

# Advanced 3D Monte Carlo Algorithms for Biophotonic and Medical Applications

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This thesis is submitted in partial fulfilment for the degree of  
PhD  
at the  
University of St Andrews

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# Declaration

I, Lewis McMillan, hereby certify that this thesis, which is approximately \*\*\*\*\* words in length, has been written by me, that it is the record of work carried out by me, or principally by myself in collaboration with others as acknowledged, and that it has not been submitted in any previous application for a higher degree.

I was admitted as a research student in September 2015 and as a candidate for the degree of PhD in September 2015; the higher study for which this is a record was carried out in the University of St Andrews between 2015 and 2019.

Date ..... Signature of candidate .....

I hereby certify that the candidate has fulfilled the conditions of the Resolution and Regulations appropriate for the degree of PhD in the University of St Andrews and that the candidate is qualified to submit this thesis in application for that degree.

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# Abstract

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# Acknowledgements

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# Abbreviations

$T_a$  ablation temperature.

**AMR** adaptive mesh refinement.

**FDM** finite difference method.

**K-M theory** Kubelka-Munk Theory.

**MCRT** Monte Carlo radiation transfer.

**MPI** Message-passing interface.

**OCT** optical coherence tomography.

**PDF** probability density function.

**PDT** photo-dynamic therapy.

**RTE** radiative transfer equation.

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# Chapter 1

# Monte Carlo Radiation Transport Technique

## 1.1 Introduction and Background

This chapter will provide an overview of the Monte Carlo method and how it is used within the context of Monte Carlo radiation transfer (MCRT). The chapter will then present the details of the MCRT code used as the basis of the subsequent chapters. Validation of this code and details of computational speed up are also presented. Subsequent chapters will expand upon the code for each individual projects needs.

### Monte Carlo Method

The Monte Carlo method is a numerical analysis technique based upon random numbers, which are used to calculate unknown variables in problems [1, 2].

The earliest use of the method is in Buffon's needle experiment of the 18<sup>th</sup> century [3–5]. Buffon asked the question;

“Suppose we have a floor made of parallel strips of wood, each the same width, and we drop a needle onto the floor. What is the probability that the needle will lie across a line between two strips?”

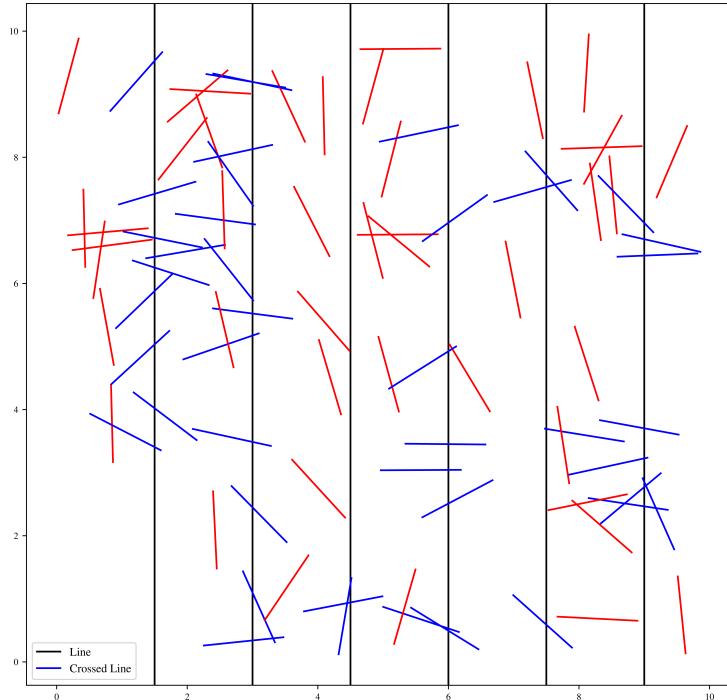
The solution to this question is: for a needle length  $l$ , strip separation  $s$ , where  $x$  is the distance from the needle to the closest line, and  $\theta$  is the angle of the needle with respect to the wood strips. Then using a simple geometrical argument, a needle crosses a strip if  $x \leq \frac{l}{2} \sin\theta$ .

$x$  is distributed uniformly in  $[0, \frac{s}{2}]$ , and  $\theta$  in  $[0, \frac{\pi}{2}]$ . Therefore the probability density function for  $x$  is  $p(x) = \frac{2}{s}$ , and  $\theta$  is  $p(\theta) = \frac{2}{\pi}$ . The probability density function (PDF), is a function of a variable that gives probability for a variable to take a given value. The PDF is normalised over the whole range of the variable, in this case  $x$ , and  $\theta$ . Thus, as  $x$  and  $\theta$  are independent variables, giving a joint probability of  $p(x, \theta) = \frac{4}{s\pi}$ . So the probability of a needle of length  $l$  ( $l < s$ ) is:

$$P = \int_0^{\frac{\pi}{2}} \int_0^{\frac{l}{2} \sin\theta} \frac{4}{s\pi} dx d\theta = \frac{2l}{s\pi} \quad (1.1)$$

Equation (1.1) can be used to carry out a Monte Carlo estimation of  $\pi$ . A simple rearrangement yields:  $\pi = \frac{2l}{sP}$  where  $P$  is the ratio of needles crossing the line over total number dropped.

Laplace was the first to suggest that Buffon's needle experiment could be used to estimate  $\pi$  [4]. Figure 1.1 shows an example of simulation of Buffon's needle experiment.



**Figure 1.1:** Sample Buffon needle experiment. 100 needles are dropped on a  $10 \times 10$  cm area with lines spaced 1.5 cm apart. If a needle lands on a line it is recorded and coloured blue, else it is red. This simulation gave a value of  $\pi \approx 3.10$ .

There are various different approaches to using the Monte Carlo method to obtain randomly sampled variables. One analytical way of achieving this is the inverted sampling method. The inverted sampling method can be summarised by the following steps for drawing a sample  $X_i$  from an arbitrary PDF  $p(x)$ :

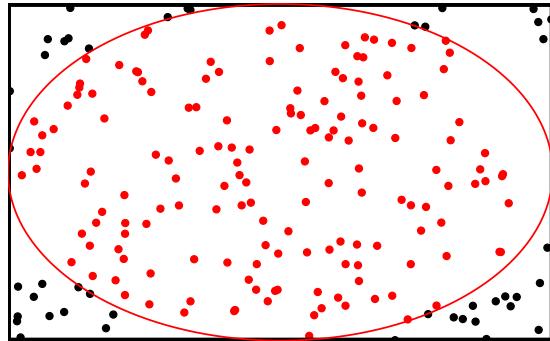
1. Compute the CDF\*  $P(x) = \int_0^x p(x')dx'$
2. Compute the inverse  $P^{-1}(x)$
3. Obtain a uniformly distributed random number  $\xi$
4. Finally, compute  $X_i = P^{-1}(\xi)$

If a given problem cannot use the inverted sampling method, as it may not be possible to get a PDF or analytically invert the CDF, then the rejection method can be used. The rejection method is essentially a dart throwing method. This means that points are drawn and compared to the function. If the point lies under the function then the point is accepted, if it lies above the function then it is rejected. For example, if a function,  $f(x)$  that does not have an analytical PDF, we can use a PDF  $p(x)$  such that  $f(x) < cp(x)$  where  $c$  is a constant. Therefore sampling from  $p(x)$ , and if the sampled point lies under  $f(x)$  it is accepted, else it is rejected. Figure 1.2 shows an example of this process.

The Monte Carlo method is used in various different disciplines. Ranging from use in the financial sector to analyse investments and stocks by simulating the sources of uncertainty which

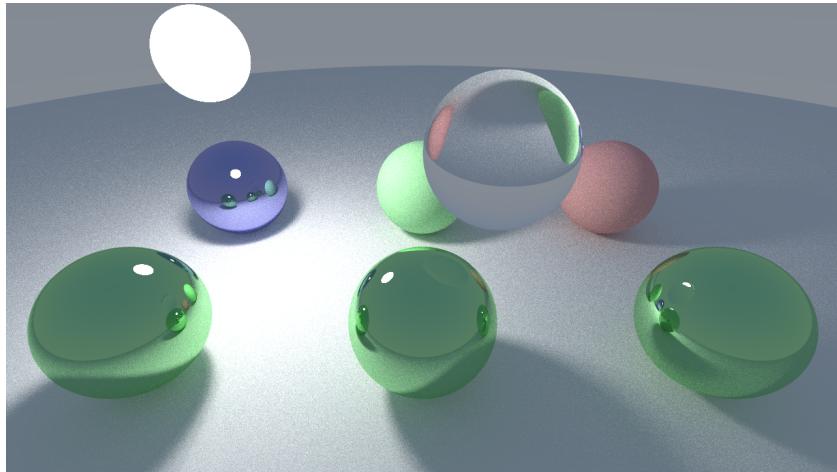
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\*The CDF is the cumulative distribution function.



**Figure 1.2:** Illustration of the rejection method for determining  $\pi$  from the area of a circle inscribed within a square. The ratio of the area of the circle to the square is  $\frac{\pi}{4}$ . Thus the ratio of darts landing in the circle to those that land outside the circle is  $\pi \approx \frac{4N_{inner}}{N_{total}}$ , where  $N_{total}$  is the total number of darts, and  $N_{inner}$  is the total number of darts that land in the circle. Using 200 darts gave a value of  $\pi \approx 3.12$

affect their values [6, 7], use in statistical analysis [8], and in modern computer generated images (see Fig. 1.3) [9, 10]. It is also widely used in astronomy [11, 12] and medicine [13, 14], in order to simulate the propagation of radiation through turbid media. This technique, MCRT, is what makes up the bulk of this thesis and is described in depth in the following sections.



**Figure 1.3:** Computer generated imagery using ray tracing. The Monte Carlo method is used to “compute radiance along ray paths between lights and the camera”, in order to generate CGI images [15].

## 1.2 Monte Carlo Radiation Transport Algorithm

### 1.2.1 Introduction & background

The technique that makes up the bulk of this thesis, is the MCRT technique. This method was developed at the end of the Second World War at the Los Alamos National Laboratory, for the purpose of calculating neutron diffusion through shielding material [16–19]. It has since found a myriad of applications from light transport through dusty galactic clouds [20], calculating doses for radiotherapy [21] to light transport through tissue [22].

The theory that governs the transport of radiation through medium is the radiative transfer equation. Before describing MCRT which is a numerical solution to the radiative transfer equation (RTE), the theory of radiation transport must be examined.

#### Radiative Transfer

Transport of photons through turbid media, can be modelled analytically using the RTE. The RTE models the radiative losses, and gains by a beam of radiation as it travels through a medium, including: loss of energy due to absorption, loss/gain of energy due to scattering, and energy gain due to emission. Before deriving the RTE, some definitions of some terms and physical quantities is required.

The first term is spectral irradiance,  $L_\nu$ . Spectral irradiance is defined as the energy flow in a direction  $\hat{\mathbf{n}}$ , for a solid angle  $d\Omega$ , per unit time per unit temporal frequency bandwidth. Irradiance is defined as the spectral irradiance over a small frequency range  $[\nu, \nu + \Delta\nu]$ :

$$L(\vec{r}, \hat{s}, t) = L_\nu(\vec{r}, \hat{s}, t)\Delta\nu \quad (1.2)$$

Where:

- $\vec{r}$  is the position;
- $\hat{s}$  is the unit normal vector;
- $t$  is the time;
- and  $L(\vec{r}, \hat{s}, t)$  is the irradiance [ $W m^{-2} sr^{-1}$ ].

The irradiance can be used to determine the energy,  $dE$ , transported across an area  $dA$ , in a solid angle  $d\Omega$  in a time  $dt$  (see Fig. 1.4) is:

$$dE = L(\vec{r}, \hat{s}, t) \cdot (\hat{s} \cdot \hat{n}) dA d\Omega dt \quad (1.3)$$

Where:

- $\hat{n}$  is the unit normal to  $dA$ ;
- and  $\hat{s} \cdot \hat{n}$  is the angle of the solid angle.

Irradiance can also be used to determine the fluence rate,  $\phi$ , which is defined as the energy flow per unit time, independent of the flow direction.

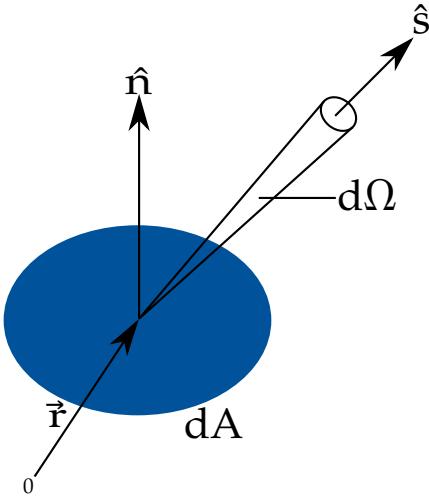
$$\phi(\vec{r}, t) = \int_{4\pi} L(\vec{r}, \hat{s}, t) d\Omega \quad (1.4)$$

Where:

- $\phi$  is the fluence rate [ $Wm^{-2}$ ].

Solving the RTE yields the irradiance which gives the distribution of light in the medium, and gives information on the state of the system and all the physical properties of it.

With the irradiance defined, as well as the other quantities that follow, the RTE can be derived [23, 24]. First considering the conservation of energy, as shown in Eq. (1.5).



**Figure 1.4:** Energy flow through area  $dA$  within solid angle  $d\Omega$  in a direction  $\hat{s}$ . Adapted from [23, 24]

$$dP = -dp_{div} - dp_{ext} + dP_{scatt} + dP_{src} \quad (1.5)$$

Where:

$dP$  is the total change in energy in the volume  $dA ds$  within the solid angle,  $d\Omega$ , per unit time (see Fig. 1.5);

$dP_{div}$  is the energy loss due to the divergence of the radiation beam per unit time;

$dP_{ext}$  is the energy loss due to absorption and scattering within  $dA ds d\Omega$ ;

$dP_{scatt}$  is the energy gain due to scattering from  $\hat{s}'$  into  $d\Omega$  per unit time;

and  $dP_{src}$  is the energy gain due to emission within the medium, per unit time.

The total change in energy,  $dP$ , in the volume element within the solid angle  $d\Omega$  is equal to:

$$dP = \frac{1}{c} \frac{\partial L(\vec{r}, \hat{s}, t)}{\partial t} dA ds d\Omega \quad (1.6)$$

Where  $c$  is the speed of light.

The first loss term,  $dP_{div}$ , is the energy loss due to divergence of the radiation beam. This is modelled as:

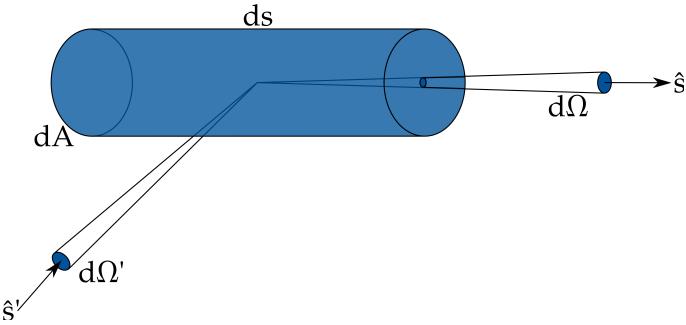
$$dP_{div} = \frac{\partial L}{\partial s} d\Omega dV \quad (1.7)$$

$$= \hat{s} \cdot \nabla L(\vec{r}, \hat{s}, t) d\Omega dV \quad (1.8)$$

$dP_{ext}$  is the second loss term, and accounts for energy loss due to scattering and absorption in the volume element within the solid angle  $d\Omega$ . This is modelled as:

$$dP_{ext} = \mu_t ds L(\vec{r}, \hat{s}, t) dA d\Omega \quad (1.9)$$

The first energy gain term,  $dP_{src}$ , is due to emission in the volume element within the solid angle  $d\Omega$ .



**Figure 1.5:** Cylindrical volume element,  $ds dA$ , with solid angle  $d\Omega$  in direction  $\hat{s}$  and solid angle  $d\Omega'$  in direction  $\hat{s}'$ . Energy flowing through this element is used to derive the radiation transfer equation. Adapted from [23, 24].

$$dP_{src} = S(\vec{r}, \hat{s}, t) dV d\Omega \quad (1.10)$$

The second energy gain term, and final term, is due to the incident energy on the volume element within the solid angle  $d\Omega$  in direction  $\hat{s}$  due to scattering from any direction  $\hat{s}'$ .

$$dP_{scatt} = N_s dV \left( \int_{4\pi} L(\vec{r}, \hat{s}', t) P(\hat{s}', \hat{s}) \sigma_s d\Omega' \right) d\Omega \quad (1.11)$$

$$= \mu_s dV \left( \int_{4\pi} L(\vec{r}, \hat{s}', t) P(\hat{s}', \hat{s}) d\Omega' \right) d\Omega \quad (1.12)$$

Where:

$N_s$  is the number density of scatters;  
 $P(\hat{s}', \hat{s})$  is the scattering phase function (see Section 1.2.2 for further discussion);  
and  $\sigma_s$  is the cross section of the scatters, thus  $\mu_s = N_s \sigma_s$ , where  $\mu_s$  is the scattering coefficient.

