A Note on the Optimal Volumetric Flow Rate During Start Up of a BSTR Performing a Michaelis-Menten Reaction

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Note
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Theoretical background for the calculation of the optimum constant volumetric flow rate for an isothermal BSTR performing a *Michaelis-Menten reaction* under transient behaviour arising from start up conditions is reported. The asymptotic kinetic behaviours of zeroth and first order were used in order to derive analytical criteria, quite useful for the predesign steps in some situations where the filling up and the overall operating time are of the same order of magnitude.

Key words:
Analytical optimization, asymptotic behaviour, BSTR, computation of optimum constant volumetric flow rate, transient conditions during start up

Introduction

Operating biochemical stirred tank reactors (BSTR's) under transient conditions demands a good knowledge of the dynamics of the system if maximum advantage of the net profit involved is to be taken. If the existing reactor is very large and the transient behaviour of the reacting system extends for a long time, special attention is to be paid to the choice of the volumetric flow rate of reacting fluid every time the reactor is started up in order to maximize the overall production of converted substrate over such a time period. This criterion is particularly relevant whenever the product of the reaction has a high market value.

It is the purpose of this Note to provide a theoretical means to calculate the optimum volumetric flow rate, including the first situation of non-steady state for both the volume of the reacting fluid and substrate concentration, and the next situation of non-steady state only for the substrate concentration inside the reactor. The asymptotic kinetic situations provide a convenient set of balance equations leading to a quick analytical estimate of the constant volumetric flow rate to be used during reactor operation.

Mathematical analysis

Two periods of operating conditions for the system will be considered:

i) the reactor is being filled up with no outflow.

ii) the reactor is already full of reacting liquid, the inlet and outlet volumetric flow rates being the same.

The inlet volumetric flow rate is assumed to remain constant in either case. Assuming that the maximum amount of mixing at the molecular level takes place according to *Zwietering's* criterion[1] allows one to write the overall and partial mass conservation laws for case i) as

$$V^* = Q^* t^*, \text{ for } 0 < t^* < t^*_f \quad (1)$$

$$\frac{dC^*}{dt^*} = \frac{Q^* (1-C^*)}{V^*} - \frac{C^*}{K^*+C^*}, \text{ for } 0 < t^* < t^*_f \quad (2)$$

together with the initial condition

$$\text{at } t^* = 0,\ C^* = 1 \quad (3)$$

A similar reasoning applied to case ii) leads to

$$V^* = 1 \quad \text{for } t^*_f < t^* \quad (4)$$

$$\frac{dC^*}{dt^*} = Q^* (1-C^*) - \frac{C^*}{K^*+C^*} \quad \text{for } t^*_f < t^* \quad (5)$$

subject to the initial condition

$$\text{at } t^* = t^*_f,\ C^* = C^*_f \quad (6)$$

Variables t^*_f and C^*_f denote the dimensionless time and the normalized substrate concentration at the very moment the reactor gets full of reacting fluid, C^*_f being easily obtained via integration of Eqn. 2.

Setting the goal of the optimization procedure at maximizing the molar flow of converted substrate leads to the following objective function

$$\max F = \int_0^{t^*_b} Q^* [1 - C^* (t^*)]\ dt^* \quad (7)$$

The optimum operating volumentric flow rate is then to be found from[2]

$$\frac{\partial F}{\partial Q^*} = \int_{t^*_f}^{t^*_b} [1 - C^* (t^*) - Q^* \frac{\partial C^* (t^*)}{\partial Q^*}] \, dt^* = 0 \quad (8)$$

where the lower limit was changed in order to account for the fact that the filling up period is related to the absence of an outlet stream.

The solution of Eqn. 8 is only possible through numerical integration leading to extensive, cumbersome computation work. The Michaelis-Menten model suggests, however, that for low concentrations of substrate the reaction can be considered to be first order with respect to the substrate, whereas for high substrate concentrations the kinetics become of zeroth order, the concentration of substrate in the vicinity of the Michaelis-Menten constant leading to a kinetic equation with an intermediate fractional order[3]. Therefore, the Michaelis-Menten rate equation is bounded by two asymptotic behaviours: $K^* + C^* \sim K^*$ and $K^* + C^* \sim C^*$, respectively.

