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BIOPROCESS COMPUTATIONS IN BIOTECHNOLOGY

volume 1

Tarun K. Ghose

BIOPROCESS COMPUTATIONS IN BIOTECHNOLOGY

Volume 1

Editor

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Foreword

Success in bioprocessing involves the combination of basic principles and methods from chemical engineering and the biological sciences. To design and operate bioprocesses efficiently, this integration must surpass conceptual and qualitative union. Rigorous quantitative description of the properties of the materials to be used and the characteristics of the processes employed are necessary for bioprocess engineering. One of the best ways for learning the intellectual and analytical strategies appropriate to the engineering description and analysis of biological systems is confrontation with well-designed problems which afford the opportunity to practise quantitative approaches to the complex materials and interactions found in bioprocesses. Further, such exercises provide a useful forum in which engineers can learn and become aware of certain biological principles and properties since, by their training, engineers are accustomed to working with systems in quantitative terms and to seeking central common properties. Problems which have been carefully prepared and selected for achieving these pedagogical purposes are few. This volume will greatly enrich the opportunities for biochemical engineers to learn about bioprocessing through excellent problems.

This collection of problems is organized into eleven chapters which cover fundamental principles as well as engineering analysis and design and bioproject engineering. The volume also includes glossary of nearly 450 different terms in biotechnology and a list of terms and symbols which many students and practitioners in the field will find extremely useful. This book is intended to be the first in a series of volumes providing instructive and informative problems to assist students in learning bioprocess engineering.

James E. Bailey
California Institute of Technology,
USA

Preface

Imparting knowledge in inter-disciplinary engineering sciences through good teaching is considered by many teachers more important than research done with empirical tools. Since learning bioprocesses principles cannot be equated with acquiring knowledge in philosophy a good teacher must be equipped with problem-solving abilities to make students appreciate what the special inputs in bioprocess engineering are that differ from teaching biology and chemical engineering separately.

At the time of my spending a year of Visiting Professorship in the Department of Chemical Engineering, University of Delaware during 1985–86 the need for a book dealing with problems in various areas of bioprocess engineering was keenly felt. Extension of the Coulson and Richardson series on Chemical Engineering by J. R. Backhurst and J. H. Harkar in separate volumes dealing with numerical problems has been very useful in the classroom teaching of chemical engineering courses. Another book entitled *Examples and Problems to the Course of Unit Operations of Chemical Engineering* by K. F. Peblov, P. G. Ramankov and A. N. Noskov, MIR Publishers, Moscow is also considered as a very useful text for first-degree students. A similar book to support the teaching of biochemical engineering was very much missed. It is believed that the application of the acquired knowledge of bioprocesses is likely to remain weak if the learners are not properly and quantitatively exposed to many and multiple questions that occur again and again at the delivery end of biotechnology. The compilation of contributions contained in this volume is therefore an attempt to reduce the gap.

The volume is designed essentially for students in a first-degree programme. Much of the material provided will drill them on fundamental principles. Graduate students and practising bioprocess engineers may find insight and satisfaction in many of these problems and the manner in which these are handled. The volume is organized in ten chapters each pertaining to the principles and application of concepts, mainly in the areas of conversion reactions and downstream processing, elaborated with the help of 125 solved problems. There are also 40 discrete problems, pertaining to most of these areas, without solutions. Nearly 250 terms and symbols used in the book are based on the recommendations of IUPAC Commission on Biotechnology as well as those prescribed by the American Institute of Chemical Engineers. These are consolidated and presented in a separate chapter provided with both SI and customary units.

In the course of preparation of this volume I have benefited from the experience and advice of many colleagues during the last three years. Assistance received from reviewers, friends, colleagues and some graduate students. In particular the late Professor H. Taguchi of Osaka University, Pradeep Roy Choudhury, T. R. Sreekrishan. Radhika Satsangee and Soma Chakraborty, and typing help from R. N. Shukla and Sunita Verma of the Centre is thankfully acknowledged. Critical reviews of many of the solved problems were made by Professors John Howell, University of Bath, UK, Prasad Dhurjati, University of Delaware, USA, Paul Peringer, Swiss Federal Institute of Technology, Lausanne, Switzerland, and T. Imanaka, University of Osaka, Japan. Special mention should be made to the dedicated work of deciphering of several hand written materials and proof reading done by Sreekrishan. My sincere thanks are due to all of them.