Finally substituting Eqs. (1.6), (1.8) to (1.10) and (1.12) into Eq. (1.5) yields the RTE:

$$\frac{1}{c} \frac{\partial L(\vec{r}, \hat{s}, t)}{\partial t} + \mathbf{s} \cdot \nabla L(\vec{r}, \hat{s}, t) = -\mu_t L(\vec{r}, \hat{s}, t) + \mu_s \int_{4\pi} p(\hat{s}, \hat{s}') L(\vec{r}, \hat{s}', t) d\Omega' + S(\vec{r}, \hat{s}, t) \quad (1.13)$$

In general, the RTE is hard to solve in arbitrary 3D geometries, however there are a number of approximations, and numerical methods available. Diffusion approximation, Kubelka-Munk Theory (K-M theory), and MCRT are the common methods used to approximate or solve the RTE.

### Kubelka-Munk Theory

K-M theory was originally developed in order to calculate the light distribution in thin layered materials, such as paint or paper [25]. The theory is rather simple and makes many assumptions about the medium and the incident light. The main assumptions of K-M theory are: only scattering and absorption take place in the medium, the incident light is already diffuse, the medium is uniform with only isotropic scattering, no external or internal reflections, and the medium is planar and infinitely wide [26–28].

These assumptions make K-M theory poor for modelling light-tissue interactions. This is because in tissue, scattering is not isotropic but rather forward biased (see Section 1.2.2). Tissue is rarely, planar and infinitely wide. Tissue also has some reflections at its external and internal boundaries, due to change in refractive indices. Many medical and biophotonic treatments/methods use laser light which is not diffuse. Finally tissue can also exhibit fluorescence, which K-M theory is not able to model, along with polarization. K-M theory does have some positive aspects. It is good at calculating the diffuse reflectance of simple media, and can be used to roughly estimate calculations. Though it is not well suited for modelling light-tissue applications [29].

### Diffusion Approximation

The diffusion approximation for the RTE, is where the irradiance is separated into two components:

$$L(\vec{r}, \hat{s}) = L_c(\vec{r}, \hat{s}) + L_d(\vec{r}, \hat{s}) \quad (1.14)$$

Where  $L_c$  is the unscattered contribution, which satisfies Beer's law<sup>†</sup>, and  $L_d$  is the diffuse contribution. The  $L_d$  component is expanded using Legendre polynomials and truncated. The diffusion approximation also has a number of assumptions and restrictions. The main assumption is that scattering dominates over absorption, and that the scattering is nearly isotropic. This restricts the types of scattering the Diffusion approximation can model, though using similarity relations can partially model scattering in tissue [30, 31].

Diffusion theory is computationally fast, and simple to implement. However it is poor at modelling light-tissue interactions due to its assumptions and restrictions, mainly the inaccurate modelling near the boundaries of the medium and its lack of modelling fluorescence and other microphysics. However it can be used to speed up MCRT in optically thick regions [32, 33].

### MCRT

The final method, MCRT, is a method that is numerically equivalent to the RTE [23]. MCRT is a flexible method, it can model arbitrary 3D geometries, various microphysics including fluorescence, and polarisation. It can also model various different light sources, from collimated laser beams, to diffuse light sources. The only downside that is noted in the literature is that the MCRT can be expensive computationally. However with computational power growing faster with each year, this is less of a problem going forward. The next several sections give an in depth description of the MCRT method and its flexibility, along with a description of the code used in this thesis to solve various medical and biophotonic problems.

### 1.2.2 Optical Properties

Before an in depth description of the MCRT method is outlined, a discussion of the optical properties of materials, which the MCRT method needs in order to simulate the transport of photons in a material.

Optical properties of a medium are the properties that describe how light is transported through that medium. Usually the optical properties of a medium are defined by three main parameters: the scattering and absorption coefficients ( $\mu_s$  and  $\mu_a$ ), and the anisotropy coefficient

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<sup>†</sup>Beer's law (or Beer-Lambert law) states that the transmission,  $T$ , is equal to  $e^{-\mu L}$ , where  $L$  is the distance and  $\mu$  is the attenuation coefficient.

( $g$ ). There are several other optical properties the medium can be defined with, however these in general are only used for specific applications, such as Raman cross-sections for Raman scattering.

## Scattering

The scattering coefficient, along with the anisotropy value (see [Anisotropy](#)), define how light is scattered in a medium. Scattering occurs in skin due to a number of different scatterers, and inhomogeneities found within the skin. The main scatters in the skin are filamentous proteins such as collagen and elastin. These proteins are generally found within the dermis and epidermis [34]. In the upper layers of the skin, the main scatters are keratins and various chromophores such as melanin. The size of the scatters affect how light is scattered and into which direction that light is scattered into.

The scattering of light within tissue is usually defined as  $\mu_s$  or  $\mu'_s$ : the scattering coefficient and the reduced scattering coefficient, where  $\mu'_s = \mu_s(1-g)$ . The scattering coefficient is defined such that the probability of transmission without scattering in a path length  $L$  is:

$$T = e^{-\mu_s L} \quad (1.15)$$

This gives units of inverse length for the scattering coefficient (usually measured in  $cm^{-1}$ ). The reduced scattering coefficient is quite often given in place of the scattering coefficient, as the reduced coefficient is more easily measured than the “normal” coefficient [35].

## Anisotropy

Anisotropy is the degree of deviation that light undergoes at each scattering event. The anisotropy value is taken from the phase function for the medium. The phase function is defined as the angular distribution of light intensity scattered by a particle. The phase function,  $\Phi(\theta, \phi)$ , is usually normalised over all angles:

$$\int_{\Omega} \Phi(\theta, \phi) d\Omega = 1 \quad (1.16)$$

Where  $\theta$ , and  $\phi$  are the usual spherical angles. Thus for Rayleigh and isotropic scattering, their phase function's are:

$$\Phi_{isotropic}(\theta, \phi) = \frac{1}{4\pi} \quad (1.17)$$

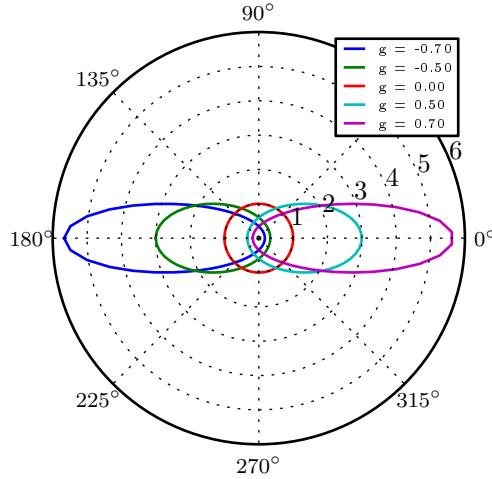
$$\Phi_{Rayleigh}(\theta, \phi) = \frac{3}{8\pi} (1 + \cos^2(\theta)) \quad (1.18)$$

For simplicity, the phase function is usually cast as the anisotropy value  $g$ , which is defined as the average angle of deflection:

$$g = \langle \cos(\theta) \rangle = \int_{\Omega} \cos(\theta) \Phi(\theta, \phi) d\Omega \quad (1.19)$$

The anisotropy factor,  $g$ , can take on any value from  $-1$  to  $1$ . Where a value of  $-1$  is highly back scattering,  $0$  is isotropic scattering, and  $1$  is highly forward scattering (see Fig. 1.6).

There are many phase functions that can be used to model the anisotropy factor in a medium. The standard phase function in biological tissue is the Henyey-Greenstein phase function. The Henyey-Greenstein phase function, was originally created to modelling diffuse radiation in the galaxy [36, 37]. It has since become the *de-facto* phase function for biological tissue. This is



**Figure 1.6:** Figure show the  $g$  factor for the Henyey-Greenstein phase function, for various configurations of back, forward or isotropic scattering.

due to the phase functions relative simplicity and due to it being regarded as a “good” phase function for accurately modelling scattering in biological tissue [38]. The Henyey-Greenstein phase function is shown in Eq. (1.20):

$$\Phi_{H.G}(\theta, \phi) = \frac{1}{4\pi} \frac{1 - g^2}{(1 + g^2 - 2g \cos(\theta))^{\frac{3}{2}}} \quad (1.20)$$

### Absorption

Absorption of light by a medium is defined by the absorption coefficient  $\mu_a$ . The absorption coefficient is defined in a similar fashion to the scattering coefficient, by considering the probability of transmission without absorbing in a path length L:

$$T = e^{-\mu_a L} \quad (1.21)$$

This, again like the scattering coefficient, gives inverse distance for the unit of the absorption coefficient (and its is also usually measured in units of  $\text{cm}^{-1}$ ).

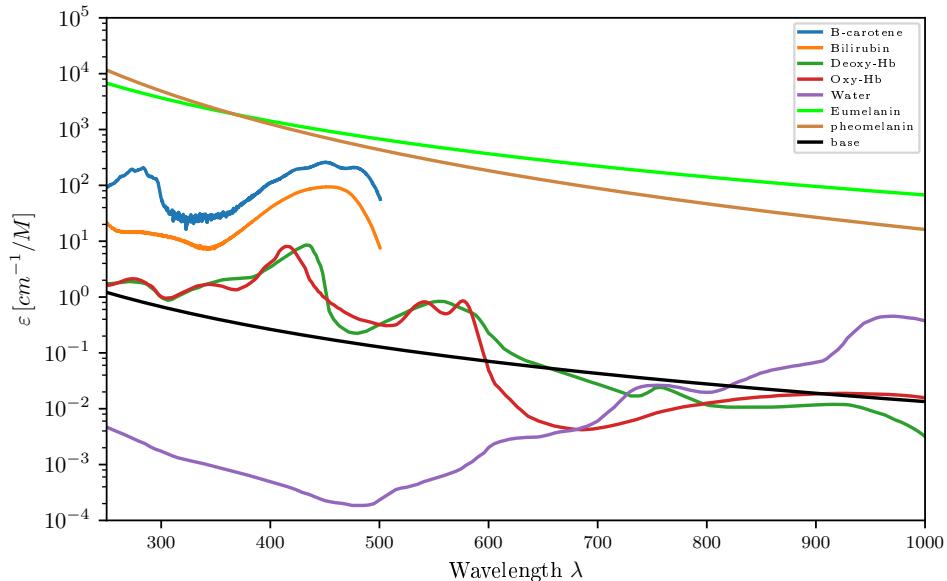
There are various sources of absorbers in tissue: blood, water, fat, melanin,  $\beta$ -carotene, bilirubin are among the more absorbing chromophores. These chromophores can all contribute, depending on the wavelength, with some more absorbing than others, see Fig. 1.7.

#### 1.2.2.1 Derived Parameters

There are also some derived parameters that are useful to use. These are the albedo and the transmission coefficient.

The transmission/attenuation coefficient is defined as the sum of the scattering coefficient and the absorption coefficient:

$$\mu_t = \mu_s + \mu_a \quad (1.22)$$



**Figure 1.7:** Spectra of some of the more common absorbers found in the skin [35, 39–47].

The albedo, or scattering probability, is defined as the ratio of the scattering coefficient to the transmission coefficient:

$$a = \frac{\mu_s}{\mu_a + \mu_s} = \frac{\mu_s}{\mu_t} \quad (1.23)$$

## Other Parameters

The preceding subsection, described the optical properties that this thesis will use in every chapter. However there are other optical properties that can be used to define a medium. These other parameters generally are used to model microphysics such as Raman scattering, polarization, fluorescence or reflection/refraction. This section will give a brief overview of these other optical properties.

### Refractive Index

The refractive index of a medium, defines how fast light propagates through that medium. Generally, for tissue, the refractive index is given as a bulk refractive index. Meaning that the medium is divided into sections, with each section given a refractive index. For example, skin's refractive indices are divided up by the different layers of skin. Details on how refraction is implemented with the code can be found in ??.

### Raman Scattering

Raman scattering is where a photon is scattered inelastically, which excites the molecule the photon scattered off, thus decreasing the energy of the photon and increasing the photons wave-

length. The optical property needed to model Raman scattering is the Raman scattering cross section. The cross section, like the absorption or scattering coefficient, is the likelihood of a photon undergoing a Raman scattering event. Raman scattering has been modelled in MCRT in order to simulate spatially offset Raman spectroscopy for breast tumour analysis [48].

### Fluorescence

Fluorescence occurs when a photon is absorbed by a fluorescent molecule and re-emitted with a new wavelength. Fluorescence is a reactively common phenomena, and is heavily utilised in biophotonics and medicine, in order to image, or monitor molecules in tissue. Again the optical property that models fluorescence is coefficient that gives the probability of absorption and re-emission of a photon by a certain molecule. Usually this is in the form of an absorption coefficient or extinction coefficient. The extinction coefficient is a measurement of absorption in terms of the concentration of that absorber. Thus if a medium has many fluorophores, then the total absorption coefficient is the bulk absorption of the medium plus the contribution from the fluorophores as in Eq. (1.24):

$$\mu_a = \ln 10 \sum_i C_i \varepsilon_i \quad (1.24)$$

Where  $C_i$  is the concentration of the  $i^{th}$  fluorophore, and  $\varepsilon_i$  is the extinction coefficient of the  $i^{th}$  fluorophore.

Fluorescence will be described in more depth in ????.

### 1.2.3 MCRT Algorithm

A MCRT algorithm can range in complexity from a simple 20 line program, to tens of thousands of lines, depending on the application. This section will provide an in depth description of the MCRT algorithm for the propagating photons thorough a spherical medium with optical properties  $\mu_s$ , and  $\mu_a$ . The section following this one, will provide details of how the MCRT algorithm is implemented in the Fortran programming language, along with the various code details, such as the parallelisation of the code.

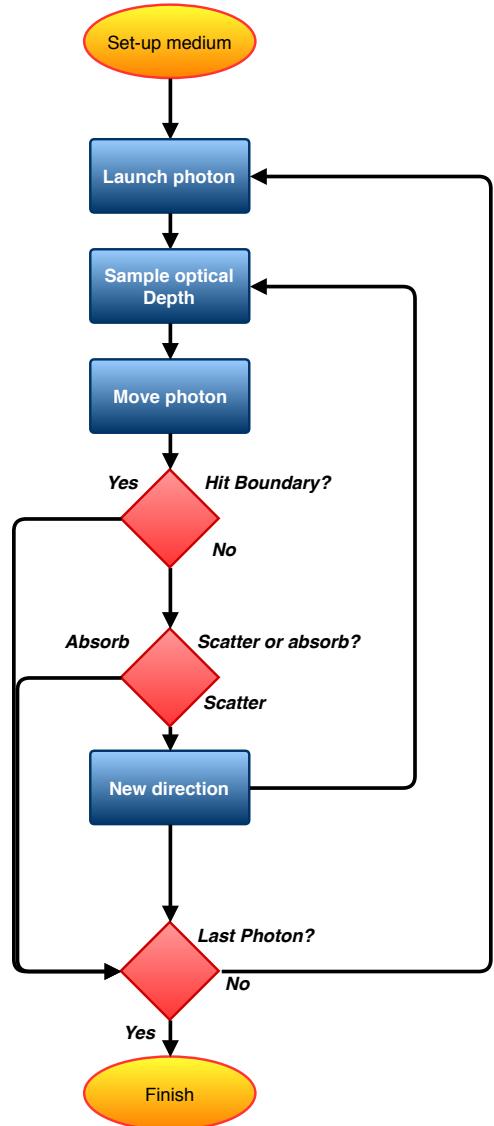
Figure 1.8 shows a flow chart of the MCRT algorithm described in this chapter.

