École doctorale Science pour l'Ingénieur

Modélisation et Commande Passive des Bioréacteurs Continus: Application aux Réactions Enzymatiques et Microbiennes

THÈSE

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***C**entre de **R**echerche en **I**nformatique, **S**ignal et **A**utomatique de **L**ille* - **UMR 9189**

École doctorale Science pour l'Ingénieur

Passivity Based Modeling and Control of Continuous Biological Reactors: Application to Enzymatic and Microbial Reactions

A THESIS

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Résumé

Cette thèse présente une modélisation et commande passive des bioréacteurs continus isothermes. Une attention spéciale est portée à la recherche de fonctions de Lyapunov ayant un sens physique ou reliées à la structure du modèle. On montre que l'énergie libre de Gibbs est une fonction Hamiltonienne appropriée pour les réacteurs enzymatiques. Un modèle basé sur une représentation énergétique est proposé qui peut être considéré comme un système quasi-Port-Hamiltonien. Le modèle se décline en une représentation dans l'espace des concentrations (SPH) et une autre dans l'espace réactionnel (RPH). La commande basée sur la passivité par interconnexion et assignation d'amortissement est obtenue en donnant une forme appropriée à l'énergie désirée, que ce soient pour des modèles SPH ou RPH. Les résultats sont validés par simulation sur un modèle d'hydrolyse enzymatique de la cellulose.

On propose ensuite un modèle passif d'un ensemble de réactions microbiennes dans un réacteur ouvert, avec un nouveau type de fonctions de stockage. Grâce à un changement de variables adéquat, le nombre d'équations du système est réduit et les propriétés de passivité sont directement démontrées. A partir de ce modèle, il est possible de déterminer une commande passive de manière systématique. Les fonctions de Lyapunov candidates peuvent présenter une certaine analogie avec l'énergie libre de Gibbs introduite dans la représentation quasi Port-Hamiltonienne des réactions enzymatiques. Par la suite, une loi de commande adaptative basée sur le modèle présenté est proposée. La validation a été effectuée à partir de simulations d'une réaction élémentaire, puis d'une digestion anaérobie. Les résultats montrent la pertinence des nouvelles lois de commandes passive et adaptative.

Abstract

This thesis proposes a passivity based formulation and control of a well-mixed CSTR model for a set of chemical and biochemical reactions taking place at constant pressure and temperature. Special care has been taken to not look loosely on the physical coherence of a system by using meaningful energy functions as Lyapunov functions and using the structure of the model while performing the control.

It is made clear that Gibbs free energy is an apt Hamiltonian function for such cases. The Bond Graph models related to Port-Hamiltonian formulation for both types of reactions are given in order to show its ability of pictorial representation and intuitive solution. An energy based model of such systems is proposed which can be said as quasi Port-Hamiltonian system (PHS) based on physical grounds. The model is taking care of the concentration space and reaction space of a chemical reaction. Stoichiometric and Reaction interconnection and damping assignment passivity based controllers (IDA-PBC) are derived from the proposed Stoichiometric and Reaction energy based models respectively by physically giving the energy function a desired form. Real application of enzymatic hydrolysis of cellulose in continuous reactor is simulated.

Then, a passivity based model of a general set of microbial reactions in open reactors with new Lyapunov functions is derived. A useful change of coordinates is done which simplifies the number of equations to be taken care of and shows directly the passivity of the system. The passivity based control is obtained from systematic controller design techniques. The Lyapunov functions can be said to be in close proximity with the Gibbs free energy function used in Port-Hamiltonian model of enzymatic reactions and are far from the traditional non-physical quadratic functions.

A general method of generating an adaptive passivity based control law with the new model which is more physical and maintains the structure of the model has been generated. Application and validation of the model through simulations is done on single and multiple reaction examples. To explore the pseudo-energetic point of view towards modeling and control of microbial reactions in open reactors with parametric uncertainty, different candidate energy functions are being tested and an adaptive controller is designed to cope with uncertainties on the specific growth rate.

In memory of my Brother

To my Parents

Acknowledgements

First and foremost I want to thank my advisor Jean-Yves Dieulot. It has been an honor to be his Ph.D. student. He has taught me, both consciously and unconsciously, how good research is done. I appreciate all his contributions of time, ideas, and funding to make my Ph.D. experience productive and stimulating. The joy and enthusiasm he has for his research was contagious and motivational for me, even during tough times in the Ph.D. pursuit. I am also thankful for the excellent example he has provided as a successful researcher and professor. The members of the Mocis group have contributed immensely to my personal and professional time at Lille. The group has been a source of friendships as well as good advice and collaboration. I specially thank Gerardo Ayala, Pushpendra Kumar and Ibrahim Abdallah for inspirational discussions with me regarding my work. Other past and present group members that I have had the pleasure to work with or alongside of are Ph.D students Nizar Chatti, Thor Morales Bieze and Mohamed Benmerikhi and the numerous summer and rotation students who have come through the lab.

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Nomenclature

Symbol	Description	Unit
A	chemical Affinity	Joules/Mole
S_t	Stoichiometric Matrix	–
n	Quantity of Chemicals	No. of Moles (Grams)
r	Rate of Reaction	–
x	Concentration of Chemicals	No. of Moles (Grams)/Liter
m	Chemical Potential	Joules/Mole
m_0	Maximum Chemical Potential	Joules/Mole
G	Gibbs Free Energy	Joules
H	Hamiltonian	–
$V, \bar{V}$	Storage Function	–
$\hat{S}$	Entropy	Joules/kelvin
T	Temperature	Kelvin
D	Dilution Rate	$Time^{-1}$
A	chemical Affinity	Joules/Mole
$\hat{V}$	Volume	Liter
Subscript f	Forward	–
Subscript in	Inlet	–
Subscript out	Outlet	–

Subscript r	Reverse	–
Superscript $*$	Steady State/Equilibrium	–
Superscript d	Desired	–
μ	Specific Growth Rate	–
μ_m	Maximum Specific Growth Rate	–
S	Substrate	–
X	Biomass	–
E	Enzyme	–
ES	Enzyme-Substrate Complex	–
P	Product	–
$y, \bar{y}$	Output	–
Y	Yield Point	–
$\bar{P}$	Pressure	Bar
$\hat{H}$	Enthalpy	Joules
U	InternalEenergy	Joules
Q	Heat	Joules
q	Flow Rate	Liters/Second
M	Mass	Grams

1
General Introduction

1.1 Thesis Framework

This Doctoral dissertation was developed in the research team "Méthodes et Outils pour la Conception Intégrée de Systèmes (MOCIS)" within the group "Conception Intégrée de Systèmes et Supervision (CI2S)" of the laboratory "Centre de Recherche en Informatique, Signal et Automatique de Lille (CRISTAL-UMR CNRS 9189)[1]". The laboratory CRISTAL is a joint research unit of *Polytech Lille*[2]*-Université Lille 1*[3], *Ecole Centrale de Lille*[4] and the *Centre National de la Recherche Scientifique* (CNRS)[5]. This research was directed by Mr. Jean-Yves Dieulot, Associate Professor (Habilité à Diriger des Recherches) at Polytech Lille-Université Lille 1. A constant guidance by Professor Iordan Nikov has been provided to validate the research work on various useful experiments.
The research team MOCIS is dedicated to energy based modeling, structural analysis, control and diagnosis of multi-domain (electrical, mechanical, chemical...) dynamic systems using tools such as Bond Graph (graphical tool) and Hamiltonian (analytical tool). The present work is focused on the energy based modeling and control of chemical reactions taking place in continuous chemical reactors with a view to apply on enzymatic and microbial reactions in bioreactors.

[1] http://www.cristal.univ-lille.fr/
[2] http://www.polytech-lille.fr
[3] http://www.univ-lille1.fr
[4] http://http://www.ec-lille.fr
[5] http://http://www.cnrs.fr

1.2 Thesis Contribution

The contribution of biotechnology to generate industrially useful products has been widely known and appreciated. Industries ranging from food processing, water treatment to biofuels are engaged in biochemical research. They study about the structures, functions, biological environment inside the bioreactors (chambers in which bioreactions take place for mass industrial production) and interactions among biological molecules like flow and dissipation of chemical energy in chemical transformation of one molecule into another. Energy flow has been a "transversal" currency (lingua franca) to know the physics of any system. Controlling the flow of energy can keep the biochemical transformations under control. But, studying the energy flow in chemistry is not so simple because of irreversible thermodynamics and it is also very complicated in biology because the kinetics of a large number of bio reactions is still unknown and their behaviors are based on purely empirical relations. This lack of physical insight of these reactions has forced researchers to rely on non-physical control methods. The research in this work was dedicated towards filling this gap by trying to give physical meaning to the kinetics of biochemical reactions using the passivity theory. Passivity brings some energy-like framework to the different exchanges takes place in the systems e.g. mass, temperature, concentration etc. and can be transposed to a wide family of systems. Also, passivity based modeling tools give systemic insight about the stability and design of controllers of the systems. It helps to design physical, self stabilising control systems which are easy to operate and understand as well.

In this work, biochemical processes were studied as the flow and dissipation of energy and then mathematical models were made to depict the energy dissipation known as energy based models. Port-Hamiltonian and Bond Graph are the energy based modeling tools used in this thesis where Bond Graph can be seen as a complimentary graphical representation of Port-Hamiltonian modeling. A system is said to be passive if it satisfies the geometrical structure of Port-Hamiltonian model. Then, passivity based controllers are obtained from the models.

The contribution of this thesis can be summarised in the following points:

- Applies the notions of chemical thermodynamics to known enzyme kinetics (Michaelis-Menten kinetics) and the empirical microbial kinetics (Monod kinetics) to explain the flow and dissipation of energy which also induces passivity.
- Models Enzymatic and microbial reactions in open bioreactors in an energetic/passive environment using two energy based modeling tools i.e. Bond Graph (BG) and Port-Hamiltonian (PH) representation.
- Designs passivity based control laws out of these energy/passivity based models.
- Designs passivity based adaptive control laws encountering the uncertainty in the unknown constant parameters.
- Applies these laws to some bioreaction experiments.

1.3 Thesis Organization

This thesis is divided into 5 chapters. Second chapter defines the general notions and terminology of chemical and biochemical systems. It explains the basics of chemistry and biochemistry which are needed to be known for better understanding of the research work. Third chapter starts with the introduction of passivity and energy based models followed by the discussion on previous research in the energetic modeling of open chemical and biochemical systems along with the new and improved BG and PH models of chemical and enzymatic reactions. The last part of the chapter will show the PH models of enzyme reactions in concentration and reaction space. Fourth chapter deals with more obvious passivity based control of enzyme reactions derived through PH formulations also known as Interconnection and Damping Assignment Passivity Based Control (IDA-PBC). Fifth chapter shows passivity based modeling and control technique being applied on microbial reaction with Monod Kinetics. The later part of the chapter will show Adaptive PBC of single reaction with Monod kinetics. It focuses mainly on the derivation of the generalized passivity based model with coordinate transformation of the bio reactions in open bioreactors with single streams. The general

Passivity Based Control (PBC) and then Adaptive PBC is designed on the basis of a general Passivity Based Model (PBM). The adaptive controller derived ensures structure preservation. All these models and controllers are applied on bio reaction experiments and simulation results are shown at the end of 4th and 5th chapter

Thesis is concluded with the conclusions and mentioning possible future work.

1.4 Publications

i) Makkar, M. & Dieulot, J.-Y. Bond graph model and Port-Hamiltonian formulation of an enzymatic reaction in a CSTR. 2nd International Conference on Systems and Computer Science (ICSCS), 2013, 68-73.

ii) Makkar, M. & Dieulot, J.-Y. Passivity based control of a chemical process in isothermal reactors: Application to enzymatic hydrolysis of cellulose. IEEE Conference on Control Applications (CCA), 2014, 753-758 .

iii) Dieulot, J.-Y. & Makkar, M. A pseudo-Port-Hamiltonian representation and control of a continuous bioreactor. 1st Conference on Modelling, Identification and Control of Nonlinear Systems.

iv) Makkar, M. & Dieulot, J.-Y. Energy Based Modeling and Control of Continuous Chemical Reactors Under Isothermal Conditions. Submitted.

v) Makkar, M. & Dieulot, J.-Y. Passivity Based Model and Adaptive Control with Structure Preservation in Continuous Bioreactors. Submitted.

2

General Notions on Chemical and Biochemical Systems

2.1 Introduction

This chapter explains about chemical and biochemical systems along with transformation and basic terminology related to these systems. It describes briefly about the composition, structure, properties and change of chemical and biochemical compounds. Then, it will discuss about how different chemical changes are optimised using different chambers known as reactors and what are the laws governing this change through mathematical equations. Later in the chapter, there is a review on what are the problems faced during the process, different control strategies to avoid such problems and how the energy flows in the process i.e. chemical thermodynamics.

2.2 Chemical Kinetics

Everything in our world is built out of atoms, from the smallest piece of paper to the biggest, most complicated electronic device. Each atom is unique in terms of mass, size and properties in comparison to other atoms. Electrostatic force of attraction between atoms, known as chemical bond, allows the formation of chemical substances that contain two or more atoms. Pure chemical substance consisting of a single type of atom not chemically bonded to each other are known as elements e.g. carbon (C). When atoms form bonds together, they make molecules e.g. molecular hydrogen (H_2). A chemical compound is a molecule that involves the chemical bond between at least two different atoms e.g. carbon dioxide (CO_2). Atoms or compounds have tendency to transform into

new compounds by chemically combining with atoms or compounds of different composition. This process of transformation of one set of chemical compounds called reactants to another set of chemical compounds called products by breaking and making new chemical bonds between atoms is known as chemical reaction e.g.

$$\underbrace{C + O_2}_{\mathrm{Reactants}} \rightarrow \underbrace{CO_2}_{\mathrm{Product}} .$$

Several chemical reactions end up in combined mixture of reactants and products. Such reactions are called reversible reactions i.e. they run in both directions and are represented as:

$$aA + bB \rightleftharpoons cC + dD,$$

The speed at which a chemical reaction takes place is known as the rate of a reaction (r). A reversible reaction has two rates of reaction, forward r_f and backward r_r.

Chemical kinetics deals with the mechanism of rates of chemical reactions. It also includes the investigation of the conditions that can influence the speed of reaction e.g. temperature, concentration as well as developing mathematical models to describe the nature of the reaction. Several theories act as basis for calculating the reaction rates at the molecular level. Some basic theories are as follows:

i) Law of conservation of mass It states that for a closed system the total mass of the system must remain constant i.e. the system mass cannot change quantity if it is not added or removed.

ii) Law of conservation of energy It states that the total energy of an isolated system is constant but it can change from one form to another.

iii) Law of mass action When two reactants, A and B, react together at a given temperature, the chemical affinity (A) between them is directly proportional to the product of concentration of $[A]$ and $[B]$, each raised to a particular power:

$$A = \alpha[A]^a[B]^b. \tag{2.1}$$

α, a and b are the empirical constants.

iv) Chemical equilibrium It is the state of reversible reactions in which the forward reaction proceeds at the same rate as the reverse reaction and both reactants and products have no further tendancy to change with time i.e. :

$$r_f = r_r. \tag{2.2}$$

v) Stoichiometry It is founded on the law of conservation of mass. It states that the relations among quantities of reactants and products form a ratio of positive integers. These positive integers are known as stoichiometric coefficients and are represented in front of the chemical compounds, for example:

$$CH_4 + 2O_2 \rightarrow CO_2 + 2H_2O$$

Here, 1 molecule of CH_4 combines with 2 molecules of O_2 to form 1 molecule of CO_2 and 2 molecules of H_2O. 1, 2, 1 and 2 are the stoichiometric coefficients.

Besides these basic laws some other methodologies are there which are purposely executed and play an important role in the chemical kinetics.

1. **Chemical synthesis** It is a deliberate execution of chemical reactions using physical and chemical manipulations to obtain the desired products. It usually increases the number of steps to obtain the desired product and/or change the intermediate product.

2. **Catalysis** It is the process of increasing the rate of a reaction through participation of an additional compound called catalyst. With catalyst, the reaction mechanism changes and reactions occur faster without the catalyst actually being consumed.

For example, consider a set of interdependent reversible chemical reaction under constant pressure and temperature (no thermal effect):

$$aA + bB \underset{k_{r1}}{\overset{k_{f1}}{\rightleftharpoons}} cC + dD,\ cC + dD \underset{k_{r2}}{\overset{k_{f2}}{\rightleftharpoons}} eE \tag{2.3}$$

where a, b, c, d, e are stoichiometric coefficients and A, B, C, D, E are the chemical species involved, k_{f1}, k_{f2} are forward rate constants and k_{r1}, k_{r2} are reverse rate constants. The rate of these reactions can be written as:

$$r_1 = k_{f1}[A]^a[B]^b - k_{r1}[C]^c[D]^d \tag{2.4}$$

$$r_2 = k_{f2}[C]^c[D]^d - k_{r2}[E]^e \tag{2.5}$$

At chemical equilibrium: $r_1 = r_2 = 0$ i.e.

$$k_{f1}[A]^a[B]^b = k_{r1}[C]^c[D]^d. \tag{2.6}$$

$$k_{f2}[C]^c[D]^d = k_{r2}[E]^e \tag{2.7}$$

Based on the rate of reaction, the rate of change of concentration of each component can be written as:

$$\begin{bmatrix} \dot{n}_A \\ \dot{n}_B \\ \dot{n}_C \\ \dot{n}_D \\ \dot{n}_E \end{bmatrix} = \underbrace{\begin{bmatrix} -a & 0 \\ -b & 0 \\ c & -c \\ d & -d \\ 0 & e \end{bmatrix}}_{S_t} \times \begin{bmatrix} r_1 \\ r_2 \end{bmatrix}. \tag{2.8}$$

S_t is the stoichiometric matrix.

General Rate Law

The general rate law according to law of mass action for a set of j reactions can be written as (5):

$$r_j = k_f \times \prod (x_i)_r{}^{c_i} - k_r \times \prod (x_i)_p{}^{c_i}, \tag{2.9}$$

$(x_i)_r$ = concentration of reactants, $(x_i)_p$ = concentration of product. $c_i's$ are the corresponding stoichiometric coefficients. For a set of j chemical reactions, the rate of change of concentration x will be:

$$[\dot{x}_i] = [S_t]_{i \times j} [r_j]. \tag{2.10}$$

$[S_t]_{i \times j}$ is the stoichiometric matrix.

2.3 Biochemical kinetics

The chemical compounds that are usually found in organisms, living things and/or are part of the makeup of living cells are called biomolecules e.g. carbohydrates, proteins. Biomolecular interactions govern the processes of life. The biomolecular interaction which leads to transformation of one biomolecule into a different biomolecule is called a biochemical reaction. Biochemical kinetics is the study of mechanism and rates of biochemical reactions.
Many biochemical reactions are mediated by enzymes which are biological catalysts that can alter the rate and specificity of these reactions. Enzymes are rather flexible structures which bind the biochemical reactant (substrate), and then carry out the reaction. This small port in an enzyme where a susbstrate molecule binds is known as active site. The study of many biomolecular binding events make them amenable to know how organisms function at the molecular level. All biomolecular interaction involves a binding event, either by enzyme-catalysed processes or by cell communications that are mediated by signalling and receptor proteins.
A typical biochemical reaction can be written as:

$$E + S \rightleftharpoons ES, \qquad ES \rightleftharpoons E + P.$$

Here, E is the enzyme which acts upon substrate S the substrate bonds with the enzyme active site, and an enzyme-substrate complex ES is formed. The substrate is transformed into one or more products P, which are then released from the active site. The active site is now free to accept another substrate molecule. The whole process is reversible with formation of product being the forward reaction. The rate at which an enzyme works is influenced by several factors e.g. the concentration of substrate molecules, temperature, presence of inhibitors, pH etc.

2.3.1 Michaelis-Menten Kinetics

Named after German biochemist Leonor Michaelis and Canadian physician Maud Menten is one of the known models of single substrate enzyme kinetics. It assumes

that the substrate is in instantaneous chemical equilibrium with the enzyme-substrate complex of reaction. Applying the law of mass action, the rate (r) of product formation is given by:

$$r = \frac{dP}{dt} = \frac{\mu_m S}{K_s + S} \tag{2.11}$$

Here, μ_m is the maximum rate and K_s is the Michaelis constant. For the basic enzyme reaction with MM kinetics, the change in concentrations with time for enzyme E, substrate S, complex ES and product P generally related to each other in the form shown in Figure 2.1 below: Similarly, another single substrate

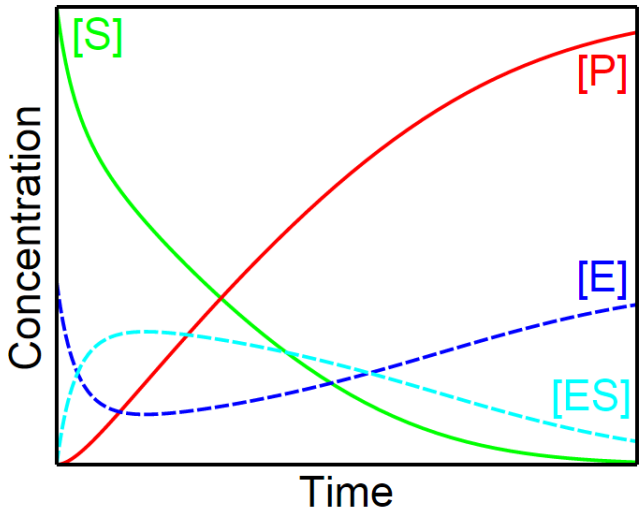


Figure 2.1: Concentration vs Time For Basic Enzyme Reaction With MM Kinetics in Batch Reactor[1]

kinetics known as Briggs and Haldane kinetics based on the assumption that the concentration of the enzyme substrate complex does not change during product formation. Biochemical reactions involving a single substrate are often assumed to follow Michaelis-Menten or Briggs-Haldane kinetics.

2.3.2 Microbial Kinetics

A living organism that cannot be seen with the naked eye is entitled to be called a microorganism e.g. bacteria. The capacity to grow, and ultimately to multi-

[1] `http://wiki.mn.wtb.tue.nl/biological_systems/man`

ply, is one of the most fundamental characteristics of microorganisms. Microbial kinetics is the branch of biochemical kinetics which deals with the growth of microorganisms. The process of microbial growth requires the coordinated synthesis of a range of complex macro molecules such as enzymes and the energy for this process derived from the growth supportive surroundings. Despite, growth being such a basic aspect of microbial behavior, a very little is known about the principles behind it. Hence, the mathematical models defining the rate of these processes are totally empirical and based on quantitative data fitting.
The simplest microbial reaction with no products of reaction can be represented as:

$$S \rightarrow X.$$

S is the substrate is directly converting into biomass X.

Monod Kinetics

Named after Jaques Monod, who proposed an empirical mathematical model for the growth of micro organisms. Basically, Monod kinetics can be understood as a first order law at high substrate concentration, the rate law changes when the substrate concentration is low. The Monod equation has the same form as Michaelis-Menten kinetics and is applicable to many growth processes. According to Monod kinetics, the rate of biomass growth (r_X) and substrate utilisation (r_S) can be given as:

$$r_X = \mu X,\ r_S = -\frac{\mu X}{Y} \tag{2.12}$$

with

$$\mu = \mu_m \frac{S}{K_s + S}. \tag{2.13}$$

μ is the specific growth rate of the microorganisms, μ_m is the maximum specific growth rate, S is the concentration of substrate, K_s is the half-velocity constant, X is the biomass concentration and Y is the yield coefficient.
Conceptually, the Monod equation is fit to the observed substrate and specific growth rate data. It follows the curve shown in Figure 2.2. The rate of change

[2] http://www.cs.montana.edu/webworks/projects/stevesbook/contents/chapters/chapter002/section002/black/page001.html

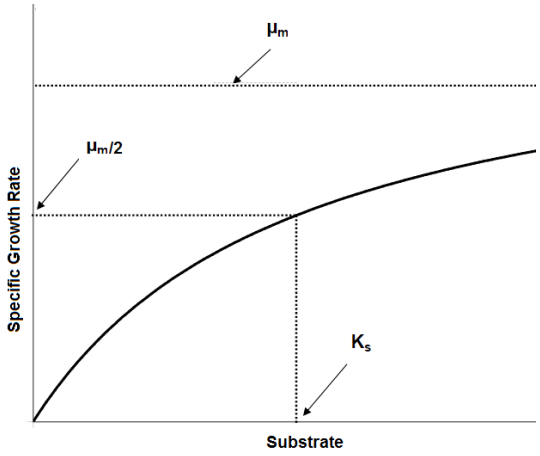


Figure 2.2: Specific Growth Rate vs Substrate Concentration [2]

of concentration in vector form can be represented as:

$$\underbrace{\begin{bmatrix} \dot{S} \\ \dot{X} \end{bmatrix}}_{\dot{\xi}} = \underbrace{\begin{bmatrix} -1 & 0 \\ 0 & 1 \end{bmatrix}}_{S_t} \underbrace{\begin{bmatrix} \frac{\mu X}{Y} \\ \mu X \end{bmatrix}}_{r}, \tag{2.14}$$

where S_t can be seen as stoichiometric matrix.

2.4 Reactors

Chemicals and biochemicals are being heavily produced and used in industries for more effective and efficient production of goods for e.g. synthetic polymers, superior alloys, pesticides etc. There are industries which are dedicated to the mass production of these chemicals which obviously arise the need that the reaction should proceed with the highest efficiency towards the desired output product, producing the highest yield of product while requiring the least amount of money to purchase and operate. This led to the design of vessels to contain reactions in the desired manner called reactors. These reactors are normally cylindrical in shape and ranging from litres to cubic metres. A chemical reactor takes care of the thermodynamics and kinetics of the chemical reactions being carried out and a bioreactor ensures the biologically active environment to grow biochemicals or cells. The important functions of reactors are:

- Mixing of substrates, contacting catalyst

- Mass transfer
- Heat transfer
- Control of environment
- Containment (protection from/of environment)

There are different types of reactors with different purposes:

1. **Batch reactor** In this, chemical process takes place in Batches. Batch operation is most flexible. Reactors can be used for multiple purposes. This is particularly important for the fine chemical industry where multiple products are produced in one plant.

2. **Fed-Batch reactor** In this, operation is semi-batch and semi-continuous and is most commonly used to conduct reactions in biochemical industries. A substrate feed stream is being slowly added to the reactor. This type of operation is also used to increase selectivity or to improve safety. Various feeding policies for reactor control would be possible.

3. **Plug flow Reactor (PFR)** There is continuous flow of reactants and products of reaction, in and out of the tubular reactor. Fluid flows through a PFR in a series of thin coherent plugs, traveling in the axial direction of the reactor. The fluid is considered to be mixed in the radial direction but not in the axial direction. Each plug of differential volume is considered as a separate entity.

4. **Continuously stirred tank reactor** Continuous reactor is used to produce very large quantities of product in various industries every year and is among the important reactors for biochemical reactions.

In a CSTR, the substrate is continuously fed to a reactor and immediately mixed with the entire reactor content. There are no gradients of concentration with respect to location. Therefore, the effluent concentration is equal to the reactor concentration. The rate of reaction of CSTR is constant throughout. In general the continuous operation has the following characteristics:

1. Continuous production
2. Steady state after start-up period (usually)
3. No variation of concentrations with time
4. In Steady State
5. Ease of balancing to determine kinetics
6. No down-time for cleaning, filling, etc.

The Figure 2.3 below is depicting the basic process which takes place in a CSTR.

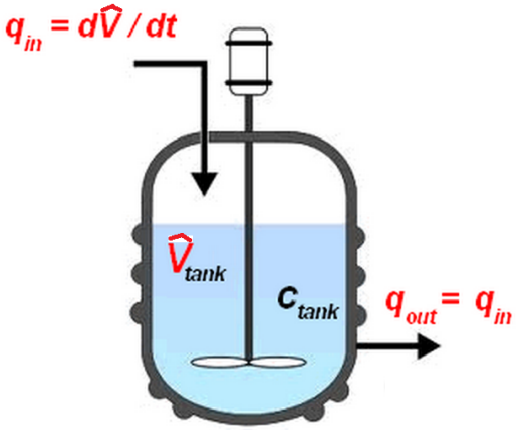


Figure 2.3: Continuously Stirred Tank Reactor[3]

Here, c_{tank} represent the total concentration of chemicals present inside the tank, q is the flow rate, q_{in} is the inflow, q_{out} is the outflow of chemicals, $\hat{V}$ is the volume, $\hat{V}_{tank}$ is the total volume of the reactor tank which is kept constant in almost all CSTRs i.e. $q_{in} = q_{out}$. All calculations performed with CSTRs assume perfect mixing. In a perfectly mixed reactor, the output composition is identical to composition of the material inside the reactor i.e. $q_{out} = q$.
The continuous process will add the additional terms of mass inflow rate and mass outflow rate in the rate of change of chemical concentrations i.e.

[3] `http://www.hydrochemistry.eu/exmpls/cstr.html`

Change of mass inside reactor = Generation/utilisation of mass + Mass in - Mass out.

Monod Kinetics in a CSTR

Consider a basic constant volume continuous bioreactor with Monod kinetics in which substrate S is directly converting into cells X i.e. $S \to X$. The dynamical model for such a system can be expressed by the equations:

$$\dot{X} = \mu X - DX, \tag{2.15}$$

$$\dot{S} = -\frac{\mu x}{y} + D\left(S_{in} - S\right), \tag{2.16}$$

where $D = q/V$ is the dilution rate, y is the cell/substrate yield coefficient and μ is the specific growth rate. For Monod kinetics:

$$\mu = \frac{\mu_m S}{K_s + S}, \tag{2.17}$$

here, μ_m is the maximum specific growth rate and K_s is the half velocity constant. As X and S are concentrations therefore $X, S \geq 0$. Also, $K_s, \mu_m, Y > 0$ always. The state space of concentration will be: $\begin{bmatrix} S & X \end{bmatrix}^T$ and the model can be represented as:

$$\begin{bmatrix} \dot{S} \\ \dot{X} \end{bmatrix} = \begin{bmatrix} -1 & 0 \\ 0 & 1 \end{bmatrix} \begin{bmatrix} \frac{\mu X}{Y} \\ \mu X \end{bmatrix} + \begin{bmatrix} DS_{in} - DS \\ -DX \end{bmatrix}. \tag{2.18}$$

2.5 Microbial Reactions in Continuous Culture

Continuous cultivation of microorganisms features addition of nutrients in a chemostat at a constant rate and simultaneous withdrawl at the same rate. This mode of cultivation is particularly useful as it results in significant improvement in productivity e.g. fermentation. Also, it is rather easy to implement process control for these systems. It is a nice tool to study the physiology of microbial reaction as the process achieves a steady state condition at a particular dilution rate. However, there are some disadvantages which limits the use of continuous process e.g. contamination in cultivation, change in characteristics of organisms. The two major issues associated with such processes are as follows:

i) Uncertainty The overall response of any continuous cultivation can be simulated by the mathematical model but quite often there is a variation in the model results and the actual results. It has been observed that Monod model is unable to perfectly simulate the transients in continuous cultivations because of lack of complete knowledge of the kinetic parameters e.g. maximum specific growth rate as the method of finding these parameters is empirical and is measured for fixed range of substrate feed rate. However, a considerable shift in dilution rate changes the metabolism and there is no proportionate increase in the cell growth as proposed by Monod's model. It is therefore necessary to incorporate this "uncertainty" in the model which cannot only quantitatively describe the metabolic reactions of the cells but adaptively graduate changes in transient conditions of continuous cultivation.

ii) Washout Condition In any cultivation it is always necessary to devise strategies which might result in high productivity. Productivity in continuous cultivation is dependent on not only the concentration of biomass /product but also on its dilution rate. For example, biomass Productivity $(Py) = D \times X$, so it is therefore necessary to increase both D and X to increase the productivity. However, if one increases the dilution rate, eventually a point comes where the cell concentration reduces to zero. This state of zero cell concentration is called washout.

Washout Derivation of Monod model in CSTR

Consider the Monod model shown in section 2.4, the steady state equations can be written as (82):

$$\mu X = DX, \tag{2.19}$$

$$\frac{\mu X}{Y} = D\,(S_{in} - S) \tag{2.20}$$

and

$$\mu = \frac{\mu_m S}{K_s + S}, \tag{2.21}$$

(2.19) shows that at steady state, $\mu = D$ i.e.

$$D = \frac{\mu_m S}{K_s + S} \tag{2.22}$$

or

$$S = \frac{DK_s}{\mu_m - D}. \tag{2.23}$$

Substituting (2.22) in (2.20) will give:

$$X = (S_{in} - S)Y. \tag{2.24}$$

Substituting (2.23) in (2.24) will give:

$$X = Y\left(S_{in} - \frac{DK_s}{\mu_m - D}\right). \tag{2.25}$$

The cell concentration will be zero in the washout condition, hence putting $X = 0$ in (2.25) will give the washout dilution rate (D_W), the washout dilution rate D_w is:

$$D_W = \frac{S_{in}\mu_m}{K_s + S_{in}}. \tag{2.26}$$

As dilution rate increases, the productivity ($Py = DX$) increases initially, reaches to a maximum level then start decreasing and ultimately becomes zero. Figure 2.4 depicts this behaviour in a graph:

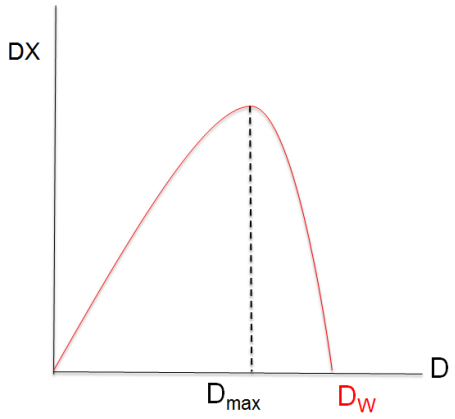


Figure 2.4: Steady State Productivity vs. Dilution Rate[4]

[4] https://controls.engin.umich.edu/wiki/index.php/Bacterial_Chemostat_Model

Here, D_{max} is the dilution rate at maximum productivity. This value of D_{max} can be calculated by putting first derivative of productivity w.r.t. dilution rate (D) equals to zero i.e. $\frac{d(DX)}{dD} = 0$. For the Monod model:

$$D_{\max} = \mu_{\mathrm{m}} \left(1 - \sqrt{\frac{K_S}{K_S + S_{in}}}\right) \tag{2.27}$$

This thesis is dedicated to the passivity based control of continuous bioreactors but in order to perform passivity based control on biochemical processes, it is really important to know the chemical reaction thermodynamics and how energy flows in a biochemical reaction. The next section will discuss the same.

2.6 Chemical Reaction and Thermodynamics

Chemical thermodynamics is the study of relation of heat, energy and work with chemical reactions. The main objective of chemical thermodynamics is to establish a criterion for the determination of the feasibility of a given reaction which is possible by predicting the energy exchanges that occur in the reaction. As discussed earlier that a chemical reaction takes place because chemical compounds in a solution has a tendancy to react with each other. This measure of the reactivity of a component in a solution is called **chemical potential**. Chemical potential is a form of potential energy that can be absorbed or released during a chemical reaction. In an ideal solution, the chemical potential m_i of each species i with concentration x_i is given by the expression:

$$m_i = m_i^o \left(T, \bar{P}\right) + RT \ln x_i. \tag{2.28}$$

In this expression, R is the molar ideal gas constant, m_i^o is the standard state chemical potential at temperature T and pressure $\bar{P}$. When the system is in chemical equilibrium, the chemical potential of each substance appearing in the system will be same.

All chemical reactions obey the law of conservation of mass and for that matter the law of conservation of numbers of atoms of each kind therefore stoichiometry of the reaction should be considered the part of the expression. This leads to a new notation which imply that the amounts of the components cannot be changed independently and is known as **chemical affinity**. Chemical affinity is

referred as the force or tendency that causes chemical reactions. The mathematical expression for chemical affinity A_i of component i is:

$$A_i = -m_i c_i, \tag{2.29}$$

c_i is the stoichiometric coefficient. The total affininty A of the reaction system will be:

$$A = -\sum_i m_i c_i \tag{2.30}$$

Total affinity gives the measure of the potential of the whole reaction. However, the measure of the extent in which the reaction proceeds is given by **extent of reaction**. It represents the degree of advancement of a process. Mathematically, the extent of reaction $d\xi$ is defined as:

$$d\xi = \frac{dx_i}{c_i}. \tag{2.31}$$

2.6.1 Energy of a Chemical Reaction

Due to the absorption of energy when chemical bonds are broken, and the release of energy when chemical bonds are formed, chemical reactions almost always involve a change in energy between products and reactants. By the law of conservation of energy, the total energy of a system must remain unchanged and that allows a chemical reaction to absorb or release energy in different forms. The energy change in a chemical reaction is due to the difference in the amounts of stored chemical energy between the products and the reactants. This stored chemical energy, or heat content, of the system is known as its **enthalpy** $\hat{H}$. Enthalpy itself is a thermodynamic potential, so in order to measure the enthalpy of a system, one must refer to a defined reference point hence it is measured as change in enthalpy $\Delta\hat{H}$. Mathematically:

$$\Delta H = \Delta U + \Delta\left(\bar{P}\hat{V}\right), \tag{2.32}$$

U is the internal energy of the system, $\bar{P}$ is the pressure of the system and $\hat{V}$ is the volume of the system.

