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Robust Nonlinear Extended Prediction Self-Adaptive Control (NEPSAC) of Continuous Bioreactors

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***Abstract*— A nonlinear predictive control strategy (NEPSAC) is formulated for a continuous bioreactor characterized by severe non-linearity and parameter time-variance, with the control objective being to regulate the fermenter operation near the optimum productivity. Robustness towards the unpredictable time-variance, which comes from cell-mass growth, is guaranteed by disturbance filter design. The dilution rate and feed substrate concentration are considered as manipulated inputs, while the state variables are the biomass, substrate and product concentrations. Results obtained with robust NEPSAC are presented and compared with those obtained with other model predictive control and various linearization based strategies.**

I. Introduction

The dynamic behavior of a biochemical system is usually characterized by severe nonlinearities and time variance of the bioprocess. This is especially valid for reactors used in biochemical processes such as ethanol fermentation [1], production of biomass [2] and treatment of wastewater through the activated sludge process [3]. The high degree of non-linearity, multivariability and parameter time variance in these processes make it extremely difficult to model and control even in the simplest cases.

The primary objective of any batch, fed-batch or continuous fermenter is to control, contain and positively influence the biochemical reactions occurring within it, although continuous operation has several advantages over batch and fed-batch operations such as minimizing equipment downtime and time loss due to the lag phase of the microbial culture [4]. Some microbial systems exhibit highly oscillatory behavior during operation. Such oscillations may result from an initial synchronization of the culture and often appear to occur spontaneously. This self-oscillating behavior caused by spontaneous synchronization is studied using segregated models [5] and is probably due to system perturbations [6]. However, these sustained oscillations are sometimes necessary depending on the metabolic considerations.

Control of such fermenters is a difficult task owing to input multiplicity and output singularity, when the production of biomass (or a product) is to be optimized at its maximum productivity rate. For example, continuous fermenters exhibit input multiplicity in the optimal operating region i.e. the operating region where identical outputs are obtained from multiple inputs [7]. Input multiplicities, in general, occur due to the presence of competing dynamic effects in a nonlinear system causing robustness problems [8].

Accurate process models are rarely available due to the complexity of the underlying biochemical processes involved [9]. Furthermore, in a continuous fermenter, the inherently unpredictable nature of microbial systems due to sudden changes in feed concentration or drifts lead to sub-optimal operating conditions. Although various approaches of analyzing and controlling continuous cultivation processes have been attempted [10], a successful control of a nonlinear continuous fermenter system is critically dependent upon the knowledge of the nonlinear dynamics of the underlying process.

Model Predictive Control (MPC) can be grouped under the family of controllers which makes explicit use of a model of the process to obtain the control signal by minimizing an objective function and predict the process output at future time instants or horizon [11]. Conventionally, MPC employs a linear deterministic model to predict the process dynamics, although a real process is usually nonlinear and uncertain [12]. Although various nonlinear model based predictive control algorithms exist (see [13] for details), they differ amongst themselves in the model used to represent the process, the disturbance dynamics and the cost function to be minimized. A built-in feature of MPC is the direct use of an explicit and separately identifiable process model [14]. It is worth mentioning that apart from the classical PID controller, the MPC strategy has found wide acceptance both in academia and in industry.

De Keyser and Van Cauwenberghe [15][16] developed an Extended Predictive Self-Adaptive Control (EPSAC) algorithm which has the advantage that the process model to be used by the control law can be either linear or nonlinear. The NEPSAC algorithm for nonlinear systems is capable of obtaining (in an iterative way) the optimal control signal, not depending on the model type. In this way, the use of complex optimizing techniques, which result in a complicated solution unsuitable for real-time implementation, can be avoided. The latest version NEPSAC is a nonlinear predictive controller which is essentially characterized by its simplicity since it consists of repetitive application of the basic linear EPSAC algorithm during the controller sampling interval and leads in an iterative way, after convergence, to the optimal solution for the underlying nonlinear problem [17].