#### Medium and Grid Set-up

The first step of any MCRT algorithm, is to set-up the medium the photons will propagate through. There are a variety of ways that the medium can be set-up, for this section, assuming the medium is an isotropic sphere, radius  $R$ , and centred at the origin. For simplicity one wavelength is considered,  $\lambda$ . As the MCRT algorithm presented here is run on a 3D Cartesian grid, the grid is setup before creating the spherical medium. The grid is composed of  $n_x \times n_y \times n_z$  voxels<sup>‡</sup>, where each voxel can have its own optical properties. The grid is setup by first setting an array that stores the locations of the voxel boundary walls in the  $x$ ,  $y$ , and  $z$  directions. The next step is to setup the actual medium. This is achieved by discretising the medium onto a grid. For this example a sphere is inscribed into a cubic volume, by setting the optical properties of a voxel to that of the medium if the sphere encloses that voxel. The voxels out with sphere are set to that of the ambient medium. An example of a voxelised medium can be seen in Fig. 1.9.

#### Photon Launch and Initialisation

The second step in the MCRT algorithm, is to initialise the photon. Initialisation of the photon involves setting its initial position and direction. Again how this is done depends on the experiments being simulated. Here the photon is initialised to the centre of the sphere. The initial direction is sampled isotropically, and set accordingly:



**Figure 1.8:** Flowchart of the Monte Carlo radiation transport algorithm as described in this section.

<sup>‡</sup>A voxel is a 3D pixel

$$n_{xp} = \sin(\theta) \cdot \cos(\phi) \quad (1.25)$$

$$n_{yp} = \sin(\theta) \cdot \sin(\phi) \quad (1.26)$$

$$n_{zp} = \cos(\theta) \quad (1.27)$$

With  $\theta$  and  $\phi$  sampled uniformly between  $[0, \cos^{-1}(2\xi - 1)]$  and  $[0, 2\pi\xi]$  respectively.

The next step is to launch a photon packet. Depending on the source of photon packets for a given simulation, this step varies from simulation to simulation. The general idea of launching a photon packet is that the packet is given an initial direction vector and position (which consists of a physical position and a voxel position)<sup>§</sup>:

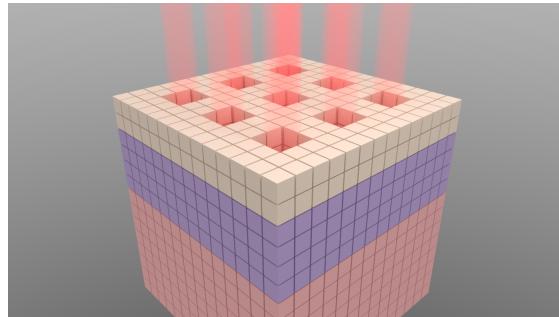
$$\text{direction} = \begin{bmatrix} n_{xp} \\ n_{yp} \\ n_{zp} \end{bmatrix} \quad (1.28)$$

$$\text{position} = [x_p, y_p, z_p] \quad (1.29)$$

$$\text{voxel} = [x_{cell}, y_{cell}, z_{cell}] \quad (1.30)$$

To set the direction vectors, the components of the direction vectors must be first set. The packets position is tracked using a Cartesian coordinate system, however for ease of computation for calculating scattering angles (see [Photon Interaction Event](#)), the direction vectors are computed in a spherical system thus the direction vectors are in Eqs. (1.25) to (1.27).

$\theta$  and  $\phi$  are generated dependant on the photon source used. The individual sine and cosine terms are saved for use in the scattering routines, see [Photon Interaction Event](#). The position is then set according to the light source used. For this example the photons are released from origin of the sphere. Using this position the voxel the packet is in is calculated.



**Figure 1.9:** Example of a possible voxel model, with three different layers, various holes due to ablative pixel beam lasers ( see Chapter 2). Each voxel can represent a different optical/thermal property of the tissue medium.

### Photon Move

The next step in the algorithm is moving a packet to the next interaction point. The probability a packet will interact over a distance  $dL$  is  $\mu_t dL$ , where  $\mu_t$  is the interaction probability (see [Optical Properties](#)). Thus, the probability of travelling  $dL$  without any interaction is  $1 - \mu_t dL$ . Therefore

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<sup>§</sup>all variables given in this section are the same as they are in the code.

over a distance  $L$ , with  $N$  segments of length  $L/N$  the probability of travelling  $L$  before any interaction:

$$P(L) = (1 - \mu_t \frac{L}{N}) \cdot (1 - \mu_t \frac{L}{N}) \dots (1 - \mu_t \frac{L}{N}) = (1 - \mu_t \frac{L}{N})^N \quad (1.31)$$

$$P(L) = \lim_{N \rightarrow \infty} (1 - \mu_t \frac{L}{N})^N = e^{-\mu_t L} = e^{-\tau} \quad (1.32)$$

Where  $\tau$  is the number of mean free paths over a distance  $L$ . Eq. (1.32) is now a PDF for the distance a packet will travel before an interaction occurs. To be able to get a random optical depth, the PDF has to be able to be sampled from either analytically or via the rejection method. Using the Monte Carlo method described in Section 1.1, with  $\xi$  as our random variable, gives:

$$\xi = \int_0^\tau e^{-\tau'} = 1 - e^{-\tau} \rightarrow \tau = -\log(1 - \xi) \quad (1.33)$$

As  $\xi$  is symmetric about 0.5,  $1 - \xi$  can be substituted for  $\xi$  yielding:

$$\tau = -\log(\xi) \quad (1.34)$$

$\tau$  is now the optical distance, however this needs to be converted into a physical distance so that the photon packet can be moved. From our definition of  $\tau$  we know that  $\tau = \int_0^L \mu_t dS$ , and if the medium is smooth and homogeneous (i.e not a gridded medium):

$$L = \frac{\tau}{\mu_t} \quad (1.35)$$

Therefore in order to update the packets position it is simply:

$$x_p = x_p + L \cdot n_{xp} \quad (1.36)$$

$$y_p = y_p + L \cdot n_{yp} \quad (1.37)$$

$$z_p = z_p + L \cdot n_{zp} \quad (1.38)$$

However as the code in this thesis is a 3D gridded Cartesian code, the method of updating and moving the packets position is slightly adjusted. As stated in [Medium and Grid Set-up](#), the medium has been discretised onto a grid, so that each voxel can have a different  $\mu_t$ , thus Eq. (1.35) becomes:

$$L = \frac{\tau}{\mu_{t,\zeta}} \quad \zeta = (x, y, z) \quad (1.39)$$

with  $\mu_{t,\zeta}$  the  $\mu_t$  for the  $\zeta^{th}$  voxel.

Moving the photon through a voxelised medium is more involved than propagating a photon through a non voxelised medium. This is mainly due to the fact the “book keeping” needed in tracking where the photon is and in what voxel it is in. The first step of moving the photon through a voxelised medium is drawing a random optical depth. This optical depth will be the full optical depth the photon travels before an interaction event. The generation of a random optical depth is as outlined above. As the photon travels through the voxel grid, a running total of the current optical distance travelled is kept. This is then compared to the randomly generated optical depth. When the running total optical depth equals the randomly generated optical depth the photon propagation is stopped, and the photon undergoes an interaction.

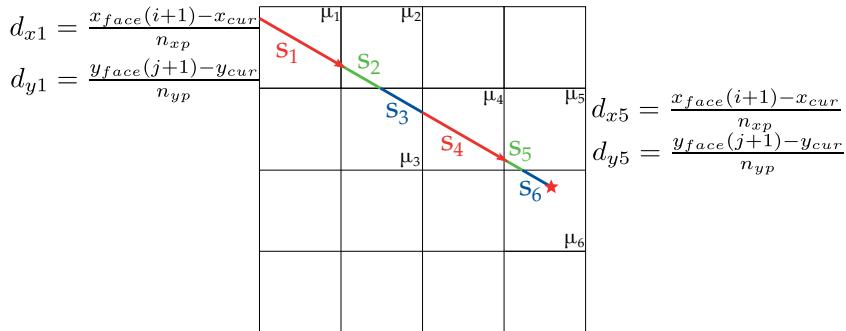
The next step is to calculate the distance to the nearest wall in the  $x$ ,  $y$ , and  $z$  directions. The distance is calculated for each direction. Equation (1.40) shows for the  $x$  direction:

$$d_x = \frac{x_{face} - x_{cur}}{n_{xp}} \quad (1.40)$$

Where  $d_x$  is the distance to the nearest wall in the  $x$  direction.  $x_{face}$  is the voxel wall position in the  $x$  direction, and  $n_{xp}$  is the  $x$  direction vector. With three distances calculated,  $[d_x, d_y, d_z]$ , the minimum of these is thus the distance to the nearest voxel wall.

The next step is to calculate the optical depth for this distance. The optical depth is calculated by rearranging Eq. (1.39) for  $\tau$ , with  $L$  now the distance to the nearest wall. With the optical distance to the nearest wall calculated, the next step is to determine if there is “enough” optical distance left to travel the full distance to the nearest wall. Therefore the running total optical distance is compared to the randomly generated optical distance. If the running total + the new optical distance to the nearest wall, is less than the randomly generated optical depth, then the photon travels to the nearest wall. The photon is then placed in the next voxel by a distance  $\delta$ , where  $\delta$  is just larger than machine precision. If the running total + the new optical distance to the nearest wall is greater than the generated optical distance then an interaction event occurs in the current voxel. The distance to the interaction event is calculated and the photon moved to this location.

Figure 1.10 illustrates this whole process for a 2D example.



**Figure 1.10:** Illustration of photon propagation through a 2D grid.  $d_{x1}$ , and  $d_{y1}$  are the distances to the voxel walls in the  $x$  and  $y$  directions in the  $\mu_1$  voxel. In this case  $S_1 = d_{x1}$  as  $d_{x1}$  is smaller than  $d_{y1}$ , thus the photon hits the voxel wall in the  $x$  direction. For the  $\mu_5$  voxel,  $d_y$  is smaller, thus the photon hits the voxel wall in the  $y^{th}$  direction.

This whole process is repeated until the photon undergoes an interaction event or leaves the voxel medium. The next step in the algorithm is the interaction event, which can consist of either: scattering, absorbing or another microphysics phenomena.

### Photon Interaction Event

The next section of the algorithm is to decide how the photon interacts with the medium, either via scattering or absorption. There are other interaction events that can occur, however descriptions of these are left for the chapters that detail these behaviours.

To decide whether a packet scatters or absorbs involves “throwing” a random number and comparing it against the albedo. The random number is compared to the albedo, and if the random number is less than the albedo then the packet scatters, otherwise the packet is absorbed.

## Packet Absorption

If the interaction event is a photon packet absorption, then the algorithm terminates the photon packets and starts the next photon packet, see [Termination](#).

## Packet Scattering

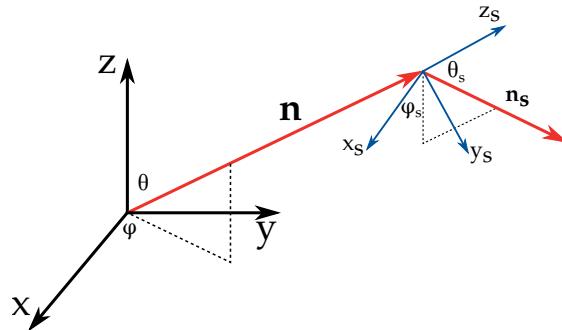
If the interaction event is a packet scattering, then the packet is scattered into a new direction and the above process are carried out until a termination clause is met, see [Termination](#).

Depending on the medium being simulated, it can either be isotropically or anisotropic scattered. For the isotropic case, new  $\theta$  and  $\phi$  angles are sampled uniformly, and the direction vectors set as in section [Photon Launch and Initialisation](#). For the case where the scattering is anisotropic the calculation of the scattering angles,  $\theta$  and  $\phi$ , is more complicated. The random sampling of the scattering angles,  $\theta$  and  $\phi$ , are valid in the “centre of mass” frame containing the scatter, incident and scattered particle. The photons position is updated in the lab frame, thus the direction vectors also have to be updated in the lab frame. This means that the scattering angles need to be rotated into the lab frame. For the isotropic case assume that the scattering is also isotropic in the lab frame, thus the new direction vector is easily calculated. However this is not the case for anisotropic scattering, as the centre of mass frame has to be rotated into the lab frame.

Figure 1.11 and Eq. (1.41) show how this process is achieved. Where  $\mathbf{n} = (n_x, n_y, n_z)$ ,  $\mathbf{n}_s = (n_x^{new}, n_y^{new}, n_z^{new})$ ,  $\theta_s$  is chosen from the phase function Eq. (1.42), and  $\varphi_s = 2\pi\xi$  with  $\xi$  being a random number in the range 0 to 1.

$$\begin{aligned} n_x^{new} &= \frac{\sin\theta_s}{\sin\theta} (n_x n_y \cos\varphi_s - n_y \sin\phi_s) + n_x \cos\theta_s \\ n_y^{new} &= \frac{\sin\theta_s}{\sin\theta} (n_y n_z \cos\varphi_s + n_x \sin\phi_s) + n_y \cos\theta_s \\ n_z^{new} &= -\sin\theta_s \cos\varphi_s + n_z \cos\theta_s \end{aligned} \quad (1.41)$$

$$\cos\theta_s = \frac{1 + g^2 - \left(\frac{1-g^2}{(1-g+2g\xi)^{3/2}}\right)^2}{2g} \quad (1.42)$$



**Figure 1.11:** Illustration of rotating the centre of mass frame to the lab frame.  $\mathbf{n}$  is the direction vector of the photon before scattering, and  $\mathbf{n}_s$  is the scattered direction vector.  $\theta$  and  $\varphi$  are the scattering angles.  $z_s$  is in the same direction as  $\mathbf{n}$ .

## Termination

The final section of the MCRT algorithm is to check if it should be terminated. This is a simple check to see if there are any more photons to run. If there are more photons to run then the algorithm goes back to the [Photon Launch and Initialisation](#) section and continues from there. If there are no more photons the algorithm terminates and any results are written out.

## Scored Quantities

As MCRT is a computational method, a wealth of information is able to be recorded during the simulation. From the paths of individual photons, to average scattering angles and more. However it is not practical to record all this information for every simulation, as this would lead to inefficient simulations, and expensive data storage solutions. Thus for a given problem only the pertinent information is stored.

One important recorded variable is fluence. Fluence is the number of photons entering a sphere per unit cross section area [2]. In practise the average fluence per area is used, Eq. (1.43), as this is easier to calculate in an MCRT code. Lucy showed that the average fluence per area is proportional to the sum of the path length through a volume [49]:

$$J_i = \frac{L}{NV_\zeta} \sum l \quad (1.43)$$

Where:

$J_i$  is the fluence or mean intensity [ $W m^{-2}$ ];

$L$  is the luminosity or power of the light source [ $W$ ];

$N$  is the total number of photon packets [-];

$V_\zeta$  is the volume of the  $\zeta^{th}$  voxel [ $m^3$ ];

and  $l$  is the path length of a photon packet through the  $\zeta^{th}$  voxel [ $m$ ].

The majority of the chapters in the thesis make use of Eq. (1.43) or modified versions of it as the main scored quantity.

Other common scored quantities are the exit location of a photon, the wavelength of an exiting photon or the distribution of photon packet absorption.

### 1.2.4 Code Details

The preceding section gave an overview of the algorithm and how it works. This section details the various code and implementation details such as how the code is parallelised.

#### Code

All code in this thesis is written in modern Fortran<sup>¶</sup>. All subroutines and functions are contained in modules (with the exception of the main program—mc polar.f90). This is done in order to be able to “hide” data from subroutines and functions, and to arrange the code that relates to other parts of the code in the same file. Having the code in modules also allows the use of runtime allocation of memory for arrays. This enables the user to specify the size of arrays depending on the need of the user for the problem at hand.

Modules are classified into three different modules types: data, routines and dependencies. Data modules are modules that contain no function or routines, but store variables that can be accessed anywhere in the program when required. Routine modules contain the subroutines

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<sup>¶</sup>modern Fortran is considered anything past Fortran 95 [50].

and functions used in the code. Finally dependency modules are the modules that have not been written by me, and thus the code depends upon them in order to run.

Figure 1.12 show the relationship between the various modules, for a basic version of the MCRT as described in [MCRT Algorithm](#).

Using Fig. 1.12 as a reference each module contains:

`mcpolar.f90` is the entry point of the code. It calls all other subroutines and functions, as well as setting up various variables and printing progress.

`ch_opt` is the module where the optical properties are set or changed.

`gridset_mod` is where the optical properties grid and voxel walls are set.

`subs` contains general purpose routines that are used in various different parts of the code.

`writer_mod` contains routines that write out the results of the simulation.

`inttau2` is the module that contains the routines that propagate the photon through the voxel grid.

`sourceph_mod` contains the routines that initialise the photon position and direction.

`stokes_mod` contains the routine that calculates the scattering direction after a scattering event.

