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An optimal control problem for controlling the cell volume in dehydration and rehydration process

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Abstract

An optimal control algorithm utilizing the conjugate gradient method (CGM) of minimization is applied successfully in the present study in determining the optimal boundary control function for a diffusion-limited cell model based on the desired cell volume. The validity of the present optimal control analysis is examined by means of numerical experiments. Different desired cell volume for dehydration, rehydration and their combination are given in three test cases with different weighting coefficients and the corresponding optimal control functions are determined. The results show that the optimal boundary control functions can be obtained with an arbitrary initial guess within one second CPU time on a Pentium III-600 MHz PC.

1. Introduction

Cryopreservation is a new technology for application in the fields of tissue engineering, biotechnology and cell and organ transplantation, where prolonged storage of living biological systems is required. Considerable works have been done in mathematical modeling and simulation for the cell freezing process [1–4], however, comparatively few works have been made in the simulation of cell damage during warming from the crypreserved state.

According to Kasharin and Karlsson [5], the models for cell dehydration during freezing process assumed that water transport is limited by membrane transport only. This is not valid during cell warming since the high solution viscosity at cryogenic temperature results in solute polarization and diffusion-limited water transport. For this reason the diffusion-limited model for cell dehydration during cryoperservation becomes important.

The first investigation of the diffusion-limited model with moving, semipermeable boundary is done by Levin et al. [6]. Recently, Kasharin and Karlsson [7] reformulated the model and examined the numerical stability requirement for the simplified model, i.e. the boundary condition at cell membrane is simplified and the moving boundary condition is ignored.

In order to consider the optimal control problem for both cell freezing (dehydration) and cell thawing (rehydration), the direct problem of the present study is based on the model used in [7] but the complete formulation for boundary condition at cell membrane and moving boundary condition are considered. The intracellular water concentration and volume of cell can be calculated simultaneously in this model by giving time-varying water concentration at the external surface of the cell.

As we may know that significant damage can occur to specimens during the procedures of freezing and thawing, this is because cells are killed when their tolerance of dehydration and rehydration is exceeded, i.e. the change of cell volume is too rapid. This is apparent due to failure of the structure of the membranes [8]. For this reason if one can devise an algorithm which the cell volume can be controlled by optimal controlling the

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Nomenclature

c_w	water concentration
c_w^{ex}	extracellular water concentration
D	the diffusion constant
J	functional defined by Eq. (7)
J'	gradient of functional defined by Eq. (20)
J_w	molar flux of water
L	the permeability of the cell membrane to water
P	direction of descent defined by Eq. (9)
P_{e0}	the initial value of Peclet number
R	cell membrane
Y	desired water concentration
y	estimated water concentration
y^{ex}	control function
Δy	sensitivity functions defined by Eq. (11)
V	cell volume
Greek symbols	
α	weighting coefficient
β	search step size
γ	conjugate coefficient
λ	Lagrange multipliers defined by Eq. (17)
Superscript	
n	iteration index

external time-varying water concentration, the cell surviving rate could be increased significantly during the procedures of freezing and thawing.

Optimal control laws have received increased attention in recent years in many engineering applications. Such system can be controlled either at the boundary (boundary control) or through the spatial domain (distributed control), or both.

Optimal control techniques can be applied in many different fields of research, especially in heat transfer engineering (or diffusion equation). This type of problems has been initiated by Butkovskii and Lerner [9]. Meric [10] used the conjugate gradient method to find the optimal boundary control temperatures for a non-linear system, i.e. temperature-dependent thermal properties. Chen and Ozisik used similar algorithm to determine the optimal heating sources for a cylinder [11] in a non-linear optimal control problem. Recently, Huang used a similar algorithm to determine the optimal boundary control functions for a non-linear heat transfer problem [12], to determine the optimal boundary control function for a concurrent flow problem based on the desired thermal entry length and fluid temperatures [13] and to optimal heating for a 3-D forced convection problem [14].

The objective of the present study is to apply the conjugate gradient method (CGM) in determining the optimal boundary control function, i.e. the external time-varying water concentration, based on the desired cell volume. To the author's best knowledge, this technique has not been seen in the literature for this type of application.

The conjugate gradient method of optimal control derives basis from the perturbational theory [15] and transforms an inverse problem to the solution of three problems, namely, the direct problem, a sensitivity problem and an adjoint problem, which will be discussed in detail in the following sections.

2. Direct problem

To illustrate the methodology for developing expressions for use in determining the optimal extracellular water concentration for controlling the desired cell volume, we consider the following optimal control problem.

The cell is modeled in a one-dimensional Cartesian coordinate with width $2R(t)$. The boundaries on each side are subjected to a semipermeable membrane. The magnitude of the osmotically driven flow of water across the cell membrane depends on the water concentration $c_w(R,t)$ at the inside surface of membrane and extracellular water concentration $c_w^{ex}(t)$. The molar flux of water J_w can be expressed as

$$J_w = L\left[c_w(R,t) - c_w^{ex}(t)\right], \tag{1}$$

where L is the permeability of the cell membrane to water.

The governing equation and boundary conditions of diffusion of water inside the cell with moving, semipermeable boundary can be expressed as follows [7]:

$$D\frac{\partial^2 c_w(r,t)}{\partial r^2} = \frac{\partial c_w(r,t)}{\partial t} \quad \text{in } 0 < r < R(t),\ 0 < z < z_f; \tag{2a}$$

$$\frac{\partial c_w(r,t)}{\partial r} = 0 \quad \text{at } r = 0; \tag{2b}$$

$$-D\frac{\partial c_w(r,t)}{\partial r} = c_w\frac{dR}{dt} + J_w \quad \text{at } r = R(t); \tag{2c}$$

$$c_w(r,t) = c_0 \quad \text{for } t = 0. \tag{2d}$$

Here D is the diffusion constant, c_0 is the initial water concentration and $c_w(r,t)$ is the water concentration inside the cell.

