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Dynamic optimization of chemical and biochemical processes using restricted second-order information

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Abstract

The extension of a recently developed method for the dynamic optimization of chemical and biochemical processes is presented. This method is based on the control vector parameterization approach and makes use of the calculation of first- and second-order sensitivities to obtain exact gradient and projected Hessian information. In order to achieve high discretization levels of the control variables with a moderate computational cost, a mesh refining technique is also presented here. The robustness and efficiency of this strategy is illustrated with the solution of several challenging case studies.

Keywords: Optimal control; Dynamic optimization; Chemical processes; Biochemical processes; Sensitivity analysis

Nomenclature

Notation:

$\mathbf{f}$	vector of differential-algebraic equations (DAE)
int_tol_i, int_tol_f	initial and final integration tolerances in the mesh refining technique
J	performance index
n	number of state variables, dimension of vectors $\mathbf{z}$,$\dot{\mathbf{z}}$ and $\mathbf{f}$
NRO	number of refining optimizations in the mesh refining technique
$\mathbf{p}$	time invariant vector
S, $\dot{\mathbf{S}}$	special matrix having as columns the vector products of individual state variable Hessians and vector $\mathbf{p}$ and its time derivative
$\mathbf{s}_i\dot{\mathbf{s}}_i$	column i of matrix $\mathbf{S}$ and $\dot{\mathbf{S}}$, respectively
t, t_0, t_f	time, initial integration time and final integration time, respectively
$\mathbf{u}$	vector of control variables
$\mathbf{v}$	vector of time invariant parameters
$\mathbf{z}$, $\dot{\mathbf{z}}$	vector of state variables and its time derivative

Special symbols:

$\mathbf{0}_{(.)}$	zero matrix (or vector) with appropriate dimensions indicated by (.)

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$\mathbf{I}_{(.)}$ identity matrix with appropriate dimensions indicated by (.)
$\otimes$ Kronecker matrix product operator

Greek letters:
η number of time invariant parameters originally present in the problem, dimension of vector $\mathbf{v}$
σ number of control variables, dimension of vector $\mathbf{u}$
$\tilde{\rho}$ total number of decision variables in the solution of the NLP, dimension of vector $\mathbf{p}$
ρ_i, ρ_f initial and final discretization value for each of the control variables in the mesh refining technique
δ_{tol} tolerance reduction step in the mesh refining

1. Introduction

Many chemical and biochemical processes are operated in batch or semi-continuous mode. In order to increase the productivity and/or profitability of these processes, many efforts have been devoted to their model-based optimization and control. Typical examples are the dynamic optimization (DO) (i.e. open loop optimal control) of batch polymerization reactors (Wang & Chiou, 1997) or fed-batch bioreactors (Banga, Alonso, & Singh, 1997). Most of these processes have highly non-linear dynamics, and constraints are also frequently present on both the state and the control variables. Hence, efficient and robust DO methods are needed in order to obtain their optimal operating policies.

A number of methods have been proposed in the literature for the solution of optimal control problems, and they are usually classified in three main groups: indirect, direct and dynamic programming approaches. Indirect approaches are based on the variational formulation (maximum principle of Pontryagin, e.g. see Bryson & Ho, 1975). This approach has been used by many authors in the context of chemical and biochemical reactors (e.g., San & Stephanopoulos, 1984; Hong, 1986; Lim, Tayeb, Modak, & Bonte, 1986; Modak, Bonte & Lim, 1989; San & Stephanopoulos, 1989; Shioya, 1992). However, it results in a two or multi-point boundary value problem, which is usually very difficult to solve.

As an alternative, direct approaches transform the original problem into a non-linear programming problem (NLP), either using control vector parameterization (Control Vector Parameterization, CVP; e.g. Vassiliadis, 1993) or complete (control and states) parameterization (e.g., Cuthrell & Biegler, 1989). These NLPs are typically solved using deterministic local methods, like sequential quadratic programming, although stochastic methods have also been suggested as alternatives in the case of multimodal NLPs (Banga & Seider, 1996).

Finally, a third group of methods is based on the use of dynamic programming techniques. Luus (1990a) presented a modification of these ideas resulting in the so-called Iterative Dynamic Programming (IDP). This method has been used by several authors for the optimal control of chemical processes (e.g. Luus, 1992; Dadebo & Mcauley, 1995; Luus, 1995; Tholudur & Ramirez, 1997). However, the reported computation times indicate that this method is computationally very costly.

