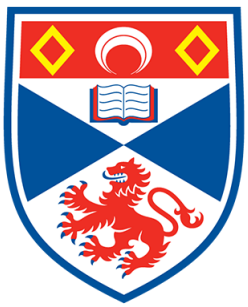
Advanced 3D Monte Carlo Algorithms for Biophotonic and Medical Applications

Lewis McMillan



University of
St Andrews

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

March 2019

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.

Date ..... Signature of supervisor .....

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Abstract

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Acknowledgements

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Abbreviations

MCRT Monte Carlo radiation transfer.

NM Nelder-Mead.

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Chapter 1

AmoebaMCRT, modelling autofluorescence in skin for novel biomarkers of cardiovascular disease

1.1 Introduction

1.2 Skin Model

So far in this thesis all tissue models have been simplified, by assuming that tissue is a homogeneous structure with uniform optical properties. However this is not the case. Tissue is very un-homogeneous, with non-uniform optical properties. However to create a 1 to 1 model of tissue in a simulation is impractical due to the resolution required to resolve all the constituent part of the tissue. Therefore we need to make a compromise between reality and what is possible to model efficiently. To this end the section presents a 5 layer model of human skin. Dermatologists usually split the skin into 5 layers: Stratum Corneum, Epidermis*, Papillary Dermis, Reticular Dermis, and Hypodermis, see Fig. 1.1.

1.3 Modelling Fluorescence

1.4 Nelder-Mead Method

The Nelder-Mead (NM) method is an algorithm for unconstrained optimisation. The algorithm is based upon iteratively updating a simplex. A simplex is a structure in $n-dimensional$ space, consisting of $n+1$ points that are not in the same plane. Therefore in 1D, the simplex is a line, in 2D a triangle, in 3D a tetrahedron, etc.. The Nelder-Mead method is a gradient free method, meaning that it does not require derivative to be calculated and that the search space does not need to be smooth.

*The epidermis can be split into several more layers, however these layers are optical similar and are rather small so we model just one layer here.

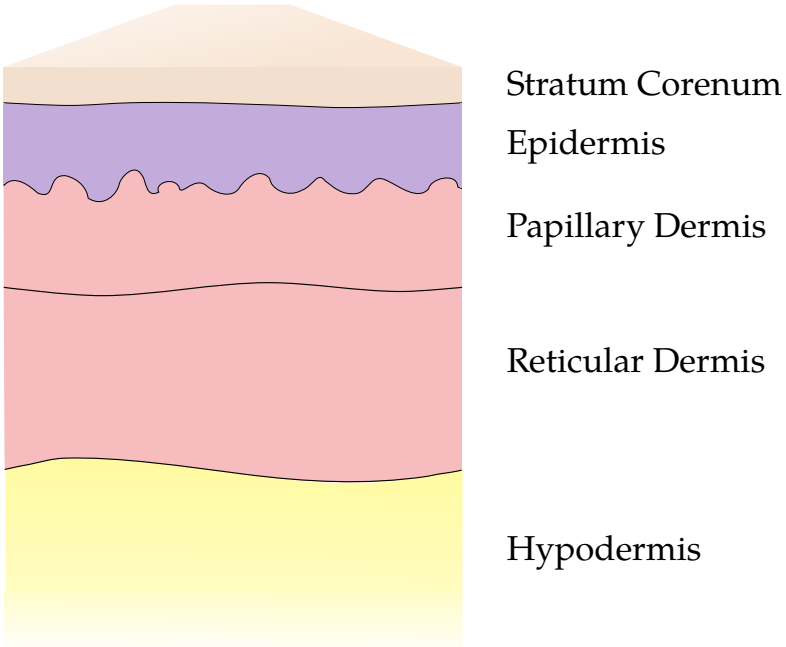

Figure 1.1: *Illustration of skin layers in human skin.*

The algorithm works by removing the worst vertex of the simplex and replacing it with a 'better' vertex calculated via a number of different operations. These operations can be seen in Fig. 1.2.

The first step of the NM method is to sort the initial vertices according to their fitness. For $n = 2$, we define x_w as the 'worst' point, x_l and the 'lousy' point, and x_b the 'best' point, such that $f(x_b) \leq f(x_l) \leq f(x_w)$, where $f(x)$ is evaluating the 'fitness' of a point x. With the vertices sorted, the centroid of the simplex is calculated as in Eq. (1.1). The centroid is the mean of all the vertices bar the 'worst' point.

