function PRSC=10

A TEMPERATURE HISTOGRAM IN ONE DIMENSION

KM2=5.0.....KM1=0.0.....LEN=40
 LAMC008 FACTOR INCLUDED.....PRSC=20

```

-3.2631424E-04-
-4.0646488E-04-
3.7407432E-04--
4.0478002E-04--
-4.4545902E-04-
-5.9609343E-04-
5.4644618E-04--
7.6308229E-04--
-7.0132129E-04-
-1.0203161E-03-
9.5944142E-04--
1.4013403E-03--
-1.4663640E-03-
-2.3494987E-03-
2.8790405E-03--
4.3063473E-03--
-4.4930613E-03-
-9.4024036E-03-
5.1128090E-02--
0.2237054  -----
0.4953703  -----
0.7797173  -----
0.9614410  -----
0.9614410  -----
0.7797174  -----
0.4953703  -----
0.2237054  -----
5.1128090E-02--
-9.4024036E-03-
-6.4930613E-03-
4.3063473E-03--
2.8790405E-03--
-3.3494987E-03-
-1.4663640E-03-
1.4013403E-03--
9.5944142E-04--
-1.0203161E-03-
-7.0132129E-04-
7.6308229E-04--
5.4644618E-04--
-5.9609343E-04-

```

THE AREA ABOVE THE
ZERO AXIS IS 5.090071

T
S
M
P
A
A
T
U
R
E
(C)

Figure #14(b)

One-dimensional step function PRSC=20

A TEMPERATURE HISTOGRAM IN ONE DIMENSION

KM2=5.0.....KM1=0.0.....LEN=40
 LAMC008 FACTOR INCLUDED.....PRSC=30

```

-8.2373263E-03-
1.3200428E-04--
-1.1204534E-04-
2.3713997E-05--
0.9302702E-05--
-1.9302809E-04-
1.9624305E-04--
-0.9302809E-05-
-1.2044163E-04-
3.3403728E-04--
-4.1427030E-04-
2.0606447E-04--
1.0306039E-04--
-6.0203210E-04-
1.2894363E-03--
-1.4963567E-03-
0.6070226E-04--
1.6418521E-03--
-9.3662273E-03-
0.1195009  -----
0.5020522  -----
0.6774503  -----
1.0068339  -----
1.0068339  -----
0.6774503  -----
0.5020522  -----
0.1195009  -----
-9.3662217E-03-
1.6418516E-03--
0.6070226E-04--
-1.4963567E-03-
1.2894363E-03--
-6.0203210E-04-
1.0306039E-04--
2.0606447E-04--
-4.1427030E-04-
3.3403728E-04--
-1.2044163E-04-
-0.9302809E-05-
1.9624305E-04--
-1.9302809E-05-

```

THE AREA ABOVE THE
ZERO AXIS IS 5.049710

T
S
M
P
A
A
T
U
R
E
(C)

Figure #14(c)

One-dimensional step function PRSC=30

A TEMPERATURE HISTOGRAM IN ONE DIMENSION

MM=5.0.....MM1=0.0.....LEN=40
 LANCOS FACTOR INCLUDED.....PREC=40

```

-7.4117704E-04-
 0.5443400E-04-
-9.4487854E-04-
 1.1980374E-04-
-1.4118591E-04-
 1.6967679E-04-
-2.0603792E-04-
 2.5469146E-04-
-3.1868026E-04-
 4.0942474E-04-
-5.2789790E-04-
 7.0833042E-04-
-9.0212708E-04-
 1.4229377E-04-
-2.1877074E-04-
 3.4641992E-04-
-5.0402811E-04-
 1.5518943E-04-
-8.0138660E-04-
 4.6776407E-04-
 0.4996763
 0.0920390
 1.003423
 1.003423
 0.9320397
 0.4996763
(C) 4.6776410E-04-
-5.0136149E-04-
 1.5518943E-04-
-6.0402811E-04-
 3.4641992E-04-
-3.1868026E-04-
 1.4229377E-04-
-9.0212708E-04-
 7.0833042E-04-
-5.2789790E-04-
 4.0942474E-04-
-3.1868026E-04-
 2.5469146E-04-
-2.0603792E-04-
 1.6967679E-04-
-1.4118591E-04-
 1.1980374E-04-
-9.4487854E-04-
 0.5443400E-04-
-7.4117704E-04-

```

THE AREA ABOVE THE
 ZERO AXIS IS 8.024946

Figure #14(d)

One-dimensional step function PREC=40

A TEMPERATURE HISTOGRAM IN ONE DIMENSION

MM=5.0.....MM1=0.0.....LEN=40
 LANCOS FACTOR INCLUDED.....PREC=100

```

-1.1882407E-03-
-1.7240714E-03-
 1.3668572E-03-
 2.0671298E-03-
-1.3363930E-03-
-2.3534647E-03-
 1.0223769E-03-
 3.2934522E-03-
-2.2438257E-03-
-4.4743312E-03-
 2.0474817E-03-
 6.3428404E-03-
-3.0428534E-03-
-1.0610568E-04-
 3.7484399E-03-
 2.0533396E-04-
-1.0710662E-04-
-3.6279417E-04-
 4.3139981E-04-
 4.8533079E-03-
 0.4997919
 0.9954755
 1.000244
 1.000244
 0.9954755
 0.4997920
(C) 4.8534430E-03-
 4.3149291E-04-
-3.6279302E-04-
-1.0715322E-04-
 2.0539806E-04-
 3.7593444E-03-
-1.0612808E-04-
-3.6304314E-03-
 6.3391007E-03-
 2.0434037E-03-
-4.4743768E-03-
-2.2395333E-03-
 3.2000304E-03-
 1.0322833E-03-
-2.5492704E-03-

```

THE AREA ABOVE THE
 ZERO AXIS IS 8.003702

Figure #14(e)

One-dimensional step function PREC=100

Figure #16

A lego plot of Figure #15. The histogram's groupings of 9 and 12 blocks with spaces in between is a property of the plotting package (ignore the spaces).

A TEMPERATURE HISTOGRAM IN ONE DIMENSION

GAUSSIAN.... A=.1257PREC=20....LEN=40
 NO DISCONTINUITY...THEREFORE....NO LANCZOS
 CONVERGENCE FACTOR....

```

    2.4766370E-04----
   -4.4415009E-04---
   -2.1175609E-04---
    5.0867698E-04----
    1.6330765E-04----
   -5.8042235E-04---
   -9.6288568E-05---
    6.5881514E-04----
    1.5261758E-06----
   -7.4049400E-04---
    1.3794930E-04---
    8.5316080E-04----
   -8.0229365E-06---
    1.2588556E-03----
    1.1426139E-02----
T    4.3981433E-02----*
E    0.1329187      ----*****
M    0.3220094      ----*****
P    0.6060254      ----*****
E    0.8821074      ----*****
R    0.8821074      ----*****
A    0.9986931      ----*****
T    0.8821074      ----*****
U    0.6060254      ----*****
R    0.3220094      ----*****
E    0.1329187      ----*****
    4.3981433E-02----*
(C) 1.1426139E-02----
    1.2588556E-03----
   -8.0229365E-06---
    8.5316080E-04---
    1.3794930E-04---
   -7.4049400E-04---
    1.5261758E-06----
    6.5881514E-04----
   -9.6288568E-05---
   -5.8042235E-04---
    1.6330765E-04----
    5.0867698E-04----
   -2.1175609E-04---
   -4.4415009E-04---
    2.4766370E-04----

```

THE AREA ABOVE THE
ZERO AXIS IS 5.007452

	Pixel Distance	Fourier	Exact
	From Center	Approx.	Value
	0	0.9987	1.0000
	1	0.8821	0.8819
	2	0.6060	0.6048
	3	0.3220	0.3226
	4	0.1329	0.1338
	5	0.0440	0.0432

Figure #17
 One-dimensional gaussian PREC=20

time taken to perform each run recorded (see Table #1). The decision as to which PREC level to be used is dependent upon the geometry involved, the desired level of accuracy, and the amount of CPU time available to the researcher. The recommended levels are between $\text{PREC} = 20$ and 30 . Since the problems at discontinuities due to the Gibbs phenomenon and the second Dirichlet condition are not reduced with an increase in precision, it is felt that beyond $\text{PREC} = 30$ the method is no longer time effective with respect to the increase in the accuracy. For the runs performed in these studies, the most time efficient precision level was felt to be $\text{PREC} = 20$.

The next step is to determine whether the method accurately describes the bioheat equation. To do so, we construct and solve the following heat conduction problem both analytically and by using the computer program.

In a two-dimensional infinite medium $-\infty < x, y < +\infty$ consider the regions $-1 < x < 1$ and $-2 < y < 2$ (where x and y are measured in centimeters) initially set at a constant temperature $T_0 = 20^\circ\text{C}$, and everywhere outside this region is set at zero celsius. This problem is evaluated for 5 time steps at three different time step sizes: 20, 60 (see figures #18(a-f)), and 100 seconds (see Table #2).

