University of Auckland

Department of Engineering Science

Part IV Project

Optimal Experimental Design for Understanding Burn Injuries

MID-YEAR TECHNICAL REPORT

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1 Background

Skin - the largest organ in the body - has multiple layers with varying thermal properties. The structure of skin can be classified into three main sections, starting from the surface: the epidermis, dermis and hypodermis (fat). The thickness of each layer averages at $0.1mm$, $\leq 1mm$ and 0.1 to several cm for the epidermis, dermis and hypodermis layers, respectively [1]. For simplicity, in the past, many attempts to study the properties of skin have adopted a one layer approach to capture the complex structure [2, 3, 4]. However, recent studies more often than not, have incorporated multiple layers to more accurately classify the behaviour of skin [5, 6].

One parameter of interest, which varies across skin layers, is the thermal diffusivity. Still, the optimal experimental design for measuring such a property is yet to be established. Whether the added complexity of a multi-dimensional and multi-layered model produces significant results is uncertain. Additional experimental design variations include the location of temperature measurement and the number of probes used in measuring the model temperature. In general these experiments typically mimic a burn to skin.

1.1 Burn Injuries

Burn injuries are ranked in four different degrees. A first-degree burn is considered the least severe, only affecting the skins epidermis, while a fourth-degree reaches past the skin, fat layer, muscle and bone [7]. Burns caused by heat are of the most common [8], thus are of the highest interest to investigate.
To enhance understanding of these conditions, experiments have been conducted using various methods, such as the use of heated water, infrared lasers, porcine (pig) skin or phantom models [5, 6].

1.2 Inverse Problems

A forward problem, with $F(x) = y$, finds y given x. An inverse problem on the other hand, estimates x given y. In essence, inverse problems start with effects then determine the causes. Inverse problems are commonly more complex. For instance, forward problems and solutions typically have an one-to-one relationship, i.e. one problem brings one solution. However, inverse problems usually have an one-to-many relationship, meaning often there are various parameters that can fit the problem. Hence, further analysis on the values would be required to decide which solution is optimal. Additionally, there may not be a solution that exists at all, and at times, if there is a solution, it could be unstable [9].

The objective of an inverse problem is to best determine parameters of a governing model where direct observation is not possible. An example of a famous inverse problem is the measurement of the Newtonian gravitational constant, G. Although, G is one of the most fundamental values in physics and over 200 experiments have been conducted to observe the constant [10, 11], there is still uncertainty around the exact value [12]. This lack of precision highlights the complexity of inverse problems and their dependency on experimental methods. Consequently, experimental designs that have considered parameter inference are best suited for inverse problems and are critical for success.

1.3 Computational Experimental Design

Experiments with the goal of parameter inference should be designed differently to ensure the best observations are made. Articles have shown the role experimental design has played a large part in parameter estimation by concluding differing results [13].

The experiment set-up and what it collects has an indirect relationship with the quality of parameter estimations. Figure 1 shows this relationship.

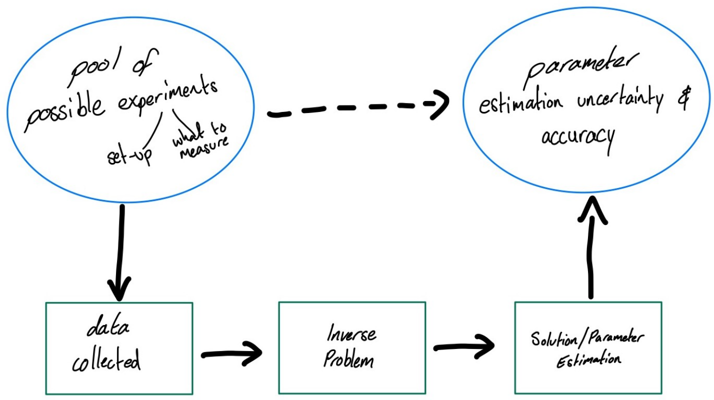


Figure 1: Relationship of Experiments to Parameter Estimates

A particular design will yield a specific parameter estimation. This value may or may not be equal to other parameter estimations from differing experiments but will likely have a different magnitude of uncertainty associated with it.
When working with an inverse problem, collecting specific parts of data may be of more use than other parts. For instance, a 2015 geothermal reservoir model study indicated that collecting data including injection pressure and matrix temperature yield lower uncertainties than others when predicting parameters [14]. Therefore, it is more worthwhile collecting one type of data than another when particularly inferring parameters.