Internal energy U is defined as the energy associated with the random, disordered motion of molecules i.e. the Kinetic Energy of the atoms due to their random

motion relative to the Center of Mass plus the binding energy (Potential Energy) that holds the atoms together. The change in internal energy of a system is given by:

$$dU = Td\hat{S} - \bar{P}d\hat{V} + \sum_i m_i dx_i. \tag{2.33}$$

Here $\hat{S}$ is the entropy of the system, T is the absolute temperature, m_i is the chemical potential of component i and x_i is the concentration of component i.

Entropy $\hat{S}$ is the quantitative measure of the amount of thermal energy not available to do work. The amount of entropy is often thought of as the amount of disorder or degree of randomness in a system. The change in entropy of a system for a thermodynamically reversible process as:

$$d\hat{S} = \frac{dQ}{T}, \tag{2.34}$$

where dQ is net transfer of heat into the system. In (2.33), $Td\hat{S}$ represent the heat dQ transfer into the system, $-\bar{P}d\hat{V}$ represent the mechanical work dW done on the system in which pressure $\bar{P}$ is the intensive generalised force and $d\hat{V}$ is the extensive generalised displacement and $\sum_i m_i dx_i$ represent the internal energy change with respect to variations in composition also known as **Gibbs Free Energy**. The Gibbs free energy is the amount of non-expansion work that can be extracted from a closed system i.e. work obtainable from a thermodynamic system at constant temperature and pressure.

2.6.2 Irreversible Thermodynamics

Classical thermodynamic relations does not enquire into the mechanism of the phenomena and thus is unconcerned with molecular structure of the systems under investigation. It is correct for equilibrium systems, for reversible (equilibrium) processes and for processes between equilibrium states. The relationships in classical thermodynamics between state variables lose their validity in non-equilibrium.

Irreversible thermodynamics (non-equilibrium thermodynamics) is a division of physics which studies the general irregularities in transport phenomena (heat transfer, mass transfer, etc.) i.e. a change in the thermodynamic state of a system cannot be precisely restored to its initial state. During this transformation, there will be a certain amount of heat energy loss or dissipation due to intermolecular friction and collisions which will not be recoverable if the process is reversed. The state of the system will not be uniform but will vary locally in those as energy, entropy, and temperature distributions as gradients are imposed by dissipative thermodynamic fluxes.
The chemical reactor models with varying temperatures belong to nonlinear non-equilibrium thermodynamic systems because of reaction kinetics and irreversibilities of the coupling between matter and temperature (59). The energy of the reactor moves irreversibly from the material domain to thermal domain. As a consequence, the links between thermodynamics and system theory have to be characterized more precisely in order to exhibit thermodynamic variables usable for modeling and control design.
However, the energy of chemical reactions taking place at constant temperatures can be reversed if the reaction is reversible. Hence, isothermal systems can be dealt with the equilibrium thermodynamics.

2.7 State-space Modeling of Reactors

The main purpose of mathematical modeling is to encode dependencies between variables. By capturing those dependencies, a model can be used to answer questions about the values of unknown variables given the values of known variables. In order to guarantee the intrinsic validity of the final mathematical model, the translation of model's specification in to equations must be based on general principles, such as mass or energy conservation. Energy in this case acts as "common currency" of exchange among systems from different domains.
A state-space representation is a mathematical model of a physical system as a set of input, output and state variables related by first-order differential equations. State variables are the set of variables that are used to describe the mathematical state of a dynamical system e.g. position, momentum etc. State variables

$x(t)$ can be reconstructed from the measured input-output data, but are not always measured during an experiment. A state-space structure is very informative about the behavior of the system. It just needs the information of input to give a quick estimation of the system. It is often easier to define a parametric state-space model in continuous time because physical laws are most often described in terms of differential equations. In continuous-time, the conventional state-space representation has the following form:

$$\begin{aligned} \dot{x} = f(x) + g(x)\,u,\ x \in \mathbb{R}^n,\ u \in \mathbb{R}; \\ y = h(x)\,,\ y \in \mathbb{R},\ y \neq 0. \end{aligned} \tag{2.35}$$

The matrices f, g and h contain elements with physical significance e.g. material constants. u, y are the input and output of the system respectively.
The state-space representation also addresses the other aspects of the system such as:

a) Observability It is the measure of ability of the system to observe the unmeasurable state variables of the system by knowledge of its external outputs.

b) Controllability It is the measure of the ability of the system to control all the state variables of the system using the system input.

c) Stability It is a measure of the ability of the system to develop forces or moments that causes it reach an equilibrium or a steady-state point when away from a condition of equilibrium or steady motion.

d) Fault Detection It is the ability of a system to identify a fault and pinpointing the type of fault and its location. It helps in monitoring the system under accidental conditions.

There are mathematical terms e.g. observability matrix, derived from state-space representation which give information about these aspects of a system. Normally, these terms are based on non-physical modifications and also state-space representation lacks on physical interpretation as it does not use energy in the system. The next section will show how energy based modeling helps in the better understanding and control of the system.

Remark 1. *This thesis will not focus on the issues related to controllability, observability, fault detection and stability theory of solution of differential equations. However, issue of stability of systems near to a point of equilibrium derived from the passivity based model will be dealt in the next chapter and the same principles will be applied while modeling and control of open biochemical systems later in the thesis.*

2.7.1 Modeling of Chemical Reactors

To ensure the successful operation of a continuous stirred tank reactor (CSTR), it is necessary to understand their dynamic characteristics. A good understanding will ultimately enable effective control systems design. To describe the dynamic behaviour of a CSTR mass, component and energy balance equations must be developed. A chemical reaction creates new components while simultaneously reduces reactant concentrations. It may give off heat or may require energy to proceed. The following methodologies are used when modeling the continuous stirred tank chemical reactor (128):

1) **The Mass Balance** Without reaction, the basic mass balance expression for a tank is written:
   Rate of mass flow in - Rate of mass flow out = Rate of change of mass within system.

2) **The component balance** To develop a realistic CSTR model the change of individual species (or components) with respect to time must be considered as shown in the chemical kinetics above. A component balance for the j^{th} chemical species is:
   Rate of flow of j^{th} component in - rate of flow of j^{th} component out + rate of formation of j^{th} component from chemical reactions = rate of change of j^{th} component
   The unit balance, reaction order and unit of the component balance expression are needed to be checked while applying component balance

3) **The Energy Balance** The energy balance expression is given by:
   Rate of energy flow in - rate of energy flow out + rate at which heat added due to reaction = rate of change of energy within system. In order to balance energy, there is a need of expression for rate of flow of energy in/out, heat of

reaction, rate of change of energy and Arrhenius temperature dependence. Apart from inside the reactor, the energy is transferred from outside the reactor. In that case, modeling of reactors has to know the rate of heat transfers through a reactor wall and its dynamics.

2.7.2 Modeling of Bioreactors

The bioreaction systems are often poorly known, even when the desired product and the main side reactions are well known, since there might exist additional poorly known or totally unknown side reactions or partial product. These problems are not trivial, because the model structure is unknown and one is faced with choosing many various candidate models. Moreover, the equations describing the system are often nonlinear differential and/or algebraic equations and the parameters may vary over a wide range of values. Three different kind of models have been used in the literature for a bioreactor (101):

1) Data-driven black box models These are empirical input-output models, often able to represent the relationship between manipulated and observed variables. These models are relatively easy to obtain, but present two main drawbacks: (i) they are, usually, inadequate for predicting the reactor behavior outside the experimental domain in which the data were collected for model building; (ii) they are able to represent only relationships between variables that are manipulated or measured; hence, key variables, such as the heat or the concentrations, are difficult to represent.

2) Knowledge-driven white box models This is the preferred approach for modeling batch reactors. It is a mechanistic, state-space representation based on stoichiometric and kinetic knowledge, as well as on energy and mass balances for the reactor. The kinetic model describes the effect that temperature and concentrations have on the rate of each reaction. The energy and mass balances relate the states (concentrations, temperature and volume) to the inlet streams and possible disturbances. The drawbacks of these models are the following: (i) no realistic model is purely mechanistic, so a few physical parameters typically need to be estimated on the basis of experimental data; (ii) their derivation is very time-consuming and they are

difficult to build for industrially-relevant reaction systems (e.g. polymerization); (iii) they cannot be derived in presence of unknown side-reactions or unknown partial products.

3) Hybrid grey-box models They are a combination of the previous ones. Typically they are characterized by a simple (simplified) structure based on some qualitative knowledge of the process. Pseudo or lumped reaction are often exercised within hybrid models, so it is necessary to identify some model parameters and, sometimes, adjust them on-line. To this purpose, tendency models have been proposed in literature. The drawback of this approach is that, often, is not possible to follow, using a simplified model, all the species involved in the reaction, but only the species of major interest.

2.7.3 Process Modeling Improvisations

There are techniques which are applied on process models in order to simplify the calculations and further control of such process. In general, some models can be big, complex and highly non linear which makes them difficult to understand, monitor and control. Some techniques or improvisations, done to simplify the model are as follows:

a) Linearization Linearization is a linear approximation of a nonlinear system that is valid in a small region around the operating point. Most chemical process models are nonlinear, but they are often linearized to perform a simulation and stability analysis. Linear models are easier to understand (than nonlinear models) and are necessary for most control system design methods. To obtain an approximate (linearized) model of the CSTR Taylor series expansion may be used (128).

b) Model Reduction Sometimes the reaction involves a great number of chemical species and a detailed model of all of them may be useless. Hence, often the kinetic model involves few real and pseudo (lumped) reaction in order to follow the behavior of the concentration of interest. To this desire, many techniques aimed at reducing the complexity of models and to identify the model parameters have been introduced in the last two decades (8).

c) Passivization In this method, the system is dicretized into sub systems to represent the dissipative component, the inlet and the outlet separately. It helps in a better understanding of the system and helps in designing a stable control law for the system (91).

2.8 Control of Reactors

Control theory is an interdisciplinary branch of engineering and mathematics that deals with the behavior of dynamical systems with inputs, and how their behavior is modified by feedback. The usual objective of control theory is to control a system so that its output follows a desired control signal, called the reference, which may be a fixed or changing value. To do this a controller is designed, which monitors the output and compares it with the reference. The difference between actual and desired output, called the error signal, is applied as feedback to the input of the system, to bring the actual output closer to the reference. A controller is basically a mathematical function block that reads the error between desired setpoint and the measured output and then computes the corrective action for the manipulated input that would steer process towards the desired setpoint.

An important part of a high-quality reactor is a process controller. It optimises the process operation or detects malfunctions. Process control systems are used to improve the product output while sustaining the delicate conditions required for chemical reaction or cultivation of microorganisms. The control of a process is most often accomplished by measuring the variable it is required to control, comparing this measurement with the value at which it is desired to maintain the controlled variable and adjusting some further variable which has a direct effect on the controlled variable. A process control system is required either to maintain the process at the operational conditions and set points and/or to transition the process from one operational condition to another. Design methodology for process control is as follows [5]:

[5] http://open.umich.edu/sites/default/files/chemical_process_dynamics_and_controls-book_1.pdf

1) **Understand the process** Before attempting to control a process it is necessary to understand how the process works and what it does.

2) **Identify the operating parameters** Once the process is well understood, operating parameters such as temperatures, pressures, flow rates, and other variables specific to the process must be identified for its control.

3) **Identify the hazardous conditions** to maintain a safe and hazard-free facility, variables that may cause safety concerns must be identified and may require additional control.

4) **Identify the measurables** It is important to identify the measurables that correspond with the operating parameters in order to control the process.

5) **Select control method** In order to control the operating parameters, the proper control method is vital to control the process effectively

6) **Select control system** Choosing between a local or distributed control system that fits well with the process effects both the cost and efficacy of the overall control

7) **Investigate effects of changes before/after** By investigating changes made by implementing the control system, unforeseen problems can be identified and corrected before they create hazardous conditions in the facility.

8) **Integrate and test with other systems** The proper integration of a new control system with existing process systems avoids conflicts between multiple systems.

2.8.1 Chemical Reactors

The key unit operation in chemical plants namely the continuous stirred tank reactor (CSTR) exhibits highly nonlinear dynamic behavior. Hence, there arises a need to develop computationally non-intensive control schemes in order to achieve tighter control of strong nonlinear processes i.e. given the current states of the process, what actions should be taken to achieve desired specifications. Depending on the form of the plant model, different control strategies can be developed

(102).

As a general statement of the basic objectives, the aim is to produce a specified product at a given rate from known reactants. The other objectives of a chemical reactor can be maintaining the desired temperature, pressure, to achieve the steady state with desired flow rate. Some other additional objectives could be to maintain specified density, viscosity, molecular weight distribution etc. or economic objectives such as conversion, yield, selectivity, etc. All the objectives boil down to control the flow rate, heat transfer, agitation speed, residence time, external pressure etc. Different control algorithms are being developed to have an efficient control on all these parameters. Some of the control strategies are discussed in the process control algorithm section (115).

2.8.2 Bioreactors

Automatic control of bioreactors, in general, aims to increase the output and/or productivity by developing methods of monitoring and control, enabling real-time optimization of the bioprocess operation. The high complexity of biological processes due to parameter uncertainty, lack of sensors for the measurement of internal variables and variations in the characteristics of the living organisms pose a greater challenge in monitoring and control of such systems. Washout and multiple equilibrium points are the major problems of a bioreactor in an attempt to optimise the productivity. In addition to that, there are other issues of structure non-linearity, large number of system states, under actuation, external disturbances, unwanted delays and incomplete knowledge of the process mechanism, which bioprocess control tries to cope with. Figure 2.5 shows the schematic presentation of a continuous bioprocess control system.

The growth and persistence of bacteria depend on the close monitoring and control of many conditions within the bioreactor. Usually, the following parameters are monitored and controlled in bioreactors:

1) **Temperature** Temperature is an important parameter to control because cell growth can be significantly affected by environmental conditions. Choosing

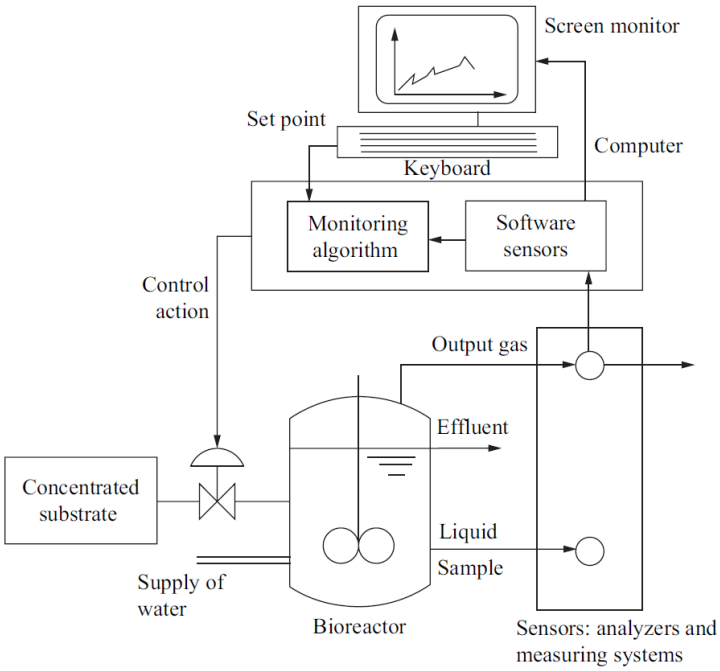


Figure 2.5: Schematic Representation of Bioprocess Control System(31)

the appropriate temperature can maximize the cell growth rate as many of the enzymatic activates function the best at its optimal temperature.

The temperature of a bioreactor can be controlled in many ways such as by using heat exchanger inside the bioreactor vessel, electrical heater on the bioreactor etc.

2) pH It is a measure of acidity or basicity of an aqueous solution. Different cells favor different pH environments. Many enzymes, that helps in microbial growth depends, function only within a narrower range of pH. Therefore appropriate action needs to be taken to restore the desired range of pH. pH change is caused by the unwanted or unavoidable side reactions taking place inside the reactor which produce acids or bases. The control of pH values is ensured with the help of feed pumps giving out the acid and the base. Normally, the pH adjustment consists of the desired pH width, i.e. between minimum pH and maximum pH values. If pH is between these values, then no influence occurs.

3) **Oxygen Transfer** Since oxygen is an essential nutrient for microbial growth which requires oxygen for respiration known as aerobic cultures. Maintaining an adequate supply of oxygen during aerobic processes is crucial. Therefore, in order to maximize the cell growth, optimization of oxygen transfer becomes extremely important. Due to low solubility of oxygen in aqueous solutions, a continuous supply is needed. Oxygen is fed from outside as a gas but can only be utilized in the liquid form. The dissolved oxygen concentration in an aqueous solution depends on the rate of oxygen transfer from the gas phase to the liquid, the rate at which oxygen is transported within the solution to the cells which consume oxygen (oxygen transfer rate (OTR)) and the rate at which oxygen is consumed (oxygen uptake rate (OUR)). Various factors can vary the oxygen supply such as inlet oxygen flow rate, oxygen content in the inlet flow, reactor pressure, stirring speed etc.

4) **Agitation speed** A stirrer, usually automated and powered with a motor, mixes the contents of the chemostat to provide a homogeneous suspension. This enables individual cells in the culture to come into contact with the substrate and to achieve optimal distribution of oxygen when aerobic cultures are present. Stirring accelerate cell growth and is sometimes required to break lumps of bacterial cells.

5) **Foam** The appearance of foam is a very undesirable phenomenon. During the foaming, it is not possible to perform high-quality analyses and measurements. Foam is eliminated by either an antifoaming agent or by using mechanical foam breaking mixer.

6) **Substrate inlet flow rate** One of the important features of the chemostat is that it allows the operator to control the cell growth rate. The common way of doing this is by controlling the inlet flow rate of substrate which is possible by controlling dilution rate, concentration of substrate in the inlet feed or both. In order to achieve this control of inlet substrate concentration, various control strategies have been developed and applied on bioprocesses

such as setpoint tracking, proportional-integral actions, extremum seeking etc. Some of these strategies are discussed in next section.

The following section will discuss and compare different feedback control algorithms used in the control of chemical and biological reactors.

2.8.3 Process Control Algorithms

An important aspect of process control is to perform a stable real time operation, less prone to disturbances, close to the desired state and compatible with optimal operating conditions. The objective is to obtain control laws, which seek the best compromise between what is well known in process dynamics (e.g. the reaction scheme and the material balance) and what is less understood (e.g. the kinetics). There has been continuous development of more sophisticated control methods for the past two decades which are accounting for uncertainties and guaranteeing the best possible operation such as optimal and adaptive control methods (1), (114). The most common strategies of continuous process control are as follows:

1) **Open-Loop Control** Also known as chemostat control. Open-loop control maintains a steady rate of reaction in a continuous process by controlling the volumetric feed rate. It calculates the value of inlet feed rate such as dilution rate from the system's model without observing the output of the process (62). This type of control does not compensate for the disturbances like parameter uncertainties in the system which leads to the risk of deflection from the desired concentration and washout state is possible if the desired state is close to optimal dilution rate. This type of control is strictly not suitable for the processes which involve very small concentrations and/or with high parametric uncertainties.

2) **Closed-Loop Control** Also known as feedback control. To overcome the limitations of the open-loop controller, a closed-loop controller is introduced which uses the ouput information to regulate the system towards the desired output or measurement and then to maintain the same state. Feedback controllers ensure optimum performance with model uncertainties, impart

stability to unstable processes, reduce sensitivity to parameter variations, improve reference tracking performance etc.

There have been different closed-loop control methodologies adopted to use the output feedback (31). A few common methodologies are as follows:

a) Set Point Control The strategy of this controller is to keep the system close to or at the desired value of the variable to be controlled called set point. The control algorithm reduces the error between the set point and the controlled variable (30). The most common control algorithms are:

i) PID Controller The PID controller algorithm is a three-term linearized control: the proportional P, the integral I and derivative D values. The weighted sum of these three actions is used to adjust the process via a control element such as a control valve etc. (102). PID controllers are for single input single output (SISO) systems. Multiple input multiple output (MIMO) systems can be controlled through PID if loops can be decoupled. They can be gain scheduled under the condition of changing operating points.It is difficult to control time delays with these controllers.

ii) Model Predictive Controller Model Predictive Control (MPC) control algorithm uses an internal dynamic model of the process, a history of past control moves and an optimization function to calculate the future control moves (4). It can handle time delays, very non-linear and multivariable systems as well. It can be both linear or non-linear. MPC is good for optimal control problems but controller can be very difficult to tune.

iii) Nonlinear Feedback Controller This controller takes the feedback (state-space, output etc.) of the plant and compares it to the desired output and provides modified input to the plant to change the output to bring it closer to the desired output or to allow the output of a system to follow a desired reference signal (49). Analyzing the output ensures the convergence of the system

to the setpoint using in general the Lyapunov stability theory and tracks the overall performance of controller.

Set point control algorithms in general are good for multivariable process and processes with known disturbance. However, they are difficult to tune, do not in general provide optimal control if the system is nonlinear and are unphysical with no knowledge of the process (129).

b) **Direct vs Indirect Measurement Control** In order to ensure complete intolerance towards disturbances and uncertainty, it is quite obvious that there is a need to measure specific performances such as yield optimization, online monitoring of environmental parameters etc. The direct control enforce this by using advanced instrumentation like automated concentration analyzers etc. (71). It is probable that the monitoring and maintenance of these instruments can be very difficult. Also, the control algorithm becomes complicated as each variable gives an additional control loop but the main problem is that there is a serious lack of sensors which could enable online measurement of key variables in some complex processes. This leads to development of **state observers** (not to be discussed in the PhD thesis) which provide an estimate of these unmeasurable variables from input, output measurements. On the other hand in indirect control, the biological variables are not directly regulated and the users merely ensure optimum conditions for the growth of micro-organisms independent of biological parameters like growth rate and concentrations (10) e.g. **turbidostat**: it is a feedback control apparatus for cultivating microorganisms which indirectly controls the turbidities in the system e.g. when the system is away from equilibrium and/or cells are mutating inside the reactor.

c) **Adaptive Control** Due to variability in kinetics of reactions, there exists substantial parameters uncertainties and also there is lack of online measurements. Control algorithms will prove efficient if they

are able to deal with the missing information without significantly deteriorate the control performance of the process. Adaptive controllers serve the purpose. They adapt to the online estimated values of uncertain parameters provided by **parameter estimators**. A parameter estimator attempts to approximate the unknown parameters using the error in the output.

The basic idea of the adaptation is that the estimated value of uncertain parameter and the tracking error are correlated. This correlation is used to generate the adaptive gain which is continued until the gain derivative tends to zero i.e. a constant gain (8). The two most common control strategies used in bioreactors are:

i) **Adaptive Linearizing Control** Since the bioprocess model is generally nonlinear, the adaptive linearising control design will result in a linearizing control structure, in which the online estimation of the unknown variables (component concentrations) and parameters (reaction rates and yield coefficients) are incorporated (6). It is explicitly used for non-linear systems with uncertainty problems and can handle multiple inputs and multiple outputs. It forms a closed reation with model with no real insight into the system. It requires special tools and is also difficult to tune.

ii) **Extremum Seeking Control** In some applications, however, the control objective could be to optimize an objective function which can be a function of unknown parameters, or to select the desired values of the state variables to keep a performance function at its extremum value. Extremum-seeking control is the method of handling these types of optimization problems. The task of extremum seeking is to find the operating set-points that maximize or minimize an objective function. It utilizes explicit structure information of the objective function that depends on system states and unknown plant parameters (26), (**?**).

Adaptive control strategies are very robust but are unphysical and their stability is also based on unphysical **Lyapunov functions**: Scalar

functions that are be used to prove the stability of an equilibrium of an ordinary differential equation.

d) Robust control Robust control involves, firstly, quantifying the uncertainties or errors in a 'nominal' process model, due to nonlinear or time-varying process behaviour. If this can be accomplished, one essentially have a description of the process under all possible operating conditions (129). The next stage involves the design of a controller that will maintain stability as well as achieve specified performance over this range of operating conditions. Robust control methods such as H_2 and $H\infty$ ensures guaranteed stabilization, optimal control and are very efficient for multivariable systems (17).

e) Energy Based Control The traditional approach towards controlling the system as discussed above involve complex computations and are signal based without any physical interpretation. Most of the problems in control stems from not using any information about the physical structure of the system. This problem is addressed in energy based control.

It is well known that energy plays an essential role in the description of physical systems. Passivity plays an important role in designing energy based controller. Passivity is a property of physical systems which means that the energy stored by a system can not exceed that supplied from outside. For such systems, passivity balances the energy of a system quantifying the external input and generated output. Passivity based control methodology aims at making the closed loop system passive. It shapes the energy of the system and change how energy flows inside the system. The energy functions can be used as Lyapunov function candidate to prove the isolated system stability properties and as a storage function to emphasize the passivity properties when the system interacts with the surroundings. Passivity based control incorporates physical knowledge for predicting and modifying the behaviour of systems (56), handles on both performance and stability and are self stabilising (96), (123). It mostly generates

non-linear control algorithm with tuning criterion and often applied to SISO systems. It can be modified to imply on MIMO systems and can generate robust and adaptive control algorithms but not very efficient in it.

With a view to optimise the control strategies there has also been superposition of different control strategies e.g. passivity based adaptive control (29), extremum seeking setpoint tracking control (28) etc.

2.9 Conclusion

This chapter tells in brief about all the basic concepts of biochemical kinetics, different modes to carry out modeling and control the chemical and biochemical reactions, the uncertainties and problems faced in control of such systems. It concludes that the passivity based control is one physical control strategy for any system if the energy of the system can be quantified. It is robust and helps in better understanding of the control methodology. The application of passivity based control methodology on chemical systems has been a bit difficult and very difficult for biochemical systems. Passivity based control of biochemical systems could be seen as an important task for the researchers in order to get a control over the energy exhange in such systems.

The next chapter will give the details about tools used for energy based modeling, which gives systematic insight about the stability of the systems and also helps in design of controllers. The later part of chapter will show the application of these tools to chemical and enzyme reactions in continuous bioreactors.

3

Port-Hamiltonian Modeling of Continuous Reactors

3.1 Introduction

This chapter focuses on the role of energy and passivity in the modeling of chemical systems. The two energy based modeling tools i.e. Bond Graph (BG) and Port-Hamiltonian (PH) will be discussed in detail in this chapter. Then, the whole bunch of literature on the energy based modeling of open chemical and biochemical systems and issues related with it will be reviewed. Subsequently, the chapter will show the most physical and best way to model such systems in PH and BG form concluded with the application of the modeling technique on an enzymatic reaction problem.

3.1.1 Role of Energy in Modeling

Energy based models (EBMs) capture dependencies between variables by associating a scalar energy to each configuration of the variables according to the different domains of represented physical processes which allows scalability and physical interpretation (70). EBM provides a unified framework for prediction, classification and control of systems. As discussed in the previous chapter energy based control (passivity based control) is among the most physical control techniques and leads to the better understanding of the system as well as its controller. The interesting fact is that modeling the system in an energetic form really complements the design of controller. The controller can be obtained directly by shaping the energy function in the model with much ease and the energy

based model itself tells a lot about the control algorithm and stability of the system at the desired state. This leads to the development of a few energy based modeling techniques and tools which makes it easier to model a system energetically. Passivity plays a central role in these energy based modeling techniques. It is really important to learn about passivity before knowing these tools. The role of passivity is discussed in detail in the next section.

3.1.2 Passivity

Passivity is a fundamental property of physical systems which are able to transform and dissipate energy. (74). A passive system is a system which cannot store more energy than is supplied by some source, with the difference between the stored energy and supplied energy, being the dissipated energy. The basic definition of a passive system goes as follows:

Definition 1. *(41), Considering the system:*

$$\begin{aligned} \dot{x} &= f(x) + g(x)\,u; \\ y &= h(x)\,. \end{aligned} \tag{3.1}$$

$f(x)$, $g(x)$ and $h(x)$ are the interconnection matrices containing elements with physical significance. u, y are the input and output of the system respectively. Which with a storage function $V(x)$:$V(x^*) = 0$, where x^* is the steady state value of x and $V(x) > 0$ at $x \neq x^*$, is passive if:

$$\frac{dV}{dt} \leq u^T y. \tag{3.2}$$

Assume that the passive system satisfying the condition presented in Definition 1 can be written in the form:

$$\begin{aligned} \dot{x} &= Q(x,u)\frac{\partial V}{\partial x} + \gamma(x)v; \\ y &= \gamma^T(x)\frac{\partial V}{\partial x}, \end{aligned} \tag{3.3}$$

Here, v is the modified input, Q and γ are the modified interconnection matrices.

Lemma 1. *(41), Considering the system shown in Equation (3.3), which with a storage function $V(x)$: $V(x^*) = 0$, where x^* is the steady state value of x and $V(x) > 0$ at $x \neq x^*$, will be passive if $Q \prec 0$.*

Storage function V is often the total energy function for electro-mechanical systems. Passivity also correlate with the stability of a system. The next section will discuss about the stability theories derived from passivity.

Stability via Passivity

A system which remains in a constant state unless affected by an external action and which returns to a constant state when the external action is removed can be considered to be stable. The stability of a control system is often very important and is generally a safety issue in the engineering of a system.

Definition 2. *(117), An autonomous system:*

$$\dot{x} = f(x), \tag{3.4}$$

where $x = [x_1, \cdots, x_n]^T$ *are local coordinates for* χ*. Let* x^* *be an equilibrium point, i.e.*

$$f(x^*) = 0. \tag{3.5}$$

The equilibrium point x^* *is stable if for any neighbourhood* X *of* x^* *there exists a neighbourhood* X' *of* x^* *such that if* $x' \in X'$*, then the solution* $x(t, 0, x')$ *belongs to* X *for all* $t \geq 0$*. The equilibrium* x^* *is unstable if not stable. The equilibrium* x^* *is asymptotically stable (i.e. the states are asymptotically approaching towards the equilibrium point) if there exists a neighbourhood* X_o *of* x^* *such that all solutions of* $x(t, 0, x')$ *with* $x' \in X_o$*, converge to* x^* *as* $t \to \infty$*. The equilibrium* x^* *is globally asymptotically stable if* $X_o = \chi$*.*

There are various theories invented which, by using the state-space representation, prove that whether a particular system is stable or not e.g. Lyapunov stability. A stable system produces a bounded output if supplied with a bounded input. Passivity is therefore related to the property of stability in the sense that it quantifies the energy balance of a system i.e. a passive system yields bounded output energy if bounded input energy is supplied to the system. A passive system is therefore a stable system, however such systems are directly linked to the Lyapunov stability as shown in Proposition 1 below.

Proposition 1. *(67), Consider a passive system shown in Equation (3.3) with a storage function* $V(x)$*:* $V(x^*) = 0$*, where* x^* *is the steady state value of* x *and* $V(x) > 0$*. The time derivative of storage function yields the dissipation equality:*

$$\frac{dV}{dt} = \frac{1}{2}\frac{\partial V}{\partial x}^T \left(Q(x) + Q(x)^T\right)\frac{\partial V}{\partial x} + \frac{\partial V}{\partial x}\gamma(x)\upsilon. \tag{3.6}$$

Hence, the system is stable if:

$$\frac{1}{2}\frac{\partial V}{\partial x}^T \left(Q(x) + Q(x)^T\right)\frac{\partial V}{\partial x} \leq 0, \tag{3.7}$$

with zero input the system is Lyapunov stable at $x = x^*$ *if:*

$$\frac{dV}{dt} \leq 0, \tag{3.8}$$

and it is asymptotically stable if:

$$\frac{dV}{dt} < 0 \quad in \quad \mathbb{R} - \{x^*\}. \tag{3.9}$$

These stability theories mostly concern about the stability of systems near to equilibrium or tending to evolve towards equilibrium as simple energy minimization principles do not seem to exist far from equilibrium.

Remark 2. *All the chemical and biochemical systems studied in this thesis are also assumed to be near to the equilibrium. The chemical processes that occur far from equilibrium are uncertain and give some intricate solutions (68).*

3.2 Energy Based Modeling Tools

Energy based modeling tools use some theories or methods while implementing the concept of energy in the modeling of the dynamical systems. These methods restraint these mathematical models to follow a particular structure. This structure divides the model into discrete parts, each part representing some attributes of the system, which offers a systematic framework for analysis of physical systems. These attributes explain many things about the inner structure and behaviour of the model. The three major energy based modeling tools or techniques are Bond Graph (BG), Port-Hamiltonian (PH) and Energetic Macroscopic Representation (EMR). EMR and BG are graphical tools for capturing the commmon energy structure of the systems. EMR is a functional representation of a system consists of mathematical functions for the description of different parts of the system and BG is a structural representation consists of physical components focusing on the system's topology. EMR is a way to organize models of subsystems to enhance some properties whereas BG does both pictorial representation and derivation of system equations from it. PH modeling tool can be said as the mathematical description of the BG technique or BG can be said as the graphical representation of the PH models (32).
All these modeling techniques come under port based approach of modeling. The next part will give details about the port based modeling.

3.2.1 Port Based Modeling

The concept of a port is generated by the fact that sub-models in a model have to interact with each other by definition and accordingly need some form of conceptual interface, for example the conceptual inerface on the interaction between a spring and mass in a spring mass system. In physical systems, such an interaction is always coupled to an exchange of power i.e. energy and such a relation is called a power bond. This bond represents a bilateral relation and connects two ports of the elements e.g. spring, mass. The bilateral nature of the power P is represented by means of a product of two conjugate variables named effort e and flow f: $P = e \times f$. The flow variable can be seen as the rate of change of some state, or equilibrium-establishing variable of the system and effort variable as equilibrium-determining variable (14). Figure 3.1 represents pictorial view of ports exchanging power between element in terms of effort and flow where direction of arrows shows the direction of effort and flow which is always opposite. Table 3.1 shows the list of most common chosen efforts and flows in various domains:

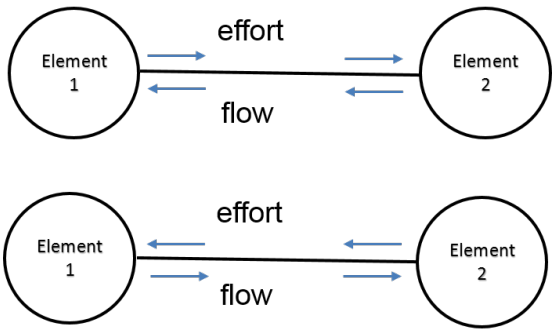


Figure 3.1: Power Bond Connecting Two Ports

The next sections will discuss in detail the BG and PH modeling tools.

3.2.2 Bond Graph Modeling

Bond Graph (BG) is an explicit graphical tool for capturing the common energy structure of systems. It is based on the idea of portraying systems in terms of power bonds, connecting the elements of the physical system to the so called junction structures (98). Bond Graph theory has been further developed on

Systems	Effort (e)	Flow (f)
Mechanical	Force (F), Torque (τ)	Velocity (v), Angular velocity (ω)
Electrical	Voltage (V)	Current (i)
Hydraulic	Pressure ($\bar{P}$)	Volume flow rate ($\dot{q}$)
Thermal	Temperature (T), Pressure ($\bar{P}$)	Entropy change rate ($\dot{\hat{S}}$), Volume change rate ($\dot{\hat{V}}$)
Chemical	chemical potential (m)	Mole flow rate ($\dot{n}$), Mass flow rate ($\dot{M}$)
Magnetic	magneto-motive force (e_m)	Magnetic flux (ϕ)

Table 3.1: List of Effort and Flow Variables in Various Domains

extending this modeling technique to power hydraulics, mechatronics, general thermodynamic systems and recently to electronics and non-energetic systems like economics and queuing theory. The basic variables in Bond Graph are effort (e), flow (f), time integral of effort (p) and the time integral of flow (x). Elements of BG are classified as passive and active elements. The passive elements are idealized elements because they contain no sources of power (15). The inertia or inductor I, compliance or capacitor C, and resistor or dashpot R are the three elements used to represent passive components in actual system. The active elements are those, which act as source of energy. For this reason, they are called active ports. There are two active elements, SE as source of effort and SF as source of flow. Power bonds which show the flow of power between elements are shown as half arrows. However, the direction of power will be same as direction of half arrows if only both the variables chosen for effort and flow, acquire positive values or else the direction will be opposite to the direction of half arrow. The elements which share either the same effort or same flow are connected together using half arrows to the junctions. There are only two kinds of junctions, the 1 and the 0 junction. They conserve power and are reversible. 1 junction has equality of flows and the efforts sum up to zero with the same power orientation. 0 junctions have equality of efforts while the flows sum up to

zero, if power orientations are taken positive toward the junction. Besides that, the other basic elemnts of BG to be considered are "Transformer" and "Gyrator". The Bond Graph symbols for these elements are TF and GY, respectively. The Bond Graphic transformer can represent an ideal electrical transformer, a mass less lever, etc. The transformer does not create, store or destroy energy. It conserves power and transmits the factors of power with proper scaling as defined by the transformer modulus. A transformer relates flow-to-flow and effort-to-effort. Conversely, a gyrator establishes relationship between flow to effort and effort to flow, again keeping the power on the ports same(84).

An important aspect of BG modeling is causality. Causality establishes the cause and effect relationships between the factors of power. In Bond Graphs, the inputs and the outputs are characterized by the causal stroke. The causal stroke indicates the direction in which the effort signal is directed (by implication, the end of the arrow or bond that does not have a causal stroke is the end towards which the flow signal is directed). Following example will give a clear idea of the Bond Graph pictorial representation (84).