`iarray` is a data module that contains all the arrays in the code.

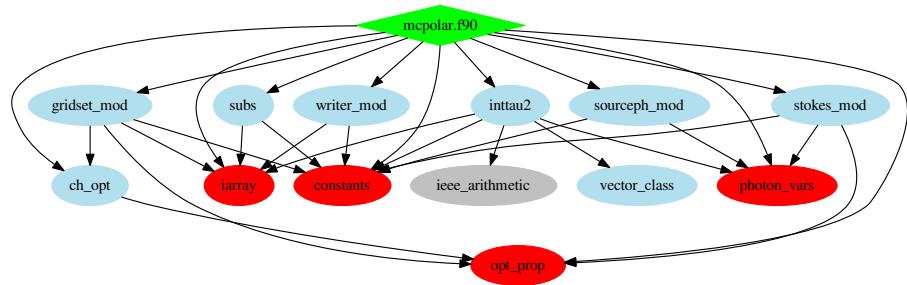
`constants` is a data module that contains all the constants and filepaths needed in the code.

`ieee_arithmetic` is an external dependency that gives various arithmetic checking routines such as `is_nan()`.

`vector_class` is a module that contains the vector type, and all its associated operation such as cross and dot products.

`photon_vars` is a data module that contains the data pertaining to each photon, such as wavelength or energy.

Finally, `opt_prop` contains the data about the current optical properties such as the albedo, and absorption coefficient.



**Figure 1.12:** Source code hierarchy, showing the relationship between different modules. Green is the entry point for the simulation. Red are the data modules, light blue are the routine modules, and grey are the external dependencies.

## Parallelisation of the MCRT Algorithm

As mentioned in the previous sections, MCRT can be computationally intensive, especially when dealing with highly scattering mediums. Fluorescence can also cause simulations times to dras-

tically increase as photons are no longer “killed” off, but rather re-emitted at a new wavelength. Other optical processes such as Raman scattering are highly unlikely events, which again can lead to a dramatic increase in simulation times, as many photons are required to be simulate in order to get “good” statistics.

Fortunately MCRT is classed as an “embarrassingly parallel” problem<sup>||</sup>. This means that it is trivial to parallelise in comparison to other algorithms. The reason that MCRT is classed as “embarrassingly parallel”, is that the algorithm can be split up onto separate processes, with little need for communication between them. In reality this means that  $n$  copies of the algorithm can run on  $n$  cores in a processor, with communication taking place at the start and end of each simulation run.

All the code in this thesis is parallelised using Message-passing interface (MPI) [52, 53], with the only communication taking place at the end, where the results are collated on to all process. The one exception to the is in Chapter 2, where the heat diffusion calculation needs communication between the process during the calculation.

The parallel efficiency of a code depends on the problem, and the number of photon packets run. To determine the speedup of a given problem Amdahl’s law is used [54]:

$$speedup = \frac{1}{(1 - P) + P/N} \quad (1.44)$$

Where  $P$  is the fraction of the code that is parallel, and  $N$  is the number of cores the code is run on. The consequence of Amdahl’s law is as  $N$  tends to infinity the speedup tends to a maximum:

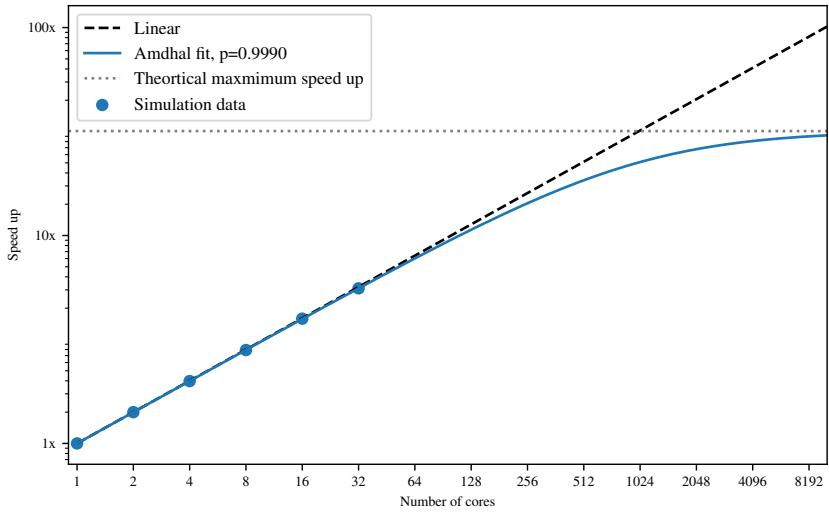
$$speedup_{max} = \frac{1}{1 - P} \quad (1.45)$$

The value of  $P$  varies from problem to problem, and the number of photon packets run. Figure 1.13 shows the results of the profiling of the code, for various numbers of cores. This test consisted of running the same number of photons, in a highly scattering medium of size  $2\text{ cm}^3$ . This yielded a  $P$  of  $0.999010 \pm 0.000045$ , and a maximum speedup of 1010.1.

There are other ways the code could be parallelised, including task farms and domain decomposition [55]. However these methods are more involved to set up and validate, so the simplest approach was taken.

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<sup>||</sup>However this is not true for all MCRT applications. For example, using the Bjorkman & Wood [51] immediate temperature corrections method, turns MCRT into a different class of parallel problem [11].



**Figure 1.13:** Performance of the parallelisation of the MCRT code using MPI.

### 1.3 Validation of MCRT Code

As the Monte Carlo method is an algorithm that depends upon random numbers, it is sometimes hard to ensure the correct result is obtained. Or to put it another way:

“Monte Carlo is easy to do wrong!” G.W. Collins III [56]

Thus the code has to be validated against various theoretical/experimental and other simulations, to determine whether the results are correct.

For the first test of a MCRT code, it is compared against a experimental expression, Eq. (1.46), for fluence as a function of depth [57]. This expression has also been matched by other MCRT simulations [58].

$$\Psi(z) = \Psi_0(C_1 e^{-k_1 z/\delta} - C_2 e^{-k_2 z/\delta}) \quad (1.46)$$

Where:

$\Psi(z)$  is the penetration of the excitation light, or equivalently the fluence rate [ $W\text{ cm}^{-2}$ ];

$\Psi_0$  is a normalisation constant [ $W\text{ cm}^{-2}$ ];

$C_n$  and  $k_n$  are fitted coefficients [-];

and  $\delta$  is the optical penetration depth, defined as  $\delta = 1/\sqrt{3\mu_a(\mu_a + \mu_s(1-g))}$ , [cm].

Jacques *et al.*, in their simulation used two different wavelengths, 420 nm and 630 nm. The medium in the simulation is a infinitely wide slab with a depth of 1 cm, with uniform optical properties. The medium has a refractive index of 1.38. The  $g$  value is in the range 0.7 – 0.9, and the optical properties are as in Table 1.1.

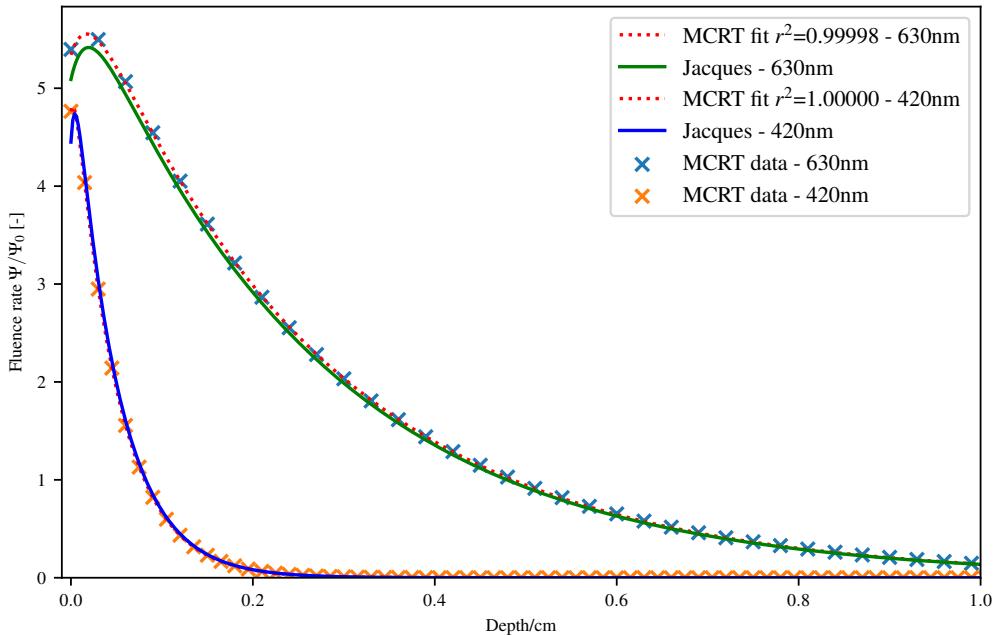
Using these values Jacques *et al.* calculated values for  $C_1$ ,  $C_2$ ,  $k_1$  and  $k_2$  using their MCRT code. The above optical properties and medium dimensions\*\* are recreated in the code and a value of 0.9 was chosen for  $g$ . 8 million photons were run for the simulation. This yielded the result as in Fig. 1.14.

---

\*\*The infinitely wide slab is implemented so that when a photon leaves the one of the sides of the voxel grid, it is moved to the other side of the grid, retaining its original direction vectors.

Wavelength/nm	Absorption $\mu_a/cm^{-1}$	Scattering $\mu_s(1-g)/cm^{-1}$	Penetration			$\delta/cm$	
	C1	k1	C2	k2			
420	1.8	82	5.76	1.00	1.31	10.2	0.047
630	0.23	21	6.27	1.00	1.18	14.4	0.261

**Table 1.1:** Table of optical properties and determined coefficients from Jacques *et al.* [58].



**Figure 1.14:** Figure shows the fluence as a function of depth. Figure also shows comparison to the Jacques MCRT simulation and the MCRT as described in this chapter.

Fitting Eq. (1.46) to the data calculated by our MCRT code for 630 nm, gave:  $C_1 = 6.425$ ,  $C_2 = 1.083$ ,  $k_1 = 1.0$ , and  $k_2 = 12.966$ . For 420 nm gave:  $C_1 = 5.600$ ,  $C_2 = 0.838$ ,  $k_1 = 1.003$ , and  $k_2 = 9.846$ . These are in good agreement with Jacques *et al.* results.

## 1.4 Conclusion

The Monte Carlo method relies on drawing random numbers in order to calculate unknown variables in problems. The Monte Carlo method can be used to calculate radiation transport in order to numerically solve the RTE. MCRT is the most flexible of the methods available to solve the RTE, allowing arbitrary geometries, light sources and turbid mediums. MCRT also allows the inclusion of various microphysics such as polarisation, Raman scattering and fluorescence. However the MCRT method does have the downside, that for some problems, many photon packets must be run in order to achieve a good signal to noise ratio. Though this is becoming less of an issue due to increased computational available capacity and MCRT being classed as an “embarrassingly parallel” problem, allowing it to be easily parallelised.

The algorithm covered in this chapter is the underpinning algorithm for this whole thesis, and validating it against experimental and simulation data from other authors. Each subsequent

chapter builds upon the algorithm in order to solve the problem at hand.

# Chapter 2

## Computational Modelling of Tissue Ablation

### 2.1 Introduction and Background

This chapter uses MCRT techniques coupled to a heat transfer simulation, to study the thermal damage to tissue due to a laser, with its power spread over many beams to leave viable tissue around zones of damaged/necrotic tissue [59]. This class of laser is called a fractionated ablative laser. This chapter presents experimental work carried out on porcine tissue by our collaborators at the University of Dundee and the photobiology department at Ninewells hospital, along side my computational model of tissue ablation.

Ablative lasers are used in a wide variety of medical procedures including: coagulating scalpels, port wine stain removal, tattoo removal, hair removal, and skin rejuvenation [60–64]. One class of laser used in these procedures are ablative lasers. Ablative lasers are usually high powered lasers ( $>30\text{ W}$ ) targeted at a specific chromophore in the skin, to partially or fully remove layers of skin. These types of lasers are commonly used for aesthetic procedures such as: skin rejuvenation [64], and removal of various diseases such as Rhinophyma [65] or lesions/nodules [66]. Ablative lasers have also been recently investigated as a means of better drug penetration into the skin for various therapies such as photo-dynamic therapy (PDT). The ablative laser “drills” holes in the skin, which allows topical treatments to better diffuse into the skin [67].

One downside to using lasers to remove tissue, is that unlike a scalpel where the surgeon has full control of the depth of the incision, ablative lasers are not as predictable. Lasers can cause thermal damage to the surrounding areas, leading to potentially unwanted effects, though some applications of ablative lasers utilise the thermal damage, particularly aesthetic procedures [68].

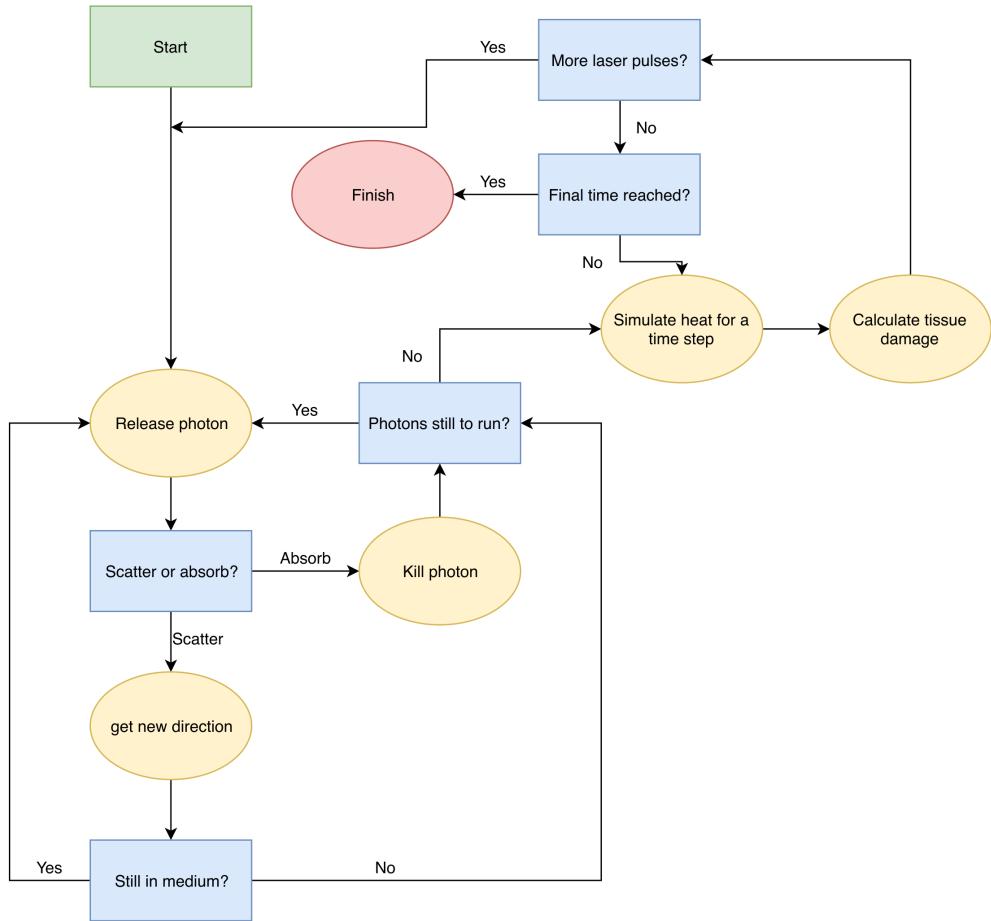
Currently the only reliable method to measure the depth of the ablative holes, is via a biopsy, which is an invasive procedure. In this work an optical coherence tomography (OCT) system is used to measure the ablative crater non-invasively *in-vivo*. The OCT measurements are then compared to a computational model developed as part of this project. It is hoped this computational model could be used to predict the depth of the ablative crater when using a certain laser power for various different applications such as: laser assisted drug delivery, and various cosmetic applications.

## 2.2 Methods

To replicate the experimental work *in silico*, the numerical model has three main portions. The first is the MCRT code that models light transport through tissue so that we can calculate the laser energy deposited as a function of time and space. The second, a finite difference method (FDM) which is used to calculate the heat diffusion within the tissue due to the absorbed laser energy. Finally, a tissue damage model to track the tissue damage caused by the laser. All these individual functions are connected together to create a full numerical model.

### 2.2.1 Monte Carlo radiation transport (MCRT)

MCRT is used here to calculate the energy deposited by the laser. This is then passed to the heat transport simulation, which calculates the heat diffusion in the medium. The algorithm for the three coupled simulations is presented in Fig. 2.1.



