Approximate Robust Optimization of Time-Periodic Stationary States with Application to Biochemical Processes

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Abstract— In this paper we present techniques to optimize periodic stationary states of processes that depend on uncertain parameters. We start with an introduction to approximate robust counterpart formulations and specialize on systems with many uncertain parameters but only a small number of inequality constraints. The presented approximate robust programming formulation has an interesting application for stable time-periodic systems where the steady state is affected by uncertainties. In order to demonstrate this, we apply our techniques to a fermentation process optimal in a periodic operation. We discuss this optimal periodic solution and robustify it with respect to unknown model parameters.

Key words: Approximate Robust Optimization, Adjoint Differential Equations, Periodic Biochemical Processes

I. INTRODUCTION

Since decades robust optimal control problems have received much attention and they have been discussed by a variety of authors (e.g [4], [8], [9], [14], [20]). Many of these approaches take uncertainties of systems into account by constructing a robust counterpart. This robust counterpart methodology, mainly developed by Ben-Tal and Nemirovski [5], [6], [7] but also independently by El-Ghaoui et al. [12] has been applied for many systems in the context of convex optimization under the additional assumption that the uncertainty enters affine. But also for nonlinear systems we can find some approaches in the literature: in [10], [11], [16] techniques are proposed that optimize the robustness of nonlinear systems in a linear approximation.

In this paper we focus on systems where we have on the one hand a large number of uncertain parameters but on the other hand only a small number of inequality constraints that should robustly be satisfied. For this aim, we start in Section II with an introduction of the basic notation for robust counterpart formulations and also the idea of approximate robust optimization. Moreover, in Section III, we transfer this formulation and the ideas in [10] to uncertain stable periodic systems where a periodic stationary state has to be optimized. This periodic stationary state is in our consideration depending on both open-loop control inputs and unknown time constant parameters. Thus, we are interested in a robust optimization of the cyclic stationary state.

In Section IV we introduce the model of a biochemical fermentation process. We discuss optimal periodic operation modes for this model which can be realized by an application of a time-varying open-loop control input as the system turns out to be asymptotically stable. Here, the average productivity is maximized for a given average amount of substrate feed input. In Section V we show that this nominally optimal solution needs to be refined if the parameters are not exactly known. The optimal robustified solution for the periodic operation requires a significantly different control input in order to guarantee robustness with respect to the parameter uncertainties.

II. APPROXIMATE ROBUST OPTIMIZATION

Let us consider an uncertain nonlinear optimization problem of the form

\[
\begin{align*}
\min_{x \in \mathbb{R}^{n_x}, u \in \mathbb{R}^{n_u}} & \quad F_0(x, u) \\
\text{subject to} & \\
& \quad G(x, u, w) = 0 \quad (1) \\
& \quad F_i(x, u) \leq 0 \quad \text{for all } i \in \{1, \ldots, n\}
\end{align*}
\]

with continuously differentiable functions

\[
F_0, F_1, \ldots, F_n : \mathbb{R}^{n_x} \times \mathbb{R}^{n_u} \to \mathbb{R}
\]
depending on an optimization variable \(u \in \mathbb{R}^{n_u}\). Furthermore, we assume that the variable \(x\) is implicitly defined by the continuously differentiable equality constraint

\[
G : \mathbb{R}^{n_x} \times \mathbb{R}^{n_u} \times \mathbb{R}^{n_w} \to \mathbb{R}^{n_x},
\]

where the partial derivative function \(\frac{\partial G}{\partial x}\) is assumed to be regular on its domain. This requirement ensures that \(x\) can at least locally be eliminated from the optimization problem such that the components of \(u\) are the remaining degrees of freedom for the optimization.

In the following we regard the case that \(G\) does not only depend on \(x\) and \(u\) but also on an uncertain parameter \(w \in W \subseteq \mathbb{R}^{n_w}\) lying in an uncertainty set \(W\) which has ellipsoidal form

\[
W := \{ w \in \mathbb{R}^{n_w} \mid (w - \overline{w})^T \Sigma^{-1} (w - \overline{w}) \leq 1 \}.
\]

where \(\Sigma \in \mathbb{R}^{n_w \times n_w}\) is a positive definite scaling matrix and \(\overline{w} \in \mathbb{R}^{n_w}\) a constant. However, for the theoretical part of this paper, we will assume that we have \(\Sigma = 1\) and \(\overline{w} = 0\).
which can always be achieved by shifting and rescaling the uncertainty \( w \). Note that in our notation the functions \( F_0, F_1, \ldots \) are not allowed to explicitly depend on \( w \), which is however not a restriction as such a dependence can always be eliminated by a suitable definition of \( x \) and \( G \).

