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Application of control theory to the hyperthermia problem

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The University of Arizona, 1992
APPLICATION OF CONTROL THEORY TO THE HYPERTHERMIA PROBLEM

by

Jon Kyle Potocki

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1992
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ABSTRACT

The objective of a hyperthermia cancer treatment is to heat the tumor tissue to a therapeutic level while limiting the detrimental effects experienced by the surrounding normal tissue. To achieve an optimal treatment requires knowledge of the resulting temperature response and an understanding of the complex interaction between the thermal response, the applied power, and the blood flow in the target tissue region. This dissertation considers model reduction to overcome the large dimensions associated with thermal modelling, extended Kalman filtering to estimate both the unmeasured temperature states and the unknown blood perfusion magnitudes, optimization of the applied power to achieve the best thermal response, and optimal servomechanism control to attain the desired regulated output tracking. A controller methodology that combines thermal estimation, applied power optimization, and optimal servomechanism control with a simple expert system shell is examined. This controller methodology is analyzed for a simulated scanned focused ultrasound system (SFUS) based upon the bioheat transfer equation (BHTE) model of the thermal response in the target region.

The results of the presented studies illustrate the following important points. First, open-loop reduced-order models based on the balanced transformation provide drastic model reduction for controller design purposes. Second, the success of thermal estimation depends on the number and the location of the thermal sensors, and the accuracy of the modelled blood perfusion profile. Third, multiple modelling in estimation provides an alternate technique for overcoming model mismatch associated with the modelling of the
blood perfusion pattern. Fourth, the choice of the set points for the optimal servomechanism controller play a crucial role in the resulting tissue temperatures. Fifth, the scan parameter sets that result in optimal SFUS power profiles need to be changed on-line during a treatment as the blood perfusion magnitude and pattern are estimated. Finally, to fully automate a hyperthermia treatment requires that the expertise of the clinician be incorporated into the controller design. Hierarchical control provides a means of incorporating the expert system shell at the higher levels of the controller, while maintaining optimal servomechanism control at the lower levels.
CHAPTER ONE

INTRODUCTION

1.0 Introductory Remarks

Hyperthermia is the process of raising the body temperature, either locally or globally, for medicinal purposes. Historically, hyperthermia has been recognized for its curative power in treating tumors and other ailments since ancient times (Singh 1991). With regard to cancer therapy, Freundlich first proposed the application of ultrasound for the treatment of animal tumors in 1932 (Freundlich et. al. 1932, Corry et. al. 1984). More recent clinical studies have shown that the success of a hyperthermia cancer treatment is related to the minimum temperature rise occurring in the tumor tissue (Hand and James 1986, Van Der Zee et. al. 1986, Oleson et. al. 1984, Dewhirst et. al. 1984). Unfortunately, prolonged exposure of normal, healthy tissue to elevated temperatures has a detrimental effect (Lindholm et. al. 1990, Barlogie et. al. 1979, Larkin et. al. 1977, Pettigrew et. al. 1974). Thus, the treatment objective is to elevate the tumor tissue volume to the target temperature while minimizing the detrimental effects experienced by the surrounding normal tissue.

Three factors have limited the success of applying hyperthermia as a localized cancer therapy and achieving the treatment objective. These factors are inefficient and inflexible heating modalities, sparse thermometry information in the treatment region, and limited control strategies. Large strides have been made in the design of applied power modalities that provide the spatial conformability of the applied power needed for
hyperthermia treatments (Roemer 1991). A wide variety of flexible heating modalities, such as scanned focused ultrasound (Lele and Parker 1982, Hynynen et. al. 1987, Shimm 1988, Harari et. al. 1990), incoherent external microwave arrays (Samulski et. al. 1990), multielement planar ultrasound arrays (Ogilvie et. al. 1990), electrically focussed ultrasound arrays (Ibbini and Cain 1990), multiple interstitial microwave antennae (Trembley et. al. 1986), multiple RF electrodes (Doss 1985), and phased arrays (Lin 1986), now exist for treating localized tumors. The advent of these new, more flexible heating modalities has provided researchers with the task of identifying the best spatial shape configurations for heating tumors. The optimization of the thermal response as a function of the applied power helps to identify the best directions and spatial shapes for the applied power deposition.

When treating cancerous tissue with hyperthermia, the inference of the resulting temperature response is a very basic requirement for evaluating the treatment success. Since clinically useful and accurate noninvasive techniques do not currently exist, temperature sensors are inserted into the treatment region. These temperature sensors provide the clinician with only a small sampling of the total thermal response of the target volume. Rarely during a treatment are the minimum tumor tissue temperature or the maximum normal tissue temperature directly measured. Instead, thermal estimation is required to predict the complete temperature field from the measured sensor information. Since estimation is closely tied to the ability to model the thermal response of the heated tissue, both thermal modelling and thermal estimation remain active areas of hyperthermia research.
The application of control techniques to hyperthermia is driven in part by the successes in improved flexibility of the heating modality, and more accurate thermal estimation. Effective utilization of control requires the analysis of the on-line thermal data to vary both the magnitude and the spatial shape of the applied power to drive the tumor tissue to its target temperature. Thus, more flexible heating modalities provide better means of reshaping the applied power to achieve a more optimal thermal response. Greater thermal information provides the controller with a better basis for changing the applied power to improve the treatment response. In addition, the computer is better able to process the huge amount of thermal information acquired during a treatment than a human operator.

1.1 Hyperthermia Control Literature

The application of hyperthermia to patients provides a variety of unique and challenging obstacles for the control designer to overcome. The human body is an extremely complex system to model, regardless of the size and speed of the computer performing the analysis. Tumors vary in type, size, location, shape, stage of growth, and proximity to significant organs and bones for each patient. The highly complex nature of the human vasculature and the inhomogeneities of the tissue complicate the model. In addition, the tolerance to pain, a limiting factor in many treatments, also varies for each patient. Mathematically, the thermal transfer in the treated tissue is a time varying, distributed parameter system. This tumor and patient variation, coupled with the mathematical complexity of the thermal transfer in the region, proves challenging to the
control designer.

To achieve the treatment objective, several investigators have proposed or applied control system theory to hyperthermia treatments. Lin et. al. (1990) designed and tested a PID plus bang-bang controller that varied the applied power of a scanned focussed ultrasound system (SFUS) along prespecified regions of the scan path. The drawback of this controller is that each region of the scan path is treated as an independent single-input, single-output (SISO) system. Thus, no allotments are made for the thermal coupling between scanning regions, and if more than one sensor is in a region, the extra temperature sensor information is not used. Nathanson (1992) improved upon this PID plus bang-bang controller by allowing for thermal sensor switching in scan path regions having multiple sensors. The sensor switching feature establishes the controlled thermocouple in a multiple sensor region as the hottest sensor in the region. Thus, the hot spots within the target tissue volume are reduced by constantly controlling the hottest thermal sensor. Knudsen and Heinzl (1986) use a multiple-input, multiple-output (MIMO) self-tuning Smith controller to vary the temperature of a surface water bolus and the applied microwave power. In their study the parameter estimation and control design is limited to a one dimensional thermal model. Knudsen and Hartmann (1986) apply optimal control with parameter estimation to the four magnitudes and three phases of a phased array RF applicator. Their seven point controller is based on a two dimensional (r,θ) thermal model, and is limited to accurate control in only a single tissue depth plane. Babbs et. al. (1986) develop an optimal power technique that minimizes the standard deviation of the measured intratumoral temperatures. The drawback of this method is that
the design is based on the positions of the thermometry gathering data and the updating is performed only at these possibly restrictive locations. Doss (1985) modelled the tumor in two dimensions, but only considered the proportional control of a single point within the region. Kress (1988) analyzed three different adaptive schemes for controlling the temperatures in the thermal regions, and made note of the computational burden required to perform on-line three dimensional adaptation. Hartov (1991) considers the MIMO adaptive controller specially designed for an intraoperative ultrasound hyperthermia system. While these controllers greatly improve the understanding of the hyperthermia control problem and its solution, none of these controllers provide a methodology for fully automating the treatment process.

1.2 Hyperthermia Estimation Literature

Thermal dosimetry, the characterization of a thermal treatment (Cetas 1984), is characterized as comparative, prospective, concurrent, and retrospective (Roemer 1984). The goal of comparative dosimetry is to evaluate the expected treatment performance as a function of the applied power modality, prospective dosimetry is used to plan a treatment for a specific patient, concurrent dosimetry refers to the dosimetry used for feedback control during a treatment, and retrospective dosimetry is applied to evaluate the success of a treatment. Several researchers (Clegg and Roemer 1992, 1989, 1985, Clegg 1988, Liauh 1991, 1988, Winget et. al. 1986) have investigated the estimation of the thermal profile of a hyperthermia treatment for retrospective purposes. One basic difference between retrospective and concurrent dosimetry is the amount of time allowed
for the estimation. Retrospective analysis allows sufficient time for a wide variety of computationally intensive schemes to be evaluated, since the analysis is performed post-treatment. Alternatively, concurrent routines have to be computed on-line during a treatment or the routine is useless (Knudsen and Hartmann 1986). Knudsen (1989) gives a concurrent algorithm based on the bioheat transfer equation restricted to a single spatial dimension. The controller proposed by Knudsen and Hartmann (1986), and Knudsen and Heinzl (1986) are concurrent techniques that directly estimate the parameters of the feedback controllers without actually performing temperature estimation. The drawback of these direct methods is that the clinician is still limited to the thermometry information measured during the treatment.

1.3 Hyperthermia Power Optimization Literature

Three questions need to be asked before an optimization of the thermal response of the treatment region with respect to the applied power can be performed (Roemer 1991). First, what is the boundary of the cancerous tissue volume to be treated? Second, what is the ideal temperature distribution within the tumor tissue and within the normal tissue that results in the most therapeutic treatment? Finally, how can the applied power be optimized to result in the ideal temperature distribution?

The goal of hyperthermia power optimization is to find the direction and spatial shape of the applied power that best heats the treatment region. Since the temperature varies as a function of the blood flow, the optimization of the power needs to consider the various possible blood flows in the region. Ocheltree and Frizzell (1987, 1988)
theoretically analyzed the optimal power deposition required to heat both spherical and cylindrical tumor volumes based on the steady state and transient thermal responses. Roemer (1991) extends this theoretical study to include the influence of thermally significant blood vessels in the treatment region. Lin et. al. (1992) performed a simulation study based on the optimization of the scan parameters dictating the spatial shape of the applied power for a scanned focussed ultrasound system. DeWagter (1986) studied the optimization of a two-dimensional temperature distribution induced by multiple electromagnetic applicators. Strohbehn et. al. (1989) studied the optimization of the absorbed power distribution for an annular phased array hyperthermia system. Tharp and Roemer (1992) studied the three dimensional optimization of the temperature field due to a finite-sized, planar hyperthermia applicator array. These studies indicate that *ad hoc* choices for the shape of the applied power will result in significant degradation in the resulting temperature field. In addition, since it is unrealistic to obtain a uniform 43°C thermal response in the tumor tissue, the choice of set points for a feedback controller plays an important role in the resulting temperature response.

1.4 Outline of Dissertation

The goal of this dissertation is to develop a controller methodology that results in the automation of hyperthermia treatments. The chapters represent a logical progression of results from the initial control motivated modelling, to estimation, and then to control design. The proposed controller methodology is a model-based and is designed for a scanned focussed ultrasound system. Significant portions of this

The background material required to understand the bioheat transfer model and the scanned focused ultrasound simulations are described in Chapter Two. Chapter Three describes the open-loop reduction of the thermal state space model for control system design purposes. Both model-reduction based on the balanced realization and criterion for choosing the reduced-order model's dimension are given. A reduced-order optimal servomechanism controller is designed and its performance is compared with that of the full-order optimal servomechanism controller. Chapters Four and Five describe the estimation of the thermal response of the simulated tissue region based on a limited set of measured output locations. Chapter Four compares the full-order extended Kalman filter with a full-order steady state Kalman filter and two reduced-order estimators as a function of the measured output number and location. Chapter Five analyzes a multiple model estimator based on the extended Kalman filter as a means of addressing model mismatch in the tissue blood perfusion pattern. Chapter Six describes the optimization of the applied scanned focused ultrasound parameters as a function of the blood perfusion magnitude. For the power optimization study, two independent scan patterns are compared simultaneously to define the globally optimal scan parameter sets that best heat the tissue for a given perfusion magnitude. Chapter Seven unifies the optimal servomechanism controller, the extended Kalman filter, and the power optimization results into a single controller methodology. The proposed methodology considers a two level hierarchical control scheme that applies optimal servomechanism control at the
lower level and an expert system at the upper level. Simulations are performed to evaluate the efficacy of using this controller methodology to automate hyperthermia treatments.
CHAPTER TWO

MODELLING AND STABILITY

2.0 Introduction

Central to the success of hyperthermia optimization, estimation, and control is the need for accurate thermal modelling. This chapter discusses the application of the bioheat transfer equation (BHTE) to model the heat transfer that occurs in the target tissue during a hyperthermia treatment. Next, the simulation of the applied SFUS power is explained, and the scan parameters that shape the resulting power are defined. Based on the BHTE and the simulated SFUS power deposition, a state space model is derived using the method of finite differences. Finally, based on this state space model, the stability of the open loop thermal models are analyzed.

2.1 The Bioheat Transfer Equation.

Before defining the BHTE it should be noted that thermal modelling remains a very active and highly debated field of hyperthermia research (Huang et. al. 1992, Roemer 1992, Chen and Roemer 1992, Crezee and Lagendijk 1992, Williams 1990, Wienbaum and Jiji 1985). The blood flow in the target tissue plays an important role in cooling the tumor during a treatment. The complex vasculature of the human body is a difficult structure to quantify for thermal modelling purposes. The BHTE is an empirically derived equation (Pennes 1948) that ignores the effects of large thermally significant blood vessels in the heat transfer process (Chen and Roemer 1992).
BHTE approximates the blood flow as a nondirectional mass blood transfer through the region called the blood perfusion term. The advantage of using the BHTE is that it has been experimentally tested in vivo (Moros 1990), and found to model the temperature behavior quite well. The goal of this dissertation is to provide a control methodology for automating hyperthermia treatments, and not to evaluate the various existing heat transfer models. Thus, for the purposes of this research the BHTE more than suffices as a thermal model for simulating hyperthermia treatments.

In 1948 Pennes published a paper analyzing the tissue and arterial blood temperature in the resting human arm (Pennes 1948). Pennes' BHTE defines the temperature of any point within the treatment volume as

$$\rho c \frac{\partial T}{\partial t} = \kappa \nabla^2 T - \omega c_b (T - T_a) + Q_a + Q_m, \quad (2.1)$$

where $\rho <\text{kg/m}^3>$ is the tissue density, $c$ and $c_b <\text{J/kg }{^\circ}\text{C}>$ are the specific heat of the tissue and the blood, $\kappa <\text{W/}^\circ\text{C m}>$ is the thermal conductivity, $w <\text{kg/m}^3 \text{ s}>$ is the blood perfusion, $T <^\circ\text{C}>$ is the tissue temperature, $T_a <^\circ\text{C}>$ is the arterial temperature, and $Q_a$ and $Q_m$ are the absorbed power and metabolic heat term, respectively. The tissue density, specific heat, thermal conductivity, and arterial temperature are all assumed homogeneous and known throughout the subsequent simulations. The metabolic term is negligible (Jain 1983) and is ignored, and the absorbed power that results from the SFUS simulations are explained in the next section. The blood perfusion term, $w$, is an unknown parameter that varies as a function of space,
but does not typically vary as a function of time after the initial heat up phase of a treatment (Anhalt et. al. 1992).

The BHTE considers both conductive and convective heat transfer in modelling the thermal process of the target tissue. The conduction term represents the heat transfer in the tissue as a result of the solid nature of the tissue. The convection term represents the heat transfer as a result of the liquid (blood) moving through the tissue. Thus, as the blood perfusion term approaches zero, the BHTE resembles the classical heat equation (Haberman 1987) driven by a nonuniform source term.

2.2 Scanned Focused Ultrasound Simulations.

The advantage of SFUS over other heating modalities is that it is an efficient and effective modality for heating deep-seated tumors (Lele 1984, Roemer et. al. 1984) regardless of perfusion rate (Hynynen et. al. 1989). In addition, studies show that the scan shape, the transducer speed, and the scan parameters can be varied to improve the heating of the target tissue (Lin et. al. 1992, Moros et. al. 1988, Hynynen et. al. 1986). The SFUS simulation routines used in this study are the culmination of simulations developed by three different researchers at the University of Arizona (Swinell 1986, Moros 1987, Lin 1990).

Briefly, the absorbed ultrasound power is calculated as

\[ Q_a(x, t) = 2\alpha_a I(x, t) \]  (2.2)
where $\alpha_s \ (m^{-1})$ is the absorption coefficient in the tissue, and $I(r,t) \ (W/m^2)$ is the intensity of the ultrasonic wave. For homogeneous absorbing media the ultrasonic intensity is calculated from

$$I(x_o, t) = \frac{1}{2} \frac{\omega^2 \rho^2}{Z} |\Psi(x_o, t)|^2$$  \hspace{1cm} (2.3)

where $\omega \ < \text{rad/s} >$ is the frequency of the sound wave, $\rho \ < \text{kg/m}^3 >$ is the density of the absorbing media, and $Z \ < \text{kg/m}^2 \text{s} >$ is the acoustic impedance. The complex velocity potential, $\Psi(r_o,t)$, is calculated from the attenuated Rayleigh-Sommerfeld diffraction integral

$$\Psi(x_o, t) = \frac{1}{2\pi} \int_S \frac{V_s}{x} e^{-i\kappa x} e^{-\alpha x'} \ ds$$  \hspace{1cm} (2.4)

where $S$ is the physical aperture of the transducer, $r \ < \text{m} >$ is the distance from the transducer to $r_o$, $r' \ < \text{m} >$ is the distance the ultrasound wave travels in the tissue, $\kappa = 2\pi/\lambda$ for ultrasound wavelength $\lambda \ < \text{m} >$, $V_s \ < \text{m/s} >$ is the normal particle velocity at $ds$, and $\alpha \ < \text{m}^{-1} >$ is the attenuation coefficient of the tissue (Hynynen 1990, Swindell 1986, Strohbehn and Roemer 1984).

Swindell (1986) codified a simulation that calculates the absorbed power, in a single R-z plane in an axially symmetric, homogeneous, cylindrical tissue volume, resulting from a single, stationary transducer as a function of transducer dimension and
frequency. Moros' (1987) simulations expanded upon the work of Swindell to convert the single R-z plane power profile into a three dimensional rectangular power profile. This three dimensional power profile can be tilted, and scanned through the target region. Lin's work (1990) extended Moros's work to include transducer rotation angle, and to convolve circular scans into single R-z symmetric cylindrical power profiles. Thus, the four SFUS scan parameters are the transducer tilt angle, rotation angle, focal depth, and scan radius. Figure 2.1 defines the transducer tilt angle, focal depth, and scan radius, and Figure 2.2 defines the transducer rotation angle.

The result of having four variable scan parameters is that it allows the user to investigate SFUS power profiles having numerous shapes. Research shows that the scan parameters can be optimized to deposit the best distribution of power to produce a given temperature (see Lin et. al. 1992 and Chapter Six). Thus, the work of Swindell, Moros, and Lin shows the transformation of the ultrasound heating modality from a stationary application, to simple scanned applications, and finally, to scans based on complex transducer configurations.
Figure 2.1. Transducer tilt angle, focal depth, and scan radius.
Figure 2.2. Transducer rotation angle and scan radius
2.3 BHTE State Space Model.

To best illustrate the results and interface with the existing SFUS power simulations, an axially symmetric cylindrical tissue model is simulated. The BHTE describing the R-z symmetric tissue volume is

\[
\rho c \frac{\partial T}{\partial t} = k \left( \frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial T}{\partial r} \right) + \frac{\partial^2 T}{\partial z^2} \right) + wc_b(T - T_a) + Q_a, \quad (2.5)
\]

with the \( r = 0 \) boundary condition

\[
\lim_{r \to 0} \frac{\partial T}{\partial r} = 0. \quad (2.6)
\]

Expanding the radial term on the right of (2.5) using the chain rule gives

\[
\frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial T}{\partial r} \right) = \frac{\partial^2 T}{\partial r^2} + \frac{1}{r} \frac{\partial T}{\partial r}. \quad (2.7)
\]

Applying the boundary condition in (2.6) to the second partial derivative term on the right of (2.7) and L’Hopital’s rule (Smith 1985) gives the boundary condition

\[
\lim_{r \to 0} \left( \frac{1}{r} \frac{\partial T}{\partial r} \right) = \frac{\partial^2 T}{\partial r^2}. \quad (2.8)
\]

Thus, the total boundary condition at \( r = 0 \) for (2.7) is
\[
\lim_{r \to 0} \left( \frac{\partial^2 T}{\partial r^2} + \frac{1}{r} \frac{\partial T}{\partial r} \right) = 2 \frac{\partial^2 T}{\partial r^2}.
\]  
(2.9)

For the purposes of state space control, equation (2.5) is infinite in spatial dimension, which eliminates much of the standard feedback design theory. A numerical approximation technique is needed to create a model of finite dimension, so that the thermal response can be represented on a computer and finite dimensional control theory can be applied.

The method of finite differences is applied to (2.5) to create a state space that is discrete in time, as well as, space. Applying forward differences (Smith 1985) to the left side of (2.5) gives

\[
\rho c \frac{\partial T}{\partial t} \rightarrow \rho c \frac{T(x, z, t+\Delta t) - T(x, z, t)}{\Delta t}
\]  
(2.10)

where \( \Delta t \) is the sampling period. Applying central differences (Smith 1985) to the second partial terms in (2.7) gives

\[
\frac{\partial^2 T}{\partial x^2} \rightarrow \frac{T(x+\Delta x, z, t) + T(x-\Delta x, z, t) - 2T(x, z, t)}{\Delta x^2}.
\]  
(2.11)

Similarly, the first partial is approximated as

\[
\frac{1}{r} \frac{\partial T}{\partial r} \rightarrow \frac{T(x+\Delta r, z, t) - T(x-\Delta r, z, t)}{2r\Delta r}.
\]  
(2.12)
The second partial with respect to \( z \) in (2.5) has the same form as (2.11) with \( z \) replacing \( r \), and \( \Delta z \) replacing \( \Delta r \).

