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Parameterising continuum models of heat transfer in heterogeneous living skin using experimental data

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ABSTRACT

In this work we consider a recent experimental data set describing heat conduction in living porcine tissues. Understanding this novel data set is important because porcine skin is similar to human skin. Improving our understanding of heat conduction in living skin is relevant to understanding burn injuries, which are common, painful and can require prolonged and expensive treatment. A key feature of skin is that it is layered, with different thermal properties in different layers. Since the experimental data set involves heat conduction in thin living tissues of anesthetised animals, an important experimental constraint is that the temperature within the living tissue is measured at one spatial location within the layered structure. Our aim is to determine whether this data is sufficient to reliably infer the heat conduction parameters in layered skin, and we use a simplified two-layer mathematical model of heat conduction to mimic the generation of experimental data. Using synthetic data generated at one location in the two-layer mathematical model, we explore whether it is possible to infer values of the thermal diffusivity in both layers. After this initial exploration, we then examine how our ability to infer the thermal diffusivities changes when we vary the location at which the experimental data is recorded, as well as considering the situation where we are able to monitor the temperature at two locations within the layered structure. Overall, we find that our ability to parameterise a model of heterogeneous heat conduction with limited experimental data is very sensitive to the location where data is collected. Our modelling results provide guidance about optimal experimental design that could be used to guide future experimental studies.

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Nomenclature

A brief description of all variables used in the document are given in Table 1.

1. Introduction

Injuries caused by accidental exposure to hot liquids are common, painful and often require extensive long-term treatment [1]. To improve our understanding of how thermal energy propagates through human skin, experimental studies often work with porcine (pig) skin because porcine skin is anatomically similar to human skin [2–8]. Many experimental studies deal with heat conduction in excised non-living tissues [6,7,9,10]. In contrast, the experimental protocols developed by Cuttle and colleagues [11–14] are unique because they quantify heat conduction in living porcine tissues. Working with living tissues is far more biologically relevant than working with excised non-living tissues. Cuttle's experimental protocol involves working with anesthetised living pigs that are given analgesia. A thermocouple probe, referred to as the *subdermal probe*, is inserted obliquely under the skin of the animal at various locations on the body [11–14]. To initiate an experiment, a cylindrical scald creation device is placed onto the surface of the skin so that the centre of the circular scald device is above the subdermal probe. Pre-heated water is pumped into the scald device and suctioned out of the device at an equal rate to ensure that a constant level of water at a particular temperature is maintained in the device at all times during the experiment. The temperature response in the living skin is measured by the subdermal probe as a function of time during the experiment. This time series data reveals information about how the thermal energy propagates through the living skin, and this experimental protocol can be used to study how thermal energy propagates through skin in different locations on the body. Further, by using pigs of different ages the same experimental protocol can be used to study how the propagation of thermal energy depends on skin thickness [2].

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Table 1
Variable nomenclature and description.

Variable	Description
t	time
t_j	jth sample in the time series
t_c	critical time
δt	time between samples
x	depth below the surface of skin
l_1	depth of the interface between the skin and fat layers
l_2	depth of the bottom of the fat tissue
p	depth of first probe
q	depth of second probe
T	non-dimensional temperature
T_1	non-dimensional temperature in skin layer
T_2	non-dimensional temperature in fat layer
$\widehat{T}$	non-dimensional synthetic temperature data, obtained using $\left(\widehat{D}_1, \widehat{D}_2\right)$
$\mathcal{T}_1$	dimensional temperature in skin layer
$\mathcal{T}_2$	dimensional temperature in fat layer
$\mathcal{T}_0$	dimensional initial temperature in the experiments
$\mathcal{T}_h$	dimensional temperature in the scald creation device
$\widehat{\mathcal{T}}$	dimensional experimental temperature data
D_1	thermal diffusivity of skin
D_2	thermal diffusivity of fat
D_{eff}	homogenised averaged thermal diffusivity
$\widehat{D}_1$	target thermal diffusivity of skin
$\widehat{D}_2$	target thermal diffusivity of fat
$D_1^{(\min)}$	minimum value of D_1
$D_1^{(\max)}$	maximum value of D_1
$D_2^{(\min)}$	minimum value of D_2
$D_2^{(\max)}$	maximum value of D_2
d	non-dimensional temperature discrepancy between model and data
ε	discrepancy threshold
$\mathcal{I}_1$	indicator function for one probe
$\mathcal{I}_2$	indicator function for two probes
A	area of the bounded (D_1, D_2) parameter space
$\mathcal{A}_1$	proportion of the bounded (D_1, D_2) parameter space where $\mathcal{I}_1 = 1$
$\mathcal{A}_2$	proportion of the bounded (D_1, D_2) parameter space where $\mathcal{I}_2 = 1$