The motion of boundary $R(t)$ is determined by considering the cell volume change due to the water efflux J_w

$$\frac{dR}{dt} = -J_w v_w, \tag{3}$$

Here v_w is the specific volume of water. $\frac{dR}{dt} < 0$ represents cell dehydration and $J_w > 0$, i.e. the cell is shrinking, $\frac{dR}{dt} > 0$ indicates cell rehydration and $J_w < 0$, i.e. the cell is swelling.

By defining the following dimensionless functions [7]

$$y(x,\tau) = \frac{c_w(x,\tau) - c_w^{ex}(\tau)}{\Delta c_0}, \tag{4a}$$

$$y^{ex}(\tau) = \frac{c_w^{ex}(\tau) - c_w^{ex}(0)}{\Delta c_0}, \tag{4b}$$

where $\Delta c_0 = [c_w(R,0) - c_w^{ex}(0)]$ and defining the following dimensionless parameters:

$$V(\tau) = \frac{R(\tau)}{R(0)}, \quad x = \frac{r}{R(\tau)}, \quad d\tau = \frac{D}{R(\tau)^2}dt.$$

The dimensionless diffusion equation for water concentration $y(x,\tau)$ inside the cell is as follows:

$$\frac{\partial^2 y(x,\tau)}{\partial x^2} = \frac{\partial y(x,\tau)}{\partial \tau} + \frac{\partial y^{ex}(\tau)}{\partial \tau} \quad \text{in } 0 < x < 1, \ 0 < \tau < \tau_f; \tag{5a}$$

$$\frac{\partial y(x,\tau)}{\partial x} = 0 \quad \text{at } x = 0; \tag{5b}$$

$$\frac{\partial y(x,\tau)}{\partial x} = -\frac{LR(\tau)}{D} y\{1 - [y\Delta c_0 + y^{ex}\Delta c_0 + c_w^{ex}(0)]v_w\} \quad \text{at } x = 1; \tag{5c}$$

$$y(x,\tau) = 1 \quad \text{for } \tau = 0; \tag{5d}$$

and the motion of cell boundary $V(\tau)$ becomes

$$\frac{dV(\tau)}{d\tau} = -P_{e0}(\Delta c_0 v_w) y(1,\tau) V(\tau)^2, \tag{6}$$

where P_{e0} is the initial value of Peclet number and is defined as $P_{e0} = \frac{LR(0)}{D}$.

We should note that the formulation of the present direct problem is identical to that for [7] except for Eq. (5c). In [7], the authors simplified the nonlinear boundary condition (5c) in terms of a modified Peclet number, this may simplify the numerical calculations but at the same time this may also lost its physical significance. For this reason we expressed the complete formulation for boundary condition at cell membrane, i.e. Eq. (5c), and solve it numerically.

Moreover, in [7] the cell volume is assumed fixed regardless its nature of moving boundary, therefore Eq. (6) is ignored, it is also not applicable to reality situation. This matter is going to be improved in the present calculations (i.e. a moving boundary problem will be considered) and is discussed in the next section.

It is obvious from Eqs. (5) and (6) that both water concentration and cell volume are unknown. This is a typical moving boundary problem and the iterative technique is needed. Here the iterative implicit finite-difference method with variable time step can be used to solve this direct problem.

3. Optimal control problem

In the optimal control problem, the control function $y^{ex}(\tau)$ is regarded as being unknown, but everything else in Eq. (5) is known. In addition, the desired cell volume as a function of time $V_d(\tau)$ (either for cell shrinking or cell swelling) is considered available. Based on the variation of desired cell volume $V_d(\tau)$, the corresponding desired water concentration at the inside surface of cell membrane can be determined from Eq. (6).

If the space domain is subdivided into fixed equal intervals Δx, but time step is varied such that the cell boundary moves a distance Δx during the time interval $\Delta\tau(\tau)$, hence always remains at a grid point at the end of each time interval $\Delta\tau(\tau)$. Moreover, once the desired cell volume $V(\tau)$ is given, the boundary moving velocity $\frac{dV(\tau)}{d\tau}$ can also be determined. For this reason, for a fixed Δx, the variable $\Delta\tau(\tau)$ can thus be calculated.

Let the desired water concentration be denoted by $Y(1,\tau)$. Then this optimal control problem can be stated as follows: by utilizing the above mentioned desired water concentration $Y(1,\tau)$, estimate the optimal values for extracellular water concentration $y^{ex}(\tau)$ over the specified time domain to control the system and to match the requirement.

The solution of the present optimal control problem is to be obtained in such a way that the following functional is minimized:

$$J[y^{ex}(\tau)] = \int_{\tau=0}^{\tau_f} [y(1,\tau) - Y(1,\tau)]^2 d\tau + \frac{\alpha}{2}\int_{\tau=0}^{\tau_f} y^{ex}(\tau)^2 d\tau. \tag{7}$$

Here α is a given weighting coefficient. $y(1,\tau)$ is the estimated or computed water concentration at the inside surface of cell membrane within the specified time domain. These quantities are determined from the solution of the direct problem given previously by using the estimated control function $y^{ex}(\tau)$.

