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Mixed Modifier-Adaptation for RTO in a Continuous Bioreactor

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Abstract: This paper deals with the problem of optimizing the performance of a process using Real Time Optimization (RTO) considering the unavoidable errors in the process models. It implements a new architecture within the modifier-adaptation methodology, presenting a nested optimization problem with two layers. With this methodology, it is possible to find a point that satisfies the KKT conditions of a process using an inaccurate model in the optimization, without the need to estimate directly the experimental gradients of the process. The suggested methodology has been tested in a continuous bioreactor example that present a washout closer to the real optimum of the simulated process. The results show that the proposed methodology is able to find the optimum of the process smoothly, avoiding unstable operating points.

Keywords: Real time optimization, Nested modifier-adaptation, Modifier adaptation, uncertainty

1. INTRODUCTION

One of the main difficulties that appear when an economic-based optimization layer (Real Time Optimization, RTO) is implemented in a process, is the uncertainty associated with the process or the model being used for computing the optimal decisions. The incertitude can have different origins: a) the measurements and the lack of reliable information provided by the instrumentation, and b) the partial knowledge of the physical and chemical phenomena or changes occurring in the process. From this perspective, under the term process, we can also include the basic control layer governing it.

To deal with the uncertainty associated with measurements and sensors, a data reconciliation procedure with enough redundancy in the plant can be implemented associated to the RTO layer following a two-step algorithm (parameter estimation and economic optimization). In the first step, the uncertainties are taken into account updating the parameters α of a process model solving a parameter estimation problem (1), where $u \in \mathrm{R}^{\mathrm{Nu}}$ is the value of the manipulated variables and $y \in \mathrm{R}^{\mathrm{Ny}}$ represents the model outputs, $f \in \mathrm{R}^{\mathrm{Nx}}$ models the process and $g \in \mathrm{R}^{\mathrm{Ng}}$ are the inequality constraints of the system. The superscript "$\bar{}$" indicates in the entire document that the variable is measured from the process.

$$\begin{aligned} &\min_{\alpha} \Phi_{id} := \left(y-\bar{y}\right)^T R\left(y-\bar{y}\right) \\ &s.t.: f\left(x,y,u,\alpha\right)=0, \quad g\left(x,u,\alpha\right)\le 0 \end{aligned} \tag{1}$$

After the model update, an economic optimization is performed (2), obtaining a new set of decision variables. Here $\phi \in \mathrm{R}$ represents an economic objective function. The solution of (2) is then applied to the process in an iterative scheme.

$$\begin{aligned} &\min_{u} \Phi_{eco} := \phi\left(x,u,\alpha\right) \\ &s.t.: f\left(x,y,u,\alpha\right)=0, \quad g\left(x,u,\alpha\right)\le 0 \end{aligned} \tag{2}$$

Nevertheless, even with the reconciled model, there is always a gap between the model used in the optimization and the process (model mismatch). This point, plus the type of interaction that takes place in the two-stage implementation of estimation and optimization, implies that the classical approach of RTO that provides an economic optimum for the model will not necessarily converge to the real optimum of the process. Several methods have been proposed in the literature to avoid this problem. Among them, the ones that iteratively modify the optimization problem with direct measurements and estimated gradients of the process, in such way that the modified optimization problem, with the same model, provides the real process optimum. See (Roberts, 1979, Tatjewski, 2002, Gao and Engell, 2005). Recently, this methodology has been generalized by Marchetti and co-workers presenting the so called *Modifier-adaptation method* (MA) (Chachuat et al., 2009, Marchetti et al., 2009))

The modifier methods can find a point that satisfies the necessary conditions of optimality (NCO) of the process, but its implementation requires estimating the real gradients of the system by performing some process experimentation, which is not a trivial task and can be time consuming. To avoid this step, Navia and co-workers have reformulated the method, introducing the *Nested Modifier-Adaptation* (Navia et al., 2013) in which an additional optimization layer provides directly the gradient modifiers in an iterative way.

In this paper, after presenting both approaches, they are combined in a mixed algorithm, including the nested and gradient-based modifier adaptation methodologies with the purpose of expanding its range applicability. The resulting algorithm is used for the optimal operation of a continuous

bioreactor with structural modelling mismatch between the model and the process, showing how the real process optimum can be attained.

