Control Engineering Practice 42 (2015) 89–94

Contents lists available at ScienceDirect

Control Engineering Practice

journal homepage: www.elsevier.com/locate/conengprac

A mid-ranging control strategy for non-stationary processes and its application to dissolved oxygen control in a bioprocess

O. Johnsson [a,*], D. Sahlin [b], J. Linde [c], G. Lidén [d], T. Hägglund [a]

[a] Department of Automatic Control, Faculty of Engineering LTH, Lund University, Sweden
[b] Novozymes A/S, Hallas Allé 1, 4400 Kalundborg, Denmark
[c] NNE Pharmaplan, Nybrovej 80, 2820 Gentofte, Denmark
[d] Department of Chemical Engineering, Faculty of Engineering LTH, Lund University, Sweden

ARTICLE INFO

Article history:
Received 16 October 2014
Accepted 8 March 2015
Available online 18 June 2015

Keywords:
Mid-ranging control
Process control
Control architecture
Industrial bioprocess
Dissolved oxygen control

ABSTRACT

In this study a modified mid-ranging strategy is proposed where the controller for the secondary manipulated variable uses its own output as its setpoint, possibly with an offset and/or re-scaling. This modification allows the manipulated variables to increase in unison so that the mid-ranging advantage of utilizing the fast dynamics of the primary controller to regulate the process can be achieved also in non-stationary processes, while not adding complexity to the controller. The proposed control strategy has been implemented in pilot-scale (500 l) industrial bioprocesses where it is used to control the dissolved oxygen level by manipulating agitator speed and aeration rate. The controller is demonstrated to perform well in these, outperforming a reference controller which has previously been shown to give satisfactory control performance. It is also shown in similar experiments that the strategy can easily be adapted to control dissolved oxygen in bioprocesses where the feed rate is controlled using an extremum-seeking controller. The proposed strategy is generally applicable to non-stationary processes where a mid-ranging approach is suitable.

1. Introduction

In an aerobic bioprocess, maintaining aerobic conditions in the liquid medium is important to ensure efficient microbial growth and production. Oxygen transfer through the medium is more efficient at low oxygen concentrations (Garcia-Ochoa & Gomez, 2009) so maintaining a low yet non-zero oxygen concentration is therefore desirable, meaning that well-designed control which allows for lower set-points can improve process efficiency (du Preez & Hugo, 1989). When using oxygen control in conjunction with other control systems it can also be highly important that a steady baseline in the oxygen level is maintained, so that disturbances in oxygen concentration do not influence these other systems (Åkesson & Hagander, 1999).

Mid-ranging control is a commonly used approach for control of a single variable using two manipulated variables (process inputs). Although model predictive control (MPC) can be more suitable to handle complex systems, mid-ranging control is often preferred due to its simplicity (Allison & Ogawa, 2003). The control of oxygen concentration in a biotechnical process in a stirred tank reactor can be regarded as such a process, where the manipulated variables are agitator speed and aeration rate. There are other variables which can be used to influence the oxygen concentration, such as oxygen concentration of inlet air and total pressure, but these are often not practical to use.

Many industrial bioprocesses are performed as fed-batch, i.e. are non-stationary (Rani & Rao, 1999). This causes certain difficulties in regard to mid-ranging control as it is then typically not desirable to maintain one manipulated variable at a predefined level for as long as possible, which is the aim of classical mid-ranging control. In this study, a modification to the classical mid-ranging scheme for the purpose of adapting it to non-stationary processes is proposed and evaluated in the context of oxygen control in a fed-batch industrial bioprocess.

2. Industrial bioprocesses

In an industrial bioprocess, the aim is commonly to maximize microbial growth and/or production of some compound produced by microorganisms. To achieve this in an efficient manner, it is necessary to maintain a suitable environment for the microorganisms at all times. This is commonly done by using stirred-tank bioreactors, where microorganisms are grown in a liquid medium

* Correspondence to: Department of Automatic Control, Faculty of Engineering LTH, Lund University, Box 118, SE-22100 Lund, Sweden. Tel.: +46 46 222 87 60.
E-mail address: ola.johnsson@control.lth.se (O. Johnsson).

http://dx.doi.org/10.1016/j.conengprac.2015.03.003
0967-0661/

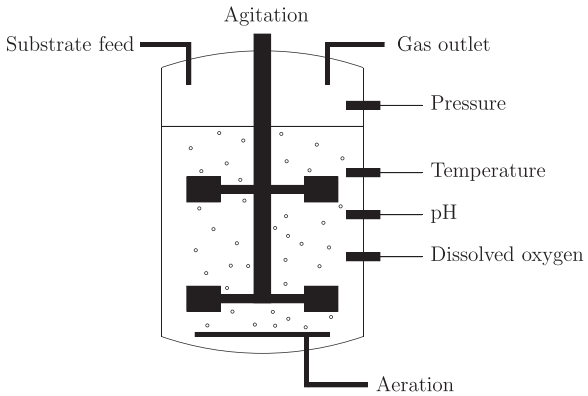

Fig. 1. Illustration of a typical fed-batch bioreactor. Liquid substrate is added continuously while air is introduced through a sparger at the bottom of the tank. Agitation ensures that the liquid medium is suitably mixed and the air bubbles small enough to allow efficient oxygen transfer. Temperature, pH and dissolved oxygen concentration are monitored continuously, while the oxygen and carbon dioxide concentrations in the gas outlet are analysed by a mass spectrometer. Total pressure is controlled by varying the gas outlet flow, temperature through cooling and pH through addition of acid/base.

which is stirred to achieve an even spatial distribution of compounds in the medium.