Example 1. *Consider the spring mass damper model shown in Figure 3.2 with mass M, spring stiffness k, damping coefficient c and external input force F.*

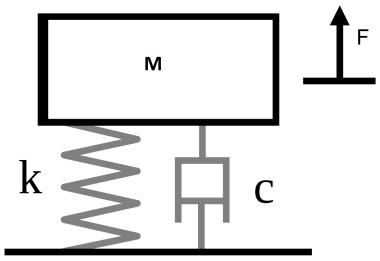


Figure 3.2: Spring Mass Damper System [1]

The Bond Graph model for such a system can be shown as in Figure 3.3. The common flow v is shown by 1 *element in the middle and the external effort F will be distributed among spring C, damper R, and mass I. The Causal stroke on any one end of each arrow is showing the direction in which the effort is flowing.*

[1] `http://en.wikipedia.org/wiki/File:Mass_spring_damper.png`

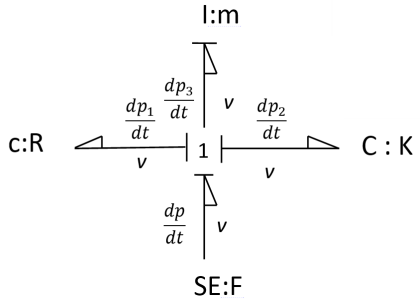


Figure 3.3: Bond Graph Model of Spring Mass Damper System

Through BG, a physical system can be represented by symbols and lines, identifying the power flow paths. The lumped parameter elements of resistance, capacitance and inertance are interconnected in an energy conserving way by bonds and junctions resulting in a network structure. The BG model can be used to derive sytem equations, design a controller (24) and is very efficient in issues of controllability, causality and fault-detection (113), (46). Also, Bond Graph can indicate if there are any serious violations of principles of conservation of energy using the concept of differential causality.

3.2.3 Port-Hamiltonian Modeling

The Hamiltonian approach, based on the principle of least action, has been used in analytical mechanics. Hamiltonian equations are the Legendre transform of Euler-Lagrange equations. This interest is mainly originated from the fact that Hamiltonian systems have a number of advantageous properties from a control point of view (96). On the other hand, the port based modeling approach also started constituting to the mathematical systems theory. While most of the analysis of physical systems is being performed within the Hamiltonian framework, the port point of view was also established in modeling and simulation of physical systems (122). The framework of Port-Hamiltonian (PH) systems combine both points of view by associating a Hamiltonian vector field with the interconnection structure of the port model.

Definition 3. *(91) Network modeling of lumped-parameter physical systems with independent storage elements leads to models of the formâĂŤcalled PCH systems:*

$$\dot{x} = (J(x) - R(x))\frac{\partial H}{\partial x} + gu, \tag{3.10}$$

$$y = g^T \frac{\partial H}{\partial x}, \tag{3.11}$$

where x is the state and $H(x)$ is the storage function called Hamiltonian. u, y are port power variables and their duality product defines the power flows exchanged. The two interconnection matrices are: $J(x)$is a skew-symmetric matrix and g. $R(x)$ is a symmetric dissipation matrix.

Port-Hamiltonian systems are thus open dynamical systems, which interact with their environment through ports. Resistive effects are included by terminating some of these ports on energy-dissipating elements. Passive systems are thus Port-Hamiltonian with non-negative Hamiltonian. Conversely every Port-Hamiltonian system with non-negative Hamiltonian can be said to be passive. Most nonlinear passive systems can be written as Port-Hamiltonian systems. The following example will give the better idea of how PH models are formulated.

Example 2. *Consider the same spring mass damper model shown in Figure 3.2. The system states, displacement x and momentum p, can be written in PH form as:*

$$\begin{bmatrix} \dot{x} \\ \dot{P} \end{bmatrix} = \left(\begin{bmatrix} 0 & 1 \\ -1 & 0 \end{bmatrix} - \begin{bmatrix} 0 & 0 \\ 0 & c \end{bmatrix} \right) \begin{bmatrix} \frac{\partial H}{\partial x} \\ \frac{\partial H}{\partial P} \end{bmatrix} + \begin{bmatrix} 0 \\ 1 \end{bmatrix} F, \tag{3.12}$$

$$y = \begin{bmatrix} 0 & 1 \end{bmatrix} \begin{bmatrix} \frac{\partial H}{\partial x} \\ \frac{\partial H}{\partial p} \end{bmatrix} \tag{3.13}$$

where H will be the total energy of the system:

$$H = \frac{1}{2}kx^2 + \frac{1}{2m}p^2. \tag{3.14}$$

The structure of a PH model itself divides the system into different parts with each part holding a physical significance. While controlling a system, these structural attributes of a PH system are forced to follow the desired behavior therefore it is more oriented towards physical controller design.

3.3 Energetic Modeling of Chemical and Biochemical Systems: Literature Review

In passivity based modeling, the main concern is to find the storage function or Hamiltonian function which can fit into the structure of a passive model or a

Hamiltonian model respectively. The most suitable storage functions or Hamiltonian functions have been energy functions which also associate low energies to the equilibrium or steady state values and higher energies to values not at equilibrium. Therefore, passivity based models are closely related to energy based models.

The class of Hamiltonian systems as a special type of passive systems have gained significant interest during the last decade (121). Port-Hamiltonian (PH) or Bond Graph (BG) have proven very successful for modeling electro-mechanical or thermal systems. Well-known examples of Hamiltonian systems are LC-circuits in electrical systems (80), (19), electromechanical models (93) and process systems (73). (84) has shown the implementation of Bond Graph on mechanical, electromechanical and electrical systems.

There exists a lot on PH and BG model for chemical and biochemical systems as well but in contrast with mechanical and electrical systems, the physics of a chemical system is quite difficult to exhibit in the geometry of a Port-Hamiltonian model (35). A chemical or biochemical system deals with three domains i.e. thermal, hydraulic and chemical. So the concern was to find the energy function which can consider all the states related to these three domains such as concentration, enthalpy, volume etc. and incorporate them into a single PH structure. For the Bond Graph part, each domain was to be assigned a set of effort-flow variables e.g. Temperature-Entropy. Different researchers tried to fit different energy function expressions to fit in the structure of the PH models which can also satisfy the necessary passivity and stability conditions. Some researchers took some arbitrary functions which are not energy functions providing pseudo PH models of chemical systems so as to satisfy the structural properties of PH system. Similarly, for the BG model, different researchers took into account different functions to act as effort and flow variables for various sub-systems. The BG models are told to be pseudo BG if the product of effort and flow does not represent power.

3.3.1 Bond Graph Review

The BG model of the flash separator, dealing with hydraulic and thermal domains, is developed in (25) and (99). It is a multi Bond Graph since several variables

of different domains exist in the same bond, and it is a pseudo Bond Graph because the product of the variables in the bonds does not represent power. The effort variables are pressure and temperature, and the flow variables are mass flow and enthalpy flow. (55) also proposed the pseudo BG model of a CSTR using Molar flow and concentration as flow and the heat flow and temperature as effort variables.

(119) gave the true Bond Graph model for a chemical reaction, instead of pseudo Bond Graph. They went through the complex affinity gateway in order to derive the equations from the Bond Graph in order to make it look coherent. They chose Entropy, molar flow and volume as flow variable and temperature, chemical potential and pressure as effort variables. The new BG elements were invented to compensate for the irreversible loss of energy in Entropy. (131) gave true BG for Enzyme kinetics where effort is chosen to be chemical potential, Chemical affinity and flow as rate of reaction and mass flow rate. (16) also improved upon the BG by (119) representing chemical transformation using new BG elements e.g. RS element as irreversible TF element. One RS element is contributing one reaction including both forward and reverse reaction rates converting concentration space to reaction space.

(21) divided the internal energy into 3 parts which have temperature-Entropy, pressure-volume and chemical potential- no of moles as effort-flow variables. The system is solved in 3 different domains connected by 0 junctions shown in Figure 3.4. The irreversible Entropy production is dealt with *RS* element.

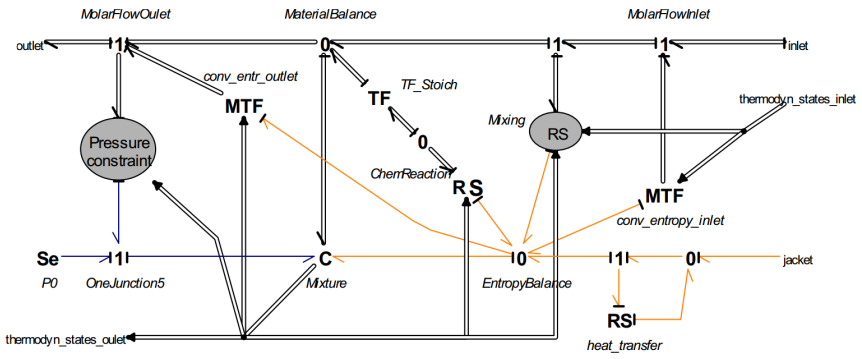


Figure 3.4: Bond Graph Model of a CSTR (21)

(22) also present the Bond Graph language by using some rather simple dynamical systems as tutorial examples and to show the potentialities of this language to build dynamical models from reusable sub-models. Their application is more directly related to the concepts of irreversible thermodynamics. (12) made it clear that in order to consider mass flow in a thermal system; it is wise to make pseudo BG and use Enthalpy and mass flow rate as effort-flow variables as suggested by (65) and used by (25). (111), (116) and (110) made pseudo BG of batch, fed-batch and continuous bioreactors. They considered the isothermal chemical reactions only assuming the temperature is either constant or being maintained constant by external means. They take inflow as SF (Source of flow), outflow as R (Resistance), accumulation as C (Capacitance) and the reaction is shown bt the TF (Transformer) element with MR (Modulated Resistance) representing the rate of reaction. Figure 3.5 will give the clear idea of the works of Roman et al. They did not focus much on stoichiometric coefficients as seperate entity and

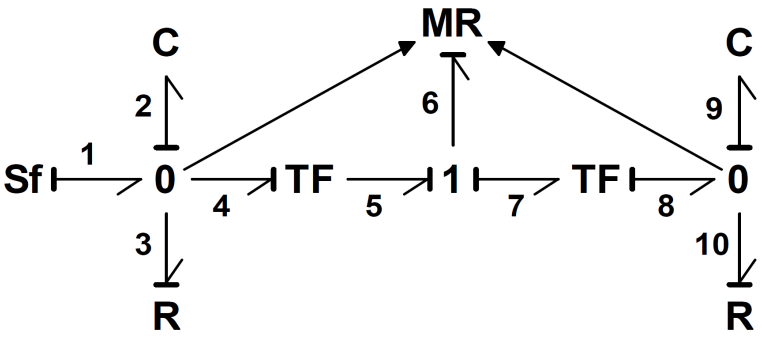


Figure 3.5: Pseudo Bond Graph Model of a CSTR Prototype (111)

considered them within the flow variable.

3.3.2 Port-Hamiltonian Review

Artificial decomposition

(122) differentiated the usual geometric approach of Hamiltonian systems. The formulation in this paper is based on the canonical symplectic structure of the phase space which is obtained by (symmetric) reduction of the phase space with the Port-Hamiltonian system whose geometric structure derives from the interconnection of its sub-systems. He considered Dirac structures which enables one

to define Hamiltonian systems with algebraic constraints.
(33) also did not consider temperature change and used quadratic functions of concentrations while formulating biochemical reactions with Monod kinetics in PH form.
(56) took Gibbs Free Energy G as Hamiltonian ($H = G$), state x equal to concentration, chemical potential $m_i = \frac{\partial G}{\partial x_i}$ for isothermal CSTR and used relation between reaction Entropy, reaction rate and chemical potential in order to introduce dissipation. They used matrix property $A = (A + A^t)/2 + (A - A^t)/2$ to get a symmetric and skew-symmetric interconnection and dissipation matrix respectively which do not justify the physical meaning behind various parts of the structure of the PH form. The formulation is in pseudo form as matrix elements should not depend on the Hamiltonian gradient. For non-isothermal CSTR they took $H = -\hat{S}$, $\hat{H}$ ($\hat{H}$ is enthalpy), input $u = Q$ as heat. He proposed that outflow can be derived as a function of inflow.
(60) linked Brayton-Moser and Port-Hamiltonian forms. They generalized the objective of formulation and control as thermal stability criterion. They used chemical affinity and Ectropy ($Ectropy = -Entropy$) as potential Hamiltonian function which satisfy the thermodynamic stability criterion. It lacked symmetry and physical meaning.

Straightforward Decomposition

(52) tried to fit the Hamiltonian model into the process systems. They chose the system states p, q and Hamiltonian H such that $\dot{q} = \frac{\partial H}{\partial p}$ and $\dot{p} = -\frac{\partial H}{\partial q}$. For a CSTR, they use system states as mass and concentration and Hamiltonian as complex quadratic functions of states in order to satisfy the above equations.
The Hamiltonian (H) function of (96), (95) contains scaled affinites involving concentration terms at equilibrium and is not an energy function. Log of ratio of reaction rate was taken as state space variables.

(37) used different Hamiltonian functions for example, sum of concentration with stoichiometric coefficients which is not an energy function but advocated the use of thermodynamic variables such as Entropy, Enthalpy, Gibbs Free Energy etc. Also, structural matrix elements in this formulation are a combination of rates of reaction. With Internal Energy, Entropy, Enthalpy as Hamiltonian, they

used different state space variables along with concentration terms as few of them and input is chosen as inlet flow - outlet flow of chosen Hamiltonian Functions.

(34) in his book insisted on the fact that in order to understand the importance of port-based approach, it is also necessary to briefly introduce some generic aspects of modeling and simulation of dynamic behavior of physical systems. The book describes the issues of thermodynamics in using various energy function e.g. Enthalpy, Entropy etc. as Hamiltonian functions.

(123) introduced the states x as $\dot{x} = s_i v_i + s_b v_b$, where s_i, s_b are the internal and boundary stoichiometric matrices and v_i, v_b are the internal and boundary fluxes respectively. The Gibbs Free Energy function used as Hamiltonian was represented in this paper as the difference of gradient of forward and reverse affinities with forward affinity always greater than reverse affinity under natural conditions. The rate of a reversible isothermal chemical reaction r can be written as $r = k(exp(A_f/RT) - exp(A_r/RT))$, where $A_f = -S_f m$, $A_r = -S_r m$. S_f, S_r are the forward and reverse stoichiometric matrices. The stoichiometric matrix is $S_t = S_r - S_f$. This formulation relates concentration space with reaction space and incurred the dynamics of chemical reaction network in his formalism. Although, it completely ignores the interconnection matrix and shows the system as a purely dissipative Hamiltonian system.
(59) shows that any thermodynamic variable fulfilling some stability criterion can be used as Hamiltonian for pseudo Hamiltonian representation of a non-isothermal Continuous Stirred Tank Reactor model. More precisely, it is shown that from Brayton-Moser formulation is obtained some Port-Hamiltonian representation with negative dissipation.
(124) improve upon the Gibbs Free Energy function provided in (123) by introducing equilibrium concentrations in the formula.

In (104), quasi Port-Hamiltonian systems are defined with respect to a structure matrix and a modulating function which depends on the thermodynamic relation between state and co-state variables of the system. This modulating function itself is the product of some positive function g and the Poisson bracket of the Entropy and the energy function. This construction guarantees that the

Hamiltonian function is a conserved quantity and simultaneously that the Entropy function satisfies a balance equation containing an irreversible Entropy creation term.

3.3.3 Conclusion from Literature review

3.3.3.1 Difficulties and Framework

Different energy functions used in chemistry were taken as Hamiltonians e.g. Internal Energy, Ectropy, Enthalpy etc. but the structure matrices are explicitly dependent on the gradient of the Hamiltonian (intensive variables) destroying the linearity between the flows and efforts (geometry of the system). In fact, the chemical reactor models belong to irreversible thermodynamic systems as there is irreversible coupling between matter and temperature i.e. energy changes are moving irreversibly from the material domain to the thermal domain. As a matter of fact, the non-isothermal systems cannot be written as pure Hamiltonian models because it does not allow to express the inherent irreversibility of the system governed by the Second Law of Thermodynamics. This implies that all formulations of thermodynamic systems as Port-Hamiltonian systems (PHS) will be quasi PH Systems. However, in the particular case of isothermal chemical/biochemichal reaction networks, since the temperature is assumed constant, there are no internal irreversible transformations (no internal irreversible Entropy production due to the reaction) and it is possible to model the reaction with a structure similar to that of a true dissipative Port-Hamiltonian system (96).

Remark 3. *This thesis will focus only on the isothermal and isobaric systems. All the chemical and biochemical reactions are supposed to take place at constant temperature and pressure. In a CSTR, seperate measures are taken to maintain a desired constant temperature and pressure in the vessel.*

3.3.3.2 Outcome

(123) expressed Gibbs Free Energy (G) as a suitable Hamiltonian function but for a closed chemical system at constant temperature and Pressure. It mentions about the energy exchange at the boundary but did not explain it and also did not apply the model to any real system. It is a mathematical interpretation needs to be extended to open systems and validated on the real system. The work of (96) also gave energetic representation in reaction space is also based on

some abstract function hence not logical on the physical grounds. The issue of bridge between reaction space and concentration space also not been solved in an energetic approach. However, this concept is well known from the chemical engineering point of view, where notions of advancement and orientations are introduced. Bond-Graphs representations seem to be more sound. (119) proposes a "real" BG representation based on total energy and use of chemical affinities. There are few - and not very interesting - representations of Monod reactions. As an example, Roman and co-workers proposed a pseudo Bond Graph with no energetic insight where the reaction rate is embedded in a special Modulated TF element. Hence, it seems difficult to obtain an exact Hamiltonian formulation. Van der shaft and Maschke Hamiltonian is very close to reality taking care of reaction stoichiometry and energy function and other chemical aspects (124). This approach also needs to keep a check on mathematical aspects. Making a Bond Graph instead of pseudo BG seems more preferable using the concepts of X. Zhang (131) and F.T. Brown (16).

3.3.3.3 Choice of Hamiltonian

Of different energy functions, the notion of G for isothermal systems seems very obvious ((124)). The Internal Energy of a chemical system is its total energy and under conditions of constant pressure, temperature and volume it reduces to G. Gibbs Free Energy (G) clearly represents the energy of a chemical reaction for such systems. G is a form of potential (Molar Potential Energy) which gets absorbed in forward reaction and released reverse reactions. The relation is shown below:

$$dG = -\hat{S}dT + \hat{V}d\bar{P} + \sum_{i=1}^{k} m_i dx_i. \tag{3.15}$$

dG is the change in Gibbs Free Energy, $\hat{V}$ is the volume of the reactor, dT is the change in temperature, $d\bar{P}$ is the change in pressure, m is the chemical potential, $\hat{S}$ is Entropy and x is the concentration of component i. When a system reaches the equilibrium, the GFE is minimum and its derivative with respect to the concentration is zero. As the focus is on chemical processes at constant temperature and pressure, G is the best suited Hamiltonian for such

systems. At constant pressure and temperature:

$$dG = \sum m_i dx_i \tag{3.16}$$

and

$$\sum m_i = \sum RT \log\left(\frac{x_i}{x_i^*}\right). \tag{3.17}$$

R is the gas constant, x_i^* is the concentration of i at equilibrium. The next sections will show the Bond Graph and PH model of basic open chemical and enzyme reactions at constant temperature and pressure. These models are derived from the literature and are further extended to apply on open systems. Some improvisations are done in the BG presentation obtained from literature which is making it more sound from the physical point of view.

3.4 Bond Graph and Port-Hamiltonian Model of Open Chemical Systems

Consider a basic chemical reaction:

$$aA + bB \underset{k_r}{\overset{k_f}{\rightleftharpoons}} cC + dD,$$

taking place at constant volume and temperature in an open reactor with single stream flow. Here a, b, c, d are stoichiometric coefficients and A, B, C, D are the chemical species involved, k_f, k_r are forward and reverse rate constants. The rate of these reactions can be written as:

$$\frac{dr_1}{dt} = k_f[A]^a[B]^b - k_r[C]^c[D]^d. \tag{3.18}$$

Using the relation of chemical potential, chemical affinity and Gibbs Free Energy showed in *Chapter 2*, the rate of reaction can be written as:

$$\frac{dr_1}{dt} = K_1\left(\exp\left(\frac{A_f}{RT}\right) - \exp\left(\frac{A_r}{RT}\right)\right) = -K_1 f\left(\frac{\partial G}{\partial n_i}\right),$$

where A_f and A_r are the forward and reverse affinities, n_i is the number of moles of constituent i. It is related to the affinities of the constituents of reaction i.e. A, B, C, D in the following way:

$$A_f = A_{oA} + A_{oB},\ A_r = A_{oC} + A_{oD}, \tag{3.19}$$

and $K_1 = f(k_f, k_r, m_{oA}, m_{oB}, m_{oC}, m_{oD}) > 0$, A_o's and m_o's are the chemical affinities and the reference chemical potentials of individual constituents respectively. Based on (97), the BG model which is not pseudo-energetic for such a reaction is shown in Figure 3.6 (76).

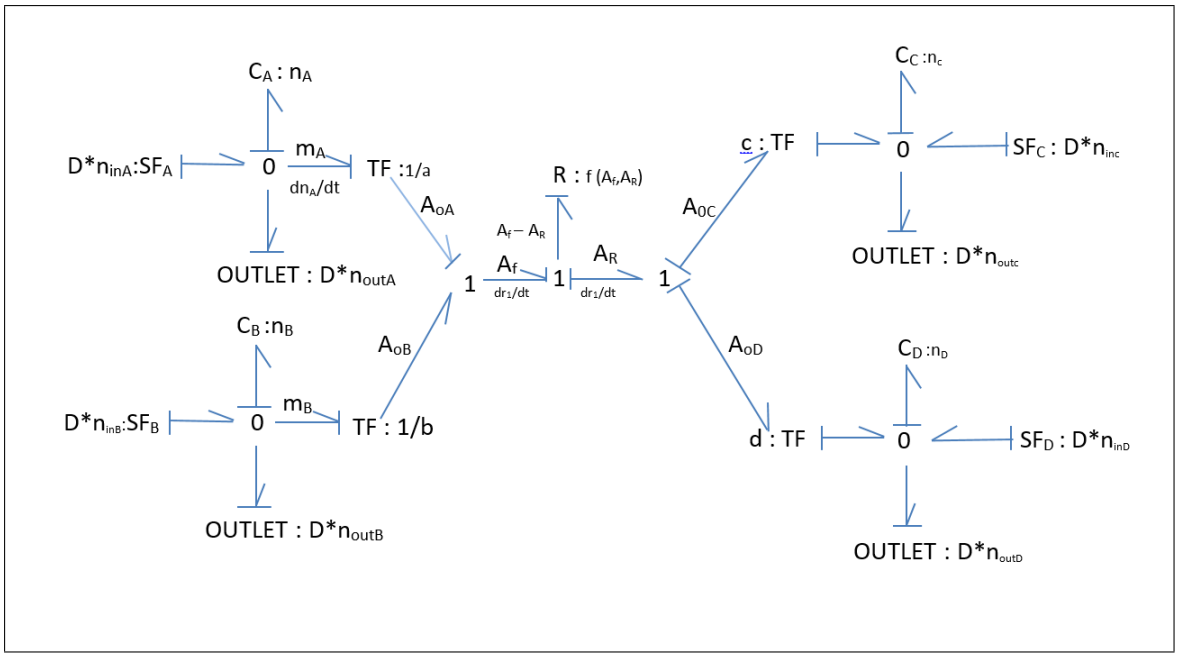


Figure 3.6: Bond Graph Model of Chemical Reaction in Open Reactor (76)

The C elements represent the quantity of chemical inside the reactor, SF elements are for flow coming in with dilution rate D, the "$OUTLET$" element is showing the flow going out with the same dilution rate to maintain constant volume. It was represented by R elemnt by (111) and physically flow going out can not be considered as dissipation of energy. 0 junctions are the flow (dn/dt) summing junction and common effort (m) junction. TF elements are accounting for reaction stoichiometry and also giving relation between rate of reaction and actual change in the quantity of each species. 1 junction is common flow (dr_1/dt) junction and effort summing junction (A_o). R element is symbolizing the loss of energy in a chemical reaction giving the relation between the rate of reaction and the forward and reverse affinity. The 1 junctions on the left and right side are giving the relation that forward and reverse affinity is equal to the sum of the individual affinities of reactants and products respectively.

In order to write the material balance equation in Port-Hamiltonian form, there is a need to define the energy function which will be the Hamiltonian function. Many attempts have been made to formulate the chemical process in and continuous modes. As discussed in literature review, the only acceptable energy function which can be used to represent an isothermal energetic model physically with effort and flow variables has been shown to be Gibbs Free Energy (119). It is clear that, for chemical process, the representation in the PH framework is not straightforward, a deviation from the standard model has to be done to take the stoichiometry of the reactions in to account (124).

Proposition 2. *(123)The PH form of an open chemical system with k chemical constituents, where n_i is the concentration of constituent i:* $[n_i] = \begin{bmatrix} n_1 & n_2 & \cdots & n_n \end{bmatrix}^T$ *and the Hamiltonian function is Gibbs Free Energy (G):* $G > 0$ *and* $G = 0$ *at steady state is:*

$$[\dot{n}_i] = -[S_t] \times [K_1 \times f(\partial G/\partial n_i)] + [I] \times [D((n_{in})_i - (n_{out})_i)], \tag{3.20}$$

$$y = [I] \times [\partial G/\partial n_i], \tag{3.21}$$

S_t is the stoichiometric matrix.

On comparing to the Port-Hamiltonian structure given in Equations (3.10) and (3.11), G is the Hamiltonian function, $[I] = [g]$, $[D(n_{in} - n_{out})] = [u]$. Instead of using partial derivative of Hamiltonian, the function of it is being used, which is justified seeing the complexity of the system:

$$(J(x) - R(x))\frac{\partial H}{\partial x} = -S_t \times K_1 \times f(\frac{\partial G}{\partial n}). \tag{3.22}$$

The stoichiometric matrix S_t describes the basic structure of the reactions. It is necessary to introduce the stoichiometric system seperately as it accounts for the passage of concentration and links them with the inner dynamics (96).

3.5 Bond Graph and Port-Hamiltonian Model of Basic Enzyme Reaction With MM Kinetics in a CSTR

Consider the basic single substrate enzyme reaction represented schematically as:

$$E + S \underset{k_{r1}}{\overset{k_{f1}}{\rightleftharpoons}} ES,$$

$$ES \underset{k_{r2}}{\overset{k_{f2}}{\rightleftharpoons}} E + P.$$

Lack of insight of an enzyme reaction i.e. true mechanism and how energy flows and dissipates in the process makes it difficult to apply an energetic approach on it. (94) tried to get the rate equation in the form of affinities. They showed that under quasi steady-state approximations and $E << S$, the concentration ES will be considered as constant and the production rate r can be simplified as (here $k_{r2} = 0$):

$$r = \frac{k_{f2} n_E n_S}{n_S + \frac{k_{r1}+k_{f2}}{k_{f1}}} = \frac{m_o n_S}{n_S + K_m}. \tag{3.23}$$

Here, m_o is the maximum rate possible and K_m is Michaelis-Menten constant. In the following sections, the basic chemical kinetics has been applied to the enzyme reaction in the same way as defined for chemical reaction and subsequently BG representation and Port-Hamiltonian formulation are obtained.

3.5.1 Bond Graph Representation

The Bond Graph of the enzyme reaction is shown in Figure 3.7. The Basic elements of Bond-Graph represent the system in a similar way as shown for the chemical reaction in Figure 3.6 (76).

3.5.2 Port Hamiltonian Formulation

Port Hamiltonian formulation of basic Enzyme reaction in an open reactor will be as:

$$\begin{bmatrix} \dot{n}_E \\ \dot{n}_S \\ \dot{n}_{ES} \\ \dot{n}_p \end{bmatrix} = - \begin{bmatrix} -1 & 1 \\ -1 & 0 \\ 1 & -1 \\ 0 & 1 \end{bmatrix} \times \begin{bmatrix} K_1 f_1 \left(\frac{\partial G}{\partial n_E}, \frac{\partial G}{\partial n_S}, \frac{\partial G}{\partial n_{ES}} \right) \\ K_2 f_2 \left(\frac{\partial G}{\partial n_{ES}}, \frac{\partial G}{\partial n_P}, \frac{\partial G}{\partial n_E} \right) \end{bmatrix} + \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} D(n_{inE} - n_{outE}) \\ D(n_{inS} - n_{outS}) \\ D(n_{inES} - n_{outES}) \\ D(n_{inP} - n_{outP}) \end{bmatrix} \tag{3.24}$$

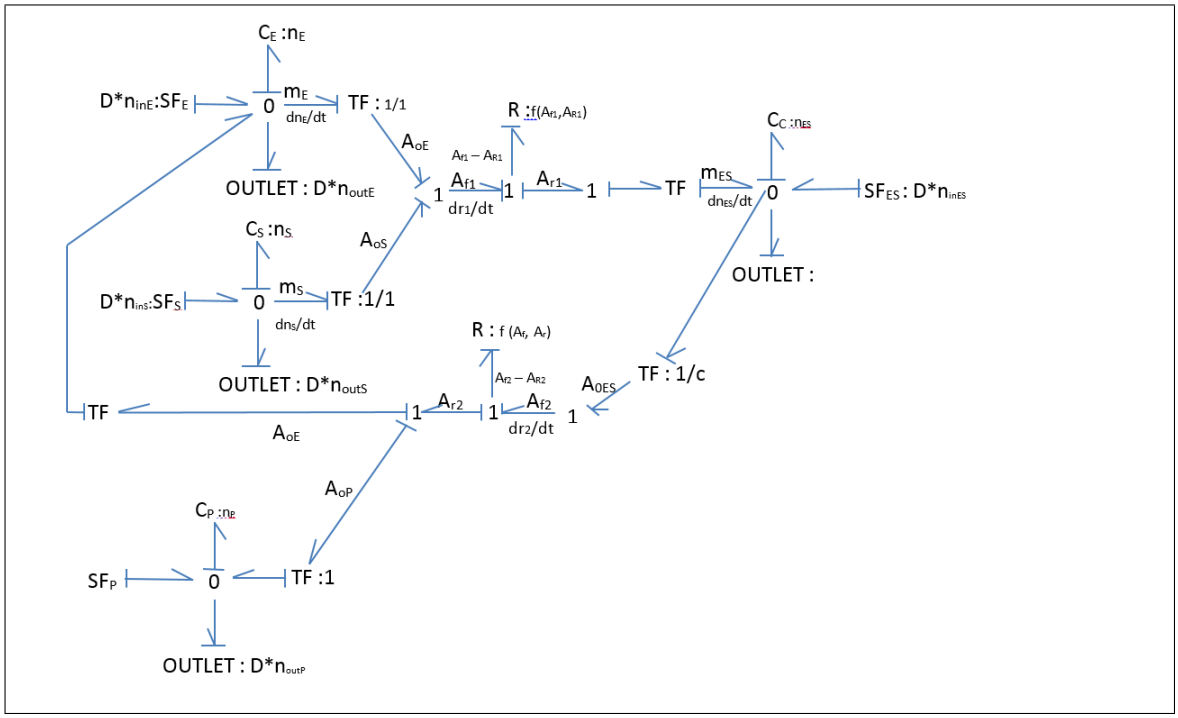


Figure 3.7: Bond Graph Model of Enzyme Reaction in a CSTR

$$y = [I]\left[\frac{\partial G}{\partial n_i}\right] \tag{3.25}$$

where,

$$-f_1\left(\frac{\partial G}{\partial n_E}, \frac{\partial G}{\partial n_S}, \frac{\partial G}{\partial n_{ES}}\right) = \exp\left(\frac{A_{f1}}{RT}\right) - \exp\left(\frac{A_{r1}}{RT}\right),$$
$$-f_2\left(\frac{\partial G}{\partial n_{ES}}, \frac{\partial G}{\partial n_P}, \frac{\partial G}{\partial n_E}\right) = \exp\left(\frac{A_{f2}}{RT}\right) - \exp\left(\frac{A_{r2}}{RT}\right)$$

and

$$A_{f1} = A_{oE} + A_{oS},\ A_{r1} = A_{oES}, \tag{3.26}$$

$$A_{f2} = A_{oES},\ A_{r2} = A_{oE} + A_{oP}. \tag{3.27}$$

$K_1 = f(k_{f1}, k_{r1}, m_{oE}, m_{oS}, m_{oES}) > 0,\ K_2 = f(k_{f2}, k_{r2}, m_{oES}, m_{oE}, m_{oP}) > 0$. In Equation (3.24), the first term on the right hand side is accounting for the structural balance of the chemical reaction system. It is the product of the stoichiometric matrix and the vector of rates of reactions. Speed of reaction is dependent

on the amount of chemical present inside the chamber, which can be controlled from outside by controlling the inlet and outlet flow of the chemical. Outflow in this case will be same as the amount present at that instant of time. The second term on the right hand side is accounting for the net input of each chemical. It can be positive, negative or zero. For example, ES complex and product is formed inside and not supplied from outside, Enzyme also remains inside the tank in many cases so n_{out} will be zero in this case. ES complex gets converted in to product very fast therefore no output for this too. The formulation of second part varies according to the inlet conditions. For example, if the incoming chemical is supplied from different tanks then dilution rate may vary for each inlet and dilution rate for outlet can also differ under various conditions like non-constant volume etc., in that case the second term will have to further split in two parts and a new formulation will be required in order to look coherent with the actual Port-Hamiltonian formulation i.e. further shaping by respecting the structure of the model. This opens the window for new ideas in energetic representation of a system with actual physical meaning.

As an immediate consequence of the Port-Hamiltonian formulation, the following energy balance could be obtained:

$$\frac{dG}{dt} = -\frac{\partial G}{\partial n} S_t f\left(\frac{\partial G}{\partial n}\right) + \frac{\partial G}{\partial n} D\left((n_{in}) - (n_{out})\right). \tag{3.28}$$

Proposition 3. *(123) From the energy balance shown in Equation (3.28), the following relation can be incurred:*

$$-\frac{\partial G}{\partial n} S_t f\left(\frac{\partial G}{\partial n}\right) = \left(A_r^T - A_f^T\right)\left(\exp\left(\frac{A_f}{RT}\right) - \exp\left(\frac{A_r}{RT}\right)\right) \leq 0, \tag{3.29}$$

thus shows passivity.

Remark 4. *The structural properties of Hamiltonian will not be completely satisfied by the given PH formulations of chemical systems. They can be seen as purely dissipative Port-Hamiltonian systems and might be called pseudo-PH for not following the exact structure.*

The next section will show a newly structured pseudo-PH model of open reaction networks using Gibbs Free Energy as Hamiltonian.

3.6 Port-Hamiltonian Model of a Continuous Reactor

As discussed in introduction, it is difficult to ideally fit an energy function associated to a chemical reaction in a Port-Hamiltonian structure. However, for reversible reaction networks which is also the case of most of the enzyme processes, (124) gave one formulation through modification of Hamiltonian as an exponential function of the energy function. This formulation is used in open systems shown in a CSTR example below. The structural properties of Hamiltonian will not be completely satisfied by the formulation so it will be a quasi or pseudo PH model.

Example 3. *A CSTR maintaining a constant volume ($\hat{V}$) with same and constant dilution rate D for both inlet flow x_{in} and outlet flow x_{out} of concentration of chemical x for the reaction:*

$$A + B \underset{k_{r1}}{\overset{k_{f1}}{\rightleftharpoons}} C, \;\; C \underset{k_{r2}}{\overset{k_{f2}}{\rightleftharpoons}} D + A.$$

Here, A,B,C are the chemical constituents. A reversible chemical reaction bears a equilibrium concentration x^* of reactants and products. The rate laws for the two reactions with equilibrium rate constants:

$$k_1 = k_{f1}[A]^*[B]^* = k_{r1}[C]^* > 0,$$

and

$$k_2 = k_{f2}[C]^* = k_{r2}[D]^*[A]^* > 0,$$

can be given as:

$$r_1 = k_1 \left(\frac{[A]\,[B]}{[A]^*[B]^*} - \frac{[C]}{[C]^*} \right),$$

$$r_2 = k_2 \left(\frac{[C]}{[C]^*} - \frac{[A]\,[D]}{[A]^*[D]^*} \right).$$

In order to fit the model of the system, it is important to express concentration in terms of energy gradient. (124) gave the relation connecting the concentration (x) with steady state concentration (x^*) and exponential function of Gibbs free energy at constant temperature and pressure. The relation is:

$$x = x^* \exp\left(\frac{1}{RT} \frac{\partial G}{\partial x} \right). \tag{3.30}$$

Here, R ($JK^{-1}mol^{-1}$) is the universal gas constant. Using (3.30), the rate terms can be written as:

$$r_1 = k_1 \left(\exp\left(\frac{1}{RT} \frac{\partial G}{\partial A} \right) \exp\left(\frac{1}{RT} \frac{\partial G}{\partial B} \right) - \exp\left(\frac{1}{RT} \frac{\partial G}{\partial C} \right) \right) \tag{3.31}$$

$$r_2 = k_2\left(\exp\left(\frac{1}{RT}\frac{\partial G}{\partial C}\right) - \exp\left(\frac{1}{RT}\frac{\partial G}{\partial A}\right)\exp\left(\frac{1}{RT}\frac{\partial G}{\partial D}\right)\right) \tag{3.32}$$

Now the whole system can be modeled as:

$$\begin{bmatrix} dA/dt \\ dB/dt \\ dC/dt \\ dD/dt \end{bmatrix} = \begin{bmatrix} -r_1 + r_2 \\ -r_1 \\ r_1 - r_2 \\ r_2 \end{bmatrix} + \begin{bmatrix} D(A_{in} - A_{out}) \\ D(B_{in} - B_{out}) \\ D(C_{in} - C_{out}) \\ D(D_{in} - D_{out}) \end{bmatrix}. \tag{3.33}$$

The inlet and outlet concentration terms can be seen as an entropy change in the system:

$$\underbrace{\sum d\hat{S}_{sys}}_{\substack{system\\ entropy\\ change}} = \underbrace{\sum x_{in}\hat{S}_{in}}_{\substack{inlet\\ flow}} - \sum \underbrace{x_{out}\hat{S}_{out}}_{\substack{outlet\\ flow}} - \underbrace{\frac{dG}{T}}_{\substack{entropy\\ generation}}. \tag{3.34}$$

Also, outgoing concentration will be equal to the concentration inside the reactor ($x_{out} = x$). Now, through integration of Equation (3.30) for Gibbs Free Energy provides the required Hamiltonian. Hamiltonian H will be:

$$H = G = \sum\left(zRTx\log\frac{x}{x^*} - zRT(x - x^*)\right) + C_o, \tag{3.35}$$

$z = \pm 1$, as G will be actually the difference between the Gibss Free Energy of reactants and products. C_o is the constant of integration chosen such that $G(x) > 0$ and $G(x) = 0$ at steady state.