In this paper, a robust NEPSAC controller based on a continuous bioreactor using the experimental data of Agrawal et al. [18], is developed to regulate the fermenter near its optimum productivity . The feed substrate concentration is employed as manipulated input, holding dilution rate to its nominal value, in a single-input/single-output (SISO) control strategy. Furthermore, the results obtained are compared with the nonlinear control strategies based on linearization of Henson and Seborg [9] and nonlinear MPC (NMPC) of Silva and Kwong [20].

The organization of this work is as follows. Section II introduces the model, the subsequent model analysis is presented in III. The NEPSAC algorithm is summarized in IV, simulation results and comparisons are in V. Section VI gives some conclusions.

II. Continuous fermenter

In order to apply the NEPSAC strategy, a simple unstructured model of the fermentation process is considered. The model has been previously developed on the basis of data from steady state experiments by assuming that the fermenter culture consists of a single, homogeneously growing organism. The microbial culture is grown in a reactor fed in a continuous mode at a constant volume under perfect mixing conditions.

A variety of isothermal, well-mixed, constant yield fermentation processes can be described by the following simple unstructured model [18]:

$$Cell - balance$$
$$\dot{X} = -DX + \mu X \quad (1)$$
$$Substrate - balance$$
$$\dot{S} = D(S_f - S) - \frac{1}{Y_{x/s}}\mu X \quad (2)$$
$$Product - balance$$
$$\dot{P} = -DP + (\alpha\mu + \gamma)X \quad (3)$$

where μ is the specific growth rate, $Y_{x/s}$ is cell-mass yield, α and γ are yield parameters for the product.

Two variables are chosen to describe the reactions which occur in the fermenter: the biomass concentration X and the limiting substrate concentration S. These along with product concentration P form the process state variables. The system has two manipulated inputs: the culture dilution rate D and the limiting feed substrate concentration S_f. D equals the flow rate F, at which existing medium is replaced with fresh medium in a continuous culture, divided by the volume of the growing culture. The specific growth rate model is assumed to exhibit both substrate and product inhibition according to Haldane kinetics:

$$\mu = \frac{\mu_m(1 - \frac{P}{P_m})S}{K_m + S + \frac{S^2}{K_i}} \quad (4)$$

The parameters of the above model are product saturation constant P_m, substrate saturation constant K_m, substrate inhibition constant K_i. The maximum specific growth rate μ_m and the cell-mass yield $Y_{x/s}$ are usually sensitive to operating conditions because they have a strong effect and could be

TABLE I
Operating conditions and parameters

Parameter	Nominal value
α	2.2g/g
γ	$0.2h^{-1}$
K_m	1.2g/l
K_i	2.2g/l
P_m	50g/l
μ_m	$0.48h^{-1}$
$Y_{x/s}$	0.4g/g
D	$0.15h^{-1}$
S_f	20g/l
X	7.038g/l
S	2.404g/l
P	24.87g/l

uncertain. These two parameters can be viewed as unmeasured disturbances because they may exhibit significant time variance. However, the other parameters K_i, K_m, P_m and α, γ mentioned in Table I are equally important but are more certain. Following the work of Henson and Seborg [9], the latter five parameters were not varied in this study.

If the biomass and substrate values are negligible when compared to that of the product, the productivity Q is defined as the amount of product cells produced per unit of time:

$$Q = DP \quad (5)$$

The model in (1)-(3) can be compactly represented as:

$$\dot{z} = F(z, D, S_f) \quad (6)$$

III. Model analysis

From a control perspective, the next step is to obtain a nominal optimum operating point of the process using the above mechanistic model [7]. The nominal values of the parameters and the operating conditions used in the present study are those reported in [9], see Table I.

