

# Adaptive Multidisciplinary Training for Engineers

*Rashad Aouf<sup>1</sup>, Vojislav Ilic<sup>2</sup>*

<sup>1,2</sup>University of Western Sydney, Locked Bag 1797, South Penrith DC, NSW 1797

*r.aouf@uws.edu.au<sup>1</sup>, v.ilic@uws.edu.au<sup>2</sup>*

## Abstract

Solution to challenges facing current and future engineers often requires a holistic approach which mandates a wide range of skills. These skills do not know discipline boundaries and therefore present educators with a challenge as well – how to accommodate this relatively recent demand for a multidisciplinary training. On one hand, and on the other, do it well within the limited resources that perpetually plague universities. For example, while Mechanical Engineering does provide a wide base of interdisciplinary skills, specialist courses have evolved from it, such as Robotics, Mechatronics, Engineering Construction, Project Management, Biomedical Engineering to mention a few. It seems to these authors that Mechanical Engineering provides the most appropriate base upon which specialist knowledge may be built in an adaptive fashion at the workplace. This approach would also reinforce the basic role of an educational institution – to provide fertile basis upon which to build future specializations. Until such times when this approach becomes commonplace, Postgraduate Training fulfils that need. This paper focuses on such a case by discussing the approaches needed to understand the mechanics of Hyperthermic Ablation of Tumours.

Index Terms æ education, heat transfer, hyperthermia, mathematical model, physics, tumour treatment

## Introduction

Nowadays, engineering provides a wide base of interdisciplinary skills in order to satisfy the recent demand of multidisciplinary training. Since decades ago, Mechanical Engineering has been evolved to produce various specialization including Robotics, Mechatronics, Engineering Construction, Project Management, Biomedical Engineering to mention a few. From the authors' point of view, Mechanical Engineering is considered as a core discipline from where an adaptive fashion at workplace can be built. In connection to this paper, this is sponsoring the development of tools that can be applied in critical medical situations including research studies, clinical trials, diagnosis, and treatment. However, the application of such technique must consider the associated effects on patients. Thus, biomedical engineers have to understand a number of scientific disciplines and establish relationships among them to solve difficult problem that may confront the specialists in various treatment circumstances.

From the oncology study, treatment of tumours remains a crucial area for researchers. Accordingly, an analysis of propagation of thermal interface in tumour tissue subject to hyper-thermal necrosis takes place at the University of Western Sydney. The development of a mathematical model is an integral part of this study to quantify temperature distribution field. This study may also use aspects of molecular dynamics (MDs) simulation to examine the mechanism of thermal wave propagation.

It can be seen that this research requires a solid background in various areas. In relation to biomedical engineering, this paper considers tumour treatments as domain problem and hyperthermia is main area of investigation. With respect to engineering education, this paper covers all scientific areas examined in this study in order to engage undergraduate students. This paper is organized as follows. Section I gives a brief introduction to Hyperthermia. Section II provides a brief overview of the research problem. Section III shows different components of this research. In Section IV, it is proposed the use of differential equation in mathematical bioheat transfer model with some theoretical outline. Shape discretisation is addressed in section V. In Section VI, we proposed the incorporation of molecular dynamics (MDs) simulation to provide a deep understanding of heat transfer and phase change processes. Finally, section VII is just to conclude.

## **THERMAL ABLATION THERAPY**

One of the effective aggressive treatments of tumours is to elevate its temperature in a controlled manner giving rise to cell apoptosis and tissue necrosis. The use of extreme temperature to kill tumours (i.e. irreversible necrosis) is not a new concept. However, preserving the normal cells has been explored in the recent years. The thermal ablation therapy, Hyperthermia [1] has been used extensively in the past, but fell into disrepute owing to gross unwanted collateral effects that inevitably accompanied such a treatment. This is attributed to the inadequate temperature distribution due to the chaotic structure of tumour tissue. In particular, tumour has a rich vascular supply acting as heat sinks, which resist heat propagation. Thus, heat transfer in living tissues is a complex process involving conduction, convection, and metabolism. However, the advent of digital imaging and novel sources of heat and their improved control, has seen re-emergence of the hyperthermic treatment. The latest technology helped minimize such side effects. However, they were not completely eliminated. Concerning this issue, an accurate bio-heat transfer modelling has to precisely quantify the temperature distribution within a complex geometry of a tumour tissue, in order to optimize side effects and recurrence of the disease in the future. Hence the examination of effective energy propagation within a volume of interest (VOI), i.e. tumour tissue, is an integral part of treatment procedure.