A visual summary of Cuttle's experimental porcine model is given in Fig. 1. The image in Fig. 1(a) shows a portion of excised skin at the conclusion of an experiment highlighting the location and size of the subdermal probe. The histology image in Fig. 1(b) highlights the layered structure of the skin. The epidermis and dermis forms the upper layer of the skin where hair follicles are present [15,16]. The epidermis and dermis are bright pink in Fig. 1(b), and throughout this study we treat the epidermis and dermis as a single layer that we call the *skin* layer. Underneath the skin layer there is a layer of fat that is a lighter shade of pink in Fig. 1(b). Throughout this work we refer to this lower layer as the *fat* layer. As indicated in Fig. 1(c), we adopt a coordinate system where $x = 0$ corresponds to the skin surface. The interface between the fat and skin is located at $x = l_1 > 0$, we have $l_1 = 1.6$ mm in this case. The interface between the fat and the underlying muscle and bone is at $x = l_2 > l_1$, and we have $l_2 = 4.0$ mm in this case. Our conceptual idealisation of the structure of the layered tissues is given in Fig. 1(c) where the subdermal probe is placed at $x = l_2$ since experimental data reported by Cuttle involves placing the probe at the bottom of the fat layer [2,17]. A summary of the kind of experimental data reported by Cuttle is given in Fig. 1(d). In this particular experiment the probe is located at the interface of the fat and muscle, $x = l_2$, and a scald creation device of diameter 50 mm is placed on the surface of the skin [2]. Water at temperature of 50 °C is maintained in the scald creation device for a duration of 120 s, and the time series data showing the temperature at the subdermal probe is recorded, as shown. It is worth noting that the total depth of the tissue (4 mm) is much smaller than the diameter of the scald creation device (50 mm), so that $4/50 = 0.08 \ll 1$, as illustrated in Fig. 1(e). Since the centre of the circular scald creation device is placed directly over the location of the probe the heat transfer downward through the skin can be idealised as a one-dimensional process [17].

A prominent feature of the skin, highlighted in Fig. 1(b), is the layered structure where we see that the fat layer is below the skin layer. This kind of histological information has been previously incorporated into mathematical descriptions of heat transfer in skin by explicitly accounting for the layered, heterogeneous structure of the tissue. These previous models have often been based on generalisations of Pennes' bioheat equation [18–20] and reformulated as a multilayer heterogeneous heat transfer model where the thermal properties can vary between the different layers [21–25]. A key limitation of working with such a heterogeneous multilayer heat transfer model is that they are more challenging to parameterise than simpler single layer models. This is a consequence of the fact that there are a greater number of unknown parameter values in a multilayer heterogeneous model compared to a simpler single layer model of heat transfer. This challenge is particularly acute if we consider parameterising a mathematical model of heat transfer using Cuttle's realistic experiments that report the temperature response at one location within the layered structure. This experimental limitation is difficult to overcome because inserting multiple probes simultaneously at different depths would risk compromising the integrity of the living tissues. Our previous work has involved calibrating the solution of much simpler single layer homogeneous models to match data from Cuttle's experiments [2,17]. However, these previous studies suffer from the limitation that they implicitly treat the thermal parameters of the skin layer and fat layer together into a simplified, vertically averaged, homogenised single layer [26]. While this approach is mathematically convenient, it is unclear whether a single layer model is appropriate since we know that one of the main biological roles of the fat layer is to provide thermal insulation [27]. Therefore, we expect that the thermal properties of the skin and fat layers could be very different.

In this work we use a two-layer heterogeneous model to describe heat conduction in living tissues. Our aim is to perform a suite of synthetic experiments with realistic parameter values to mimic data generated by Cuttle's experimental protocol. With this synthetic data we explore the extent to which we can confidently estimate the thermal diffusivity in each layer when we have limited experimental observations where the temperature is reported at one single location within the layered tissues. To achieve this, we use the solution of the two-layer heterogeneous model, parameterised with biologically-relevant estimates of the thermal diffusivity of skin and fat, to generate synthetic data that mimics Cuttle's experimental protocol where a single probe is placed at the bottom of the fat layer. Given that the synthetic data is generated with known estimates of the thermal diffusivity in the skin and fat layers, we then systematically explore the parameter space to investigate whether the kind of data can be used to reliably determine parameters in the heterogeneous mathematical model. Once we have demonstrated how delicate this parameter estimation task can be, we turn our attention to the question of experimental design. First, we explore whether our ability to determine the parameters in the two-layer model varies when we alter the location of the single subdermal probe. Second, we explore the extent to which our ability to estimate the parameters improves when we consider synthetic experiments with two probes so that the temperature is recorded simultaneously at two different positions within the layered skin.

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