

# Method for Evaluating Changing Blood Perfusion

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# New Method for Changing Blood Perfusion Estimation

Baoyi Sheng

(ABSTRACT)

This thesis provides insight into methods for estimating blood perfusion, emphasizing the need for accurate modeling in dynamic physiological environments. The thesis critically examines conventional error function solutions used in steady state or gradually changing blood flow scenarios, revealing their shortcomings in accurately reflecting more rapid changes in blood perfusion. To address this limitation, this study introduces a novel prediction model based on the finite-difference method (FDM) specifically designed to produce accurate results under different blood flow perfusion conditions. A comparative analysis concludes that the FDM-based model is consistent with traditional error function methods under constant blood perfusion conditions, thus establishing its validity under dynamic and steady blood flow conditions. In addition, the study attempts to determine whether analytical solutions exist that are suitable for changing perfusion conditions. Three alternative analytical estimation methods were explored, each exposing the common thread of inadequate responsiveness to sudden changes in blood perfusion. Based on the advantages and disadvantages of the error function and FDM estimation, a combination of these two methods was developed. Utilizing the simplicity and efficiency of the error function, the prediction of contact resistance and core temperature along with the initial blood perfusion was first made at the beginning of the data. Then the subsequent blood perfusion values were predicted using the FDM, as the FDM can effectively respond to changing blood perfusion values.

# New Method for Changing Blood Perfusion Estimation

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## (GENERAL AUDIENCE ABSTRACT)

Blood perfusion, the process of blood flowing through our body's tissues, is crucial for our health. It's like monitoring traffic flow on roads, which is especially important during rapid changes, such as during exercise or medical treatments. Traditional methods for estimating blood perfusion, akin to older traffic monitoring techniques, struggle to keep up with these rapid changes. This research introduces a new approach, using a method often found in engineering and physics, called the finite-difference method (FDM), to create more accurate models of blood flow in various conditions. This study puts this new method to the test against the old standards. We discover that while both are effective under steady conditions, the FDM shines when blood flow changes quickly. We also examined three other methods, but they, too, fell short in these fast-changing scenarios. This work is more than just numbers and models; it's about potentially transforming how we understand and manage health. By combining the simplicity of traditional methods for initial blood flow estimates with the dynamic capabilities of the FDM, we're paving the way for more precise medical diagnostics and treatments.

# Contents

<b>List of Figures</b> .....	<b>vi</b>
<b>List of Tables</b> .....	<b>viii</b>
<b>1 Introduction and Background</b> .....	<b>1</b>
<b>2 Measurement System</b> .....	<b>3</b>
<b>3 Blood Perfusion Model</b> .....	<b>5</b>
3.1 Finite Difference Solution Method .....	5
3.2 Analytical Solution Method (Error Function Method).....	7
3.2.1 One Step of Input Heat Flux.....	7
3.2.2 Sum of All Solution to Heat Flux Input .....	7
3.3 Parameter Estimation.....	8
<b>4 Evaluation with Simulated Data</b> .....	<b>9</b>
4.1 Prove the FDM is Grid Independent.....	10
4.2 Prove the FDM is Same as the Error Function for Blood Perfusion Calculation .....	11
<b>5 Varying Blood Perfusion Evaluation with Simulated Data</b> .....	<b>13</b>
5.1 Error Function Method in Varying Blood Perfusion Value .....	13
5.2 Additional Analytical Methods .....	14
5.2.1 Case 1 Constant Heat Flux.....	15
5.2.2 Case 2 Heat Flux Step.....	16
5.2.3 Changing Heat Flux.....	19
5.3 Combined Error Function and FDM Estimation .....	21
<b>6 Evaluation with Real data</b> .....	<b>24</b>
6.1 Find the Best $kpC$ for Real data with constant perfusion .....	24
6.2 Compare Three Methods with Real Data for Varying Perfusion .....	32
6.2.1 Nearly Constant Blood Perfusion Data.....	32
6.2.2 Restricted Blood Perfusion Data.....	33
6.3 Experiment Date Testing .....	35
6.4 Time Period Length for Transient Estimation .....	38

6.5 Sensitivity of Transient Stage Estimation for Estimation Result .....	41
<b>7 Discussion of Results.....</b>	<b>44</b>
<b>8 Conclusion .....</b>	<b>46</b>
<b>9 References.....</b>	<b>47</b>
<b>10 Appendix.....</b>	<b>48</b>

# List of Figure

Figure 1. contact diagram and the <i>CHFT+</i> sensor.....	4
Figure 2. Heat flux steps .....	7
Figure 3. Constant Heat flux vs time for the simulated data.....	9
Figure 4. Comparison of FDM and error function method with constant heat flux..	11
Figure 5. Varying Heat flux vs time for simulated data. ....	12
Figure 6. Comparison of FDM and error function method with varying heat flux...	12
Figure 7. Varying blood perfusion value .....	13
Figure 8. Comparison of FDM and error function method with varying blood perfusion value .....	14
Figure 9. Temperature results of Case 1 constant heat flux.....	15
Figure 10. Equation 13 validation. ....	16
Figure 11. Sensor Temperature Calculated by FDM with decrease $w_b$ . ....	17
Figure 12. Calculated results compare with set blood perfusion data. ....	17
Figure 13. Sensor Temperature Calculated by FDM with increased $w_b$ . ....	18
Figure 14. Calculated results compare with set blood perfusion data. ....	19
Figure 15. Constant increase in heat flux of simulated data. ....	20
Figure 16. Sensor Temperature Calculated by FDM with changing $w_b$ . ....	20
Figure 17. Comparison of three different methods .....	21
Figure 18. Schematic diagram of the parameter estimation processes. ....	22
Figure 19. Combine Method estimation comparison. ....	23
Figure 20. Data with constant blood perfusion .....	24
Figure 21. Responds to $k$ change from 0.1 W/m <sup>2</sup> *K to 1.0 W/m <sup>2</sup> *K ( $C = 3500$ J/kg- K). ....	25
Figure 22. Responds to $C$ change from 1000 J/kg-K to 6000 J/kg-K ( $k = 0.5$ W/m <sup>2</sup> *K).....	26
Figure 23. Responds to Blood perfusion from 0.001 (ml/s)/ml to 0.01 (ml/s)/ml. ...	27
Figure 24. Real data two method comparison.....	28
Figure 25. Real data two method comparison.....	29
Figure 26. Estimation results with $R=0.0043$ m <sup>2</sup> ·K/W and $w_b=0.0047$ (ml/s)/ml...	29
Figure 27. Real data two method comparison.....	30
Figure 28. Real data two method comparison.....	31
Figure 29. Estimation results with $R=0.0037$ m <sup>2</sup> ·K/W and $w_b=0.0043$ (ml/s)/ml...	31
Figure 30. Constant $w_b$ Estimation result comparison for three methods.....	33
Figure 31. Data with varying blood perfusion values .....	34
Figure 32. Varying $w_b$ Estimation result comparison for three methods.....	35
Figure 33. Experiment data .....	36
Figure 34. Compare three methods with 80 seconds transients. ....	37

Figure 35. Compare three methods with 120 seconds transients. ....	38
Figure 36. Estimation for 1 min .....	39
Figure 37. Estimation for 2 mins.....	39
Figure 38. Estimation for 3.5 mins.....	40
Figure 39. Estimation with change of transient stage estimation.....	42
Figure 40. Estimation with change of transient stage estimation 2.....	43

# List of Tables

Table 1. Assumed tissue properties. ....	9
Table 2: the RMS of difference node numbers with blood perfusion of 0.001 (ml/s)/ml. ....	10
Table 3: the RMS of difference node numbers with blood perfusion of 0.03 ml/ml/s. .....	10
Table 4. Initial rough assumption tissue properties. ....	24
Table 5. Modification tissue properties. ....	28
Table 6. Final tissue properties.....	32
Table 7- Estimation for different time periods.....	40
Table 8- Estimation for different time periods.....	40
Table 9- Estimation for different time periods.....	40
Table 10- Estimation for different time periods.....	41
Table 11- Estimation for different time periods.....	41
Table 12- Estimation for different time periods.....	41
Table 13 - Original transient stage estimation .....	42

# Chapter 1 Introduction and Background

Temperature sensors and thermal sensing systems have been indispensable across a plethora of technological domains. These systems play pivotal roles not just in gauging surface temperatures but also in discerning deeper, intricate properties of objects and physiological entities. Among these, non-invasive thermal sensors and systems stand out for their potential to provide insights without any physical intrusion [1]. The prominence of non-invasive tools is accentuated by their myriad advantages, encompassing attributes such as improved reliability, enhanced accuracy, cost-effectiveness, user-friendliness, and quick response times, to name a few.

One pioneering avenue in the realm of non-invasive thermal sensing is the Non-Invasive Thermal Interrogation (NITI). Fundamentally, NITI facilitates non-destructive testing and monitoring via thermal sensing mechanisms [2]. This methodology involves a concurrent measurement of both surface temperature and surface heat flux. When synergistically analyzed, these dual measurements can unveil a wide array of internal parameters of an object or a biological system. Parameters such as thermal conductivity, density, heat capacity, and the convection coefficient can be gleaned, alongside insights into the internal temperature distribution. Notably, in biological systems like the human body, this temperature distribution and the associated parameters can be intricately linked to physiological processes, notably blood perfusion.

Blood perfusion, characterized as the non-directional blood flow per tissue volume, is a cornerstone of physiological homeostasis. This flow, mediated through the capillary network and intercellular spaces, is indispensable for nutrient delivery, waste removal, and overall cellular health [3]. However, the nature of blood perfusion – acting volumetrically with no distinct entrance or exit – makes its testing and modeling exceptionally challenging. Variations in blood perfusion often serve as indicators of physiological or pathological states, underscoring the importance of accurate estimation methods. With its ability to deduce internal properties non-destructively, NITI offers a promising avenue for blood perfusion estimation [2].

Recent work, such as the research by Alkhwaji et al. (2012), has laid the groundwork for analytical methods targeting blood perfusion estimation. A new analytical model is proposed to simplify data processing and provide correct initial conditions for the bioheat equation. In addition, a robust parameter estimation method has been developed that can simultaneously solve for local core temperature, thermal contact resistance, and blood

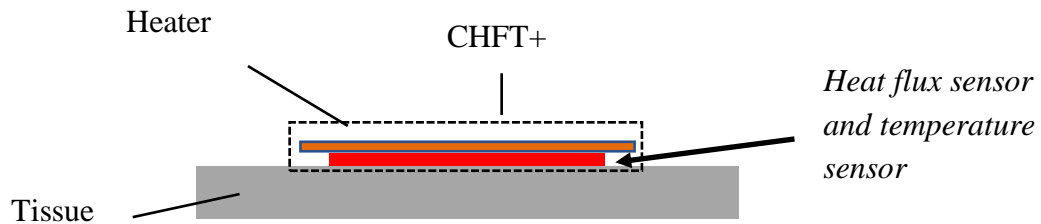
perfusion values. The measured sensor temperature data is used to estimate the heat flux compared to the measured heat flux data. Cooling is applied to the skin to take away the heat [4]. After research based on the Alkhwaji's groundwork, a new method is developed to generate better and more stable data: heat is applied to the skin by using the heater on top of the temperature sensor and heat flux sensor [5]. Finally, the research done by Alanazi is a new method to measure the energy flow rate in the pipe. However, it is a similar idea to measure the blood perfusion for the tissue and gave inspiration for a new estimation method for blood perfusion. Instead of using the sensor temperature to estimate the heat flux, the heat flux sensor data is used to estimate the sensor temperature [6]. The patent of Roghanizad has come out with an analytical equation for real-time measurements without any parameter estimation for blood perfusion [2]. In this paper, the equations from Roghanizad's works will be used and compared to the different estimation methods for blood perfusion.

Building upon such foundational research and leveraging the potential of NITI, there emerges an opportunity to advance our understanding and precision in estimating blood perfusion, thereby enriching our tools for physiological monitoring and diagnosis.

## Chapter 2 Measurement System

All the real data are measured using the thermally activated non-invasive blood perfusion measurement systems [7]. The data obtained from this device is a time history of the heat flux and sensor temperature. The Combined Heat-Flux Temperature Sensor (CHFT+) is a cutting-edge non-invasive measurement system tailored for assessing peripheral perfusion [8]. Utilizing the core principle of bio-heat transfer, the CHFT+ administers a controlled amount of heat to the skin surface and monitors resulting temperature changes, offering real-time insights into blood flow. These temperature changes, representative of the balance between tissue heat conduction and convective blood flow, are then analyzed using bio-heat transfer models to deduce tissue perfusion characteristics. The sensor's ability to provide immediate, depth-specific, and non-invasive data makes it a valuable tool for clinical evaluation and patient comfort.

CHFT+ is a combination of heat flux sensor and thermocouple into a sleek, pliable, and water-resistant sensor shown in Fig. 1 [8]. When looking from the top, the combined heat flux sensor and thermocouple are visible, while the heater and its power connections are situated below. The resistance heater, responsible for the thermal disturbance, along with the sensor pairing, are specialty components from FluxTeq. When measuring, the tissue would be placed over the sensor, ensuring direct contact of the heat flux sensor with the skin.



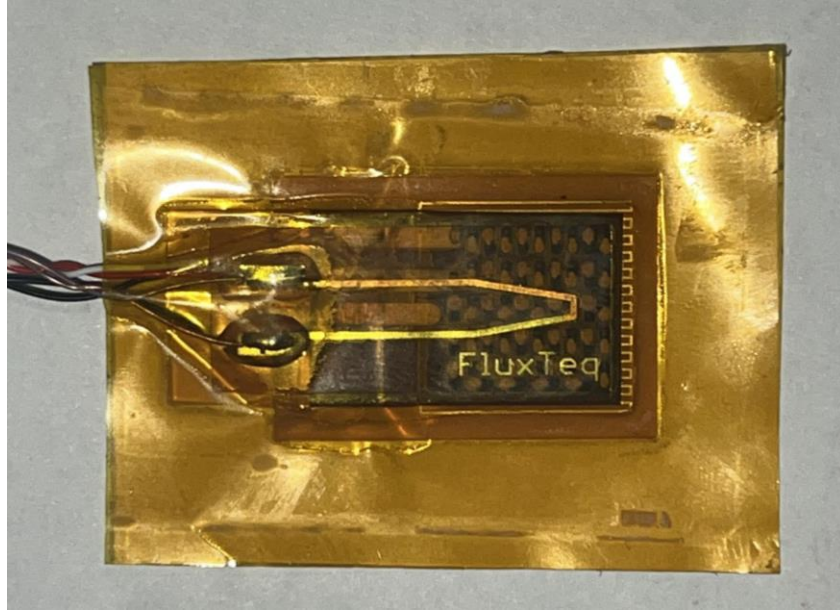


Figure 1. contact diagram and the *CHFT+* sensor.

## Chapter 3 Blood Perfusion Model

In biological tissues, the temperature distribution is notably influenced by blood perfusion. The heat imposed onto the tissue is carried away by the perfusion flow through the tissue and it is conducted into the tissue. This process is described by the Pennes bio-heat equation with a few simplifying assumptions. Assume all heat transfer between the tissue and the blood occurs in the capillaries, the metabolic heat generation can be neglected, and the core body temperature and tissue properties is constant.

$$\rho C \frac{\partial T}{\partial t} = k \frac{\partial^2 T}{\partial x^2} - \rho C w_b (T - T_b) \quad (1)$$

The surface boundary condition is described in terms of thermal contact resistance between the sensor where the measurements occur, and the tissue surface specified at  $x = 0$ .

$$q''_s = -k \frac{\partial T}{\partial x} \Big|_{x=0} = \frac{1}{R''} (T_s - T|_{x=0}) \quad (2)$$

where

$w_b$  = blood perfusion in (ml/s/ml)

$k$  = tissue thermal conductivity (W/m-K)

$\rho$  = tissue density (kg/m<sup>3</sup>)

$C$  = tissue specific heat (J/kg-K)

$q''_s$  = measured heat flux (W/m<sup>2</sup>)

$T_s$  = measured surface temperature (°C)

$T_b$  = blood temperature (°C)

There are several approaches to solve these equations.

