APPLICATION OF ESTIMATION TECHNIQUES TO BIOTECHNICAL PROCESSES

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ABSTRACT

It is acknowledged that to significantly improve biochemical system performance control should be implemented in real-time. Control algorithms, particularly modern control algorithms, require knowledge of the process dynamics and continuous measurement or detection of the system states and outputs. In many processes state variables cannot be measured on-line due, for example, to the non-availability of on-line sensors. Estimation techniques can be applied to estimate nonmeasurable state variables. Such techniques in general require the use of accurate system models.

In this thesis simplified yet nonlinear models of fed-batch and batch fermentation processes are presented. Details of modelling and simulation studies carried out on a Baker's Yeast fermentation process are included. Variations of the basic models are considered and tested using computer simulation with a view to evaluating the effect of different influences on the specific biomass growth rates.

Results presented using experimental data and computer simulation results indicate the validity of a number of estimation procedures including an observer, extended Kalman filter and an iterative extended Kalman filter. Adaptive recursive least squares is applied to identify the uncertain parameters which influence the growth phases of biomass (e.g. the yeast organism).

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I must especially thank Dr. Charles McCorkell, who gave me the time, space and the funding resources to complete this research.

DECLARATION

I hereby declare that this thesis is entirely of my own work under the supervision of Mr. Jim Dowling, Dr. Charles McCorkell and Dr Hugh McCabe and has not been submitted as an exercise to any other Universities.

Liang Tan

Liang Tan

DEDICATION

Dedicated to my parents and my wife.

NOMENCLATURE

A : system matrix of the linearized model.

C : bulk-liquid CO_2 concentraiton (g/l).

C_1 : dissolved CO_2 concentration (g/l).

CER : CO_2 evolution rate. (g/l·hr).

CTR : CO_2 transfer rate. (g/l·hr).

OUR : oxygen uptake rate. (g/l·hr).

OTR : oxygen transfer rate. (g/l·hr).

D : dilution rate. (hr^{-1}).

E : ethanol concentration in the broth. (g/l).

EPR : ethanol production rate. (g/l·hr).

ECR : ethanol concentration rate. (g/l·hr).

F : volumetric flow rate. (hr^{-1}).

H : Henry's constant for gases.

K : absolute temperature in Kelvin.

K_1 : $= 1/Y_{x/s}$.

K_2 : $= 1/Y_{x/o}$.

K_c : Contois' constant.

K_{c2} : constant of proportionally for cell mass production.

K_d : factor by which the volumetric absorption coefficient for CO_2 is greater than that of oxygen.

K_{O2} : saturation constant for dissolved oxygen concentration. (g/l)

K_{la} : mass transfer or absorption coefficient. (hr^{-1}).

Kp_o : ethanol consumption rate per unit volume.(g/l·hr)

K_s : Blackman's constant. (g/l)

K_{et} : rate limiting constants for ethanol.(g/l)

M : output matrix of the linearized model.

O_1 : saturation concentration of dissolved O_2 in the liquid.(g/l).

O : dissolved oxygen concentration in the liquid. (g/l).

P : filter covariance matrix.

R : gas constant.

S : substrate concentration. (g/l).

S_{fi} : substrate concentration in the influent.(g/l)

V : volume of liquid in the vessel. (l).

ζ_{max}: maximum ethanol production rate per unit volume.(g/l·hr)

X : biomass (cell) concentration. (g/l).

Y : output vector

$Y_{x/s}$: yield coefficient of biomass on substrate. (g/g).
$Y_{x/o}$: yield coefficient of O_2 on biomass. (g/g).

μ : specific growth rate. (g/g·hr).
μ_{max}: maximum of μ
θ : state vector.

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PART I INTRODUCTION

I– 1 Biotechnology

The science of biochemistry underlies all mathematical treatment of fermentation processes, particularly kinetics which is at the core of all dynamic models of bioreactors. Biochemistry is concerned with the particular types of chemical reactions found in all living organisms, and which underly all biological processes. The challenge in learning biochemical engineering is to understand and analyze the processes of biotechnology so that we can design and operate them in a rational way. To reach this goal however, a basic working knowledge of cell growth and function is required. [1][2]

Microorganisms grow by converting substrates (e.g. glucose) present in a liquid medium into cell mass (e.g. yeast) and possibly products such as alcohol and carbon-dioxide. Growth, which is characterised by an increase in cell mass, occurs only where certain chemical and physical conditions are satisfied, such as acceptable temperature and pH as well as the availability of required nutrients. For the development of mathematical models, however, the influence of temperature and pH are usually neglected because they are assumed constant and controlled during a fermentation run.[1]

Biotechnology is the application of microbiology, biochemistry and genetics. Most biotechnical processes consist of fermentation, oxidation and/or reduction of feedstuff by microorganisms such as yeasts or bacteria. Fermentation engineering has been widely applied to daily requirements, e.g., to produce penicillium chrysogenum, alcohol, beer and baker's yeast. The principle of fermentation processes can be simply described as follows: the micro-organisms (bacteria, fungi, yeast, etc) grow with the consumption of certain nutrients (carbon derivatives etc.) assuming that the environmental conditions (temperature, pH, agitation, aeration, etc) are favourable.

The aim of microbial growth is biomass production (e.g., antibiotics, pesticides methane, hydrogen, etc), biological depollution, i.e., consumption of certain polluting matters by the micro-organism.

Fermentation processes may be conveniently classified according to the mode chosen for process operation: either batch, fed-batch or continuous. [2][5]

* Batch : The liquid, microorganisms and substrate are all put into the vessel at the beginning of the batch run, and no further additions are made. Only environmental

variables such as temperature and pH value are manipulated during the batch-run.

* Fed-batch : This is similar to the batch process, except that substrates are fed continuously into the fermentor during the batch run.

* Continuous : With this method liquid substrates, synthetic products and microorganisms are continuously fed in and drawn off. The aim is to keep these variables in a steady state. (e.g., total concentrations of products, substrates and microbes in fermentor are kept constant).

Of these techniques, fed-batch poses the greatest challenge to the control engineer. In the fed-batch fermentation process the substrate is usually fed straight into the batch with dilution. Batch fermentation processes allow only trivial set-point control of temperature, pH value etc., while continuous fermentation allows its variables only to be kept at a steady state. However, in fed-batch the control engineer must devise an algorithm to obtain an optimal substrate feed-rate for a given control objective. In fed batch fermentation the variables directly controlled are usually substrate feed rate, agitator feed rate and aeration rate. Measurements are made of the composition of exit gas from the fermentor (partial fractions of carbon dioxide and oxygen) and dissolved oxygen concentration.[2][5] Note that none of the primary variables which concern the control engineer (cell growth rate and concentration of products in the liquid phase) are mentioned above. This highlights the non-availability of sensors which are capable of accurately measuring these variables. Thus estimation techniques must often be applied to obtain pseudo measurements of the main system states.

I– 2 Control Problems of Biotechnical Processes

In recent years it has been acknowledged that to significantly improve biotechnical process performance productivity and efficiency, or to reject noisy disturbances in process operation, control (including optimal control) should be implemented on-line. On-line control in a biotechnical process is usually based on the measurement of physical, chemical or biochemical properties and the manipulation of physical and chemical environmental parameters such as temperature, pH, dissolved oxygen and nutrient concentrations. It is very important to separate the control of biotechnical and environmental parameters because of the difference between them.[34]

The dynamics of a biotechnical process are usually multivariable, highly non-linear and more complicated than other chemical processes. It is difficult, for example, to develop reliable on-line models to describe every factor which influences the specific bacterial growth rate and yield coefficients which characterize microorganism growth in the fermentation process. Furthermore the parameters of such models are often uncertain.

Because of nonmeasurability of many important state variables, such as biomass and substrate concentrations, control problems are made more complicated. To apply any modern control method state variables and parameters must be measured or at least estimated on-line. The absence of suitable, accurate and reliable sensors for the measurement of these important process variables is the essence of the problem. As an aid to contributing solutions to the twin difficulties of complex dynamics and measurement difficulty a relatively simple mathematical model has been presented for the purposes of simulation and estimation algorithm evaluation.

I– 3 On-line State Estimation for Biotechnical Processes

The dynamics of biotechnical processes are usually difficult to describe so it is necessary to use relatively simple (non-linear) mathematical models instead of models embracing the complete dynamics of these processes. For the purposes of simulation simplifying assumptions are used in conjunction with real-time data collected from a pilot plant and the resulting models provide the basis for application of on-line estimation techniques. Simulation models are employed as a testing ground for all estimation algorithms.

Although the linear estimation problem with continuous time measurements has been solved many years ago, very few exact finite dimensional filters and observers have been discovered for non-linear problems. In this thesis, many estimation techniques, such as observers, extended Kalman filter and the iterative extended Kalman filter, have been successfully applied to fed-batch and batch fermentation processes. In most cases it is assumed that some of the nonmeasurable state variables are known and that then the others can be estimated on-line using the different techniques, based on prior knowledge of parameters, such as yield coefficients or growth rate μ. Many results have been derived using different models of the specific growth rate μ considering various influencing factors.

Estimation error can be significantly reduced through use of a high-order estimation technique if nonlinearities are sufficiently important.[29] The iterative extended Kalman filter can yield substantially better estimates of nonmeasurable state variables when a system is non-linear. In addition, the iterative filter can show a faster convergence because of improved approximation.

I– 4 Parametrization and Identification of Biological Processes

Parameter estimation techniques have had their greatest success with linear systems. Very few methods have been used successfully for identification of non-linear systems. In this thesis, an adaptive recursive least squares (ARLS) method has been applied to the identification of a biotechnical process. In practice, the procedure of system identification is iterative: when investigating a biotechnical process, which is non-linear and where a priori knowledge is poor, it is reasonable to start with transient or frequency-response analysis to get crude estimates of dynamics and the disturbances; the results can then be applied to plan further experiments. The data obtained are then used to estimate the unknown parameters in the model. Based on the results, the model structure can be improved and new experiments may be designed.

I– 5 Thesis Structure

Part II : The dynamics of fermentation processes are described. The specific growth rate μ is presented by considering different factors.

Part III : Non-linear state estimation problems are presented. A series of methods, such as observers, non-linear filters, extended Kalman filter, iterative extended Kalman filter, are developed to estimate unobserved quantities, such as biomass and substrate concentrations in the fermentation processes. This part is organised as follows.

Chapter 2 : A non-adaptive state estimation algorithm is used to estimate one of the nonmeasurable variables, assuming other state variables and the yield coefficients are known.

Chapter 3 : In the absence of prior knowledge of the parameters like the yield coefficients or growth rate μ, an adaptive observer algorithm is applied to estimate one of the nonmeasurable variables assuming other state variables can be measured on-line.

Chapter 4 : Assuming that the system is observable, a non-linear observer may be used to estimate one of the nonmeasurable variables assuming other quantities are known.

Chapter 5 : Assuming none of the state variables are known, the extended Kalman filter can be applied to the fermentation processes based on some known information in real-time, such as on-line measurements of oxygen and carbon-dioxide concentrations.

Chapter 6 : Assuming the nonlinearities of the processes are sufficiently important or if a long delay in the estimation cannot be permitted for a particular process, then the iterative extended Kalman filter can be applied.
rate instead of supposing any further model for the specific growth rate μ.

Part IV : Adaptive recursive least squares is developed for non-linear identification of biotechnical process parameters, such as yield coefficient $Y_{X/S}$, the maximum of the specifc growth rate μ and Blackman's constant K_S.

Part V : Conclusions and discussion on modelling, simulation, state estimation, and identification of the non-linear biotechnical processes.

Appendix A : A reported example of a non-linear filter is presented for estimation of parameters and states. It is usually easy to measure continuously the total oxygen utilization rate instead of supposing any further model for the specific growth rate μ.

PART II MODELLING AND SIMULATION OF THE FERMENTATION PROCESSES

Chapter 1 Introduction

In a baker's yeast process the basis of the reaction during fermentaion is metabolism. The metabolism is very similiar to metabolisms within other organisms. It is important to remember that every step in the metabolic conversion process is controlled by enzymes, and thus is described by the Monod equation. It is also important to realise that in a series chain of reactions, the slowest reaction determines the overall rate.[1]

The main substrates supplied by the organism to effect metabolic conversions are ATP (Adenosine diphosphate) and NADH (Nicotinamide adenine dinucleoide). These substrates supply much of the energy required to carry out the conversions. At the beginning of the metabolism, the substrate glucose (a type of sugar) is absorbed into the cell from the surrounding environment. With the aid of ATP, the glucose is converted into glucose-E-phosphate. This substance can enter two pathways, one of which recycles the substance. The other pathway leads to it's conversion into pyruvate. At this stage, two important branches in metabolism appear, both of which eventually lead to production of Acetyl-Coenzyme-A.

The intermediate and final pathways are important in the determination of the final product. Pathways lead to the production of ethanol and CO_2, which are released into the environment. Generally, in the presence of plentiful glucose, a large amount of pyruvate is formed. This in turn leads to saturation of the pathway leading to acetyle-CoA production and drives the excess pyruvate into production of large amounts of ethanol. The net result is that in the presence of excess glucose, ethanol accumulates in the environment.

If glucose levels are then brought down, the amount of pyruvate also decreases. This means that the cell looks to ethanol to produce the Acetyl-CoA needed by the metabolism. Thus in the absence of glucose, the available ethanol is consumed. However, since the first part of the metabolism is inactive in this mode, it is less efficient in promoting growth. In addtion, in the presence of excess glucose, the production of ethanol means that much of the glucose has been inefficiently converted to alcohol instead of cell mass.

The acetyl-CoA enters a cycle called TCA, the detailed of which are unimportant, save that CO_2 and NADH are produced. The NADH then enters into the so-called

Respiratory Chain (R.Ch). In this chain, O_2 is taken up, and ATP and water (H_2O) are released. Thus in the presence of oxygen, the respiratory chain deactivates and since the R.Ch is in series with the other main metabolic reactions, the oxygen level becomes growth-rate limiting. This leads to an effect similiar to the deficiency of glucose.

Overall, then the metabolism takes in glucose, oxygen and ethanol; to produce CO_2, H_2O, ethanol and cell growth.[1][2]

The baker's yeast fermentaion involved inputs : a yeast innoculum and the biomass growth medium. The innoculum was used to seed a production medium batch and incubated over 20 hrs. The actual production batch stage was the stirred aerated fermentation process under the condition of dilution rate D (for batch, D = 0) and was run in the 10-litre New Brunswick SF-116 pilot plant fermentor. The outputs of the process involved the oxygen and carbon-dioxide concentrations (on-line measurements) and substrate (glucose) and biomass concentrations (off-line measurements using the technique of dry weights for biomass and a sugar reducing test for levels of glucose). The experimental results provided the basis for validating the system model.

In this part, two mathematical models of the fed-batch and batch fermentation processes (baker's yeast) are presented. These system models are based on different models of the specific growth rate μ which is influenced by many factors such as pH, temperature, biomass and substrate concentrations. Several mathematical models exist at different cell levels and their environments. Many approaches have been tried arising from the difficulty of developing models covering every factor which can influence the specific bacterial growth rate and the yield coefficients which characterize microorganism growth.[2][3] The reproduction of experiments are often uncertain because of the twin difficulties of unobservability of the important process state variables and the complex dynamics of the process. The improvement of these mathematical models depends on gathering more and better experimental data.

In order to solve the model equations classical first order *Euler* and a fourth order *Runge-Kutta* computer algorithms were used for the integration of the non-linear differential equations. The state models include the various nonlinearities of the processes.

Chapter 2 Dynamics of Fermentation Processes

2.1 Modelling of Kinetics

Kinetics, in chemistry, deals with the behaviour of chemical systems when reactants come together and react to give rise to products. Since these reactions are the fundamental activities by which changes in biochemical systems (e.g. microorganisms) occur (such changes include growth in cell concentration and product concentration), the laws governing the kinetics of biochemical reactions form the basis of all mathematical models of reactors, including fermentors.[2]

From knowledge of the metabolism a mathematical description of uptake of substrates and their utilisation within the cell can be developed.[6] In addition to the substrate (glucose), aerobic bakers-yeast fermentation also utilizes oxygen dissolved in the liquid to enable growth. A model of usage of dissolved oxygen is presented.[6] In addition to extra cell mass/growth, the products of baker's yeast [5] are a type of ethanol and CO_2. The modelling of formation and utilisation of these products is also considered.

2.2 Basic Dynamical Models of Bioreactors

The dynamics of the process are described by a series of expanded models. In fact, a fed-batch, batch or continuous culture of baker's yeast, can be described in fully aerobic conditions by the non-linear models described in the following section. [3][4]

2.2.1 Cell Mass (Biomass X):

The microorganisms or biomass concentration are the main feature of a fermentation affecting the growth rates, substrate consumption and product formation. The intereaction of the microorganism with its environment is a complex one. The following model will be employed to characterise the biophase in order to model cell population kinetics. The nett rate of cell mass growth r_X is often written as [6]

$$r_X = \mu(t)\cdot X(t). \qquad \textbf{(2.2–1)}$$

where $\mu(t)$ is the specific growth rate of cells (hr^{-1}). X(t) is the cell mass per unit culture volume (g/l). For a fermentation process a useful definition of the dilution rate in which the culture is being diluted at a rate D(hr^{-1}) has been given, allowing a mass balance using the above model giving:

$$dX(t)/dt = [\mu(t) - D(t)]\cdot X(t); \qquad \textbf{(2.2–2)}$$

$$D(t) = F(t)/V(t); \qquad \textbf{(2.2–3)}$$

where F(t) is the volumetric feed flowrate of input substrate (hr^{-1}) and V(t) is the culture volume (litre). Section 2.3 will discuss $\mu(t)$ in detail.

2.2.2 Substrate Utilisation (S)

The substrate (e.g., glucose) concentration (S, (g/l)), which is usually the growth-limiting factor, is used to synthesise new cellular and extracellular products and also to provide the energy necessary to drive the reactions for microorganisms. Thus growth and substrate utilisation are both closely related. For a fed-batch fermentation process the model of the substrate consumption can be presented as follows:

$$dS(t)/dt = -K_1 \cdot \mu \cdot X(t) + D(t) \cdot [S_{fi} - S(t)]; \qquad (2.2\text{-}4)$$

where S_{fi} is the substrate concentration in input. K_1 is a yield coefficient of cell mass on substrate. If a yield factor is approximately constant for a particular cell cultivation system it provides useful knowledge of biomass and substrate concentrations.[5]

2.2.3 Fermentor Volume of the Growth Culture (V) :

The model of fermentor volume (V, (litre)) of the growth culture can be described as follows:

$$dV/dt = F_{in} - F_{out}; \qquad (2.2\text{-}5)$$

where F_{in}, F_{out} are the volumetric flowrates of input and output flows respectively. The differentoperating conditions for a fermentor, e.g., batch, fed-batch and continuous operations are treated as follows: [3]

Batch :

The fermentor in a batch condition is a reactor without inflow and outflow:

$$F_{in} = F_{out} = 0; \qquad (2.2\text{-}6)$$

A large amount of substrate and a small amount of biomass are initially filled into the fermentor. During fermentation no substrate is produced, only biomass (cell mass) is produced. The culture volume is constant with D = 0.

Fed-batch :

The fermentor in a fed-batch condition is a reactor without outflow:

$$F_{out} = 0; \qquad (2.2\text{-}7)$$

A small amount of substrate and biomass are firstly contained in the fermentor and augmented with the influent substrate.

$$F(t) = D(t) \cdot V(t); \qquad (2.2\text{-}8)$$

Continuous :

In a continuous cultivation of microorganisms, the reactor is continuously fed with the substrate influent. The rate of outflow is equal to the rate of inflow, and the fermentor is filled in order to keep the volume of culture constant:

$F_{in} = F_{out} = F = \text{Constant}$; (2.2-9)

$dV/dt = 0$; (2.2-10)

$D(t) = F/V$; (2.2-11)

2.2.4 *Oxygen Uptake Rate (OUR)*

The dissolved oxygen is similar to substrate utilization since the substrate reaction occurs by oxygen reaction. The oxygen level in the environment is also a growth-limiting factor. Only oxygen dissolved in the liquid and not in gaseous state can be utilized by the cells.

The rate at which oxygen is taken up by the cells from the liquid is assumed proportional to the cell mass growth rate and is called the oxygen uptake rate OUR (g/l·hr).

$OUR = -1/Y_{X/O} \cdot dX/dt = -\ K_2 \cdot dX/dt$; (2.2-12)

where $Y_{X/O}$, K_2 is the yield coefficient of oxygen on biomass.

The rate of change of dissolved oxygen concentration is presented by

$dO/dt = OUR + OTR$; (2.2-13)

where OTR is the Oxygen Transfer Rate (g/l·hr), i.e. the rate at which oxygen is transfered from air bubbles within the fluid into the dissolved state. The OTR will be discussed in detail in Section 2.2.6.1.

2.2.5 *Carbon-Dioxide Evolution Rate (CER)*

During the fermentation carbon-dioxide (CO_2) is produced or evolved by the cell as well as ethanol. This carbon-dioxide is secreted by the cell and becomes dissolved in the liquid. The CO_2 produced is assumed proportional to the cell-mass produced, i.e. the growth-rate. Thus the CER (g/l·hr) is presented by

$CER = K_{C2} \cdot \mu \cdot X$; (2.2-14)

K_{C2} is the constant of proportionally for cell mass production.

Overall the level of dissolved-CO_2 is described by

$dC/dt = CER + CTR$; (2.2-15)

where CTR is the rate at which CO_2 is transferred from the air bubbles in the fluid into the dissolved state. CTR will be introduced in Section 2.2.6.2.

Although the growth rate is not directly affected by the dissolved CO_2, it is important to model the amount of dissolved-CO_2 because measurements of the CO_2 concentration in the exit gas can be related to dissolved CO_2 levels.

2.2.6 Modelling of Transport

Whether transport becomes important depends on the magnitude of the rate of transport compared to the rate of reaction. [2] If the rate of transport (i.e. the rate at which some substance is transferred to the area of interaction) is of similiar or lesser magnitude than the rate of reaction (the rate at which that substance is taken up by the reaction) then, because the transport mechanism is in series with the reaction mechanism, the rate of transport becomes a rate-determining-step. If, on the other hand, the transport rate is faster than the rate of reaction, then there will always be substance available for reaction and transport effects can be neglected.

Substrate fed into the fluid becomes dissolved immediately, unlike gases which are held in air bubbles before dissolving. Since it is a reasonable assumption that the rate of transfer of substrate from the dissolved state into the inside of the cell is rapid compared to the rate at which the substrate is used, the transport of substrate (i.e. glucose) is ignored in the model.

In this section a comprehensive model of transport of O_2 and CO_2 from gas (air bubbles) to liquid (dissolved) state will be introduced.

2.2.6.1 Oxygen Transfer Rate (OTR) and K_{la}

In an aerobic fermentation, the supply of oxygen into the broth must be sufficient to meet the demand of the organisms. The volumetric oxygen transfer rate (OTR, g/l·hr) is given by the equation

$$OTR = K_{la} \cdot (X_{O_2} \cdot O_1 - O\ ); \qquad (2.2\text{–}16)$$

where K_{la} = mass transfer coefficient (hr^{-1}).
$X_{O_2} \cdot O_1$ = dissolved oxygen in the fermentor.
X_{O_2}= the partial fraction of O_2.
O_1 = saturation concentration of dissolved O_2 in the liquid.(g/l)

***K_{la}* :**

Equation (2.2–16) contains the term K_{la}, or volumetric absorption coefficient for oxygen, the same as equation (2.2–19). This term is highly variable, depending principally on air flow rate (aeration) into the fermentor, and agitation rate (the rate at which the fermentor stirrer revolves).

Many methods can be used to estimate K_{la}. One of the techniques usually referred to as the dynamic technique, estimates K_{la} from dissolved oxygen measurements during transient conditions. The technique involves errors due to the dynamic response of the dissolved oxygen probe which itself is affected by the resistance to the liquid film which covers the membrane. The dissolved oxygen may not be consistent in the broth, unless it is well mixed.[7]

The transient conditions may be initiated by changing the air flow rate or the stirrer speed.

The solubility of oxygen in aqueous media is small compared with the oxygen requirements of a culture. The solubility is affected by the partial pressure of oxygen, temperature and other solutes in the medium.[7]

The partial pressure is also called oxygen tension and is related to the equilibrium oxygen consumption ($X_{O_2} \cdot O_1$) by Henry's law

$$X_{O_2} \cdot O_1 = H \cdot P_g \; ; \qquad \textbf{(2.2–17)}$$

where H is Henry's constant.

P_g is the oxygen pressure in the gas phase.

The value of ($X_{O_2} \cdot O_1$) in pure water at 1 atmosphere can be evaluated by the equation (Truesdale [8])

$$X_{O_2} \cdot O_1 = 14.16 - 0.3943T + 0.007714T^2 - 0.00006467T^3; \qquad \textbf{(2.2–18)}$$

where T is the temperature in $^\circ$C.

2.2.6.2 Carbon-Dioxide Transfer Rate (CTR)

Carbon-dioxide transfer rate CTR (g/l·hr) can be developed in exactly the same way as OTR given in section 2.2.6.1. The similiar equation for carbon-dioxide transfer rate CTR can be written:[9]

$$CTR = K_d \cdot K_{la} \cdot (X_{co_2} \cdot C_1 - C); \qquad \textbf{(2.2–19)}$$

where $X_{co_2} \cdot C_1$ is the bulk-liquid concentration of CO_2 that is in equilibrium with the bulk gas, C is the bulk-liquid CO_2 concentration, and K_d is the factor by which the volumetric absorption coefficient for CO_2 is greater than that for O_2. X_{CO_2} is the partial fraction of CO_2. C_1 is the dissolved CO_2 concentration.

2.2.7 *Respiratory Quotient (RQ)*

RQ is an excellent indicator of the cells' physiological condition. For example for the baker's yeast fermentation.[7]

(1) $RQ > 1.05$ indicates ethanol production
(2) $1.05 > RQ > 0.9$ indicates oxidative growth
(3) $0.9 > RQ > 0.7$ indicates endogenous metabolism
(4) $RQ > 0.6$ indicates ethanol utilisation

Knowing the oxygen uptake rate and carbon-dioxide evolution rate, the respiratory quotient may be evaluated from

$$RQ = CPR/OUT; \qquad \textbf{(2.2–20)}$$

2.2.8 *Ethanol Production and Consumption*

A major cause for a decline in cellular yield in a yeast fermentation is the formation of ethanol which may occur due to oxygen limitation (Pasteur effect) and/or high sugar concentration (Crabtree effect).[10] To examine the ethanol (E) production and consumption effects, the metabolism should be included by both absorption of glucose to the production of alcohol (the ethanol production rate EPR (g/l·hr)) and the consumption of alcohol to the production of H_2O (the ethanol consumption rate ECR (g/l·hr)).

The ethanol is produced when excess substrate causes one branch of the metabolism to be saturated, and the branch which produces ethanol to activate (Crabtree Effect). The rate at which ethanol is produced depends on the level of glucose as well as on the cell mass. However, the presence of ethanol in the medium inhibits the further production of ethanol. At low concentrations, this effect is negligible, but at higher concentrations inhibition becomes significant. This effect can be incorporated in an overall EPR equation by: [1][5]

$$EPR = [\zeta_{max}/(1+E/K_{et})]\cdot[S/(K_S + S)]; \qquad \textbf{(2.2–21)}$$

where ζ_{max} = the maximum ethanol production rate per unit volume.(g/l·hr)
K_{et} = a rate limiting constant for ethanol. (g/l)
E = the ethanol concentration.
K_S = Blackman's constant.

Ethanol consumption occurs when ethanol acts as a substrate, cutting out the part of the metabolism that acts on glucose. Thus the consumption rate depends on ethanol concentration, and also on oxygen as a rate-limiting substrate since oxygen consumption occurs in series with ethanol consumption :[1][5]

$$ECR = [K_{po} \cdot O/(O+K_{o_2})] \cdot [E/(K_{et}+E)]; \qquad (2.2\text{–}22)$$

where K_{po} = the maximum value of ethanol consumption rate per unit volume. (g/l·Hr)

K_{o_2} = the saturation constant for dissolved oxygen.

The overall ethanol concentration is described by

$$\begin{aligned} dE/dt &= EPR - ECR; \\ &= [\zeta_{max}/(1+E/K_{et})] \cdot [S/(K_s+S)] - \\ &\quad [K_{po} \cdot O/(O+K_{o_2})] \cdot [E/(K_{et}+E)]; \end{aligned} \qquad (2.2\text{–}23)$$

In the above model (in section II–3) there are two nonmeasurable state variables: biomass (X), substrate (S) and four measurable variables: oxygen concentration (O), carbon-dioxide concentration (C), ethanol concentration (E).

2.3 The Specific Growth Rate (μ)

The specific growth rate μ (g/g·hr) is the key parameter for the description of biomass growth, substrate consumption and products formation. μ is time-varying and is influenced by many physico-chemical and biological environmental factors. The general goal in making a good medium is to support good growth of biomass and/or high rates of product synthesis such as alcohol production depending on the type of fermentation in progress. This does not mean that all nutrients should be supplied in great excess. For one thing, excessive concentrations of a nutrient can inhibit or poison cell growth. Moreover, if the cell grows too extensively their accumulated metabolic end product will often disrupt the normal biochemical processes of the cell. Consequently it is common practice to limit total growth by limiting the amount of one nutrient in the medium. The control of the specific growth rate by limiting substrate concentration in the broth is often critical to a process. [1][3]

2.3.1 Monod's Model

Monod's model of cell growth can be presented by [11]

$$\mu(S) = \mu_{max} \cdot S/(K_s + S); \qquad (2.3\text{–}1)$$

where μ = the specific growth rate.

Monod's model is found to be generally the most applicable. It forms the basis for the modelling of all enzyme-based aspects of the fermentor model used in the simulation in this thesis because it is simple and fits the experimental results very well in most cases.

In a high substrate concentration, the specific growth rate reaches a maximum level beyond which further increases have no effect. This is due to saturation of enzyme activity i.e. all the enzyme is being fully utilized, and there is no spare capacity to cope with further increases in substrate concentration.

In a relatively low substrate concentration, the specific growth rate increases linearly with substrate concentration. This is because there is plenty of spare enzyme for additions of substrate to react with.[11]

2.3.2 Ollson's Model

As consideration of the metabolism demonstrates, oxygen levels in the environment can be a growth-limiting factor, in the same way as glucose. In such cases, the dissolved-oxygen in the liquid can be used by the cell. Thus the dissolved oxygen in the culture medium can be considered an additional substrate and it can be shown that when two substrates are rate-limiting in a single enzyme-controlled reaction series, then the overall specific growth rate is refered as the Ollson's model, which is the product of the individual rates.[11]

$$\mu(S,O) = \mu_{max}\cdot[S/(K_s + S)]\cdot[O/(K_{O_2}+O)]; \qquad (2.3\text{–}2)$$

2.3.3 Contois' Model

The specific growth rate μ of biomass production and substrate inhibition kinetics is also presented by a combination of Contois' kinetics [12]

$$\mu(S,X) = \mu_{max}\cdot S/(K_c.X+S); \qquad (2.3\text{–}3)$$

where

K_c = the Contois' constant

Both biomass and substrate concentration are considered in Contois' model. The biomass growth is often presumed to slow down at high biomass concentration and this has been experimentally observed in particular instances.

Chapter 3 Computer Simulation of Fermentation Processes

3.1 Introduction

To study the dynamics of the process and to facilitate future controller design, the model of the biotechnical process was simulated on a digital computer using numerical integration techniques. The principle of all numerical integration methods is to compute the system states at time (t+Δt) given the state at time t where Δt is the sampling period [25]. For a general state equation of the form,

$$\dot{\theta} = f(\theta,\ u,\ t); \qquad (3.1\text{–}1)$$

At each step computations are performed using some algorithm normally based upon a Taylor series expansion of (3.1–1);

$$\theta(t+\Delta t) = \theta(t) + \Delta t\cdot\dot{\theta}(t) + (\Delta t)\cdot 2/2!\cdot\ddot{\theta}(t)\cdots\cdots \qquad (3.1\text{–}2)$$

If Δt is chosen to be sufficiently small and if sufficient higher order derivatives of θ and powers of θ are taken, then the value θ(t+Δt) can be accurately found, and thus the equation (3.1–1) can be solved iteratively. In practice an algorithm based on an approximation to (3.1–2) must be used.

The dynamic models of a fed-batch and batch fermentation processes have been previously described in detail in this work [Chapter 2]. A classical first order *Euler* approximation and a fourth order *Runge-Kutta* approximation are chosen for integrating the non-linear differential equations. The state models include the various non-linearities.

The advantages of simulating the dynamics of a non-linear system are great : e.g., having a virtual non-linear system allows one to try experimental control algorithms. It is convenient optimising controllers and improve the real system performance. Also, It is the basis of applying the estimation techniques.

3.2 Euler Approximation

The *Euler* method is the simplest. For equation (3.1–2), only a first power of Δt is considered assuming the terms in Δt^n (n > 1) are very small compared to Δt. This is valid only if Δt << 1. The *Euler* method has the form,

$$\theta(t + \Delta t) = \theta(t) + \Delta t\cdot f(\theta,\ u,\ t); \qquad (3.2\text{–}1)$$

Applying a simple *Euler* approximation to the process model, the equations (2.2–2), (2.2–4), (2.2–5), (2.2–12), (2.2–13), (2.2–14), (2.2–15), (2.2-16), (2.2–19), (2.2–21), (2.2–22), (2.2–23), (2.3–1), (2.3–2), (2.3–3) have the following forms:

3.2.1 System Model

Biomass:

$$X(k+1) = X(k) + \Delta t\cdot\mu\cdot X(k) - \Delta t\cdot D(k)\cdot X(k); \tag{3.2–2}$$

Substrate :

$$S(k+1) = S(k) - K_1\cdot\Delta t\cdot\mu\cdot X(k) + [\Delta t\cdot D(k)\cdot(S_{fi} - S(k))]; \tag{3.2–3}$$

Volume of Fermenter :

$$V(k+1) = V(k) + \Delta t\cdot(F_{in} - F_{out}); \tag{3.2–4}$$

$$F_{in} = D\cdot V(k);$$

$$F_{out} = 0\ ; \quad \text{(in Fed-batch)}$$

Oxygen :

$$O(k+1) = O(k) + \Delta t\cdot(OUR + OTR); \tag{3.2–5}$$

$$OUR = -K_2\cdot(\mu - D)\cdot X(k); \tag{3.2–6}$$

$$OTR = K_{la}\cdot[X_{o_2}\cdot O_1 - O(k)]; \tag{3.2–7}$$

Carbon-Dioxide :

$$C(k+1) = C(k) + \Delta t\cdot(CER + CTR); \tag{3.2–8}$$

$$CER = K_{c_2}\cdot\mu\cdot X(k); \tag{3.2–9}$$

$$CTR = K_d\cdot K_{la}\cdot[X_{co_2}\cdot C_1 - C(k)]; \tag{3.2–10}$$

Ethanol:

$$E(k+1) = E(k) + \Delta t\cdot X(k)\cdot(EPR - ECR); \tag{3.2–11}$$

$$EPR = [\zeta_{max}/(1 + E(k)/K_{et})]\cdot[S(k)/(K_s + S(k))]; \tag{3.2–12}$$

$$ECR = [K_{po}\cdot O(k)/(O(k) + K_{o_2})]\cdot[E(k)/(K_{et}+E(k))]; \tag{3.2–13}$$

3.2.2 The Specific Growth Rate μ :

Monod's model :

$$\mu(k) = \mu_{max}\cdot S(k)/[K_s + S(k)]\ ; \tag{3.2–14}$$

Ollson's model :

$$\mu(k) = \mu_{max}\cdot[S(k)/(K_s + S(k))]\cdot[O(k)/(K_{O_2} + O(k)]; \qquad \textbf{(3.2–15)}$$

Contois' model :

$$\mu(k) = \mu_{max}\cdot S(k)/[K_c\cdot X(k) + S(k)]; \qquad \textbf{(3.2–16)}$$

These discretized equations were successfully simulated by computer. The simulation programme structure will be described in section **3.4.** This gives an overview of the simulation programme implemented. This routine (Fig 3.4.1) is called periodically at times determined by the integration interval. An integration interval of 0.05 hours is found to be adequate. The value of each state is printed out to a data file at periods of 10 minutes.

3.3 The Runge-Kutta Technique

The *Runge-Kutta* methods attempt to obtain a more accurate approximation to Taylor's expansion **(3.1–2)**, while avoiding the need for higher derivatives, by evaluating the function f(θ, u, t) in **(3.1–1)** at selected points within each integration interval. The simplest *Runge-Kutta* algorithm (fourth-order) is presented here.

Again for a general equation **(3.1–1)** the formula for advancing the solution step is:

$$\theta_{n+1} = \theta_n + 1/6\cdot(K_1 + 2K_2 + 2K_3 + K_4); \qquad \textbf{(3.3–1)}$$

Assuming : $\alpha = f(\theta, u)$, $\alpha(\theta_0) = \alpha_0$;

where

$$K_1 = \Delta t\cdot f(\theta_0, \alpha_0) \qquad \textbf{(3.3–2)}$$

$$K_2 = \Delta t\cdot f(\theta_0+\Delta t/2, \alpha_0+ K_1/2); \qquad \textbf{(3.3–3)}$$

$$K_3 = \Delta t\cdot f(\theta_0+\Delta t/2, \alpha_0+ K_2/2); \qquad \textbf{(3.3–4)}$$

$$K_4 = \Delta t\cdot f(\theta_0+\Delta t/2, \alpha_0+K_3); \qquad \textbf{(3.3–5)}$$

The *Runge-Kutta* algorithm does not require calculation of the higher derivatives of θ as is indicated in the Taylor series method. For the fermentation process model f(θ, u, t) at various points can be calculated based on this algorithm.

3.4 Structure of the Simulation Programme

The simulation programme flow-chart is shown on Fig 3.4.1. The programme is written using C language on PC-proturbo 386 computer. The routine (Fig 3.4.2) is called periodically at times determined by integration interval. This routine calls a further routine (deriv) which returns the values of the derivatives of the state, as given by the differential equations of the model. Based on the experimental data from the pilot plant an integration interval of 0.05 hours for simulation is found to be adequate, and the value of each state is printed out to a data file at periods of 10 minutes. A total run-time can be chosen in terms of each simulation. The flow-charts (Fig. 3.4.2. and Fig 3.4.3) gives an overview of the simulation programme implemented. The data is then plotted as shown in Chapter 5.

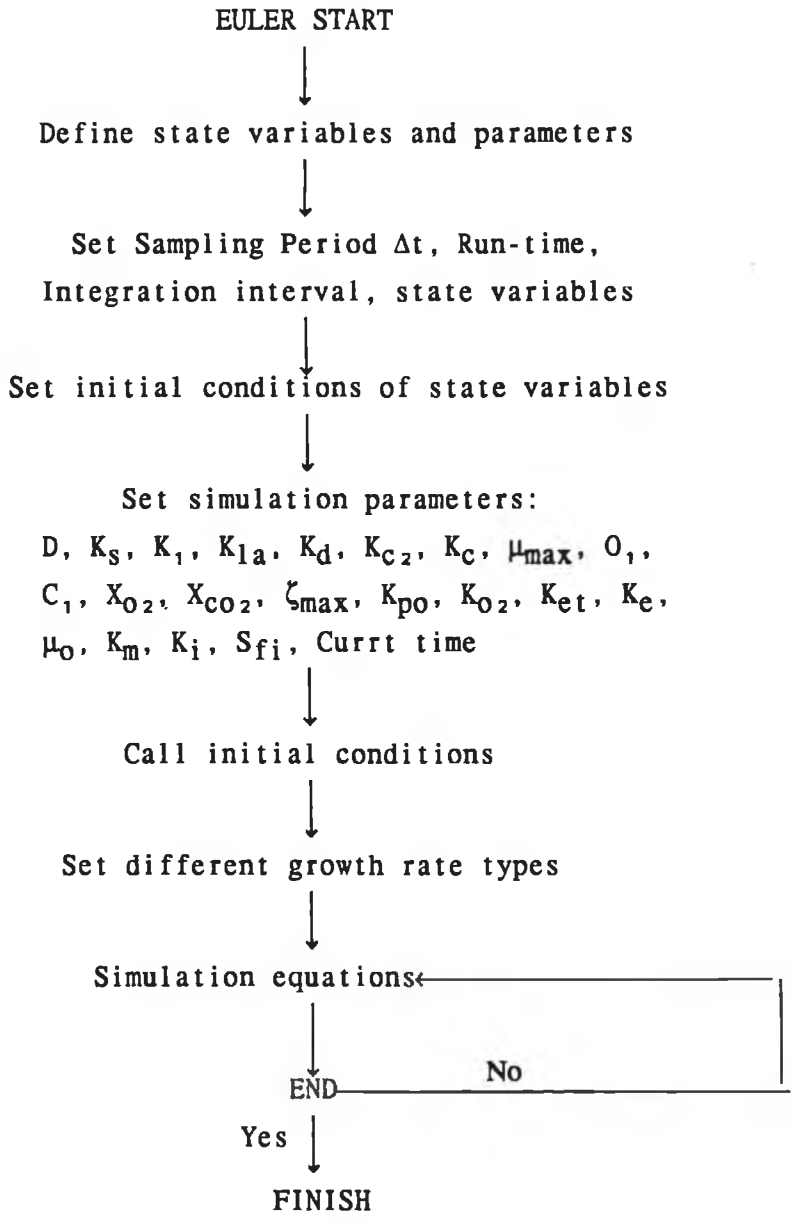


Fig 3.4.1. Euler Program Flow-chart

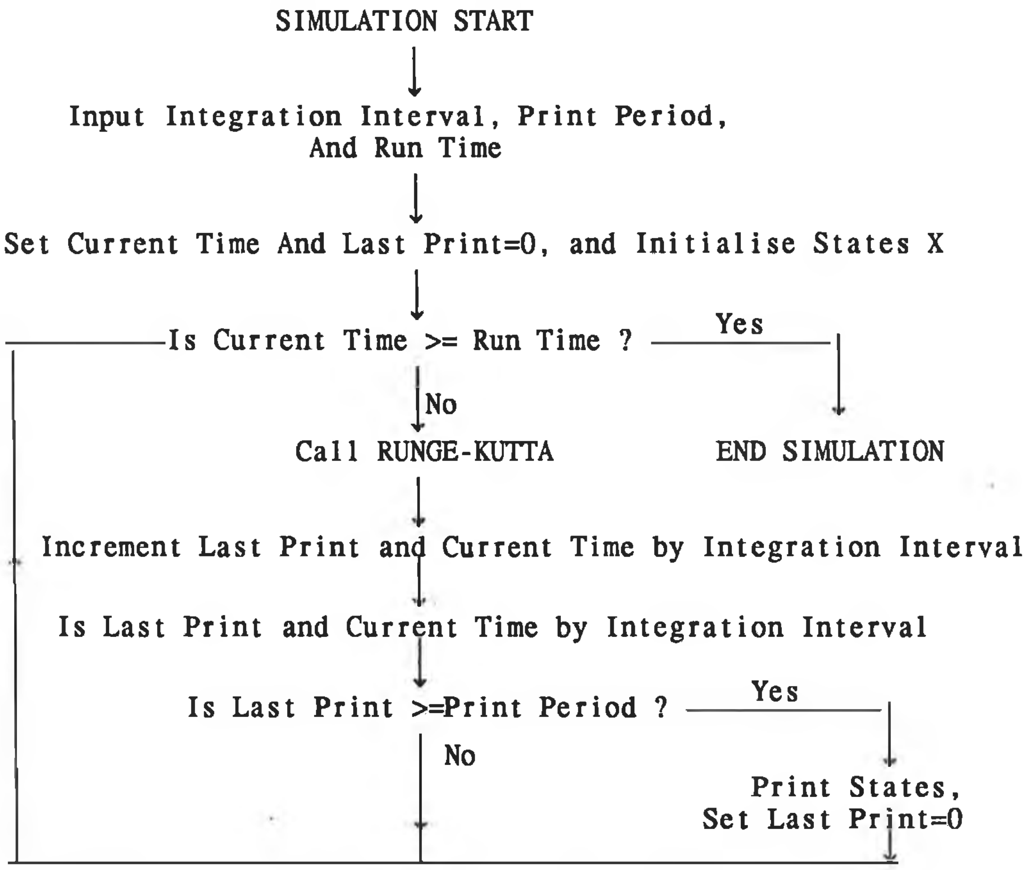


Fig 3.4.2. Runge-Kutta Simulation Flow-chart

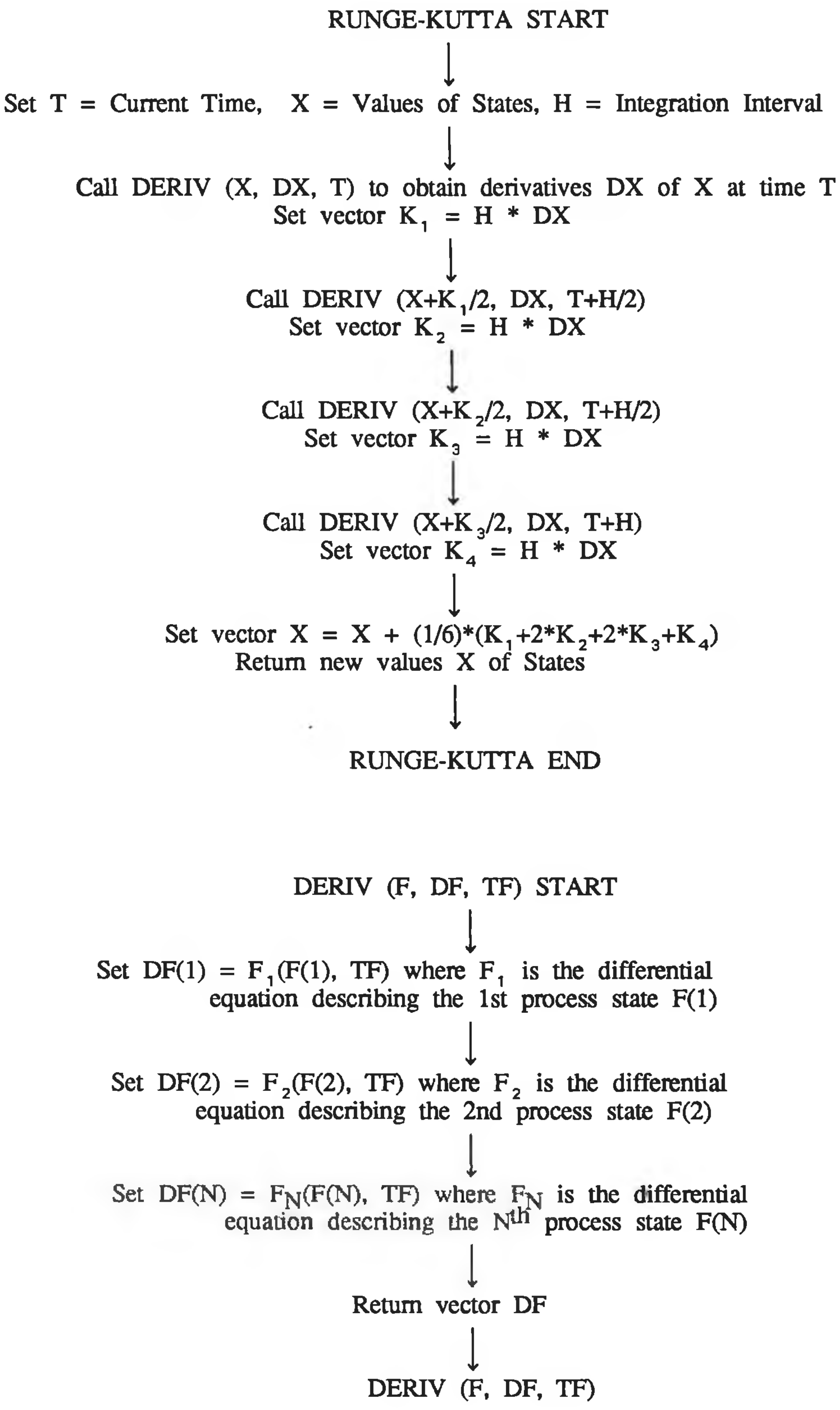


Fig 3.4.3. A 4th-order Runge-Kutta Subroutine Flow-chart

Chapter 4 Summary and Comments

Basically, the fermentation processes considered are multi-input multi-output, batch or fed-batch processes. The inner dynamics of these processes are always time-varying. It's difficult to develop models taking into account the numerous factors which can influence the specific bacterial growth rate and the yield coefficients which characterise micro-organism growth.