The tissue volume analyzed in this dissertation has a 6.0 cm depth and a 6.0 cm diameter. For a grid spacing of 0.5 cm (\( \Delta s = \Delta r = \Delta z = 0.5 \text{ cm} \)), the model will have 7 nodes in the radial direction and 12 nodes in the depth direction, for a total of 84 nodes or state variable components. Figure 2.3 shows the tissue volume and the numbering of states as a function of their locations in the tissue. Combining the SFUS simulation results, the equations (2.10) through (2.12), and the node definition in Figure 2.3, a state space equation of the form

\[
\begin{align*}
    x(k+1) &= Ax(k) + Bu(k) \\
    y(k) &= Cx(k)
\end{align*}
\]  

(2.13)

(2.14)

is derived. For \( n \) finite difference nodes, \( m \) independent inputs, and \( p \) measured outputs, \( x \in \mathbb{R}^n \) is the state vector representing the temperatures at the finite difference node, \( u \in \mathbb{R}^m \) is the magnitude of the applied power, and \( y \in \mathbb{R}^p \) is the measured outputs. The sampling index, \( k \), relates discrete-time to continuous-time as \( t = k\Delta t \). \( A \in \mathbb{R}^{nxn} \) is the system matrix, or the state transition matrix in discrete-time, that represents the thermal coupling between the states, \( B \in \mathbb{R}^{nxm} \) is the input matrix that maps the applied power to the states, and \( C \in \mathbb{R}^{pxn} \) is the output matrix that maps the states to the measured outputs. Appendix A shows how equations (2.10) through (2.12) combine to give the elements of
the state transition matrix, and reviews the input and the output matrices. Figure 2.4 shows a SFUS absorbed power profile for 40° tilt angle, 80° rotation angle, 3.0 cm focal depth, and 0.5 cm scan radius for the tissue volume defined in Figure 2.3. The columns of the input matrix represent the mapping of the individual transducer SFUS absorbed power profiles (evaluated at 1 watt of applied power) such as Figure 2.4 to the state locations. The output matrix reconstructs the measured outputs by linearly combining the states in locations surrounding the measured output locations.
Figure 2.3. Tissue region and the location of the 84 states.
Figure 2.4. Power profile for a tilt angle of 40°, a rotation angle of 80°, a focal depth of 3.0 cm, and a scan radius of 0.5 cm. The power profile for this set of scan parameters is shown in increments of 20% starting with the 10% contour.
2.4 Open-loop Stability Analysis.

Central to control theory is the stability of the open-loop and closed-loop processes. The stability of the open-loop plant influences the considerations made when designing an appropriate feedback controller. For the linear time-invariant system defined in (2.13) and (2.14) the system is both bounded-input, bounded-output (BIBO) stable and globally asymptotically stable if

$$|\lambda_i(A)| < 1.0 \ \forall \ i = 1, ..., n$$

(2.15)

where $\lambda_i(A)$ is the $i$th eigenvalue of the state transition matrix (Vidyasagar 1978).

The state transition matrix, described spatially in Figure 2.3 and defined numerically in Appendix A, is calculated using the parameters defined in Table 2.1.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\rho$</td>
<td>1000.0 kg/m$^3$</td>
</tr>
<tr>
<td>$c$</td>
<td>4000.0 J/kg °C</td>
</tr>
<tr>
<td>$c_0$</td>
<td>4000.0 J/kg °C</td>
</tr>
<tr>
<td>$\kappa$</td>
<td>0.5 W/°C m</td>
</tr>
<tr>
<td>$w$</td>
<td>[0.0,10.0] kg/m$^3$ s</td>
</tr>
<tr>
<td>$\Delta t$</td>
<td>15 s</td>
</tr>
<tr>
<td>$T_s$</td>
<td>37.0 °C</td>
</tr>
</tbody>
</table>

Table 2.1. Values of BHTE thermal parameters used in simulations.
Note that the blood perfusion term is allowed to vary from 0.0 kg/m$^3$ s to 10.0 kg/m$^3$ s.

The eigenvalues of the state transition matrix defined by the parameters in Table 2.1 were found and analyzed for stability purposes. For a uniform perfusion of 0.0 kg/m$^3$ s, the 84 eigenvalues are positive, real, and bounded between 0.341 and 0.987. Thus, for a uniform perfusion of 0.0 the BHTE is stable as all of its eigenvalues are bounded between 0.0 and 1.0 on the real axis of the complex plane. Since the blood perfusion term influences only the diagonal terms of the state transition matrix, a uniform increase in perfusion of $\Delta w_u$ will move all the eigenvalues in the complex plane by an amount

$$\lambda_v(A(w+\Delta w_u)) = \lambda_v(A(w)) - \frac{c_p \Delta c}{\rho c} \Delta w_u.$$  

For a uniform perfusion of 10.0 kg/m$^3$ s, the eigenvalues move left on the complex plane an amount 0.15 from the original eigenvalues when the perfusion was a uniform 0.0 kg/m$^3$ s. Thus, for the uniform 10.0 kg/m$^3$ s perfusion plant the eigenvalues are positive, real and fall between 0.191 and 0.837.

Since the perfusion is bounded between 0.0 and 10.0, for nonuniform perfusion magnitudes the eigenvalues are positive, real and bounded between 0.191 and 0.987. As a result, for all perfusion patterns and magnitudes of interest the open-loop BHTE state space model is stable. This eigenvalue behavior is intuitively acceptable as application of bounded power in the clinic results in bounded temperature responses.

As a consequence of these stability results, the application of control theory to hyperthermia is more for performance enhancement purposes than stability enhancement.
When using the SFUS the problem for the control designer is described as finding the applied ultrasonic power shape and magnitude to bring about the most therapeutic thermal response in the target region.

2.5 Summary.

The BHTE is an empirically derived equation that has been successfully tested experimentally. The BHTE approximates the convective heat transfer associated with the blood flow through the target region with the blood perfusion term. The method of finite differences is applied to the BHTE to create a state space representation that has finite dimension, and is discrete in both time and space. Figure 2.3 describes the numbering and location of the states in the cylindrical axisymmetric R-z tissue volume analyzed in this dissertation.

The SFUS is an efficient and effective modality for controlling the heating of deep-seated tumors. Four transducer scan parameters exist for shaping the applied SFUS power in the target region. These scan parameters are transducer tilt angle, rotation angle, focal depth, and scan radius, and are defined graphically in Figures 2.1 and 2.2. Modelling packages exist for developing absorbed power profiles for the R-z tissue volume as a function of the transducer scan parameters.

Analysis of the open-loop stability of the state space model with parameters given in Table 2.1 shows that for the perfusion magnitudes of interest the BHTE is a stable system. Thus, the goal of the control designer is to improve the therapeutic response of the treatment by manipulating the shape and the magnitude of the applied power.
CHAPTER THREE

MODEL REDUCTION AND CONTROL

3.0 Introduction

This chapter investigates the application of model reduction techniques as a viable approach to the development of hyperthermia control systems. Model reduction is a significant issue since typical tissue masses in hyperthermia require hundreds and even thousands of grid point (state variable components) to accurately describe numerically the thermal response of the tissue volume. Without reducing the model dimension prior to the control algorithm design, numerically unsolvable design problems may arise. Also, there is little insight or intuition that exists for the control designer when the system is of such high dimension. Thus, reduced-order modelling should be a useful tool in the development of the sophisticated control algorithm designs that are needed for current and future heating modalities.

One of the main objectives of this reduced-order modelling study is to produce a simple controller. Simple controllers are easier to develop, implement, debug, understand, and require fewer on-line computations than more complex controllers (Anderson and Lui 1989). To fully utilize both the flexibility in the current hyperthermia power deposition devices and the extracted thermometry information, a MIMO controller is desired. This MIMO controller should be designed using a model that includes the physical coupling between the inputs and the outputs of the thermal process and the power process. A state space model is more capable of incorporating this coupling and
is more amenable to sophisticated control design techniques and estimation algorithms than other modelling structures. For this reason MIMO reduced-order models based on the balanced realization are investigated because they yield state space models of low dimension whose impulse response match that of the full-order model within prespecified bounds (Hinrichsen and Pritchard 1990).

This chapter is organized as follows. First, the balanced realization is described as a reduced-order modelling technique. Based on the balanced realization three methods for choosing the dimension of the reduced-order model are described. To evaluate reduced-order modelling as a viable control technique a reduced-order optimal servomechanism controller is designed. A series of simulations are run for both a full-order and a reduced-order optimal servomechanism controller. Finally, the results of these simulations are compared and contrasted for the full-order and the reduced-order optimal servomechanism controllers.

3.1 Reduced-Order Modelling Using the Balanced Realization.

Two different approaches for designing reduced-order controllers exist and are illustrated in Figure 3.1 (Anderson and Lui 1989). In the first methodology the full-order model of the system is reduced and a controller is designed based on this reduced-order model. In the second methodology a full-order controller is designed using the full-order system model and this controller is then reduced to a desired dimension. The advantage of the first methodology is that it requires less computation to design the controller. Also, it may be numerically ill-posed to design a full-order controller for the full-order thermal
model. The advantage of the second methodology is that errors between the reduced-order and the full-order thermal model are not amplified in the controller design as the controller is designed on the full-order model (Anderson and Lui 1989). For this study a comparison is made of a reduced-order model based controller and a full-order model based controller applied to the hyperthermia problem. The results validate the use of the first model reduction methodology in hyperthermia control design.

A variety of model reduction techniques exist for both frequency domain and time domain system models (Rivera and Morari 1987, 1992, Glover 1984, Shamash 1974, Bosley and Lees 1972, Chuang and Shieh 1968, Davison 1966). One useful state space reduction technique, called balancing (Moore 1981), requires transforming the state space into a representation where the controllability and observability grammians are diagonal and equal. Using the controllability and observability grammians, and the singular value decomposition, it is possible to derive the transformation that balances the state space in (2.13) and (2.14). The details associated with calculating the transformation matrix are found in Appendix B.
Figure 3.1 Block diagram of reduced-order controller construction.

Using the balancing transformation, $T \in \mathbb{R}^{nn}$, the balanced realization is described by

$$\tilde{X}(k+1) = \tilde{A}\tilde{X}(k) + \tilde{B}u(k) \quad (3.1)$$
\[ y(k) = \bar{C}\bar{x}(k) \]  

(3.2)

with \( \bar{x} = Tx, \bar{A} = TAT^{-1}, \bar{B} = TB, \) and \( \bar{C} = CT^{-1}. \) The controllability and observability grammians are given as

\[
\bar{A}\Sigma \bar{A}^T + \Sigma = -\bar{B}\bar{B}^T \tag{3.3}
\]

\[
\bar{A}^T \Sigma \bar{A} + \Sigma = -\bar{C}^T \bar{C} \tag{3.4}
\]

where

\[
\Sigma = \begin{bmatrix}
\sigma_1 & 0 & 0 \\
0 & \ddots & 0 \\
0 & 0 & \sigma_n
\end{bmatrix}, \tag{3.5}
\]

and the \( \sigma_i \) are the second order modes of the system with \( \sigma_1 \geq \sigma_2 \geq \ldots \geq \sigma_n. \)

The importance of having equal and diagonal grammians is that the relative magnitude of the diagonal elements of \( \Sigma \) dictate the influence that a particular balanced state component has on the impulse response of the system. Model reduction is achieved by removing those state components with the smaller grammian values, because they have little effect upon the impulse response of the system (Moore 1981). Therefore, the reduced-order model is found by truncating (3.1) and (3.2) at some desired dimension, thus eliminating the least controllable and observable state components. The reduced-
order balanced realization is described by

\[ z(k+1) = A_x z(k) + B_x u(k) \]  \hspace{1cm} (3.6)

\[ y(k) = C_x z(k) \]  \hspace{1cm} (3.7)

where \( z \in \mathbb{R}^j \) is the first \( j \) states of \( x \), and \( A_x \in \mathbb{R}^{j \times j} \), \( B_x \in \mathbb{R}^{j \times m} \), and \( C_x \in \mathbb{R}^{p \times j} \) are truncations of \( \bar{A} \), \( \bar{B} \), and \( \bar{C} \), respectively.

3.2 Dimension of Reduced-Order Model.

The question that naturally arises is what dimension is acceptable for matching the open-loop responses of the reduced-order and the full-order models? Three criteria, based on the second order modes, of the system exist for determining the reduced-order model dimension for truncating a balanced system. An advantage of using the second order modes is that an analysis of the reduced-order dimension can be performed before the balanced realization is calculated.

The first criterion compares the relative sizes of neighboring second order modes as a cutoff for choosing model order. If \( \sigma_j \gg \sigma_{j+1} \), then \( j \) represents a good dimension for truncating the balanced realization (Moore 1981). The second criterion, the degree of internal dominance is given by the ratio
where ID(j) is the degree of internal dominance for dimension j. For the impulse response of a jth-order model to match that of the full-order model, an ID(j) ≪ 1.0 is needed with smaller degrees of internal dominance being better (Moore 1981). The third criterion gives a bound on the error between the frequency response of the full-order and the reduced-order models (Hinrichsen and Pritchard 1990). This bound is given as

\[
\|E(j)\| = \max_{\theta \in [0, 2\pi]} \|G(e^{i\theta}) - G_j(e^{i\theta})\| \leq 2 \sum_{i=j+1}^{n} \sigma_i
\]  

(3.9)

where G is the transfer function of the full-order system, and G_j is the transfer function for the jth-order balanced realization.

### 3.3 Optimal Servomechanism Controller.

After calculating the balanced realization to develop a model for reduction and choosing an appropriate order, the next step is to incorporate the reduced-order model into the controller design. A servomechanism controller is used because it exhibits good tracking capabilities, a desirable characteristic in hyperthermia control. An optimal
servomechanism is used because optimal control generates the MIMO gains, which automatically account for the system coupling, in an analytical framework. Figure 3.2 shows a block diagram of the closed-loop system. Notice the limiting term at the input of the plant. This limit is the consequence of SFUS only being able to heat and not cool the target tissue. In addition, the number of outputs that can be freely controlled by the optimal servomechanism controller is equal to the number of independent inputs. Thus, the control designer must choose reference inputs and regulated output locations that both keep the controller in its linear operating region and result in a therapeutic response in the target tissue.
Figure 3.2. Block diagram of optimal servomechanism applied to the hyperthermia system.
Since the number of measured outputs need not equal the number of regulated outputs, a distinction is made between the measured output \( y(k) \) and the regulated output \( y_r(k) \). The measured outputs represent the information gathered at the thermal sensor locations, and the regulated outputs are the locations to be tracked. For a state space system described by (2.13) and having regulated outputs \( y_r(k) \), the compensator dynamics are given as

\[
 u(k) = -K_2 x(k) + K_1 v(k) \tag{3.10}
\]

\[
 v(k) = v(k-1) + (r(k) - y_r(k)) \tag{3.11}
\]

where \( K_1 \in \mathbb{R}^{m \times m} \) and \( K_2 \in \mathbb{R}^{m \times m} \) are the feedback gains, \( v \in \mathbb{R}^m \) is the compensator state, and \( r \in \mathbb{R}^m \) is the reference input taken as the temperature rise above the normal tissue temperature of 37°C. Appendix C shows how to calculate the above feedback gains given in (3.10) and (3.11).

The reduced-order controller is designed using a reduced-order model of the nominal system in place of the full-order model. For a reduced-order model of dimension \( j \), the reduced-order controller has \( K_1 \in \mathbb{R}^{m \times j} \), \( K_2 \in \mathbb{R}^{j \times j} \), and \( z \) replaces \( x \) in (3.10).

3.4 Simulations.

The axially symmetric R-z tissue volume in Figure 2.3 is modified to include a 2.0 cm in depth, 2.0 cm diameter tumor centered 3.0 cm from the skin surface. The
extra nodes around the tumor are retained to eliminate the impact of the boundary conditions on the thermal response. In general, we are only interested in the thermal response of the tumor and its surrounding tissue. Therefore, only the 40 states (5 radial and 8 in depth) spatially within and surrounding the tumor are selected as possible regulated outputs. Figure 3.3 shows the tissue volume including the tumor tissue and the 40 possible regulated output locations. Note that equation (3.10) assumes full state feedback, so it is assumed that this information is available to the controller.
Figure 3.3. Tumor and normal tissue region showing the 40 critical output locations.
For the design of the controller a perfusion pattern is needed to fully describe the dynamics of the thermal model. For this study a nominal pattern is picked as a uniform perfusion of 5.0 kg/m³ s in the normal tissue (w_N) and a uniform perfusion of 1.0 kg/m³ s in the tumor (w_T). For an ultrasound transducer with a 25.0 cm radius of curvature, 13.0 cm diameter, and 1.0 Mhz frequency, a set of scan parameters are required to generate the SFUS power profile. For the \([w_N, w_T] = [5.0,1.0] \text{ kg/m}^3 \text{s}\) perfusion profile, the 40° tilt angle, 80° rotation angle, 3.0 cm focal depth, and 0.5 cm scan radius shown in Figure 2.4, is an optimal set of scan parameters for a single transducer (Lin et. al. 1992). Simulations show that the single scan is incapable of heating the entire tumor region to a minimum of 43°C without attaining excessively high temperatures inside the tumor. Thus, to better heat the tissue and analyze the effects of using multiple inputs in the design methodology, a second scan is added. This second scan has a 45° tilt angle, 90° rotation angle, a 2.0 cm focal depth and a 1.0 cm scan radius, and is shown in Figure 3.4. Figure 3.5 shows the full-order open-loop, steady-state, thermal response of the nominal perfusion model to constant inputs of 5.0 W and 3.0 W applied to the first and second scan, respectively. Figure 3.6 shows the open-loop transient responses of the outputs for locations 13 and 22 of Figure 3.3 for the fourth-order and the full-order two input models. This open-loop transient response is overdamped with steady state temperatures of 46.14°C and 43.19°C, and an 8.60 minute rise time (the time needed to go from 10% to 90% of the steady state temperature). The open-loop steady state responses of the 40 critical nodes for the fourth-order model match those of the full-order model shown in Figure 3.5, and will not be repeated.
Figure 3.4. The second applied power profile having scan parameters tilt angle 45°, rotation angle 90°, focal depth 2.0 cm, and scan radius 1.0 cm. The power profile for this set of scan parameters is shown in increments of 20% starting with the 10% contour.
Figure 3.5. The nominal open-loop, two input, full-order models' steady state regulated output responses to step inputs of 5.0 watts and 3.0 watts.
Figure 3.6. The nominal open-loop, two input, full-order and fourth-order models' transient measured output responses for step inputs of 5.0 and 3.0 watts. The responses are plotted over a 20 minute period. The steady state output temperatures are 46.14°C and 43.20°C, and the rise time is 8.60 minutes.
Balanced realizations were calculated for the nominal perfusion pattern for both the single and the two input models. Table 3.1 shows the second order modes, the degree of internal dominance, and the frequency matching dimension criterion for these balanced realizations. Analysis of Table 3.1 shows that reduced-order models of third and fourth order adequately match the full-order model responses for the one and the two input systems. The two input model requires more dynamics (than the single input system) in the reduced-order model to match the response of the full-order model. This increase in dimension is not surprising as the addition of another independent input results in stronger coupling with more of the dynamics of the system. This increased input structure coupling with the system dynamics translates to greater dynamic requirements in the reduced-order model.

Using Table 3.1 as a guide, a fourth-order model adequately represents the open-loop dynamics of the two input full-order model, and a controller based on this fourth-order model is designed. The steady state response of the 40 critical outputs in Figure 3.5 is considered the desired heating pattern for raising the tumor to 43.0°C while keeping the normal nodal tissue temperature at 40.0°C or cooler. The outputs are chosen at locations (13,22) in Figure 3.2, as these locations are the focal points of the two transducer scans. The steady state temperatures at the measured regulated output locations are used to select the set points (r(k) values) as inputs to both the reduced-order and the full-order optimal servomechanism controllers. The actual set point values that are used in all the subsequent simulations are r(k) = \{9.1, 6.2\}, respectively. These set point values correspond to 37° + 9.1° = 46.1° and 37° + 6.2° = 43.2° at the
regulated output locations.

<table>
<thead>
<tr>
<th>j</th>
<th>$\sigma_j$</th>
<th>ID(j)</th>
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Two Input System

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Table 3.1. The first 10 singular values, degrees of internal dominance, and the frequency response bounds for the nominal single input and two input balanced systems.
A series of computer simulations are run to analyze the success of the fourth-order controller's ability to heat the tumor as the size, the perfusion, and the input-output structure of the simulated model representing the actual tissue are changed. The nominal controllers are designed using the nominal perfusion model described above, the two transducer SFUS power profiles, and the regulated output locations (13,22) shown in Figure 3.3. Initially, control is applied to the simulated tissue model having the nominal perfusion profile, power profile, and output locations to see if the controllers are capable of heating the tissue volume for which they are specifically designed. Figure 3.7 shows the transient temperature response of the measured regulated outputs when the fourth-order controller and the full-order controller are applied to the nominal plant. Comparison of the transients in Figures 3.6 and 3.7 show that the rise time for the closed-loop (controlled) system is a factor of 2.2 faster. The steady state responses of the 40 critical nodes for the two closed-loop systems matched that shown in Figure 3.5, and are not repeated. Figure 3.8 shows the first 5 minutes of the closed-loop applied power magnitude that results from the fourth-order controller (the response for the full-order controller is nearly identical and is not repeated). Based on the closed-loop transient and the steady state temperature responses of the 40 critical nodes, both controllers performed well when applied to the nominal plant.

The simulated tissue region is varied to evaluate the robust nature of the fourth-order controller. The tumor size and shape, and the input-output structure are maintained, and the perfusion of the simulated tissue model is varied to compare the responses of the two nominal controllers. Figure 3.9 shows the controlled steady state temperatures when
the nominal controllers are applied to a tissue model with a uniform perfusion of 1.0 kg/m³ s. The transient response for this case showed the same overdamped response as the nominal case in Figure 3.7, with measured output temperatures of 46.09°C and 43.19°C and a rise time of 4.14 minutes. The controlled steady state temperatures for a 5.0 kg/m³ s tumor perfusion and a 10.0 kg/m³ s normal tissue perfusion shows a slight degradation in the 43°C contour near the z = 2 cm face of the tumor when compared with Figure 3.3. The transient response is overdamped with measured steady state output temperatures of 46.10°C and 43.20°C, and a rise time of 3.78 minutes. Next, the perfusion is kept at the nominal values, but the diameter of the tumor in the simulated tissue model is increased from 2.0 cm to 3.0 cm. Figure 3.10 shows the controlled steady state temperature response for the plant with the larger tumor. The transient response of the regulated outputs for the plant with the larger tumor is overdamped with measured steady state output temperatures of 46.10°C and 43.20°C, and a 3.84 minute rise time.

Changing either the perfusion or the tumor size alters the size of the diagonal elements of the state transition matrix, A. The simulated tissue model can also be perturbed by changing the input or the output structure of the plant. The input structure can be changed by varying the scan parameters of the transducers which apply power to the system. Power profiles with scan parameters including a tilt angle of 0.0°, a rotation angle of 0.0°, focal depths of 3.0 and 2.5 cm, and scan radii of 0.5 and 1.0 cm, respectively, are simulated. Figure 3.11 shows the controlled steady state regulated output temperatures for the input perturbed system under the control of the nominal
fourth-order and the full-order controllers. The transient response is overdamped with measured steady state output temperatures of 46.10°C and 43.20°C, and a rise time of 4.17 minutes.