### 3.1 finite difference solution method

The finite-difference solution of equation 1 is given in terms of the derivatives.

$$\frac{dT}{dt} \simeq \frac{T_i^{p+1} - T_i^p}{t_i^{p+1} - t_i^p}$$

$$\frac{d^2T}{dx^2} \simeq \frac{T_{i+1}^p - 2T_i^p + T_{i-1}^p}{\Delta x^2}$$

$$\rho C \frac{T_i^{p+1} - T_i^p}{\Delta t} = k \frac{T_{i+1}^p - 2T_i^p + T_{i-1}^p}{\Delta x^2} - \rho C w_b (T_i^p - T_b)$$

$$T_i^{p+1} - T_i^p = \alpha \Delta t \frac{T_{i+1}^p - 2T_i^p + T_{i-1}^p}{\Delta x^2} - w_b \Delta t (T_i^p - T_b) \quad (3)$$

Solving for

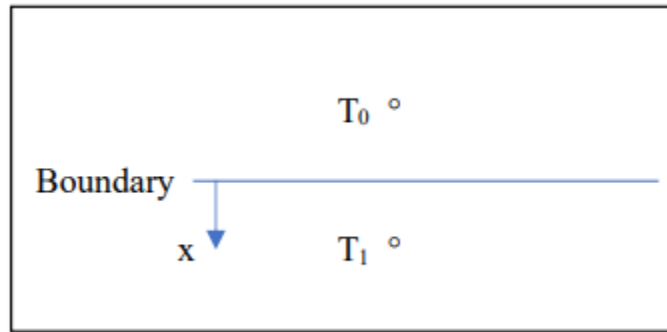
$$T_i^{p+1} = T_i^p + Fo(T_{i+1}^p - 2T_i^p + T_{i-1}^p) - w_b \Delta t (T_i^p - T_b)$$

$$T_i^{p+1} = (1 - Fo - w_b \Delta t) T_i^p + Fo(T_{i+1}^p + T_{i-1}^p) + w_b \Delta t T_b \quad (4)$$

where the requirement is that

$$(Fo + w_b \Delta t) < 1$$

The surface node is special and must be handled separately with an imaginary node, called  $T_0$ . The boundary nodes are shown in the diagram.



The temperature at the boundary is  $T|_{x=0} = \frac{T_0 + T_1}{2}$

The spatial derivative at the boundary is  $\frac{\partial T}{\partial x}|_{x=0} = \frac{T_1 - T_0}{\Delta x} = \frac{T_S - T_0}{\frac{\Delta x}{2}}$

$$q''_s = -k \frac{T_1 - T_0}{\Delta x} = \frac{1}{R''} \left( T_S - \frac{T_0 + T_1}{2} \right)$$

Consequently, the two unknowns in terms of the other variables are.

$$T_0 = T_1 + \frac{q''_s \Delta x}{k}$$

$$T_S = q''_s R'' + \frac{T_0 + T_1}{2} = T_0 \left( \frac{1}{2} + \frac{kR''}{\Delta x} \right) + T_1 \left( \frac{1}{2} - \frac{kR''}{\Delta x} \right) \quad (5)$$

### 3.2 Analytical Solution Method (Error Function Method)

#### 3.2.1 One step of input heat flux

For an input of  $q''_s$ , the analytical solution for the complete temperature distribution is.

$$\theta(x, t) = q''_s \frac{1}{2k} \sqrt{\frac{\alpha}{w}} e^{-x\sqrt{\frac{w}{\alpha}}} \left[ \operatorname{erfc}\left(\frac{x-2t\sqrt{w\alpha}}{2\sqrt{\alpha t}}\right) - e^{2x\sqrt{\frac{w}{\alpha}}} \operatorname{erfc}\left(\frac{x+2t\sqrt{w\alpha}}{2\sqrt{\alpha t}}\right) \right] \quad (6)$$

$$\theta(0, t) = q''_s \frac{1}{k} \sqrt{\frac{\alpha}{w}} \operatorname{erf}(\sqrt{wt}) \quad (7)$$

At steady state ( $t \rightarrow \infty$ )

$$\theta(0, \infty) = q''_s \frac{1}{k} \sqrt{\frac{\alpha}{w}} \quad (8)$$

To find the core blood temperature from the steady sensor measurements before the heat flux is applied.

$$T_b = T_s - q''_s \frac{1}{k} \sqrt{\frac{\alpha}{w}} - q''_s R'' \quad (9)$$

where heat flux is defined as positive into the tissue.

#### 3.2.2 sum of all solution to heat flux input

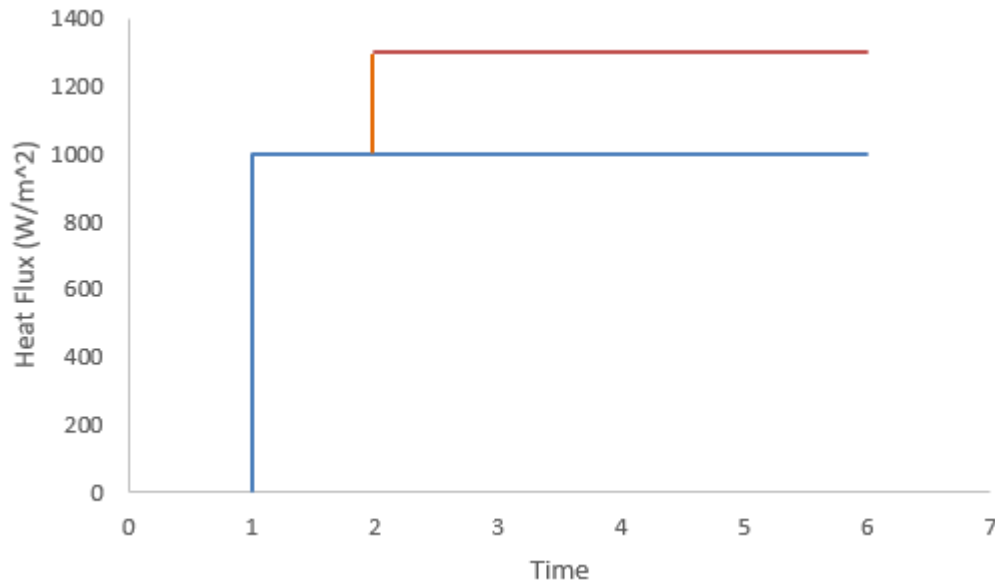


Figure 2. Heat flux steps

For a step function input of  $q''_s$  as shown in Fig. 2, The digital data are naturally represented as a series of heat flux step functions  $H(t-t_n)$ , and the final temperature is calculated by using eq. 6 is shown below:

$$T(t) = T_{initial} + \sum_{m=1}^{m=max} \Delta q''_s \times \frac{1}{k} \sqrt{\frac{\alpha}{w}} \operatorname{erf}(\sqrt{wt}) H(t) \quad (10)$$

$$T_{initial} = T_b + \frac{q''_{s,0}}{\sqrt{w\rho ck}}$$

### 3.3 Parameter Estimation

The task involves adjusting the parameters  $w$ ,  $R$ , and  $T_b$  to ensure that the measured sensor temperatures align closely with those forecasted by a theoretical model. An objective function, denoted as  $S$ , is defined by eq.11, which represents the sum of the squared discrepancies between the actual measurements and the model's forecasts. The objective is to fine-tune these parameters so that the value of  $S$  is minimized, indicating a high degree of correlation between the model's predictions and the observed data [9]. This fine-tuning is accomplished through a systematic approach known as sequential search. This strategy incrementally tests different parameter combinations to find the one that reduces  $S$  to its lowest possible value.

$$S = \sum_{m=1}^M (T_{pred,m} - T_{s,m})^2 \quad (11)$$

Sequential search method is used to find the minimum of the least square estimation. A sequential search, also known as a linear search, is one of the simplest search algorithms [10]. It is a method for finding a particular value in a list that checks each element in sequence until the desired value is found, or the list is exhausted. It does not require the list to be sorted, which differentiates it from binary searches that require a sorted list to operate efficiently.

## Chapter 4 Evaluation with Simulated Data

First start by using Simulate data is first used to examine solutions provided by the finite difference method (FDM) and analytical method for simple data sets. The parameters used for the simulated data are common values of the tissue properties as shown in Table 1.

Table 1. Assumed tissue properties.

Thermal conductivity (k)	density( $\rho$ )	Heat capacity (C)	Core body temperature (Tb)	Contact Resistance (R)
0.4 W/m*K	900 kg/m <sup>3</sup>	4000 J/kg-K	34 °C	0.0015 m <sup>2</sup> ·K/W

The values of the above tissue properties will be used in all simulated data validations. The simulated data is a set of heat flux measurement values with a time step of 0.687 seconds (normal time step for the heat flux sensor) from zero to 3000 seconds. The system is assumed to be at steady state before the heater is turned on and has a set initial heat flux value. For this validation, the heat flux is set to 70 W/m<sup>2</sup> before turning on at 137 seconds, remaining 550 W/m<sup>2</sup> after the heater turns on for the rest of the time, as illustrated in Fig. 3.

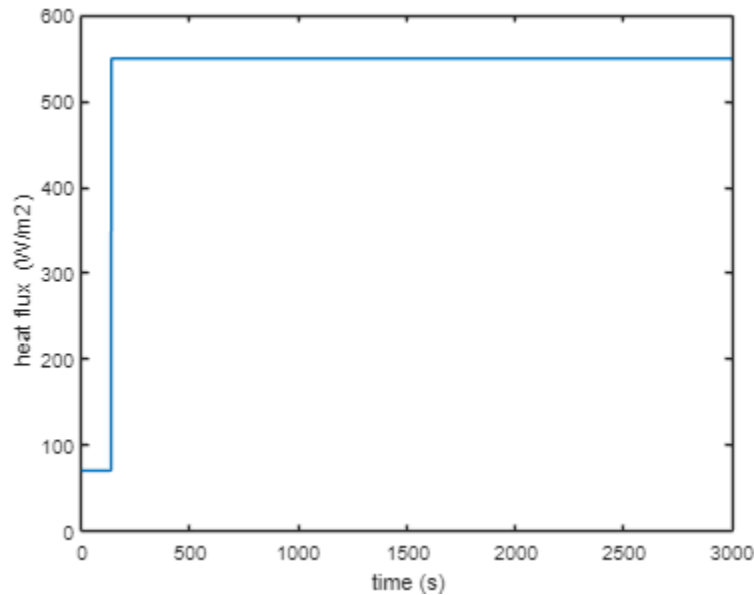


Figure 3. Constant Heat flux vs time for the simulated data.

### 4.1 Prove the FDM is grid independent.

First, this study needs to prove that the finite difference method (FDM) is grid-independent for the normal range of blood perfusion values (From  $W_b=0.001$  (ml/s)/ml) to  $W_b=0.03$  (ml/s)/ml). Grid independence is a crucial aspect of numerical methods because it ensures that finite difference solution is not heavily dependent on the choice of grid, making it more reliable and accurate [12].

The grid spacing (dx - distance between two nodes (meter)) is the first value to determine. With a smaller dx, the FDM results will be much more accurate. Of course, a smaller dx is better but when decreasing the grid spacing (dx) in the finite difference method to a very small value, the system may not be able to produce results due to numerical instability. Some finite-difference schemes are stable only within a certain range of grid spacings and time steps. If the time step is too small for the grid spacing used, the solution will become unstable and diverge. For this whole Chapter, the smallest dx is 0.0004 m for this set of tissue properties and time step.

Then node number is the next value to determine for the system is grid independent. Start with an initial grid size with 20 nodes and compute a numerical solution using FDM. Then, systematically refine the grid by doubling the number of nodes and computing the solution again. Then calculate the numerical error for each node number. RMS of difference shown in eq 12, is used to calculate the difference between the numerical solution obtained with the current node numbers and the solution obtained with a double node number [11]. Which x is the sensor temperature:

$$RMS = \sqrt{\frac{\sum_{t=1}^n (x_{1,t} - x_{2,t})^2}{n}} \quad (12)$$

The RMS of difference between the node numbers is shown in the tables below:

Table 2: the RMS of difference node numbers with blood perfusion of 0.001 (ml/s)/ml.

Node numbers	RMS (°C)
20-40	3.1485
40-80	0.6952
80-160	0.0141
160-320	5.615e-6
320-640	1.528e-14

Table 3: the RMS of difference node numbers with blood perfusion of 0.03 ml/ml/s.

Node numbers	RMS (°C)
20-40	0.0015

40-80	3.737e-7
80-160	1.099e-14
160-320	0
320-640	0

Therefore, with the consideration of the range of the blood perfusion value, the best choice of the node number is 160 for best performance. The RMS of difference is significantly small for this system.

#### 4.2 Prove the FDM is the same as the error function for blood perfusion calculation.

Through the above process, the most suitable grid size and node number have been found these parameters will be used to verify that the FDM and the error function solutions get the same value in the blood perfusion calculation. First, use the same heat flux data from Figure 3 (constant heat flux after the heater turns on). The resulting sensor temperature results are shown in Fig. 4 for both methods. The difference in values between them is not visible. The parameter estimation routine was used to calculate with the perfusion value ( $W_b=0.001$  (ml/s)/ml and  $W_b=0.03$  (ml/s)/ml). The RMS (Root mean square) value for both blood perfusion values is significantly small. Therefore, for constant heat flux, two different methods can output similar results.

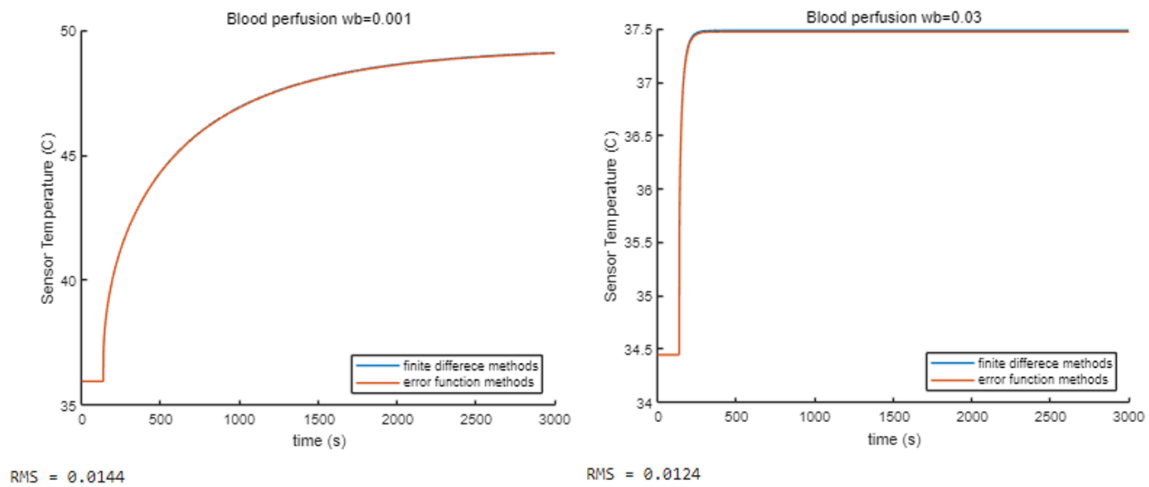


Figure 4. Comparison of FDM and error function method with constant heat flux.

The RMS (Root mean square) value for both blood perfusion values is significantly small. Therefore, for constant heat flux, two different methods can output similar results.

Then verify the two methods are still the same with changing heat flux. Another simulated heat flux data is shown in Figure 5.

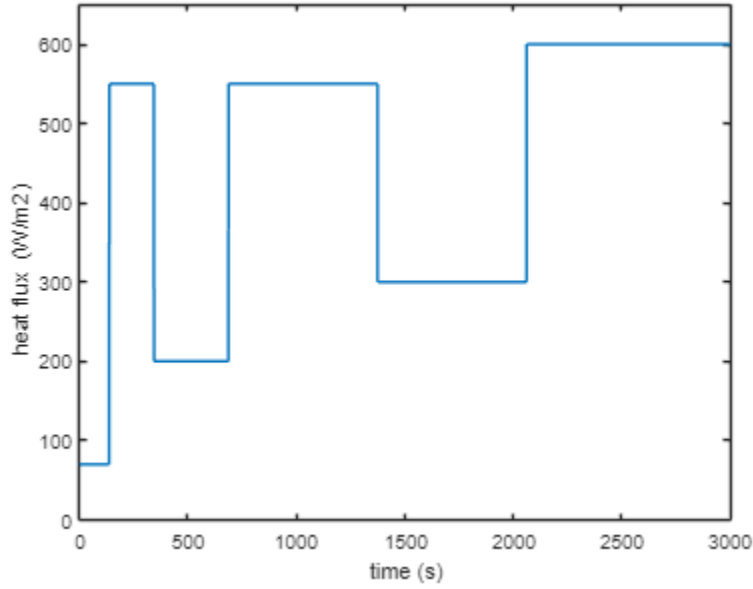


Figure 5. Varying Heat flux vs time for simulated data.

With all other parameters kept the same, the sensor temperature results were calculated by FDM and error function method. Again, the results match with no visible difference in values. The blood perfusion values with  $W_b=0.001$  (ml/s)/ml and  $W_b=0.03$  (ml/s)/ml using for the entire data set. The RMS value for both blood perfusion values is significantly small. Therefore, for varying heat flux, two different methods can also output similar results.

