Control System Development for Integrated Bioreactor and Membrane Separation Process

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Abstract
A bioreactor integrated with an electrically driven membrane separation process (Reverse Electro-Enhanced Dialysis - REED) is under investigation as potential technology for enhancing lactic acid bioproduction. In order to reveal the operation of the integrated process to achieve a specific production goal, a methodology for goal driven control system development is expanded to handle periodically operating systems. In this paper the pH control issue is addressed. A sensitivity analysis is used as criterion for the conceptual design of the control structure.

Keywords: Lactic acid production, REED, sensitivity analysis

1. Introduction
Lactic acid is mostly produced using fermentation of carbohydrates by Lactic Acid Bacteria (LAB). Improvements in the design of the lactic acid bioproduction have been studied extensively driven by an increasing number of applications of the fermentation products. The main limitation for this bioprocess is that LAB normally are impaired by product inhibition at a certain concentration level of the main metabolic product. Therefore, the fermentation can be intensified by continuous lactate removal from the cultivation broth during a pH controlled fermentation, this will result in a higher productivity and product yield. An integrated bioreactor and a novel electrically driven membrane separation processes (Reverse Electro-Enhanced Dialysis - REED and Electrodialysis with Bipolar membranes - EDBM) has been recently proposed as a method for in situ continuous lactate removal from the fermentation broth, the first extraction stage is depicted in fig. 1 [5]. Additional productivity is achieved by the continuous recycle of biomass and unconsumed substrates, which allow working at higher cell densities and exploitation of the substrate.

The novelty of the process is the innovative electro-membrane separation process employed which selectively extracts the lactate and simultaneously facilitates the pH control in the fermenter. This is possible since the lactate ions are exchanged by hydroxyl ions in the REED module. In addition, the adverse influence of the membrane fouling is diminished by periodically reversing the polarity of the electrical field, ensuring longer operation compared to continuously operated membrane based separations.

Fig 1. Integrated bioreactor and REED module sketch for intensified lactic acid cultivation
The cleaning effect in the REED module, by alternating the polarity of the potential gradient, has been attributed to an effective destabilization mechanism generated by the hydroxyl flux [5]. The periodic operation of the REED module implies a lost of lactate recovery when the current is reversed. However, the enhanced cleaning enables a higher productivity of the REED module compared to a traditional continuously operating membrane separation process.

The present contribution is part of our efforts on modeling and operational design of a novel process for lactic acid production, where the fermentation and product removal are tightly integrated. To reveal the operation of the integrated system according to different fermentation goals, a systematic procedure for control system design is employed. In this paper, a conceptual pH control structure is proposed based on a systematic but non trivial sensitivity analysis for the periodically operated process.

2. Conceptual control system design methodology

The employed methodology to control structure design is based on ideas for plantwide control design [6]. Existing guidelines for the conceptual control structure design of a goal driven control system needs extension especially when the selection of manipulated variables is not evident for a periodically operated process

2.1. Functionality

The starting point of the control structure design procedure is to define the desired functionality of the process which is the plant operating goal. Interesting industrially relevant primary objective functions are: lactate production as potential feedstock for the production of the biodegradable Poly-Lactic Acid (PLA), probiotic culture production (>10 times higher activity) or extracellular protein production based on genetically modified lactic acid bacteria. To achieve these goals an important subgoal is to achieve pH control in the fermenter. This is selected as a main subgoal and further investigated in this contribution.

2.2. Top-down analysis

The degrees of freedom (DOF) for the integrated system are determined. The DOF which can ensure that the goals and subgoals can be achieved will become actuator variables and define the axes of the operating window for the process. The remaining degrees of freedom are considered as disturbances. In linear systems, the selection of the manipulated variables according to a specific goal can be handled in a relatively simple way based on prior knowledge and guidelines i.e. that large and fast effects on the controlled variables are desired, corresponding to a large steady state gain and relatively small time constants. However, in this integrated periodically operated system it is desirable to define an index that can quantify the mentioned guidelines. As a case study the pH control structure design is chosen.

The selected criterion is the dynamic sensitivity of the controlled variable to changes in the potential manipulated variables. Stationary simulations of the periodically operated system within the operating window are performed and the sensitivity is evaluated. The simulation results additionally provide useful information concerning the type of operating surface for the system and the operational constraints. Simulations have been performed for the fermentation and REED module separately.

2.3. Bottom-up design

Once the conceptual control structure is designed, the controllers can be designed. Usually a multilevel hierarchical structure is employed. It is of particular interest to
reveal the potential benefit of multivariable control over a fully decentralized control structure.

2.4. Evaluation of the control structure performance

The implemented control structure is tested through dynamic simulations. Performance indicators provide relevant indicators for the integrated plant monitoring.

