Optimization of a Fed-Batch Bioreactor

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Introduction and Objective

Fed-Batch Bioreactor: A bioreactor where substrates are continuously added over time, while the culture medium is not removed. This method allows for more control over microbial growth and product formation..
Applications: Used in pharma, biofuels, and fermentation processes.

Objective: Maximize the final concentration of product P at a given time tf .

$$\max_{u(t)} \quad J = P(t_f)$$

Manipulated Variable: The feed rate of substrate u, which influences both the substrate concentration S and biomass concentration X.
Constraints:
▶ Input bounds on feed rate: $u_{min} \leq u \leq u_{max}$.
▶ Biomass concentration constraint: X(t) ≤ Xmax to avoid oxygen depletion.

Reactions and Conditions

Reactions:
▶ Substrate S is converted into Biomass X and Product P:

$$S \xrightarrow{X} P.$$

Conditions:
▶ Fed-batch bioreactor, isothermal.

Model Equations

Biomass: $\frac{dX}{dt} = \mu(S)X - \frac{u}{V}X$

Substrate: $\frac{dS}{dt} = -\frac{\mu(S)}{Y_x}X - \frac{\nu}{Y_p}X + \frac{u}{V}(S_{in} - S)$

Product: $\frac{dP}{dt} = \nu X - \frac{u}{V}P$

Volume: $\frac{dV}{dt} = u$

Variables:

- S = Substrate concentration
- X = Biomass concentration
- V = Volume of the culture
- P = Product concentration
- u = Feed rate of substrate

Parameters:

▶ $\mu_m,\ K_m,\ K_i,\ \nu$: Kinetic parameters
▶ $Y_x,\ Y_p$: Yield coefficients
▶ S_{in}: Inlet substrate concentration
▶ $X_{\max}$: Maximum biomass concentration
▶ $u_{\min},\ u_{\max}$: Feed rate bounds

Parameters and Initial Conditions

Kinetic Parameters:

- $\mu_m = 0.53\,h^{-1}$, $K_m = 1.2\,g/L$, $K_i = 22\,g/L$
- $Y_x = 0.4$, $Y_p = 1$, $\nu = 0.5\,h^{-1}$

Feed Conditions:

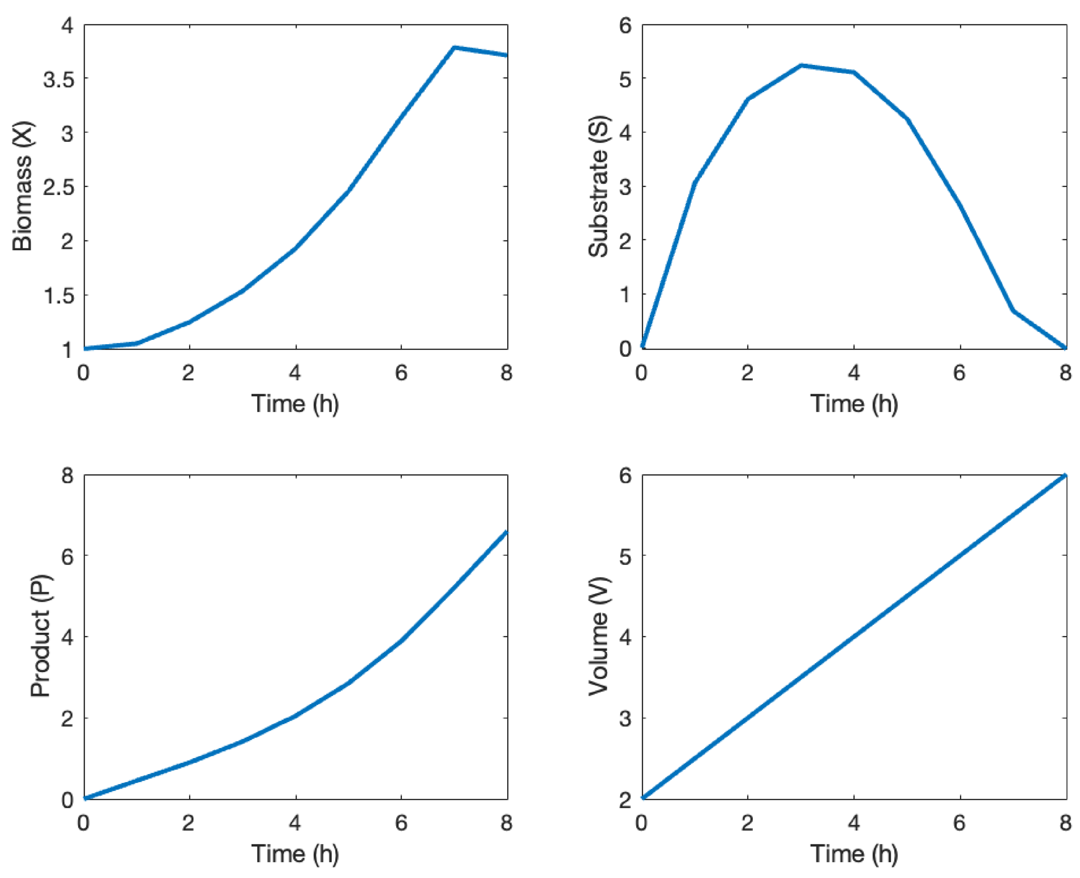
- $S_{\text{in}} = 20\,g/L$, $u_{\min} = 0$, $u_{\max} = 1\,L/h$
- $X_{\max} = 3\,g/L$

