MEASUREMENT AND CONTROL IN BIOPROCESSING

Edited by
K.G. Carr-Brion

ELSEVIER APPLIED SCIENCE

MEASUREMENT AND CONTROL IN BIOPROCESSING

Edited by

K. G. CARR-BRION

Cranfield Institute of Technology, Cranfield, Bedfordshire, MK43 OAL, UK

ELSEVIER APPLIED SCIENCE
LONDON and NEW YORK

ELSEVIER SCIENCE PUBLISHERS LTD
Crown House, Linton Road, Barking, Essex IG11 8JU, England

Sole Distributor in the USA and Canada
ELSEVIER SCIENCE PUBLISHING CO., INC
655 Avenue of the Americas, New York, NY 10010 USA

WITH 26 TABLES AND 88 ILLUSTRATIONS

© 1991 ELSEVIER SCIENCE PUBLISHERS LTD

British Library Cataloguing in Publication Data

Measurement and control in bioprocessing
1. Biotechnology
I. Carr-Brion, K.
660.6

ISBN 1-85166-620-6

Library of Congress Cataloging-in-Publication Data

Measurement and control in bioprocessing/edited by K. Carr-Brion.
p. cm.
Includes bibliographical references and index.
ISBN 1-85166-620-6
1. Biotechnology—Measurement. 2. Biotechnology—Quality control.
I. Carr-Brion, K.
TP248.25.M43M4 1991
660'.6'0287—dc20 91-13737
CIP

No responsibility is assumed by the Publisher for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions or ideas contained in the material herein.

Special regulations for readers in the USA
This publication has been registered with the Copyright Clearance Center Inc. (CCC), Salem, Massachusetts. Information can be obtained from the CCC about conditions under which photocopies of parts of this publication may be made in the USA. All other copyright questions, including photocopying outside the USA, should be referred to the publisher.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without the prior written permission of the publisher.

Typeset and printed in Northern Ireland by The Universities Press (Belfast) Ltd.

MEASUREMENT AND CONTROL IN BIOPROCESSING

ELSEVIER APPLIED BIOTECHNOLOGY SERIES

Other Titles in this Series:

M. Y. Chisti:	Airlift Bioreactors
W. M. Fogarty & C. T. Kelly (eds):	Microbial Enzymes and Biotechnology, 2nd Edition
T. J. R. Harris (ed):	Protein Production by Biotechnology
R. Isaacson (ed):	Methane from Community Wastes
A. M. Martin (ed):	Bioconversion of Waste Materials to Industrial Products
A. M. Martin (ed):	Biological Degradation of Wastes
E. J. Vandamme (ed):	Biotechnology of Vitamins, Pigments and Growth Factors

此为试读,需要完整PDF请访问: www.ertongbook.com

PREFACE

This book contains eight chapters, each authored by one well versed in the chapter topic, chosen by the editor to give a broad view of measurement and control in bioprocessing. The authors have been given the freedom to produce work that reflects their own interests and emphases—since this is considered to give the most valuable material for the reader. However, some overlap and duplication is inevitable, hopefully fully covered by the index. The volume starts with two introductory chapters on process control and measurement, then follows with six on specific areas of interest.

The intended readers include biochemists, biologists, chemists and others without specialist knowledge in these areas, along with practitioners in these fields requiring to update their knowledge in some of these topics. Bioprocessing is used in its broadest sense to include all operations using biological routes to products, thus including effluent treatment and water purification. It is hoped that this may be of value in providing that much hoped for virtue, cross-fertilisation, and stimulate the introduction of measurement and control into industries that have often been backward in accepting what was commonplace in areas such as chemical manufacture and petroleum refining.

My thanks are due to all the co-authors both for their texts and the many helpful suggestions made in discussion with them.