Figure 3.7. The transient temperature response of the measured outputs for the fourth-order and the full-order optimal servomechanism controllers applied to the nominal system over a time span of 20 minutes. The steady state measured output temperatures are 46.10°C and 43.20°C, and the rise time is 3.95 minutes.
Figure 3.8. The first 5 minutes of the transient closed-loop applied power magnitude for the nominal simulated plant due to the fourth-order controller.
Figure 3.9. The controlled steady state temperature profile for the two controllers when applied to a plant with a uniform perfusion of 1.0 kg/m³ s.
Figure 3.10. The controlled steady state temperature profile for the two controllers when applied to a plant with the nominal perfusion magnitude but a tumor radius of 1.5 cm.
Figure 3.11. The controlled steady state temperature profile for the two controllers when applied to a plant with perturbed scan parameters.
The output structure of the simulated model is varied by perturbing the regulated output information with temperatures at adjacent measurement locations. The servomechanism controller was designed based on the regulated output information measured at locations (13,22). To investigate the impact of errors in the sensor locations, the two measured regulated outputs are moved to the locations (16,18) and the controllers are applied assuming the nominal locations are still being measured. Figure 3.12 shows the controlled steady state temperatures associated with the output perturbed system. The transient response is overdamped with steady state output temperatures at the original regulated output locations, (13,22), of 48.19°C and 42.30°C, and a rise time of 3.39 minutes. Since the optimal set point temperature for the first component of the perturbed measured output locations should be \( r_1(k) = 8.0 \), which is more than a degree less than that for the first nominal set point temperature value of \( r_1(k) = 9.1 \), it is not surprising that the entire steady state temperature field is considerably higher. Using the locations (16,18) as the desired regulated outputs and with a correction to the set point temperatures of \( r(k) = \{8.0,6.5\} \), a redesign of the fourth-order and full-order controllers gives an overdamped transient response with steady state temperatures at the original (13,22) regulated locations of 46.12°C and 43.25°C, and a 3.87 minute rise time.
Figure 3.12. The controlled steady state temperature profile for the two controllers when applied to a plant with perturbed outputs. The two perturbed outputs are located at (16,18) in Figure 3.3.
3.5 Results

One advantage of using the reduced-order models is that the significant three dimensional coupling effects within the full-order model are retained in the low-order model. To date very few proposed hyperthermia controllers are designed using three dimensional models, probably because of the large dimensions encountered during the design. Many model based designs use one or two dimensional models, or assume a model structure and use estimation to fit the control model to the actual system. The drawback of using one and two dimensional thermal models is that the controller is designed for a model that does not include conduction in all directions. The drawback of learning the model on-line is that the identification process requires highly exciting inputs and sufficient time to gather the thermal information. Typically, patient tolerance and pain limit both the time of the treatment and the amount of input variation that can be applied during a treatment. Reduced-order models consider the complete coupling in the thermal process, and provide structure and considerable a priori information for system identification purposes.

Lower-order models give a more intuitive understanding of the dynamics describing a given system. It should be noted that reduced-order modelling is not merely an increase in the finite difference grid size to reduce the number of nodes to a manageable size. Increasing the grid size leads to a dynamic structure that does not accurately represent the thermal response of the tissue. The objective of model reduction in general is to retain an aggregate of the dynamics that best fit, in some manner, the dynamics of the full-order model. For reduced-order models based on the balanced
realization, the most controllable and observable portion of the full-order model is retained in the reduced-order model. This portion of the full-order model is a dimensionally manageable system that is compatible with the sophisticated control algorithm strategies and estimation schemes needed for hyperthermia.

There are several advantages of the balanced reduced-order modelling algorithm over other model reduction techniques. First, for an asymptotically stable system with unique second order modes, the reduced-order model is guaranteed to be stable. Second, the balanced realization is based on the singular value decomposition, a numerically stable algorithm. Finally, once the transformation matrix that places the system in a balanced representation has been constructed, reduced-order models of any order from one to \( n \) can be obtained using this one transformation matrix. Also, the singular values of the system provide indicators on how effective a particular reduced-order model will be before actually constructing the reduced-order model.

One drawback of reduced-order modelling is that a certain amount of intuitive physical meaning is lost in the reduction process. The full-order state space model gives a simple relationship between the state components and the thermal grid points of the control volume. The coupling from one grid point to another is given by the off-diagonal elements of the system matrix, \( A \). Changes in the relative magnitudes of the diagonal elements of the system matrix directly relate to changes in the perfusion pattern. The input matrix shows to what extent each transducer scan pattern applies power to the grid points. During the model reduction process, this nice spatially defined model is replaced with a model whose impulse response matches that of the full-order model. However,
reduced-order modelling is a control design tool, and this spatial knowledge is an acceptable trade-off for having such low-order models.

A second drawback of the reduced-order model is the sensitivity of these models to changes in the system model. The balanced realization is a function of the controllability and the observability structure of the thermal models. Assuming that the perfusion magnitude is the only variable physiological parameter, changes in perfusion change the system matrix which changes both grammian calculations. Changes in the shape of the applied power result in changes in the input matrix which changes the controllability grammian calculation. Similarly, changes in the location of the output sensors changes the output matrix which changes the observability grammian calculation. A systematic comparison of the effectiveness of these reduced-order models when subject to these input and output uncertainties is an important topic for further research. How sensitive the reduced-order models are to these uncertainties must always be considered during the physical implementation of any control scheme. However, as the results show, a certain amount of model mismatch associated with these perturbed tissue models can be accommodated by the controller.

The reduced-order optimal servomechanism controller described in Appendix C gives good results when the applied power is similar to the simulated power and the thermocouple positions match the measured output locations of the model. However, the optimal servomechanism controller, which assumes the input can be both positive and negative is a linear controller that is being applied to a input constrained system, i.e., the input in the hyperthermia system is constrained to be positive. As a result, the set point
temperatures for the controller have to be selected to maintain linear operation of the controller. For this reason the set points for the controller are taken from the steady state nominal plant temperature response shown in Figure 3.5, as the controlled steady state applied powers applied to the nominal plant should be close to those constant powers of 5.0 W and 3.0 W.

Perturbing the perfusion of the plant changes the steady state temperature response of the non-controlled outputs. To improve the response for uncertain perfusion magnitudes, the set points for the controller have to be changed to values that provide an acceptable steady state temperature response for that particular perfusion pattern.

Perturbations in the scan parameters reshape the applied power and the steady state response of the system changes accordingly. Manipulation of the set points will not result in an optimal thermal response, because the optimal response is a function of the optimal applied power. However, acceptable responses are still possible for power patterns that are not optimal.

Finally, perturbations in the regulated output information resulted in the largest deviations from the desired transient and steady state responses. The controller is more sensitive to shifts in the sensor locations in regions of large thermal gradients. With inaccurate measured output locations, the transient data expected by the controller is incorrect and the set points do not reflect the values needed for an optimal thermal response.

Comparison of the results for the reduced-order and the full-order controllers show very similar responses in all cases. Both controllers forced the desired measured
outputs to the specified set point temperatures, and the differences in the measured transient responses are negligible. The results of the full-order controller validate the use of the reduced-order model of the original system as a control design tool. These results indicate that for the hyperthermia problem, little would be gained by calculating the full-order controller and then reducing it.

The model reduction techniques described here are applicable to a wide variety of tumor thermal models and hyperthermia modalities. The R-z symmetric model can be replaced by a cartesian based model that incorporates more complicated inhomogeneous tissue and perfusion structures. In addition, other modalities such as RF and EM applicators can easily be incorporated into the model reduction process. The relative orders of the reduced-order models will change from modality to modality, but the criteria for choosing the order, and the results of the reduced-order controllers will not change.

3.6 Summary

Based on the results given in this chapter the following points have been reached. First, the open-loop reduced-order models based on the balanced realization provide sufficient information for reduced-order controller design. Second, drastic model reduction is possible by truncating the balanced realization of a BHTE state space model with known perfusion parameters. Third, the reduced-order models are sensitive to tissue perfusion changes, shifts in the applied power pattern, and perturbations in the regulated output information. However, the reduced-order controllers are more robust than the
reduced-order models and perform satisfactorily under a variety of perturbations in the actual system. Finally, reduced-order modelling gives a low-order model that characterizes the coupling inherent to the thermal process without ignoring spatial dimensions or requiring extensive estimation.
CHAPTER FOUR

CONCURRENT THERMAL ESTIMATION

4.0 Introduction

This chapter investigates the application of the extended Kalman filter (EKF) estimation techniques to the on-line (concurrent) reconstruction of the tissue thermal response during a hyperthermia treatment. Thermal estimation is a significant issue since accurate and clinically useful noninvasive techniques are currently unavailable for measuring the temperature distribution in the heated region during a treatment. Consequently, invasive temperature sensors are generally used to provide the clinician with a small sampling of the thermal information needed for controlling the applied power. The number and the location of these temperature sensors that can be inserted into the tumor region are limited by various patient considerations. Thus, the minimum tumor tissue temperature and the maximum normal tissue temperature are rarely measured during a treatment. As a result, the complete temperature profile of the treated region has to be estimated using the information gathered from the limited number of temperature sensors.

Knowledge of the thermal response of the tumor volume during a hyperthermia treatment is an important factor in determining the treatment's success and in determining the applied power modification required to improve that response. How closely the treatment objective has been reached can only be evaluated if an accurate thermal profile exists for the tumor and its surrounding tissue. Reconstructing this thermal profile is
hindered, however, by unknown and variable blood flows that cool the tissue, and the limited input excitation.

This chapter considers estimation based on the complex thermal transfer associated with nonuniform power applied to nonuniformly perfused tissue regions. Simulations of the complex tissue model allow a systematic evaluation of the success of the estimators, and addresses such issues as sensor number and location. The basic scheme underlying the estimators presented is the EKF. The EKF is used because it leads to a recursive estimator that isolates the significant unknown tissue parameters in an efficient manner that retains the major features of the thermal model. However, similar to the controller design, the large dimension of the thermal state space models places limits on the hardware required to perform the on-line calculations for the full-order EKF. To circumvent the problems associated with high model dimensionality, reduced-order models are used to develop lower order estimators. The reduced-order models given in Chapter Three can be used in a variety of ways to reduce the computational requirements associated with concurrent dosimetry. Two such reduced-order estimation schemes and two full-order estimation schemes are presented here.

This chapter is organized as follows. The methods section discusses the specifics of the full-order EKF, the steady state Kalman filter, and the two reduced-order estimators. The simulation section details the simulations that compare the estimators as a function of various blood perfusion magnitudes, and the number and the locations of the output sensors. The discussion section compares the results obtained from the simulations. The EKF’s results are compared with a full-order steady state Kalman
filter’s results to show the added need for parameter estimation associated with concurrent state estimation. The two reduced-order estimators are compared based on their thermal accuracy and the computational efforts required.

4.1 Methods

Two full-order estimators are designed to reconstruct the temperature response of the heated region from a limited number of measured outputs. A full-order steady state Kalman filter is designed for comparison purposes, and illustrates the pitfalls of hyperthermia estimation when only the states (temperatures) are reconstructed. The EKF extends the estimation in the Kalman filter to include the reconstruction of the parameters (unknown perfusion magnitudes), as well as, the states (temperatures).

Examination of (A.1) through (A.5) of Appendix A shows that the perfusion influences only the diagonal elements of the state transition matrix, A. Based on this observation, the discrete-time EKF (Ljung 1979) for this process simplifies to

\[
\begin{align*}
\mathbf{x}(k+1) &= A(\hat{\mathbf{x}}(k)) \mathbf{x}(k) + B u(k) + K(k) [y(k) - C \mathbf{x}(k)] ; \\
\mathbf{x}(0) &= 0 \\
\hat{\mathbf{x}}(k-1) + L(k) [y(k) - C \mathbf{x}(k)] ; \\
\hat{\mathbf{x}}(0) &= \hat{\mathbf{x}}_0
\end{align*}
\] (4.1) (4.2)

where \( \hat{\mathbf{x}} \in \mathbb{R}^n \) is the estimate of the states in (2.13), \( \hat{\mathbf{w}} \in \mathbb{R}^d \) is the estimate of the \( d \) unknown perfusion magnitudes, and \( K(k) \in \mathbb{R}^{nxp} \) and \( L(k) \in \mathbb{R}^{dxp} \) are time varying Kalman
feedback gains described in Appendix D. The equations for the Kalman filter are similar to those of the EKF except that $\hat{\psi}$ is a constant, and $L(k)$ in (4.2) is set to zero. For the steady state Kalman filter, the optimal steady state Kalman gain is applied to (4.1) instead of the optimal time-varying Kalman gain, i.e., $K$ replaces $K(k)$ in (4.1) (see Ogata (1987) for a steady state Kalman gain calculation technique).

In this study the spatial pattern for the perfusion profile is divided into two possible regions ($d=2$). The perfusion in the tumor tissue takes one uniform value, and the normal tissue perfusion takes a second uniform value. This choice of perfusion pattern is reasonable when dealing with brain tumors where xenon gas studies have shown typically two to four different perfusion zones in the tumor region (Toglia et. al. 1992). For the purposes of the present simulations, no model mismatch exists between the actual system's spatial perfusion pattern and the model's spatial perfusion pattern. Thus, the unknown perfusion magnitudes represent the only model mismatch in the present problem.

Two reduced-order estimators are designed to test the feasibility of reducing the computational burden associated with hyperthermia estimation. The reduced-order models, described in Chapter Three, are designed based on the truncation of the balanced realization of the open-loop state space model. These open-loop, reduced-order models are used to design the two reduced-order estimators. The application of the reduced-order models to thermal estimation design increases the understanding of the sensitivity of the reduced-order models to perfusion magnitude mismatch.

In the first reduced-order estimator, the dynamics of the full-order model
appearing in the EKF are replaced by the reduced-order model. Thus, the computation of the matrices in the EKF are reduced in dimension to that of the reduced-order model. In the second reduced-order estimator, only the perfusion estimates gathered by the reduced-order EKF are retained. These perfusion estimates are then inserted into a full-order, steady state Kalman filter to estimate the states. Here, the full-order Kalman gain is calculated before the treatment, and the reduced-order EKF is used to change the full-order dynamics on-line. Thus, the computational burden of the second estimator is that of a reduced-order EKF, plus the full-order solution of the steady state Kalman gain. Table 4.1 summarizes the four estimators designed in this chapter.

<table>
<thead>
<tr>
<th>Estimator Name</th>
<th>Estimator Model Dimension</th>
<th>Temperature Estimation</th>
<th>Parameter Estimation</th>
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<td>Optimal Steady State Feedback Gain</td>
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<td>Extended Kalman Filter</td>
<td>Full-Order</td>
<td>Feedback Gains Vary as Parameters are Estimated</td>
<td>Incorporated into Filter Structure</td>
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<tr>
<td>Reduced-Order Extended Kalman Filter</td>
<td>Reduced-Order</td>
<td>Feedback Gains Vary as Parameters are Estimated</td>
<td>Incorporated into Filter Structure</td>
</tr>
<tr>
<td>Reduced-Order EKF and Full-Order Steady State Kalman Filter</td>
<td>Both Full-Order and Reduced-Order Models</td>
<td>Optimal Full-Order Steady State Feedback Gains</td>
<td>Performed by Reduced-Order EKF</td>
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Table 4.1. A comparison showing the differences between the four estimators.
4.2 Simulations

A variety of simulations have been performed to evaluate the proposed estimation schemes for the tissue volume described in Figure 3.2. The magnitude of the applied power profiles described in Figures 2.4 and 3.4 are chosen to result in a 46 °C steady state temperature at the center of the tumor (location 22 in Figure 3.3). This normalization procedure enables comparisons of the results from simulations having different perfusion profiles to be made for similar tumor treatment conditions. Figure 4.1 shows a block diagram of the simulated plant with the estimators.

The first simulation tests the ability of the full-order estimators to estimate a variety of different perfusion magnitudes. The temperatures at locations 7 and 22 of the simulated plant represent the measured output locations generating the transient information used by the estimators. Table 4.2 shows the perfusion estimates and the maximum temperature difference (MTD) at the 10 minute and 20 minute points of the transient response defined by

\[
MTD(k) = \max_i |T(k, i) - T_e(k, i)|; \quad i = 1, \ldots, 40
\]  

(4.3)

where \(T(k, i)\) is the simulated temperature at time sample \(k\) and at output location \(i\), and \(T_e(k, i)\) is the estimated temperature at the same time and location.
Figure 4.1. Block diagram of the simulated plant and estimators.
The success of a single simulation is categorized into one of four possible classes based on the MTD at the 10 and 20 minute points of the transient. The simulation is considered i) unacceptable (U) if the MTD at 20 minutes is greater than 1.0 °C, ii) marginally acceptable (MA) if the MTD at 20 minutes is less than 1.0 °C, iii) acceptable (A) if the MTD at 10 and 20 minutes are both less than 1.0 °C, and iv) superior (S) if the MTD is less than 1.0 °C at 10 minutes and less than 0.5 °C at 20 minutes. The 20 minute point of the transient is considered since most SFUS treatments reach steady state in approximately 20 minutes. This classification is summarized in Table 4.2.

<table>
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<td>&gt;1.0°</td>
</tr>
<tr>
<td>MA</td>
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</tr>
<tr>
<td>A</td>
<td>&lt;1.0°</td>
<td>&lt;1.0°</td>
</tr>
<tr>
<td>S</td>
<td>&lt;1.0°</td>
<td>&lt;0.5°</td>
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Table 4.2. Classification of the estimation results based on MTD at 10 and 20 minutes.
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<th>MTD (10)</th>
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<td>4.32</td>
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<td>[4.9,1.0]</td>
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</tr>
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<td>-</td>
<td>3.20</td>
<td>-</td>
<td>U</td>
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<tr>
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<td>0.74</td>
<td>-</td>
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<td>[0.9,0.9]</td>
<td>0.03</td>
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<td>SSKF</td>
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<td>S</td>
</tr>
<tr>
<td>SSKF</td>
<td></td>
<td>2.46</td>
<td>-</td>
<td>2.74</td>
<td>-</td>
<td>U</td>
</tr>
<tr>
<td>EKF</td>
<td>[5.0,10.0]</td>
<td>0.10</td>
<td>[4.8,9.6]</td>
<td>0.04</td>
<td>[4.9,9.8]</td>
<td>S</td>
</tr>
<tr>
<td>SSKF</td>
<td></td>
<td>4.41</td>
<td>-</td>
<td>4.49</td>
<td>-</td>
<td>U</td>
</tr>
</tbody>
</table>

Table 4.3. The MTD and the perfusion estimates for both the full-order EKF and the full-order steady state Kalman filter (SSKF) as a function of plant perfusion. All results have been obtained using the measured output locations (7,22).

For all cases in Table 4.3, the perfusion values for the full-order steady state Kalman filter are [0.0,0.0], and the \( \hat{w}_0 \) values (initial conditions) for the full-order EKF are taken as [0.0,0.0]. Figure 4.2 shows that for the selected measured outputs (at locations 7 and 22) the choice of \( \hat{w}_0 \) is not critical in the EKF, since by 20 minutes the estimated perfusion magnitudes converge to within 10% of the desired plant perfusion.
values for all the initial perfusion magnitudes studied. Figures 4.3a and 4.3b show the steady state estimated temperature profiles for the full-order EKF and the Kalman filter applied to the \( w = [8.0, 2.0] \) plant, respectively. The steady state temperatures in Figure 4.3a are within 0.05 °C of the steady state profile generated by the simulated (actual) plant.

Having established that the full-order EKF is capable of estimating the perfusion for a variety of different perfusion magnitudes, a second study is performed to evaluate the effects of thermocouple number and location on the EKF. Table 4.4 shows the perfusion estimates and the MTD for the \([8.0,2.0]\) kg/m³ s perfusion pattern for different output locations. Table 4.5 shows similar results for larger numbers of measured outputs, and Table 4.6 shows results for plants \([8.0,2.0]\) kg/m³ s and \([2.0,1.0]\) kg/m³ s for a single measured output. Table 4.7 shows the MTD at 20 minutes for the \([8.0,2.0]\) kg/m³ s plant, and measured output 13 for a ramp to step input and a sinusoid plus step input.