For the case where the biochemical reaction approaches zeroth order kinetics, Eqn. 2 can be integrated to give[4]

$$C^* (t^*) = 1 - \frac{1}{2} t^*, \qquad \text{for } 0 < t^* < t^*_f < 2 \quad (9)$$

whereas asymptotic first order kinetics yields

$$C^* (t^{**}) = \frac{1 - \exp (-t^{**})}{t^{**}}, \text{ for } 0 < t^{**} < t^{**}_f \quad (10)$$

Equation 5 then becomes

$$C^* (t^*) = \frac{Q^* - 1}{Q^*} - \left[\frac{Q^* - 1}{Q^*} - 1 + \frac{1}{2} t^*_f\right] \times$$

$$\times \exp [-Q^* (t^* - t^*_f)], \quad \forall t^* > t^*_f, \; Q^* > 1$$

$$\text{or: } t^*_f < t^* < t^*_f + \frac{1}{Q^*} \ln \left[\frac{Q^* t^*_f - 2}{2(Q^* - 1)}\right],$$

$$\text{for } 0 < Q^* < 1 \quad (11)$$

by using Eqn. 9 for zeroth order kinetics ($t^* > t^*_f$), and

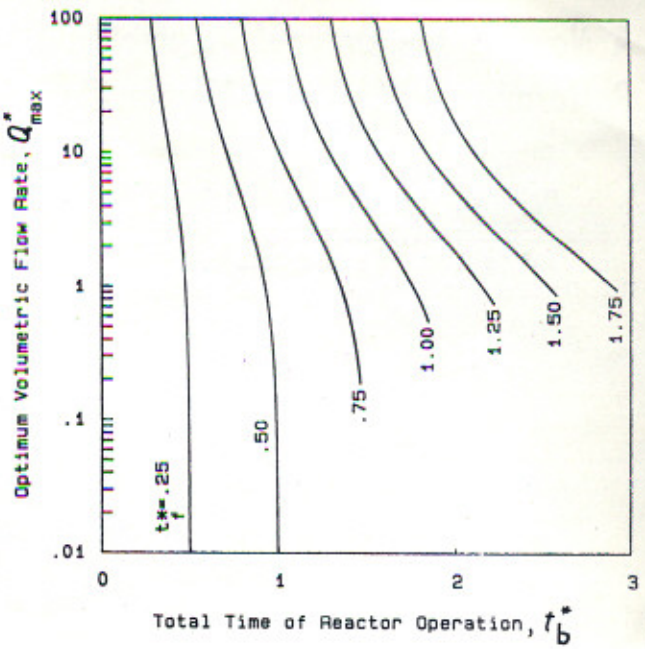

Fig. 1 — *Optimum volumetric flow rate vs. total time of reactor operation, for the case of asymptotic zeroth order kinetics, using a few values for parameter* t^*_f.

$$C^* (t^{**}) = \frac{Q^{**}}{1 + Q^{**}} - \left[\frac{Q^{**}}{1 + Q^{**}} - \frac{1 - \exp (-t^{**}_f)}{t^{**}_f}\right]$$

$$\times \exp [-(1 + Q^{**}) (t^{**} - t^{**}_f)] \quad (12)$$

by using Eqn. 10 for its first order counterpart ($t^{**} > t^{**}_f$).

Using Eqn. 11 in Eqn. 8 and performing some algebraic work gives

$$\left[1 + Q^*_{max} (t^*_b - t^*_f) \left[1 + \frac{Q^*_{max} t^*_f}{2}\right]\right] \times$$

$$\times \exp [-Q^*_{max} (t^*_b - t^*_f)] - 1 = 0 \quad (13)$$

for the case of zeroth order kinetics. The values for Q^*_{max} vs. t^*_b for several values of parameter t^*_f are sketched in Fig. 1, a zero finding subroutine having been used to solve Eqn. 13.

The other asymptotic case leads to the following equation

$$\frac{\partial F}{\partial Q^{**}_{max}} = \frac{1}{(1 + Q^{**}_{max})^2} \left[t^{**}_b - t^{**}_f + \left[\frac{Q^{**}_{max}}{1 + Q^{**}_{max}} - \frac{1 - \exp (-t^{**}_f)}{t^{**}_f}\right] \times \left[1 - \exp[-(1 + Q^{**}_{max}) (t^{**}_b - t^{**}_f)]\right] + \right.$$

$$\frac{Q^{**}_{max}}{1 + Q^{**}_{max}} \left[1 - \exp. [-(1 + Q^{**}_{max}) (t^{**}_b - t^{**}_f)]\right] + Q^{**}_{max} (t^{**}_b - t^{**}_f) \left[Q^{**}_{max} - \frac{1 - \exp (-t^{**}_f)}{t^{**}_f} (1 + Q^{**}_{max})\right]$$

$$\times \exp [-(1 + Q^{**}_{max}) (t^{**}_b - t^{**}_f)] \quad (14)$$

which enables one to state that the larger Q^{**}_{max} the larger the objective function F in the range with physical significance.