K. G. CARR-BRION

LIST OF CONTRIBUTORS

R. BRIGGS
Measurement and Instrumentation Centre, City University, Northampton Square, London, EC1V 0HB, UK

K. G. CARR-BRION
Cranfield Institute of Technology, Cranfield, Bedfordshire, MK43 0AL, UK

S. W. COOK
SmithKline Beecham Pharmaceuticals, Shewalton Road, Irvine, Ayrshire, KA11 5AP, UK

H. HÅKANSON
Department of Biotechnology, Chemical Centre, University of Lund, PO Box 124, S-221 00 Lund, Sweden

M. KELLY
Millipore SA, Waters Chromatography Division, Molsheim, France. Present address: *53 Rue du Donjon, 67530 St Nabor, France*

A. LIVINGSTONE
SmithKline Beecham Pharmaceuticals, Shewalton Road, Irvine, Ayrshire, KA11 5AP, UK

B. MATTIASSON
Department of Biotechnology, Chemical Center, University of Lund, PO Box 124, S-221 00 Lund, Sweden

D. M. RAWSON
ARCC, Luton College of Higher Education, Putteridge Bury, Hitchin Road, Luton, Bedfordshire, LU2 8LE, UK

P. N. C. Royce
Advanced Centre for Biochemical Engineering, University College London, Torrington Place, London, WC1E 7JE, UK

N. F. Thornhill
Advanced Centre for Biochemical Engineering, University College London, Torrington Place, London, WC1E 7JE, UK

J. A. Wilson
Department of Chemical Engineering, University of Nottingham, University Park, Nottingham, NG7 2RD, UK

CONTENTS

Chapter 1

INTRODUCTION TO CONTROL IN BIOPROCESSING

J. A. WILSON

Department of Chemical Engineering, University of Nottingham, University Park, Nottingham, NG7 2RD, UK

NOTATION

a	Process dead-time or transport lag (min)
D	Derivative action
$e(t)$	Error between measured value and set point
F	Fluid flow-rate
I	Integral action time (min)
K	Loop gain factor ($K = K_c \times K_p$)
K_c	Proportional controller gain factor
$K_c$crit	Critical controller gain factor (promotes continuous oscillation)
K_f	Feedforward controller gain factor
K_p	Process gain factor
L	Liquid level
P	Proportional action
PBW	Proportional bandwidth of controller
PI	Proportional plus integral action
PID	Proportional plus integral plus derivative action
R	Derivative action time (min)
t	Time (min)
$T(t)$	Temperature measured value
T_p	Period of oscillation at controller gain $K_c$crit (min)
$T_{sp}(t)$	Set point for temperature control
τ	Time constant for first-order transfer lag (min)

1 INTRODUCTION

At an outward level, the problem of controlling biochemical engineering processes is similar to that of controlling any other process system. For example, a biochemical process could be viewed as being analogous to one involving chemical reaction. The same external factors such as temperature, the proportions and addition rates of the reactants (i.e. substrate or nutrients), and perhaps even the pH level, are potentially important. In the case of reaction systems at least, quite standard methods have been developed for handling control of such variables and particular scenarios can be identified and matched against associated, well proven control strategies. To be sure even in the case of reaction processes there are significant control problems that remain to be solved but in the main the techniques already available can and do provide acceptable performance much of the time. More advanced methods are in general only called on where unusually difficult features arise. Thus, application of these same proven techniques to biochemical process control might be expected to meet with reasonable success. The purpose of this introductory chapter is to review some of the basic techniques available to the process control engineer and to identify their main limitations and extensions. The treatment is deliberately non-mathematical, aiming to give a reader with no previous background in control aspects a feel for the practical factors of prime importance in process systems, coupled with sufficient understanding to allow an appreciation of the function of any particular process control system encountered. A selection of references is given for those interested to pursue specific areas in greater depth but at a broader level Luyben (1990) provides coverage with emphasis on process aspects.