Proposition 4. *The general quasi Port-Hamiltonian form for a CSTR with $H = G$, as shown in Equation 3.35, will be passive and can be written in the form:*

$$\begin{aligned}[\dot{x}] &= -S_t\,[K]\exp\left[f\left(\partial G/\partial x\right)\right] + (D(x_{in} - x))\,; \\ y &= I\frac{\partial G}{\partial x}.\end{aligned} \tag{3.36}$$

$f\left(\partial G/\partial x\right)$ *is the function of state space gradient of Gibbs Free Energy.* $[K]$ *is the diagonal matrix of equilibrium rate constants. Where:*

$$-\frac{\partial G}{\partial x}S_t\,[K]\,f\left(\frac{\partial G}{\partial x}\right) = \left(A_r^T - A_f^T\right)\left(r_f - r_r\right) \leq 0, \tag{3.37}$$

r_f *and* r_r *forward and reverse rates of reaction.*

In the series of reactions where product formation from one reaction acts as the reactant in the other reaction, there has to be a basic topological structure show-

ing the effect of one reaction with the other. The speed of final product formation depends on speed of individual reaction. This structure is called stoichiometry expressing the conservation laws of chemical reaction. The Stoichiometric matrix S connects all the individual concentrations with the rates of reaction. In concentration space, S should be treated as a different entity. It is a connection matrix which should not be a part of classical PH formulation.

3.7 Stoichiometric Port-Hamiltonian Formulation of Open Reaction Networks

This formulation is further improvisation in the representation of the rate terms in Port-Hamiltonian of chemical reaction. It takes stoichiometry into account seperately in the rate terms (124) as well. It is exploring $f\left(\frac{\partial G}{\partial n}\right)$ and introducing new matrices such as incidence matrix. The representation itself is more clear and more close to the Real PH form. The following example will give a clear idea of the representation.

Example 4. *Consider a simple enzyme reaction with single enzyme-substrate (ES) complex. In an Enzyme reaction after the substrate (S) has been transformed into product (P), the enzyme is free to catalyze the next reaction. Below is the reaction:*

$$E + S \underset{k_{r1}}{\overset{k_{f1}}{\rightleftharpoons}} ES, \;\; ES \underset{k_{r2}}{\overset{k_{f2}}{\rightleftharpoons}} E + P.$$

The stoichiometric matrix S_t for this reaction will be:

$$S_t = \begin{bmatrix} -1 & 1 \\ -1 & 0 \\ 1 & -1 \\ 0 & 1 \end{bmatrix}$$

and the rates of reaction will be:

$$r_1 = k_1 \left(\frac{x_E x_S}{x_E^* x_S^*} - \frac{x_{ES}}{x_{ES}^*} \right), \;\; r_2 = k_2 \left(\frac{x_{ES}}{x_{ES}^*} - \frac{x_E n_P}{x_E^* x_P^*} \right). \tag{3.38}$$

where $k_1 = k_{f1} x_E^* x_S^* = k_{r1} x_{ES}^*$, $k_2 = k_{f2} x_{ES}^* = k_{r2} x_E^* x_P^*$. Using (3.30), the expanded stoichiometric PH (SPH) form (124) for this reaction can be written as

follows (77):

$$\begin{aligned}\begin{bmatrix} \dot{x}_E \\ \dot{x}_S \\ \dot{x}_{ES} \\ \dot{x}_P \end{bmatrix} &= -\begin{bmatrix} -1 & 1 \\ -1 & 0 \\ 1 & -1 \\ 0 & 1 \end{bmatrix}\begin{bmatrix} k_1 & 0 \\ 0 & k_2 \end{bmatrix} B_m \\ \exp\left(Z\frac{1}{RT}\begin{bmatrix} {}^{\partial G}/_{\partial x_E} \\ {}^{\partial G}/_{\partial x_S} \\ {}^{\partial G}/_{\partial x_{ES}} \\ {}^{\partial G}/_{\partial x_P} \end{bmatrix}\right) &+ \begin{bmatrix} d(x_{inE}-x_E) \\ d(x_{inS}-x_S) \\ d(x_{inES}-x_{ES}) \\ d(x_{inP}-x_P) \end{bmatrix}.\end{aligned} \tag{3.39}$$

B_m is called the incidence matrix and Z is called the complex stoichiometric matrix, their values for this case are:

$$B_m = \begin{bmatrix} -1 & 1 & 0 \\ 0 & -1 & 1 \end{bmatrix}$$

$$Z = \begin{bmatrix} 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 1 \end{bmatrix}$$

There is a close relation of the two matrices with the stoichiometry of the reaction network ((124)) which is $S_t = Z \times B_m$.

It is quite easy to find the B_m and Z matrices of any reaction network. Z includes the stoichiometric coefficients and B_m assigns either positive, negative sign them or assign zero to them. These matrices discretise the rate functions into a matrix of individual gradient of Gibbs Free Energy directly relating each concentration term with it.

Proposition 5. *The general SPH form for a CSTR can be written as:*

$$\begin{aligned}\dot{x} = -S_t K B_m \exp\left(Z\frac{1}{RT}\frac{\partial G}{\partial x}\right) + D\,(x_{in} - x)\,; \\ y = [I]\left[\frac{\partial G}{\partial n_i}\right].\end{aligned} \tag{3.40}$$

This formulation also emphasize on the fact that stoichiometry of the set of reactions is not part of the system for fitting in to the structure and does not have any impact on stability and passivity properties. It should be taken as separate entity though it is also not having any impact on input and output as well.
Only individual concentrations are being dealt in this formulation. The next section will deal with the reaction space and what if the progress of reaction is

the state to be monitored which is also the case in many examples. The following formulation will give an easy way to peek into the reaction space and is derived from the SPH formulation.

3.8 Reaction Port-Hamiltonian Formulation of Open Reaction Networks

A complex reaction network possesses an underlying potential structure on a state space that will be referred to as the reaction space. The Reaction space is the state space where one is not talking about individual concentration and views the reaction as a whole. It was important to reformulate the structure in to reaction terms and yet maintaining the physical essence of the formulation plus huge concern was to justify the change in input and output terms. In this section, the reaction space's PH structure will be produced using matrix transformations and referred to as a RPH formulation. The Reaction Port-Hamiltonian structure of an open chemical system can be written as:

$$\underbrace{\eta}_{\substack{\text{Reaction}\\ \textit{state}\,\text{space}}} = \underbrace{r}_{\substack{\text{Reaction}\\ \textit{rate}}} + \underbrace{(w_{in} - w)}_{\substack{\text{Reaction}\\ \textit{input}}} \tag{3.41}$$

The link which connects the two spaces is the stoichiometric matrix S. One can mathematically find the left inverse of a rectangular matrix. On pre-multiplication of SPH formulation with (3.40) by ${S_t}^{-1}$: $S_t {S_t}^{-1} = I$, one obtains:

$${S_t}^{-1}\dot{x} = -KB_m \exp\left(Z\frac{1}{RT}\frac{\partial G}{\partial x}\right) + {S_t}^{-1}D\left(x_{in} - x\right). \tag{3.42}$$

The rate of reaction r can be written in terms of extent of reaction ξ as:

$$r = -f\left(\frac{\partial G}{\partial \xi}\right), \tag{3.43}$$

where $d\xi = \frac{dx_i}{v_i}$. Also, ${S_t}^{-1}\dot{x} = \dot{\xi}_o$. ξ_o is the new variable related to extent of reaction in an indirect sense.

Proposition 6. *The general Reaction PH (RPH) form for a CSTR can be written as:*

$$\underbrace{\dot{\xi}_o}_{\substack{\text{Reaction}\\ \textit{state space}}} = \underbrace{-Kf\left(\frac{\partial G}{\partial \xi}\right)}_{\substack{\textit{Reaction}\\ \textit{rate}}} + \underbrace{(w_{in} - w)}_{\substack{\textit{Reaction}\\ \textit{input}}}. \tag{3.44}$$

Here, $(w_{in} - w) = {S_t}^{-1}(D(x_{in} - x))$, ${S_t}^{-1}\dot{x} = \dot{\xi}_o$, S^{-1} *is the inverse of stoichiometric matrix* S_t.

The reaction statespace and the reaction input and output is the sum of concentrations multiplied by some coefficients. These coefficients solely depend on the stoichiometric matrix as $S_t {S_t}^{-1} = I$. The extent of reaction will vary with individual concentration but will be calculated collectively as is expected to be in reaction space (95). For the enzyme reaction given in Example 4, The inverse stoichiometric matrix will be:

$${S_t}^{-1} = \frac{1}{5}\begin{bmatrix} -3 & -2 & 0 & 3 \\ 3 & -1 & 2 & 4 \end{bmatrix}$$

The RPH form for these reactions in a CSTR can be written as (77):

$$[S_t]^{-1}\begin{bmatrix} \dot{x}_E \\ \dot{x}_S \\ \dot{x}_{ES} \\ \dot{x}_P \end{bmatrix} = -\begin{bmatrix} k_1 & 0 \\ 0 & k_2 \end{bmatrix}\exp\left(\frac{1}{RT}\begin{bmatrix} {\partial G}/{\partial \xi_1} \\ {\partial G}/{\partial \xi_2} \end{bmatrix}\right) + [S_t]^{-1}\begin{bmatrix} D\,(x_{inE} - x_E) \\ D\,(x_{inS} - x_S) \\ D\,(x_{inES} - x_{ES}) \\ D\,(x_{inP} - x_P) \end{bmatrix}. \tag{3.45}$$

3.9 Conclusion

It can be concluded that the open chemical and biochemical systems at constant temperature and pressure can be formulated in pseudo PH form only, but in many ways. The most suitable and physical Hamiltonian function is Gibbs Free Energy for the reaction part. One can show input and output as variation in Internal Entropy. BGs for such systems are most physical when understood through the gateway of chemical potential and chemical affinity which falls under the same category of Gibbs Free Energy. SPH and RPH form are a nice addition to the previous PH formulations. Actually SPH and RPH can be said to be more close to the physical representation and good for overall understanding of the systems. Writing rate terms in the form of equilibrium concentrations is really a need for the PH formulation and control.

The next section will review about the control of systems based on passivity theory and design of controller using the PH form. Interconnection and Damping Assignment-Passivity Based Control will be discussed in detail and derived from the PH formulation shown in this chapter.

4

Interconnection and Damping Assignment-Passivity Based Control of Continuous Reactors

4.1 Introduction

This chapter will deal with the issues related to control of continuous reactors with more focus on Passivity Based Control (PBC). The basic definitions of Passivity Based Control (PBC) and then Interconnection and Damping Assignment-Passivity Based Control (IDA-PBC) strategy will be discussed in detail. The application of PBC and IDA-PBC of open chemical and biochemical systems will be reviewed from the literature. General IDA-PBC control laws will be derived for the Port-Hamiltonian formulations of open chemical and biochemical systems proposed in *chapter 3*. Then the PH modeling and IDA-PBC control law of SPH system will be applied on the example of enzymatic hydrolysis of cellulose. The simulation results at the end will illustrate the modeling and control strategy.

4.2 Role of Energy in Control

Control problems, approached traditionally by adopting a signal-processing viewpoint, have been very useful for linear time-invariant systems where signals can be discriminated via filtering. However, for nonlinear systems, frequency mixing makes things harder due to undesirable signals and very involved computations. Most of the problems stems from not using any information about the physical structure of the system.
Energy plays a central role in exploiting the structure of physical systems for their

control since energy is related to the stability of the system. It is well known from physics that every configuration characterized by a local minimum of the energy exhibits a local stable behavior. Energy based controller shapes the energy of the system and even changes how energy flows inside the system. The controller is interpreted as a device which exchanges energy with the plant and it has to be designed in such a way that the controlled system can still be interpreted as a physical system which has an energy function whose minimum corresponds to the desired configuration of the system (34). The link between stability of the controlled system and energetic properties of a physical system can be formalised by means of passivity theory. Passivity can be seen as a restatement of energy conservation for physical systems, hence energy based control is also called Passivity Based Control (PBC). The aim in PBC is to render the closed loop system passive. The energy shaping stage accomplishes the objective of rendering the closed loop system passive with a desired energy function. The damping injection reinforces the passivity property to output strict passivity. Lastly, Lyapunov stability follows from the input-output stability of the passive system (74).
Passivity Based Control (PBC) if compared to other types of control handles more on performance, incorporates physical knowledge and provides a logical interpretation to the control action. Passivity based control (PBC), as discussed above, exploits system's physical properties while exploring the possibilities of managing its energy. PBC is very interesting and sound because one can actually think on physical terms while choosing the control action. (121) explored a complete and excellent exposition about passivity. Passivity Based Control has been extensively used in electro-mechanical systems. It is an interesting method to determine the control input of Passivity Based Models (PBM). The structure itself imparts stability to the control methodology. The possibilities of passivization of nonlinear systems by means of regular aÂĄffine feedback have been shown to be equally valid for monovariable and multivariable cases by (118).
Before performing the Passivity Based Control, there are some observability properties which are needed to be satisified for the internal stability and passivity of the input-output Passivity Based Controlled system . The conditions are as follows:

Definition 4. *(88):* ***(Zero-state observability and detectability)*** *A state-space system:*

$$\begin{aligned} \dot{x} &= f(x) + g(x)\,u; \\ y &= h(x), \end{aligned} \tag{4.1}$$

is zero-state observable from the output $y = h(x)$, if for all initial conditions $x(0)$, we have $y(t) = 0 \Rightarrow x(t) = 0$. It is zero-state detectable if $y(t) = 0 \Rightarrow \lim_{t\to\infty} x(t) = 0$.

Proposition 7. *(88): Suppose the system:*

$$\dot{x} = Q(x)\frac{\partial H}{\partial x} + gu, \tag{4.2}$$

$$y = g^T \frac{\partial H}{\partial x}, \tag{4.3}$$

where $H(x) \geq 0$ represents the storage function is output strictly passive and the system is zero-state detectable then $x = 0$ is a locally asymptotically stable equilibrium of $\dot{x}$.

Lemma 2. *(33):A general system given in (4.2) with zero input will have an asymptotically stable equilibrium point x^* if $H(x)$ has an isolated minimum at equilibrium point x^*.*

Assuming that the above conditions of stability are satisfied, the following definitions will give general formulations of Passivity Based Control.

Proposition 8. *(105) Consider the passive system of the form:*

$$\dot{x} = Q(x,u)\frac{\partial V}{\partial x} + \gamma(x)v; y = \gamma^T(x)\frac{\partial V}{\partial x}, \tag{4.4}$$

where, $V(x)$ is a storage function $V(x)$: $V(x^*) = 0$, $x^* \neq 0$ is the steady state value of x and $V(x) > 0$, $Q \prec 0$. Suppose that the model is zero state detectable, then the feedback $v = -C(x,t)y$ with $C(x,t) \geq eI > 0$ and constant e renders $x = x^*$ globally asymptotically stable.

Lemma 3. *Consider the passive system shown in* (4.4)*, which with some algebraic manipulation can be written in form:*

$$\dot{\bar{x}} = \bar{Q}(\bar{x},\bar{u})\frac{\partial \bar{V}}{\partial \bar{x}} + \bar{\gamma}(\bar{x})\bar{v}; \bar{y} = \bar{\gamma}^T(\bar{x})\frac{\partial \bar{V}}{\partial \bar{x}}, \tag{4.5}$$

where $\bar{x} = x - x^d$, x^d is the desired state, $\bar{V}$ is the desired storage function: $\bar{V} \geq 0$ with minimum at $\bar{x} = 0$ i.e. $x = x^d$. If $\bar{Q} \prec 0$ then the system (4.5) *will be passive and the feedback $\bar{v} = -C\bar{y}$ with $C \geq eI > 0$ and constant e renders $x = x^d$ globally asymptotically stable.*

A geometric formulation of passive systems and feedback equivalence to passivity was given in the work of (18). Non-trivial applications of passivity-based

control, to the areas of robotics, synchronous motors and power electronics, have been given by Ortega and his co-workers over the years ((40), (85), (87), (88), (89), (90), (91)). In Energy Based Control, the storage functions and desired storage functions used in PBC will be the energy functions and the desired energy functions respectively. The interconnection matrices will be dependent on the system characteristics and will follow the mentioned conditions if the system is physical and energy dissipating. So, Energy Based Control approach hinges upon the fundamental and universal property of passivity and can be extended to many applications.

4.3 Energy Based Control Tools

The Energy Based Control approach is a very appealing approach to design feedback controllers for nonlinear systems which provides by construction of energy function as a storage function for the closed-loop equilibrium. Energy Based Control has shown to be very powerful to design robust controllers for physical systems described by Euler-Lagrange (EL) equations of motion. Different energy based control tools or techniques were developed to incorporate energy in monitoring and stability of the system. Some of the major techniques are as follows:

4.3.1 Energy Balancing Control

Proposition 9. *(88) Consider a system with states $x \in R^n$, inputs $u \in R$ and outputs $y \in R$. The map $u \to y$ is passive if there exists an energy function $H(x)$, bounded from below and we set $u = 0$, $H(x(t))$ will decrease in presence of dissipation and the system will eventually reach the point of minimum energy. The rate of convergence can be increased if we extract energy from the system with $u = -Ky$ with $K^T = K > 0$ a so called damping injection.*

4.3.2 Energy Shaping Control

Energy balancing will guide the system towards its minimum energy level. However, the minimum of the energy of the system is not a very interesting point from an engineering perspective. Energy shaping control deals with such situations.

Proposition 10. *(92) Consider a passive system of the form:*

$$\begin{aligned} \dot{x} = f(x) + g(x)\,u, x \in R^n, u \in R \\ y = h(x), y \in R, y \neq 0, \end{aligned} \tag{4.6}$$

with energy function $H(x)$. If there exists a vector function $\beta(x)$ such that the matching equation:

$$\left(\frac{\partial H_a}{\partial x}\right)^T (f(x) + g(x)\,\beta(x)) = -h^T(x)\,\beta(x) \tag{4.7}$$

can be solved for $H_a(x)$, where the desired energy function $H_d(x) : H_d(x) = H(x) + H_a(x)$ has a minimum at desired steady state x^d, then the control action $u = \beta(x) + v$ is an energy balancing PBC.

Setting $v = 0$ will assure that the x^d is a stable equilibrium with difference between the stored and the supplied energies constituting a Lyapunov function.

There is no damping injection in energy shaping PBC, hence the control strategy depends only on the natural dissipation of the system. The next section will introduce the damping injection in the energy shaping control.

4.3.3 Energy Shaping plus Damping Injection Control

This control methodology introduce damping injection with energy shaping in order to direct system towards desired path by inducing damping and the system should not rely on natural damping only.

Proposition 11. *(125) Consider the passive system shown in Equation 4.6, If there exists a vector function $\beta(x)$ such that equation:*

$$H_d(x(t)) - H_d(x(0)) = \int_0^t v^T(s)\,z(s)ds - d_d(x,t) \tag{4.8}$$

can be solved, where $H_d(x)$ is the desired total energy function having a minimum at desired state x^d, $d_d(x,t) \geq 0$ is the desired damping and z (which may be equal to y) is the new passive output, then the control action $u = \beta(x) + v$ is an energy balancing PBC.

4.3.4 Power Shaping Control

Energy-balancing stabilization cannot be applied to some systems such as systems with pervasive dissipation which refers to the existence of dissipative elements

whose power does not vanish at the desired equilibrium point. To overcome this obstacle, a power shaping control tool was introduced in (86). The starting point for the method is a description of the system using Brayton-Moser equations (13):

$$Q(x)\dot{x} = \nabla P + G(x)u \tag{4.9}$$

where $Q : R^n \to R^{n\times n}$ is a full rank matrix and $P : R^n \to R$ is the mixed potential which has units of power.

Proposition 12. *(44) Consider the general nonlinear system shown in Equation 4.6. Assume, there exists a matrix $Q : R^n \to R^{n\times n}, |Q| \neq 0$, that solves the the PDE $\frac{\partial}{\partial x}(Q(x)f(x)) = \left[\frac{\partial}{\partial x}(Q(x)f(x))\right]^T$ and verifies $Q + Q^T \leq 0$ and there exists a scalar function $P_a : R^n \to R$ verifying $g^{\perp}Q^{-1}\nabla P_a = 0$, where $g^{\perp}(x)$ is a full- rank left annihilator of g where $P_d(x) = \int [Q(x)f(x)]^T dx + P_a(x)$ and x^d is an isolated minimum of P_d and the large invariant set contained in the set $\left\{x \in R^n, \nabla P_d\left(Q^{-1} + Q^{-1T}\right)\nabla P_d = 0\right\}$ is x^d. Under these conditions, the control law:*

$$u = \left(g^T Q^T Q g\right)^{-1} g^T Q^T \nabla P_a \tag{4.10}$$

ensures x^d is an asymptotically stable equilibrium with Lyapunov function (power function) P_d.

The resulting controller is power-balancing, in the sense that the power function assigned to the closed-loop system is the difference between the total power of the system and the power supplied by the controller. Also, in contrast with energy based control, the power of dissipative element in power balancing can always be brought to zero at equilibrium.

4.3.5 Energy Shaping via Control by Interconnection

So far, to regulate the behavior of passive systems, it is natural to adopt a Passivity-Based Control (PBC) perspective, where the control objectives are achieved shaping the energy function and adding dissipation. In control by interconnection (CBI), the controller is another passive system connected to the plant through a power preserving interconnection to add up their energy functions, while in standard PBC energy shaping is achieved by static feedback. The control by interconnection imposes a severe restriction on the plant dissipation

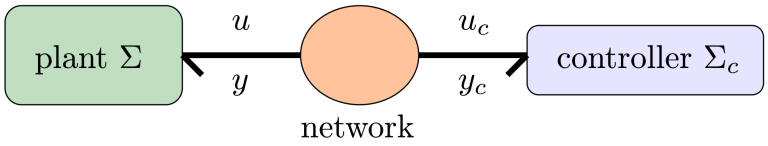


Figure 4.1: Block Diagram of CBI (9)

structure that obstructs its practical application (90). The configuration used by CBI is shown in Figure 4.1. The interconnection is power continuous if:

$$u_c^T(t)\,y_c(t) + u^T(t)\,y(t) = 0 \quad \forall t \tag{4.11}$$

Proposition 13. *(9) Assume, there is an interconnection with extra inputs v and v_c in the plant and the controller respectively such that $u \to u + v$, $u_c \to u_c + v_c$. Let plant and controller have state variables x and ξ, and let the maps $u \to y$ and $u_c \to y_c$ be passive with energy functions $H(x)$ and $H_c(\xi)$ respectively. Then the map $(v, v_c) \to (y, y_c)$ is passive for the interconnected system, with energy function $H_d(x,\xi) = H(x) + H_c(\xi)$.*

If the energy function of the resulting system doesnot depend only on x then the dynamics are restricted to a submanifold of the (x,ξ) space parametrized by x: $\xi = F(x) + K$ and dynamically invariant: $(\partial F \dot{x})_{\xi = F(x)+K} = 0$.
The analytical control results shown in different Energy Based Control tools above, although quite general, are of limited interest. The reason is that the models do not reveal the role played by the energy function in the system dynamics. Hence it is difficult to incorporate prior information to select an input function to solve the partial differential equation.
However, Port-Hamiltonian modeling deals with these issues as explained in previous chapter. PH models give physical insight to the passive system by properly interconnecting a set of multi-dimensional elements, each of them characterized by a particular energetic property. Since every PH system is passive, an immediate consequence is that control techniques already developed for the stabilization of passive systems can be easily extended and specified in order to deal with PH systems. This came out to be a good point for the development of control strategies that can be applied in order to solve the regulation (and, eventually, the tracking) problem for Port-Hamiltonian systems. Improvements are possible since the PH formulation of a physical systems provides a deep insight on the

structural properties of the system itself. If the controller is developed in order to properly modify these inner characteristics of the plant, then more complex and powerful control schemes can be implemented, whose behavior can be suitable for (nice) physical interpretations (75). The following control algorithms are based on PH models.

4.3.6 Casimir Functions and Control by Interconnection

Instead of solving the control by interconnection problem through a general model, it is better to formulate the systems in PH form.

Definition 5. *(75) Consider the PH system given by:*

$$\dot{x} = (J(x) - R(x))\frac{\partial H}{\partial x} + gu, \tag{4.12}$$

$$y = g^T \frac{\partial H}{\partial x}, \tag{4.13}$$

where x is the state and $H(x)$ is the storage function called Hamiltonian. u, y are port power variables and their duality product defines the power flows exchanged. The two interconnection matrices are: $J(x)$is a skew-symmetric matrix and g. $R(x)$ is a symmetric dissipation matrix. Assume that the controller can be defined in PH form as:

$$\dot{\xi} = (J_c(\xi) - R_c(\xi))\frac{\partial H_c}{\partial \xi} + g_c(\xi)u, \tag{4.14}$$

$$y_c = g_c^T \frac{\partial H_c}{\partial \xi}. \tag{4.15}$$

With the power preserving, standard negative feedback interconnection $u = -y_c$, $u_c = -y$, one gets

$$\begin{bmatrix} \dot{x} \\ \dot{\xi} \end{bmatrix} = \begin{bmatrix} J - R & -g(x)\, g_c(\xi)^T \\ g_c(\xi)\, g(x)^T & J_c - R_c \end{bmatrix} \begin{bmatrix} \partial H_d(x) \\ \partial H_d(\xi) \end{bmatrix}, \tag{4.16}$$

where $H_d(x,\xi) = H(x) + H_c(\xi)$ For the invariant manifold of the form:

$$C_K(x,\xi) = F(x) - \xi + K, \tag{4.17}$$

$\dot{C}_K = 0$ *yields,*

$$\begin{bmatrix} \partial F & I_m \end{bmatrix}^T \begin{bmatrix} J - R & -g(x)\, g_c(\xi)^T \\ g_c(\xi)\, g(x)^T & J_c - R_c \end{bmatrix} = 0, \tag{4.18}$$

Function $C_k(x,\xi)$ such that F satisfies the PDE on $C_k = 0$ are called Casimirs.

It appears that no Casimir functions exist in presence of dissipation, so dissipation is only admissible for those coordinates which do not require energy

shaping. For regulation problems in mechanical systems, where the state consists of positions and velocities, dissipation only appears associated to the velocities, while energy shaping is necessary only in the position part, since the kinetic energy already has the minimum at the desired point (that is, at velocity equal to zero).

4.3.7 Interconnection and Damping Assignment-Passivity Based Control (IDA-PBC)

The previous section has exposed some shortcomings of the passivity based control method by means of control as interconnection. One can get a method with more freedom if not only the energy function is changed but also the interconnection J and dissipation R. The key idea is that using the Hamiltonian framework, solving the PDE associated to the energy-balance equation can be done with an appropriate selection of the interconnection J and dissipation R matrices and the energy function H of the desired closed-loop system (which will be denoted with J_d, R_d and H_d).

Definition 6. *(91) Consider the dissipative Port-Hamiltonian system given in Equation 4.12 and 4.13 and a desired equilibrium point x_d. Assume there are matrices $J_d = -J_d^T$, $R_d = R_d^T \geq 0$ and a smooth function H_d such that it verifies the equation:*

$$\dot{x} = (J_d - R_d)\frac{\partial H_d}{\partial x}. \tag{4.19}$$

The control input $u = \beta(x)$

$$\beta(x) = \left(g^T g\right)^{-1} g^T \left((J_d - R_d)\frac{\partial H_d}{\partial x} - (J - R)\frac{\partial H}{\partial x}\right) \tag{4.20}$$

is asymptotically stable.

It is thus clear that the problem is how to solve the *matching equation*:

$$(J(x) - R(x))\frac{\partial H}{\partial x} + gu = (J_d - R_d)\frac{\partial H_d}{\partial x} \tag{4.21}$$

Notice that there is a huge amount of freedom in selecting J_d, R_d and H_d satisfying the previous assumptions. Several techniques are being use in different control problems:

1) **In Non-Parameterized IDA** the structure and damping matrices ($J_d(x)$ and $R_d(x)$) are fixed, the matching equation is pre-multiplied by a left annihilator of $g(x)$ and the resulting PDE in H_d is then solved.

2) **In Algebraic IDA** the desired Hamiltonian function H_d is first selected and then the resulting algebraic equations are solved for J_d and R_d.

3) **In Parameterized IDA** the knowledge of a priori structure of the desired Hamiltonian is used to obtain a more easy to solve PDE, giving constraints on J_d and R_d.

4) **In Interlaced Algebraic-Parameterized IDA** the PDE is evaluated in some subspace and then matrices J_d, R_d are found which ensure a valid solution of the matching equation.

There is not a best method to solve the matching equation. Each control problem requires an individual study to find out which of the above strategies provides an acceptable solution of the matching equation.
IDA-PBC can prove very handy for controlling the systems modeled in Port-Hamiltonian form as it is utilising the structural properties of the system as well. IDA-PBC is one such technique which can be derived straight away from the PH models and in comparison with what is more logical and can be interpreted physically. IDA-PBC is very interesting and sound because it is actually overcoming the short comings of other PBC techniques such as pervasive dissipation etc. and one can think on energy terms while choosing the control action unlike the nonphysical techniques.

Proposition 14. *A general IDA-PBC Controlled Port-Hamiltonian system:*

$$\dot{x} = -\left[J_d - R_d\right] f\left(\frac{\partial H_d}{\partial x}\right), \tag{4.22}$$

guarantees stability at desired steady state point x_d if it is zero-state detectable and:

I $H_d(x)$ has an isolated minimum at x_d

II $-((J_d - R_d) + (J_d - R_d)^T)$ is negative definite.

4.3.8 Energy Based Control Using Graphical Tools

4.3.8.1 Bond Graph

The Bond Graph approach is used for the analysis of structural properties of linear multivariable time invariant systems (24) and can be said as a graphical approach towards control. Physical model based control using Bond Graph has been first suggested by Karnopp (64). (46) represented controllers by Bond Graph and thus designed in the graphical domain. In (48), the control was taken to the next level by using Bond Graph in monitoring and interconnecting small subsystems of a big system. It allows the controller to have access to the measurement of any variable within the system, but can only manipulate variables corresponding to physical sources present in it. In (83), an augmented Bond Graph model is obtained associated with the optimal control problem. This augmented Bond Graph, consisting of the original model representation coupled to an optimizing Bond Graph directly provides the solution of the optimal control problem cutting the analytical steps needed to follow for such problems. The advantage of working in the (physical) Bond Graph domain is that a clear physical interpretation can be given to each controller coefficient.

4.3.8.2 Energetic Macroscopic Representation

The other graphical control tool is control through Energetic Macroscopic Representation (EMR). The control structure of a system is based on inversion based control theory, as for the Causal Ordering Graph (53), because the control has to define the appropriated inputs to apply to the system from the desired output. Because the derivative causality is forbidden, a direct inversion of time-dependence relationships is not possible. An indirect inversion is thus made using a controller and measurements. These inversion rules then extended to EMR. EMR has been devoted to modeling of electro-mechanical systems so far and not used on chemical and biochemical systems.
The graphical control techniques i.e. BG and EMR are also not physical in the sense that they are based on inversion principles and partly use the structure of system to monitor and control. These graphical tools are physical for modeling but not much physical in control.

4.4 Energetic Control of Continuous Chemical and Biochemical Reactors: A review

Energy Based Control techniques discussed above originate from the Energy Based Models only. EBM's are Passivity Based Models with more physical storage functions. In Energy Based Modeling of chemical systems, the storage functions used in passivizing are the various energy functions belonging to chemical thermodynamics, for example Internal Energy, Enthalpy, Entropy, Gibbs Free Energy, etc. Although Internal Energy represents the total energy of chemical systems, it has been difficult to physically fit the Internal Energy function in the structure of Passivity Based Models due to complexity of the relation. So, researchers tried other energy functions and some physical functions (which will not be called energy functions) to render the system passive and then tried to give the physical angle to the system based on the chosen storage function.
In case of bioprocess models, it is not possible to assign a true energy function for the passivization because of lack of knowledge about kinetics and how energy flows. These systems are modeled using random storage functions which may or may not explain the physical phenomena of the process e.g. quadratic functions etc.
Bond Graph has also been used for chemical and biochemical systems for control as well as issues of controllability, parameter estimation of kinetic parameters of bioprocess systems. The review of Energy Based modeling of chemical systems was discussed in previous chapters. Based on these models, the Energy Based Control strategies have been designed.

4.4.1 Bond Graph Control

There has been very little work in the actual control of continuous reactors using Bond Graph but rather on the issues related to control. In (47), a physical interpretation of the inverse dynamics of linear and non-linear systems is shown using a Bond Graph in which the BG itself gives information about system zeros in case of linear systems and system zero dynamics in case of nonlinear systems. The methodology was applied on chemical systems and yielded physical insight about the inverse dynamics and controllability of the control system with respect

to the possible input/output pairings.
The physical model based control, which includes a Bond Graph, has also been used on continuous tank reactors for the determination of the configuration of the control system in the sense of determining inputs, outputs and feed-forward terms but not feedback control (20). As mentioned earlier, Bond Graph works better on the issues related to control such as parameter estimation, controllability, observability. (116) has done some online estimation of waste water bio degradation process. (100) used pseudo Bond Graph to design PI observers of a CSTR. (130) proposed concepts on control design and fault detection and isolation of many chemical and biochemical processes using Bond Graph framework.

4.4.2 Energetic Control of Continuous Chemical Systems

As mentioned, in order to obtain a physical control there is a need to consider a physical storage function. The complexity of thermodynamic relations between the system states (concentration, temperature etc.) and energy functions (Internal Energy etc.) has forced researchers to opt for nonphysical storage functions for control. Also, the reactions taking place in a CSTR have been the subject of a large number of stability and advanced control studies which was taken into account by system theory. These systems are nonlinear and exhibit multiple steady states and complex dynamic behavior. All this leads to nonphysical control algorithms. The theoretical issues in connecting passivity and thermodynamics have been discussed in (2). So, the control strategy can be divided into two types:

4.4.2.1 Control Using Artificial Energy Functions

Most of the researchers in the Passivity Based Control of chemical systems have control strategies involving energy shaping with damping injection or IDA-PBC control through PH models. The researchers which opt for easy to formulate but nonphysical storage functions (Lyapunov functions) for chemical processes have mostly chosen quadratic functions of chemical concentrations for isothermal systems and some complex sum of quadratic functions of concentration and temperature. For non-isothermal systems, the storage function consists of quadratic temperature terms. (33) also used quadratic function for a CSTR but formulated

the chemical system in PH form by artificial splitting of matrix into interconnection and damping matrices and performed IDA-PBC control. With IDA-PBC, it was easy to stabilize and passify these kind of nonlinear systems. (105) used quadratic function of concentration for isothermal systems and performed energy shaping with damping injection control with desired storage function as $(x - x_d)^2/2$, where x_d is the desired concentration. It proves that Passivization is achievable for mono variable system by means of control input space by keeping the energy storage function of the system of strictly relative degree one in the region of interest. Passivity-based regulation can be easily compared against linearization techniques in terms of the controller complexity. (106) also applied IDA-PBC on a multiple-input/multiple-output non-isothermal continued stirred tank reactor that exhibit non minimum phase behavior. An additional degree of freedom is introduced in the controller design by the use of non-exact matching closed-loop storage functions. By a proper closed-loop interconnection assignment, the proposed controller achieves total decoupling between outputs and since no inversion of the process dynamics is made in the design, it is equally applicable to minimum phase and non minimum phase systems. Power shaping control has also been considered in (72) and (36). The potential function which is supposed to have the units of power was a quadratic term that is linked to the convection phenomena (Temperature change) and a more complex term that is linked to the reaction kinetics. Although the potential function has a physical meaning for the Brayton-Moser formulation of electrical or mechanical systems, the physical interpretation of the potential function in a continuous reactor has still to be found.