A. Control objectives

A fermenter under operation should maximize the production of a desired product. This in turn can be achieved by optimizing the steady state operating conditions of the fermentation process. It can be solved analytically based on the physical model equations. The productivity Q can be maximized if both the feed substrate concentration and dilution rate are available for manipulation. The optimum can be formalized as:

$$max_{\bar{D}\bar{S_f}}\bar{Q} = \bar{D}\bar{P} \quad (7)$$

subject to the system constraints i.e.

$$F(\bar{z}, \bar{D}, \bar{S_f}) = 0 \quad (8)$$

which can be obtained by setting $\bar{D} = D^* = 0.164h^{-1}$ and $\bar{S_f} = S_f^* = 23.4g/l$. The effect of variations in μ_m and $Y_{x/s}$ in various combinations on the characteristic curves between D, Q and S_f, Q are shown in Figs. 1 and 2 respectively. As is evident, small changes in μ_m and/or $Y_{x/s}$ have drastic effects on optimal Q. Note that the optimum region is quite flat, meaning the productivity would still remain optimal, even if not operated at exact D^* and S_f^*, and rather regulated to its nominal operating conditions of table I.

However, at higher values of D and S_f, Q goes to 0 and such a state also satisfies the steady state optimum derived in (7) and (8). This phenomenon is called washout, and unfortunately resides very near to the optimum productivity. Therefore a good control action must regulate the system to its optimal steady state and at the same time avoid washout. The washout is farther away from optimum in case of S_f than for D. This coupled with the fact that S_f is directly controllable over D which occurs where the cells exit, makes S_f a suitable input to regulate the productivity Q. This makes it necessary that the product concentration P be measured, so that Q can be computed from:

$$Q = \bar{D}P \tag{9}$$

This computation of Q is precise because we hold the dilution rate D to its optimal $\bar{D}$ and measure P.

Notice that the nominal values of $\mu_m = 0.48$ and $Y_{x/s} = 0.4$ are chosen to be higher than the true values [18]. Due to this adjustment, in our analysis we only consider the uncertainty in these parameters as a decrease from their nominal values.

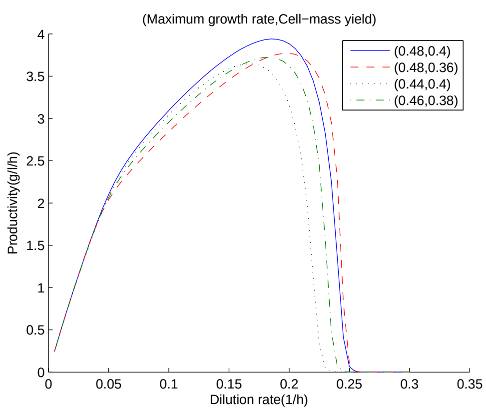

Fig. 1. Dilution effect on optimal productivity

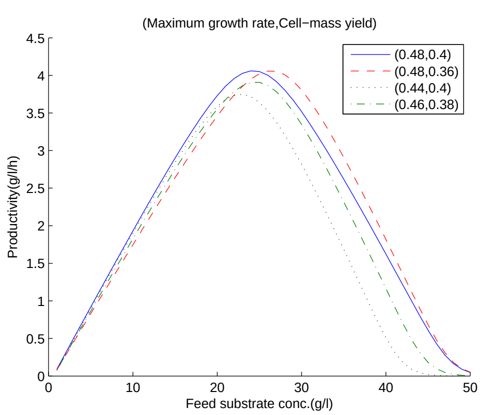

Fig. 2. Feed effect on optimal productivity

B. Open-loop characteristics

The response of Q to step changes in D and S_f are shown in Figs. 3 and 4 respectively. Though the plant behaves practically linearly for input D, to output P in the range $\pm 25\%$ as the response is symmetric (not plotted), the same behavior is not replicated when Q is to be regulated, which is a direct consequence of its nonaffine property. The inverse response seen can be explained by the change in sign of process gain.

In case of S_f as manipulated input, the responses for $\pm 25\%$ step changes are skewed, which highlights the presence of nonlinearity. However, if the signal changes within $\pm 10\%$, the productivity transients and steady states are comparable which makes it a good idea to keep the control actions in this range in order to guarantee faster convergence of NEPSAC.