Here, we present the extension of a recently developed method based on the CVP concept which makes use of exact restricted second-order information. As it will be shown, this new method is able to solve challenging problems very efficiently. A mesh refining technique is used to achieve high levels of control discretization with a low computational cost. This is of special interest in this context, as most optimal control policies of (bio)chemical units present a quite wild shape, requiring fine control discretizations in order to ensure optimality.

2. General optimal control problem

A general DO problem, i.e. open loop optimal control problem (OCP), considering lumped parameter processes, can be stated as follows:Find $\mathbf{u}(t)$ and $\mathbf{v}$ to minimize (or maximize) a performance index $J(\mathbf{z}, \mathbf{u})$:

$$J(\mathbf{z},\mathbf{u}) = \psi(\mathbf{z}(t_f)) + \int_{t_0}^{t_f} \phi(\mathbf{z}(t),\mathbf{u}(t),t)\,\mathrm{d}t, \tag{1}$$

subject to the dynamics of the process, described by a set of differential-algebraic equations (DAEs):

$$\mathbf{f}(\dot{\mathbf{z}},\mathbf{z},\mathbf{u},\mathbf{v}) = \mathbf{0}. \tag{2}$$

Initial conditions are also especified in order to assure the solvability of the DAEs:

$$\mathbf{z}(t_0) = \mathbf{z}_0(\mathbf{v}), \tag{3}$$

where $\mathbf{z}\in\mathbb{R}^n$ is the vector of state variables, $\mathbf{u}\in\mathbb{R}^\sigma$, the vector of control variables and $\mathbf{v}\in\mathbb{R}^\eta$, the vector of time invariant parameters.

Path equality and inequality constraints may also be imposed to the system to express certain conditions of operation:

$$\mathbf{h}(\mathbf{z}(t),\mathbf{u}(t),\mathbf{v},t)=\mathbf{0}, \tag{4}$$

$$\mathbf{g}(\mathbf{z}(t),\mathbf{u}(t),\mathbf{v},t)\leqslant\mathbf{0}. \tag{5}$$

Finally, bounds on the control variables and the time invariant parameters might also be present:

$$\mathbf{u}^{\mathrm{L}}(t)\leqslant\mathbf{u}(t)\leqslant\mathbf{u}^{\mathrm{U}}(t), \tag{6}$$

$$\mathbf{v}^{\mathrm{L}}\leqslant\mathbf{v}\leqslant\mathbf{v}^{\mathrm{U}}. \tag{7}$$

3. Solution of optimal control problems using a second-order method

As it was mentioned previously, the method presented here for the solution of the OCP is based on the CVP approach due to its ability to handle large DO problems without solving very large NLPs. It proceeds dividing the duration of the process into a number (ρ) of elements and approximating the control function using a low order polynomial ($\mathbf{u}=\mathbf{u}(\mathbf{v})$). In this work, piecewise constant approximations defined by ρ elements of fixed length were used. Therefore, the decision variables in the solution of the outer NLP will be the levels (steps) of the control variables and the time invariant parameters originally present in the problem (η). An inner initial value problem (IVP), i.e. the DAEs of the system, is solved for each function evaluation.

Here, we will focus our attention on deterministic methods for the solution of the outer NLP. Although derivative-free methods are recently becoming more respectable (Wright, 1996), they usually require a large number of function evaluations and this may result in excessively large computation times, especially in the case of large dynamic systems. The speed of convergence is rapidly increased if the gradient, or both the gradient and the Hessian of the objective function, are given to the optimization algorithm for the calculation of the search direction.

In the case of dynamic systems, the use of sensitivity analysis within CVP methods allows the efficient calculation of the gradient (Vassiliadis, 1993) and the Hessian (Vassiliadis, Balsa-Canto, & Banga, 1999) of the performance index.

3.1. Sensitivity analysis

Several methods have been proposed in the literature for the calculation of first- and second-order information of dynamic systems. The use of adjoint equations allows the computation of first-order information, but this has proved to be very inefficient when trying to solve large problems. Rosen and Luus (1991) compared sensitivity and adjoint implementations as well as finite difference methods for the evaluation of gradients, concluding that using the trajectory sensitivity and finite difference approaches can be computationally more efficient. Finite difference methods allow the calculation of both first- and second-order information. However, in the context of CVP methods, and especially in the case of second-order information, the finite difference approach becomes impracticable. Moreover, finite difference calculations are dependent on the selection of parameter perturbations.