4.4.2.2 Control Using True Energy Functions

(56), (58) used Gibbs Free Energy, square of chemical affinity for isothermal CSTR and Ectropy (- Entropy) for non-isothermal case but performed IDA-PBC with availability function as it induced smoother variations of the control variable. (57) illustrated his theory of physical Lyapunov functions on the control of a multiple steady state chemical reaction in a CSTR. They used a part of availability function as a Lyapunov function and derived asymptotically and exponentially stable control laws. (2) have explored this research area and resulted

in very insightful works on the control design of process systems to develop stabilizing controllers and to derive general structural stability conditions for chemical process networks. In their paper, they used the first and second laws of thermodynamics to motivate a theory for nonlinear process control and promoted Helmholtz Free Energy as a storage function for zero state detectability and stability of chemical processes. (52) used a nonlinear extension of the curvature of the entropy function as it has been proposed within the framework of passivity theory for processes. (37) took multiple steady states and complex dynamic behavior of a CSTR into account to address the stability issue by using a number of thermodynamics based approaches. It appears that even for simple reactions, analysis and control issues using thermodynamic properties are still open problems. (95) used entropy as a legitimate Lyapunov function candidate to derive stability conditions for kinetic networks in closed systems. They also formulated a local Hamiltonian description of the open reaction kinetic system in the reaction space. Passivity based methods are given for the systematic design of globally stabilizing feedback controllers in both the concentration space and a the reaction space. (45) showed that Internal Entropy production can be used as a storage function to emphasize the passivity properties of open systems. They formulated a port-controlled Hamiltonian representation of this class of systems and did the stability analysis of chemical reactors based on the internal entropy production. (38) used Entropy function while performing power shaping control which is not a power function but makes more sense physically.

4.4.3 Biochemical systems

Though microbial kinetics is not known, (54),(126) made the analogy of microbial kinetics with chemical kinetics. They tried to formulate the change in Gibbs Free Energy Function during a microbial reaction. These formulations will be pseudo-energetic only as there is no physical insight into the mechanism of reactions. Passivity based control of isothermal continuous bioreactors has never been done using Gibbs Free Energy function. (41) have proposed a systematic design of a real PH structure with an efficient control design. However, the energy function is given a quadratic form, and the PH model is given by an artificial decomposition, as explained in the literature review of previous chapter, of the

nonlinear model without any real world insight. They addressed the need to attach some logical strings from the passivity based model to the control design applying a useful change of coordinates. (120) designed an output feedback passivity controller for Microalgae cultivation based on the storage function provided in the work of Fossas (41). In the discrete case, the passivization mode control presents a quick stabilization time and provides sufficient precision for the tolerance margins used in bioreactors. (33) used quadratic function of states to form PH system and then performed IDA-PBC Control for the basic Monod kinetics. It was also shown that with IDA-PBC design, the stability analysis may increase significantly for larger and more complicated model equations. With simple ideas and physical considerations it is not only possible to stabilize nonlinear systems but also to passify them. This passivity-based approach to nonlinear systems can physically interpret canceling out nonlinearities and assigning high gain feedback. Once a system is passified, passivity-based techniques from the literature can be applied easily.
(61) used total mass of all components in wastewater treatment plant as storage function and proposed dissipative control which comes out to better than proprtional flow control in terms of efficiency in achieving desired state and effectivenss of the dissipative design. In (95), a PBC strategy on Enzyme Reaction networks is used which took stoichiometry into account but with usual reaction rate terms and not physical energy function. Passivity Based Control laws based on the new pseudo-PH formulations were proposed in this paper.

(63) made robust control with L_2 gain of PH systems with quadratic Hamiltonian to impart stability to model uncertainties in a biochemical fermenter model. (72) applied power shaping control and used complex terms involving quadratic functions of states for bioreactors.

4.4.4 Conclusion From Literature Review

BG is being used to make model of the controller which gives a physical angle to the control design issues but BG control has a limitation of using only physical sources present in the system to manipulate control variables. Hence, it is not used much and also not very suitable for complex systems like chemical and biochemical systems. On the other hand, BG gives very easy and physical approach

to the issues of controllability, fault detection etc.
It is also clear that PBC of chemical and biochemical sytems is more suitable from the physical point of view than other non physical control techniques. Also, the stability conditions are easy to derive from PBC. Overall, PBC provides the systematic design of globally stabilizing feedback controllers. Out of different types of PBC techniques for chemical and biochemical systems, IDA-PBC techniques derived from the Port-Hamiltonian models seem the most convenient and able to tackle the issues of pervasive dissipation, damping injection etc. very efficiently. IDA-PBC has been shown to have the ability of physically solving fully actuated non-linear MIMO systems and SISO systems like open chemical systems through various strategies discussed in literature. The main problem of IDA-PBC is in tuning under-actuated MIMO systems (51).
As the physical understanding of the system and control lies in using physical energy function and following the exact structure of the PH form, the basic idea is to find a physical Lyapunov function candidate which can prove the isolated system stability properties and can act as a storage function to emphasize the passivity properties for open systems. It has been really difficult to assign an energy function as storage function for open chemical systems. Specially for non-isothermal systems, it is impossible to formulate the system in a real PH form because of irreversible thermodynamics. Many attempts have been made in recent years to obtain a not pseudo passive or PH formulation for isothermal chemical systems. The chemical and enzyme reactions in closed system have been modeled in PH form by (123), (124) using Gibbs Free Energy function but not extended to open system and not applied to perform PBC or IDA-PBC.
Assigning an energy function to the microbial reaction will not be right because the kinetics is not known and any PH formulation of such systems will be pseudo-physical only, so it is better to create an analogy of energy exchange in chemical reaction with microbial reaction but that will be purely artificial. Though, it will help in better understanding of the system from the control point of view.
In the previous chapter, the physical PH models of open chemical and enzyme reactions at constant temperature were formulated using Gibbs Free Energy and it would be interesting to apply IDA-PBC technique on those models and simulate them with real data.

4.5 IDA-PBC of Open Chemical Reactors

Proposition 15. *Consider the general quasi Port-Hamiltonian form of a CSTR with dilution rate D:*

$$[\dot{x}] = -[K]\exp\left[f\left({}^{\partial G}/_{\partial x}\right)\right] + (D(x_{in} - x)). \tag{4.23}$$

The IDA-PBC controlled equation for the PH form of the CSTR can be written as:

$$\dot{x} = -[J_d - R_d]\, f\left(\frac{\partial H_d}{\partial x}\right), \tag{4.24}$$

where the net input $D(x_{in} - x)$ will be equal to:

$$D\,(x_{in} - x) = -\,(J_d - R_d)\, f\left(\frac{\partial H_d}{\partial x}\right) + (K)\, f\left(\frac{\partial G}{\partial x}\right) \tag{4.25}$$

Proof: *On Matching equation (4.23) with (4.24), the value of net input will be same as (4.25).*

The important task is to choose the desired Hamiltonian and assign values to the elements of desired interconnection J_d and dissipation R_d matrices. The general Hamiltonian and desired Hamiltonian for IDA-PBC of continuous chemical process chosen in this thesis are:

$$H = G = \sum\left(zRTx\log\frac{x}{x^*} - zRT(x - x^*)\right) + C_o, \tag{4.26}$$

$$H_d = \sum\left(zRTx\log\frac{x}{x^d} - zRT(x - x^d)\right) + C_o. \tag{4.27}$$

$z = \pm 1$.

The compulsory conditions of stability and passivity put some constraints in choosing them will be discussed in the next section.

Passivity and Stability Conditions

Proposition 16. *Consider the PH and PCH form for a chemical process in continuous reactors given in (4.23) and (4.24) respectively. The PH system is said to be passive and asymptotically stable towards x^* if the square matrix of $-[K]$ is negative definite and H is minimum at steady state point x^*. For the input given in (4.25), the PCH system is said to be stable if H_d is minimum at desired steady state point x_d and for a system with zero input, the time derivative of Hamiltonian $\frac{dG}{dt} \leq 0$.*

Proof: *With reference to conditions i, ii and I, II given above for the general dissipative PH and PCH systems respectively and comparing the equations*

of General PH and PCH model with chemical process model, the negative definiteness of $-K$ and $-(J_d - R_d)$ can be justified. Now, K is the diagonal matrix of equilibrium rate constants, rate constants are positive , hence $-K$ is negative definite. Also, the elements of $(J_d - R_d)$ are chosen such that J_d and R_d satisfies the necessary conditions. (4.26) and (4.27) are chosen such that $H(x)$ will have its minimum at x^* and the chosen function H_d will be strictly minimum at desired concentration x_d respectively.
Lastly, the time derivative of Hamiltonian G corresponding to respective models with zero input yields the following dissipation equality:

$$\frac{dG}{dt} = -\frac{\partial G}{\partial x} K f\left(\frac{\partial G}{\partial x}\right).$$

Hence, for the system to be passive one needs $-\frac{\partial G}{\partial x} f\left(\frac{\partial G}{\partial x}\right) \leq 0$. On substitution (Section 4.2 in (124)) and expansion:

$$\frac{dG}{dt} = -\sum \left[m_p - m_r\right] \left[exp\left(\mu_p\right) - \exp\left(\mu_r\right)\right] K \leq 0.$$

Here, m_p is the chemical potential of products and m_r is the chemical potential of the reactants where the expression of chemical potential m is:

$$m = \frac{\partial G}{\partial x} = RT \log\left(\frac{x}{x^*}\right).$$

Hence, the system is passive and asymptotically stable towards $x = x^*$ and in the similar way stability conditions can be proved at the desired $x = x_d$ using H_d.

4.6 IDA-PBC of SPH Systems

Proposition 17. *(78) For a continuous reactor at constant temperature and pressure with concentration inflow (x_{in}), outflow (x_{out}), a constant dilution rate D, the SPH form can be written as:*

$$\dot{x} = -S_t K \exp\left(f\left(\frac{\partial G}{\partial x}\right)\right) + D(x_{in} - x_{out}) \tag{4.28}$$

$$y = \frac{\partial G}{\partial x} = -T\frac{\partial S_{sys}}{\partial x}. \tag{4.29}$$

$\hat{S}_{sys}$ is the entropy of the system. Assume that the desired steady state point is x_d and there are matrices $J_d = -J_d^T, R_d = R_d^T \geq 0$ and a smooth function H_d in a closed-loop system with input $D(x_{in} - x) = \beta(x)$, such that:

$$\beta(x) = -S_t\left(\left(J_d - R_d\right) f\left(\frac{\partial H_d}{\partial x}\right) - K f\left(\frac{\partial G}{\partial x}\right)\right) \tag{4.30}$$

leads to an asymptotically stable IDA-PBC design of the form (4.30)

Proof: *Comparing the IDA-PBC design of SPH system:*

$$\dot{x} = -S\,(J_d - R_d)\,f\left(\frac{\partial H_d}{\partial x}\right), \tag{4.31}$$

with (4.28) *and using some mathematical manipulations, the value of* $\beta(x)$ *shown in in (4.28) can be obtained.*

Passivity and Stability of SPH Systems

The Stoichiometric matrix describes the basic chemical structure of the reactions. It is necessary to introduce the stoichiometric system in order to account for the passage from the concentration space to the reaction space, which governs the inner dynamics. Hence, the stoichiometric matrix does not influence the passivity and stability properties. Therefore, the properties of PH systems of open chemical systems can be applied on SPH systems.

4.7 IDA-PBC of RPH Systems

Proposition 18. *(78) Consider the general Reaction PH (RPH) form of a CSTR:*

$$\underbrace{\dot{\xi}_o}_{\substack{\text{Reaction}\\ \text{state space}}} = \underbrace{-K f\left(\frac{\partial G}{\partial \xi}\right)}_{\substack{\text{Reaction}\\ \text{rate}}} + \underbrace{(w_{in} - w)}_{\substack{\text{Reaction}\\ \text{input}}}. \tag{4.32}$$

Here, $(w_{in} - w) = {S_t}^{-1}(D(x_{in} - x))$, ${S_t}^{-1}\dot{x} = \dot{\xi}_o$, ${S_t}^{-1}$ *is the inverse of stoichiometric matrix* S_t. *, Assume there are matrices* $J_d = -J_d^T, R_d = R_d^T \geq 0$ *and a smooth function* H_d *in a closed-loop system with input* ${S_t}^{-1}D(x_{in} - x) = \beta(x)$, *such that:*

$$\beta(x) = -(J_d - R_d)\,f\left(\frac{\partial H_d}{\partial \xi}\right) + K f\left(\frac{\partial G}{\partial \xi}\right) \tag{4.33}$$

approach asymptotically towards the desired steady state point ξ_d .

Proof: *Using IDA-PBC design of the form:*

$${S_t}^{-1}\dot{x} = -\,(J_d - R_d)\,f\left(\frac{\partial H_d}{\partial \xi}\right). \tag{4.34}$$

and comparing (4.34) *with RPH form shown in* (4.32)*, the value of* $\beta(x)$ *shown in (4.32) can be obtained after some mathematical manipulations.*

The stability and passivity conditions of concentration space are also valid for the reaction space.

4.8 PH Formulation and IDA-PBC of Enzymatic Hydrolysis of Cellulose in an Open Reactor

Application to a real system is very important to validate the model. At first, this section is explaining about the problem in details and the assumptions used. Then the simulations based on real data are presented.
Biological conversion of fermentable reducing sugars to fuels and chemicals offers the high yields of these products at low costs (43), (103). Enzymatic hydrolysis of cellulosic material is a way of producing these sugars. However, commercial application of enzymatic cellulose hydrolysis may be the most difficult step in this process due to lack of an effective reactor system to cater for the interfacial heterogeneous catalysis and complex reaction kinetics.
Earlier, hydrolysis process used to take place in conventional batch reactors (50). (42) Recent modifications such as using purpose-built integrated membrane reactors featuring simultaneous and continuous product removal have shown promising results. The integrated operation improves reaction kinetics, reducing enzyme inhibition and immobilization of enzymes which leads to high product yield.
Kinetics of cellulose hydrolysis also involves action of several cellulase components. Cellulose materials are insoluble, structured, and comprised of multicomponents which arise complexities like composition of cellulosic materials, the mechanism of the enzymes and inhibition by intermediates and end product. A lot of research has been done but the current understanding the overall mechanism is still limited.
The mechanism given in (42) is being taken and modeled and then IDA-PBC is applied. Figure 4.2 is showing the shcematic view of the process.

The integrated membrane reactor is assumed similar to a continuous stirred tank reactor. Also, the perfect mixing in the reactor and zero rejection of reducing sugar by the membrane assures that outgoing concentration of reducing sugar and substrate is same as the concentration inside the reactor.

4.8.1 Reaction Mechanism

There have been plenty of assumptions made before finally arriving to the mathematical representation of hydrolysis process ((42)). The assumptions are:

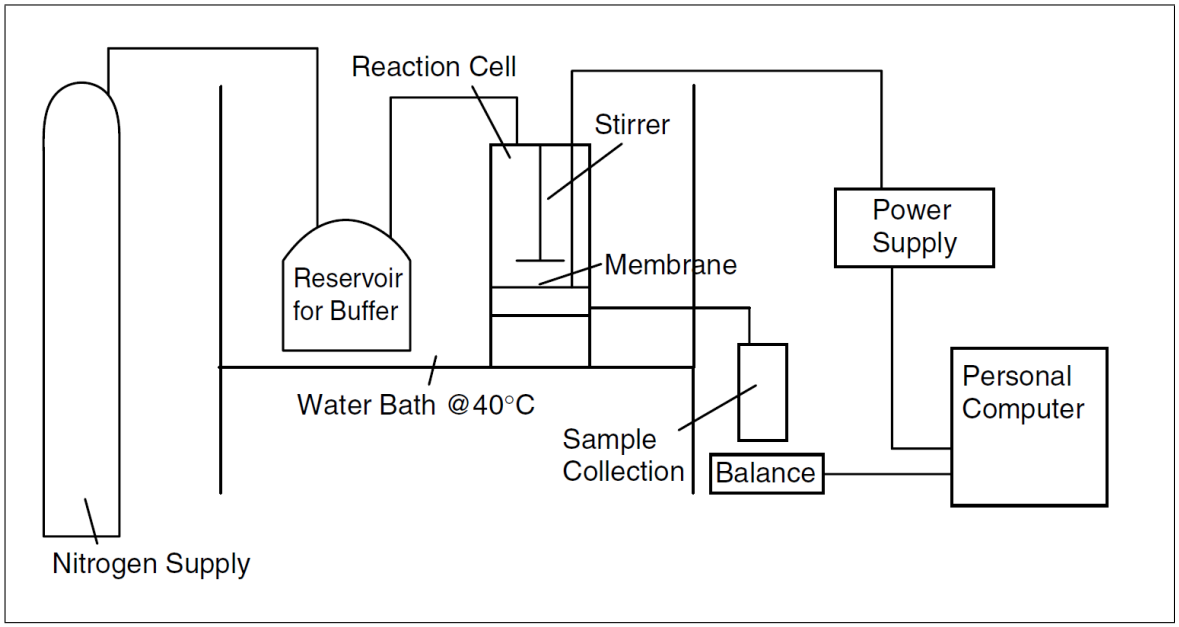


Figure 4.2: Schematic Flow Diagram of the Integrated Membrane Reactor System (43)

1) Multi components of Enzyme E are combined and assumed to have a unified catalytic effect and multiple reducing sugars produced are also supposed as single product P.

2) The different reaction intermediates are divided in to two types: Enzyme-substrate complexes E_{Sc} which leads to final product formation and other act as inhibitors E_{Sx}.

3) The substrate concentration taken in to account will be measured according to the surface concentration of active cellulose enzyme.

4) Final product is also inhibiting enzyme through a reversible reaction leading to EP complex.

5) All the reactions are reversible.

6) The operation is assumed to be smooth and rate of change of interfacial inert and appearance of new cellulose is ignored.

The following set of reactions represent the series of events in the process:

$$E + S_c \underset{k_{Sc2}}{\overset{k_{Sc1}}{\rightleftharpoons}} ES_c, E + S_x \underset{k_{Sx2}}{\overset{k_{Sx1}}{\rightleftharpoons}} ES_x,$$

$$ES_c \underset{k_{P2}}{\overset{k_{P1}}{\rightleftharpoons}} E + P, E + P \underset{k_{EP2}}{\overset{k_{EP1}}{\rightleftharpoons}} EP.$$

E is the cellulase system, S_c is cellulose, S_x is cellobios and P is glucose. k_{Sc1} and k_{Sc2} are the primary rate constants for the reversible formation of the active ES_c intermediate, k_{Sx1} and k_{Sx2} are the primary rate constants for the reversible formation of the non-productive ES_x complex, k_{P1} and k_{P2} are the rate constants of reversible product formation, and k_{EP1} and k_{EP2} are the forward and reverse reaction rate constants for the formation of the EP complex.

The kinetics of the process is seen to have followed the basic Michaelis-Menten (MM) kinetics with no inhibition to the initiation reaction forming the complex ES_c, which in this case will be helpful to find the correct values of steady state concentrations. So, the basic MM kinetics leads to the following equality for the closed system:

$$k_{Sc1} x_E x_{S_c} = k_{Sc2} x_{ES_c} \tag{4.35}$$

Also, the total enzyme concentration E^{tot} at any time will be:

$$E^{tot} = x_E + x_{ES_c} + x_{ES_x} + x_{EP} \tag{4.36}$$

The mass action reaction rates for the four reactions are as follows:

$$r_1 = k_{Sc1} x_E x_{S_c} - k_{Sc2} x_{ES_c}, \tag{4.37}$$

$$r_2 = k_{Sx1} x_E x_{S_x} - k_{Sx2} x_{ES_x}, \tag{4.38}$$

$$r_3 = k_{P1} x_{ES_c} - k_{P2} x_E x_P, \tag{4.39}$$

$$r_4 = k_{EP1} x_E x_P - k_{EP2} x_{EP}. \tag{4.40}$$

In terms of steady state concentrations, the rate equations become:

$$r_1 = k_1 \left(\frac{x_E}{x_E^*} \frac{x_{S_c}}{x_{S_c}^*} - \frac{x_{ES_c}}{x_{ES_c}^*} \right), \tag{4.41}$$

$$r_2 = k_2 \left(\frac{x_E}{x_E^*} \frac{x_{S_x}}{x_{S_x}^*} - \frac{x_{ES_x}}{x_{ES_x}^*} \right), \tag{4.42}$$

$$r_3 = k_3 \left(\frac{x_{ES_c}}{x_{ES_c}^*} - \frac{x_E}{x_E^*} \frac{x_P}{x_P^*} \right), \tag{4.43}$$

$$r_4 = k_4 \left(\frac{x_E}{x_E^*} \frac{x_P}{x_P^*} - \frac{x_{EP}}{x_{EP}^*} \right). \tag{4.44}$$

Here, $k_1 = {}^{k_{Sc1}}/_{k_{Sc2}}$, $k_2 = {}^{k_{Sx1}}/_{k_{Sx2}}$, $k_3 = {}^{k_{P1}}/_{k_{P2}}$ and $k_4 = {}^{k_{EP1}}/_{k_{EP2}}$. For the state space of concentrations in this order:
$[x] = \begin{bmatrix} x_E & x_{S_c} & x_{ES_c} & x_{S_x} & x_{ES_x} & x_P & x_{EP} \end{bmatrix}^T$, Stoichiometric matrix S_t will be:

$$S_t = \begin{bmatrix} -1 & -1 & 1 & -1 \\ -1 & 0 & 0 & 0 \\ 1 & 0 & -1 & 0 \\ 0 & -1 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & -1 \\ 0 & 0 & 0 & 1 \end{bmatrix}. \tag{4.45}$$

Its inverse for the reaction space is:

$${S_t}^{-1} = \begin{bmatrix} -1 & 0 & 0 & 0 & 1 & 1 & 0 \\ -1 & 1 & 0 & 0 & 0 & 1 & 0 \\ 1 & -1 & 0 & -1 & 0 & 0 & 1 \\ -1 & 1 & 0 & 1 & 0 & 1 & 1 \end{bmatrix} \tag{4.46}$$

The incidence matrix (B_m) and complex stoichiometric matrix (Z) are as follows:

$$B_m = \begin{bmatrix} -1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & -1 & 1 & 0 & 0 \\ 0 & -1 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & -1 & 1 \end{bmatrix}$$

$$Z = \begin{bmatrix} 1 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

4.8.2 SPH and RPH formulation of Enzymatic Hydrolysis of Cellulose in a Continuous Bioreactor

The SPH form for an open system with dilution rate D and net input as $x_{in} - x$ will be:

$$[\dot{x}]_{7\times1} = -[S_t]_{7\times4} \begin{bmatrix} k_1 & 0 & 0 & 0 \\ 0 & k_2 & 0 & 0 \\ 0 & 0 & k_3 & 0 \\ 0 & 0 & 0 & k_4 \end{bmatrix} [B_m]_{4\times6} \exp\left[[Z]_{6\times7} \frac{1}{RT} \left[{}^{\partial G}/_{\partial x}\right]_{7\times1}\right] + [D(x_{in} - x)]_{7\times1} \tag{4.47}$$

The RPH form can be formulated as:

$$[S_t]^{-1}_{4\times7}[\dot{x}]_{7\times1} = -\begin{bmatrix} k_1 & 0 & 0 & 0 \\ 0 & k_2 & 0 & 0 \\ 0 & 0 & k_3 & 0 \\ 0 & 0 & 0 & k_4 \end{bmatrix} \exp\left[\frac{1}{RT}\left[{}^{\partial G}/_{\partial \xi}\right]_{2\times1}\right] + [S]^{-1}_{4\times7}[D(x_{in} - x)]_{7\times1} \tag{4.48}$$

4.8.3 Interconnection and Damping Assignment-Passivity Based Control of Enzymatic Hydrolysis of Cellulose in a Continuous Bioreactor

Assigning the desired interconnection and damping matrices which also satisfy their structural conditions, the matrices are as follows:

$$J_d = \begin{bmatrix} 0 & x' & y' & z' \\ -x' & 0 & w' & v' \\ -y' & -w' & 0 & t' \\ -z' & -v' & -t' & 0 \end{bmatrix} \tag{4.49}$$

$$R_d = \begin{bmatrix} a' & e' & f' & g' \\ e' & b' & h' & i' \\ f' & h' & c' & j' \\ g' & i' & j' & d' \end{bmatrix} \tag{4.50}$$

The elements of J_d, R_d matrices i.e. $x', y', z', w', y', a', b', c'$ etc. are tuning parameters and are constant values. The IDA-PBC controlled input for the chemical system modeled through SPH form will be:

$$\begin{aligned} D\left(x_{in} - x\right) = \\ -S_t \begin{bmatrix} -a' & x'-e' & y'-f' & z'-g' \\ -x'-e' & -b' & w'-h' & v'-i' \\ -y'-f' & -w'-h' & -c' & t'-j' \\ -z'-g' & -v'-i' & -t'-j' & -d' \end{bmatrix} B_m \exp\left(Z \frac{1}{RT}\left[\frac{\partial G_d}{\partial x}\right]\right) - \\ S \begin{bmatrix} k_1 & 0 & 0 & 0 \\ 0 & k_2 & 0 & 0 \\ 0 & 0 & k_3 & 0 \\ 0 & 0 & 0 & k_4 \end{bmatrix} B_m \exp\left(Z \frac{1}{RT}\left[\frac{\partial G}{\partial x}\right]\right) \end{aligned} \tag{4.51}$$

(4.51) is the generalised control law. The derivation of the control law for this application is shown in section 4.8.4. For a 4×4 $J_d - R_d$ matrix, the constraints of positive definiteness are very complex in which one parameter depending on

the value of many parameters therefore few parameters are assigned 0 value to reduce the complexity maintaining the symmetricity and skew-symmetricity of R_d and J_d matrices. The next section will show the derivation of the relation of the inlet substrate concentration for the case.

4.8.4 Inlet Substrate Concentration Derivation

As it is known that there are only one or two inlet concentrations which can be monitored and also not all the constituents go out. Specially enzymes stay inside the reactor in most of the bioreactions which is the case in this example also therefore equation (4.51) can be reduced to be written in the following form:

$$D\left[x_{in}-x\right]=-S_t\left(\left[J_d-R_d\right]\left[\frac{r_d}{k}\right]-\left[K\right]\left[\frac{r_{eq}}{k}\right]\right) \tag{4.52}$$

Here, $[K]$ is a positive definite matrix of rate constants, r_d and r_{eq} are the rate equations at desired and steady state concentrations respectively. The main concern in this case is to get a relation for the inlet concentration of active cellulose. Solving above equation for $x = Sc$, substituting S_t given in (4.45), the equation formed is as follows:

$$\begin{aligned} D\left(Sc_{in}-Sc\right)=a'\left(\frac{v_{1d}}{k_1}\right)+\left(-x'+e'\right)\left(\frac{v_{2d}}{k_2}\right)+\\ \left(-y'+f'\right)\left(\frac{v_{3d}}{k_3}\right)+\left(-z'+g'\right)\left(\frac{v_{4d}}{k_4}\right)+v_{1eq}, \end{aligned} \tag{4.53}$$

and Sc_{in} will be:

$$\begin{aligned} Sc_{in}=\left(\frac{1}{D}\right)\left(a'\left(\frac{v_{1d}}{k_1}\right)+\left(-x'+e'\right)\left(\frac{v_{2d}}{k_2}\right)+\right.\\ \left.\left(-y'+f'\right)\left(\frac{v_{3d}}{k_3}\right)+\left(-z'+g'\right)\left(\frac{v_{4d}}{k_4}\right)+v_{1eq}\right)+Sc. \end{aligned} \tag{4.54}$$

The next section will show the simulation results of the Enzymatic Hydrolysis of Cellulose based on this control law.

4.8.5 Simulations

There are broadly two control variables, dilution rate and inlet substrate concentration. Only one parameter can be controlled at a time. As there is only one dilution rate in single stream flow, hence it gives only one degree of freedom for the manifold of various parameters to be controlled. There is only one substrate

as inlet in this case therefore the control variable will be either substrate concentration or dilution rate.

The IDA-PBC control simulations are obtained for the desired concentration of reducing sugars. Before it, the steady state concentrations (x_{eq}) are obtained at given initial conditions (x_0) of various constituents taking part in reaction and dilution rate. The values of initial concentration, steady state concentration, desired concentration of all the constituents and dilution rate and rate constants are given in Table 4.1. The desired concentration is chosen from the steady state model for a constant value of inlet substrate concentration. The desired inlet concentration (Sc_{ind}) and the manifold of desired concentration(x_d) is then obtained through the IDA-PBC control methodology explained above. As only substrate is fed from outside the reactor so inlet substrate concentration will be the parameter to control. This will reduce (4.51) to a single algebraic equation in which inlet substrate concentration S_{cin} will be linear fuction of desired rate laws and actual rate laws having tuning parameters as multiplying coefficients to these rate laws. The final equation of S_{cin} derived from equation (4.51) can be seen in section 4.8.4. The simulations obtained for the various concentrations with respect to time and inlet substrate concentration are shown below:

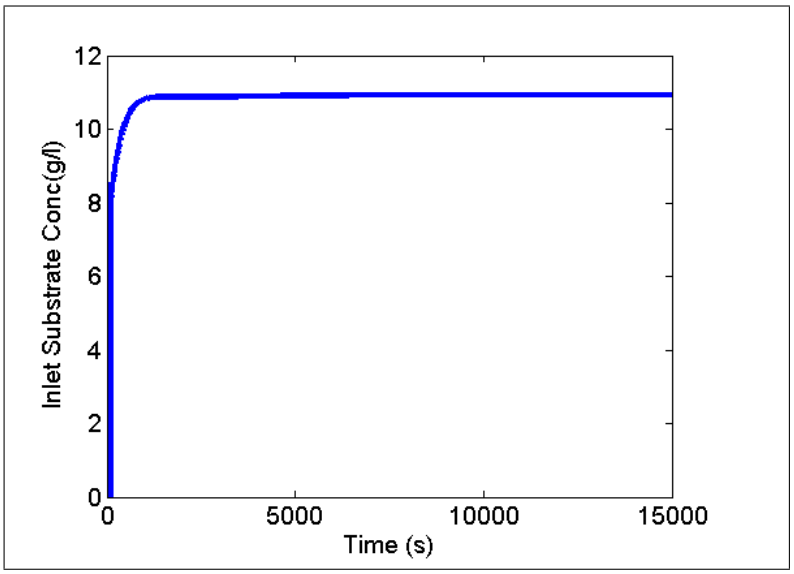


Figure 4.3: Inlet Substrate Concentration with Time.

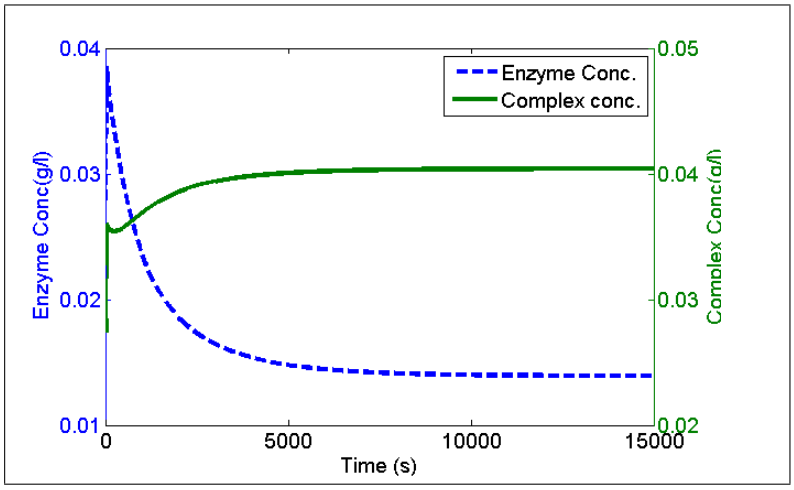


Figure 4.4: Enzyme and Active Cellulose Concentration with Time.

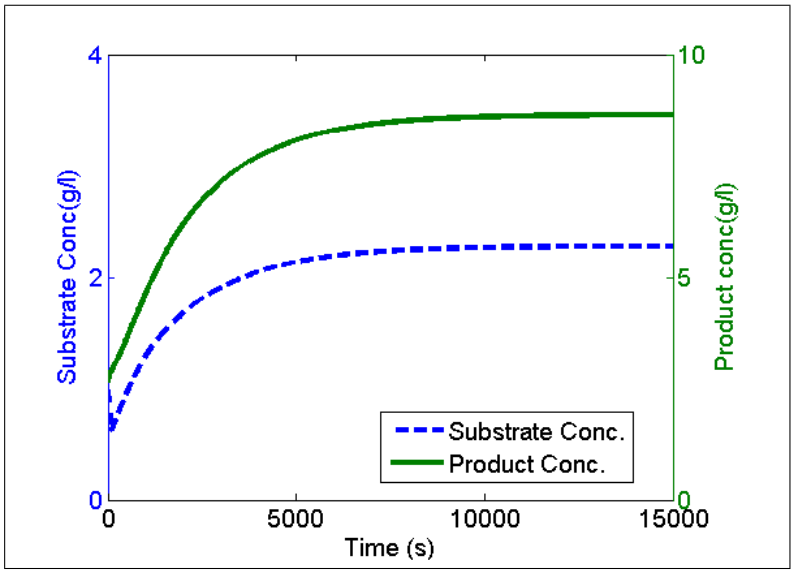


Figure 4.5: Active Subsrate and Product Concentration with Time.

The full kinetics of the process is modeled and controlled without any reduction. The results obtained are actual and smooth hence prove the potential of the modeling and controling technique for open systems. The SPH and RPH model can be made of almost all reactions in chemical and biochemical world with very few neglectable assumptions. The IDA-PBC is very much physical, easy to understand and apply. It can be used to generate the control law of the real processes through simulations. The assumptions taken are from the biochemical

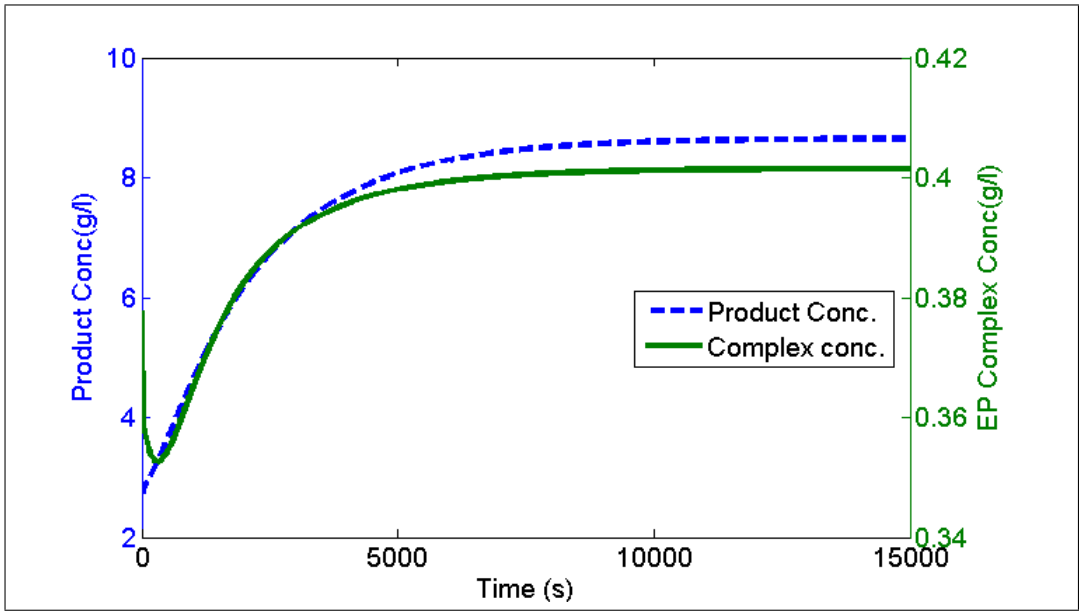


Figure 4.6: Product and Enzyme-Product Complex Concentration with Time.

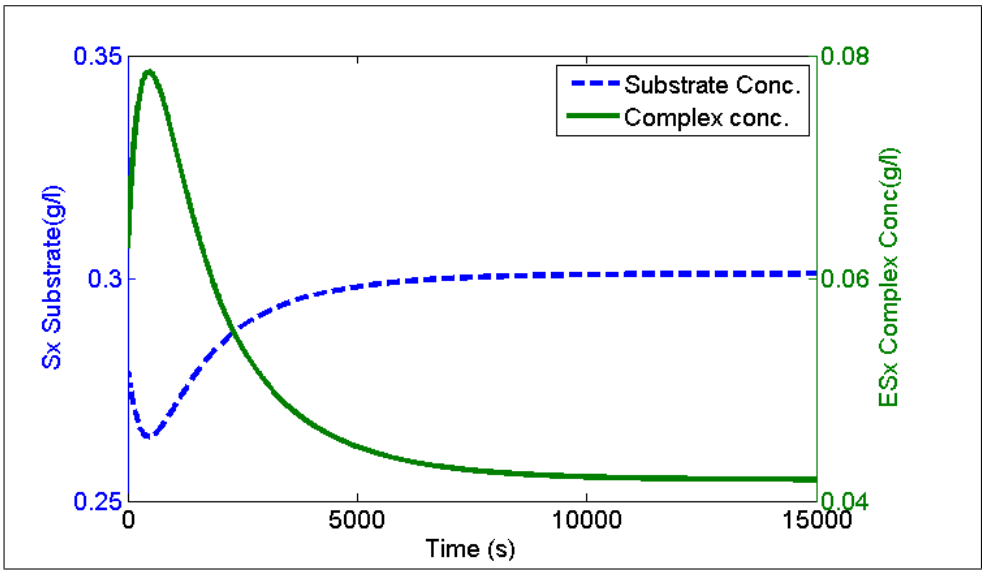


Figure 4.7: Inert Subsrate and Enzyme-Inert Complex Concentration with Time.

kinetics only.