Having looked at the feasibility of using the full-order EKF, simulations were run to analyze the effectiveness of reduced-order estimators. To create a reduced-order model, the perfusion profile for the full-order model has been assumed known. For both reduced-order estimators, the reduced-order balancing transformation is calculated from a full-order \([0.0,0.0]\) kg/m³ s model of the plant. Figure 4.4 shows a plot of the MTD at the 20 minute point versus model dimension of the reduced-order estimators for the \([8.0,2.0]\) kg/m³ s plant. In the cases where the dimension of the reduced-order estimator is less than 40 (number of estimated outputs), the balancing transformation is used to generate the remaining output values. Table 4.6 shows a comparison of the reduced-order
estimators as the perfusion profile of the simulated plant is varied. Table 4.7 compares the four estimators for the [8.0,2.0] kg/m³ s plant. This comparison includes an estimate of the number of floating point multiplications needed at each sampling period. Figure 4.5 compares the transient response of the four estimators at output 13 for the [8.0,2.0] kg/m³ s plant.
Figure 4.2. Results of the full-order EKF showing the affect of various initial perfusion values on the perfusion estimation of the [8.0,2.0] kg/m³ s plant.
Figure 4.3a. The 40 steady state estimated outputs for the full-order EKF applied to the [8.0,2.0] kg/m³ s plant.
Figure 4.3b. The 40 steady state estimated outputs for the full-order steady state Kalman filter applied to the [8.0,2.0] kg/m³ s plant.
Figure 4.4. Plot of the MTD at 20 minutes versus the model dimension for the two reduced-order models applied to the \([8.0,2.0]\) kg/m\(^3\) s plant.
Figure 4.5. Plot of the transient temperature for output 13 for the actual and the estimated profiles for the [8.0,2.0] kg/m³ s plant.
<table>
<thead>
<tr>
<th>Sensor Locations</th>
<th>Sensor Tissue Type</th>
<th>MTD (10)</th>
<th>Estimated Perfusion (10 min)</th>
<th>MTD (20)</th>
<th>Estimated Perfusion (20 min)</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>(11,40)</td>
<td>TB,N</td>
<td>0.26</td>
<td>[6.7,1.9]</td>
<td>0.13</td>
<td>[7.2,2.0]</td>
<td>S</td>
</tr>
<tr>
<td>(22,29)</td>
<td>T,NB</td>
<td>0.15</td>
<td>[7.2,1.9]</td>
<td>0.07</td>
<td>[7.7,2.0]</td>
<td>S</td>
</tr>
<tr>
<td>(16,22)</td>
<td>T,T</td>
<td>2.23</td>
<td>[2.5,2.3]</td>
<td>1.99</td>
<td>[3.4,2.4]</td>
<td>U</td>
</tr>
<tr>
<td>(21,22)</td>
<td>T,T</td>
<td>2.81</td>
<td>[1.9,2.2]</td>
<td>1.89</td>
<td>[3.4,2.2]</td>
<td>U</td>
</tr>
<tr>
<td>(3,5)</td>
<td>N,N</td>
<td>0.53</td>
<td>[7.3,1.5]</td>
<td>0.07</td>
<td>[7.7,1.9]</td>
<td>S</td>
</tr>
<tr>
<td>(10,36)</td>
<td>N,N</td>
<td>0.86</td>
<td>[7.1,2.4]</td>
<td>0.67</td>
<td>[7.6,2.4]</td>
<td>A</td>
</tr>
<tr>
<td>(16,23)</td>
<td>T,TB</td>
<td>0.54</td>
<td>[5.6,2.0]</td>
<td>0.28</td>
<td>[6.7,2.0]</td>
<td>S</td>
</tr>
<tr>
<td>(21,28)</td>
<td>T,TB</td>
<td>0.31</td>
<td>[6.5,1.9]</td>
<td>0.14</td>
<td>[7.3,1.9]</td>
<td>S</td>
</tr>
<tr>
<td>(11,13)</td>
<td>TB,TB</td>
<td>0.89</td>
<td>[4.4,2.2]</td>
<td>0.56</td>
<td>[5.6,2.1]</td>
<td>A</td>
</tr>
<tr>
<td>(13,23)</td>
<td>TB,TB</td>
<td>0.81</td>
<td>[4.7,2.2]</td>
<td>0.52</td>
<td>[5.8,2.1]</td>
<td>A</td>
</tr>
<tr>
<td>(2,7)</td>
<td>N,NB</td>
<td>0.32</td>
<td>[7.3,2.1]</td>
<td>0.17</td>
<td>[7.7,2.1]</td>
<td>S</td>
</tr>
<tr>
<td>(24,36)</td>
<td>NB,N</td>
<td>1.15</td>
<td>[6.8,2.8]</td>
<td>0.75</td>
<td>[7.4,2.5]</td>
<td>MA</td>
</tr>
<tr>
<td>(6,8)</td>
<td>NB,NB</td>
<td>1.16</td>
<td>[6.6,2.8]</td>
<td>0.66</td>
<td>[7.2,2.4]</td>
<td>MA</td>
</tr>
<tr>
<td>(14,24)</td>
<td>NB,NB</td>
<td>1.17</td>
<td>[6.7,2.8]</td>
<td>0.70</td>
<td>[7.3,2.4]</td>
<td>MA</td>
</tr>
<tr>
<td>(24,31)</td>
<td>NB,NB</td>
<td>2.24</td>
<td>[5.6,4.1]</td>
<td>2.30</td>
<td>[5.8,4.1]</td>
<td>U</td>
</tr>
<tr>
<td>(13,28)</td>
<td>TB,TB</td>
<td>1.64</td>
<td>[3.1,3.4]</td>
<td>1.52</td>
<td>[3.6,3.4]</td>
<td>U</td>
</tr>
</tbody>
</table>

Table 4.4. The performance of the full-order EKF as a function of output location for the [8.0,2.0] kg/m³ s plant. The four tissue types for the sensor locations are T tumor tissue, TB tumor tissue bordering the normal tissue, N normal tissue, and NB normal tissue bordering the tumor tissue.
<table>
<thead>
<tr>
<th>Sensor Locations</th>
<th>Sensor Tissue Type</th>
<th>MTD (10)</th>
<th>Estimated Perfusion (10 min)</th>
<th>MTD (20)</th>
<th>Estimated Perfusion (20 min)</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>(17,21,22)</td>
<td>T,T,T</td>
<td>1.69</td>
<td>[3.1,2.2]</td>
<td>1.17</td>
<td>[4.5,2.1]</td>
<td>U</td>
</tr>
<tr>
<td>(16,17,21,22)</td>
<td>T,T,T</td>
<td>1.59</td>
<td>[3.3,2.2]</td>
<td>1.13</td>
<td>[4.6,2.1]</td>
<td>U</td>
</tr>
<tr>
<td>(6,8,10)</td>
<td>NB,NB,N</td>
<td>0.50</td>
<td>[7.3,2.2]</td>
<td>0.25</td>
<td>[7.7,2.1]</td>
<td>S</td>
</tr>
<tr>
<td>(11,13,22)</td>
<td>TB,TB,T</td>
<td>0.62</td>
<td>[5.4,2.4]</td>
<td>0.43</td>
<td>[6.2,2.2]</td>
<td>S</td>
</tr>
<tr>
<td>(6,16,26)</td>
<td>NB,T,TB</td>
<td>0.09</td>
<td>[7.5,1.9]</td>
<td>0.03</td>
<td>[7.8,2.0]</td>
<td>S</td>
</tr>
<tr>
<td>(6,18,21,33)</td>
<td>NB,TB,T,NB</td>
<td>0.06</td>
<td>[7.7,1.9]</td>
<td>0.02</td>
<td>[7.9,2.0]</td>
<td>S</td>
</tr>
</tbody>
</table>

Table 4.5. The performance of the full-order EKF as a function of multiple measured output locations for the [8.0,2.0] kg/m³ s plant. The four tissue types are the same as in Table 4.4.
<table>
<thead>
<tr>
<th>Sensor Location</th>
<th>Sensor Tissue Type</th>
<th>Sensor MTD (10)</th>
<th>MTD Estimated Perfusion (10 min)</th>
<th>MTD Estimated Perfusion (20 min)</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>N</td>
<td>0.15</td>
<td>[7.2, 1.7]</td>
<td>0.54</td>
<td>[7.6, 2.3]</td>
</tr>
<tr>
<td>8</td>
<td>NB</td>
<td>1.50</td>
<td>[6.5, 3.1]</td>
<td>2.88</td>
<td>[6.8, 3.5]</td>
</tr>
<tr>
<td>13</td>
<td>TB</td>
<td>1.67</td>
<td>[3.0, 3.3]</td>
<td>1.61</td>
<td>[3.5, 3.5]</td>
</tr>
<tr>
<td>21</td>
<td>T</td>
<td>3.53</td>
<td>[1.3, 2.5]</td>
<td>2.73</td>
<td>[2.5, 2.5]</td>
</tr>
<tr>
<td>3</td>
<td>N</td>
<td>0.85</td>
<td>[1.9, 0.4]</td>
<td>0.72</td>
<td>[2.0, 0.6]</td>
</tr>
<tr>
<td>8</td>
<td>NB</td>
<td>0.19</td>
<td>[1.8, 0.8]</td>
<td>0.04</td>
<td>[1.9, 1.0]</td>
</tr>
<tr>
<td>13</td>
<td>TB</td>
<td>0.48</td>
<td>[1.1, 1.3]</td>
<td>0.37</td>
<td>[1.5, 1.3]</td>
</tr>
<tr>
<td>21</td>
<td>T</td>
<td>1.12</td>
<td>[0.4, 1.1]</td>
<td>0.81</td>
<td>[1.1, 1.2]</td>
</tr>
<tr>
<td>28</td>
<td>TB</td>
<td>0.47</td>
<td>[1.1, 1.3]</td>
<td>0.34</td>
<td>[1.5, 1.2]</td>
</tr>
</tbody>
</table>

Table 4.6. Sensor location, MTD, perfusion estimates and classification of the results for the [8.0,2.0] kg/m³ s plant and the [2.0,1.0] kg/m³ s plant for a single measured output location.
Table 4.7. MTD results for the [8.0,2.0] kg/m³ s plant and measured output 13 with greater input excitation. For the transition between the ramp input to the step input, the input power is ramped up to the desired level over the $T_{ramp}$ time frame. For the sinusoid inputs plus a step input $u_1(k) = u_{1o} + \sin(\omega k)$, $u_2(k) = u_{2o} + \sin(2\omega k)$.

<table>
<thead>
<tr>
<th>$T_{ramp}$</th>
<th>MTD(20)</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 min</td>
<td>1.62</td>
<td>U</td>
</tr>
<tr>
<td>10 min</td>
<td>1.71</td>
<td>U</td>
</tr>
<tr>
<td>15 min</td>
<td>1.79</td>
<td>U</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>$\omega$</th>
<th>MTD(20)</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>1°</td>
<td>1.83</td>
<td>U</td>
</tr>
<tr>
<td>5°</td>
<td>1.56</td>
<td>U</td>
</tr>
<tr>
<td>10°</td>
<td>1.66</td>
<td>U</td>
</tr>
<tr>
<td>Estimator</td>
<td>Actual Perfusion</td>
<td>MTD (10)</td>
</tr>
<tr>
<td>-----------</td>
<td>------------------</td>
<td>----------</td>
</tr>
<tr>
<td>ROE1</td>
<td>[10.0,5.0]</td>
<td>0.41</td>
</tr>
<tr>
<td>ROE2</td>
<td></td>
<td>0.29</td>
</tr>
<tr>
<td>ROE1</td>
<td>[5.0,1.0]</td>
<td>0.44</td>
</tr>
<tr>
<td>ROE2</td>
<td></td>
<td>0.23</td>
</tr>
<tr>
<td>ROE1</td>
<td>[0.75,0.25]</td>
<td>0.08</td>
</tr>
<tr>
<td>ROE2</td>
<td></td>
<td>0.10</td>
</tr>
<tr>
<td>ROE1</td>
<td>[1.0,1.0]</td>
<td>0.08</td>
</tr>
<tr>
<td>ROE2</td>
<td></td>
<td>0.11</td>
</tr>
<tr>
<td>ROE1</td>
<td>[1.0,5.0]</td>
<td>0.60</td>
</tr>
<tr>
<td>ROE2</td>
<td></td>
<td>0.53</td>
</tr>
<tr>
<td>ROE1</td>
<td>[5.0,10.0]</td>
<td>0.58</td>
</tr>
<tr>
<td>ROE2</td>
<td></td>
<td>0.42</td>
</tr>
</tbody>
</table>

Table 4.8. The reduced-order estimator results as a function of perfusion at the measured output locations (7,22). ROE1 is the 19th-order EKF, ROE2 is the ninth-order EKF with the full-order steady state Kalman filter.
Table 4.9. Comparison of the MTD and the floating point multiplication count of the four estimators for the [8.0,2.0] kg/m³ s plant and the measured output locations (7,22).

### 4.3 Discussion

The perfusion magnitudes in Table 4.3 include larger ([10.0,5.0], [8.0, 2.0]), medium ([5.0,1.0]) and smaller ([0.75,0.25]) perfusion magnitudes, uniform ([1.0,1.0]) perfusion magnitudes, and magnitudes where the tumor perfusion is higher than the normal perfusion ([1.0,5.0], [5.0,10.0]). The results of Table 4.3 show that the full-order EKF is capable of successfully estimating the thermal response for a variety of possible perfusion magnitudes. In addition, Figure 4.2 shows that for outputs (7,22) the full-order EKF is insensitive to the initial perfusion values chosen.

In contrast with the EKF, the choice of initial perfusion is crucial to the success of the full-order steady state Kalman filter. Since the perfusion parameters are not
estimated by the Kalman filter, the initial choice of perfusion dictates the shape of the resulting steady state temperature profile. Thus, the Kalman filter can change the temporal response of the estimated temperatures, but can not properly change the spatial pattern of the steady state estimated temperatures. When the perfusion spatial distribution and magnitude for the estimation model is similar to that of the plant, the standard Kalman filter performs satisfactorily. As the differences between the estimator's perfusion and the plant's perfusion grow, the standard Kalman filter fails to estimate the unmeasured temperatures accurately. Increasing the number of measured outputs fed back through the Kalman filter fails to improve the estimates. Figure 4.3 further illustrates the advantages of the state and the parameter estimation of the EKF over the state estimation of the Kalman filter.

Analysis of Tables 4.4 and 4.5 shows that the convergence of the EKF output is a function of the number, as well as, the locations of the measured outputs. Table 4.4 lists several illustrative examples taken from a large number of simulations comparing the affects of output locations on the results of the \([8.0, 2.0]\) kg/m³ s case with an initial perfusion of \([0.0,0.0]\) kg/m³ s. These results are shown because the \([8.0,2.0]\) kg/m³ s plant has the highest perfusion gradient and is the most difficult plant to estimate perfusion values, as shown by the results in Table 4.3. Consistently, the best estimation results occur when one measured output is placed in the normal tissue perfusion zone, and the other measured output is placed in the tumor tissue perfusion zone (outputs (7,22), (11,40), and (22,29), refer to Figure 3.2 for the output locations). This is not surprising since the measured outputs are in locations where the unknown perfusion
parameters are directly sampled.

Simply having two measured outputs in the treatment region does not guarantee the convergence of the full-order EKF to the correct thermal profile, however. The thermal response represents a highly complex interaction of the conduction process, the perfusion process, and the SFUS power applied to the region. Here the success of the estimator is based on the MTD evaluated after 20 minutes of heating. An unsuccessful result for the full-order EKF (except in the underdetermined case) does not imply that the EKF converged to the incorrect perfusion values. Instead, insufficient information was extracted for the EKF to converge to the correct values in just 20 minutes. Simulations showed that for the cases that were classified as unacceptable the MTD fell below 1.0 °C after 20 minutes of estimation.

To compare the results of the EKF as a function of measured output location consider four classes of locations. The 40 critical outputs in Figure 3.2 are classified as (T) totally inside the tumor (outputs 16,17,21,22), (TB) inside the tumor but bordering the normal tissue (outputs 11,12,13,18, 23,26,27,28), (NB) inside the normal tissue but bordering the tumor (outputs 6,7,8,14,19,24,29,31,32,33), and (N) totally inside the normal tissue (remaining outputs). The results of the EKF after placing the measured outputs totally within the tumor tissue (outputs (16,22) and (21,22)) are unacceptable. Conversely, placing the measured outputs totally inside the normal tissue ((3,5) and (10,36)) gives acceptable results. For the [8.0,2.0] kg/m³ s plant, the states totally inside the tumor are more influenced by the applied power than by the coupling associated with the tumor perfusion-normal perfusion interface. As a result, for measured outputs located
totally inside the tumor, the normal perfusion is not accurately estimated in 20 minutes, and the resulting thermal estimates are unacceptable. The states located totally inside the normal tissue are influenced more by the relative thermal transfer from the tumor to the normal tissue than the applied power. Thus, the estimates for the measured outputs located totally in the normal tissue give better perfusion estimates and acceptable temperature profiles. Note that for plants with higher tumor tissue perfusion (the [1.0,5.0] kg/m³ s plant), the thermal energy from the given SFUS applied power profiles is transferred very quickly from the tumor tissue to the normal tissue. As a result, the tumor tissue is influenced more by the thermal transfer into the normal tissue than the applied power. Thus, the EKF results for the higher tumor perfusion plants are reversed, and the acceptable profiles arise from the measured outputs located totally inside the tumor tissue.

Placing one measured output totally inside the tumor tissue and the other measured output in the tumor tissue bordering on the normal tissue (outputs (16,23) and (21,28)) gives superior results. The results are acceptable when both measured outputs are placed inside the tumor tissue bordering on the normal tissue (outputs (11,13) and (13,23)). Similarly, placing one measured output totally inside the normal tissue and the other measured output inside the normal tissue bordering on the tumor (outputs (2,7) and (24,36)) gives marginally acceptable results. However, placing both outputs inside the normal tissue bordering on the tumor gives at best marginally acceptable results (outputs (6,8) and (14,24)), and possibly unacceptable results (outputs (7,24) and (24,31)). These unacceptable results are probably a function of the small amount of information about the
tumor tissue perfusion magnitude that can be gathered from the normal tissue region locations. For these measured output locations, which are inside the normal tissue but border the tumor, the estimated tumor perfusion is inaccurate giving rise to unacceptable thermal estimation.

Unacceptable results also occur when the two measured output locations are chosen with respect to each other in a structurally symmetric location about the \( z = 3.0 \) cm line (outputs \((13,28)\) and \((2,37)\)). For these symmetric output locations the coupling of the corresponding states in the state transition matrix is symmetric. This structural and transition matrix symmetry may explain why the EKF is unable to converge for these locations. (In a real tumor, the various shapes of the perfusion zones will reduce the number of transition matrix symmetries).

Simulation results for one measured output shown in Table 4.6, the underdetermined estimator, do not provide sufficient information for the successful estimation of the \([8.0,2.0]\) kg/m\(^3\) s plant. The estimation of unknowns is related to the variability of the input excitation applied (Goodwin and Sin 1984), the number of sampled outputs, and the magnitude of the perfusion gradients. Thus, it is not surprising that the estimation of the two perfusion magnitudes for the \([8.0,2.0]\) kg/m\(^3\) s plant, from a single measured output generated from constant applied power, gives unsatisfactory results. Increasing the input excitation poses additional problems for the clinician as patient pain has to be considered. Varying the applied power to increase the input excitation may cause overheating, and may increase the duration of the treatment. The application of ramp inputs and sinusoidal variations in the applied power, shown in Table
over the first 20 minutes of the treatment did little to change the results of the single output simulations. In cases where the magnitude of the perfusion gradient is small, i.e., the \([2.0,1.0]\) kg/m\(^3\) s plant in Table 4.6, single measured output locations exist that result in acceptable thermal estimation. When the magnitude of the perfusion gradient is small, uniform perfusion patterns exist that keep the MTD for the EKF within an acceptable tolerance. A single measured output is capable of estimating such nearly uniform perfusion characteristics.

The results in Table 4.5 illustrate that the greater the number of measured outputs, the better the thermal estimation. However, the addition of thermal sensors does not guarantee acceptable thermal estimation. The results for outputs \((17,21,22)\) and \((16,17,21,22)\) are better than the results for outputs \((21,22)\) and \((16,22)\), but are still unacceptable. Similarly, the results for output \((7,24,31)\) are better than those for \((7,24)\) and \((24,31)\), but they are also unacceptable. Thus, care is needed in placing the output sensors so that the results are improved and give acceptable results. For example, the results for \((6,8,10)\) and \((11,13,22)\) are classified as superior and are better than the results for \((6,8)\) and \((11,13)\). For cases where sensors exist in all the unknown perfusion zones, the addition of sensors improves the rate of convergence of the EKF (outputs \((6,16,26)\) and \((6,18,21,33)\)).

The design of the reduced-order estimators results in a natural tradeoff between accuracy and computational requirements. Figure 4.4 shows a comparison of the MTD of the reduced-order estimators as a function of the reduced-order model dimension. The results of the reduced-order EKF combined with the full-order steady state Kalman filter
are more attractive than those of the reduced-order EKF. The reconstruction of the temperatures at the final stage of each reduced-order estimator gives rise to the differences seen in Figure 4.5. For the reduced-order EKF, the balancing transformation is used to reconstruct the 40 estimated outputs from a state space model having a dimension less than 40. The choice of the perfusion profile required for calculation of the reduced-order model influences the resulting balancing transformation. Thus, the perfusion choice used to calculate the balancing transformation impacts upon the reconstruction of the estimated temperature profile. The reduced-order models applied to the EKF produce an accurate reconstruction of the dynamics, but are limited by the ability of the balancing transformation to reconstruct temperature profiles for which they were not designed. The results of the reduced-order EKF to plants whose perfusion profiles give rise to temperature profiles with shapes similar to the design perfusion temperature profile are much better than those having widely differing temperature profiles. However, the results in Table 4.9 show that acceptable responses do exist for the reduced-order EKF at great computational savings. Table 4.8 shows that acceptable and superior results exist for the reduced-order EKF estimator based on a 19th-order thermal model.

The reduced-order EKF combined with the full-order steady state Kalman filter seeks to combine the dynamics of the reduced-order EKF with the temperature reconstruction capabilities of the full-order steady state Kalman filter. The results of the reduced-order EKF in Table 4.8 indicate that perfusion estimation is possible using EKF’s of greatly reduced dimension. The steady state Kalman filter is computed before
the simulated treatment and only requires the calculation of equation (D.3) for a static gain K. Table 4.8 shows that acceptable and superior results exist for the reduced-order EKF combined with the steady state Kalman filter when a ninth-order thermal model is used by the reduced-order EKF to estimate the perfusion magnitudes. Figure 4.5 shows that both reduced-order estimation schemes result in acceptable alternatives to the full-order EKF.

Note that the location of the measured outputs dictates the dimension required by the reduced-order model for estimation purposes. The results of Table 4.8 are indicative of the greatest amount of model reduction expected based on the two measured outputs (7,22). Results (not shown) based on other less desirable ((N,N), (T,T), (N,NB), (T,TB), (NB,NB), (TB,TB)) measured output locations showed that the dimension of the reduced-order models had to be increased to match the full-order EKF results. However, these results also indicate that as a worst case the reduced-order estimators reduce the computational burden of the full-order EKF by at least a factor of 10.

4.4 Summary

First, the success of the EKF when applied to the concurrent hyperthermia problem is a function of the number of perfusion zones, the sign and magnitude of the perfusion gradients, the limited input excitation, the finite time of the heat up transient, and the number and the location of the measured outputs. The best results occur when at least one measured output exists in each unknown perfusion zone. When a measured output exists in each unknown perfusion zone, all the unknown parameters are directly
sampled. The magnitudes of the perfusion gradients influence the thermal estimation when the number of measured outputs is less than the number of unknown perfusion zones. In this case, the more uniform the unknown perfusion profile, the better the thermal reconstruction. The addition of sensors into the region improves the thermal response, but does not always guarantee acceptable results. Locations within unmeasured perfusion zones provide better information for the EKF and such locations should be considered when adding extra sensors. Second, the steady state Kalman filter (used only to estimate the temperatures and not the perfusion values) does not provide the flexibility required for accurate temperature estimation when uncertainty in the perfusion field exists. Finally, reduced-order modelling allows the design of accurate thermal estimators having significantly reduced computational effort.
CHAPTER FIVE

MULTIPLE MODELLING FOR ESTIMATION

5.0 Introduction

Unfortunately, many estimated parameters, like blood perfusion, are allowed to vary only within prespecified spatial regions to help simplify the models of the treated tissue volume. Results show that the mismatch due to incorrect spatial perfusion zone characterization can create significant errors in the resulting estimation scheme (Clegg and Roemer 1985). While spatial model mismatch has been identified as a problem in hyperthermia estimation, little has been proposed to reduce its impact upon concurrent dosimetry.

This chapter analyzes a concurrent scheme that combines thermal estimation and spatial discrimination based on multiple modelling. The boundary of the blood perfusion zone associated with the tumor tissue is assumed known within some spatially bounded region. Estimators based on the (EKF) are designed for a variety of thermal models having different spatial perfusion zone relationships. The outputs of the multiple EKFs are linearly combined based on each filter's output error. This linear combination is performed by assigning more weight (acceptance) to the EKFs having smaller output errors. As a result of this error weighted combination, the scheme reconstructs thermal responses very similar to the actual tissue responses. This multiple model estimation scheme represents an alternative to acquiring spatial perfusion information by adding more spatial perfusion zones to the estimation model.
This chapter is organized as follows. The methods section discusses the thermal models, and the multiple model EKF estimator. Two multiple model estimators and two estimators based on greater perfusion segmentation are designed. Simulations are performed to show the efficacy of using multiple modelling in bioheat transfer based concurrent estimation. Simulations allow for a systematic evaluation of the success of the multiple model EKF estimator. The simulations section details the simulations that compare the four estimators as a function of blood perfusion profile, and measured output location and number. The discussion section compares the results obtained from the simulations, and evaluates the multiple model hyperthermia estimator.