2 FUNDAMENTALS

In general the objective of any production process is to achieve the desired volume of production at a quality that falls within the specified constraints. The process control system implements a strategy for concerted operation of the production plant equipment so as to meet this process objective in a safe and cost-effective manner. A fully automatic process control system would aim to implement such a control strategy without ever calling for the intervention of a human operator but such a system has yet to be achieved in practice and a blend of manual and automatic control action is more usual. The most effective implementation for a complete process control system will generally involve a balance between the manual and automatic elements so as to take advantage of the strengths of both. Instrumentation technology and practice have now been developed to a level where automatic systems can be relied upon to provide

accurate repetitive actions,
consistency of response to a given disturbance,
precise recording of measurements,
continuous operation,
operation in a hostile environment,
rapid action compared with humans,

whilst in contrast a human operator (with varying levels of individual skill) will generally be more effective in providing higher level functions such as

decision making on partial and disparate information,
adaption to unforeseen or unusual situations,
diagnosis of fault conditions.

此为试读,需要完整PDF请访问: www.ertongbook.com

However, more recent developments in artificial intelligence are making even some of these activities look like potential candidates for automation.

Process variables are defined as conditions or states of the process material or its environment that are subject to change with time. They can be classified as either (i) independent or forcing variables, or (ii) dependent or response variables. Their relationship is represented schematically in Fig. 1. In order to exercise control over such a process two indispensable features must always be available; (i) measurements of appropriate response variables, (ii) mechanisms for manipulation of appropriate forcing variables.

Whilst today's measurement technology is highly developed, the rigours of the process control environment mean that in practice measurement options that provide the required safety and reliability are few in number. Because measurement is the fundamental basis for any control system the restricted choice of suitable measuring elements represents a prime practical constraint on the structure and performance of process control systems. As for manipulation of process variables for control purposes, this is most frequently achieved by means of adjustable valves that throttle the flow in pipelines supplying service or process fluids to the process equipment. In order to exercise control over the process, an adjustment to the setting of such valves must result in appropriate modulation of the fluid flow-rate concerned and through that in turn the variable of interest.

Because of their importance, both of these areas are covered in more detail later but meanwhile, assuming that both are available to us, we can proceed to consider more precisely how they can be used to implement a control strategy. Process systems can be classified broadly as being conducted in either a batchwise or continuous fashion, bioprocesses often arising as batch or fed-batch systems. In operating a batch plant (or indeed during start-up or shut-down phases in operating a continuous one) action must be taken according to a strict sequence of events or steps. A decision to move to the next step in the sequence is made on pre-set conditions. This may involve, for example, waiting for a set length of time to pass or waiting for a particular process variable to attain a defined value before moving on. This type of control activity is called 'sequence control'. In contrast to this, whilst operating continuous plant, or within certain sequence steps in batch processing, the immediate objective is to maintain operation as close as possible to a desired steady state (e.g. the design condition for continuous plant). The control valves must be continually manipulated to achieve this steady state in the face of variations either in feed- or supply-stream qualities, in the process equipment itself or even in its environment. This type of control activity is

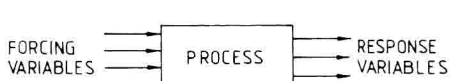

Fig. 1. Relationship between forcing and response variables in a process.

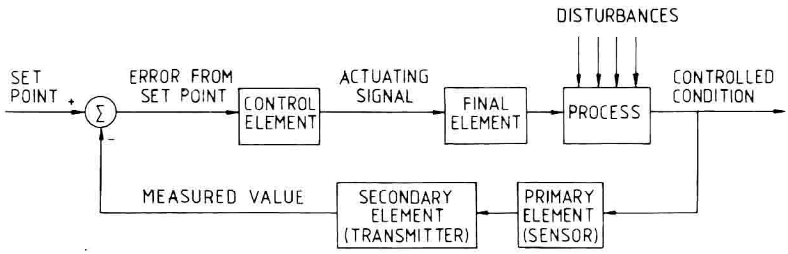

Fig. 2. Information flow in a feedback control system.