The paper is organized as follows: Section two presents a summary of the modifier-adaptation approaches. In section three, a simulated continuous Bioreactor case-study is presented and used for implementation of the gradient-based and the nested algorithms. Section four describes and applies the mixed procedure proposed in this paper in the example already mentioned. Finally, section five gives some concluding remarks.

2. NESTED MODIFIER-ADAPTATION METHODOLOGY

2.1 Original Modifier-Adaptation

In order to guarantee convergence to a point that satisfies the KKT conditions of the process, the modifier-adaptation approach changes the original cost function and inequality constraints of problem (2) to new ones $\Phi_{mod} \in R$ and $G_{mod} \in R^{Ng}$ as in (3):

$$\begin{aligned} &\min_{u\in U} \Phi_{mod} := \phi(x,u,\alpha) + \lambda_k^{\,T} u \\ &s.t. \\ &f(x,y,u,\alpha) = 0 \\ &G_{mod} := g(x,u,\alpha) + \gamma_k^{\,T}(u-u_{k-1}) + \varepsilon_k \le 0 \end{aligned} \tag{3}$$

Here, λ_κ are the modifiers of the cost function at iteration k and γ_κ and ε_κ the ones of the constraints. They are given by the errors between the process and the model in the cost function gradient, the constraints gradients and the constraints values, respectively as in (4). It is important to mention that they have fixed values when solving (3), since they are computed with values from the previous iteration.

$$\begin{aligned} \lambda_k &:= \nabla_u \bar{\phi} - \nabla_u \phi(x_{k-1},u_{k-1},\alpha) \\ \gamma_k &:= \nabla_u \bar{G} - \nabla_u G(x_{k-1},u_{k-1},\alpha) \\ \varepsilon_k &:= \bar{g} - g(x_{k-1},u_{k-1},\alpha) \end{aligned} \tag{4}$$

Under the assumption of convergence of the algorithm, it is possible to show that the NCO conditions for (3) correspond to the ones of the process optimum. In order to solve (3), at every iteration of the RTO layer, it is necessary to estimate the modifiers of the cost function and the constraints using process data. The bias ε is not difficult to obtain, but the estimation of the gradient of the cost and constraints measured on the process is the key issue of this methodology (Mansour and Ellis, 2003). Typically, a first order filter is applied to the modifiers in (4) for implementation. Then, the implementation of the modifier-adaptation methodology proceeds as in Fig. 1: after estimating the modifiers, the optimization problem (3) is solved and the optimal actions u_k are applied to the process. Once the process has reached the new steady state, the procedure is repeated until no further changes in the decision variables are observed, which implies, according to the MA assumptions, that a KKT point of the process has been found (Chachuat et al., 2009).

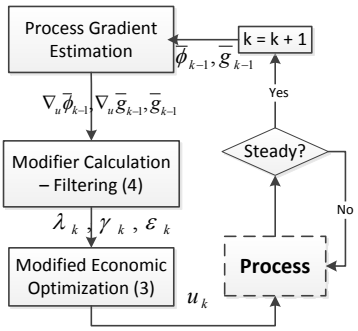

Fig. 1. Implementation of the Modifier Adaptation Methodology.

2.2 The Nested Modifier Adaptation

The main idea behind the Nested Modifier Adaptation (NMA) approach is that, in principle, any policy for updating the modifiers could be used provided that it improves the process objective function and respects the constraints of the process. With this idea in mind, one can replace the gradient estimation and the modifier calculation steps of Fig.1 by other method designed for decreasing the cost function measured directly from the process iteratively. In particular, it is possible to implement an upper optimization layer that have the modifiers λ_k and γ_k as decision variables as represented in Fig.2 and the process cost function as cost function. The solution of this layer are the modifiers to be applied directly in the inner modified optimization (3), while (3) provides the decision variables to be applied into the process and takes direct care of the constraints.

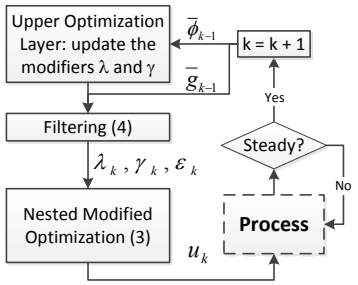

Fig. 2. Implementation of the Nested Modifier Adaptation Methodology.