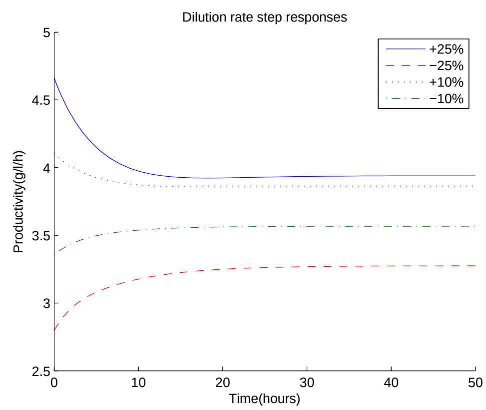

Fig. 3. Productivity response to dilution steps

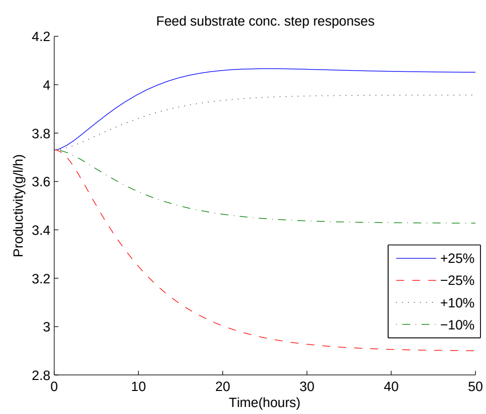

Fig. 4. Productivity response to feed steps

IV. NEPSAC STRATEGY

Among the diversity of control engineering principles available in the last few decades, model based predictive control strategy (MPC) has gained significant acceptability and industrial applicability [11][14]. MPC has clearly some useful characteristics to tackle nonlinear models: it is a multi-variable control strategy and it takes into account the system constraints a priori by using constrained optimization methods [19]. However, applying advanced control techniques is not straightforward and therefore, it must be first analyzed whether MPC is really necessary from the application point-of-view. Selection of a model gives an insight into the process which is further improved by the development of an on-line optimizing strategy using an appropriate control algorithm. Thus, advanced control requires a comprehensive approach, based primarily on a model.

The advantages of NEPSAC over other Nonlinear MPC (NMPC) strategies is its real-life applicability and underlying ease of implementation as it does not demand significant modification of the basic linear EPSAC concept which is computationally simple and fast, making it suitable for real-time online control. The shortcoming is that the convergence of the iterative approach and closed loop stability remain yet to be rigorously proven.

A. EPSAC

The process is modeled as [19]:

$$y(t) = x(t) + n(t) \tag{10}$$

with $y(t), x(t), n(t)$ as process output, model output, process/model disturbance respectively. The fundamental step is based on the prediction over the basic process model given by:

$$y(t+k|t) = x(t+k|t) + n(t+k|t) \tag{11}$$

where $y(t+k|t)$ is the prediction of process output at time instant t, over prediction horizon N_2, based on prior measurements and postulated values of inputs. Prediction of model output $x(t+k|t)$ and of colored noise process $n(t+k|t)$ can be obtained by the recursion of process model and filtering techniques respectively.

The future response can then be expressed as:

$$y(t+k|t) = y_{base}(t+k|t) + y_{optimize}(t+k|t) \tag{12}$$

The two contributing factors have the following origins:

- $y_{base}(t+k|t)$ is the cumulative effect of past control inputs $u(t-1), u(t-2)\ldots$, base future control scenario $u_{base}(t+k|t)$ which is defined a priori and predicted disturbances $n(t+k|t)$.
- $y_{optimize}(t+k|t)$ is the effect of optimizing future control actions $\delta u(t|t), \ldots \delta u(t+N_u-1|t)$ with $\delta u(t+k|t) = u(t+k|t) - u_{base}(t+k|t)$.