The only sizeable disagreement between the analytically and numerically calculated solutions, is found at the early time steps near the edges of the heat square. This is a direct result of the Fourier series difficulty in simulating a two dimensional square. As the region cools, the discontinuities disappear, and at time steps of 60 seconds and more there is excellent agreement between the numerical and analytical solutions. In addition, it was found that the step size had no bearing on the accuracy of the solution. The results after one time step of 60 seconds was identical to that of three time steps of 20 seconds. This is the result of forcing the final temperature solution $\bar{T}_{mn}(t)$ to conform to equation (18).

The effectiveness of forcing the temperature to an exponential fit is tested by comparing it to a linear fit (see figure #19(d)). This was done by replacing the exponential fit in the

Table #1

Four computer runs using the program
FMETHOD each with 5 time steps, and
varying precision (PREC) levels.

+++++		
+	+	+
+	PREC LEVEL	+
+		TIME
+		Hours:Minutes:Seconds
+		+
+++++		
+		+
+	10	0:04:21
+		+
+++++		
+		+
+	20	0:45:36
+		+
+++++		
+		+
+	30	2:32:51
+		+
+++++		
+		+
+	40	6:39:52
+		+
+++++		

Table #2

=====

Heat distributions at four different times due
to a 2x4 cm block centered at the (0,0) axis
with an initial temperature of 20 degrees
celsius (everywhere else at zero celsius).

Time Interval (sec)	Coordinate Points (x,y) (cm)	Analytical Solution (°C)	Numerical Solution (°C)
20	(0, 0)	8.39	8.17
	(-1, 1)	6.08	5.96
	(1, 2)	4.12	3.33
	(.5, -1)	7.06	6.53
60	(0, 0)	3.51	3.47
	(-1, 1)	3.06	3.03
	(1, 2)	2.53	2.43
	(.5, -1)	3.23	3.17
100	(0, 0)	2.21	2.19
	(-1, 1)	2.03	2.01
	(1, 2)	1.79	1.76
	(.5, -1)	2.10	2.08
300	(0, 0)	0.775	0.780
	(-1, 1)	0.751	0.758
	(1, 2)	0.718	0.726
	(.5, -1)	0.760	0.766

A comparison of the error between the linear and exponential fits.

Figure #19(d)

Error comparisons at different time steps between the exponential and linear fits at the point $x, y = (.5, 1.5)$, for the problem in 19(a to c). The error is the % difference between the numerical and exact solutions. Note that the linear fit threatens to diverge almost immediately, and the exponential fit error remains relatively constant. The initial error of 10% is due to the Fourier series approximation.

above test, to a linear one. As can be seen in figures #19(a-c), the linear fit is seriously disturbed by the initial discontinuities in the temperature field to the point that it diverges. It should be noted that in the case of an initial discontinuity in the temperature field, or a jump in the blood perfusion or thermal conductivity fields, there is the possibility that a diverging term may appear in equation (18). This term occurs when an Ω element becomes negative. When this element is extremely small (in magnitude) it has little effect on the equation. However, when the discontinuity in Fourier space is large with respect to the size of the Fourier field the temperature function will diverge. Since this phenomenon occurs in only a handful (out of nearly five hundred) of elements, it is eliminated by extracting any OMEGA terms that are less than (-0.001). A more elegant method for removing these diverging terms has not been developed, and is suggested for further research.

The final computer simulation to be performed is to solve a problem involving a heat deposition term, a blood perfusion rate, and a thermal conductivity term. There are ten time steps involved, with the first five involving a thermal deposition of 0.1 Watts per square centimeter followed by five cooling steps where the power deposition is removed. The region being heated has the same properties as that of muscle, where the thermal conductivity $K = 6.4E-3 \text{ J/cm/g/C}$ and the blood perfusion rate is held constant at $2.0E-3 \text{ cm}^3/\text{g/sec}$. The PREC level used is 20 and the final CPU time was found to be 1:22:54.

As seen in figures #20(a-k), the qualitative temperature distribution is as expected.

One of the benefits of using the Fourier method lies in the simplicity in constructing different geometries. Once the program was operational it was very easy to insert different configurations and geometries for a given test. Hence, if so desired, the program can be modified to be menu driven and then with a little practice, anyone can run different thermal configurations.

There are a number of factors which must be taken into consideration when deciding whether to use the Fourier method in solving a given problem. If there are a large number

The temperature at two points over a period of 10 minutes, with heat applied for the first five minutes, and removed for the next five

Figure #20(k)
 Temperature profile at the points $x, y = (0, 0)$ and $x, y = (1, 1)$, after 0.1 Watt/cm^2 power deposition in the region $-1 < x < 1$, $-2 < y < 2$, for 5 minutes. Power is then turned off for 5 minutes.
 Thermal cond. = $6.4 \times 10^{-3} \text{ J/cm/g/C}$, and
 blood perf. rate = $2 \times 10^{-3} \text{ cm}^3/\text{g/sec}$

of discontinuities in the field, or a high degree of accuracy is required at the point of a discontinuity, then the Finite Element method should be used instead. Likewise, if speed (this involves complete construction of the problem and run-time within a few hours) with reasonable accuracy - in a field with few or no discontinuities - are the priorities, then the Fourier method is a superior technique. In addition, if the heat is deposited using a method which is wave-like in nature (ultrasound, E.M. waves, etc.) then a Fourier series would be an extremely effective technique for modeling, due to its wave-like nature.

In comparison with the Finite Difference method, the Fourier method's strength lies in that the function is being fit to an exponential curve resulting in a greatly improved approximation to heat conduction problems. In addition, the divergences which can occur near a discontinuity by using a linear fit are suppressed by the exponential fit. Hence, for many problems fewer time steps are needed when using the Fourier method. The Finite Difference method however, has the benefit of being easier to learn and modify than the Fourier technique. Therefore, programming and predicting the run-time speeds are more difficult in the case of the Fourier method than the Finite Difference.

In order to properly determine which method is superior for a given problem, computer simulations should be run for all three techniques and the results compared. Once this is done, the Fourier method should be applied to a real life situation to make a final determination as to whether it is accurate and quick enough to be used for modelling in the laboratory and eventually the clinic.

CHAPTER 5

Conclusion

It has been shown that the Fourier method presented here, is capable of determining a solution to the non-linear bioheat equation. The method provides an excellent approximation to smooth functions, with very few iterations needed to perform the calculation. It was also found that using an exponential fit was an extremely efficient technique in modelling heat conduction problems.

The drawbacks to using Fourier series modelling occurs when a discontinuity is encountered. The smooth, continuous nature of the sine and cosine waves makes it intrinsically difficult for them to accurately approximate a sharp discontinuity. In addition, since the pixels along an axis must all be the same size, we cannot increase the precision at the point of a specific phenomenon. Instead, the precision of the entire field must be changed.

It was found that for a problem involving a power deposition term, with ten time steps at a reasonable level of precision ($PREC=20$), the total CPU time was 1:22:54, which is within the time frame necessary for most clinical situations. It is felt that the Fourier method has proved to be successful enough to warrant further study and development.

APPENDIX 1
A Detailed Explanation of the
Fourier Series Method

A1.1 The Theory of Fourier Series Expansions

The Fourier series is based on the premise that a function $f(x)$ can be expressed in terms of a sum of sines and cosines with the same period:

$$f(x) = \frac{a_0}{2} + \sum_{n=1}^{+\infty} (a_n \cos(nx) + b_n \sin(nx))$$

where $f(x)$ has a finite number of finite discontinuities, a finite number of maxima and minima, and where a_n and b_n are Fourier coefficients defined as:

$$a_n = \frac{1}{\pi} \int_0^{2\pi} f(t) \cos(nt) dt$$

$$b_n = \frac{1}{\pi} \int_0^{2\pi} f(t) \sin(nt) dt$$

(For further information see [60-64].)

Using Euler's identities $e^{ix} = \cos(x) + i \sin(x)$ the complex notation for the Fourier series becomes

$$f(x) = \sum_{n=-\infty}^{+\infty} c_n e^{inx} \quad \text{where} \quad c_n = \frac{1}{2\pi} \int_{-\pi}^{+\pi} f(x) e^{-inx} dx$$

For the period L we find the series becomes

$$f(x) = \sum_{n=-\infty}^{+\infty} c_n e^{\frac{in\pi x}{L}} \quad \text{and} \quad c_n = \frac{1}{2L} \int_{-L}^{+L} f(x) e^{-\frac{in\pi x}{L}} dx$$

which is the form that will be used.

For the case of two variables in two-dimensional space the series are independent. Therefore, we can write the double Fourier series as:

$$f(x,y) = \sum_{n=-\infty}^{+\infty} c_n e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}}$$

$$\text{and} \quad c_{mn} = \frac{1}{4LH} \int_{-H}^{+H} \int_{-L}^{+L} f(x,y) e^{-\frac{in\pi x}{L}} e^{-\frac{im\pi y}{H}} dx dy$$

There are several important properties of Fourier series which create difficulties at points of discontinuity. Since the Fourier series is a combination of sine and cosine waves - which are continuous and repetitive functions - it is difficult for them to properly represent a discontinuous function.