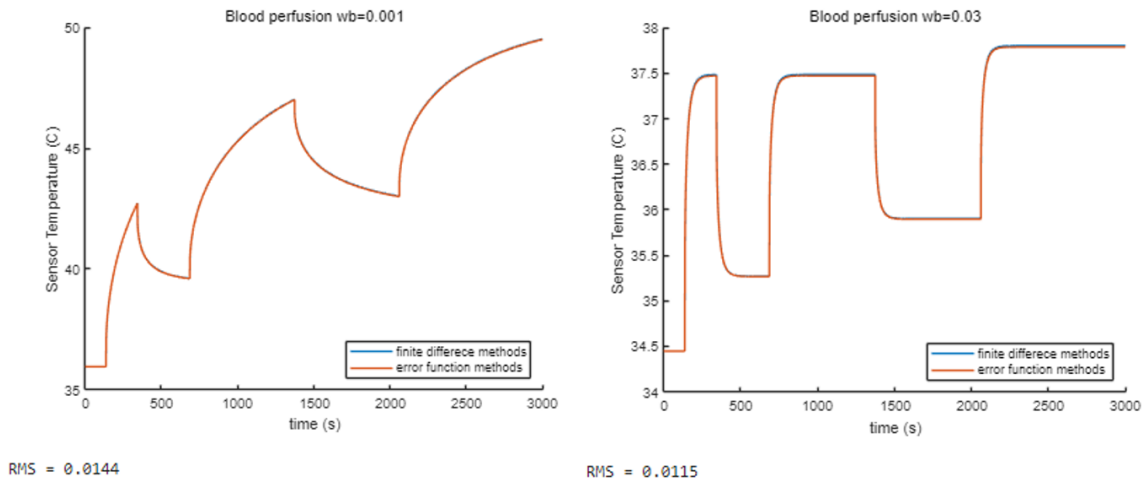


Figure 6. Comparison of FDM and error function method with varying heat flux.

## Chapter 5 Varying Blood Perfusion Evaluation with Simulated

### Data

As can be seen from the above Chapter, for the case of constant blood perfusion, both solution methods show the same results. However, the current challenge of interest is for varying values of blood perfusion. First, the error function method is tested. Then, other possible analytical methods are tested.

#### 5.1 Error function method in varying blood perfusion value.

The simplest case is to assume that the heat flux is constant with a value of  $70 \text{ W/m}^2$  and that the initial conditions at time zero are steady state. The initial blood perfusion is  $0.01 \text{ (ml/s)/ml}$ . This gives an initial steady-state temperature of  $34.47^\circ\text{C}$ . A new set of blood perfusion values is created for validation with the blood perfusion specified in Fig. 7.

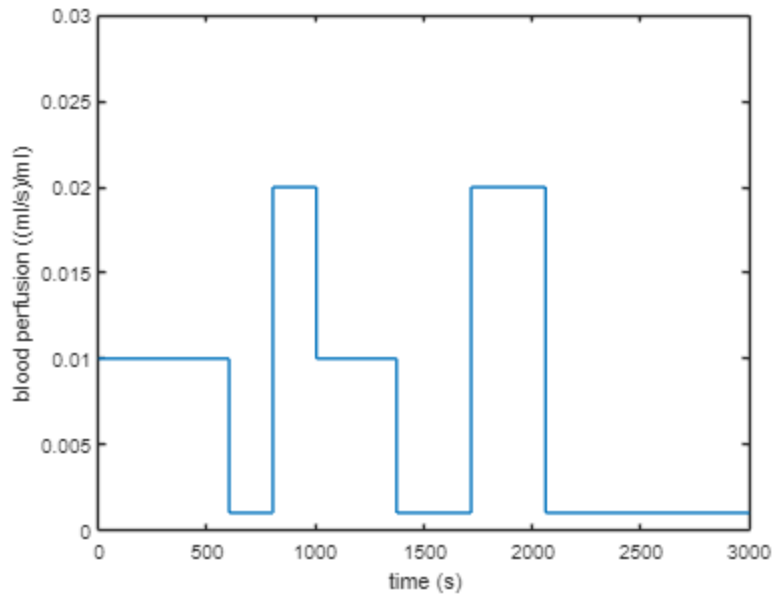
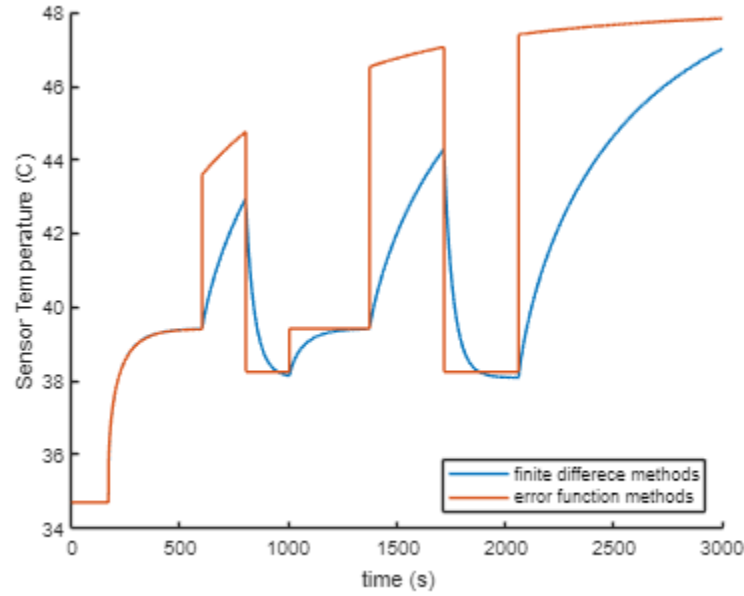


Figure 7. Varying blood perfusion value

This new blood perfusion value is changing from  $0.001 \text{ (ml/s)/ml}$  to  $0.02 \text{ (ml/s)/ml}$  for the whole period. The varying blood perfusion value is used to do the temperature calculation with both the FDM and the error function method as shown in Fig.8.



RMS = 2.8950

Figure 8. Comparison of FDM and error function method with varying blood perfusion value

Both methods aim to predict the sensor temperature over time, the results significantly diverge, with the error function method typically showing higher temperatures and more abrupt changes, while the FDM is smoother and more gradual. This should not be surprising because the error function method must assume constant coefficients in equation 10 to be valid for superpositions. In a temperature system, sudden temperature changes are unreasonable. FDM can produce smooth results with varying blood perfusion values, whereas the error function method does not work properly with changing blood perfusion values.

## 5.2 Additional analytical methods

The above validation shows that the error function does not work properly with changing blood perfusion values. However, if an analytical equation can be found to estimate the blood perfusion value, it will make the work easier and more efficient.

Below are two analytical equations to estimate the blood perfusion value. The first is from the steady state of equation 8:

$$w = \left( \frac{q}{T_{skin} - T_b} \right)^2 \times \frac{1}{k\rho c} \quad (13)$$

A second equation is taken from equation 47 of Roghanizad [2]:

$$w = \left[ kpc \left( \frac{(T_{s,m} - q_{s,m} \times R) - (T_{s,0} - q_{s,0} \times R)}{q_{s,m} - q_{s,0}} \right)^2 \right]^{-1} \quad (14)$$

where  $T_{s,m}$  is the real-time sensor temperature,  $q_{s,m}$  is the real-time sensor heat flux,  $T_{s,0}$  is the initial of the sensor temperature,  $q_{s,0}$  is the initial heat flux of the sensor. These equations are evaluated for predicting varying blood perfusion by using the FDM to calculate the corresponding sensor temperature curves. Three different cases are documented.

### 5.2.1 Case 1 Constant heat flux

Both equations 13 and 14 are specified for steady-state situations. However, equation 14 cannot work if the heat flux is constant because the denominator will be zero. To test equation 13, a steady-state heat flux of  $550 \text{ W/m}^2$  is used and the blood perfusion value is changed at 1030 seconds from  $0.001 \text{ (ml/s)/ml}$  to  $0.01 \text{ (ml/s)/ml}$ . The temperature from the FDM for this case is shown in Fig. 9. Using this with equation 13 results in the blood perfusion shown in Fig. 10. It gives a very slow response.

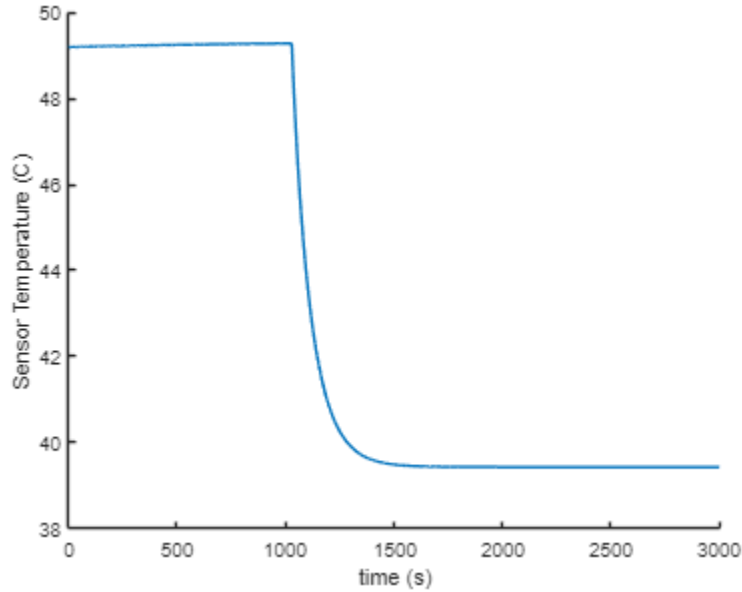


Figure 9. Temperature results of Case 1 constant heat flux.

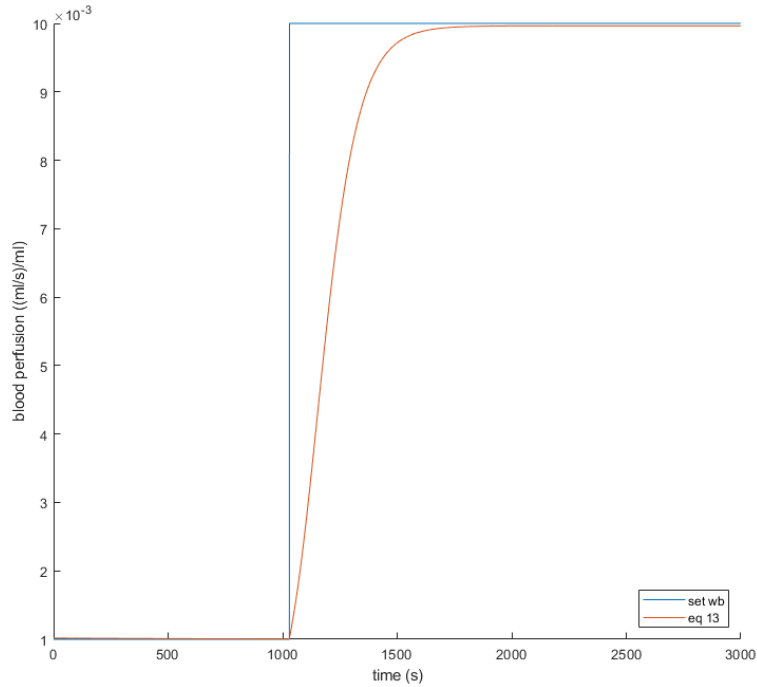


Figure 10. Equation 13 validation.

### 5.2.2 Case 2 Heat flux step

To accommodate equation 14, the heat flux must change. Consequently, case 2 has the heat flux is set to  $70 \text{ W/m}^2$  at steady state. At 137 seconds the heat flux is increased to  $550 \text{ W/m}^2$  as shown in Figure 3.

Set the blood perfusion value change at 1030 seconds from  $0.01 \text{ (ml/s)/ml}$  to  $0.001 \text{ (ml/s)/ml}$ . The sensor temperature is calculated by using the FDM and the calculated result is used to estimate the blood perfusion by using the two analytical equations.

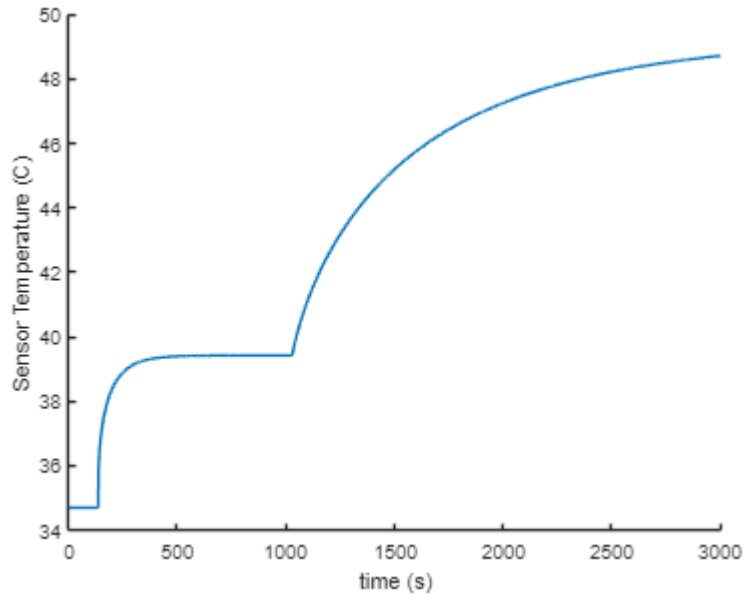


Figure 11. Sensor Temperature Calculated by FDM with decrease wb.

The calculated result is shown in the Figure 12. Again, the response is very slow.

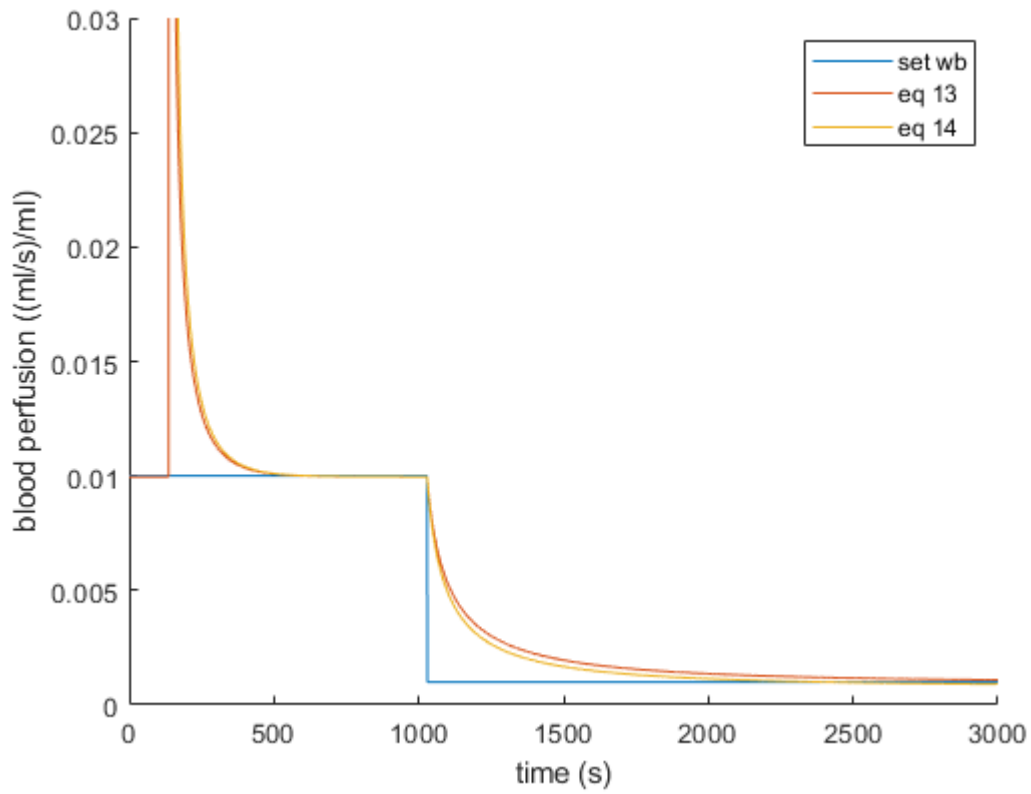


Figure 12. Calculated results compare with set blood perfusion data.

Next, use the same heat flux data but set the blood perfusion change at 1030 second the opposite direction from 0.001 (ml/s)/ml to 0.01 (ml/s)/ml. FDM is again used to calculate the sensor temperature data as shown in Fig. 13.