The purpose of the upper optimization layer is to obtain the optimum of the process iterating with the modifiers. When selecting the optimization method, one can take into account the fact that their decision variables (the gradient modifiers) are not constrained, so that any unconstrained method can be used. In particular the choice of a gradient-free algorithm, such as the simplex method, allows avoiding the need of estimating the process gradients directly from measurements.

Notice that the proposed methodology only uses the modifiers λ and γ as the decision variables, and the cost function of the process as the objective function for the upper optimization layer. The value of ε, on the other hand, is computed in the same way than in the original modifier

adaptation methodology because are obtained as a direct calculation from the process measurements. The process constraints are not considered in the upper optimization, but they are enforced in the inner one that incorporates the modifiers.

The upper optimization layer is continuously iterating with the modifiers λ and γ, with the purpose of driving the whole system closer and closer to the optimum of the process. At every iteration of the algorithm, for the set of modifiers provided by the upper optimization, it is necessary to solve the inner constrained one and then apply its solution to the process to obtain the value of the real cost function. The main advantage of the NMA reformulation is that, as a gradient-free algorithm is implemented in the upper layer, it is neither necessary to estimate the process derivatives in order to look for the real optimum, nor to apply additional perturbations into the real system to estimate the gradient of the measured cost function. However, as a drawback, an additional optimization problem has to be solved with N_u (N_g+ *1*), decision variables, being N_u the number of decision variables and N_g the number of the constraints of the nested problem, unlike the original MA where the number of perturbations (new or previous), needed to estimate the gradient of the process, is only proportional to the number of decision variables. Nevertheless, this is not an important disadvantage if the Nelder-Mead (NM) algorithm is implemented in the upper layer, since it is particularly parsimonious in function evaluations per iteration and zero initial values are a sensible choice for λ and γ. This property is very important considering that each function evaluation implies changing the operation point of the real process (Walters et al., 1991).

If the upper layer converges to an optimal stationary point, the feasibility of the process is ensured by the definition of ε. Moreover, if its cost function cannot be improved, it means that the real optimum of the constrained process (local if the problem is not convex) has been found, as the cost function of the upper layer is the process cost function.

Starting from the KKT conditions of (3), it is clear that, under stationary assumption, the definition of ε allows to ensure primal feasibility of the process. On the other hand, dual feasibility is given by the solution of the nested problem, assuming the same set of Lagrange multipliers for the nested problem and the process (Marchetti et al., 2009). Also, complementary slackness for the inequality constraints of the process is given by the definition of ε and the dual feasibility.

Regarding the optimum of the measured objective function, it is possible to manipulate the complementary slackness condition and the gradient of the Lagrangean function of (3) from its KKT conditions to obtain:

$$\left(\nabla_u \phi - \lambda^T\right)\nabla_\lambda u = 0, \qquad \left(\nabla_u \phi - \lambda^T\right)\nabla_\gamma u = 0 \tag{5}$$

Equation (5), holds for any value of λ and γ, independently of the definition of the gradient modifiers. In particular, if we replace these values with the expression from equation (4), and apply the chain rule, we get:

$$\nabla_\lambda \overline{\phi} = 0, \qquad \nabla_\gamma \overline{\phi} = 0 \tag{6}$$

This means that the application of the modifier adaptation policy leads to a (local) unconstrained optimum of the process economic cost function with respect to the modifiers λ and γ, which is also the point given by the upper optimization layer of the nested approach after convergence.

3. IMPLEMENTATION IN A CONTINUOUS BIOREACTOR

The nested modifier-adaptation methodology has been tested in an example of a continuous bioreactor with structural modelling mismatch between the model and the process. This example has been used previously to test RTO methodologies (Zhang and Forbes, 2006, Golden and Ydstie, 1989). It was selected as a proper candidate to be used in the implementation of the NMA algorithm, taking into account the increase of the decision variables explained later, since this is an unconstrained problem in the state variables.

3.1 Process Description

The system contains a continuous culture that grows inside a bio-CSTR. With adequate constant aeration (Air), mixing conditions, substrate concentration at the feed (S_0) and pH (NaOH), the dilution rate D of the reactor can be modified in order to change the concentration of the cells (or biomass) at the effluent of the reactor (X), which is the process output. To be more precise, the real manipulated variable of the system is the flow rate of the feed (F); nevertheless, if the volume of the reactor (V) is constant, these two variables are equivalent ($D=F/V$). Fig. 3 schematizes the process.

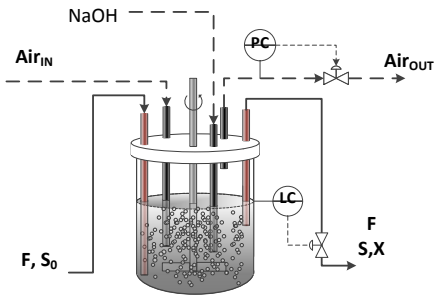

Fig. 3. Diagram of the continuous bioreactor

The operational goal of the system is to maximize the production of cells in steady state. This can be expressed as a product of the dilution rate and the concentration of the microorganisms:

$$f_{Bio} := XD \tag{7}$$

The bio-CSTR can be described with a first principle model that will be used as a simulation of the real process (Golden and Ydstie, 1989). Combining the mass balance applied to the cells and substrate, and using a Monod-type kinetic, the concentration of biomass in steady state can be described using eq. (8). Here it is assumed that there is not biomass in the influent and that the reaction volume remains constant. In (8) K_S and μ_{max} are kinetic parameters, m_c a maintenance coefficient and Y the yield of the biomass w.r.t. the substrate.

$$X = \underbrace{\frac{YD}{m_C + D}}_{Y_{Obs}} \underbrace{\left(S_0 - \frac{K_S D}{\mu_{\max} - D} \right)}_{\Delta S} \tag{8}$$

Feasible dilution rates are constrained by μ_{max} as (8) becomes singular for that value. Eq. (8) can be viewed as a product between the consumed biomass (ΔS) and an observed yield (Y_{Obs}) which depends on the dilution rate. In order to test the modifier methods using an incorrect model, we will consider the following optimization problem (9).

$$\begin{aligned} &\min_{D \in [D^L, D^U]} \; -f_{Bio} \\ &s.t. \\ &X = \widetilde{Y}_{Obs} \left(S_0 - \frac{\widetilde{K}_S D}{\widetilde{\mu}_{\max} - D} \right) \end{aligned} \tag{9}$$

Where the parameters have different values (see Table 1) and the model presents also structural mismatch with respect to the equations used to model the process, since the observed yield does not depend on other variables.

Table 1. Value of the Parameters

Parameter	Value	Parameter	Value
D^L	0	Y	0.5
D^U	0.42	$\mu_{\max}$	0.35
S_0	5	$\widetilde{K}_S$	0.19
m_c	0.025	$\widetilde{Y}_S$	0.4
K_S	0.09	$\widetilde{\mu}_{\max}$	0.42

3.2 Results of the Modifier – Adaptation and NMA Methods

The mismatch of the bioreactor produces an interesting effect with respect to the real behaviour of the system illustrated in Fig. 4. This Figure shows a comparison of the cost function value f_{Bio} and output X corresponding to the process (P) and to the model (M), as a function of D.

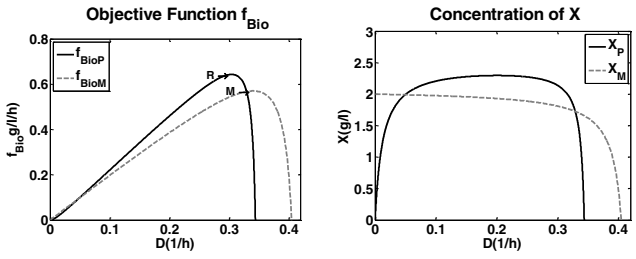

Fig.4. Comparison of the process and the model

Because of the modelling mismatch, the optimum of the process (marked R) does not match with the one computed with the model (marked M), situation that is quite expectable. However, it can be observed that the dilution rate that optimizes the performance index of the approximated model of the reactor causes a washout in the steady state of the real process. Washout is a peculiar phenomenon for continuous culture systems. It consists in a complete removal of the cells inside the reactor ($X=0$) when the dilution rate is greater than the cell growth rate. Taking this into account, it is clear that the model of the process is a poor representation of the behaviour of the process.

To help avoiding the washout phenomenon, a trust region with ΔD = 0.01 was incorporated to D in (9), so that at iteration k

$$D_k \in \left[\max(D^L, D_{k-1} - \Delta D/2), \min(D^U, D_{k-1} + \Delta D/2) \right] \tag{10}$$

This small value was required to assure convergence to the optimum, increasing as a consequence the number of iterations. Fig. 5 shows the evolution of the decision variable D and cost function f_{Bio} over time, obtained when the modified adaptation methodology was applied to (9). The process derivatives have been estimated using finite differences.

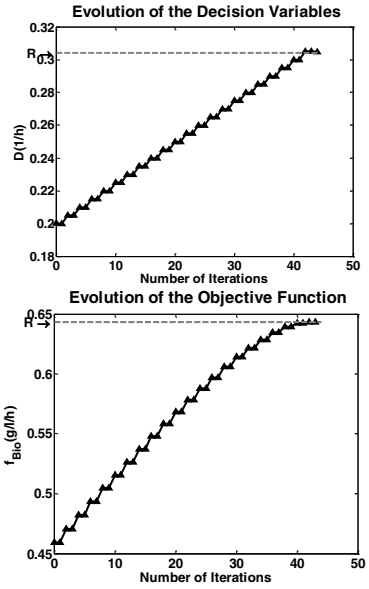

Fig.5. Evolution with the modifier -adaptation algorithm

The convergence to the real optimum of the process in the gradient-based approach took around 40 iterations. The method showed a high sensitivity to the value of ΔD which could be a significant drawback in practice. Regarding the detection of the optimum of the process, the shrinking of the local feasible region with the thrust region, allows to converge to the desired point (R) avoiding the occurrence of the washout phenomenon. It is important to mention that if the feasible region is not constrained, the next operating point suggested by the RTO layer, could pass the optimum of the process (not detecting it) and falling in the region closer to the washout phenomenon. In this case, the process derivative will be more negative than the gradient of the model, moving the system again into the region before the optimum of the process, repeating this behaviour over and over bouncing around the real optimum.

The NMA algorithm was also applied to the bioreactor optimization, with the *fminsearch* function from MATLAB used in the upper optimization layer (Mathworks, 2007). Fig. 6 shows its evolution. The real optimum of the process was also reached, this time in one half of iterations. Nevertheless, Fig.6 shows that the algorithm did not stop in this point as

expected. This behaviour can be explained based in the fact that there is an important difference in the rate of change of the objective function on both sides of the process optimum. As a consequence of this, if the system starts from a point below the optimum of the process, the size of the simplex of the NM method will be bigger than the one required when the process pass the real optimum, because of the rate of change is increased after this point. This implies that the next RTO iteration will be farther from the required point and closer to the washout zone, producing the removal of all the biomass.

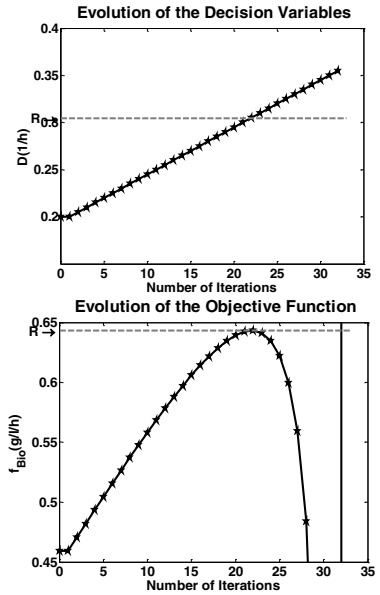

Fig.6. Evolution with the NMA approach

4. MIXED MODIFIER-ADAPTATION METHODOLOGY

With the purpose of improving the behaviour of the methods and the applicability of the modifier methodology in this case, we have used the previous knowledge of the system to help stopping the algorithm when a situation of possible optimum is detected, combining both approaches.

Even when the point of washout is not known a priori, these kinds of systems exhibit this phenomenon for some value of the dilution rate. Furthermore, starting from a suboptimal operation point (on the left side of the process optimum in Fig. 6) an increment of the dilution rate will rise the concentration of the cells inside the vessel because there is additional available subtract to produce more biomass. This increase is maintained until D exceeds the maximum growth rate (an unknown parameter). After this point, the cells inside the reactor have not enough residence time to create more microorganisms, decreasing the concentration of the biomass and producing the washout. As this is an expectable behaviour of the continuous cell cultures, we can try to detect the point when the change in the performance of the bioreactor is produced, postulating it as a point (or a region) close to the real optimum. So, the change in the tendency of the objective function can be used as a criterion to detect a candidate for process optimum and stopping the iterations.

Alternatively, we could refine the search, adding a gradient based methodology after the gradient free algorithm, following the analogy that some global optimization solvers, like the SSm GO (Egea et al., 2007), implement in their routines. The possibility of mixing the two approaches (gradient free with gradient-based) is one of the contributions that the reinterpretation of the modifiers in NMA presents, giving an additional degree of adaptation to the modifier method depending on the particular characteristics of the system (Navia et al., 2013).

The implementation of the *Mixed* (Nested and Gradient-based) *modifier-adaptation* methodology is summarized in Fig. 7.

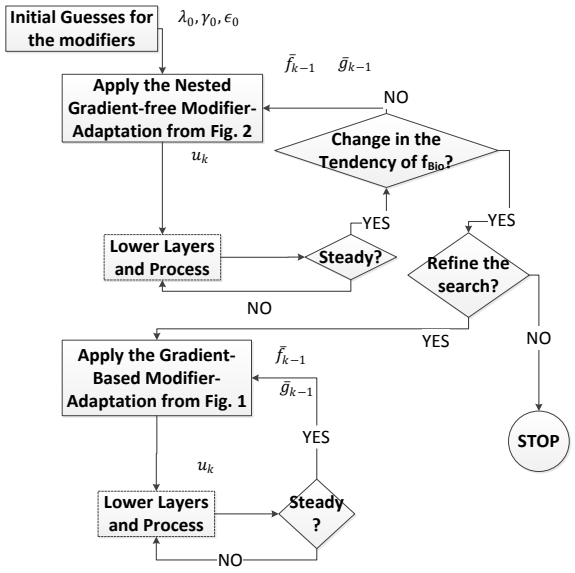

Fig.7 Diagram of the Mixed Approach

The outcomes obtained applying the previous idea, are summarized in Fig. 8, showing that it is possible to reach the process optimum in a stable way and within shorter time. We have tested the early detection of a possible optimum for two scenarios: using the change of tendency as a stopping criterion and refining the search using the mixed modifier-adaptation methodology to find the optimum of the process. The arrow in Fig.8 shows the point where the process stops in the first scenario, while the iterations continue till the end in the second case.

If the early detection is implemented without the refining in the search of the optimum of the process, the nested methodology is able to stop once the change in the tendency of the objective function is detected. As a result of this, the washout phenomenon is no longer observed and the iterations finish in a neighbourhood of the process optimum. The last decision variable proposed by the nested methodology is not exactly the real optimum of the process but it is an operating point that is slightly above this value, producing a mild deterioration of the objective function corresponding to a 0.35% with respect to the real optimum value. This worsening in the objective function can be understood as a trade-off with respect to the number iterations obtained with the gradient-based algorithm, and it can be a good indicator regarding if it is necessary the refining of the search using the gradient-based methodology or not.

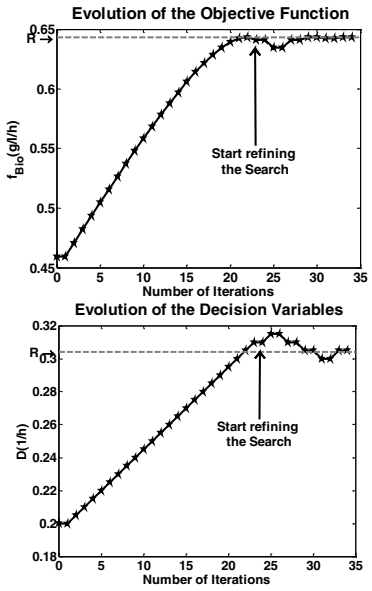

Fig.8. Evolution of the Mixed Approach

Even when the worsening obtained in the objective function can be acceptable for a real application, taking into account the reduction in the number of iterations of 50%, there is always a danger of stopping the algorithm prematurely, due to wrong measurements or other events.

Nevertheless, as it can be observed, the mixed approach finds the optimum of the process by adjusting the results given by the NMA algorithm with the early optimum detection, using a gradient based algorithm. Starting from the end of the gradient-free methodology, 11 iterations were necessary to converge to the real optimum of the process. In this case, to reduce 0.35% in the objective function measured from the process, it was necessary to increase the number of iterations in 45% with respect to the previous approach.

In real applications the optimum of the process is not known a priory. Therefore, when the NM algorithm stops the operator does not know how far is from this point, but only the progresses in the performance index with respect to the starting point. Hence, the decision of applying the refinement or using directly the outcomes from the NMA algorithm cannot be taken based in the distance with respect to the final goal, and it must be based in the criterion of the operator and in its previous knowledge of the system considering the progress achieved. In any case, the nested methodology with the early stop criterion only is able to find a region where the optimum could be according to the expected behaviour around this point. While the mixed approach is in charge to refine the search and find the required point.

5. CONCLUSIONS

This paper has discussed two methods within the modifier-adaptation approach to uncertainty management in RTO, evaluating them in a bioreactor case study and proposing a mixed algorithm that presents some advantages over them.

As a remark of the implementation of the modifier adaptation methodology in the continuous bioreactor example, we can say that the mixed approach proposed, combining the nested reformulation with the former gradient-based procedure, allows finding the optimum of a process reducing the requirements of additional perturbations of the process and avoiding unstable operating zones.

Other associated topics remain as open problems, e.g. the increase in complexity when the number of decision variables and the number of inequality constraints grow, or the sensitivity of the refining part of the search with the process noise. But we hope it contribute to the advance in the practical solution of process optimization problems.

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REFERENCES

Chachuat, B., Srinivasan, B. & Bonvin, D. 2009. Adaptation Strategies for Real-Time Optimization. *Computers & Chemical Engineering,* 33**,** 1557-1567.

Egea, J. A., Rodríguez-Fernández, M., Banga, J. R. & Martí, R. 2007. Scatter Search for Chemical and Bio-Process Optimization. *J. of Global Optimization,* 37**,** 481-503.

Gao, W. & Engell, S. 2005. Iterative Set-Point Optimization of Batch Chromatography. *Computers & Chemical Engineering,* 29**,** 1401-1409.

Golden, M. P. & Ydstie, B. E. 1989. Adaptive Extremum Control Using Approximate Process Models. *AIChE Journal,* 35**,** 1157-1169.

Mansour, M. & Ellis, J. E. 2003. Comparison of Methods for Estimating Real Process Derivatives in on-Line Optimization. *Applied Mathematical Modelling,* 27**,** 275-291.

Marchetti, A., Chachuat, B. & Bonvin, D. 2009. Modifier-Adaptation Methodology for Real-Time Optimization. *Industrial & Engineering Chemistry Research,* 48**,** 6022-6033.

Mathworks, I. 2007. *Matlab Optimization Toolbox 6 User's Guide,* Natick, Mass., The MathWorks.

Navia, D., Gutierrez, G. & de Prada Moraga, C. 2013. Nested Modifier-Adaptation Methodology for Rto in the Otto Williams Reactor. *10th International Symposium on Dynamics and Control Process Systems (DYCOPS 2013).* Mumbai, India: IFAC.

Roberts, P. D. 1979. An Algorithm for Steady-State System Optimization and Parameter-Estimation. *Int. J. Syst. Sci.,* 10**,** 719-734.

Tatjewski, P. 2002. Iterative Optimizing Set-Point Control - the Basic Principle Redesigned. *15th Triennial World Congress, Barcelona, Spain.* IFAC.

Walters, F. H., Parker, L. R., Morgan, S. L. & Stanley, D. N. 1991. *Sequential Simplex Optimization: A Technique for Improving Quality and Productivity in Research, Development, and Manufacturing,* Boca Raton, Fla., CRC Press.

Zhang, Y. & Forbes, J. F. 2006. Performance Analysis of Perturbation-Based Methods for Real-Time Optimization. *The Canadian Journal of Chemical Engineering,* 84**,** 209-218.