The Dirichlet conditions state that:

(1) $f(x)$ is a single valued function defined in the range $[-\pi, +\pi]$.

(2) $f(x)$ is bounded and sectionally continuous.

In a finite number of points $f(x+) \neq f(x-)$.

At these points, $f(x)$ is the arithmetic mean

$$f(x) = \frac{1}{2} [f(x+) + f(x-)]$$

(3) $f(x)$ has only a finite number of maxima and minima in the range $[-\pi, +\pi]$.

These conditions are sufficient, but not necessary. If they are satisfied the series converges, however, it does not necessarily diverge if they are not. In the heat flow case, they are satisfied.

The second condition, that of averaging the arithmetic mean, creates a problem at points of discontinuity. A sharp discontinuity cannot be perfectly approximated, since the region is the average between the top and bottom of the discontinuity.

Another problem arising from discontinuities is the Gibbs phenomenon. This was discovered in 1898 by Albert Michelson and explained a year later by Josiah Gibbs [65]. It states simply, that at the point of a discontinuity, the absolute error does not converge as the number of terms n approaches but does not reach infinity (for proof see [62]).

As an example of this effect, consider a sawtooth function. The Fourier series expansion is:

$$S(x) = \frac{1}{\pi} \sum_{n=1}^{\infty} \frac{\sin nx}{x}$$

and the finite expansion is:

$$S_m(x) = \frac{1}{\pi} \sum_{n=1}^m \frac{\sin nx}{x}$$

We find that the error in the finite Fourier series expansion is:

$$E(x) = \frac{\cos(m + 1/2)x}{(m + 1/2)\pi x}$$

Obviously, as m approaches infinity, the error becomes zero. But, the error is entirely dependent upon $(m + 1/2)x$, which means that as n increases, the error oscillations are not diminished, but are compressed into a smaller range.

The actual height of the Gibbs phenomenon remains at an 8.949% error at both ends of the discontinuity (see figure #21).

A possible correction to the Gibbs phenomenon is through the use of the Lanczos convergence factor. It is based on taking an average derivative of the Fourier series:

$$D_m f(x) = \frac{f(x+\pi/m) - f(x-\pi/m)}{2\pi/m}$$

where, $\lim_{m \rightarrow \infty} D_m = \frac{d}{dx}$

When this term is applied to a complex Fourier series we find that:

$$\begin{aligned} D_m e^{inx} &= \lim_{m \rightarrow \infty} \left[\frac{\sin(n\pi/m)}{n\pi/m} \right] e^{inx} \\ &= \left[\frac{\sin(n\pi/m)}{n\pi/m} \right] \frac{d}{dx} e^{inx} \end{aligned}$$

Hence, differentiating a function in this way, is equivalent to multiplying it by a factor:

$$G_n = \left[\frac{\sin(n\pi/m)}{n\pi/m} \right]$$

which is called the Lanczos convergence factor. The end result of applying this factor is to reduce the Gibbs phenomenon from 8.949% to 1.187%. However, as can be seen in figure

**Figure # 21: The Gibbs' phenomenon
for a step -1 to 1.**

**Figure # 22: The effect of Lanczos convergence
factors on a square wave [53].**

22, this factor slows down the rate at which the Fourier series converges. Therefore, in the case of smooth functions where the Gibbs phenomenon is absent, the Lanczos convergence factor is not only unnecessary, but is detrimental to finding the proper solution.

A1.2 The Fourier Method in Detail

The rewritten bioheat equation has the form:

$$\rho_t c_t \frac{\partial \bar{T}(r,t)}{\partial t} = \nabla (K \nabla \bar{T}(r,t)) - W_b c_b \bar{T}(r,t) + Q(r,t) \quad (20)$$

The thermal conductivity K is separated into a constant and a spatial component.

$$K = K_N + K_a(r)$$

Hence, for (20) we have

$$\rho_t c_t \frac{\partial \bar{T}(r,t)}{\partial t} = \nabla [(K_N + K_a(r)) \nabla \bar{T}(r,t)] - W_b c_b \bar{T}(r,t) + Q(r,t) \quad (18)$$

The spatial component is separated from the temporal via Fourier series expansions:

$$\bar{T}(r,t) = \sum_{mn=-\infty}^{+\infty} \bar{T}_{mn}(t) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}}$$

$$Q(r,t) = \sum_{mn=-\infty}^{+\infty} Q_{mn}(t) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}}$$

$$W_b(r) = \sum_{mn=-\infty}^{+\infty} W_{mn} e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}}$$

$$K_a(r) = \sum_{mn=-\infty}^{+\infty} A_{mn} e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}}$$

substituting into the bioheat equation, we obtain

$$\begin{aligned} \rho_t c_t \frac{\partial}{\partial t} \left[\sum_{mn=-\infty}^{+\infty} \bar{T}_{mn}(t) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right] = \\ \nabla \left[\sum_{mn=-\infty}^{+\infty} A_{mn} e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right] + \nabla \left[\sum_{mn=-\infty}^{+\infty} \bar{T}_{mn}(t) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right] \\ + \left[K_N + \sum_{mn=-\infty}^{+\infty} A_{mn} e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right] \nabla^2 \left[\sum_{mn=-\infty}^{+\infty} \bar{T}_{mn}(t) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right] \\ + c_b \left[\sum_{mn=-\infty}^{+\infty} W_{mn} e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right] \left[\sum_{mn=-\infty}^{+\infty} \bar{T}_{mn}(t) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right] \\ + \left[\sum_{mn=-\infty}^{+\infty} Q_{mn}(t) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right] \end{aligned}$$

Taking the spatial derivatives, we find:

$$\rho_t c_t \frac{\partial}{\partial t} \left[\sum_{mn=-\infty}^{+\infty} \bar{T}_{mn}(t) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right] =$$

$$\begin{aligned}
& \left[\frac{i m \pi}{H} + \frac{i n \pi}{L} \right]^2 \left[\sum_{m n = -\infty}^{+\infty} A_{m n} e^{\frac{i m \pi y}{H}} e^{\frac{i n \pi x}{L}} \right] \left[\sum_{m n = -\infty}^{+\infty} \bar{T}_{m n}(t) e^{\frac{i m \pi y}{H}} e^{\frac{i n \pi x}{L}} \right] \\
& + \left[\left(\frac{i m \pi}{H} \right)^2 + \left(\frac{i n \pi}{L} \right)^2 \right] \left[K_N + \sum_{m n = -\infty}^{+\infty} A_{m n} e^{\frac{i m \pi y}{H}} e^{\frac{i n \pi x}{L}} \right] \\
& \times \left[\sum_{m n = -\infty}^{+\infty} \bar{T}_{m n}(t) e^{\frac{i m \pi y}{H}} e^{\frac{i n \pi x}{L}} \right] \\
& - c_b \left[\sum_{m n = -\infty}^{+\infty} W_{m n} e^{\frac{i m \pi y}{H}} e^{\frac{i n \pi x}{L}} \right] \left[\sum_{m n = -\infty}^{+\infty} \bar{T}_{m n}(t) e^{\frac{i m \pi y}{H}} e^{\frac{i n \pi x}{L}} \right] \\
& + \left[\sum_{m n = -\infty}^{+\infty} Q_{m n}(t) e^{\frac{i m \pi y}{H}} e^{\frac{i n \pi x}{L}} \right]
\end{aligned}$$

Taking a Taylor series expansion of $\bar{T}_{m n}(t)$ and $Q_{m n}(t)$ to first order, we obtain

$$\bar{T}_{m n}(t) = \bar{T}_{m n}(t_0) + t \bar{T}'_{m n}(t_0)$$

$$Q_{m n}(t) = Q_{m n}(t_0) + t Q'_{m n}(t_0)$$

Then

$$p_t c_t \frac{\partial}{\partial t} \left[\sum_{m n = -\infty}^{+\infty} \bar{T}_{m n}(t) e^{\frac{i m \pi y}{H}} e^{\frac{i n \pi x}{L}} \right] =$$