**Figure 2.1:** Flowchart of the tissue ablation algorithm.

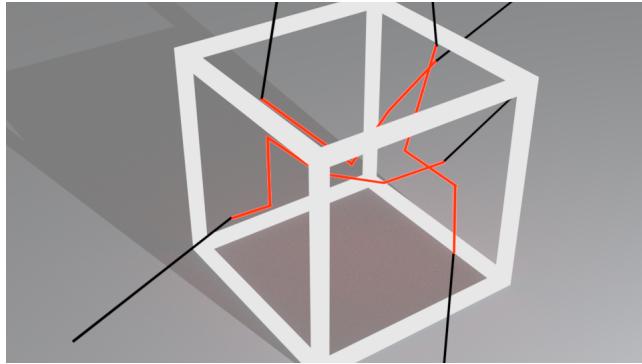
The MCRT algorithm is largely the same as described in Chapter 1, with some important adjustments.

The first adjustment is that the path length counter for fluence is changed to track absorbed energy. This is achieved by multiplying the pathlength in a voxel by the absorption coefficient of that voxel. Figure 2.2 show this process graphically, and Equation (2.34) shows the mathematical expression:

$$E_i^{abs} = \frac{P}{NV_i} \sum \mu_{a,i} s \quad (2.1)$$

Where:

- $E_i^{abs}$  is the energy absorbed in the  $i^{th}$  voxel [ $J s^{-1} m^{-3}$ ];
- P is power [W];
- N is the number of packets, representing a power, P;
- $V_i$  is the volume of the  $i^{th}$  voxel [ $m^{-3}$ ];
- $\mu_{a,i}$  is the absorption coefficient of the  $i^{th}$  voxel [ $cm^{-1}$ ];
- and s is the pathlength of a packet through the  $i^{th}$  voxel [cm].



**Figure 2.2:** Red lines are packet paths within a voxel. Black lines packet paths out with the voxel. Red packet paths, weighted by  $\mu_a$ , are summed up to calculate the absorbed energy within each voxel.

This grid of absorbed energy is then passed to the heat transport portion of the simulation, so that the heat diffusion in the porcine tissue can be calculated.

The next adjustment to the MCRT algorithm, is that the MCRT algorithm is run for every heat simulation time step, as the medium could change at every time step due to the optical, and thermal properties changing as a function of tissue damage.

Finally, to match the experiment undertaken the medium and laser for the *in-silico* experiments must match the practical experiments. As the laser used in the experiments emits an infra-red wavelength ( $10.6 \mu m$ ), the optical properties are dominated by the water content of the tissue. Due to this it is assumed that there is just absorption in the medium, with no scattering. Further discussion can be found in Section 2.3.1. The laser in some of the *in silico* modelling, has multiple beams and the source photon packet routine is adjusted to accommodate this when needed.

## 2.2.2 Heat Transport

The diffusion of heat can be modelled using the heat equation (Eq. (2.2)), which is derived from Fourier's law and the principle of conservation of energy [69]. The standard heat equation is a partial differential equation of the parabolic form. Solutions and analytical methods are readily

available for lower dimensions (i.e. 1D heat diffusion), but for higher dimensions, numerical models must be used for all except the simplest problems. The simplest form of the heat equation is shown below:

$$\rho c_p \frac{\partial T}{\partial t} = \nabla \cdot (\kappa \nabla T) + \dot{q} \quad (2.2)$$

Where:

- $T(x, y, z, t)$  is the temperature as a function of time and space [K];
- $\kappa$  is the thermal conductivity [ $Wm^{-1}K^{-1}$ ];
- $\rho$  is the density [ $Kgm^{-3}$ ];
- $c_p$  the specific heat capacity [ $JK^{-1}$ ];
- $\dot{q}(x, y, z, t)$  is the source/sink term as a function of time and space [ $Wm^{-3}$ ].

Equation (2.2) is for a homogeneous system where the thermal properties do not change as a function of time, space and temperature. However in order to model a moving ablation front the nonlinear heat equation must be used, where the thermal properties can be a function of time, space and temperature (Eq. (2.3)).

$$\frac{\partial T}{\partial t} = \frac{1}{(\rho c_p)_\xi} (\nabla k_\xi T + k_\xi \nabla^2 T) + \dot{q}, \quad \text{where } \xi = (i, j, k) \quad (2.3)$$

Included in Eq. (2.3) is a source and sink term,  $\dot{q}$  to allow the modelling of heat loss/gain from external sources/sinks. The heat source in this simulation is due to the laser, and it is assumed that the only loss of heat to the surrounding medium is via conduction.

The medium is considered to be at a constant temperature of 5°C, as the porcine skin was kept cooled prior to experimental work and the simulation volume is smaller than the porcine tissue samples.

Where:

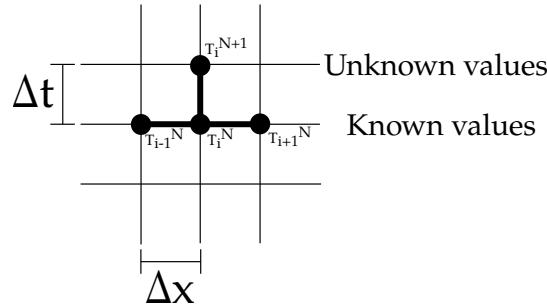
- $h$  is the heat transfer coefficient [ $Wm^{-2}K$ ];
- $A$  is the area of the grid element, that is radiating/convicting heat away [ $m^{-2}$ ];
- and  $T$ , and  $T_\infty$  are the temperature in a voxel and the surrounding medium temperature respectively [K].

As Eq. (2.3) is generally hard to solve in arbitrary geometries with complex boundary conditions a numerical method is employed to solve it. The numerical method employed is a FDM, derived from the Taylor series, see Eq. (2.4).

A function  $f(x)$  is discretised onto a grid with  $N$  nodes a distance  $\Delta x$  apart. Equation (2.4) is then truncated and rearranged and it is assumed that the remainder term  $R_1$  is sufficiently small enough, to yield an approximation for the first derivative of a function  $f(x)$  at a point  $x_0 + \Delta x$ , see Eq. (2.5). Equation (2.5) is the so called forward difference, due to it using a point in the ‘forward’ direction. The “backward” and central difference terms can be calculated by using a node at  $x_0 - \Delta x$  for the backward difference Eq. (2.6b). The central difference ( Eq. (2.6c)) is an average of the forward and backwards differences. Expressions can also be given for the 2<sup>nd</sup> derivatives for backward, forward and central (forward and backward 2<sup>nd</sup> order equations omitted for brevity) Eq. (2.6d).

$$f(x_0 + \Delta x) = f(x_0) + \frac{f'(x_0)}{1!} \Delta x + \frac{f''(x_0)}{2!} \Delta x^2 + \dots + \frac{f^{(n)}(x_0)}{n!} \Delta x^n + R_n(x) \quad (2.4)$$

$$f'(x_0) \approx \frac{f(x_0 + \Delta x) - f(x_0)}{\Delta x} \quad (2.5)$$



**Figure 2.3:** Finite difference method stencil for simple explicit scheme

$$\frac{df}{dx} = \frac{f_{i+1} - f_i}{\Delta x} \quad (\text{forward}) \quad (2.6a)$$

$$\frac{df}{dx} = \frac{f_i - f_{i-1}}{\Delta x} \quad (\text{backward}) \quad (2.6b)$$

$$\frac{df}{dx} = \frac{f_{i+1} - f_{i-1}}{2\Delta x} \quad (\text{central}) \quad (2.6c)$$

$$\frac{d^2f}{dx^2} = \frac{f_{i-1} - 2f_i + f_{i+1}}{\Delta x^2} \quad (\text{central}) \quad (2.6d)$$

Thus the linear heat equation Eq. (2.2), in 1D, taking a 1<sup>st</sup> order forward time derivative, and a 2<sup>nd</sup> order central spatial derivative gives:

$$\frac{T_i^{n+1} - T_i^n}{\Delta t} = \alpha \frac{T_{i-1}^n - T_i^n + T_{i+1}^n}{\Delta x^2} + \frac{\dot{q}}{\rho c_p} \quad (2.7a)$$

$$T_i^{n+1} = \alpha \Delta t \frac{T_{i-1}^n - 2T_i^n + T_{i+1}^n}{\Delta x^2} + \frac{\Delta t \dot{q}}{\rho c_p} \quad (2.7b)$$

Where  $\alpha = \frac{\kappa}{\rho c}$ .

Equation (2.7b) is called the “simple explicit form of finite-difference approximation” [70]. Figure 2.3 shows the “stencil” of this scheme, where there are three known points at time  $N$ , and just one unknown at time  $N+1$ . There are various other schemes that can be used to calculate the temperature at the next time step. However a simple explicit scheme is used here, due to its ease of implementation despite there being a constraint on the stability in comparison to an implicit method. This method is also easily scaled up to 3D with little difficulty.

For the more complicated nonlinear heat equation there is a possibility that the medium is not continuously smooth between nodes, in terms of optical and thermal properties. The two easiest methods [70] of achieving this are: (1), lag the value behind by one step, i.e  $c_p^{n+1} = c_p^n$ . (2), average  $\kappa$ ,  $\rho$ , and  $c_p$  using a half difference scheme where the thermal property used in the calculation is the thermal property half way between two nodes, i.e the average of the two nodes:

---

\*For brevity  $f(x_0 + \Delta x)$  is defined as  $f_{i+1}$ , and  $f(x_0 - \Delta x)$  as  $f_{i-1}$ , etc.

$$\kappa^\pm = \frac{\kappa_i + \kappa_{i\pm 1}}{2} \quad (2.8)$$

$$\rho^\pm = \frac{\rho_i + \rho_{i\pm 1}}{2} \quad (2.9)$$

$$c_p^\pm = \frac{c_{p,i} + c_{p,i\pm 1}}{2} \quad (2.10)$$

Thus for the simple 1D case as in Eq. (2.7b), the thermal properties are averaged between nodes when computing the coefficients of the temperature nodes, and lag the thermal properties when adding the heat from the laser:

$$T^{N+1} = \Delta t (AT_{i-1}^N - 2BT_i^N + DT_{i+1}^N) + T_i^N + \frac{\Delta t}{\rho c_p} q_L \quad (2.11)$$

Where (in the  $x$  direction):

$$\begin{aligned} A &= \frac{\kappa^-}{\rho^- c_p^- 2\Delta x^2} \\ B &= \frac{\kappa^+}{\rho^+ c_p^+ 2\Delta x^2} \\ D &= \frac{(A + B)}{2} \end{aligned} \quad (2.12)$$

Equation (2.11) is straightforward to generalise to higher dimensions. The 3D case gives:

$$U_{xx} = (AT_{i-1,j,k}^N - 2BT_{i,j,k}^N + DT_{i+1,j,k}^N) \quad (2.13)$$

$$U_{yy} = (AT_{i,j-1,k}^N - 2BT_{i,j,k}^N + DT_{i,j+1,k}^N) \quad (2.14)$$

$$U_{zz} = (AT_{i,j,k-1}^N - 2BT_{i,j,k}^N + DT_{i,j,k+1}^N) \quad (2.15)$$

$$T_{i,j,k}^{N+1} = \Delta t (U_{xx} + U_{yy} + U_{zz}) + T_{i,j,k}^N + \frac{\Delta t}{\rho c_p} q_L \quad (2.16)$$

Where:

$T_{i,j,k}^{N+1}$  is the new temperature at node  $i, j, k$  [K];

$T_{i,j,k}^N$  is the temperature at node  $i, j, k$  at the current time step [K];

$\alpha$  is the thermal diffusivity [ $m^2 s^{-1}$ ];

$\kappa$  is the thermal conductivity [ $W/mK$ ];

$\Delta x$  etc. is the size of the grid element in the  $p^{th}$  direction [m];

and  $A, B, D$  are the coefficients in their respective dimension (Eq. (2.12)).

Equation (2.16) gives the full numerical solution to the nonlinear heat equation with a laser heat source. This will allow the calculation of the heat diffusion in the porcine tissue due to laser heating.

As the laser used in the experimental work, operates in a pulsed mode, this is accounted for this in the simulation. The laser pulse shape is a triangular pulse, with the peak power,  $P_{peak}$ , and pulse length,  $\tau$  [71]. In the heat simulation there has to be an additional variable in the term  $laserOn(t) \cdot \frac{\alpha \Delta t}{\kappa} q_L$  in Eq. (2.16). This additional variable,  $laserOn(t)$ , is a boolean value and a function of time, which is defined as:

$$laserOn = \begin{cases} 1, & \text{Laser on} \\ 0, & \text{Laser off.} \end{cases}$$

In the instance where there is a train of laser pulses, the laser is turned on and off based upon the pulse frequency.

Due to a simple explicit FDM being used, the time step is constrained in order to make the solution stable. For a cubic 3D FDM without prescribed flux boundary conditions, this yields the constraint:  $\Delta t \leq \frac{1}{\delta_\alpha}$  where  $\delta = \frac{1}{\Delta x^2} + \frac{1}{\Delta y^2} + \frac{1}{\Delta z^2}$ . Along with this time constraint, the pulse length of the laser also has to be considered. If the time step of the heat simulation is too large it will not account for the heat deposited by the laser. Thus, the timestep has to be at least an order of magnitude smaller than the shortest laser pulse.

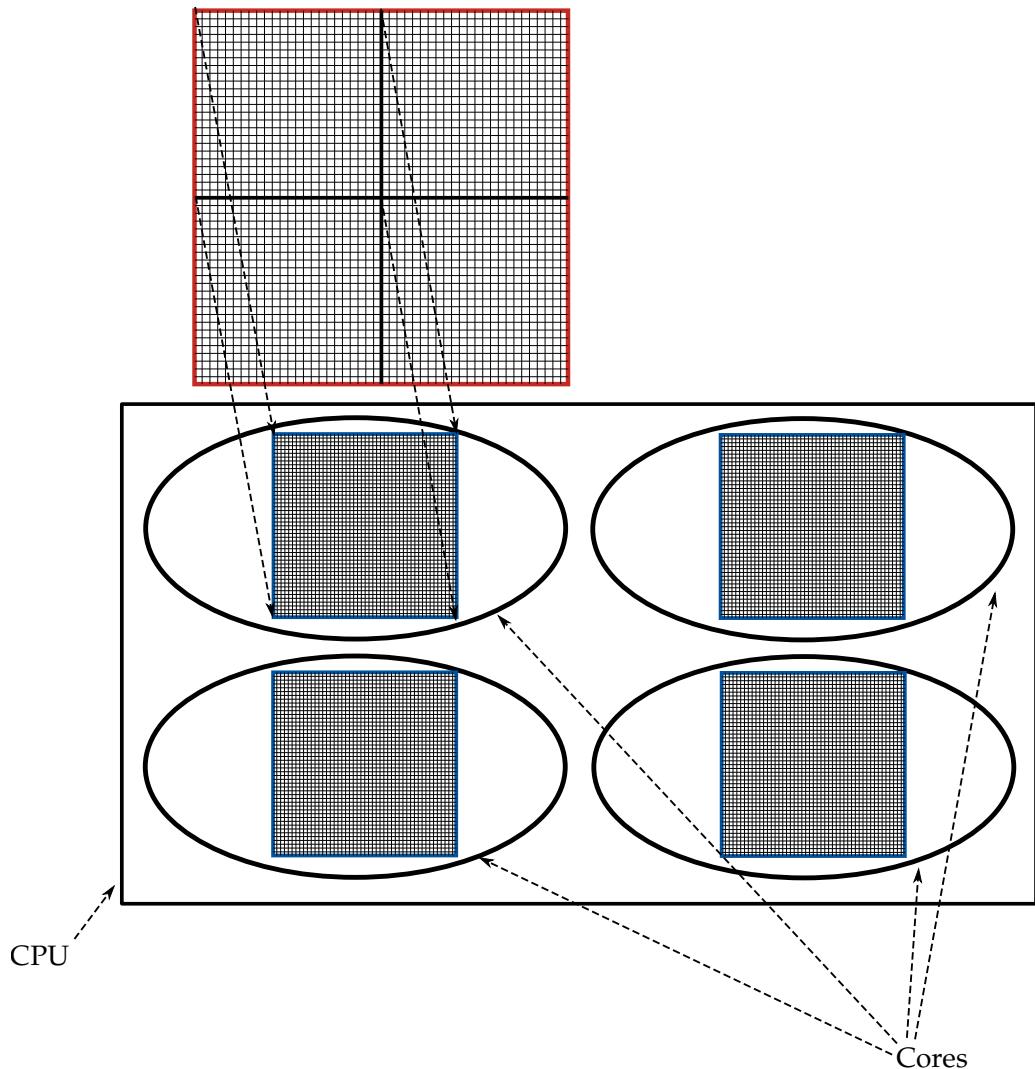
As the time step is small, and the grid resolution large, the resultant simulation is slow. Thus the code has been fully parallelised to improve performance. Both the MCRT and heat simulation are independently parallelised.

