TECHNICAL REPORT

DOTcvpSB: application to biochemical engineering problems

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CHAPTER 1

Biochemical engineering problems

1.1 LEE-RAMIREZ BIOREACTOR

DOTcvp: cdop_LeeRamirezBioreactor.m

Considering a bioreactor, which was first solved in [7] and later slightly modified in [9]. The objective is to maximize the profitability of the process using the nutrient u_1 and the inducer feeding rates u_2. Different scenarios with the various value of Q are considered.

The mathematical formulation of the problem is as follow: find the control trajectories that maximize the cost function at the final time

$$\max_{u_i} J_0 = x_1(t_F)x_4(t_F) - Q\int_{t_o}^{t_F} (u_2)\,\mathrm{d}t \tag{1.1}$$

subject to

$$\dot{x_1} = u_1 + u_2 \tag{1.2}$$

$$\dot{x_2} = g_1 x_2 - \frac{u_1+u_2}{x_1}x_2 \tag{1.3}$$

$$\dot{x_3} = \frac{100u_1}{x_1} - \frac{u_1+u_2}{x_1}x_3 - \frac{g_1}{0.51}x_2 \tag{1.4}$$

$$\dot{x_4} = R_{fp}x_2 - \frac{u_1+u_2}{x_1}x_4 \tag{1.5}$$

$$\dot{x_5} = \frac{4u_2}{x_1} - \frac{u_1+u_2}{x_1}x_5 \tag{1.6}$$

$$\dot{x_6} = -k_1 x_6 \tag{1.7}$$

$$\dot{x_7} = k_2(1 - x_7) \tag{1.8}$$

where

$$g_1 = \left(\frac{x_3}{14.35 + x_3(1 + x_3/111.5)}\right)\left(x_6 + \frac{0.22x_7}{0.22 + x_5}\right) \tag{1.9}$$

$$R_{fp} = \left(\frac{0.233x_3}{14.35 + x_3(1 + x_3/111.5)}\right)\left(\frac{0.0005 + x_5}{0.022 + x_5}\right) \tag{1.10}$$

$$k_1 = k_2 = \frac{0.09x_5}{0.034 + x_5} \tag{1.11}$$

The scenario with $Q = 0$ and 2.5 is considered. The final time is specified as 10 h and the vector process and decision initial conditions as $x(0) = [1; 0.1; 40; 0; 0; 1; 0; 0]$ and $u_{1,2}(0) = [0.5; 0.5]$, respectively. The additional constrains on the decision variables are the following: $u_{1,2} \in [0; 1]$

```
Final results [single-optimization; Q=0.0]:
 ............ Problem name: Lee-RamirezBioreactor
 ...... NLP or MINLP solver: FMINCON
 . Number of time intervals: 25
 ... IVP relative tolerance: 1.000000e-007
 ... IVP absolute tolerance: 1.000000e-007
 . Sens. absolute tolerance: 1.000000e-007
 ........... NLP tolerance: 1.000000e-005
 ....... Final state values: 4.182486e+000 6.413670e+000 3.893872e+001 1.470736e+000 1.367472e+000 7.134128e-001 2.865872e-001 1.429858e+000
 ...... 1th optimal control: ...
 ...... 2th optimal control: ...

 ........... Final CPUtime: ... seconds
 . Cost function [max(J_0)]: 6.15123355
```

```
Final results [single-optimization; Q=2.5]:
 ............ Problem name: Lee-RamirezBioreactor
 ...... NLP or MINLP solver: FMINCON
 . Number of time intervals: 25
 ... IVP relative tolerance: 1.000000e-007
 ... IVP absolute tolerance: 1.000000e-007
 . Sens. absolute tolerance: 1.000000e-007
 ........... NLP tolerance: 1.000000e-005
 ....... Final state values: 1.910086e+000 1.479996e+001 3.497523e+001 3.131412e+000 1.878273e-001 7.134005e-001 2.865995e-001 8.969161e-002
 ...... 1th optimal control: ...
 ...... 2th optimal control: ...

 ........... Final CPUtime: ... seconds
 . Cost function [max(J_0)]: 5.75694021
```