In this work, exact first- and second-order trajectory sensitivities are used. The set of first-order sensitivities can be obtained by a chain rule differentiation applied to the original DAE system with respect to the time-invariant parameters:

$$\frac{\partial\mathbf{f}}{\partial\dot{\mathbf{z}}}\frac{\partial\dot{\mathbf{z}}}{\partial\mathbf{v}}+\frac{\partial\mathbf{f}}{\partial\mathbf{z}}\frac{\partial\mathbf{z}}{\partial\mathbf{v}}+\frac{\partial\mathbf{f}}{\partial\mathbf{u}}\frac{\partial\mathbf{u}}{\partial\mathbf{v}}+\frac{\partial\mathbf{f}}{\partial\mathbf{v}}=\mathbf{0}_{n\times\tilde{\rho}}, \tag{8}$$

where $\mathbf{f}$, $\dot{\mathbf{z}}$ and $\mathbf{z}\in\mathbb{R}^n$, $\mathbf{u}\in\mathbb{R}^\sigma$ and $\mathbf{v}\in\mathbb{R}^{\tilde{\rho}}$with $\tilde{\rho}=\sigma\rho+\eta$ and the initial conditions given by:

$$\frac{\partial\mathbf{z}}{\partial\mathbf{v}}(t_0)=\frac{\partial\mathbf{z}_0}{\partial\mathbf{v}}(\mathbf{v}). \tag{9}$$

The use of second-order sensitivities was first presented by Guay and McClean (1995) for ODE systems, and afterwards extended by Vassiliadis et al. (1999), who presented a rigorous tensorial formulation for general DAE systems derived using a second differentiation of the original DAE system:

$$\begin{aligned}&\left\{\left[\frac{\partial\mathbf{f}}{\partial\dot{\mathbf{z}}}\otimes\mathbf{I}_{\tilde{\rho}}\right]\frac{\partial^2\dot{\mathbf{z}}}{\partial\mathbf{v}^2}+\left[\frac{\partial\mathbf{f}}{\partial\mathbf{z}}\otimes\mathbf{I}_{\tilde{\rho}}\right]\frac{\partial^2\mathbf{z}}{\partial\mathbf{v}^2}\right\}+\left[\mathbf{I}_n\otimes\left(\frac{\partial\dot{\mathbf{z}}}{\partial\mathbf{v}}\right)^{\mathrm{T}}\right]\\&\left[\frac{\partial^2\mathbf{f}}{\partial\dot{\mathbf{z}}^2}\frac{\partial\dot{\mathbf{z}}}{\partial\mathbf{v}}+\frac{\partial^2\mathbf{f}}{\partial\mathbf{z}\partial\dot{\mathbf{z}}}\frac{\partial\mathbf{z}}{\partial\mathbf{v}}+\frac{\partial^2\mathbf{f}}{\partial\mathbf{u}\partial\dot{\mathbf{z}}}\frac{\partial\mathbf{u}}{\partial\mathbf{v}}+\frac{\partial^2\mathbf{f}}{\partial\mathbf{v}\partial\dot{\mathbf{z}}}\right]+\\&\left[\mathbf{I}_n\otimes\left(\frac{\partial\mathbf{z}}{\partial\mathbf{v}}\right)^{\mathrm{T}}\right]\left[\frac{\partial^2\mathbf{f}}{\partial\dot{\mathbf{z}}\partial\mathbf{z}}\frac{\partial\dot{\mathbf{z}}}{\partial\mathbf{v}}+\frac{\partial^2\mathbf{f}}{\partial\mathbf{z}^2}\frac{\partial\mathbf{z}}{\partial\mathbf{v}}+\frac{\partial^2\mathbf{f}}{\partial\mathbf{u}\partial\mathbf{z}}\frac{\partial\mathbf{u}}{\partial\mathbf{v}}+\frac{\partial^2\mathbf{f}}{\partial\mathbf{v}\partial\mathbf{z}}\right]\\&+\left[\frac{\partial\mathbf{f}}{\partial\mathbf{u}}\otimes\mathbf{I}_{\tilde{\rho}}\right]\frac{\partial^2\mathbf{u}}{\partial\mathbf{v}^2}+\\&\left[\mathbf{I}_n\otimes\left(\frac{\partial\mathbf{u}}{\partial\mathbf{v}}\right)^{\mathrm{T}}\right]\left[\frac{\partial^2\mathbf{f}}{\partial\dot{\mathbf{z}}\partial\mathbf{u}}\frac{\partial\dot{\mathbf{z}}}{\partial\mathbf{v}}+\frac{\partial^2\mathbf{f}}{\partial\mathbf{z}\partial\mathbf{u}}\frac{\partial\mathbf{z}}{\partial\mathbf{v}}+\frac{\partial^2\mathbf{f}}{\partial\mathbf{u}^2}\frac{\partial\mathbf{u}}{\partial\mathbf{v}}+\frac{\partial^2\mathbf{f}}{\partial\mathbf{v}\partial\mathbf{u}}\right]+\\&\left[\frac{\partial^2\mathbf{f}}{\partial\dot{\mathbf{z}}\partial\mathbf{v}}\frac{\partial\dot{\mathbf{z}}}{\partial\mathbf{v}}+\frac{\partial^2\mathbf{f}}{\partial\mathbf{z}\partial\mathbf{v}}\frac{\partial\mathbf{z}}{\partial\mathbf{v}}+\frac{\partial^2\mathbf{f}}{\partial\mathbf{u}\partial\mathbf{v}}\frac{\partial\mathbf{u}}{\partial\mathbf{v}}+\frac{\partial^2\mathbf{f}}{\partial\mathbf{v}^2}\right]=\mathbf{0}_{n\cdot\tilde{\rho}\times\tilde{\rho}}.\end{aligned} \tag{10}$$