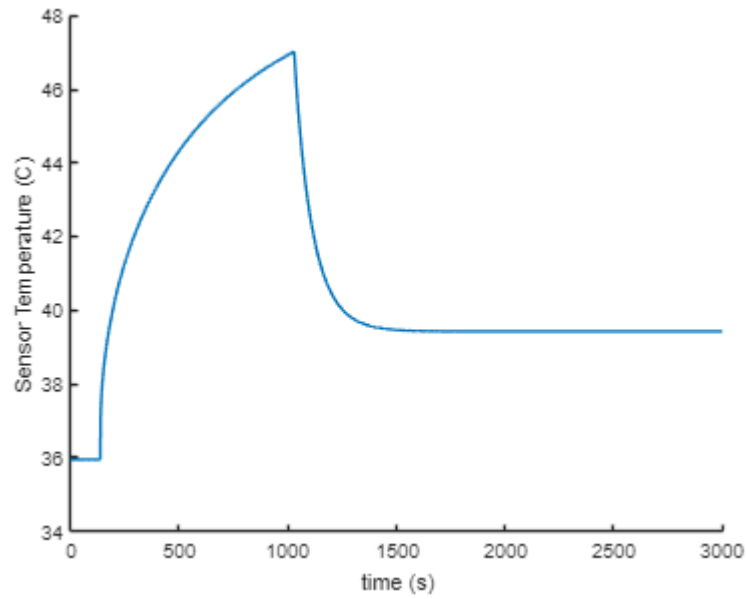


Figure 13. Sensor Temperature Calculated by FDM with increased wb.

The calculated results are shown in Fig. 14. They are particularly bad for eq. 14.

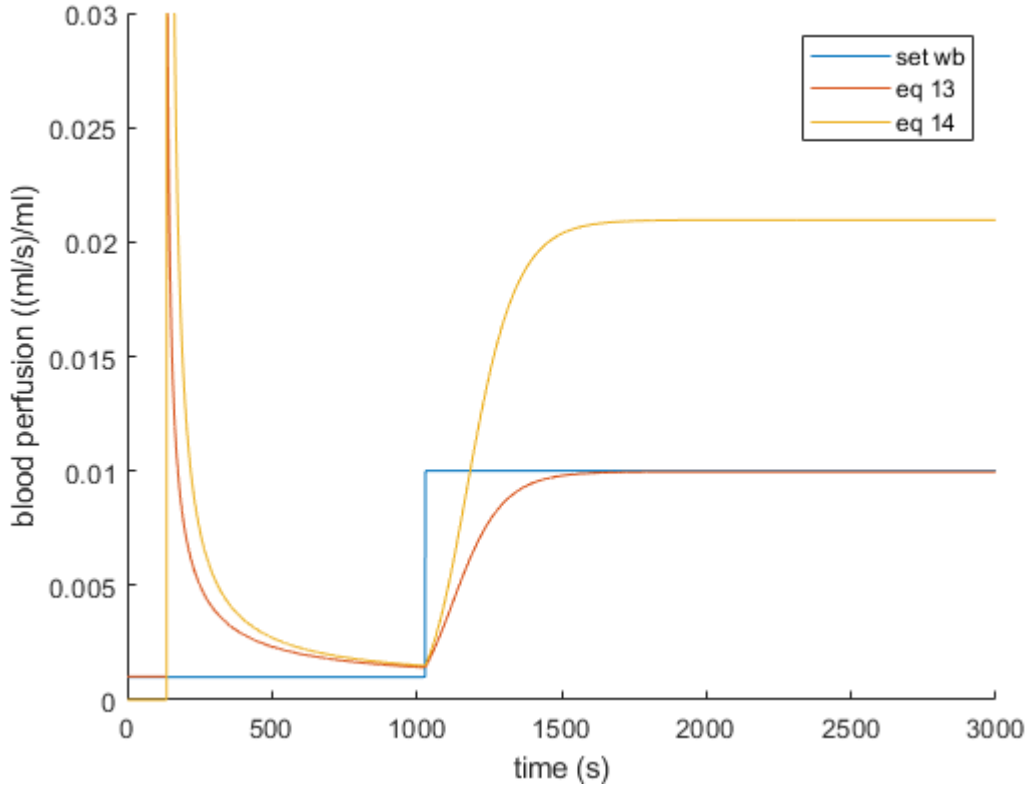


Figure 14. Calculated results compare with set blood perfusion data.

From the comparison figure of the results, equation 13 is doing well at a steady state of the system, no matter changing the blood perfusion from low to high or high to low.

If the temperature reaches a steady state, the calculation result is close to the set blood perfusion value.

For Equation 14, if the blood perfusion value is increased, the estimation value at steady state is not accurate. For decreased blood perfusion value, Equation 14 has a slightly faster response than Equation 13.

### 5.2.3 Changing heat flux.

The most realistic simulation is for constantly changing heat flux. An additional solution is available only for this case, equation 46 from Roghanizad [2].

$$w = \left[ kpc \left( \frac{(Ts, m - qs, m \times R) - (Ts, 0 - qs, 0 \times R)}{\sum_{j=1}^m \Delta qs, j \times Erf(\sqrt{w}(t_m - t_{j-1}))} \right)^2 \right]^{-1} \quad (15)$$

where  $Ts, m$  is the real time sensor temperature,  $qs, m$  is the real time sensor heat flux,  $Ts, 0$  is the initial sensor temperature,  $qs, 0$  is the initial heat flux of the sensor,  $qs, j$  is the

iteration heat flux,  $t_m$  is real-time,  $t_{j-1}$  is the previous iteration time. The blood perfusion  $w$  on the right side is updated by every new blood perfusion value calculated with the time. For this case a constant increase in heat flux is specified starting  $70 \text{ W/m}^2$  to  $550 \text{ W/m}^2$  as shown in Fig. 14.

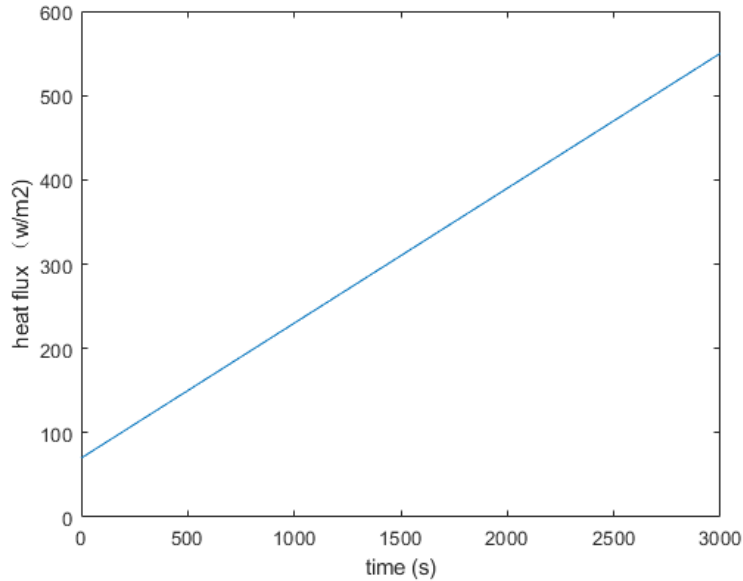


Figure 15. Constant increase in heat flux of simulated data.

Then the blood perfusion changes with time several times in the 3000 seconds shown in Figure 7. The sensor temperature is calculated by using the FDM as shown in Fig. 16.

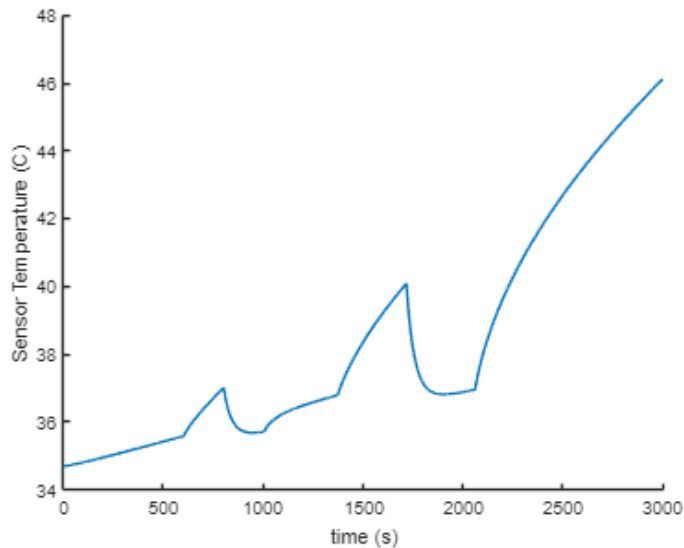


Figure 16. Sensor Temperature Calculated by FDM with changing  $w_b$ .

All three equations are used to estimate the blood perfusion value and compare with the set value as shown in Fig. 17.

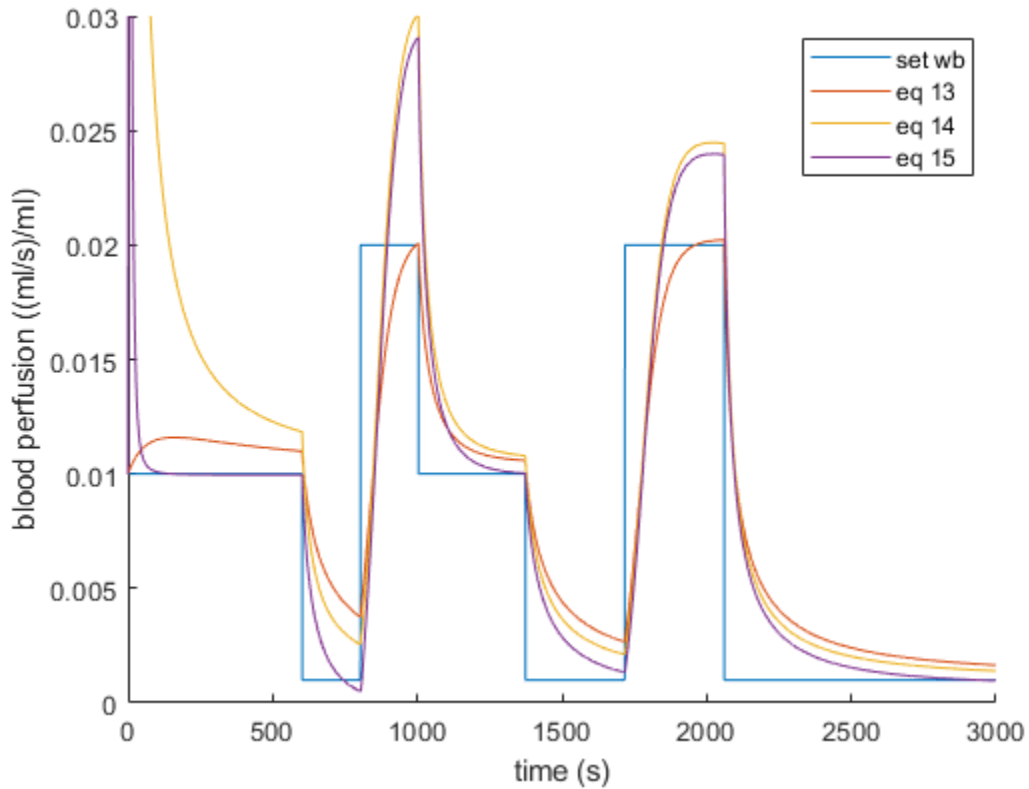


Figure 17. Comparison of three different methods

Equation 15 behaves like Equation 14, but the Equation 15 response is the fastest for the decreasing blood perfusion value. For the increased blood perfusion value, Equation 15 is slightly better than Equation 14 but still not close to the actual value. Both Equation 14 and Equation 15 overshoot at increasing points. For decreased blood perfusion value, Equation 15 has the best estimate of value with the fastest response time. For increasing blood perfusion value, Equation 13 has the best estimate of value compared to two other methods.

### 5.3 Combined error function and FDM estimation

Based on all the validations for different methods of estimating, none of these methods work well during the transients and around the blood perfusion changing point. So, a new method needs to be developed to estimate those stages.

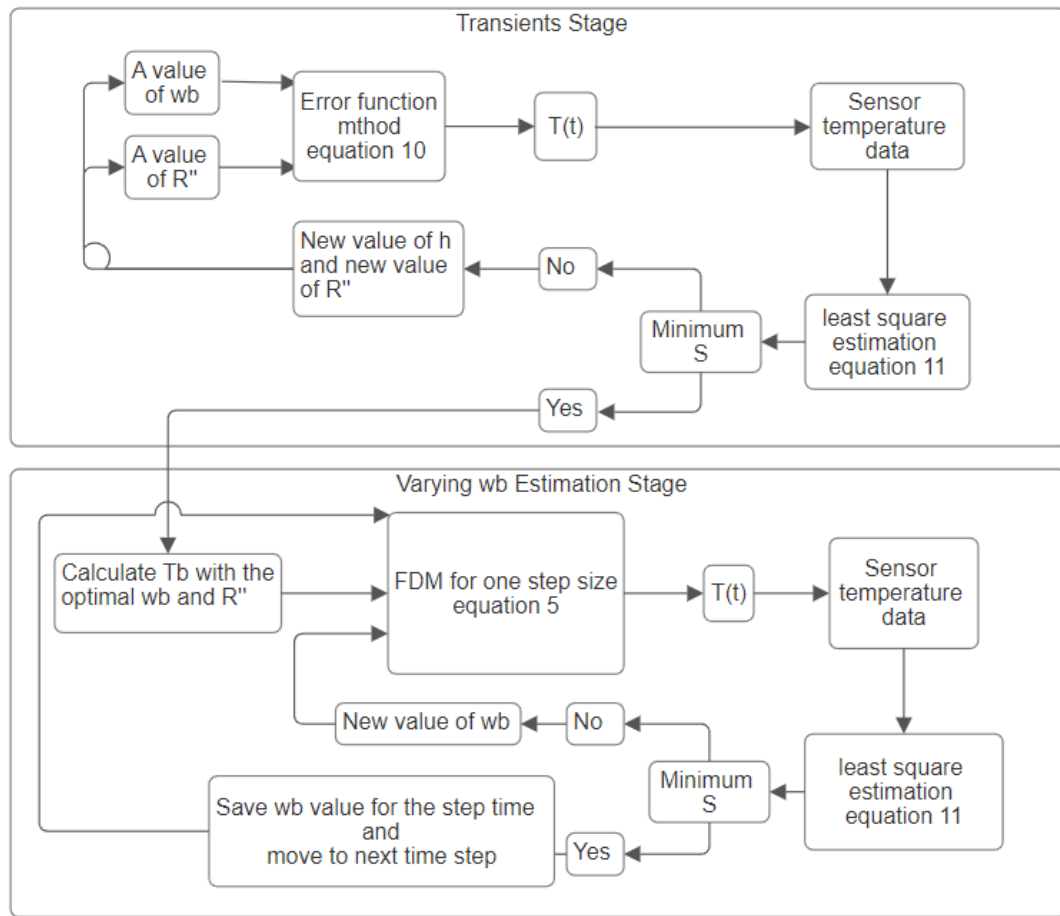


Figure 18. Schematic diagram of the parameter estimation processes.

A combination of the error function and FDM will be used for the new estimation method. For the transient stage before 412 seconds, the error function is used to estimate the  $R$  and  $w_b$ . Both  $R$  and  $w_b$  values will be used to calculate the  $T_b$  by using Eq. 10. The estimated  $R$  and  $T_b$  are assumed to be constant for this system and will be used for later estimation by using FDM. For the rest of the time, 68.7 seconds of step size is used for each estimation of new blood perfusion value.

A constant increase in heat flux from Figure 15 and changing blood perfusion the same as in Figure 16 are used for the comparison. Below is the estimation from the combined method compared to the set value.

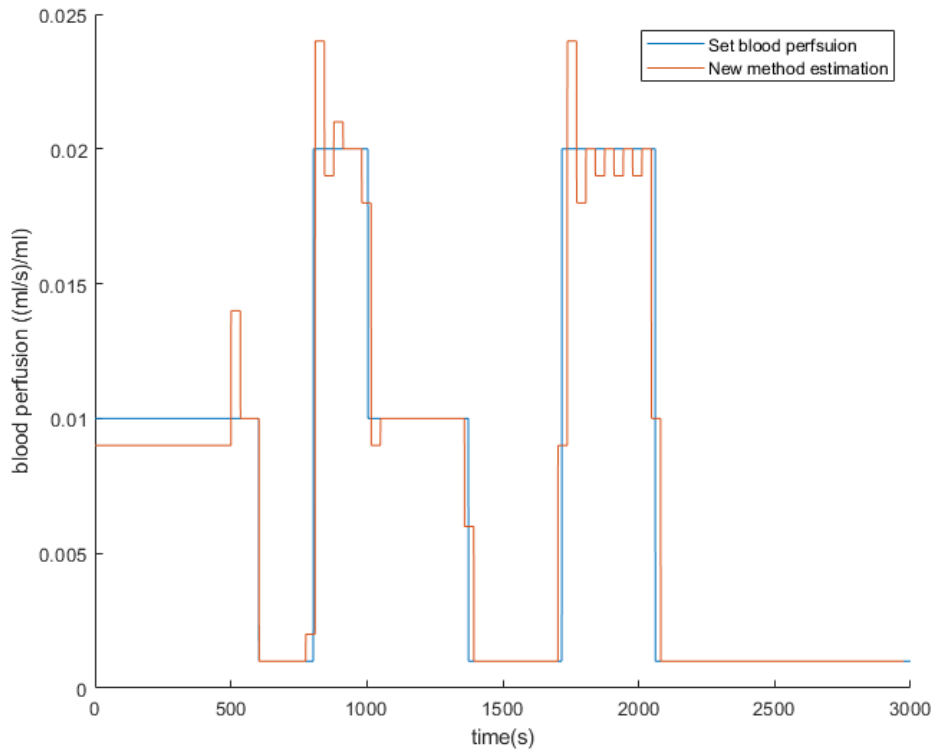


Figure 19. Combine Method estimation comparison.