In order to incorporate the uncertainty into the optimization problem we follow the classical approach \([6], [7]\) and formulate the robust counterpart problem. I.e. we assume that whatever \( u \) the optimizer chooses, the adverse player “nature” chooses the worst possible value \( V(u) \) defined by \( V_i(u) := \max_{w,x} F_i(x, u, w) \) s.t. \( G(x, u, w) = 0 \) \( w \in W \). Our aim is now to solve the associated worst-case minimization problem

\[
\min_{u \in \mathbb{R}^{n_u}} V_0(u) \\
\text{subject to} \quad V_i(u) \leq 0 \quad \text{for all} \quad i \in \{1, \ldots, n\}.
\]

As this problem is, due to its bi-level structure, for general non convex large scale optimization problems extremely hard to solve it has e.g. in \([10], [13], [16]\) been suggested to replace the functions \( V_i(u) \) by approximations \( \tilde{V}_i(\pi, u) \) (for all \( i \in \{1, \ldots, n\} \)) which are obtained by a linearization technique. For this aim, the functions \( G \) and \( F_i \) are for all \( i \in \{1, \ldots, n\} \) linearized around a reference \( \pi \in \mathbb{R}^{n} \) satisfying \( G(\pi, u, 0) = 0 \).

Now the approximation \( \tilde{V}_i(\pi, u) \) is defined by

\[
\tilde{V}_i(\pi, u) := \max_{w, x} F_i(\pi, u) + \frac{\partial F_i(\pi, u)}{\partial x} x_i \left( \frac{\partial G(\pi, u, 0)}{\partial x} x_i + \frac{\partial G(\pi, u, 0)}{\partial w} w_i = 0 \right) w_i \leq 1 \nonumber \]

\[
= F_i(\pi, u) + \left| \frac{\partial F_i(\pi, u)}{\partial x} \left( \frac{\partial G}{\partial x} \right)^{-1} \frac{\partial G}{\partial w} \right|_2 \nonumber \]

where \( \cdot \) denotes the Euclidean norm. For the last transformation we have explicitly solved the linearized maximization problem. In \([10]\) several approaches have been presented on how to numerically deal with the appearance of the inverse \( \left( \frac{\partial G}{\partial w} \right)^{-1} \) and in \([6], [7]\) the above explicit solution is discussed under the more general assumption that \( W \) is an intersection of a finite number of ellipsoids.

However, in this paper we like to specialize on the computation of the derivatives in equation (5) for the case that \( n \) is small, i.e. we have only very few uncertain constraints while the number \( n_w \) of uncertain parameters might be very large. In this case it is advisable to use automatic differentiation in the adjoint mode to evaluate the margin terms of the form

\[
\left| \frac{\partial F_i(\pi, u)}{\partial x} \left( \frac{\partial G}{\partial x} \right)^{-1} \frac{\partial G}{\partial w} \right|_2 = \left| \frac{\partial F_i(\pi, u)}{\partial w} \right|_2 \frac{\partial G}{\partial w} \quad (\text{for} \quad i \in \{0, \ldots, n\})\nonumber \]

(7)

Summarying \( \mu := (\mu_0, \ldots, \mu_n) \in \mathbb{R}^{n_u} \times (n+1) \) we can formulate the approximate robust counterpart problem in the form

\[
\min_{\pi, u, \mu} F_0(\pi, u) + \left| \frac{\partial G}{\partial w} \right|_2 \text{ s.t.} \quad G(\pi, u, 0) = 0 \nonumber \]

\[
F_i(\pi, u) + \left| \frac{\partial F_i(\pi, u)}{\partial w} \right|_2 \leq 0 \quad \text{f. a.} \quad i \in \{1, \ldots, n\} \nonumber \]

\[
\mu_i^T \frac{\partial G}{\partial w} \left| \frac{\partial F}{\partial x} \right|_2 = 0 \quad (8)\nonumber \]