In addressing heat transfer problem in tumour tissue subject to necrosis, this paper also postulates an advanced study of molecular dynamics (MDs) analysis in the hope of enhancing the thermal ablation therapy: hyperthermia. This approach aims to provide benchmarks for bioheat transfer mathematical models, perhaps quantify deviations from macroscopic approaches at the scale of very thin (nanometer) films. From this, we obtain a comprehensive understanding of hyperthermic treatment in sense of temperature distribution, hence trying to optimize collateral damage.

## **PROPOSED ONGOING RESEARCH**

Application of hyperthermia in treatment of tumours was established in the seventies, peaking in the eighties, and decreasing in the nineties [1]. The collateral damage accompanied such treatment represents a crucial challenge for research studies and clinical trials due to misdirected heat delivery. Recently, this type of treatment has witnessed a significant progress depicted by the use of digital imaging and minimally-invasive heat sources to enhance heat propagation control. However, this progress lacks to numerically approximate temperature distribution field (e.g.  $T(x,y,z)$  in the Cartesian coordinate system) of the time-dependent phenomena. Thus patients who undergo hyperthermic treatment remain subject to side effects and complications. Consequently the examination of energy propagation within a volume of interest (VOI) is an integral part of treatment procedure.

Accordingly, bio-heat transfer mathematical modeling had been recently adopted by researchers in order to optimize unwanted damage to healthy tissue. A major challenge facing such a model is that heat transfer in living tissue is a complex process involving complex process conduction, convection, and cell metabolism. Therefore, the accuracy of a model can be measured by its ability to convey the realistic geometrical structure and biological environment for tumour.

Analysis of propagation of thermal interface in tumour tissue subject to hyperthermal necrosis is ongoing research in the University of Western Sydney. Necrosis or death of cancer cells procedures at high temperature requires a precise treatment of tumour tissue. The ultimate aim of hyperthermia is to elevate the temperature of affected tissue to beyond a therapeutic value ( $>50^{\circ}\text{C}$ ) while maintaining surrounding normal tissue at sublethal temperature values [2-4]. However, the collateral damage accompanied such treatment represents a crucial challenge for research studies and clinical trials due to inadequate heat delivery. This can be attributed to the inaccurate imaging of the topological surface of the tumour tissue that causes undesirable side effects rather than benefits to patient undergoing hyperthermic treatment [5, 6]. Subsequently, one of the major problems of this procedure is the recurrence of the disease after treatment due to insufficient heating of tumour [7, 8].

The objective of this research is to optimize hyperthermic procedure by simulation & imaging of the temperature dis-

tribution before surgery that will serve as the basis for optimization of the proper probe placement at the targeted site. In this context, it is planned the development of an accurate mathematical model to predict temperature distribution field with incorporation of blood perfusion information both as a steady state phenomenon and time dependent thermal wave propagation. Depending on its strength, the latter may give rise to tissue necrosis and thus be also viewed as a propagation of a phase change interface. Hence, heat transfer in living tissues is a complex process involving conduction, convection, and metabolism.

Arising from this discussion, it can be seen that this research is a multidisciplinary area. With respect to engineering education, this paper covers various scientific areas in order to engage undergraduate students.

## MANAGEABLE COMPONENTS

By addressing the complex structure of the tumour tissue, this research project is divided into manageable components including bio-heat transfer formulation, discretisation of tumour tissue, and then application of gathered knowledge. The latter may lead to prospects of commercial application and patents (i.e. generating 3D algorithm that combines data depicted in a 2-D image taken from two different angles). In order to determine temperature distribution field within a living tissue exposed to high temperature a discretisation approach will be followed such as the finite element method (FEM). Currently, there is a dedicated effort to generate an accurate mathematical model with incorporation of blood perfusion information. This component is well represented in the following section.