Initial Conditions:

- $X_0 = 1\,g/L$, $S_0 = 0\,g/L$, $P_0 = 0\,g/L$, $V_0 = 2\,L$

ODE Solutions at Fixed Feed Rate

- at u = 0.5 L/h

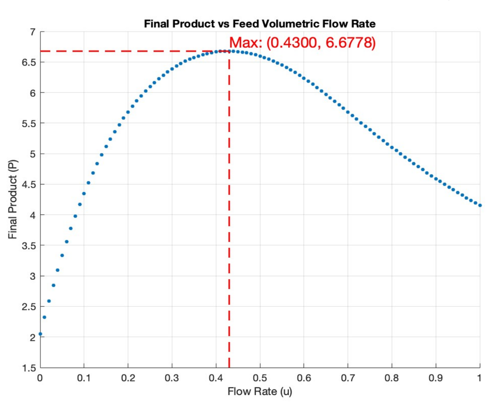


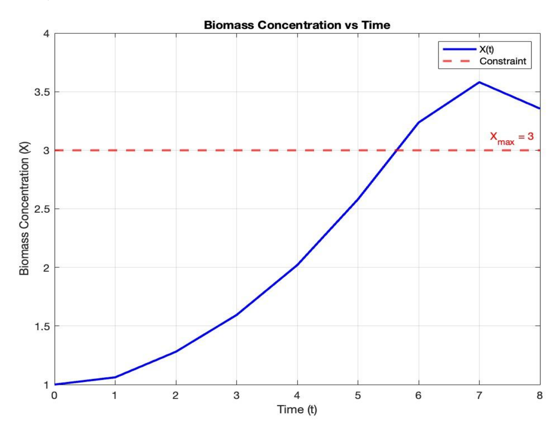
Maximum Product P =6.5964 g/L

Feed Rate Optimization

Optimization Methods
(a) Iterative Method:
- Try multiple constant values of $u \in [0,1]$
- Solve ODEs and record $P(tf)$
- Select uu giving maximum product

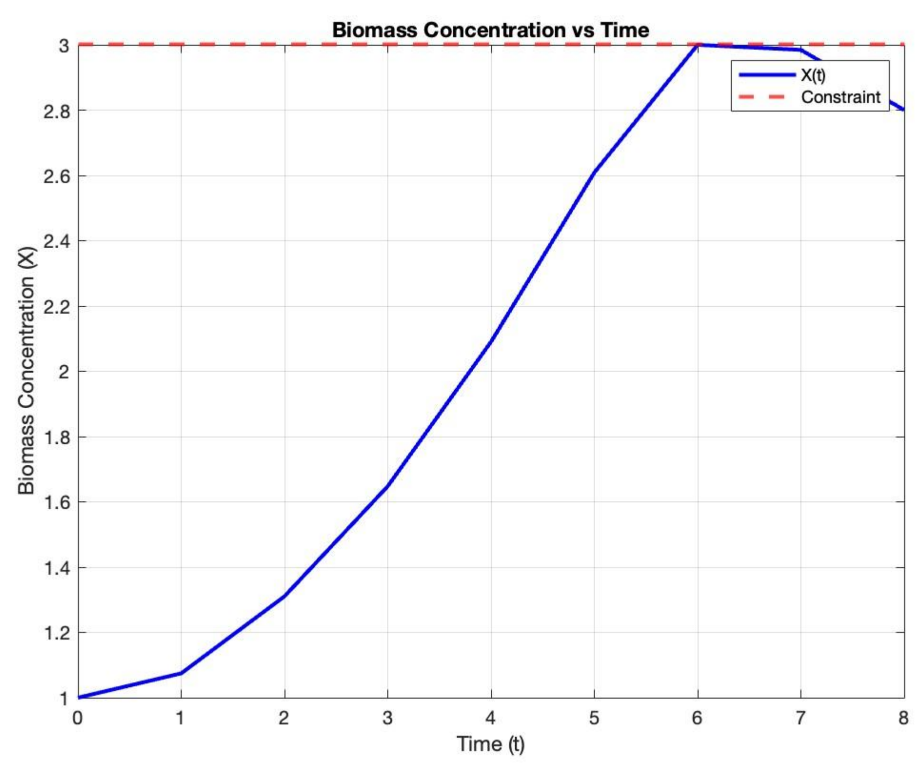
(b) Fmincon method (without constraint)





- Iterative method: u = 0.4284 L/h, P = 6.6778 g/L.
- fmincon: u = 0.4284 L/h, P = 6.6778 g/L.