The design parameter N_u is the control horizon. Further, the colored noise can be modeled as:

$$n(t) = \frac{C(q^{-1})}{D(q^{-1})} e(t) \tag{13}$$

This disturbance model must be designed to achieve robustness of the control loop against unmeasured disturbances and modelling errors. These disturbances have a stochastic nature with non-zero bias. $e(t)$ is white noise, C and D are polynomials in backward shift operator q^{-1}.

The optimizing signal can be expressed as a discrete time convolution of impulse response coefficients $h_1, h_2, \ldots$ and step response coefficients $g_1, g_2, \ldots$ of the system as follows:

$$\begin{aligned} y_{optimize}(t+k|t) = \quad & h_k \delta u(t|t) + h_{k-1} \delta u(t+1|t) + \ldots \\ & + g_{k-N_u+1} \delta u(t+N_u-1|t) \end{aligned} \tag{14}$$

Using (13) and (14), the key EPSAC-MPC formulation becomes:

$$Y = \bar{Y} + GU \tag{15}$$

where $Y, \bar{Y}$ are the vector of outputs, base responses through N_2 respectively. U is the vector of future controls upto $N_u - 1$. G is a special matrix with impulse and step response coefficients with dimension upto $(N_2 - N_1 + 1) \times N_u$. The optimal control is then obtained by minimizing the following cost function:

$$\begin{aligned} V(U) = \quad & \Sigma_{k=N_1}^{N_2} [r(t+k|t) - y(t+k|t)]^2 \\ & + \lambda \Sigma_{k=0}^{N_u-1} [u(t+k|t)]^2 \end{aligned} \tag{16}$$

with λ being the control penalty and $r(t+k|t)$ the desired reference trajectory. N_1 is the process dead time. A closed form solution can be obtained for the unconstrained case to be:

$$U^* = [G^T G + \lambda I]^{-1} [G^T (R - \bar{Y})] \tag{17}$$

Only the first optimal control input is applied to the plant and the whole procedure is repeated at the next sampling instant $t+1$.

B. NEPSAC

When a nonlinear system $f[.]$ is used for $x(t)$, as the case in this paper, the above superposition is still valid only if the term $y_{optimize}(t+k|t)$ is small enough compared to $y_{base}(t+k|t)$, which is true if $\delta u(t+k|t)$ is small. This can in turn only happen if $u_{base}(t+k|t)$ is close to the optimal $u^*(t+k|t)$. Notice that, in the nonlinear case the step responses are different for each operating point, and hence unlike the linear controller, NEPSAC requires recomputation of the G matrix at every sampling instant. However, the exact values of the matrix are not critical, since the effect of G would gradually disappear.

This can be realized iteratively by going over the following steps for each sampling interval:

1) Initialize $u_{base}(t+k|t)$ to the previous optimal control sequence i.e. $u^*(t+k|t-1)$.
2) Compute $\delta u(t+k|t)$ using the linear EPSAC procedure.
3) Calculate corresponding $y_{optimize}(t+k|t)$ with (14) and compare it to $y_{base}(t+k|t)$
   - In case the difference is not small enough, redefine $u_{base}(t+k|t)$ as $u_{base}(t+k|t) + \delta u(t+k|t)$ and return to 2. The underlying concept is this optimal input can act as a 2^{nd} estimate for the nonlinear system.
   - In case the difference is within certain tolerance, $u(t) = u_{base}(t|t) + \delta u(t|t)$ is the optimal control for the current sampling instant.

The algorithm after convergence results in the optimal control for a given nonlinear system. The number of iterations required depends on how far the optimal control is from its prior value.

V. Closed loop simulations

As discussed in section II, μ_m and $Y_{x/s}$ are the parameter uncertainties for the process model, and the controller with feed substrate concentration S_f as manipulated input needs to be robust in rejecting these unmeasured variations and show good performance for setpoint regulation of optimal productivity Q, by measuring P.