This volume, dedicated to my wife, Atreyee, who has been a constant source of inspiration and indulgence to what I have been doing in biochemical engineering all my life, will grow and prosper only with the help, advice and comments from the students, teachers and engineers associated with the design of bioprocesses. The second volume will provide integrated process problems handling both old and new biotechnology.

Tarun K. Ghose

1

Thermodynamics of biosystems

Contributors: Tarun Ghose, V. S. Bisaria, Subhash Chand

PROBLEM 1.1

The equilibrium constant (K_{eq}) for the reaction:

Fumarate + $H_2O \rightleftharpoons$ L-malate

has been reported as a function of temperature by Scott and Powell (1948) (Table 1). From these data, calculate the values of ΔH°, ΔG° and ΔS° for the above enzyme-catalysed reaction at 30°C, where ΔH° is the standard heat of reaction, ΔG° is the standard free energy change and ΔS° is the standard entropy change.

Table 1.1 — K_{eq} as a function of temperature for the hydrolysis of fumarate

Temp (°C)	15.0	20.2	25.0	30.0	34.6	40.0	44.4	49.6
K_{eq}	4.78	4.46	3.98	3.55	3.27	3.09	2.75	2.43

Gas constant $R = 8.314$ J mol^{-1} K^{-1}.

Reference

Scott, E. M. & Powell, R. (1948) *J. Amer. Chem. Soc.* **70**, 1104.

Solution

Second law of thermodynamics gives the relationship:

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ \tag{1.1.1}$$

Also, standard free energy change (ΔG°) is related to the equilibrium constant as

$$\Delta G^\circ = -RT \ln K_{eq} \tag{1.1.2}$$

Therefore,

$$\frac{d(\ln K_{eq})}{dT} = -\frac{1}{R}\frac{d(\Delta G^\circ/T)}{dT} \tag{1.1.3}$$

from equation (1.1.1),

$$\frac{\Delta G^\circ}{T} = \frac{\Delta H^\circ}{T} - \Delta S^\circ$$

substituting in equation (1.1.3), we get,

$$\frac{d\,(\ln K_{eq})}{dT} = \frac{\Delta H^\circ}{RT^2} \qquad (1.1.4)$$

assuming that ΔH° is constant over the range of temperature used, or,

$$\ln K_{eq} = -\frac{\Delta H^\circ}{RT} + I \qquad (1.1.5)$$

where, I is an integration constant. ΔH° can, therefore, be determined from a plot of ($\ln K_{eq}$) versus ($1/T$) the slope of which is equal to ($-\Delta H^\circ/R$). Such a plot for the data in the given problem is shown in Fig. 1.1.