2.1. Fed-batch bioprocesses

In order to control microbial growth a limiting compound, i.e. one which does not exist in excess in the medium, can be added by means of a continuous feed throughout the process. This mode of operation is termed fed-batch and is commonly used in large-scale industrial bioprocesses today (Lidén, 2002). An illustration of a fed-batch bioreactor showing some common measurements and actuators is given in Fig. 1.

A fed-batch bioprocess can be divided into at least two distinct phases, an initial growth phase in which microbial growth is emphasized followed by a production phase where as much as possible of the product compound is produced. During the growth phase, exponential growth of the biomass at a high rate is desired as a higher biomass concentration will be able to generate more product. The growth phase ends when the mass transfer capacity of the bioreactor limit biomass growth, i.e. when if the biomass would increase further it would not be possible to supply oxygen at a high enough rate, transport away heat fast enough or some other transport limitation occurs. This leads to a change in control objective and typically means that it is necessary to decrease the substrate feed rate to limit growth.

2.2. Oxygen dynamics in a fed-batch bioreactor

Exponential growth of microorganisms can in the right environment be very rapid, with a doubling time lower than 10 minutes (Eagon, 1962). This means that in the case of microorganisms using oxygen as a substrate, termed aerobes, the oxygen consumption during the initial growth phase of a fed-batch bioprocess will be exponentially increasing at a high rate.

Maintaining a steady concentration of oxygen above zero in the liquid bioreactor medium is required in aerobic bioprocesses, as oxygen deficiency leads to either cessation of growth (obligate aerobes) or less efficient metabolism as well as production of undesirable by-products (facultative anaerobes) (Villadsen et al., 2011). As the consumption of oxygen increases with both biomass concentration and specific growth rate, the supply of oxygen must also increase to maintain a desired concentration. The supply of oxygen can be described as in (1), where q_O is the volumetric mass transfer rate of oxygen, k_l is the mass transfer coefficient, a is the specific surface area, c_O^* is the oxygen concentration when at equilibrium with the gas phase and c_O is the current oxygen concentration (Villadsen et al., 2011).

$$q_O = k_l a(c_O^* - c_O) \tag{1}$$

As seen in Eq. (1) the oxygen supply is determined by several factors, which can be manipulated in order to vary the supply. In a stirred tank reactor (STR) $k_l a$ can be increased by increasing the aeration rate and the agitator speed, but it is also possible to increase the transfer by increasing the partial pressure of oxygen in the gas phase and hence c_O^* or decreasing the dissolved oxygen level c_O. However, increasing the partial pressure of oxygen in the gas phase is often not feasible as it either requires increased total pressure which increases strain on the bioreactor or addition of pure oxygen which is costly compared to using pure air. Decreasing c_O does not come with these practical limitations but brings the process closer to oxygen deficiency, meaning that stricter control is required to avoid this undesirable state.

Empirical correlations for the effects of aeration (AR) and agitation (AG) on $k_l a$ exist, but coefficient values will vary depending on the size and geometry of the bioreactor. Most of them can be written in the form given in (2), where u_s is the superficial gas flow (proportional to aeration rate), P_g/V_l is the power input per volume of gassed medium and k, α and β are coefficients which will depend on medium properties (Villadsen et al., 2011).

$$k_l a = k \cdot u_s^{\alpha} \left(\frac{P_g}{V_l}\right)^{\beta} \tag{2}$$

A correlation between the power input into gassed medium P_g and the power input into ungassed medium P was suggested by Hughmark (1980), as given in (3) where V_l is the liquid volume, g is the acceleration of gravity and d_s and w_s are the diameter and width of the stirrer respectively.

$$P_g = P \cdot 0.1 \left(\frac{AR}{AG \cdot V_l}\right)^{-1/4} \left(\frac{AG^2 \cdot d_s^4}{g \cdot w_s \cdot V_l^{2/3}}\right)^{-1/5} \tag{3}$$

The power input into ungassed medium, P, can be expressed as in (4) where N_p is the dimensionless power number which depends on the viscous and inertial forces and ρ_l is the density of the liquid.

$$P = N_p \cdot \rho_l \cdot AG^3 \cdot d_s^5 \tag{4}$$

Eqs. (3) and (4) give that the power input per volume of gassed medium relates to AG and AR as in (5).

$$\frac{P_g}{V_l} \propto AG^{2.85} \cdot AR^{-0.25} \tag{5}$$

Villadsen et al. (2011) give examples of coefficient values in (2) for different settings, the values for α are in the range 0.2–0.5 and the values for β 0.4–0.7. Inserting this into (2) and using the relation in (5), it can be seen that $k_l a$ depends on AG and AR as in (6) where a is in the range 1.14–2.00 and b 0.0250–0.400. As the exponent for AG is at least 2.85 times greater than that for AR, variations in AG will have a larger impact on $k_l a$. In a setting where a primary control variable should be chosen, AG is therefore the most suitable choice.

$$k_l a \propto AG^a \cdot AR^b \tag{6}$$

3. Control strategies

For a process with two inputs and one output, mid-ranging control as illustrated in Fig. 2 is a classical solution to the control problem. Utilizing one input to control the output directly and the