3. pH control structure design

3.1. pH model in the REED module

The question to answer at this stage is: what is the most appropriate manipulated variable which can control pH? Previously, a dynamic model was developed to describe simultaneous ion transport across anion exchange membranes in a dialysis cell [4]. Investigations were performed for operation without imposing current density, operation applying an external potential gradient and operation under current reversal conditions [2, 3, 4]. In those contributions, the operating window of the device was explored. Here, we investigate pH changes in the outlet of the REED module as a function of the potential manipulated variables, therefore the pH model is highlighted.

The mass balances within the boundary layers and membranes in the REED model can be summarized as follows. A mass balance for component $k$ in phase $p$ is:

$$
\frac{\partial C_{k,p}}{\partial t} + \nabla \cdot J_{k,p} - R_k = 0
$$

The reaction term ($R_k$) is used to introduce the acid dissociation into the model. The flux $J_{k,p}$ is estimated using the Nernst-Planck equation for ideal solutions, neglecting convective transport [7]:

$$
J_{k,p} = -D_{k,p} \left( \frac{\partial C_{k,p}}{\partial x} + \frac{z_k F C_{k,p} \psi}{RT} \frac{\partial}{\partial x} \right)
$$

Where $D_{k,p}$ is the diffusion coefficient, $z_k$ the valence, $F$ the Faraday number, $R$ is the ideal gas constant, $T$ is temperature and $\psi$ is the electrical potential. The potential gradient can be calculated using the assumption that all current $I_p$ is carried by ions:

$$
I_p = \sum_{k} z_k F A_{k,p}
$$

Donnan equilibrium is used to describe the concentration and potential discontinuities at the membrane surface. The bulk channel models are approximated using tanks in series model where in each tank there is mass transport towards the membrane and the dissociation reactions are present. Experimentally, it has been verified that a pH buffer effect is induced by the presence of biomolecules in a fermentation broth. When those components are modeled as highly charged macromolecules, multiple dissociation reactions must be introduced. That increases unnecessarily the complexity of the model. To deal with this situation, the proton acceptor groups in the proteins are considered in terms of equivalents, i.e. the protein concentration is represented as mol of acid equivalents per volume. Therefore, the dissociation of a polyprotic species is simplified to a monoprotic acid reaction [1]. The protein species represents a wide range of components in the fermentation broth from low molecular weight proteins to colloidal material. The system of reactions is given by the following equilibrium expressions:

- $HL + OH^- \rightarrow \frac{1}{n} L^- + H_2O$
- $HP + OH^- \rightarrow \frac{1}{n} P^- + H_2O$
Where the dissociation constants for those reactions (K_d) correspond to the acid dissociation constant (K_a) divided by the ionic product of water (K_w). Using a stoichiometric matrix, the dissociation reaction rates are systematically introduced into the model.

3.2. Degrees of freedom

The potential manipulated variables to control hydroxyl flux towards the REED feed channel are: the feed and dialysate input flow rates (q_feed and q_dia), the polarity reversal time (t_rev), the imposed current density (I_d) and the inlet hydroxyl concentration in the dialysate channel (C_{in, dia}). A first screening is performed based in the knowledge earned from previous investigations [2, 3, 4]. The first variables discarded are the flow rates, the reason is the lack of information about how the thickness of boundary layers change as a function of the flow conditions. Therefore, the model predictive power during flow rate changes is very limited. The reversal time, or operation time before the polarity of the potential gradient is inversed, is not investigated since it is a design variable that is chosen by trading off lactate recovery and the energy consumption subject to the power source constrains [3]. These choices leave the current density and the inlet base concentration to the dialysate channel as potential manipulated variables.

3.3. pH sensitivity estimation

In order to evaluate the influence of the REED module operation on the pH of the fermenter, a simulation scenario is proposed. Feed channel input concentrations to REED are assumed constant, corresponding to hypothetical fermentation broth at constant pH. Simulations are performed to estimate the pH at the end of the feed channel based on changes of the potential manipulated variables. The dynamic sensitivity of the pH to the potential manipulated variables is approximated using forward finite differences:

\[
NS_{I_d} = \left[ \frac{I_d}{pH} \right] \frac{dpH(t)}{dI_d} \\
\frac{dpH(t)}{dI_d} \approx \frac{pH(I_d, t) - pH(I_d + \Delta I_d, t)}{\Delta I_d}
\]

(4)

\[
NS_{C_{in, dia}} = \left[ \frac{C_{in, dia}}{pH} \right] \frac{dpH(t)}{dC_{in, dia}} \\
\frac{dpH(t)}{dC_{in, dia}} \approx \frac{pH(C_{in, dia}, t) - pH(C_{in, dia} + \Delta C_{in, dia}, t)}{\Delta C_{in, dia}}
\]

(5)