The second term on the right hand side of Eq. (7) is the integration with respect to time of the square of the control function $y^{ex}(\tau)$ multiplied by the weighting coefficient α. The square of the control function (i.e. the quadratic form) guarantees the existence of the minimum and avoids the cancellation effect between the positive and negative values.

The weighting coefficient α is the design parameter that controls the closeness of the estimated concentration to the desired concentration. For example, $\alpha = 0$ implies estimated cell volume close to the desired cell volume, but the estimated optimal control function may exist oscillatory behavior. Therefore a finite value for α is needed to damp such an oscillation. Moreover, it can also be used as the adjustment factor of the control function $y^{ex}(\tau)$.

4. Conjugate gradient method for minimization

The following iterative process based on the conjugate gradient method [15] is now used for the estimation of control function $y^{ex}(\tau)$ by minimizing the above functional $J[y^{ex}(\tau)]$:

$$y^{ex\,n+1}(\tau) = y^{ex\,n}(\tau) - \beta^n P^n(\tau), \quad n = 0, 1, 2, \ldots, \tag{8}$$

where β^n is the search step size in going from iteration n to $n+1$, and $P^n(\tau)$ is the direction of descent (i.e. search direction) given by

$$P^n(\tau) = J'^n(\tau) + \gamma^n P^{n-1}(\tau), \tag{9}$$

which is a conjugation of the gradient direction $J'^n(\tau)$ at iteration n and the direction of descent $P^{n-1}(\tau)$ at iteration $n-1$. The conjugate coefficient is determined from

$$\gamma^n = \frac{\int_{\tau=0}^{\tau_f} [J'^n(\tau)]^2 \, d\tau}{\int_{\tau=0}^{\tau_f} [J'^{n-1}(\tau)]^2 \, d\tau} \quad \text{with } \gamma^0 = 0. \tag{10}$$

To perform the iterations according to Eq. (8), we need to compute the step size β^n and the gradient of the functional $J'^n(\tau)$. In order to develop expressions for the determination of β^n and $J'^n(\tau)$, a "sensitivity problem" and an "adjoint problem" are constructed as described below.

5. Sensitivity problem and search step size

It is assumed that when the control function $y^{ex}(\tau)$ undergoes a variation $\Delta y^{ex}(\tau)$, $y(x,\tau)$ is perturbed by $\Delta y(x,\tau)$. Then replacing in the direct problem $y^{ex}(\tau)$ by $y^{ex}(\tau) + \Delta y^{ex}(\tau)$, $y(x,\tau)$ by $y(x,\tau) + \Delta y(x,\tau)$, subtracting from the resulting expressions the direct problem and neglecting the second-order terms, the following sensitivity problem for the sensitivity function $\Delta y(x,\tau)$ is obtained:

$$\frac{\partial^2 \Delta y(x,\tau)}{\partial x^2} = \frac{\partial \Delta y(x,\tau)}{\partial \tau} + \frac{\partial \Delta y^{ex}(\tau)}{\partial \tau} \quad \text{in } 0 < x < 1, \; 0 < \tau < \tau_f; \tag{11a}$$

$$\frac{\partial \Delta y(x,\tau)}{\partial x} = 0 \quad \text{at } x = 0; \tag{11b}$$

$$\frac{\partial \Delta y(x,\tau)}{\partial x} = -\frac{LR(\tau)}{D}\left\{\Delta y - \left[2y\Delta y \Delta c_0 + (y\Delta y^{ex} + \Delta y y^{ex})\Delta c_0 + \Delta y c_w^{ex}(0)\right] v_w\right\} \quad \text{at } x = 1; \tag{11c}$$

$$\Delta y = 0 \quad \text{for } \tau = 0. \tag{11d}$$

We should note that the above sensitivity problems can be solved by using the implicit finite-difference method. Here the boundary condition (11c) becomes linear and the iterative technique is not needed.

The functional $J(y^{ex\,n+1})$ for iteration $n+1$ is obtained by rewriting Eq. (7) as

$$J[y^{ex}(\tau)] = \int_{\tau=0}^{\tau_f} [y(1,\tau; y^{ex\,n} - \beta^n P^n) - Y(1,\tau)]^2 \, d\tau + \frac{\alpha}{2}\int_{\tau=0}^{\tau_f} (y^{ex\,n} - \beta^n P^n)^2 \, d\tau, \tag{12}$$

where we replaced $y^{ex\,n+1}(\tau)$ by the expression given by Eq. (8). If the estimated concentration $y(1,\tau; y^{ex\,n} - \beta^n P^n)$ is linearized by a Taylor expansion, Eq. (12) takes the form

$$J[y^{ex}(\tau)] = \int_{\tau=0}^{\tau_f} [y(1,\tau; y^{ex\,n}) - \beta^n \Delta y(P^n) - Y(1,\tau)]^2 \, d\tau + \frac{\alpha}{2}\int_{\tau=0}^{\tau_f} (y^{ex\,n} - \beta^n P^n)^2 \, d\tau, \tag{13}$$

where $y(1,\tau; y^{ex\,n})$ is the solutions of the direct problem by using estimate control function $y^{ex}(\tau)$. The sensitivity function $\Delta y(p^n)$ is taken as the solutions of problem (11) by letting $\Delta y^{ex}(\tau) = p^n(\tau)$.