The simulation results have demonstrated here that computer simulation can be successfully applied to a biological process, which is a complex non-linear system, in order to assess the bioreactor model's accuracy and to facilitate controller appraisal. Although many important system variables cannot be measured on-line directly estimation methods based on simulation technique can be applied to solve this problem, and the basis of such method is to run computer models of the system in real-time.

The *Euler* method is of limited practical use due to its large truncation error per step of order Δt^2. This is exaggerated when a large step length Δt is used. The *Euler* method would satisfy most requirements only if using small step Δt. But it always remains strongly dependent on the sample period. The selection of Δt is based on the simulation results and the experimental data from a pilot plant.

The *Runge-Kutta* method attempts to obtain greater accuracy then the *Euler* method but without requiring the calculation of the higher derivatives of θ in the Taylor series. From the simulation results in this part of work, both of the *Euler* and *Runge-Kutta* can be applied to a biotechnical process while *Euler* method is much more simpler.

Arising from the results obtained in this part of the work a paper on computer simulation techniques was presented by the auther at the IECON'91 International Conference on Industrial Electronics, Control and Instrumentation, which was held in Kobe, Japan from October 28 to November 1, 1991.[52]

Chapter 5 Simulation Results (I)

Experimental data from previous work by Comferford [54] was used for model parameter "tunning". This data was obtained from a baker's yeast fermentation as follows. The baker's yeast fermentation involved inputs: a yeast innoculum and the biomass growth medium. The innoculum was used to seed a production medium batch and incubated over 20 hrs. The actual production batch stage was the stirred aerated fermentation process under the condition of dilution rate D (for batch, D=0) and was run in the 10-litre New Brunswick SF-116 pilot plant fermentor. The outputs of the process involved the oxygen and carbon-dioxide concentrations (on-line measurements) and substrate (glucose) and biomass concentrations (off-line measurements using the technique of dry weights for biomass and a sugar reducing test for levels of glucose). The experimental results provided the basis for validating the system model.

The dissolved O_2 probe (New Brunswich SS 900 and DO-50 transmitter) when connected to its measuring instrument has a 0— 100 % output range, with 100% corresponding to a saturation level of 0.5 g/l. This saturation level is based on the saturation level of dissolved O_2 in distilled water at 30^{0}C.[1][2]

An analyser SS206 (Manufacturer's name) was used to monitor CO_2 levels in the exhaust gas stream between 0 — 100%. For comparison with simulation values, 100% CO_2 was taken as 0.4 g/l. The exhaust gas for CO_2 measurement was first passed through a drying column containing calcium chloride to remove excess moisture before entering the infra-red analyser.

The results of modelling and simulation of a batch fermentation process will be shown in this chapter.

The same initial conditions and parameter values was used for both of the Euler and Runge-Kutta methods. These initial conditions and parameter values were chosen to tune the simulation model (in each case) to the experimental data.

5.1 Euler's method:

Fig 1 to Fig 6 show the simulation experimental results of specific growth rate (μ), biomass (X), substrate (S), the volume of growth culture (V), dissolved oxygen concentration (O) and exhaust CO_2 concentration (C) under the following conditions:

(i) Common Initial Conditions :

$X(0)=0.35$ g/l; $S(0)=12.2$ g/l; $V(0)=3.0$ l; $O(0)=0.18$ g/l ; $C(0)=0.07$ g/l; $\mu(0)=0.06$ g/g·hr.

(ii) Parameters:

$D=0.0$; $K_s=0.8$; $K_1=2.0$; $K_2=1.0$; $K_{la}=2.0$; $K_d=0.4$; $K_{c2}=1.15$; $K_c=0.5$; $\Delta t=0.05$; $\mu_{max}=0.03$; $O_1=0.3$; $C_1=0.10$; $X_{o2}=2.50$; $X_{co2}=0.0033$; $\zeta_{max}=0.15$; $K_{po}=0.05$; $K_{o2}=0.006$; $K_{et}=71.5$; $K_e=0.5$; $\mu_o=0.4$; $K_m=0.4$; $K_i=2.5$; $S_{fi}=12$; Currt= 0.0.

5.2 Runge-Kutta method:

Fig 7 to Fig 12 show the simulation results of μ, $X(t)$, $S(t)$, $V(t)$, $O(t)$, $C(t)$ under the following conditions :

(i) Common Initial Conditions :

$X(0)=0.35$ g/l; $S(0)=12.2$ g/l; $V(0)=3.0$ l; $O(0)=0.18$ g/l; $C(0)=0.07$ g/l; $\mu(0)=0.06$ g/g·hr.

(ii) Parameters:

$D=0.0$; $K_s=2.0$; $K_1=2.0$; $K_{la}=3.5$; $K_d=0.8$; $K_c=3.0$; $\Delta t=0.05$; $\mu_{max}=0.4$; $O_1=0.4$; $C_1=0.1$; $X_{o2}=0.50$; $X_{co2}=0.0033$; $\zeta_{max}=0.15$; $K_{po}=0.05$; $K_{o2}=0.009$; $K_{et}=71.5$; $K_e=0.5$; $\mu_o=0.4$; $K_m=0.4$; $K_i=2.5$, $S_{fi}=12$; Currt=0.0.

It has been demonstrated here that computer simulation techniques can be applied to a batch fermentation process.

A model for ethanol concentration is also presented because it may be involved in some fed-batch and batch fermentation process.

In our pilot plant, the experimental data for a fed-batch fermentation process is not available at this time. The simulation model for a batch fermentation process should be extended to a fed-batch using the same parameters (only modifying some values of the parameters if the experimental data is available). Also, a dilution rate for a fed-batch should be given.

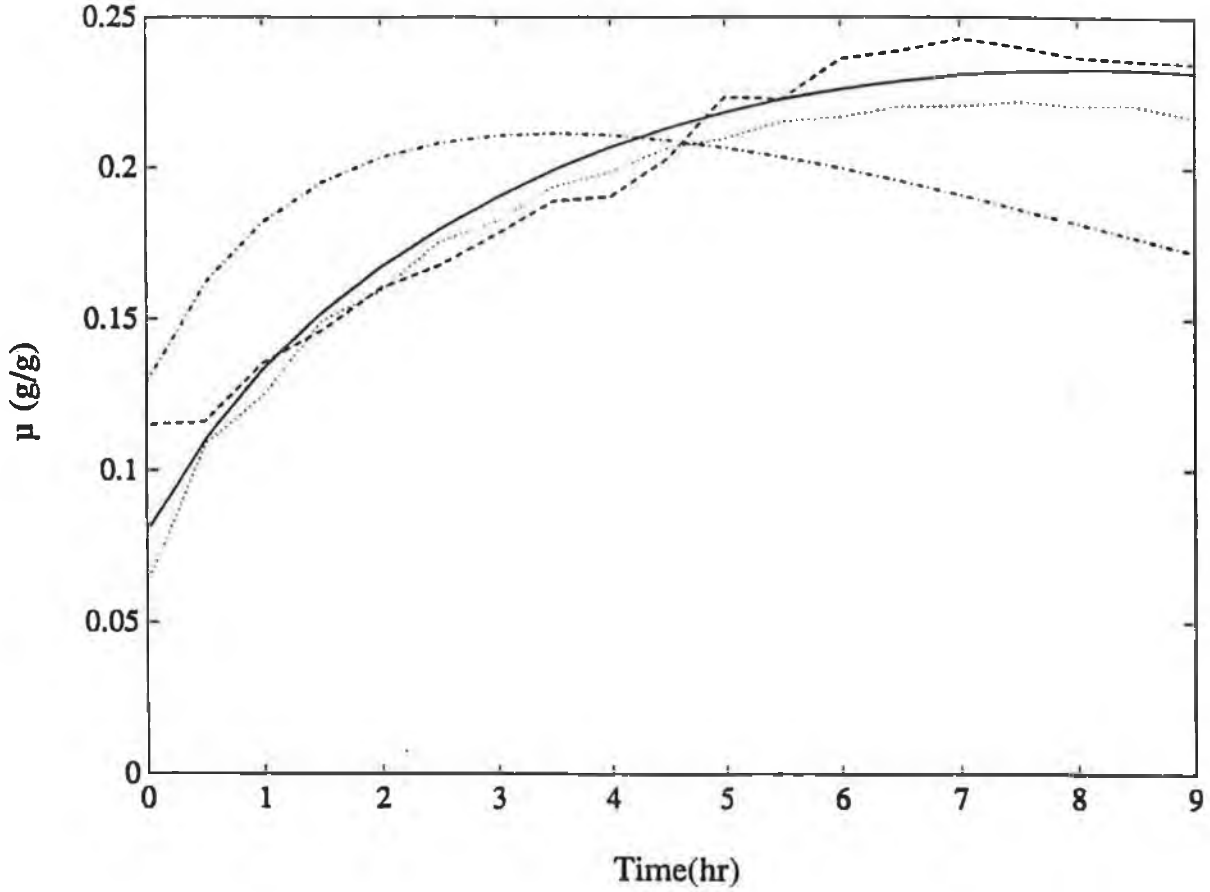


Fig 1 : The specific growth rate (μ) for simulation using *Euler* method based on different options of μ

---------- The experimental result μ (g/g·hr)

________ The Monod's model μ (g/g·hr)

.... The Ollson's model μ (g/g·hr)

_._._._._ The Contois' model μ (g/g·hr)

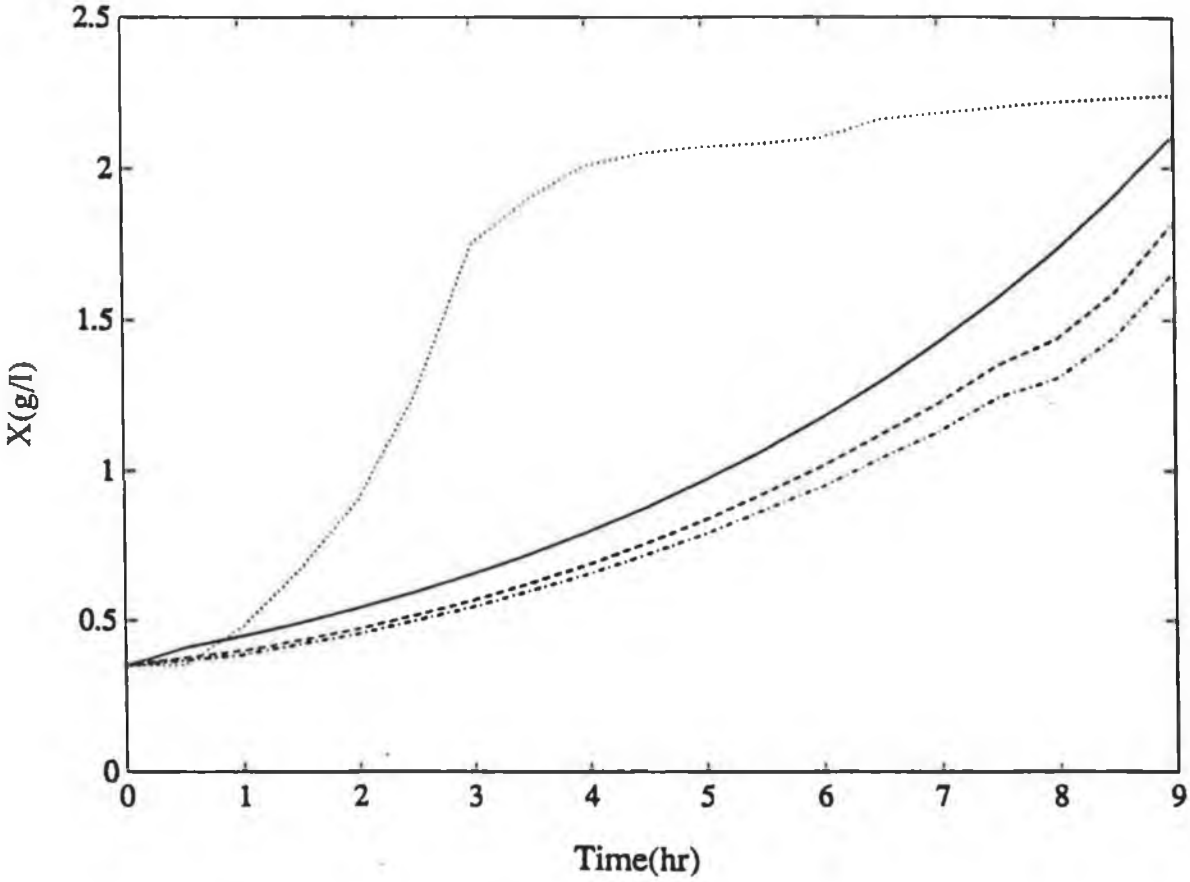


Fig 2 : The biomass concentration X for simulation using *Euler* method based on different options of μ

....	The experimental data X from pilot plant (g/l)
______	The simulation result X using Monod's model (g/l)
-----------	The simulation result X using Ollson's model (g/l)
_._._._	The simulation result X using Contois' model (g/l)

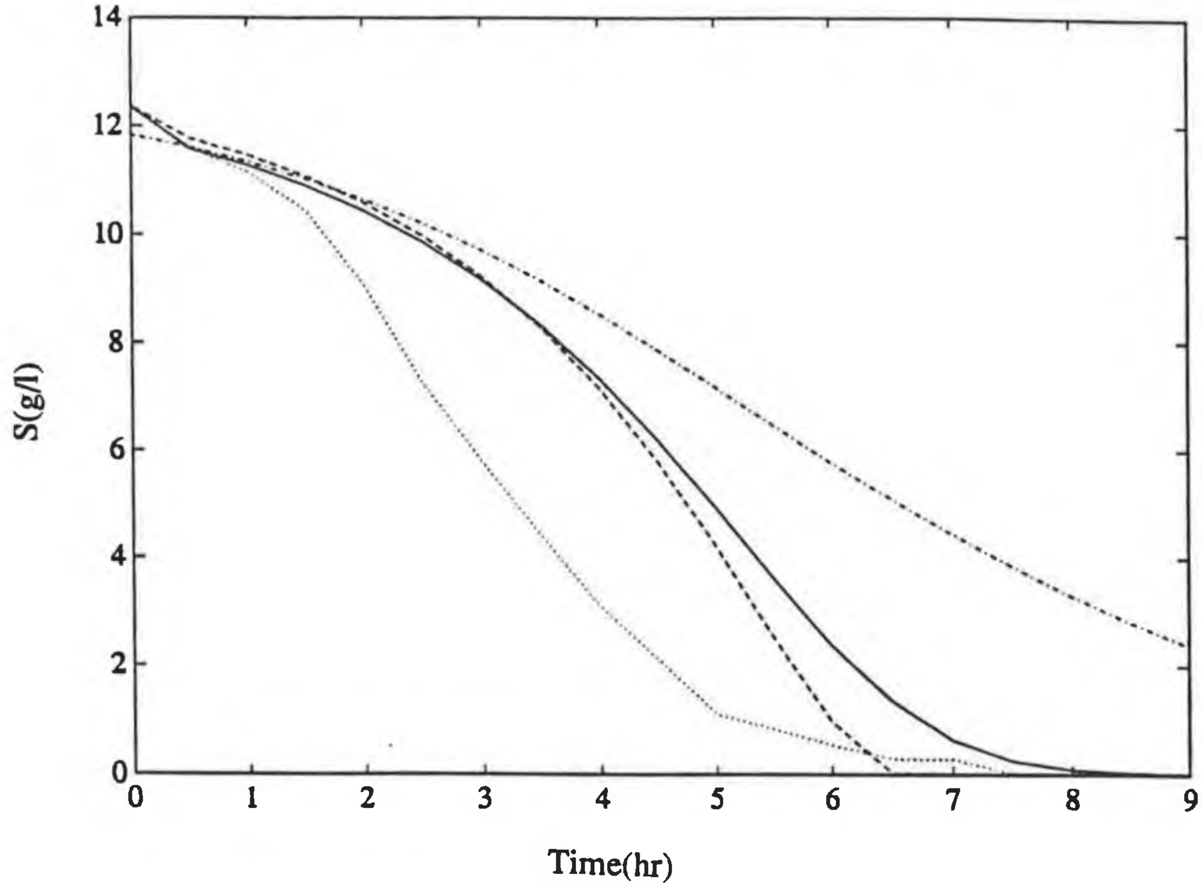


Fig 3 : The substrate concentration S for simulation using *Euler* method based on different options of μ

…………	The experimental data S from pilot plant (g/l)
————	The simulation result S using Monod's model (g/l)
-----------	The simulation result S using Ollson's model (g/l)
.—.—.—.—	The simulation result S using Contois' model (g/l)

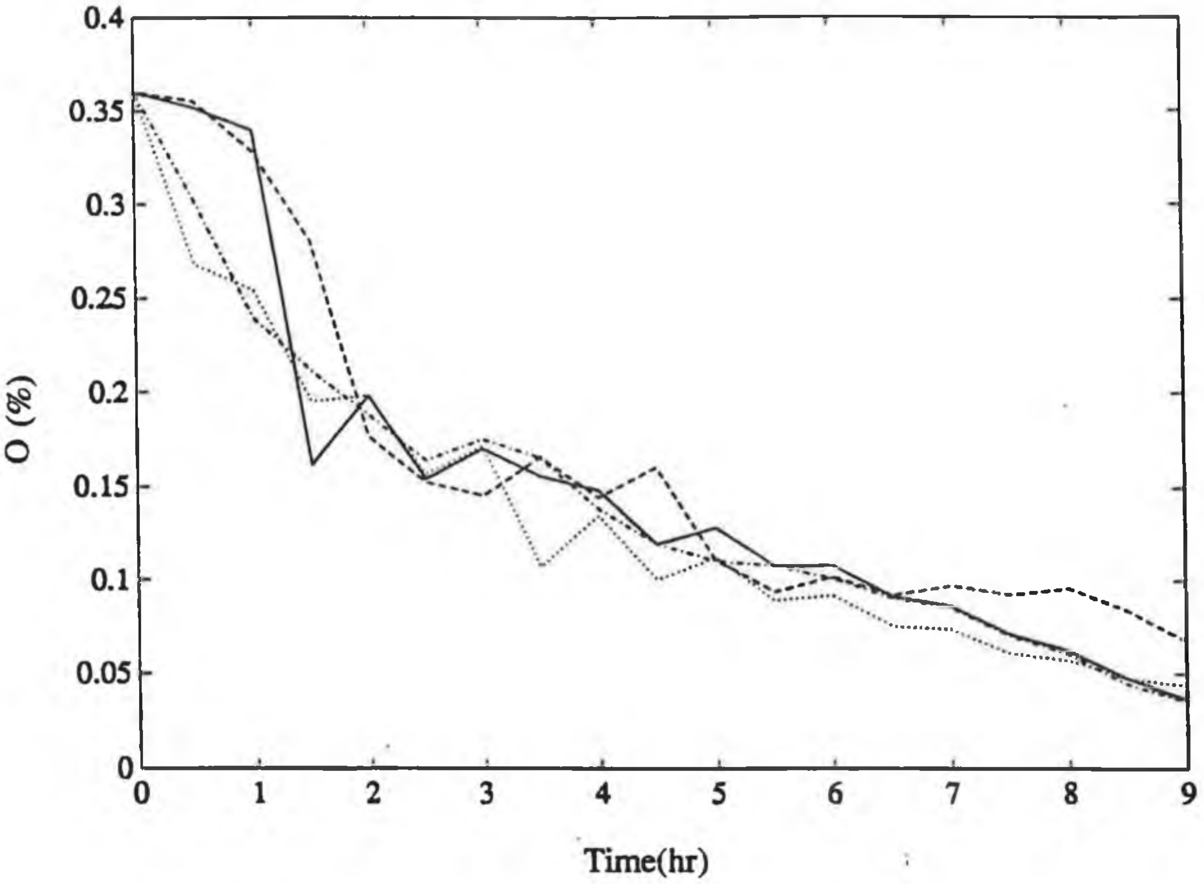


Fig 4 : Dissolved oxygen concentration O for simulation using *Euler* method based on different options of µ

____________The experimental data O from pilot plant (%   )

_._._._._._ The simulation result O using Model's model (%   )

.... The simulation result O using Ollson's model (%   )

-------------- The simulation result O using Contois' model (%   )

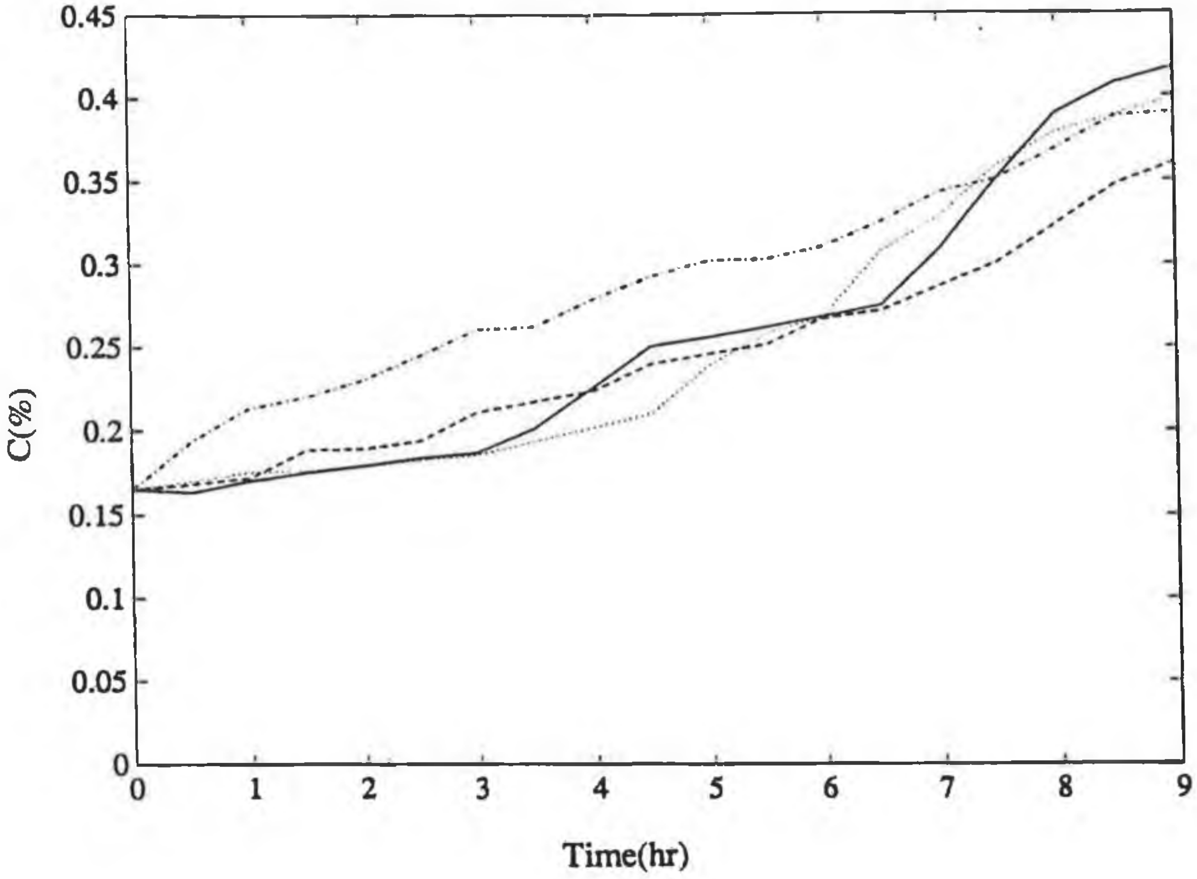


Fig 5 : Exhaust CO_2 concentration C for simulation using *Euler* method based on different options of μ

-.-.-.-.-.- The experimental data C from pilot plant (% age)

------------ The simulation result C using Monod's model (% age)

.... The simulation result C using Ollson's model (%age)

____________ The simulation result C using Contois' model (%age)

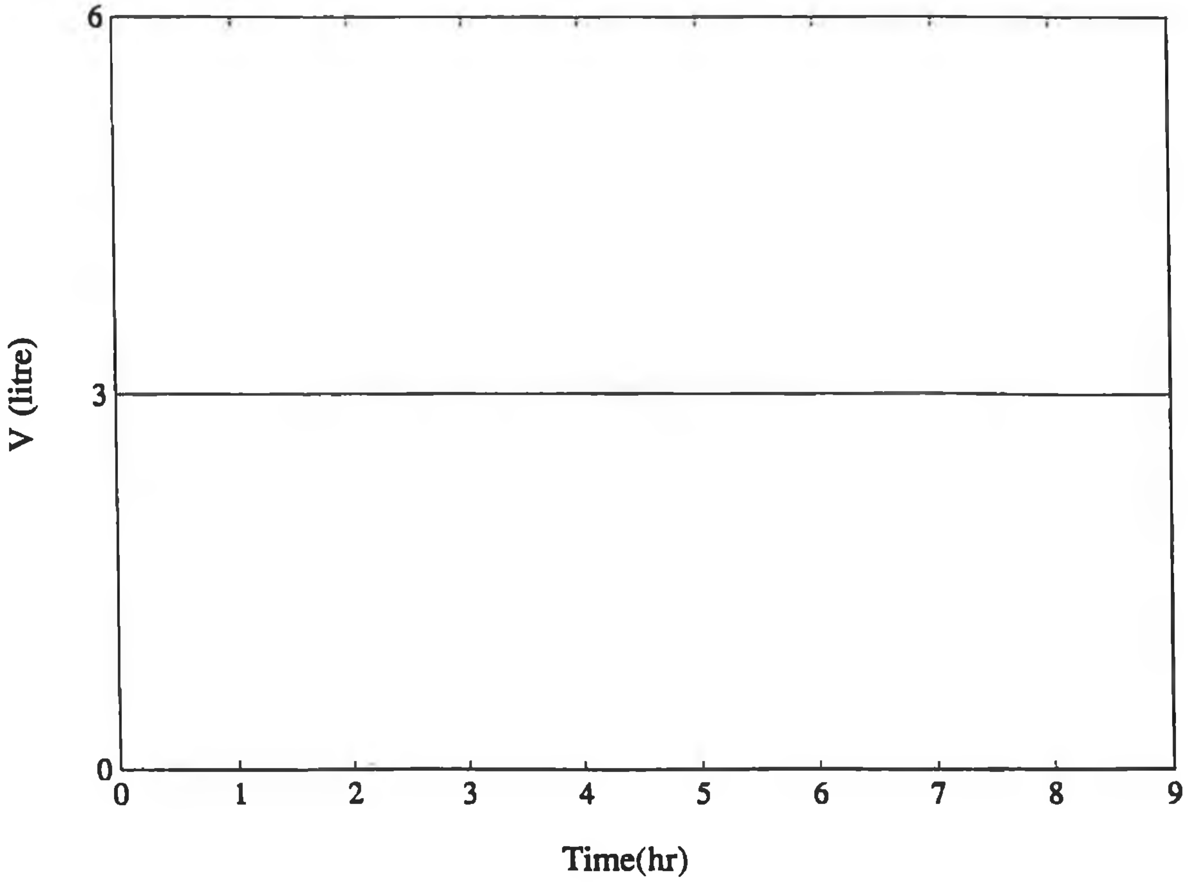


Fig 6 : The fermenter volume of the growth culture V using *Euler* method based on different options of µ

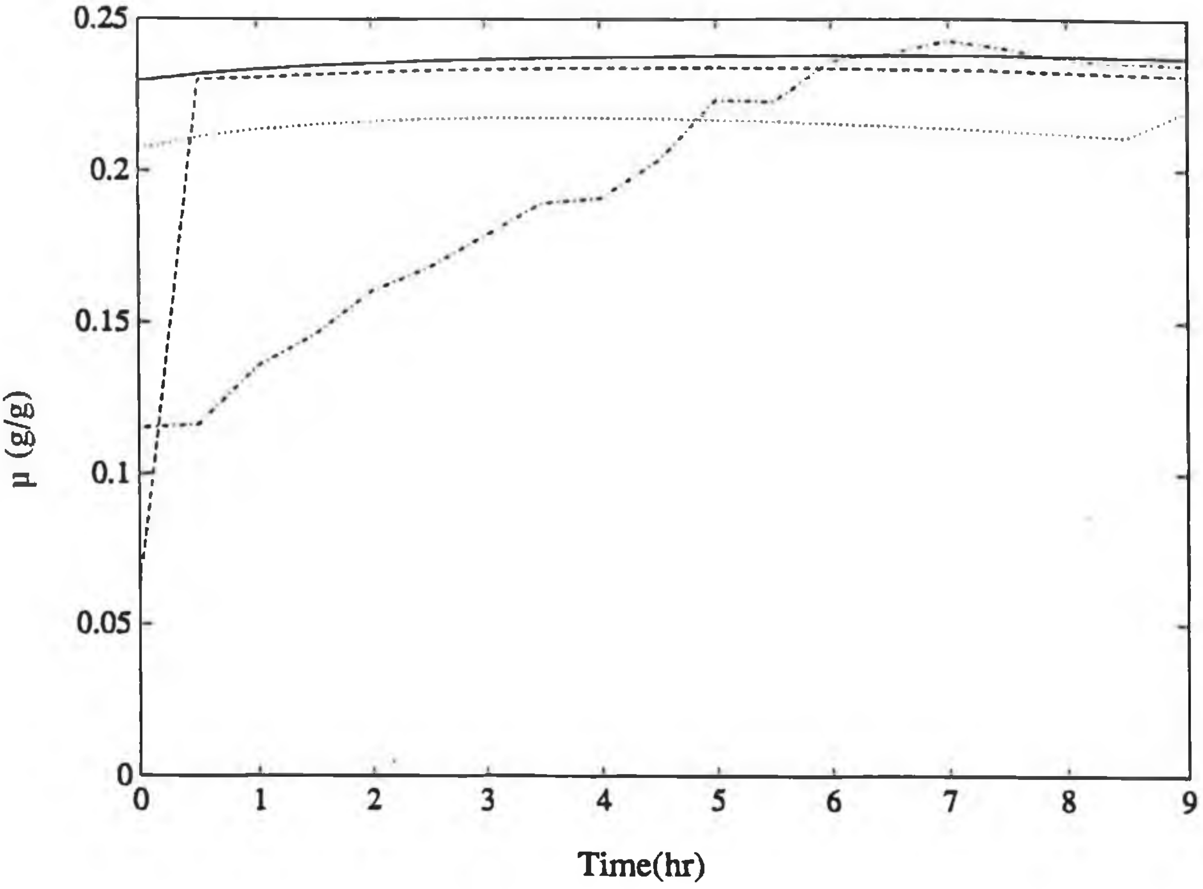


Fig 7 : The specific growth rate (μ) for simulation using *Runge-Kutta* method based on different options of μ

–·–·–·–·– The experimental result μ (g/g.hr)

——————— The Monod's model μ (g/g.hr)

– – – – – – The Ollson's model μ (g/g.hr)

……… The Contois' model μ (g/g.hr)

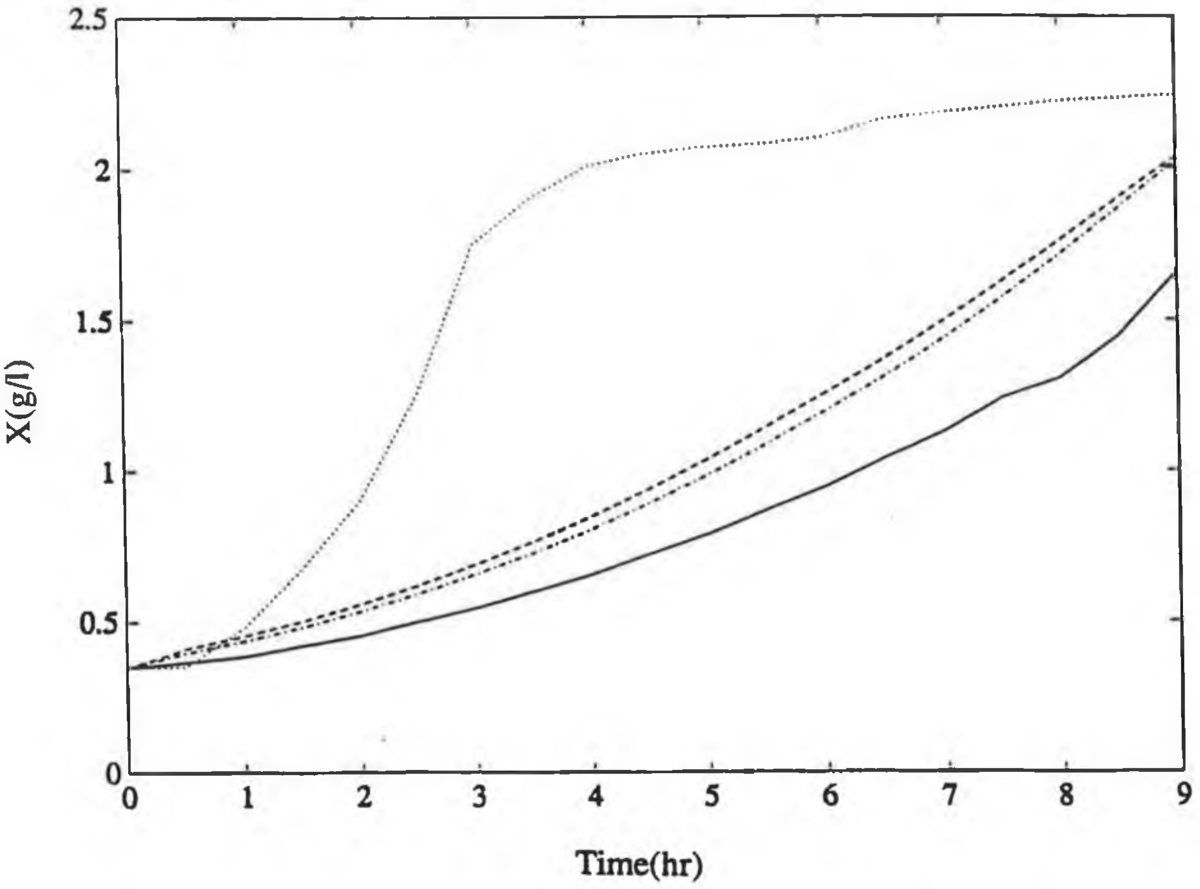


Fig 8 : The biomass concentration X for simulation using *Runge-Kutta* method based on different options of μ

....	The experimental data X from pilot plant (g/l)
————	The simulation result X using Contois' model (g/l)
-----------	The simulation result X using Monod's model (g/l)
_._._._._	The simulation result X using Ollson's model (g/l)

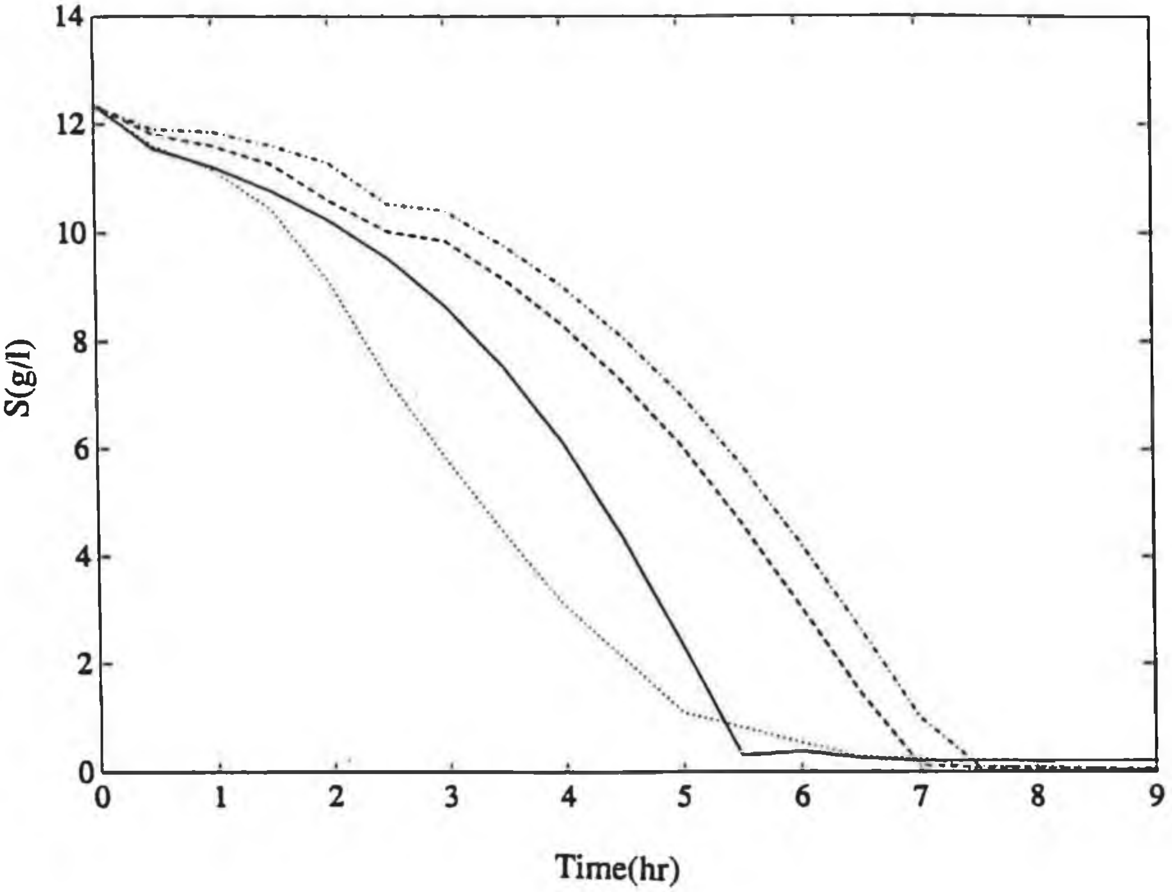


Fig 9 : The substrate concentration S for simulation using *Runge-Kutta* method based on different options of μ

.... The experimental data S from pilot plant (g/l)

———— The simulation result S using Monod's model (g/l)

------------ The simulation result S using Ollson's model (g/l)

—.—.—.— The simulation result S using Contois' model (g/l)

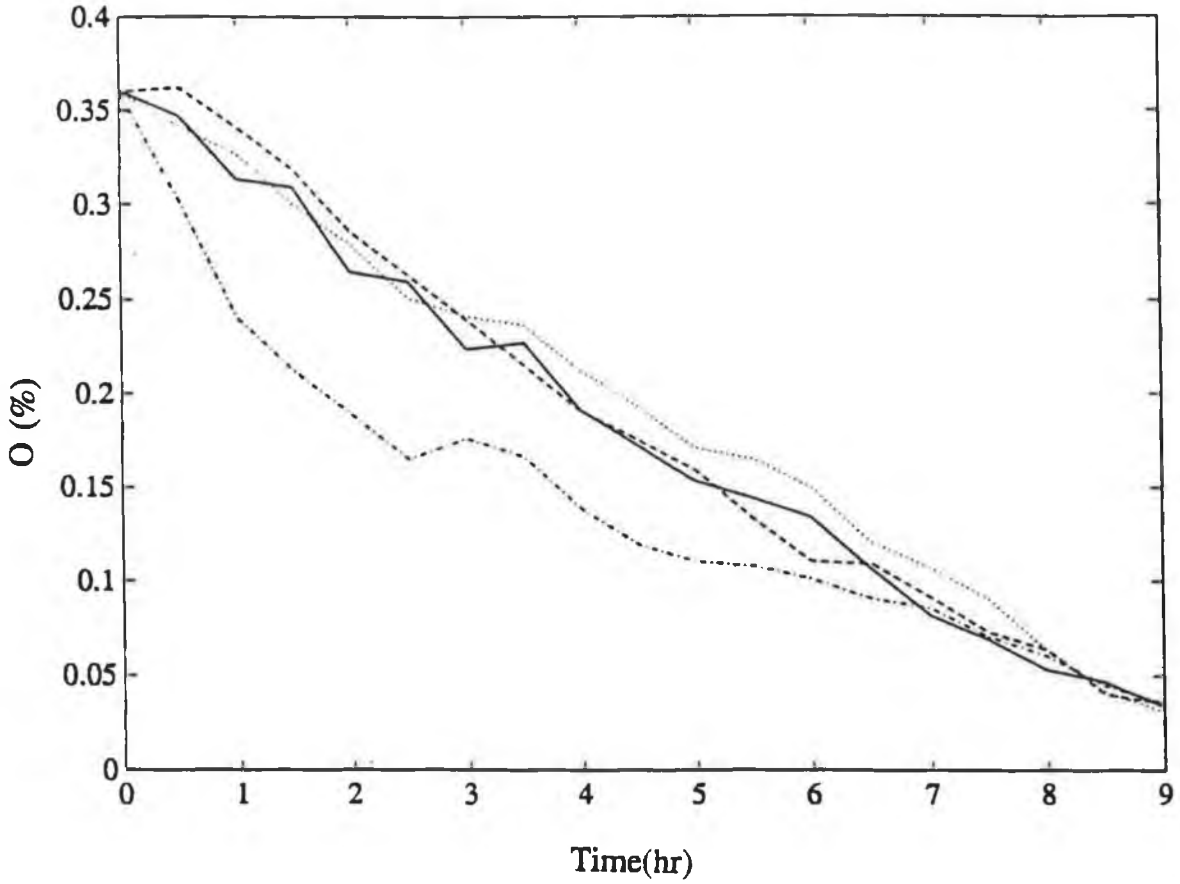


Fig 10 : Dissolved oxygen concentration O for simulation using *Runge-Kutta* method based on different options of µ

________	The experimental data O from pilot plant (%)
_._._._._.	The simulation result O using Contois' model (%)
....	The simulation result O using Ollson's model (%)
-------------	The simulation result O using Monod's model (%)

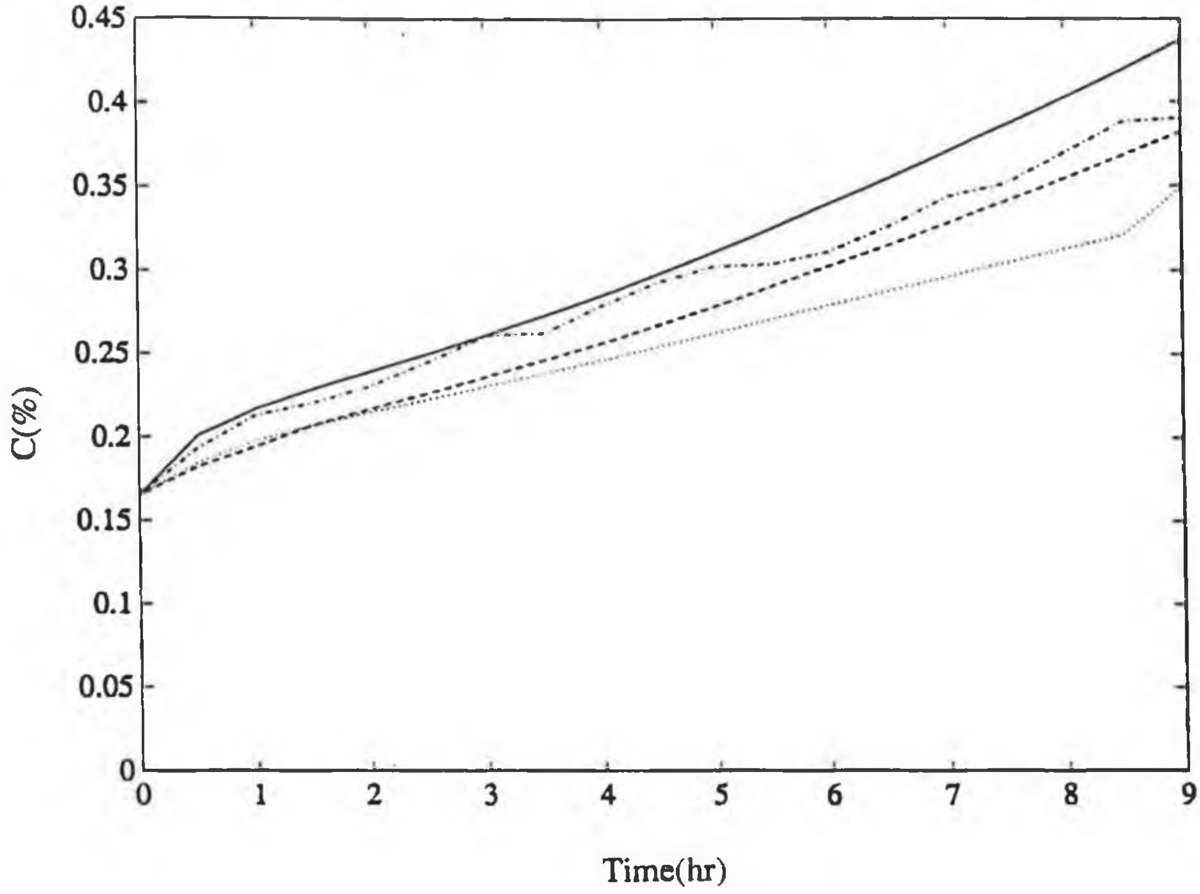


Fig 11 : Exhaust CO_2 concentration C for simulation using *Runge-Kutta* method based on different options of µ

_._._._._ The experimental data C from pilot plant (%)

------------ The simulation result C using Monod's model (%)

.... The simulation result C using Ollson's model (%)

____________ The simulation result C using Contois' model (%)

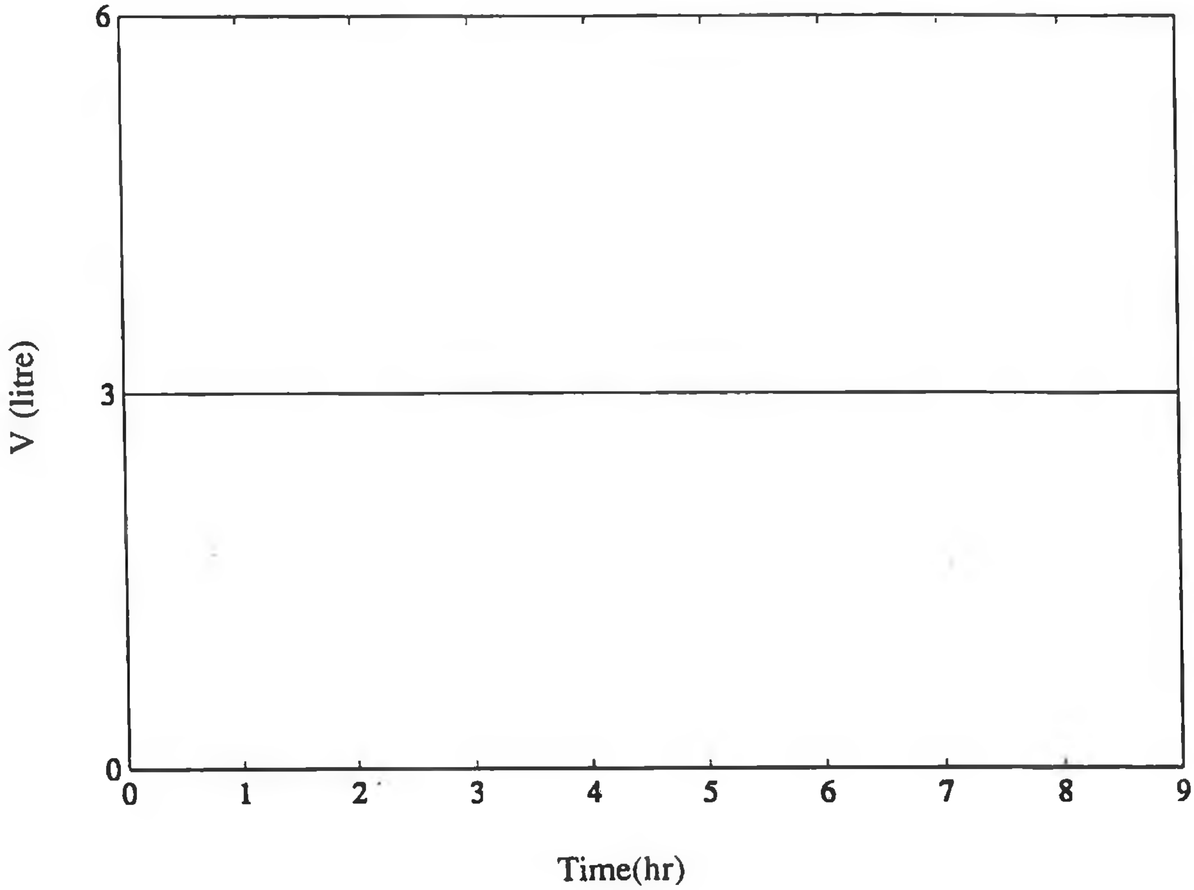


Fig 12 : The fermenter volume of the growth culture V using *Runge-Kutta* method based on different options of µ

PART III STATE ESTIMATION TECHNIQUES FOR THE FERMENTATION PROCESSES

Chapter 1 Introduction

The success of a fermentation process depends on the control of specific environmental conditions for cell mass or biomass, substrate and product formation. It is necessary to obtain reliable on-line data for all the variables involved for the purpose of control. The biomass and substrate concentrations cannot be measured on-line because suitable biochemical sensors are not available for on-line measurements. It is always much more difficult to control these variables without relevant measurements. In this part of the thesis the application of estimation techniques to the solution of the above problem is described.