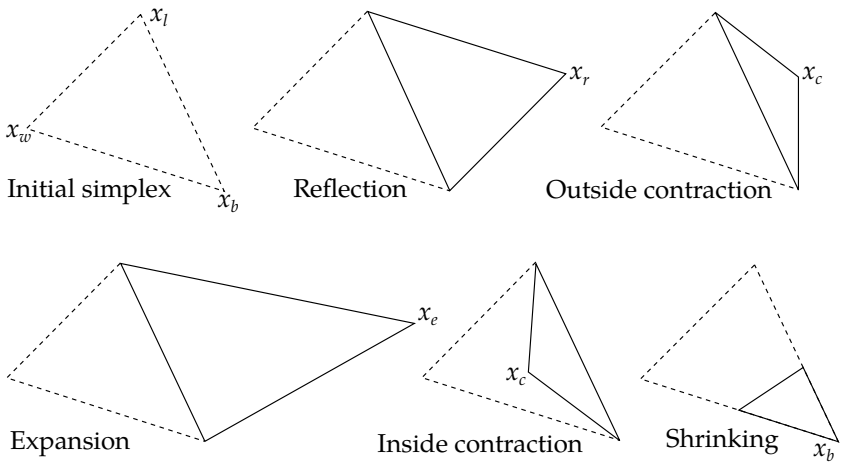

Figure 1.2: *Operations that can be preformed on a simplex for $n = 2$.*

The next step is to move the simplex via a reflection. To calculate the new vertex via reflection Eq. (1.2) is used, where α is the reflection factor. If this new point, x_r, is better[†] than the current 'best' point then we calculate a new point in the same direction but further using the expansion operation Eq. (1.3), where γ is the expansion factor. If this new point, x_e, is better than the 'best' point then we replace x_w with x_e and start the process again. However is x_e is not better than the 'best' point, then we discard it and replace the worst point with x_r the reflected point.

If when calculating x_r, we find that is worse than the 'best' point, we then check if x_r is better than the 'lousy' point. If x_r is better than x_l then we replace the 'worst' point and start the process again. However if the x_r is worse than x_l, we then compare it to the 'worst' point. If x_r is better than the 'worst' point then we preform and inside contraction Eq. (1.5), where β is the contraction factor. If this new point, x_{ic}, is better than the 'worst' point then we keep it, otherwise we preform the shrink operation, shrinking the whole simplex around the 'best' point.

If x_r is not worse than the 'worst' point then we preform an outside contraction Eq. (1.4). This computes a new point x_{oc}. If x_{oc} is better than x_w, then we keep it, otherwise again we shrink around the 'best' point.

The process described above is summarised in Fig. 1.3. Standard values for the factors are: $\alpha = 1$, $\beta = \frac{1}{2}$, and $\gamma = 2$. Though in practise these values are adjusted for the problem at hand.

$$c = \frac{1}{n} \sum_{i=1, i \neq w}^{n+1} x_i \tag{1.1}$$

$$x_r = c + \alpha(c - x_w) \tag{1.2}$$

$$x_e = c + \gamma(x_r - c) \tag{1.3}$$

$$x_{oc} = c + \beta(x_r - c) \tag{1.4}$$

$$x_{ic} = c + \beta(x_w - c) \tag{1.5}$$

As the Nelder-Mead method has no inbuilt convergence criteria, this must be added. We use two different criteria based upon simplex size, and vertex fitness. The criteria for the simplex size is as; if the size of the simplex(Eq. (1.6)) Where p_i and p_{i+1} are vertices in the simplex that are connected by and edge.

$$size = \sum_{i=1}^{n+1} |p_i - p_{i+1}| \tag{1.6}$$

If the size of the simplex falls below a pre-set value, then we preform a factorial test to see if the simplex should be restarted or if the algorithm should terminate. The factorial test checks the space around the current simplex to ensure that we have converged to a global minima. If the check fails then the algorithm is restarted with the current best point kept, and new vertices generated.

The other convergence criteria is the a check to see if the best point is 'good enough'. The current best point is compared to a pre-set fitness value. If the best point is better than the pre-set value then the algorithm terminates.

[†]Here better means the point has a lower fitness score, as we use χ^2 metric to assess the fitness of a point.