Eq. (13) is differentiated with respect to β^n, and equating it equal to zero to obtain the following expression for the search step size β^n as

$$\beta^n = \frac{\int_{\tau=0}^{\tau_f} [2(y - Y)\Delta y(P^n) + \alpha y^{ex\,n} P^n] \, d\tau}{\int_{\tau=0}^{\tau_f} [2(\Delta y)^2 + \alpha (P^n)^2] \, d\tau}. \tag{14}$$

6. Adjoint problem and gradient equation

To obtain the adjoint problem, Eq. (5a) is multiplied by the Lagrange multiplier (or adjoint function) $\lambda(x,\tau)$ and the resulting expression is integrated over the specified space and time domains. Then the result is added to the right hand side of Eq. (7) to yield the following expression for the functional $J[y^{ex}(\tau)]$:

$$J[y^{ex}(\tau)] = \int_{\tau=0}^{\tau_f} [y(1,\tau) - Y(1,\tau)]^2 \, d\tau + \frac{\alpha}{2}\int_{\tau=0}^{\tau_f} y^{ex}(\tau)^2 \, d\tau + \int_{x=0}^{1}\int_{\tau=0}^{\tau_f} \lambda \times \left\{\frac{\partial^2 y(x,\tau)}{\partial x^2} - \frac{\partial y(x,\tau)}{\partial \tau} - \frac{\partial y^{ex}(x,\tau)}{\partial \tau}\delta(x-1)\right\} d\tau \, dx \quad \text{in } 0 < x < 1, \; 0 < \tau < \tau_f. \tag{15}$$

Here $\delta(\cdot)$ represents a Dirac Delta function. Firstly, the variation ΔJ is obtained by perturbing $y^{ex}(\tau)$ by

$y^{ex}(\tau)+\Delta y^{ex}(\tau)$, $y(x,\tau)$ by $y(x,\tau)+\Delta y(x,\tau)$ in Eq. (15), subtracting from the resulting expression the original Eq. (15) and neglecting the second-order terms. We thus find

$$\Delta J[y^{ex}(\tau)] = \int_{\tau=0}^{\tau_f} 2[y(1,\tau)-Y(1,\tau)]\Delta y\,d\tau + \alpha\int_{\tau=0}^{\tau_f} y^{ex}\Delta y^{ex}\,d\tau + \int_{x=0}^{1}\int_{\tau=0}^{\tau_f}\lambda\times\left\{\frac{\partial^2\Delta y(x,\tau)}{\partial x^2}-\frac{\partial\Delta y(x,\tau)}{\partial\tau} - \frac{\partial\Delta y^{ex}(x,\tau)}{\partial\tau}\delta(x-1)\right\}d\tau\,dx$$
$$\text{in } 0<x<1,\ \ 0<\tau<\tau_f. \tag{16}$$

In Eq. (16), the double integral terms are integrated by parts; the boundary conditions of the sensitivity problem are utilized. The vanishing of the integrands leads to the following adjoint problem for the determination of $\lambda(x,\tau)$:

$$\frac{\partial^2\lambda(x,\tau)}{\partial x^2}+2(y-Y)\delta(x-1)+\frac{\partial\lambda(x,\tau)}{\partial\tau}=0$$
$$\text{in } 0<x<1,\ \ 0<\tau<\tau_f; \tag{17a}$$

$$\frac{\partial\lambda(x,\tau)}{\partial x}=0 \quad \text{at } x=0; \tag{17b}$$

$$\frac{\partial\lambda(x,\tau)}{\partial x}=-\frac{LR(\tau)}{D}\lambda\left\{1-\left[2y\Delta c_0+y^{ex}\Delta c_0+c_w^{ex}(0)\right]v_w\right\}$$
$$\text{at } x=1; \tag{17c}$$

$$\lambda=0 \quad \text{for } \tau_f=0. \tag{17d}$$

The adjoint problem is different from the direct problem in that the final time conditions condition at $\tau=\tau_f$ is specified instead of the customary initial value condition. However, this problem can be transformed to a standard problem by the transformation of the variable as $\tau^*=\tau_f-\tau$. Then the standard techniques of implicit finite differences method can be used to solve the above adjoint problem, moreover, boundary condition (17c) also becomes linear.

Finally, the following integral term is left

$$\Delta J=\int_{\tau=0}^{\tau_f}\left[\frac{\partial\lambda}{\partial\tau}+\frac{\lambda LR(\tau)}{D}y\Delta c_0 v_w+\alpha y^{ex}\right]\Delta y^{ex}\,d\tau. \tag{18}$$

From definition [15], the functional increment can be presented as

$$\Delta J=\int_{\tau=0}^{\tau_f}(J')\Delta y^{ex}\,d\tau. \tag{19}$$

A comparison of Eqs. (18) and (19) leads to the following expression for the gradient of functional $J'[y^{ex}(\tau)]$:

$$J'(y^{ex})=\left[\frac{\partial\lambda}{\partial\tau}+\frac{\lambda LR(\tau)}{D}y\Delta c_0 v_w+\alpha y^{ex}\right]. \tag{20}$$

7. Computational procedure

The computational procedure for the solution of this optimal control problem may be summarized as follows:

Suppose $y^{ex}(\tau)$ is available at iteration n.

Step 1. Solve the direct problem given by Eq. (5) for $y(x,\tau)$.

Step 2. Solve the adjoint problem given by Eq. (17) for $\lambda(x,\tau)$.

Step 3. Compute the gradient of the functional $J'[y^{ex}(\tau)]$ from Eq. (20).

Step 4. Compute the conjugate coefficients γ^n and the direction of descent $P^n(\tau)$ from Eqs. (10) and (9), respectively.

Step 5. Set $\Delta y^{ex}(\tau)=P^n(\tau)$ and solve the sensitivity problems given by Eq. (11) for $\Delta y(x,\tau)$.