Although linear feedback control strategy, such as PI control has been traditionally used for continuous bioreactors [21], Henson and Seborg [9] showed that the response of a conventional PI controller is sluggish with lower disturbance rejection capabilities and neglects the nonlinearities inherent in fermentation models, as compared to nonlinear control strategies. According to [22], linear PI controller results in wash out condition or switch over from initial lower input dilution rate to higher input dilution rate or vice versa. As such, PI controller with input multiplicities may give unstable, less economical or oscillatory responses. In contrast, with a model based NMPC strategy like NEPSAC, the optimization function can be formulated to be cost effective, and the optimal control can be computed taking into account the predictions of the output deviations caused by parameter uncertainty. This motivates us to design a robust NEPSAC controller, presented in section IV, for the control of bioreactor of sections II, III.

The only way to get robustness against nonlinear plant-model mismatch for NEPSAC is by the design of a suitable linear disturbance filter, in our case is of the form:

$$\frac{C(q^{-1})}{D(q^{-1})} = \frac{(1-\beta q^{-1})^{N_1}}{1-q^{-1}} \tag{18}$$

However, in the absence of any significant delay N_1 remains fixed to 1. The parameter β must be chosen inside the unit circle, its distance from the origin is roughly proportional to the aggression in the control action. In our case we keep it to null for faster response. The control penalty λ arguably has a similar effect of damping the response with increasing λ. This would be also held at null for better performance.

The sampling time has been chosen as $T_s = 1$ hour to cover the plant's transient dynamics. With these settings, two closed loop configurations would be investigated, the one with control horizon $N_u = 1$, prediction horizon $N_2 = 3$ called $rNEPSAC_1^3$ and the other with $N_u = 2, N_2 = 4$ hours called $rNEPSAC_2^4$. Our controller's performance is compared to the best among the existing controllers for the same process in literature, i.e. dynamic matrix control (DMC), NMPC1, NMPC2 of Silva and Kwong [20] and state-space, exact, approximate and modified input-output linearization of Henson and Seborg [9]. NMPC1 is based on orthogonal collocation on finite elements and NMPC2 on equidistant collocation; with parameters $N_u = 1, N_2 = 5$ for both [20].

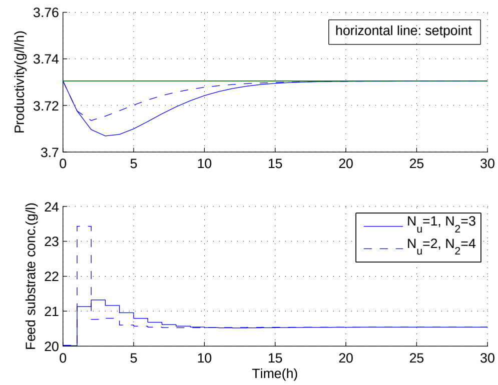

Fig. 5. Robust control against maximum growth rate = 0.46/h

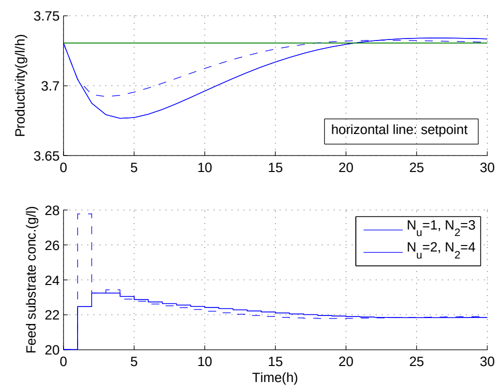

Fig. 6. Robust control against maximum growth rate = 0.44/h

A. *Uncertainty in maximum growth rate μ_m*

The case when plant parameter μ_m is perturbed to $0.46/h$ from its nominal modeled value of $0.48/h$ is demonstrated in Fig. 5. The productivity Q deviation from optimum is shorter for the $rNEPSAC_2^4$ controller, but the control effort is larger. Note that, the computation time, which though is not a factor here, rises marginally with the increase in N_u. In this scenario, the best performance was given by state-space linearization [9], and NEPSAC results are a close match to it. Further, the control effort of $rNEPSAC_2^4$ can be decreased by raising either β or λ.