5.1 Methods

The blood perfusion term in the BHTE is a spatially dependent variable having both unknown pattern and magnitude. The results of Chapter Four show that the full-order EKF is capable of successfully estimating the temperature profile when the spatial pattern for the perfusion is known, and there are as many measured outputs as perfusion zones. However, these results degrade as the uncertainty of the spatial perfusion pattern increases in regions having high perfusion magnitude gradients. In cases where the perfusion magnitude gradient is very small, mismatch due to spatial perfusion pattern has a less significant impact upon the estimation since the tissue resembles a more uniform perfusion pattern.

Assuming that the perfusion is piece-wise constant, at least two methods exist for dealing with the model mismatch due to the uncertain spatial perfusion pattern. One
method would be to segment the estimator's perfusion model representing the treatment volume into a large number of perfusion zones in the hope of improving the spatial resolution of the perfusion pattern. However, greater segmentation may result in estimator convergence problems. An alternate method would be based on a set of thermal models possessing different spatial perfusion patterns. An EKF could then be designed for each model with each EKF processed in parallel. The results of each EKF are compared and a weighted average of the outputs from each EKF is formed based on the output error statistics of the individual filters. The resulting thermal profiles would be summed based on this weighted average to create the output estimate. Figure 5.1 shows a block diagram of the multiple model EKF estimator.

Let \( N \) be the number of independent hypothesis models to be incorporated into the multiple model estimator, and let \( \hat{w}_j \) denote the jth model in the set \( \{ \hat{w}_1, \hat{w}_2, \ldots, \hat{w}_N \} \). The likelihood function, \( P(y(k) \mid \hat{y}_j(k-1), \hat{w}_j(k)) \), is the probability that the measured outputs match the estimated outputs conditioned on hypothesis model \( \hat{w}_j \), and the estimated output of the jth model, \( \hat{y}_j \). Based on the gaussian structure of the EKF, the likelihood function is given as

\[
P(y(k) \mid \hat{y}_j(k-1), \hat{w}_j(k)) = \frac{1}{\sqrt{(2\pi)^P|S_j(k)|}} \exp(-\frac{1}{2} \mathbf{x}_j^T(k) S_j^{-1}(k) \mathbf{x}_j(k))
\]

(5.1)

where \( \mathbf{r}_j(k) = y(k) - C\hat{x}_j(k) \), \( S_j(k) \) is the output error covariance (see (D.7) of Appendix D), and \( | \cdot | \) is the determinant.
Figure 5.1. Block diagram of the multiple model EKF estimator.
Two methods, based on the same derivation, exist for calculating the estimator weights. In the first method the temperatures are averaged based on the individual error statistics at each time increment. These error weights, \( \gamma_j^*(k) \), are calculated as

\[
\gamma_j^*(k) = \frac{P(y(k) | y_j(k-1), \varphi_j(k))}{\sum_{j=1}^{N} P(y(k) | y_1(k-1), \varphi_1(k))},
\]  

(5.2)

where the numerator is given by (5.1). In the second method the weights are based on the a posteriori probabilities and consider the entire transient. Thus, the weights are chosen in an attempt to detect the estimator that maximizes the a posteriori density. For a unimodal distribution, like the assumed gaussian form of the EKFs, the maximum a posteriori estimate and the minimum mean-square error estimate are equal (Van Trees 1968). The a posteriori probability is given as

\[
p(\varphi(k) | \hat{y}_j(k)) = \frac{p(y(k), \hat{y}_j(k-1), \varphi(k))}{p(y(k), \hat{y}_j(k-1))}.
\]  

(5.3)

After manipulation (Papoulis 1984) (5.3) gives

\[
p(\varphi_j(k) | \hat{y}_j(k)) = \gamma_j^*(k) = \frac{p(y(k) | \hat{y}_j(k-1), \varphi_j(k)) p(\varphi_j(k) | \hat{y}_j(k-1))}{\sum_{j=1}^{N} p(y(k) | \hat{y}_1(k-1), \varphi_1(k)) p(\varphi_1(k) | \hat{y}_1(k-1))}
\]  

(5.4)

where \( \gamma_j^d \) are the detecting weights. Thus, a comparison of (5.2) and (5.4) shows that the
averaging weights are the same as the detecting weights having weight resetting at each sampling interval.

The multiple model estimator calculates the resulting thermal profile as

\[ T_e(k, i) = \sum_{j=1}^{N} \gamma_j(k) \mathcal{R}_j(k, i), \quad i = 1, \ldots, 40, \quad (A.15) \]

where \( i \) represents the 40 critical temperature states given in Figure 5.2, and \( \gamma \) are the estimator weights either averaging or detecting.

5.2 Simulations

Simulations are run to evaluate the multiple model EKF estimators and compare them with estimators having greater perfusion segmentation. During estimation the tumor is assumed to have a 2.0 cm depth, centered 3.0 cm from the skin, and the radius of the tumor is known to be between 0.5 cm and 1.5 cm. Figure 5.2 contains a diagram of the tissue model showing the uncertain tumor region, and the 40 critical measured output locations.
Table 5.1. The four estimators \((A,B,C,D)\) are described based on the number of EKFs per estimator, the spatial perfusion characterization as given in Figure 5.3 of each model for each EKF, and the number of unknown parameters per model.

A variety of perfusion configurations exist for describing the uncertain tumor perfusion region shown in Figure 5.2. Figure 5.3 shows five possible perfusion patterns that fit within this uncertain tumor region. Table 5.1 gives the models and the perfusion configurations associated with the four estimators \((A,B,C,D)\) analyzed in this study. The actual tumor radius used in the calculation of the simulated thermal plant’s response is 1.0 cm (model (i) in Figure 5.3). Thus, estimator \(A\) contains a model having the perfusion pattern that matches the actual perfusion pattern. In addition, the perfusion pattern in estimator \(D\) allows the reconstruction of the correct perfusion pattern. For estimators \(B\) and \(C\), spatial mismatch exists between the estimator’s expected perfusion pattern(s) and the actual perfusion pattern. As a result, one would expect the thermal reconstruction of estimators \(A\) and \(D\) to outperform those of estimators \(B\) and \(C\).
Figure 5.2. Diagram of the tissue model showing the uncertain tumor region, and the 40 critical measured output locations.
Figure 5.3 shows five possible perfusion patterns that fit within the uncertain tumor region.
The applied power magnitudes for the scans shown in Figures 2.4 and 3.4 are chosen to result in a 46 °C steady state temperature at output 22 in Figure 5.2. This choice of magnitudes enables an equivalent comparison of the results from simulations having different perfusion profiles. The success of a single simulation is categorized into one of the four possible classes given in Table 4.2, based on the MTD defined in (4.3).

The first simulations, shown in Table 5.2, compare the four estimators as a function of perfusion magnitude, where $A^a$ and $B^a$ denote the multiple model estimators based on the averaging weights. Plants having large perfusion magnitudes ([10.0, 5.0] and [8.0,2.0]), average magnitudes ([5.0, 1.0]), small magnitudes ([0.75,0.25]), uniform magnitudes ([1.0,1.0]), and tumor magnitudes greater than normal tissue magnitudes ([1.0,5.0] and [5.0,10.0]) are simulated. For all estimators the perfusion for each zone is initialized to zero, and the thermal reconstruction of each estimator is based on the two measured outputs at locations (7,22).

Next, the number of measured outputs is increased to three and simulations are run for the [8.0,2.0] kg/m$^3$ s plant as a function of measured output location. Table 5.3 compares the four estimators as a function of measured output locations. For each set of measured output locations in Table 5.3, one measured output is placed in the known tumor zone, one in the known normal tissue zone, and the last measured output is placed anywhere. The third measured output is included to improve both the calculation of the weights used in estimators $A$ and $B$, and the perfusion reconstruction used in estimators $C$ and $D$. The [8.0,2.0] kg/m$^3$ s plant is simulated as it has the greatest perfusion magnitude difference of the seven plants compared in Table 5.2.
Table 5.4 compares the four estimators as the number of measured outputs is increased to four and greater. Three measured outputs give acceptable results for models A, B, and C, but estimator D has five unknown perfusion zones. Thus, a greater number of measured outputs are required for the accurate reconstruction of the unknown perfusion magnitudes in estimator D. Table 5.4 compares the multiple model estimators with the estimators having more perfusion zones in situations where a greater number of thermal sensors exist.
Table 5.2. Comparison of the four estimators as a function of perfusion magnitude based on the two measured outputs (7,22).

<table>
<thead>
<tr>
<th>Actual Perfusion</th>
<th>Estimator</th>
<th>MTD (10)</th>
<th>MTD (20)</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>[10.0,5.0]</td>
<td>$A^*$</td>
<td>0.34</td>
<td>0.36</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^*$</td>
<td>0.51</td>
<td>0.76</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>$C$</td>
<td>1.49</td>
<td>1.49</td>
<td>U</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>1.71</td>
<td>1.69</td>
<td>U</td>
</tr>
<tr>
<td>[8.0,2.0]</td>
<td>$A^*$</td>
<td>0.46</td>
<td>0.49</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^*$</td>
<td>0.69</td>
<td>0.74</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>$C$</td>
<td>1.06</td>
<td>1.12</td>
<td>U</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>1.40</td>
<td>1.41</td>
<td>U</td>
</tr>
<tr>
<td>[5.0,1.0]</td>
<td>$A^*$</td>
<td>0.33</td>
<td>0.38</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^*$</td>
<td>0.50</td>
<td>0.57</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>$C$</td>
<td>0.86</td>
<td>0.99</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>1.03</td>
<td>1.12</td>
<td>U</td>
</tr>
<tr>
<td>[0.75,0.25]</td>
<td>$A^*$</td>
<td>0.09</td>
<td>0.06</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^*$</td>
<td>0.09</td>
<td>0.08</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$C$</td>
<td>0.15</td>
<td>0.20</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>0.19</td>
<td>0.26</td>
<td>S</td>
</tr>
<tr>
<td>[1.0,1.0]</td>
<td>$A^*$</td>
<td>0.09</td>
<td>0.03</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^*$</td>
<td>0.09</td>
<td>0.03</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$C$</td>
<td>0.34</td>
<td>0.36</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>0.33</td>
<td>0.33</td>
<td>S</td>
</tr>
<tr>
<td>[1.0,5.0]</td>
<td>$A^*$</td>
<td>0.48</td>
<td>0.53</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>$B^*$</td>
<td>0.69</td>
<td>0.78</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>$C$</td>
<td>1.46</td>
<td>1.54</td>
<td>U</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
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<td>1.41</td>
<td>U</td>
</tr>
<tr>
<td>[5.0,10.0]</td>
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<td>0.50</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>$B^*$</td>
<td>0.74</td>
<td>0.74</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>$C$</td>
<td>2.55</td>
<td>2.52</td>
<td>U</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>2.39</td>
<td>2.33</td>
<td>U</td>
</tr>
<tr>
<td>Sensor Locations</td>
<td>Estimator</td>
<td>MTD (10)</td>
<td>MTD (20)</td>
<td>Class</td>
</tr>
<tr>
<td>------------------</td>
<td>-----------</td>
<td>----------</td>
<td>----------</td>
<td>-------</td>
</tr>
<tr>
<td>(16,18,20)</td>
<td>A</td>
<td>0.55</td>
<td>0.50</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>0.86</td>
<td>0.87</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>0.90</td>
<td>0.90</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>0.45</td>
<td>0.32</td>
<td>S</td>
</tr>
<tr>
<td>(6,16,26)</td>
<td>A</td>
<td>0.46</td>
<td>0.51</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>0.71</td>
<td>0.77</td>
<td>A</td>
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<td>C</td>
<td>0.81</td>
<td>0.88</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>1.51</td>
<td>1.57</td>
<td>U</td>
</tr>
<tr>
<td>(7,18,22)</td>
<td>A</td>
<td>0.49</td>
<td>0.49</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>B</td>
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<td>0.96</td>
<td>A</td>
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<td>C</td>
<td>0.94</td>
<td>0.95</td>
<td>A</td>
</tr>
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<td></td>
<td>D</td>
<td>1.32</td>
<td>1.33</td>
<td>U</td>
</tr>
<tr>
<td>(2,17,32)</td>
<td>A</td>
<td>0.46</td>
<td>0.53</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>0.72</td>
<td>0.80</td>
<td>A</td>
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<td>C</td>
<td>1.12</td>
<td>1.14</td>
<td>U</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>1.75</td>
<td>1.79</td>
<td>U</td>
</tr>
<tr>
<td>(3,22,23)</td>
<td>A</td>
<td>0.63</td>
<td>0.70</td>
<td>A</td>
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<td></td>
<td>B</td>
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<td>A</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>0.87</td>
<td>0.89</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>1.10</td>
<td>1.10</td>
<td>U</td>
</tr>
</tbody>
</table>

Table 5.3. Comparison of the four estimators as a function of three measured output locations for the [8.0,2.0] kg/m³ s plant.
<table>
<thead>
<tr>
<th>Sensor Location</th>
<th>Estimator</th>
<th>MTD (10)</th>
<th>MTD (20)</th>
<th>Class</th>
</tr>
</thead>
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<td>(16,17,18,19)</td>
<td>A</td>
<td>0.18</td>
<td>0.20</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>0.69</td>
<td>1.08</td>
<td>U</td>
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<td></td>
<td>C</td>
<td>1.31</td>
<td>1.64</td>
<td>U</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>0.72</td>
<td>0.81</td>
<td>A</td>
</tr>
<tr>
<td>(3,13,16,31)</td>
<td>A</td>
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<td>0.55</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>1.07</td>
<td>1.13</td>
<td>U</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>0.99</td>
<td>1.00</td>
<td>U</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>1.42</td>
<td>1.40</td>
<td>U</td>
</tr>
<tr>
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<td>0.49</td>
<td>0.47</td>
<td>S</td>
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<tr>
<td></td>
<td>B</td>
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<td>0.91</td>
<td>A</td>
</tr>
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<td>C</td>
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<td>0.32</td>
<td>S</td>
</tr>
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</tr>
<tr>
<td></td>
<td>B</td>
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<td>1.04</td>
<td>U</td>
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<td>1.05</td>
<td>1.06</td>
<td>U</td>
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<tr>
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<td>0.34</td>
<td>0.24</td>
<td>S</td>
</tr>
<tr>
<td></td>
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<td>0.73</td>
<td>A</td>
</tr>
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<td></td>
<td>C</td>
<td>0.66</td>
<td>0.77</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>0.29</td>
<td>0.15</td>
<td>S</td>
</tr>
</tbody>
</table>

Table 5.4. Comparison of the four estimators as a function of four and five measured output locations for the [8.0,2.0] kg/m³ s plant.
Finally, simulations are performed for the multiple model estimators based on the
detecting weights, denoted $A^d$ and $B^d$. Table 5.5 reconstructs the $[8.0,2.0]$ kg/m$^3$ s plant
results shown in Tables 5.2 through 5.4 for these detecting schemes.

<table>
<thead>
<tr>
<th>Sensor Location</th>
<th>Estimator</th>
<th>MTD (10)</th>
<th>MTD (20)</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>(7,22)</td>
<td>$A^d$</td>
<td>0.15</td>
<td>0.16</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^d$</td>
<td>1.34</td>
<td>1.43</td>
<td>U</td>
</tr>
<tr>
<td>(16,18,20)</td>
<td>$A^d$</td>
<td>0.25</td>
<td>0.10</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^d$</td>
<td>0.92</td>
<td>0.93</td>
<td>U</td>
</tr>
<tr>
<td>(6,16,26)</td>
<td>$A^d$</td>
<td>0.55</td>
<td>0.47</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^d$</td>
<td>0.90</td>
<td>0.99</td>
<td>A</td>
</tr>
<tr>
<td>(7,18,22)</td>
<td>$A^d$</td>
<td>0.36</td>
<td>0.14</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^d$</td>
<td>0.95</td>
<td>0.97</td>
<td>A</td>
</tr>
<tr>
<td>(2,17,32)</td>
<td>$A^d$</td>
<td>1.03</td>
<td>1.05</td>
<td>U</td>
</tr>
<tr>
<td></td>
<td>$B^d$</td>
<td>1.35</td>
<td>1.40</td>
<td>U</td>
</tr>
<tr>
<td>(3,22,23)</td>
<td>$A^d$</td>
<td>0.19</td>
<td>0.06</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^d$</td>
<td>0.87</td>
<td>0.90</td>
<td>A</td>
</tr>
<tr>
<td>(16,17,18,19)</td>
<td>$A^d$</td>
<td>0.09</td>
<td>0.04</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^d$</td>
<td>1.41</td>
<td>1.76</td>
<td>U</td>
</tr>
<tr>
<td>(3,13,16,31)</td>
<td>$A^d$</td>
<td>0.35</td>
<td>0.03</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^d$</td>
<td>1.10</td>
<td>1.15</td>
<td>U</td>
</tr>
<tr>
<td>(15,18,21,34)</td>
<td>$A^d$</td>
<td>0.18</td>
<td>0.05</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^d$</td>
<td>0.92</td>
<td>0.93</td>
<td>A</td>
</tr>
<tr>
<td>(5,9,13,17,21)</td>
<td>$A^d$</td>
<td>0.26</td>
<td>0.04</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^d$</td>
<td>1.04</td>
<td>1.07</td>
<td>U</td>
</tr>
<tr>
<td>(21,22,23,24,25)</td>
<td>$A^d$</td>
<td>0.14</td>
<td>0.06</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>$B^d$</td>
<td>0.66</td>
<td>0.77</td>
<td>A</td>
</tr>
</tbody>
</table>

Table 5.5. Results due to detecting weights for the $[8.0,2.0]$ kg/m$^3$ s plant.
5.3 Discussion

Model mismatch is a significant source of estimator error arising in concurrent hyperthermia dosimetry (Clegg and Roemer 1992). Due to issues such as the variability in tumor sizes, locations, and types, and the differences from patient to patient, model mismatch is an ever present problem. One source of model mismatch in the bioheat transfer models is the inability to exactly model the spatial perfusion characteristic. Mismatch, resulting from incorrect spatial perfusion zone designation in the estimator model, becomes a problem when the perfusion gradient is large. Four estimators are designed based on two methods of dealing with spatial model mismatch. Estimators A and B use multiple models to reconstruct the temperature when spatial mismatch exists. Estimators C and D try to reduce the effects of zonal mismatch by increasing the number of unknown perfusion regions. The four estimators are designed for a tissue region having unknown but spatially bounded perfusion zone information.

The advantage of multiple modelling is that it leads to an optimal parallel processing adaptive estimation scheme when the unknown parameters belong to a finite, discrete set (Anderson and Moore 1979). The weights of the multiple model estimators are typically chosen to detect the closest estimate and eliminate the remaining models (see Anderson and Moore 1979, and Mealy and Tang 1983). Here, the weights are picked to both average the estimator outputs and detect the correct model. The goal of thermal dosimetry is to reconstruct the temperature profile as exactly as possible. Two measured output results for estimator B showed that the MTD increased to unacceptable levels when the weights were chosen for detection of the best model in the set of models. The
models in estimators \( A \) and \( B \) are assumed to be crude approximations to the actual tissue perfusion profile. Thus, rather than throw away information associated with less exact estimators, the estimator results are averaged. Consequently, the results for estimator \( B^a \) are generally better than the results of either of the two individual EKFs comprising estimator \( B^a \). The results of estimator \( A^a \) are slightly degraded when compared to those for the EKF based on model (i) in Figure 5.3. However, the results of estimator \( A^a \) for all simulations shown in Tables 5.2, 5.3, and 5.4 are superior or acceptable. Thus, in situations where a high degree of confidence exists in the choice of models, the weights should be chosen to detect the proper model. For situations where the models are more crude or limited in number, the weights should average the individual EKF outputs.

The results in Table 5.2 compare the four estimators as a function of perfusion magnitude based on the information gathered at measured output locations (7,22). As noted in Chapter Four, for a known two zone perfusion pattern, two temperature sensors, one in the tumor perfusion zone and one in the normal tissue perfusion zone, provide sufficient information for superior thermal reconstruction. Since estimators \( A \) and \( B \) are comprised of two perfusion zone models, the EKFs in estimators \( A \) and \( B \) converge to the best perfusion magnitudes for their given zonal structure. Estimators \( C \) and \( D \) require three and five sensors, respectively, to guarantee convergence of the estimated perfusion magnitudes. Thus, the results in Table 5.2 for estimators \( A^a \) and \( B^a \) are much better than those of \( C \) and \( D \) for the cases having one of the perfusion magnitudes greater than 1.0 kg/m\(^3\)\(\cdot\)°C. For the cases having both perfusion magnitudes less than or equal to 1.0 kg/m\(^3\)\(\cdot\)°C, the initial perfusion of zero in estimators \( C \) and \( D \) is close enough to the
actual perfusion to give acceptable results.

The results of Table 5.3 compare the four estimators as a function of three measured output locations for the [8.0,2.0] kg/m³ s perfusion model. Placing one measured output in the known tumor perfusion zone and one in the known normal perfusion zone guarantees parameter convergence of the individual EKFs in estimators $A^*$ and $B^*$. The third measured output adds information for calculating the output weights for estimators $A^*$ and $B^*$, and improves the parameter convergence in estimators $C$ and $D$. With the exception of measured outputs (16,18,20) the results of estimator $A^*$ are the best, estimators $B^*$ and $C$ are very similar, and estimator $D$ are unacceptable. For measured outputs (16,18,20) sufficient information exists for good parameter convergence in estimator $D$. The remaining measured output locations do not provide sufficient information for accurate parameter reconstruction in estimator $D$.

The results in Table 5.4 compare the estimators when greater numbers of thermal sensors exist providing sufficient information for accurate parameter estimation in all four estimators. Again the results of estimators $B^*$ and $C$ are very similar. Estimator $B^*$ is based on two estimators whose perfusion profiles bound the uncertain tumor boundary region. Estimator $C$ treats the uncertain boundary region as an additional unknown perfusion zone to be estimated. For estimator $B^*$, the results for the (16,17,18,19), (3,13,16,31) and (5,9,13,17,21) cases are unacceptable because sufficient error information exists to essentially eliminate the influence of model (ii) in Figure 5.3 on the thermal reconstruction. Similarly, for these same measured output locations, the results for estimator $C$ are also unacceptable. Here estimator $C$ is unable to construct an
acceptable perfusion in the uncertain boundary region that satisfies the thermal requirements on each side of the tumor - normal tissue interface.

With the exception of the $(3,13,16,31)$ case, the results given in Table 5.4 are very similar for estimators $A^*$ and $D$. For the $(3,13,16,31)$ case, insufficient radial information exists for accurate perfusion reconstruction in estimator $D$. A comparison of the spatial patterns in estimators $A^*$ and $D$ shows that the five zone model in estimator $D$ is capable of recreating the thermal profile of each spatial model in estimator $A$. However, the accurate reconstruction of the thermal profile in estimator $D$ requires a greater number of measured outputs than in estimator $A^*$.