Compared to the other estimation methods in Fig. 17, the combined method is much better at the transient stage and blood perfusion changing point. And the overall performance was the best.

## Chapter 6 Evaluation with Real data

Several sets of data were measured by using the combined heat flux and temperature sensor (CHFT+). The CHFT+ is attached to the inner forearm, and before the sensor has taken any data, the forearm was given time to reach steady state. After data acquisition begins, initial conditional data is recorded, followed by activation of the heater. In some cases, a pressure cuff is applied to the upper arm, to block blood flow.

### 6.1 Find the best $kpC$ for real data with constant perfusion.

The first set of data was taken for 2300 seconds with supposedly a constant blood perfusion. This set of data was used to obtain more accurate thermodynamic parameters for human tissue. The data as time, heat flux, and sensor temperature, which need to be analyzed to derive the appropriate parameter based on the equation for the blood perfusion model. The error function method (equation 10) was used for this process.

The blood perfusion value for this data is known to be constant, but the value is uncertain. The data has an almost constant heat flux after 70 seconds, which peaks when the heater turns on. The heat flux and sensor temperature are shown below:

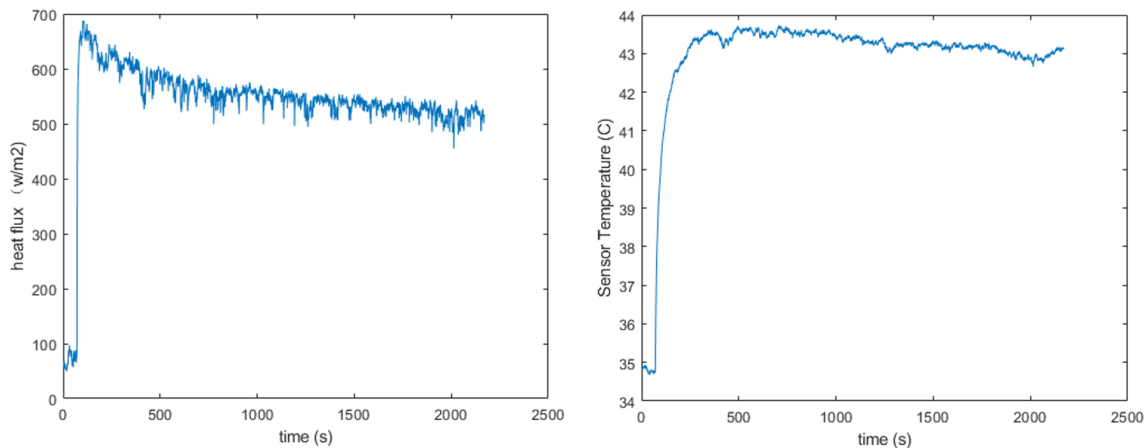


Figure 20. Data with constant blood perfusion

There are five key parameters to be determined, which are  $R$ ,  $w$ ,  $k$ ,  $p$ , and  $c$ . First, it is important to observe the effect of different parameters on the calculation results.

First, an initial rough assumption was made about the five parameters shown in Table 4.

Table 4. Initial rough assumption tissue properties.

Thermal conductivity ( $k$ )	density( $\rho$ )	Heat capacity ( $C$ )	Blood perfusion value	Contact Resistance ( $R$ )
---------------------------------	-------------------	--------------------------	--------------------------	-------------------------------

0.5 W/m*K	950 kg/m <sup>3</sup>	3500 J/kg-K	0.003	0.0015 m <sup>2</sup> ·K/W
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For contact resistance, changing R will only shift the overall result up or down and will have no effect on the overall graph shape. Therefore, the analysis of the different contact resistances will not be repeated here.

For density, this program mainly deals with human tissues, so the values of 950 kg/m<sup>3</sup> will not deviate much from the actual. Therefore, effect of different densities on the results will also not be considered here.

The thermal conductivity, k, was set from 0.1 W/m\*K to 1 W/m\*K (increased by 0.05 W/m\*K), and the other values were kept the same as the initial assumptions. The following figure shows the effect of different k on the results.

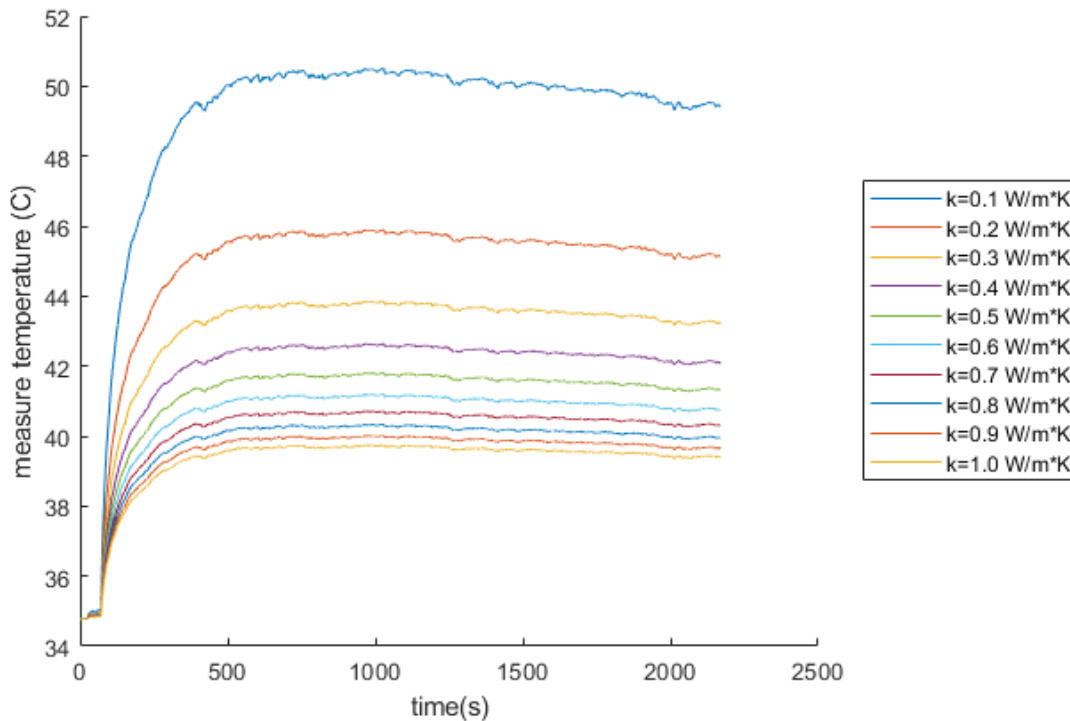


Figure 21. Responds to k change from 0.1 W/m\*K to 1.0 W/m\*K (C = 3500 J/kg-K).

The thermal heat capacity, C, was set from 1000 J/kg-K to 6000 J/kg-K (increased by 500 J/kg-K) and the other values were kept the same as the initial assumptions. The following figure shows the effect of different C on the results.

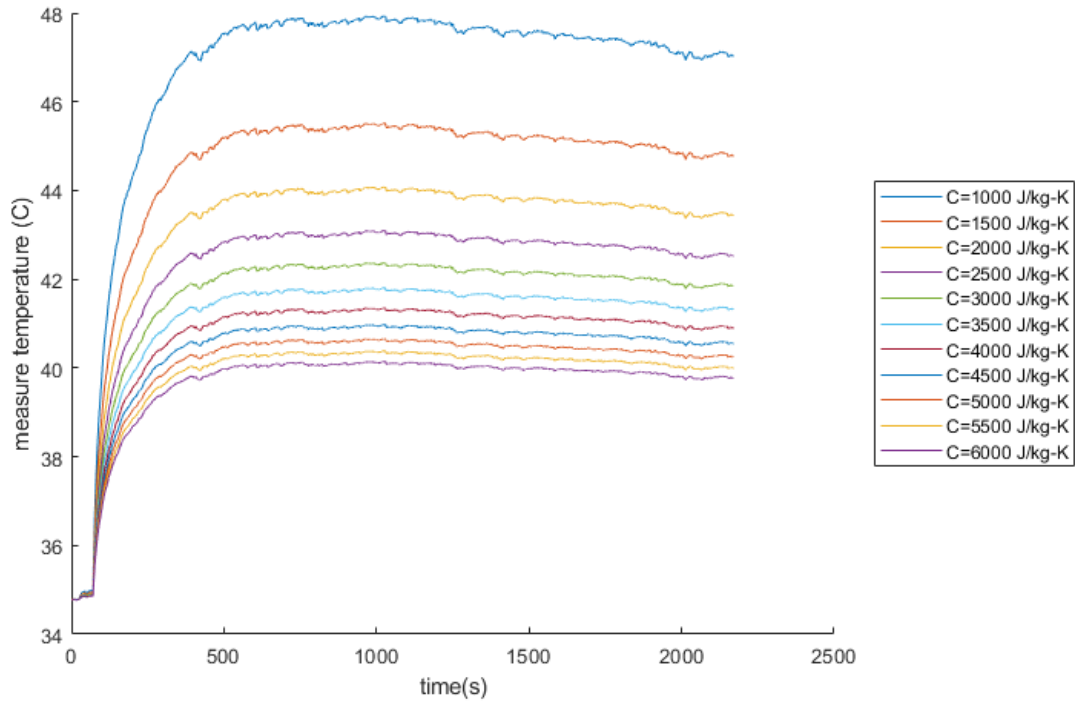


Figure 22. Responds to C change from 1000 J/kg-K to 6000 J/kg-K ( $k = 0.5 \text{ W/m}^2\text{K}$ ).

The comparison shows that  $k$  and  $C$  have very similar effects on the results. The effect on the final steady state is significant, but not decisive for the overall trend. By analyzing the Error Function method, the three values of  $k$ ,  $p$ ,  $C$  do not appear separately in the formula, so  $kpC$  can be viewed as a whole parameter. The larger the  $kpC$  is, the smaller the final steady state temperature is.

For different  $w_b$  effects,  $w_b$  was set from  $0.001(\text{ml/s})/\text{ml}$  to  $0.01 (\text{ml/s})/\text{ml}$  (increases by  $0.001 (\text{ml/s})/\text{ml}$ ), and the other values were kept the same as the initial assumptions. The following figure shows the effect of different  $w_b$  on the results.

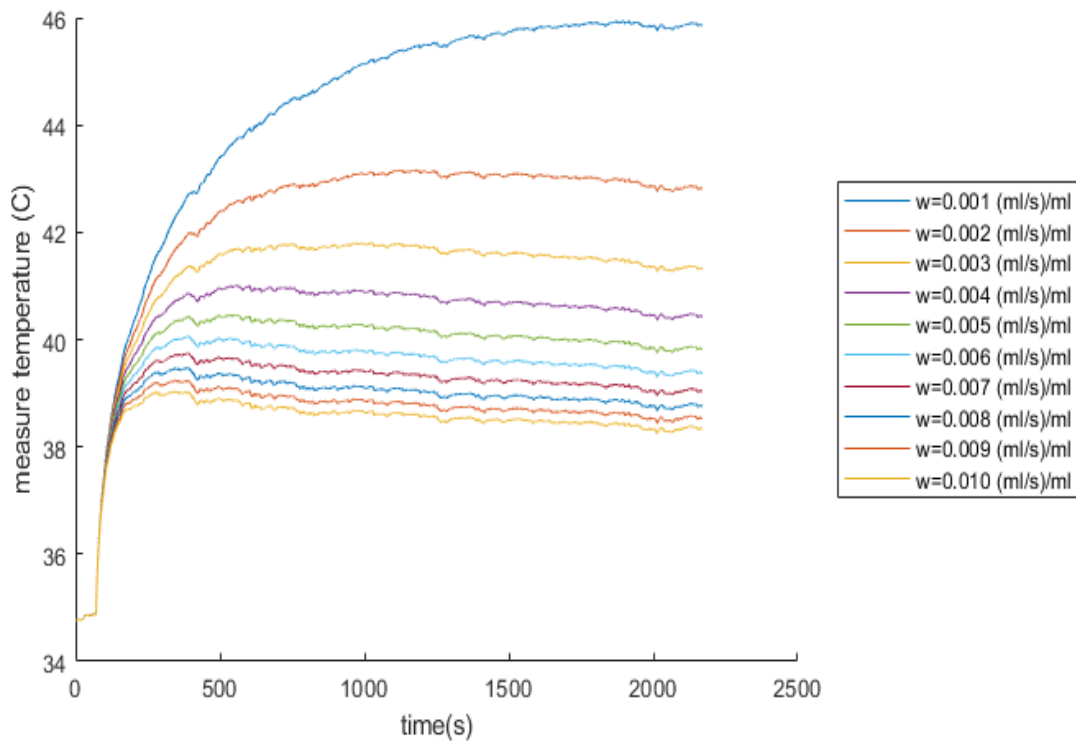


Figure 23. Responds to Blood perfusion from 0.001 (ml/s)/ml to 0.01 (ml/s)/ml.

As can be seen from the above figure,  $w_b$  has a large effect on the rate of reaching the steady state. The smaller the  $w_b$ , the slower it is to reach the steady state. The value of the  $w_b$  largely determines the sensitivity of the system's response to heat flux.

First, calculations are done by using the values of the initial assumptions, and the results are compared with the measured temperature data.

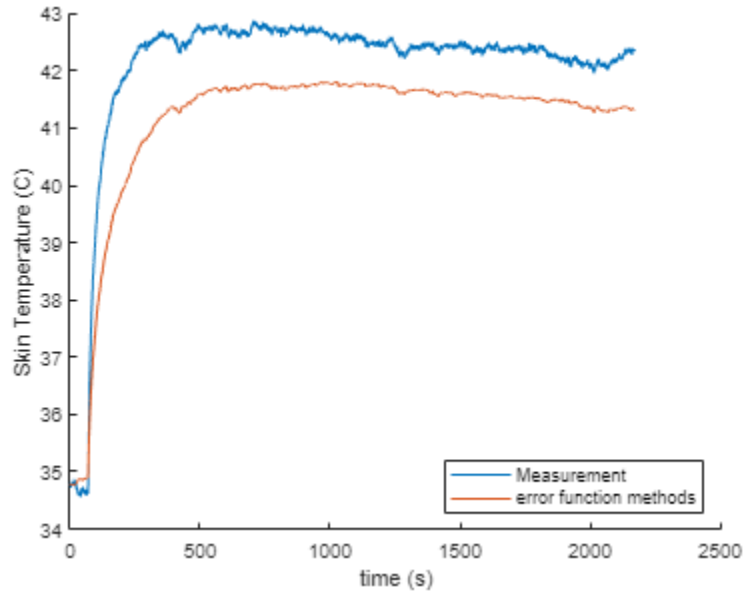


Figure 24. Real data two method comparison.

As you can see from the above figure there is still a big difference in the final steady state. By shrinking the kpc, the results of the calculations are made closer to the measured values.

Now, the parameters after modification are now shown in Table 5:

Table 5. Modification tissue properties.

Thermal conductivity (k)	density( $\rho$ )	Heat capacity (C)	Blood perfusion value	Contact Resistance (R)
0.4 W/m*K	950 kg/m <sup>3</sup>	3500 J/kg-K	0.003	0.0015 m <sup>2</sup> ·K/W

The result is calculated by using the above parameters is shown below:

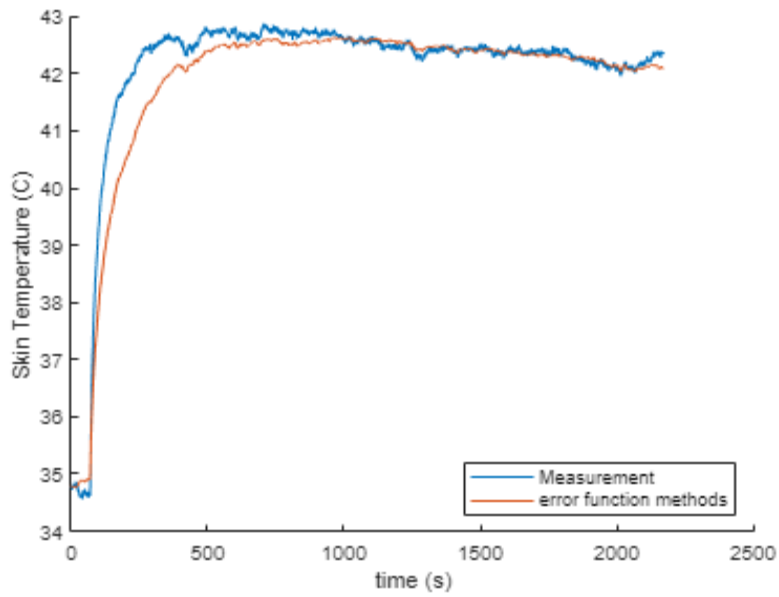


Figure 25. Real data two method comparison.