The corresponding initial conditions for the above system are:

$$\frac{\partial^2\mathbf{z}}{\partial\mathbf{v}^2}(t_0)=\frac{\partial^2\mathbf{z}_0}{\partial\mathbf{v}^2}(\mathbf{v}), \tag{11}$$

where $\otimes$ is the Kronecker matrix-product operator, and the second-order derivatives result in tensors of

third-order. To clarify the similarity between the first- and second-order sensitivities, we present the product of a time-invariant vector $\mathbf{p}\in\mathbb{R}\tilde{\rho}$ with the Hessians for each state. The result of Eq. (10) is post-multiplied by $\mathbf{p}$ and by comparing terms the equivalent form is derived:

$$\frac{\partial \mathbf{f}}{\partial \dot{\mathbf{z}}}\dot{\mathbf{S}}^{\mathrm{T}}+\frac{\partial \mathbf{f}}{\partial \mathbf{z}}\mathbf{S}^{\mathrm{T}}+\mathbf{A}(\dot{\mathbf{z}},\mathbf{z},\mathbf{u},\mathbf{v})=\mathbf{0}_{n\cdot\tilde{\rho}\times 1}, \tag{12}$$

with initial conditions given by

$$\mathbf{S}(t_0)=\left(\mathbf{p}^{\mathrm{T}}\left[\frac{\partial^2\mathbf{z}_{01}}{\partial\mathbf{v}^2}(\mathbf{v})\right]\quad\cdots\quad\mathbf{p}^{\mathrm{T}}\left[\frac{\partial^2\mathbf{z}_{0n}}{\partial\mathbf{v}^2}(\mathbf{v})\right]\right), \tag{13}$$

where S, $\dot{\mathbf{S}}\in\mathbb{R}\tilde{\rho}\times n$ and the set of correspondent initial conditions is given in Eq. (13). From the above results, it is clear that Eq. (12) is a set of first-order sensitivity equations, similar to Eq. (8).

The results reported in Vassiliadis et al. (1999) showed that the performance of quasi-Newton methods within the CVP approach was considerably enhanced by using exact Hessians, obtained via Eq. (10), of the objective function. However, it was also noted that the computational cost in evaluating full Hessians grows rapidly both with the problem size and the discretization level (ρ). Therefore, the use of algorithms requiring Hessian-vector inner products only (as computed in Eq. (12) above), such as those using conjugate gradient methods, will be clearly more efficient for large dynamic systems and higher ρ values.

Another interesting feature of this exact restricted second-order information is that the resulting DAE has the same Jacobian as the original DAE and the first-order sensitivity systems, and this can be exploited to efficiently evaluate the gradient and the required Hessian vector product for dynamic systems.

In order to fully automate the application of this restricted second-order information method, a Mathematica™ 3.0 notebook has been developed to derive symbolically the extended initial value problem (EIVP, Eq. (2), Eq. (8) and Eq. (12)). The resulting set of equations is also transformed into a suitable format (e.g. Fortran or C) ready to be used with standard IVP solvers.

Table 1
Summary of results for case study I (PR bioreactor)

Sub-case	Authors	Performance index	CPU time (s)
PR-a	Yang and Wu (1994)	32.681	Not reported (NR)
	Luus (1995)	32.686	3651
	Banga et al. (1998)	32.562	13–40
	This work	32.632 ($\rho=40$)	9
		32.691 ($\rho=120$)	200
PR-b	Tholudur and Ramirez (1997)	32.31–32.47	NR
	This work	32.388 ($\rho=40$)	23
		32.480 ($\rho=320$)	316

3.2. Solution of the outer NLP problem. Mesh refining technique

In order to solve efficiently the outer NLP problem, the TN (Truncated Newton) large-scale optimization code of Nash (1984) was selected because it makes use of gradient and Hessian dot vector product. This TN code was modified so that the first-order and projected second-order information are calculated exactly via the solution of the EIVP mentioned above.