Where NS is the dimensionless sensitivity. It is selected in order to make a fair comparison between both actuator variables. The scaling values chosen are the initial conditions before the disturbance is applied, i.e. at \( t_0 = 0 \). The simulation procedure to estimate the sensitivity around each operating point involves three steps:

a. The dynamic model is initialized from a known operating point to periodically stationary operation. This point is function of \( I_d \) and \( C_{in, dia} \). The other input variables are fixed. The last simulation point during the period is selected as the initial condition for the following simulations.

b. The model is solved from the new initial conditions and the previous input variables. The simulation results correspond to the stationary operation, and become the reference to estimate the sensitivity. The main variable stored is either \( pH(I_d, t) \) or \( pH(C_{in, dia}, t) \).

c. The model is solved again introducing the disturbance in the potential manipulated variable. The main variable stored is either \( pH(I_d + \Delta I_d, t) \) or \( pH(C_{in, dia} + \Delta C_{in, dia}, t) \).
4. Results and discussion

4.1. Cultivation broth pH behavior during REED operation

Under constant \( I_d \) and \( C^{\text{Oh,dis}} \) operation, the system is driven by the periodicity and strength of the current. The pH behavior at the outlet of the feed channel during a step change in the operating current of 100 A/m\(^2\) is depicted in fig. 2. The period to period dynamics is visible before a periodic stationary operation is achieved after a few cycles in the open loop simulation. After the polarity is reversed, there is a reduction in the pH due to a temporal flux inversion in the system. Due to the symmetry of the unit, the pH behavior is not a function of the polarity of the electrical field under stationary operation, but of the absolute current density.

![Fig 2. Feed channel pH behavior for \( t_{rev}=5 \) min, \( C^{\text{Oh,dis}}_d=50 \) mol/m\(^3\). When \( I_d \) is changed from 100 A/m\(^2\) to 200 A/m\(^2\). The highlighted points indicate the time just before the current is reversed.](image)

4.2. pH Sensitivity

The pH sensitivity is evaluated dynamically, however a comparison is only performed when the derivative has been approximated at the same point in time within subsequent periods. The chosen points are at the time just before the polarity is reversed - shown highlighted in fig. 2. Following the simulation procedure described above, the sensitivity is investigated within a selected operating window of the potential manipulated variables. The sensitivity response is underdamped and overdamped, after introducing disturbances in \( I_d \) and \( C^{\text{Oh,dis}} \) respectively, while the settling time for both responses is comparable. The ratio between the dimensionless sensitivities was investigated at one point during the transient response -the first middle point- and under stationary operation after the transient has settled as shown in fig. 3 and 4.

![Fig 3. Stationary sensitivity ratio at different operating points](image)

![Fig 4. First middle point sensitivity ratio at different operating points](image)

Fig. 3 shows that the stationary normalized sensitivity does not change radically by introducing disturbances either in the current density or the base concentration. At low current densities there are no practical differences. At high current densities, the pH is between 5 and 10 times more sensitive to \( I_d \) than to \( C^{\text{Oh,dis}} \).
On the other hand, larger differences are evident in the first middle point after a step change where normalized pH sensitivity is approx. 20 to 50 times higher for current density than for base concentration changes (fig. 4). These results indicate that $I_d$ is an appropriate manipulated variable to handle the dynamic response; while $C_{\text{out, dial}}$ can control the stationary behavior to achieve optimal operation. From a practical point of view, both potential manipulated variables have operating constraints. The current density should not be larger than the current saturation value, for this system which is around 280 A/m² [2]. The base concentration has a larger operating range, but low concentrations are desired since that prolong the anion exchange membrane life time.

5. Conclusions

This paper illustrates how to perform a quantitative systematic analysis that lead us to select an appropriate manipulated variable to satisfy a specific control goal for a highly non-linear and dynamic system, when the selection is neither intuitive nor trivial. As case study, we have selected as goal the pH control at the end of the feed channel of the REED module. A defined operative window was explored using a dynamic model derived from first principles. The model describes the simultaneous transport of multiple ions across anion exchange membranes in a REED cell during lactate recovery from a fermentation broth. The solution of the system of multiregion partial differential equations was approximated numerically [2, 3, 4]. In this contribution, the pH model in the cultivation is highlighted including a pH buffer effect which was been experimentally validated [5]. A dimensionless pH sensitivity, towards $I_d$ and $C_{\text{in, dial}}$, was used as the quantitative criterion. The sensitivity was evaluated at a specific point within the periodic shifting of the imposed gradient polarity. The results show that pH can be controlled, during stationary operation, by both manipulated variables; especially around low current densities. However, pH has shown a considerably higher sensitivity towards current density in the first middle period point after a step change in the actuator. That behavior leads us to propose that the dynamic pH response can be controlled by manipulating the current density. Additionally, the base concentration in the inlet of the dialysate channel can control the stationary response since the $I_d$ operative window more narrow than for the $C_{\text{out, dial}}$. Our current investigation is focused on the control implementation.

References