It is clearly visible that the system is reaching to the desired value of product concentration asymtotically with an initial hiccup and that is due to the choice of initial conditions. The tuning parameters can be changed to change the path

towards the desired concentration.

4.9 Conclusion

IDA-PBC method is the most obvious and suitable alternative to energy based models but its way better alternative to non-physical controlling ways. Simulation results obtained for the enezymatic hydrolysis of cellulose are smooth and showing the potential of IDA-PBC in the chemical systems. The results also prove that the application of Port-Hamiltonian models and IDA-PBC control to open systems based on Gibbs Free Energy function as storage function is the most physical methodology for isothermal systems. The IDA-PBC on SPH and RPH formulation are the wonderful addition to the Passivity Based Control of open chemical and biochemical systems. The approach towards PH model and control in reaction space which has been hardly touched is opening the new way to look to control such systems. Port-Hamiltonian modeling and IDA-PBC can prove handy in modeling and control of microbial reactions.
The next chapter will focus of passivity based modeling and passivity based adaptive control of microbial reactions in continuous reactors.

Table 4.1: Table of Adopted Values With Notations

SYMBOL	NAME	UNIT	VALUE
K_{Sc1}	Enzyme Adsorption Constant	l/g-s	.2
K_{Sc2}	Enzyme Desorption Constant	s^{-1}	.05
K_{Sx1}	Inert Enzyme Adsorption Constant	l/g-s	.02
K_{Sx2}	Inert Enzyme Desorption Constant	s^{-1}	.002
K_{P1}	Product Formation Constant	s^{-1}	9.05
K_{P2}	Product Dissociation Constant	l/g-s	3
K_{EP1}	Forward Product Inhibition Constant	l/g-s	.1
K_{EP2}	Reverse Product Inhibition Constant	s^{-1}	.03
D	Dilution Rate	s^{-1}	.0005
E_0	Initial free soluble Enzyme Conc.	g/l	.02759
Sc_0	Initial Active Cellulose Conc.	g/l	1.035
ESc_0	Initial Enzyme-Cellulose Conc.	g/l	.0297
Sx_0	Initial Inert Material Conc.	g/l	.2802
ESx_0	Initial Enzyme-Inert Conc.	g/l	.06275
P_0	Initial Product Conc.	g/l	2.649
EP_0	Initial Enzyme-Cellulose Conc.	g/l	.3777
E_{eq}	Steady state Free Soluble Enzyme Conc.	g/l	.02271
Sc_{eq}	Steady state Active Cellulose Conc.	g/l	.7291
ESc_{eq}	Steady state Enzyme-Cellulose Conc.	g/l	.01352
Sx_{eq}	Steady state Inert Material Conc.	g/l	.2852
ESx_{eq}	Steady state Enzyme-Inert Conc.	g/l	.06477
P_{eq}	Steady state Product Conc.	g/l	5.271
EP_{eq}	Steady state Enzyme-Cellulose Conc.	g/l	.399
Sc_{ind}	Desired Inlet Active Cellulose Conc.	g/l	11
E_d	Desired Free Soluble Enzyme Conc.	g/l	.01379
Sc_d	Desired Active Cellulose Conc.	g/l	2.327
ESc_d	Desired Enzyme-Cellulose Conc.	g/l	.04058
Sx_d	Desired Inert Material Conc.	g/l	.3076
ESx_d	Desired Enzyme-Inert Conc.	g/l	.04241
P_d	Desired Product Conc.	g/l	8.773
EP_d	Desired Enzyme-Cellulose Conc.	g/l	.4032

5

Passivity Based Modeling and Passivity Based Adaptive Control of Microbial Reactions in Continuous Bioreactors

5.1 Introduction

In this chapter, a passive model and a Passivity Based Adaptive Control technique have been designed for a general set of single stream continuous bioreactors. Thermodynamics allows passive models of chemical systems using its kinetics whereas, in the literature, passive models of microbial reactions mostly use quadratic functions as storage function with no link to kinetics. In this chapter we will use the specific kinetic structure of the microbial reactions to passivize them. We will consider the case when the set of reactions can be written as a linear combination of functions of single state variable or when decoupling control allows to achieve such a transformation. A change of coordinates has been found for general bioreactors for general continuous bioreactors makes a partition between a nonlinear control-affine subsystem and a bilinear subsystem. The bilinear subsystem is shown to be always stable and converging to zero, thereby reducing the complexity of the problem. Also, the passivity notion is also being used in this chapter to design an adaptive control law for microbial reactions. One cannot ignore the fact the properties of organisms vary by virtue of the fact that the environment is changing continuously which is explained in kinetics through uncertainty in some parameters. This led to the need of adaptive control for microbial systems. We derive to take advantage of passive model structure to design an adaptive controller. However, so far, there has been little work, as

will be seen, that use the passivity properties or PCH systems to design such adaptive controllers. Their application to bioreactors has not been done so far. The new model is applied on single reaction aniline degradation by *Pseudomonas putida* in a CSTR and simulations obtained are validating the model proposed. The later part of the chapter is discussing an alternative passivity based adaptive control strategy i.e. IDA-PBC for Single reactions and exploring the options of different possible Hamiltonians which can serve the purpose and applied on the basic Monod model. The Multiple reaction digestor example has been shown in the end to validate the model for MIMO systems.

5.2 Passivization of Bioreactor System

5.2.1 The General Dynamical Model of a Single Stream Bioreactor

Suppose there are j number of reactions involving n components, taking place inside a perfectly mixed continuous reactor at constant volume and temperature. The bioreactor has only one single stream for all the concentrations coming in or going out which is common and can be seen happening in many real examples of microbial reactions e.g. wastewater treatment. The inlet dilution rate will be equal to outlet dilution rate to maintain constant volume. Dilution rate D will also be the control parameter and inlet concentrations will remain constant throughout. Let's suppose the state space of the concentrations as:

$$[\xi] = [\xi_1, \xi_2 \cdots \xi_n]^T.$$

$[\xi]$ comprises of a set of $\begin{bmatrix} S & X & P \end{bmatrix}^T$. S represent substrates, X are biomasses, P are products of reaction. The general dynamical model (GDM) of bioreactions introduced in (8) is as follows:

$$\frac{d\xi}{dt} = \sum_{i,k=1}^{n,j} c_{ij} r_k(\xi) + F - D\xi, \tag{5.1}$$

where, ξ represents the concentration of $i\,th$ components, F represents the inlet flow rate of component ξ, c_{ik} represents the yield coefficients and r_k is the rate of the $k\,th$ reaction.

Remark 5. *The GDM in this chapter can be said to be a specific case of the GDM shown in* (5.1) *in which there is only single inlet stream $D\xi$ with only one feed instead of multiple inlet flow rates* (F).

A generalised first order time derivative of concentration model of a set of bioreactions in an open reactor with single dilution rate at constant volume and temperature can be written as:

$$\left[\dot{\xi}\right] = [c]\,[r_k] + [D\xi_{in} - D\xi_{out}] \tag{5.2}$$

ξ's are the n components, c is the matrix of constant yield coefficients associated with the reaction. r_k's are the j rates of reaction. ξ_{in}'s, and ξ_{out}'s are the inlet and outlet concentrations of n components. ξ_{in}'s are mostly substrates altogether coming in one stream with dilution rate D. For the concentrations not fed from outside such as products and biomasses, ξ_{in} will be zero. Similarly, ξ_{out} is the concentration coming out of the reactor which will be same as the concentration inside the reactor i.e. ξ. The general model shown in (5.2) is valid for all types of microbial kinetics. The inputs u will be: $u \in [D, D\xi_{in}]$.

5.2.2 A Useful Coordinate Transformation

This coordinate transformation is chosen to simplify the model and making it easier to passify and will help in clear interpretation of the model. The important point here is that the new set of coordinates will be independent of kinetics which are restricted to appear in the kinetics and can be used to analyze various properties of biological systems.
Suppose, state vector ξ can be divided into two parts a and b, $n = a + b$, $[\xi] = \begin{bmatrix} \xi_a & \xi_b \end{bmatrix}^T$, $[c] = \begin{bmatrix} c_a & c_b \end{bmatrix}^T$ such that:

$$\left[\dot{\xi}_a\right] = [c_a]\,[r] + [D\xi_{ain} - D\xi_a] \tag{5.3}$$

and

$$\left[\dot{\xi}_b\right] = [c_b]\,[r] + [D\xi_{bin} - D\xi_b]\,. \tag{5.4}$$

The coordinate transformation will lead to a new vector of b elements and will be represented by state W where:

$$[W]_{b\times 1} = [A]_{b\times a}\left([\xi_{ain} - \xi_a]_{a\times 1}\right) + [\xi_{bin} - \xi_b]_{b\times 1}. \tag{5.5}$$

Here, $[A]$ is a constant.

Proposition 19. *For the relation of W proposed in (5.5) and under the assumptions of single dilution rate and constant inlet concentrations, If matrix $[A]$ and functions of ξ_{ain} and ξ_{bin} are chosen in a way that $[A][c_a]+[c_b]=0$ and $[A]\dot{\xi_{ain}}+\dot{\xi_{bin}}=0$, the state space model takes the form:*

$$\begin{bmatrix} \dot{\xi}_a \\ \dot{W} \end{bmatrix} = \begin{bmatrix} [c_a]_{a\times j} & [0]_{a\times b} \\ [0]_{b\times j} & [-DI]_{b\times b} \end{bmatrix}_{(a+b)\times(j+b)} \begin{bmatrix} r_k \\ W \end{bmatrix}_{(j+b)\times 1} + \begin{bmatrix} D(\xi_{ain})-D\xi_a \\ 0 \end{bmatrix} \tag{5.6}$$

***Proof**: On differentiating (5.5) with respect to time we get:*

$$\left[\dot{W}\right] = [A]\left(\dot{\xi_{ain}}-\dot{\xi}_a\right)+\left(\dot{\xi_{ain}}-\dot{\xi}_b\right). \tag{5.7}$$

Further substitution for $\left[\dot{\xi}_a\right]$, $\left[\dot{\xi}_b\right]$ from (5.3) and (5.4) respectively will lead to:

$$\left[\dot{W}\right] = [A]_{b\times a}\left(-[c_a]_{a\times j}[r]_{j\times 1}+[D\xi_{ain}-D\xi_a]_{a\times 1}\right)-[c_b]_{b\times j}[r]_{j\times 1}+[D\xi_{bin}-D\xi_b]. \tag{5.8}$$

substituting $[A][c_a]=-[c_b]$ and $[A]\dot{\xi_{ain}}=-\dot{\xi_{bin}}$ in (5.8) will give:

$$\dot{W}=-DW. \tag{5.9}$$

With state space as $[\ \xi_a \quad W\ ]^T$, the Bioreactor model becomes same as shown in (5.6).

Note that this solution necessarily needs c_a to be a full rank square matrix which is possible by careful choice of the components of ξ_a.

Corollary 1. *If $\forall D : D \geq D_{\min} > 0$, W will exponentially converge to zero.*

***Proof**: Considering a continuously differentable non-negative storage function $H=\frac{1}{2}W^2$ and $H:W\to R$ with $H(0)=0$. Differentiating H w.r.t. time and substituting (5.9) will give $\dot{H}=-DW^2=-2DH\leq -2D_{\min}H$.*

Remark 6. *For the general dynamical model shown in (5.1), the model representation after coordinate transformation was referred to as a "'Nice" representation of the biosystem in (7) as it was independent of kinetics. However, the representation in (5.9), which considers the case of a single stream input flow, is independent of kinetics as well as concentration of the feed and allows the partition of state space for which one subsystem will always converge to zero. The new model has two types of states, one is bilinear W, will always approach to zero and other is control affine part ξ_a. The convergence of W to zero is what exactly called the useful change of coordinates.*

5.2.3 Decoupling of Coupled Bioreactions

The following procedure of decoupling the coupled bioreactor system is applicable to the microbial reactions which can be decoupled using some valid assumptions.

A decoupled reaction has its rate terms depending only on single state or many states if they can be separated (decoupled) algebraically such that they become a linear combination of functions of single state only (79).

The bioreactor systems chosen here are single stream bioreactors having inlet concentration of each component to be constant. Dilution rate D is the only control input in such systems. The following procedure can be followed to decouple a microbial reaction.

The main aim here is to modify the rate function matrix $c_a[r]$: $c_a[r] = \bar{c_a}\bar{r} + \begin{bmatrix} f'(\xi'_a, W) & f''(\xi_a, W) \end{bmatrix}^T$, where $\bar{r} = \begin{bmatrix} r' & p'' \end{bmatrix}^T$, in which $[r']$ is a matrix of modified rates of reaction whose each element is a function of single state ξ'_i and $\bar{c}_a$ is the improvised stoichiometric matrix. The elements of $[p'']$ are the functions of single state ξ''_i. $f'(\xi_a, W)$ is the decoupled function of ξ_a, W, $f''(\xi_a, W)$ is the function of ξ_a, W which cannot be decoupled. Mathematically:

$[r']^T = \begin{bmatrix} r'_1(\xi'_1) & r'_2(\xi'_2) & \cdots & r'_{a'}(\xi'_{a'}) \end{bmatrix}$

and

$[p'']^T = \begin{bmatrix} p''_1(\xi''_1) & p''_2(\xi''_2) & \cdots & p''_{a''}(\xi''_{a''}) \end{bmatrix}$. The nominal model shown in (5.6) can be elaborated to be written in the form:

$$\begin{bmatrix} \dot{\xi}'_a \\ \dot{\xi}''_a \\ \dot{W} \end{bmatrix} = \begin{bmatrix} \bar{c}_a & 0 \\ 0 & -DI \end{bmatrix} \begin{bmatrix} r'(\xi') \\ p''(\xi'') \\ W \end{bmatrix} + \begin{bmatrix} f'(\xi_a, W) \\ f''[\xi_a, W] \\ 0 \end{bmatrix} + \begin{bmatrix} D(\xi'_{ain} - \xi'_a) \\ D(\xi''_{ain} - \xi''_a) \\ 0 \end{bmatrix}, \tag{5.10}$$

where ξ'_a is the subset of ξ_a which has decoupled rate terms, $\xi_a{}''$ is the subset of ξ_a which is the sum of decoupled rate terms and $f''(\xi_a, W)$.

Lemma 4. *Assuming that $\dot{\xi''}_a$ is discreted in such a way that the function $f''(\xi_a, W) < 0$ and the steady state values of ξ''_{ain}, D, ξ''_a in the input term are compensating for $f''(\xi_a, W)$ such that $D(\xi''_{ain} - \xi''_a) + f''(\xi_a, W) = 0$,*

Using *Lemma* 4, the nominal model shown in (5.10) can take the following

form:

$$\begin{bmatrix} \dot{\xi}'_a \\ \dot{\xi}''_a \\ \dot{W} \end{bmatrix} = \begin{bmatrix} \bar{c}_a & 0 \\ 0 & -DI \end{bmatrix} \begin{bmatrix} r'(\xi') \\ p''(\xi'') \\ W \end{bmatrix} + \begin{bmatrix} f'({\xi'}_a, W) \\ 0 \\ 0 \end{bmatrix} + \begin{bmatrix} D({\xi'}_{ain} - {\xi'}_a) \\ 0 \\ 0 \end{bmatrix}. \tag{5.11}$$

5.2.4 Passivity Based Model of a Decoupled Bioreactor System

Proposition 20. *(79) Suppose that $f'(\xi_a, W)$ is a vanishing perturbation i.e. $\lim_{t\to\infty} f'(\xi_a, W) = 0$. Assume that there exists a neighbourhood Z of ${\xi'}_a^*$ such that the unperturbed system $\dot{\xi}'_a = \bar{c}_a r'({\xi'}_a) + D({\xi'}_{ain} - {\xi'}_a)$ has ${\xi'}_a^*$ as an exponentially stable equilibrium point and the Lyapunov function $V(\xi'_a, t)$ of the system satisfies the conditions:*
$\exists k_3, k_4 > 0, k_3 \parallel {\xi'}_a \parallel \leq \frac{\partial V}{\partial {\xi'}_a} \leq k_4 \parallel {\xi'}_a \parallel$,
$\exists \gamma > 0 \parallel f'(W) \leq \gamma \parallel {\xi'}_a \parallel$.

Then the perturbed system $\dot{\xi}'_a = \bar{c}_a r'({\xi'}_a) + f'(\xi_a, W) + D({\xi'}_{ain} - {\xi'}_a)$ is locally exponentially stable if $(-\lambda_{\min} k_3 - k_3 + k_4 \gamma \lambda_{\max}) < 0$, where $\lambda_{\min}$, $\lambda_{\max}$ are the minimum and maximum eigenvalues of $-\bar{c}_a$.

Proof: One knows from the exponential stability conditions that
$k_1 \parallel {\xi'}_a \parallel \leq V \leq k_2 \parallel {\xi'}_a \parallel$ *where* $k_1, k_2 > 0$. *Since,* $\frac{dV}{dt} = \frac{\partial V}{\partial {\xi'}_a} \frac{\partial {\xi'}_a}{\partial t}$, *then from the assumptions:*
$[\frac{\partial V}{\partial {\xi'}_a}^T \bar{c}_a r'({\xi'}_a) \leq (-\lambda_{\min} - 1) k_3 \parallel {\xi'}_a{}^2 \parallel$,
$\frac{\partial V}{\partial {\xi'}_a}^T f'(\xi_a, W) \leq k_4 \gamma \lambda_{\max} \parallel {\xi'}_a{}^2 \parallel$
Now, $\frac{dV}{dt} = (-\lambda_{\min} k_3 - k_3 + k_4 \gamma \lambda_{\max}) \parallel {\xi'}_a{}^2 \parallel$.
Hence, from Theorem 3.12 in (67), the system will be exponentially stable.

Now, from *Corollary* 1, and from the *Proposition* 20, $f'(\xi_a, W) = 0$, the unperturbed system can be written as:

$$\begin{bmatrix} \dot{\xi}'_a \\ \dot{\xi}''_a \\ \dot{W} \end{bmatrix} = \begin{bmatrix} \bar{c}_a & 0 \\ 0 & -DI \end{bmatrix} \begin{bmatrix} r'(\xi') \\ p''(\xi'') \\ W \end{bmatrix} + \begin{bmatrix} D({\xi'}_{ain} - {\xi'}_a) \\ 0 \\ 0 \end{bmatrix}. \tag{5.12}$$

5.2.4.1 Passivity at Zero Equilibrium

Proposition 21. *Assume that there exists a neighbourhood* Z *of* $\xi = 0$ *such that* $\sum {r'}_i({\xi'}_i) > 0$ *and* $\sum r_i(0) = 0$. *Consider the storage function* $V = \sum_{k=1}^{a+b} V_k = \sum_{i=1}^{a'} \int ({r'}_i({\xi'}_i))\, \partial {\xi'}_i + \sum_{t=1}^{a''} \int ({p''}_t({\xi''}_t))\, \partial {\xi''}_t + \sum_{j=1}^{b} \frac{1}{2} {W_j}^2$, $V(0) = 0$. *Then if* $\bar{c}_a \prec 0$ *and* V_k *has its minimum at* $\xi_k = 0$, *the system* (5.12) *will be passive.*

Proof: *On partially derivating* V *w.r.t. states* ${\xi'}_a$, ${\xi''}_a$ *and* W, *the system in* (5.12) *can be written in the form:*

$$\underbrace{\begin{bmatrix} \dot{\xi'}_a \\ \dot{\xi''}_a \\ \dot{W} \end{bmatrix}}_{\dot{\xi}} = \underbrace{\begin{bmatrix} \bar{c}_a & 0 \\ 0 & -DI \end{bmatrix}}_{Q} \underbrace{\begin{bmatrix} \frac{\partial V}{\partial {\xi'}_a} \\ \frac{\partial V}{\partial {\xi''}_a} \\ \frac{\partial V}{\partial W} \end{bmatrix}}_{\frac{\partial V}{\partial \xi}} + \underbrace{[I]}_{g} \underbrace{\begin{bmatrix} D({\xi'}_{ain} - {\xi'}_a) \\ 0 \\ 0 \end{bmatrix}}_{u}. \tag{5.13}$$

The output y *of the system will be* $y = g^T \frac{\partial V}{\partial \xi}$. *Also,* $\xi_a, W, V > 0$ *and the time derivative of* V *will be:*

$$\dot{V} = \frac{\partial V}{\partial \xi}\dot{\xi} = \frac{\partial V}{\partial \xi}^T Q \frac{\partial V}{\partial \xi} + \frac{\partial V}{\partial \xi}^T gu = \frac{\partial V}{\partial \xi}^T Q \frac{\partial V}{\partial \xi} + y^T u; \tag{5.14}$$

Since, $\bar{c}_a \prec 0, D > 0$ *making matrix* Q *negative definite,* (5.14) *with zero input will be negative. Also,* $V_i(0) = r_i(0) = 0$, *the system* (5.12) *will be passive and will have an asymptotically stable equilibrium point* $\xi = 0$.

5.2.4.2 Passivity at Non-zero Equilibrium

Considering the system (5.12), suppose the non-zero equilibrium point of this system is ξ^*: $\xi^* = \begin{bmatrix} {\xi'}_a{}^* & {\xi''}_a{}^* & 0 \end{bmatrix}$. At equilibrium $\dot{\xi} = 0$, i.e. $\bar{c}_a r'\left({\xi'}_a{}^*\right) = -D^*\left({\xi'}_{ain}{}^* - {\xi'}_a{}^*\right)$. It would be interesting to introduce the rate term at equilibrium point in the equation to have a clear view about the system being passive at non-zero equilibrium point. Adding and subtracting $r'({\xi'}_i{}^*)$ in the corresponding

equation, the model (5.13) with ${\xi'}_{ain} = {\xi'}^*_{ain}$ becomes:

$$\begin{bmatrix} \dot{\xi}'_a \\ \dot{\xi}''_a \\ \dot{W} \end{bmatrix} = \begin{bmatrix} \bar{c}_a & 0 \\ 0 & -DI \end{bmatrix} \begin{bmatrix} r'({\xi'}_a) - r'\left({\xi'}_a^*\right) \\ p''({\xi''}_a) - p''\left({\xi''}_a^*\right) \\ W \end{bmatrix} + \begin{bmatrix} {\xi'}^*_{ain}(D - D^*) + \left(D^*{\xi'}_{ain}^* - D{\xi'}_a\right) \\ \bar{c}_a p''\left({\xi''}_a^*\right) \\ 0 \end{bmatrix} \tag{5.15}$$

The new input as shown in (5.15) will also have only D as an actual input. The above presentation is very straightforward and clearly physically understandable from the passivity point of view.

Proposition 22. *Considering the system* (5.15) *with* $\bar{c}_a \prec 0$. *Assuming that there exists a neighbourhood* Z *of* $\xi = \xi^*$ *such that* $\sum r'_i(\xi'_i) > 0$, $\sum {r'}_i\left(\xi'^*\right) = 0$, $\sum p''_i(\xi''_i) > 0$ *and* $\sum p''_i\left(\xi''^*\right) = 0$ *then the storage function* $V' = \sum_{k=1}^{a+b} {V'}_k = \sum_{i=1}^{a'} \int \left(r'_i(\xi'_i) - r'_i({\xi'}_i^*)\right) \partial {\xi'}_i + \sum_{t=1}^{a''} \int \left(p''_i({\xi''}_i) - p''_i({\xi''}_i^*)\right) \partial {\xi''}_i + \sum_{j=1}^{b} \frac{1}{2} {W_j}^2$ *satisfying the conditions:* $V' > 0$, $V'(\xi^*) = 0$ *and* ${V'}_k$ *is minimum at* $\xi_k = {\xi_k}^*$ *will make the system* (5.15) *passive and asymptotically stable at* $\xi = \xi^*$.

Proof*: One has* V' *is always positive around* ξ^*. *On partially derivating* V' *w.r.t. states* ξ'_a,ξ''_a *and* W*:*

$$\frac{\partial V'}{\partial \xi'_a} = r'\left(\xi'_a\right) - r'\left({\xi'}_a^*\right) : \frac{\partial V'}{\partial {\xi''}_i} = p''\left({\xi''}_a\right) - p''\left({\xi''}_a^*\right) : \frac{\partial V'}{\partial W} = W \tag{5.16}$$

the system in (5.15) *can be written in the form:*

$$\underbrace{\begin{bmatrix} \dot{\xi}'_a \\ \dot{\xi}''_a \\ \dot{W} \end{bmatrix}}_{\dot{\xi}} = \underbrace{\begin{bmatrix} \bar{c}_a & 0 \\ 0 & -DI \end{bmatrix}}_{Q'} \underbrace{\begin{bmatrix} \frac{\partial V'}{\partial {\xi'}^g} \\ \frac{\partial V'}{\partial {\xi''}^g} \\ \frac{\partial V'}{\partial W} \end{bmatrix}}_{\frac{\partial V}{\partial \xi}} + \underbrace{\underbrace{[I]}_{g} \underbrace{\begin{bmatrix} {\xi'}_{ain}^*(D - D^*) + \left(D^*{\xi'}_{ain}^* - D{\xi'}_a\right) \\ \bar{c}_a p''\left({\xi''}_a^*\right) \\ 0 \end{bmatrix}}_{u'}}_{} \tag{5.17}$$

The output of the system will be $y' = g^T \frac{\partial V}{\partial \xi}$. *The time derivative of* V' *will be:*

$$\dot{V'} = \frac{\partial V'}{\partial \xi}\dot{\xi} = \frac{\partial V'}{\partial \xi}^T Q' \frac{\partial V'}{\partial \xi} + \frac{\partial V'}{\partial \xi}^T g u' = \frac{\partial V'}{\partial \xi}^T Q \frac{\partial V'}{\partial \xi} + y'^T u'; \tag{5.18}$$

Since, $\bar{c}_a \prec 0, D > 0$ *making matrix* Q' *negative definite,* (5.18) *with zero input will be negative .Also,* ${V'}_k$ *is minimum i.e. 0 at* ${\xi_k}^*$, *the system* (5.17) *will be passive and will have an asymptotically stable equilibrium point* $\xi = \xi^*$.

The Passivity Based Model derived in this section is physically more viable as rate terms are chosen as storage function.

Remark 7. *The left term in* (5.16) *will include the specific growth rate* μ *terms and these can be seen "analogous" with the terms in* (5.19) *for passive enzymatic reactors with MM kinetics as both stand for reaction potential. Hence, the left term on storage function* (5.16) *can be viewed as a "pseudo- thermodynamical" energy.*

$$\frac{\partial G}{\partial x} = \underbrace{m_c}_{\substack{chemical \\ potential}} - \underbrace{m_c^*}_{\substack{steadystate \\ potential}} \tag{5.19}$$

5.3 Passivity Based Control of Bioreactor System

To render the system stable at the desired point, the feedback control of a passive system is shown below. The control is designed in such a way that the controlled is also passive and asymptotically reach the desired equilibrium point.

Proposition 23. *(29) Consider the PBM described in* (5.13). *Suppose that* $V(x,t) \geq 0$ *and the model is zero state detectable. Then, the feedback* $u = -C(x,t)y$ *with* $C(x,t) \geq eI > 0$ *and constant* e *renders* $x = 0$ *globally asymptotically stable.*

Proposition 24. *Considering the desired storage function* $\bar{V}$*:*

$$\bar{V} = \sum_{k=1}^{a+b} \bar{V}_k = \sum_{i=1}^{a'} \left(r'\left({\xi'}_i\right) - r'\left({\xi'}_i^d\right)\right) + \sum_{t=1}^{a''} \left(p''\left({\xi''}_i\right) - p''\left({\xi''}_i^d\right)\right) + \sum_{j=1}^{b} \frac{1}{2} W_j^2, \tag{5.20}$$

where $\bar{V} > 0, \bar{V}\left({\xi'}_i^d\right) = 0$ ${\xi_i}^d$ *is the desired state of* ξ_i. $\bar{V} > 0$, $\bar{V}(\xi^d) = 0$ *and* $\bar{V}_k$ *is minimum at* $\xi_k = {\xi_k}^d$. *Then the system* (5.17) *is passive and the feedback* $\bar{u} = -C(x,t)\bar{y}$ *with* $C(x,t) \geq eI > 0$ *renders* (5.17) *globally asymptotically stable at* $\xi = \xi^d$.

Proof: *Replacing the non-zero equilibrium point ξ^* with desired equilibrium point ξ^d, the system* (5.17) *can take the form:*

$$\underbrace{\begin{bmatrix} \dot{\xi}'_a \\ \dot{\xi}''_a \\ \dot{W} \end{bmatrix}}_{\dot{\xi}} = \underbrace{\begin{bmatrix} \bar{c}_a & 0 \\ 0 & -DI \end{bmatrix}}_{Q} \underbrace{\begin{bmatrix} \frac{\partial \bar{V}}{\partial \xi'_a} \\ \frac{\partial \bar{V}}{\partial \xi''_a} \\ \frac{\partial \bar{V}}{\partial W} \end{bmatrix}}_{\frac{\partial \bar{V}}{\partial \xi}} + \underbrace{[I]}_{g} \underbrace{\begin{bmatrix} {\xi'_{ain}}^d \left(D - D^d\right) + \left(D^d {\xi'_{ain}}^d - D\xi'_a\right) \\ d''_a p'' \left({\xi''_a}^d\right) \\ 0 \end{bmatrix}}_{\bar{u}} \tag{5.21}$$

From the Proposition 22, the new system is passive. The new input of the system is $\bar{u}$ and ouput $\bar{y}$ of the system can be written as:$\bar{y} = [g]\frac{\partial \bar{V}}{\partial \xi}$. From the Proposition 8, the feedback $\bar{u} = -C(x,t)\bar{y}$ with $C(x,t) \geq eI > 0$ will render (5.21) *globally asymptotically stable at $\xi = \xi^d$.*

Lemma 5. *Consider system* (5.21) *with input $\bar{u}$ and output $\bar{y}$. Let the practical control u, a vector of independent inputs $u = (U_1 \cdots U_m)^T \in \{D\xi_{ain}\}$. Then, there exists a vector of independent inputs $u = (U'_1 \cdots U'_m)^T \in \{D, D.\xi_{ain}\}$, a matrix $\lambda(\xi_a)$ and a vector $\omega(\xi_a)$ such that $\bar{u} = \lambda(\xi_a)U' + \omega(\xi_a)$*

Proof: *One has $\bar{u} = \xi'_{ain}\left(D - D^d\right) + \left(D^d \xi'_{ain} - D\xi'_a\right)$. As $D \in u$, the right hand term is an affine function of D. When $\{D\xi_{ain}\} \in u$, one can use D and $D.\xi_{ain}$, which belong to u . This Lemma means that, in practice, one can retrieve the practical control u from $\bar{u}$ if the linear system of equations $\bar{u} = \lambda(\xi_a)u + \omega(\xi_a)$ has at least one solution.*

Corollary 2. *Consider the bioreactor* (5.21) *that verifies Proposition 24, and let a vector of independent inputs $u = (U_1 \cdots U_m)^T \in \{D\xi_{ain}\}$. If there exists a positive definite matrix $C(\xi_i) > eI > 0$, such that the equation, called the matching equation: $\bar{u} = -C\bar{y} = \lambda(\xi_a)u + \omega(\xi_a)$, has at least one solution, then the system is asymptotically stable.*

Proof: *From Proposition 24, the system is passive, from 5, one can retrieve the set of solutions u from $\bar{u}$. Then from Proposition 23, the system* (5.21) *is asymptotically stable. An obvious case arises when $m = a$ and λ is invertible.*

Thus, *Proposition* 24 and *Corollary* 2 ensures that the controlled system will remain passive throughout the control process.

5.4 Passivity Based Adaptive Control of Bioreactor Systems

Microbial growth, substrate utilization and product formation in bioreactors have traditionally been described by algebraic or differential equations derived on the

principles of chemical reactions. Such bioreactors are usually operated under largely ideal conditions, implying that the fermentation broth is homogeneous, there are no disturbances, there is approximately balanced growth, and data acquisition and control systems are sufficiently elaborate, fast and accurate. These ideal conditions do not, however, prevail in the more real situations of pilot-scale and production-scale bioreactors. These larger reactors have spatial variations within the vessel, influx of noise from the environment, and restricted use of monitoring and control devices because of practical considerations. Culture behavior in such non ideal situations is often quite different from that in ideal reactors, and mechanistic mathematical models developed on the basis of laboratory-scale observations become inapplicable or too approximate or may require frequent adjustments of the parameters during the fermentation process.This develops the need of online adaptive control of such systems which can rectify the unwanted variation in the desired path of the product formation.

The parameters or the structure of the bioreactor's model are often not perfectly known and also the working conditions vary from time to time. This leads to a big problem in implementing reliable bioreactor control strategies to perform Adaptive Control (107), (114), (8). Adaptive control techniques that allow controller parameter tuning on the site along with the control around optimal or non-optimal productivity set-points are necessary and has become a key issue in case of bioreactors. Hence, there exists a huge bunch of papers on adaptive control of bioreactors. There are mainly two types of adaptive control laws for bioreactors, extremum seeking dedicated to maximise biomass production (23), (26) and setpoint tracking (28). One would like to take advantage of a passive or Port-Hamiltonian structure to propose a new kind- if possible passive or PH- of adaptive controller. However, there exists very little literature on adaptive Port-Hamiltonian systems of microbial reactions in bioreactors.

5.4.1 Passivity Based Adaptive Control Review With a Possible Application to Microbial Reactions in Continuous Bioreactors

(3) introduced a new adaptive controller for solving the tracking problem of linear systems that are subject to large parametric uncertainty and sudden exogenous

disturbances. The design of the proposed adaptive controller is based on Lyapunov control design approaches. Its application to the biomass concentration speed control of biotechnological processes shows excellent reference tracking and disturbance rejection capabilities at the expense of less effort as compared to known adaptive control techniques. (112) made the adaptively controlled model of *Enzymatic Synthesis of Ampicillin* using Bond Graph and did estimation of kinetic parameters. It, as usual, gives the physical interpretation of the whole system but control strategy is not influenced by the Bond Graph. (39) used passivity approach for the parameter estimation of the unknown parameters in biochemical reaction networks.

Some other works has been done by researchers in the field of Passivity Based Adaptive Control. These works are not applied to the bioreactors but the general models seem interesting to apply on bioreactors. Some of them are discussed below.

The works of (127) proposed the adaptive PCH based stabilisation controllers for parametric uncetainities while maintaining the Hamiltonian structure. Simulations show that the simultaneous stabilization controllers obtained in this paper work very well. In (29), the adaptive control scheme is combined with canonical transformation theory for PH systems. This allows the adaptive control scheme to be applied on a large class of systems and for being included in the PH framework. The results show that the adaptive control estimates and compensates for the errors of the uncertain constant parameters such that trajectories converge to the desired trajectories.

Extensions to include passivity based adaptive feedback control schemes can be found in an article by (66) and in that of (69).

Conclusion From Literature Review

Passivity Based Adaptive Control has not been developed much and when applied to bioreactors, it is based on nonphysical storage functions with absolutely no link from the kinetics. Though, the Passivity Based Adaptive design of PH models in (29) seems very interesting and can be applied on bio reactor models but it donot really take the advantage of the mechanism. The physical storage functions for the bioreactor model shown in this chapter can be further modified to accomodate

the error in the constant parameters of the model and one can still obtain a storage function which let the whole adaptively controlled system be passive. The important thing here to note is that the kinetics of reaction will be taking part in the design of the Passivity based Adaptive controller.

5.4.2 The Adaptive Controller Design

The Adaptive Control proposed here will be designed in such a way that the closed loop system with adaptive control will still be passive. The algorithm will be based on an augmented system that will rely on the passive bioreactor representation in (5.21) but before that the following assumptions are needed to be taken care of:

1. The dilution rate is the control input.
2. The inlet concentration is measured externally and is known.
3. The output concentrations of all the constituents are also measurable which are same as the concentrations inside the reactor.
4. The yield coefficients are considered to be known.
5. The controller can be split into a nominal part and an additional term comes from the discrepancies between the nominal and the real model with uncertain constant terms.

Theorem 1. *Assume that the controller is under the form:*

$$u'' = -C\bar{y} + \lambda(\xi,t)\,\bar{z}, \tag{5.22}$$

the term $\lambda(\xi,t)\,\bar{z}$ is the error in the control that comes from the parameteric uncertainties in the model which are fed to the control design. $\lambda(\xi,t)$ is the matrix of known functions, z is a vector of unknown constant parameters with an estimate $\hat{z}$, $\bar{z} = \hat{z} - z$ is the parameter estimation error. Consider system (5.21) *along with control* (5.22) *and assume that $Q \prec 0$ for $D \geq D_{min} > 0$. Assume that the modified Lyapunov candidate function $V''(\xi,\bar{z}) = \bar{V}(\xi) + \frac{1}{2}\bar{z}^T K_a^{-1}\bar{z}$ is such that $\bar{V}(\xi_a^d) = 0$, then the closed loop adaptation law:*

$$\dot{\bar{z}} = \dot{\hat{z}} = -K_a\lambda(\xi,t)\,\bar{y}; K_a \succ 0 \tag{5.23}$$

renders the system asymptotically stable.