2 Introduction

This project aims to investigate and understand the reality of burn injuries by performing real-time heat transfer experiments to recover the significant thermal parameters of skin. Experiments to understand burn injuries are currently associated with problems and complications such as using porcine skin, using a single measuring probe and ignoring possibly important factors (e.g. blood perfusion). The limitations of recent studies raise protocol ambiguity. This project aims to investigate the optimal experimental design by clarifying the following matters: the effect of including the blood perfusion term; the optimal number of measuring probes; the location of these probes; the response of additional layers, and; the impact of additional spatial dimensions.

The importance of each factor will be quantified by examining each protocol's ability to recover the model's thermal diffusivity. Thermal diffusivity can be retrieved where the temperature distribution is known. The temperature of several models will be measured in a parallel project conducted by Anthony Zemke (see [15]). This parallel project will calculate thermal diffusivity

by measuring the parameter's individual components (from equation 2). The calculated thermal diffusivity will then be used as a comparison for all *computed* thermal diffusivity estimates for each experiment conducted.
The precision of the computed parameter (if any) is also considered. If for instance, the additional accuracy provided by including multiple spatial dimensions cannot be justified by the additional computational complexity, it may be concluded a single dimension will suffice.

3 Modelling and Solving the Problem

Heat traveling through skin can be mathematically modelled and solved in a number of different ways. Two solvers are examined and implemented in this section. Both use the general heat equation - originally developed by Joseph Fourier [16]. The parabolic heat equation in one dimension is given by:

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2} \tag{1}$$

where D is the thermal diffusivity of the medium [17]. Thermal diffusivity is a constant calculated from density, ρ, thermal conductivity, λ and the specific heat capacity, c where:

$$D = \frac{\lambda}{c\rho} \tag{2}$$

To solve this partial differential equation (PDE), boundary and initial conditions must be specified. The conditions used throughout this model are:
boundary conditions:

$$u\left(0,t\right) = T \qquad\qquad \frac{\partial u}{\partial x}\left(L,t\right) = 0 \tag{3}$$

initial condition:

$$u\left(x,0\right) = 0 \tag{4}$$

where T is the temperature being applied to the model and L is the length of the model. T and L are set to 30°C and $1m$ respectively in the following simulations as arbitrary values.

The numerical methods used to solve the equation include the finite difference (FD) method and the Finite Element Method (FEM). Each have their relative advantages, however, finite differences was initially implemented due to its simplicity while FEM was later adopted as it is more robust.

3.1 Finite Differences

Finite difference solvers are either explicit or implicit in nature. A review of the methods is discussed below.
Ultimately, an explicit finite differences method was coded to solve the heat equation. For validation, the results were then compared against an equivalent working explicit finite differences method.

3.1.1 Comparison of Explicit and Implicit Methods

Both methods have their respective trade offs. Explicit methods are easier to implement and come at a lower computational cost. Although, explicit methods have conditionally stability.

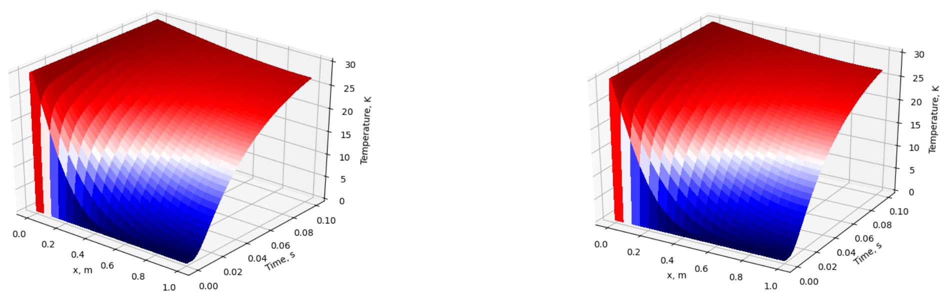
The numerical solution is guaranteed to converge only if equation 5 below is satisfied.

$$0 < \frac{K\Delta t}{(\Delta x)^2} \leq \frac{1}{2} \tag{5}$$

Given a high thermal diffusivity, a small time step must be used to satisfy equation 5. The additional computational cost from smaller time steps could bring explicit methods to be as expensive as implicit methods. For this reason, implicit methods may be of more use.
Implicit methods also have drawbacks. In general, implicit methods come at a greater computational cost compared to an explicit method. However, the solution has unconditional stability meaning a larger time step could be used. Nonetheless, the solution's numerical accuracy depends on r. Hence, it isn't clear which method would be optimal in every situation. Each method should be examined and used based on the respective problem.

