ABSTRACT
The objective of this study is to develop a generic numerical model to simulate the coupled solute and solvent transport process during the addition and removal of cryoprotective agents (CPAs) in biological tissue systems. The model accounts for the axial and radial diffusion of the solute as well as axial convection. In addition, the model also accounts for the radial movement of the solvent (water) into the vascular spaces. Although not shown in the present study, the model developed has the capability to simulate the radial diffusion of both the solute and the solvent in the interstitial spaces as well. Osmotic responses of the tissue cells are simulated by the numerical model with different solute permeability coefficients \( \omega \), water permeability coefficients \( L_p \), reflection coefficients \( \sigma \) and the diffusion coefficients of the solute in the vascular space (D). The results indicate that these parameters play an important role in the osmotic response of embedded tissue cells.

INTRODUCTION
The use of low temperature to preserve or store viable biological systems such as cell and tissue in the frozen state for a long period of time has been successfully applied in practice. And researchers continue to develop cryopreservation protocols to improve the post-thaw viability of the biological system. During a typical cryopreservation protocol the cells tolerate five non-physiological conditions: (i) addition of molar concentrations of cryoprotective additives (CPAs), causing “osmotic” injury; (ii) cooling to subzero temperatures, causing “chilling” injury; (iii) removal or conversion of almost all liquid cell water into the solid state, or the freezing process, (iv) warming to room temperature, causing both “recrystallization” and other “thawing” injury; (v) removal of CPAs, causing “osmotic” injury [2].

The rates of introduction and removal of cryoprotective additives (CPAs) affect the successful freeze preservation of biomaterial. On the basis of a nonequilibrium model for the transport of water and permeable solute across cell membranes, Levin and Miller [5] devised an optimum method for the introduction and the removal of permeable cryoprotectants from single, isolated cells so that “osmotic” injury can be minimized. This original work has been extended for other isolated single cells [3, 7]; Levin [6] also investigated the osmotic effects of introducing and removing cryoprotectants for perfused tissues and organs; transport of a non-permeating CPA in a liver tissue was studied recently with experimental and theoretical techniques by Bhowmick et. al. [1]. In this project, we focus on the development of a numerical model to simulate the individual tissue cell osmotic response during conditions (i) and (v) of a typical cryopreservation protocol in the presence of both permeable and impermeable solutes.

MATHEMATICAL MODEL
The description of the mass (solute) transport process uses a coupled convection-diffusion equation.

\[
\frac{\partial C}{\partial t} + \frac{\partial (VC)}{\partial x} = D \frac{\partial^2 C}{\partial x^2}
\]

where \( C \) denotes the concentration of the solute or the CPA; \( V \) denotes the velocity vector field and \( D \) is the assumed constant diffusion coefficient. We also use Kedem and Katchalsky equations [4] to analyze nonequilibrium osmotic flows and net solute movements in our model.

\[
J_V = L_p[\Delta p - RT\sigma \Delta C_{\text{cpa}}]
\]

\[
J_{\text{cpa}} = \Delta C_{\text{cpaave}} (1 - \sigma) J_V + RT\omega \Delta C_{\text{cpa}}
\]

where \( J_V \) and \( J_{\text{cpa}} \) are the water flux and the solute flux, respectively. The terms \( \Delta p \) and \( \Delta C_{\text{cpa}} \) represent, respectively, the difference in the hydrostatic pressures and the osmolalities of the solutes across the cell membrane. \( \Delta C_{\text{cpaave}} \) represents the “log mean” osmolality of the permeable solute.

\[
\Delta C_{\text{cpaave}} = \frac{\Delta C_{\text{cpa}}}{\ln(C_{\text{cpa}}^O / C_{\text{cpa}}^I)}
\]

where the superscripts \( O \) and \( I \) represent the extracellular and intracellular space, respectively. A more detailed description of the
RESULTS AND DISCUSSION

The horizontal arrows in the Fig 1(A) represent solute convection flow in the axial direction; and the vertical arrows represent solvent (water) movement into the vascular space. And the arrows shown in Fig 1 (B) represent the CPAs or solute movement into the intracellular space in the radial direction.

CONCLUSION

The goal of this project is to simulate the coupled solute and solvent transport, and analyze the effects of various parameters on the process. The mathematical model is based on 3 basic equations and uses a finite difference discretization scheme [1]. The model developed in this study has the unique capability to predict the osmotic response of individual tissue cells within a tissue slice exposed to different concentration CPAs. In addition, preliminary data indicates that we can calculate, for the first time, the individual tissue cell membrane values \( \sigma \), \( L_p \) and \( \sigma \), by fitting our model results to experimentally obtained osmotic response at various locations in a tissue system [8].

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REFERENCE: