Robust Economic Model Predictive Control For Continuous Fermentation Processes ⋆

Ali Ghodba [*], **Chris McCready** [**], **Mahshad Valipour** [**], **Luis Ricardez-Sandoval** [*], **Hector Budman** [**]

[*] *Chemical Engineering Department, University of Waterloo, Waterloo, Canada (*Email: hbudman@uwaterloo.ca)*
[**] *Sartorius Corporate Research, Toronto, Canada*

Abstract: We propose an Economic Model Predictive Control (EMPC) framework that is robust to model structure error. The approach integrates parameter estimation with gradient correction to improve controller performance. At each sampling time, the algorithm performs parameter estimation over past samples, followed by a gradient correction step that updates model parameters to match the gradients of the model and plant using transient measurements. To match the gradients while maintaining model accuracy, a correction term is added, which ensures an upper bound on the model error. The approach is validated on a continuous penicillin production process subject to model-plant mismatch. Results demonstrate that the proposed EMPC with gradient correction drives the process closer to the true plant optimum values and achieves better convergence to optimal operating conditions than a similar EMPC without gradient correction.

Keywords: Robust Economic Model Predictive Control (EMPC), Gradient Correction, Model-Plant Mismatch, System Identification, Penicillin Fermentation

1. INTRODUCTION

Fermentation processes in the pharmaceutical sector are typically operated in batch, fed-batch, or perfusion modes. While such operations were reasonable in the past due to the lower risk of contamination, they may be unsustainable as the demand for pharmaceuticals increases and their cost exceeds the purchasing power of the public. Continuous manufacturing is an alternative manufacturing strategy that relies less on human labor and transitioning steps between unit operations, requires potentially smaller facilities, and is more suitable for automation and adaptation across different drug products. Continuous manufacturing is gaining increasing popularity in the pharmaceutical industry (Khanal and Lenhoff, 2021). Hence, there is an increasing interest in the optimization of continuous pharmaceutical operations. Since optimization algorithms generally rely on mathematical models, the accuracy of such models is crucial for finding the true optimum. Models of pharmaceutical processes are particularly prone to model structure errors due to either model simplification or a lack of prior information about certain phenomena and, if not accounted for, they can lead to sub-optimal results.

Optimization of an economic cost for batch and fed-batch operations in the presence of model structure errors has been extensively tackled with batch-to-batch optimization algorithms, which involve successive identification and optimization steps until convergence (Bonvin, 1998; Mandur and Budman, 2015). These batch-to-batch algorithms uniformly required matching of the measured and predicted gradients in order to ensure convergence to the true economic optimum in the presence of model errors.

Economic Model Predictive Control (EMPC) has been proposed for the economic optimization of continuous processes. EMPC integrates economic process optimization and process control into one optimization layer instead of the traditional two-layer optimization approach involving a real-time optimization of set-points followed by Model Predictive Control (MPC) about the calculated set points(Darby et al., 2011). Different formulations of EMPC have been reported (Rawlings et al., 2012), and studies on the robustness of EMPC with respect to an error in model parameters have been reported (Santander et al., 2016; Schwenkel et al., 2020).

In view of the ability of batch-to-batch algorithms to find an economic optimum in the presence of model structure errors, researchers have investigated the application of these algorithms to continuous processes. A key contributor to the ability of batch-to-batch techniques to deal with model structure error is the matching of measured and model gradients of the cost with respect to the decision variables, which is not done in traditional EMPC algorithms.

A widely used batch-to-batch optimization approach is the Modifier Adaptation (MA), which adjusts the cost function and constraints of the optimization problem to account for differences between measured and expected gradients (Marchetti et al., 2009). More recently, the MA methodology was used in real-time optimization (Patrón and Ricardez-Sandoval, 2023) and also integrated into EMPC algorithms for continuous processes (Vaccari and

⋆ This work is supported by MITACS Grant IT-23368 through MITACS-Accelerate Program and Sartorius Canada Inc.

Pannocchia, 2016, 2018) based on steady-state gradients of the cost and constraints. To address problems with slow convergence to a steady state, transient measurements have also been used to estimate the plant's gradients (François and Bonvin, 2014; Speakman and François, 2020; Oliveira-Silva et al., 2021). A common feature of all MA algorithms is the use of a filter to reduce sensitivity to noise that must be tuned in an ad-hoc fashion.

Another approach that was previously applied for batch-to-batch economic optimization in the presence of model-plant mismatch (MPM) was originally proposed in Mandur and Budman (2015) and then extended by Ghodba et al. (2025) to deal with unmeasured disturbances. The algorithm involves 4 sequential steps that are repeated until convergence to the optimum: model identification, gradient matching, model-based optimization, and experimentation in the neighborhood of the calculated optimum.

The current work modifies and extends the algorithm of Ghodba et al. (2025), previously used solely in batch processes, for application to continuous operations. Distinctive features of the current approach are:

- It does not require a tunable filter in contrast to the MA method; instead, it relies on performing model adaptation to provide such filtering ability.
- The algorithm provides a good model approximation in the neighborhood of the optimum, which may be useful for state estimation or for testing critical constraints.
- The economic objective function does not have to be modified.

The approach includes an identification step at each sampling time to identify model parameters and is followed by a gradient correction step that updates model parameters to match the model and measured plant gradients. A model correction term is introduced to match gradients while ensuring a user selected upper bound on the prediction error. Dynamic gradients are calculated in this work using transient measurements. Then, the model is updated by the identification and gradient matching steps and is used in the EMPC to determine the optimum input variables for the next control horizon. Since gradient matching is a salient feature of the proposed EMPC as compared to conventional EMPC, the focus of this study will be to test whether this matching contributes to improve closed-loop performance.

The paper is organized as follows. The structure of the proposed EMPC used in the paper is presented in Section 2. Then, Section 3 describes the case study of Penicillin production. The results of the proposed methodology are presented in Section 4. Finally, Section 5 presents the conclusions and future work.

2. PROPOSED ROBUST EMPC METHODOLOGY

The new proposed method involves four steps: i—a model is updated based on measured plant inputs along an identification horizon; ii—measured and predicted cost gradients with respect to decision variables are matched along a time horizon subject to an upper bound on the prediction error; iii—EMPC is used to optimize an integral cost over a prediction horizon; iv—a square pulse signal

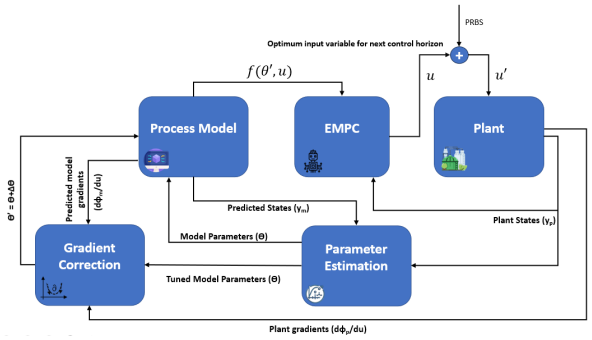

Fig. 1. The general schematic of proposed EMPC

is added to the calculated optimal inputs, and the entire procedure is again repeated from step i above.

A general schematic representation of the proposed EMPC is illustrated in Fig.(1). In the following, each step is detailed.

2.1 Step i: Parameter Estimation

In this step, the sum of squared errors between model predictions and the measurements is minimized according to Eq.(1).

$$\Theta = \underset{\Theta}{argmin} \sum_{k=\lambda}^{n_k} \left\| \mathbf{y}_p(t_k) - \mathbf{y}(\mathbf{x}, t_k) \right\|^2 \tag{1a}$$

$$s.t. \quad \dot{\mathbf{x}} = f(\mathbf{x}, \Theta, \mathbf{u}) \tag{1b}$$

$$\mathbf{y} = h(\mathbf{x}) - \mathbf{C} \tag{1c}$$

$$\Theta \in [\Theta_{lb}, \Theta_{ub}] \tag{1d}$$

$$\lambda = (n_k - LIH) \cdot H\,(n_k - LIH) \tag{1e}$$

where the subscript p refers to plant. $\mathbf{x} \in \mathbb{R}^{n_x}$ is the vector of states evaluated at sampling times t_k with $k \in \{\lambda, ..., n_k\}$ where n_x and n_k represent the number of state variables and total time intervals by current sampling instance. $\Theta \in \mathbb{R}^{n_\Theta}$, where n_Θ represents the number of parameters, are model parameters at the current sampling time that are calibrated to minimize the sum of square error between plant and model outputs. The bounds $\Theta_{lb} \in \mathbb{R}^{n_\Theta}$ and $\Theta_{ub} \in \mathbb{R}^{n_\Theta}$ provide a permissible range of parameter values. $u \in \mathbb{R}^{n_u}$, where n_u represents the number of input variables, are determined input variables of the process. $\mathbf{y}_p \in \mathbb{R}^{n_y \times (n_k - \lambda)}$ are the plant measurements whereas $\mathbf{y} \in \mathbb{R}^{n_y \times (n_k - \lambda)}$ is the model prediction where n_y represents the number of outputs. Also, $f \in \mathbb{R}^{n_x}$ is a set of differential equations representing the correlation between model states and process inputs and $h \in \mathbb{R}^{n_y}$ is a mapping between model states and predicted outputs. $\mathbf{C}$ is a correction term that will be explained in Section 2.2. Also, λ indicates the starting point of the identification horizon that is determined by the Heaviside function, H, and the length of the identification horizon is shown by LIH. The LIH is chosen according to the largest time constant expected in the process. For simplicity, in the current study, a straightforward least squares regression was used. We are currently investigating the use of an Extended Kalman Filter or a Moving Horizon Estimator to identify the states and model parameters.

2.2 Step ii: Gradient Matching

In the presence of structural MPM, the model parameters estimated by Eq.(1) do not necessarily result in correct predictions of the plant gradients. Thus, the predicted gradients from the model must be matched to the measured gradients of the process to drive the optimization search toward the plant optimum. To do this, the parameters' values that were obtained in the identification step are perturbed by an amount $\Delta\Theta$ to fit the predicted to the measured gradients of the cost function and constraints as follows:

$$\begin{aligned}\Delta\Theta = \quad & \arg\min_{\Delta\Theta}\Big(\sum_{t_i=\gamma}^{n_k}\mathbf{w}_{\phi}^{T}\left|\frac{\partial\phi_p(t_i)}{\partial\mathbf{u}}-\frac{\partial\phi(\mathbf{y}(\mathbf{x}),t_i)}{\partial\mathbf{u}}\right| \\ & +\sum_{t_i=\gamma}^{n_k}\sum_{j=1}^{n_g}\mathbf{w}_{g,j}^{T}\left|\frac{\partial g_{p,j}(t_i)}{\partial\mathbf{u}}-\frac{\partial g_j(\mathbf{y}(\mathbf{x}),t_i)}{\partial\mathbf{u}}\right|\Big) \quad (2a)\end{aligned}$$

$$s.t. \quad \dot{\mathbf{x}} = f\left(\mathbf{x},\Theta+\Delta\Theta,\mathbf{u}\right) \quad (2b)$$

$$\mathbf{y} = h\left(\mathbf{x}\right)-\mathbf{C} \quad (2c)$$

$$\left\|\epsilon^{T}\right\|_{\infty}\leq\epsilon_{max}^{T} \quad (2d)$$

$$\Theta+\Delta\Theta\in[\Theta_{lb},\Theta_{ub}] \quad (2e)$$

$$\gamma = (n_k-GCH)\cdot H\left(n_k-GCH\right) \quad (2f)$$

where $\Delta\Theta\in\mathbb{R}^{n_\Theta}$ is the change introduced in the parameter estimates, with respect to Θ, required to minimize the difference between the predicted and measured gradients along the gradient correction horizon (GCH). $\frac{\partial\phi}{\partial u}\in\mathbb{R}^{n_k-\gamma}$ and $\frac{\partial g_j}{\partial u}\in\mathbb{R}^{n_k-\gamma}$ with $j=1,...,n_g$ are the gradients of cost and constraints, respectively. The measured gradients are denoted by the subscript p. The plant gradients are obtained with a dynamic perturbation method using the finite difference method between the values of the cost function at two consecutive time steps with respect to the difference between input variables. $\mathbf{w}_\phi\in\mathbb{R}^{n_k-\gamma}$ and $\mathbf{w}_g\in\mathbb{R}^{n_g\times(n_k-\gamma)}$ are used to weight the gradient-matching objectives.

Finding parameter values that simultaneously satisfy both the minimization of square errors and gradient-matching objectives is impeded in the presence of model structure error because these objectives are conducted separately (the advantage of this approach over combining Eqs.(1) and (2) is that weighting each objective function is challenging, and in the proposed method, parameters can be identified without the need to determine appropriate weights.) In other words, parameters estimated to reduce gradient differences may not simultaneously minimize prediction error. To approximately reconcile these objectives, a first-order Taylor expansion is used to estimate the difference between the model outputs generated by the model identification step (Section 2.1) and the output generated by the current gradients' matching step.

$$\mathbf{y}(\mathbf{x}(\Theta+\Delta\Theta,t_k))-\mathbf{y}(\mathbf{x}(\Theta,t_k))\cong D\mathbf{y}(\mathbf{x}(\Theta,t_k))\cdot\Delta\Theta \quad (3)$$

where $D\mathbf{y}(\mathbf{x}(\Theta,t_k))\in\mathbb{R}^{n_y\times n_\Theta}$ is the Jacobian matrix of the states with respect to model parameters at sampling time t_k. Then, to maintain a similar fitting accuracy to that obtained in the parameter estimation step, a correction term $\mathbf{C}\in\mathbb{R}^{n_k\times n_y}$, is subtracted in (Eq.(2c)) from the output resulting from the gradient matching step. This correction term is recursively calculated as follows:

$$\mathbf{C}(t_k) = \mathbf{C}(t_{k-1})+D\mathbf{y}(\mathbf{x}(\Theta,t_{k-1}))\cdot\Delta\Theta \quad (4)$$

where $\mathbf{C}(t_k)$ is the current correction term. Then, the truncation error introduced by the linear correction term in Eq.(3) can be calculated as follows

$$\epsilon^{T} = \frac{\mathbf{y}(\mathbf{x}(u,\Theta+\Delta\Theta))-D\mathbf{y}(\mathbf{x}(u,\Theta))\cdot\Delta\Theta-\mathbf{y}(\mathbf{x}(u,\Theta))}{\mathbf{y}(\mathbf{x}(u,\Theta))} \quad (5)$$

Accordingly, inequality (Eq.(2d)) imposes an upper bound on the prediction error, thus ensuring a pre-specified level of accuracy in the model prediction despite the changes in parameters' values that were required to match the gradients. Low epsilon values restrict the flexibility of gradient correction, while high values may cause the model to diverge significantly from the parameter estimation step. $\epsilon_{max}^{T}=0.05$ has been selected in this study.

2.3 Step iii: EMPC calculation

The dynamic model updated based on the previous model identification and gradient matching steps, i.e. $\Theta'=\Theta+\Delta\Theta$, is used in the EMPC algorithm to calculate optimal input variables along a prediction horizon based on the current measured states of the system. The corresponding EMPC formulation is as follows:

$$\min_{u} \quad \int_{t}^{t+T_P} l_e(\widetilde{\mathbf{x}}(\tau),\widetilde{\mathbf{u}}(\tau))d\tau \quad (6a)$$

$$s.t. \quad \dot{\widetilde{\mathbf{x}}}(\tau) = f(\widetilde{\mathbf{x}}(\tau),\widetilde{\mathbf{u}}(\tau),\theta',w(\tau)) \quad (6b)$$

$$\widetilde{\mathbf{y}} = h\left(\widetilde{\mathbf{x}}\right)-\mathbf{C} \quad (6c)$$

$$g(\widetilde{\mathbf{x}}(\tau),\widetilde{\mathbf{u}}(\tau),\theta',w(\tau))\leq 0 \quad (6d)$$

$$\widetilde{\mathbf{x}}(t) = \mathbf{x}(t) \quad (6e)$$

$$\widetilde{\mathbf{u}}(\tau)\in U, \quad \forall\tau\in[t,t+T_C] \quad (6f)$$

$$\widetilde{\mathbf{u}}(\tau) = \widetilde{\mathbf{u}}(t+T_C), \quad \forall\tau\in[t+T_C,t+T_P] \quad (6g)$$

where T_P and T_C are the prediction and the control horizon with $T_C\leq T_P$. Eq.(6a) represents the economic stage cost (l_e). $\widetilde{\mathbf{x}}$ denotes the predicted state sequence, which is the solution of Eq.(6b) driven by the input signal $\widetilde{\mathbf{u}}(.):[t,t+T_P]\longrightarrow U$ under the initial condition $x(t)$. At each sampling instance, the state measurements are used via Eq.(6e), so the dynamic model is initialized by the actual system state and predicts future system behavior. In this preliminary study, the full state vector is assumed to be measured. Future studies will consider state estimation based on a limited set of measurements. Eq.(6f) fixes the input beyond the control horizon.

2.4 Step iv: Addition of square pulse and data collection

In batch-to-batch optimization, several experiments are run simultaneously with nominal values of input variables and perturbations with respect to these nominal values to calculate the plant's gradients. However, in a continuous process, running simultaneous experiments is not possible

since there is a single process, and experiments must be collected from this single process. Instead, perturbations must be introduced in the form of a square pulse signal entering the process at each time interval. The purpose of this signal is twofold: i– to provide persistent excitation for parameter estimation and ii– to excite the process sufficiently to permit the calculation of meaningful gradients. Accordingly, the pulse signal must be large enough to overcome the noise but not too large so as to avoid significant deviation from optimal performance. The dither is particularly crucial when the process approaches a steady-state operation, so the signal provides excitation to avoid convergence to a suboptimal condition. In this study, a square pulse whose frequency matches the control horizon. That is done to avoid the occurrence of the same input variables at two consecutive points, leading to an undefined (or infinite) gradient. After the addition of this signal to the input variable, it is applied to the system, and state variables in the next sampling instance are measured. Then, the entire procedure is repeated starting from Section 2.2 above.

3. CASE STUDY: CONTINUOUS PENICILLIN PROCESS

A continuous operation of a penicillin fermentation process is used to illustrate the proposed algorithm. An unstructured model for penicillin production in a batch/fed-batch process was developed by (Birol et al., 2002), and it was modified to a continuous process to test the proposed methodologies. This model is used for the generation of *in silico* data needed for the current study. This process is described by the following set of equations:

$$\frac{dX}{dt} = \left(\frac{\mu_X S X}{K_X X + S}\right) - \frac{FX}{V} \tag{7a}$$

$$\frac{dP}{dt} = \left(\frac{\mu_P S X}{K_P + S + \frac{s^2}{K_I}}\right) - K_H P - \frac{FP}{V} \tag{7b}$$

$$\frac{dS}{dt} = -\frac{1}{Y_{X/S}}\left(\frac{\mu_X S X}{K_X X + S}\right) - \frac{1}{Y_{P/S}}\left(\frac{\mu_P S X}{K_P + S + \frac{s^2}{K_I}}\right) - m_X X + \frac{F s_f}{V} - \frac{FS}{V} \tag{7c}$$

where X, P, and S represent biomass concentration (g/l), penicillin concentration (g/l), and substrate concentration (g/l), respectively. F is the feed flow rate of the substrate (l/h). Model parameters (kinetic parameters) are shown in Table 1. The initial conditions are shown in Table 2.

Table 1. Model Parameters for Eq.(7)

Parameter	Value
Yield constant: $Y_{x/s}$ (g biomass/g glucose)	0.45
Yield constant: $Y_{p/s}$ (g penicillin/g glucose)	0.9
Maintenance coefficient on substrate: m_x (per h)	0.014
Maximum specific growth rate: μ_x (per h)	0.092
Contois saturation constant: K_x (g/l)	0.15
Specific rate of penicillin production: μ_p (per h)	0.005
Inhibition constant: K_p (g/l)	2e-4
Inhibition constant for product formation: K_I (g/l)	0.1
Penicillin hydrolysis rate constant: K_H (per h)	0.04
Feed substrate concentration: s_f (g/l)	5
Reactor volume: V (l)	120

Table 2. Initial operating conditions for the simulations

Biomass conc. (X_0)	0.1 (g/l)
Product conc. (P_0)	0 (g/l)
Substrate Concentration (S_0)	15 (g/l)
Initial Substrate Feed rate (F_0)	6 (l/h)

The structural model-plant mismatch is intentionally introduced into the model used by EMPC by eliminating the penicillin consumption term occurring via hydrolysis and substrate consumption for the maintenance requirements of the microorganism. Thus, the model used for EMPC is given Eq.(8):

$$\frac{dP}{dt} = \left(\frac{\mu_P S X}{K_P + S + \frac{s^2}{K_I}}\right) - \frac{FP}{V} \tag{8a}$$

$$\frac{dS}{dt} = -\frac{1}{Y_{X/S}}\left(\frac{\mu_X S X}{K_X X + S}\right) - \frac{1}{Y_{P/S}}\left(\frac{\mu_P S X}{K_P + S + \frac{s^2}{K_I}}\right) + \frac{F s_f}{V} - \frac{FS}{V} \tag{8b}$$

4. RESULTS AND DISCUSSION

The simulations assume 5% uniform noise in all process states (X, P, S) generated by the process simulator. The objective of the optimization problem is the maximization of penicillin production ($\int P(t)dt$) during the operation time. The decision variable is the substrate feed rate, F(t). The MATLAB function $fmincon$ was utilized for all optimization problems considered in this section using the interior-point algorithm as the optimization solver. The processor of the system is 12th Gen Intel(R) Core(TM) i7-12700 and is equipped with 16GB of RAM. Seven parameters are considered for parameter estimation and gradient matching;

- $Y_{x/s}$, $Y_{p/s}$, μ_x , K_x , μ_p , K_p , K_I

Their initial guesses in the first iteration are selected as shown in Table 1. In this study, the sampling time interval is 4 hours. This sampling interval duration is typical in fermentation processes because of the lack of some online sensors for faster data acquisition. Also, the identification horizon (LIH) and gradient correction horizon (GCH) are chosen according to the estimated largest time constant, which is 200 hours, and the prediction horizon is 160 hours. The control horizon is 8 hours to allow the system enough time to exhibit meaningful dynamic changes and make gradient estimation reliable.

First, we tested the effect of model structural errors by comparing the proposed EMPC that used a model with structural errors with an EMPC that used a perfect model. Fig.(2) presents a comparison between these two cases. In the dynamic model without structural errors, the process model (Eq.(7)) is used as the model simulator, and no MPM is present. As shown in Fig.(2), the proposed EMPC drives the process close to the real optimum of the process, and both converge to the same optimal state variables. This shows that the gradient correction step, in combination with the identification step, could model the correct gradients of the plant in the presence of model structural errors. However, Fig(2c) exhibits that in the

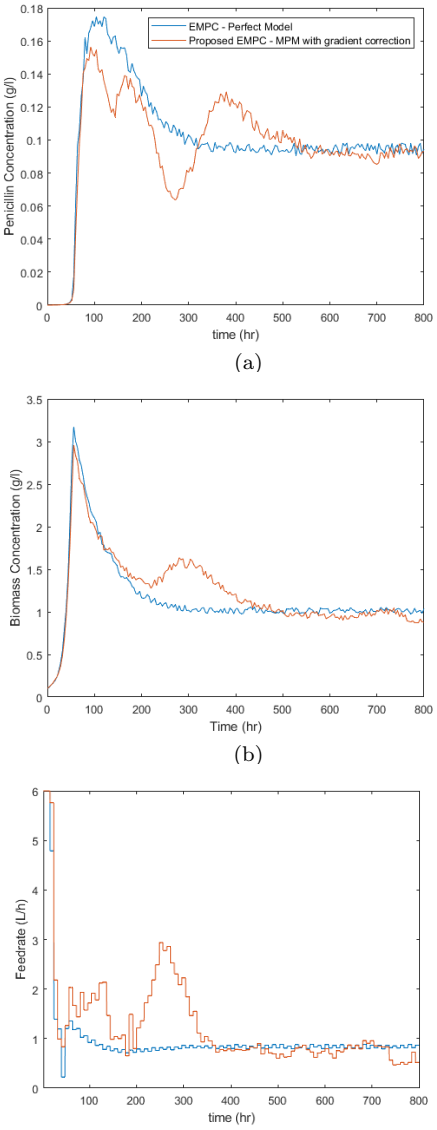

Fig. 2. Comparison of the proposed EMPC using the model structural errors with EMPC using perfect model, in terms of a) specific productivity, b) biomass density, and c) input variables

presence of model structure error, the robust EMPC controller needs larger control actions to keep the process close to optimum values compared to the case without error. Fig.(2a) shows that the penicillin concentrations have fallen below optimal values at some time intervals due to inaccurate predictions of the system's actual behavior. This may be due to insufficient excitation (pulse signal) in the system for estimating parameters and gradients, which will be examined in future work. Nevertheless, the controller attempted to increase biomass—and subsequently penicillin production—by injecting more feed at certain time intervals.