## MATHEMATICAL BIOHEAT TRANSFER MODEL

This study is investigating into the development of an accurate mathematical model to predict temperature distribution field with incorporation of blood perfusion information both as a steady state phenomenon and time dependent thermal wave propagation. Depending on its strength, the latter may give rise to tissue necrosis and thus be also viewed as a propagation of a phase change interface. Three processes are involved in modeling energy propagation: conduction, convection, and metabolism. The major advantage of this combination is to introduce students to these processes and how to apply them in real situation using theoretical analysis.

Traditionally, feedback of temperature propagation inside a volume of interest (VOI) was given by invasive monitoring [9]. Thus, limited knowledge can be deduced concerning temperature distribution field. Therefore, in addition to the experimental approach [10-16], mathematical modeling has been introduced as an integral approach to enhance treatment procedure in which three-dimensional information of temperature can be recorded [17].

The theory of heat flow has been initially evaluated by Pennes (1948) to quantify the relationship between arterial blood and tissue temperature in the resting human forearm [18]. Many research studies have incorporated Pennes equation to measure temperature distribution during hyperthermic treatment [18] [19] [20]. Pennes' equation is defined as follows:

$$\nabla(k\nabla T) + (\rho c) \omega_b (T_a - T) + q_{met} = \rho c_p \frac{\partial T}{\partial t} \quad (1)$$

From the left hand side of the equation, the first term refers to net conduction heat flux (W/m<sup>2</sup>) into the control volume (i.e. tissue). The second term represents the rate of heat transfer from blood to tissue (W/m<sup>3</sup>). Finally, the third term is the rate of tissue heat production. The time rate at which thermal energy of the tissue changed per unit volume is represented by the right hand side term (J/m<sup>3</sup>/s).

The chaotic structure of tumour tissue is the cause of inadequate heat transfer from induced hyperthermia treatment. Therefore, it can be seen in (1) the combination of three terms of heat transfer process at the left hand side: conduction, convection, and metabolism. The conduction term is included in order to quantify heat flux within the tissue regardless blood perfusion. Conduction is viewed as transfer of energy from the more energetic to the less energetic

particles of the living tissue due to interactions between the particles. This is followed by another term to measure the resistance of blood vessels to heat transfer. Blood perfusion within a living tissue is governed by the convection mode that moves from one position to another due to blood motion. Finally the third term represents the metabolic of the chemical substance reaction.

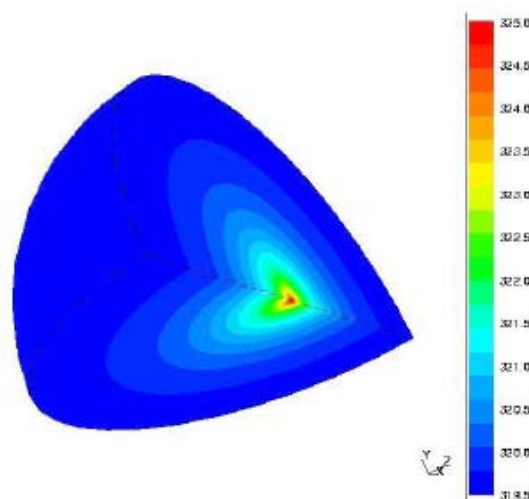
## DISCRETISATION

Finite element method (FEM) is one of the most commonly used numerical procedures to obtain solutions to a large class of engineering problems. As a consequent, the solution domain is divided into a number of smaller regions, called elements. Thus, the continuum problem is simplified with FEM discretization. As resultant, it is also reduced to a finite number of unknowns at specified points referred to as nodes. In FEM, the behavior of a field variable within an element is called interpolation functions, shape functions, or approximating functions [21, 22]. The complete solution is then generated by assembling the individual solutions, allowing for continuity at the interelemental boundaries. FEM uses integral formulation to create a system of algebraic equations. This numerical approach is originally used in stress analysis until recently; it also finds its usefulness in heat transfer, fluid flow, electric magnetic field, and etc.