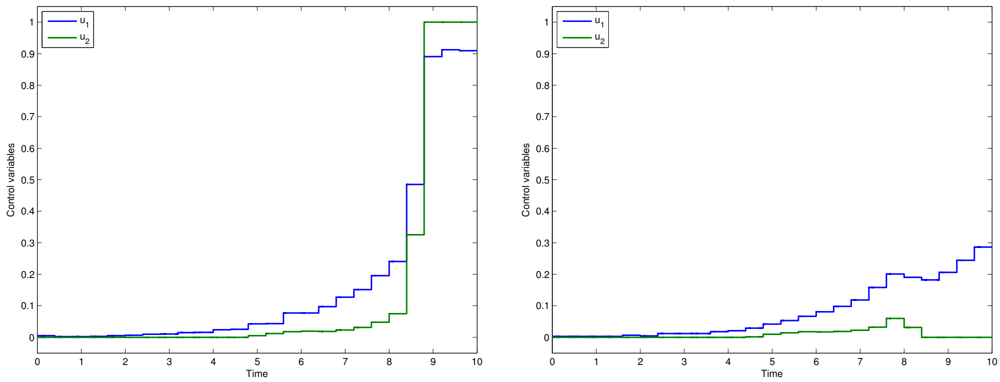

Figure 1.1 – Optimal control trajectories for the Lee-Ramirez bioreactor, left for $Q = 0$ and right for $Q = 2.5$ case.

1.2 OPTIMAL PRODUCTION OF PROTEIN IN THE FED-BATCH REACTOR

DOTcvp: cdop_OptimalProductionOfSecretedProtein.m

Consider a fed-batch reactor where the goal of the optimization is to achieve the maximum amount of the secreted protein at the end of the batch time. This optimal control problem has been studied by many authors [1; 8; 4]. The cost function is defined as follows

$$\max_{u_i} J_0 = x_1(t_F)x_5(t_F) \tag{1.12}$$

where x_1 is the concentration of the protein (L^{-1}) and x_5 is the culture volume (L) at the final time $t_F = 15\,\mathrm{h}$. The optimal control problem is solved subject to

$$\dot{x_1} = g_1(x_2 - x_1) - \frac{u}{x_5}x_1 \tag{1.13}$$

$$\dot{x_2} = g_2x_3 - \frac{u}{x_5}x_2 \tag{1.14}$$

$$\dot{x_3} = g_3x_3 - \frac{u}{x_5}x_3 \tag{1.15}$$

$$\dot{x_4} = -7.3g_3x_3 + \frac{u}{x_5}(20 - x_4) \tag{1.16}$$

$$\dot{x_5} = u \tag{1.17}$$

where

$$g_1 = \frac{4.75g_3}{0.12 + g_3} \tag{1.18}$$

$$g_2 = \frac{x_4 e^{-5x_4}}{0.1 + x_4} \tag{1.19}$$

$$g_3 = \frac{21.87x_4}{(x_4 + 0.4)(x_4 + 62.5)} \tag{1.20}$$

with the vector of a process initial conditions: $x(0) = [0; 0; 1; 5; 1]$ and the initial control trajectory: $u(0) = [0.5]$. The value of u is the feed flow rate $(\mathrm{L\,h^{-1}})$, x_2 is the concentration of the total protein $(\mathrm{L^{-1}})$, x_3, and x_4 are the glucose and the substrate concentration $(\mathrm{g\,L^{-1}})$. The lower and upper bounds on the decision variables are defined as follows: $u \in [0; 2]$.

```
Final results [single-optimization]:
 ............ Problem name: OptimalProductionOfSecretedProtein
 ...... NLP or MINLP solver: FMINCON
 . Number of time intervals: 15
 ... IVP relative tolerance: 1.000000e-007
 ... IVP absolute tolerance: 1.000000e-007
 . Sens. absolute tolerance: 1.000000e-007
 ........... NLP tolerance: 1.000000e-005
 ....... Final state values: 2.347980e+000 2.699309e+000 2.643206e+000 1.445502e-001 1.374892e+001
 ...... 1th optimal control: ...

 ........... Final CPUtime: ... seconds
 . Cost function [max(J_0)]: 32.28218810
```