The results of Table 5.5 support the reasoning that the averaging weights should be used when the multiple modelling set is incomplete, and the detecting scheme should be used when there is high confidence in the modelling set including the exact model. With the exception of output locations $(2,17,32)$, estimator $A^d$ outperformed both estimators $A^*$ and $D$. For locations $(2,17,32)$ the gathered information is in the depth direction and the model mismatch is in the radial direction. As a result, estimator $A^d$ detects the incorrect model and the thermal estimate is incorrect. For estimator $B^d$ all the results are slightly worse than those of estimator $B^*$, with the exception of the two measured output simulations (like locations $(7,22)$) and locations $(2,17,32)$ and $(16,17,18,19)$ which are noticeably worse.

The greatest disadvantage of multiple modelling estimation is the increased computational effort required. Instead of calculating a single EKF, a block of $N$ EKFs ($N$ equals the number of multiple models) are calculated on-line at each sample period.
However, the reduced-order estimators designed in Chapter Four can be applied to the EKF to reduce the computational effort required for multiple model concurrent dosimetry. In addition, the computation of the $N$ EKFs can be performed in parallel using distributed computing architectures (Gelende 1989, Rhodes 1990, Chui et al. 1990).

5.4 Summary

In this chapter we have constructed multiple model hyperthermia estimators based on the EKF solution of a bioheat transfer state space model. The multiple models are designed to reduce the effects of model mismatch resulting from uncertain but bounded perfusion pattern information. Simulations are performed to evaluate multiple model estimation applied to the concurrent hyperthermia dosimetry problem. The results of two multiple model estimators are compared with two single model estimators having greater perfusion pattern segmentation.

Based on the results given in this chapter the following points have been reached. First, multiple model estimation is a viable technique for dealing with the spatial mismatch associated with hyperthermia dosimetry. Second, multiple model estimation reduces the need for high numbers of sensors to reconstruct the thermal response when uncertain perfusion regions exist. Spatial resolution is achieved by varying the spatial characterization of the perfusion zones associated with the uncertain regions. As a result, the number of thermal sensors does not need to be increased to guarantee parameter convergence in the individual EKFs. Finally, the multiple model estimators compare...
favorably with the estimators based on models having greater zonal segmentation when greater numbers of measured outputs exist.
CHAPTER SIX

POWER OPTIMIZATION

6.0 Introduction

Modern control theory provides a wide variety of algorithms for modifying the magnitude of the applied power (Brogan 1991, Ogata 1987, Maciejowski 1989), but does not explain how to vary the directionality or the structure of the input coupling of the applied power into the system dynamics (i.e., the elements of the input matrix). Thus, an understanding of how the shape of the applied power influences the temperature in the target tissue volume is required. Optimization of the applied power is one method for defining acceptable power profiles that result in desirable thermal responses. Note that the goal of the power optimization is to find the power profiles that result in optimal thermal responses, and is not just optimization of the power to some ideal shape.

Power optimization studies based on the four transducer scan parameters defined in Figures 2.1 and 2.2 are described in this chapter. Unlike the optimization in (Lin et. al. 1992) here two independent transducer scans are optimized simultaneously to produce an optimal thermal response. The methods section describes the cost function used in the optimization study. The simulation section details the simulations and results of the power optimization studies. The discussion section summarizes the results of the power optimization studies.
6.1 Methods

A variety of cost functions exist for determining the optimal thermal response of a given perfusion magnitude profile \((w)\) as a function of the admissible scan parameters \((s)\) (Lin et al. 1992, Roemer 1991). In this study the cost function, \(J\), is defined as

\[
J(w, s) = \sqrt{T_c(w, s) + T_b(w, s) + T_n(w, s)}
\]  
(6.1)

where

\[
T_c(w, s) = \left\{ \begin{array}{ll}
\sum (x-46)^2, & \text{for } x > 46°, \ x \in L_t, \\
\sum (x-43)^2, & \text{for } x < 43°, \ x \in L_t,
\end{array} \right.
\]  
(6.2)

\[
T_b(w, s) = \sum (x-43)^2 \text{ for } x \neq 43°, \ x \in L_b,
\]  
(6.3)

\[
T_n(w, s) = \sum (x-40)^2 \text{ for } x > 40°, \ x \in L_n.
\]  
(6.4)

In the above equations, \(L_t = \{\text{state located totally inside the tumor}\}\), \(L_b = \{\text{states located inside the tumor but bordering the normal tissue}\}\), and \(L_n = \{\text{all states located in the normal tissue}\}\). Thus, \(J\) constrains the tumor states to temperatures between 46°C and 43°C, it restricts the tumor boundary states to 43°C, and it limits the normal tissue states to 40°C.
6.2 Simulations

The simulation results given in this chapter are based on the axially symmetric tissue volume defined in Figure 3.3. For the 1.0 cm tumor shown in Figure 3.3, \(L_t = \{36, 37, 43, 44\}, L_o = \{29, 30, 31, 38, 45, 50, 51, 52\}, \) and \(L_a = \{\text{the remaining 72 states}\} \). It is assumed that the tumor perfusion \((w_T)\) and the normal tissue perfusion \((w_N)\) are bounded and lie in the set \(w \in [0.0, 10.0] \text{ kg/m}^3 \text{ s}\), and such that \(w_T \leq w_N\). This range of perfusion values and relationship between \(w_T\) and \(w_N\) is consistent with treatment data (Toglia et. al. 1992). The perfusion is varied in increments of 1.0 \text{ kg/m}^3 \text{ s}\) starting with the \([0.0, 0.0] \text{ kg/m}^3 \text{ s}\) perfusion combination.

For the optimization study the scan parameters are constrained to vary within a limited set of values to speed the search for optimal combinations. The following parameter value sets were used: the tilt angle set was \(\{25^\circ, 35^\circ, 45^\circ\}\), the rotation angle set was \(\{70^\circ, 80^\circ, 90^\circ, 100^\circ, 110^\circ, 120^\circ, 130^\circ\}\), the focal depth set was \(\{3.0 \text{ cm}, 3.5 \text{ cm}\}\), and the scan radius set was \(\{0.5 \text{ cm}, 1.0 \text{ cm}, 1.5 \text{ cm}\}\). Since the rotation angle does not influence profiles having a 0.0 cm scan radius, the tilt angle set for the 0.0 cm scan radius was \(\{0^\circ, 5^\circ, 10^\circ, 15^\circ, 20^\circ, 25^\circ, 30^\circ, 35^\circ, 40^\circ, 45^\circ\}\). In addition, the magnitude of the applied power is constrained to a maximum of 20.0 W, and is varied in increments of 0.25 W.

To better heat the target tissue volume, two independent transducers are evaluated in the optimization. An exhaustive search algorithm is used to find the optimal scan parameters for each transducer that result in a globally minimum steady state cost for a given perfusion magnitude. The four possible scan radii and the two possible focal
depths result in eight possible transducer focal points within the tissue region. With two transducers and eight focal point locations there are a total of 28 possible focal point combinations to be investigated. Thus, for a given focal point combination, the tilt and rotation angles are varied and a minimum scan parameter set is found. Thus, 28 locally minimum scan parameter sets are found for a given perfusion magnitude, and the globally optimal scan parameter set is picked as the smallest of the 28 local minimums.

Table 6.1 shows the 19 resulting globally optimal scan parameter sets that arise for the 1.0 cm tumor and the perfusion magnitudes investigated. Figure 6.1 shows spatially the location of the optimal scan parameter sets shown in Table 6.1 as a function of the tumor and the normal tissue perfusion magnitude. Table 6.2 shows the seven locally minimum scan parameter sets that have steady state cost values of less than 1.0 for the [8.0,2.0] kg/m³ s plant. Table 6.3 shows the five largest locally minimum steady state cost values for the [8.0,2.0] kg/m³ s plant. Table 6.4 codifies the optimal scan sets given in Figure 6.1 and gives the steady state cost for each perfusion magnitude investigated. Note that the optimal steady state cost for the 66 perfusion magnitudes investigated falls between 0.6 and 1.65. Figure 6.2, 6.3, and 6.4 show the optimal steady state thermal responses for the [8.0,2.0] kg/m³ s, [1.0,1.0] kg/m³ s, and [10.0,9.0] kg/m³ s plants, respectively.
<table>
<thead>
<tr>
<th>Power Profile</th>
<th>Tilt Angle (°)</th>
<th>Rotation Angle (°)</th>
<th>Focal Depth (cm)</th>
<th>Scan Radius (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>(45,45)</td>
<td>(100,130)</td>
<td>(3.0,3.5)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>b</td>
<td>(45,25)</td>
<td>(130,70)</td>
<td>(3.5,3.5)</td>
<td>(1.0,1.5)</td>
</tr>
<tr>
<td>c</td>
<td>(45,45)</td>
<td>(110,120)</td>
<td>(3.0,3.5)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>d</td>
<td>(45,25)</td>
<td>(110,80)</td>
<td>(3.0,3.0)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>e</td>
<td>(45,35)</td>
<td>(100,110)</td>
<td>(3.0,3.5)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>f</td>
<td>(35,25)</td>
<td>(90,100)</td>
<td>(3.0,3.5)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>g</td>
<td>(45,35)</td>
<td>(110,80)</td>
<td>(3.0,3.0)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>h</td>
<td>(25,25)</td>
<td>(80,100)</td>
<td>(3.0,3.5)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>i</td>
<td>(35,45)</td>
<td>(130,130)</td>
<td>(3.5,3.5)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>j</td>
<td>(25,25)</td>
<td>(70,100)</td>
<td>(3.0,3.5)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>k</td>
<td>(25,45)</td>
<td>(120,130)</td>
<td>(3.5,3.5)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>l</td>
<td>(45,25)</td>
<td>(110,90)</td>
<td>(3.0,3.5)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>m</td>
<td>(35,35)</td>
<td>(120,120)</td>
<td>(3.5,3.5)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>n</td>
<td>(45,25)</td>
<td>(110,80)</td>
<td>(3.0,3.0)</td>
<td>(0.5,1.5)</td>
</tr>
<tr>
<td>o</td>
<td>(25,25)</td>
<td>(120,100)</td>
<td>(3.5,3.5)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>p</td>
<td>(25,25)</td>
<td>(120,90)</td>
<td>(3.5,3.0)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>q</td>
<td>(35,35)</td>
<td>(130,120)</td>
<td>(3.5,3.0)</td>
<td>(0.5,1.0)</td>
</tr>
<tr>
<td>r</td>
<td>(15,35)</td>
<td>(0,120)</td>
<td>(3.0,3.5)</td>
<td>(0.0,1.0)</td>
</tr>
<tr>
<td>s</td>
<td>(35,25)</td>
<td>(130,110)</td>
<td>(3.5,3.5)</td>
<td>(0.5,1.0)</td>
</tr>
</tbody>
</table>

Table 6.1. Scan parameters for the globally optimal results given in Figure 6.1. The scan parameters for the first input are the first element of every pair.
Figure 6.1. Spatial location of the scan parameter sets given in Table 6.1 as a function of tumor and normal tissue perfusion.
Table 6.2. Comparison of the seven local minimum scan parameter sets having a steady state cost less than 1.0 for the [8.0,2.0] kg/m³ s plant.

<table>
<thead>
<tr>
<th>Tilt Angle</th>
<th>Rotation Angle</th>
<th>Focal Depth</th>
<th>Scan Radius</th>
<th>Steady State Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>110</td>
<td>3.0</td>
<td>0.5</td>
<td>0.85</td>
</tr>
<tr>
<td>25</td>
<td>80</td>
<td>3.0</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>110</td>
<td>3.0</td>
<td>0.5</td>
<td>0.86</td>
</tr>
<tr>
<td>25</td>
<td>90</td>
<td>3.5</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>120</td>
<td>3.0</td>
<td>0.5</td>
<td>0.91</td>
</tr>
<tr>
<td>25</td>
<td>100</td>
<td>3.5</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>110</td>
<td>3.0</td>
<td>0.5</td>
<td>0.91</td>
</tr>
<tr>
<td>25</td>
<td>80</td>
<td>3.0</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>120</td>
<td>3.5</td>
<td>0.5</td>
<td>0.92</td>
</tr>
<tr>
<td>25</td>
<td>90</td>
<td>3.0</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>0</td>
<td>3.0</td>
<td>0.0</td>
<td>0.93</td>
</tr>
<tr>
<td>25</td>
<td>110</td>
<td>3.5</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>100</td>
<td>3.0</td>
<td>0.5</td>
<td>0.99</td>
</tr>
<tr>
<td>25</td>
<td>90</td>
<td>3.5</td>
<td>1.5</td>
<td></td>
</tr>
</tbody>
</table>
Table 6.3. The five largest locally minimal steady state cost function scan parameter sets for the [8.0,2.0] kg/m³ s plant.

<table>
<thead>
<tr>
<th>Tilt Angle</th>
<th>Rotation Angle</th>
<th>Focal Depth</th>
<th>Scan Radius</th>
<th>Steady State Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>0°</td>
<td>0°</td>
<td>3.0 cm</td>
<td>0.0 cm</td>
<td>6.21</td>
</tr>
<tr>
<td>5°</td>
<td>0°</td>
<td>3.5 cm</td>
<td>0.0 cm</td>
<td></td>
</tr>
<tr>
<td>0°</td>
<td>0°</td>
<td>3.0 cm</td>
<td>0.0 cm</td>
<td>5.16</td>
</tr>
<tr>
<td>25°</td>
<td>0°</td>
<td>3.5 cm</td>
<td>0.5 cm</td>
<td></td>
</tr>
<tr>
<td>0°</td>
<td>90°</td>
<td>3.5 cm</td>
<td>0.0 cm</td>
<td>5.16</td>
</tr>
<tr>
<td>25°</td>
<td>90°</td>
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<td>0.5 cm</td>
<td></td>
</tr>
<tr>
<td>45°</td>
<td>70°</td>
<td>3.0 cm</td>
<td>1.5 cm</td>
<td>4.75</td>
</tr>
<tr>
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<td>130°</td>
<td>3.5 cm</td>
<td>1.5 cm</td>
<td></td>
</tr>
<tr>
<td>25°</td>
<td>120°</td>
<td>3.0 cm</td>
<td>1.0 cm</td>
<td>2.84</td>
</tr>
<tr>
<td>35°</td>
<td>70°</td>
<td>3.0 cm</td>
<td>1.5 cm</td>
<td></td>
</tr>
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<td>Perfusion</td>
<td>Cost</td>
<td>Scan Set</td>
<td>Perfusion</td>
<td>Cost</td>
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<td>-------</td>
<td>----------</td>
<td>-----------</td>
<td>-------</td>
</tr>
<tr>
<td>[0.0,0,0]</td>
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<td>a</td>
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</tr>
<tr>
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</tr>
<tr>
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</tr>
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</tr>
<tr>
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<td>[8.0,3,0]</td>
<td>0.79</td>
</tr>
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</tr>
<tr>
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<td>[8.0,5,0]</td>
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<td>c</td>
<td>[8.0,6,0]</td>
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</tr>
<tr>
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<td>f</td>
<td>[8.0,7,0]</td>
<td>0.82</td>
</tr>
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<td>1.01</td>
</tr>
<tr>
<td>[4.0,4,0]</td>
<td>0.73</td>
<td>i</td>
<td>[9.0,2,0]</td>
<td>0.89</td>
</tr>
<tr>
<td>[5.0,0,0]</td>
<td>0.97</td>
<td>j</td>
<td>[9.0,3,0]</td>
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<tr>
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<td>[9.0,4,0]</td>
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</tr>
<tr>
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</tr>
<tr>
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<td>d</td>
<td>[9.0,6,0]</td>
<td>0.78</td>
</tr>
<tr>
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<td>k</td>
<td>[9.0,7,0]</td>
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</tr>
<tr>
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<td>k</td>
<td>[9.0,8,0]</td>
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</tr>
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<td>l</td>
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<td>l</td>
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</tr>
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</tr>
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<td>k</td>
<td>[10.0,4,0]</td>
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</tr>
<tr>
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<td>k</td>
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<td>0.82</td>
</tr>
<tr>
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<td>[10.0,6,0]</td>
<td>0.81</td>
</tr>
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<td>[7.0,1,0]</td>
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</tr>
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<td>0.80</td>
<td>d</td>
<td>[10.0,8,0]</td>
<td>0.86</td>
</tr>
<tr>
<td>[7.0,3,0]</td>
<td>0.75</td>
<td>d</td>
<td>[10.0,9,0]</td>
<td>0.89</td>
</tr>
<tr>
<td>[7.0,4,0]</td>
<td>0.76</td>
<td>m</td>
<td>[10.0,10,0]</td>
<td>0.92</td>
</tr>
</tbody>
</table>

Table 6.4. The steady state cost for the result shown graphically in Figure 6.1.
Figure 6.2. The optimal steady state response for the [8.0,2.0] kg/m³ s plant.
Figure 6.3. The optimal steady state response for the \([1.0, 1.0]\) kg/m\(^3\) s plant.
Figure 6.4. The optimal steady state response for the [10.0, 9.0] kg/m³ s plant.
6.3 Discussion

Ideally, the most desirable thermal response would result in a uniform 43°C temperature in the tumor tissue, and a uniform 37°C temperature in the normal tissue. In this idealized situation the tumor is heated to the desired therapeutic temperature and none of the normal tissue is harmed. Unfortunately, the applied SFUS power cannot replicate the power profile required to create such an ideal thermal response (Ocheltree and Frizzell 1987, 1988). Instead, a more realistic thermal response is chosen as the basis for the cost function to be optimized. The harm to the normal tissue is limited by allowing only maximum normal tissue temperatures of 40°C. Since attaining a uniform temperature of 43°C in the inner tumor tissue is somewhat unrealistic, a more attainable thermal response is one that is bounded between 43°C and 46°C. Thus, the inner tumor tissue is maintained at a therapeutic temperature, but is not allowed to rise to extremely high temperatures. By placing the tumor boundary nodes at 43°C, a tradeoff is made between the tumor temperature and the normal tissue temperature. The tumor boundary is maintained at a therapeutic level, but is not allowed to rise to the temperatures of the inner tumor as this would result in greater normal tissue temperatures. In addition, the equality constraint in (6.3) is useful in the choice of the regulated output locations and the optimal set point temperatures discussed in Chapter Seven.

The creation of Figure 6.1 was nontrivial as the exhaustive search for a single perfusion magnitude required up to four hours of CPU time on a Cray Y-MP machine (Cray Research Minn.). For this reason the perfusion magnitude in the tumor tissue was constrained to be less than or equal to those in the normal tissue, and only a complete
search was considered for the 1.0 cm radius tumor. An exhaustive search was performed because of the large number of local minimum values that exist when two independent transducers are used to heat the tumor region.

The results of Table 6.2 suggest that several scan parameter sets exist that result in desirable steady state cost values. Having more than a single desirable scan parameter set adds flexibility to the choices that the controller can make when changing the shape of the applied power. For example, if the anatomy of the treatment region constrains the shape of the applied power, having multiple scan parameter sets for a single perfusion magnitude increases the probability that a single desirable scan parameter set exists for the region. Alternatively, Table 6.3 shows that having two transducers heating the treatment volume does not guarantee a good treatment. In addition, no single scan parameter set resulted in desirable steady state cost values for all the perfusion magnitudes investigated. Thus, an understanding of how the applied power influences the resulting thermal response is crucial to the success of the treatment. Optimization of the simulated treatment volume is one useful method for gaining insight into the influences of the shape of the applied power.

6.4 Summary

Simulations have been run to develop an understanding of how the transducer scan parameters influence the thermal response of the treatment region as a function of the perfusion magnitude. Unlike similar previous studies (Lin et. al. 1992), two independent transducers are applied and their power is optimized simultaneously. The results indicate
that for a single perfusion magnitude several scan parameter sets exist that result in acceptable steady state cost values. However, no single scan parameter set exists that results in desirable steady state cost values for all the perfusion magnitudes studied. Thus, to attain an optimal thermal response, the scan parameters need to be varied online during the treatment in accordance with the estimated perfusion information.
CHAPTER SEVEN

NEW CONTROLLER METHODOLOGY

7.0 Introduction

The success of a hyperthermia treatment is directly related to the temperature response achieved in the tissue being heated. This chapter describes a model based controller methodology that combines power optimization, thermal estimation, and modern feedback control into a unified approach for performing SFUS hyperthermia treatments. Power optimization is important because successful heating of the tissue region requires more than simply varying the magnitude of the applied power for an ad hoc set of ultrasound transducer scan parameters. The successful heating of the target region depends strongly on the shape of the applied power. Thus, ultrasound transducer scan parameters that result in shapes that best heat the target region need to be identified and used in the control process. Thermal estimation is required as accurate and clinically useful noninvasive techniques are currently unavailable for measuring the temperature distribution of the heated region during a treatment. In addition, parameter estimation provides useful information on the choice of the transducer scan parameters and the gains of the feedback controller. Modern feedback control is needed to effectively process the large amount of thermal information gathered during the estimation process.

In this chapter a new controller methodology is developed to advance the level of automation achieved during a hyperthermia cancer treatment. This controller methodology is model-based, and combines pretreatment power optimization results with
an on-line state and parameter estimator, and a hierarchical feedback controller. Simulation results presented here are based on a BHTE thermal model and a SFUS heating modality. However, this controller methodology is not limited to just BHTE thermal models or SFUS power systems. In addition, other power optimization criteria, and thermal estimation and feedback control schemes can be easily incorporated into the presented methodology.

This chapter is organized as follows. The methods section describes the overall controller methodology and the specifics of the hierarchical feedback controller. The simulations section describes the thermal model and the simulations generated to evaluate the proposed controller methodology. The discussion section evaluates the controller methodology based on the results given in the simulation section.

7.1 Method

Figure 7.1 shows a diagram of the interaction of each block of the proposed controller methodology during a treatment. The hierarchical controller interacts with both the power optimization block and the state and parameter estimator. The optimization block and the state and parameter estimator do not interact directly with each other. However, the state and parameter estimator provides the hierarchical controller with the information needed to choose the correct optimal scan parameters. By changing the scan parameters, the optimization block indirectly influences the dynamics of the state and parameter estimator.
Figure 7.1. Block diagram of the interaction of the power optimization, the state and parameter estimator and the hierarchical controller.
A two level hierarchical feedback control scheme is designed to combine the optimal thermal power profiles with the estimated state and parameter information. Figure 7.2 shows the information transfer associated with the two levels of the hierarchical controller. The controller decision block, which forms the higher level of the controller, contains all the information required to vary the scan parameters, update the controller, and change the regulated output locations. This information is partitioned into a decision tree that relates possible perfusion spatial patterns and magnitudes to desired controller strategies. The decision block chooses the optimal scan parameters, the appropriate feedback gains, and the regulated output locations based on the perfusion information estimated by the state and parameter estimator. This controller decision block is not turned on until an initial identification phase is complete and more accurate perfusion estimates exist. After the initial heat up phase (typically 10 minutes) the controller decision block modifies the scan parameters in accordance with the estimated parameters, and initializes the appropriate lower level feedback controller. The controller decision block can be thought of as an expert system that varies the shape of the applied power as the tissue information is learned.