called 'regulatory control' because the controlled conditions are regulated to the required steady state. Because of its importance this forms the main area of attention in this chapter. Regulatory control is applied uniformly over an extended period of operation (perhaps minutes or hours in the case of a batch plant extending to months in the case of a continuous one). At each instant the available measurements are used to calculate any necessary movement in the manipulated variables (i.e. the control valve positions) according to a set strategy which in turn can be classed as either 'feedback' or 'feedforward' in nature. The information flows within these two types of system are illustrated in Figs 2 and 3. A separate issue, outside the scope of the control aspects covered here, is that of automatic safety systems and the strategies for coping with alarm conditions on a manual or automatic basis. Generally a quite separate set of instrumentation will be specified for important alarm or automatic shut-down systems perhaps calling in addition for high levels of instrumentation integrity.

2.1 Structure for Feedback Control

The feedback control system in Fig. 2 is directed at maintaining a steady state in the 'controlled condition' of the process. This is the process variable we wish

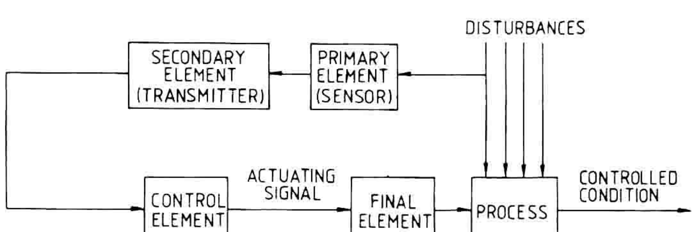

Fig. 3. Information flow in a feedforward control system.

to regulate at a specific desired steady state value called the 'set point'. The current value of the controlled condition is sensed automatically on a continuous basis by a measuring or 'primary element'. Such a sensing device interfaces directly with the process fluid and is mounted locally on the plant item. This primary measurement must usually be relayed to a point remote from the plant item (perhaps to a centralised control room) and a 'secondary element' or signal 'transmitter' is required to derive a higher level signal from that of the primary element in a form suitable as a basis for transmission over some distance. At the receiving end, the transmitted value of the measurement is first compared with the set point. If the two coincide (i.e. if there is no error between measured value and set point) then no change to the control valve position will be necessary. However, if an error is present then corrective action is needed. The precise form of this corrective action is decided on by the 'control element' which acts according to a fixed strategy, usually a simple calculation based on the size of the set-point error. The result of this calculation is generated in the form of an actuating signal that is transmitted back locally to the plant item where it is used to manipulate the 'final element'. This, as has already been stated, usually amounts to altering the flow restriction in an automatic control valve. As a result of changing the fluid flow-rate through the valve the controlled condition will be affected, hopefully for the better. In the system shown, information is travelling continuously around the 'control loop' in an endless cycle. Provided a suitable control strategy has been implemented in the control element the objective of regulating the controlled condition as its set point will in the course of time be achieved. Because the measurements are fed back around the loop to the control element, this type of arrangement is called a 'feedback' control system. Such systems can always be recognised in requiring both a set point and a measurement of the controlled condition.

2.2 Structure for Feedforward Control

Fig. 3 shows the relationships in a 'feedforward' control system. In this case no direct measurement of the controlled condition is taken. The intention is to react immediately against disturbances detected in specific forcing variables by making appropriate changes to other inputs. 'Seeing' major disturbances as they enter provides for rapid correction without awaiting the development of any deviation in the controlled condition. Thus, no reference to a set point should be necessary. The variables most likely to be the source of a major disturbance problem are measured (primary and secondary elements as before) and their measured values are then acted on by a feedforward controller calculation, the controller output signal being linked as before to an automatic control valve on the plant. The term 'feedforward' implies simply that the control element acts on one input in response to another, the control action being chosen in such a way that once having passed forwards through the process the respective effects of the two changes will cancel exactly, leaving no residual disturbance to affect the controlled condition.