Although the linear estimation problem with continuous time measurements has been solved many years ago, very few exact finite dimensional filters and observers have been developed for non-linear problems. It is necessary to develop new estimation methods because the classical estimation methods do not prove very efficient in overcoming these basic difficulties in non-linear systems such as the fermentation processes.

In this work, several different algorithms are applied to fed-batch and batch fermentation processes using on-line real-time information and off-line data, for the purposes of estimating (non-linear) system states, such as biomass and substrate, and uncertain model parameters. After slight modification of the parameter estimation the algorithm worked with experimental data. The results of several experiments are presented. These results demonstrate that estimation techniques can be successfully applied to a complex biological process.

The basis of many estimation methods is to run the simulation models of the processes. The basic dynamical model of a bioreactor has been presented in PART II–Chapter 2.

Chapter 2 Non-Adaptive State Estimation

2.1 Introduction

Assuming one of state variables (e.g., biomass and substrate in a fermentation process) and the yield coefficients are known, a simple algorithm such as non-adaptive state estimation can be used to estimate another state variable. These algorithms have the advantage of converging asymptotically in the noise-free case, but their speed of convergence completely depends on the experimental conditions and cannot be assigned through appropriate design parameter choices. (Based on the work of Dochain [3])

Based on this algorithm and the non-linear structure of the system, some estimation results of state variables are presented.

2.2 Non-Adaptive Algorithm

This algorithm was applied assuming one of state variables, biomass or substrate, is measured on-line and the yield coefficient K_1 (= $1/Y_{X:S}$) is known, and was used to estimate another state variable.

2.2.1 Estimate Substrate $\hat{S}(t)$

Assuming:

(1) Biomass (X) can be measured on-line,
(2) The yield coefficient K_1 is known,
Estimate substrate $\hat{S}(t)$.
Define :

$$K = K_1 \cdot X = 1/Y_{X:S} \cdot X \; ; \qquad \textbf{(2.2.1–1)}$$

Combine **(2.2.1–1)** with **II–(2.2-2), II–(2.2–4), II–(2.3–1)**, that is,

$$dX(t)/dt = [\mu - D(t)] \cdot X(t); \qquad \textbf{II–(2.2–2)}$$

$$d\hat{S}(t)/dt = D(t) \cdot [S_{fi}(t) - \hat{S}(t)] - K_1 \cdot \mu \cdot X(t); \qquad \textbf{II–(2.2–4)}$$

$$\mu = \mu_{max} \cdot \hat{S} / (K_S + \hat{S}); \qquad \textbf{II–(2.3–1)}$$

(Note: the equations in part **II** used in this part contained **'II- '**)
Using them we can get:

$$d[K(t) + \hat{S}(t)]/dt = D(t) \cdot [\, S_{fi}(t) - (K(t) + \hat{S}(t))]; \qquad \textbf{(2.2.1–2)}$$

Assuming :

Z(t) is an auxiliary state variable and is defined by the following equation

$$dZ(t)/dt = D(t)\cdot[S_{fi}(t) - Z(t)]; \qquad (2.2.1\text{–}3)$$

with $0 \leq Z(t) < \infty$, arbitrary-function,

Comparing equations (2.2.1–2) with (2.2.1–3), Obviously we have

$$\begin{aligned} Z(t) &= K(t) + \hat{S}(t) \\ &= K_1\cdot X + \hat{S}(t); \qquad (2.2.1\text{–}4) \end{aligned}$$

From (2.2.1–4) we get:

$$\hat{S}(t) = Z(t) - K_1\cdot X(t); \qquad (2.2.1\text{–}5)$$

A simple discrete time version of this algorithm has been derived by using a first order Euler approximation for dZ/dt.

$$Z(k) = Z(k-1) + \Delta t\cdot D(k-1)\cdot[\ S_{fi}(k-1) - Z(k-1)]; \qquad (2.2.1\text{–}6)$$

$$\hat{S}(k) = Z(k) - K_1\cdot X(k)\ ; \qquad (2.2.1\text{–}7)$$

Where k is the time index and T is the sampling period.

In these equations, the initial values of all the parameters were determined by the simulation. We can get the solution for Z(t) from equation (2.2.1-3). The estimated value of $\hat{S}(t)$ can be calculated from (2.2.1-5) in conjunction with initial assumptions (1) and (2). The result was presented in Chapter 8 (Fig 3, 8, 12)

Using Monod's model (in part II) (equation II–(2.3-1)), Ollson's model (equation II–(2.3–2)), Contois' model (equation II–(2.3–3)) respectively, different results of estimation of substrate $\hat{S}(t)$ were obtained.

2.2.2 *Estimate Biomass* $\hat{X}(t)$[3]

Assuming:

(1) Substrate S can be measured on-line,

(2) The yield coefficient K_1 is known,

The following equation is obtained using the same technique as above:

$$Z(t) = K_1\cdot\hat{X}(t) + S(t)\ ; \qquad (2.2.1\text{–}4)$$

From (2.2.1–4), on-line estimation of biomass (X) can also be computed as follows:

$$\hat{X}(t) = 1/K_1\cdot[\ Z(t) - S(t)\ ]\ ; \qquad (2.2.2\text{–}1)$$

Using a first order Euler approximation and (2.2.1–6), we get

$$\hat{X}(t) = 1/K_1\cdot[Z(k) - S(k)]; \qquad (2.2.2\text{–}2)$$

The results of on-line estimated biomass based on Monod's model, Ollson's model and Contois's model are presented in Chapter 8 (Fig 2, 6, 10) respectively.

2.2.3 *Estimate Dissolved Oxygen Concentration* $\hat{O}(t)$

Assuming:

(1) Biomass X(t) can be measured on-line.
(2) Yield coefficient K_2 ($=1/Y_{X:O}$) and K_{la} are known.
Considering the following equations :

$$d\hat{O}/dt = OTR + OUR\ ;$$

$$= K_{la}\cdot(X_{O2}\cdot O_1 - \hat{O}) - K_2\cdot dX/dt; \tag{2.2.3–1}$$

$$dX/dt = [\mu - D(t)]\cdot X(t); \tag{II–(2.2–4)}$$

$$\mu = \mu_{max}\cdot S(t)/[K_S + S(t)]; \tag{II–(2.3–1)}$$

$$K(t) = K_2\cdot X(t); \tag{2.2.1–1}$$

Using the same non-adaptive algorithm as above:

$$d[K(t)+\hat{O}(t)]/dt = K_{la}\cdot[X_{O2}\cdot O_1 - (K(t)+\hat{O}(t))] + K_{la}\cdot K_2\cdot X(t); \tag{2.2.3–1}$$

Let the auxiliary state variable Z(t) be defined by the following equations:

$$dZ(t)/dt = K_{la}\cdot[X_{O2}\cdot O_1 - Z(t)] + K_{la}\cdot K_2\cdot X(t)\ ; \tag{2.2.3–2}$$

Comparing **(2.2.3–1)** with **(2.2.3–2)**, gives:

$$Z(t) = K_2\cdot X(t) + \hat{O}(t); \tag{2.2.3–3}$$

From **(2.2.3–3)**: the on-line estimated dissolved oxygen concentration $\hat{O}(t)$ can be computed as follows:

$$\hat{O}(t) = Z(t) - K_2\cdot X(t); \tag{2.2.3–4}$$

Using a first Euler approximation and **(2.2.1–6)**, we get

$$\hat{O}(k) = Z(k) - K_2\cdot X(k); \tag{2.2.3–5}$$

The estimated $\hat{O}(t)$ based on Monod's model, Ollson's model and Contois' model are presented in Chapter 8 (Fig 13, 14, 15) respectively.

2.2.4 *Error Dynamics*

The validity of the estimation algorithms is demonstrated by the extensive set of results comparing the outcome of the estimation algorithms with the output of the simulation.

Furthermore, in the case of oxygen estimation, the actual error would in practice be available since on-line oxygen measurements are common. This error signal could then be employed in an adaptive manner to improve the estimation of either biomass or substrate concentrations.

2.2.5 *Comments*

Similar algorithms can also be developed to estimate different state variables, such as synthesis product concentration, exhaust carbon-dioxide concentration, ethanol concentration. These algorithms have some drawbacks:

(1) Its speed of convergence is completely determined by the experimental conditions (through the dilution rate D(t)).

From equations (1.1-1), (1.1–3), (1.1–21), (2.2.1–1) and (2.2.1–3) and (2.2.1–4), the following error equation can be obtained:

$$dE/dt = -D(t)\cdot E(t); \qquad (2.2.5\text{–}1)$$

Clearly (2.2.1–3), (2.2.1–4) is stable (since $D(t) > 0$). (Anderson 1977).

(2) Its lack of robustness: for example in section 2.2.2, if the available measurements of S(t) are noisy ($S_m(t) = S(t) + \epsilon(t)$), the estimate $\hat{X}(t)$ is directly corrupted by the noise $\epsilon(t)$:

$$\hat{X}(t) = 1/K_1\cdot[\, Z(t) - S(t) - \epsilon(t)\,]; \qquad (2.2.5\text{–}1)$$

The noise influence could of course be attenuated by filtering the data of S(t) but this would further slow down the estimation algorithm's dynamics.[3]

Chapter 3 Adaptive Observer

3.1 Introduction

If a priori knowledge of the parameters is not available, such as the yield coefficients or growth rate μ, some estimation algorithm, like adaptive observers, can be used. This algorithm was obtained from the work of Dochain (1986)[13] and Goodwin et al[14].

3.2 Structure of Algorithm

The adaptive observer algorithm can be described as follows:

3.2.1 Estimate Substrate $\hat{S}(t)$

Assuming:

(1) Biomass X(t) can be measured on-line,

(2) The system parameters (μ, K_1,etc) are unknown.

Define the auxiliary time-varying parameters:

$$\varphi_1(t) = S(t) - \mu(t); \qquad (3.2.1\text{–}1)$$

$$\varphi_2(t) = K_1 \cdot \mu(t); \qquad (3.2.1\text{–}2)$$

Then the following state-space representation is equivalent to (1.1–1), (1.1–3):

$$dX(t)/dt = -\varphi_1(t) \cdot X(t) + X(t) \cdot S(t) - D(t) \cdot X(t); \qquad (3.2.1\text{–}3)$$

$$dS(t)/dt = -\varphi_2(t) \cdot X(t) + D(t) \cdot S_{fi}(t) - D(t) \cdot S(t); \qquad (3.2.1\text{–}4)$$

From these equations, the following adaptive observer can be derived to estimate on-line the substrate concentration $\hat{S}(t)$:

$$\begin{aligned} d\hat{X}(t)/dt = & -\hat{\varphi}_1(t) \cdot X(t) + X(t) \cdot \hat{S}(t) - D(t) \cdot X(t) \\ & + C_1 \cdot [X(t) - \hat{X}(t)]; \qquad (3.2.1\text{-}5) \\ d\hat{S}(t)/dt = & -\hat{\varphi}_2(t) \cdot X(t) - D(t) \cdot \hat{S}(t) + D(t) \cdot S_{fi}(t) \\ & + [C_2 + C_3 \cdot X(t) \cdot \lambda^2(t)\ ][X(t) - \hat{X}(t)] \qquad (3.2.1\text{–}6) \end{aligned}$$

$$d\lambda(t)/dt = -D(t)\cdot\lambda(t) + \mathring{X}(t); \tag{3.2.1–7}$$

$$d\mathring{\varphi}_1(t)/dt = -C_3\cdot X(t)\cdot[X(t) - \mathring{X}(t)]; \tag{3.2.1–8}$$

$$d\mathring{\varphi}_2(t)/dt = -C_3\cdot X(t)\cdot\lambda(t)\cdot[X(t) - \mathring{X}(t)] \tag{3.2.1–9}$$

where C_1, C_2, C_3 are the design parameters and $\lambda(t)$ is an auxiliary filtered value of $X(t)$. $\varphi_1(t)$ and $\varphi_2(t)$ are the auxiliary time-varying parameters. $\mathring{X}(t)$, $\mathring{\varphi}_1(t)$ and $\mathring{\varphi}_2(t)$ are the solutions from **(3.2.1–5, 6,7,8,9)**. Simulation results of estimation of substrate $\hat{S}(t)$ have been carried out by using the models **II–(2.2–3), II–(2.2–4)** under the following initial conditions: $S_{fi} = 10.0$; $D = 0.2$; $X(0) = 0.35$; $\mathring{X}(0) = 2.63$; $\hat{S}(0) = 0.35$.

3.2.2 *Estimate Biomass* $\hat{X}(t)$

Assuming:

(1) Substrate $S(t)$ can be measured on-line,
(2) The system parameters (μ, K_1, etc.) are unknown.
Using the above adaptive algorithm **(equations (3.2.1– 3-9)** the biomass $\hat{X}(t)$ can be estimated.

In [13] Dochain claimed that C_1, C_2 and C_3 could be tuned by simulation. Unsuccessful attempts were made to tune these designed parameters. Further investigation would be necessary to ascertain the validity of the algorithm.

Chapter 4 Non-linear Observer

4.1 Introduction

For a non-linear system, like a fermentation process, a non-linear observer can be applied to state estimation if only one of the states must be estimated and others can be measured on-line. In this chapter, the theorem in section 4.2 will be used to estimate the state vectors of the models **II–(2.2–3)**, **II–(2.2–4)**, of the fermentation process.

4.2 Observation Of A Non-Linear System

If a system is observable, for each pair of initial states $\theta_1(0)$, $\theta_2(0)$, we can find an input variable $\Psi(t)$ such that θ_1, θ_2, are distinguishable by observations of the corresponding output variables $Y_1(t)$ and $Y_2(t)$. There are some works dealing with theoretical aspects of observers for non-linear systems and a theorem about the observability of non-linear systems is firstly presented. The theorem presented by Gallegos [15]is an extension of a lemma given by Williamson [16] and deals with the observability of a non-linear system.

Theorem

A necessary and sufficient condition for the system

$$d\theta/dt = f(\theta) + \sum_{i=1}^{m} g_i(\theta)\cdot\Psi_i ; \qquad \Psi = (\Psi_1, \ldots \Psi_m)^T \in R^m \tag{4.2–1}$$

$$Y = h(\theta) \quad ; \qquad \theta \in R^n; \; Y \in R; \tag{4.2–2}$$

to be completely, uniformly, locally, observable is that there exists a system of local coordinates on R^n such that **(4.2–1)** is of the form

$$d\theta/dt = \begin{vmatrix} \theta_2 \\ , \\ , \\ \theta_n \\ F(\theta) \end{vmatrix} + \sum_{i=1}^{m} \begin{vmatrix} g_{i1}(\theta_1) \\ g_{i2}(\theta_1, \theta_2) \\ , \\ , \\ g_{in}(\theta_1, \theta_2, \ldots, \theta_n) \end{vmatrix} \cdot \Psi_i \tag{4.2–3}$$

$$Y = \theta_1 \tag{4.2–4}$$

From (4.2–3) and (4.2–4), it is possible to estimate the state vector through successive derivatives of the output and input variables. [15][16].

4.3 Summary Of Non-Linear Observer

Based on above theorem, equations II–(2.2–3), II–(2.2–4), have the form given by (4.2–3) and (4.2–4) with,

$$f(\theta) = \begin{bmatrix} \mu\cdot X \\ \\ -K_1\cdot\mu X \end{bmatrix}; \qquad g_1(\theta) = \begin{bmatrix} -X \\ \\ -S \end{bmatrix}; \qquad g_2(\theta) = \begin{bmatrix} 0 \\ \\ 1 \end{bmatrix}; \tag{4.3–1}$$

and Ψ_1=D, Ψ_2 =D·S_i. The system is completely, uniformly, locally observable because it is of the form given by equations (4.2–3), (4.2–4),. The fermentation model may therefore be written as:

$$\begin{bmatrix} \dot{z}_1 \\ \\ \dot{z}_2 \end{bmatrix} = \begin{bmatrix} z_2 \\ \\ F(z) \end{bmatrix} + \begin{bmatrix} g_{11}(z_1) \\ \\ g_{12}(z_1,z_2) \end{bmatrix}\cdot\Psi_1 + \begin{bmatrix} g_{21}(z_1) \\ \\ g_{22}(z_1,z_2) \end{bmatrix}\cdot\Psi_2 ; \tag{4.3–2}$$

$$Y = z_1 \tag{4.3–3}$$

with

$$z_1 = X ;$$

$$z_2 = \mu X ;$$

$$g_{11}(z_1) = -z_1;$$

$$g_{12}(z_1, z_2) = z_2\cdot\left(\frac{z_2}{\mu_m\cdot z_1} - 2\right) ;$$

$$g_{21}(z_1) = 0 ;$$

$$g_{22}(z_1, z_2) = \frac{(\mu_m\cdot z_1 - z_2)^2}{\mu_m\cdot K_S\cdot z_1} ;$$

$$F(z) = \frac{z_2}{z_1}\cdot\left[z_2 - \frac{(\mu_m\cdot z_1 - z_2)^2\cdot K_1}{\mu_m\cdot K_S}\right];$$

From equation (4.3–2), (4.3–3), it is possible to estimate the state vector since it follows:

$$z_2 = \dot{z}_1 - g_{11}(z_1)\cdot D = \dot{Y} + D\cdot Y \; ; \qquad (4.3\text{–}4)$$

Assuming:

Biomass X can be measured on-line.

Using the above way, it will only be necessary to estimate the substrate concentration $\hat{S}(t)$. The following estimate of substrate $\hat{S}(t)$ can be obtained:

$$\hat{S} = \frac{K_S\cdot z_2}{\mu_m\cdot z_1 - z_2} \; ; \qquad (4.3\text{–}5)$$

From equation (4.3–4), it can be observed that the derivative of the process output is required. It is possible to approximate the output derivative if we use:

$$\dot{Y} \approx \frac{Y(t) - Y(t-T)}{T} \; ; \qquad (4.3\text{–}6)$$

with T small. compared with the process dynamics. From equations (4.3–4), (4.3–5), (4.3–6), we have

$$\hat{S}(t) = \frac{K_S/T\cdot[Y(t) - Y(t-T) + T\cdot D(t)\cdot Y(t)]}{\mu_m\cdot Y(t) - 1/T\cdot[Y(t) - Y(t-T) + T\cdot D(t)\cdot Y(t)]} \; ; \qquad (4.3\text{–}7)$$

Equation (4.3–7) in discrete form becomes:

$$\hat{S}(k) = \frac{K_S\cdot\alpha\cdot(Y_k - Y_{k-1} + T\cdot D\cdot Y_k)}{\mu_m\cdot Y_k - \alpha\cdot(Y_k - Y_{k-1} + T\cdot D_k\cdot Y_k)} \; ; \qquad (4.3\text{–}8)$$

where $\alpha = 1/T$.

The estimation result of substrate concentration has been shown on Fig 21 (Chapter 8).

Chapter 5 Extended Kalman Filter

5.1 Introduction

Kalman and Bucy solved the linear estimation problem with continuous time measurements in 1961. Despite a quarter-century of intensive research, very few exact finite dimensional filters have been discovered for non-linear problems. Such filters will exist only in certain special cases. In this chapter, the extended Kalman filter was applied.

In designing an Extended Kalman Filter (EKF), simulation techniques can be used to select suitable process model and to test the performance of the EKF. Compared to experimental tests the time effort is remarkably reduced. In addition the influence of sampling interval, of measurement noise and of model errors can be examined by simulation.

In what follows, an iterative solution to the non-linear model of a fed-batch fermentation process is reported using a developed Extended Kalman Filter based on some information available in real-time, such as the measurements of oxygen concentration, carbon dioxide concentration. For simulations of the EKF behaviour, the real process was replaced by a dynamic nonlinear model. Simulation results for EKF with and without experimental data are presented.

5.2 Description Of Extended Kalman Filter [27][29]

Let us consider continuous nonlinear systems of the form

$$\dot{\theta}(t) = f(\theta, u, t) + G(t)\cdot\omega(t) ; \qquad \textbf{(5.2–1)}$$

with measurements at discrete times k given by

$$Z(k) = h[\theta(k), k] + \upsilon(k) \qquad \textbf{(5.2–2)}$$

Jacobians :

$$F(\theta, t) = \partial f(\theta, u, t)/\partial\theta; \qquad \textbf{(5.2–3)}$$

$$H(\theta) = \partial h(\theta, k)/\partial\theta; \qquad \textbf{(5.2–4)}$$

In the model **(5.2–1)** and **(5.2–2)**, the $\omega(t)$ and $\nu(t)$ represent uncorrelated zero mean white noise with covariance

$$E[\omega(t)\omega(t)^T] = Q ; \qquad \textbf{(5.2–5)}$$

and

$$E[\upsilon(t)\upsilon(t)^T] = R \; ; \qquad (5.2\text{–}6)$$

where

Q = the 2 x 2 positive definite state noise covariance.
R = the 1 x 1 positive definite state observation noise covariance.

where $\omega(t) \sim (0, Q)$, $\upsilon(k) \sim (0, R)$ are white noise processes uncorrelated with each other and with $\theta(0) \sim (\tilde{\theta}_0, P_0)$. For simplicity the process noise matrix $G(t)$ is assumed to be independent of $\theta(t)$. $\theta(t)$ is a state vector. f and G are non-linear functions.

Since the state vector $\theta(t)$ is unmeasurable on-line and in the presence of state and observation noise (or model inacuracies) the question is how to find an on-line estimation algorithm based on on-line available measurements of oxygen and carbon dioxide. The extended Kalman filter application will be presented as a technique for optimal on-line estimation of state variables based on a model of the process.

Initialization:

$$P(0) = P_0, \quad \hat{\theta}(0) = \tilde{\theta}_0 \; ; \qquad (5.2\text{–}7)$$

where $\hat{\theta}(0)$ is initial estimation. $\tilde{\theta}_0$ is initial value.

Time update:

estimate: $$\dot{\theta} = f(\hat{\theta}, u, t) \; ; \qquad (5.2\text{–}8)$$

where

$\hat{\theta}$ is updated estimation.

error covariance :

$$\dot{P} = F(\hat{\theta}, t)\cdot P + P\cdot F^T(\hat{\theta}, t) + GQG^T \; ; \qquad (5.2\text{–}9)$$

This equation represents an approximate, computationally feasible time update for the estimate and error covariance. The estimate simply propagates according to the non-linear dynamics, and the error covariance propagates like that of a linear system with plant matrix $F(\hat{\theta}, t)$. Note that Jacobian F is evaluated for each t at the current estimate, which is provided by **(5.2–8)**, so that there is coupling between **(5.2–8)** and **(5.2–9)**. To eliminate this coupling it is possible to introduce a further approximation and solve not **(5.2–9)** but instead

$$\dot{P}(t) = F(\hat{\theta}(t_k), t)\cdot P(t_k) + P(t)F^T[\hat{\theta}(t_k), t] + G(t)QG^T(t); \qquad (5.2\text{–}10)$$

$t_k \leqslant t \leqslant t_{k+1}$.

In this equation, the Jacobian F is evaluated once using the estimate $\hat{\theta}(t_k)$ after updating at t_k to include Z(k). This is used as the plant matrix for the time propagation over the entire interval until the next measurement time t_{k+1}.

Measurement update:

Kalman gain:

$$K_k = \underline{P}(t_k)\cdot H^T(\hat{\theta}_k^-)\cdot[H(\hat{\theta}_k^-)\cdot\underline{P}(t_k)\cdot H^T(\hat{\theta}_k^-) + R]^{-1}\ ; \tag{5.2-11}$$

$$P(t_k) = [I - K_k\cdot H(\hat{\theta}_k^-)]\cdot\underline{P}(t_k)\ ; \tag{5.2-12}$$

estimate:

$$\hat{\theta}_k = \hat{\theta}_k^- + K_k\cdot[Z_k - h(\hat{\theta}_k^-,\ k)]; \tag{5.2-13}$$

These equations represent an approximate, computationally feasible linear measurement update for the estimate and the error covariance. The residual is computed using the nonlinear measurement function h evaluated at the previous estimate $\hat{\theta}_k^-$. The error covariance is found using the Jacobian matrix $H(\hat{\theta}_k^-)$.

5.3 Application Of The Extended Kalman Filter

For on-line estimation of the generally nonmeasurable biomass X(t) and substrate S(t) in fed-batch fermentation processes, an extended Kalman filter was chosen. A number of alternative approaches have been developed and described below. The results of estimated biomass and substrate concentrations have been obtained with simulation or experimental data.

Problem Formulation

Assume the biomass and substrate concentrations and the specific growth rate for a fed-batch fermentation process have been modelled by the following stochastic non-linear differential equations :

$$dX(t)/dt = (\mu - D)\cdot X(t) + \omega_1(t)\ ; \tag{5.3-1}$$

$$dS(t)/dt = -K_1\cdot\mu\cdot X(t) + D\cdot(S_{fi} - S(t)) + \omega_2(t)\ ; \tag{5.3-2}$$

$$\mu = \mu_{max}\cdot S(t)/[K_s + S(t)]\ ; \tag{5.3-3}$$

where $\omega(t) = (\omega_1(t),\ \omega_2(t))^T$ is the state noise.

5.3.1 System Equations

Based on equation (5.2–1), the system equations (5.3–1), (5.3–2), (5.3–3) are written as follows:

$$\dot{\theta}(t) = f(\theta,\mu,t) + \omega(t) \; ; \qquad (5.3.1\text{–}1)$$

where

$\theta(t)$ is the 2 x 1 state vector, where $\theta_1(t)$ is biomass $X(t)$, $\theta_2(t)$ is substrate $S(t)$.

$f(\theta,\mu,t)$ is the 2 x 1 function, where

$$F_1(\theta(t)) = \mu_{max}\cdot X(t)\cdot S(t)/[K_S+S(t)] - D\cdot X(t) \; ; \qquad (5.3.1\text{–}2)$$

$$F_2(\theta(t)) = -\mu_{max}\cdot K_1\cdot X(t)\cdot S(t)/[K_S+S(t)] + D\cdot[S_{fi}-S(t)] \; ; \qquad (5.3.1\text{–}3)$$

5.3.2 Measurement Equations

In the fed-batch fermentation process, a linear function of biomass and substrate concentrations in conjunction with the on-line oxygen and carbon-dioxide measurements can be developed with the aid of simulation techniques :

$$Z(\theta) = H\cdot\theta(t) + \upsilon(t); \qquad (5.3.2\text{–}1)$$

H is 2 x 2 observation matrix, which can be obtained heuristically by simulation from the relationships between experimental data of biomass and substrate concentrations, and on-line measurements of oxygen and carbon-dioxide concentrations.

$$H = \begin{bmatrix} K_{X1} & K_{S1} \\ K_{X2} & K_{S2} \end{bmatrix} = \begin{bmatrix} 0.5 & 0.22 \\ 0.4 & 0.12 \end{bmatrix} \; ; \qquad (5.3.2\text{–}2)$$

$Z(\theta)$ is 2 x 1 output; evolved oxygen and carbon dioxide concentrations.

K_{X1}, K_{S1} are the observation yield coefficients of carbon dioxide measurement.

K_{X2}, K_{S2} are the observations yield coefficients of oxygen measurement.

In these equations, other nomenclature of alphabet are the same as PART II.

The initial state of the model is assumed to be a normally distributed stochastic variable with mean

$$E[\hat{\theta}(0)] = \theta(0) \; ; \qquad (5.3.2\text{–}5)$$

and covariance

$$E[\;(\hat{\theta}(0) - \bar{\theta}(0))\cdot(\hat{\theta}(0) - \bar{\theta}(0))^T\;] = \underline{P}_0 \; ; \qquad (5.3.2\text{–}6)$$

$\upsilon(t)$ is assumed to have zero mean and to satisfy

$$E[\upsilon(t)\upsilon(t)^T] = R(t) \; ; \qquad (5.3.2\text{–}7)$$

5.4 Summary of Structure of Algorithm

Before going to the details of the derivation of the extended Kalman filter algorithm, it's worthwhile to understand the structure of the algorithm. The fed-batch fermentation process model is non-linear and in continuous time form. It needs to be in linearised discrete-time form for use with EKF. The flow chart of the EKF algorithm will be shown in section 5.4.5.

5.4.1 Linearisation And Discretisation

Applying simple Euler approximation to the continuous models **(5.3.1–1)**, **(5.3.2–1)**, we can derive the following discrete non-linear stochasic model of biomass and substrate consumption for the fed-batch fermentation process:

$$\theta(k+1) = g(\theta(k),\ T) + \omega(k)\ ; \tag{5.4.1–1}$$

$$Z(k) = H\cdot\theta(k) + \upsilon(k)\ ; \tag{5.4.1–2}$$

where

$$E[\hat{\theta}(0)] = \theta(0)\ ;$$

$$E[(\hat{\theta}(0) - \tilde{\theta}(0)(\hat{\theta}(0) - \tilde{\theta}(0)^T\ ] = \underline{P}o\ ;$$

$$g(\theta(0),\ T) = \theta(0) + T\cdot F(\theta(0)); \tag{5.4.1–3}$$

ampling time, g is the function of the system model in discrete form, $\hat{\theta}$ and $\tilde{\theta}$ are updated and previous estimation repectively, θ(k/k) is the prediction estimate at time k, and other values are in models **(5.3.1–1)**, **(5.3.2–2)**. The extended Kalman filter equations for discrete non-linear stochastic model **(5.4.1–1)** can be written as follows

$$\hat{\theta}(k+1/k+1) = \tilde{\theta}(k+1/k) + K(k+1)\cdot[Z(k+1) - H\cdot\tilde{\theta}(k+1/k)] \tag{5.4.1–4}$$

$$\tilde{\theta}(k+1/k\ \ ) = g(\tilde{\theta}(k/k),\ T);$$

For system models **(5.3.1–1)**

$$\dot{\theta}(t) = F(\theta(t))\ ;$$

then, in discrete time with sample interval T,

$$\Delta\theta(k+1) = \Phi(T)\cdot\Delta\theta(k)\ ;$$

where Φ is the transition matrix for state vector θ.

Note that if Φ(T) is approximated by the truncated series $\Phi(T)= I + J\cdot T$, where I is 2 x 2 identity matrix, this is equivalent to the Euler solution of the original equations. The Kalman gain and error covariance are decribed as follows:

$$K(k+1) = \underline{P}^*(k+1)\cdot H\cdot[H\cdot P^*(k+1)\cdot H^T + R\ ]^{-1}\ ; \tag{5.4.1–6}$$

$$\underline{P}^*(k+1)= \Phi(k)\cdot\underline{P}(k)\cdot\Phi^T(k) + Q\ \ ; \tag{5.4.1–7}$$

$$\underline{P}(k) = (1 - K(k)\cdot H)\cdot\underline{P}^*(k)\ ;$$

where

$\hat{\theta}(k+1/k+1)$ = the 2 x 2 optimal state estimation at time k+1.

$\tilde{\theta}(k+1/k)$ = the 2 x 1 state estimate at time k+1 based on estimate $\tilde{\theta}(k/k)$ at time k only (prediction).

Z(k+1) = the 2 x 2 output (observation) vector at time k+1.

H = the 2 x 2 observation matrix .

K(k+1) = the 2 x 1 optimal Kalman matrix gain at time k+1.

$K(k+1)[Z(k+1) - H\tilde{\theta}(k+1/k)]$

= the so-called innovation sequence(correction).

$\underline{P}(k)$ = the 2 x 2 positive definite symmetric error filtering covariance matrix.

$$= E[((\hat{\theta}(k) - \tilde{\theta}(k/k))\cdot((\hat{\theta}(k) - \tilde{\theta}(k/k))^T]; \qquad (5.4.1\text{–}8)$$

$\underline{P}^*(k+1)$ = the 2 x 2 positive definite symmetric error prediction covariance matrix:

$$= E[(\hat{\theta}(k+1) - \tilde{\theta}(k+1/k))(\hat{\theta}(k+1) - \tilde{\theta}(k+1/k))^T]; \qquad (5.4.1\text{–}9)$$

$\Phi(k)$ = the 2 x 2 transition matrix of linearised perturbation model evaluated at time k for estimate $\tilde{\theta}(k/k)$.

$g(\tilde{\theta}(k/k),T)$= the function from equations **(5.4.1–1)**, **(5.4.1–2)**, **(5.4.1–3)**

The transition matrix $\Phi(k)$ can be obtained by linearising of non-linear madels equations **(5.4.1–1)**, **(5.4.1–2)**) around estimate $\theta(k)$.

$$\begin{aligned}\hat{\theta}(k+1) &= \tilde{\theta}(k) + T\cdot F(\tilde{\theta}(k)) \\ &= [I + T\cdot J|_{\theta(k)}]\cdot\Delta\theta(k) + \omega(k)\ ; \qquad (5.4.1\text{–}10)\end{aligned}$$

$J|_{\theta(k)}$ = the Jacobian of f (equations (5.3.1–1), (5.3.1–2), (5.3.1–3), (5.3.2–1)) evaluated for estimate $\theta(k)$.

$\Delta\theta(k)$ = $[\hat{\theta}(k) - \tilde{\theta}(k)]$is the 2 x 1 state perturbation vector.

The matrix $\Phi(k)$ can be described as follows

$$\Phi(k) = I + T\cdot J|_{\theta(k)}\ ; \qquad (5.4.1\text{–}11)$$

5.4.2 Jacobian Matrix

Considering a fed-batch fermentation process model ((5.3.1–1), (5.3.1–2), (5.3.1–3), (5.3.2–1)). The Jacobian $J|\theta(k)$ matrix can be evaluated as follows:

$$J_{11} = \frac{\partial F_1[\theta(t)]}{\partial\theta_1(t)}\Big|_{\theta(k/k)} = \frac{\partial F_1[X(t),\ S(t)]}{\partial X(t)}\Big|_{\theta(k/k)}$$

$$= \frac{\mu_{max}\cdot S(k/k)}{K_S + S(k/k)} - D\ ; \qquad (5.4.2\text{–}1)$$

$$J_{12} = \frac{\partial F_1[\theta(t)]}{\partial\theta_2(t)}\Big|_{\theta(t)} = \frac{\partial F_1\ [X(t),\ S(t)]}{\partial S(t)}\Big|_{\theta(k/k)}$$

$$= \frac{\mu_{max}\cdot K_S\cdot X(k/k)}{(Ks+\ S(k/k))^2}\ ; \qquad (5.4.2\text{–}2)$$

$$J_{21} = \frac{\partial F_2[\theta(t)]}{\partial \theta_1}\Big|_{\theta(k/k)} = \frac{\partial F_2\ [X(t),\ S(t)]}{\partial X(t)}\Big|_{\theta(k/k)}$$

$$= -\frac{K_1 \cdot \mu_{max} \cdot S(k/k)}{K_S\ +\ S(k/k)}\ ; \qquad (5.4.2\text{–}3)$$

$$J_{22} = \frac{\partial F_2[\theta(t)]}{\partial \theta_2(t)}\Big|_{\theta(k/k)} = \frac{\partial F_2[X(t),\ S(t)]}{\partial S(t)}\Big|_{\theta(k/k)}$$

$$= -\frac{K_1 \cdot \mu_{max} \cdot K_S \cdot X(k/k)}{K_S\ +\ S(k/k)} - D\ ; \qquad (5.4.2\text{–}4)$$

5.4.3 Initial Conditions

The initial conditions $\theta_1(0)$, $\theta_2(0)$ of the process are assumed to be normally distributed with co-variance $\underline{P}_0$, which was presented in **(5.3.2–6)**.

where

$\theta(0)$ = mean of initial process state vector.

$\underline{P}(0)$ = initial value of estimate error covariance matrix.

Favourable initial values of the EKF variables for the on-line estimation were determined by simulation. The developed filter worked satisfactory on the fed-batch process after slight modification of the parameter estimation procedure. The simulation data and experimental data are separately used in the EKF algorithm for obtaining the estimation results.

5.4.4 Error Dynamics

The comparison of predicted values and measurements leads to an estimated error

$$\epsilon(k+1) = \theta(k+1) - \hat{\theta}(k+1)\ ; \qquad (5.4.4\text{–}1)$$

The error is minimised by an internal feedback loop with Kalman gain K(k+1). (equation **(5.4.1–6)**)

5.4.5 EKF Algorithm Flowchart

The on-line optimal state estiamtion based on the EKF technique can be represented as follows:

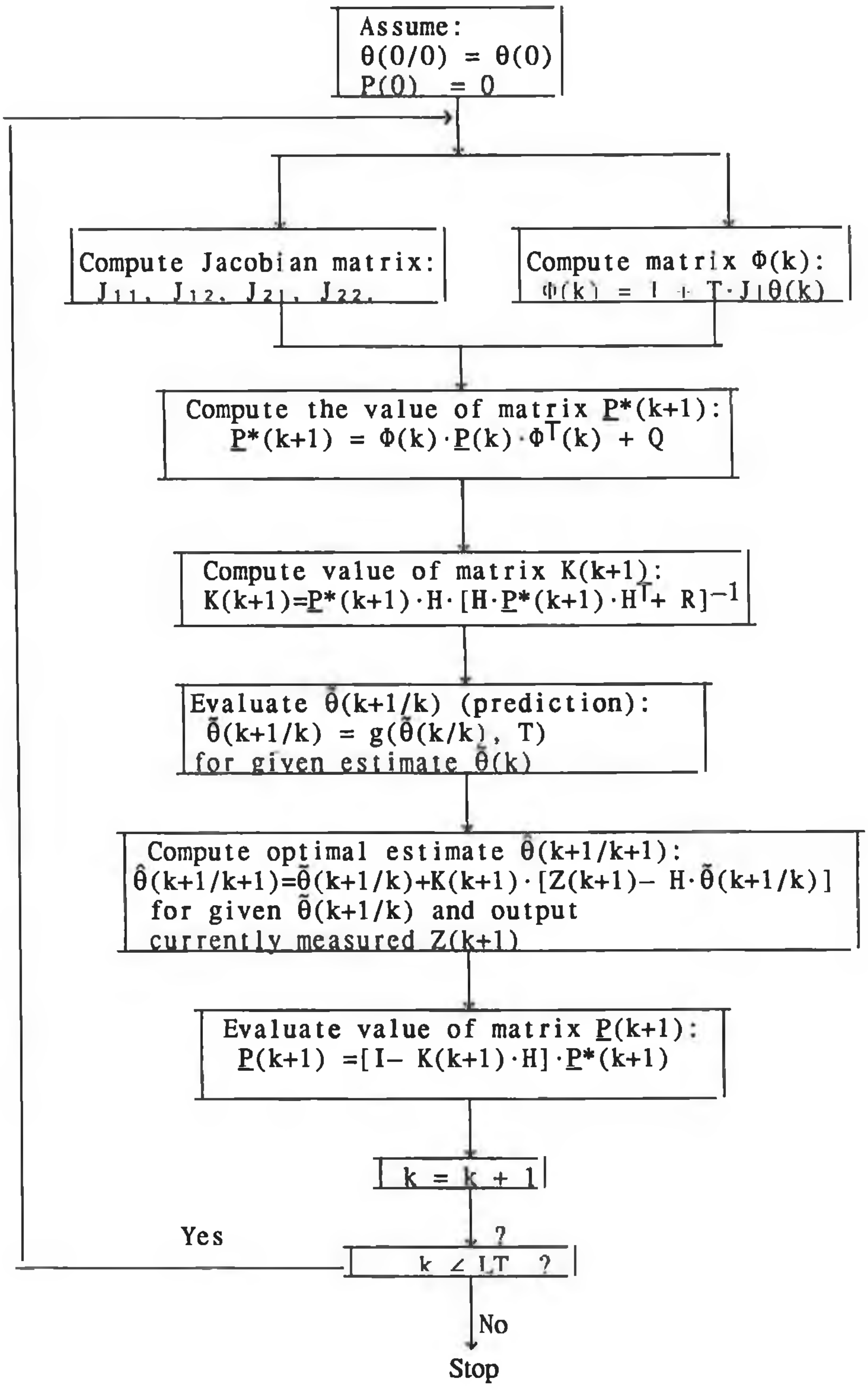


Fig 5.4.5 EKF Algorithm Flowchart

5.5 Experimental Results

With the algorithm of the described extended Kalman filter parameter and state estimations were carried out for a fed-batch and a batch fermentation processes.