In this general form, the above nonlinear optimization problem can be interpreted as a nonlinear Second Order Conic Program (SOCP). However, we should be aware of the fact that e.g. \( \frac{\partial G}{\partial w} \) is vanishing in the optimal solution, our approximation is obviously too optimistic as higher order terms might dominate the linear approximation even for small uncertainties - this is a known general drawback of linear approximation techniques. On the other hand, if the terms of the form \( \mu_i^T \frac{\partial G}{\partial w} \) are for all \( i \in \{0, \ldots, n\} \) not equal to zero we can at least guarantee that the approximation is valid for sufficiently small uncertainty sets \( W \). In this case the norms in the above formulation are also differentiable in a neighborhood of the optimal solution.

\section{Robustified Optimal Control for Periodic Processes}

In this section we apply the considerations from the previous section for the case that we like to optimize the stationary state of a stable time periodic dynamic system. Let \( y: \mathbb{R} \rightarrow \mathbb{R}^{n_y} \) be the differential state of the system

\[
\forall t \in [0, \infty) : \quad \dot{y}(t) = g(y(t), v(t), w) \nonumber \]

\[
y(0) = y_0 \quad (9)\nonumber \]

where \( v: \mathbb{R} \rightarrow \mathbb{R}^{n_u} \) is a time dependent but periodic control input satisfying \( v(t) = v(t + T) \) for a cycle duration \( T > 0 \) and \( w \in \mathbb{R}^{n_w} \) a time-constant but unknown parameter.

Now we assume that we have the additional knowledge about the system that the state \( y \) converges (independent of the initialization \( y_0 \)) for \( t \rightarrow \infty \) to a time-periodic limit cycle \( z: \mathbb{R} \rightarrow \mathbb{R}^{n_y} \) satisfying

\[
\forall t \in [0, T] : \quad \dot{z}(t) = g(z(t), v(t), w) \nonumber \]

\[
z(0) = z(T) \quad (10)\nonumber \]

We are now interested in the behavior of this limit cycle in dependence on the periodic open-loop control input \( v \) but also on the uncertain parameter \( w \).
In order to transfer the ideas from the previous section, we consider an uncertain periodic optimal control problem of the following form:

\[
\begin{align*}
\text{minimize} & \quad f_0(z(T)) \\
\text{subject to:} & \\
& \forall t \in [0, T]: \quad \dot{z}(t) = g(z(t), v(t), w) \\
& \forall i \in \{1, \ldots, n\}: \quad 0 \geq f_i(z(T)) \\
& z(0) = z(T)
\end{align*}
\] (11)

To discretize this problem we replace the function \( v \) by a piecewise constant approximation

\[
\tilde{v}(t) := \sum_{i=0}^{N-1} u_i I_{[i, i+1]}(t),
\]

where \( I_{[a, b]}(t) \) is equal to 1 if \( t \in [a, b] \) and equal to 0 otherwise. The time sequence \( 0 = t_0 < t_1 < \ldots < t_N = T \) can e.g. be equidistant. In the following we summarize

\[
u := (u_0, \ldots, u_{N-1})^T
\]
to achieve a convenient notation.

In the next step, we regard \( z(T) = Z(u, w, x) \) as a function depending on the control input \( u \), the uncertain parameter \( w \), as well as the initial value \( z(0) = x \). In other words, \( Z \) is the solution operator of the differential equation, which can numerically be evaluated by using an integrator.

As we have \( x = z(0) = z(T) \) we define \( F_i(x) := f_i(z(T)) \) for all \( i \in \{0, \ldots, n\} \). Finally, the periodic boundary condition can be written as

\[
G(x, u, w) := Z(u, w, x) - x = 0.
\] (12)

Obviously, the functions \( F_0, \ldots, F_n \) and \( G \) are now defined in such a way that the discretized version of the problem (11) takes the form (1). Thus, also the associated robust counterpart formulation (8) transfers immediately.

Note that for the computation of the terms \( \mu^T \frac{\partial G}{\partial x} \) and \( \mu^T \frac{\partial G}{\partial w} \), automatic differentiation in backward mode can be used:

\[
\mu^T \left( \frac{\partial G}{\partial x}, \frac{\partial G}{\partial w} \right) = \mu^T \frac{\partial Z}{\partial (x, w)} (u, w, x) - \mu^T (1, 0)
\] (13)

For the numerical evaluation of this expression we can use an integrator which is able to store intermediate values during the forward evaluation of \( Z \) such that the associated adjoint variational equation can later be solved by a backward run. However, for the details of adjoint differentiation for differential equations we refer the reader to [3].