In connection to our study, finite element analysis (FEA) is used to determine an approximate solution for bio-heat transfer problem from nanoparticles heat source into liver tissue. Since that, FEM is widely used for modelling of soft tissues [23, 24] i.e. liver. This can be attributed to the high demand of researchers for supporting techniques to simulate surgeries, particularly of deformable models, for training in virtual environments. Concomitant with this, we choose the liver as solution region in which temperature distribution is discretized. The thickness of the layer of tissue coagulation form around the nanoparticles is an integral part of this study, stated as the physical problem. The last is denoted as the start point to establish the numerical model designated in the figure below. It can be seen, that one part of the model deals with the discretization of the domain and the other carries out the discrete approximation of the partial differential equations. Finally, by combining both, the numerical solution to the problem is achieved.

The following example shows the benefit of using mathematical model to simulate thermal behavior in biological system.

FIGURE 1: Damage in tumour model tissue



## MOLECULAR DYNAMICS (MDS) SIMULATION

In this section, authors aim to involve engineering students in more advanced study concerning heat transfer. Propagation of thermal energy within a given matter is originally attributed to atomic/molecular motion [25] in form of vibration or migration of free electrons. Temperature is only an indication of the energy level. Therefore, molecular dynamics (MDs) simulation is theoretically outlined below.

In the context of our study, front phase change or gel formation corresponds to the thermal tissue coagulation in the field of treatment of tumours. Such correspondence will guide the design for a successful molecular model for biological tissue. Modeling, prediction, and simulation of behavior of assembly of finite number of molecules (N) require detailed information about intermolecular interactions. Accordingly, it is essential in MDs to emphasize the motion of individual particle (atoms or/and molecules) within an assembly of N atoms or molecules. From this, the dynamical theory employed to derive the equation of motion is the Newtonian deterministic dynamics. Consequently, the particles are assumed to be like points, are moved according to the Newton's equation of motion, given by:

$$\vec{F}_i = m_i \frac{d^2 \vec{r}_i}{dt^2} \quad (2)$$

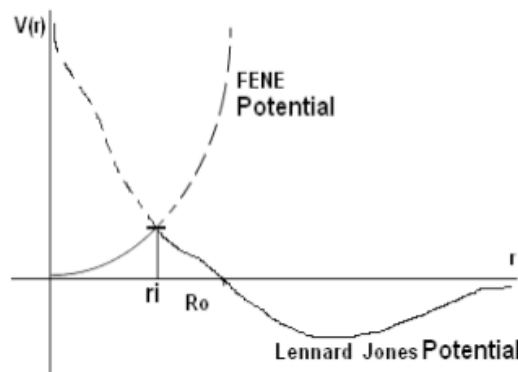
where  $F_i$  is the force coming from the interparticle interaction.

Following this discussion, the proposed potential interaction model is defined as:

$$V(r) = \begin{cases} V^{FENE}(r) = -0.5kR_0^2 \ln \left[ 1 - \left( \frac{r}{R_0} \right)^2 \right] & r < r_i < R_0 \\ V^{LJ}(r) = 4\epsilon \left[ \left( \frac{\sigma}{r} \right)^{12} - \left( \frac{\sigma}{r} \right)^6 \right] & r_i < r < r_c \end{cases} \quad (3)$$

The Lennard-Jones interaction potential acts between any pair of particles separated by a distance less than  $r_c = 2.5\sigma$ . The FENE bonding potential [23] acts only between adjoining particles, and has the effect of limiting the bond length to  $R_0$ . The parameters in the FENE potential are taken to be  $R_0 = 1.5\sigma$  and  $k = 30 \epsilon / \sigma^2$ , following Kremer and Grest [24]. The energy barrier is numerically approximated to  $13.65k_B T$  at  $r_i = 0.8636\sigma$  pair separation. The characteristic time for particle dynamics is defined by the LJ parameters,  $\tau = \sqrt{m/\epsilon}$ , where  $m$  is the particle mass. In the study, all the dimensions are given in LJ units where  $\sigma$  is the unit of length;  $\tau$  is the unit of time, and  $\epsilon$  the unit of energy. Diagram below (Fig. 4) shows the interaction potential versus distance among particles creating bond then crossing energy barrier.

