OPTIMISATION AND CONTROL OF FED-BATCH YEAST PRODUCTION USING Q-LEARNING

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Helen Chuo Sin Ee
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ABSTRACT

OPTIMISATION AND CONTROL OF FED-BATCH YEAST PRODUCTION USING Q-LEARNING

In this work, the optimal production of yeast with minimal production of ethanol in fed-batch yeast fermentation is investigated. Q-learning (QL) is a heuristic approach suggested for the process dynamic handling to achieve the multiobjective optimisation. The QL agent interacts with the fermentation environment will gain experience on the state transitions, which are represented by the change of substrate, yeast, oxygen and ethanol concentration and the system volume. In the present study, multistep action (MSA) has been implemented in consideration of the inborn process delay for the substrate feeding to take effect on the yeast growth. Parameter deviated model has been implemented in the QL to test the robustness of the algorithm besides to identify the process disturbance. From the result, QL was able to perform multiobjective decision making for the optimal substrate feeding profile. The final yeast production using QL-optimised feeding profile is 20.86% higher compare to the nominal exponential feeding (EF), and 19.59% higher compare to EF with process disturbance. To cater for the process disturbance, Q-learning with exploration (QLE) has been included in this work for online optimisation. QLE signifies the importance of exploration from time to time based on the developed "past experience" in Q-table to optimise the process. The performance of QLE in both nominal and disturbance cases yielded 51.00% and 46.87% higher yeast production than EF respectively, while maintaining low ethanol production. In a nutshell, QL is an alternative that can be considered to perform multiobjective optimisation in a frequently changing bioenvironment and suggest a substrate feeding profile that satisfied the process goal. The QLE can cope better with the process disturbance.

ABSTRAK

Kajian ini membincangkan pengoptimuman produksi ragi di samping mengurangkan produksi etanol untuk fermentasi ragi semi kelompok. Pembelajaran-Q (QL) merupakan satu kaedah heuristik yang digunakan untuk mengatasi masalah dinamik sistem fermentasi bagi mencapai optimisasi berbilang objektif (multiobjektif) iaitu memaksimumkan produksi ragi dan meminimumkan penghasilan etanol yang menjejaskan qualiti ragi. Ejen pembelajaran berinteraksi dengan persekitaran proses fermentasi untuk menimba ilmu dan pengalaman mengenai keadaan peralihan sistem yang menggambarkan perubahan dalam kepekatan substrat, ragi, oksigen dan etanol, serta pertukuran isipadu sistem. Dalam kajian ini, tindakan berbilang langkah (MSA) telah diimplimentasikan menimbangkan kelewatan proses semula jadi yang menyebabkan pembekalan substrat lambat berkesan terhadap pertumbuhan ragi. Model yang berparameter terpesong juga telah diimplimentasikan di dalam QL untuk menguji keberkesanan dan kekukuhannya di samping mengidentifikasikan gangguan proses. Daripada keputusan kajian, QL berupaya berfungsi dalam penentuan profil pembekalan substrat optimum berdasarkan berbilang objektif. Produksi akhir ragi bagi QL dalam kes nominal mencapai 20.86% produksi lebih tinggi daripada pembekalan eksponen (EF), dan mencapai 19.59% produksi ragi lebih tinggi berbanding dengan EF bagi kes semasa gangguan proses berlaku. Demi menyelesaikan masalah gangguan proses, QL dengan eksplorasi (QLE) telah dikembangkan untuk pengoptimuman secara 'online'. QLE menunjukkan kepentingan eksplorasi lanjutan dari semasa ke semasa berdasarkan "pengalaman" dalam jadual-Q yang bagi mengoptimumkan proses fermentasi. Pencapaian QL dengan eksplorasi menunjukkan 51.00% dan 46.87% produksi ragi lebih tinggi berbanding dengan pembekalan eksponen dalam kes nominal serta kes ganguan proses masing-masing, sementara mengekalkan kepekatan etanol yang rendah sepanjang proses fermentasi. Secara keseluruhan, QL merupakan satu pilihan yang boleh dipertimbang untuk bertindak terhadap biopersekitaran yang kerap berubah dan menentukan pembekalan substrat yang memuaskan objektif-objektif proses. QLE juga menunjukkan prestasi yang lebih memuaskan walaupun di bawah pengaruh gangguan proses untuk mencapai pengoptimuman berbilang objektif.