An even bigger uncertainty would mean $\mu_m = 0.44/h$ and the results in this case produces an overshoot for the $rNEPSAC_1^3$ controller as shown in Fig. 6. The best performing controller in this class from literature is NMPC2 [20]. Comparatively, the $rNEPSAC_2^4$ controller achieves 50% reduction in settling time and $0.03g/l/h$ reduction in undershoot, with a marginal rise in control effort.

B. *Uncertainty in cell-mass yield $Y_{x/s}$*

Now, the mismatch is in $Y_{x/s}$, the actual process uses $0.38g/g$ whereas modeled value is $0.4g/g$. The deviation in the output is much smaller in case of $rNEPSAC_2^4$ controller than that of $rNEPSAC_1^3$ with almost the same control effort, refer Fig. 7. In fact, when raising the control horizon

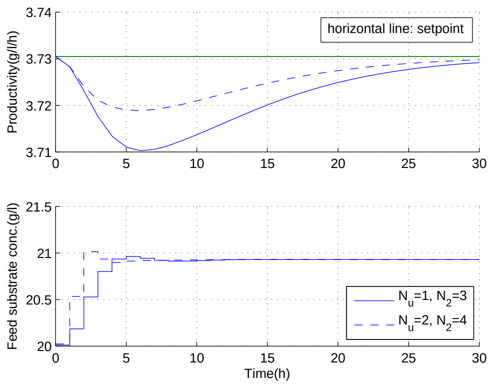

Fig. 7. Robust control when cell-mass yield = 0.38g/g

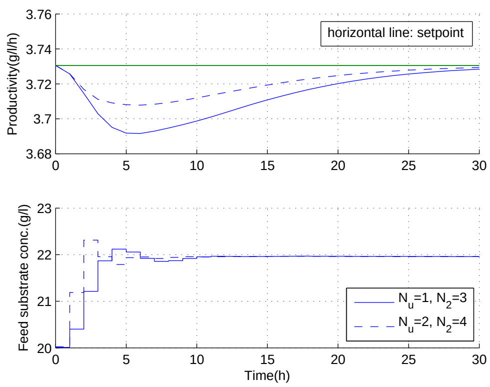

Fig. 8. Robust control when cell-mass yield = 0.36g/g

further or reducing the prediction horizon, the plant goes into the washout region, which is to be avoided. There is no data from literature available for a comparison, however the performance is in tune with the other scenarios presented before.

If there is even greater disturbance i.e. $Y_{x/s} = 0.36g/g$, it takes a bit more control effort to achieve similar response, for exactly the same horizon settings as the one before. The settling times for both the investigated controllers are the same. The best performer in this category was NMPC1 [20], which has an undershoot of $-0.06g/l/h$ and 40 hours settling time. The $rNEPSAC_2^4$ on the other hand has an undershoot of only $-0.02g/l/h$ and 30 hours settling time (Fig. 8), with very similar control effort, thus achieving a massive performance improvement.

Note that, the control horizon N_u has a strong effect on the convergence of the system towards its equilibrium point in this case. This is understandable, as a higher $N_u = 2$ increases the bandwidth of the closed loop, thus the controller reacts faster to limit the undershoot. However, a further increase in N_u introduces oscillations which drives the system into washout, and is thus not advised.