Parallelisation of the heat simulation is more involved than the “embarrassingly parallel” class of problems where MCRT belongs. This is due to the heat simulation being dependent on neighbouring nodes to update the temperature at the current node. Thus if the medium were to be split up on to separate cores, there would have to be communication between the cores, in order for the simulation to be completed successfully. Therefore it is not possible to take the ‘easy’ route of running the simulation concurrently  $N$  times and collating the result at the end of all the simulations.

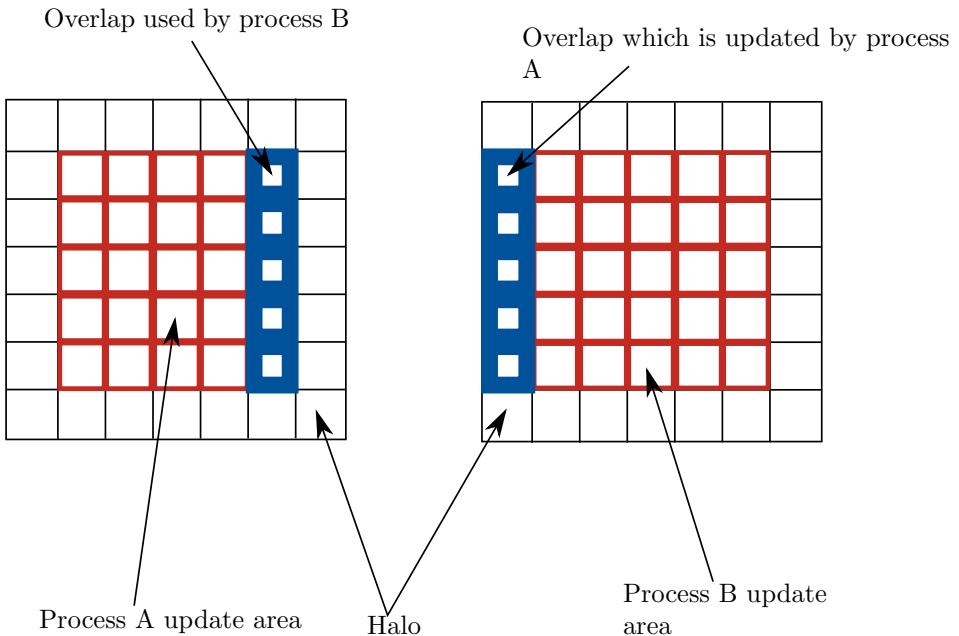
The heat simulation is parallelised using a technique called “halo swapping”. This involves splitting up the computational domain (see Fig. 2.4), in this case the tissue medium, and doing the calculations on each domain on a separate core. The “halo swapping” comes in when cores need to communicate with each other about updating their boundary temperature nodes (see Fig. 2.5).

Figure 2.6 shows the speed up gained from using the technique. The “halo swapping” technique is efficient for situations where the computational domain can be split up with large ‘chunks’ being calculated on each core. However if the computational domain is small, and the number of cores large then bottlenecks occur due to too much communication between cores taking place. Thus to efficiently use ‘halo swapping’ careful thought has to be given to the size of the computational domain, and the number of cores running the simulation. Evidence of this bottlenecking can be seen in Fig. 2.6 for problems where the size of the grid, in voxels, is  $40^3$  and  $24^3$ . These problems also show superlinear speed up, for certain number of cores. This is not unfeasible, due to a number of reasons, in particular the underlying computer architecture [72].

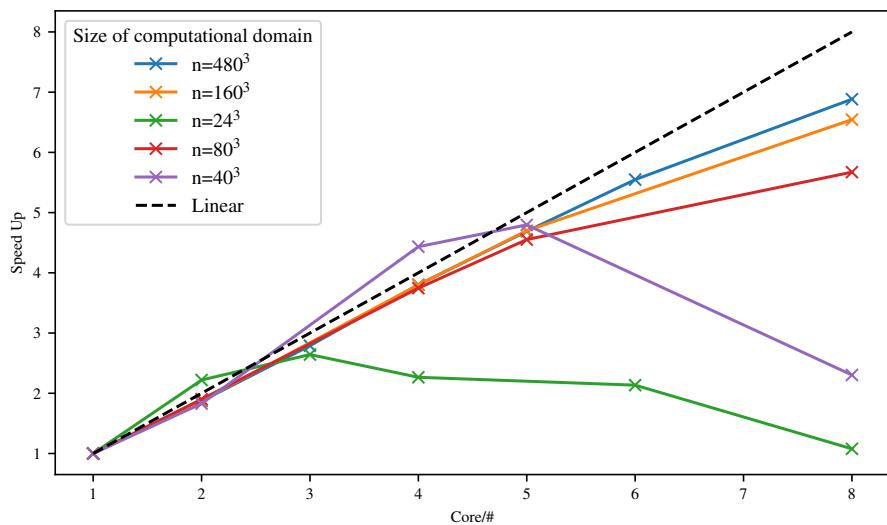
After one time step of the heat simulation has been completed, the temperature grid is passed to the tissue damage portion of the simulation to calculate the tissue damage that may have accrued during the heat simulation time step.



**Figure 2.4:** Computational domain decomposition. Total computational domain (red outline) is evenly divided between cores in the CPU. This is done via layers of the domain in the  $z$  direction. Information is passed to/from cores via the “halo swap” process (see Fig. 2.5).



**Figure 2.5:** Halo swapping. Process A updates the area in red and blue on the left. It updates the blue area which is sent to process B as B's "halo". Process B cannot update its own halo, but rather updates the halo for process A.



**Figure 2.6:** Figure show the speed up gained by parallelisation of the heat simulation using the "halo" swapping technique, for various sizes of computational domain (voxels). Data taken from a Intel Xeon E3-1245 v5, 8 cores @ 3.5GHz machine.

### 2.2.3 Tissue Damage

#### Introduction

The final portion of the simulation is the tissue damage model. To be able to model damage to the tissue, the process tissue undergoes upon heating due to the laser needs to be able to be described.

When the laser is turned on, the temperature starts to rise within the tissue due to the absorption of photons by the tissue. The temperature rise causes damage to the tissue when above a threshold temperature,  $T_d$ , approximately  $43^\circ\text{C}$  [73]. From the temperature,  $T_d$ , four main areas of tissue damage are defined:

$$T = \begin{cases} \text{coagulation}, & T_d \leq T \leq 100^\circ\text{C} \\ \text{water boils}, & T = 100^\circ\text{C} \\ \text{carbonisation}, & 100^\circ\text{C} \leq T \leq T_a \\ \text{ablation}, & T = T_a. \end{cases} \quad (2.17)$$

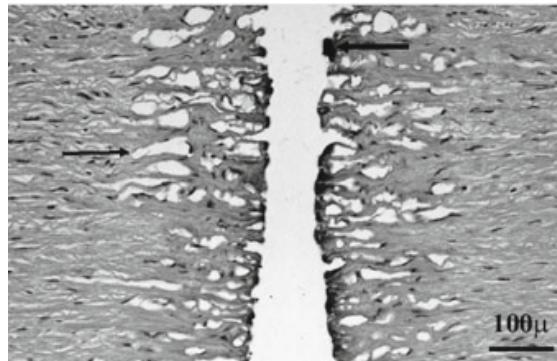
The area of tissue damage termed “coagulation” is a multifaceted process. At  $43^\circ\text{C}$  -  $50^\circ\text{C}$ , bonds break within cell membranes, causing ruptures, and some cell death [73, 74]. This process is usually termed *hyperthermia*. Around  $50^\circ\text{C}$ , enzyme activity decreases, cells become immobile, and various cell repair mechanisms are disabled, leading to increased cell death. When temperatures exceed  $60^\circ\text{C}$ , proteins become denatured. Thermal denaturation is a structural and functional change in a protein due to the heating it undergoes. This means they change from a highly organised structure with specific purposes, to disorganised structures with little to no function at all [75].

The next stage in the tissue damage process is the vaporisation of water. As the temperature of the tissue starts to approach  $100^\circ\text{C}$  (at 1 atm), water starts to vaporise. If the vaporised water cannot escape the tissue it forms steam vacuoles, small pockets of steam. These vacuoles can easily been seen when viewing tissue samples after tissue has been treated with a high powered laser (see Fig. 2.7). In certain conditions these steam pockets can explode [76].

The third stage of tissue damage is carbonisation of the tissue. This occurs when most of the water has boiled off, leaving the remaining tissue to heat up and reduce to its elemental carbon form. This carbonisation of tissue, when it occurs, is generally only a thin layer of 5-20  $\mu\text{m}$  [73, 77].

The final stage of tissue damage is the removal of the remaining tissue, i.e tissue ablation. There is no agreement in the literature how tissue undergoes ablation with a number of methods proposed. The three main methods are: photochemical, thermal, and explosive [78–80]. Photochemical ablation is when the energy of a photon from the irradiating laser, is sufficient enough that it excites the electronic state of the tissues molecules into an anti-boding state, leading to broken bonds and conversion from electronic energy into kinetic energy, and thus ablation. Thermal ablation is where tissue is heated sufficiently so that tissue vaporisation takes place. Finally, explosive ablation is an extreme version of thermal ablation. Explosive ablation occurs when large amounts of energy is deposited in a small time scale, so that none of the energy can thermally diffuse away, resulting in explosive ablation. Photochemical ablation, is usually applied to UV laser ablation, whereas thermal and explosive ablation regimes are the more likely candidates for IR ablation which is considered here.

The theoretical models behind explosive and thermal ablation models are also not well understood, with many models proposed in order to try to and explain experimental results. These models range from heuristic models to sophisticated models that relate the underlying physical mechanisms to ablation damage. The two main heuristic models are: the blow off model, and



**Figure 2.7:** Ablation of a dog aorta, as viewed under a microscope. Steam vacuoles are clearly visible either side of the ablation area. Carbonisation is also evident at the edges of the ablation fronts. Adapted from [73].

the steady state model. The blow off model, assumes that there is thermal confinement (i.e no propagation of heat in time  $t$ ), that material is removed after the laser irradiation. There is a radiant threshold that has to be met in order to ablate material, and that Beer-Lambert's law describes the spatial distribution of light. For laser pulses of  $< 10$  ns, these conditions are normally met. However for lasers with pulse length larger than this, these conditions are not usually met [81–83].

The steady state heuristic model, assumes that the pulse length is of the order of  $ms$  or larger, that material starts to be removed shortly after laser irradiation begins, and that some radiant threshold exists in order for ablation to begin. The steady state model also assumes that a fixed energy is required to remove a unit of tissue [81]. However this does not always hold, as there are many circumstances where there is no one fixed energy, but rather many energies (due to various phase changes) that must be met in order for ablation to occur. There are also many other sophisticated models, that try to describe what happens physically when ablation occurs [84–86].

Due to the above mentioned reasons, there is no defined ablation temperature. The literature however, does suggest that it takes place when the tissue temperature is between 177 °C and 500 °C [85, 87, 88].

To model all these tissue damage processes the tissue damage model is split into two sections: “physical” damage and coagulation damage. “Physical” damage changes the tissue optical and thermal properties. Coagulation damage has no effect on the tissue’s bulk optical or thermal properties.

### Modelling coagulation damage

With the description of the various process that tissue undergoes during ablation, a numerical model of these processes can be created. First, in order to model the full extent of the damage done under 100°C, i.e in the coagulation regime, the Arrhenius damage model is used. The Arrhenius damage model was originally used as a kinetic model of reaction products in chemistry [89]. It has since been adapted by various authors for modelling tissue damage, and is the *de facto* standard [90, 91]. These authors and various others, adapted this model by fitting Eq. (2.18) to experimental data for burn damage. The two parameters fitted are  $A$ , the frequency factor, and  $\Delta E$ , the activation energy.

$$\Omega(t) = \int_{t_i}^{t_f} Ae^{(-\frac{\Delta E}{RT})} d\tau \quad (2.18)$$

Where:

- $\Omega$  is the damage value [-];
- A is “frequency factor” [ $s^{-1}$ ];
- $\Delta E$  is activation energy [ $Jmol^{-1}$ ];
- R is the universal gas constant [ $Jmol^{-1}K^{-1}$ ];
- T is the temperature [K];
- and  $t_i$  and  $t_f$  are the initial time and final time at  $t_{crit}$ .

It is reported that a value of  $\Omega$  of 0.53, 1.0, and  $10^4$  relate to first, second, and third degree burns respectively [92]. The Arrhenius damage model is used to better understand the amount of damage caused by the laser in the non-ablated areas of tissue. Values of  $A = 3.1 \times 10^{98}$  and  $\Delta E = 6.3 \times 10^5$  are adopted [88, 90, 93].

### Modelling physical tissue damage

As tissue mostly consists of water [94] when the temperature of the tissue approaches  $100^\circ C$  (at 1 atm), water in the tissue begins to boil off. This acts as a large heat sink for the absorbed laser energy, slowing down the rate of ablation. The energy required to boil the water is  $Q_{vapor} = m_v \cdot L_v$ , where  $m_v$  is the mass of a voxel, and  $L_v$  is the latent heat of vaporisation. The energy to boil off the water is provided via the laser and heat diffusing into the voxel:

$$Q_{vapor} = \underbrace{laserOn(t) \cdot \dot{q} \cdot \Delta t \cdot V_{i,j,k}}_{\text{laser heating}} + \underbrace{c \cdot M_{i,j,k} \cdot \Delta T}_{\text{heat diffusion}} \quad (2.19)$$

Where:

- $Q_{vapor}$  is the current energy in Joules that has been used to boil off the water in the voxel [J];
- $laserOn$  is a boolean variable that determine if the laser is on or off [-];
- $\dot{q}$  is the energy absorbed by the voxel due to the laser [ $Wm^{-3}$ ];
- $\Delta t$  is the timestep [s];
- $V_{i,j,k}$  is the volume of the voxel labelled  $i, j, k$  [ $m^3$ ];
- $c$  is the heat capacity of the voxel [ $JK^{-1}$ ];
- $M_{i,j,k}$  is the mass of the voxel labelled  $i, j, k$  [ $kg$ ];
- and  $\Delta T$  is the change in temperature the voxel would undergo, if the water was not boiling off.

As water boils off, the water content of each voxel changes. This affects the absorption coefficient, density, thermal conductivity, and heat capacity. Each of these vary with water content per voxel [95];

$$W = W_{init} - \left( W_{init} \cdot \left( \frac{Q_{current}}{Q_{vaporisation}} \right) \right) \quad (2.20)$$

$$\rho = \frac{1000}{W + 0.649 \cdot P} \quad (2.21)$$

$$c_p = 4.2 \cdot 10^3 \cdot W + 1.09 \cdot 10^3 \cdot P \quad (2.22)$$

$$\kappa = \rho \cdot (6.28 \cdot 10^{-4} \cdot W + 1.17 \cdot 10^{-4} \cdot P) \quad (2.23)$$

$$\mu_a = W \cdot \mu_{water} + \mu_{protein} \quad (2.24)$$

$$(2.25)$$

Where:

$W$  is the water content (i.e  $W = 0.7$  equates to 70% water content);

$W_{init}$  is the initial water content;

$Q_{current}$  is the total energy absorbed by the  $i^{th}$  voxel since the temperature reached 100°C [J];

$P$  is the protein content (i.e  $P = 1.0 - W$ );

$\kappa$  is the Thermal conductivity [ $Wm^{-1}K^{-1}$ ];

$c_p$  is the heat capacity [ $Jkg^{-1}K^{-1}$ ];

and  $\mu_a$  is the total absorption coefficient, and  $\mu_{water}$  and  $\mu_{protein}$  are the absorption coefficients of water and protein respectively.

$T_a$  is defined as occurring between 177 and 500 °C [85, 87, 88]. At  $T_a$  the tissue is removed and the thermal, optical, and physical properties set to that of air.

The updated damaged tissue structure is then fed back to the MCRT model and the whole process repeats until the predefined time limit is reached. This whole process of photon propagation, heat diffusion and tissue damage is outlined in Fig. 2.1.