The feedforward strategy is, in essence, predictive and embodies a model of the process which must be exact in order to produce perfect control. Furthermore, feedforward control alone can only work if all possible disturbances to the process are measured on entry to the plant. Otherwise, deviations in the controlled condition could arise that would not be countered by the feedforward system. In practice models never fit perfectly and measurement of only a small number of disturbance variables is practical. As a result feedforward action is never perfect and is never used alone. It is always combined with a feedback control strategy which has the long-term capability of returning the controlled condition to its set point following any disturbance (manual feedback may sometimes be adequate), thus compensating for the shortcomings of pure feedforward action. Whilst inevitably inaccurate in the long term, the feedforward element contributes, in the short term, approximate but very rapid corrective action to specific major disturbances, thus leaving less for the feedback controller to cope with.

2.3 Dynamic Characteristics of Processes

Before looking at the performance of different control strategies we first need to consider the types of dynamic behaviour that may arise in the uncontrolled process itself, since this has some implications for choice of an appropriate control form. The dynamic behaviour of a system can be directly assessed from a plot of response variable value against time following a deliberate disturbance in a forcing variable (e.g. a step change). In many processes, a set stimulus will always provoke the same response. Such systems are said to possess 'stationary' dynamics. In addition a step increase away from an initial steady state will sometimes provoke an equal but opposite perturbation in the response variable as does a step decrease. Such systems are described as being 'linear'.

The response of systems that are both stationary and linear can be characterised as a combination of simple dynamic elements that are easily understood and quantified. The response behaviour of the most common examples is shown in Fig. 4 following a forcing variable step change. If nothing happens for a while and then suddenly there is a response with the same form as the input (i.e. a step response) the process exhibits a pure time delay, referred to as either 'dead-time' or 'transport lag' (arising from the fact that the effects of the disturbance have had to be carried, usually spatially, from one point in the process to another). A good example arises in the response of a temperature probe at one end of a long run of pipework to a change in feed-stream temperature at the other. With minor heat losses and plug flow along the pipe the dead-time will equal the fluid transit time.

As distinct from this a 'transfer lag' will arise in a process wherever a flow (of energy or material) is being driven through a resistance from one reservoir

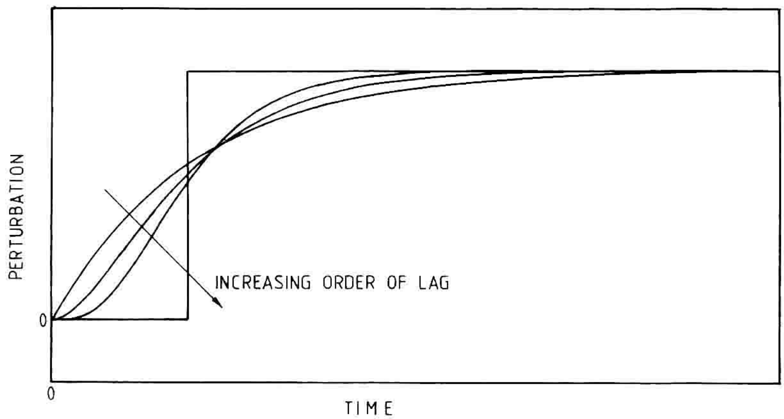

Fig. 4. Step response of transport lag and transfer lags of increasing order.

to another. In this case the rate of transfer relates to the potential difference between the two reservoirs that provides the driving force for flow. As the transfer proceeds, material or energy will accumulate or deplete leading to a gradual reduction of driving force and hence of rate of movement. Following a step change the result is a gradually slowing response of exponential form. A good example is the response of a temperature probe when suddenly immersed in hot process fluid. A rapid initial rate of response will gradually slow exponentially towards the steady state where the probe and process fluid reach the same temperature. Such behaviour is represented by a first-order differential equation (or a single exponential term) and is referred to as a 'first-order' transfer lag, a single 'time constant' parameter, τ, fixing its time scale of response. When several such elements are linked together in series then their combined effects produce a characteristic S-shaped response, the higher the order or the number of transfer lags present, the more pronounced the S-shape. On this basis, a transport lag can be viewed as equivalent to an infinite series of infinitesimal transfer lags (i.e. dead-time behaves like an infinite order transfer lag). Viewed on a microscopic scale, flow along our pipeline involves a transfer of fluid between minute segments of pipe, each linked to its nearest neighbours by the main flow.

