

## OPTIMIZATION OF PERFUSION/CONDUCTION FREEZING PROTOCOLS FOR PRESERVATION OF THREE-DIMENSIONAL ORGANS

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### ABSTRACT

In this substantiated proof-of-concept study it has been successfully demonstrated that it is possible to numerically simulate the entire freezing protocol of realistic three-dimensional organs using simultaneously heat conduction via external cooling and heat convection via internal perfusion. It has been successfully demonstrated numerically that it is possible to control the thermoelastic stresses during freezing of organs by periodically optimizing time-varying temperature distribution on the surface of the freezing container. This suggests that it may be possible to develop optimally controlled protocols for freezing organs. Using more diverse tissue sub-domains, more accurate non-isotropic thermophysical tissue data, finer spatial and temporal discretization, and more geometrically complicated configurations of organs and containers is a relatively straightforward future extension of this work. However, a considerably more challenging extension of this work would be to incorporate effects of viscoplasticity of the freezing tissue.

### INTRODUCTION

One of the serious difficulties encountered by surgeons involved with organ transplantation is the shortage of available organs. It would be invaluable to establish organ banks that could store organs with different immunological properties in a frozen state for lengthy periods of time. The organs could be cooled in a special gelatin while being internally perfused by a cooling liquid. Because of the difficulties in controlling the local cooling rates within a three-dimensional organ, extreme thermal stresses develop that cause fractures of the organ tissue. Consequently, over the past four decades, experimental attempts at viably freezing organs have been unsuccessful. However, there is the possibility that mathematically optimum

freezing protocols could be determined that will maximize the survivability of organs. The authors have developed a preliminary mathematical model and computer simulation and optimization of this process. A time-accurate finite element computer program was used to predict unsteady heat conduction with phase change, thermal stresses and coolant flow within the realistically shaped organs. A micro-genetic optimization algorithm and a robust response surface based self-adapting optimizer were then used to achieve nonlinear constrained optimization of time-varying container wall temperature distribution so that the prescribed maximum allowable thermal stress levels are never exceeded throughout the organ.

The objective of this paper is to present a fully automatic computational procedure that can determine the optimum time variation of temperature distribution on the surface of the freezing container and the optimum time variation of temperature and flow rate of the perfusing coolant so that the local thermal stresses can be maintained below a specified level at each instant of time at every point in the arbitrarily shaped and sized organ. Most significantly, the results of this research will offer substantial evidence towards answering the still open question: is freezing of three-dimensional organs possible without causing irreparable damage due to fracturing of the organ tissue?

### MULTILEVEL PARALLELISM IN OPTIMIZATION

The usual approach to parallel optimization is to run a single analysis on each processor per optimization iteration. However, a mesh for a geometrically complex design may be large; sometimes the finite element analysis requires more memory than is available on a single processor. For this reason, the finite element analysis must be distributed among several processors. If a large number of processors are available, we

can use all of them by running several simultaneous parallel analyses to evaluate several candidate design configurations. We have developed an optimization communication module with the MPI library that utilizes this multilevel hierarchy of parallelism. This module can be used with any parallel optimization method including GA and IOSO algorithms.

## THERMAL AND FLUID FLOW ANALYSIS

The thermal, thermoelastic, and coolant fluid flow analysis is performed by a set of parallelized finite element analysis computer codes. The finite element analysis codes and tools for mesh generation, mesh partitioning, and others are freely available as a part of the ADVENTURE project lead by the University of Tokyo. The finite element solvers are geared towards large-scale parallel analysis and are well suited to the efficient analysis of complicated geometries.