$$\begin{aligned}
& \left[\frac{i\pi\pi}{H} + \frac{i\pi\pi}{L} \right]^2 \left[\sum_{mn=-\infty}^{+\infty} A_{mn} e^{\frac{i\pi\pi y}{H}} e^{\frac{i\pi\pi x}{L}} \right] \left[\sum_{mn=-\infty}^{+\infty} \bar{T}_{mn}(t_0) e^{\frac{i\pi\pi y}{H}} e^{\frac{i\pi\pi x}{L}} \right] \\
& + \left[\left(\frac{i\pi\pi}{H} \right)^2 + \left(\frac{i\pi\pi}{L} \right)^2 \right] \left[K_N + \sum_{mn=-\infty}^{+\infty} A_{mn} e^{\frac{i\pi\pi y}{H}} e^{\frac{i\pi\pi x}{L}} \right] \\
& \times \left[\sum_{mn=-\infty}^{+\infty} \bar{T}_{mn}(t_0) e^{\frac{i\pi\pi y}{H}} e^{\frac{i\pi\pi x}{L}} \right] \\
& - c_b \left[\sum_{mn=-\infty}^{+\infty} W_{mn} e^{\frac{i\pi\pi y}{H}} e^{\frac{i\pi\pi x}{L}} \right] \left[\sum_{mn=-\infty}^{+\infty} \bar{T}_{mn}(t_0) e^{\frac{i\pi\pi y}{H}} e^{\frac{i\pi\pi x}{L}} \right] \\
& + \left[\sum_{mn=-\infty}^{+\infty} Q_{mn}(t_0) e^{\frac{i\pi\pi y}{H}} e^{\frac{i\pi\pi x}{L}} \right] \\
& + \left[\frac{i\pi\pi}{H} + \frac{i\pi\pi}{L} \right]^2 \left[\sum_{mn=-\infty}^{+\infty} A_{mn} e^{\frac{i\pi\pi y}{H}} e^{\frac{i\pi\pi x}{L}} \right] \left[\sum_{mn=-\infty}^{+\infty} \bar{T}'_{mn}(t_0) e^{\frac{i\pi\pi y}{H}} e^{\frac{i\pi\pi x}{L}} \right] \\
& + \left[\left(\frac{i\pi\pi}{H} \right)^2 + \left(\frac{i\pi\pi}{L} \right)^2 \right] \left[K_N + \sum_{mn=-\infty}^{+\infty} A_{mn} e^{\frac{i\pi\pi y}{H}} e^{\frac{i\pi\pi x}{L}} \right] \\
& \times \left[\sum_{mn=-\infty}^{+\infty} \bar{T}'_{mn}(t_0) e^{\frac{i\pi\pi y}{H}} e^{\frac{i\pi\pi x}{L}} \right] \\
& - c_b \left[\sum_{mn=-\infty}^{+\infty} W_{mn} e^{\frac{i\pi\pi y}{H}} e^{\frac{i\pi\pi x}{L}} \right] \left[\sum_{mn=-\infty}^{+\infty} \bar{T}'_{mn}(t_0) e^{\frac{i\pi\pi y}{H}} e^{\frac{i\pi\pi x}{L}} \right]
\end{aligned}$$

$$+ \left[\sum_{mn=-\infty}^{+\infty} Q'_{mn}(t_0) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right]$$

The products of two convergent series

$$a = a_1 + a_2 + a_3 + \dots + a_n + \dots$$

$$b = b_1 + b_2 + b_3 + \dots + b_n + \dots$$

is $ab = a_1 b_1 + (a_1 b_2 + a_2 b_1) + \dots$

$$\dots + (a_1 b_n + a_2 b_{n-1} + \dots + a_{n-1} b_2 + a_n b_1) + \dots$$

$$= \sum_{n=1}^{+\infty} (a_1 b_n + a_2 b_{n-1} + \dots + a_{n-1} b_2 + a_n b_1)$$

$$= \sum_{n=1}^{+\infty} c_n \quad \text{where} \quad c_n = \sum_{m=1}^n a_m b_{n-m+1}$$

which holds when the last series converges, and always holds when a and b converge absolutely.

Using this method in two dimensions:

$$ab = a_{11}b_{11} + (a_{11}b_{12} + a_{12}b_{11}) + (a_{21}b_{11} + a_{11}b_{21})$$

$$+ (a_{11}b_{22} + a_{12}b_{21} + a_{21}b_{12} + a_{22}b_{11}) + \dots$$

we combine the series such that:

$$\sum_{mn=-\infty}^{+\infty} D I_{mn}(t_0) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} =$$

$$\left[\sum_{mn=-\infty}^{+\infty} A_{mn} e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right] \left[\sum_{mn=-\infty}^{+\infty} \bar{T}_{mn}(t_0) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right]$$

$$\sum_{mn=-\infty}^{+\infty} D2_{mn}(t_0) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} =$$

$$\left[\sum_{mn=-\infty}^{+\infty} W_{mn} e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right] \left[\sum_{mn=-\infty}^{+\infty} \bar{T}_{mn}(t_0) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right]$$

$$\sum_{mn=-\infty}^{+\infty} E1_{mn}(t_0) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} =$$

$$\left[\sum_{mn=-\infty}^{+\infty} A_{mn} e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right] \left[\sum_{mn=-\infty}^{+\infty} \bar{T}'_{mn}(t_0) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right]$$

$$\sum_{mn=-\infty}^{+\infty} E2_{mn}(t_0) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} =$$

$$\left[\sum_{mn=-\infty}^{+\infty} W_{mn} e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right] \left[\sum_{mn=-\infty}^{+\infty} \bar{T}'_{mn}(t_0) e^{\frac{im\pi y}{H}} e^{\frac{in\pi x}{L}} \right]$$

Inserting these into the bioheat equation, and canceling away the Fourier space terms, we find:

$$\begin{aligned}
p_t c_t \frac{\partial}{\partial t} \bar{T}_{mn}(t) = & \left[\frac{im\pi}{H} + \frac{in\pi}{L} \right]^2 D1_{mn}(t_0) + \left[\left(\frac{im\pi}{H} \right)^2 + \left(\frac{in\pi}{L} \right)^2 \right] \\
& \times \left[K_N \bar{T}_{mn}(t_0) + D1_{mn}(t_0) \right] - c_b D2_{mn}(t_0) + Q_{mn}(t_0) \\
& + t \left[\left[\frac{im\pi}{H} + \frac{in\pi}{L} \right]^2 E1_{mn}(t_0) + \left[\left(\frac{im\pi}{H} \right)^2 + \left(\frac{in\pi}{L} \right)^2 \right] \right. \\
& \left. \times \left[K_N \bar{T}'_{mn}(t_0) + E1_{mn}(t_0) \right] - c_b E2_{mn}(t_0) + Q'_{mn}(t_0) \right] \quad (21)
\end{aligned}$$

Expanding $\bar{T}_{mn}(t)$ into a MacLaurin expansion, we get:

$$\bar{T}_{mn}(t) = \bar{T}_{mn}(t_0) + \beta_{mn} t + \frac{\mu_{mn}}{2} t^2 \quad (22)$$

where $\beta_{mn} = \bar{T}'_{mn}(t_0)$ and $\mu_{mn} = \bar{T}''_{mn}(t_0)$.

Therefore,

$$\frac{\partial}{\partial t} \bar{T}_{mn}(t) = \beta_{mn} + \mu_{mn} t. \quad (23)$$

Equating (21) and (23) we find that

$$\begin{aligned}
\beta_{mn} = & \frac{1}{p_t c_t} \left[\left[\frac{im\pi}{H} + \frac{in\pi}{L} \right]^2 D1_{mn}(t_0) + \left[\left(\frac{im\pi}{H} \right)^2 + \left(\frac{in\pi}{L} \right)^2 \right] \right. \\
& \times \left[K_N \bar{T}_{mn}(t_0) + D1_{mn}(t_0) \right] - c_b D2_{mn}(t_0) + Q_{mn}(t_0) \left. \right]
\end{aligned}$$

$$\mu_{mn} = \frac{1}{p_t c_t} \left[\left[\frac{im\pi}{H} + \frac{in\pi}{L} \right]^2 E1_{mn}(t_o) + \left[\left(\frac{im\pi}{H} \right)^2 + \left(\frac{in\pi}{L} \right)^2 \right] \right. \\ \left. \times \left[K_N \bar{T}'_{mn}(t_o) + E1_{mn}(t_o) \right] - c_b E2_{mn}(t_o) + Q'_{mn}(t_o) \right]$$

Since thermal conductivity causes heat flow to behave exponentially, we set:

$$\bar{T}_{mn}(t) = \left[\bar{T}_{mn}(\infty) - \bar{T}_{mn}(t_o) \right] \left[1 - e^{-\Omega_{mn} t} \right] + \bar{T}_{mn}(t_o) \quad (18)$$

Equating (22) and (18) we obtain

$$\beta_{mn} t + \frac{\mu_{mn}}{2} t^2 = \left[\bar{T}_{mn}(\infty) - \bar{T}_{mn}(t_o) \right] \left[1 - e^{-\Omega_{mn} t} \right] \\ = \left[\bar{T}_{mn}(\infty) - \bar{T}_{mn}(t_o) \right] \left[1 - \left(1 - \Omega_{mn} t + \frac{(\Omega_{mn} t)^2}{2!} \right) \right] \\ = \left[\bar{T}_{mn}(\infty) - \bar{T}_{mn}(t_o) \right] \left[\Omega_{mn} t - \frac{(\Omega_{mn} t)^2}{2} \right]$$

Equating terms we find:

$$\beta_{mn} = \left[\bar{T}_{mn}(\infty) - \bar{T}_{mn}(t_o) \right] \Omega_{mn}$$

$$\mu_{mn} = \left[\bar{T}_{mn}(\infty) - \bar{T}_{mn}(t_o) \right] \Omega_{mn}^2$$

$$\text{Hence, } \Omega_{mn} = \frac{\mu_{mn}}{\beta_{mn}} \text{ and } \bar{T}_{mn}(\infty) = \frac{\beta_{mn}^2}{\mu_{mn}} + \bar{T}_{mn}(t_o)$$

which can be substituted into (18) to find the solution for $\bar{T}_{mn}(t)$, for a given time step t .