The following identified model parameters which refer to a laboratory scale fermentor in a pilot plant have been used.

Common initial Conditions :

$X(0) = 0.35$ g/l ; $S(0) = 1.0$ g/l ;(for a fed-batch); $S(0)=12.2$ g/l (for a batch)

The initial condition of filter covariance matrix :

$$P(0) = \begin{vmatrix} 0.01 & 0 \\ 0 & 0.01 \end{vmatrix} \quad ;$$

R and Q are supposed to be uncorrelated zero mean white noise covariances. The choise of the different covariance matrices (i.e. P, Q, R) is one of the most difficult task of the implementation of EKF. They can be approximately set from examination of previous runs data but they have to be considered as important tuning parameters affecting the filter covariance. After tests on simulated processes it appeared that precautions have to be taken to deal with numerical information losses. It is especially important to verify that the P matrix is keeping its symmetry. These initial values of covariances can be determined empirically by simulations and experiments, which are based on the experimental samples of biomass and substrate concentrations.

Parameters :

$K_s = 2.0$; $\Delta t = 0.05$; $\mu_{max} = 0.4$; $S_{fi} = 12$; $Currt = 0.0$; $D = 0.2$;

The on-line estimation results of biomass and substrate have been shown in Chapter 8 (Fig 16, 17) using the data from simulation results.

The on-line estimation results of biomass and substrate using experimental data are also presented in Chapter 8 (Fig 18, 19, 20).

5.6 Conclusion

It has been successfully demonstrated that the states of a complex biotechnical process can be estimated on-line by extended Kalman filter methods. The observability of the process must be carefully taken into consideration to avoid estimation problems. For this process it is necessary to measure the oxygen and carbon-dioxide concentrations.

All algorithms are observed to be sensitive to errors in initial estimation of biomass and substrate and on-line measurements, such as oxygen and carbon-dioxide concentrations. There is a serious problem of finding an initial estimate of the error covariance. The application of computer simulation techniques for the development of a Kalman filter has been demonstrated here for a fed-batch and a batch fermentation process. The inherent delay for running an estimation algorithm can be permitted in the control of a fermentation process.

Chapter 6 Iterative Extended Kalman Filter

6.1 Introduction

The extended Kalman filter is a popular method for treating non-linear estimation problems.(e.g., Chapter 5). However, if nonlinearities are sufficiently important, the estimation error can be significantly reduced through use of a high-order estimation technique.[29] The iterative extended Kalman filter can yield substantially better estimates of nonmeasurable state variables.

6.2 Summary of Algorithm

This algorithm is based on the extended Kalman filter algorithm. The estimated state variables $\hat{\theta}(k+1/k+1)$ given in equation **(5.4.1–4)** can be improved by repeatedly calculating $\hat{\theta}(k+1/k+1)$, $K(k+1)$ and $\underline{P}(k)$, each time linearizing about the most recent estimate. To develop this algorithm, denote the ith estimate of $\hat{\theta}(k+1/k+1)$ by $\hat{\theta}(k+1/k+1)^i$, i=0, 1, 2, ..., and expand the estimated state at time k at the ith iteration of the output equation in the form:

$$\hat{\theta}(k+1/k+1)^{i+1} = \hat{\theta}(k+1/k) + K[\hat{\theta}(k+1/k+1)^i,\ k+1]\cdot\{Z(k+1)^i - h[\hat{\theta}(k+1/k+1)^i,\ u_k] - M[\hat{\theta}(k+1/k)^i]\cdot[\hat{\theta}(k+1/k) - \hat{\theta}(k+1/k+1)^i]\}\ ; \qquad \textbf{(6.2–1)}$$

The iteration with starting value $\hat{\theta}(k+1/k+1)^1 = \hat{\theta}(k+1/k)$ proceeds until
$|\hat{\theta}(k+1/k+1)^i - \hat{\theta}(k+1/k+1)^{i-1}| \leqq \epsilon_f$.
is reached. The bound ϵ_f must be chosen. The actual Kalman gain is given by

$$K[\hat{\theta}(k+1/k+1)^i,\ k+1] = P^*(k+1/k)\cdot M^T[\hat{\theta}(k+1/k+1)^i] \cdot\{M[\hat{\theta}(k+1/k+1)^i]\cdot P^*(k+1/k)\cdot M^T[\hat{\theta}(k+1/k+1)^i] + R(k+1)\}^{-1}; \qquad \textbf{(6.2–2)}$$

and the filter covariance by

$$P(k+1/k) = \{I - K[\hat{\theta}(k+1/k+1),k+1]\cdot M[\hat{\theta}(k+1/k+1)]\}\cdot P^*(k+1/k); \qquad \textbf{(6.2–3)}$$

The predictions of state and filter covariances are

$$\hat{\theta}(k+1/k) = \Phi[\hat{\theta}(k/k),T]\ ; \qquad \textbf{(6.2–4)}$$

$$P^*(k+1/k) = A(\hat{\theta}(k/k)]\cdot P(k/k)\cdot A^T[\hat{\theta}(k/k)] + Q(k)\ ; \qquad \textbf{(6.2–5)}$$

where

$$M[\theta(k),T] = \left.\frac{\partial H[\theta(k),\ T]}{\partial \theta(k)}\right|_{(\theta(k),\ T)} \quad ; \qquad (6.2\text{–}6)$$

and

$$A[\theta(k),\ T] = \left.\frac{\partial \Phi[\theta(k),\ T]}{\partial \theta(k)}\right|_{(\theta(k),\ T)} \qquad (6.2\text{–}7)$$

are the matrices of the linearised system. The noniterative filter can be seen as a special case of these last equations.

6.3 Algorithm Flowchart

The on-line optimal estimation of state variables based on the iterative EKF can be written as follows:

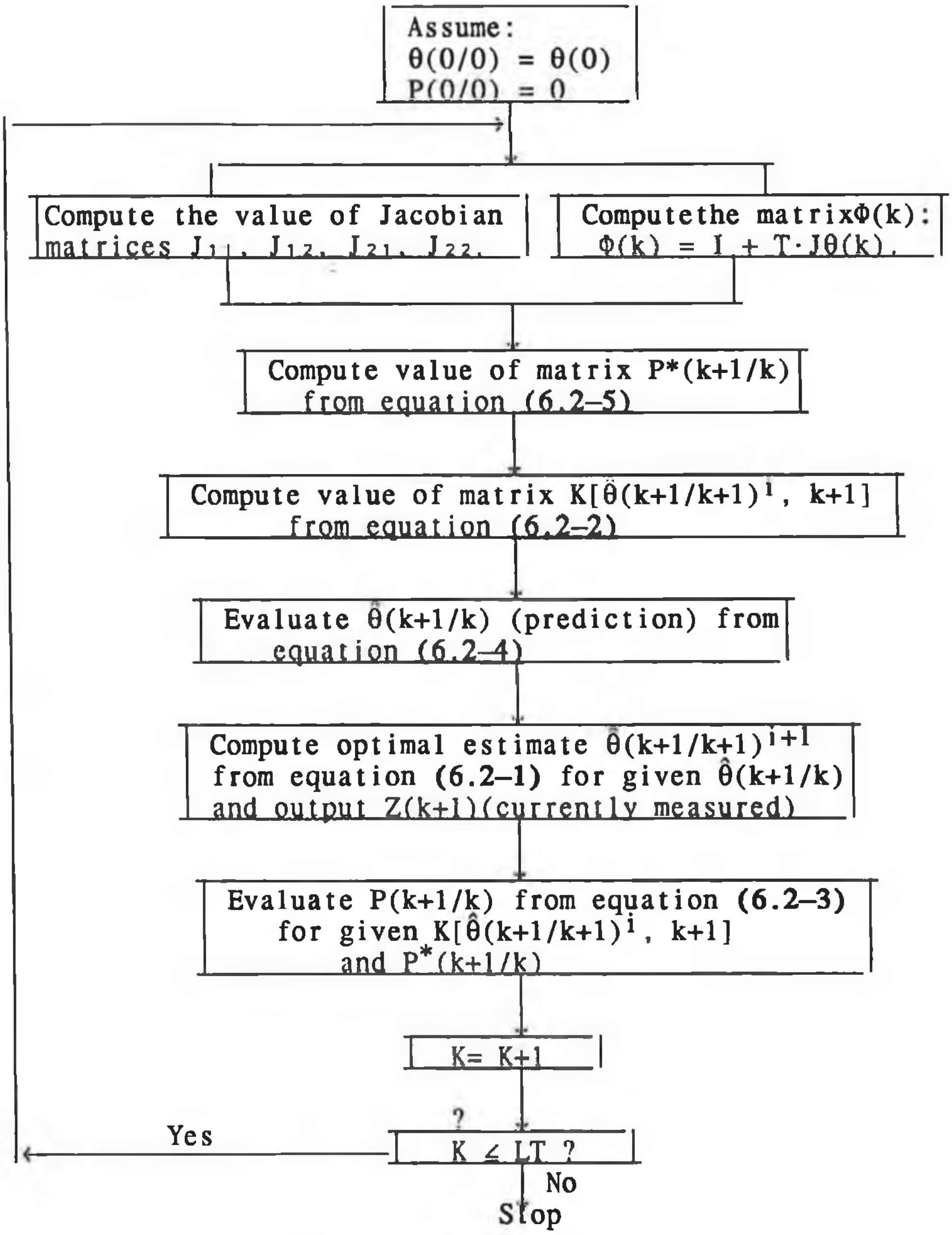


Fig 6.3 Iterative EKF Algorithm flowchart

6.4 Comments

The performance of the filter algorithm for on-line estimation of state variables of a fed-batch fermentation process was investigated by simulation. Due to the adaption of the system parameters, the estimation of biomass and substrate is very insensitive to an incorrect model. To improve the transient behaviour of the estimation error, which is dominated by the parameter estimation, further investigations will be necessary. It could be advantageous to include other parameters in the on-line estimation, to reduce the accuracy requirements of off-line identification. The errors of measurements of on-line oxygen and carbon-dioxide concentrations have also a slight effect on the estimation. For other non-linear fermentation processes, higher-order models could be used to estimate nonmeasurable states. The estimation results based on second order IEKF algorithm using same initial conditions of the state variables ,parameters and the covariance matrices with EKF are shown on Fig 22, 23 (Chapter 8). In this part of work, both of the results based on EKF and IEKF algorithms are satisfied.

Chapter 7 Conclusions

When one of state variables can be measured on-line, then a non-linear adaptive observer,an adaptive observer, or a non-linear observer,(introduced in chapter 2, 3, 4) can be applied to estimate another state variables.

When the specific growth rate is the only unknown parameter, the non-adaptive observer can be applied to on-line estimation of state variables. However, at present an important drawback is that the rate of convergence is completely determined by the experimental conditions (via the dilution rate D(t)). In particular the choice of the initial conditions may be very critical.

When all the paramaters are unknown, an adaptive observer can be applied to on-line estimation of state variables. It is also worth noting that all the proposed algorithms do not imply any analytical expression for the parameters, such as the specific growth rate $\mu(t)$ and the yield coefficients.

It can be observed that the application of a non-linear observer for the estimation of substrate and biomass concentration has led to realizability problems. It's necessary to build differentiators. However, the use of approximate differentiators has given good results.

It has been demonstrated that states and parameters of a complex biotechnical process can be estimated on-line by extended Kalman filter (EKF) methods. The estimation of substrate and biomass in fermentation processes is based on some known information (e.g., oxygen and carbon-dioxide concentration can be measured on-line). The experimental and computer simulation results show that the extended Kalman filter gives satisfactory results during computer simulation.

When state noise covariance and observation noise covariance are not known a priori, the adaptive EKF algorithm can be used on-line to identify the unknown covariances.

If nonlinearities are sufficiently important and the estimation error cannot satisfy the industrial demands, then the iterative extended Kalman filter can be applied to on-line estimation. Because of the better approximation for non-linear system, the iterative filter shows a faster convergence when estimating the state variables or parameters.

There is a serious problem in finding an initial estimate of the error covariances. It can be observed that all algorithms are sensitive to errors in initial estimate of substrate and biomass in conjunction with on-line measurements, such as oxygen and carbon-dioxide concentrations. This is possible even with very simple mathematical models which are based on extensive simplifications. The observability of the process must be carefully taken into consideration to avoid estimation problems.

In appendix A, a non-linear filtering algorithm will be introduced to estimate state variables. This algorithm should have some better computation and robustness properties which are clear improvements than other standard algorithms, such as extended Kalman filter, adaptive observer.

Arising from the results obtained in this part of the work a paper on state estimation techniques was presented by the auther at IECON' 91 International Conference on Industrial Electronics, Control and Instrumentation, which was held at Kobe in Japan from October 28 to November 1, 1991.[53]

Chapter 8 Simulation and Experimental Results (II)

The on-line state estimation results for fed-batch and batch fermentation processes will be shown in this chapter.

The following common initial conditions which refer to the laboratory scale fermentor in a pilot plant have been used :

The state variables:

$X(0)=0.35$ g/l; $S(0)= 12.2$ g/l; $O(0)= 0.18$ g/l;

$K_{X_1}= 0.5$; $K_{S_1}= 0.22$; $K_{X_2}= 0.4$; $K_{S_2} = 0.12$.

The parameters values:

$K_S=0.8$; $\Delta t=0.05$; $\mu_{max}=0.45$; $S_{fi}=10$; $Currt=0.01$; $D(0)=0.2$; $K_{O_2}=0.006$; $K_C=0.5$; $K_1 = 2.0$; $K_2 =1.0$.

Some of estimation results of substrate concentration for a fed-batch, which are based on an assumption that the simulation data can be available, are also presented.

Fig 1 to Fig 4 show the on-line estimation results of biomass and substrate concentrations using Monod's model, which are based on the Observer algorithms assuming one of state variable can be measured on-line.

Fig 5 to Fig 8 show the on-line estimation results of biomass and substrate concentrations using Ollson's model, which are based on the Observer algorithms assuming one of state variable can be measured on-line.

Fig 8 to Fig 12 show the on-line estimation results of biomass and substrate concentrations using Contois' model, which are based on the Observer algorithms assuming one of state variable can be measured on-line.

Fig 13 to Fig 15 show the on-line estimation results of dissolved oxygen concentration using Monod's model, which are based on the Observer algorithms assuming biomass concentration can be measured on-line. These results can be used to minimise the estimation errors of biomass and substrate concentrations indirectly.

Fig 16 to Fig 17 show the on-line estimation results of biomass and substrate concentrations for a fed-batch using the data from simulation results, which are based on the extended Kalman filter algorithm in conjunction with the measurements of dissolved oxygen and exhaust carbon-dioxide concentrations.

Fig 18 to Fig 20 show the on-line estimation results of biomass and substrate concentrations for a fed-batch and batch using the data from pilot experimental results, which are based on the extended Kalman filter algorithm in conjunction with the measurements of dissolved oxygen and exhaust carbon-dioxide concentrations.

Fig 21 shows the on-line estimation result of substrate concentration only for a batch fermentation process using the data from a pilot plant, which are based on the non-linear observer assuming biomass concentration can be measured on-line.

Fig 22 and Fig 23 show the on-line estimation results of biomass and substrate concentrations for a batch using the data from pilot plant, which are based on the second order IEKF algorithm in conjunction with the measurements of dissolved oxygen and exhaust carbon-dioxide concentrations.

These results demonstrated that the estimation technique can be successfully applied to a complex biotechnical process and I.E.K.F. has a faster convergence rate.

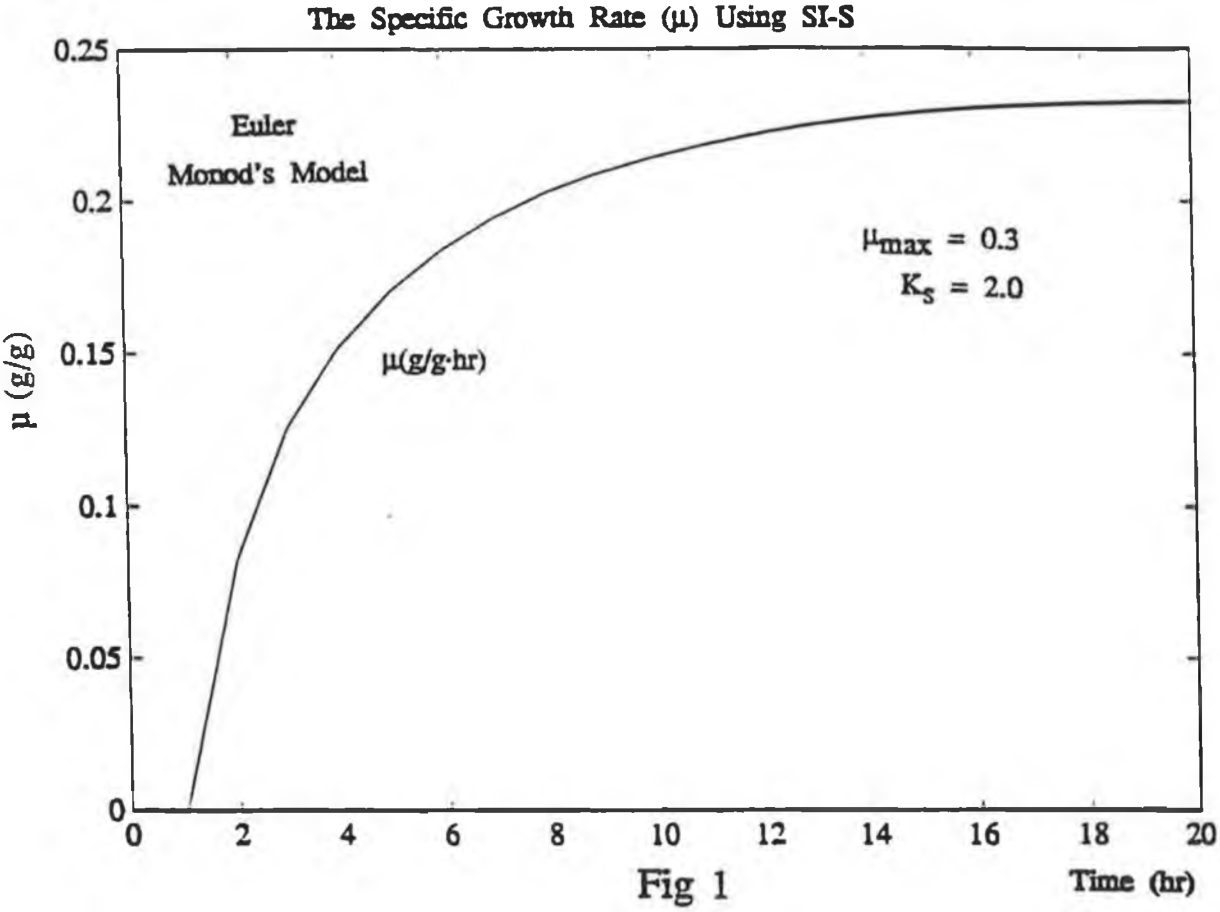

The Specific Growth Rate (μ) Using SI-S
Euler
Monod's Model
μ_{max} = 0.3
K_S = 2.0
μ(g/g·hr)
μ (g/g)
0.25
0.2
0.15
0.1
0.05
0
0
2
4
6
8
10
12
14
16
18
20
Time (hr)

Fig 1

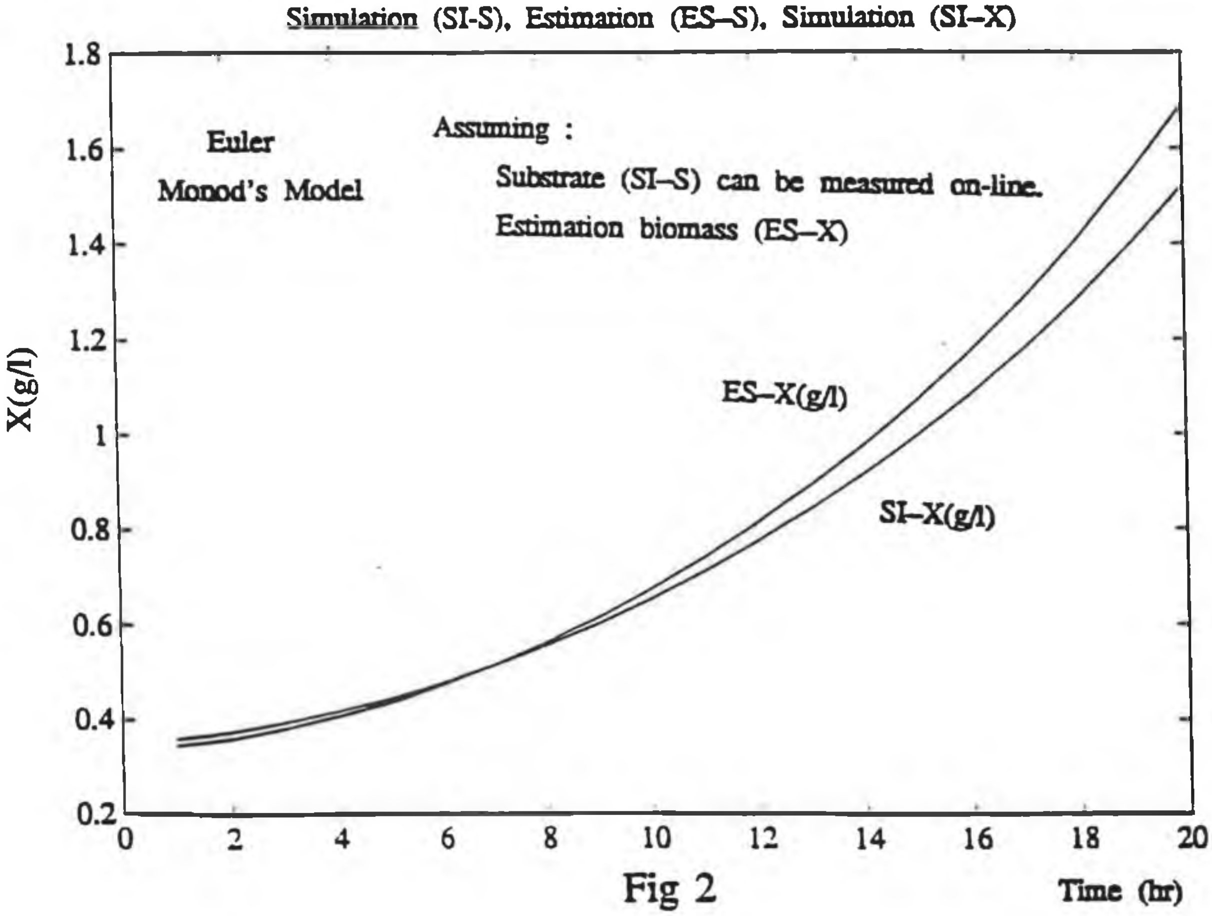

Simulation (SI-S), Estimation (ES–S), Simulation (SI–X)
Euler
Monod's Model
Assuming :
Substrate (SI–S) can be measured on-line.
Estimation biomass (ES–X)
ES–X(g/l)
SI–X(g/l)
X(g/l)
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
2
4
6
8
10
12
14
16
18
20
Time (hr)

Fig 2

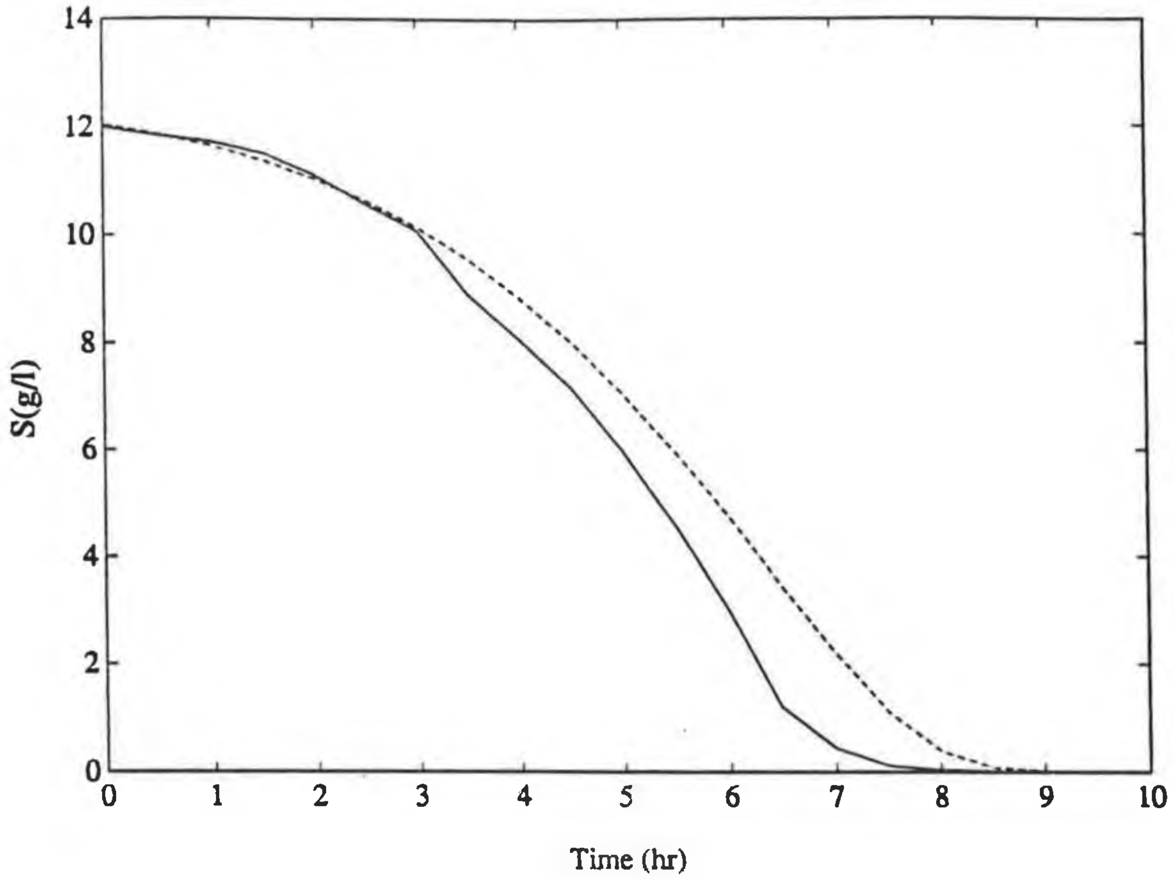


Fig 3 Estimation results of sustrate concentrations using Monod's model and Euler method based on non-adaptive algorithm assuming biomass concentration can be measured on-line.

-------- Simulation result of substrate concentration using Monod's model (g/l)

———— Estimation result of substrate concentration using Monod's model based on non-adaptive algorithm (g/l)

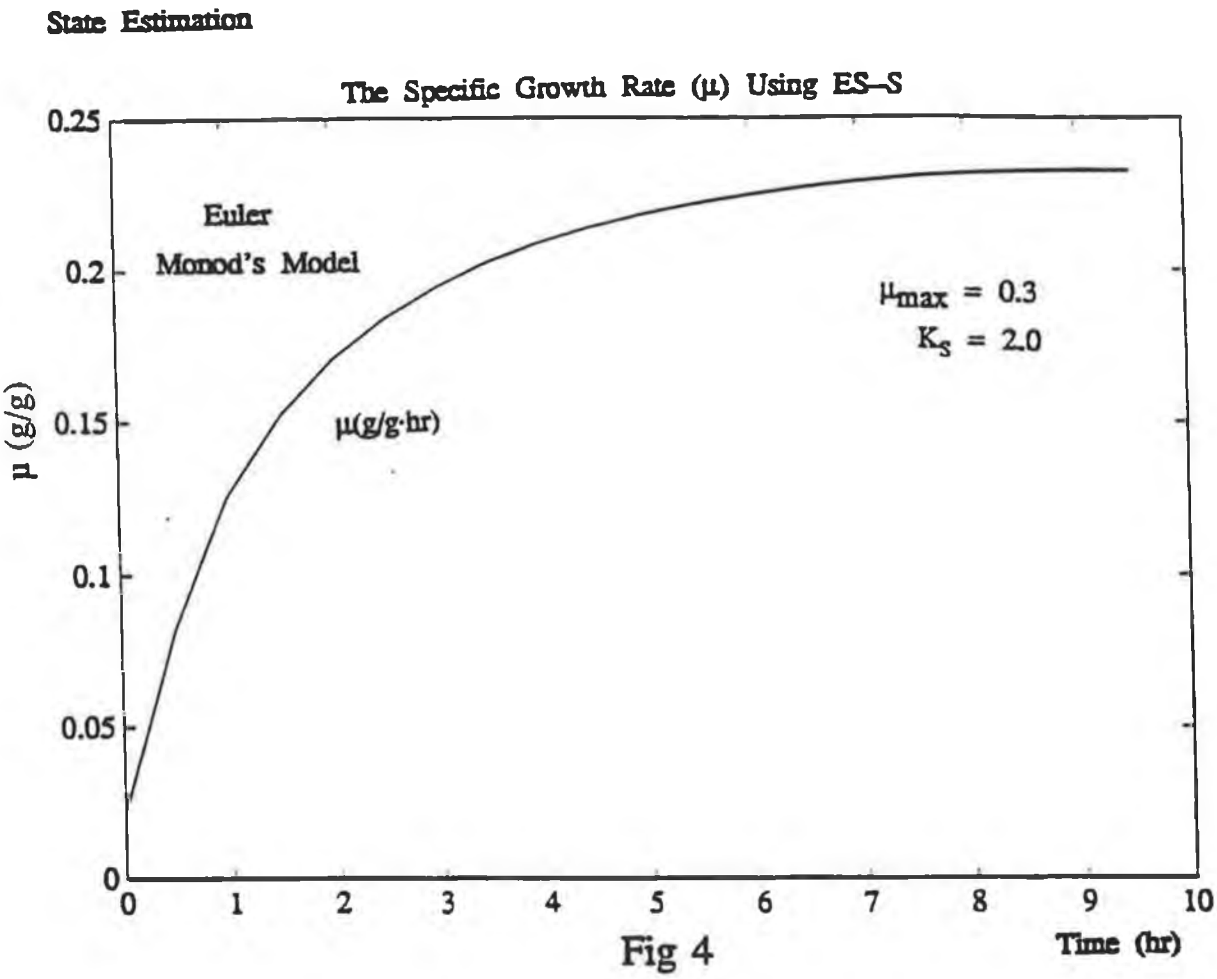

State Estimation
The Specific Growth Rate (μ) Using ES–S
Euler
Monod's Model
μmax = 0.3
Ks = 2.0
μ(g/g·hr)
μ (g/g)
0.25
0.2
0.15
0.1
0.05
0
0
1
2
3
4
5
6
7
8
9
10
Time (hr)

Fig 4

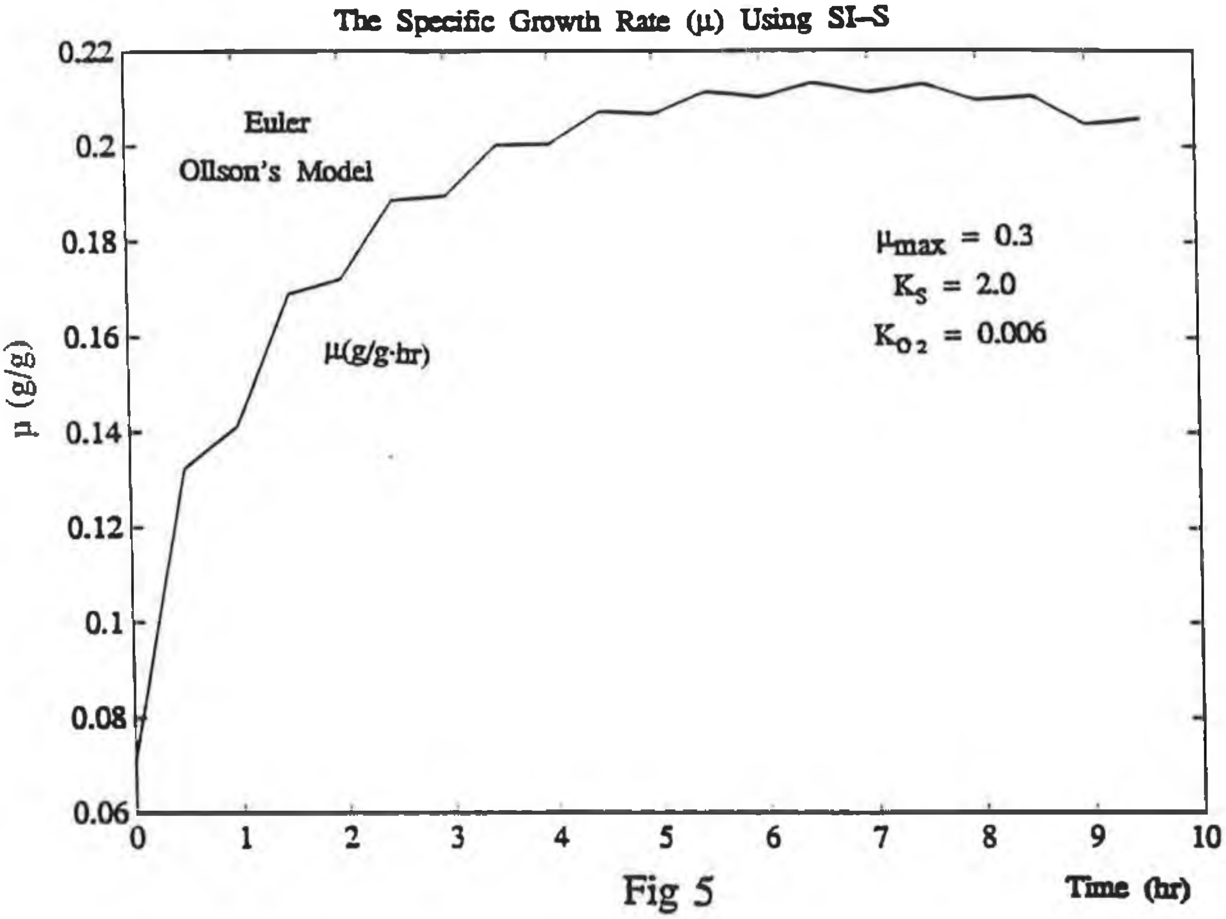

The Specific Growth Rate (μ) Using SI–S
Euler
Ollson's Model
μ(g/g·hr)
μmax = 0.3
Ks = 2.0
KO2 = 0.006
μ (g/g)
0.22
0.2
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0
1
2
3
4
5
6
7
8
9
10
Time (hr)

Fig 5

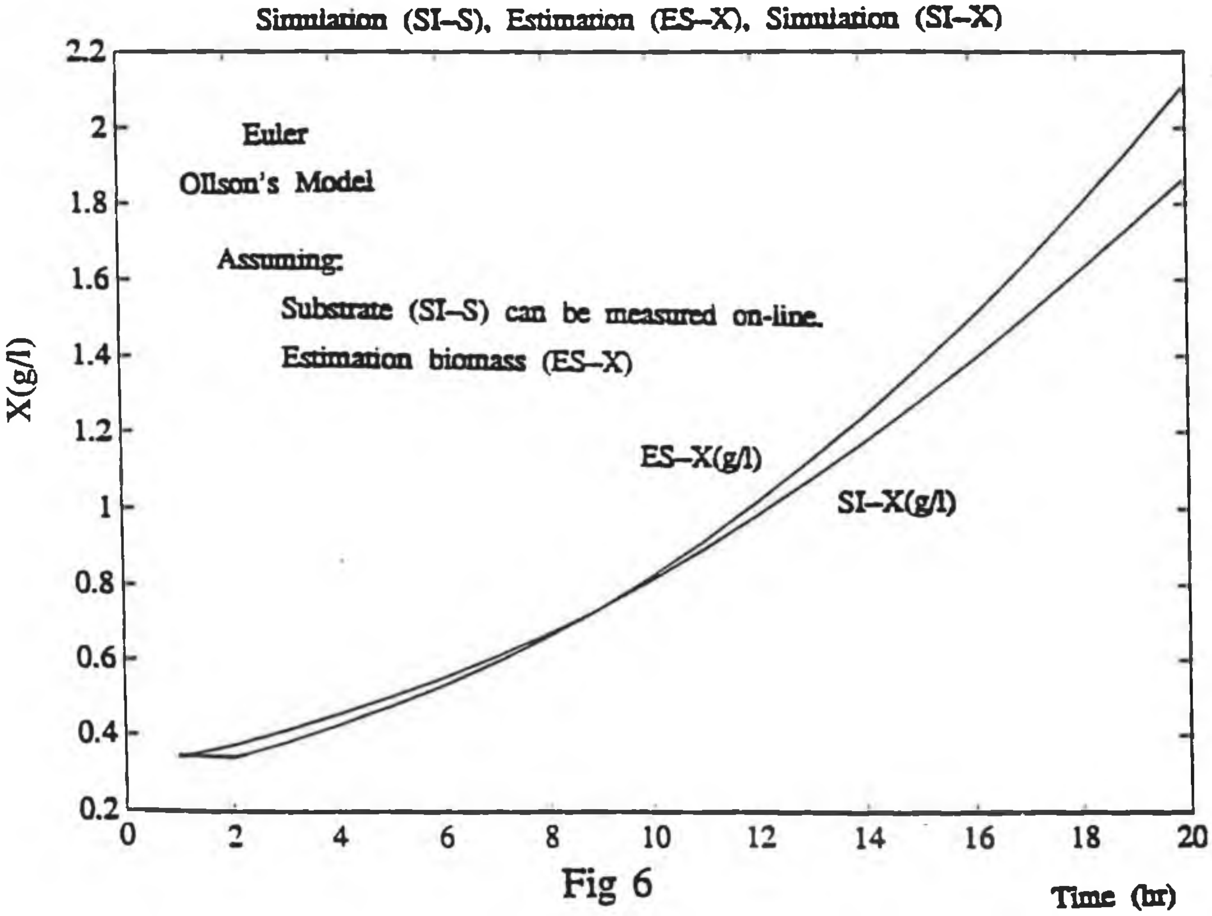

Simulation (SI–S), Estimation (ES–X), Simulation (SI–X)
Euler
Ollson's Model
Assuming:
Substrate (SI–S) can be measured on-line.
Estimation biomass (ES–X)
ES–X(g/l)
SI–X(g/l)
X(g/l)
2.2
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
2
4
6
8
10
12
14
16
18
20
Time (hr)

Fig 6

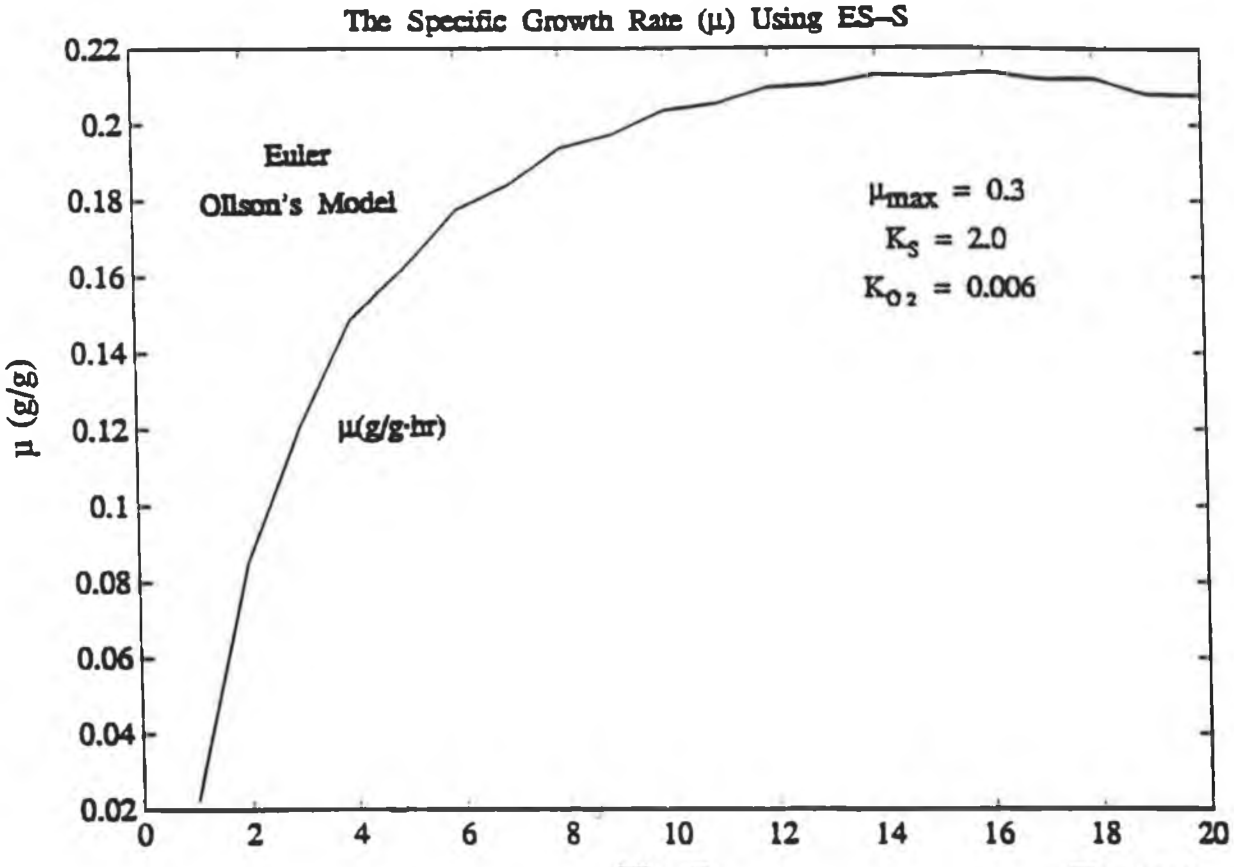

The Specific Growth Rate (µ) Using ES–S
Euler
Ollson's Model
μ_{max} = 0.3
K_S = 2.0
K_{O_2} = 0.006
µ(g/g·hr)
µ (g/g)
0.22
0.2
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
2
4
6
8
10
12
14
16
18
20

Fig 7

Time (hr)

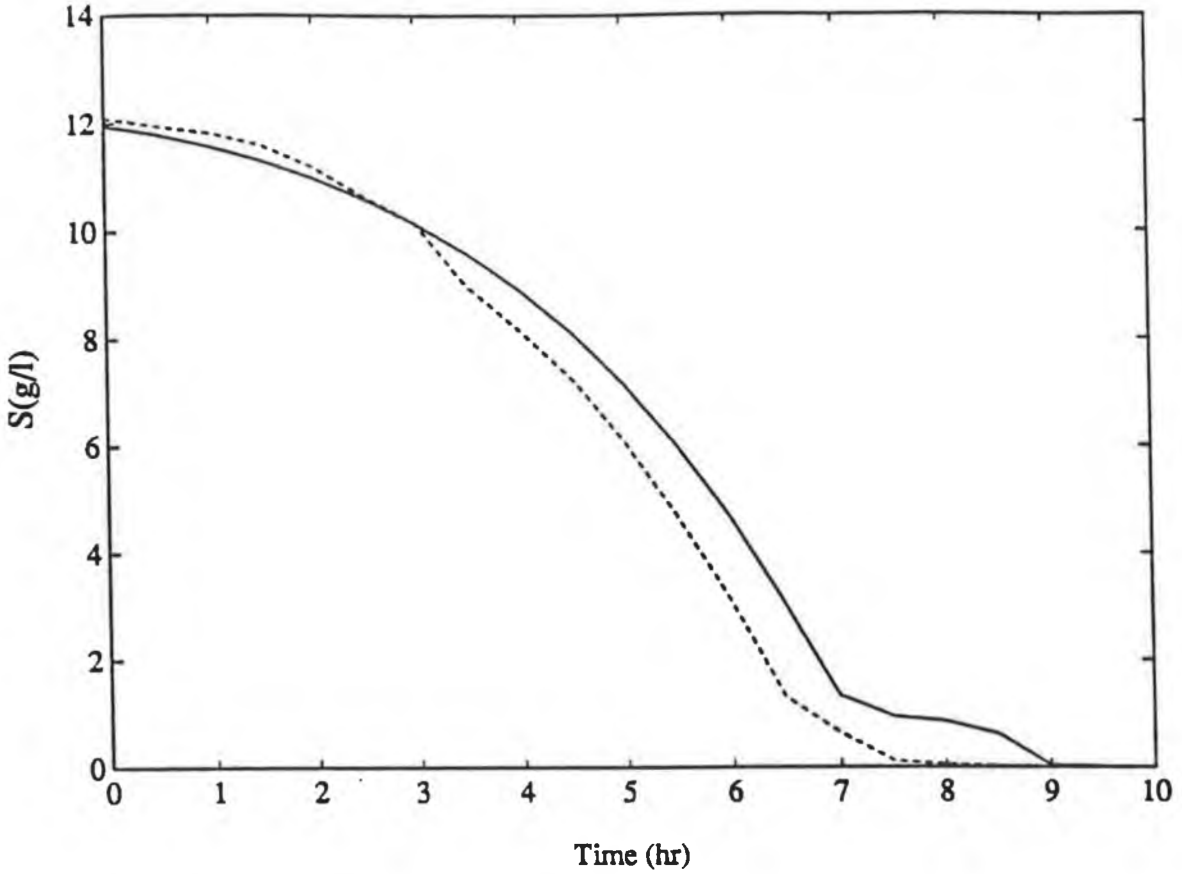


Fig 8 Estimation results of substrate concentration using Ollson's model and Euler method based on non-adaptive algorithm assuming biomass concentration can be measured on-line.