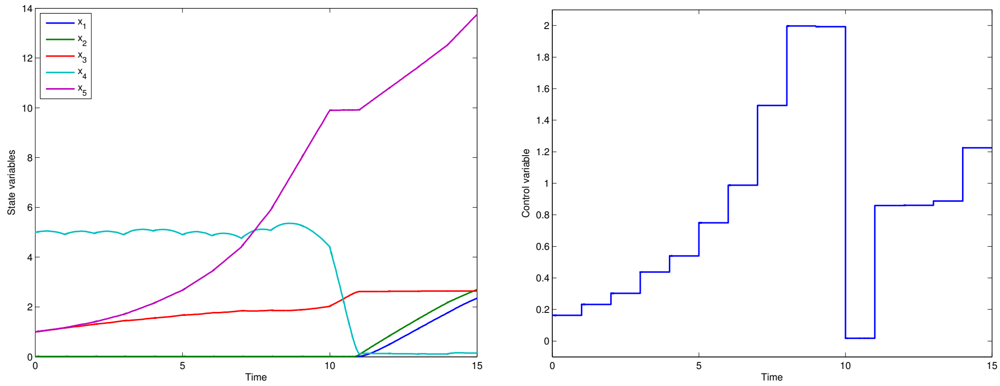

Figure 1.2 – Optimal state trajectories (left) and the control profile (right) for the fed-batch reactor.

1.3 FED-BATCH FERMENTER FOR PENICILLIN PRODUCTION

DOTcvp: cdop_FedBatchFermenterForPenicillinProduction.m

The problem of the feed batch fermenter for the penicillin production has been solved e.g. in [6; 3]. The scenario with fixed final time is considered. The aim is to maximize until the final time ($t_F = 132$) the cost function of the form

$$\max_{u_i} J_0 = x_2(t_F)x_4(t_F) \tag{1.21}$$

subject to

$$\dot{x}_1 = g_1 x_1 - u\left(\frac{x_1}{500x_4}\right) \tag{1.22}$$

$$\dot{x}_2 = g_2 x_1 - 0.01x_2 - u\left(\frac{x_2}{500x_4}\right) \tag{1.23}$$

$$\dot{x}_3 = -\left(\frac{g_1 x_1}{0.47}\right) - \frac{g_2 x_2}{1.2} - x_1\left(\frac{0.029x_3}{0.0001 + x_3}\right) + \frac{u}{x_4}\left(1 - \frac{x_3}{500}\right) \tag{1.24}$$

$$\dot{x}_4 = \frac{u}{500} \tag{1.25}$$

where

$$g_1 = 0.11 \left(\frac{x_3}{0.006x_1 + x_3} \right) \tag{1.26}$$

$$g_2 = 0.0055 \left(\frac{x_3}{0.0001 + x_3(1 + 10x_3)} \right) \tag{1.27}$$

with the vector of process and control initial conditions: $x(0) = [1.5; 0; 0; 7]$, $u(0) = [11.25]$. The values of the biomass, penicillin, substrate concentration (g/L), and volume (L) are marked as x_1, x_2, x_3, and x_4, respectively.