Step 6. Compute the search step size β^n from Eq. (14).

Step 7. Compute the new estimation for $y^{ex\,n+1}(\tau)$ from Eq. (8) and return to step 1 until the given specified stopping criteria is satisfied.

8. Results and discussion

The physical model for the cell will be modeled as a one-dimensional planar compartment with width $2R(\tau)$. The osmotically active solution is assumed to be pseudo-binary, consisting of water and a solute, of which only water is allowed to pass through the membrane.

The initial concentration c_0 is assumed constant, thus the initial water concentration y (x,0) equals to unity and the initial $y^{ex}(0)$ equals to zero, moreover, $P_{e0}=0.5$, $\Delta c_0=1.0$, $D=2.0$ and $v_w=1.0$ are used in the following calculation.

It is required that the cell volume be satisfied with the variation of desired volume for cell shrinking or cell swelling such that the cell's tolerance for dehydration and rehydration is not exceeded, i.e. the cells will not be killed during the change of cell volume. Once the desired time-varying cell volume is available, the desired water concentration at cell membrane $Y(1,\tau)$ can be calculated from Eq. (6), i.e. the equation of motion for cell boundary. The present optimal control problem is to find the optimal $y^{ex}(\tau)$ such that the desired water concentration $Y(1,\tau)$ can be satisfied.

The boundary of cell is always taken as unity in the present study, the space increment used in numerical calculations are fixed and taken as $\Delta x=0.005$, the time increment is calculated by using $\Delta\tau(\tau)=\Delta x\Big/\frac{dV(\tau)}{d\tau}$, i.e. the system always remains at a grid point at the end of each time interval $\Delta\tau$. $\frac{dV(\tau)}{d\tau}<0$ represents cell dehydration, i.e. the cell is shrinking; $\frac{dV(\tau)}{d\tau}>0$ indicates cell rehydration, i.e. the cell is swelling; $\frac{dV(\tau)}{d\tau}=0$ implies the volume is fixed and time increment for this case can not be calculated from the above equation, it must be assigned artificially based on the duration of time for $\frac{dV(\tau)}{d\tau} = 0$.

To illustrate the accuracy of the conjugate gradient method in predicting $y^{ex}(\tau)$ with optimal control analysis from the knowledge of the desired water concentration at cell membrane $Y(1,\tau)$, we consider following three specific examples.

One of the advantages of using the conjugate gradient method is that the initial guesses of the unknown control function $y^{ex}(\tau)$ can be chosen arbitrarily. In all the test cases considered here, the initial guesses of control function used to begin the iteration are taken as $y^{ex}(\tau)^0 = 0.0$.

We now present below the numerical experiments in determining $y^{ex}(\tau)$ by the optimal control analysis:

8.1. Numerical test case 1: dehydration process

The optimal control problem is firstly performed by examining the monotonically decreasing cell volume during dehydration. The desired cell volume with time $V_d(\tau)$ is given as

$$V_d(\tau) = 1 - 0.5\tau, \quad 0 \leqslant \tau \leqslant \tau_f. \tag{21}$$

The desired water concentration at cell membrane $Y(1,\tau)$ can be calculated based on Eqs. (6) and (21).

For $\alpha = 0.0$, by setting the stopping criteria $\varepsilon = 2 \times 10^{-3}$, after 9 iterations the functional is calculated as $J = 1.7 \times 10^{-3}$ (CPU time at Pentium III-600 MHz PC is about one second) and the solutions for the optimal control function $y^{ex}(\tau)$ can be obtained. Fig. 1 shows the estimated control functions $y^{ex}(\tau)$. Fig. 2 illustrates the desired and estimated water concentration at cell membrane, i.e. $Y(1,\tau)$ and $y(1,\tau)$, respectively, and Fig. 3 shows the desired and estimated cell volume, i.e. $V_d(\tau)$ and $V(\tau)$, respectively.

From those Figures we learned that in order to let cell volume shrinking linearly with time, in accordance with Eq. (6), the desired membrane water concentration is increased parabolically with time with concave up

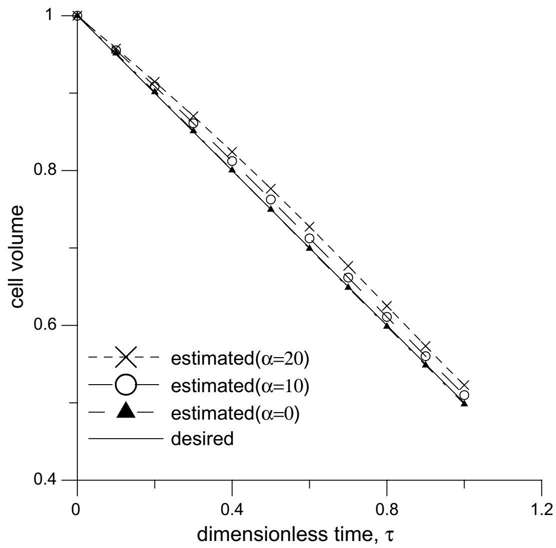

Fig. 2. The desired and estimated cell volume in test case 1.