The difference between calculated and measured data in the steady state phase is now small, but there is still a big difference in the rising phase.

So, the rising phase is presented separately (0-700 seconds), and the previous RW prediction program is used for the better prediction of R and W.

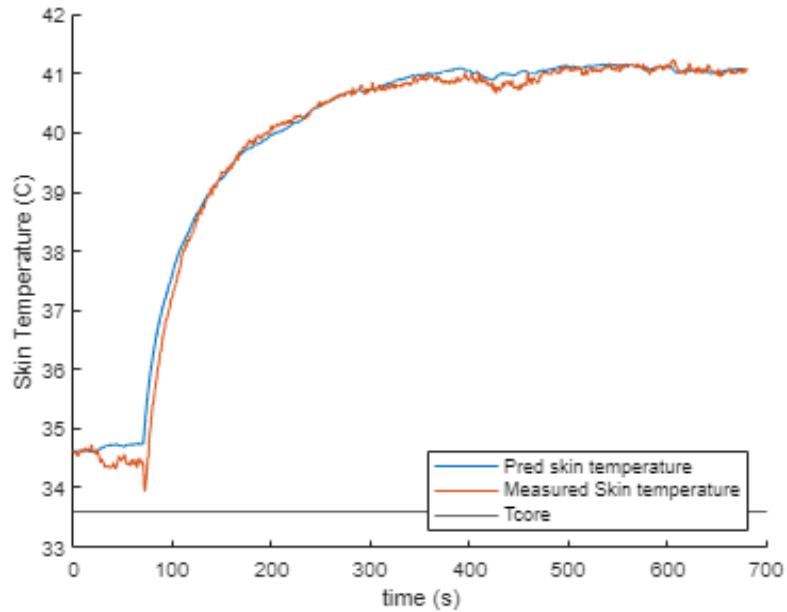


Figure 26. Estimation results with  $R=0.0043 \text{ m}^2 \cdot \text{K/W}$  and  $w_b=0.0047 \text{ (ml/s)/ml}$ .

By using the prediction program, now in the rising phase the calculation result is much closer to the measurement. Therefore, change the R to 0.0043 m<sup>2</sup>·K/W and Wb to 0.0047 for later calculation. The core body temperature is 33.60 °C by using the average of data before the heater turns on.

The result calculated by using the changing R and W values is shown below:

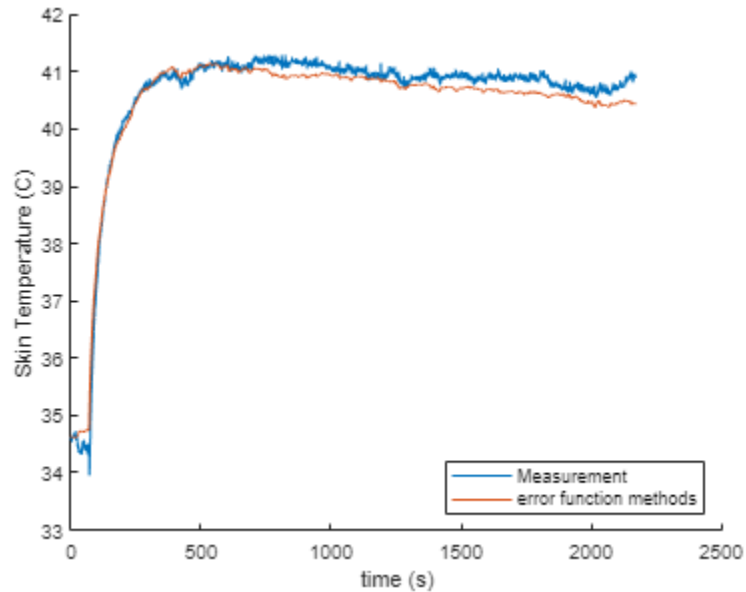


Figure 27. Real data two method comparison.

Looking at the overall result, the first half of the calculation does fit the actual data better, but there is still a gap in the final steady state phase.

By using the equation:

$$w = \left( \frac{q}{T - T_b} \right)^2 \times \frac{1}{k \rho c} \quad (13)$$

Wb is 0.0043 for this set of parameters which is close to the estimation of the program. But it's not the same, so it may result in a slightly different steady-state phase. Small adjustment is needed to make the steady state to be closer.

Therefore, change the C to 3300 J/kg-K, making the steady state closer. The result is shown below with another parameter that remains the same as the last one.

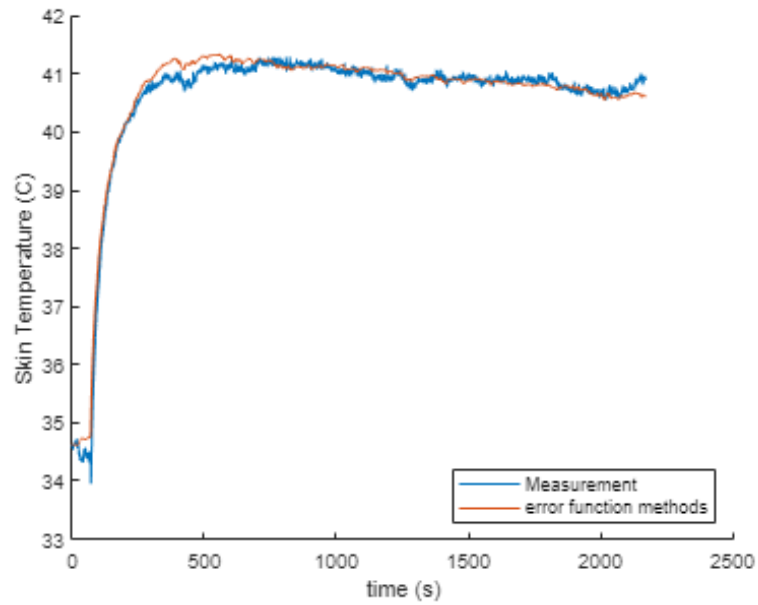


Figure 28. Real data two method comparison.

Then repeat the same process and use the new kpc value for the estimation of the RW program. But this time, use all the data to do the prediction (from 0 to 2300 seconds) The new R and W estimation is shown below:

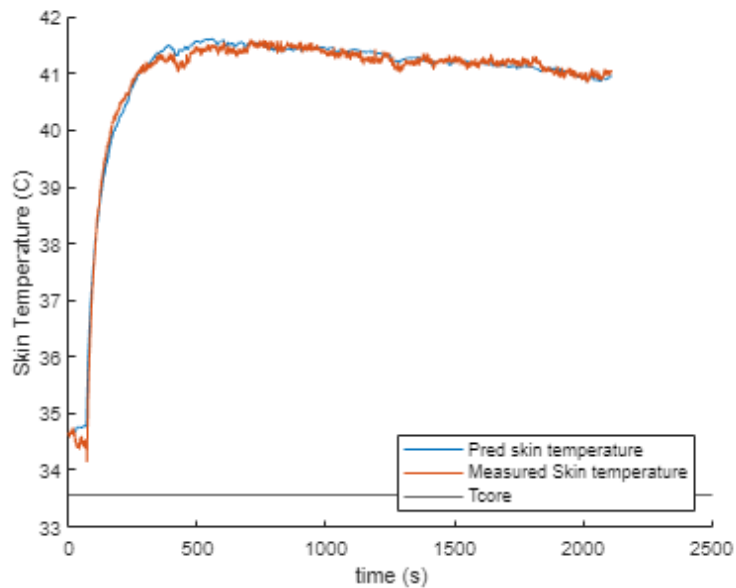


Figure 29. Estimation results with  $R=0.0037 \text{ m}^2 \cdot \text{K}/\text{W}$  and  $w_b=0.0043 \text{ (ml/s)/ml}$

By using eq. 13 the calculated  $w$  for the steady state is  $0.0044 \text{ (ml/s)/ml}$  which is close to the estimation. The overall result is close to the real measurement data.

Finally, all the parameter estimations are shown in Table 6:

Table 6. Final tissue properties.

Thermal conductivity (k)	density( $\rho$ )	Heat capacity (C)	Blood perfusion value	Contact Resistance (R)	Core body temperature (Tb)
0.4 W/m*K	950 kg/m <sup>3</sup>	3300 J/kg-K	0.0043	0.0037 m <sup>2</sup> ·K/W	33.5754 °C

k and c can also be adjusted, since for this formula, as long as KPC remains consistent it will not affect the result. To keep the same KPC, increasing k would require decreasing c.

## 6.2 Compare three methods with real data for varying perfusion.

### 6.2.1 Nearly constant blood perfusion data

Use the real data with constant blood perfusion first (Fig. 20) and compare all three different method results of estimating time-varying blood perfusion.

All the parameters are the same as the best value found in Table 6. The real data has measured sensor temperature and heat flux shown below:

Heat flux used from Fig. 20. Heat flux before the heater turns on is around 50 W/m<sup>2</sup>. The heater turns on at around 200 seconds, then the heater remains on. Heat flux is almost steady at a steady state around 550 W/m<sup>2</sup>.

The figures show all the method comparisons.

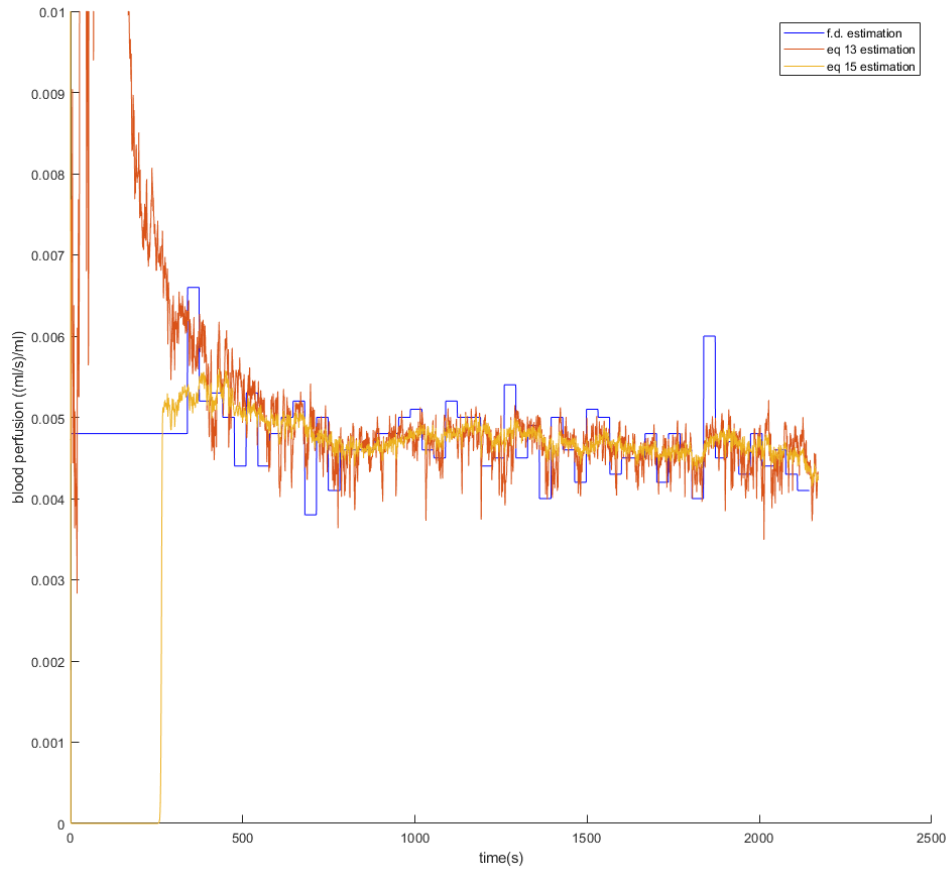


Figure 30. Constant  $w_b$  Estimation result comparison for three methods

Both analytical equation estimation is also not good at the raising phase. The results from two different equations have similar results after the system reaches the steady state (equation 14 has higher temperature results). The finite difference in results matches Equation 13 very well. Therefore, for the constant blood perfusion, Equation 13 is a better analytical solution to use.

### 6.2.2 Restricted blood perfusion data

All the parameters are the same as the constant perfusion case. The heat flux and sensor temperature of the real data are shown below:

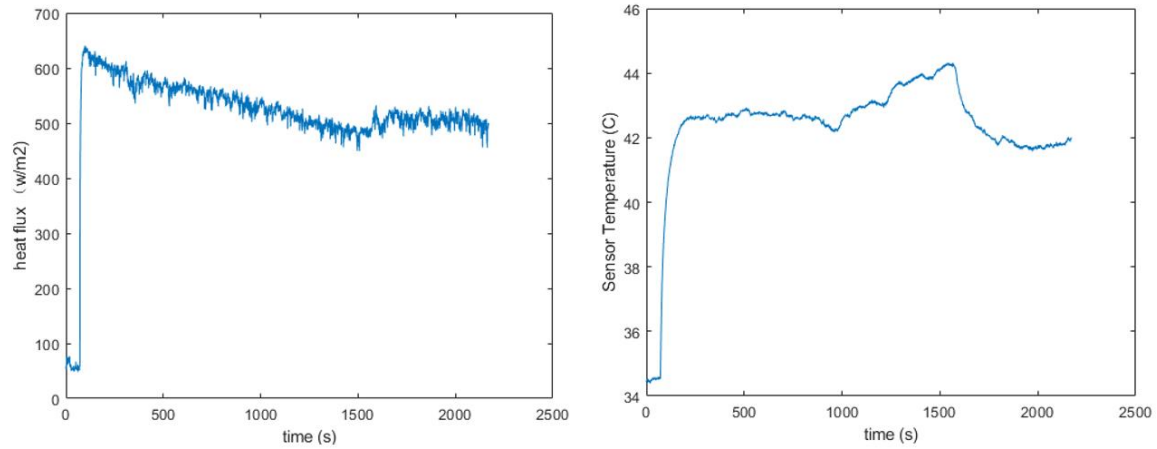


Figure 31. Data with varying blood perfusion values

The blood perfusion is changed by experimental design.

For the finite-difference estimation, the first 340 seconds are estimated as a whole with error function method. The result for that raising phase  $w_b$  is around 0.0075 (ml/s)/ml. After 340 seconds, a period of 34.35 seconds is used to do the estimation in the FDM ( $w_b$  is calculated by using 34.35 seconds of data).

The results from the finite difference method, Equation 14 estimation, and Equation 13 estimation are shown below:

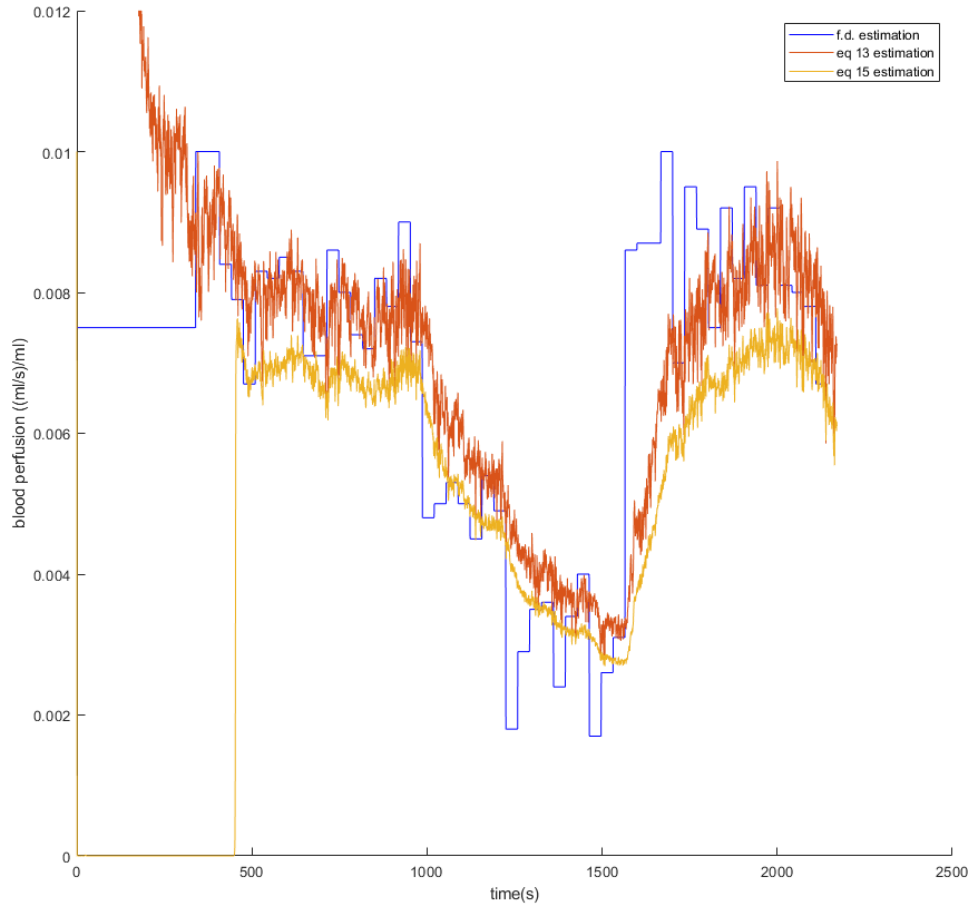


Figure 32. Varying  $w_b$  Estimation result comparison for three methods

Both analytical equation estimation is not good at the raising phase. The results from two different equations have similar results after the system reaches the steady state. Even in the changing blood perfusion period, both equations output similar results.