FIGURE 2: The Potential Interaction during the Gelation Process. (Dimensions Expressed in Lennard-Jones Units)



## CONCLUSION

This paper provides an overview of the heat transfer mechanism focusing on bio-heat and its role in the palliative

medicine. Hence, aspects of hyperthermal treatment have been introduced in the context of biomedical engineering education. A significant attention has been given to fundamental and theoretical basis of this multidisciplinary area including heat transfer, mathematical modeling, discretisation, and molecular dynamics (MDs) simulation. It also shows the need to connect research with education of undergraduates.

Finally, the specific educational spin-offs that come from this research project are widely recommended to be integrated into the curriculum. Adaptive curriculum and the need to be relevant-readiness to create new academic offerings in place of old is an integral trend (e.g. Place of a Biomedical Engineering discipline in UWS academic offerings.)

## References

01. Pietro, G. and R. Cristina, Results of Hyperthermia Alone or With Radiation Therapy and/or Chemotherapy, in *Hyperthermia in Cancer Treatment: A Primer*, G.F. Baronzio, Editor. 2006, Landes Bioscience and Springer Science+Business Media, LLC New York. p. 119-127.
02. Field SB and Hand JE, *An Introduction to the practical aspects of clinical hyperthermia*. London: Pub. Taylor and Francis, 1990.
03. Dewhirst MW and Samulski TV, *Hyperthermia in the treatment of cancer. Current concepts*. Kalamazoo (MI): Upjohn, 1988.
04. Oleson et al., Regional Hyperthermia by Magnetic Induction in a Beagle Dog Model: Analysis of Thermal Dosimetry,. *Radiation Research*, 1984. 98: p. 445-455.
05. Schmidt J. D., P.C.L., Casola G. F. et al., Transperineal cryoablation for prostate cancer. *Urol.*, 1995. 153: p. 502.
06. Onik E.M., C.J.K., Reyes G.D. et al., Transrectal ultrasound guided percutaneous radical cryosurgical ablation of the prostate cancer. *PubMed*, 1993. 72: p. 1291-1298.
07. Tortal E.R., L.-P.R., Ilic V., Gunawardana, U., Monitoring of the coalesced ice ball in cryosurgery. in *IEEE Tencon Conference*. 2005. Melbourne, Vic.: IEEE.
08. Lee F., B.D., McHugh T. et al., Ultrasound guided percutaneous cryoablation of prostate cancer. *Radiology*. 192: p. 769-776.
09. Clegg S T, et al., Hyperthermia treatment planning and temperature distribution reconstruction: a case study. *Int. J. Hyperth*, 1996. 12: p. 65-76.
10. S. Weinbaum and L. Jiji. A New Simplified Bioheat Equation for the Effect of Blood Flow on Average Tissue Temperature. in *J. of Biomech. Eng.* 1985.
11. Charny, C.K. and R.L. Levin. Bioheat transfer in a branching counter-current network during hyperthermia. in *ASME Journal of Biomechanical Engineering* 1989.
12. C.K. Charny, S. Weinbaum, and R.L. Levin. An Evaluation of the Weinbaum-Jiji Bioheat Equation for Normal and Hyperthermic Conditions. in *ASME J. Biomech. Eng.* 1990.
13. Baish, J.W. Heat transport by countercurrent blood vessels in the presence of an arbitrary temperature gradient. in *J. Biomech. Engr.* 1990.
14. Zhu, M., S. Weinbaum, and L.M. Jiji. Heat exchange between unequal countercurrent vessels asymmetrically embedded in a cylinder with surface convection in *Int. J. Heat Mass Transfer* 1990.
15. Chen, Z.D. and R.B. Roemer. The effects of large blood vessels on temperature distributions during simulated hyperthermia. in *ASME Journal of Biomechanical Engineering*. 1992.
16. Creeze, J. and J.J.W. Lagendijk. Temperature uniformity during hyperthermia: the impact of large vessels. in *Phys. Med Bio.*, . 1992.
17. Clegg, S. and R.B. Roemer, Reconstruction of experimental hyperthermia temperature distributions: Applications of state and parameter estimation. *ASME J. BME*, 1993. 115: p. 380-388.
18. Pennes, H.H. Analysis of Tissue and Arterial Blood Temperature in the Resting Human Forearm. in *J. of Applied Physiology*. 1948.
19. C.X. Zhang, et al. Effects of Large Blood Vessels Locations During High Intensity Focused Ultrasound Therapy for Hepatic Tumors: a finite element study. in *Proceeding on the 2005 IEEE Engineering in Medecine and Biology*