To solve the same equation linearly, we use the fact that:

$$B_{mn} = \bar{T}'_{mn}(t_0)$$

Since to first order

$$\bar{T}_{mn}(t) = \bar{T}_{mn}(t_0) + t \bar{T}'_{mn}(t_0)$$

then $\bar{T}_{mn}(t) = \bar{T}_{mn}(t_0) + t B_{mn}$ for a given time step t .

APPENDIX 2

A Computer Program using the Fourier Method

The program FMETHOD was developed to solve the bioheat equation using the Fourier method described in Appendix 1. It is controlled by the main routine FMETHOD, where the temperature is calculated using (18). The three main subroutines that are called are INPAR, EQUAN, and PPACK. The first, INPAR, is where the initial parameters are declared and the Time=0 temperature distribution is constructed. The second, EQUAN, determines the Ω and $T(\infty)$ parameters in (18), by first determining β and μ (see Appendix 1). Finally, PPACK is simply the printing package, which is rather primitive, but like the entire program has the ability to be transferable to any computer system using FORTRAN. The rest of the subroutines are called by these four, and are explained in the program.

PROGRAM FMETHOD

The following program determines the heat flow in a given biological medium. It does this by solving the bioheat equation using a numerical technique based on Fourier series expansion.

The include statement 'HYPO' contains the common blocks and parameter statements.

```
INCLUDE 'HYPO.CMM'
COMPLEX SU(-NX:NX,-NX:NX),KA(-NX:NX,-NX:NX)
COMPLEX W(-NX:NX,-NX:NX),Q(-NX:NX,-NX:NX)
COMPLEX QP(-NX:NX,-NX:NX),BACK(-NX:NX,-NX:NX)
COMPLEX TZERO(-NX:NX,-NX:NX)
```

Set up the input parameters by calling the subroutine 'INPAR'

```
CALL INPAR(KA,W,Q,QP,TZERO,BACK)
```

The number of time steps used is NUMIT

```
NUMIT=10
WRITE(2,*) '..POWER DEP IN MIDDLE FOR 3 MIN...'
WRITE(2,*) '..POWER DEP REMOVED FOR 3 MIN....PREC=20'
WRITE(2,*) 'TIME STEP 60.0 SEC...DIM -1*1..-2*2'
```

Within the following DO loop we calculate the new temperature values T(X+1) by forcing them to conform to an exponential function.

```
DO 99 X=0,NUMIT
```

The power deposition term is turned off at a certain time

```
IF(X.EQ.5) THEN
  CALL NULSUB(Q)
END IF
```

Calculate the bioheat equation and by determining the values for OMEGA and T(infinity). This is done in the subroutine EQUAN

```
CALL EQUAN(KA,W,Q,QP,TZERO,BACK)
```

Set the time increment TINCR between each time step NUMIT.

```
TINCR=60.
```


C
C Calculate the new temperature $T(x+1)$ by forcing them to
C conform to an exponential function. This allows for greater
C time increments $TINCR$ than if a linear fit were to be used.
C The Fourier space range is $M \times N$ in size.
C

```

          DO 98 M=-PREC,PREC
            DO 97 N=-PREC,PREC
              T(X+1,M,N)=( (TINF(X,M,N)-T(X,M,N)) ) *
+              (1.-EXP(-OMEGA(X,M,N)*TINCR))+T(X,M,N)
97          CONTINUE
98          CONTINUE

```

C
C Set the new temperature equivalent to the old one.
C This allows the process to be repeated, and standardizes
C the dimension size of the array when calling the printing
C package.
C If desired, the total history of the heat flow can be
C viewed, and reconstructed by recalling T , $OMEGA$, and $T(infinity)$.
C

```

          DO 399 M=-PREC,PREC
            DO 398 N=-PREC,PREC
              TZERO(M,N)=T(X+1,M,N)
398          CONTINUE
399          CONTINUE
99          CONTINUE

```

C
C
C
C After the entire history of the heat flow is calculated,
C it is called up for printing on the subroutine PPACK.
C

```

          DO 96 X=0,NUMIT
            DO 90 M=-PREC,PREC
              DO 91 N=-PREC,PREC
                SU(M,N)=T(X,M,N)
91          CONTINUE
90          CONTINUE

          WRITE(2,92)
          WRITE(2,*) 'HEAT DISTRIBUTION T=',X
          CALL PPACK(SU)

96          CONTINUE
92          FORMAT('1')
          STOP
          END

```



```

C      State the thermal conductivity of the normal tissue (J/cm/g/C)
        KN=6.4E-3

C      State the normal tissue volumetric blood flow rate (cm**3/g/sec)
        W1=2.0E-3
        WNEW=W1

C      (WNEW acts as a flag in EQUAN)

C
C
C      Construct the exponential components of the fourier
C      and inverse fourier transforms.
C
        CALL SETUP
        CALL ARRAY

C
C
C      What is the initial temperature distribution?
C      Where T1 is the temperature, and TXN# & TYN#
C      are the bounds of the distribution
C      FACT constructs a rectangular function in two
C      dimensions.
C
        T1=0.0
        TXN1=LENX
        TXN2=-LENX
        TYN1=LENY
        TYN2=-LENY
        CALL FACT(TXN1, TXN2, TYN1, TYN2, T1, TZERO)

C
C
C      What is the distribution of the medium?
C      (Tumors, bones, fat, or other non-homogeneities
C      in the background)
C
C      If there is a space dependency for the thermal
C      conductivity, then state it in KA1.
C
        KA1=0.0
        KANEW=KA1

C
C      The space dependency for W1 is constructed
C      as well as a general background term TB.
C
C      These background terms can be extended, to gaussian
C      shapes, or whatever continuous form desired.
C      This can be accomplished quite easily.
C      In the cases studied, only simple geometries were
C      used, but the same principles can be applied for
C      more complex ones.
C

```

TB=0.0

BXN1=LENX
 BXN2=-LENX
 BYN1=LENY
 BYN2=-LENY

CALL FACT(BXN1,BXN2,BYN1,BYN2,KA1,KA)
 CALL FACT(BXN1,BXN2,BYN1,BYN2,W1,W)
 CALL FACT(BXN1,BXN2,BYN1,BYN2,TB,BACK)

C
 C
 C
 C
 C
 C
 C
 C
 C

The power deposition form is constructed.
 Once again, whatever shape is desired.
 Note however, that due to Nyquists theorem, a point
 source power deposition will not be properly described
 by a fourier approximation.

C
 C
 C
 C

The term Q1 is the power deposition term assuming
 it is a constant, and QP is the derivative over time.
 The term QP (and its shape) must be calculated seperately.

Q1=0.1
 QP1=0.0

QXN1=-1.
 QXN2=1.
 QYN1=-2.
 QYN2=2.

CALL FACT(QXN1,QXN2,QYN1,QYN2,Q1,Q)
 CALL FACT(QXN1,QXN2,QYN1,QYN2,QP1,QP)

C
 C
 C
 C
 C
 C

The initial temperature TZERO is now stored, and
 redimensionalized for insertion into the exponential
 fitting equation.

DO 199 M=-PREC,PREC
 DO 198 N=-PREC,PREC
 T(0,M,N)=TZERO(M,N)
 198 CONTINUE
 199 CONTINUE
 195 FORMAT('1')
 RETURN
 END

```

C          SUBROUTINE NEW(A,B,C)
C          -----
C          This subroutine is used in assembling background,
C          and complex geometries. It simply superimposes one
C          configuration onto another.
C          It has not been called in this example, but is
C          usually called from INPAR.
C
C          Dimensionalize, and declare the variables
C          INCLUDE 'HYPO.CMM'
C          COMPLEX A(-NX:NX,-NX:NX),B(-NX:NX,-NX:NX)
C          COMPLEX C(-NX:NX,-NX:NX)
C
C          Add the fourier field elements
C
C          DO 999 M=-PREC,PREC
C            DO 998 N=-PREC,PREC
C              A(M,N)=B(M,N)+C(M,N)
998          CONTINUE
999          CONTINUE
C
C          RETURN
C          END

```

```

C          SUBROUTINE ARRAY
C          -----
C          This subroutine constructs the exponential term in
C          the fourier transformations.
C
C          Dimensionalize and declare the variables
C
C          INCLUDE 'HYPO.CMM'
C
C          Calculate the exponential terms and insert them
C          into arrays.
C
C          DO 200 M=-PREC,PREC
C            ZGX(M)=(-1.)*ZI*FLOAT(M)*PI/LENX
C            ZGY(M)=(-1.)*ZI*FLOAT(M)*PI/LENY
200          CONTINUE
C
C          RETURN
C          END