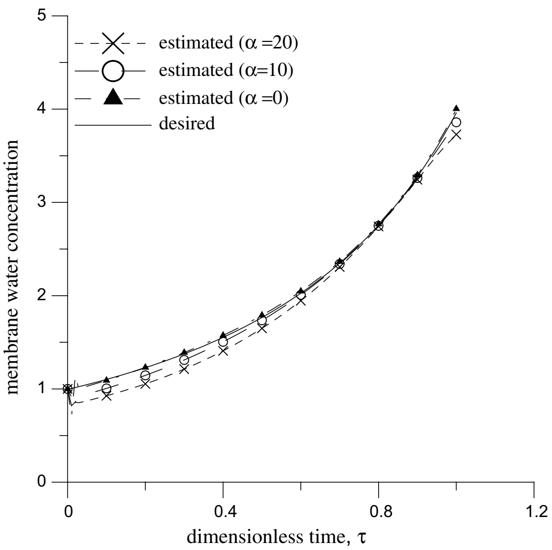

Fig. 1. The desired and estimated water concentration at cell membrane in test case 1.

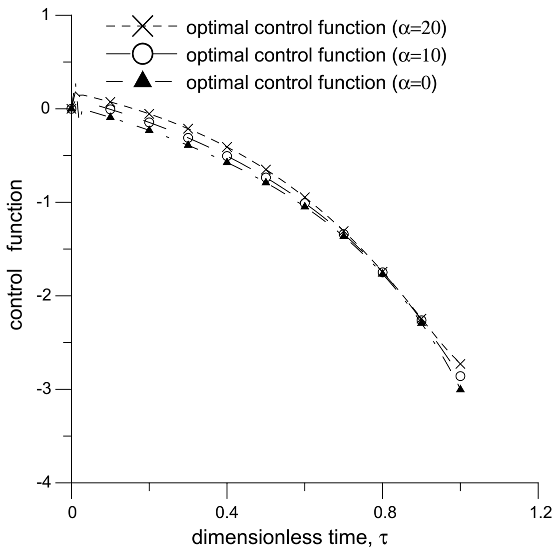

Fig. 3. The estimated optimal control functions using different weighting coefficients in test case 1.

shape (i.e. increases more as time increases) and the optimal control function should be decreased parabolically with time with concave down shape (i.e. decreases more as time increases). This implies that the molar flux is not varying linearly even though the cell volume varying linearly, i.e. more and more molar flux is required during the cell shrinking process.

It is obvious from Figs. 1 and 2 that the control function and the estimated membrane concentration exist some oscillatory behavior in the beginning time, this is quite normal for optimal control problem. It has been shown from these Figures that the oscillatory behavior is gone very soon with time, this implies that the present algorithm has good ability in controlling the cell volume.

The average errors for the estimated water concentration at cell membrane $y(\tau)$ and cell volume $V(\tau)$ are calculated as ERR1 = 0.97% (by neglecting first two oscillatory data) and ERR2 = 0.16%, respectively. The definitions of average error ERR1 and ERR2 are given as

$$\mathrm{ERR1\%} = \left[\sum_{J=1}^{\mathrm{NT}}\left|\frac{y(J)-Y(J)}{Y(J)}\right|\right]\Big/\mathrm{NT}\times 100\%, \qquad (22a)$$

$$\mathrm{ERR2\%} = \left[\sum_{J=1}^{\mathrm{NT}}\left|\frac{V(J)-V_{\mathrm{d}}(J)}{V_{\mathrm{d}}(J)}\right|\right]\Big/\mathrm{NT}\times 100\%. \qquad (22b)$$

Here NT represents the total number of discreted time while NT indicates the index of discreted time.

In order to examine the effectiveness of the weighting coefficient α to the control function we consider the following numerical experiments: The numerical parameters are the same as the original conditions except that $\alpha = 10$ and 20 are used. By setting the stopping criteria $\varepsilon = 4\times10^{-3}$ and 1.5×10^{-2} for $\alpha = 10$ and 20, respectively, after 7 iterations for both cases, the optimal control function $y^{\mathrm{ex}}(\tau)$ can be determined. The results are also shown in Figs. 1–3 for estimated control function, estimated membrane water concentration and estimated cell volume, respectively. For $\alpha = 10$ and 20, the relative errors ERR1 are calculated as 3.38% and 7.42%, and ERR2 are calculated as 1.44% and 3.03%, respectively.

It is clear from these figures that as the weighting coefficient increases, the oscillatory behavior is damped and the absolute value of maximum strength of the control function is decreased, this implies that it is easier to obtain the control function. However, the accuracy of the estimated membrane water concentration and estimated cell volume are both decreased. This implies that as $\alpha = 0$ we can always obtain the best control function to control the cell volume but at the same time more complicated control function is needed.

8.2. Numerical test case 2: rehydration process

In the second test case the numerical parameters are the same as were used in numerical test case 1 except that the desired cell volume $V_{\mathrm{d}}(\tau)$ is now monotonically increasing with time, i.e. rehydration process. The desired cell volume with time $V_{\mathrm{d}}(\tau)$ is given as

$$V_{\mathrm{d}}(\tau) = 1 + 0.2\tau^2, \quad 0 \leqslant \tau \leqslant \tau_{\mathrm{f}}. \qquad (23)$$

The desired water concentration at cell membrane $Y(1,\tau)$ can be calculated based on Eqs. (6) and (23).

For $\alpha = 0.0$, by setting the stopping criteria $\varepsilon = 2.5\times10^{-4}$, after 8 iterations the functional is calculated as $J = 2.4\times10^{-4}$ (CPU time at Pentium III-600 MHz PC is about one second) and the solutions for the optimal control function $y^{\mathrm{ex}}(\tau)$ is shown in Fig. 4. Fig. 5 illustrates the desired, $Y(1,\tau)$, and estimated water concentration at cell membrane, $y(1,\tau)$, and Fig. 6 shows the desired, $V_{\mathrm{d}}(\tau)$, and estimated cell volume, $V(\tau)$.