IV. PERIODIC OPTIMAL CONTROL OF A BIOCHEMICAL PROCESS

In this section we apply the approximate robust formulation of periodic optimal control problems to a biochemical process. More precisely, we consider the following model of continuous culture fermentation which is often used in the literature [2], [15], [17], [19]:

\[
\begin{align*}
\dot{X}(t) &= -DX(t) + \mu(t)X(t) \\
\dot{S}(t) &= D(S(t) - S(t)) - \frac{\mu(t)X(t)}{Y_{X/S}} \\
\dot{P}(t) &= -DP + (\alpha \mu(t) + \beta)X(t)
\end{align*}
\] (14)

This model consists of 3 states: here, \( X \) denotes the biomass concentration, \( S \) the substrate concentration, and \( P \) the product concentration of a continuous fermentation process. Furthermore, the process can be controlled by the input \( S_T : \mathbb{R} \to \mathbb{R} \) representing the feed substrate concentration. While the dilution rate \( D \), the biomass yield \( Y_{X/S} \), and the product yield parameters \( \alpha \) and \( \beta \) are assumed to be constant and thus independent of the actual operating condition, the specific growth rate \( \mu : \mathbb{R} \to \mathbb{R} \) of the biomass is a function of the states:

\[
\mu(t) = \mu_m \left( 1 - \frac{P_i(t)}{P_m} \right) S(t) K_m + S(t) + \frac{(S(t))^2}{K_i}
\] (15)

This specific growth rate equation is constructed to allow a description of both the product and the substrate inhibition. For the product an associated saturation constant \( P_m \) has been introduced while \( K_m \) denotes a saturation constant associated with the substrate. The constant \( K_i \) is the substrate inhibition constant and \( \mu_m \) can be interpreted as the maximum specific growth rate.

In the next step we consider the following optimal control task for our fermentation model: our aim is to maximize the average productivity

\[
Q := \frac{1}{T} \int_{0}^{T} DP(\tau) d\tau
\]

for a given amount of substrate \( S_T \). It has already been suggested in [17], [19] that this aim can efficiently be achieved by operating the system in a periodic mode. The corresponding optimal control problem takes the form

\[
\begin{align*}
\min_{z(\cdot), S_T(\cdot)} & \quad \frac{1}{T} \int_{0}^{T} DP(\tau) d\tau \\
\text{subject to:} & \\
& \forall t \in [0, T]: \quad \dot{z}(t) = g(z(t), S_T(t), w) \\
& \frac{1}{T} \int_{0}^{T} S_T(\tau) d\tau = S_T \\
& z(0) = z(T) \\
& X(0) = 0 \\
& \forall t \in [0, T]: \quad S_T^\min(t) \leq S_T(t) \leq S_T^\max \\
& \frac{1}{T} \int_{0}^{T} X(\tau) d\tau \leq X^\max
\end{align*}
\] (16)

Here, we have summarized the states into one differential state vector \( z : \mathbb{R} \to \mathbb{R}^3 \) given by

\[
z := (X, S, P)^T
\]
Fig. 1. A locally optimal result for the three states of the optimal control problem (16).
while the corresponding right-hand side of the differential equation (14) has been denoted by $g$. Moreover, the parameters are summarized in a vector $w \in \mathbb{R}^8$ given by

$$w := \left(D, K_i, K_m, P_m, Y_{x/p}, \alpha, \beta, \mu_m\right)^T,$$

while the corresponding nominal values for $w$, which are used in this section, are listed in Table I.

Note that the optimization problem (16) additionally regards a maximum and a minimum bound ($S_{f_{\text{min}}}$ and $S_{f_{\text{max}}}$) on the input $S_f$ as well as a constraint on the maximum average of the biomass concentration $X := \frac{1}{T} \int_0^T X(\tau) d\tau$ over one periodic cycle. Moreover, the equation $\frac{d}{d\tau} X(0) = 0$ has been introduced to remove the indefiniteness with regard to phase shifts. For the numerical solution of the periodic optimal control problem (16) we use the single shooting method with a piecewise constant parameterization (here 30 pieces) of the control input in combination with an Sequential Quadratic Programming (SQP) algorithm which has been implemented in the automatic control and dynamic optimization software ACADO [1]. A corresponding locally optimal solution is shown in Figure 1.