-------- Simulation result of substrate concentration using Ollson's model (g/l)

———— Estimation results of substrate concentration using Ollson's model based on non-adaptive algorithm (g/l)

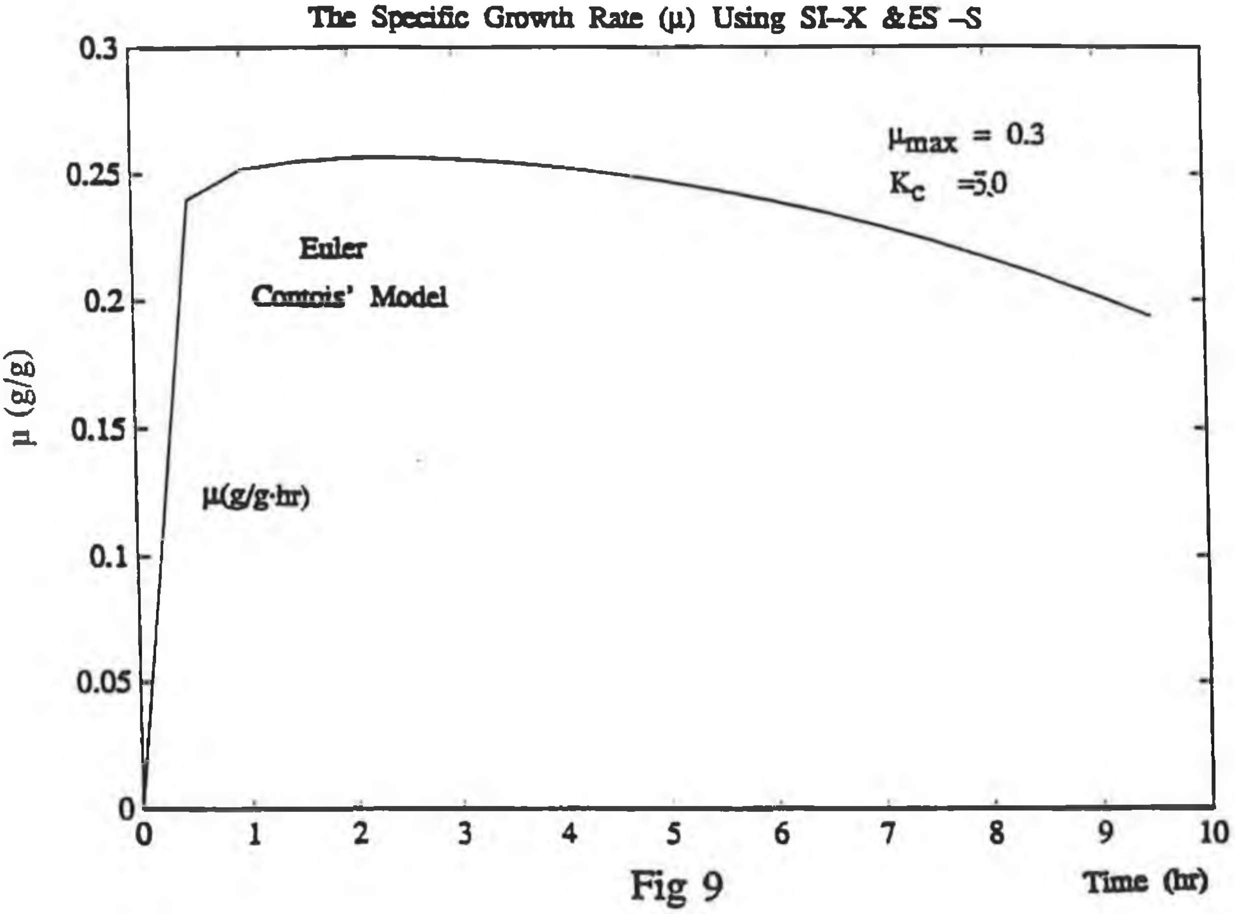

The Specific Growth Rate (μ) Using SI–X &ES –S
μ (g/g)
0.3
0.25
0.2
0.15
0.1
0.05
0
0
1
2
3
4
5
6
7
8
9
10
Time (hr)
μmax = 0.3
Kc =5.0
Euler
Contois' Model
μ(g/g·hr)

Fig 9

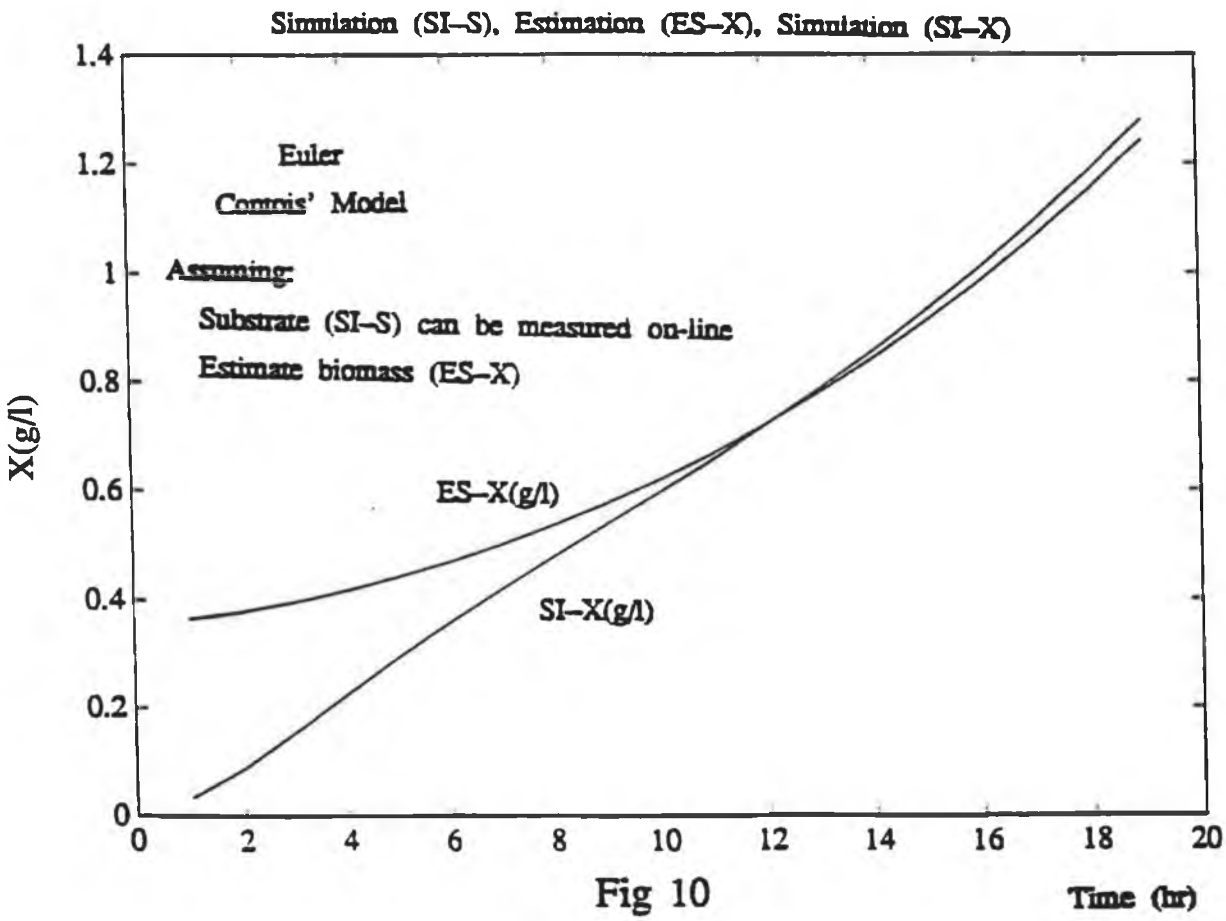

Simulation (SI–S), Estimation (ES–X), Simulation (SI–X)
Euler
Contois' Model
Assuming:
Substrate (SI–S) can be measured on-line
Estimate biomass (ES–X)
ES–X(g/l)
SI–X(g/l)
X(g/l)
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
2
4
6
8
10
12
14
16
18
20
Time (hr)

Fig 10

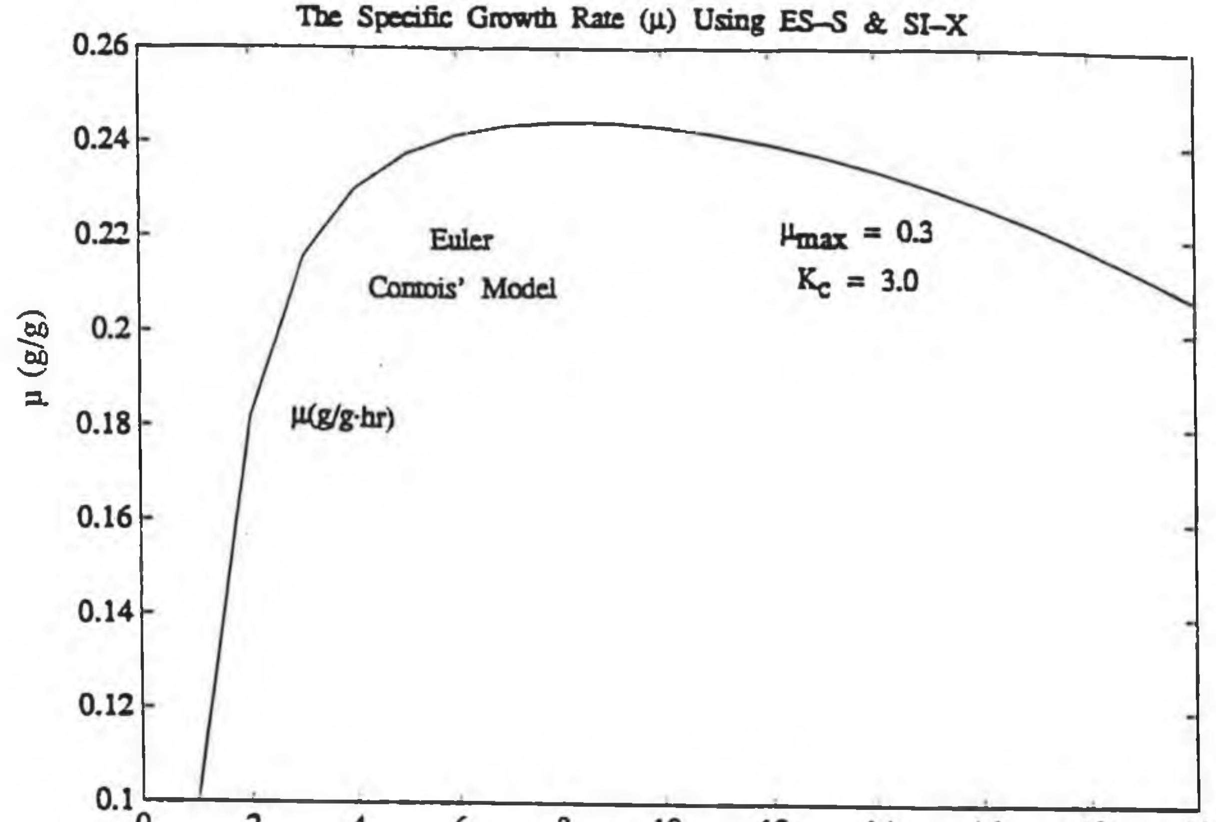

The Specific Growth Rate (μ) Using ES–S & SI–X
0.26
0.24
0.22
0.2
0.18
0.16
0.14
0.12
0.1
μ (g/g)
0
2
4
6
8
10
12
14
16
18
20
Euler
Contois' Model
μ_{max} = 0.3
K_c = 3.0
μ(g/g·hr)
Time (hr)

Fig 11

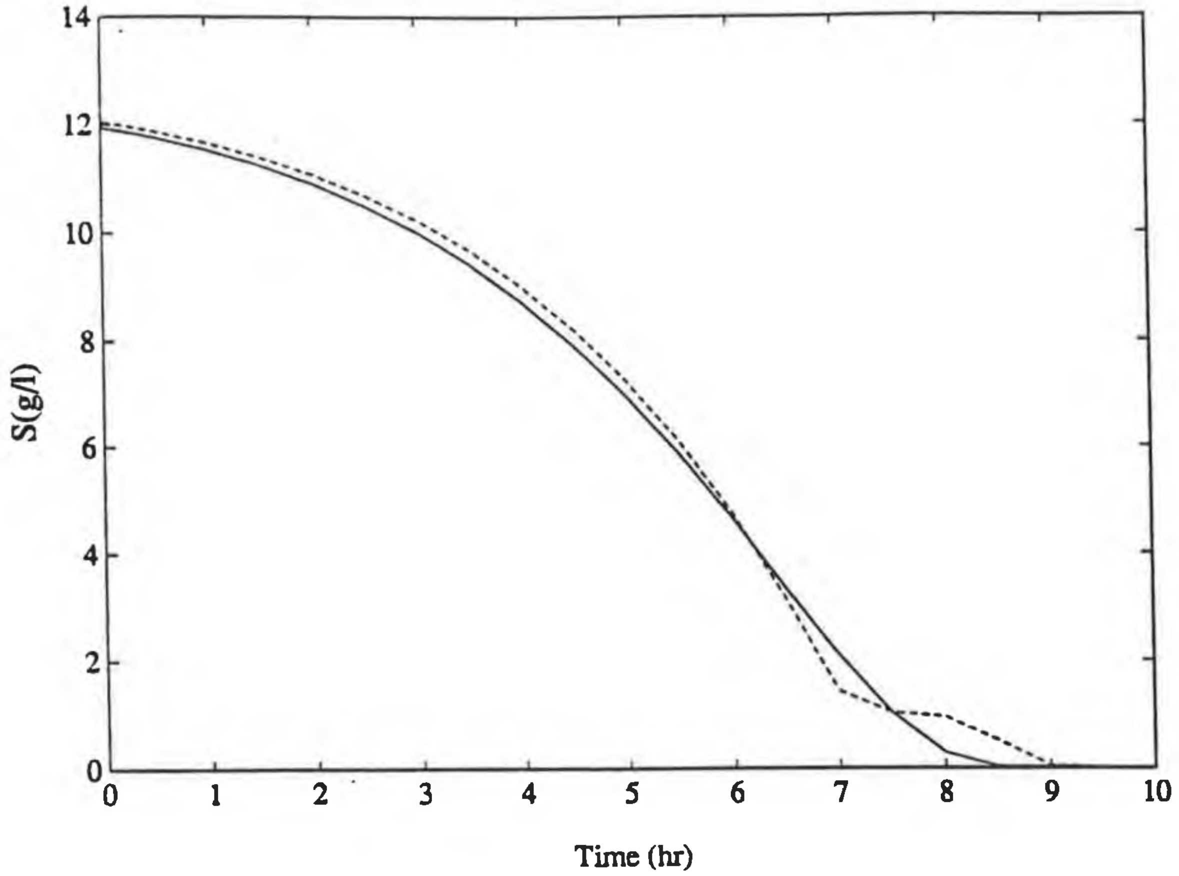


Fig 12 Estimation results of substrate concentration using Contois' model and Euler method based on non-adaptive algorithm assuming biomass concentration can be measured on-line.

------- Simulation result of substrate concentration using Contois' model (g/l)

________ Estimation result of substrate concentration using Contois' model based on non-adaptive algorithm (g/l)

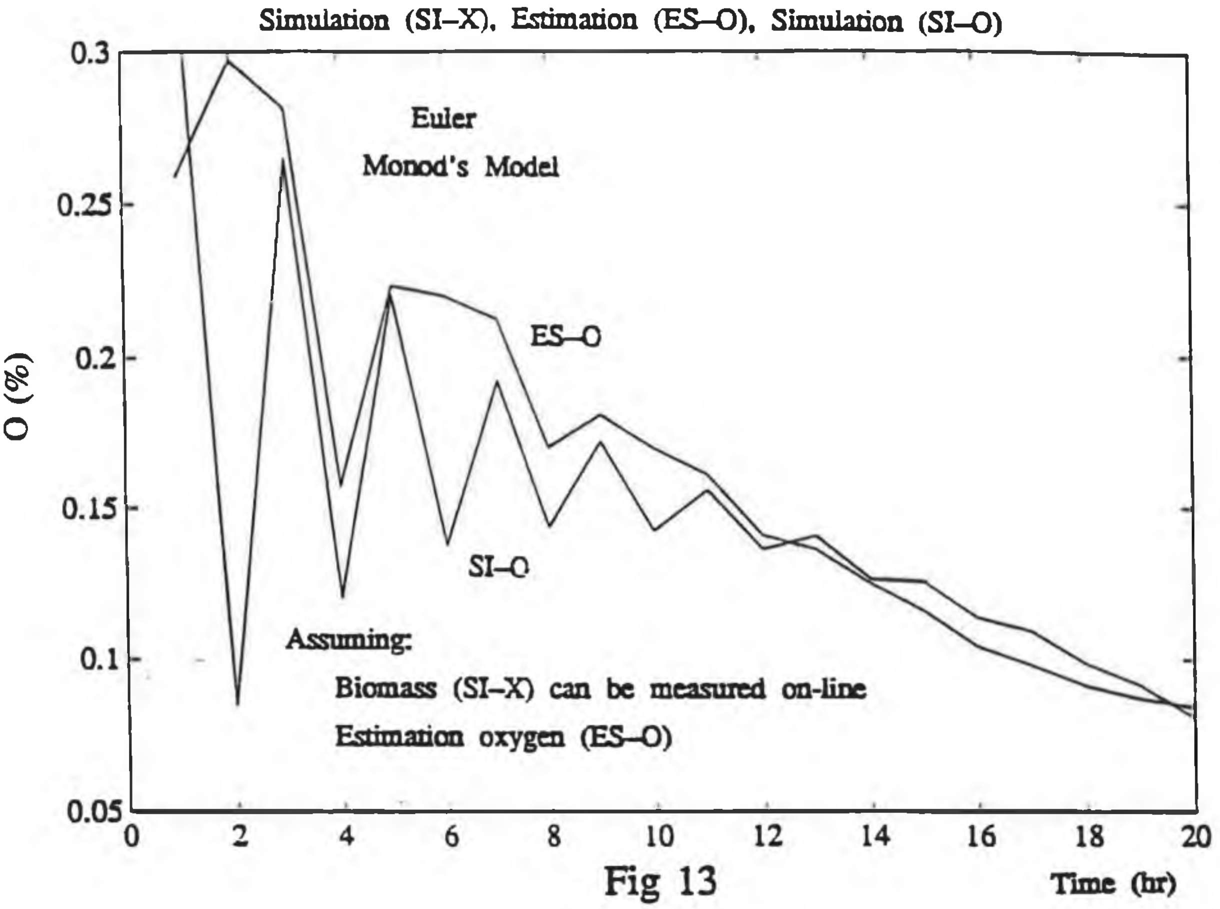

Simulation (SI–X), Estimation (ES–O), Simulation (SI–O)
Euler
Monod's Model
ES–O
SI–O
Assuming:
Biomass (SI–X) can be measured on-line
Estimation oxygen (ES–O)
O (%)
0.3
0.25
0.2
0.15
0.1
0.05
0
2
4
6
8
10
12
14
16
18
20
Time (hr)

Fig 13

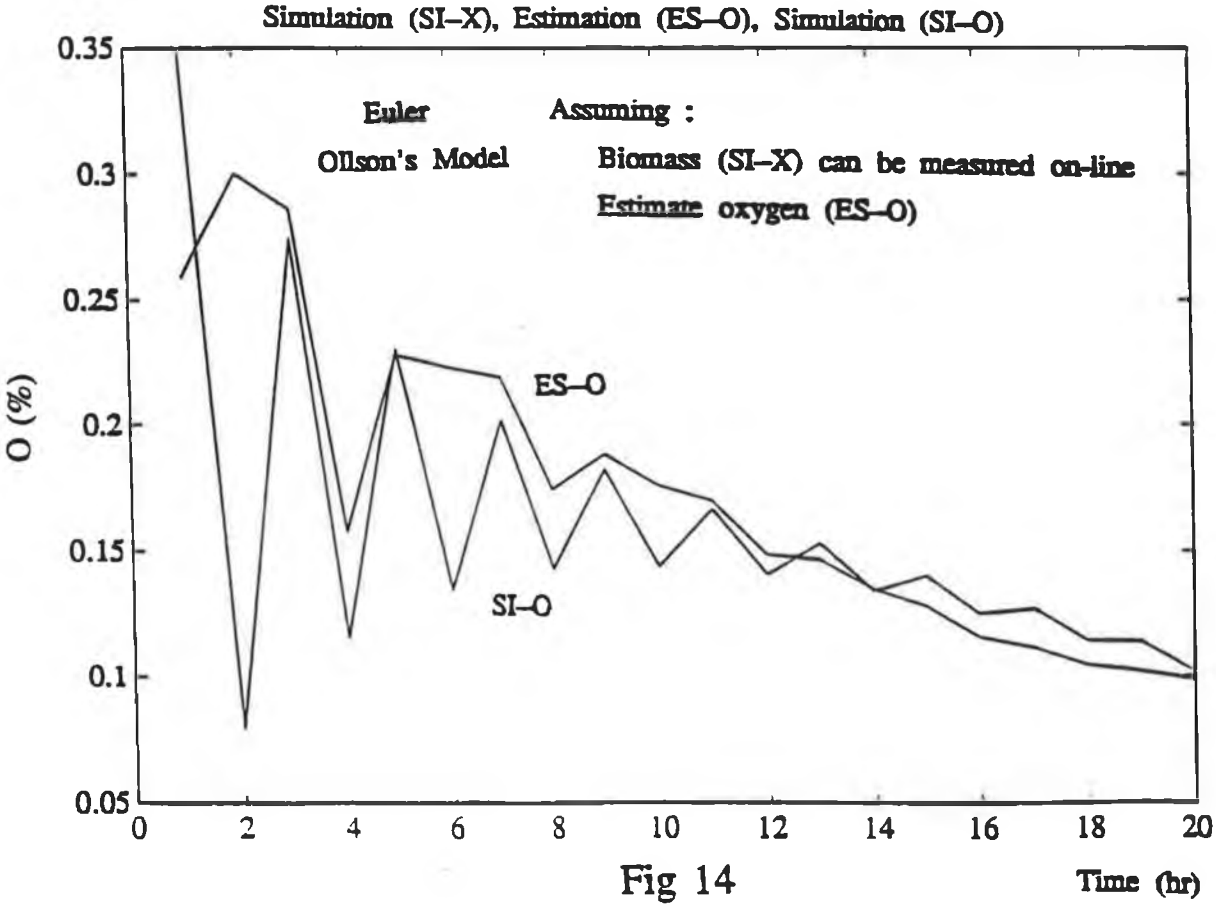

Simulation (SI–X), Estimation (ES–O), Simulation (SI–O)
Euler
Ollson's Model
Assuming :
Biomass (SI–X) can be measured on-line
Estimate oxygen (ES–O)
ES–O
SI–O
O (%)
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
2
4
6
8
10
12
14
16
18
20
Time (hr)

Fig 14

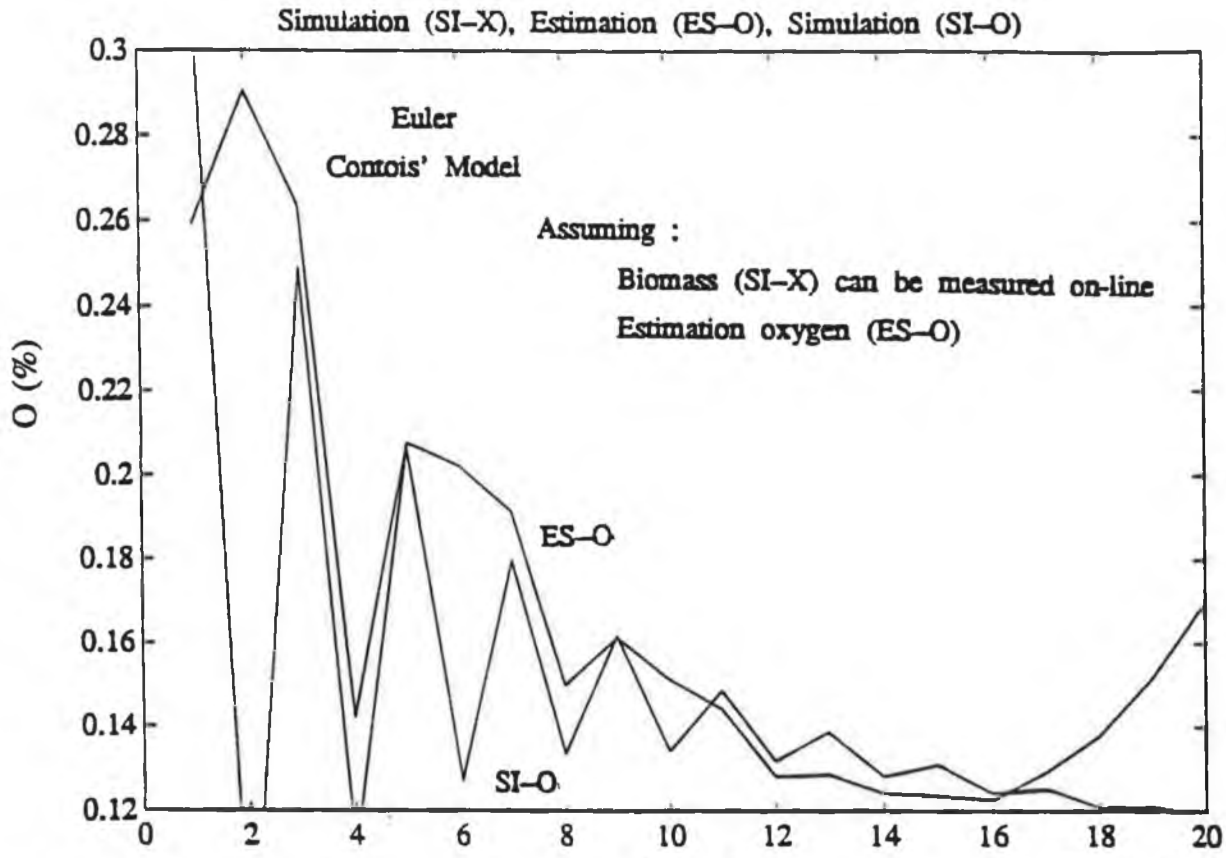

Simulation (SI–X), Estimation (ES–O), Simulation (SI–O)
Euler
Contois' Model
Assuming :
Biomass (SI–X) can be measured on-line
Estimation oxygen (ES–O)
ES–O
SI–O
O (%)
0.3
0.28
0.26
0.24
0.22
0.2
0.18
0.16
0.14
0.12
0
2
4
6
8
10
12
14
16
18
20
Time (hr)

Fig 15

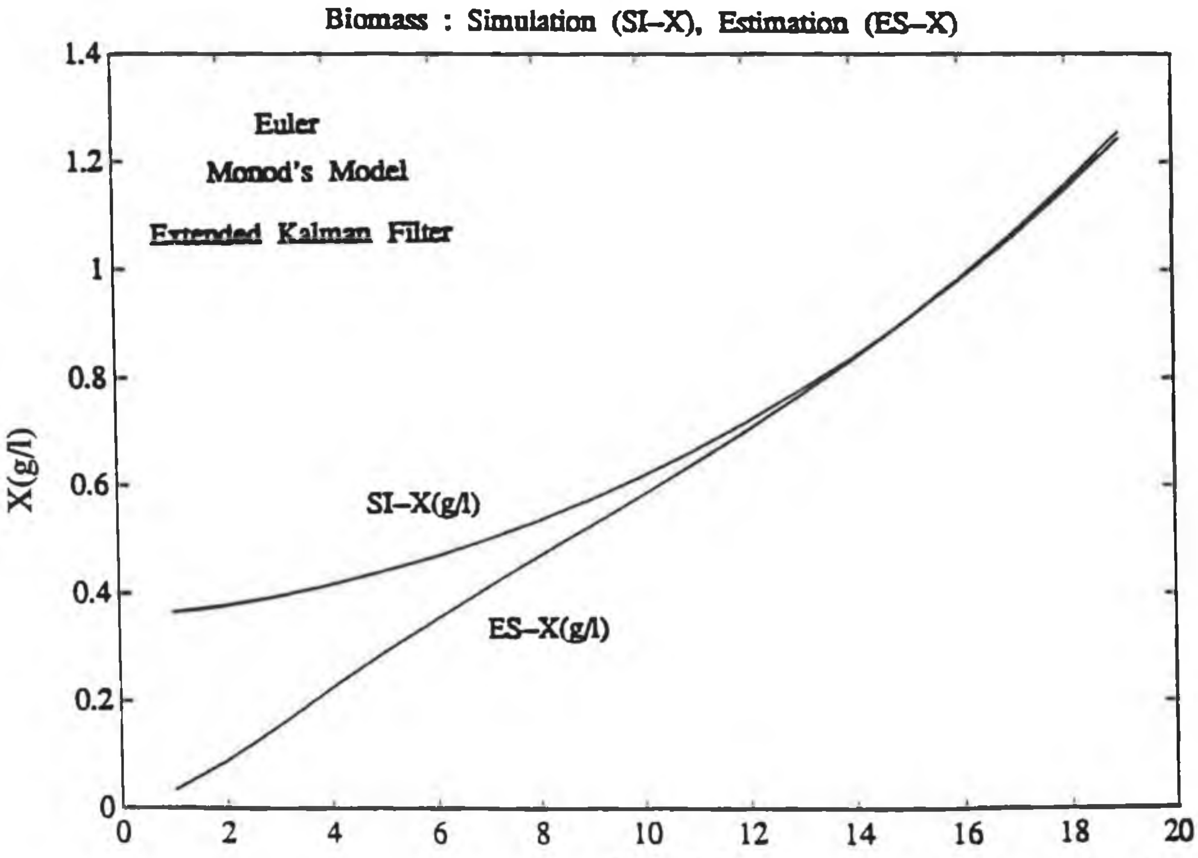

Biomass : Simulation (SI–X), Estimation (ES–X)
Euler
Monod's Model
Extended Kalman Filter
SI–X(g/l)
ES–X(g/l)
X(g/l)
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
2
4
6
8
10
12
14
16
18
20
Time (hr)

Fig 16

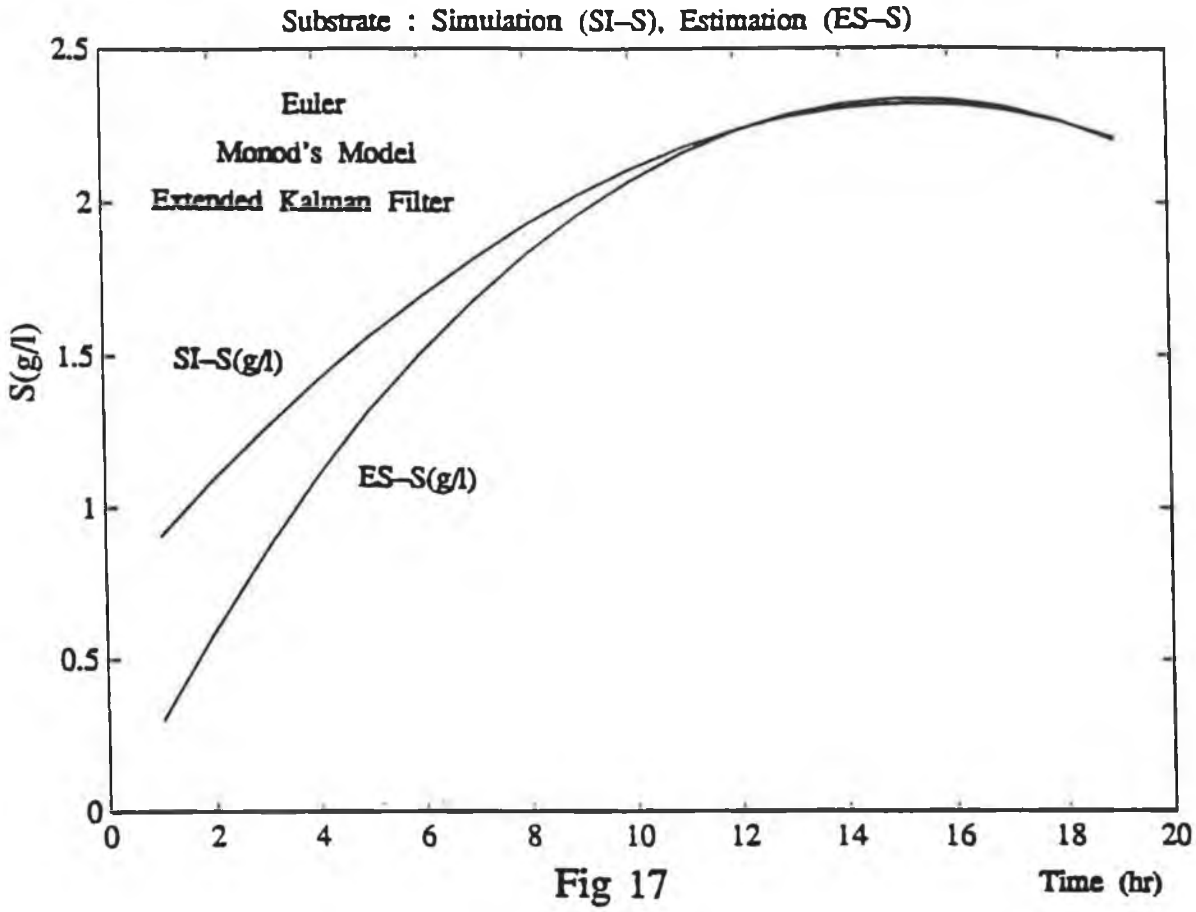

Substrate : Simulation (SI–S), Estimation (ES–S)
Euler
Monod's Model
Extended Kalman Filter
SI–S(g/l)
ES–S(g/l)
S(g/l)
2.5
2
1.5
1
0.5
0
0
2
4
6
8
10
12
14
16
18
20
Time (hr)

Fig 17

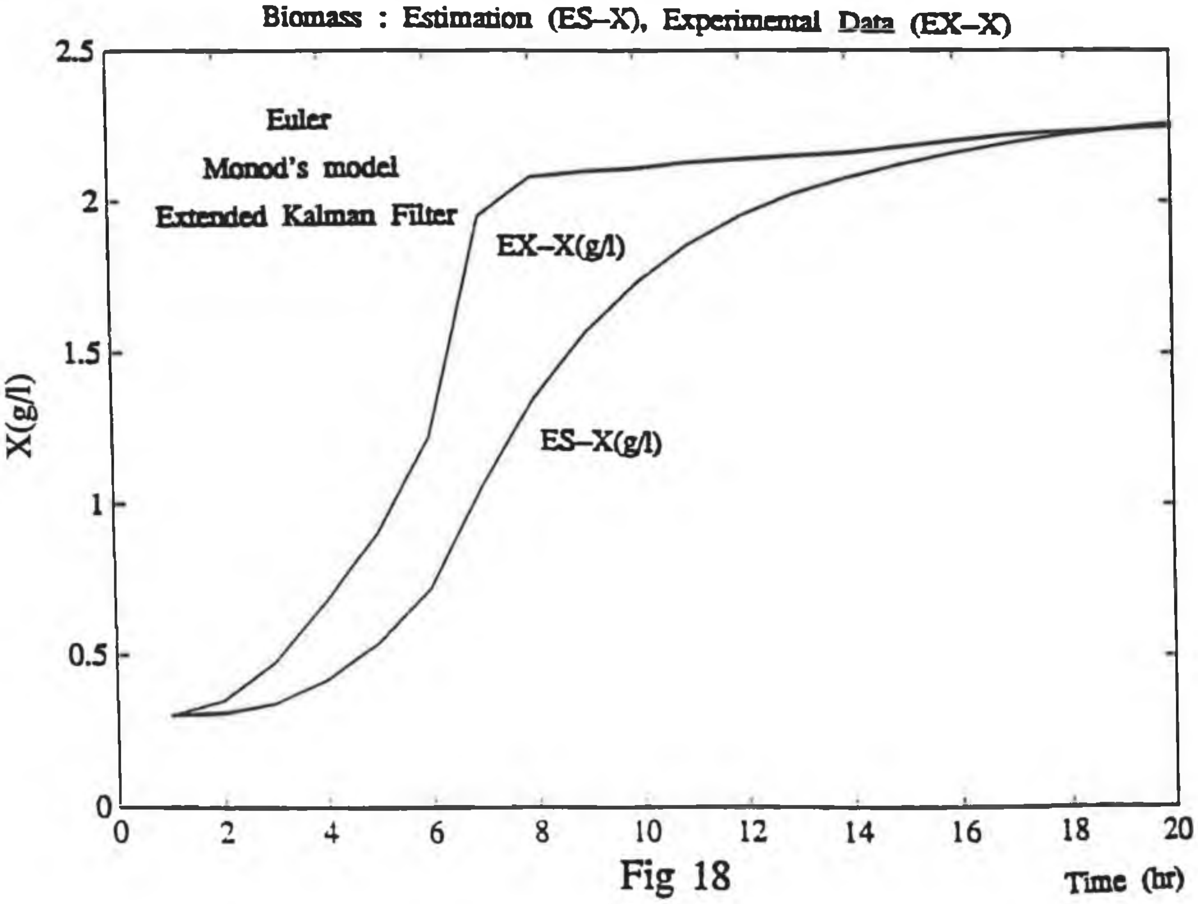

Biomass : Estimation (ES–X), Experimental Data (EX–X)
Euler
Monod's model
Extended Kalman Filter
EX–X(g/l)
ES–X(g/l)
X(g/l)
2.5
2
1.5
1
0.5
0
0
2
4
6
8
10
12
14
16
18
20
Time (hr)

Fig 18

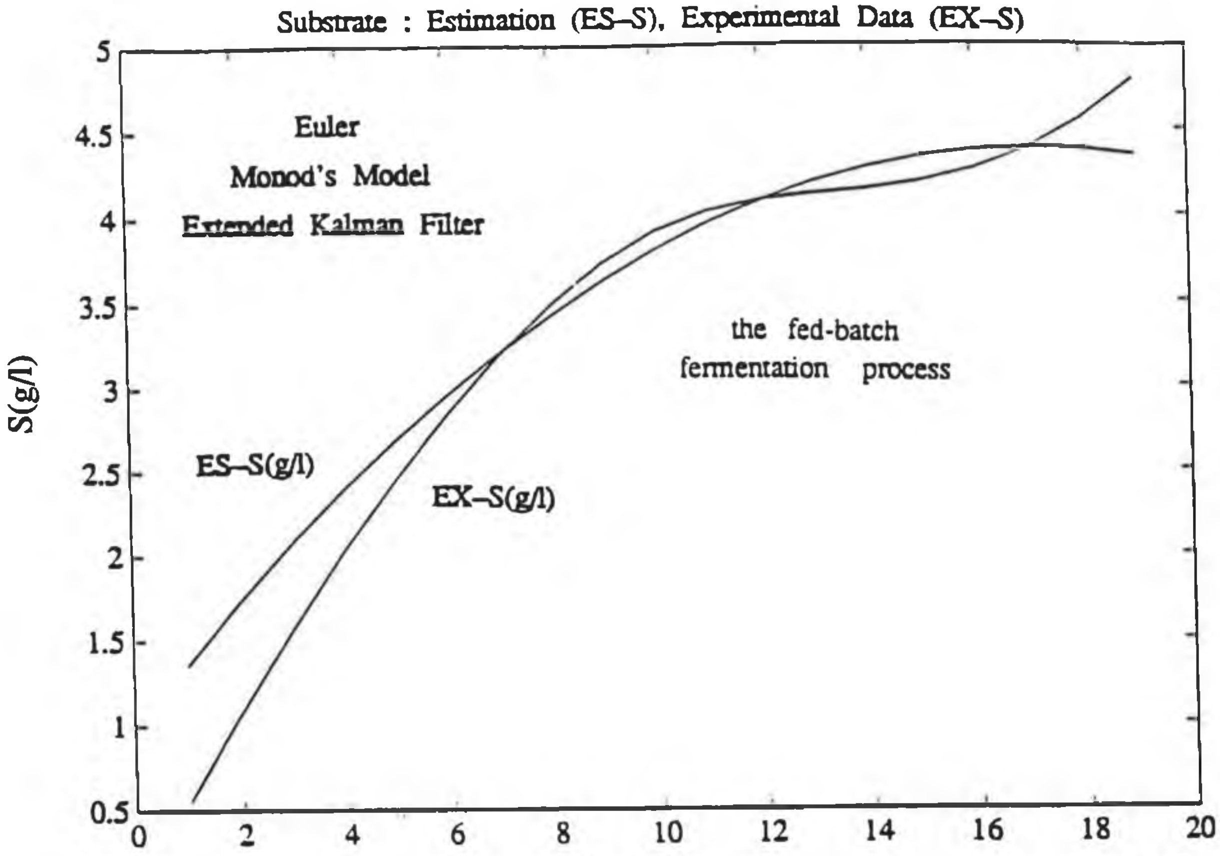

Substrate : Estimation (ES–S), Experimental Data (EX–S)
Euler
Monod's Model
Extended Kalman Filter
the fed-batch fermentation process
ES–S(g/l)
EX–S(g/l)
S(g/l)
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
2
4
6
8
10
12
14
16
18
20
Time (hr)

Fig 19

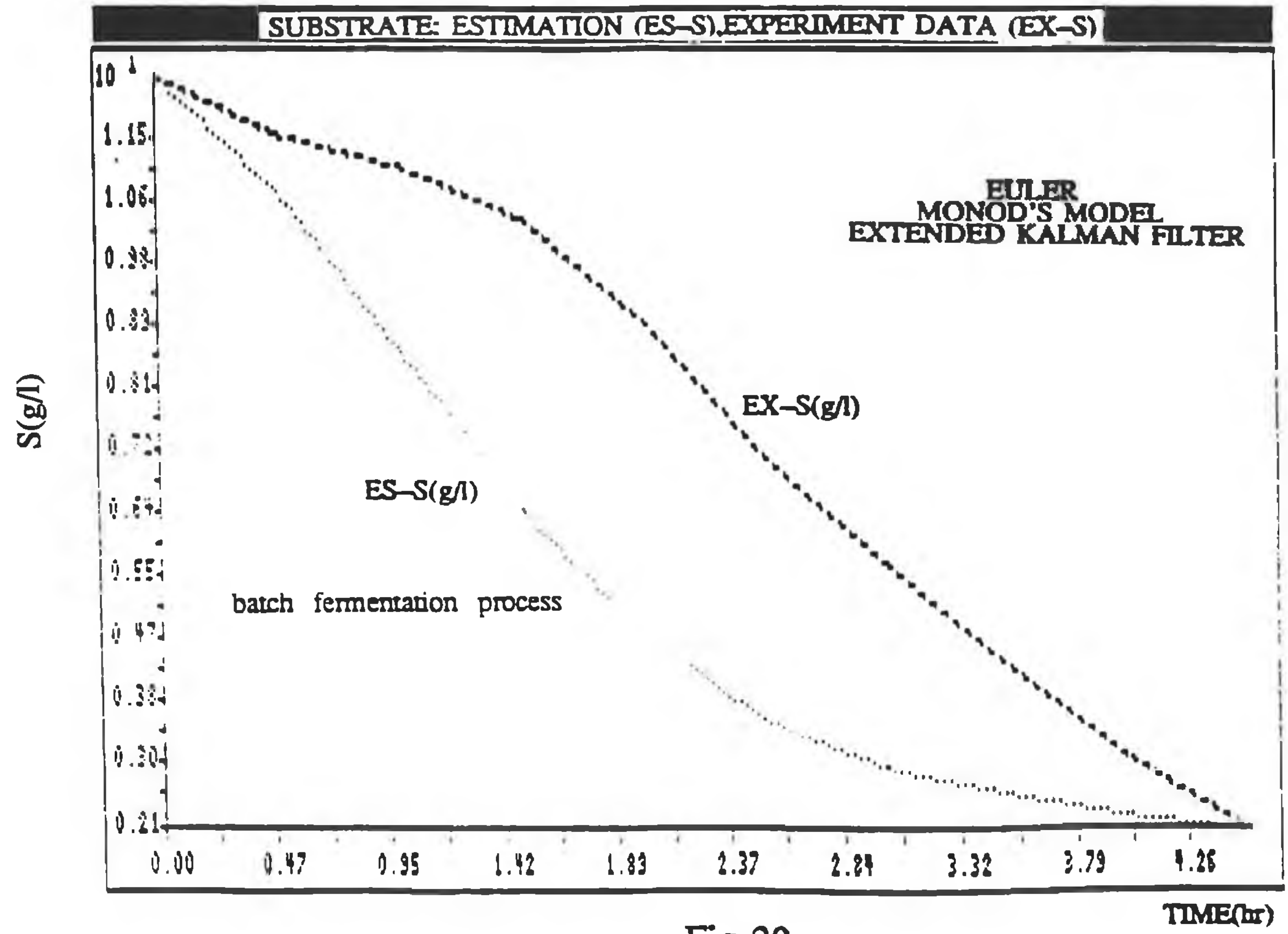

SUBSTRATE: ESTIMATION (ES–S),EXPERIMENT DATA (EX–S)
EULER
MONOD'S MODEL
EXTENDED KALMAN FILTER
EX–S(g/l)
ES–S(g/l)
batch fermentation process
S(g/l)
10 1
1.15
1.06
0.98
0.89
0.81
0.72
0.64
0.55
0.47
0.38
0.30
0.21
0.00
0.47
0.95
1.42
1.89
2.37
2.84
3.32
3.79
4.26
TIME(hr)