## REFERENCES

1. Madison, J. V., Dulikravich, G. S. and Hayes, L. J., 1987, "Optimization of Container Wall Temperature Variation During Transplant Tissue Cooling," *Proc. of International Conference on Inverse Design Concepts and Optimization in Eng. Sciences (ICIDES-II)*, (ed: G. S. Dulikravich), Pennsylvania State University, University Park, PA, Oct. 26-28, 1987, pp. 321-336.
2. Dulikravich, G. S., 1988, "Inverse Design and Active Control Concepts in Strong Unsteady Heat Conduction," *Appl. Mech. Rev.*, Vol. 41, No. 6, pp. 270-277.
3. Dulikravich, G. S. and Hayes, L. J., 1988, "Control of Surface Temperatures to Optimize Survival in Cryopreservation," ASME Winter Annual Meeting, Chicago, Illinois, Nov. 27 - Dec.2, 1988, *Proceedings of the Symposium on Computational Methods in Bioengineering*, (eds: Spilker, R. L. and Simon, B. R.), ASME BED-Vol. 9, pp. 255-265.
4. Dulikravich, G. S., Madison, J. V., and Hayes, L. J., 1989, "Control of Interior Cooling Rates in Heterogeneous Materials by Varying, Surface Thermal Boundary Conditions," 1st Pan-American Congress of Applied Mechanics (PACAM), eds: C. R. Steele and L. Bevilacqua, Rio de Janeiro, Brazil, January 3-6, 1989, pp. 420-423.
5. Ambrose, C., Hayes, L. J., and Dulikravich, G. S., 1989, "An Active Control System for Thermal Fields in Hypothermic Processes," ASME National Heat Transfer Conference, Philadelphia, PA, Aug. 6-9, 1989, eds: S. B. Yilmaz, *AICHE Symposium Series 269*, Vol. 85, pp. 440-405.
6. Dennis, B. H., and Dulikravich, G. S., 2000, "Determination of Unsteady Container Temperatures During Freezing of Three-dimensional Organs With Constrained Thermal Stresses," *Internat. Symposium on Inverse Problems in Engineering Mechanics - ISIP'2k*, (eds: M. Tanaka and G. S. Dulikravich), Nagano, Japan, March 7-10, 2000, Elsevier Science Ltd, Amsterdam, pp. 139-148.
7. Dennis, B. H., Eberhart, R. C., Dulikravich, G. S. and Radons, S. W., 2002, "Finite Element Simulation of Cooling of 3-D Human Head and Neck", ASME IMECE 2002, paper IMECE2002-HT-32045, New Orleans, LA, November 17-22, 2002.
8. Dennis, B. H., Dulikravich, G. S. and Rabin, Y., 2000, "Optimization of Organ Freezing Protocols With Specified Allowable Thermal Stress Levels", Symposium on Advances in Heat and Mass Transfer in Biotechnology, (eds: Scott, E. P. and Bischof, J. C.), ASME IMECE 2K, Orlando, FL, Nov. 5-10, 2000, HTD-Vol. 368/BED-Vol. 47, pp. 33-48.
9. Han, Z.-X., Dennis, B. H. and Dulikravich, G. S., 2001, "Simultaneous Prediction of External Flow-Field and Temperature in Internally Cooled 3-D Turbine Blade Material", *International Journal of Turbo & Jet-Engines*, Vol. 18, No. 1, pp. 47-58.
10. Dulikravich, G. S., Martin, T. J., Dennis, B. H. and Foster, N. F., 1999, "Multidisciplinary Hybrid Constrained GA Optimization", Chapter 12 in *EUROGEN'99 - Evolutionary Algorithms in Engineering and Computer Science: Recent Advances and Industrial Applications*, (editors: K. Miettinen, M. M. Makela, P. Neittaanmaki and J. Periaux), John Wiley & Sons, Ltd., Jyvaskyla, Finland, May 30 - June 3, 1999, pp. 231-260.
11. Egorov, I. N., 1998, "Indirect Optimization Method on the Basis of Self-Organization", Curtin University of Technology, Perth, Australia., *Optimization Techniques and Applications (ICOTA'98)*, Vol.2, pp. 683-691.
12. Egorov, I. N., Kretinin, G. V., Leshchenko, I. A., Kostiuk, S. S., 1999, "The Methodology of Stochastic Optimization of Parameters and Control Laws for the Aircraft Gas-Turbine Engines Flow Passage Components", ASME paper 99-GT-227.
13. Gropp, W., Lusk, E., and Skjellum, A., 1994, *Using MPI: Portable Parallel Programming with the Message-Passing Interface*, MIT Press.
14. ADVENTURE Project Homepage, <http://adventure.q.t.u-tokyo.ac.jp>.
15. Shewchuk, J.R., 1996, "Triangle: Engineering a 2D Quality Mesh Generator and Delaunay Triangulator," First Workshop on Applied Computational Geometry, Philadelphia, PA.
16. Marcum, D. L. and Weatherhill, N. P., 1995, "Unstructured Grid Generation Using Iterative Point Insertion and Local Reconnection", *AIAA Journal*, Vol. 33, No. 9, pp. 1619-1625.