As a second comparative case study, the improvement of the proposed EMPC algorithm with gradient correction is compared to the EMPC without gradient matching. In both cases, the model was assumed to have structural errors as discussed above. Fig.(3a) illustrates the

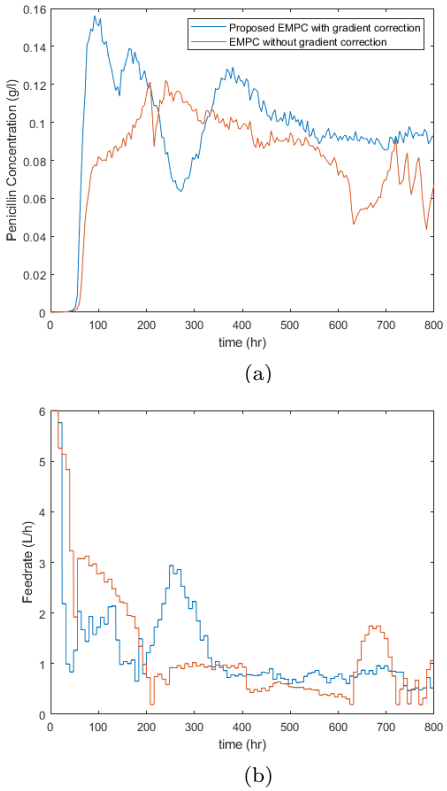

Fig. 3. Comparison between the proposed EMPC with gradient correction and regular EMPC without gradient correction in the presence of model-plant mismatch in terms of a) specific productivity, and b) input variables

plant production of penicillin. As shown in this figure, the EMPC without gradient correction is unable to reach the optimum economic cost and fast dynamic behavior in the initial moments (0-100 hr) because the dynamic model has errors and there has not been sufficient data for training. These errors also lead to discrepancies between the gradients of the model and the system, ultimately resulting in incorrect predictions of input variables. In contrast, with the controller incorporating the gradient correction step, despite the lack of data for model training in the initial time, it is able to improve the economic cost function after matching the gradients of the model with the plant. Another notable point is the deviations from the optimum along the continuous operation. In the regular EMPC without gradient correction, a significant deviation from the optimal input trajectory occurred after 400 hours. This deviation is not observed in the proposed EMPC with gradient correction, underscoring the effectiveness of gradient correction in steering the process toward optimality. Fig.(3b) also shows the deviation in the feed rate in EMPC without a gradient in the presence of MPM. As discussed earlier, in this case, the system deviates from the optimum after 400 hours, and the model's higher uncertainty also led to some significant deviations in the last 200 hours. In contrast, the identified model is more accurate with gradient correction, contributing to greater robustness around the optimal points.

As a last case study, we evaluate the ability of the proposed method to drive the system to the true economic optimum.

Table 3. Comparison of the obtained economic function using noise-free measurement of penicillin concentration

Scenario	Value
Steady-state optimum of the plant	79.36
EMPC using the perfect model	80.32
EMPC using model structural errors with gradient correction	77.21
EMPC using model structural errors without gradient correction	63.55

The steady-state optimum of the plant (optimum economic function) is determined by optimizing the steady-state of Eq.(7) and compared for three different strategies: regular EMPC with the perfect model, regular EMPC with MPM, and the proposed EMPC with MPM and gradient correction. The results are given in Table 3. To calculate the steady-state optimal economic function of the plant, it is assumed that the process starts at the optimal steady state. However, in EMPC with a perfect model, a transition period is required to reach this steady-state optimum, during which the optimum can be increased as compared to steady state optimum. Hence, EMPC with a perfect model yields a slightly higher economic function value than the steady-state optimum of the plant. Also, the proposed EMPC with gradient correction approaches the steady-state optimum of the process, and it reaches an optimal cost that is very close to the one achieved by an EMPC with a perfect model. In contrast, the optimal solution for the regular EMPC without gradient correction is approximately 20% lower than the true optimum. The introduction of disturbances into the process will resemble the initial period of operation in terms of the expected deviations of the identified model from the process behavior. Similar to the initial period of operation considered in this study, significant model updates will be required to compensate for these disturbances correctly. Future studies will be conducted on the ability of the proposed algorithm to reject disturbances.

5. CONCLUSION

A novel robust EMPC methodology for continuous processes in the presence of structural model-plant mismatch is proposed. The method is inspired by methodologies previously used in batch-to-batch optimization procedures, which involve the matching of gradients of the cost function of the process and the model with respect to decision variables. It is shown that the gradient correction significantly improves the economic optimum as compared to a similar algorithm that does not employ such a correction. The methodology was validated on a continuous penicillin production process with the intentionally introduced model-plant mismatches. The case study involved relatively large sampling intervals that are typical in fermentation processes due to the unavailability of online sensors in such systems. Future studies will investigate the optimal design of dithering signals for a selected sampling interval and the effect of disturbances on the performance of the algorithm.

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