***Proof**: Substituting the relations* (5.22), (5.23), $\bar{y} = g^T\frac{\partial\bar{V}}{\partial\xi}$ *and* $\frac{\partial V''}{\partial\xi} = \frac{\partial\bar{V}}{\partial\xi}$ *in*

(5.21), (5.21) *along with adaptation law can be written in the form:*

$$\underbrace{\begin{bmatrix} \dot{\xi} \\ \dot{\bar{z}} \end{bmatrix}}_{\dot{\xi}''} = \underbrace{\begin{bmatrix} Q - gCg^T & g\lambda K_a \\ -K_a\lambda g^T & 0 \end{bmatrix}}_{Q''} \underbrace{\begin{bmatrix} \frac{\partial V''}{\partial \xi} \\ \frac{\partial V''}{\partial \bar{z}} \end{bmatrix}}_{\frac{\partial V''}{\partial \xi''}}. \tag{5.24}$$

Here, $Q'' \prec 0$ *and* $V'' \geq 0$ *and* $V''({\xi''}^d) = 0$. *According to Proposition 23 and Proposition 24, the system* (5.24) *can be said to be compensating for the unknown parameter error and reducing it to zero. The adaptively controlled system* (5.24) *will be uniformly asymptotically stable at* $\bar{z} = 0$ *and* $\xi = \xi^d$.

Theorem 1 shows how any input disturbance expressed in terms of unknown constant terms can be cancelled by applying an adaptive control which can be realized into a passivity based framework in order to estimate and compensate for the unknown term. The passivity properties are self stabilising hence making this adaptive control stable.

5.5 Application to a Single Reaction with Monod kinetics: Aniline Degradation by *Pseudomonas putida* in CSTR

Aniline is among the constituents of many industrial effluents (e.g. wastewaters in chemical and dyeing industries). It is toxic and may cause severe health effects for living organisms. Hence, process streams containing such compounds should not be released in the environment without proper treatment. Current chemical removal processes such as solvent extraction, chemical oxidation, etc. are costly and further generate toxic byproducts. Biological processing for aniline degradation has been considered suitable for slightly low concentrations e.g. Aniline degradation by *Pseudomonas putida*. It is very important to model and control the kinetics of such processes for large scale industrial use.
(81) has studied the model of aniline degradation by *Pseudomonas putida* ATCC 21812 cells in batch reactors following a modified Monod model. We will only consider the case of a simplified Monod model. The time course of biomass Pseudomonas putida growth X and simultaneous aniline degradation S in a constant

volume CSTR with dilution rate D can be represented by the differential equations:

$$\dot{X} = \mu X - DX, \tag{5.25}$$

$$\dot{S} = -\frac{\mu x}{Y} + D\left(S_{in} - S\right), \tag{5.26}$$

where D is the dilution rate, Y is the cell/substrate yield coefficient and μ is the specific growth rate. For Monod kinetics:

$$\mu = \frac{\mu_m S}{K_s + S}, \tag{5.27}$$

here, μ_m is the maximum specific growth rate and K_s is the half velocity constant. As X and S are concentrations therefore $X, S \geq 0$. Also, $K_s, \mu_m, Y > 0$ always. The state space will be $[\xi] = \begin{bmatrix} S & X \end{bmatrix}^T$ and the model can be represented as:

$$\underbrace{\begin{bmatrix} \dot{S} \\ \dot{X} \end{bmatrix}}_{\dot{\xi}} = \underbrace{\begin{bmatrix} -1 & 0 \\ 0 & 1 \end{bmatrix}}_{c} \underbrace{\begin{bmatrix} \frac{\mu X}{Y} \\ \mu X \end{bmatrix}}_{r} + \underbrace{\begin{bmatrix} DS_{in} - DS \\ -DX \end{bmatrix}}_{D(\xi_{in} - \xi_{out})}. \tag{5.28}$$

5.5.1 Coordinate transformation And a Passivity Based Model

Dividing state space in to two parts ξ_a and ξ_b such that:

$$\left[\dot{\xi}_a\right] = \left[\dot{S}\right] = \underbrace{[-1]}_{c_a} \underbrace{\left[\frac{\mu X}{Y}\right]}_{r} + \underbrace{[DS_{in} - DS]}_{D(\xi_{ain} - \xi_a)}, \tag{5.29}$$

$$\left[\dot{\xi}_b\right] = \left[\dot{X}\right] = \underbrace{[1]}_{c_b} \underbrace{[\mu X]}_{r} + \underbrace{[-DX]}_{D(\xi_{bin} - \xi_b)}. \tag{5.30}$$

The new coordinate W can be written as:

$$W = A\left(S_{in} - S\right) + \left(X_{in} - X\right), \tag{5.31}$$

where $A = 1$, $X_{in} = 0$ and S_{in} is a constant. Hence, derivating (5.31) w.r.t. time and substituting (5.29),(5.30) will give $\dot{W} = -DW$. With the new state space $\begin{bmatrix} S & W \end{bmatrix}^T$ and the substitution $X = S_{in} - S - W$ the bioreactor model becomes:

$$\begin{bmatrix} \dot{S} \\ \dot{W} \end{bmatrix} = \begin{bmatrix} -1 & 0 \\ 0 & -D \end{bmatrix} \begin{bmatrix} \mu \frac{(S_{in}-S)}{Y} \\ W \end{bmatrix} + \begin{bmatrix} -\mu \frac{W}{Y} \\ 0 \end{bmatrix} + \begin{bmatrix} D(S_{in}-S) \\ 0 \end{bmatrix} \tag{5.32}$$

Corollary 1 and from the *Proposition* 20, we know that $\lim_{t\to\infty} W = 0$ and hence $-\mu\frac{W}{Y} = 0$ Using the storage function:

$$V = \int \mu(S) \frac{(S_{in}-S)}{Y} \partial S - \int \mu^*(S^*) \frac{(S_{in}-S^*)}{Y} \partial S + \frac{1}{2} W^2, \tag{5.33}$$

here μ^*, S^* are the steady state values of μ, S, and doing some algebraic modifications, the bioreactor model can be rewritten as:

$$\underbrace{\begin{bmatrix} \dot{S} \\ \dot{W} \end{bmatrix}}_{\dot{\xi}} = \underbrace{\begin{bmatrix} -1 & 0 \\ 0 & -D \end{bmatrix}}_{Q} \begin{bmatrix} \frac{\partial V}{\partial S} \\ \frac{\partial V}{\partial W} \end{bmatrix} + \underbrace{[I]}_{\gamma} \underbrace{\begin{bmatrix} D(S_{in}-S) - \mu^*(S^*) \frac{(S_{in}-S^*)}{Y} \\ 0 \end{bmatrix}}_{v}. \tag{5.34}$$

The matrix Q will always be negative definite and it can be seen through careful observation that if $V \geq 0$ and 0 at $S = S^*$ making the system (5.34) passive.

5.5.2 Passivity Based Control Design

Replacing the steady state S^* with desired steady state S^d and the new storage function V':

$$V' = \int \mu(S) \frac{(S_{in}-S)}{Y} \partial S - \int \mu^d\left(S^d\right) \frac{\left(S_{in}-S^d\right)}{Y} \partial S + \frac{1}{2} W^2, \tag{5.35}$$

here μ^d is the desired steady state values of μ, and doing some algebraic modifications, the bioreactor model can be rewritten as:

$$\underbrace{\begin{bmatrix} \dot{S} \\ \dot{W} \end{bmatrix}}_{\dot{\xi}} = \underbrace{\begin{bmatrix} -1 & 0 \\ 0 & -D \end{bmatrix}}_{Q} \underbrace{\begin{bmatrix} \frac{\partial V'}{\partial S} \\ \frac{\partial V'}{\partial W} \end{bmatrix}}_{\frac{\partial V'}{\partial \xi}} + \underbrace{[I]}_{\gamma} \underbrace{\begin{bmatrix} D(S_{in}-S) - \mu^d\left(S^d\right) \frac{\left(S_{in}-S^d\right)}{Y} \\ 0 \end{bmatrix}}_{v'}; y' = \gamma^T \frac{\partial V'}{\partial \xi}. \tag{5.36}$$

The matrix $Q \prec 0$ if $D > 0$ and if $V' \geq 0$, this makes the system (5.36) passive. $V' = 0$ at $S = S^d$ and $W = 0$. Since the system (5.36) is zero state detectable if the desired concentration of substrate $S^d = 0$, the feedback $v' = -Cy'$ will assure asymptotical stability at $S = S^d$.

5.5.3 Passivity Based Adaptive Control Design

Suppose μ_m is the unknown constant parameter in the bioreactor model shown in (5.36), then the estimation error is $\bar{\mu}_m = \hat{\mu}_m - \mu_m$, where $\hat{\mu}_m$ is the estimated value of the μ_m. Using the controller:

$$\bar{v} = -Cy' + \bar{\mu}_m \lambda(S, W, t), \tag{5.37}$$

where $C = \begin{bmatrix} c_1 & 0 \\ 0 & c_2 \end{bmatrix}; C \succ 0$ and $\lambda = \begin{bmatrix} \lambda_1 \\ \lambda_2 \end{bmatrix}$ is a function of known parameters, the adaptation law:

$$\dot{\bar{\mu}_m} = -K_a \lambda^T y', \tag{5.38}$$

Where $K_a > 0$ is a constant, and the adaptive storage function:

$$\bar{V} = \int \mu(S) \frac{(S_{in} - S)}{Y} \partial S - \int \mu^d\left(S^d\right) \frac{\left(S_{in} - S^d\right)}{Y} \partial S + \frac{1}{2} W^2 + \frac{1}{2} K_a^{-1} \bar{\mu}_m^2, \tag{5.39}$$

where $\bar{V} \geq 0$ and $\bar{V}(0) = 0$, the system (5.36) can be written as:

$$\begin{bmatrix} \dot{S} \\ \dot{W} \\ \dot{\bar{\mu}_m} \end{bmatrix} = \underbrace{\begin{bmatrix} -1 - c_1 & 0 & K_a \lambda_1 \\ 0 & -D - c_2 & K_a \lambda_2 \\ -K_a \lambda_1 & -K_a \lambda_2 & 0 \end{bmatrix}}_{\bar{Q}} \begin{bmatrix} \frac{\partial \bar{V}}{\partial S} \\ \frac{\partial \bar{V}}{\partial W} \\ \frac{\partial \bar{V}}{\partial \bar{\mu}_m} \end{bmatrix}. \tag{5.40}$$

$\bar{Q} \prec 0$ as $D > 0$, therefore the feedback adaptive controlled system (5.40) will be asymptotically stable towards $S = S^d$, $W = 0$ and $\bar{\mu_m} = 0$.

5.5.4 Simulations

The problem of industrial incident, where 9 tons of anilin leaked from a chemical plant into a river (single stram), is considered here, where the initial aniline concentration is 70 mg/l. It is aimed to reach 1 mg/l or less. Monod parameters are $K_s = 3.1$ mg/l, $\mu_m = .12h^{-1}$, $Y = 0.74$. Substrate concentration is assumed to be the only measurement, the dilution rate D is the control input.

The simulation results comparing the three control strategies i.e. chemostat control with steady state dilution rate, passivity based control with assumed value of μ_m and passivity based adaptive control are shown below (79): Fig 5.1

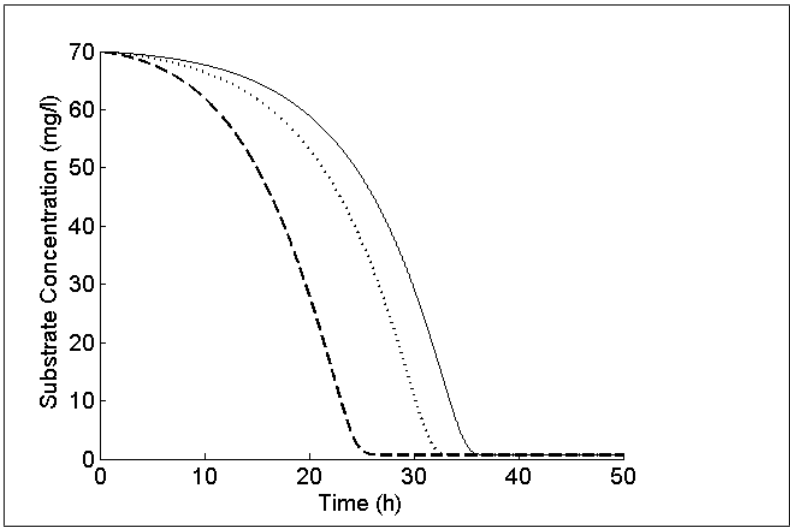


Figure 5.1: Substrate Concentration; Bold: Chemostat; Dotted: Passivity Based; Dashed: Adaptive.

shows the substrate concentration pattern reaching to the desired concentration level of $1mg/l$. It is clear that the Adaptive control strategy allows to reach the desired level at a faster rate with same smoothness. W is the new coordinate

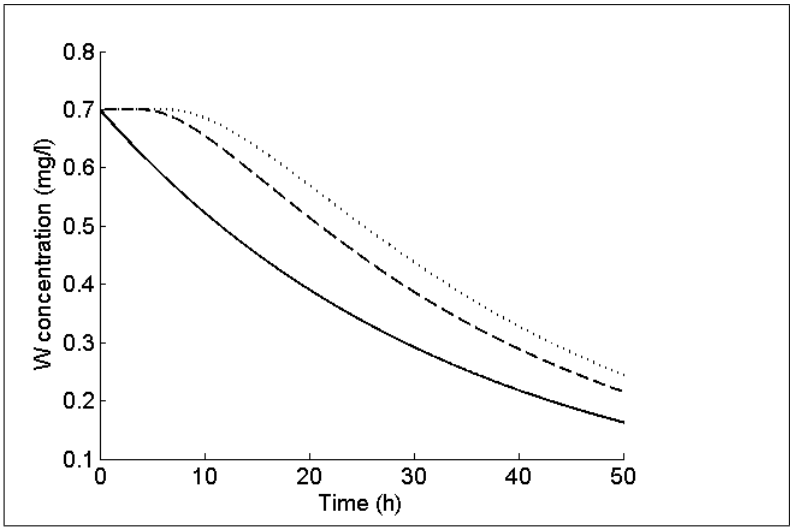


Figure 5.2: W Concentration; Bold: Chemostat; Dotted: Passivity Based; Dashed: Adaptive.

which is proportional to the negative of the substrate concentration and. It will eventually converge to zero shown in Fig 5.2. The adaptive controller reaching the

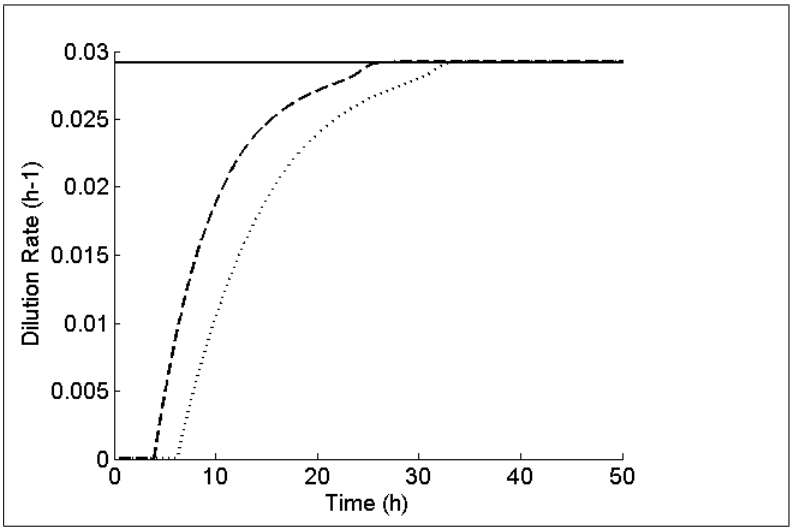


Figure 5.3: Dilution Rate; Bold: Steady state, Dotted: Passivity Based; Dashed: Adaptive.

desired steady state of dilution rate quickly same as in substrate concentration in Fig 5.3. The adaptive control is making it possible to reach the assumed

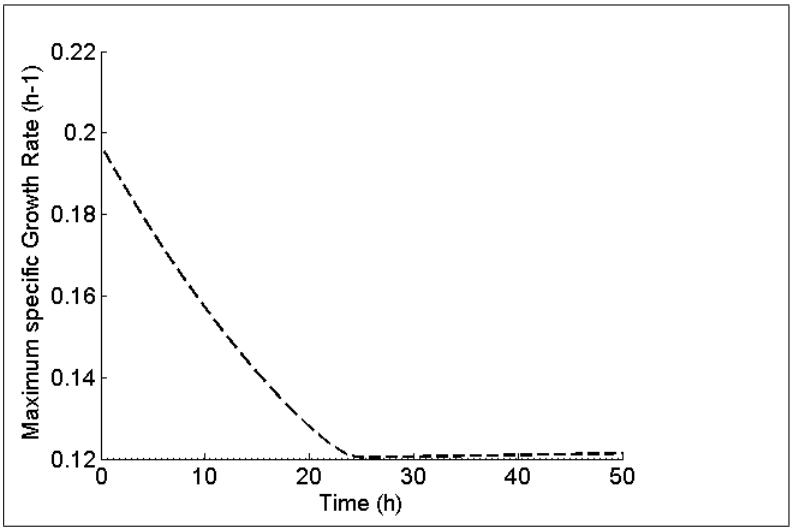


Figure 5.4: Maximum Specific Growth Rate; Dotted: Assumed; Dashed: Adaptive.

value of maximum specific growth rate shown in Fig 5.4. Fig 5.5 shows the variation in specific growth rate under different types of strategies. clearly the adaptive control strategy is more spontaneous towards the steady state. The cell

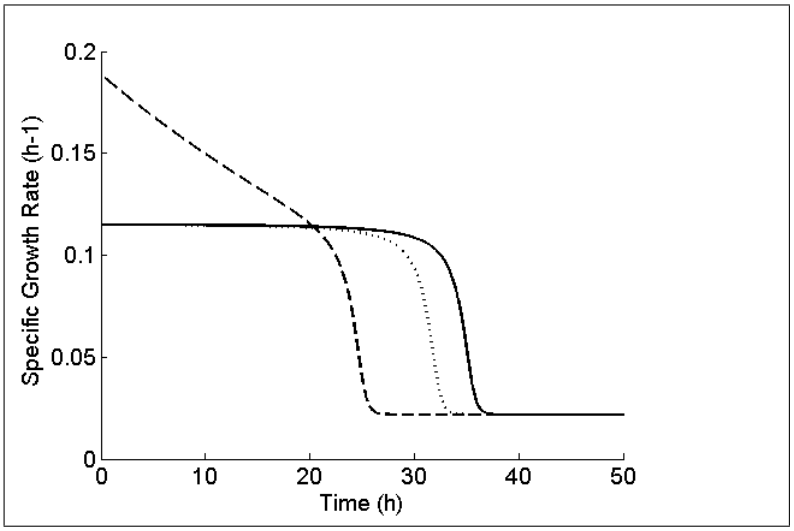


Figure 5.5: Specific Growth Rate; Bold: Chemostat; Dotted: Passivity Based; Dashed: Adaptive.

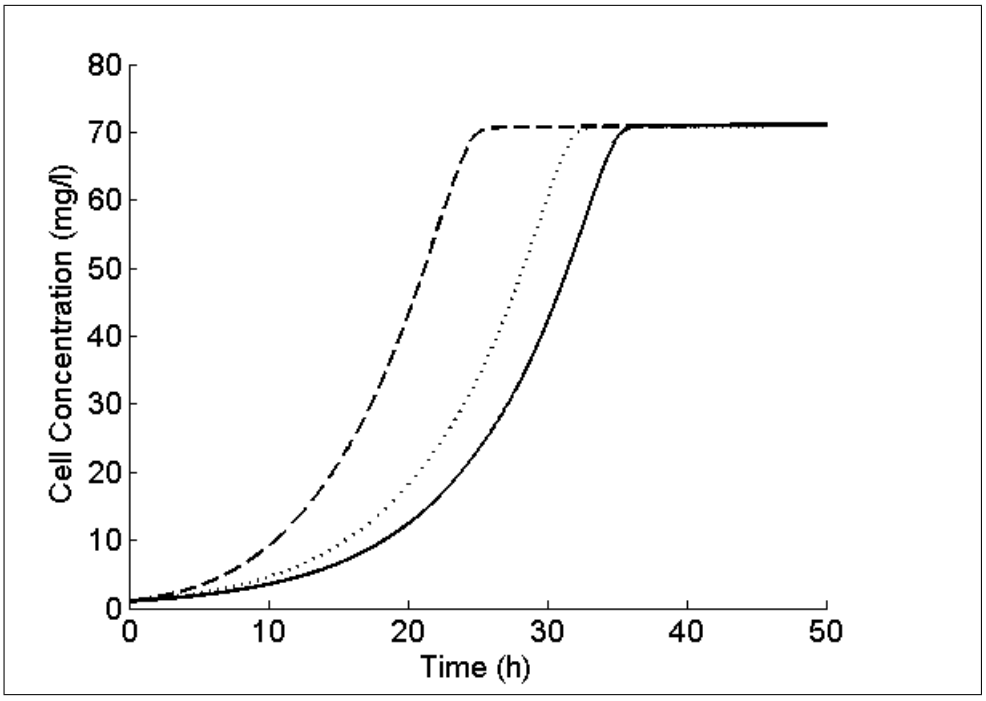


Figure 5.6: Cell Concentration; Bold: Chemostat; Dotted: Passivity Based; Dashed: Adaptive.

concentration will obviously increase at a similar rate as substrate concentration will decrease as visible in Fig 5.6.

5.5.5 Alternative Storage Functions

This section is showing the possibility of having some other storage functions for the single reaction application. These storage functions may not be physical but can serve the purpose of passivizing the model and perform the Passivity Based Adaptive Control. More focus is done here to perform PH formulation and IDA-PBC Control using different storage functions. The important point is that these storage functions do not need decoupling of the reactions hence such technique can be applied to the systems which cannot be decoupled. However, the latter methodology is more physical and one can relate to the kinetics while performing control. Consider the system (5.32), passivity can be shown for this model at $(W,S,D)=(0,0,0)$ (which corresponds to near-batch operating conditions) using such a very simple energy function such as a sum of quadratic terms $H=W^2+S^2$ and taking $y=S$ as a possible output.
Nevertheless, in this case, one will not have the nice symmetry properties given for PH systems, which need an appropriate energy function to be shown. There could be other Hamiltonian functions and can be derived using the following proposition.

Proposition 25. *The system in equation* (5.32) *with* $\mu=f(S)S$*, where* f *is non-singular at* $S=0$*, can be written in a PH form with an energy function* H *such that* $\delta H=\frac{\partial H}{\partial S}=\frac{\partial H}{\partial W}$ *, where* $\lim_{X\to 0}\frac{S}{\delta H}\neq 0$*. Assuming that the system is zero-state detectable, then a simple output feedback* $v=-ky$*, where* $k>0$*, stabilizes asymptotically the system at the equilibrium point* $y=0$*.*

Proof: *Note* $H_{(.)}=\frac{\partial H}{\partial (.)}$*. From* (5.32) *one has the pseudo-PH form :*

$$\begin{pmatrix}\dot{W}\\ \dot{S}\end{pmatrix}=\begin{pmatrix}0 & -\frac{\mu(S)W}{\delta H}\\ \frac{\mu(S)W}{\delta H} & 0\end{pmatrix}\begin{pmatrix}H_W\\ H_S\end{pmatrix}+\begin{pmatrix}-W\\ S_0-S\end{pmatrix}v \tag{5.41}$$

$$y=\begin{pmatrix}-W\\ S_0-S\end{pmatrix}^T\begin{pmatrix}H_W\\ H_S\end{pmatrix} \tag{5.42}$$

The output feedback property is inherent to PH systems ((91)).

Remark 8. *Many functions qualify. Instead of a standard quadratic function, one can take* $H=(W+S)^2$*. It seems all the more interesting to use* $H_W=H_S=(W+S+1)log(W+S+1)-(S+W)$*,which is inspired from a scaled Gibbs free energy (note that, in this case, there is no physical background; even if this function could be interpreted - with multiplication by RT - as an energy). In this*

case, the output will be
$y = \begin{pmatrix} -W \\ S_0 - S \end{pmatrix}^T \begin{pmatrix} logW + S + 1 \\ logW + S + 1 \end{pmatrix}$ *which finally reduces to*

$$y = \frac{Xlog(1 + S_0 - X)}{Y}, \tag{5.43}$$

which is a function of the biomass concentration corresponding to some kind of an "energetic" rate.

5.5.5.1 IDA-PBC Scheme Using Alternative Storage Functions

(27) One can easily apply the IDA-PBC control to the PH system in (5.41). Different simple configurations of Hamiltonians can be considered :

1. $H = \frac{1}{2}(W + S)^2$ and $H_d = \frac{1}{2}(W + \frac{S}{S_d} - 1)^2$
2. $H = (1 + W + S)log(1 + W + S)$ and $H_d = (\frac{W+S}{s_d})log(\frac{W+S}{S_d}) - (\frac{W+S}{S_d})$

The main problem consists of finding the matching condition; assume that the matrices J_d, R_d are under the form:
$J_d - R_d = \begin{pmatrix} \beta & -\alpha \\ \alpha & \beta \end{pmatrix}$.
Following basic IDA-PBC rule mentioned in previous chapter, one has simply the matching condition:

$$\alpha = \beta \frac{w - s0 + s}{-w - s0 + s} - \frac{\mu w}{\delta H_d}$$

The control will be chosen directly as a function of δH_d , for example:

$$v = -K \frac{\delta H_d}{x},$$

which yields $\beta = KY$. the control ensures that (S, W) will converge to $(S_d, 0)$.

5.5.5.2 Adaptive Control Scheme Using Alternative Storage Functions

(27) Typically, for the single reaction example chosen, the dilution rate D can be split in three parts,

$$D = \hat{\mu} + v + (\mu_m - \hat{\mu}_m)\Delta,$$

where $\hat{\mu}$ is an estimate of the specific growth rate, μ_m is the maximum specific growth rate which is a constant parameter, and $\Delta(S) = \frac{\mu}{\mu_m}$. v is the remaining

part of the controller that will stabilize the biosystem around the desired equilibrium point. Of course, when the specific growth rate is perfectly known, the third part which accounts for uncertainties vanishes.
Note $\tilde{\mu_m} = \hat{\mu_m} - \mu_m$, then we have the following proposition

Proposition 26. *The system in equation* (5.41) *with* $\dot{\tilde{\mu_m}} = -K_\theta \Delta y, K_\theta > 0$ *and energy function* $\mathscr{H} = H + \frac{1}{2K_\theta}(\hat{\mu_m} - \mu_m)^2$ *is Port-Hamiltonian.*

Proof: *First note that* $\dot{\hat{\mu_m}} = -K_\theta \Delta y$*, where the value of* y *can be replaced by its Port-Hamiltonian description. Then one has to take into account the additional term* $\Delta(S,W)(\mu_m - \hat{\mu_m})$ *in the dynamics of* S *and* W*. One has now straightforward, replacing the value of* $\hat{\mu_m}$ *in equation* (5.41) *and augmenting the system with* $\hat{\mu_m}$*,*

$$\begin{pmatrix} \dot{W} \\ \dot{S} \\ \dot{\hat{\mu_m}} \end{pmatrix} = \begin{pmatrix} 0 & -\frac{\mu(S)W}{H_W} & +WK_\theta\Delta \\ \frac{\mu(S)W}{H_S} & 0 & (S_0 - S)K_\theta\Delta \\ -WK_\theta\Delta & -(S_0 - S)K_\theta\Delta & 0 \end{pmatrix} \begin{pmatrix} \mathscr{H}_W \\ \mathscr{H}_S \\ \mathscr{H}_z \end{pmatrix} + \begin{pmatrix} -W \\ S_0 - S \\ 0 \end{pmatrix} v$$
$$y = \begin{pmatrix} -W \\ S_0 - S \\ 0 \end{pmatrix}^T \begin{pmatrix} \mathscr{H}_W \\ \mathscr{H}_S \\ \mathscr{H}_{\tilde{\mu_m}} \end{pmatrix} \tag{5.44}$$

This system is indeed Port-Hamiltonian and thus is stable at the equilibrium point $(D_d, S_d, W_d, \hat{\mu_m}^d, y_d)$ *and origin* $(D, \bar{S}, \bar{W}, \tilde{\mu_m}, y) = (0,0,0,0,0)$ *such that* $\bar{W} = W - W_d$*,* $\bar{S} = S - S_d$ *which implies that* $\dot{\bar{S}} = \dot{S}$ *and* $\dot{\bar{W}} = \dot{W}$*.*

Remark 9. *The equilibrium point can be shifted to origin by taking states as* $W = W - W_d$*,* $S = S - S_d$*. In this case IDA-PBC control as defined in the previous section can be designed using Hamiltonian:*
$\mathscr{H}_d = H_d + \frac{1}{2K_\theta}(\hat{\mu_m} - \mu_m)^2$ *with the same update law. An adequate controller will replace the expression of* y *arising from the Port-Hamiltonian model by a value directly obtained from measurements of the biomass concentration* X*.*

5.5.6 Simulations Comparing Different Storage Functions

Assuming that the substrate concentration and biomass concentration can be measured. One has $K_s = 0.22g/l, \mu_{max} = 0.3\ h^{-1}, Y = 0.6$, the goal, in this study case, would be simply to cut the substrate concentration by 2.
The controlled input is dilution rate D. The substrate feed concentration S_0 is constant, i.e. $S_0 = 2g/l$ (27).

One can see that there is a good improvement with respect to a chemostat strategy (open-loop control with constant dilution rate), as shown in Fig. (5.7).

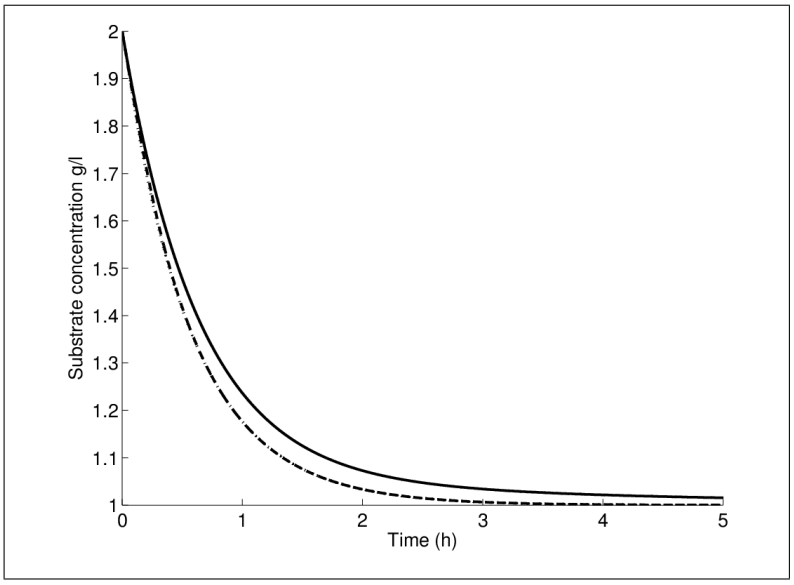


Figure 5.7: Substrate concentration; Bold: constant; Dotted : logarithmic function; Dash-dot : quadratic function

However, a change in the energy function, with comparable convergence rate, leads to similar results. Mainly, the differences can be shown during the onset of tracking with a difference in the W auxiliary variable and the dilution rate as can be seen in figures (5.8) and (5.9)

Note that, as expected, the auxiliary variable converges asymptotically to zero.

One can see that the adaptive law allows to follow in an adequate way the specific growth rate (Fig. 5.10). The estimated values reach the steady state value (for the desired operating point). In the simulations, it happens that the logarithmic function offers a better tracking than the quadratic function, but a generalization of this specific case would have to be proven. Tracking is indeed quite acceptable for this algorithm, as the estimation error is always below 5 %.

The impact regarding tracking errors for the logarithmic function (with real specific growth rate and estimated specific growth rate) is rather small (see Fig. 5.11). However, these errors could be more significant when optimal productivity is desired. In this latter case, the set-point may be sensitive to parametric

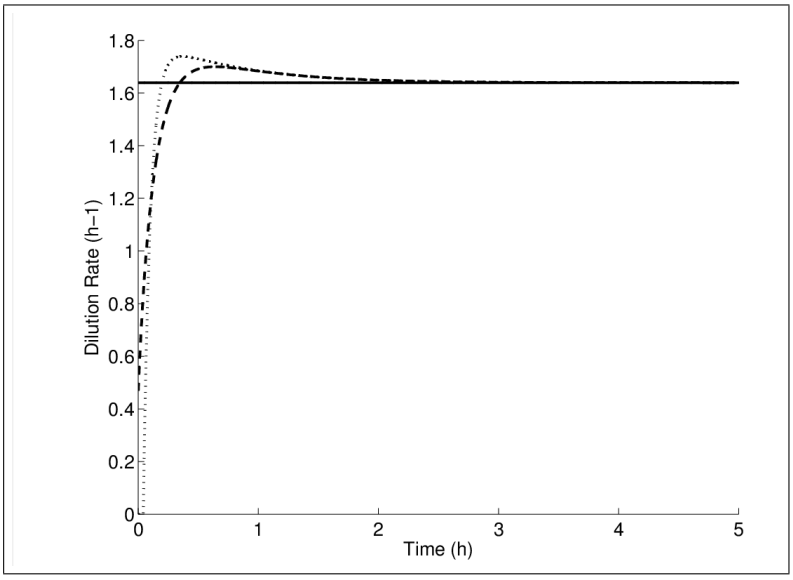


Figure 5.8: Dilution Rate; Bold: constant; Dotted : logarithmic function; Dash-dot : quadratic function

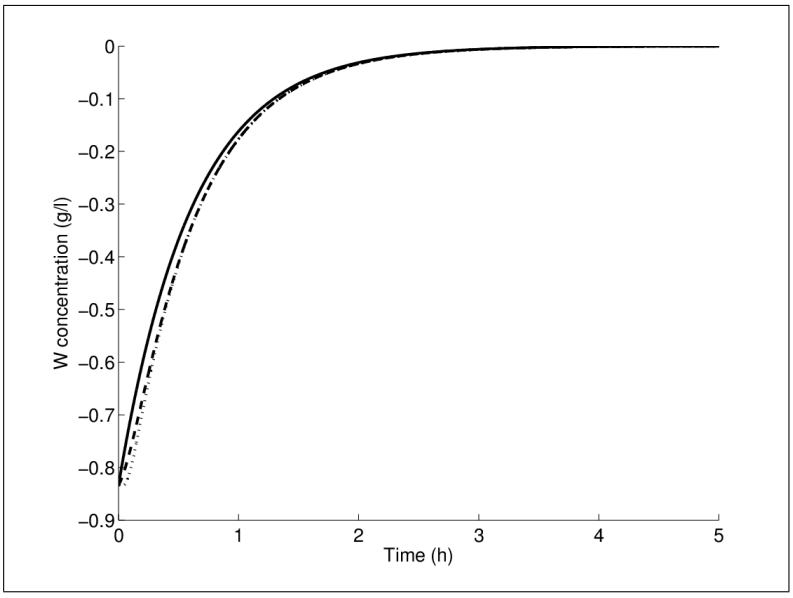


Figure 5.9: Auxiliary variable; Bold: constant; Dotted : logarithmic function; Dash-dot : quadratic function

variations, as the optimal productivity operating point is very often close to the washout. This controller thus better fit to applications such as wastewater treatment, and extensions can be done for extremum tracking.