The controller feedback block, which forms the lower level of the controller, updates the applied power based on the measured and the estimated thermal information. In this study the controller feedback block consists of an optimal servomechanism controller described in Appendix C. Since the applied power for each scan parameter set is unique, an optimal servomechanism controller is designed for each set. Thus, if the decision controller block considers a set of $M$ optimal scan parameter combinations, $M$
optimal servomechanism controllers are designed.

Figure 7.2. Block diagram of the hierarchical controller.
7.2 Simulations

Table 7.1 shows the resulting set of optimal scan parameters and their cost as a function of the perfusion magnitudes. Figure 7.3 shows the segmentation of the perfusion field associated with the scan parameters shown in Table 7.1. In addition, the results in Table 7.1 and Figure 7.3 graphically represent the scan parameter choices made in the decision control block of the hierarchical controller.

After defining the set of optimal scan parameters and the perfusion magnitudes associated with their application, the EKF and the optimal servomechanism controllers are designed. Based on Table 7.1 a total of five optimal servomechanism controllers are designed. An optimal proportional state feedback controller is designed for the initial 10 minute identification heat up phase of the thermal transient. This optimal feedback controller is calculated based on the Riccati equation solution described in Appendix C with no integrator terms. After the initial heat up phase, the decision control block determines the best set of scan parameters from Figure 7.3 based on the perfusion estimates from the EKF. Based on these scan parameters, the appropriate optimal servomechanism controller is sent to the feedback control block of the hierarchical controller. To make the controller change as smooth as possible, bumpless transfer is used to initialize the integral action in the optimal servomechanism term (Astrom and Wittenmark 1984).
Figure 7.3. Plot of scan parameter set versus normal tissue and tumor tissue perfusion magnitudes.
Table 7.1. Scan parameters for the power profiles given in Figure 7.3. The scan parameter set for the first input is associated with the top line for each power profile.

<table>
<thead>
<tr>
<th>Power Profile</th>
<th>Tilt Angle</th>
<th>Rotation Angle</th>
<th>Focal Depth</th>
<th>Scan Radius</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>45° 25°</td>
<td>110° 80°</td>
<td>3.0 cm</td>
<td>0.5 cm</td>
</tr>
<tr>
<td></td>
<td>45°</td>
<td>110° 120°</td>
<td>3.0 cm</td>
<td>0.5 cm</td>
</tr>
<tr>
<td></td>
<td>25°</td>
<td>120°</td>
<td>3.5 cm</td>
<td>0.5 cm</td>
</tr>
<tr>
<td>III</td>
<td>25°</td>
<td>120°</td>
<td>3.5 cm</td>
<td>0.5 cm</td>
</tr>
<tr>
<td></td>
<td>45°</td>
<td>130°</td>
<td>3.5 cm</td>
<td>1.0 cm</td>
</tr>
<tr>
<td>IV</td>
<td>35°</td>
<td>130°</td>
<td>3.5 cm</td>
<td>0.5 cm</td>
</tr>
<tr>
<td></td>
<td>35°</td>
<td>120°</td>
<td>3.5 cm</td>
<td>1.0 cm</td>
</tr>
<tr>
<td>V</td>
<td>45°</td>
<td>110° 80°</td>
<td>3.0 cm</td>
<td>0.5 cm</td>
</tr>
<tr>
<td></td>
<td>45°</td>
<td>120°</td>
<td>3.0 cm</td>
<td>1.0 cm</td>
</tr>
</tbody>
</table>

For regulation purposes two set points are required to drive the optimal servomechanism controller. The set points have to be chosen in a manner that results in an optimal thermal response and that keeps the controller within its linear mode of operation (the controller is in its linear mode of operation when all controlled ultrasound inputs are greater than zero). Since the profiles given in Table 7.1 are picked to minimize the cost function in (6.1), the set points are picked as 43°C at two tumor boundary locations ($L_n$) to satisfy (6.3). Table 7.2 shows the steady state cost as a function of the boundary location for a plant having a $[8.0,2.0]$ kg/m³ s perfusion and measured outputs (7,13,22). Based on Table 7.2 the set points for the 1.0 cm radius tumor are picked as 43°C at locations 11 and 28. Figure 7.4 shows a plot of the cost versus time for the $[8.0,2.0]$ kg/m³ s plant for set point locations 11 and 28, and
measured outputs (7,13,22).

<table>
<thead>
<tr>
<th>Regulated Output Location</th>
<th>Steady State Cost</th>
<th>Regulated Output Location</th>
<th>Steady State Cost</th>
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</thead>
<tbody>
<tr>
<td>(11,12)</td>
<td>5.8</td>
<td>(13,23)</td>
<td>9.4</td>
</tr>
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<td>(11,13)</td>
<td>1.5</td>
<td>(13,26)</td>
<td>1.5</td>
</tr>
<tr>
<td>(11,18)</td>
<td>1.0</td>
<td>(13,27)</td>
<td>2.0</td>
</tr>
<tr>
<td>(11,23)</td>
<td>1.1</td>
<td>(13,28)</td>
<td>2.4</td>
</tr>
<tr>
<td>(11,26)</td>
<td>1.6</td>
<td>(18,23)</td>
<td>1.3</td>
</tr>
<tr>
<td>(11,27)</td>
<td>2.1</td>
<td>(18,26)</td>
<td>1.1</td>
</tr>
<tr>
<td>(11,28)</td>
<td>1.1</td>
<td>(18,27)</td>
<td>1.0</td>
</tr>
<tr>
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<td>4.1</td>
</tr>
<tr>
<td>(12,18)</td>
<td>1.1</td>
<td>(23,26)</td>
<td>1.1</td>
</tr>
<tr>
<td>(12,23)</td>
<td>1.2</td>
<td>(23,27)</td>
<td>1.1</td>
</tr>
<tr>
<td>(12,26)</td>
<td>37.7</td>
<td>(23,28)</td>
<td>503.2</td>
</tr>
<tr>
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<td>4.5</td>
</tr>
<tr>
<td>(12,28)</td>
<td>1.2</td>
<td>(26,28)</td>
<td>1.1</td>
</tr>
<tr>
<td>(13,18)</td>
<td>34.6</td>
<td>(27,28)</td>
<td>1.2</td>
</tr>
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</table>

Table 7.2. The steady state cost versus regulated output location for the [8.0,2.0] kg/m³ s plant, measured output locations (7,13,22), and set points 43.0°C. The optimal steady state cost for the [8.0,2.0] kg/m³ s plant and scan parameter set I is 0.85.

Next, the output locations and the perfusion magnitudes were varied to evaluate the results of the proposed controller methodology. Table 7.3 shows the steady state cost, and the power profile choice made by the hierarchical controller as a function of the
measured output for the [8.0, 2.0] kg/m³ s plant. In addition, the MTD at the 70 minute point (10 minutes of heat up plus 60 minutes of treatment) of the treatment is shown in Table 7.3. Table 7.4 shows the steady state cost and the power profile choice made by the hierarchical controller as a function of the perfusion magnitude for the measured outputs (7, 13, 22).

Finally, it is assumed that the radius of the tumor is uncertain but is bounded between 0.5 cm and 1.5 cm. A multiple model EKF is designed based on the three models having radii of 0.5 cm, 1.0 cm, and 1.5 cm, respectively. The perfusion is constrained to \( w \in [0, 10] \) kg/m³ s and \( w_T < w_N \). Table 7.5 gives the desired scan parameters and set point locations for the three possible tumor models. The multiple model EKF is designed to detect the correct tumor spatial pattern from the three possible tumor models. The decision block of the hierarchical controller chooses the power profile given in Table 7.5 based on the most probable model predicted by the multiple model EKF. Table 7.6 shows the steady state cost and the model choice as a function of the perfusion and the tumor radius.
<table>
<thead>
<tr>
<th>Measured Output Location</th>
<th>Steady State Cost</th>
<th>Power Choice</th>
<th>MTD (70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(11,28)</td>
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<td>II</td>
<td>0.04</td>
</tr>
<tr>
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<td>0.04</td>
</tr>
<tr>
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<td>I</td>
<td>0.20</td>
</tr>
<tr>
<td>(22,29)</td>
<td>1.1</td>
<td>I</td>
<td>0.08</td>
</tr>
<tr>
<td>(16,22)</td>
<td>1.6</td>
<td>II</td>
<td>1.83</td>
</tr>
<tr>
<td>(21,22)</td>
<td>1.4</td>
<td>II</td>
<td>1.44</td>
</tr>
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<td>1.3</td>
<td>I</td>
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<td>1.3</td>
<td>II</td>
<td>0.47</td>
</tr>
<tr>
<td>(21,28)</td>
<td>1.0</td>
<td>I</td>
<td>0.24</td>
</tr>
<tr>
<td>(11,13)</td>
<td>1.3</td>
<td>V</td>
<td>0.27</td>
</tr>
<tr>
<td>(13,23)</td>
<td>1.1</td>
<td>I</td>
<td>0.27</td>
</tr>
<tr>
<td>(2,7)</td>
<td>1.6</td>
<td>I</td>
<td>0.39</td>
</tr>
<tr>
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<td>0.44</td>
</tr>
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<td>I</td>
<td>0.50</td>
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<td>I</td>
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<td>I</td>
<td>1.48</td>
</tr>
<tr>
<td>(24,31)</td>
<td>5.7</td>
<td>III</td>
<td>2.77</td>
</tr>
<tr>
<td>(13,28)</td>
<td>2.0</td>
<td>II</td>
<td>1.02</td>
</tr>
<tr>
<td>(2,37)</td>
<td>5.5</td>
<td>I</td>
<td>2.29</td>
</tr>
</tbody>
</table>

Table 7.3. The steady state cost and the scan parameter set choice for the 1.0 cm radius tumor as a function of measured output locations for the [8.0,2.0] kg/m³ s plant and regulated outputs (11,28).
<table>
<thead>
<tr>
<th>Perfusion</th>
<th>Steady State Cost</th>
<th>Power Choice</th>
<th>Desired Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>[8.0, 2.0]</td>
<td>1.1</td>
<td>I</td>
<td>I</td>
</tr>
<tr>
<td>[5.0, 1.0]</td>
<td>1.1</td>
<td>I</td>
<td>I</td>
</tr>
<tr>
<td>[10.0, 5.0]</td>
<td>1.2</td>
<td>IV</td>
<td>I</td>
</tr>
<tr>
<td>[0.75, 0.25]</td>
<td>1.3</td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>[1.0, 1.0]</td>
<td>1.3</td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>[10.0, 10.0]</td>
<td>1.0</td>
<td>III</td>
<td>III</td>
</tr>
<tr>
<td>[3.0, 2.0]</td>
<td>0.9</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>[2.0, 0.0]</td>
<td>1.0</td>
<td>I</td>
<td>I</td>
</tr>
<tr>
<td>[9.0, 0.0]</td>
<td>1.5</td>
<td>I</td>
<td>I</td>
</tr>
<tr>
<td>[5.0, 4.0]</td>
<td>0.9</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>[6.0, 0.0]</td>
<td>1.4</td>
<td>I</td>
<td>I</td>
</tr>
</tbody>
</table>

Table 7.4. The steady state cost and the scan parameter set choice as a function of perfusion for the 1.0 cm radius tumor, measured outputs (7, 13, 22), and regulated outputs (11, 28).
Table 7.5. Scan parameters for power profiles as a function of tumor radius for $w_T < w_N$. The scan parameter set for the first input is on the top line for each power profile. In addition, the location of the regulated output locations are also given.

<table>
<thead>
<tr>
<th>Tumor Radius</th>
<th>Tilt Angle</th>
<th>Rotation Angle</th>
<th>Focal Depth</th>
<th>Scan Radius</th>
<th>Regulated Outputs</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 cm</td>
<td>35° 25°</td>
<td>70° 130°</td>
<td>3.5 cm 3.0 cm</td>
<td>0.5 cm 1.0 cm</td>
<td>(11,27)</td>
</tr>
<tr>
<td>1.0 cm</td>
<td>45° 25°</td>
<td>110° 80°</td>
<td>3.0 cm 3.0 cm</td>
<td>0.5 cm 1.0 cm</td>
<td>(11,28)</td>
</tr>
<tr>
<td>1.5 cm</td>
<td>45° 25°</td>
<td>110° 90°</td>
<td>3.0 cm 3.5 cm</td>
<td>0.5 cm 1.5 cm</td>
<td>(11,29)</td>
</tr>
</tbody>
</table>

Table 7.6. Steady state cost for the uncertain tumor radius as a function of tumor radius and perfusion for measured outputs (7,13,22) and the scan parameters and the regulated outputs given in Table 7.5. The last three columns represent the steady state cost if single models of radius 0.5 cm, 1.0 cm and 1.5 cm, respectively, are applied to the system.

<table>
<thead>
<tr>
<th>Tumor Radius</th>
<th>Perfusion</th>
<th>Detected Tumor Radius</th>
<th>Steady State Detected Tumor Cost</th>
<th>Cost for 0.5 cm Tumor</th>
<th>Cost for 1.0 cm Tumor</th>
<th>Cost for 1.5 cm Tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 [8.0,2.0]</td>
<td>0.5</td>
<td>0.6</td>
<td>0.6</td>
<td>7.0</td>
<td>8.8</td>
<td></td>
</tr>
<tr>
<td>1.0 [8.0,2.0]</td>
<td>1.0</td>
<td>1.1</td>
<td>3.0</td>
<td>1.1</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>1.5 [8.0,2.0]</td>
<td>1.5</td>
<td>0.9</td>
<td>7.7</td>
<td>6.0</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>0.5 [6.0,0.0]</td>
<td>0.5</td>
<td>0.6</td>
<td>0.6</td>
<td>5.9</td>
<td>8.0</td>
<td></td>
</tr>
<tr>
<td>1.0 [5.0,1.0]</td>
<td>1.0</td>
<td>1.1</td>
<td>3.0</td>
<td>1.1</td>
<td>1.9</td>
<td></td>
</tr>
<tr>
<td>1.5 [10.0,1.0]</td>
<td>1.5</td>
<td>1.1</td>
<td>7.6</td>
<td>5.7</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>0.5 [7.0,3.0]</td>
<td>0.5</td>
<td>1.1</td>
<td>1.1</td>
<td>6.9</td>
<td>8.2</td>
<td></td>
</tr>
<tr>
<td>1.0 [10.0,5.0]</td>
<td>1.0</td>
<td>1.4</td>
<td>3.1</td>
<td>1.3</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>1.5 [2.0,0.0]</td>
<td>1.5</td>
<td>1.0</td>
<td>6.6</td>
<td>4.2</td>
<td>1.0</td>
<td></td>
</tr>
</tbody>
</table>
Figure 7.4. Plot of cost versus time for the [8.0,2.0] kg/m³ s plant, with measured output locations (7,13,22) and regulated output locations (11,28).
7.3 Discussion

The proposed controller methodology combines many different control design techniques into an intelligent control package. One part of the package is concerned with parameter estimation. A recent article on set-membership identification that may be useful in future hyperthermia based parameter estimation studies is Kosut et. al. (1992). Another part of the control package consists of a multivariable controller based on the servomechanism principle. This part of the package is useful for set point tracking. The critical component of the control package is the decision making block which utilizes the information that is made available through the parameter estimation component of the control package. This decision making part of the controller could place this overall controller methodology in the class of intelligent control systems (Shourechi 1991a, 1991b, Astrom 1989, 1991, Narendra 1991, Narendra and Mukhopadhyay 1992, Antsaklis et. al. 1991, Sartori and Antsaklis 1992). In set-membership identification, the model that most closely compares with the actual plant is identified and a more robust controller can be picked based on the model choice. Here, the perfusion is representative of the performance variable and the closest spatial pattern and magnitude is identified. Based on this perfusion identification, an optimal scan parameter set and appropriate controller is implemented to enhance the performance of the system. Intelligent control has as its basis the incorporation of expert systems, neural networks, or artificial intelligence into the closed-loop system. Thus, the heuristics, learning, and expertise of the clinician can be incorporated into the control of the tumor tissue temperature. This intelligence is incorporated into the closed-loop in the decision controller block of the
The results of the power optimization in Table 6.4 indicate that a variety of scan parameter sets exist that give acceptable steady state cost function values. Figure 7.3 represents an effective lumping of the optimization results into regions of like scan parameters. The segmentation of the scan parameter sets shown in Figure 7.3 was chosen for three reasons. First, the choice of the desired scan parameters is made based on the perfusion estimated by the EKF. By lumping the similar scan sets into larger regions the decision block becomes less sensitive to estimation errors. Second, the difference between many of the globally minimum costs and the locally minimum costs was negligible in many of the optimization studies. Finally, reducing the number of upper level decisions reduced the complexity of the controller decision block.

The incorporation of the EKF into the closed-loop required a change in tuning when compared with the open-loop results given in Chapters Four and Five. In the open-loop settings the dynamics of the EKF can be very fast to speed the convergence of the results to the actual thermal response. In the closed-loop settings the thermal estimates of the EKF influence the choice of the controlled inputs, and the dynamics of the EKF influence the noise rejection and the closed-loop stability margin (Doyle and Stein 1979). If the closed-loop EKF dynamics are too fast, the perfusion parameters are estimated in 10 minutes, but the temperature estimates become too sensitive to power changes. For example, if the dynamics are too fast and an increase in the applied power is made, the resulting temperature estimates will overshoot the actual temperatures. As a result, this overshoot can cause the feedback controller to lower the applied power in situations
where the power should remain unchanged. Figure 7.5 shows the controlled power based on an EKF that was tuned to dynamics that were too fast for the 1.0 cm tumor with the $[8.0, 2.0]$ kg/m³ s plant, measured outputs $(7, 13, 22)$, and regulated outputs $(11, 28)$. Figure 7.6 shows the transient power for a correctly tuned EKF.

Figure 7.5a. Transient applied power $u_1(k)$ for the $[8.0, 2.0]$ kg/m³ s plant with measured outputs $(7, 13, 22)$, regulated outputs $(11, 28)$ and the EKF tuned to the open-loop values.
Figure 7.5b. Transient applied power $u_2(k)$ for the [8.0,2.0] kg/m$^3$ s plant with measured outputs (7,13,22), regulated outputs (11,28) and the EKF tuned to the open-loop values.
Figure 7.6. Transient applied power for the \([8.0, 2.0] \text{ kg/m}^3 \text{ s}\) plant with measured outputs \((7, 13, 22)\), regulated outputs \((11, 28)\) and the EKF tuned to the desired closed-loop values.
Since the tumor tissue being heated is an open-loop stable system, the goal of the proposed controller methodology is to improve the performance of the treatment. It has been noted that for performance enhancement the difficulty in achieving an optimal result depends more on the choice of the optimal set points than the form of the regulation (Garcia and Morari 1982, Shin and Cui 1991). To assist in the proper choice, an equality constraint is placed on the tumor boundary to provide both the magnitude of the optimal set points and the location of the regulated outputs. Due to the wide variation of the acceptable temperature responses in the inner tumor tissue and normal tissue, these locations pose difficulties in picking an optimal set point. However, the equality constraint in (6.3) does not guarantee that simply picking a tumor boundary node and setting it to 43°C will result in an optimal response. Table 7.2 shows that the six regulated output locations, (11,12), (12,26), (13,18), (13,23) (18,28), and (23,28), resulted in large cost functions values. For these cases the choice of 43°C at both locations is too strict to result in an acceptable cost, and in all six cases the controller left its linear operating range. For example, changing the set point for (13,18) to \{42.5°,43.0°\}, respectively, resulted in a steady state cost of 2.4 and the controller remained in its linear operating range. When the controller leaves its linear operating range it attempts to regulate the outputs by driving one or more of the inputs to negative values. Ultrasound can only heat and not cool the region, so the inputs are constrained to be positive. Significant performance degradation, as in the (23,28) case occur when the controller leaves its linear operating range. Thus, as a rule the set points should be picked on the tumor border with an emphasis on locations that are insensitive to small
changes in the set point temperatures.

The choice of the optimal set point values and the regulated output location on the tumor boundary improves the closed-loop performance, but creates problems for the clinician. A tradeoff exists between the location of the regulated outputs to result in acceptable thermal regulation, and the location of the regulated outputs to result in accurate thermal reconstruction. Ideally, the set of regulated outputs should be contained in the set of measured outputs to reduce the affects of estimator error on the closed-loop system. However, placing thermal sensors on perfusion boundaries can significantly degrade the performance of the thermal estimation (Liauh 1991). Thus, the clinician has to place the probes in locations that give both acceptable thermal regulation and accurate thermal reconstruction.

From a control designer's viewpoint the location of the thermal sensors has an influence upon the resulting robustness properties of the closed-loop system. A strongly robust closed-loop system in one in which perturbations $A \rightarrow A + \delta A$, $B \rightarrow B + \delta B$, and $C \rightarrow C + \delta C$ will not influence the stability of the system. For a weakly robust system only perturbations $A \rightarrow A + \delta A$ and $B \rightarrow B + \delta B$ will not influence the stability of the system. For a strongly robust controller the regulated outputs must be contained in the set of the measured outputs of the system (see Davison and Goldenberg 1975 for further explanation). Thus, the clinician has to place the thermal sensors on the tumor boundary region to guarantee a strongly robust closed-loop system. Alternatively, in a weakly robust system the regulated output need not be a subset of the measured output, the regulated outputs can be estimated from the measured outputs. Thus, the results given
here represent a weakly robust closed-loop system, which requires that the measured output locations be known accurately throughout the treatment to maintain acceptable performance.

The results of Table 7.3, 7.6 and Figure 7.4 collectively define several sources of performance degradation. The most significant form of degradation occurs when the controller leaves its linear mode. For the results of Tables 7.3, 7.6, and Figure 7.4 the performance degradation is not as significant as the loss of linear performance, but still warrant investigation. Tables 7.3 and 7.6 demonstrate the problems associated with poor perfusion estimation and erroneous thermal reconstruction. For Table 7.3 different measured output locations are used to determine their impact on the performance of the closed-loop system (see Table 4.4 for open-loop estimation results for these same measured output locations). For all measured output locations in Table 7.3, the desired scan parameter set is set I. For measured output locations (11,28), (16,22), (21,22), (16,23), (11,13), (24,31), and (13,28), the EKF produces inaccurate perfusion estimates which lead to an incorrect choice for the scan parameter set. Thus, the results with the sensors located at (11,28) are slightly degraded when compared to sensors located as (7,22), because a less desirable scan parameter set is used. However, if the decision to select the scan parameter set is made after 10 minutes, then the performance with the sensors at (11,28) will be improved. This improvement in performance is a result of the estimated perfusion values actually converging to the true perfusion values after more than 10 minutes. Thus, one modification to the decision control block would be to continue to monitor the perfusion estimates after the heat up phase of the treatment.
Errors in the estimation of the states also has an impact on the steady state performance of the closed-loop system. In general, the higher the MTD the higher the steady state cost. However, the reconstruction of the temperatures at the regulated output locations is more significant than the value of the MTD. For measured outputs (16,22) the MTD is larger than the MTD with measured outputs at (13,28), but the steady state cost with the outputs at (16,22) is smaller. Similarly, the MTD for sensors at (10,36) is significantly smaller than the MTD with sensors at (21,22), but again the steady state cost is larger. In these two cases the error in the estimates of the regulated output locations is larger even though the maximum error for the entire volume is smaller.