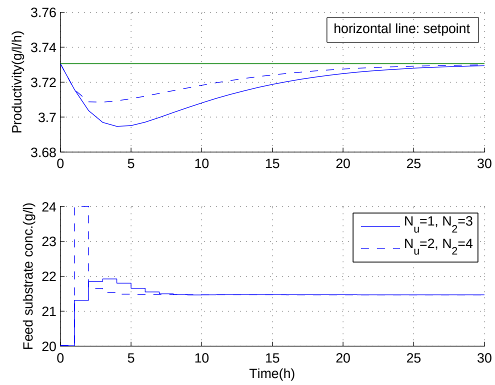

Fig. 9. Robust regulation when $\mu_m = 0.46/h$ and $Y_{x/s} = 0.38g/g$

C. *Uncertainty in both μ_m and $Y_{x/s}$*

In case there is a variation in both time varying parameters from their nominal values simultaneously to $\mu_m = 0.46/h, Y_{x/s} = 0.38g/g$, the robust performance of NMPC towards this realistic scenario is highlighted in Fig. 9. The $rNEPSAC_2^4$ controller exhibits lesser productivity loss but with higher effort, whereas $rNEPSAC_1^3$ controller has greater undershoot but uses less energy. It is worthwhile to mention here that although the results of this case study have not been reported in literature before and neither with NESPAC, the results obtained are in the same range as the other control strategies mentioned earlier, and is hence deemed satisfactory.

As mentioned before, the trajectories can be further shaped by manipulating β and/or λ, to achieve a desired trade-off between control effort and performance. In each case, the number of iterations within one sampling time before the control action converges to an arbitrary precision, is at a maximum of 10 in the beginning when we are away from the setpoint and takes just 1 step to converge near the setpoint.

D. *Control under uncertainty and additive measurement noise*

Until now, we analyzed the nonlinear control performance against various model parameter uncertainties. No measurement noise was considered in order to make a fair comparison with the other control mechanisms from literature who neither take into consideration any measurement noise.

However, in reality, we can expect some noise on the output originating from sensor or any other source of interference. Let us consider such a case where we have an additive noise over the measured product concentration P. Since P is regulated within deviation values of around ± 0.1, it is reasonable to consider a normally distributed random additive noise with standard deviation of 0.01 over true P value. It is trivial to see that this noise would directly manifest itself into the productivity through the relationship of (9).

In order to to demonstrate our control design with the considered additive measurement noise, we select one representative test case of subsection V-C with uncertainties in both μ_m and $Y_{x/s}$ amongst the three test-cases analyzed before.

As can be expected, in order to reduce the sensitivity

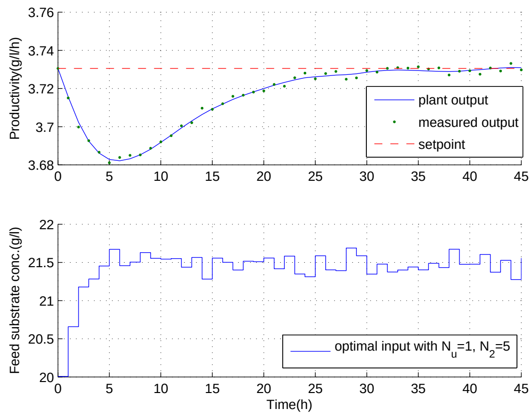

Fig. 10. Robust NEPSAC Control under uncertainty and additive measurement noise

towards noise, our control action has to be less aggressive which results in a slight increase in the prediction horizon to $N_2 = 5$. The control horizon is kept at $N_u = 1$ for the same reasons. All other control settings remain the same as before and hence, in our terminology, we call this the $rNEPSAC_1^5$ controller. Though we have a slight increase in the undershoot, which is $0.02g/l/h$ lower than the case with no measurement noise, the good news is that the settling time still remains low at $30h$, refer Fig. 10. The number of iterations for the convergence of optimal control input remains same as before.

VI. Conclusions

The open loop characteristics of a continuous fermenter demonstrates the presence of nonlinearities. The optimal productivity curves are shown to be highly sensitive towards time varying parameters. A robust nonlinear predictive control (NEPSAC) strategy has been successfully applied to this process with various parameter mismatches, and in majority of cases has been proven to perform better than the best of the existing controllers from literature. The presented control mechanism achieves fast regulation with marginal overshoot, is robust against uncertainty and measurement noise, uses less control energy, has flexibility in tuning and is easier to implement. These make it an ideal choice for bio-process control.

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