## 2.2.4 Validation

### Heat transport validation

To thoroughly validate the numerical method employed to solve the heat equation, the numerical method is compared against an easily solvable analytical case. The heat equation is solved on a cube, side  $L$ , in a surrounding medium of 0°C. The cube is initially at temperature 20°C and the temperature is calculated at various times. Thus the boundary conditions are:

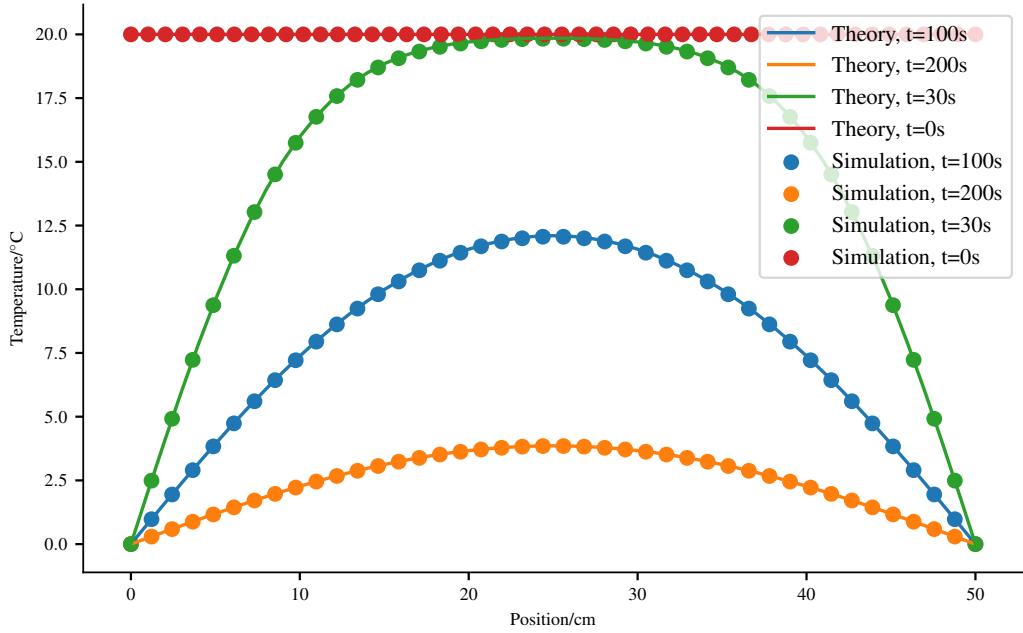
$$T(0, y, z, t) = T(x, 0, z, t) = T(x, y, 0, t) = 0^\circ\text{C} \quad (2.26)$$

$$T(L, y, z, t) = T(x, L, z, t) = T(x, y, L, t) = 0^\circ\text{C} \quad (2.27)$$

The thermal diffusivity ( $\alpha$ ), density ( $\rho$ ), and heat capacity ( $c_p$ ) are all set to 1. This corresponds to a material which has the thermal diffusivity between copper and aluminium [96, 97]. Assuming a separable solution in Cartesian coordinates yields:

$$\begin{aligned} T(x, y, z, t) = & (A_1 \cos(\alpha x) + A_1 \sin(\alpha x)) \cdot \\ & (B_1 \cos(\beta y) + B_1 \sin(\beta y)) \cdot \\ & (C_1 \cos(\gamma z) + C_1 \sin(\gamma z)) \cdot e^{-\alpha \mu^2 t} \end{aligned} \quad (2.28)$$

$$\mu^2 = \alpha^2 + \beta^2 + \gamma^2 \quad (2.29)$$



**Figure 2.8:** Temperature of the cube for various times, comparing between analytical solution and numerical method.

Applying the boundary conditions (Eqs. (2.26) and (2.27)) gives:

$$A_1 = B_1 = C_1 = 0 \text{ and } \alpha = \frac{\pi n}{L}, \beta = \frac{\pi m}{L}, \gamma = \frac{\pi p}{L} \quad (2.30)$$

$$\therefore T_{nmp}(x, y, z, t) = A_{nmp} \cdot \sin\left(\frac{\pi nx}{L}\right) \cdot \sin\left(\frac{\pi my}{L}\right) \cdot \sin\left(\frac{\pi pz}{L}\right) \quad (2.31)$$

This yields the following solution for the heat equation using the principle of superposition, and solving Eq. (2.32) with  $f(x, y, z)$  as the initial temperature profile of the cube:

$$A_{nmp} = \frac{8}{L^3} \int_0^L \int_0^L \int_0^L f(x, y, z) \cdot \sin\left(\frac{\pi nx}{L}\right) \cdot \sin\left(\frac{\pi my}{L}\right) \cdot \sin\left(\frac{\pi pz}{L}\right) dx \cdot dy \cdot dz \quad (2.32)$$

$$T(x, y, z, t) = \sum_{n=1,3,\dots}^{\infty} \sum_{m=1,3,\dots}^{\infty} \sum_{p=1,3,\dots}^{\infty} \frac{2368}{\pi^3 nmp} \cdot \sin\left(\frac{\pi nx}{L}\right) \cdot \sin\left(\frac{\pi my}{L}\right) \cdot \sin\left(\frac{\pi pz}{L}\right) \cdot e^{(-\lambda^2 t)} \quad (2.33)$$

Where:

$$\lambda^2 = \alpha\pi^2\left(\frac{n^2}{L^2} + \frac{m^2}{L^2} + \frac{p^2}{L^2}\right);$$

$n, m, p$  are odd integers;

and  $L$  is the length of the cube.

A slice through the middle of the cube,  $L = 50 \text{ cm}$ , yields Fig. 2.8, which shows that the numerical method matches the analytical solution closely.

## MCRT & heat transport validation

As a first test of the code, both MCRT and heat simulation, is compared to a simple analytical model of ablation. The simple model of ablation is as: The ablation energy ( $E_a$ ), is defined as the minimum energy required to raise the temperature of the medium to 100 °C, and then boil off the water in a volume  $dV$ , mass  $M$ . Thus in one dimension Eq. (2.34), where the symbols have their usual meanings. If the energy for ablation is delivered in a time  $dt$  by a laser of intensity ( $W\text{cm}^{-2}$ ),  $P$ , this gives Eq. (2.35). Equation (2.35) can be rearranged in order to give an ablation front velocity, Eq. (2.36).

$$E_a = c_p \rho dx \Delta T + L_v \rho dx \quad (2.34)$$

$$P \cdot dt = \rho dx (c_p \Delta T + L_v) \quad (2.35)$$

$$u = \frac{P}{\rho(c_p \Delta T + L_v)} \quad (2.36)$$

Assuming the ablation front moves with constant velocity during the ablation, and using  $L_v = 2.53 \cdot 10^6 \text{ Jkg}^{-1}$ ,  $c_p = 4181 \text{ J} \cdot \text{kg}^{-1} \cdot \text{K}^{-1}$  and the medium is a cube side 2 mm, with a starting temperature is 37 °C with a water content of 70% giving a density of  $700 \text{ kg} \cdot \text{m}^{-3}$ . For these parameters this gives an ablation velocity,  $u \simeq 0.77 \text{ cm} \cdot \text{s}^{-1}$ , and a time to ablate through 2 mm of tissue of  $\simeq 0.26 \text{ s}$ . As the code developed in this chapter simulates the diffusion of heat in a medium due to an incident laser, the expected time to ablate through the same medium should be slightly larger as heat diffuses away from the voxel while it is being heated. When the full heat + MCRT code is used to simulate this experiment, it gives a time,  $t \simeq 0.33 \text{ s}$ .

## 2.3 *In silico* results

### 2.3.1 Introduction

To match the experimental results, an accurate model of the experimental setup *in silico* must be created. However due to computational constraints, such as memory and time available, some approximations to the experimental set-up have to be made. The porcine skin was a large thin slice of the top most layers of the skin. However as the area of interest is where the ablation occurs, initially the porcine skin is modelled as a cuboid, dimensions:  $1.1 \times 1.1 \times 0.5 \text{ cm}$ . The initial temperature of the porcine skin is assumed to be around 5°, as the tissue was kept on ice or was kept cooled. As mentioned in the previous sections, there are several unknowns in the model:  $T_a$ , water content, temperature of air after ablation, and the exact thermal and optical properties of the porcine tissue. Therefore several models are run so that the full parameter space of these unknowns can be explored. Results from these *in silico* experiments are presented in this section along with a comparison of the model to the experimental work carried out in collaboration with the University of Dundee and the Photobiology department at Ninewells hospital.

### Optical & thermal properties

The thermal and optical properties of porcine tissue are not known exactly for any given tissue sample. As such the thermal and optical properties used in this section are taken from various literature sources.

The laser used in the experimental work is a CO<sub>2</sub> laser operating at 10.6  $\mu\text{m}$ . This means that the optical properties of the tissue are dominated by water absorption. The laser used in the experiment is the Pixel CO<sub>2</sub> [98]. The Pixel CO<sub>2</sub> laser has a wavelength 10.6  $\mu\text{m}$  which

	Thermal conductivity, $\kappa$	Density, $\rho$	Heat capacity, $c$
Tissue	$\rho \cdot (6.28 \cdot 10^{-4} \cdot W + 1.17 \cdot 10^{-4} \cdot P)$	$\frac{1000}{W+0.649 \cdot P}$	$4.2 \cdot 10^3 \cdot W + 1.09 \cdot 10^3 \cdot P$
Air	$a e^{-b(T-273.15)} + c$	$\frac{p_{atm}}{R_{spec} T}$	1006

**Table 2.1:** Optical and thermal properties for porcine tissue and air.  $W$  and  $P$  are the percentage of water and protein respectively.  $\rho$  is the density of the skin,  $p_{atm}$  is the pressure of air at 1 atmosphere, and  $R_{spec}$  is the gas constant.  $a$ ,  $b$ , and  $c$  are constants.

corresponds to an absorption of coefficient in water of  $\sim 850 \text{ cm}^{-1}$ . As the absorption coefficient is large, it is assumed that scattering is negligible at these wavelengths. Table 2.1 summarises the thermal properties for tissue and air used in the simulations.

The laser was used in “Pixel beam” mode. This means that the laser beam is split into an array of smaller beams. The laser used an array  $9 \times 9$  of 81 pixel beams, each with a diameter of  $250 \mu\text{m}$ . The Pixel CO<sub>2</sub> rated laser power is  $\sim 70 \text{ W}$ .

The laser delivered one single pulse of varying total energy delivered over the range  $50 \text{ mJ}$  to  $400 \text{ mJ}$ , in so called “super pulsed mode”. The experiment consisted of ablating the porcine tissue, as a function of energy per “pixel” beam. This was achieved by adjusting the pulse length of the laser,  $\tau$ , so that the energy per pulse was varied over a range  $50 \text{ mJ}$  to  $400 \text{ mJ}$ . The energy range for the laser was kept the same pre and post-upgrade, with the pulse length differing.

### Computational speed up:

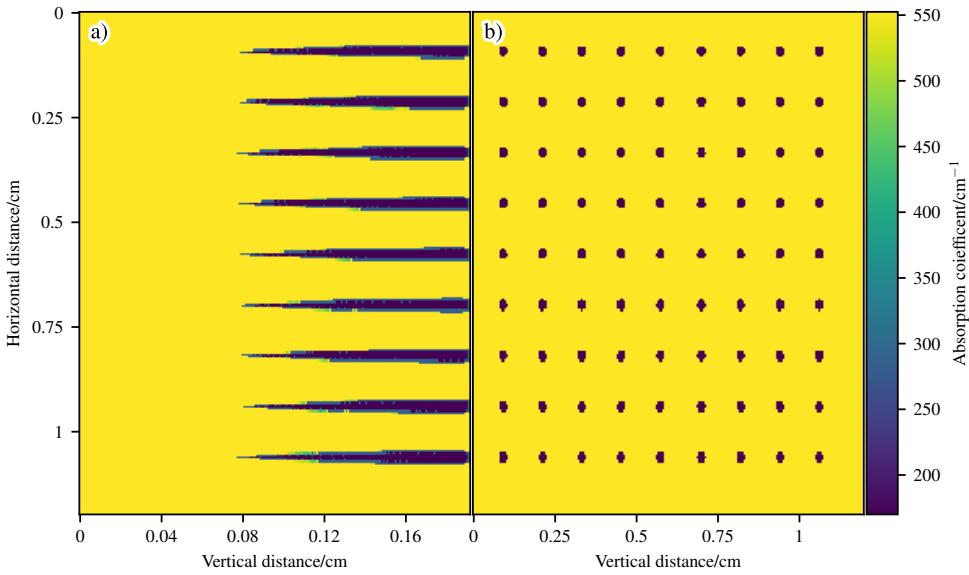
As discussed in the Section 2.1, the volume of interest is the area around the ablation craters. The volume is  $1.1 \text{ cm} \times 1.1 \text{ cm} \times 0.5 \text{ cm}$ . However, in order for the simulation to have good resolution of the ablation craters, this volume would require a large number of voxels for the tissue model. This is unfeasible due to: the memory required to store the various counters, grids, and variables, and the time that would be required in order to carry out the computation. Thus the volume of interest is reduced to focus on just one of the ablation craters that is created by the laser (a volume of  $0.06 \text{ cm} \times 0.06 \text{ cm} \times 0.18 \text{ cm}$ ) As a check to ensure that no physical phenomena are omitted by focusing on just one ablation crater, an initial simulation that models the full volume of interest was carried out to investigate the possibility of overlapping craters or other related phenomena. The simulation, as shown in Fig. 2.9, gives reassurance that the shrinking of the volume of interest is a valid approximation to make, as there is no overlap between the separate ablation crater.

### 2.3.2 Results

#### Investigating ablation temperature, $T_a$

Various literature sources report the ablation temperature ranging widely from  $177^\circ$  to  $500^\circ$  [85, 87, 88]. Thus, several models are run over this range in order to establish the  $T_a$  which fits the experimental results. Figures 2.10 and 2.11 show how  $T_a$ , and beam profile affect the crater depth as a function of pixel beam energy for the CO<sub>2</sub> laser. The data suggests that, a  $T_a$  around  $T_a = 500^\circ \text{C}$  is appropriate for the studies carried out, the upper limit of  $T_a$  from the literature.

Increasing the ablation temperature, has the obvious effect of requiring more energy to be deposited by the laser before ablation takes place. This also allows more heat to diffuse away from the ablation crater increasing the thermal damage done to the surrounding tissue. Decreasing the ablation temperature has the converse affect, and allows the ablation crater to become deeper.



**Figure 2.9:** Simulation of 81 pixel beams. Figure a) shows a slice through the optical properties at the end of the simulation in the z-y plane. Figure b) shows the optical properties in the x-y plane at the top surface. Yellow is unchanged tissue, and purple is completely ablated tissue. Figure shows that the ablation craters do not overlap one another.

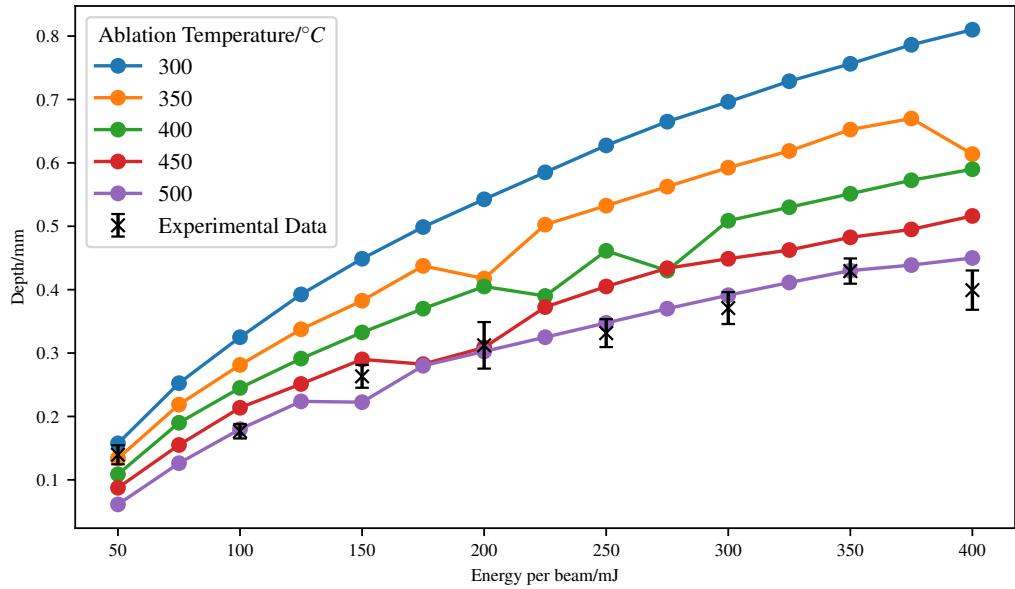
Over the full range of  $T_a$ , as the energy per pixel beam increases, there is a trend that at higher energies the crater depth begins to taper off. This is potentially due to a number of reasons. As the ablation craters grows the volume of tissue that is ablated is replaced with air, allowing more heat loss from the tissue to the environment. As well as heat loss to the environment, more heat is diffused away into the surrounding tissue as the crater grow, due to the availability of more tissue for the heat to diffuse into.