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LIST OF ABBREVIATIONS

AI	Artificial Intelligence
ANN	Artificial Neural Network
CER	Carbon dioxide Evolution Rate
CPR	Carbon dioxide Production Rate
CSTR	Continuous Stirred Tank Reactor
DE	Differential Evolution
EA	Evolutionary Algorithm
EF	Exponential Feeding
FDA	Food and Drug Administration
FL	Fuzzy Logic
GA	Genetic Algorithm
GRAS	Generally Recognised As Safe
MDP	Markov Decision Process
MSA	Multistep Action
NBP	National Biotechnology Policy
OUR	Oxygen Uptake Rate
PI	Proportional-Integral
POMDP	Partial Observable Markov Decision Process
QL	Q-learning
QLE	Q-learning with Exploration
RL	Reinforcement Learning

LIST OF SYMBOLS

α	Learning rate
β	Weight of preference index of QL reward function
δ	Stoichiometric coefficient for hydrogen
γ	Discount factor
μ	Total specific growth rate
μ_{max}	Critical specific growth rate
μ_{cr}	Maximum specific growth rate
θ	Stoichiometric coefficient for nitrogen
ζ	Stoichiometric coefficient for oxygen
A	Action space
a'	Maximum rewarded action
a_t	Action at time t
C_e	Ethanol concentration
C_o	Oxygen concentration
C_o^*	Oxygen saturation coefficient
C_s	Substrate concentration
C_x	Yeast concentration
DO	Dissolved oxygen
F_0	Initial substrate feed flow rate
F	Substrate feed flow rate
K_e	Saturation constant for ethanol
K_i	Inhibition constant
$k_L a_o$	Mass transfer coefficient

K_o	Saturation constant for oxygen
K_s	Saturation constant for substrate
Q_C	Carbon dioxide production rate (CPR)
$Q_{e,max}$	Maximum oxidative ethanol metabolism
$Q_{e,ox}$	Respiratory ethanol consumption
$Q_{e,pr}$	Ethanol production rate
$Q_{e,up}$	Ethanol uptake rate
Q_o	Oxygen uptake rate (OUR)
Q_m	Cell maintenance
$Q_{o,lim}$	Oxidation capacity of yeast
$Q_{o,max}$	Maximum oxidation capacity of the yeast
Q_s	Substrate uptake rate
$Q_{s,lim}$	Limiting substrate flux
$Q_{s,max}$	Maximum substrate consumption rate of yeast
$Q_{s,red}$	Reductive glucose consumption
$Q_{s,ox}$	Oxidative glucose consumption
R	Reward function
RQ	Respiratory quotient
r_t	Reward generated from reward function at time t
S	State space
s'	Resulting state, s of maximum rewarded action, a'
S_o	Substrate concentration of the feed flow input
s_t	State at time t
T	State transition function
t	Time (s)

t_d	Time delay in substrate consumption
U	Input
V	Fermentation system volume
y	Output
$Y_{p/q}$	Yield coefficient of p over q
$Y_{o/s}^{ox}$	Oxidative yield coefficient of oxygen over substrate
$Y_{n/s}^{ox}$	Oxidative yield coefficient of nitrogen over substrate
$Y_{x/s}^{ox}$	Oxidative yield coefficient of biomass over substrate
$Y_{c/s}^{ox}$	Oxidative yield coefficient of carbon dioxide over substrate
$Y_{w/s}^{ox}$	Oxidative yield coefficient of water over substrate
$Y_{n/s}^{red}$	Reductive yield coefficient of nitrogen over substrate
$Y_{x/s}^{red}$	Reductive yield coefficient of yeast over substrate
$Y_{e/s}^{red}$	Reductive yield coefficient of ethanol over substrate
$Y_{c/s}^{red}$	Reductive yield coefficient of carbon dioxide over substrate
$Y_{w/s}^{red}$	Reductive yield coefficient of water over substrate
$Y_{o/s}^{eth}$	Oxidative yield coefficient of oxygen over substrate based on ethanol consumption
$Y_{n/s}^{eth}$	Oxidative yield coefficient of nitrogen over substrate based on ethanol consumption
$Y_{x/s}^{eth}$	Oxidative yield coefficient of biomass over substrate based on ethanol consumption
$Y_{c/s}^{eth}$	Oxidative yield coefficient of carbon dioxide over substrate based on ethanol consumption
$Y_{w/s}^{eth}$	Oxidative yield coefficient of water over substrate based on ethanol consumption

CHAPTER 1

INTRODUCTION

1.1 The Growing Importance of Fermentation in Bioindustry

In the 21st century, the remarkable growth in industrial biotechnology has represented the breakthrough of the efforts of bridging up the industrial science to the environment, without compromising the depleting natural resources. The development of the industry has been focusing more on the sustainability and value-adding to the production line, at the same time contributing to the competitiveness of existing industries.

The importance of bioindustry is proven in its globally growing development over the past 10 – 15 years and its ability to boost the economy of a country. The trend of increment in investment is bursting from United States to all around the world (Pefile, 2009; Strategic direction literature review, 2005). The chain reaction swifts towards the developing countries including India and China, who leverages the strength of trained manpower, cost-effective technologies, lower operational costs, and the richness in the raw materials. In Malaysia, since the launching of National Biotechnology Policy (NBP) in 2005, Malaysian government had provided a development framework for the implementation of biotechnology up to the highest investment dollars close to USD$ 300 million (RM 1 billion), as reported in the Malaysian Biotechnology country report 2009/2010.