There are defined several path constraints

$$0 \leq x_1 \leq 40 \tag{1.28}$$

$$0 \leq x_2 \leq 25 \tag{1.29}$$

$$0 \leq x_3 \leq 10 \tag{1.30}$$

with bounds on the decision variables (feed rate of the substrate) $u \in [0; 50]$.

```
Final results [single-optimization]:
 ............. Problem name: FedBatchFermenterForPenicillinProduction
 ...... NLP or MINLP solver: FMINCON
 . Number of time intervals: 10
 ... IVP relative tolerance: 1.000000e-006
 ... IVP absolute tolerance: 1.000000e-006
 . Sens. absolute tolerance: 1.000000e-006
 ............ NLP tolerance: 1.000000e-004
 ....... Final state values: 2.802555e+001 8.796238e+000 1.511141e-003 1.000434e+001
 ...... 1th optimal control: ...

 ............ Final CPUtime: ... seconds
 . Cost function [max(J_0)]: 88.00031256
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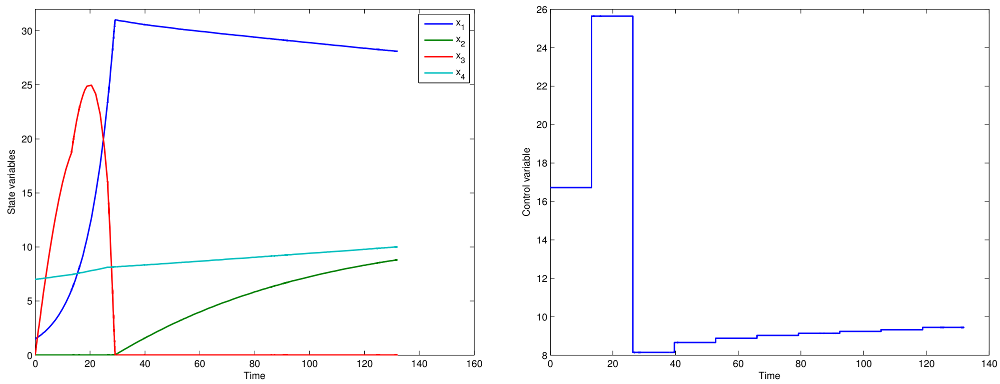

Figure 1.3 – Optimal state trajectories (left) and the control profile (right) for the fed-batch fermenter for penicillin production.

1.4 FED-BATCH REACTOR FOR ETHANOL PRODUCTION

DOTcvp: cdop_FedBatchReactorForEthanolProduction.m

The problem of the fed-batch reactor which was initially solved by [5] with final time $t_F = 54$ was considered. This problem was later solved in e.g. [2] and it consists of the finding of the optimal control policy over the whole time $t \in [t_0; t_F]$ that maximizes

$$\max_{u_i} J_0 = x_3(t_F)x_4(t_F) \tag{1.31}$$

subject to

$$\dot{x}_1 = g_1 x_1 - u\left(\frac{x_1}{x_4}\right) \quad (1.32)$$

$$\dot{x}_2 = -10 g_1 x_1 + u\left(\frac{150 - x_2}{x_4}\right) \quad (1.33)$$

$$\dot{x}_3 = g_2 x_1 - u\left(\frac{x_3}{x_4}\right) \quad (1.34)$$

$$\dot{x}_4 = u \quad (1.35)$$

where

$$g_1 = \left(\frac{0.408}{1 + x_3/16}\right)\left(\frac{x_2}{0.22 + x_2}\right) \quad (1.36)$$

$$g_2 = \left(\frac{1}{1 + x_3/71.5}\right)\left(\frac{x_2}{0.44 + x_2}\right) \quad (1.37)$$

The state values x_1, x_2, x_3, and x_4 are the cell mass, the substrate, the ethanol concentration (g/L), and the volume (L), respectively. The initial conditions for the process and decision variables were initially set at the value of: $x(0) = [1; 150; 0; 10]$ and $u(0) = [6]$. The lower and upper bound of the decision variables (feed rate) was defined as follows: $u \in [0; 12]$. The volume of the container (x_4) is bound with the equation as follows

$$0 \leq x_4(t) \leq 200 \quad (1.38)$$

```
Final results [single-optimization]:
 ............. Problem name: FedBatchReactorForEthanolProduction
 ...... NLP or MINLP solver: FMINCON
 . Number of time intervals: 25
 ... IVP relative tolerance: 1.000000e-007
 ... IVP absolute tolerance: 1.000000e-007
 . Sens. absolute tolerance: 1.000000e-007
 ........... NLP tolerance: 1.000000e-005
 ....... Final state values: 1.504808e+001 1.916873e-002 1.021811e+002 2.000084e+002
 ...... 1th optimal control: ...
______________
 ........... Final CPUtime: ... seconds
 . Cost function [max(J_0)]: 20437.07128407
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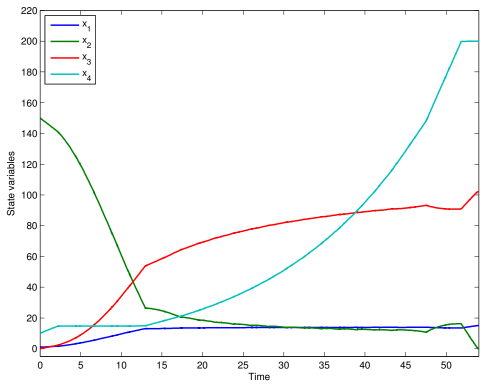

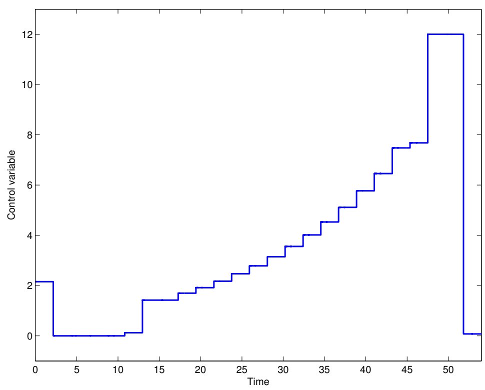

Figure 1.4 – Optimal state trajectories (left) and the control profile (right) for the fed-batch reactor for ethanol production.

Bibliography

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