Fig 20

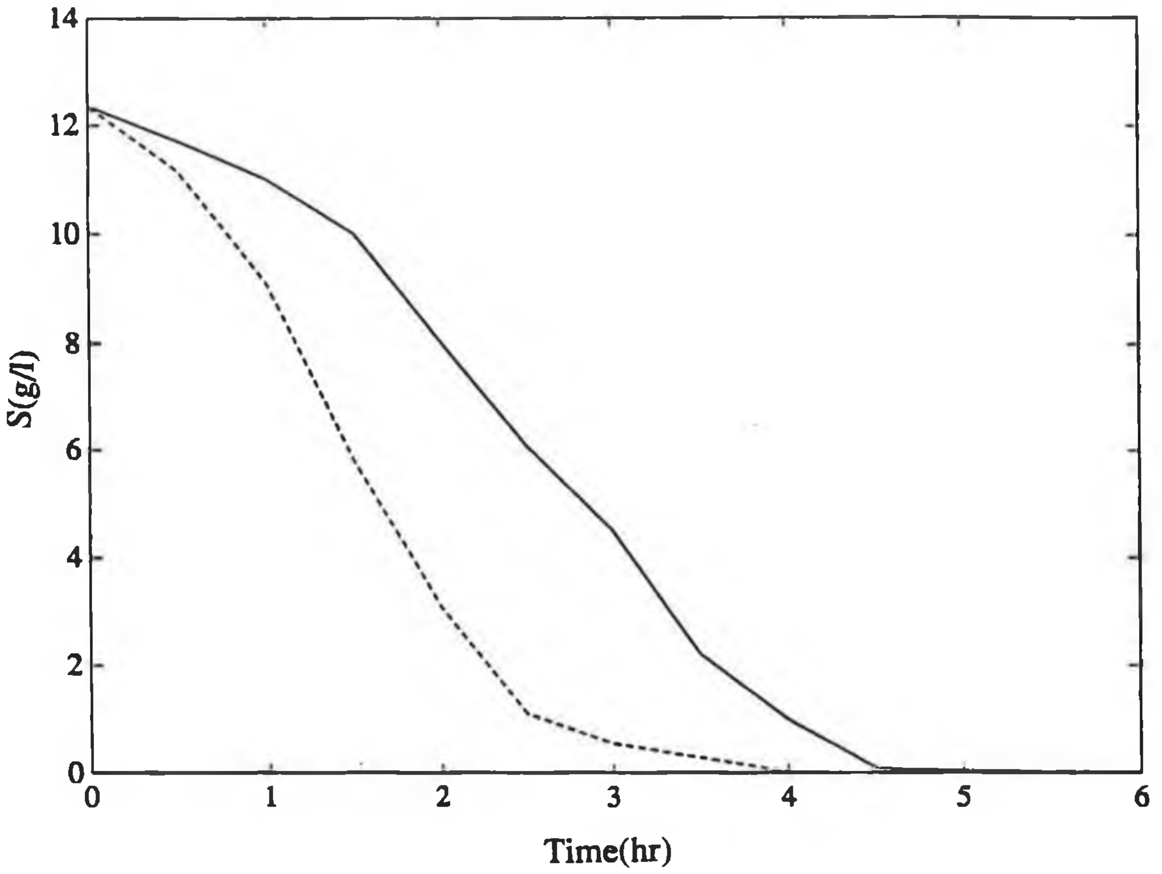


Fig 21 The estimation result of substrate concentration (S) based on a non-linear observer using Monod's model

-----------	The experimental result of substrate (g/l)
————	The estimation result of substrate concentration (g/l)

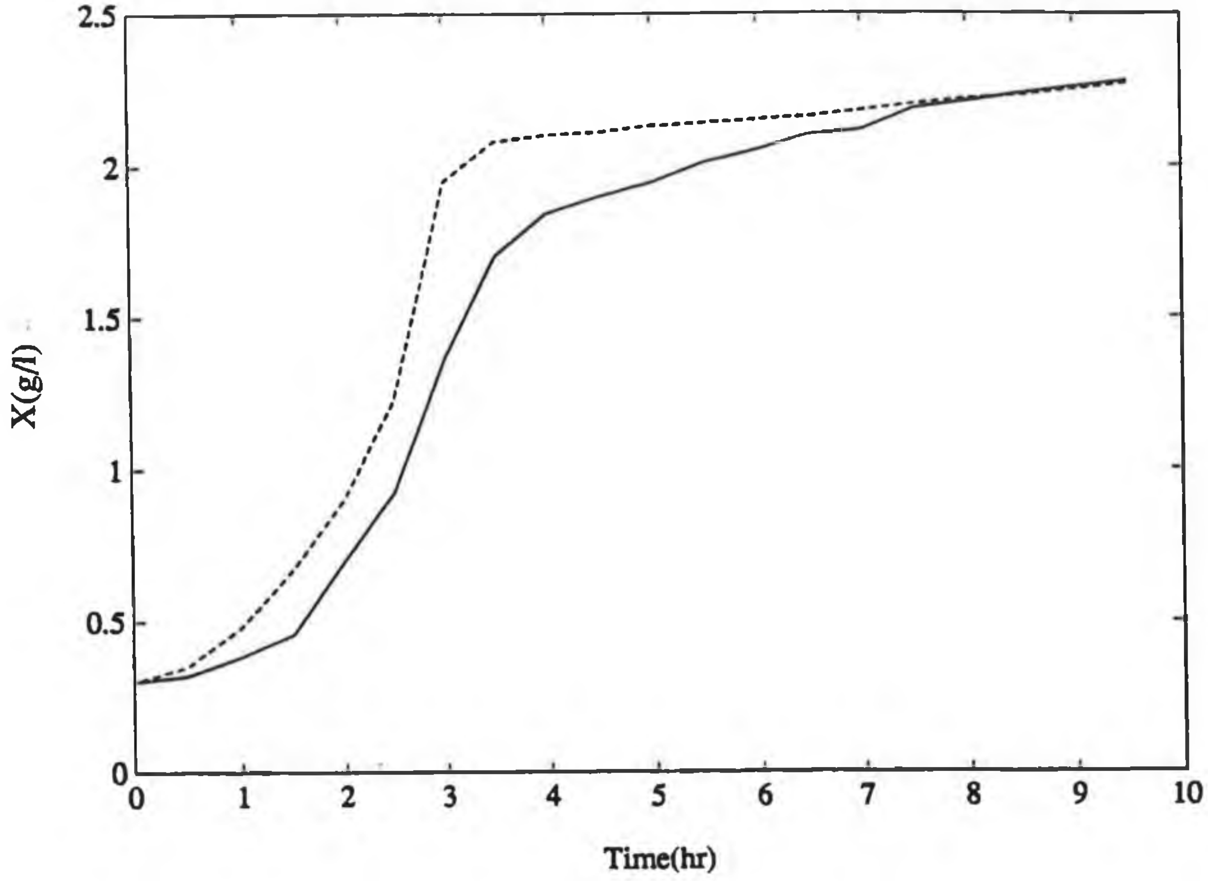


Fig 22 The estimation result of biomass concentration (X) based on an IEKF algorithm using a Monod's model

----------- The experimental data of biomass concentration from a pilot plant (g/l)

——— The estimation result of biomass concentration (X) based on an IEKF algorithm (g/l)

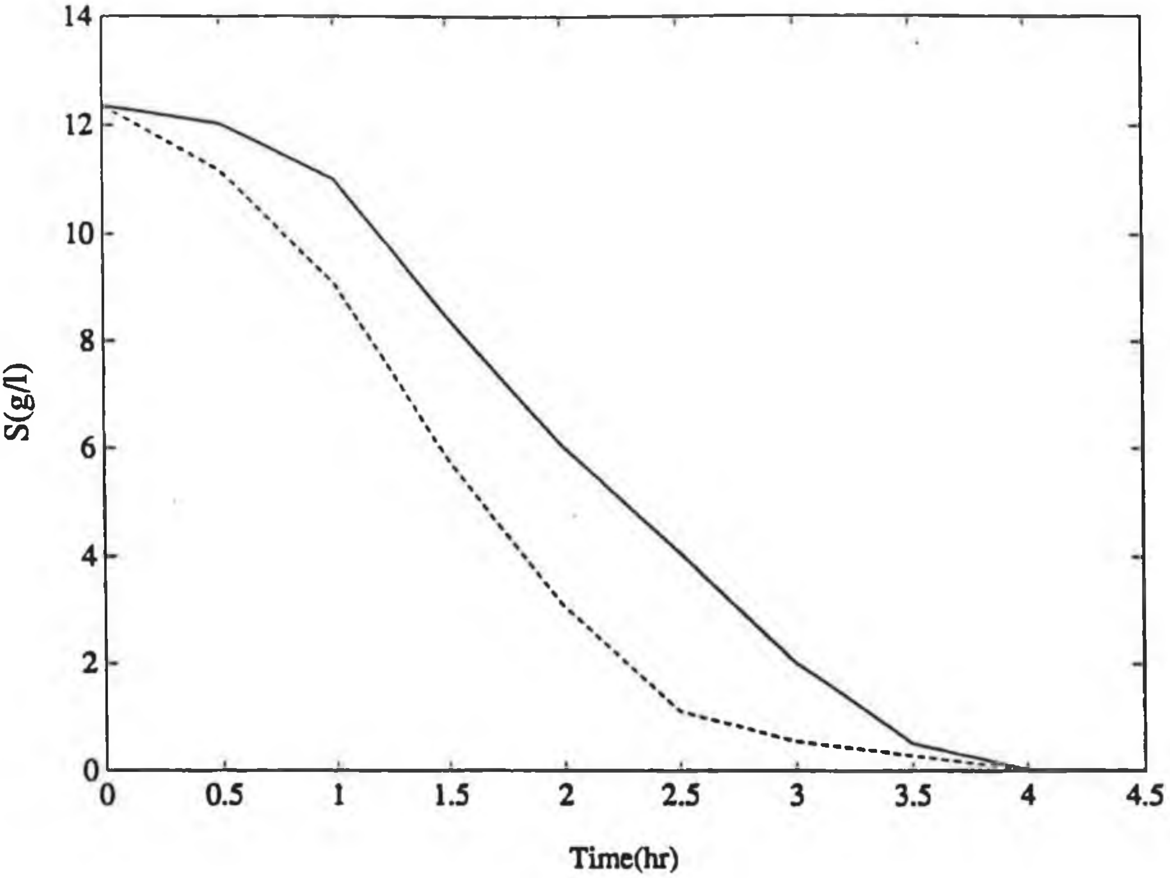


Fig 23 The estimation result of substrate concentration (S) based on an IEKF algorithm using a Monod's model (g/l)

------------ The experimental data of substrate concentration (S) from a pilot plant (g/l)

———— The estimation result of biomass concentration (X) based on an IEKF algorithm using a Monod's model (g/l)

PART IV PARAMETERIZATION AND IDENTIFICATION FOR FERMENTATION PROCESSES

Chapter 1 Introduction

The goal in process identification is to infer a model (estimates of the model parameters) given a process input or output data record. When there is parameter uncertainty in a dynamic system (e.g., in a fermentation process), one way to reduce it is to use parameter estimation. This activity can be carried out in an "off-line" or by using "on-line" techniques where the addition of a new data point is employed to update the model parameters. Off-line estimation may be preferable if the parameters are constant (e.g., the yield coefficient of a fermentation process) and there is sufficient time for estimation before control. However, for parameters which vary (even though slowly. e.g., the biomass specific growth rate of a fermentation process) during operation, on-line parameter estimation is necessary to keep track of the parameter values. In this section, a method of on-line estimation will be shown. Different models for the identification of the specific growth rate μ and yield coefficient K_1 are also presented.

In part III, it was assumed that most of process parameters were known. Actually it is often difficult and costly to experiment with industrial processes. Therefore, it is desirable to have identification methods that do not require special input signals. Many " classic " methods depend strongly on having the input be of a precise form, e.g., sinusoid or impulses. It is sometimes possible to base system identification on data obtained under closed-loop control of the process. Adaptive controllers are based mostly on closed-loop identification. The main difficulty with data obtained from a process under feedback is that it may be impossible to determine all the parameters in the desired model. i.e., the system is not identifiable, even if the parameters can be determined from an open-loop experiment. Identifiability can be recovered if the feedback is sufficiently complex. It helps to make the feedback nonlinear and time-varying and to change the set-points. [20]

Chapter 2 Adaptive Recursive Least Squares

2.1. Introduction

The least-squares method can be used to identify parameters in dynamic systems. A major reason for the interest in the methods of recursive identification is, of course, that they are a key instrument in adaptive control, adaptive filtering, adaptive prediction, and adaptive signal-processing problems. In addition to on-line demands, we also have the following two reasons for using recursive identification. [23]

(1) *Data compression.* With the processing of data deing made on-line, old data can be discarded. The final result is then a model of the system rather than a big batch of data. Since many recursive identification algorithms provide an estimate of the accuracy of the current model, a rational decision of when to stop data acquisition can be made on-line.

(2) *Application to off-line identification.* Methods for off-line identification may process the measured data in different ways. Often, several passes are made through the data to iteratively improve the estimated models. Depending on the complexity of the model, the number of necessary iterations may range from less than ten to a couple of hundred. An alternative to this iterative batch processing is to let the data be processed by a recursive identification algorithm. Then, one would normally go through the data a couple of times to improve the accuracy of the recursive estimates. This has proved to be an efficient alternative to conventional off-line procedures (Young, 1976).[23]

2.2. The Recursive Least Squares

According to Gauss the principle of least squares is that the unknown parameters of a model should be chosen. Let a linear system be described by : [22]

$$A(q)Y(k) = B(q)u(k) + C(q)e(k) \; ; \qquad \textbf{(2.2-1)}$$

where $u(k)$ is the input, $Y(k)$ is the output, and $e(k)$ is a white-noise disturbance. The parameters, as well as the order of the models, are considered as the unknown parameters. Assume that

$C(q) = 1$. The parameters A and B are of order n and n–1, respectively.

The applied inputs:

$$u(k) = [\ u(1)\ u(2)\ u(3) \cdots\cdots u(N)]; \qquad (2.2\text{–}2)$$

The observed outputs:

$$Y(k) = [\ Y(1)\ Y(2)\ Y(3) \cdots\cdots Y(N)]\ ; \qquad (2.2\text{–}3)$$

The unknown-parameters :

$$\theta = [\ a_1\ \cdots\ a_n\ :\ b_1\ \cdots\ b_n\ ]^T\ ; \qquad (2.2\text{–}4)$$

Further

$$\varphi(k+1) = [-Y(k) \cdots -Y(k-n+1)\ :\ u(k-n+1)] \qquad (2.2\text{–}5)$$

and

$$\Phi = [\ \varphi(n+1) \cdots\cdots \varphi(N)\ ]^T\ ; \qquad (2.2\text{–}6)$$

The least squares estimate is then given by the following equation if $\Phi^T\Phi$ is nonsingular. This is the case, for instance, if the input signal is, loosely speaking, sufficiently rich.

$$\hat{\theta} = (\Phi^T\Phi)^{-1}\ \Phi^T\ Y\ ; \qquad (2.2\text{–}7)$$

The matrix $(\Phi^T\Phi)^{-1}\ \Phi^T$ is called the *pseudoinverse* of Φ if the matrix $\Phi^T\Phi$ is nonsingular.

If the parameters are time-varying, it is necessary to eliminate the influence of old data. This can be done by using a loss function with exponential weighting, i.e.,

$$J(\theta) = \sum_{k=1}^{N} \lambda^{N-K}[Y(k) - \theta\cdot\varphi(k)]^2 \quad ; \qquad (2.2\text{–}8)$$

The "forgetting factor", λ, is less than one and is a measure of how fast old data are forgetten. For $\lambda < 1$, more weight is placed on recent measurements than on old measurements. The least-square estimate when using the loss function of (2.2–8) is given by

$$\hat{\theta}(k+1) = \hat{\theta}(k) + K(k)[Y_{k+1} - \varphi(k+1)\hat{\theta}(k)]\ ; \qquad (2.2\text{–}9)$$

$$K(k) = P(k)\varphi^T(k+1)[\lambda + \varphi(k+1)P(k)\varphi^T(k+1)]^{-1}\ ; \qquad (2.2\text{–}10)$$

$$P(k+1) = [I - K(k)\varphi(k+1)]P(k)/\lambda\ ; \qquad (2.2\text{–}11)$$

2.3. U–D Covariance Factorization

Equation (2.2– 9–11) is one way to mechanize the recursive update of the estimates and the covariance matrix. These equations are not well-conditioned from a numerical point of view, however. A better way of doing the calculation is to update the square root of P instead of updating P. Another way to do the calculations to use the *U–D* algorithm by Bierman and Thornton. This method is based on a factorization of P as [23][20]

$$P = U\,D\,U^T\ ; \qquad (2.2\text{–}12)$$

where D is diagonal and U is an upper-triangular matrix. This method is a square-root type as $UD^{1/2}$ is the square root of P. The U–D factorization method does not include square-root calculations and is therefore well suited for small computers and real-time applications. In this part, the U–D method is applied.

The exponential forgetting factor $\lambda=\lambda^{N-i}$ where N is the total number of data points and i the current data or iteration point is commonly used. In the simulation results that follow a variable forgetting factor approach is sometimes taken based on the nature of the expected parameter variation [24]. Also in the simulation, a suitable choice of the initial covariance matrix P(0) must be made. For P(0), a diagonal matrix with large elements (e.g. 10^5 or larger) implies that the users confidence in the initial set of parameter estimates is poor, while small values for the diagonal elements implies good initial estimates.

Chapter 3 Identification Models

3.1 Introduction

In this chapter, the model of the fermentation process (presented in PART II -Chapter 2) is selected, and the topics of parametrization of this model is also covered. It is assumed that the measurements of biomass (X), substrate (S), dissolved oxygen (O) and carbon-dioxide (C) concentrations are available.

The expressions for the system (2.2–1) which are linear in the parameters must be first obtained in order to use recursive least squares type identification algorithms. The system equations can be rewritten as,

$$Y(t) = \theta^T \cdot \Phi(t) \qquad (3.1\text{–}1))$$

where

$Y(t)$ = known measurement vectors.
$\Phi(t)$ = known regressor.
$\theta(t)$ = unknown parameter vector.

It is the function of the ARLS routine to identify the elements of parameter vector given a set of process input and output measurements, a known regressor $\Phi(t)$ and an unknown parameter vector $\theta(t)$.

3.2 The Unstructured Model Of The Process

The unstructured model of the fermentation process was described in part II– chapter 2. A discrete-time model of the biomass and substrate concentrations can be written as,

$$X(k+1) - X(k) + \Delta t \cdot D(k) \cdot X(k) = \mu \cdot \Delta t \cdot X(k) \; ; \qquad (3.2\text{–}1)$$

$$S(k+1) - S(k) - \Delta t \cdot D(k) \cdot [S_{fi} - S(k)] = -K_1 \cdot \Delta t \cdot \mu \cdot X(k) \; ; \qquad (3.2\text{–}2)$$

Substituting equation (3.1–1) into (3.2–1) gives:

$$Y(k+1) = \theta^T(k+1) \cdot \Phi(k+1) \; ;$$

where

$Y(k+1) = \{X(k+1) - X(k) + \Delta t \cdot D(k) \cdot X(k)\}$;
$\Phi(k+1) = \{\Delta t \cdot X(k)\}$;
$\theta(k+1) = \{ \mu \}$

The biomass specific growth rate μ can be identified based on above ARLS algorithm. (See results III, Fig 1)

Substituting equation (3.1–1) into (3.2–2) gives :

$$Y(k+1) = \theta^T(k+1)\cdot\Phi(k+1) \ ;$$

where

$$Y(k+1) = \{S(k+1) - S(k) - \Delta t\cdot D(k)\cdot[S_{fi}-S(k)]\} \ ;$$

$$\Phi(k+1) = \{-\Delta t\cdot\mu\cdot X(k)\} \ ;$$

$$\theta(k+1)= \{ K_1\} \ ;$$

The yield coefficient K_1 can also be identified. (See results III: Fig 2)

3.3 Monod's Model

Monod's model is found to be generally the most applicable. Monod's model of cell growth is repeated here for convenience: (See details in part II-chapter 2)

$$\mu(S) = \mu_{max}\cdot S/(K_s + S) \ ; \qquad (3.3\text{–}1)$$

where K_s = the "Michaelis-Manter's" constant.

Substituting equation (3.3–1) into (3.2–1) and (3.2–2), we get

$$X(k+1)-X(k)+\Delta t\cdot D(k)\cdot X(k) = \Delta t\cdot\mu_{max}\cdot S(k)\cdot X(k)/[K_s+S(k)] \ ; \qquad (3.3\text{–}2)$$

$$S(k+1)-S(k)-\Delta t\cdot D(k)\cdot[S_i(t)-S(k)]$$
$$=-\Delta t\cdot\mu_{max}\cdot S(k)\cdot X(k)\cdot K_1/[k_s+S(k)] \ ; \qquad (3.3\text{–}3)$$

The equations (3.3–2) can be rewritten as,

$$[X(k+1)-X(k)+\Delta t\cdot D(k)\cdot X(k)]\cdot S(k)$$
$$=\Delta t\cdot\mu_{max}\cdot S(k)\cdot X(k)+[X(k)-X(k+1)-\Delta t\cdot D\cdot X(k)]\cdot K_s \ ; \qquad (3.3\text{–}4)$$

Substituting equation (3.1–1) into (3.3–4) gives:

$$Y(k+1) = \theta^T(k+1)\cdot\Phi(k+1) \quad ;$$

where

$$Y(k+1) =\{[X(k+1)-X(k)+\Delta t\cdot D(k)\cdot X(k)]\cdot S(K)\} \ ;$$

$$\Phi(k+1) =\{ \Delta t\cdot S(k)\cdot X(k),\ X(k)-X(k+1)-\Delta t\cdot D(k)\cdot X(k)\}^T;$$

$$\theta^T(k+1)=\{\mu_{max} \ , \ K_s\} \ ;$$

μ_{max} and K_s can be identified. (See results III: Fig 3) part III)

3.4 *Ollson's Model*

This model for μ was introduced in part II– chapter 2– section 2.3.2. This model is repeated here:

$$\mu(S,O) = \mu_{max}\cdot[S/(K_s+S)]\cdot[O/(K_{O2}+O)] \; ; \qquad (3.4\text{–}1)$$

where K_{O2} = the saturation constant.

Substituting (3.4–1) into equs (3.2–1) and (3.2–2) give,

$$X(k+1)=X(k)-\Delta t\cdot D(k)\cdot X(k) +\Delta t\cdot\mu_{max}\cdot S(k)\cdot O(k)\cdot X(k)/[K_s+S(k)]\cdot[K_{O2}+O(k)] \; ; \qquad (3.4\text{–}2)$$

$$S(k+1)=S(K)+\Delta t\cdot D(k)\cdot[S_{fi}-S(k)] -\Delta t\cdot\mu_{max}\cdot S(k)\cdot X(K)\cdot O(K)\cdot K_1/[K_s+S(K)]\cdot[K_{O2}+O(K)] \; ; \qquad (3.4\text{–}3)$$

An RLS structure linear in the parameters gives

$$Y(k+1) = \theta^T(K+1)\cdot\Phi(k+1) \quad ;$$

where

$$Y(k+1) = \{[X(k+1)-X(k)+\Delta t\cdot D(k)\cdot X(k)]\cdot O(k)\cdot S(k)\} \; ;$$

$$\Phi(k+1) = \{\Delta t\cdot X(k)\cdot S(k)\cdot O(K),\ -O(K)\cdot\alpha,\ S(k)\cdot\alpha,\ -\alpha\}^T$$

$$\theta^T(k+1)= \{\mu_{max},\ K_s,\ K_{O2},\ K_s\cdot K_{O2}\}$$

$$\alpha = \{X(k+1)-X(k)+\Delta t\cdot D(k)\cdot X(k)\} \; ;$$

μ_{max}, K_s, K_{O2}, $K_s\cdot K_{O2}$ can be identified.

3.5 *Contois' Model*

This model for μ was introduced in part II– chapter 2– section 2.3.3. The model is also repeated here:

$$\mu(S,\ X) = \mu_{max}\cdot S/(K_c\cdot X+S) \; ; \qquad (3.5\text{–}1)$$

where K_c = the Contois' constant.

Substituting equation (3.5–1) into (3.2–1) and (3.2–2), we get,

$$X(k+1)-X(k)+\Delta t\cdot D(k)\cdot X(k)=\mu_{max}\cdot S(k)\cdot X(k)/[K_c\cdot X(k)+S(k)]; \qquad (3.5\text{–}2)$$

$$S(k+1)-S(k)-\Delta t\cdot D(k)\cdot[S_{fi}-S(k)] =-K_1\cdot\Delta t\cdot\mu_{max}\cdot S(k)\cdot X(k)/[K_c+S(k)] \; ; \qquad (3.5\text{–}3)$$

Substituting equation (3.1–1) into (3.5–2) gives:

$$Y(k+1) = \{ \beta \cdot S(k) \} ;$$

$$\Phi(k+1) = \{S(k) \cdot X(k),\ \beta \cdot X(k)\}^T;$$

$$\theta^T(k+1) = \{\mu_{max},\ K_c\} ;$$

$$\beta = \{ [X(k+1) - X(k) + \Delta t \cdot D(k) \cdot X(k)] \cdot S(k)\} ;$$

μ_{max}, K_c can also be identified using ARLS algorithm.

Chapter 3 Discussion

This part has outlined various model structures that may be used in the identification of fermentation systems. The unstructured model, Monod's model, Ollson's model and Contois' model have been presented and their respective simulation results show good parameter identification. The type of model structure chosen for the parameter estimation algorithm will ultimately depend on the type of fermentation run in operation.

Most parameter identification techniques have had their greatest success with linear systems. Biotechnical processes are inherently non-linear and time-varying. Therefore the model to describe these processes (sometimes with extensive simplifying assumption in real-time) must be structured in a linearised form for use in a parameter identification procedure. In this part, the adaptive recursive Least Squares (ARLS) have been successfully applied to fed-batch and batch fermentation processes.

Chapter 5 Simulation Results (III)

The following common initial conditions which refer to the pilot plant have been used :

λ=0.99; μ_{max}=0.4; K_1=2.0; K_S=2.0; $Y_{X/S}$=0.5; D=0.1;

μ is the time-varying parameter. In these identification studies a constant forgetting factor refers to simulation in which λ is kept constant. The data of biomass and substrate concentrations have been used from simulation results. Fig 1 to Fig 4 show the results of the specific growth rate μ, the yield coefficient K_1, the maximum of the μ. The following results of the identification procedure have been obtained,

μ_{max}= 0.4 ; K_1= 2.0; $Y_{X/S}$ =0.5;

These results demonstrated that the popular estimation technique of recursive least squares will exhibit good convergence when properly applied.

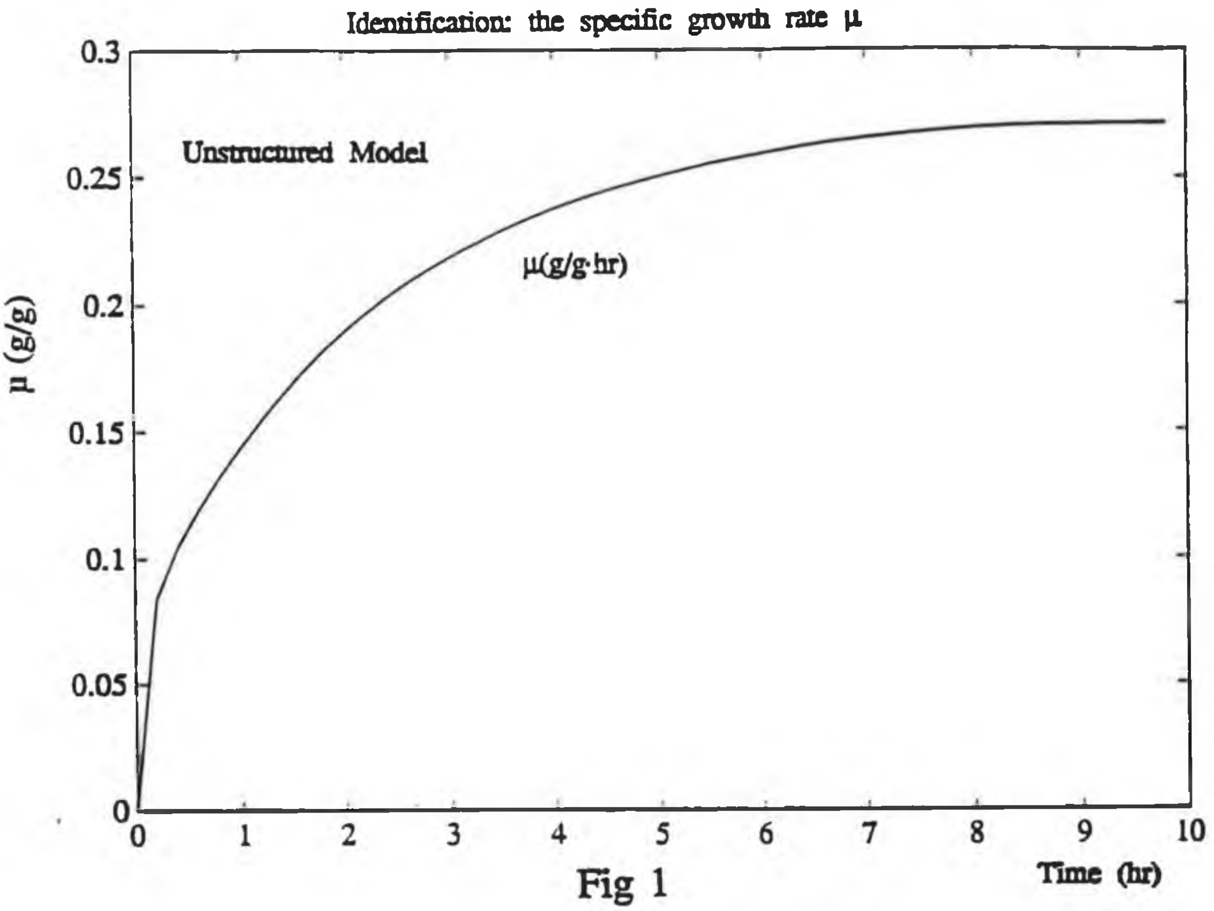

Identification: the specific growth rate μ
Unstructured Model
μ(g/g·hr)
μ (g/g)
0.3
0.25
0.2
0.15
0.1
0.05
0
0
1
2
3
4
5
6
7
8
9
10
Time (hr)

Fig 1

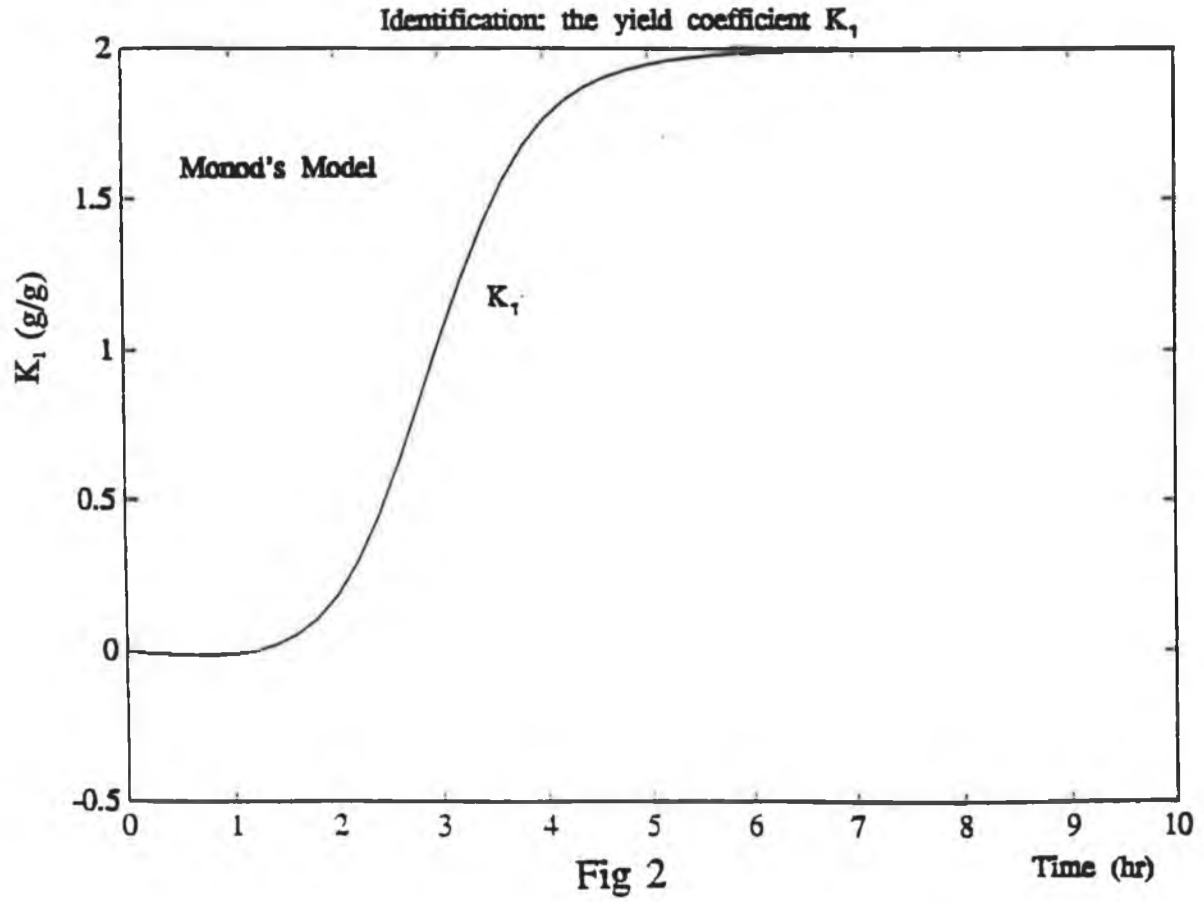

Identification: the yield coefficient K_1
Monod's Model
K_1
K_1 (g/g)
2
1.5
1
0.5
0
-0.5
0
1
2
3
4
5
6
7
8
9
10
Time (hr)

Fig 2

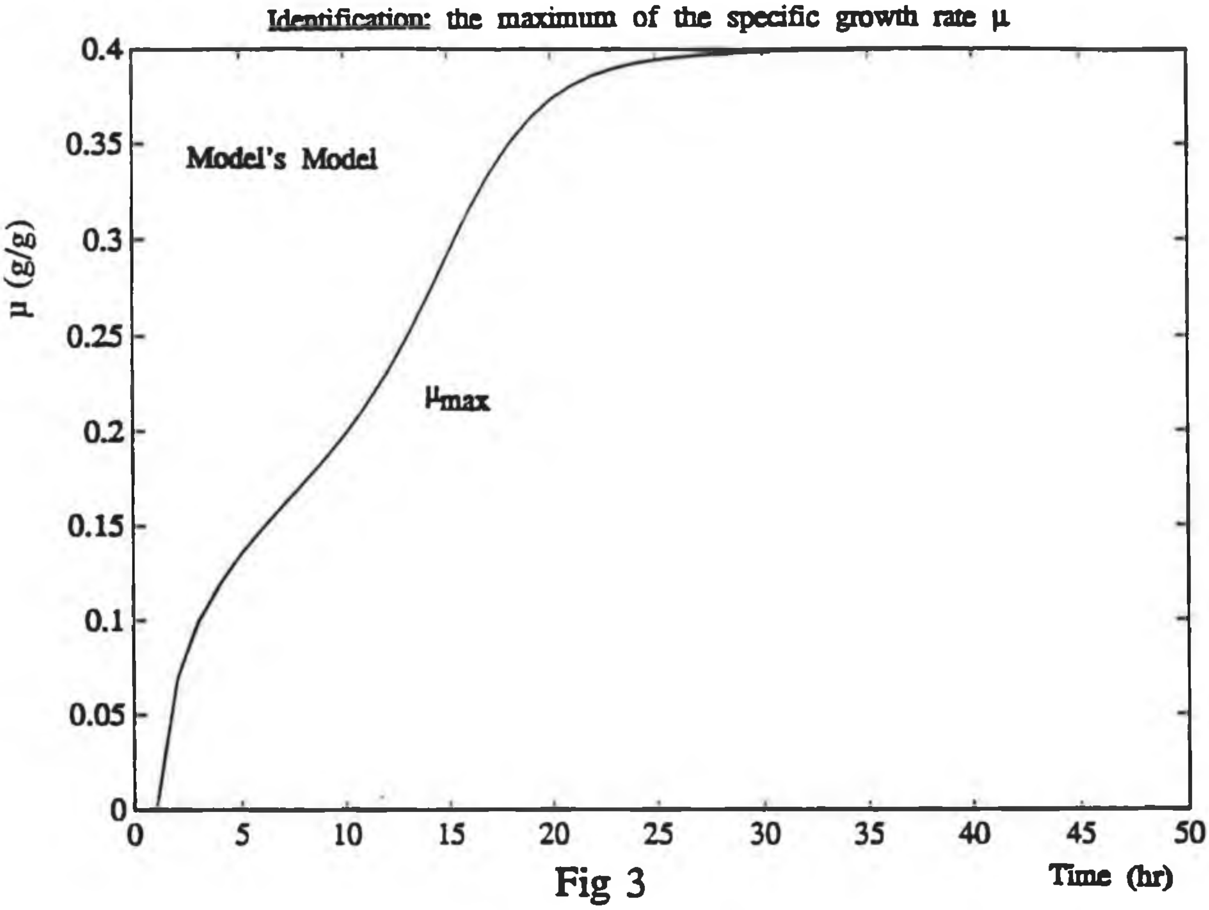

Identification: the maximum of the specific growth rate μ
Model's Model
μ_{max}
μ (g/g)
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
5
10
15
20
25
30
35
40
45
50
Time (hr)

Fig 3

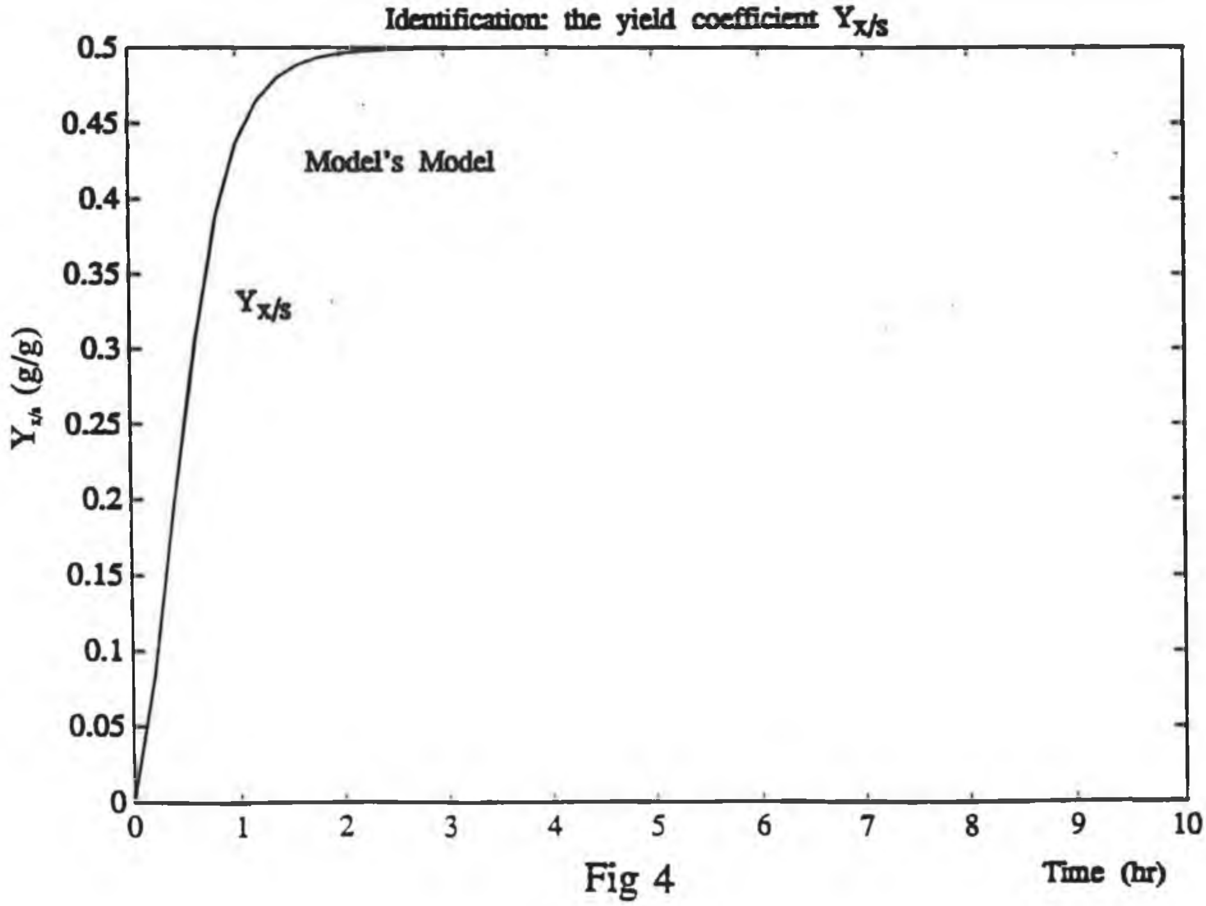

Identification: the yield coefficient $Y_{x/s}$
Model's Model
$Y_{x/s}$
$Y_{x/s}$ (g/g)
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
1
2
3
4
5
6
7
8
9
10
Time (hr)

Fig 4

PART V CONCLUSIONS

The control of a biotechnical process is based on the measurements of physical, chemical or biochemical properties and environmental parameters of the process. Classical control strategies are ineffective when applied to the task of controlling multivariable non-linear, time-varying systems, particularly, as in biotechnical processes, where some of the important state variables are not measurable, due to the non-availability of accurate and reliable sensors. The simulation technique can be applied to these kinds of systems in conjunction with some real-time data for optimal control. Often many important variables and parameters have to be calculated or estimated because of their unmeasurability, such as cell mass and substrate concentrations in a fermentation process.

It is difficult to develop models taking into account the numerous factors which can influence the specific bacterial growth rate and the yield coefficients which characterise micro-organism growth. In this thesis a model for a biotechnical process has been presented for simulation purposes with (sometimes extensive) simplifying assumptions. This model is used in conjunction with some real-time data as the basis for on-line estimation techniques. The simulation model is employed as a testing ground for estimation algorithms.

A number of state estimation algorithms based on the assumption that some of, or none, of their system quantities can be measured on-line are successfully applied to a fed-batch and a batch fermentation processes. The results have demonstrated that states and parameters of a complex biotechnical process can be estimated on-line by extended Kalman filter, iterative Kalman filter, and many observers. Many estimation algorithms must be based on some known information, such as the on-line measurements of dissolved oxygen and exhaust carbon-dioxide concentrations. In this work the experiments and computer results show especially that the extended Kalman filter gives satisfactory results during computer simulation. The iterative Kalman filter can be used to reduce estimation errors and also to produce a faster convergence rate.

In addition, it has been observed that all algorithms are sensitive to error in initial estimation of biomass and substrate. There is also the serious problem of finding an initial estimate of the error covariance. The observability of a system must be carefully considered to avoid estimation problems.

In practice, the procedure of system identification is iterative. Based on the results, the model structure can be improved and new experiments may be necessary. In this thesis an *Adaptive Recursive Least Squares* algorithm for the identification on time-varying system parameters based on on-line measurements of states has been presented. The results have especially shown good tracking of time-varying parameters with a variable forgetting factor.

In further estimation schemes consideration should also be given to more complex algorithms. The relatively large sampling time associated with the control of fermentation processes ensures adequate processing time is available for any increase in complexity of algorithms. These algorithms may consist of using a combined state and parameter estimators rather than the presently separate ARLS and EKF techniques. Consideration should also be given to cases where the state noise covariance Q and observation noise covariance R are not known a priori. Algorithms are available that can be used on-line to identify the unknown covariances.

The use of modelling and optimization for on-line computer control, coupled with the increasing use of available sensors for monitoring fermentation processes will continue to be of interest to industry. The progress in control techniques must be influenced in a positive manner by academic efforts and hopefully the research undertake for this thesis will contribute to the increasingly important field of the control of biological processes.

Also, two papers, arising from the work described in this thesis, were presented at IECON' 91 International Conference on Industrial Electronics, Control and Instrumentation, which was held at Kobe in Japan from October 28 to November 1, 1991. in Japan. [52][53]

REFERENCES

[1] **Bailey J.E.** and **Ollis D.F.**, "Biochemical Engineering Fundamentals", *McGraw-Hill, New York, (1977).*

[2] **Brauer. H.**, "Biotechnology Vol.2. Fundamentals of Biochemical Engineering." *VCH, (1985).*

[3] **D. Dochain**, " On-line Parameter Estimation, Adaptive State Estimation and Adaptive Control of Fermentation Processes", *Ph.D. thesis, 1986.*

[4] **Tan, Liang.** " Modelling and Simulation of A Fermetation Process", *RPN, 90/EE/001, Dublin City University, Ireland. 1990.*

[5] **Aiba S.**, **Humphrey A.**, and **Millis N.F.**, " Biochemical Engineering ", *Second Edition. Academic Press. (1973)*

[6] **Sinclair C.** and **Kristiansen B.**, "Fermentation Kinetics and Modelling. ", *Open University Press, 1987.*

[7] **D.Williams**, "On–line Eatimation of Variables and Adaptive Control", Chapter 15. 1980.

[8] **Truesdale, G.A.**, **Downing, A.L.**, **and Lowden, G.F.**, 1955, "J. Appl. Chem., 5, 53-62".

[9] **Bellgardt K.H.Kuhlmann W.,Meyer H.D.**, " Deterministic Growth Model of Saccharomyces Cerevisiae, Parameter Identification and Simulation", *IFAC Modelling and Control of Biotechnical Processes, 1982. (Conference, Helsinki).*

[10] **Wang, D.I.C.**, **Cooney, C.L.**, **Demain, A.L.**, **Dunnill, P.,Humphrey, A.E.**, **and Lilly, M.D.**, **1979**, " Fermentation and Enzyme Technology ", *J.Wiley & Sons, New York.*

[11] **Monod J.**, "On the Growth of Bacterial Cultures", *Annual Review of Microbiology P.371, 1949.*

[12] **Contois D.** " Kinetics of Bacterial Growth Relationship Between Population Density and Specific Growth Rate of Continuous Cultures. ", *Journ. of Gen. Microb., 21, 40. 1959.*

[13] **Goodwin G.C. Mc Innis and R.S. Long** (1980), "Adaptive Control Algorithms for Waste Water Treatment and PH Neutralization", Opt. Control Appl. Math., 3, 443-459.

[14] **Bastin G., D.Dochain,** (1986), "On-line Estimation of Microbial Specific Growth Rates", Automatica, Nov.