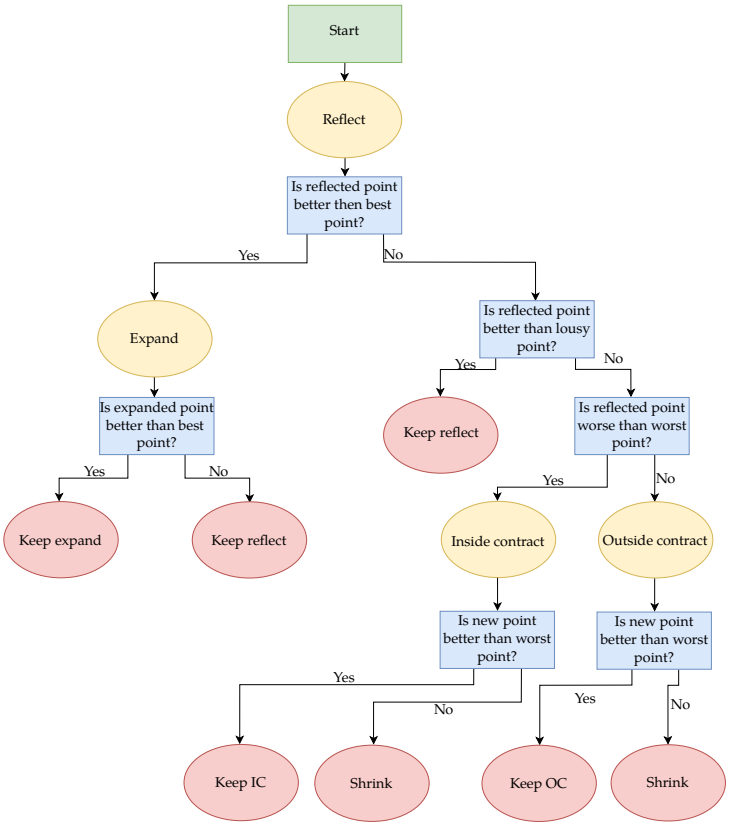

Figure 1.3: *Nelder-Mead decision tree*

1.5 Validation

The NM method was coded in Fortran, so that it could be easily interfaced with the Monte Carlo radiation transfer (MCRT) code developed as part of this thesis. To test that the method works as intended a number of trial functions were tested, see Table 1.1. This was achieved by selecting an initial simplex, and the method allowed to iterate until it converged. The results of this are shown in Fig. 1.4.

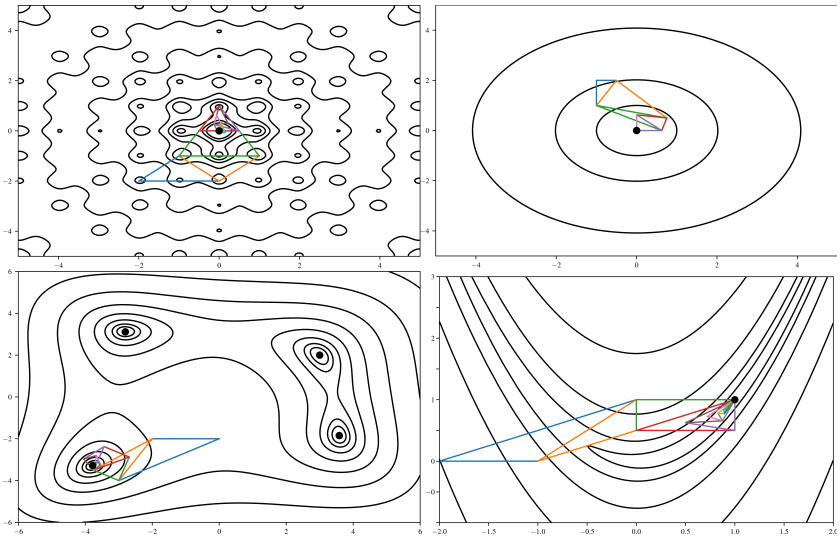

Figure 1.4: *Contour plots of test functions with Nelder-Mead simplexes over plotted. Top left is the Ackely function, top right is the sphere function, bottom left is the Himmelblau's function, and the bottom right is the Rosenbrock function. Blue simplex is the initial simplex, and the large black dots represent the Global minima.*

To ensure that the NM method can be used to find the unknown concentrations of the autoflurophores, we test the method with a known model. This model consists of three different fluorophores: NADH, FAD, and a fictions fluorophore that has similar properties to NADH and tyrosine. We first run this model through the MCRT to get an output spectrum. We then test the NM method for $n = 2$ and $n = 3$.

Name	Formula	Global Minumum
Sphere	$x^2 + y^2$	$f(0,0) = 0.$
Rosenbrock	$(a-x)^2 + b(y-x^2)^2$	$f(1,1) = 0.$
Ackely	$-20\exp\left[-0.2\sqrt{0.5\left(x^2+y^2\right)}\right] -$ $\exp\left[0.5\left(\cos 2\pi x + \cos 2\pi y\right)\right] + e + 20$	$f(0,0) = 0.$
Himmelblau's	$(x^2 + y - 11)^2 + (x + y^2 - 7)^2$	$f(3,2) = 0.,$ $f(-2.805118, 3.131312) = 0.,$ $f(-3.779310, -3.283186) = 0.,$ $f(3.584428, -1.848126) = 0.$

Table 1.1: *Table of standard test functions for numerical optimisation.*

1.6 Results

1.7 Discussion

1.8 Conclusion

We have presented out code, AmoebaMCRT, which combines the Nelder-Mead method and MCRT in order to determine the concentrations of naturally occurring fluorophores in human skin.

Bibliography