From those Figures we learned that in order to let cell volume swelling parabolically with time, based on Eq. (6), the desired membrane water concentration is decreased parabolically with time with concave up shape (i.e. decreases less as time increases) and the optimal control function increased parabolically with time with concave down shape (i.e. increases less as time increases). This implies that less and less molar flux is required during the cell rehydration process.

Again, the estimated membrane concentration and control function exist some oscillatory behavior in the beginning time, but the oscillatory behavior is damped quickly.

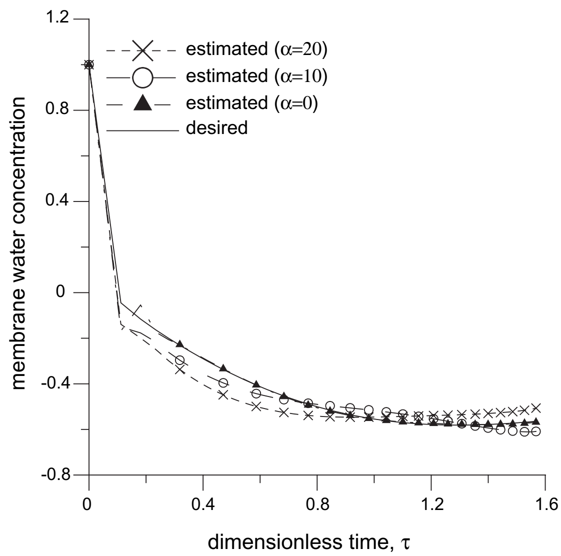

Fig. 4. The desired and estimated water concentration at cell membrane in test case 2.

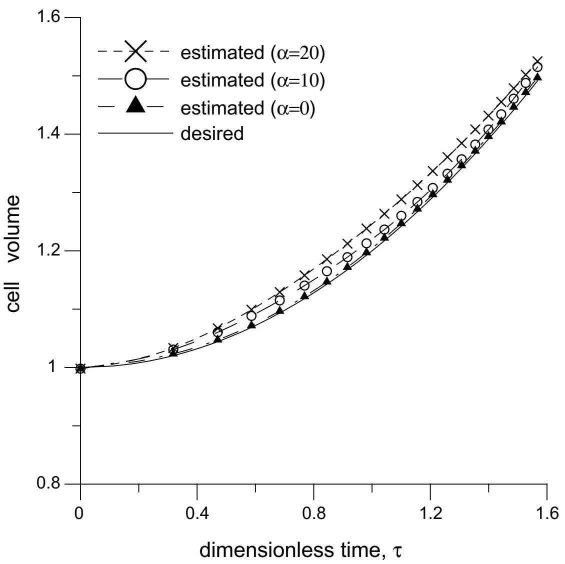

Fig. 5. The desired and estimated cell volume in test case 2.

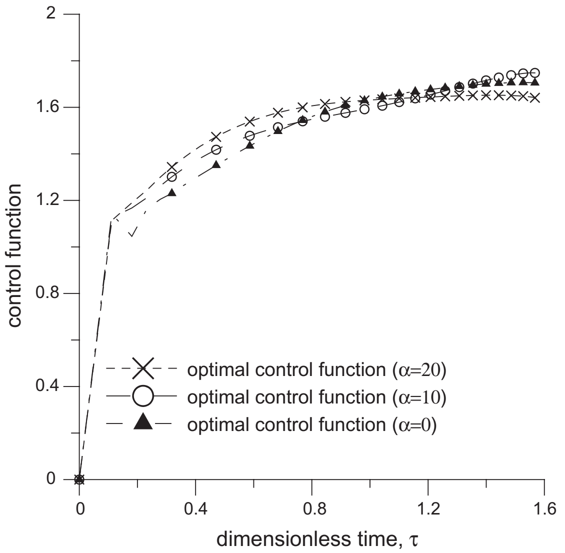

Fig. 6. The estimated optimal control functions using different weighting coefficients in test case 2.

The average errors for the estimated water concentration at cell membrane $y(\tau)$ and cell volume $V(\tau)$ are calculated as ERR1 = 0.62% (by neglecting first two oscillatory data) and ERR2 = 0.35%, respectively.

Next, when the weighting coefficients $\alpha = 10$ and 20 are used, after 5 ($\varepsilon = 1.5 \times 10^{-3}$) and 5 ($\varepsilon = 4 \times 10^{-3}$) iterations for each case, the estimated results are shown in Figs. 4–6 for estimated control function, estimated membrane water concentration and estimated cell volume, respectively. For $\alpha = 10$ and 20, the relative errors ERR1 are calculated as 9.36% and 13.87%, and ERR2 are calculated as 1.53% and 3.31%, respectively.

Again as the weighting coefficient increases, the oscillatory behavior is disappeared and the absolute value of maximum strength of the control function is decreased, at the same time, the accuracy of the estimated membrane water concentration and estimated cell volume are both decreased.

8.3. Numerical test case 3: rehydration and dehydration processes

A stricter situation is examined in the third test case where cell freezing (dehydration) and cell thawing (rehydration) are both allowed during the process, i.e. the cell is not monotonically increasing or decreasing during the process, it is allowed to have the volume of cell shrinking and swelling with time. The desired cell volume with time $V_d(\tau)$ is assumed as a sinusoidal function and is given as

$$V_d(\tau) = 1 - 0.1 \times \sin\left(\frac{\tau}{\tau_f}\right), \quad 0 \leqslant \tau \leqslant \tau_f. \tag{24}$$

The desired water concentration at cell membrane $Y(1, \tau)$ can be calculated based on Eqs. (6) and (24).