### Investigating beam type

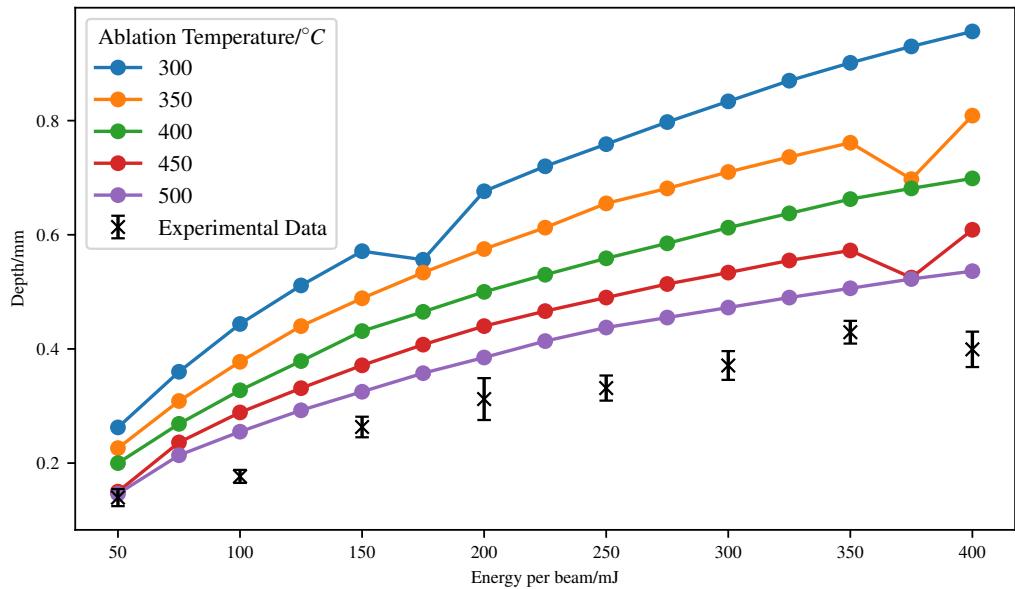
As the manufacturer does not provide information on the beam profile of the pixel beams and the lack of equipment available to measure the beam profile, the shape of the beam profile has to be assumed. Two different beam types are tried: Gaussian, and circular (top-hat). Figures 2.10 and 2.11 show the result of these *in-silico* experiments. The Gaussian beam ablates deeper holes than the circular beam type, which is to be expected due to the distribution of power in the Gaussian beam. The beam that best fits the data, is the circular beam. For the Gaussian beam to fit the data ablation would have to take place at temperatures above 500 °C which does not fit with the literature. Without knowing the exact profile of the beam, it is assumed for the rest of the *in-silico* experiments that the beam profile is circular.

### Investigating thermal damage

As stated in Section 2.2.3, the Arrhenius damage integral is used to estimate the thermal damage due to the laser. To calculate the tissue damage around the ablation craters, Eq. (2.18) is first



**Figure 2.10:** Simulation of 70 W  $CO_2$  ablative laser, with a circular beam profile. Crater depths as a function of pixel beam energy for various  $T_a$ 's.



**Figure 2.11:** Simulation of 70 W  $CO_2$  ablative laser, with a Gaussian beam profile. Crater depths as a function of pixel beam energy for various  $T_a$ 's.

transformed into a summation:

$$\Omega(t) = \int_{t_p}^{t_f} A e^{-\frac{\Delta E}{RT}} d\tau \quad (2.37)$$

$$\Omega(t) = \sum_{m=m_p}^{m_f} A e^{-\frac{\Delta E}{RT_\xi^m}} \Delta t \quad (2.38)$$

Where:

$\Delta E$ ,  $R$ ,  $T$ , and  $A$  have the same meanings as before;

$\xi$  is the  $i^{th}$ ,  $j^{th}$ ,  $k^{th}$  node;

and  $m_p$  is the  $p^{th}$  timestep when the  $\xi^{th}$  node is above the threshold temperature.

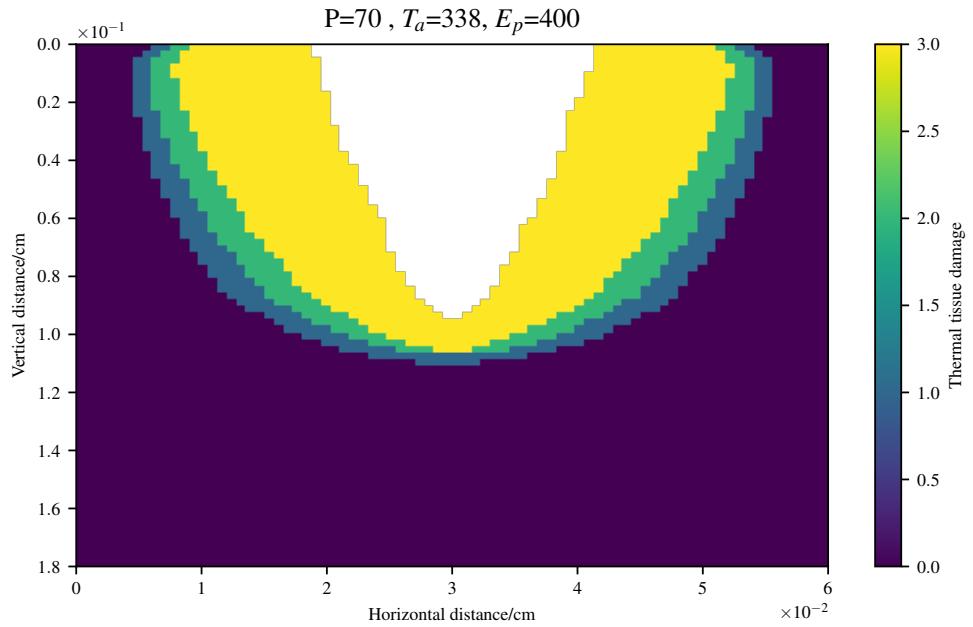
Using Eq. (2.38) it can thus be estimated that the damage to the tissue on a voxel basis. Figure 2.12 show how far the thermal damage extends around the ablation crater. For ease of visualisation 1-3 is mapped to their respective burns via the following scheme, with  $\eta$  as burn severity:

$$\eta = \begin{cases} 3, & \Omega \geq 10000 \\ 2, & 1 \leq \Omega < 10000 \\ 1, & 0.53 \leq \Omega < 1 \\ 0, & 0.0 \leq \Omega < 0.53. \end{cases} \quad (2.39)$$

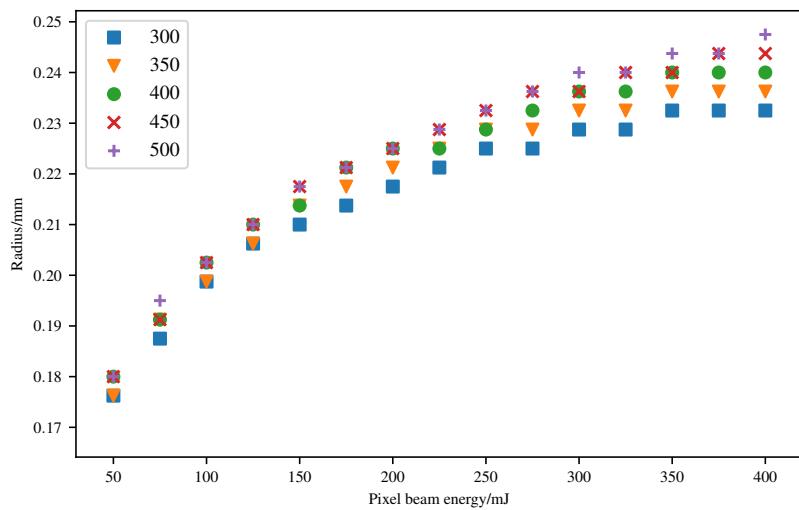
As shown in Fig. 2.12, the thermal damage zone extends for a small distance around the ablation crater, due to the diffusion of heat into these areas. Figure 2.13 shows the maximum horizontal thermal damage distance as a function of  $T_a$ , and pixel beam energy. For values of  $T_a$  less than  $\sim 425$  °C, it appears that the maximum horizontal extent of the thermal damage tapers off. This is most likely because for lower values of  $T_a$ , there is a larger ablation crater, meaning that the energy from the laser is deposited deeper in the tissue in comparison to higher values of  $T_a$ . The higher values of  $T_a$  allow greater diffusion of the heat, thus yielding larger zones of damage. Overall there is little difference in the maximum horizontal extent of thermal injury, when using different energies (of the order of  $\sim 0.01$  mm).

Investigations for the time it takes for different areas of the tissue to become thermally damaged, were also carried out. This can be easily achieved by saving the time each voxel passes one of the damage boundaries in Eq. (2.39). Figures 2.14 and 2.15 show the minimum time taken for 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> degree burns to occur as a function of depth. Figure 2.14 shows that there is little to no time (upon the order of 0.5 ms) between 1<sup>st</sup> and 2<sup>nd</sup>, and 3<sup>rd</sup> degree burns. Figure 2.15 shows there is a slightly greater time difference between 1<sup>st</sup> and 2<sup>nd</sup>, and 3<sup>rd</sup> degree burns, however this is almost as negligible as the 400 mJ case.

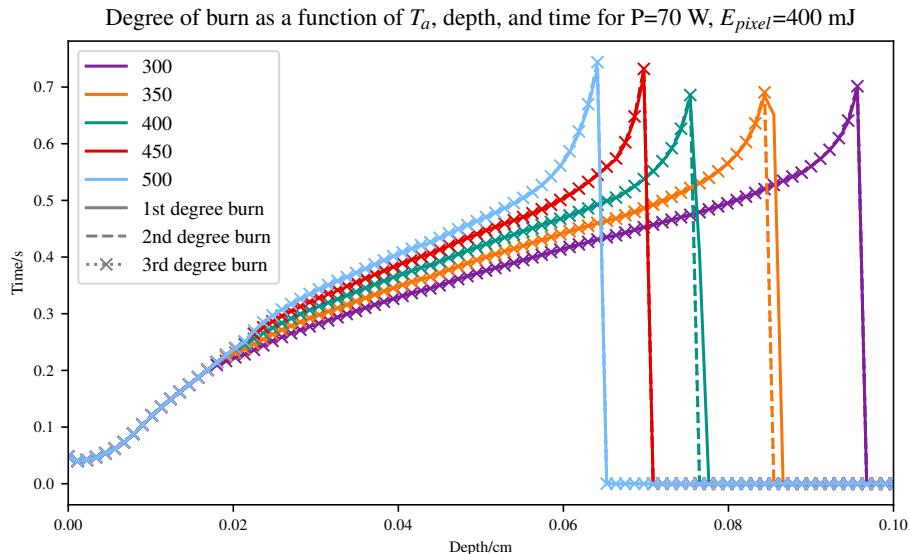
The reason that there is almost no time between 1<sup>st</sup> and 2<sup>nd</sup>, and 3<sup>rd</sup> degree burns, is most likely because there is little time for heat to diffuse, whilst the laser is still illuminating the medium. The laser pulses are on the order of seconds, and tissue is not thermally conductive. This leads to the results presented here.



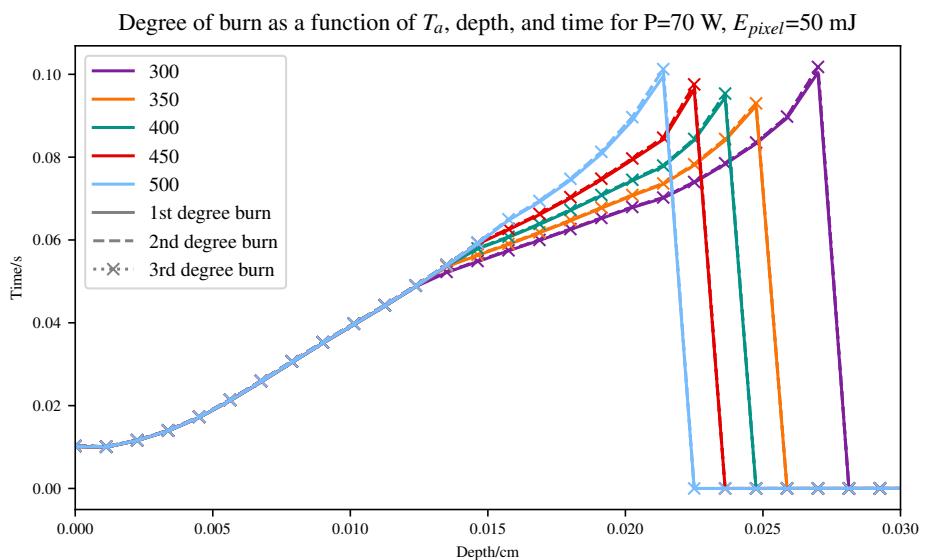
**Figure 2.12:** Tissue thermal damage around the ablation crater (white). Thermal tissue damage values of 3 refer to 3<sup>rd</sup> degree burns, 2 to 2<sup>nd</sup>, and 1 to 1<sup>st</sup> degree burns respectively.  $P$  is the power in Watts,  $T_a$  is the ablation temperature in Kelvin, and  $E_p$  is the energy per pixel beam in mJ.



**Figure 2.13:** Figure shows the maximum horizontal extent of thermal damage as a function of energy per pixel beam, for different  $T_a$ 's.



**Figure 2.14:** Figure show the time taken for 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> to occur as a function of depth, for a range of  $T_a$ 's at 400 mJ.



**Figure 2.15:** Figure show the time taken for 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> to occur as a function of depth, for a range of  $T_a$ 's at 50 mJ.

## 2.4 Conclusion

Using MCRT and a finite difference method, a fully 3D model of photon and heat transport within tissue has been created. This model can be used to simulate the heat deposited by laser, the ablation craters formed via high powered lasers and the resultant thermal damage surrounding the ablation crater.

The model has been fully compared with both analytical solutions and experimental results. The model was found to match with experimental results that a tissue ablation temperature  $T_a$  of around 500 °C has to be adopted, towards the higher end of the range previously observed in the literature.

The simulations allow us to predict for a given laser power and pulse length, how much thermal damage is caused in the tissue, and how deep an ablation crater that will form. The computational model could be used in future to help develop treatment regimes for both aesthetic and medical procedures. For example, currently there is considerable amount of “down time” after skin rejuvenation, in which the patient displays inflammation, erythema, edema, pain, and crusting [99–101]. Simulations of thermal damage due to fractional ablation could help design treatment regimes that minimise these effects, whilst still delivering skin rejuvenation. The model can also be applied to help optimise laser assisted drug delivery. Laser assisted drug delivery consists of using a laser to “drill” holes into the skin in order to help topical medicines diffuse into the skin better, than just applying the medicines to skin with no holes. Our model can help predict the laser parameters needed to reach a certain hole depth, thus minimising thermal damage and pain to patients.

There are many avenues available with regards to future work on this model. The model presented here in this chapter was on a initially homogeneous skin model. In reality skin is compromised of several distinctive layers, with each layer containing varying amounts of different chromophores. Our model can easily incorporate an multi-layered skin model complete with various fractions of chromophores. However as the laser used in these studies is an infra-red laser, water is the highest absorbing chromophore, meaning that a physically accurate model, with various chromophores is not need for this application. The current model is a voxel based model, where all the voxels are the same size. This allows the model presented in this chapter to be easily set-up, with regards to parallelisation, optical/thermal properties and ease of programming. However voxel models, where all the voxels are the same size, are not computationally efficient. Particularly in order to achieve good resolution, many voxels are needed, which requires large amounts of RAM, due to a  $\sim n^3$  scaling of voxels to memory in 3D. A more efficient way, would be to allow different sizes of voxels, depending on parts of the model which need high resolution, and parts that do not need high resolution. Such a voxel model is called an adaptive mesh refinement (AMR). There are downsides to AMR: complex implementation for parallelisation and set-up of optical/thermal properties, slower optical depth integration routines due to neighbour lookups.

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