[15] **Gallegos, J.A. and Gallegos, J.,** " Estimation and Control Techniques for Continuous Culture Fermentation Processes." , *Biotechnology and Bioengineering, Vol. 16, pp442–451 (1984).*

[16] **Williamson, D.,** " Observation of Bilinear Systems with Application to Biological Control. ", *Automatica, 13. 243-225. (1977).*

[17] **A. Halme,** " Measurement and Estimation in Bioreactors ", *" One Day International Workshop on Control of Biotechnical Processes. ", 1987.*

[18] **A. Halme,** " Some New Algorithm for Non-linear State Estimation and Filtering ", *University of Oulu, Finland, 1980.*

[19] **A. Halme, J. Selkäinaho and J. Soininen,** "Adaptive Control with A Non-linear Filtering.", Automatica, Vol.,21, No.4, pp.453–463, 1985.

[20] **Karl J.Åström, Björn Wittenmark,** "Computer Controlled Systems: theory and design", *Prentice-Hall International Editions, 1984.*

[21] **Wieslander. J, Wittenmark, B.,** " An Approach to Adaptive Control Using Real Time Identification ", *Automatica, Vol 7, pp 211-217, 1971.*

[22] **Åström, K J and Wittenmark, B.,** "On-Line Self-Tuning Regulators ", *Automatica, Vol 9, pp 185-199, 1973.*

[23] **Lennart Ljung, Torsten Söderström,** " Theory and Practice of Recursive Identification. ", *The MIT Press, Cambridge, Massachusetts, London, England. 1983.*

[24] **Clarke D.W.,** "Implementation of Self-Tuning Controllers, Chapter 6 in Self-Tuning & Adaptive Control Theory and Applications.", *Harris. S. and Billings (Eds) Peter Peregrinus Ltd. (1981).*

[25] **Hombeck R.,** " NUMERICAL METHODS ", *Quantum Publishers, New York, 1975.*

[26] **Atkinson L., and Harley P.,** " AN INTRODUCTION TO NUMERICAL METHODS WITH PASCAL ", *Addison Wesley, London, 1983.*

[27] **Frank L. Lewis,** " Optimal Estimation with an introduction to stochastic control theory.", *New York, 1986.*

[28] **Proceedings of the** "American Control Conference ", 1987.

[29] **Simon Haykin,** " Modern Filters ", *McMaster University, Hamilton, Ontario, Canada, 1989.*

[30] **Arthur Gelb,** " Applied Optimal Estimation ", *M.I.T. Press.* 1987

[31] The first European Conference on Computer Control in Fermentations. *Dijion, France. 1973.*

[32] **Arminger W.,** "Computer Applications in Fermentation Technology.", *Biotechnology and Bioengineering Syposium No 9, Wiley, New York. 1979.*

[33] **Alford J.S.,** "Evolution of the Fermentation Computer System at Eli Lilly and Co.", *Third International Conference on Computer Applications in Fermentation Technology, Manchester, 1981.*

[34] **Johnson A.,** " The Control of Fermentation Processes ", *IFAC Conference on Modelling and Control of Biotechnical Processes, Conference, Noordwijkerhout, 1985.*

[35] **Nagai S.,** " Mass Energy Balances for Microbial Growth Kinetics." *Advances in Biochemical Eng. Vol 11, p53, 1979.*

[36] **Vardar-Sukan F.,** "Dynamics of Oxygen Mass Transfer in Bioreactors." *Process Chemistry Vol 21, p40, 1986.*

[37] **Wang D., Cooney C.** and **Demain A.,** "Fermentation and Enzyme Technology.", *Wiley and Sons, 1979.*

[38] **Ljung L. and Soderstrom,** " Theory and Practice of Recursive Identification ", *Cambridge Mass., MIT press, 1985.*

[39] **Isermann R,** " Parameter Adaptive Control Algorithms – A Tutorial", *6th IFAC Conference, Digital Computer Applications to Process Control, Dusseldorf, 1980.*

[40] **Åström K. J. and Witenmark B.**, " *Computer Control Systems, Theory and Design", Prentice Hall, 1984.*

[41] **Dochain, D. and Bastin, G.**, " Adaptive Identification and Control Algorithms For Non-Linear Bacterial Growth Systems ", *Automatica, 20,621–634, 1984.*

[42] **Stephanopoulos G. and Ka–Yiu San.**, " On-Line Estimation of Time Varying Parameters. " " Application to Biochemical Reactors. ", *IFAC Conference on Modelling and Control of Biotechnical Processes, (Helsinki, Finland), 1982.*

[43] **Tan, Liang,** " On–line State Estimation For the Fermentation Processes.", *RPN. 90/EE/002, Dublin City University, 1990.*

[44] **Dekkers R.M.**, " State Estimation of A Fed-Batch Bakera yeast Fermentation.", IFAC Conference Modelling and Control of Biotechnical Processes, (Helsinki, Finland), 1982.

[45] **Jazwinski A.H.**, " Stochastic Processes and Filtering Theory. ", *Academic Press, New York, 1970.*

[46] **Wang, H., Wang, D., Cooney, C.**, " Computer Aided Penicillin Fermentation", *Biotechnology and Bioeng., 19, 69-86, 1977.*

[47] **Wang H., Wang, D., Cooney, C.**, "Computer Aided Penicillin Fermentation.", Biotechnology and Bioeng., 21, 975–995, 1979.

[48] **Constantntindes, A. et al**, " Optimization of a Fed-Batch Fermentation Process.", Part 1, Development of Mathematical Models For Batch Penicillin. Biotech and Bioeng, 12, 803-830, 1970.

[49] **Peringer, P., Blachers, H.T.**, " Modelling and Optimal Control of Bakers Yeast Production in Repeated Fed-Batch Culture. ", *Proc.2th Int. Conf. on Computer Appl. in Ferm. Tech., Univ. of Pennsylvania, Philadelphia.*

[50] **Raimerez, A., et al**, "Optimization of Fermentation Plants.", *Biotechnology Letters, 3, (10), 205-560.*

[51] **Wohrer, W., et al**, " Ethanol and RQ Based Computer Control in Bed-Batch Cultures of Bakers Yeast.", *6th International Fermentation Symposium on Advances in Biotechnology, London, Canada, 1980.*

[52] **Tan, L., Dowling, J., McCorkell, C., McCabe, H.,** "Application of A Computer Simulation Technique For Optimal Control Of A Non-linear System", IEEE IECON' 91. *1991 International Conference on Industrial, Electronics, Control and Instrumentation. Japan.*

[53] **Tan, L., Dowling, J., McCorkell, C., McCabe, H.,** "State Estimation Technique For OptimalControl Of A Non-Linear System", IEEE IECON'91. *1991 International Conference on Industrial, Electronics, Control and Instrumentation. Japan.*

[54] **Comferford, P.,** "Self-tunning Control of A Fermentation Process", Report, Dublin City University, 1990.

APPENDIX A:

A Reported Example of A Non-Linear Filtering

A.1 Introduction

In this appendix, a non-linear filtering has been applied to a fed-batch fermentation process. In loose terms, any non-linear operation on observed data is referred to as **"non-linear filtering"**. The basic models for observed data are of a well-defined stochastic process ("signal" or "system response") with an additive "noise" process to account for the unavoidable error due to measurement.

Non-linear state estimation and filtering problems with Gaussian statistics are often treated with the aid of Bayesian maximum likelihood or maximum a *posteriori* (MAP) technique.

Non-linear filters are not commonly used for estimation of parameters and states. The reason seems to be the stochastic properties of the nonlinearity. In the following a nonlinear filter will be discussed which has many desirable properties. It gives, for a quite general class of non-linear filtering problems, a finite dimensional solution, which is exact in the discrete-time case. The filter was originally introduced by Halme(1980)[18] in the continuous-time form and later on in the discrete-time form by Selkäinaho (Selkäinaho, Halme and Behbehani, 1983, Selkäinaho 1984).[19]

A.2 The Summary Of Structure Of Algorithm

A.2.1 Problem Statement

The non-linear system is supposed to be the form:

$$d\theta(t)/dt = f(\theta(t),\ u(t),\ a(t)) + \omega(t); \qquad \textbf{(A.2.1–1)}$$

$$Y(t) = h(\theta(t),\ t,\ a(t)) + \upsilon(t)\ ; \qquad \textbf{(A.2.1–2)}$$

where $\boldsymbol{\theta}$ is an n-dimensional state vector, **a** a L-dimensional parameter vector, **u** an m-dimensional control vector and **Y** an r-dimensional observation vector. The functions f and h are supposed to be properly well-behaved non-linear functions. Equation **(A.2.1–1)** in discrete-time form is:

$$\theta(k+1) = f(\theta(k),\ u(k),\ a(k)) + \omega(k); \qquad \text{(A.2.1–3)}$$

where ω is a disturbance modelled by an independent zero mean Gaussian stochastic process having covariance:

$$E[\ \omega(k)\omega(k)^T\ ] = Q_1\ ; \qquad \text{(A.2.1–4)}$$

Information about θ is obtained through the observation equation:

$$Y(k) = h(\theta(k),\ k,\ a(k)) + \upsilon(k)\ ; \qquad \text{(A.2.1–5)}$$

where υ is an independent zero mean Gaussian stochastic process having the covariance

$$E[\upsilon(k)\upsilon(k)^T\ ] = R\ ; \qquad \text{(A.2.1–6)}$$

The parameter vector includes the biochemical (or other) parameters, like the specific growth rate μ, yield coefficients etc., which are defined as the estimated parameters. Here we suppose the dynamics of the parameters can be modelled as follows:

$$a(k+1) = a(k) + \omega_a(k); \qquad \text{(A.2.1–7)}$$

which means that slow variations are permitted in practice. The disturbance ω_a is supposed to have a white gaussian character:

$$E[\ \omega_a(k)\omega_a(k)^T\ ] = Q_2\ ; \qquad \text{(A.2.1–8)}$$

A.2.2 Estimation Algorithm

It is further assumed that both the dynamics and observation equations are supposed to have linear parts as follows:

$$\theta(k+1) = A(k)\cdot\theta(k) + f_1(\theta(k),\ k)\ ; \qquad \text{(A.2.2–1)}$$

$$Y(k) = C(k) + h_1(\theta(k)\ ; \qquad \text{(A.2.2–2)}$$

where the pair (A(k), C(k)) is supposed to be completely observable in real-time. f_1 and h_1 are linearized f and h. It can be shown that under these circumstances the state estimate can be given in the form [19]

$$\hat{\theta}(k+1/k) = \hat{\theta}(k+1/k-1)+K_{\theta}[\hat{\theta}(k/k-1)]\cdot\{Y(k) - h[\hat{\theta}(k/k-1), k]\} \qquad (A.2.2\text{–}3)$$

$$\hat{\theta}(k+1/k-1) = f(\hat{\theta}(k/k-1), u(k), k) ; \qquad (A.2.2\text{–}4)$$

where the gain K_{θ} is calculated from the equation

$$K_{\theta}[\hat{\theta}(k/k-1)] = [A(k)P(k)C^T(k)+R]^{-1} + A(k)[P(k)^{-1} + C^T(k)R^{-1} C(k)]^{-1} \cdot[\partial h_1(\theta,k)/\partial\theta|_{\theta=\theta(k/k-1)} - C(k)]R^{-1} ; \qquad (A.2.2\text{–}5)$$

where in turn the covariance matrix P is calculated off-line from the **Riccati** equation:

$$\left| \begin{array}{l} P(k) = A(k)[P(k-1)^{-1} + C(k)\cdot R^{-1}\cdot C^T(k)]\cdot A^T(k) + Q_{\theta} ; \\ P(0) = P_0 ; \end{array} \right. \qquad (A.2.2\text{–}6)$$

where Q_{θ} is positive the state noise covariance.
Equation **(A.2.2–6)** can be solved independently from the prediction-correction equations **(A.2.2–3), (A.2.2–4).**
In the case where A and C are time invariant the limit gain becomes:

$$K_{\theta(k)} = K_1+ A\cdot P_2\cdot[\partial h_1(\theta)/\partial\theta - C]^T\cdot R^{-1} ; \qquad (A.2.2\text{–}7)$$

where

$$K_1 = A\cdot P_3\cdot C\cdot[C\cdot P_3\cdot C^T + R]^{-1} ; \qquad (A.2.2\text{–}8)$$

The covariance before measurement:

$$P_3 = A\cdot P_2\cdot A^T + Q_{\theta} ; \qquad (A.2.2\text{–}9)$$

The covariance after measurement:

$$P_2 = (P_3^{-1} + C\cdot R^{-1}\cdot C^T)^{-1} ; \qquad (A.2.2\text{–}10)$$

can be used.

When applying the filter to the simultaneous parameter and state estimation the standard state extension method is not used because it may lead to extensive calculations due to increased dimensions, but instead the state and parameter estimation tasks are separated for different filters. The state filter is in the form given above in the equations **(A.2.2–3-6).** The parameter filter uses the dynamic equation **(A.2.1–7),** but the observation equation is written in the form:

$$Y(k) = h\{f[\hat{\theta}(k/k-1), u(k-1), a(k-1)]\} ; \qquad (A.2.2-11)$$

where the parameter vector a is in an explicit position. The gain Ka for the parameter estimator:

$$\hat{a}(k/k) = \hat{a}(k/k-1) + K_a[Y(k)-h(\hat{\theta}(k/k-1))] ; \qquad (A.2.2-12)$$

$$\hat{a}(k/k-1) = \hat{a}(k-1/k-1) ; \qquad (A.2.2-13)$$

can be calculated now following the general equations(A.2.2– 5-10).

In the biological processes, like in many other chemical processes, the original continuous state dynamics are non-linear. It is difficult or even impossible to obtain the corresponding exact discrete-time version analytically. One can then choose either to use the original continuous time model and a small integration step or to use discretising form of the model. In practice the most convenient way to work out a discrete-time version is to use a linearized model of the form

$$\theta(k+1) = A(a)\cdot\theta(k) + B(a)\cdot u(k) ; \qquad (A.2.2-13)$$

$$Y(k) = C(a)\theta(k) \qquad (A.2.2-14)$$

where the matrix A, B, and C have been formed via derivation so that an explicit dependence on the parameter vector is known. This is important because it is better to estimate directly the biotechnical parameters such as yields, the specific growth rate etc., and not the parameters of a linear black-box model.

APPENDIX B :

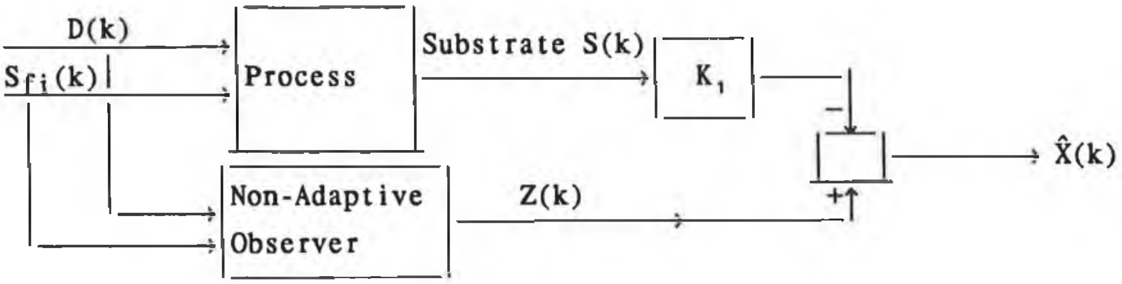


Fig III-Cha 2 Non-Adaptive Observer Scheme

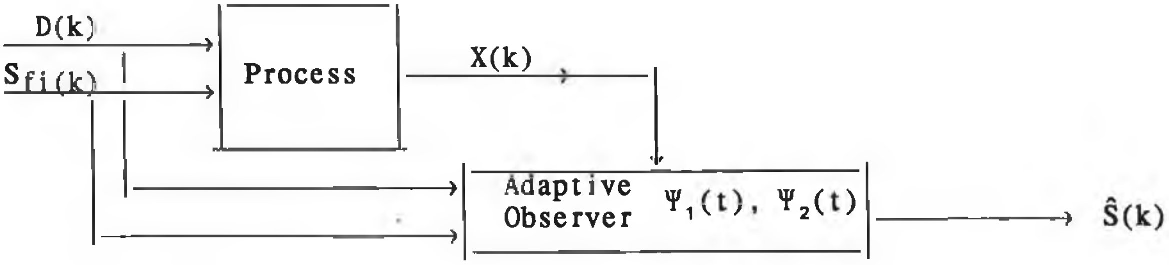


Fig III-Cha 3 Adaptive Observer Scheme

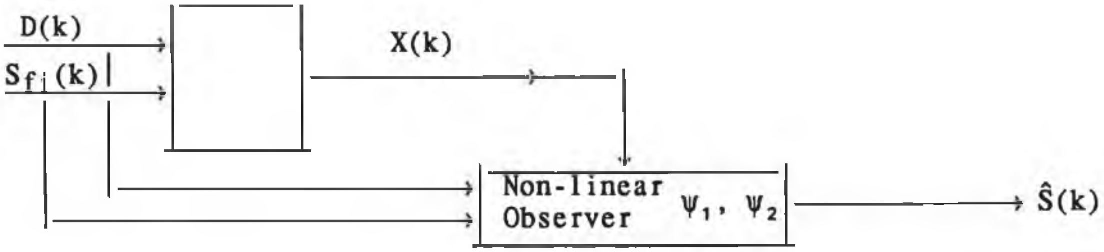


Fig III-Cha 4 Non-linear Observer Scheme

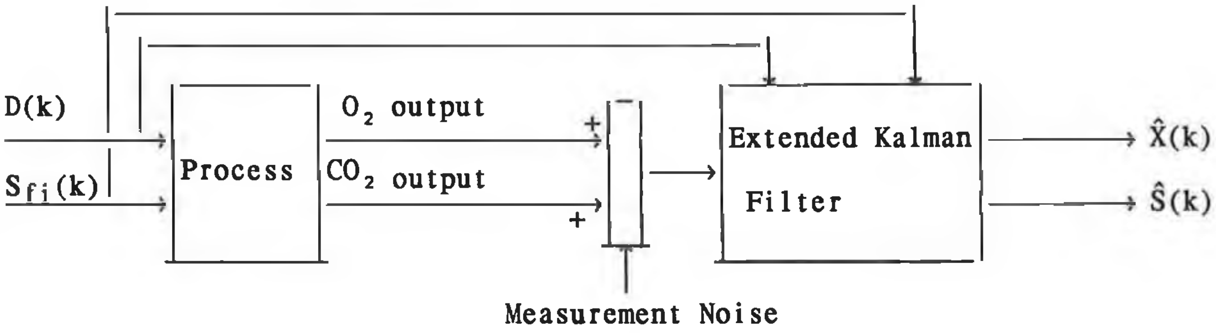


Fig III-Cha 5 Extended Kalman Filter Scheme

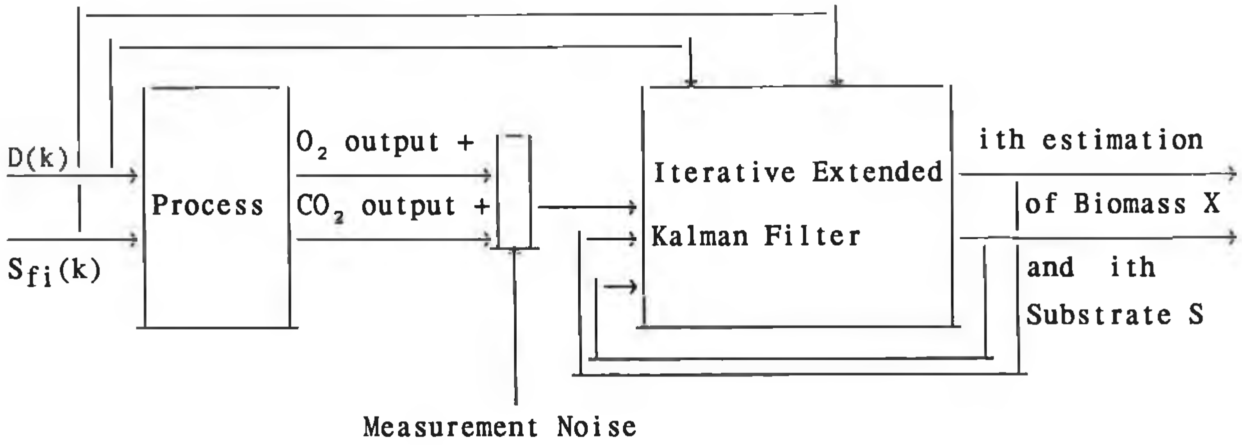


Fig III-Cha 6 Iterative Extended Kalman Filter Scheme

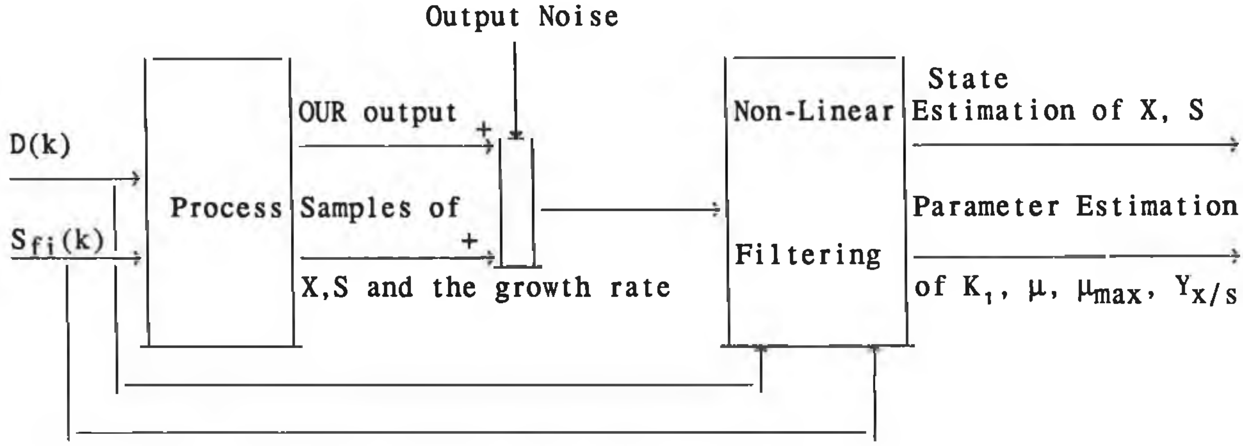
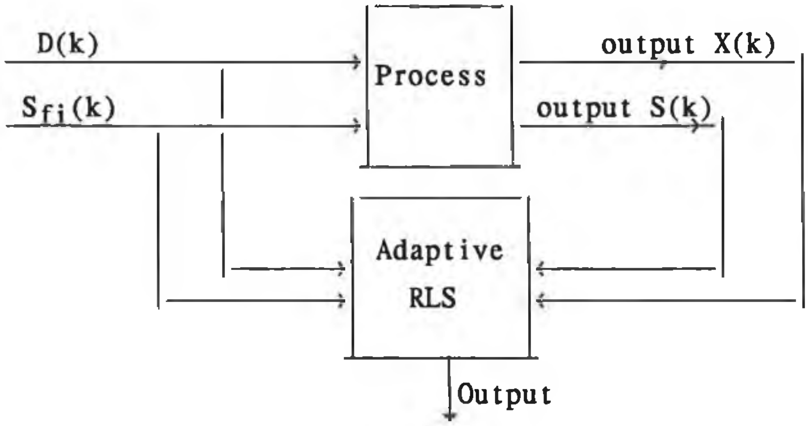


Fig III–Cha 7 Non-Linear Filtering Scheme



Parameter Estimation of
K_1, μ, μ_{max}, $Y_{x/s}$.

Fig IV-Cha 3 Parameter Estimation Scheme

APPENDIX C

APPLICATION OF A COMPUTER SIMULATION TECHNIQUE FOR OPTIMAL CONTROL OF A NON-LINEAR SYSTEM

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ABSTRACT: *In recent years it has been acknowledged that to significantly improve biological system performance and productivity, control, including optimal control, should be implemented on-line.*

The dynamics of biological processes are highly non-linear and key variables are difficult to measure. As an aid to contributing solutions to the twin difficulties of complex dynamics and measurement difficulty a relatively simple mathematical model has been developed for the purposes of evaluating optimal controllers.

A simulation of a fed-batch fermentation process is developed which includes the non-linear dynamics of the process.

KEYWORDS: *Modelling, Simulation, Bioreactors, Control.*

1. INTRODUCTION

The control of a biological process is based on the measurements of physical, chemical or biochemical properties and environmental parameters of the process. Often many important variables and parameters have to be calculated or estimated because of their unmeasurability, such as cell mass and substrate concentrations in a fermentation process. Basically the estimation technique adopted involves running, in real time, a (simulation) model of the process in parallel with, and receiving the same inputs as, the real process. Instead of the actual dynamics of a system, the simulated dynamics are often used for optimal control because many non-linear systems are generally very complex and not completely known, like a fermentation process.

This paper describes in detail the dynamic models of two non-linear systems, fed-batch and batch fermentation processes and discusses results of the analysis. In order to solve the state equations for the non-linear systems a classical first order ***Euler*** and a fourth order ***Runge-Kutta*** computer algorithm for the integration of the nonlinear differential equations were developed. The state models have been expanded to include the various nonlinearities.

2. SUMMARY OF STRUCTURE OF A NON-LINEAR SYSTEM

2.1. Description of Dynamics

A fermentation process is a complicated, non-linear, time-varying system. Its dynamics are not completely known. In this process some state variables are nonmeasurable, such as biomass and substrate concentrations. The following (non-linear) model [7] can be used to represent (in fully aerobic conditions) the dynamics of a fed-batch, batch or continuous fermentation process.(e.g. a baker's yeast fermentation).

(i) Biomass:

$$dX(t)/dt = [\mu - D(t)]\cdot X(t); \qquad (1)$$

(ii) Substrate :

$$dS(t)/dt = - K_1\cdot\mu\cdot X(t) + D(t)\cdot[S_{fi} - S(t)]; \qquad (2)$$

(iii) Fermentor volume of the growth culture:

$$dV/dt = F_{in} - F_{out} ; \qquad (3)$$
$$F_{in} = D\cdot V ;$$
$$F_{out} = 0 ;$$

(iv) Oxygen concentration:

$$dO/dt = OTR + OUR ; \qquad (4)$$
$$OUR = - dX(t)/dt\cdot(1/Y_{x:o}) ;$$
$$OTR = K_{la}\cdot(X_{o_2}\cdot O_1 - O) ;$$

(v) Carbon dioxide concentration:

$$dC/dt = CEP + CTR ; \qquad (5)$$
$$CEP = K_{c_2}\cdot\mu\cdot X(t);$$
$$CTR = K_d\cdot K_a\cdot(X_{co_2}\cdot C_1 - C) ;$$

(vi) Ethanol concentration:

$$dE/dt = EPR - ECR ; \qquad (6)$$
$$EPR = [\xi_{max}/(1+E/K_{ct})]\cdot[S/(K_s+S)] ;$$
$$ECR = [K_{po}\cdot O/(O+K_{o_2})]\cdot[E/(K_e+E)] ;$$

Where: X, S, O, C and E are the concentrations of biomass, substrate, oxygen, carbon-dioxide and ehanol respectively. X and S

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are nonmeasurable; O, C and E can be measured on-line; Other variables and parameters are: OUR — the oxygen uptake rate. OTR — the oxygen transfer rate. CEP — the CO_2 evolution rate. CTR — the CO_2 transfer rate. EPR — the ethanol production rate. ECR — the ethanol concentration rate. D — the dilution rate. S_{fi} — the substrate in the influent. μ — the specific growth rate with maximum value μ_{max}. K_1 — the yield coefficient. O_1 — the saturation concentration of dissolved oxygen in the liquid. C_1 — the saturation concentration of CO_2. K_s, K_a, K_{c1}, K_{c2}, K_{et}, K_{la}, K_c, K_{po}, ξmax will be presented in section 4.

2.2 Models Of The Specific Growth Rate (μ)

The specific growth rate μ is a key time-varying parameter for description of biomass growth, substrate consumption and products formation. For a fermentation process, the most commonly used models for μ are presented as follows:[6] [7]

(i) Monod's model :

A functional relationship between the specific growth μ and an essential compound's concentration was proposed by Monod.

$$\mu(S) = \mu_{max} \cdot S(t)/[K_s + S(t)]; \qquad (7)$$

This model is widely used to describe cell growth limited by a single substrate in a fermentation process. [7]

(ii) Ollson's model:

Aerobic fermentation are processes where the microorganism need oxygen to develop properly. In such case, dissolved oxygen (O) in the culture medium can be considered an additional substrate. This law which has Monod similarities is often referred to as the Ollson model for specific growth rate μ.

$$\mu(S, O) = \mu_{max} \cdot [S/(K_s+S)] \cdot [O/(K_{O_2}+O)] \; ; \qquad (8)$$

This model considers the influence of substrate S and dissolved oxygen concentration O.[7]

(iii) Contois' model :

The biomass growth is often presumed to slow down at high biomass concentrations. A possible model in this case is the following form :

$$\mu(S, X) = \mu_{max} \cdot S/(K_c \cdot X + S) \; ; \qquad (9)$$

This model considers the influence of substrate concentration S and biomass concentration X. [7]

3. COMPUTER SIMULATION

In order to assess the system dynamics and to optimise controller design, the system models were simulated in computer software. The principle of all numerical integration methods is to estimate the system states at time ($t+\Delta t$) given the state at time t where Δt is the sampling period [2]. For a general equation of the form ,

$$\dot{\theta} = f(\theta, u, t); \qquad (10)$$

At each step computations are done by some formula normally based upon the Taylor series,

$$\theta(t+h) = \theta(t) + \Delta t \cdot \dot{\theta}(t) + (\Delta t)^2/2! \cdot \ddot{\theta}(t) \cdots\cdots \qquad (11)$$

If Δt is chosen to be sufficiently small and if sufficient higher order derivatives of θ and powers of θ are taken, then the value $\theta(t+\Delta t)$ can be accurately found.

A classical first order ***Euler*** method and a fourth order ***Runge-Kutta*** technique have been applied to the model for integration. These techniques are widely used in engineering for a non-linear system.

3.1 Euler Approximation Methods

The ***Euler*** method is the simplest. For equation (11), only a first power of Δt is considered assuming the terms in Δt^n ($n > 1$) are very small compared to Δt. This is valid only if $\Delta t \ll 1$. The ***Euler*** method has the form,

$$\theta(t+\Delta t) = \theta(t) + \Delta t \cdot f(\theta, u, t) \; ; \qquad (12)$$

Applying a simple ***Euler*** approximation to the system model , the equations (1), (2), (3), (4), (5), (6), (7), (8), (9) have the followling forms,

3.1.1. System Model:

Biomass:

$$X(k+1) = X(k) + \Delta t \cdot \mu \cdot X(k) - \Delta t \cdot D \cdot X(k); \qquad (13)$$

Substrate:

$$S(k+1) = S(k) - K_1 \cdot \Delta t \cdot \mu \cdot X(k) + \Delta t \cdot D \cdot [S_{fi} - S(k)]; \qquad (14)$$

Volume of fermentor:

$$V(k+1) = V(k) + \Delta t \cdot (F_{in} - F_{out}); \qquad (15)$$

$$F_{in} = D \cdot V(k);$$

$$F_{out} = 0 \; ;$$

Oxygen:

$$O(k+1) = O(k) + \Delta t \cdot (OUR + OTR) \; ; \qquad (16)$$

$$OUR = - K_1 \cdot (\mu - D) \cdot X(k) \; ;$$

$$OTR = K_{la} \cdot [X_{O_2} \cdot O_1 - O(k)] \; ;$$

Carbon-dioxide:

$$C(k+1) = C(k) + \Delta t \cdot (CEP + CTR) \; ; \qquad (17)$$

Ethanol:

$$E(k+1) = E(k) + \Delta t \cdot X(k) \cdot (EPR - ECR) \; ; \qquad (18)$$

$$EPR = [\xi_{max}/(1 + E(k)/K_{et})] \cdot [S(k)/(K_s + S(k))] \; ;$$

$$ECR = [K_{po} \cdot O(k)/(O(k) + K_{O_2})] \cdot [E(k)/(K_e+E(k))] \; ;$$

3.1.2. The Specific Growth Rate μ:

Monod's model : [7]

$$\mu = \mu_{max}\cdot S(k)/[K_s + S(k)] \; ; \tag{19}$$

Ollson's model : [7]

$$\mu = [\mu_{max}\cdot S(k)/(K_s+S(k))]\cdot[O(k)/(K_{O_2}+ O(k))] \; ; \tag{20}$$

Contois' model : [7]

$$\mu(S, X) = \mu_{max}\cdot S(k)/[K_c\cdot X(k) + S(k)] \; ; \tag{21}$$

These equations discritized using ***Euler*** method were successfully simulated by computer. The simulation programme flow-chart is shown on **Fig 3.1**. This gives an overview of the simulation program implemented. This routine is called periodically at times determined by the integration interval. An integration interval of 0.05 hours is found to be adequate. The value of each state is transferred to a data file at periods of 10 minutes.

3.2 The Runge-Kutta Technique

The ***Runge-Kutta*** methods attempt to obtain higher accuracy based on Taylor's algorithm (eqn (11)), and at the same time avoiding the need for higher derivatives, by evaluating the function f(θ,u,t) (eqn(10)) at selected points on each subinterval. The simplest ***Runge-Kutta*** method is used here. Again for a general equation (10) of the form,

$$\dot{\theta} = f(\theta, u, t) \; ;$$

The formula for advancing the solution step is

$$\theta_{n+1} = \theta_n + 1/6\cdot(K_1 + 2K_2 + 2K_3 + K_4) \; ; \tag{22}$$

Assuming : $\dot{\alpha} = f(\theta, u)$; $\alpha(\theta_0) = \alpha_0$;

where

$$K_1 = \Delta t\cdot f(\theta_0, \alpha_0) \; ; \tag{23}$$

$$K_2 = \Delta t\cdot f(\theta_0 + \Delta t/2, \alpha_0 + K_1/2) \; ; \tag{24}$$

$$K_3 = \Delta t\cdot f(\theta_0 + \Delta t/2, \alpha_0 + K_2/2) \; ; \tag{25}$$

$$K_4 = \Delta t\cdot f(\theta_0 + \Delta t , \alpha_0 + K_3) \; ; \tag{26}$$

The ***Runge-Kutta*** algorithm does not require calculation of the higher derivatives of θ as is indicated in the Taylor series method. For the above system models (1), (2), (3), (4), (5), (6), f(θ, u, t) at various points can be calculated based on this algorithm. The discretized system model using a fourth-order ***Runge-Kutta*** method results in a more accurate computer simulation.

The simulation programme flow-chart is shown on Fig 3.2.1. The programme is written in PC C language. This routine is called periodically at times determined by the integration interval. This routine called a further routine (deriv) which returned the values of the derivatives of the states, as given by the differential equations of the model. An integration interval of 0.05 hours is found to be adequate, and the value of each state is printed out to a data file at periods of 10 minutes. A total run-time can be chosen in terms of each simulation. The flow-chart (Fig 3.2.2.) gives an overview of the simulation programme implemented. The data is then ploted as shown.

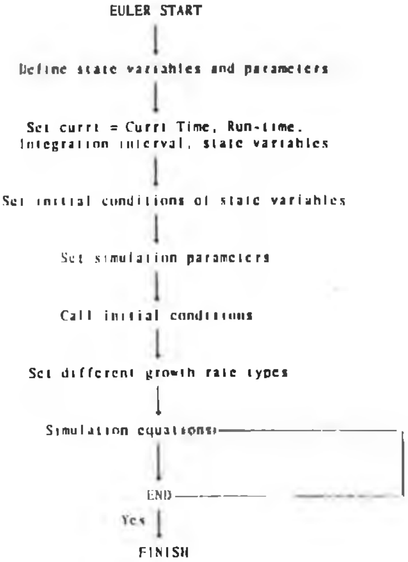


Fig 3.1 *Euler* Program Flow-chart

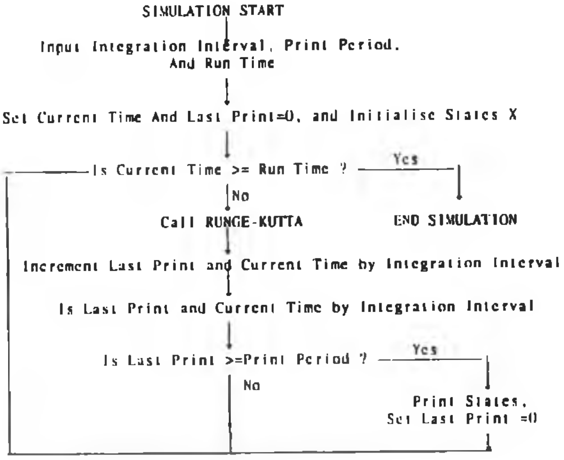
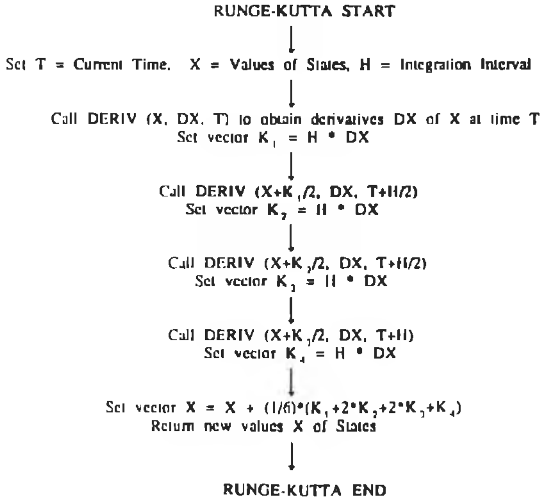


Fig 3.2.1 Runge-Kutta Simulation Flow-chart



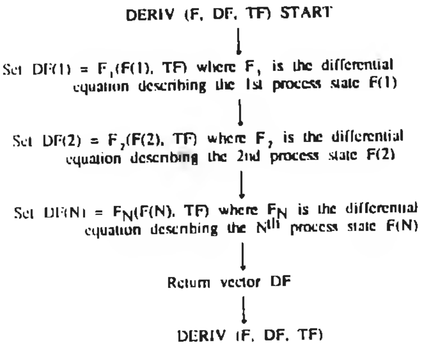


Fig 3.2.2. A 4th-order *Runge-Kutta* Subroutine Flow-chart.

4. SIMULATION RESULTS

* ***Euler's*** **method :**

——— Fig 1 to Fig 6 show the simulation experiment results of biomass (SI–X), substrate (SI-S), the volume of growth culture (SI-V), dissolved oxygen concentration (SI-O), CO_2 concentration (SI-C) and ethanol concentration (SI-E) under the following conditions:

(a) Common initial conditions:

$X(0) = 1.0$; $S(0) = 0.4$; $V(0) = 1.0$; $O(0) = 0.0040$; $C(0) = 0.0$; $E(0) = 0.0$; $\mu(0) = 0.0$;

(b) Parameters :

$D = 0.2$; $k_s = 0.8$; $K_1 = 2.0$; $K_{la} = 2.0$; $K_d = 0.4$; $K_{c_2}=1.15$; $K_c = 0.5$; $\Delta t=0.05$; $\mu_{max}= 0.03$; $O_1= 0.3$; $C_1= 0.10$; $X_{o_2}= 2.50$; $X_{co_2}=0.0033$; $\xi_{max}= 0.15$; $K_{po}= 0.05$; $K_{o_2} = 0.006$; $K_{et} = 71.5$; $K_e = 0.5$; $\mu_o = 0.4$; $K_m = 0.4$; $K_i = 2.5$; $S_{fi} = 10$; curnt = 0.0;

The experimental data (EX-) has been got from the pilot plant. The simulation technique can be successfully used to describe the dynamics of the system by comparing the simulation results and experimental results.

* ***Runge-Kutta*** **method:**

——— Fig 7 to Fig 12 show the simulation results using the same above initial conditions and parameters.

From above results, the *Runge-Kutta* method does not require calculation of the higher derivatives of θ as is indicated in the Taylor series and attempt to obtain greater accuracy. This algorithm utilizes the computation of $f(\theta, u)$ at various points.

The *Euler* method is of limited practical use due to its large truncation error per step of order Δt^2. This is exaggerated when a large step length Δt is used. The *Euler* method would satisfy most requirements only if using small step Δt and if round off error did not occur in the calculations. But it always remains strongly dependant on the sample period.

5. DISCUSSION AND CONCLUSION

It has been demonstrated here that the computer simulation technique can be successfully applied to a biological process, which is a classical complex non-linear system, in order to assess the bioreactor model's accuracy and to facilitate controller appraisal. Although many important system variables cannot be measured on-line directly, the estimation methods based on simulation technique can be applied to solve this problem and the basis of this method is to run a computer model of the system in real-time.

6. REFERENCES

[1] **James E.Bailey, and David F. Ollis,** " BIOCHEMICAL ENGINEERING FUNDAMENTALS ", *McGraw-Hill international editions, Chemical Engineering Series.*

[2] **Hornbeck R.,** " NUMERICAL METHODS ", *Quantum Publishers, New York, (1975).*

[3] **Atkinson L., and Harley P.,** " AN INTRODUCTION TO NUMERICAL METHODS WITH PASCAL", *Addison Wesley, London, (1983).*

[4] **C.G.Sinclair and B Kristiansen,** "FERMENTATION KINETICS AND MODELLING ", *I D Bu'lock, 1987.*

[5] **A. G. Fredrickson, R.D.megee III and H.M.Tsuchiya,** " MATHEMATICAL MODELS FOR FERMENTATION PROCESSES".