The finite differences estimation can be used for the raising phase, and after the blood perfusion changes back to the normal level, the estimation can respond faster than the analytical equation (after 1500 seconds). However, the result of the finite difference method is noisy with the smaller estimation period.

### 6.3 Experiment data testing.

To verify if this prediction method works in other real data as well. Another set of data measured will be carried out to verify the new prediction method. This data set was measured on the outside of the lower arm. This data set was shorter overall, and the arm

was restrained at 150 seconds in an attempt to minimize blood perfusion then release at around 200 seconds. The data is shown in Fig.33.

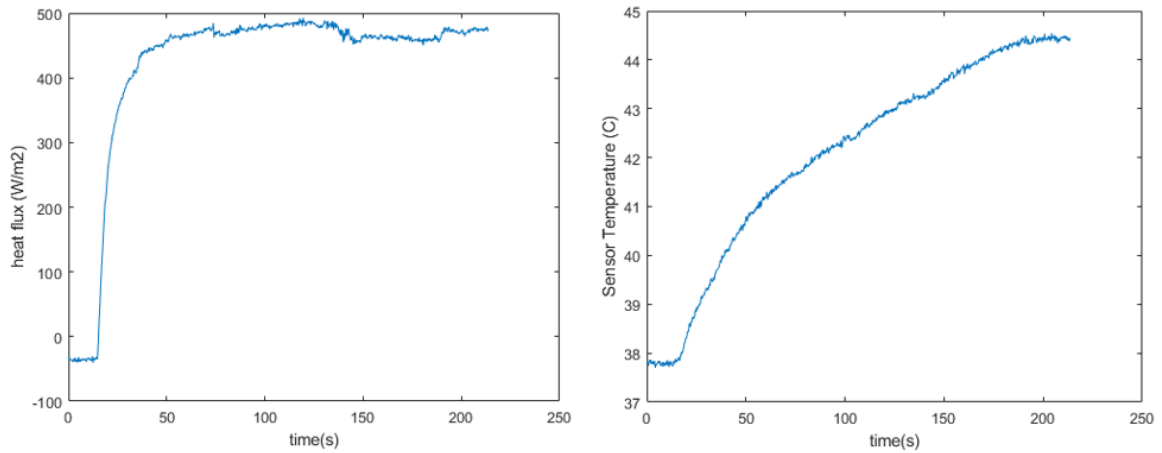


Figure 33. Experiment data.

As shown in Figure 33 above, the temperature never reaches a steady state. So only a transient time of 80 seconds is assumed for the prediction of contact resistance and blood perfusion.

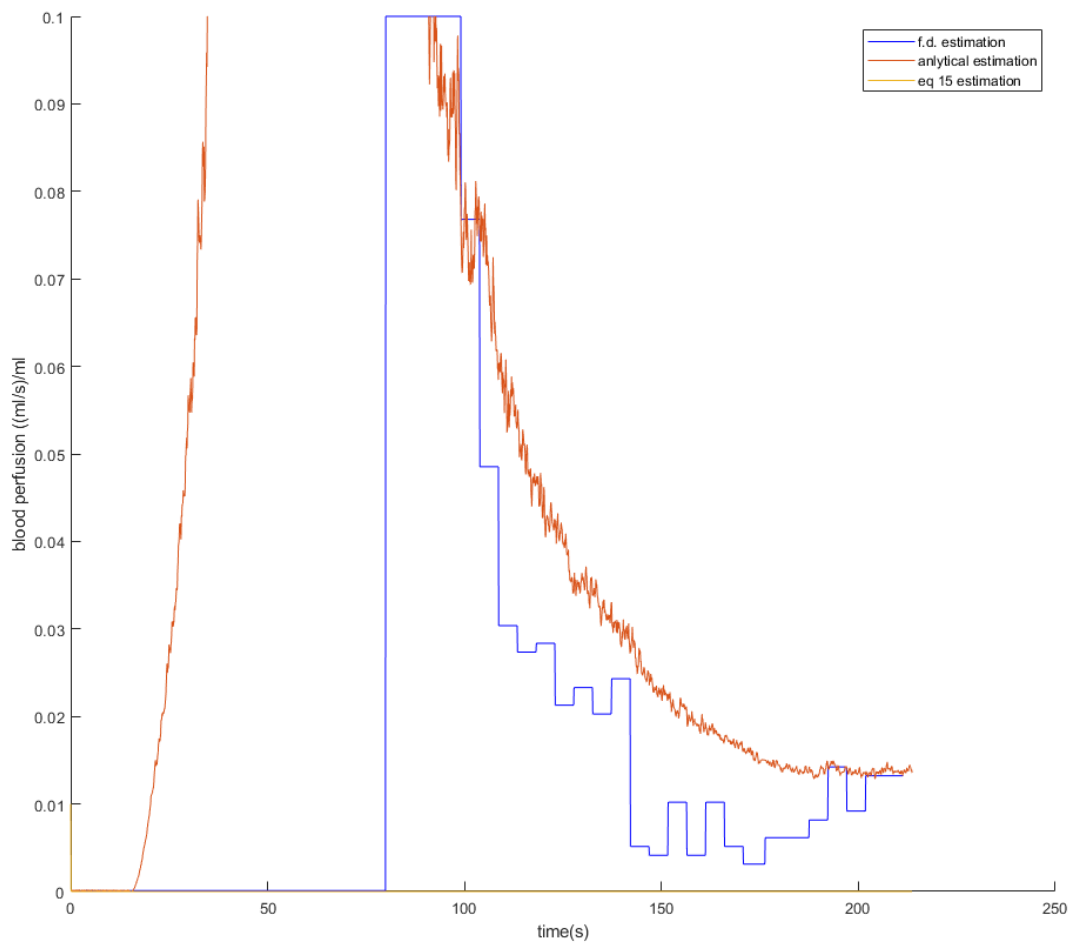


Figure 34. Compare three methods with 80 seconds transients.

From Fig.34 the estimation for the blood perfusion value is abnormal, so increase transient time to 120 seconds and try to find a better value.

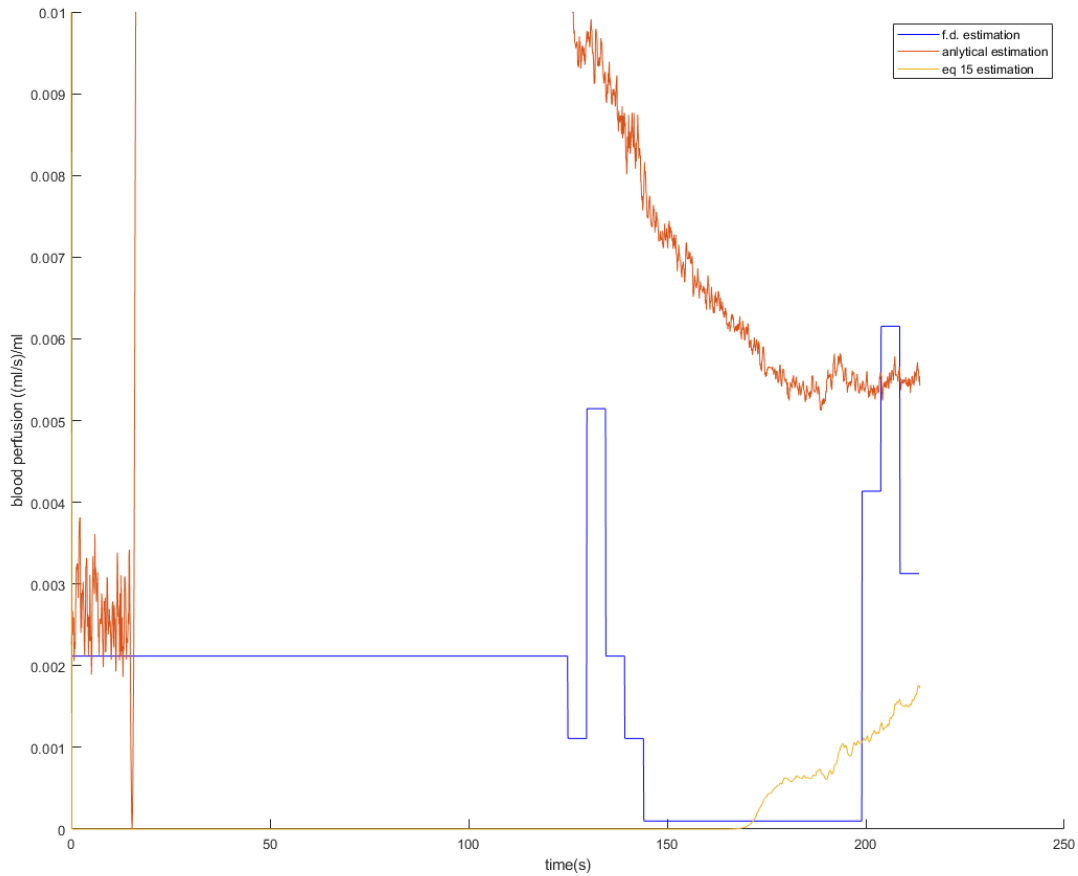


Figure 35. Compare three methods with 120 seconds transients.

Shown in Fig.35, the transient state of blood perfusion value is 0.0021(ml/s)/ml. This value is within the normal range, and the predicted value is lower at 150 seconds and higher at 200 seconds, which is consistent with the restraint behavior in the experiment. However, it can also be seen that the predictions of Equation 14 and Equation 15 cannot be considered valid results at all. Therefore, the timing of the transient is very critical and can greatly affect the overall prediction.

#### 6.4 Time period length for transient estimation

For the transient stage, making separate predictions for each data point will yield very unreasonable values for blood perfusion. Therefore, the best way to deal with the transient stage is to treat it as a whole and use the error function method to make predictions. But how long is the transient stage data needed? This will be analyzed in this Chapter. There are six different tests for this data set. The data was sampled every 1.8 s. Predictions will be made for each test for 1 minute, 2 minutes and 3.5 minutes in length. The predictions

use the best kpc found previously. The RMS from Equation 12 is used to compare the estimation and measured temperature.

Test 1-1 min:

```
The estimated contact resistance (m2·K/W) :  
R_estimate = 0  
The estimated blood perfusion value ((ml/s)/ml) :  
w_estimate = 0.0070  
The core body temperature (°C)  
Tb = 33.1060  
  
RMS = 0.3493 (°C)
```

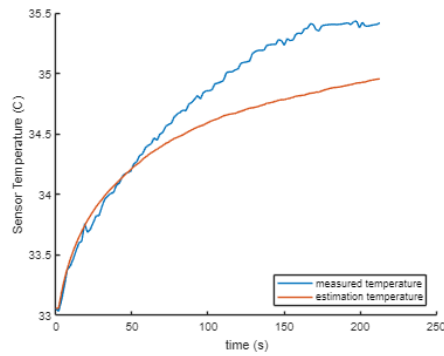


Figure 36. Estimation for 1 min

Test 1-2 mins:

```
The estimated contact resistance (m2·K/W) :  
R_estimate = 0  
The estimated blood perfusion value ((ml/s)/ml) :  
w_estimate = 1.0000e-03  
The core body temperature (°C)  
Tb = 33.1917  
  
RMS = 0.0942 (°C)
```

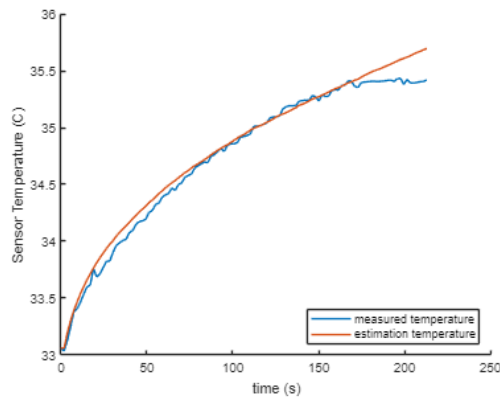


Figure 37. Estimation for 2 mins

Test 1-3.5 mins

The estimated contact resistance ( $m^2 \cdot K/W$ ) :

$R_{estimate} = 1.0101e-04$

The estimated blood perfusion value ( $(ml/s)/ml$ ) :

$w_{estimate} = 0.0020$

The core body temperature ( $^{\circ}C$ )

$T_b = 33.1513$

$RMS = 0.0762$  ( $^{\circ}C$ )

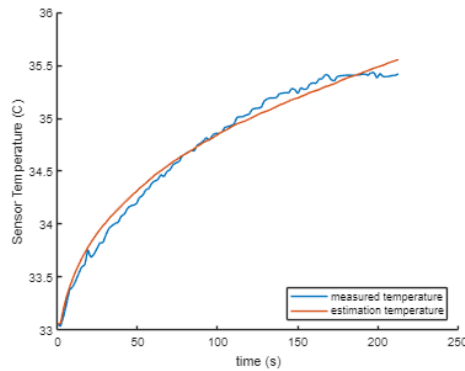


Figure 38. Estimation for 3.5 mins.

Test 1

Table 7- Estimation for different time periods

Time period	R ( $m^2 \cdot K/W$ )	Wb ( $(ml/s)/ml$ )	Tb ( $^{\circ}C$ )	RMS ( $^{\circ}C$ )
1 min	0	0.007	33.1060	0.3493
2 mins	0	0.001	33.1917	0.0942
3.5 mins	0	0.002	33.1513	0.0759

Test 2

Table 8- Estimation for different time periods

Time period	R ( $m^2 \cdot K/W$ )	Wb ( $(ml/s)/ml$ )	Tb ( $^{\circ}C$ )	RMS ( $^{\circ}C$ )
1 min	0.0001	0.001	33.7467	0.2231
2 mins	0.0002	0.003	33.6889	0.1562
3.5 mins	0.0003	0.003	33.6889	0.1565

Test 3

Table 9- Estimation for different time periods

Table 9- Estimation for different time periods

Time period	R ( $m^2 \cdot K/W$ )	Wb ( $(ml/s)/ml$ )	Tb ( $^{\circ}C$ )	RMS ( $^{\circ}C$ )
-------------	-----------------------	--------------------	--------------------	---------------------

1 min	0.0002	0.001	34.6045	0.1132
2 mins	0.0004	0.001	34.6045	0.1313
3.5 mins	0.0004	0.002	34.5645	0.0902

#### Test 4

Table 10- Estimation for different time periods

Time period	R (m <sup>2</sup> ·K/W)	Wb ((ml/s)/ml)	Tb (°C)	RMS (°C)
1 min	0.0018	0.001	34.8339	0.6481
2 mins	0.0024	0.022	34.7270	0.1742
3.5 mins	0.0019	0.017	34.7310	0.1606

#### Test 5

Table 11- Estimation for different time periods

Time period	R (m <sup>2</sup> ·K/W)	Wb ((ml/s)/ml)	Tb (°C)	RMS (°C)
1 min	0	0.001	34.5688	0.2572
2 mins	0.0012	0.001	34.5688	0.1754
3.5 mins	0.0015	0.002	34.5290	0.1780

#### Test 6

Table 12- Estimation for different time periods

Time period	R (m <sup>2</sup> ·K/W)	Wb ((ml/s)/ml)	Tb (°C)	RMS (°C)
1 min	0	0.001	34.4655	0.2486
2 mins	0.0001	0.003	34.4082	0.1100
3.5 mins	0.0003	0.005	34.3906	0.0574

By comparing the above data, it can be concluded that the longer the period, the more accurate predictions are usually obtained (smaller RMS). But in some data, such as test2, there is not a big difference between 2 minutes and 3.5 minutes. In most cases, the predictions for 2 minutes and 3.5 minutes can be considered close to each other.