To achieve high control discretization levels (ρ) with moderate computation times, a mesh refining approach has been developed, consisting of successive re-optimizations with increasing ρ values. The basic steps of this approach are outlined in the following pseudo-code:

Step 1. Set initial guess (usually a flat control value) and choose initial and final values for the discretization and the integration tolerance. Choose also a parameter (r_ρ) used to increase the discretization level from one run to the next.

Step 2. Compute the number of refining optimizations (NRO) and the tolerance reduction step δ_{tol} using the expressions: $\frac{\rho_{\mathrm{f}}}{\rho_{\mathrm{i}}}=r_\rho^{\mathrm{NRO\text{-}1}}$ and $\delta_{\mathrm{tol}}=\frac{1}{\mathrm{NRO}}(\mathrm{int\_tol_i}-\mathrm{int\_tol_f})$.

Step 3. Initial optimization run ($k=1$): compute, using TN, the optimal control profile $\mathbf{u}_1(t)$ corresponding to the initial control discretization ρ_{i} and the tolerances $\mathrm{int\_tol_i}$ and $\mathrm{opt\_tol_i}$.

Step 4. Optimization loop refining the control discretization

From $k=2$ to $k=\mathrm{NRO}$

Adjust discretization level and tolerances: $\rho_k=\rho_{k\text{-}1}\,r_\rho$

Adjust the tolerances: $\mathrm{int\_tol}_k=\mathrm{int\_tol}_{k-1}-\delta_{\mathrm{tol}}$, $\mathrm{opt\_tol}_k=\mathrm{int\_tol}_k\ \mathrm{tol\_ratio}$

Optimization run k: using $\mathbf{u}_{k-1}$ as initial guess, compute $\mathbf{u}_k$ using the modified TN

Next k

4. Case studies

In order to illustrate the performance of the restricted second-order method presented here, several challenging case studies taken from the literature are considered. Results are presented in Tables 1–3. For the sake of comparison, results from other authors are

Table 2
Summary of results for case study II (LR bioreactor)

Sub-case	Author	Performance index	CPU time (s)
$Q = 0.0$	Tholudur and Ramirez (1997)	6.16	NR
	This work	6.15	5.0
$Q = 2.5$	Tholudur and Ramirez (1997)	5.77	NR
	This work	5.76	3.5
$Q = 5.0$	Tholudur and Ramirez (1997)	5.58	NR
	This work	5.57	4.0

Table 3
Summary of results for case III (non-linear CSTR)

Sub-case	Authors	Performance index	CPU time (s)
CSTR	Luus (1990)	20.0895 ($\rho = 10$), 20.0953 ($\rho = 40$)	1278
3 control variables	This work	20.0895 ($\rho = 10$)	3.4
		20.0953 ($\rho = 40$)	22.0
CSTR 4 control variables	Luus (1990)	21.757 ($\rho = 11$)	NR
	Bojkov et al. (1993)	21.744	7.8
	This work	21.757 ($\rho = 11$)	17.0
		21.807 ($\rho = 80$)	119.0

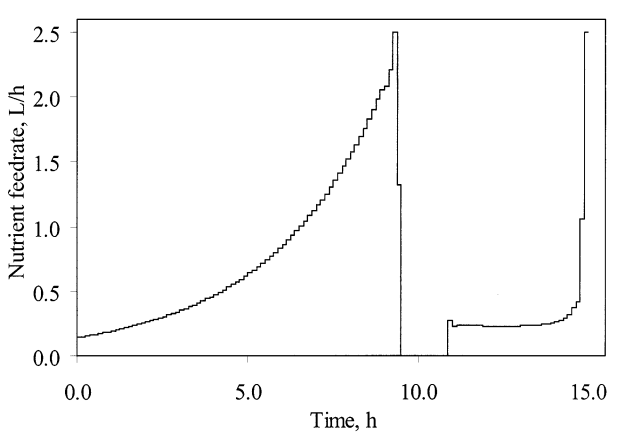

Fig. 1. Optimal control profile for case I (PR-b).

also reported. The computation times (CPU time) were converted from the original values reported by the different authors to values of the PC Pentium/III (450 MHz) computer used in this work, based on their relative performance values as measured by the Linpack-100 benchmark. Examples of the optimal control profiles obtained are presented in Figs. 1–4.