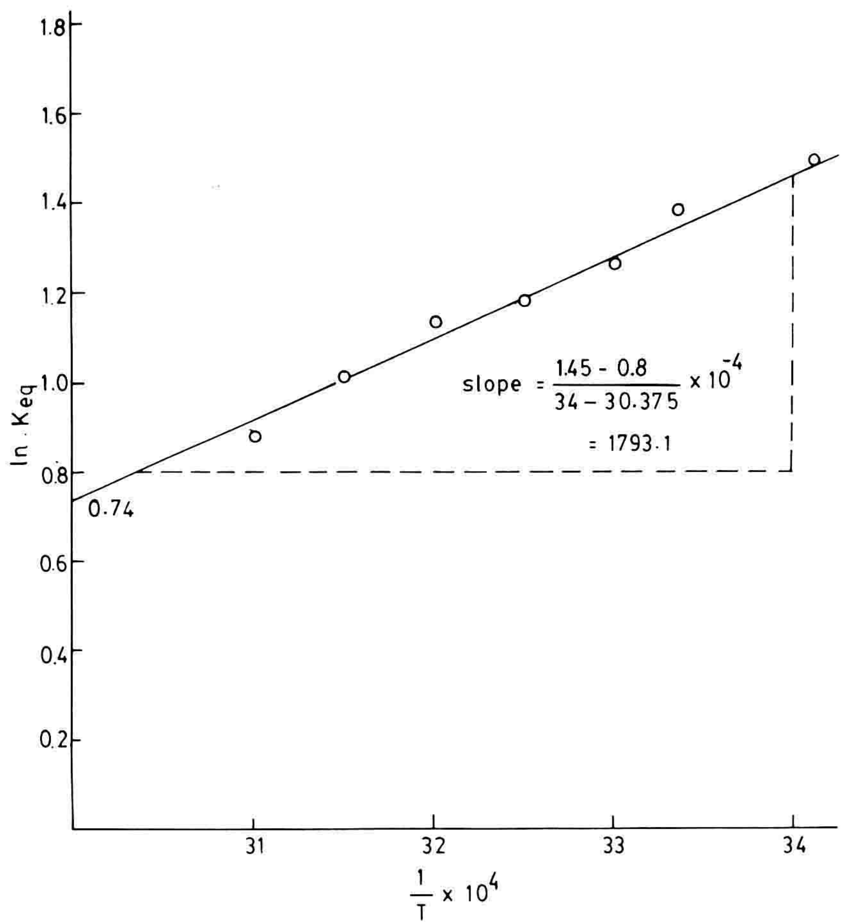

Fig. 1.1.

The slope of the straight line obtained $= 1793.1 = -\Delta H°/R$. Hence,

$$\Delta H° = -1793.1 \times 8.314$$
$$= \underline{-14907.833 \text{ J mol}^{-1}}$$

To calculate $\Delta G°$ (at 30°C), substituting values of K_{eq} and T(K) in the equation (1.1.2), we get,

$$\Delta G° = -(8.314) \times (303) \times (1.267)$$
$$= \underline{-3191.753 \text{ J mol}^{-1}}$$

The standard entropy change ($\Delta S°$), from the equation (1.1.1) will be,

$$(303)\ \Delta S° = -14907.833 + 3191.753$$

$$\therefore \Delta S° = -\frac{11716.08}{303}$$
$$= \underline{-38.667 \text{ J K}^{-1} \text{ mol}^{-1}}$$

Thus, the effect of temperature on the equilibrium constant for an enzyme-catalysed reaction can give information on the thermodynamic parameters for the reaction (free energy change, enthalpy and entropy change).

PROBLEM 1.2

Association of ATP–ADP cycle is essential in almost all biochemical reactions catalysed by enzyme *in vitro* and *in vivo*. It is therefore necessary to understand this participation in terms of both rate and equilibrium. In a typical situation in which intracellular ATP is hydrolysed by ATPase, the hydrolysis rate, Q_r is related to intracellular concentration of ATP as

$$\frac{Q_r}{Q_m} = \frac{C_{ATP}}{K_m + C_{ATP}}$$

where Q_m = maximum hydrolysis rate, C_{ATP} = intracellular concentration of ATP, and K_m = Michaelis–Menten constant.

Cultivation of a bacterium gave the data shown in Table 1.2 at different concentrations of pantothenic acid in two different media.

Table 1.2

Culture medium	Pantothenic acid (mg ml^{-1})	$Y_{x/s}$ (g cell mol^{-1} glucose)	μ (h^{-1})	ATP pool (mg ATP g^{-1} cell)
Complex	—	7	0.37	1.54
Synthetic	5×10^{-3}	6.4	0.39	1.55
Synthetic	1×10^{-7}	2.8	0.20	3.15
Mineral	5×10^{-3}	4.5	0.28	3.55
Mineral	1×10^{-4}	2.9	0.16	4.52