- 27th Annual Conference 2005. Shanghai, China: IEEE.
20. Zienkiewicz O.C. and Taylor R.L., *The Finite Element Method*. 5th ed. 2000, Butterworth-Heinemann, Woburn.
  21. Huebner K.H., et al., *Finite Element Method for Engineers*. 4th ed. 2001, NY: John Wiley & Sons.
  22. Reddy J.N., *An Introduction to the Finite Element Method*. 1984, USA: Mc.Graw-Hill.
  23. Huang, S., et al., A Common Framework for Generating Liver Tetrahedral FEM Models from CT Slices. *IEEE Xplore*, 2008.
  24. Kim, C., et al., Finite-Element Analysis of Ex Vivo and In Vivo Hepatic Cryoablation. *IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING*, 2007. 54(7): p. 1177-1185.
  25. Incropera, F.P. and D.P. Dewitt, *Fundamentals of Heat and Mass Transfer* 4ed. 1996: John Wiley & Sons.
  26. El-Bastawissy, E., M.H. Knaggs, and I.H. Gilbert, Molecular dynamics simulations of wild-type and point mutation human prion protein at normal and elevated temperature. *Journal of Molecular Graphics and Modelling*, 2001. 20: p. 145–154.
  27. Kolomeisky, A.B., Channel-Facilitated Molecular Transport Across Membranes: Attraction, Repulsion and Asymmetry. Los Alamos National Laboratory, Preprint Archive, Condensed Matter, 1-13, arXiv:cond-mat/0610086, 2006.
  28. R. Koradi a, M. Billeter b, and P. Güntert c, Point-centered domain decomposition for parallel molecular dynamics simulation. *Computer Physics Communications*, 2000. 24: p. 139–147.
  29. Huh, J. and J.W. Ho., Simulations of self-assemble structures in macromolecular systems: from atomistic model to mesoscopic model. . Hyperstructured Organic Materials Research Center, Seoul National University, Seoul, S. Korea. *Polymer (Korea)*, 2006. 30(6): p. 453-463.
  30. McGuffee, S.R. and A.H. Elcock, Atomically Detailed Simulations of Concentrated Protein Solutions: The Effects of Salt, pH, Point Mutations, and Protein Concentration in Simulations of 1000-Molecule Systems *J. Am. Chem. Soc.*, 2006. 128(37): p. 12098 -12110.
  31. Lin, D.T.W. and Y.-C. Hu. A Molecular Dynamics Study of Thermal Ablation. in *Proceedings of the 1st IEEE International Conference on Nano/Micro Engineered and Molecular Systems*. 2006. Zhuhai, China: IEEE.
  32. Colombani, J., et al., A molecular dynamics study of thermal diffusion in a porous medium. *Phys. Chem. Chem. Phys.*, 2002. 4: p. 313–321.
  33. Sonnenberg, E.V., W. McMullen, and L. Silbiati, *Tumor Ablation*. 2005: Springer.
  34. D.A. McQuarrie, *Statistical Mechanics*. Harper Collins, New York, 1976.
  35. J. de Andrade and H. Stassen, Molecular Dynamics Studies of Thermal Conductivity Time Correlation Functions. *J. Molecular Liquids*, 2004. 110: p. 169-176.