3.1.2 Validation of Finite Differences Method

To ensure the created solver works correctly, the solution was compared against a validated finite difference solver. Using identical boundary and initial conditions, the solution was obtained from both the implemented FD solver and the known working FD solver. The results are shown below in figure 2.

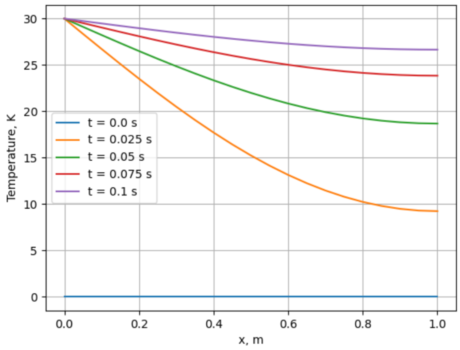


(a) Implemented Solver

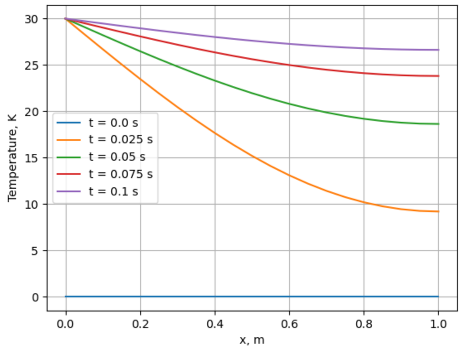
(b) Known Working Solver

Figure 2: Comparison of Solutions

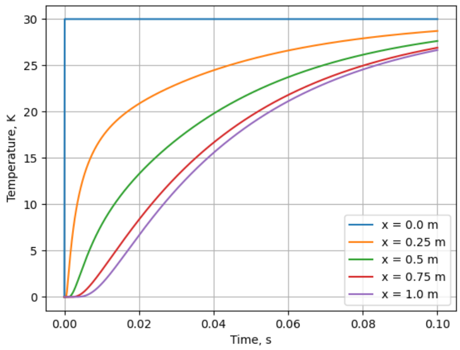
Although three-dimensional graphs are difficult to compare - it is clear both (a) and (b) are similar in nature. To grasp a better comparison, two-dimensional graphs are shown below in figure 3.



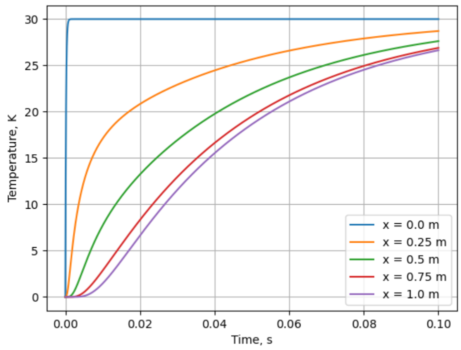
(a) Implemented Solver Δx



(b) Known Working Solver Δx



(c) Implemented Solver Δt



(d) Known Working Solver Δt

Figure 3: Two-dimensional Comparisons

To quantify the validation the main validation tools used were the mean absolute errors (mae) and the root mean squared errors (rmse) between solutions. These values are shown in table 1 given to 4 d.p.

	Error
mae	0.0031
rmse	0.0558

Table 1: Error Comparison Values

Both error values show adequate values. The mae shows overall, the difference between the validated and implemented solver is small. The rmse shows there are likely no areas with large magnitudes of differences. Therefore, it is likely the implemented solver is behaving as expected.

3.2 Finite Element Method

The FEM was ultimately deemed the more suitable approach for solving this PDE. FEM provides flexibility given its ability to handle functions of diffusivity rather than a constant. Passing a function for the diffusivity coefficient simulates multiple skin layers - better reflecting reality.

Presently, FEM is being explored and is in the implementation stage. The method will be applied in one spatial dimension, however the effect of additional dimensions will be examined with inbuilt solvers. If a large difference in accuracy is observed, the method will be revised. A FiPy library will be used to validate and evaluate the FEM implementation.