[6] **D. Dochain** " ON-LINE PARAMETER ESTIMATION, ADAPTIVE STAET ESTIMATION AND ADAPTIVE CONTROL OF FERMENTATION PROCESSES", *Ph.D thesis, University of Louvain, 1986.*

[7] **Tan, Liang.** " MODELLING AND SIMULATION OF A FERMENTATION PROCESS". *RPN. 90/EE/001, Dublin City University, Ireland. 1990.*

[8] **L.Tan, J.Dowling, C.McCorkell, H.McCabe,** "STATE ESTIMATION FOR OPTIMAL CONTROL OF A NON-LINEAR SYSTEM ", *1991 International Conference on Industrial Electronics, Control and Instrumentation. Kobe, Japan.*

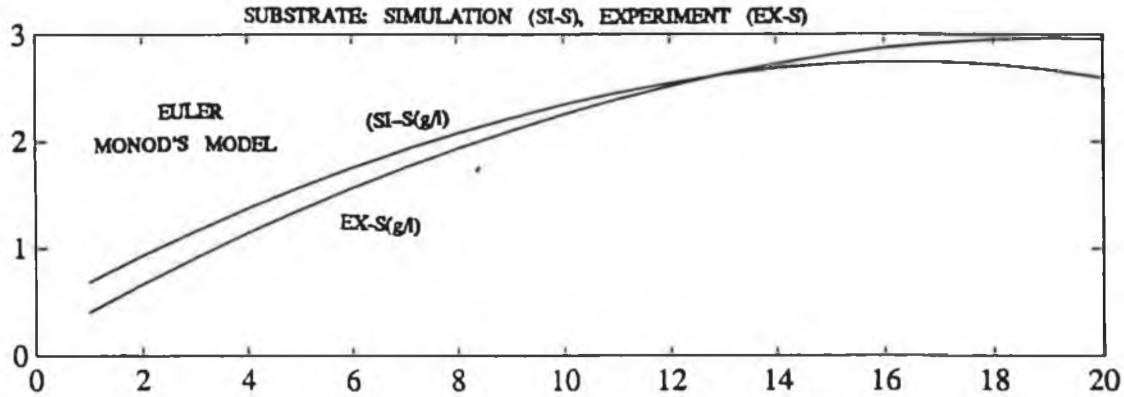


Fig 1

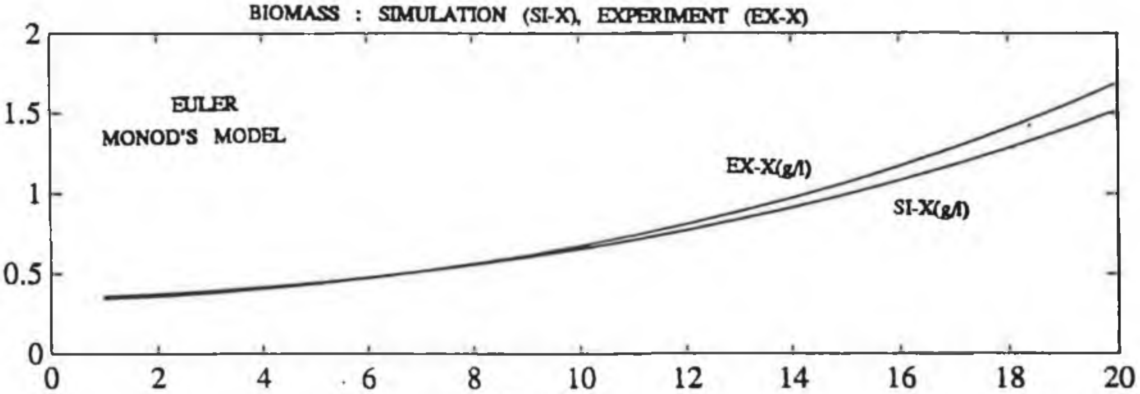


Fig 2

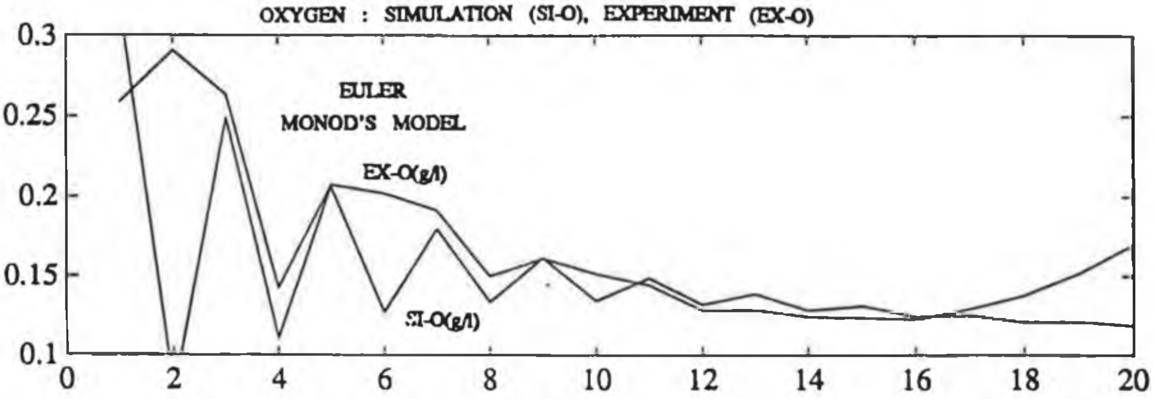


Fig 3

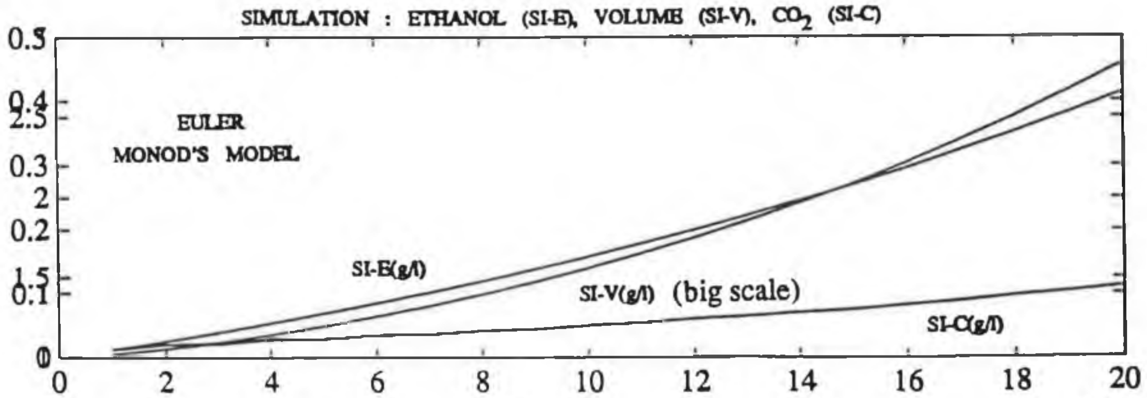


Fig 4

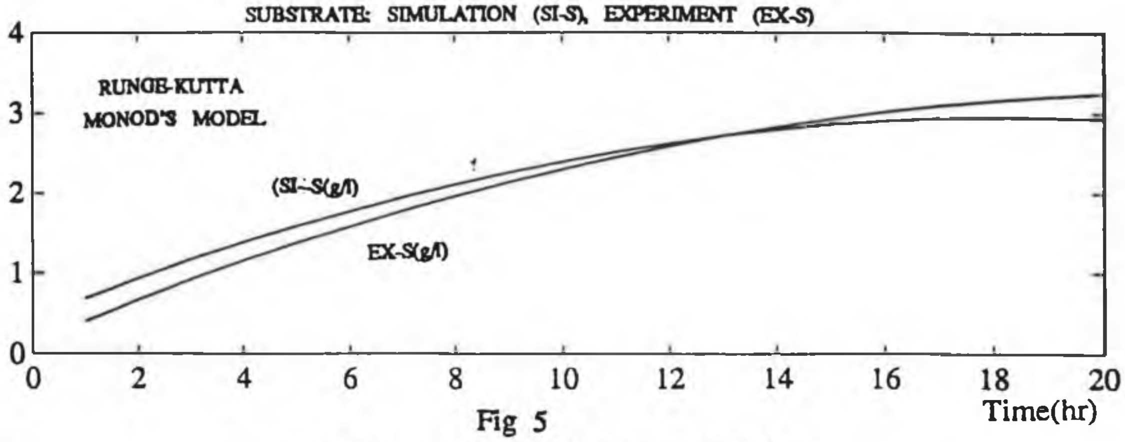


Fig 5

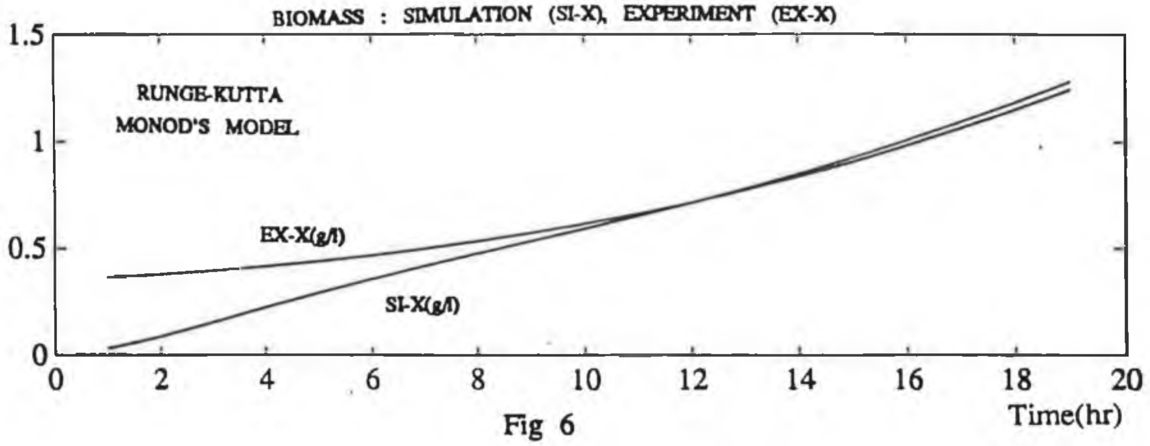


Fig 6

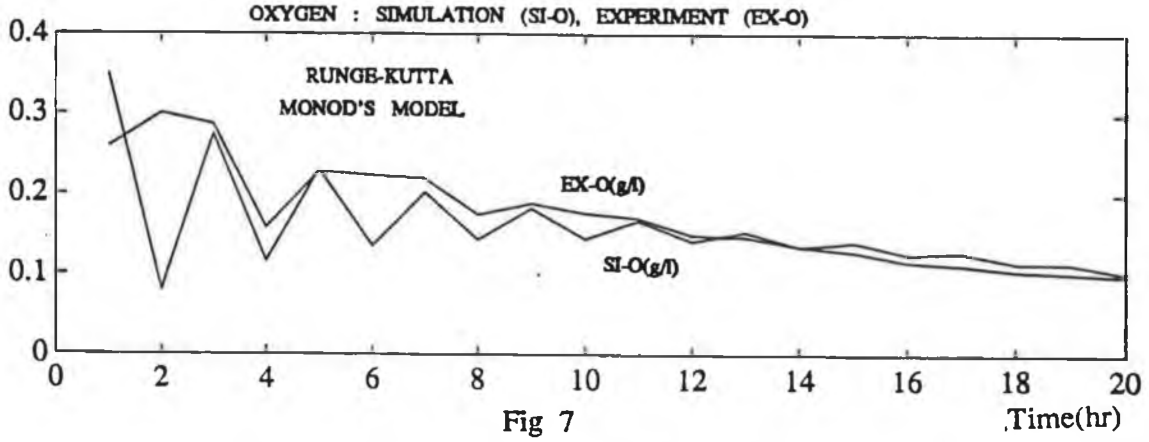


Fig 7

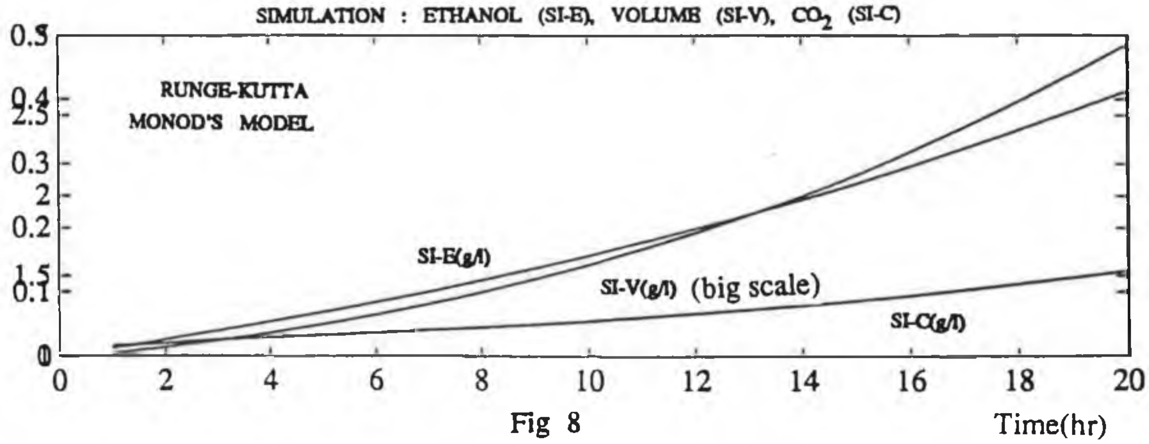


Fig 8

APPENDIX D

STATE ESTIMATION FOR OPTIMAL CONTROL OF A NON-LINEAR SYSTEM

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ABSTRACT: *Two estimation techniques, namely the extended Kalman filter (E.K.F) and the iterative extended Kalman filter (I E.K.F), have been applied to a non-linear time-varying system that has nonmeasurable state variables. An iterative solution to a fed-batch fermentation process is reported using the E.K.F. based on measurements of the oxygen and carbon-dioxide concentrations. The results demonstrate that this estimation technique can be successfully applied to complex biological processes. If the nonlinearities of these systems are sufficiently important or if a long delay in the estimation cannot be permitted for a particular process, then the I.E.K.F. can be selected.*

KEYWORDS: Non-linear state estimation, Biotechnical process, Extended Kalman filter, Iterative extended Kalman filter.

1. INTRODUCTION

Classical control strategies are ineffective when applied to the task of controlling multivariable non-linear, time-varying systems, particularly, as in biotechnical processes, where some of the important state variables are not measurable, due to the non-availability of accurate and reliable sensors. In this paper, state estimation techniques are used to estimate such unobserved quantities in the context of developing optimal control strategies.

The dynamics of a non-linear system, such as a biotechnical process, are usually complex and not completely known. It is often useful or necessary to develop relatively simple (non-linear) mathematical models to describe these systems. With (sometimes extensive) simplifying assumptions, such models might be developed for simulation purposes or for use in conjunction with some real-time input-output data as the basis for on-line estimation of states and parameters. Simulation models are employed as a testing ground for estimation algorithms.

In this paper, the extended Kalman filter (E.K.F.) method is applied to the task of state and parameter estimation for fed-batch and batch fermentation processes. These processes are well-known to be non-linear with time-varying parameters, and the state variables that must be controlled (biomass and substrate concentrations) are generally not measurable.

Using oxygen and carbon-dioxide concentrations, both of which can be measured on-line, the estimation equations are solved iteratively and compared to simulation and pilot plant experimental results.

If nonlinearities are sufficiently important, the estimation error can be significantly reduced through use of a high-order estimation technique. The iterative extended Kalman filter can yield substantially better estimates of nonmeasurable state variables when a system is non-linear. In addition, the iterative filter can show a faster convergence because of improved approximation.

2. SUMMARY OF NON-LINEAR SYSTEM STRUCTURE

2.1 Model Of Non-Linear System

Fermentation processes are non-linear time-varying systems. In these processes some state variables, such as biomass and substrate concentrations, are nonmeasurable. The following (non-linear) model [7][10] can be used to represent (in fully aerobic conditions) the dynamics of a fed-batch, batch or continuous fermentation process (e.g. a baker's yeast fermentation).

(i) Biomass:

$$dX/dt = (\mu - D)\, X; \qquad (1)$$

(ii) Substrate:

$$dS/dt = -K_1 \cdot \mu \cdot X + D \cdot (S_{fi} - S); \qquad (2)$$

(iii) Oxygen:

$$dO/dt = OTR + OUR; \qquad (3)$$

$$OUR = -dX/dt \cdot (1/Y_{x:o});$$

$$OTR = K_{la} \cdot (X_{o2} \cdot O_1 - O);$$

(iv) Carbon dioxide:

$$dC/dt = CEP + CTR; \qquad (4)$$
$$CEP = K_{c2} \cdot \mu \cdot X;$$
$$CTR = K_d \cdot K_a \cdot (X_{co2} \cdot C_1 - C);$$

Where X, S, O and C are the concentrations of biomass, substrate, oxygen and carbon-dioxide respectively. X and S are nonmeasurable. O and C can be measured. Other variables and parameters are : μ — the specific growth rate with maximum value μ_{max}. S_{fi}— the substrate in the influent. K_1 — the yield coefficient. OUR — the oxygen uptake rate. OTR — the oxygen transfer rate. $Y_{x:o}$ — the yield coefficient of biomass on oxygen. CER — the CO_2 evolution rate. CTR — the CO_2 transfer rate. O_1, C_1 are the saturation concentrations of dissolved oxygen and CO_2. X_{o2}, X_{co2} are partial fraction of O_2 and CO_2. D, K_s, K_d, K_{c1}, K_{c2}, K_{la} are known.

2.2. Models Of The Specific Growth Rate (μ)

The specific growth rate μ is a key time-varying parameter for description of biomass growth, substrate consumption and products formation. For a fermentation process, the most commonly used models for μ are Monod's model, Ollson's model, Contois' model. The Monod's model is used in this paper. [4], [7].

(i) Monod's model : [7]

$$\mu(S) = \mu_{max} \cdot S/(K_s + S); \qquad (5)$$

This model formulas are widely used to describe cell growth limited by a single substrate in a fermentation process.[7]

(ii) Ollson's model: [7]

$$\mu(S, O) = \mu_{max} \cdot S \cdot O/[(K_s + S)(K_{o2} + O)]; \qquad (6)$$

This model considers the influence of substrate S and dissolved oxygen concentration O .

(iii) Contois' model: [7]

$$\mu(S, X) = \mu_{max} \cdot S/(K_c \cdot X + S); \qquad (7)$$

This model considers the influence of substrate concentration S and biomass concentration X.

In this paper, Monod's model has been used to estimation technique.

3. APPLICATION OF EXTENDED KALMAN FILTER

3.1 Problem Formulation

The dynamics of fed-batch and batch fermentation processes can be replaced by the following stochastic non-linear differential equations based on equations (1) and (2):

$$\dot{\theta}(t) = F(\theta, \mu, t) + \omega(t); \qquad (8)$$

where

$$F = \begin{vmatrix} F_1 \\ F_2 \end{vmatrix}; \quad \theta(t) = \begin{vmatrix} X(t) \\ S(t) \end{vmatrix}; \quad \omega(t) = \begin{vmatrix} \omega_1(t) \\ \omega_2(t) \end{vmatrix};$$

The system models can be described as follows:[7]

$$F_1(\theta(t), \mu, t) = \mu_{max} \cdot X(t) \cdot S(t)/[K_s + S(t)] - D \cdot X(t) + \omega_1(t); \qquad (9)$$

$$F_2(\theta(t), \mu, t) = \mu_{max} \cdot K_1 \cdot X(t) \cdot S(t)/[K_s + S(t)] + D \cdot [S_{fi} - S(t)] + \omega_2(t); \qquad (10)$$

3.2 Measurement Equations

In a fed-batch fermentation process, when oxygen O and carbon-dioxide C concentrations appear as linear functions of X and S, the following equation is presented:[7]

$$Z(\theta(t)) = H \cdot \theta(t) + \upsilon(t); \qquad (11)$$

θ(t) is a 2 x 1 state vector, H is a 2 x 2 observation matrix:

$$H = \begin{vmatrix} K_{x1} & K_{s1} \\ K_{x2} & K_{s2} \end{vmatrix}; \quad \theta(t) = \begin{vmatrix} \theta_1(t) \\ \theta_2(t) \end{vmatrix}; \qquad (12)$$

Z(t) is a 2 x 1 output evolved on-line measurements of oxygen and carbon dioxide concentrations. K_{x1}, K_{s1} are the observation yield coefficients of carbon dioxide measurement. K_{x2}, K_{s2} are the observation yield coefficients of oxygen measurement.

ω(t) and υ(t) represent uncorrelated zero mean white noise with covariance:

$$E[\omega(t)\omega(t)^T] = Q \cdot \delta_{ij}; \quad E[\upsilon(t)\upsilon(t)^T] = R \cdot \delta_{ij}; \qquad (13)$$

$$\delta_{ij} = \left(\begin{array}{ll} 1 & \text{for } i = j \\ 0 & \text{for } i \neq j \end{array} \right);$$

The initial state of the system model is assumed to be a Normally distributed stochastic random variable with mean:

$$E[\hat{\theta}(0)] = \theta(0); \qquad (14)$$

and covariance:

$$E[(\hat{\theta}(0) - \bar{\theta}(0))(\hat{\theta}(0) - \bar{\theta}(0))^T] = P_0; \qquad (15)$$

υ(t) is assumed to have zero mean and covariance:

$$E[\upsilon(t)^2] = R(t); \qquad (16)$$

θ(t) is unmeasurable on-line. $\hat{\theta}(t)$ is updated estimate. $\bar{\theta}(t)$ is previous estimate. In the presence of state and observation noise (or model inacuracies) the question is how to find an on-line estimation algorithm based on on-line available measurements of oxygen and carbon-dioxide in order to estimate θ(t). The extended Kalman filter is employed for optimal on-line estimation of state variables based on system models.

3.3 Structure of Algorithm

3.3.1 Linearisation and Discretisation

Applying simple Euler approximation to the continuous models (8) and (11), the following discrete-time non-linear stochastic model of biomass, substrate and consumption for a fermentation process has been got:

$$\theta(k+1) = g(\theta(k/k),\ T) + \omega(k); \qquad (17)$$

$$z(k) = H\cdot\theta(k) + \upsilon(k); \qquad (18)$$

where H is defined in section (3.2).

$g(\theta(k/k),\ T) = \theta(k/k) + T\cdot F(\theta(k/k))$;

$E[\hat{\theta}(0)] = \theta(0)$; $E[(\hat{\theta}(0) - \bar{\theta}(0))(\hat{\theta}(0) - \bar{\theta}(0))^T] = P_0$;

$$g(\theta(0),\ T) = \theta(0) + T\cdot F(\theta(0)); \qquad (19)$$

T is the sample time, and other values are in models (8), (11).

3.3.2 Jacobian Matrix

In terms of E.K.F. algorithm, the Jacobian matrix must be precalculated. Considering a fed-batch fermentation process models (8), (9), (10), the Jacobian $J|_{\theta(k)}$ matrix can be derived as follows:

$$J_{11} = \frac{\partial f_1[\theta(t)]}{\partial \theta_1(t)}\bigg|_{\theta(k/k)} = \frac{\partial f_1[X(t),\ S(t)]}{\partial X(t)}\bigg|_{x(k/k)} = \frac{\mu_{max}\cdot S(k/k)}{K_s + S(k/k)} - D; \qquad (20)$$

$$J_{12} = \frac{\partial f_1[\theta(t)]}{\partial \theta_2(t)}\bigg|_{\theta(k/k)} = \frac{\partial f_1[X(t),\ S(t)]}{\partial S(t)}\bigg|_{s(k/k)} = \frac{\mu_{max}\cdot K_s\cdot X(k/k)}{[K_s + S(k/k)]^2}; \qquad (21)$$

$$J_{21} = \frac{\partial f_2[\theta(t)]}{\partial \theta_1(t)}\bigg|_{\theta(k/k)} = \frac{\partial f_2[X(t),\ S(t)]}{\partial X(t)}\bigg|_{x(k/k)} = -\frac{K_1\cdot\mu_{max}\cdot S(k/k)}{K_s + S(k/k)}; \qquad (22)$$

$$J_{22} = \frac{\partial f_2[\theta(t)]}{\partial \theta_2(t)}\bigg|_{\theta(k/k)} = \frac{\partial f_2[X(t),\ S(t)]}{\partial S(t)}\bigg|_{s(k/k)} = -\frac{K_1\cdot\mu_{max}\cdot K_s\cdot X(k/k)}{K_s + S(k/k)} - D; \qquad (23)$$

3.3.3 EKF Algorithm Flowchart

The on-line optimal state estimation based on the extended Kalman filter technique can be written as follows:

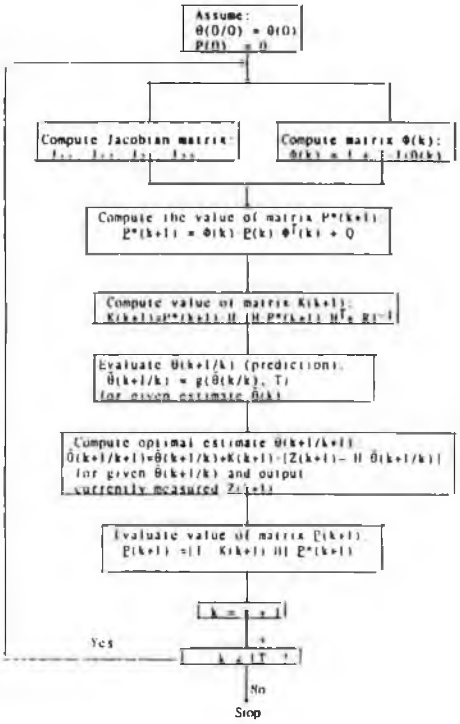


Fig 3.3.3 EKF Algorithm Flowchart

For system models (8) :

$$\dot{\theta}(t) = F(\theta(t)).$$

then, in discrete time with sample interval T,

$$\Delta\theta(k+1) = \Phi(T)\cdot\Delta\theta(k).$$

where: Φ is the transition matrix. If Φ(T) is approximated by the truncated series: Φ(T)= I + J·T, this is equivalent to the Euler solution of the original equations. The transition matrix Φ(k) can be obtained by linearising of non-linear discrete models (17), (18) around estimate θ(k).

$$\Phi(k) = I + T\cdot J|_{\theta(k)}; \qquad (24)$$

$$\hat{\theta}(k+1) = \bar{\theta}(k) + T\cdot F[\bar{\theta}(k)] = [I + T\cdot J|_{x(k)}]\cdot\Delta\theta(k) + \omega(k); \qquad (25)$$

where : I is the 2 x 2 identity matrix, $J|_{\theta(k)}$ is the Jacobian of system models,

$\Delta\theta(k) = [\hat{\theta}(k) - \bar{\theta}(k)]$ is the 2 x 2 state perturbation vector.

$\hat{\theta}(k+1/k+1)$ is the 2 x 1 optimal state estimation at time k+1.

$\bar{\theta}(k+1/k)$ is the 2 x 1 state estimate at time k+1 based on estimate $\hat{\theta}(k/k)$ at time k only (prediction).

Z(k+1) is the 2 x 1 output (observation) vector at time k+1.

H is the 2 x 2 observation matrix.

K(k+1) is the 2 x 1 optimal Kalman gain at time k+1.

$K(k+1)[Z(k+1) - H\cdot\bar{\theta}(k+1/k)]$ is the so-called innovation sequence (correction).

P(k) is the 2 x 2 positive definite symmetric error filtering covariance matrix.

P*(k+1) is the 2 x 2 positive definite symmetric error prediction covariance matrix.

Φ(k) is the 2 x 2 transition matrix of linearised perturbation model evaluated at time k for estimate $\bar{\theta}(k/k)$.

$g(\hat{\theta}(k/k), T)$ is the function from equations (17), (18) and (19).
Q is the 2 x 2 positive definite state noise covariance.
R is the 1 x 1 positive definite observation noise covariance.

3.4. Initial Conditions

The initial conditions $\theta_1(0)$, $\theta_2(0)$ of the process are assumed to be Normally distributed with covariance P_0 :

$$P_0 = E[(\begin{vmatrix} \hat{\theta}_1(0) \\ \hat{\theta}_2(0) \end{vmatrix} - \begin{vmatrix} \bar{\theta}_1(0) \\ \bar{\theta}_2(0) \end{vmatrix})(\begin{vmatrix} \hat{\theta}_1(0) \\ \hat{\theta}_2(0) \end{vmatrix} - \begin{vmatrix} \bar{\theta}_1(0) \\ \bar{\theta}_2(0) \end{vmatrix})^T]; \quad (26)$$

$\theta(0)$: mean of initial process state vector.
$P(0)$: initial value of estimate error covariance matrix.

Initial values of the EKF variables for the on-line estimation were determined by the simulations. (See discussion of resullt for specific values)

3.5. Error dynamics

Estimated error: $\varepsilon(k+1) = \theta(k+1) - \hat{\theta}(k+1)$; (27)
The error is minimised by an internal feedback loop with Kalman gain K(k+1).

4. APPLICATION OF ITERATIVE KALMAN FILTER

The extended Kalman filter is a popular method for treating non-linear estimation problems. However, if nonlinearities are sufficiently severe, the iterative extended Kalman filter can yield substantially better estimates of nonmeasurable state variables.

4.1 Summary of I.E.K.F. Algorithm

This algorithm is based on extended Kalman filter algorithm. The estimated state variables $\hat{\theta}(k+1/k+1)$ can be improved by repeatedly calculating $\hat{\theta}(k+1/k+1)$, K(k+1) and P(k), each time linearizing about the most recent estimate to develop this algorithm, denote the ith estimate of $\hat{\theta}(k+1/k+1)$ by $\hat{\theta}^i(k+1/k+1)$, i=0, 1, 2...., and expand the estimated state at time k at the ith iteration of the output equation in the form:

$$\hat{\theta}^{i+1}(k+1/k+1) = \hat{\theta}(k+1/k) + K[\hat{\theta}^i(k+1/k+1), k+1] \cdot \{Z^i(k+1) - C[\hat{\theta}^i(k+1/k)] \cdot [\hat{\theta}(k+1/k) - \hat{\theta}^i(k+1/K+1)]\}; \quad (28)$$

The iteration with starting value $\hat{\theta}^i(k+1/k+1) = \hat{\theta}(k+1/k)$ proceeds until $|\hat{\theta}^i(k+1/k+1) - \hat{\theta}^{i-1}(k+1/k+1)| \leq \varepsilon_f$
is reached. The bound ε_f must be preselected. The actual Kalman gain is given by

$$K[\hat{\theta}^i(k+1/k+1), k+1] = P^*(k+1/k) \cdot C^T[\hat{\theta}^i(k+1/k+1)] \cdot \{C[\hat{\theta}^i(k+1/k+1)] \cdot P^*(k+1/k) \cdot C^T[\hat{\theta}^i(k+1/k+1)] + R(k+1))]^{-1}; \quad (29)$$

and the filter covariance by:

$$P(k+1/k) = [I - K[\hat{\theta}(k+1/k+1), k+1] \cdot C[\hat{\theta}(k+1/k+1)]] \cdot P^*(k+1/k); \quad (30)$$

The predicted state and filter covariances are:

$$\hat{\theta}(k+1/k) = \Phi[\hat{\theta}(k/k), T]; \quad (31)$$

$$P^*(k+1/k) = A[\hat{\theta}(k/k)] \cdot P(k/k) \cdot A^T[\hat{\theta}(k/k)] + Q(k) \quad (32)$$

where

$$C[\theta(k), T] = \frac{\partial H[\theta(k), T]}{\partial \theta(k)}\bigg|_{[\theta(k), T]}; \quad (33)$$

and

$$A[\theta(k), T] = \frac{\partial \Phi[\theta(k), T]}{\partial \theta(k)}\bigg|_{[\theta(k), T]}; \quad (34)$$

are the matrices of the linearised system. The noniterative filter can be seen as a special case of these last equations.

4.2 Algorithm Flowchart

The on-line optimal estimation of state variables based on the iterative EKF are shown in Fig 4.2.

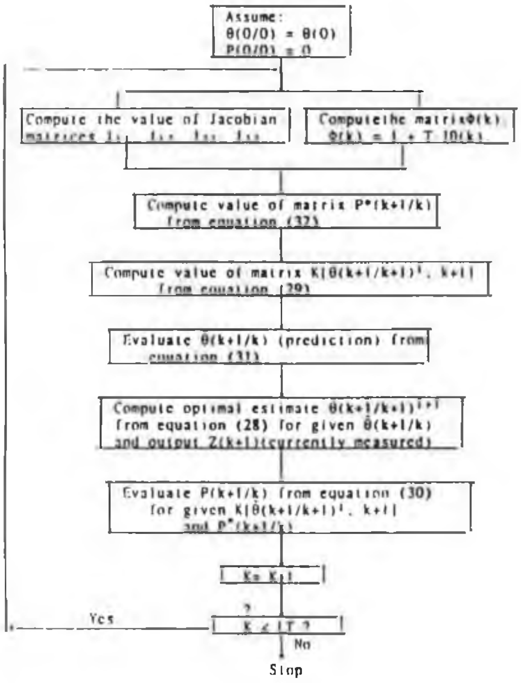


Fig 4.2 Iterative EKF Algorithm Flowchart

5 DISCUSSION OF RESULTS

The following common initial conditions which refer to the laboratory scale fermenter have been used:

The state variables: $X(0)=0.35$ and $S(0)=1.0$.

The parameters: $K_s=2.0$; $\Delta t=0.05$; $\mu_{max}=0.4$; $S_{fi}=10$; Curr=0.01; D=0.2.

Fig 1 and **Fig 2** shows the on-line estimation results of biomass and substrate using the data from simulation results. The on-line estimation results of biomass and substrate using experimental data are presented in **Fig 3** and **Fig 4**.

These experimental results demonstrate that the estimation technique can be successfully applied to a complex biological process and I.E.K.F. has a faster convergence rate. (the results of I.E.K.F. were not included in this paper)

6. CONCLUSIONS

It has been demonstrated that states and parameters of a complex biotechnical process can be estimated on-line by the extended Kalman filter (EKF). The estimation of substrate and biomass concentrations in fermentation processes is based on oxygen and carbon-dioxide concentrations which can be measured on-line. The experiments and computer results show that the extended Kalman filter gives satisfactory results during computer simulation.

The iterative extended Kalman filter can be used to reduce estimation errors and also to produce a faster convergence rate.

In addition, it has been observed that all algorithms are sensitive to error in initial estimation of biomass and substrate. There is a serious problem of finding an initial estimate of the error covariance. The observability of a system must be carefully considered to avoid estimation problems.

7. REFERENCES

[1] **Frank L.Lewis**, " OPTIMAL ESTIMATION " WITH AN INTRODUCTION TO STOCHASTIC CONTROL THEORY." *New York, 1986.*

[2] **Bailey J.E. and Ollis D.F.** " BIOCHEMICAL ENGINEERING FUNDAMENTALS". *McGraw - Hill, New York, (1977).*

[3] **A.Halme**, " MEASUREMENT AND ESTIMATION IN BIOREACTORS ", " ONE DAY INTERNATIONAL WORKSHOP ON CONTROL OF BIOTECHNICAL PROCESSES", *7th October, 1987.*

[4] **Dochain, D.**, " ON-LINE PARAMETER ESTIMATION, ADAPTIVE STATE ESTIMATION, " *PhD thesis, University of Louvain (1986).*

[5] **Proceedings of the** "AMERICAN CONTROL CONFERENCE", *1987.*

[6] **Simon Haykin**, " MODERN FILTERS ", *McMaster University, Hamilton, Ontario, Canada. 1989.*

[7] **Tan, Liang**, " ON–LINE STATE ESTIMATION OF A FERMENTATION PROCESS ", *RPN. 90/EE/002, Electronic Engineering Department. Dublin City University, Ireland. 1990.*

[8] **Comerford, P.**, " SELF-TUNING CONTROL OF FERMENTATION PROCESSES " , *Electronic Eng. Dept., Dublin City University. 1990.*

[9] **Arthur Gelb**, "APPLIED OPTIMAL ESTIMATION", *M.I.T press. 1987.*

[10] **L. Tan, J.Dowling, C.McCorkell, H.McCabe**, "APPLICATION OF A COMPUTER SIMULATION TECHNIQUE FOR OPTIMAL CONTROL OF A NON-LINEAR SYSTEM", *1991 International Conference in Industrial Electronics, Control and Instrumentation, Kobe, Japan. 1991.*

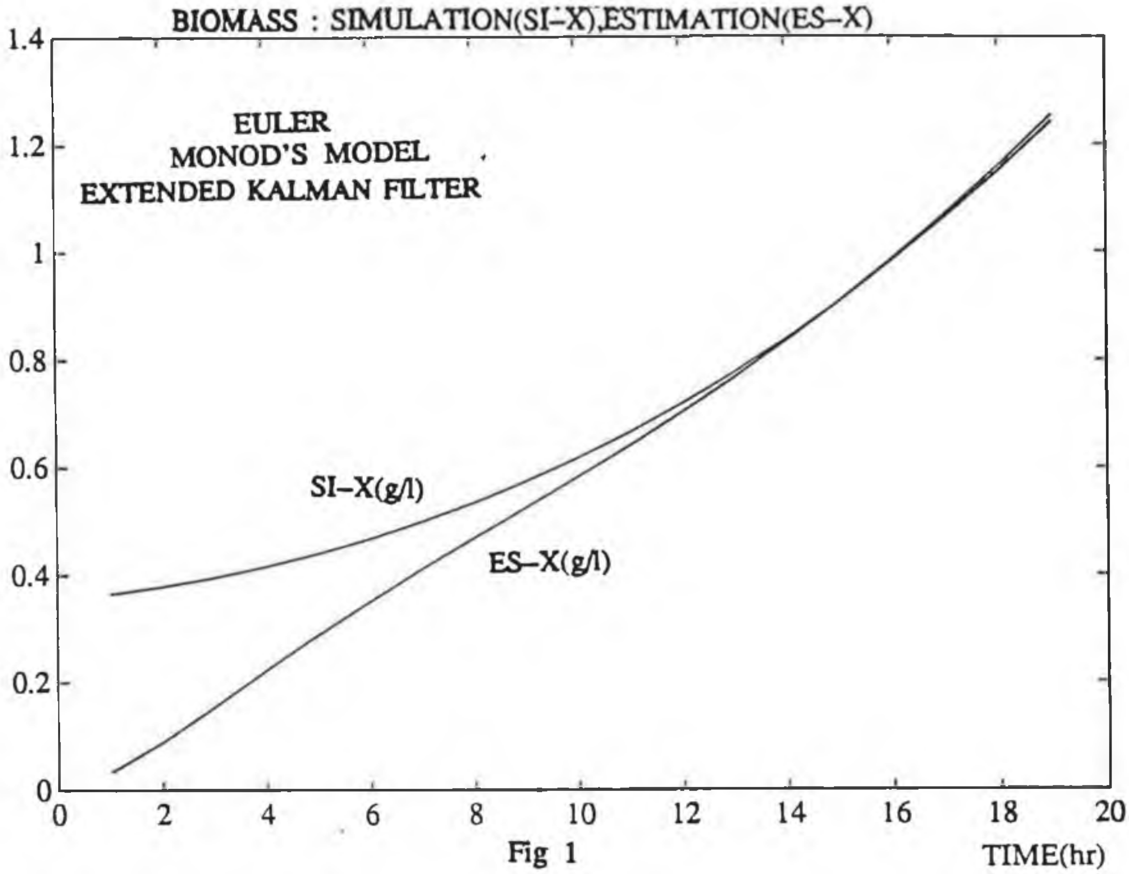

BIOMASS : SIMULATION(SI-X),ESTIMATION(ES-X)
EULER
MONOD'S MODEL
EXTENDED KALMAN FILTER
SI-X(g/l)
ES-X(g/l)
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
2
4
6
8
10
12
14
16
18
20
TIME(hr)

Fig 1

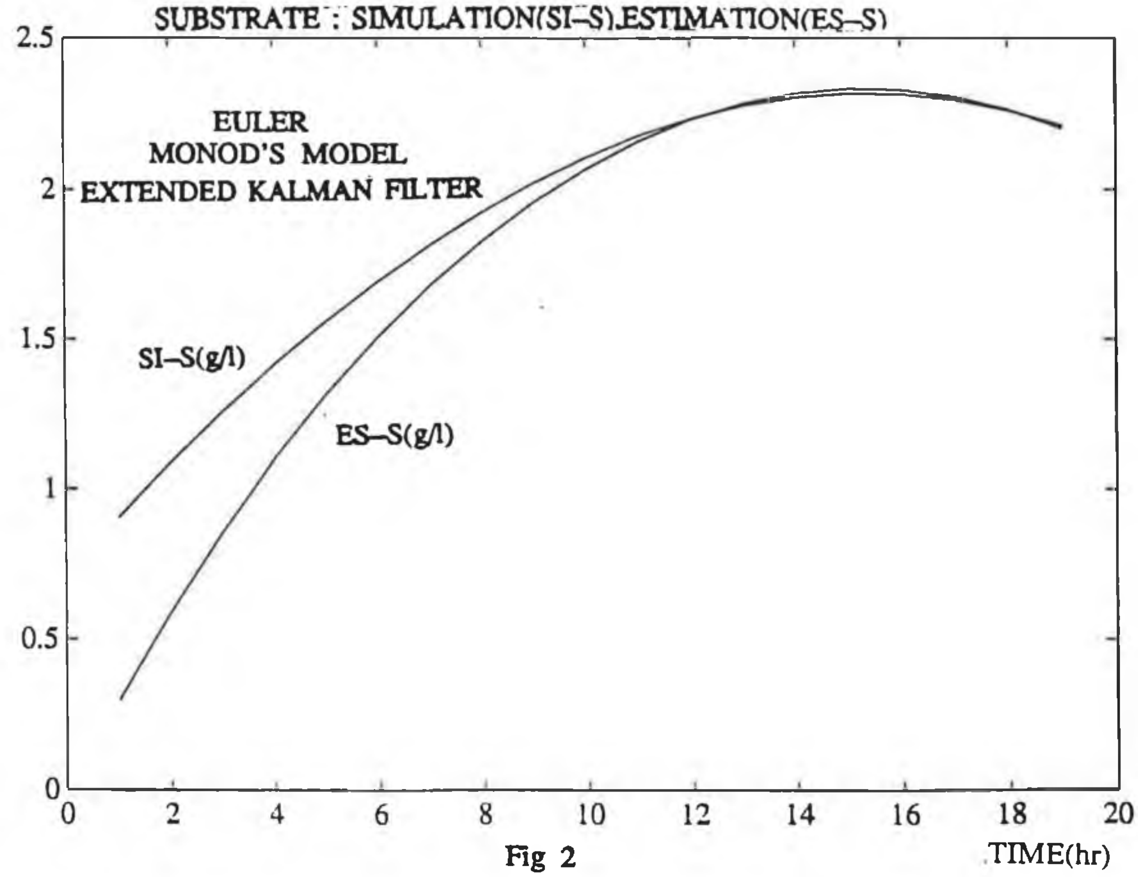
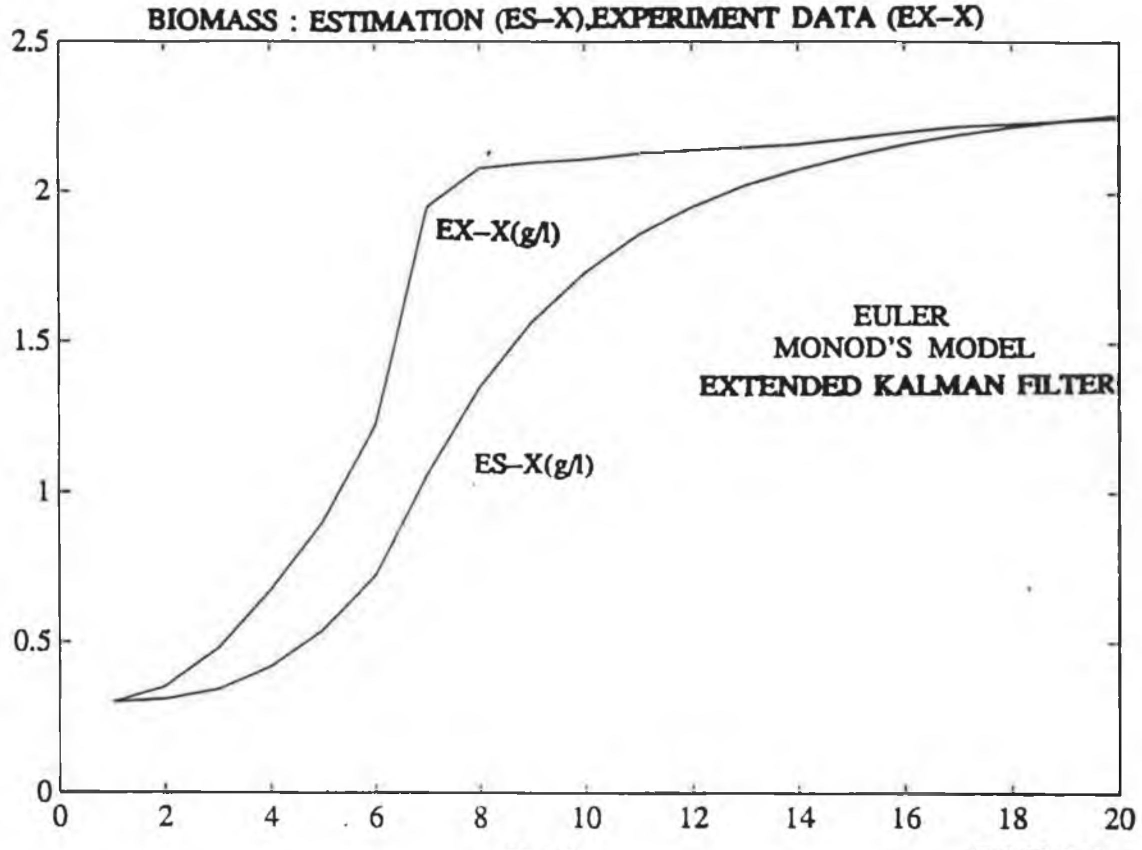
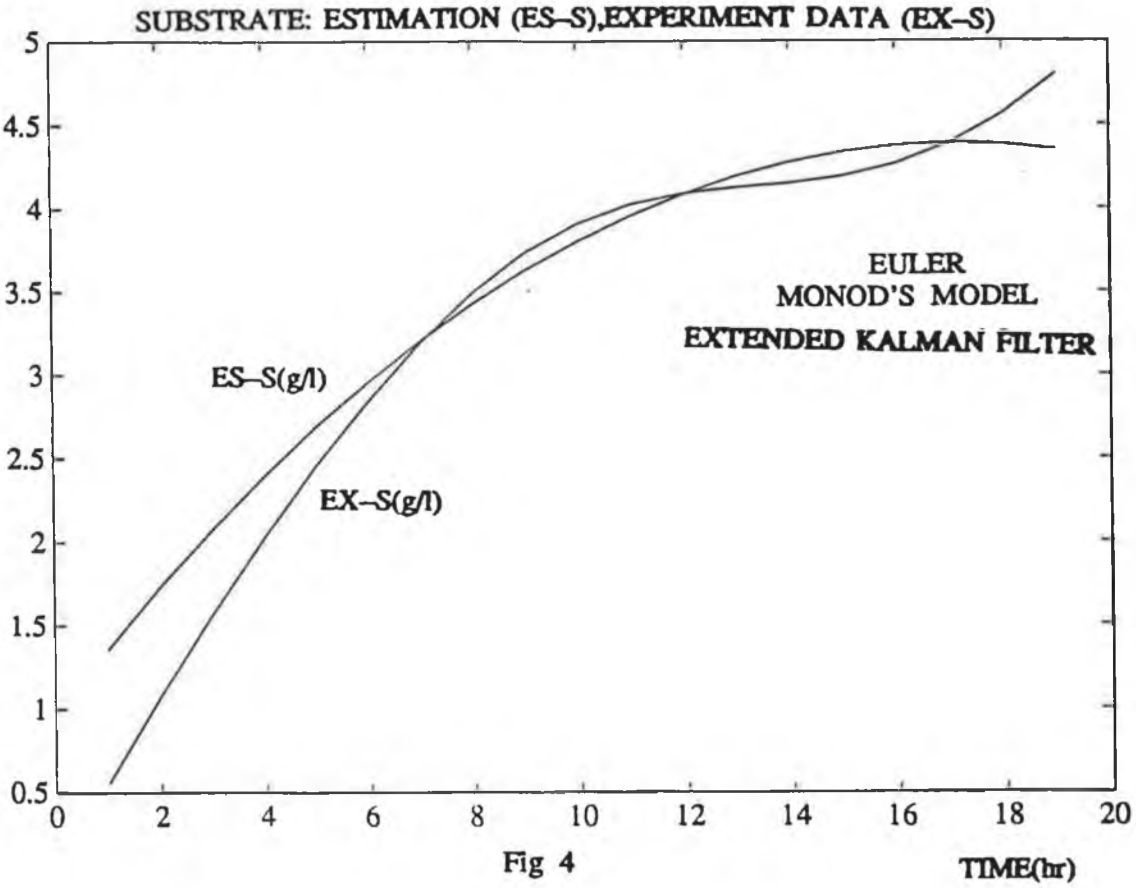

SUBSTRATE : SIMULATION(SI-S),ESTIMATION(ES-S)
EULER
MONOD'S MODEL
EXTENDED KALMAN FILTER
SI-S(g/l)
ES-S(g/l)
2.5
2
1.5
1
0.5
0
0
2
4
6
8
10
12
14
16
18
20
TIME(hr)

Fig 2



BIOMASS : ESTIMATION (ES-X),EXPERIMENT DATA (EX-X)
2.5
2
1.5
1
0.5
0
0
2
4
6
8
10
12
14
16
18
20
EX-X(g/l)
ES-X(g/l)
EULER
MONOD'S MODEL
EXTENDED KALMAN FILTER
TIME (hr)

Fig 3



SUBSTRATE: ESTIMATION (ES-S),EXPERIMENT DATA (EX-S)
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
2
4
6
8
10
12
14
16
18
20
ES-S(g/l)
EX-S(g/l)
EULER
MONOD'S MODEL
EXTENDED KALMAN FILTER
TIME(hr)

Fig 4