### 6.5 Sensitivity of transient stage estimation for estimation result

From the above 6.3 and 6.4 sections, the transient stage estimation result will significantly affect the later estimation accuracy. In this section, some simple values will test the estimation sensitivity to transient stage results. The data from Figure 31 will be used. The original estimate of R and wb for the transient stage is shown in Table 13.

Table 13 - Original transient stage estimation

R (m <sup>2</sup> ·K/W)	Wb ((ml/s)/ml)	Tb (°C)
0.0055	0.0072	33.82

If the wb value is changed to 0.001 ((ml/s)/ml), the Tb changes to 32.81 °C, which is a temperature change of 1.02 °C. The corresponding estimated blood perfusion values are shown in Figure 39. The results using equation 13 again match closely with the FDM results for most of the time following the transient region. Equation 15 is higher, but still follows the trend. The FDM is unstable initially because the steady blood perfusion has changed from 0.0072 (ml/s)/ml to 0.0055 (ml/s)/ml.

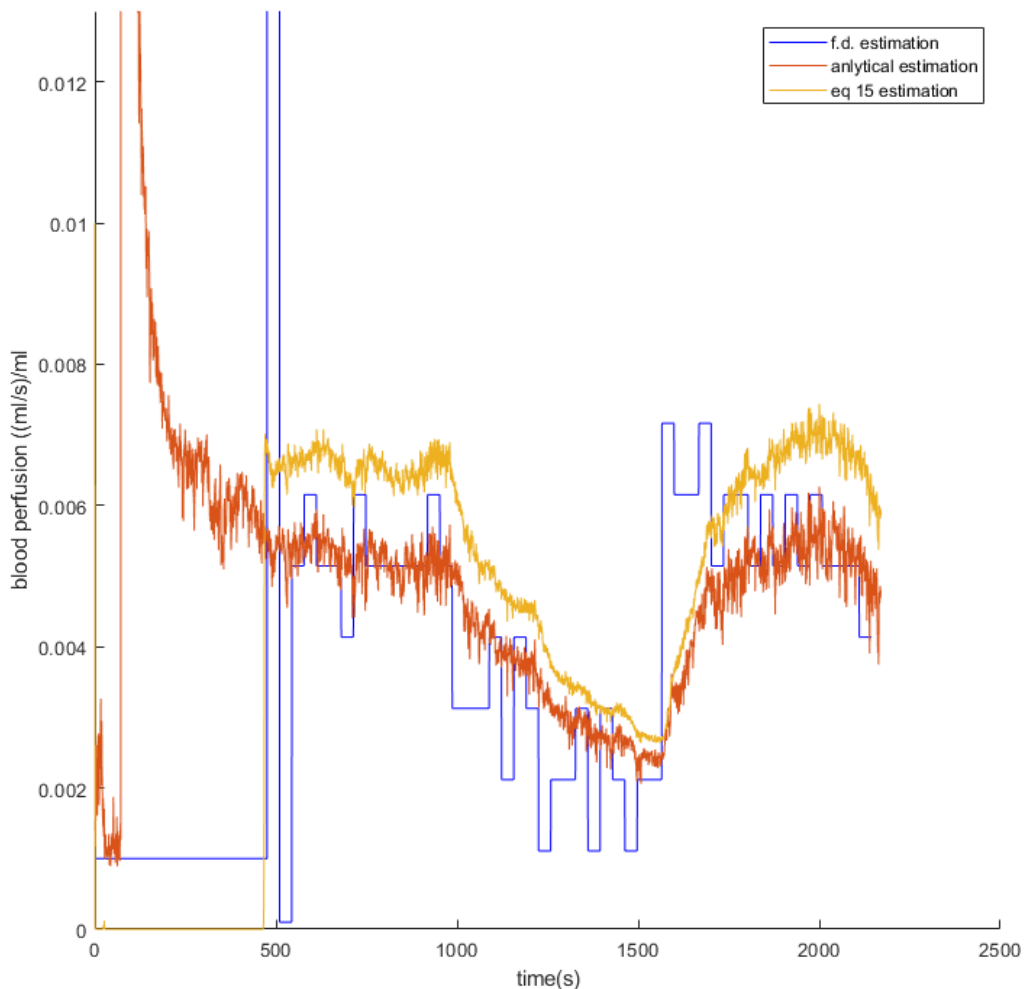


Figure 39. Estimation with change of transient stage estimation

Conversely, if the wb value is increased to 0.02 (ml/s)/ml, the Tb value increases to 34.07 °C, an increase of only 0.25 °C. The corresponding estimated blood perfusion results are shown in Figure 40. The results with equation 13 are close to the FDM results, with the

equation 15 results now lower. The steady value of blood perfusion has a small change from 0.0072 (ml/s)/ml to 0.008 (ml/s)/ml.

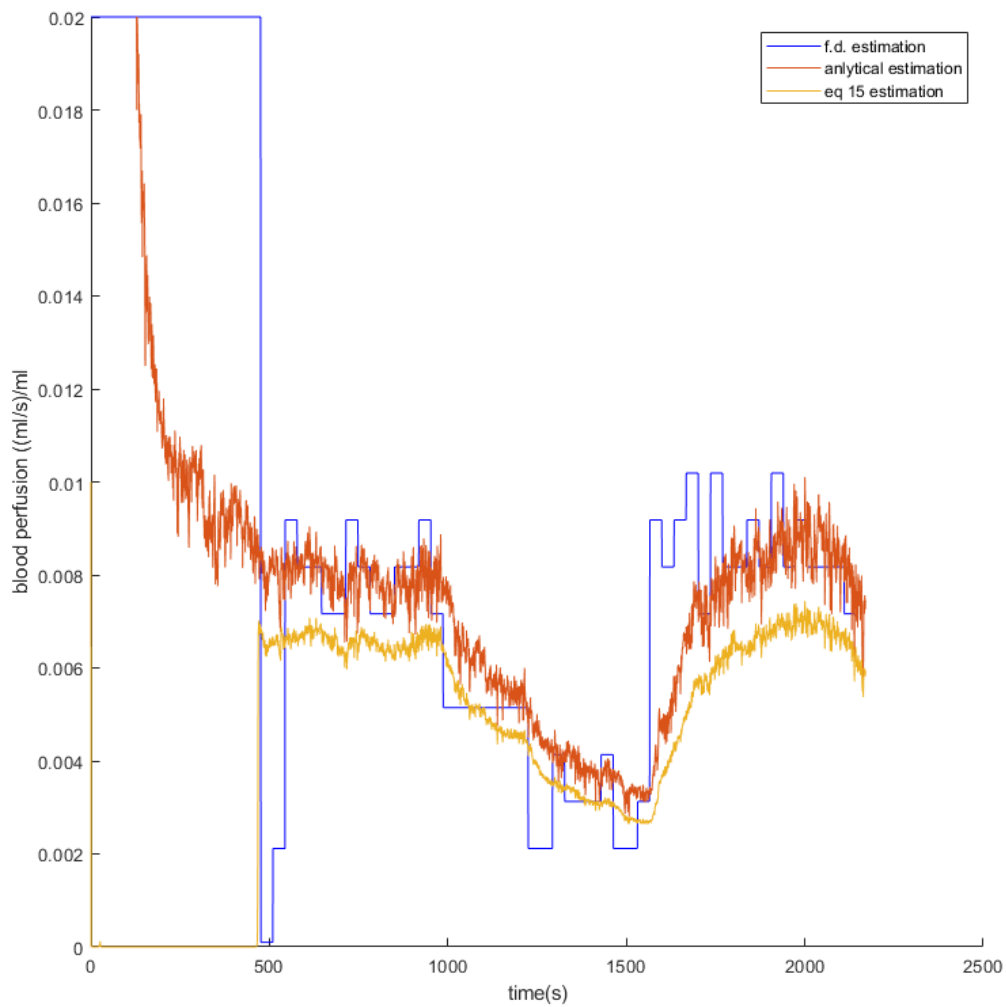


Figure 40. Estimation with change of transient stage estimation 2

The estimation of transient stage results will affect the later estimation of blood perfusion value. However, if the difference of transient stage blood perfusion value estimates is not too much different from the actual value, the effects are small.

## Chapter 7 Discussion of Results

From Chapter 5, FDM (finite difference method) is used to create the simulated temperature data with varying  $w_b$ . Comparing three other analytical solutions (two in steady state and one for all situations) that they claim are capable of calculating blood perfusion in real-time. However, the three analytical solutions do not respond quickly to rapidly changing perfusion values. The results showed that each of the three different analytical solutions for changing blood perfusion did not work well. However, the finite differences method was used to predict the varying  $w_b$  which requires much more calculation for the initial (constant blood perfusion stage with only heat flux change) . Therefore, a combination estimation method was developed for predicting blood perfusion value in changing situations. The error function method is easy and fast for estimating parameters but does not work in changing blood perfusion situations. FDM is working at changing blood perfusion situations but requires much more complicated calculations. So, the error function is used for estimating the initial condition parameters, then for the rest of the time the FDM is used for estimating the changing blood perfusion value. For simulated data, the combination estimation method results are not stable in the point close to step change in blood perfusion value, but overall, the prediction results are better than all the other three analytical methods.

In Chapter 6, the same combination estimation method is used for comparing the other two analytical solutions in real data. For real data in section 6.2, the estimation result of the combination method is better at the step change blood perfusion value point. And for the transient heat flux stage can be correctly interpreted by the newly developed estimation method. In section 6.2.2, the data have the longest transient of heat flux state data with 1000 seconds before changing the blood perfusion. However, in section 6.3, only 200 seconds in total for the whole measurement data. In section 6.3, two different assumptions of transient heat flux stage time are used for the comparison. 80 seconds and 120 seconds of transient heat flux stage shows that more transient stage data is needed to correctly estimate the initial parameter. Both sections 6.2 and 6.3 have similar heat flux values, but the time for the transient heat flux state is 10 times different. However, in predictions on real data, the accuracy strongly depends on the length of the available transient data. Only when the estimation of core temperature and contact resistance close (both are important initial parameters) to the actual value obtained from the transient data, subsequent predictions for changing blood perfusion value will be more accurate. In section 6.4, the

results provide more evidence that transient heat flux stage prediction requires longer data to have a better estimation of the blood perfusion. For some case 2 mins is good but more is better like section 6.2 data which have almost 15 mins of the transient data before making any change of blood perfusion value. The above conclusion explains why Section 6.2 can have good prediction results while Chapter 6.3 has poor results. Section 6.3 poor result is caused by the short transient of heat flux data so the estimation for core body temperature and contact resistance is too much deviation from the actual value.

## Chapter 8 Conclusion

This study of methods for estimating blood perfusion reveals important insights relevant to physiological modeling, especially in situations involving dynamic changes in human blood flow. The results show that while conventional analytic functions are effective under steady-state or slowly varying conditions, they are unable to accurately capture rapid changes of blood perfusion. When  $w$  is not constant, the superposition of Greens function solutions cannot be used. This limitation of the analytical solutions highlights a significant shortcoming of current modeling approaches, especially in real-time or dynamic physiological monitoring. To address this shortcoming, this paper explored three different analytical estimation methods. However, these methods share a common shortcoming: a lack of responsiveness to sudden changes in blood perfusion values. This shortcoming highlights the need for a more adaptive and dynamic approach to physiologic monitoring. To address this need, an estimation method based on the finite difference method (FDM) was developed. The results of the study show that the FDM is more effective in tracking rapid changes in blood perfusion variability, which is a significant improvement over the previous model. However, the FDM estimation method is not without its challenges. A major issue is its time-consuming nature, which creates limitations in scenarios where rapid decision-making is required. This shortcoming foreshadows an important area for future research and development. Improving computational efficiency and optimizing the algorithms of the FDM method could greatly improve its practical applicability. Potential avenues for improvement include improved algorithms and integration of advanced data processing techniques, which would significantly reduce the time required to compute parameters.

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## Appendix

MATLAB code of combine estimation method.

```
%This is code file to calculate the blood perfusion value
%Baoyi Sheng
```

```
clc
clear
close all
```

```
%input data section (change this section to calculate different data)
data=readmatrix('Two heaters on.xls');
time=data(:,1);
q=data(:,2);
Tmeas=data(:,3);

figure
plot(time,q)
xlabel('time(s)')
ylabel('heat flux (W/m2)')
figure
plot(time,Tmeas)
xlabel('time(s)')
ylabel('Sensor Temperature (C)')
start=700; %position to start varying wb estimation (where to use finited different method estimation)
```

```
%properties section (tissie properties)
k=0.4;
P=950;
c=3300;

a=k/(P*c);
Kpc=k*P*c;

%initial data calculation
q_0=q(1);
T_0=Tmeas(1);
```

```
%error function estimation for rising phase
R_range=linspace(0,0.01,50); %change this for conctect resistantce range
w_range=linspace(0.0001,0.1,100); %change this for blood perfusion range
for ii=1:length(R_range)
    R=R_range(ii);
    for jj=1:length(w_range)
        w=w_range(jj);

        T_first=T_0-q_0*R;
        S=0;
        for i=2:start
            t=time(i);
            T_tc=0;
            for p=2:i
                T_c=(q(p)-q(p-1))*sqrt(1/(Kpc*w))*erf(sqrt(w*(t-time(p-1))));
                T_tc=T_tc+T_c;
            end
            T_pred=T_first+T_tc;
            T_skin=Tmeas(i)-q(i)*R;
            Si=sqrt((T_skin-T_pred)^2);
            S=S+Si;
        end
        S_est(ii,jj)=S;
    end
end

[min_val,idx]=min(S_est(:));
[row,col]=ind2sub(size(S_est),idx);
disp('The conctect resistance and blood perfison estimation value for raising phase:')
R_estimate=R_range(row)
w_estimate=w_range(col)
disp('The core body temperature:')
Tb=T_0-q_0/sqrt(w_estimate*Kpc)
```

```
wb(1:start)=w_estimate;
R=R_estimate;
```

```
%parameter for finite differece method
dx=0.0005;
dt=time(4)-time(3);
Fo=a*dt/(dx^2);
n_node=150;
```

```
%initial node temperature calculation for f.d. method
q_i=q_0;
w=wb(1);
inf=5000;
T(n_node+1,length(time))=zeros;
Ti(n_node,inf)=zeros;
for i=1:n_node
    Ti(i,1)=Tb;
end
Ti(n_node+1,:)=Tb;

for i=2:inf
    for j=2:n_node
        Ti(j,i)=(1-2*Fo-w*dt)*Ti(j,i-1)+Fo*(Ti(j+1,i-1)+Ti(j-1,i-1))+w*dt*Tb;
    end
    Ti(1,i)=Ti(2,i)+(q_i*dx)/k;
end

T(:,1)=Ti(:,end);
T(end,:)=T(end,1);
Ts(1)=q_i*R+(T(1,1)+T(2,1))/2;
```

```
%step size for the varying wb estimation
n=50; %change this to change the step size of one estimation loop
step_size=n*dt %(s)
step=floor((length(time)-start)/n);
```

```
%finite differece method estimation for each step size after raising phase
for m=1:step
    for p=1:length(w_range)
        wb(start+(m-1)*n:start+m*n)=w_range(p);
        S_s=0;
        for i=2:length(wb)
            for j=2:n_node
                T(j,i)=(1-2*Fo-wb(i)*dt)*T(j,i-1)+Fo*(T(j+1,i-1)+T(j-1,i-1))+wb(i)*dt*Tb;
            end
            T(1,i)=T(2,i)+(q(i)*dx)/k;
            Ts(i)=q(i)*R+(T(1,i)+T(2,i))/2;
            Si_s=(Tmeas(i)-Ts(i))^2;
            S_s=S_s+Si_s;
        end
        S_wb(p)=S_s;
    end
    [~,index]=min(S_wb);
    wb(start+(m-1)*n:start+m*n)=w_range(index);
end
```

```
%result plot section
figure
plot(time(1:length(wb)),wb,'b')
xlabel('time(s)')
ylabel('blood perfusion')
```

```

Tskin=Tmeas-q*R;

%equation 13
for i=1:length(time)
w_1(i)=(q(i)/(Tskin(i)-Tb))^2*1/Kpc;
end

%equation 15
w_2(1)=0.01;
for i=2:length(time)
    bottom=0;
    for j=2:i
        bottom=bottom+(q(j)-q(j-1))*erf(sqrt(w_2(i-1)*(time(i)-time(j-1))));
    end
    w_2(i)=(Kpc*(((Tmeas(i)-q(i)*R)-(Tmeas(1)-q(1)*R))/bottom)^2)^-1;
end

figure
hold on
plot(time(1:length(wb)),wb,'b')
plot(time,w_1)
plot(time,w_2)
xlabel('time(s)')
ylabel('blood perfusion ((ml/s)/ml)')
ylim([0,0.013])
legend('f.d. estimation','analytical estimation','eq 15 estimation')

```