4 Parameter Recovery

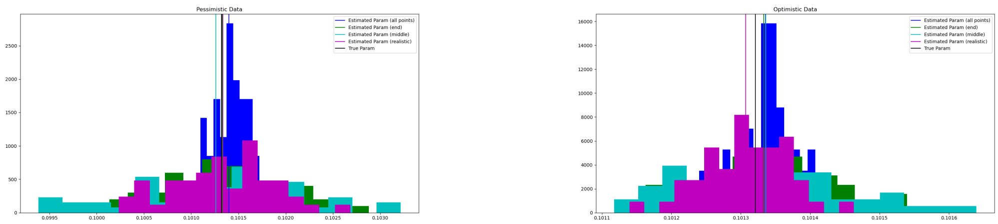
Given New Zealand and the world's struggles, experiments are yet to be conducted. Therefore, data was fabricated by solving the problem, adding noise to the solution and passing points of interest. The noise was randomly distributed with a mean of 0 and a standard deviation of 0.3 as the optimistic scenario. A pessimistic scenario was also modelled with a standard deviation of 2.3. This gave the noise an approximately 70% chance of being within |0.3| and |2.3| for the optimistic and pessimistic cases, respectively. These noise values are roughly what is expected from the experiments given a systematic variation (from equipment) of 0.2 and a general temperature variation of $1 - 2°C$.
Four experiments were simulated:

1. A single probe measuring temperature in the middle of the model, i.e. $x = 0.5$
2. A single probe measuring temperature at the end of the model, i.e. $x = 1.0$
3. Three probes measuring temperatures at three evenly spaced locations within the model, i.e. $x \in${0.15, 0.5, 0.85}
4. 22 probes measuring temperatures every $0.05m$ in the model (used as a control)

The parameter from each simulation is recovered using SciPy's "Least Squares" function. The function aims to minimise the sum of squares value from the originally inputted temperature array (collected/experimental data) and the calculated temperature values using a guess for the thermal diffusivity (the parameter attempting to be recovered).

5 Optimal Experimental Design

Both the location and the number of points to take temperature measurements are of interest when comparing parameter recovery estimates.
From the test data, it is clear measuring closer to the end of the model (@x=1, where x=0 is the heat source location) produced more accurate results than if the data was collected closer to/at the heat source. It is unclear whether this can be further applied to a data set collected from an actual experiment.
In terms of the number of points to measure from, it was evident an increase of measuring probes produced more accurate results. Figure 4 illustrates these results.



(a) Pessimistic Simulations

(b) Optimistic Simulations

Figure 4: Parameter Recovery of Experiments

However, given the simulations produced similar results, the graph cannot clearly capture performance. Hence, tables 2 and 3 better reflect contrast between simulations.

	μ	σ^2 (x10^{-7})
Middle	0.101260	8.158
End	0.101327	3.823
Realistic	0.101337	2.827
All	0.101398	0.364
Actual	0.101321	-

Table 2: Pessimistic Simulations

	μ	σ^2 (x10^{-8})
Middle	0.101336	1.519
End	0.101333	0.897
Realistic	0.101307	0.376
All	0.101335	0.147
Actual	0.101321	-

Table 3: Optimistic Simulations

The data sets were also passed to an analysis of variance (ANOVA) to investigate whether there are any statistical differences between the means of the four groups. The results of the analysis is shown in table 4.

	F-value	p-value
Pessimistic	0.417	0.741
Optimistic	1.331	0.266

Table 4: One-Way ANOVA Results

Given the $p - value$ is larger than 0.05 in both cases (pessimistic and optimistic), it cannot be deduced there are any significant statistical differences between the group means. Although, these simulation results have shown experiment protocol is not as significant with an abundant and continuous stream of temperature measurements across time, it is important to note the simulation cannot accurately replicate a real experimental situation. Therefore, the program is of more use as validation check - it does produce values that are appropriate and therefore, can be used with real collected data.

6 Future Endeavours

The implementation and validation of the FEM solver would be the next immediate step for the project. FEM will also allow flexible exploration of including a blood perfusion term and multiple layers in the mathematical model. Simulating these additional factors could give a beneficial starting point for their respective experiments in the future.

An in-depth statistical analysis - such as Bayesian inference, uncertainty analysis and sensitivity analysis - should be set-up for the collected data to better understand the differences of results and also their significance. This will aid in determining the optimal experimental design. The analysis will also provide invaluable evidence for any conclusions drawn on preferable protocols.

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