Table 7.6 shows how the results degrade when spatial mismatch is introduced into the estimation of the perfusion. The results based on the multiple model EKF are analogous to those for the correct spatial pattern. However, sufficient measured output information existed for correct model detection from the multiple model EKF results. The remaining columns in Table 7.6 indicate the expected performance degradation when the incorrect tumor model is assumed. Since the decision controller block is based on applying the results of Table 7.5 to the detected tumor model, a problem arises when the tumor region has a nearly uniform perfusion magnitude. In these nearly uniform perfusion situations, the multiple model EKF cannot detect the correct tumor model and changes to the power profile cannot be made. Note that with nearly uniform perfusion, the tumor tissue is nearly indistinguishable from the normal tissue and boundaries are much more difficult to discern.

Figure 7.4 shows an additional source of performance degradation over the
transient of the treatment. As noted, the set points are set to 43°C, but 43°C may not be the exact optimal set point for the system. Analysis of Figure 7.4 shows that the cost actually has a minimum value of 0.89 around the eighteenth minute of the transient. This minimum occurs because the thermal response transitions through the optimal thermal response in the eighteenth minute. When the set points are set to their optimal values of (42.80, 42.67), the steady state cost is reduced to 0.86.

The results of Table 7.4 show that for sufficient measured outputs the closed-loop performance as a function of perfusion is superior. From the optimization study, the optimal cost typically lies in the interval from 0.7 to 1.7. The steady state cost values in Table 7.4 fall very close to the desired optimal values. With the exception of the [10.0, 5.0] kg/m³ s perfusion case the EKF provided accurate enough perfusion estimates to select the proper scan parameter set choice. In the [10.0, 5.0] case the perfusion could not be accurately reconstructed in just 10 minutes. In general, the smaller perfusion magnitudes can be estimated in 10 minutes, but the larger perfusion magnitudes require an additional five minutes for convergence. Thus, for larger perfusion magnitudes the selection of the optimal scan parameter set should be made after 10 minutes.

The advantage of the proposed controller methodology is that it combines elements of power optimization, thermal estimation, and modern feedback control design with a decision making process that provides the performance enhancement required for successful hyperthermia treatments. The reshaping of the applied power to improve the response of the treatment requires more advanced techniques than standard classical and modern control provides. By incorporating an expert system shell into the controller
loop, the decision process of the clinician can be included in the automation process.

7.4 Summary

Based on the results given in this chapter the following points have been reached. First, the most significant source of controller degradation results when the controller leaves its linear operating range. Second, the optimal set points dictate whether or not the controller will remain in its linear operating range during the treatment. Third, the choice of optimal set points is nontrivial as the optimal thermal response varies as a function of the perfusion pattern and magnitude. Fourth, optimization can be used to find power profiles that best heat a given tumor region as a function of perfusion magnitude. Fifth, the inclusion of equality constraints in the thermal cost function significantly aids in the choice of optimal set points and regulated output locations. Sixth, the variation of the scan parameters requires perfusion information, and this perfusion information must be estimated. Seventh, in general as the MTD gets bigger, the closed-loop performance degrades. Finally, the proposed controller methodology incorporates the important optimization, estimation, control, and expert system techniques required for realistic hyperthermia automation.
CHAPTER EIGHT

CONCLUSIONS

8.0 Conclusions

This work represents a progression, away from classical SISO controllers, towards viable model-based MIMO control schemes that incorporate power optimization, thermal estimation and modern control into a framework that automates hyperthermia treatments. A set of state space tools were applied to the problem of hyperthermia control to provide building blocks for incorporating modern control techniques into the clinic. These tools include: model reduction to create thermal models of workable dimension; optimal servomechanism control to provide accurate tracking of the regulated outputs; state and parameter extended Kalman filtering to estimate both the unmeasured temperatures and the unknown perfusion magnitudes; multiple modelling as a means of addressing spatial mismatch between the actual perfusion pattern and the modelled perfusion patterns; power optimization to produce scan parameter sets that best heat the tumor region as a function of perfusion; and hierarchical control to combine the expertise of the clinician with the data management power of computer based control systems.

The following important topics have been discussed in this dissertation. First, the BHTE is a stable system, and consequently, the goal of the control designer is to enhance the performance of the treatment. This performance enhancement requires the combination of power optimization and the appropriate choice of optimal set points and regulated output locations. Placing an equality constraint on the tumor boundary locations
provides guidelines for picking the optimal set points, so long as the scan parameter sets that provide optimal heating are used during the treatment.

Second, ultrasound can only heat (and not cool) the treatment region, and as a result, the controlled input is constrained to positive values. For successful optimal servomechanism control of the treatment volume, the controller must remain in its linear operating range, or the performance will degrade significantly. To maintain linear operation the regulated outputs must be picked at locations that are insensitive to small changes about the optimal set point temperatures. If such locations do not exist, then the set points need to be manipulated to keep the applied power positive and the controller in its linear operating range.

Third, the accuracy of the estimated temperatures influences the accuracy of the tracking of the regulated outputs by the controller. The number of measured outputs and the amount of model mismatch are two issues that significantly influence the accuracy of the estimated temperatures. In cases where the number of measured outputs is less than the number of unknown perfusion zones, the estimator is underdetermined and the performance degradation is greater. In general, the larger the gradients between perfusion zones the less likely the convergence of the EKF will be in underdetermined situations. Acceptable results occur when a thermal sensor exists in each unknown perfusion zone in the treatment volume. Having a greater number of sensors than perfusion zones speeds the convergence rate of the EKF, but to improve the MTD to superior levels requires a sensor in every perfusion zone. Model mismatch can manifest itself in a variety of ways including perfusion spatial pattern mismatch, errors in the applied power shapes, errors
in the locations of the measured outputs, and dynamical differences between the mathematical model and the actual heat transfer in the tissue. Multiple modelling schemes offer a means of reducing the affects of perfusion pattern mismatch, power shape mismatch, and measured output location mismatch. However, dynamic differences between the model and the actual system remain a significant source of error between the estimated and the actual thermal responses.

Fourth, the successful control of the treatment region requires more information than just the reconstruction of the entire temperature field. The reconstruction of the entire temperature field determines the success of the treatment, but does not explain how to reshape the power. The reshaping of the power requires an understanding of the thermally significant heat sink terms in the treatment region. Thus, knowing the reason for the cold spots arising in the treatment region is just as important as knowing the location and the temperature of the cold spots in the treatment region.

Fifth, the open-loop reduced-order models based on the truncation of the balanced realization provide sufficient information for reduced-order controller design. In addition, two methods were given for creating reduced-order state and parameter estimators based on a reduced-order EKF.

Finally, the automation of hyperthermia treatments requires the incorporation of the experience of the clinician into the feedback loop. Due to the wide variety of tumor types, sizes, locations, patient pain thresholds and the like, feedback control alone cannot cope with the myriad of possibilities that arise during a treatment. An expert system shell that incorporates the expertise of the clinician and leads to an intelligent control scheme
is required. The hierarchical controller described here represents the first step towards such an intelligent control scheme.

8.1 Future Work

Based on the research given in this dissertation, several topics need to be investigated further before such a system can be implemented in the clinic. Most importantly, the model reduction, EKF estimation, power optimization, and feedback control need to be investigated using a more complex three dimensional tissue model. The blood flow characteristic in actual tumors tend to be more complex than the axisymmetric two perfusion zone models examined. In addition, thermally significant blood vessels should be incorporated into the model to determine the influence of blood vessels on the controlled treatment response.

For estimation purposes a well defined criterion for sensor placement is needed to guarantee that the maximum amount of information is extracted during a treatment. In addition, the application of multiple modelling to estimation requires that the unknown parameters fall within some bounded parameter space (Anderson and Moore 1979). In hyperthermia the unknown parameters are bounded in magnitude and regionally bounded in space. Thus, a better understanding of how to spatially segment thermal models in regions of uncertainty would aid in the accuracy of multiple model estimation results.

The generation of the optimal scan parameter sets in Figure 6.4 was far too computationally intensive for use in the clinic. While a dynamically more complex power optimization is required for clinical use, the computational time to generate optimal scan
sets needs to be reduced. Thus, faster search routines and a better understanding of the interaction between the applied modality and the expected thermal response is required.

Since the applied ultrasound power is constrained to be positive, control algorithms need to be investigated that incorporate this input constraint. Here, linear optimal servomechanism control was applied and the set points were manipulated to maintain operation in the linear range. Alternatively, the input constraint could be incorporated into the controller in an attempt to eliminate the performance degradation associated with the loss of linear operation. A comparison could be made of the performance and robustness of the linear controller and the input constrained controller.

Finally, the decision controller block will require a more complex expert system than simply changing the scan parameters and set point locations as a function of the perfusion spatial pattern and magnitude. The decision controller block incorporates the expertise of the clinician into the automation process. The controller decision block needs to maintain linear operation of the controller, and deal with patient motion and pain. Patient pain is a significant issue because pain varies as a function of the scan path, and pain thresholds vary from patient to patient (Nathanson 1992). Work by Nathanson represents an excellent starting point for incorporating pain issues into an expert shell.
APPENDIX A

STATE SPACE

This appendix describes the equations for calculating the state space evaluated in this dissertation. Recall that the method of finite differences was applied to the R-z symmetric BHTE in (2.5), resulting in equations (2.10) through (2.12). The state transition matrix, A, is defined using the numbering convention in Figure 2.3 as

\[
A(i, i) = \begin{cases} 
-6Kt + 1 - \frac{w(i)c_b\Delta t}{\rho c} & \text{if } r_i = 0 \\
\frac{-4Kt + 1 - \frac{w(i)c_b\Delta t}{\rho c}}{\rho c\Delta s^2} & \text{if } r_i > 0
\end{cases}
\]  

(A.1)

\[
A(i, i-1) = \frac{Kt}{\rho c\Delta s^2} \left(1 - \frac{1}{2r_i\Delta s}\right) \text{ if } r_i > 0
\]  

(A.2)

\[
A(i, i+1) = \begin{cases} 
\frac{4Kt}{\rho c\Delta s^2} & \text{if } r_i = 0 \\
\frac{Kt}{\rho c\Delta s} \left(1 - \frac{1}{2r_i\Delta s}\right) & \text{if } 0 < r_i < r_{\max}
\end{cases}
\]  

(A.3)

\[
A(i, i+n) = \frac{Kt}{\rho c\Delta s^2} \text{ if } z_i < z_{\max}
\]  

(A.4)
where \( r_i \) and \( z_i \) are the radial and the depth locations of state \( i \), \( r_{\text{max}} \) and \( z_{\text{max}} \) are the radial and depth dimensions of the tissue volume, \( n_r \) is the number of grid points in the radial direction; and \( \Delta s = \Delta r = \Delta z \).

The grid spacing, \( \Delta s \), and the sampling period, \( \Delta t \), are two design parameters within the state space model. The grid size is chosen as a function of the hyperthermia heating modality being used in the treatment. As the grid size gets smaller the state space model will better approximate the contiguous solution given in (2.5). However, if the gradients of the applied power are very small, as in the case of nearly uniform power, continued reduction of the grid size will show little improvement in the accuracy of the resulting temperature fields. Thus, the greater the applied power gradients resulting from a given modality, the smaller the grid size required to maintain the numerical accuracy of the state space model. The choice of the sampling period is bounded by the size of the grid spacing. It has been shown that

\[
\Delta t < \frac{\rho c \Delta s^2}{6 \kappa}
\]  

(A.6)

is an upper bound for maintaining a numerically stable explicit finite difference expansion (Swindell 1986).

The input matrix is the mapping of the absorbed power of the individual
transducers to the states. The absorbed power can be thought of as the summation of the contribution due to each transducers as

$$Q_a = \sum_{j=1}^{m} Q_j(q_j),$$  \hspace{1cm} (A.7)

where $q_j$ is the magnitude of the applied power of the $j$th transducer. Based on (A.7) the input matrix is given as

$$B = \frac{\Delta T}{\rho C} [Q_1(1) : \ldots : Q_m(1)].$$  \hspace{1cm} (A.8)

The individual transducers outputs are evaluated at $q_j = 1$, because the input, $u$, varies the magnitude of the applied power in the state space.

The measured outputs are the temperatures gathered by the thermometry devices in the tissue regions. Since the state components represent the temperatures at a given node location of the model, thermal sensors falling on a grid point map that state to the output. For thermal sensors that fall between node locations, the temperature is constructed as a linear combination of the surrounding states weighted according to geometrical considerations. Thus, if the output matrix, $C$, is the mapping of the states $x$ to the measured outputs $y$, then the rows of $C$ are the combinations of states resulting in the measured output temperature.
APPENDIX B

BALANCING TRANSFORMATION

This appendix describes the algorithm used to calculate the balancing transformation used for model reduction. The algorithm requires the calculation of the controllability and observability grammians, and the singular value decomposition (SVD). Controllability and observability are two system properties defined in (Chen 1984, Kailath 1980).

For a stable discrete-time system the controllability and observability grammians, $G_c$ and $G_o$, are the solutions of the discrete-time Lyapunov equations

$$AG_cAT + G_c = -BB^T$$  \hspace{1cm} (B.1)

$$A^TG_oA + G_o = -C^TC$$ \hspace{1cm} (B.2)

where the grammians are symmetric and positive semidefinite (Chen 1984). Since the state space for the BHTE is stable, the Lyapunov equations in (B.1) and (B.2) can be calculated without having to consider the situation when the system matrix is unstable. Numerically, the Lyapunov equations are calculated recursively as per (Chen 1984).

The calculation of the balancing transformation requires the application of the SVD. The SVD is defined as follows, for any $A \in \mathbb{R}^{m \times m}$ with rank $r$, unitary matrices $U$ and $V$ exist such that
where

\[ G = U \begin{bmatrix} \Sigma & 0 \\ 0 & 0 \end{bmatrix} V^T \]  \quad (B.3)

\[ \Sigma = \begin{bmatrix} \sigma_1 & 0 & 0 \\ 0 & \ddots & 0 \\ 0 & 0 & \sigma_r \end{bmatrix} \]  \quad (B.4)

\( \sigma_1 \geq \sigma_2 \geq \ldots \geq \sigma_r \), and the \( \sigma \)'s are the singular values of \( G \) (Horn and Johnson 1990).

Further, for a symmetric, positive semidefinite matrix \( G \in \mathbb{R}^{n \times n} \), the SVD becomes

\[ G = U \begin{bmatrix} \Sigma & 0 \\ 0 & 0 \end{bmatrix} U^T \]  \quad (B.5)

where \( U \) is unitary (Horn and Johnson 1990). Numerically, the SVD was calculated using the IMSL routine LSVRR (IMSL 1987).

The balancing transformation is calculated by first constructing the SVD of the controllability and observability grammians in (3.1) and (3.2) as

\[ G_c = U_c \Sigma_c^2 U_c^T \]  \quad (B.6)

\[ G_o = U_o \Sigma_o^2 U_o^T \]  \quad (B.7)

The matrix product
\[ H = \Sigma_o U_o^T U_c \Sigma_c \]  
(B.8)

is calculated and its SVD is found as

\[ H = U_H \Sigma_H^2 U_H^T. \]  
(B.9)

The balancing transformation, \( T \in \mathbb{R}^{nn} \) is given as (Laub 1980)

\[ T = U_o \Sigma_o U_H^T \Sigma_H. \]  
(B.10)
APPENDIX C

OPTIMAL SERVOMECHANISM CONTROLLER

This appendix describes the equations required to calculate the gains for the optimal servomechanism controller used in this dissertation. The servomechanism problem refers to the class of control problem where the plant outputs follow a class of desired trajectories (Anderson and Moore 1971). A variety of solution techniques exist for solving the servomechanism problem (Anderson and Moore 1971, Miller and Davison 1989, Davison 1976, Davison and Goldenberg 1975). The servomechanism controller designed here is a proportional-plus-integral controller where the feedback gains are chosen in an optimal manner (Ogata 1987). For this problem the number of outputs to be tracked must equal the number of independent control inputs. The gains can be found by constructing the augmented closed-loop state space

\[
\begin{align*}
\begin{bmatrix}
x_e(k+1) \\
u_e(k+1)
\end{bmatrix} &= \begin{bmatrix} A & B \\ 0 & 0 \end{bmatrix} \begin{bmatrix} x_e(k) \\
u_e(k)
\end{bmatrix} + \begin{bmatrix} 0 \\ I \end{bmatrix} \omega(k) \\
\end{align*}
\]

where \( x_e(k) = x(k) - x(\infty) \), \( u_e(k) = u(k) - u(\infty) \), and

\[
\omega(k) = -[K - K_1 CA : I - K_2 B - K_1 CB] \begin{bmatrix} x_e(k) \\
u_e(k)
\end{bmatrix} = -\bar{K} \xi(k)
\]

Equations (C.1) and (C.2) are combined to give the equation
\( \xi(k) = \begin{bmatrix} x_o(k) \\ u_o(k) \end{bmatrix} \). \hspace{1cm} (C.3) \\

\( \xi(k+1) = \bar{A} \xi(k) + \bar{B} \omega(k) \). \hspace{1cm} (C.4) \\

The optimal gain in (C.2) is chosen to minimize the cost function

\[
J = \sum_{k=1}^{m} \xi^T Q \xi + \omega^T R \omega 
\]  \hspace{1cm} (C.5) \\

\[
Q = \begin{bmatrix} C^T \\ 0 \end{bmatrix} [C \ 0]. 
\]  \hspace{1cm} (C.6) \\

where \( Q \in \mathbb{R}^{(n+m) \times (n+m)} \) is positive semidefinite, and \( R \in \mathbb{R}^{m \times m} \) is positive definite. \( Q \) is picked as the outer product of the output matrix to emphasize the state components in the regulated outputs more than those not influencing the regulated output. The minimizing steady state solution of (C.4) is the state feedback term that takes the form of a linear quadratic regulator

\[
\omega(k) = -(R + \bar{B}^T P \bar{B})^{-1} \bar{B}^T P \bar{A} \xi(k) = -\bar{R} \xi(k) 
\]  \hspace{1cm} (C.7) \\

where \( P \) is the solution of the steady state discrete-time Riccati equation (Ogata 1987)
The discrete-time Riccati equation is solved numerically using the method of doubling (Anderson 1978). The gains $K_1$ and $K_2$ are found from equation (C.2) as

$$
[K_1 : K_2] = (\bar{R} + [0 : I]) \begin{bmatrix} A - I_n & B \\ C & CB \end{bmatrix}^{-1}
$$

Note that in the case of the reduced-order controller, the state feedback terms in the $K_2$ gain are transformed into an output feedback term. By transforming $K_2$ into an output feedback term the reduced-order controller is always feeding back temperature information.
This appendix describes the equations defining the calculation of the EKF applied to the BHTE state space model. Consider the state space system perturbed by gaussian noise

\[ x(k+1) = A(w)x(k) + Bu(k) + v(k) \] \hspace{1cm} (D.1)
\[ y(k) = Cx(k) + \eta(k) \] \hspace{1cm} (D.2)

where \( v \) is an independent zero mean gaussian process with correlation \( R_1 \), and \( \eta \) is an independent zero mean gaussian process with correlation \( R_2 \). In this study the bioheat transfer based state space model is assumed deterministic, but the EKF derivation assumes the noisy system defined in (D.1) and (D.2). The EKF that solves for the unknown temperature states and the perfusion magnitudes in (D.1), based on the measured outputs in (D.2) simplifies to

\[ \hat{x}(k+1) = A(\hat{w}(k)) \hat{x}(k) + Bu(k) + K(k) [y(k) - C\hat{x}(k)] ; \] \hspace{1cm} (D.3)
\[ \hat{x}(0) = 0 \]
\[ \dot{\Theta}(k) = \dot{\Theta}(k-1) + L(k) [y(k) - C\Theta(k)] ; \quad \Theta(0) = \Theta_0 \]  
(D.4)

\[ K(k) = [A(\dot{\Theta}(k)) P_1(k) C^T + M_k P_2^T(k) C^T] S^{-1}(k) \]  
(D.5)

\[ L(k) = P_2^T(k) C^T S^{-1}(k) \]  
(D.6)

\[ S(k) = C P_1(k) C^T + R_2 \]  
(D.7)

\[ P_1(k+1) = A(\dot{\Theta}(k)) P_1(k) A^T(\dot{\Theta}(k)) + A(\dot{\Theta}(k)) P_2(k) M_k^T + M_k P_2^T(k) A^T(\dot{\Theta}(k)) + M_k P_3(k) M_k^T - K(k) S(k) K^T(k) + R_1 ; \]  
(D.8)

\[ P_1(0) = \Pi(\Theta_0) \]

\[ P_2(k+1) = A(\dot{\Theta}(k)) P_2(k) + M_k P_3(k) - K(k) S(k) L^T(k) , \]  
\[ P_2(0) = 0 \]  
(D.9)

\[ P_3(k+1) = P_3(k) - L(k) S(k) L^T(k) , \quad P_3(0) = P_0 \]  
(D.10)
In the above equations $\hat{w}$ is the vector of unknown perfusion magnitudes, $d$ is the number of unknown perfusion magnitudes to be estimated, $S$ is the output error covariance, $P_1$ is the state error covariance, $A(\hat{w}(k))$ is the state matrix modified by the estimated parameters, and $M_k$ is the Jacobian matrix that determines the effect of the unknown perfusion magnitudes upon the state space. The covariance matrices are picked as $R_1 = qCCT$, and $R_2 = r_oI$, where $I$ is the pxp identity matrix, and $q$ and $r_o$ are design parameters that are chosen to tune the EKF. Typically, the value of $q$ is picked to be 10 to 100 times larger than the value of $r_o$ to improve the robustness of the EKF's response (Doyle and Stein 1981, 1979).

For a given spatial perfusion pattern the calculation of the Jacobian matrix can be performed prior to the treatment. Since the perfusion only influences the diagonal terms of the state transition matrix (see (A.1) through (A.5) of Appendix A), $M_k$ is given by

$$M_k = \frac{\partial}{\partial w} \left( A(w) \dot{X}(w) \right) \bigg|_{w = \hat{w}(k)} = \left( \frac{\partial A(w)}{\partial w} \dot{X}(k) \right) \bigg|_{w = \hat{w}(k)} \quad (D.12)$$

where

$$\frac{\partial A(w)}{\partial w} \in R^{nxd}. \quad (D.13)$$
Based on (A.1) and (D.12)

\[
\left( \frac{\partial A(w)}{\partial \omega} \right)(i, j) = \begin{cases} 
-\frac{c_b \Delta t}{\rho c} & \text{if } x_i \in \text{zone}(j) \\
0 & \text{if } x_i \notin \text{zone}(j)
\end{cases}
\]  

(D.14)

where zone(j) refers to the jth spatial perfusion zone out of d total zones. Thus the calculation of \( M_k \) is simplified to updating (D.14) by the state vector at every time increment.
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