```

```
SUBROUTINE FACT(XN1,XN2,YN1,YN2,CONST,FC)
```

```
-----
```

```
C
C
C      This subroutine performs a fourier transformation
C      on the initial parameters. Thereby transferring the
C      initial geometry into fourier space.
```

```
C      This particular subroutine constructs a rectangular
C      shape. Other subroutines can be written for different
C      geometries.
```

```
C
C      Declare the variables
```

```
C      INCLUDE 'HYPO.CMM'
```

```
C      REAL XN1,XN2,YN1,YN2,CONST
```

```
C      COMPLEX FC(-NX:NX,-NX:NX),FA(-NX:NX),FB(-NX:NX)
```

```
C
C      Since the fourier terms are independent in real
C      space, they can be constructed seperately and
C      then multiplied together (they are not linearly
C      independent in real space).
```

```
C
C      DO 89 M=-PREC,PREC
```

```
C      Each of the fourier transformation is evaluated
C      where one of the terms ( m or n) is equal to zero.
```

```
C      IF(M.EQ.0) THEN
```

```
C          FA(M)=(1./(2.*LENX))*(YN2-XN1)
```

```
C          FB(M)=(1./(2.*LENY))*(YN2-YN1)
```

```
C      ELSE
```

```
C      Each of the fourier transformation is evaluated
C      where neither term is zero.
```

```
C          FA(M)=(1./(2.*PI*FLOAT(M)*(-ZI)))
```

```
+          *(EXP(ZGX(M)*XN2)-EXP(ZGX(M)*XN1))
```

```
C          FB(M)=(1./(2.*PI*FLOAT(M)*(-ZI)))
```

```
+          *(EXP(ZGY(M)*YN2)-EXP(ZGY(M)*YN1))
```

```
C      END IF
```

```
89      CONTINUE
```

```
C
C      The fourier terms are multiplied together
C      to form the total transform FC.
```

```
C      DO 88 M=-PREC,PREC
```

```
C      DO 87 N=-PREC,PREC
```

```
C          FC(M,N)=CONST*FA(M)*FB(N)
```

```
87      CONTINUE
```

```
88      CONTINUE
```

```
C      RETURN
```

```
C      END
```

```

SUBROUTINE EQUAN(KA,W,Q,QP,TZERO,BACK,
++++
C
C
C      This subroutine determines the values of OMEGA
C      and T(infinity) by evaluating the bioheat equation
C      in fourier space.
C
C
C      Declare the variables
C
C      INCLUDE 'HYPO.CMM'
C      COMPLEX KA(-NX:NX,-NX:NX),TZERO(-NX:NX,-NX:NX)
C      COMPLEX W(-NX:NX,-NX:NX),Q(-NX:NX,-NX:NX)
C      COMPLEX DA1(-NX:NX,-NX:NX),DA2(-NX:NX,-NX:NX)
C      COMPLEX EA1(-NX:NX,-NX:NX),EA2(-NX:NX,-NX:NX)
C      COMPLEX BACK(-NX:NX,-NX:NX)
C      COMPLEX BETA(-NX:NX,-NX:NX),QP(-NX:NX,-NX:NX)
C      COMPLEX MU,LAMDA
C      REAL FRONTA(-NX:NX,-NX:NX),CON1,CON2
C      REAL FRONTB(-NX:NX,-NX:NX)
C
C      If there is a homogeneous background, then there is
C      a constant thermal conductivity, and KA equals zero.
C      If this occurs, then there is no need to multiply it
C      with the temperature term. Therefore, it is set to zero
C      using the subroutine NULSUB.
C      This is done to avoid using the subroutine CRAM, since
C      it is CRAM which consumes the most CPU time.
C      (The term KANEW acts as a flag for KA)
C
C      IF(KANEW.EQ.0.0) THEN
C          CALL NULSUB(DA1)
C      ELSE
C          CALL CRAM(DA1,KA,TZERO)
C      END IF
C
C
C      If there is no blood flow, (the problem is strictly
C      a conductivity one) then the blood flow rate is set
C      to zero by calling NULSUB.
C
C      IF(WNEW.EQ.0.0) THEN
C          CALL NULSUB(DA2)
C      ELSE
C          CALL CRAM(DA2,W,TZERO)
C      END IF
C
C
C      The constants in the bioheat equation are calculated.
C
C      CON1=1./(ROWT*CT)
C      CON2=CB*ROWB/CT

```

C
C
C
C
C

The beta term used to calculate the bioheat equation is evaluated in fourier space.

DO 77 M=-PREC,PREC
DO 76 N=-PREC,PREC
FRONTA(M,N)=- (PI**2) * ((REAL(M)/LENX) + (REAL(N)/LENY)) **2)
FRONTB(M,N)=- (PI**2) * ((REAL(M)/LENX) **2 + (REAL(N)/LENY) **2)
BETA(M,N)=FRONTA(M,N)*CON1*DA1(M,N)-CON2*DA2(M,N)+
+ FRONTB(M,N)*CON1*(KN*TZERO(M,N)+DA1(M,N))+CON1*Q(M,N)
76 CONTINUE
77 CONTINUE

C
C
C
C
C
C

Once again, if the thermal conductivity is constant then its spatial dependent component is set to zero.

IF (KANEW.EQ.0.0) THEN
CALL NULSUB(EA1)
ELSE
CALL CRAM(EA1,KA,BETA)
END IF

C
C
C
C
C
C
C

Once again, if there is no blood flow, then the blood flow rate is set to zero.

IF (WNEW.EQ.0.0) THEN
CALL NULSUB(EA2)
ELSE
CALL CRAM(EA2,W,BETA)
END IF

C
C
C
C
C

The MU term is calculated, by evaluating the time derivative of the bioheat equation in fourier space

DO 75 M=-PREC,PREC
DO 74 N=-PREC,PREC
MU=FRONTA(M,N)*CON1*EA1(M,N)-CON2*EA2(M,N)+
+ FRONTB(M,N)*CON1*(KN*BETA(M,N)+EA1(M,N))+CON1*QP(M,N)

C
C
C
C
C
C

The following IF statements act as flags, to prevent any unexpected divergences from aborting the run.
If desired, a list of where any divergent term occurs can be inserted.

```
IF (BETA (M,N) .EQ. 0) THEN
  OMEGA (X,M,N) = 999999999.
```

```
ELSE
  OMEGA (X,M,N) = -MU/BETA (M,N)
END IF
```

```
IF (REAL (OMEGA (X,M,N)) .LT. (-.001)) THEN
  OMEGA (X,M,N) = 0.0
END IF
```

```
IF (OMEGA (X,M,N) .EQ. 0.) THEN
  TINF (X,M,N) = TZERO (M,N)
ELSE
  TINF (X,M,N) = TZERO (M,N) + (BETA (M,N) / OMEGA (X,M,N))
END IF
```

74 CONTINUE
75 CONTINUE

70 FORMAT (' 1')

RETURN
END

SUBROUTINE NULSUB (ONLY)

C
C
C
C
C
C
C
C

This subroutine sets all the elements in a fourier space array to zero.

Declare the variables

```
INCLUDE 'HYPO.CMM'
COMPLEX ONLY (-NX:NX, -NX:NX)
```

C
C
C

Set all the elements to zero.

```
DO 555 M=-PREC,PREC
  DO 556 N=-PREC,PREC
    ONLY (M,N) = (0.0, 0.0)
556 CONTINUE
555 CONTINUE
```

RETURN
END

SUBROUTINE CRAM(A,B,C)

This subroutine multiplies two 2-dimensional fourier space terms together. It is the most time consuming subroutine in the program.

Declare the variables

INCLUDE 'HYPO.CMM'

COMPLEX A(-NX:NX, -NX:NX), B(-NX:NX, -NX:NX), C(-NX:NX, -NX:NX)

Multiply the two converging series together, using the method described in chapter 4 of the thesis.

L, I, M, and N are all dummy variables

DO 21 L=-PREC, 0

DO 20 M=-PREC, 0

A(L, M)=0

A(-L, -M)=0

A(L, -M)=0

A(-L, M)=0

DO 31 I=-PREC, PREC+L

DO 30 N=-PREC, PREC+M

A(L, M)=A(L, M)+B(I, N)*C(L-I, M-N)

IF(L.EQ.0) GOTO 40

A(-L, M)=A(-L, M)+B(-I, N)*C(-(L-I), M-N)

IF(M.EQ.0) GOTO 30

A(-L, -M)=A(-L, -M)+B(-I, -N)*C(-(L-I), -(M-N))

IF(M.EQ.0) GOTO 30

A(L, -M)=A(L, -M)+B(I, -N)*C(L-I, -(M-N))

CONTINUE

CONTINUE

CONTINUE

CONTINUE

RETURN

END

SUBROUTINE SETUP

This subroutine constructs the exponential terms for the inverse fourier transformation. It does so by using trigonometric identities, rather than a direct construction. This saves on CPU time.