4.1. Case I: Park–Ramirez bioreactor

This case study deals with the optimal production of secreted protein in a fed-batch reactor. It was originally formulated by Park and Ramirez (Park & Ramirez, 1988) and it has also been considered by other researchers (Vassiliadis, 1993; Yang & Wu, 1994; Banga, Irizarry & Seider, 1995; Luus, 1995; Tholudur &

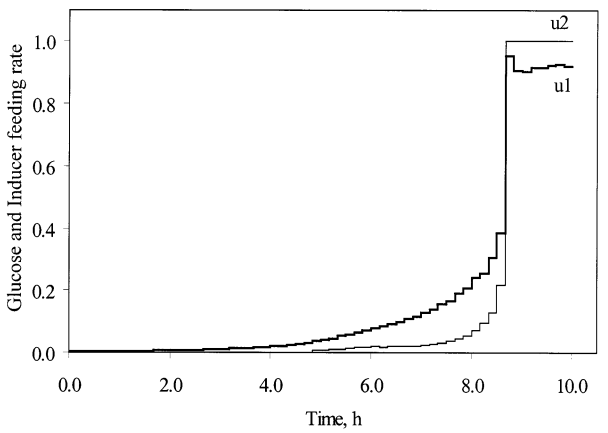

Fig. 2. Optimal control profile for case II ($Q = 0.0$).

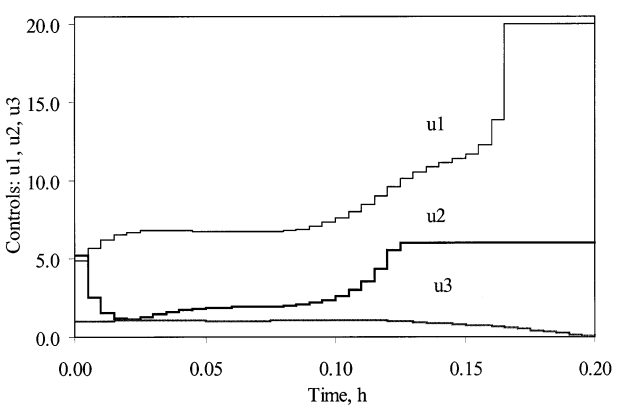

Fig. 3. Control profile for case III (3 control variables).

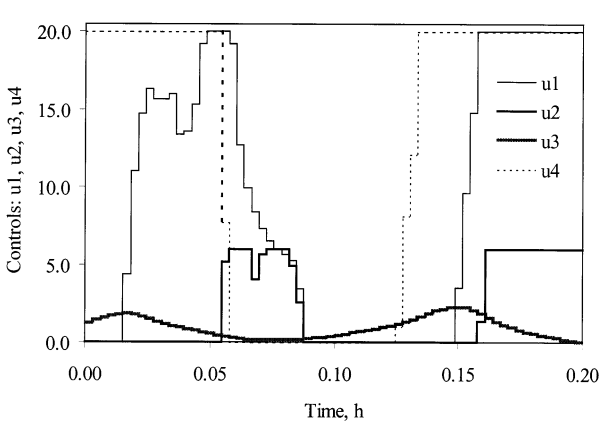

Fig. 4. Control profile for case III (4 control variables).

Ramirez, 1997). The objective is to maximize the secreted heterologous protein by a yeast strain in a fed-batch culture. The dynamic model accounts for host-cell growth, gene expression, and the secretion of expressed polypeptides. The mathematical statement is as follows: Find $\mathbf{u}(t)$ over $t\in[t_0,t_f]$ to maximize:

$$J = z_1(t_f)z_5(t_f), \tag{14}$$

subject to:

$$\frac{dz_1}{dt} = g_1(z_2 - z_1) - \frac{u}{z_5}z_1, \tag{15}$$

$$\frac{dz_2}{dt} = g_2 z_3 - \frac{u}{z_5}z_2, \tag{16}$$

$$\frac{dz_3}{dt} = g_3 z_3 - \frac{u}{z_5}z_3, \tag{17}$$

$$\frac{dz_4}{dt} = -7.3g_3z_3 + \frac{u}{z_5}(20 - z_4), \tag{18}$$

$$\frac{dz_5}{dt} = u, \tag{19}$$

with:

$$g_1 = \frac{4.75g_3}{0.12 + g_3}, \tag{20}$$

$$g_2 = \frac{z_4}{0.1 + z_4}\exp(-5.0z_4), \tag{21}$$

$$g_3 = \frac{21.87z_4}{(z_4 + 0.4)(z_4 + 62.5)}, \tag{22}$$

where z_1 and z_2 are, respectively, the concentration of the secreted protein and the total protein (l^{-1}), z_3 is the culture cell density ($g\,l^{-1}$), z_4 is the substrate concentration ($g\ l^{-1}$), z_5 is the holdup volume (l), u is the nutrient (glucose) feedrate ($l\,h^{-1}$), and J is the mass of protein produced (in arbitrary units). The initial conditions are:

$$z(0) = [0 \quad 0 \quad 1 \quad 5 \quad 1]^T. \tag{23}$$

Two different sub-cases are presented (PR-a, PR-b) which differ in the time horizon and control bounds used.