It can be seen that the optimal result shows indeed a periodic behavior. In this example the time horizon was fixed to $T = 48$ h. The result for the objective in the optimal solution, which is shown in Figure 1, is given by

$$\frac{1}{T} \int_0^T DP(\tau) d\tau = 3.11 \frac{g}{L \cdot h}.$$  \hspace{1cm} (18)

This value for the objective is clearly larger than the average productivity of $3.00 \frac{g}{L \cdot h}$ which would be obtained in a time-constant steady state operation mode.

Moreover, the periodic process is open-loop stable as the spectral radius $\rho$ of the monodromy matrix associated with the periodic process is $\rho \approx 0.003 < 1$ in the optimal solution. I.e. it is possible to start the fermentation process close to the shown periodic solution applying the optimal control $S_f(t)$ blindly without needing any feedback. This is not surprising as this is clearly what we would expect from such a process - independent of the specific control. Finally, we observe that the inequality constraint on the average biomass concentration

$$\frac{1}{T} \int_0^T DX(\tau) d\tau = 5.73 \frac{g}{L} \leq 5.8 \frac{g}{L}$$  \hspace{1cm} (19)

is not active in the optimal solution. In contrast to that, the inequality constraints for the input are almost all active: the optimal solution for $S_f$ shows partially a bang-bang structure.

In the first phase, where the feed substrate is close or equal to the upper bound, we observe a substrate accumulation while the biomass concentration as well as the product concentration decrease. In the second phase, where the lower

<table>
<thead>
<tr>
<th>Name</th>
<th>Symbol</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>dilution rate</td>
<td>$D$</td>
<td>0.15 h(^{-1})</td>
</tr>
<tr>
<td>substrate inhibition constant</td>
<td>$K_i$</td>
<td>22 (\mu g/L)</td>
</tr>
<tr>
<td>substrate saturation constant</td>
<td>$K_m$</td>
<td>1.2 (g/L)</td>
</tr>
<tr>
<td>product saturation constant</td>
<td>$P_m$</td>
<td>50 (\mu g/L)</td>
</tr>
<tr>
<td>yield of the biomass</td>
<td>$Y_{x/s}$</td>
<td>0.4</td>
</tr>
<tr>
<td>first product yield constant</td>
<td>$\alpha$</td>
<td>2.2</td>
</tr>
<tr>
<td>second product yield constant</td>
<td>$\beta$</td>
<td>0.2 h(^{-1})</td>
</tr>
<tr>
<td>specific growth rate scale</td>
<td>$\mu_m$</td>
<td>0.48h(^{-1})</td>
</tr>
<tr>
<td>average feed substrate</td>
<td>$\bar{S}_f$</td>
<td>32.9 (\mu g/L)</td>
</tr>
<tr>
<td>minimum feed substrate</td>
<td>$S_{f_{\text{min}}}$</td>
<td>28.7 (\mu g/L)</td>
</tr>
<tr>
<td>maximum feed substrate</td>
<td>$S_{f_{\text{max}}}$</td>
<td>40.0 (\mu g/L)</td>
</tr>
<tr>
<td>maximum average biomass concentration</td>
<td>$\bar{X}_{\text{max}}$</td>
<td>5.8 (\mu g/L)</td>
</tr>
</tbody>
</table>
bound for the input is active, a growth of the biomass and, with a small delay, a growth of the product concentration can be seen.

V. ROBUST OPTIMIZATION OF A BIOCHEMICAL PROCESS

In the next step we are interested in the question what happens if the eight parameters stacked in the vector $w$ are not exactly known but bounded by an ellipsoidal set $W$ given by equation 2. Here, we choose a diagonal scaling matrix $\Sigma \in \mathbb{R}^{8 \times 8}$, whose diagonal elements are given as:

$$\Sigma_{ii} := \left( \frac{1}{20} w_i \right)^2$$

(20)
i.e. we regard 5\% of uncertainty for each parameter. For the nominal parameter $w \in \mathbb{R}^8$ we use the values from Table I.