The involvement of bioprocess, especially fermentation, covers up to a wide range of fields. As quoted in the SusChem agenda (2005), "Fermentation engineering is at the heart of industrial biotechnology." For example, fermentation offers strategies for sustainable management of degraded or contaminated sites and wastewaters. In the energy field, biofuel is the most promising future energy source as a constituent for the depleting fossil fuels. Meanwhile in agriculture, biocrops increase the production of edible food source to all mankind and living creatures while the world population keeps boosting up. In medical and healthcare production, yeast is involved in the production of enzymes, antibiotics and recombinant genes (El-Mansi *et al.,* 2007). Since yeast is the raw material for the fermentation process for many uses, the price of yeast can be skyrocketing, up to USD$ 2000/mg. Figure 1.1 shows the prices of various fermentation products with increasing process complexity.

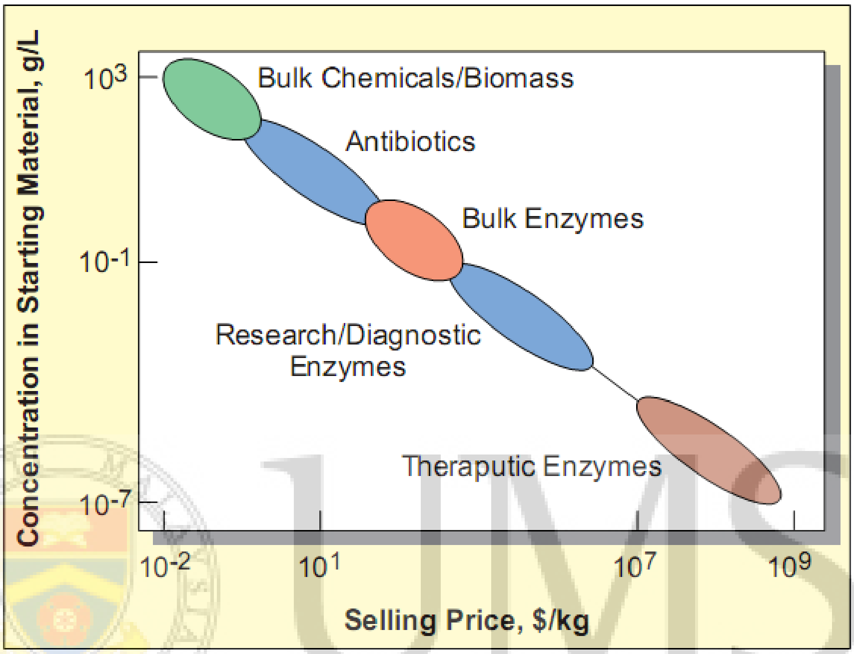

Figure 1.1: Correlation between product concentration and selling price for common fermentation products.

Source: Hoek *et al.* (2003)

In this work, the optimisation of the yeast production is of major concern. In industrial bioprocess, fed-batch operation is one of the most common modes of operation used to optimise the input stream in the fermentation process. The operation theories, the merits and the challenges of using fed-batch operation in yeast fermentation will be further discussed in Chapter Two.

Among the most studied yeast strains in microbiology, *Saccharomyces cerevisiae*, also known as the baker's yeast, is used for the studies of optimisation in this work. Research based on the fermentation of baker's yeast is very important as it serves as a benchmark for the fermentation of other yeast strains of similar metabolic behaviour. This yeast strain has achieved proven safety record in GRAS ('generally recognised as safe') for human consumption approved by US Food and Drug Administration (FDA) (Querol and Fleet, 2006), therefore it is widely utilised for all sorts of bioproductions.

1.2 Problem Statement and Rationale of the Study

Yeast fermentation process is highly nonlinear in nature due to the switching consumption and growth behaviour of yeast that causes difficulties in yeast production optimisation. Furthermore, the increasing yeast production could trigger the production of an unwanted product, i.e. ethanol production, which will toxify the fermentation system and inhibit the production of yeast. Unless the dynamic metabolic behaviour of yeast is well-captured and understood, the optimisation of such process can hardly be achieved. The optimisation strategies developed therefore has to base on multiobjective optimisation: to maximise yeast and minimise ethanol simultaneously when dealing with the metabolic behaviour of yeast.

Most feeding strategies that have been developed for yeast fermentation in the literature are based on: (i) the prior knowledge of the process, which heavily depends on the experience of the human operator to predetermine the feeding strategies, (ii) theoretical or empirical modelling of the process, including the first principle models, which is good for general predictions on the dynamic process response but insufficient for precise control and optimisation, (iii) stochastic searching and converging to optimisation, which requires strong algorithm computation and reasonable settings to seek for optimal but with less primitive knowledge regarding the process, and (iv) supervised learning of dynamic nonlinear process, whereby sufficient data training is essential. The major reason that unsupervised Q-learning (QL) is suggested in this work is to lessen the dependence on human operators for their inconsistent decision making to optimise this dynamic process, besides studying the potential and possibility of applying QL in yeast fermentation process optimisation. QL is able to self-decide for the optimal solution based on the process objectives and its "experience" through interactions with the