The conditions of validity of the two approximations developed can then be stated as follows:

if $K^* + C^*_{ss} \sim C^*_{ss}$ then the approximation of zeroth order kinetics is valid, C^*_{ss} being obtained from a mass balance to the reactor under steady state operating conditions,

$$C^*_{ss} = \frac{1 + \left[\left[\frac{1}{Q^*_{max}} + K^* - 1\right]^2 + 4K^*\right]^{1/2} - \frac{1}{Q^*_{max}} - K^*}{2} \quad (15)$$

For the case where $K^* + 1 \sim K^*$, the approximation of first order kinetics is valid.

The minimum yield of product for the reactor can be obtained from the definition of the objective function using the second form of the *Euler-Lagrange* equation[3,5], and assuming $Q^* = Q^*(t^*)$, according to

$$\frac{d}{dt^*}\left[Q^*(1 - C^*) - \beta Q^* - \left[\frac{dC^*}{dt^*}\right]\frac{\partial\,[Q^*(1 - C^*) - \beta Q^*]}{\partial\left[\frac{dC^*}{dt^*}\right]}\right] = 0 \quad (16)$$

where β is a constant Lagrangian multiplier. This auxiliary variable was introduced because the total volume of the fluid treated must be positive, thus creating a global restriction to the final solution. Performing some algebra on Eqn. 16 (cf. *Loncin* and *Merson*[3]) and using Eqns. 5 and 6 in the suitable asymptotic form enables one to obtain

$$Q^*_{min} = \frac{2}{t_f^*} \quad (17)$$

for zeroth order kinetics, and

$$Q^*_{min} = \frac{1 - \exp(-t_f^{**})}{K^*\,[t_f^{**} + \exp(-t_f^{**}) - 1]} \quad (18)$$

for first order kinetics.

Discussion

Although very simple, the Michaelis-Menten model furnishes results in excellent agreement with the practice[3]. The usefulness of the conclusions drawn for the cases where inhibition phenomena are absent is, therefore, apparent.

The local optimization in the case of first order asymptotic kinetics is not possible, the final selected volumetric flow rate lying on an operating constraint; nevertheless, the optimization pattern in the case of zeroth order asymptotic kinetics leads to an actual value for the volumetric, flow rate of reacting fluid whenever the total time of reactor operation is of the same magnitude of the time required for completely filling up the reactor. This fact leads to the definition of the optimum for reactor operation which may be very useful in the predesign steps of slow biochemical reactions, as long as the validity conditions referred to above are fulfilled.

The reasoning developed extends previous theoretical works concerning the design of reactors for operation in steady state conditions[6] by providing a tool for the heuristic computation of the volumetric flow rate in some particular situations of industrial practice.

The optimum value for the volumetric flow rate can be compared to the value that would give the minimum yield of product in the reactor in order to estimate how far from the worst conditions the operating pattern is. The values leading to minimum yield are constant volumetric flow rates, so taking the volumetric flow rate as a constant over the entire optimization procedure seems to have a certain physical background.

List of symbols

- C — Substrate concentration mol m^{-3}
- C^* — Normalized substrate concentration $= \frac{C}{C_o}$
- F — Objective function
- K — Michelis-Menten saturation constant, mol m^{-3}
- K^* — Dimensionless Michaelis-Menten saturation constant $= \frac{K}{C_o}$
- Q — Volumetric flow rate, m^3 s^{-1}
- Q^* — Dimensionless volumetric flow rate $= \frac{Q\,C_o}{V_f\,r_m}$
- Q^{**} — Dimensionless auxiliary volumetric flow rate $= Q^*\,K^*$
- r — Maximum kinetic rate, mol m^{-3} s^{-1}
- t — Time elapsed since the beginning of reactor operation, s
- t^* — Dimensionless time elapsed since the beginning of reactor operation $= \frac{t\,v_m}{C_o}$
- t^{**} — Dimensionless auxiliary time $= \frac{t^*}{K^*}$
- V — Volume of reacting fluid inside the reactor, m^3
- V^* — Dimensionless volume of reacting fluid inside the reactor $= \frac{V}{V_f}$

Greek symbol

- β — Lagrangian multiplier

Subscripts

- o — at the inlet conditions
- b — when the total time of reactor operation is over
- f — when the reactor gets completely full
- m — for the Michaelis-Menten rate equation
- min — leading to a minimum yield of product
- max — leading to a maximum yield of product
- ss — at steady state conditions