Declare variables

```
INCLUDE 'HYPO.CMM'
REAL XSSN,XCCS
DIMENSION XSSN(0:40,-NX:NX),XCCS(0:40,-NX:NX)
```

Construct the exponential terms.
(Note the .25 in the RXV term. This is inserted because the real space field is 40 pixels across and in this situation, 10 cm. Hence, each pixel is .25 cm. This adjustment must also be made in the subroutine PPACK)

The individual sine and cosine terms are calculated.

```
DO 630 XV=1,40
  RXV=(-20.+FLOAT(XV))*PI*.25/LENX
  XSSN(XV,0)=0.
  XSSN(XV,1)=SIN(RXV)
  XSSN(XV,-1)=-XSSN(XV,1)
  XCCS(XV,0)=1.
  XCCS(XV,1)=COS(RXV)
  XCCS(XV,-1)=XCCS(XV,1)

DO 631 M=2,PREC
  XSSN(XV,M)=2*XSSN(XV,M-1)*XCCS(XV,1)-XSSN(XV,M-2)
  XSSN(XV,-M)=-XSSN(XV,M)
  XCCS(XV,M)=2*XCCS(XV,M-1)*XCCS(XV,1)-XCCS(XV,M-2)
  XCCS(XV,-M)=XCCS(XV,M)
```

631 CONTINUE

630 CONTINUE

The sine and cosine terms are added to give the total function. This is a result of Euler's identity.

```
DO 633 XV=1,40
  DO 634 M=-PREC,PREC
    PART1(XV,M)=XCCS(XV,M)+ZI*XSSN(XV,M)
```

634 CONTINUE

633 CONTINUE

RETURN
END

```

C      SUBROUTINE PPACK(SU)
C      ++++++
C
C      This subroutine is the printing package.
C      The real space points are printed on a 40 x 40 pixel
C      grid, where the values 0 to 9 represent the increased
C      temperature. On a color graphics screen, the numbers
C      can be replaced with color pixels, for easier viewing.
C
C      Declare the variables
C
C      INCLUDE 'HYPO.CMM'
C      INTEGER J
C      REAL TIN, TP, TM, TEMP, TEMPN, LANC, GOOP
C      COMPLEX SU
C      CHARACTER*40 LINE
C      CHARACTER*1 COL
C      DIMENSION COL(0:9), TEMP(40,40), SU(-NX:NX, -NX:NX), LANC(-NX:NX)
C
C      Set the temperature pixel values.
C
C      COL(0)='0'
C      COL(1)='1'
C      COL(2)='2'
C      COL(3)='3'
C      COL(4)='4'
C      COL(5)='5'
C      COL(6)='6'
C      COL(7)='7'
C      COL(8)='8'
C      COL(9)='9'
C
C      The Lanczos convergence factor is included here, to
C      shrink the effect of the Gibbs phenomenon. For functions
C      without a discontinuity, it is not required.
C
C      DO 444 M=-PREC,PREC
C        IF (M.EQ.0) THEN
C          LANC(M)=1.
C        ELSE
C          GOOP=REAL(M)*PI/REAL(PREC)
C          LANC(M)=SIN(GOOP)/GOOP
C        END IF
C      CONTINUE
444
C
C      The inverse fourier transformation is performed
C      on the fourier space temperature values, to obtain
C      the temperature in real space.
C      (see subroutine SETUP for a comment on the .25 values)
C

```

```
DO 698 YV=1,40
  RYV=(-20.+FLOAT(YV))*.25
```

```

7) 697 XV=1,40
    RXV=(-20.+FLOAT(XV))*.25
    ZTEMP=(0,0)

```

The real space temperature is calculated, with the Lanzcos convergence factor included.

```

DO 696 M=-PREC,PREC
DO 695 N=-PREC,PREC
ZTEMP=ZTEMP+SU (M,N) *LANC (M) *LANC (N) *PART1 (XV,M) *PART1 (YV,N)
CONTINUE
CONTINUE

```

The complex component of the temperature is removed.

TEMP (YV, XV) = REAL (ZTEMP)

CONTINUE
CONTINUE

The maximum, and minimum temperatures in the field are determined. The temperature field is divided into ten equal parts, and a number assigned to each. In this case, the field is divided into ten .5 degree intervals.

TP=-1000.0
TM=1000.0

```
DO 620 YV=1,40
  DO 619 XV=1,40
    TP=MAX(TP,TEMP(YV,XV))
    TM=MIN(TM,TEMP(YV,XV))
  CONTINUE
CONTINUE
```

The term TIN is the size of each temperature increment.

$$TIN = (TP - TM) / 10.$$

```
WRITE(2,*) 'THE MAXIMUM TEMPERATURE IS',TP
WRITE(2,*) 'THE MINIMUM TEMPERATURE IS',TM
WRITE(2,*) 'THE TEMPERATURE FIELD IS DIVIDED'
WRITE(2,*) 'INTO TEN INCREMENTS; EACH 0.5 CELSIUS'
```

```

C
C      The term TIN is overided to form a .5 celsius increment
      TIN=0.5
      TP=5.0
      TM=0.0
C
C      The value for each pixel is determined, and the temperature
C      plot is written line by line.
C
      DO 618 YV=1,40
        DO 617 XV=1,40
          LINE(XV:XV)=COL(0)
          DO 694 J=0,9
            TEMPN=TM+(FLOAT(J)*TIN)
            IF ((TEMP(YV,XV)-TEMPN).GT.(0.0001)) LINE(XV:XV)=COL(J)
694          CONTINUE
617        CONTINUE

          WRITE(2,13) LINE

618      CONTINUE

650      FORMAT('1')
13      FORMAT(' ',A40)

      RETURN
      END

```

C
C
C
C
C
C
C

The INCLUDE statement HYPO.CMM

This shortens the written length of the program.

```

INTEGER PREC,NX,X,NUMIT,M,N,XV,YV
REAL TINCX,LENX,LENY,TB,CB,CT
REAL KN,ROWB,ROWT,KANEW,WNEW
REAL PI,RXV,RV
COMPLEX ZI,ZGX,ZGY,ZTEMP,OMEGA,TINF,T,PART1
PARAMETER (NX=50,ZI=(0,-1.),PI=3.14159265359)
COMMON LENX,LENY,ZGX(-NX:NX),ZGY(-NX:NX),PREC
COMMON T(0:12,-NX:NX,-NX:NX),OMEGA(0:12,-NX:NX,-NX:NX)
COMMON TINF(0:12,-NX:NX,-NX:NX),PART1(0:40,-NX:NX)
COMMON TB,CB,CT,ROWB,ROWT,KN,X,KANEW,WNEW

```

C
C
C

References

- 1 W.B. Coley, "The treatment of malignant tumor by repeated inoculations of erysipelas with a report of original cases.", *Amer. J. Med. Sci.*, 105: 487-511, 1893.
- 2 G.L. Rohdenburg, "Fluctuations in the growth of malignant tumors in man, with special reference to spontaneous recession.", *J. Can. Res.*, 3:193-225, 1918.
- 3 H.N. Stevenson, "The effect of heat upon tumor tissues." *J. Can. Res.*, 4:54, 1919.
- 4 G. Pincus, and A. Fischer, "The growth and death of tissue cultures exposed to supranormal temperatures.", *J. Exp. Med.*, 54: 323-332, 1931.
- 5 O. Selawry, M. Goldstein, and T. McCormick, "Hyperthermia in tissue-cultured cells of malignant origin." *Can. Res.*, 17: 785-791, 1957.
- 6 G. Crile Jr., "Selective destruction of cancers after exposure to heat." *Ann. of Surg.*, 156: 404-407, 1962.
- 7 G. Crile Jr., "The effects of heat and radiation on cancers implanted into the feet of mice.", *Can. Res.*, 23: 372-380, 1963.
- 8 R. Cavaliere, et. al., "Selective heat sensitivity of cancer cells - biochemical and clinical studies.", *Cancer*, 20: 1351-1381, 1967.
- 9 F.K. Storm, Ed., "Hyperthermia in Cancer Therapy.", G.K. Hall, Boston, 1983.

- 10 G.M. Hahn, "Hyperthermia and Cancer.", Plenum Press, New York, 1982.
- 11 C. Streffer, Ed., "Cancer Therapy by Hyperthermia and Radiation: Proceedings of the 2nd International Symposium.", Urban & Schwarzenberg, Munich, 1978.
- 12 P. Greenwald, Ed., "Cancer Therapy by Hyperthermia, Drugs, and Radiation: Third International Symposium.", U.S. Dept. Health & Human Serv., 1980.
- 13 R. Jain, and P. Gullino, Ed., "Thermal Characteristics of Tumors: Applications in Detection and Treatment. Annals of the New York Academy of Sciences. Vol. 335." N.Y. Academy of Sciences, N.Y., 1980.
- 14 H. I. Robins, et al, "Whole body hyperthermia with a microwave regional boost: unexpected toxicity in the pig.", Int. J. Rad. Biol., 44, 469, 1983.
- 15 D. E. Lee, et al, "Internal organ hypoxia during hyperthermia cancer therapy in humans.", Natl. Can. Inst. Mon., 61, 399, 1982.
- 16 R. T. Pettigraw, J. M. Galt, C. M. Ludgate, and A. N. Smith, "Clinical effects of whole-body hyperthermia in advanced malignancy.", Br. Med. J., 2, 679, 1974.
- 17 B. Barlogie, et al, "Total-body hyperthermia with and without chemotherapy for advanced human neoplasms.", Can. Res., 39, 1481, 1979.
- 18 E. R. Atkinson, "Assessment of current hyperthermia technology.", Can. Res., 39, 2314, 1979.