Processes, which exhibit inertial or drag effects in addition to resistance to transfer, can also produce oscillatory behaviour as shown in Fig. 5. A good example of this is a liquid-filled manometer measuring a pressure differential. The reading of a water-filled instrument will oscillate following a step change in pressure, whereas one filled with a viscous oil will produce a sluggish S-shaped response with no overshoot (as in Fig. 4). These are characteristic 'second-order' transfer lag responses defined by a time constant and a damping parameter (e.g. the decay ratio shown in Fig. 5).

Aside from the shape of response, the size of response provoked by a given forcing disturbance is also important as a measure of the extent to which

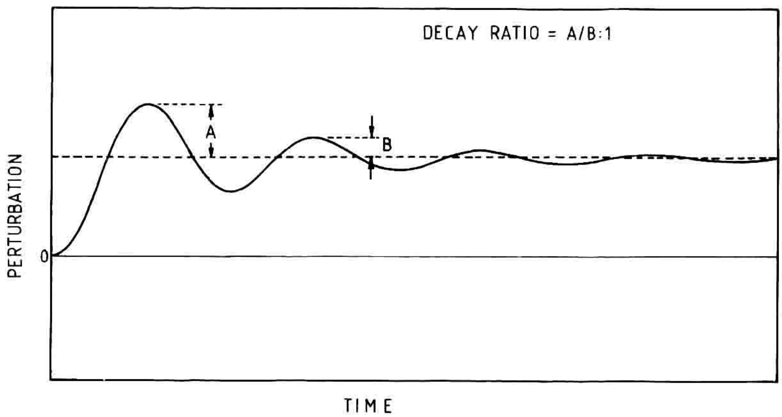

Fig. 5. An oscillatory step response (exhibiting a decay ratio of 4:1 between adjacent peaks).

perturbations are amplified or attenuated by the process. In a linear system this feature of the response is represented by the 'steady-state gain factor' for the process which can be calculated simply as the ratio of the steady perturbation in response variable to that in the forcing variable following a step change. For the response shown in Fig. 6 the process 'gain' K_p would be A/B.

In practice, processes react with a combination of these simplified characteristics. For example Fig. 6 shows the step response of a process involving a pure dead-time and at least a second-order (non-oscillatory) transfer lag. If this process is linear and stationary then the parameters defining its response are

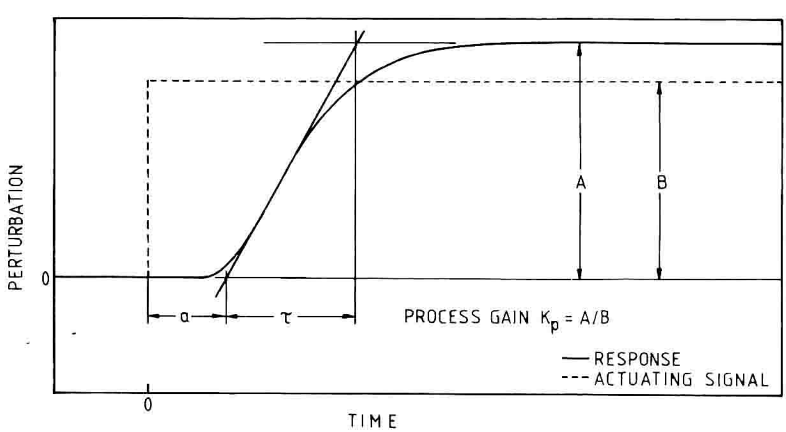

Fig. 6. Determination of process parameters for Ziegler–Nichols controller tuning from the process reaction curve (generated by a step change in control valve actuating signal).

此为试读，需要完整PDF请访问：www.ertongbook.com