Now, we can solve the robustified optimal control problem of the form (8) which is associated with the periodic optimal control problem (16) from the previous section. Note that only one inequality constraint as well as the objective needs to be robustified in this example as the inequality bounds on the control input $S_f$ are not affected by the uncertainty. As we have eight uncertain parameters we are exactly in the situation where the formulation (8) using the adjoint mode of automatic differentiation is beneficial.

We use again the ACADO toolkit [1] to solve the robustified problem. For the integration an explicit Runge-Kutta integrator of order 7 (with step-size control of order 8) has been used to discretize the dynamic system. This integrator coming with ACADO toolkit is also suitable to compute first and second order derivatives in forward and backward mode with high accuracies. The corresponding numerical optimization results for the robustified problem are shown in Figure 2. In comparison to the nominal results, the biomass concentration $X$ is, due to the robustified constraint, lower but shows still some cyclic behaviour. The substrate concentration $S$ as well as the product concentration $P$ have in the robust solution a smaller amplitude. Finally, for $S_f$ there are no active constraints anymore, but the solution shows still phases of accumulation.

The price that needs to be paid for the robustification can be discussed by an evaluation of the nominal average productivity in the optimal robustified solution:

$$Q^* \approx \frac{1}{T} \int_0^T DP(\tau) \, d\tau = 2.98 \frac{g}{L \cdot h}.$$  (21)

Comparing this result with the nominal result from equation (18) we find that we need to pay approximately 4 – 5\% of productivity if we regard the nominal amounts. Finally, we write the result for the robustified objective in the form

$$Q \approx (2.98 \pm 0.19) \frac{g}{L \cdot h},$$

(22)

where the size of the worst case interval is given by the linear approximation $\| \frac{dQ}{dw} \Sigma \|_2 \approx 0.19 \frac{g}{L \cdot h}$.

The main reason for the fact that the robustified optimal solution is, compared with the results from the previous section, significantly different, is that we have to keep a certain security distance with respect to the inequality constraint if the parameters are uncertain. Indeed, the inequality constraint of the form

$$X + \left\| \frac{dX}{dw} \Sigma \right\|_2 \leq 5.8 \frac{g}{L}$$

(23)

was active in our example.

Finally, we note that in this small example the computation
times are not critical: with the adjoint sensitivity generation the computations took approximately 2.0 ms per SQP iteration, if we use a modern Desktop PC (Intel Pentium, 1.5GHz). In most situations, between 3 and 10 SQP iterations were necessary until an accuracy in the order of $10^{-6}$ is achieved depending on how close the initialization of the algorithm is to the optimal solution. Just to check that the adjoint mode is not only from a theoretical point of view advisable in our example we have also computed the sensitivities by using the forward mode of automatic differentiation, of course obtaining the same solution, but with the forward mode we need approximately 6.8 ms per SQP iteration. The reason for this difference in the computation times is that $n_w = 8$ forward directions need to be computed in contrast to only $n + 1 = 2$ backward directions that were needed for an evaluation of the model using the adjoint formulation. In any case, these computation times for our small example show that the method has a large potential to be scaled up for larger dynamic systems that are, e.g., arising in the field of chemical and biochemical engineering, which will be the subject of further studies.

VI. CONCLUSIONS AND OUTLOOK

In this paper we have presented approximate robust optimization strategies with a main focus on periodic optimal control problems with a large number of uncertain parameters. One of the main ideas in this paper was to apply this approximate robust counterpart formulation to optimize the periodic stationary state (or limit cycle) of a dynamic system. We have formulated a corresponding periodic optimal control problem and its approximate counterpart formulation which can efficiently be solved by making use of adjoint automatic differentiation techniques. Finally, we have applied our results to a biochemical fermentation process which is optimally operated in a periodic mode. Comparing the results for the nominal and the robustified optimal control problem we have found that significantly different control inputs are suitable depending on whether the parameters are known or uncertain.

In the future, we will scale up the method for larger systems that arise in the context of chemical or biochemical processes. The results presented here, with their promising computation times, give us the chance to treat much larger systems than discussed in this paper. Furthermore, we have not yet completely used the fact that the considered system is stable. In [18] Newton Picard inexact SQP methods are presented that can be suitable for the robust optimization of stable periodic systems of the kind discussed in this paper.

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