- 19 B. C. Giovanella, "Summary of the informal discussion of future clinical and basic research needs.", *Can. Res.*, 39, 2339, 1979.
- 20 A. Westra, and W.C. Dewey, "Heat shock during the cell cycle of Chinese hamster cells in vitro.", *Int. J. Rad. Biol.*, 19: 467-477.
- 21 K.J. Henle, and L.A. Dethlefsen, "Time-temperature relationship for heat induced killing of mammalian cells.", *Ann. N.Y. Acad. Sci.* [335], 234-253, 1980.
- 22 S.A. Sapareto, et. al., "Effect of hyperthermia on survival and progression of Chinese hamster ovary cells.", *Can. Res.*, 38: 393-400, 1978.
- 23 K.J. Henle, "Sensitization to hyperthermia below 43 Celsius induced in Chinese hamster ovary cells by step-down heating.", *J. Nat. Can. Inst.*, 64: 1479-1483, 1980.
- 24 O.S. Nielsen, K.J. Henle, and J. Overgaard, "Arrhenius analysis of survival curves from thermotolerant and step-down heated L1A2 cells in vitro.", *Rad. Res.* 91:468-482 1982.
- 25 B.K. Bhuyan, "Kinetics of cell kill by hyperthermia." *Can. Res.* 39: 2277-2284 1979.
- 26 M. J. Schlesinger, M. Ashburner, and A. Tissieres, Eds., "Heat Shock From Bacteria to Man.", Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., 1982.
- 27 Lee Gerig, *Conversations with Dr. Gerig*, 1988.

2 of/de 2

MicroD

- 28 E.P. Clark, W.C. Dewey, and J.T. Lett, "Recovery of CHO cells from hyperthermic potentiation to x-rays: Repair of DNA and Chromatin.", *Rad. Res.* 85: 302-313, 1981.
- 29 G.P. Raaphorst, et al., "Intrinsic differences in heat and/or x-ray sensitivity of seven mammalian cell lines cultured and treated under identical conditions." *Can. Res.* 39: 396-401, 1979.
- 30 E. Dikomey, "Differential cytotoxic effects of hyperthermia below and above 43 Celsius alone or combined with X irradiation." *Rad. Res.* 88: 489-501, 1981.
- 31 J.S. Stehlin Jr., et al., "Eleven years experience with hyperthermic perfusion for melanoma of the extremities.", *World J. Surg.* 3: 305-307, 1979.
- 32 W. C. Dewey, S. A. Sapareto, and D. A. Betten, "Hyperthermic radiosensitization of synchronous Chinese hamster cells: relationship between lethality and chromosomal aberrations.", *Rad. Res.*, 76, 48, 1978.
- 33 D.A. Christensen, and C.H. Durney, "Hyperthermia production for cancer therapy: A review of fundamentals and methods." *J. Micro. Power.* 16(2): 89-105, 1981.
- 34 H.H. Pennes, "Analysis of tissue and arterial blood temperatures in the resting human forearm.", *J. Applied Physiology* 1: 93-122, 1948.
- 35 E. Cravalho, et al., "The application of the bioheat equation to the design of thermal protocols for local hyperthermia." *Ann. N.Y. Acad. Sci.* [335]: 86-97, 1980.

36 S. Weinbaum, L.M. Jiji, and D.E. Lemons, "Theory and experiment for the effect of vascular microstructure on surface tissue heat transfer. Part 1: Anatomical foundation and model conceptualization." *Am. Soc. Eng. J. Biomech. Eng.*

37 J.W. Strohben, "Calculation of absorbed power in tissue for various hyperthermia devices." *Can. Res. (Suppl.)*, 44: 4781s-4.87s, 1984.

38 R.K. Jain, J.M. Weissbrod, and J. Wei, "Mass transport in tumors: Characterization and application to chemotherapy.", *Adv. in Can. Res.* 33: 251-310, 1980.

39 H.G. Klinger, "Heat transfer in perfused biological tissue-II. The 'macroscopic temperature distribution' in tissue.", *Bull. Math. Biol.* 40: 183-199, 1978.

40 H.F. Bowman, E.G. Cravalho, and M. Woods, "Theory, measurement, and application of thermal properties of biomaterials.", *Ann. Rev. Biophys. and Bioeng.* 4: 43-76, 1975.

41 A.B. Elkowitz, A. Shitzer, and R.C. Eberhart, "Transient temperature profiles in tissue with non-uniform blood flow distributions.", *J. of Biomech. Eng.*, 104: 202-208, 1982.

42 J.C. Chato, "Measurement of thermal properties of growing tumors.", *Ann. N.Y. Acad. Sci.* [335]: 67-85, 1980.

43 T.V. Samulski, "Correlations of thermal washout rate, steady state temperatures, and tissue type in deep seated recurrent or metastatic tumors.", *Int. J. Rad. Oncology Biol. Phys.* 13: 907-916, 1987.

- 44 A. Shitzer, and M.K. Kleiner, "On the relationship between blood perfusion, metabolism, and temperature in biological tissue heat balance.", *J. of Biomech. Eng.* 102: 162-169, 1980.
- 45 A.J. Milligan, et al., "Predictions of blood flow from thermal clearance during regional hyperthermia.", *Int. J. Rad. Oncology Biol. Phys.* 9: 1335-1341, 1983.
- 46 J. Patterson, and R. Strang, "The role of blood flow in hyperthermia.", *Int. J. Rad. Oncology Biol. Phys.* 5:235-241, 1979.
- 47 T.S. Sandhu, "Measurement of blood flow using temperature decay: effect of thermal conduction.", *Int. J. Rad. Oncology Biol. Phys.* 12: 373-378, 1986.
- 48 R. Strang, and J. Patterson, "The role of thermal conduction in hyperthermia.", *Int. J. Rad. Oncology Biol. Phys.* 6: 729-735, 1980.
- 49 J.M. Hill, and J.N. DeWynne, "Heat Conduction.", Blackwell Scientific Publications, Oxford, 1987.
- 50 E.B. Becker, G.F. Carey, and J.T. Oden, "Finite Elements. An Introduction: Vol. I.", Prentice Hall Inc., Englewood Cliffs, New Jersey, 1981.
- 51 C.A. Brebbia, "The Boundary Element Method for Engineers.", Pentech Press, London, 1978.

- 52 P.K. Banerjee, R. Butterfield, "Boundary Element Methods in Engineering Science.", McGraw-Hill Book Company (U.K.), London, 1981.
- 53 W.M. Rohsenow, J.P. Hartnett, and E.N. Ganic ed., "Handbook of Heat Transfer Fundamentals 2nd Ed.", McGraw-Hill Book Company, N.Y., 1985.
- 54 W.J. Minkowycz, E.M. Sparrow, G.E. Schneider, and R.H. Pletcher, "Handbook of Numerical Heat Transfer.", John Wiley & Sons, N.Y., 1988.
- 55 M. Ozisik, "Heat Conduction.", John Wiley & Sons, N.Y., 1980.
- 56 T.M. Shih, "Numerical Heat Transfer.", Hemisphere Publishing Co., Washington, 1984.
- 57 B.A. Finlayson, "The Method of Weighted Residuals and Variational Principles, with Application in Fluid Mechanics, Heat, and Mass Transfer.", Academic Press, N.Y., 1972.
- 58 R.D. Richtmyer, and K.W. Morton, "Difference Methods for Partial Differential Equations.", John Wiley, New York, 1960.
- 59 O.C. Zienkiewicz, "The Finite Element Method in Engineering Science 2nd ed.", McGraw-Hill, London, 1971.
- 60 H.S. Carslaw, "Introduction to the Theory of Fourier's Series and Integrals 3rd ed.", Dover Publishing Inc., 1930.
- 61 A. Kufner, and J. Kadles, "Fourier Series.", Iliffe Books, London, 1971.

62 H. Dym, and H.P. McKean, "Fourier Series and Integrals.", Academic Press, New York, 1972.

63 G. Arfken, "Mathematical Methods for Physicists 2nd ed.", Academic Press, New York, 1970.

64 C. Lanczos, "Discourse on Fourier Series.", Hafner Publishing Co., N.Y., 1966.

65 J.W. Gibbs, Nature 59: 606, 1899.

END

1 8/02-90

FIN