The optimal control problem is performed firstly by using $\alpha = 0.0$. For $\varepsilon = 1.5 \times 10^{-4}$, after 6 iterations the functional is calculated as $J = 1.4 \times 10^{-4}$ (CPU time at Pentium III-600 MHz PC is less than one second) and the solutions for the optimal control function $y^{ex}(\tau)$ is shown in Fig. 7. Fig. 8 illustrates the desired, $Y(1, \tau)$,

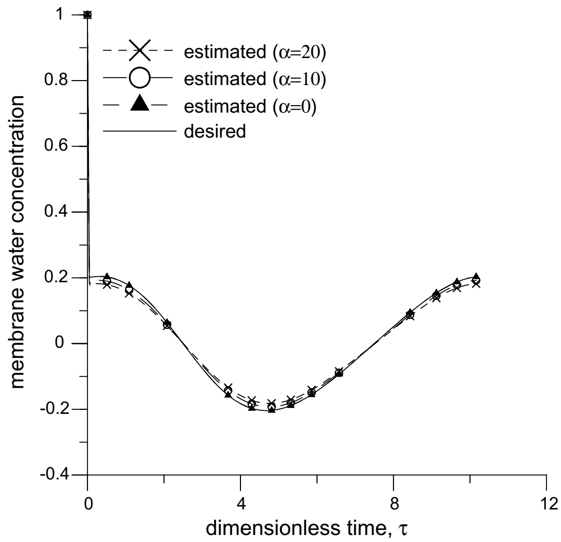

Fig. 7. The desired and estimated water concentration at cell membrane in test case 3.

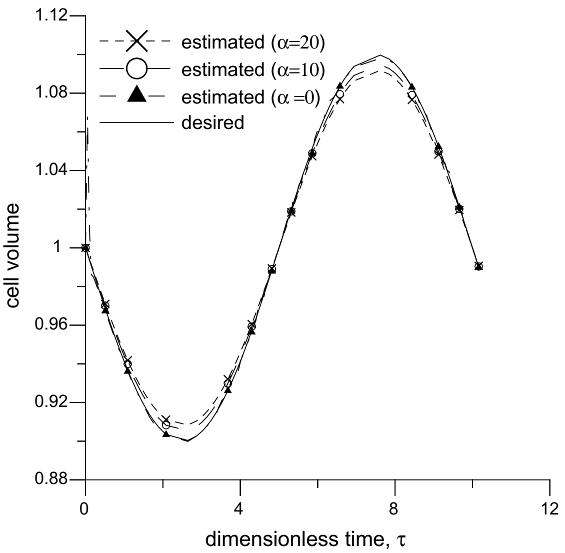

Fig. 8. The desired and estimated cell volume in test case 3.

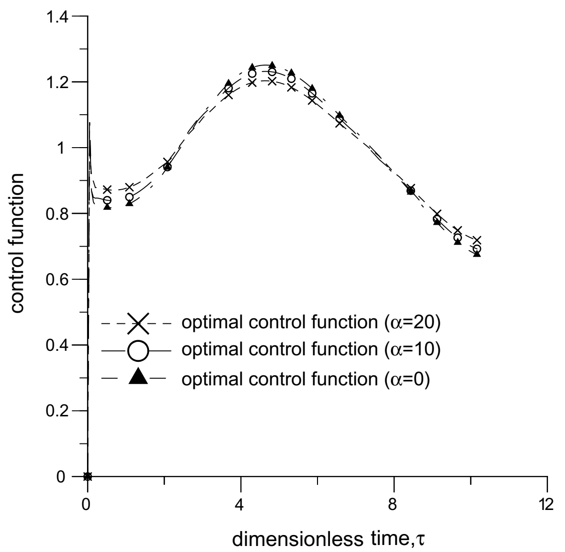

Fig. 9. The estimated optimal control functions using different weighting coefficients in test case 3.

and estimated, $y(1,\tau)$, water concentration at cell membrane and Fig. 9 shows the desired, $V_d(\tau)$, and estimated, $V(\tau)$, cell volumes. From those Figures we learned that the requirement for the desired cell volume can be satisfied. The average errors for the estimated cell volume $V(\tau)$ are calculated as ERR2 = 0.15%.

Then the weighting coefficients $\alpha = 10$ and 20 are utilized, after 5 ($\varepsilon = 1.5 \times 10^{-2}$) and 5 ($\varepsilon = 2.5 \times 10^{-2}$) iterations for each case, the estimated results are shown in Figs. 7–9 for estimated control function, estimated membrane water concentration and estimated cell volume, respectively. For $\alpha = 10$ and 20, the relative errors ERR2 are calculated as 1.21% and 2.06%, respectively. The accuracy of the estimated membrane water concentration and estimated cell volume are both decreased as the weighting coefficient is increased.

From above three numerical test cases we concluded that the conjugate gradient method can be applied successfully in this optimal control problem for predicting the optimal boundary control function to obtain the desired cell volume with time.

9. Conclusions

An optimal control algorithm in controlling the cell volume during dehydration, rehydration or their combination was successfully developed based on the conjugate gradient method with adjoint equation. Three test cases involving different desired cell volumes and weighting coefficients were considered. The results show that the conjugate gradient method does not require a priori information for the functional form of the unknown control functions and the optimal control functions can be obtained within a very short computer time.

Acknowledgements

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