(b) fmincon Optimization (With Constraints)
Biomass constraint: X(t) ≤ 3



- Optimal feed rate u = 0.3173 L/h.
- Final product concentration P = 6.4633 g/L.

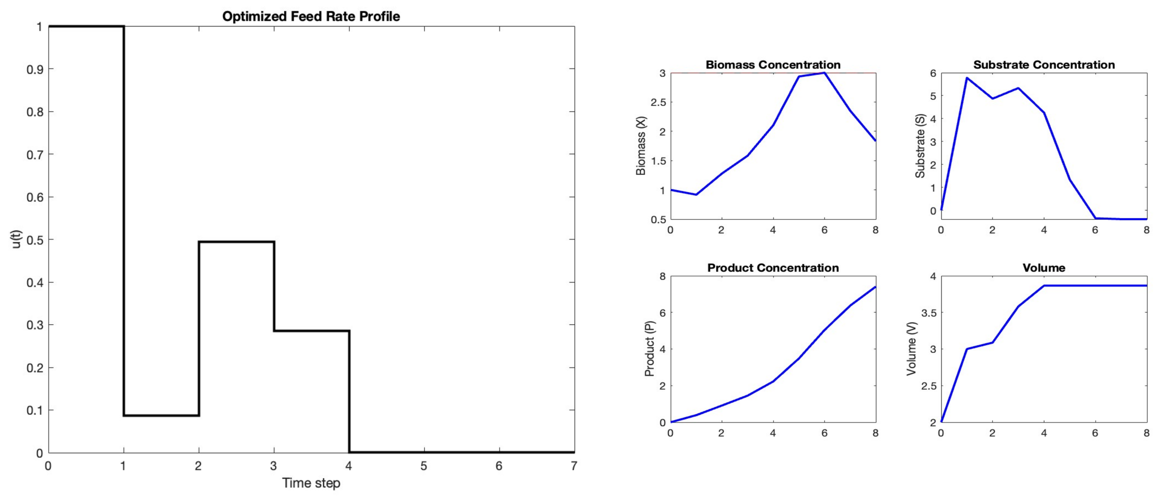
Initial Condition Optimization

Methods:
- Used fmincon in Matlab for linear constrained optimization
- Objective: **Maximize final product** P(tf)
- Bounds were set for physical and operational feasibility

Parameter	Symbol	Lower Bound	Upper Bound	Optimized
Initial Biomass (g/L)	X0	0.5	2	2
Initial Substrate (g/L)	S0	0	4	0
Initial Volume (L)	V0	0.1	4	2.8
Feed Rate (L/h)	u	0	1	0.5
Maximum Product (g/L)	P(tf)	–	–	8.0671

Hourly Feed Rate Optimization:

Optimize the feed rate u(t) at each hour to maximize the product concentration P(tf) at the final time tf = 8 hours.



Maximum Product Achieved:$P(tf)$=7.4124g/L

Result

Case No.	Optimization Type	X_0 (g/L)	S_0 (g/L)	V_0 (L)	u (L/h)	t (h)	P(tf) (g/L)
1	Fixed Feed Rate (Iterative)	1	0	2	0.4284	8	6.6778
2	Fixed Feed Rate (fmincon, with constraint)	1	0	2	0.3173	8	6.4633
3	Hourly Feed Rate (8 u_s)	1	0	2	$\{u_1, u_2, \ldots, u_8\}$	8	7.4124
4	Optimized Initial Conditions + Feed	2	0	2.7809	0.4569	8	8.0671
5	Hourly Feed (8 u_s) with Optimized Initial condition	1	0	2	$\{u_1, u_2, \ldots, u_8\}$	8	8.7371

Conclusion

- **Optimizing initial conditions** significantly enhances product yield, even when using a constant feed rate.
- **Hourly feed rate control** improves product formation compared to a single constant feed, but its effectiveness increases further when **paired with optimized initial states**.
- The **best product concentration**(P(tf)=8.7371 g/L) was achieved by combining **hourly feed rate control** with **optimized initial conditions**.
- Across all strategies, maintaining the **biomass constraint** was critical for stable and sustainable bioprocess operation.
- These results demonstrate the value of **joint optimization of initial conditions and control strategies** in fed-batch bioreactor design.

References

1. B. Srinivasan, S. Palanki, and D. Bonvin, "Dynamic Optimization of Batch Processes: I. Characterization of the Nominal Solution," Institut d'Automatique, École Polytechnique Fédérale de Lausanne, Switzerland, and Florida State University, USA, Jun. 21, 2001.