References

1. *Zwietering Th.*, The Degree of Mixing in Continuous Flow Systems. Chem. Eng. Sci. **9** (1959) 1—15
2. *Stephenson G.*, Mathematical Methods for Science Students, Longman, London, 1973
3. *Loncin M.* and *Merson R.*, Food Engineering — Principles and Selected Applications, Academic Press, New York, 1979
4. *Kreyszig E.*, Advanced Engineering Mathematics, John Wiley and Sons, New York, 1979
5. *Clegg J.*, Calculus of Variations, Oliver and Boyd, London, 1968
6. *Luyben K.* and *Tramper J.*, Optimal Design for Continuous Stirred Tank Reactors in Series Using Michaelis-Menten Kinetics. Biotechnol. Bioeng. **24** (1982) 1217—1220

Letters to the Editor

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In their reply to our recent letter[1], Noworyta and Krotki feel that we have reacted too strongly to what they consider to be a relatively unimportant error. They suggest letting the scientific world judge the validity of their [2,3] proposed method. In this respect they quote the work of Kehat and Letan[4] who experimentally investigated the variation in the local hold-up in a spray column. For one type of column they did indeed find that the hold-up decreased along the dispersion height particularly at high continuous phase throughputs. However, as they carefully point out this is because the continuous phase is injected into the middle of the dispersion thus lowering the hold-up there and creating considerable turbulence and circulation. For a column operated under more normal conditions in which the continuous phase is introduced at the top of the dispersion under calm conditions (within the widened disengaging section) so the velocities of both phases are constant over the cross-section, the same authors[5] demonstrated thad the hold-up alays increased along the dispersion height. This type of column is precisely that used by Noworyta and Krotki[2,3] as shown clearly in Figures 2 and 4 of their first paper and in their flow diagram (Figure 1 of their second paper). They also referred to the work of Vidjaja who correctly used the average hold-up as is made clear in the figures immediately following his equations. For plug flow, the increase in dispersed phase hold-up along the height in coalescing dispersions is a natural consequence of the sedimentation equation[7–12] in which the relative velocity is proportional to the product of the drop size and continuous phase hold-up (or appropriate functions thereof) for both laminar and turbulent flow. The equation applies to both counter-current flow in spray columns (in which the velocities of both phases are constant over the cross-section) and when the continuous phase is stagnant as in dense-packed dispersions in settlers.

In an effort to justify their model, Noworyta and Krotki[1] neglect the term $h\,d\varepsilon/dh$ in equation (13) to obtain equation (13a) whilst retaining the term $d\,d\varepsilon/dh$ in equation (15) (though this is not explicitly stated). Unfortunately, this lands them in deeper water as the rederived equations all contain algebraic errors (u_d should be replaced by $2u_d$ in equations (17a), (18a), (21a), (25a), (26a), and (27a) and the exponent in equations (18a) and (27a) should be 1/3 instead of 1/6) thus further confusing the issue. In any case equations (17a) and (25a) still incorrectly predict that the hold-up decreases along the dispersion height in a coalescing dispersion.

Neglecting selected terms in $d\varepsilon/dh$ without justification or replacing the average hold-up $\bar{\varepsilon}$ by the local hold-up ε in order to simplify the equations controlling the variation in hold-up along the height of the dispersion is equivalent to assuming that the earth is flat in order to make navigation easier-with predictable consequences!

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References

1. *Hartland, S., Jeelani, S. A. K.* Chem. Biochem. Eng Q. **2** (1988) 49
2. *Noworyta, A., Krotki, M.* Chem. Biochem. Eng. Q **1** (1987) 63
3. *Noworyta, A., Krotki,* M. Chem. Biochem. Eng. Q **1** (1987) 69
4. *Kehat, E., Letan, R.* Ind. Eng. Chem. Process Des. dev. **7** (1968) 385
5. *Letan, R., Kehat, E.* A. I. Ch. E. J. **13** (1967) 443
6. *Widjaja, H. Ph. D.* Thesis, ETH, Zürich (1977)
7. *Richardson, J. F., Zaki, W. N.* Trans. Inst. Chem. Eng. **32** (1954) 35
8. *Maude, A. D., Whitmore, R. L. J.* Appl. Phys. **9** (1958) 477
9. *Hanratty, T. J., Bandukwala, A.* A. I. Ch. E. J. **3** (1958) 293
10. *Chong, Y. S., Ratkowsky, D. A.*, Epstein, N. Powder Technol. **23** (1979) 55
11. *Kumar, A., Vohra, D. K., Hartland, S.* Can. J. Chem. Eng. **58** (1980) 154
12. *Reed, C. C., Anderson, J. L.* A. I. Ch. E. J. **26** (1980) 816