PR-a: as considered by Luus (1992), Luus (1995) and Banga, Irizarry, and Seider (1998) for final time $t_f = 15$ h, and the following constraints on the control variable:

$$0 \leqslant u \leqslant 2.0. \tag{24}$$

PR-b: same as PR-a, with the slight modifications to the model introduced by Tholudur and Ramirez (1997) and the following constraints on the control variable:

$$0 \leqslant u \leqslant 2.5. \tag{25}$$

The results obtained for several control discretizations are summarized in Table 1, where a comparison with the results provided by other authors is also given. Clearly, the method presented in this work is able to arrive to very good performance index values with a very low computational cost, even for high levels of control discretization. As an example, the optimal control profile obtained for PR-b is shown in Fig. 1. Note the smooth approximation of the arcs due to the use of a high discretization level.

4.2. Case II: Lee–Ramirez bioreactor

This problem considers the optimal control of a fed-batch reactor for induced foreign protein production by recombinant bacteria, as presented by Lee and Ramirez (1994) and considered afterwards by Tholudur and Ramirez (1997) and Carrasco and Banga (1998). The objective is to maximize the profitability of the process using the nutrient and the inducer feeding rates as the control variables. Three different values for the ratio of the cost of inducer to the value of the protein production (Q) were considered.

The mathematical formulation, following the modified parameter function set presented by Tholudur and Ramirez (1997) to increase the sensitivity to the controls, is as follows:

Find $u_1(t)$ and $u_2(t)$ over $\in[t_0,t_f]$ to maximize:

$$J = z_4(t_f)z_1(t_f) - Q\int_{t_0}^{t_f} u_2(t)\,dt, \tag{26}$$

subject to:

$$\frac{dz_1}{dt} = u_1 + u_2, \tag{27}$$

$$\frac{dz_2}{dt} = \mu(z_3,z_5,z_6,z_7)z_2 - \frac{u_1 + u_2}{z_1}z_2, \tag{28}$$

$$\frac{dz_3}{dt} = \frac{u_1}{z_1}C_n^f - \frac{u_1 + u_2}{z_1}z_3 - Y^{-1}\mu(z_3,z_5,z_6,z_7)z_2, \tag{29}$$

$$\frac{dz_4}{dt} = R_{fp}z_2 - \frac{u_1 + u_2}{z_1}z_4, \tag{30}$$

$$\frac{dz_5}{dt} = \frac{u_2}{z_1}C_i^f - \frac{u_1 + u_2}{z_1}z_5, \tag{31}$$

$$\frac{dz_6}{dt} = -k_1z_6, \tag{32}$$

$$\frac{dz_7}{dt} = k_2(1 - z_7), \tag{33}$$

where the state variables are the reactor volume (z_1), the cell density (z_2), the nutrient concentration (z_3), the foreign protein concentration (z_4), the inducer concentration (z_5), the inducer shock factor on cell growth rate (z_6) and the inducer recovery factor on cell growth rate (z_7). The two control variables are the glucose rate (u_1) and the inducer feeding rate (u_2). Q is the ratio of the cost of inducer to the value of the protein production, and the final time is considered fixed as $t_f = 10$ h. The

model parameters were described by Lee and Ramirez (1994).The initial conditions are:

$$\mathbf{z}(0) = [1 \quad 0.1 \quad 40 \quad 0 \quad 0 \quad 1 \quad 0]^{\mathrm{T}}. \tag{34}$$

The following constraints on the control variables are considered:

$$0 \leqslant u_1 \leqslant 1, \tag{35}$$

$$0 \leqslant u_2 \leqslant 1. \tag{36}$$

Tholudur and Ramirez (1997) solved this problem using the IDP method of Luus and also their FIDP (Filtered IDP) method, a modification of IDP developed in order to obtain smoother control profiles. These authors considered three different values of the parameter Q: $Q = 0$ (not considering the cost of inducer), 2.5 and 5.0.

This problem was solved successfully, for the three Q values, using our restricted second-order method. The results are reported in Table 2, showing that this method was able to obtain performance indexes equivalent to those of Tholudur and Ramirez (1997) in just a few seconds of computation time. As an example, the optimal control profiles for case $Q = 0.0$ are presented in Fig. 2.

4.3. Case III: Non-linear CSTR

The problem was first introduced by Jensen (1964) and consists of determining the four optimal controls of a chemical reactor in order to obtain maximum economic benefit. The system dynamics describe four simultaneous chemical reactions taking place in an isothermal continuous stirred tank reactor. The controls are the flowrates of three feed streams and an electrical energy input used to promote a photochemical reaction. Luus (1990) and Bojkov, Hansel, and Luus (1993) considered two sub-cases using three and four control variables respectively.

The problem is formulated as follows:Find $u_1(t)$, $u_2(t)$, $u_3(t)$ and u_4(t) over $t \in [t_0, t_f]$ to maximize:

$$J = z_8(t_f). \tag{37}$$

Subject to:

$$\frac{dz_1}{dt} = u_4 - (u_1 + u_2 + u_4)z_1 - 17.6z_1z_2 - 23z_1z_6u_3, \tag{38}$$

$$\frac{dz_2}{dt} = u_1 - (u_1 + u_2 + u_4)z_2 - 17.6z_1z_2 - 146z_2z_3, \tag{39}$$

$$\frac{dz_3}{dt} = u_2 - (u_1 + u_2 + u_4)z_3 - 73z_2z_3, \tag{40}$$

$$\frac{dz_4}{dt} = -(u_1 + u_2 + u_4)z_4 + 35.2z_1z_2 - 51.3z_4z_5, \tag{41}$$

$$\frac{dz_5}{dt} = -(u_1 + u_2 + u_4)z_5 + 219z_2z_3 - 51.3z_4z_5, \tag{42}$$

$$\frac{dz_6}{dt} = -(u_1 + u_2 + u_4)z_6 + 102.6z_4z_5 - 23z_1z_6u_3, \tag{43}$$

$$\frac{dz_7}{dt} = -(u_1 + u_2 + u_4)z_7 + 46z_1z_6u_3, \tag{44}$$

$$\frac{dz_8}{dt} = 5.8[(u_1 + u_2 + u_4)z_1 - u_4] - 3.7u_1 - 4.1u_2 + (u_1 + u_2 + u_4)(23z_4 + 11z_5 + 28z_6 + 35z_7) - 5u_3^2 - 0.09, \tag{45}$$

with the initial conditions:

$$\mathbf{z}(0) = [0.1883 \quad 0.2507 \quad 0.0467 \quad 0.0899 \quad 0.1804 \quad 0.1394 \quad 0.1046 \quad 0.000]^{\mathrm{T}}. \tag{46}$$

And the following bounds on the control variables:

$$0 \leqslant u_1 \leqslant 20, \tag{47}$$

$$0 \leqslant u_2 \leqslant 6, \tag{48}$$

$$0 \leqslant u_3 \leqslant 4, \tag{49}$$

$$0 \leqslant u_4 \leqslant 20. \tag{50}$$

The final time is considered fixed as $t_f = 0.2$. For the sake of comparison with the results previously reported in literature, we will consider two different sub-cases: (i) one with three control variables, as considered by Luus (1990), fixing u_4 to a constant value of 6.0, and (ii) another with the four control variables as stated above.

The two sub-cases were successfully solved using the restricted second-order method described here. A summary of results, including the solutions reported by other authors, is presented in Table 3. Regarding the sub-case with three controls, our method was able to arrive to the same value reported by Luus (1990) much faster. Regarding the sub-case with four controls, we were able to obtain a significantly better performance index in only 2 min of computation time using a PC. The optimal controls for these sub-cases are shown in Figs. 3 and 4.

5. Conclusions

The use of exact first- and second-order information resulted in two major differences with existing CVP algorithms. Firstly, a significant reduction in function and gradient evaluations was observed due to the use of second-order information, which although requires the more expensive second-order information evaluation, results in overall computational savings. Secondly, the ability to consider very fine discretization levels for the underlying controls has been enhanced both by the high precision and speed of convergence but also by the use of the mesh-refining technique.In terms of performance

and quality of solutions for the examples presented here, results achieved are comparable or better than the ones found in literature. The results also indicate that the algorithm is capable of identifying clearly singular arcs in the optimal control profiles (e.g. in the case of fermentation processes) and is also efficient enough to be used in low-cost computing platforms with very competitive computation times.

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