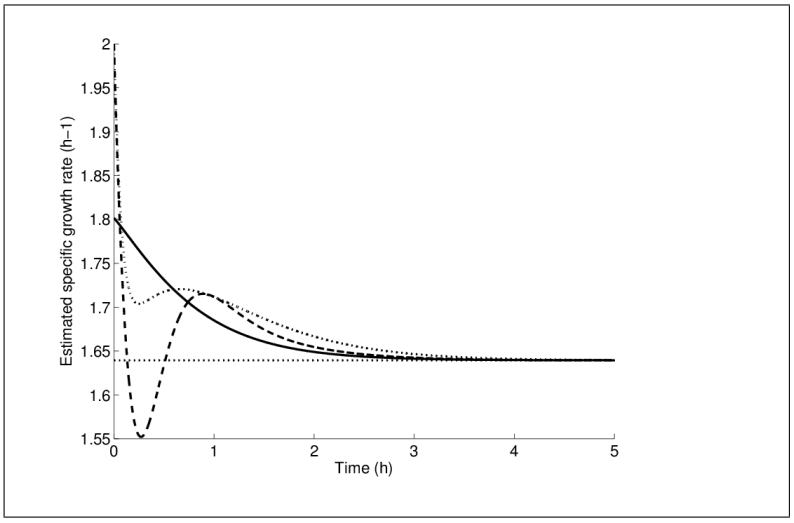


Figure 5.10: Estimated Specific Growth Rate; Bold: true value (with quadratic-based control); Dotted : adaptive / logarithmic function; Dash-dot : adaptive / quadratic function; Small dots: constant final value

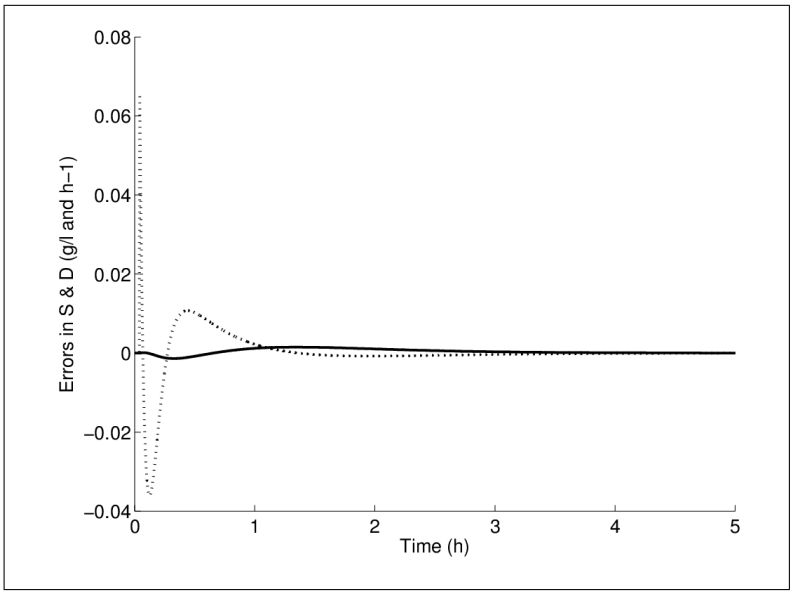


Figure 5.11: Errors in S and D; Bold: Error in substrate concentration; Dotted: Error in Dilution Rate

5.6 Application to Multiple Reactions: The Dynamics of Volatile Fatty Acids in Anaerobic Digester

The anaerobic wastewater treatment process presents very interesting advantages. It has a high capacity to degrade concentrated and difficult substrates (plant residues, animal wastes, food industry wastewater), produces very few sludges, requires little energy and can recover energy using methane combustion (108). Despite all, the anaerobic treatment plants are stil very rare at the industrial scale because of their instability under variations of operating conditions. Indeed, large variation of dilution rate or the influent organic load may lead to the so-called biomass washout. Washout phenomenon involves the inactivation of biomass and the accumulation of volatile fatty acids (109). Hence, the process needs to be stabilised via feedback adaptive control loop (109). The upflow anaerobic fixed bed reactor is considered here. The anaerobic digestion can be explained as follows: the biomass degrades the organic substrate to produce biogas (a mixture of CO2 and CH4) and for growth. The mass balance model is:

$$\dot{X}_1 = X_1 \left(\mu_1 - \alpha D\right), \tag{5.45}$$

$$\dot{X}_2 = X_2 \left(\mu_2 - \alpha D\right), \tag{5.46}$$

$$\dot{S}_1 = -k_1 \mu_1 X_1 + \left(S_{1in} - S_1\right) D, \tag{5.47}$$

$$\dot{S}_2 = -k_3 \mu_2 X_2 + k_2 \mu_1 X_1 + \left(S_{2in} - S_2\right) D, \tag{5.48}$$

$$\mu_1 = \mu_{1m} \frac{S_1}{S_1 + K_{S1}}, \tag{5.49}$$

$$\mu_2 = \mu_{2m} \frac{S_2}{S_2 + K_{S2} + \left({}^{S_2}/_{K_I}\right)^2}. \tag{5.50}$$

Here, $X_1(g/l)$ represents the concentration of acidogenic biomass, $X_2(g/l)$ represents the concentration of methanogenic biomass, $S_1(g/l)$ represents the concentration of organic substrate characterized by its chemical oxygen demand, and

$S_2(mmol/l)$ represents the concentration of volatile fatty acids. $D(day^{-1})$ represents the dilution rate and α is the proportion of biomass not attached to the reactor. $\alpha = 1$ for the case of CSTRs. k_1, $k_2(mmol/g)$, $k_3(mmol/g)$ are the yield coefficients for substrate degradation, Volatile fatty acids production and consumption respectively. $K_I(mmol/l)$ is the inhibition constant and $K_{S1}(g/l)$, $K_{S2}(mmol/l)$ are the saturation constants associated with S_1 and S_2 respectively. $\mu_{1m}(day^{-1})$ and $\mu_{2m}(day^{-1})$ are the maximum bacterial growth rates whose values will be considered to be unknown and the Adaptive control will be designed for the process. Using the coordinate transformation, W_1,W_2 can be assigned the following values:

$$W_1 = (S_{1in} - S_1) - k_1 X_1, \tag{5.51}$$

$$W_2 = (S_{2in} - S_2) + k_2 X_1 - k_3 X_2. \tag{5.52}$$

In turn,

$$X_1 = \frac{S_{1in} - S_1 - W_1}{k_1}, \tag{5.53}$$

$$X_2 = \frac{S_{2in} - S_2 + k_2\left(S_{1in} - S_1 - W_1/k_1\right) - W_2}{k_3} \tag{5.54}$$

In the system, dilution rate D is the only control input i.e. S_{1in}, S_{2in} are constant and $\alpha = 1$. Derivating (5.51), (5.52) w.r.t. time and substituting (5.45) ,(5.46),(5.47) and (5.48) in it, we get:

$$\dot{W}_1 = -DW_1$$
$$\dot{W}_2 = -DW_2$$

The modified space model of the above system can be written as:

$$\begin{bmatrix} \dot{S}_1 \\ \dot{S}_2 \\ \dot{W}_1 \\ \dot{W}_2 \end{bmatrix} = \begin{bmatrix} -k_1 & 0 & 0 & 0 \\ k_2 & -k_3 & 0 & 0 \\ 0 & 0 & -D & 0 \\ 0 & 0 & 0 & -D \end{bmatrix} \begin{bmatrix} \mu_1 X_1 \\ \mu_2 X_2 \\ W_1 \\ W_2 \end{bmatrix} + \begin{bmatrix} D\left(S_{1in} - S_1\right) \\ D\left(S_{2in} - S_2\right) \\ 0 \\ 0 \end{bmatrix} \tag{5.55}$$

From the decoupling methodology explained in this chapter, $S_1 = \xi_a'$ and $S_2 = \xi_a''$. Substituting X_1, X_2 using (5.53), (5.54), the model shown in (5.55) can be written

as:

$$\begin{bmatrix} \dot{S}_1 \\ \dot{S}_2 \\ \dot{W}_1 \\ \dot{W}_2 \end{bmatrix} = \begin{bmatrix} -k_1 & 0 & 0 & 0 \\ k_2 & -k_3 & 0 & 0 \\ 0 & 0 & -D & 0 \\ 0 & 0 & 0 & -D \end{bmatrix} \begin{bmatrix} \mu_1 \frac{S_{1in}-S_1-W_1}{k_1} \\ \mu_2 \frac{S_{2in}-S_2-W_2}{k_3} \\ W_1 \\ W_2 \end{bmatrix} + \begin{bmatrix} 0 \\ -k_2\mu_2 \frac{S_{1in}-S_1-W_1}{k_1} \\ 0 \\ 0 \end{bmatrix} + \begin{bmatrix} D(S_{1in}-S_1) \\ D(S_{2in}-S_2) \\ 0 \\ 0 \end{bmatrix} \tag{5.56}$$

Using *Lemma* 4, it can be said that $-k_2\mu_2 \frac{S_{1in}-S_1-W_1}{k_1} + D(S_{2in}-S_2) = 0$. Hence the model will become:

$$\underbrace{\begin{bmatrix} \dot{S}_1 \\ \dot{S}_2 \\ \dot{W}_1 \\ \dot{W}_2 \end{bmatrix}}_{\dot{\xi}} = \underbrace{\begin{bmatrix} -k_1 & 0 & 0 & 0 \\ k_2 & -k_3 & 0 & 0 \\ 0 & 0 & -D & 0 \\ 0 & 0 & 0 & -D \end{bmatrix}}_{Q} \underbrace{\begin{bmatrix} \mu_1 \frac{S_{1in}-S_1-W_1}{k_1} \\ \mu_2 \frac{S_{2in}-S_2-W_2}{k_3} \\ W_1 \\ W_2 \end{bmatrix}}_{r} + [\gamma] \underbrace{\begin{bmatrix} D(S_{1in}-S_1) \\ 0 \\ 0 \\ 0 \end{bmatrix}}_{u} \tag{5.57}$$

Since, $Q \prec 0$ and with storage function V:

$$V = \int \mu_1 \frac{S_{1in}-S_1-W_1}{k_1} \partial S_1 + \int \mu_2 \frac{S_{2in}-S_2-W_2}{k_3} + \frac{1}{2}W_1^2 + \frac{1}{2}W_2^2,$$

the system will be passive at zero equilibrium and can take the form:

$$\underbrace{\begin{bmatrix} \dot{S}_1 \\ \dot{S}_2 \\ \dot{W}_1 \\ \dot{W}_2 \end{bmatrix}}_{\dot{\xi}} = \underbrace{\begin{bmatrix} -k_1 & 0 & 0 & 0 \\ k_2 & -k_3 & 0 & 0 \\ 0 & 0 & -D & 0 \\ 0 & 0 & 0 & -D \end{bmatrix}}_{Q} \underbrace{\begin{bmatrix} \frac{\partial V}{\partial S_1} \\ \frac{\partial V}{\partial S_2} \\ \frac{\partial V}{\partial W_1} \\ \frac{\partial V}{\partial W_2} \end{bmatrix}}_{\frac{\partial V}{\partial \xi}} + [I] \underbrace{\begin{bmatrix} D(S_{1in}-S_1) \\ 0 \\ 0 \\ 0 \end{bmatrix}}_{u},$$

With output $y = [I]^T \frac{\partial V}{\partial \xi}$. The Passivity of the system at non-zero equilibrium and Passivity Based Adaptive Control can be performed in a similar way as done for single reaction with Monod kinetics. Based on the data available from (11), the next section will show the simulation results.

Simulations

The values of all the constants were obtained from (11). The initial conditions were chosen manually but are taken according to the context of the problem. The results obtained are smooth and clearly showing that adaptive control is more smooth and spontaneous than the normal passivity based control. The values of both the maximum bacterial growth rates also reach to the average constant values.The system achieves the steady state after approximately 50 days. The simulations are as follows (79):

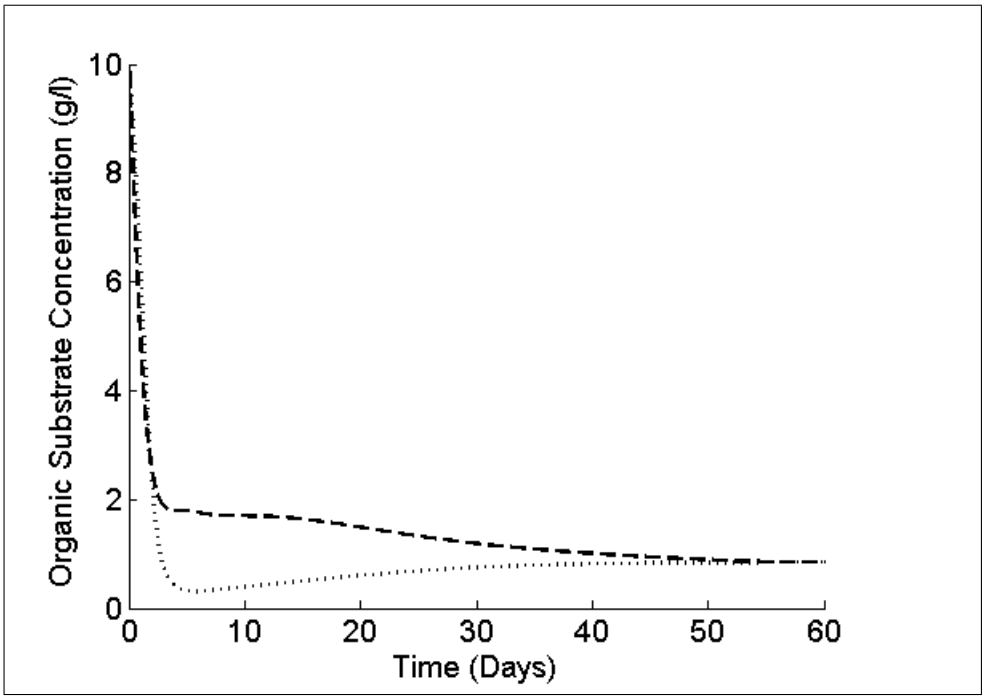


Figure 5.12: Organic Substrate Concentration; Dotted: Passivity Based; Dashed: Adaptive.

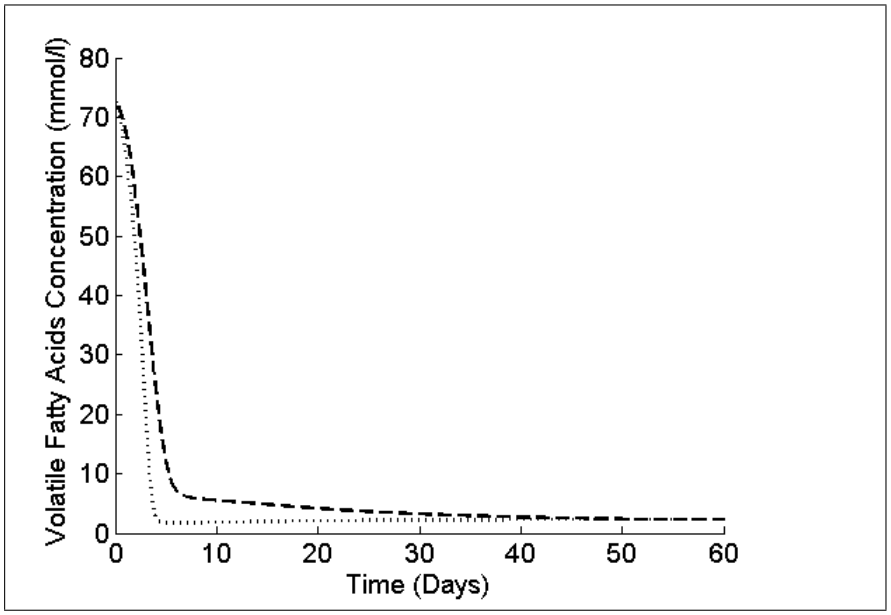


Figure 5.13: Volatile Fatty Acids Concentration; Dotted: Passivity Based; Dashed: Adaptive.

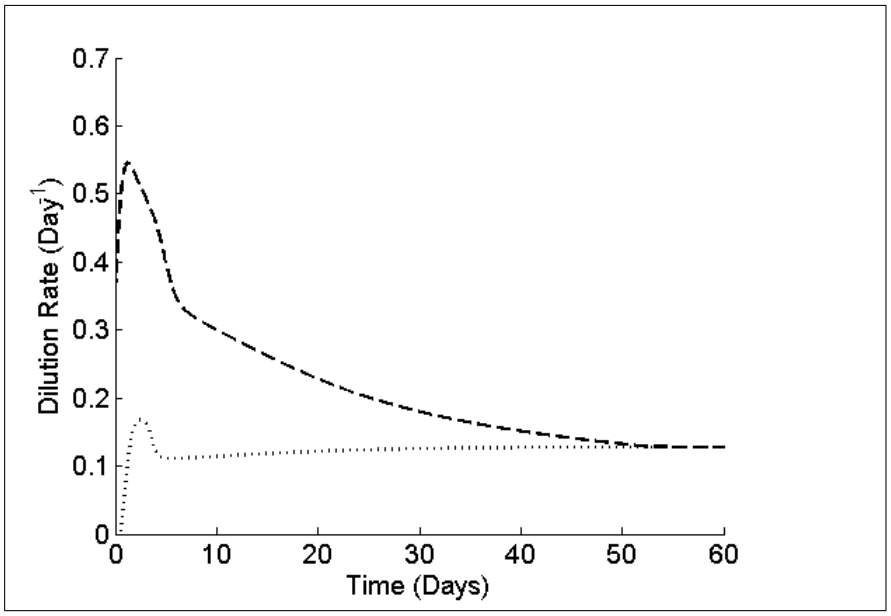


Figure 5.14: Dilution Rate ; Dotted: Passivity Based; Dashed: Adaptive.

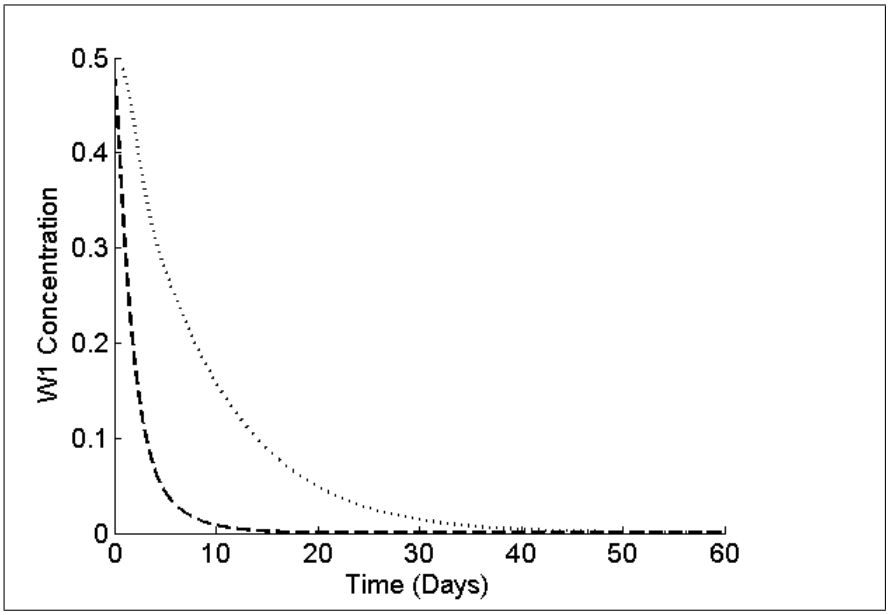


Figure 5.15: W1 Concentration; Dotted: Passivity Based; Dashed: Adaptive.

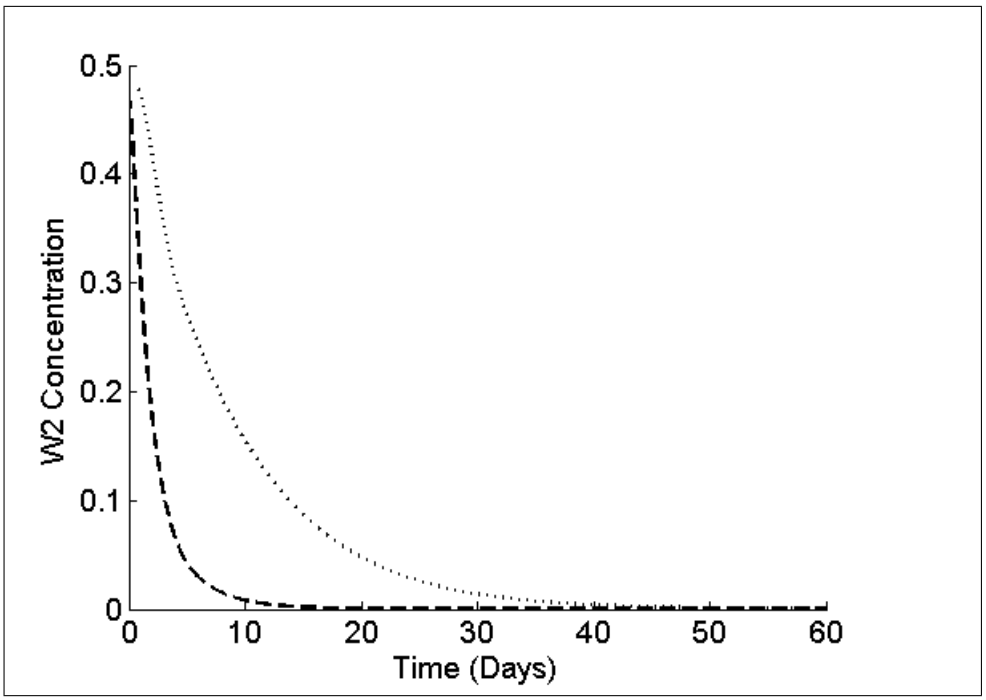


Figure 5.16: W2 Concentration; Dotted: Passivity Based; Dashed: Adaptive.

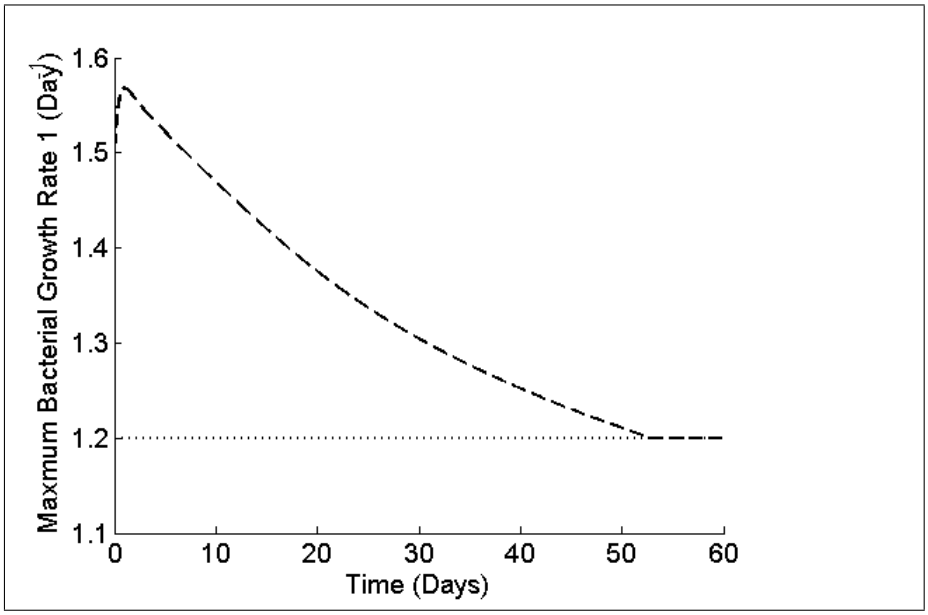


Figure 5.17: Maxmum Bacterial Growth Rate 1; Dotted: Actual; Dashed: Adaptive.

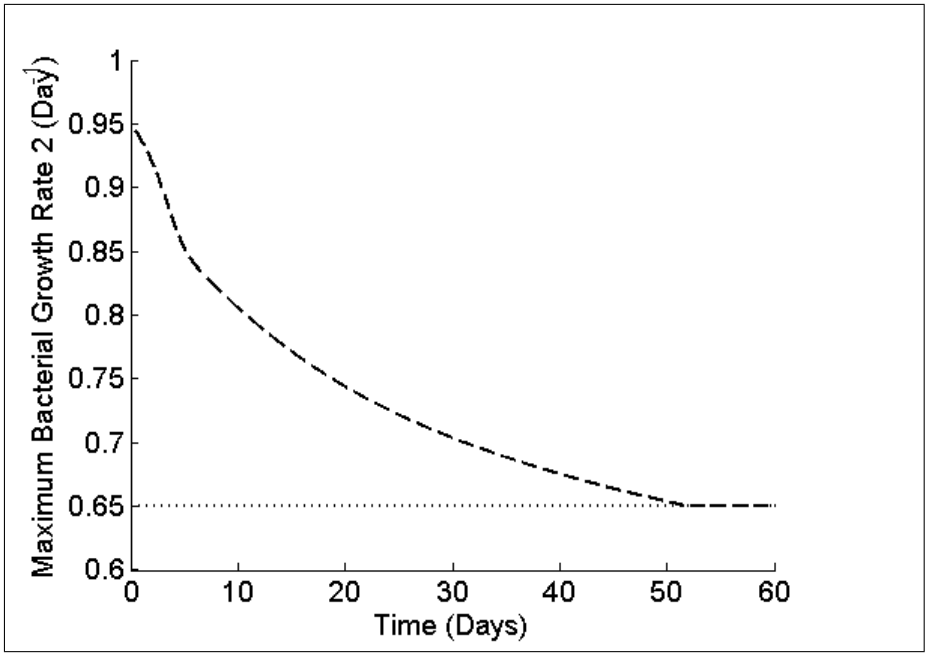


Figure 5.18: Maxmum Bacterial Growth Rate 2; Bold: Chemostat; Dotted: Actual; Dashed: Adaptive.

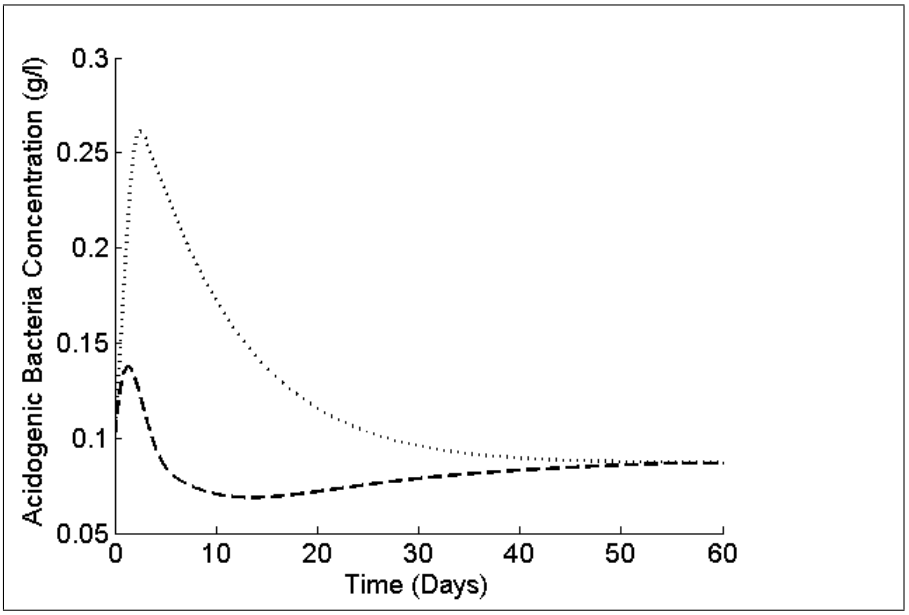


Figure 5.19: Acidogenic Bacteria Concentration; Dotted: Passivity Based; Dashed: Adaptive.

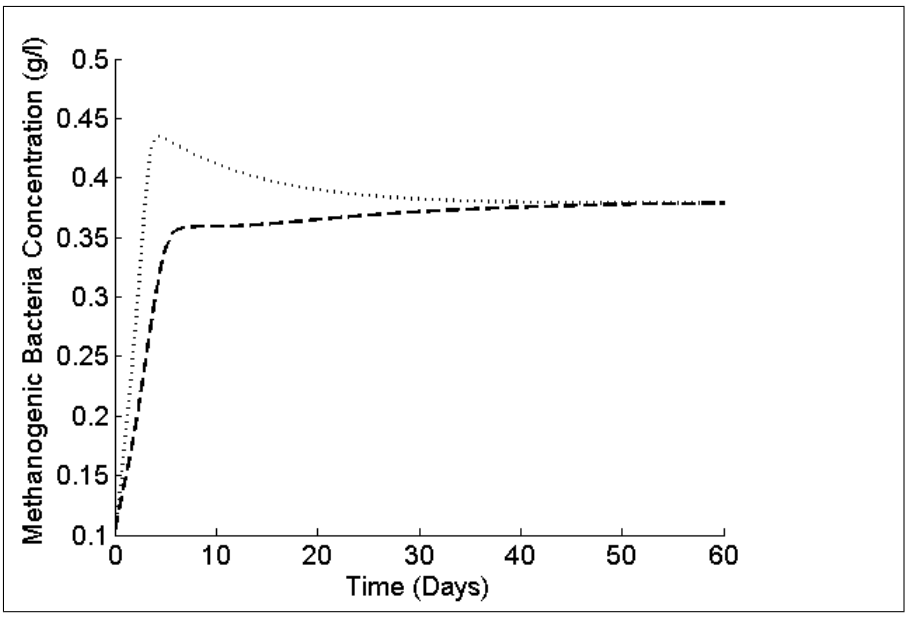


Figure 5.20: Methanogenic Bacteria Concentration; Dotted: Passivity Based; Dashed: Adaptive.

5.7 Conclusion

This chapter is a successful attempt to maintain the structure and physical meaning of the passivity based model of microbial reactions with Monod kinetics in

continuous reactors by using meaningful Lyapunov functions and obvious coordinate transformation on the grounds of passivity. Owing to a change of variable, it has been possible to split a simple bioreaction into a stable subsystem converging to zero, and another subsystem which involves primarily the substrate. It has been shown that this system is passive and to derive passivity based controllers from the modified model. A first attempt to propose more meaningful energetic functions than quadratic ones has been made. Moreover, it is shown that an adaptive controller can be designed using the passivity framework. The general model implies that this technique can be directly applied to huge set of reactions. It is providing a physical view to all issues related to robust control of a bioreaction. Results from simulations show that estimation leads to adequate results and that control using the storage function derived from general model is effective. Also, different other candidate energy functions are being tested and an adaptive controller is designed to cope with uncertainties on the specific growth rate. Simulations show the relevance of the approach. In future, this technique can be extended to other kinetics involved and to different types of reactors like plug flow etc. The physical meaning given to design of observers and parameter estimation could be an interesting job to work on.

Concluding Remarks and Future Perspective

The current work has shown fruitful approaches towards energetic and physical model of the chemical and biochemical reactions in continuous reactors. It can be concluded that the open chemical and biochemical systems at constant temperature and pressure can be formulated in pseudo PH form only. The most suitable and physical Hamiltonian function is Gibbs Free Energy for the reaction part. The input and output can be given energetic view by seeing them as variation in Internal Entropy. The attempt of giving an energetic point of view to the reaction process in open systems has been successfully achieved. A Port-Hamiltonian (PH) formulation in closed system extended to open system and is derived for the open chemical systems. The two new PH formulations for open chemical and biochemical enzyme reactions are also derived i.e. in concentration space as Stoichiometric PH model and in the reaction space as Reaction PH model. SPH and RPH form are a nice addition to the previous PH formulations. SPH and RPH formulations are perhaps the most appropriate and physical ways to model reversible chemical and enzymatic reactions. They can be said to be more close to the physical representation and good for overall understanding of the systems. Writing rate terms in the form of equilibrium or steady state concentrations is really a need for the PH formulation and passivity based control. BGs for such systems are most physical when understood through the gateway of chemical potential and chemical affinity which falls under the same category of Gibbs Free Energy. The Bond Graph model represented here is clearly complementing the Port-Hamiltonian formulation.

For the control part, the thesis concludes that the passivity based control is one physical control strategy for any system if the energy of the system can be quantified. It is robust and helps in better understanding of the control methodology.

The application of passivity based control methodology on chemical systems has been a bit difficult and very difficult for biochemical systems. Passivity based control of biochemical systems could be seen as an important task for the researchers in order to get a control over the energy exhange in such systems. IDA-PBC method is the most obvious and suitable alternative for controlling energy based models but its way better alternative to non-physical controlling ways. All bio-processes in batch and continuous modes can be covered under this approach. The IDA-PBC done on SPH and RPH formulation are the wonderful addition to the Passivity Based Control of open chemical and biochemical systems. The approach towards PH model and control in reaction space which has been hardly touched is opening the new way to look to control such systems. Simulation results obtained are showing the potential of IDA-PBC in the chemical systems and also proving the point of application to open systems and real systems. Simulation results of enzymatic hydrolysis of cellulose are smooth and the results also prove that the application of Port-Hamiltonian models and IDA-PBC control to open systems based on Gibbs Free Energy function as storage function is the most physical methodology for isothermal systems.
The later part of the thesis has shown an effective effort to maintain the structure and physical meaning of the passivity based model of microbial reactions in continuous reactors by using meaningful Lyapunov functions and obvious coordinate transformation on the grounds of passivity. Owing to a change of variable, it has been possible to split a simple bio-reaction into a stable subsystem converging to zero, and another subsystem which involves primarily the substrate. It has been shown that this system is passive and can be used to derive passivity based controllers from the modified model. A first attempt to propose more meaningful energetic functions than quadratic ones has been made.

Moreover, it is shown that an adaptive controller can be designed using the passivity framework. Passivity properties were maintained while performing general adaptive control on microbial reactions. The control takes care of all the basic concepts of biochemical kinetics, the uncertainties and problems faced in control of such systems. The general model implies that this technique can be directly applied to huge set of reactions. It is providing a physical view to all

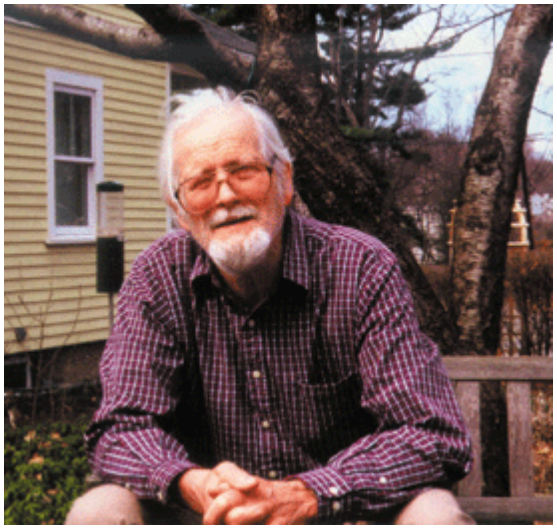
issues related to robust control of microbial reactions. Results from simulations show that estimation leads to adequate results and that control using the storage function derived from general model is effective.
Also, different other candidate energy functions are being tested and an adaptive controller is designed on a single reaction with Monod kinetics to cope with uncertainties on the specific growth rate. Simulations showed the relevance of the approach.

Future Perspective For the future work, the IDA-PBC control of a bioreaction using RPH form should be explored. Port-Hamiltonian modeling and IDA-PBC can prove handy in modeling and control of microbial reactions. The general formalisation of modeling and control of microbial reactions with Monod Kinetics can be extended to other kinetics involved and to different types of reactors like plug flow etc. The physical meaning given to design of observers and parameter estimation could be an interesting job to work on. The future work can also be concentrated on establishing a connection between the Michaelis-Menten kinetics and microbial reactions, validating it for a reaction, formulating in the Port-Hamiltonian form as the duality between Enzyme kinetics and Microbial kinetics are well known. The design of control laws in a bioreactor using IDA-PBC approach and appropriate energy shaping can be expected to derive from such representations.

Appendix

Bond Graph Modeling

The Bond Graph modeling approach was invented by H. M. Paynter in 1959. Bond Graph is a unified graphical approach for modeling systems of different domain like mechanical, thermal, electrical, etc. This approach is based on the power exchange phenomena between elements of a system. The key feature of the Bond Graph modeling is the representation of exchange power (by a bond with half-headed arrow) as the product of generalized efforts (e) and generalized flows (f) with elements acting between these variables and junction structures (algebraic constraints) to reproduce the global model as interconnected subsystems.



Professor Henry M. Paynter (1923-2002)

Bond Graphs are labeled as directed graphs, in which the vertices represent sub-models (or elements) and the edges represent an ideal energy connection between elements. Any physical system can be modeled with the following generalized Bond Graph elements:

- Active elements which provide input power to the system (source of effort Se and source of flow Sf).

- Passive elements transform input power into dissipated energy (resistance R) and stored energy (capacitance C and inductance I).
- Power conserving elements (common effort junction 0, common flow junction 1, transformer TF, and gyrator GY).

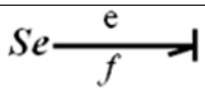
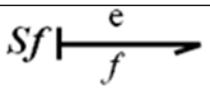
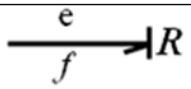
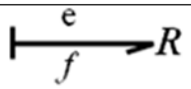
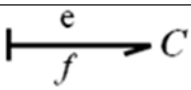
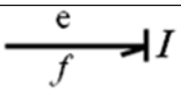
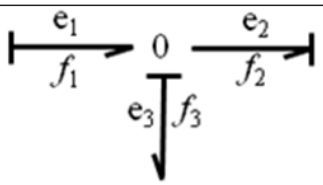
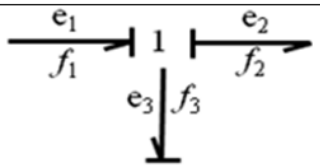
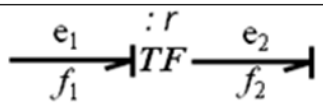
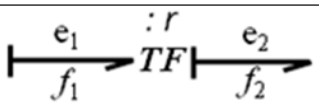
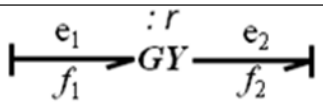
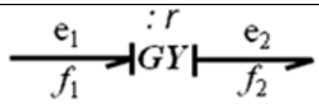
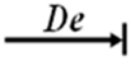
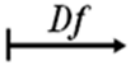
Besides these elements, the various outputs of a system are measured using sensors which are represented by the full-headed arrows in Bond Graph. These full-headed arrows are flow/effort activated bonds (not power bonds). The activated bonds are used only for measurements (detector of effort De and detector of flow Df) and do not contribute to any power flow. The values of some Bond Graph elements may depend on the system states and other variables of a system, in this case, the elements are called modulated elements, for example modulated source of effort MSe, modulated transformer MTF, etc. In this way, Bond Graph enables to develop the dynamic model of any system using Bond Graph elements and power exchange among these elements, while information exchange can be modeled using activated bonds. The description of Bond Graph elements in integral causality is given in the table below with their constitutive relations.

Causality

An important property of the Bond Graph is the causality. The latter enables to define the cause-effect relations in a system. Causal analysis determines the direction of effort and flow information exchange in a Bond Graph. The type of causality used in a model is related to the causality assigned to the storage elements I and C. Indeed, the causality assigned to these elements determine if either an integration or a differentiation with respect to time is required. For the storage elements the causal strokes in preferred integral causality are assigned. Computationally it means that the inertia element accepts an effort as input and produces a flow as output, while the capacitor accepts flow as input and produces effort (*Figure (a)*).

$$\begin{cases} f_I = \frac{1}{I}\int e_I dt, \\ \\ e_c = \frac{1}{C}\int f_C dt \end{cases}$$

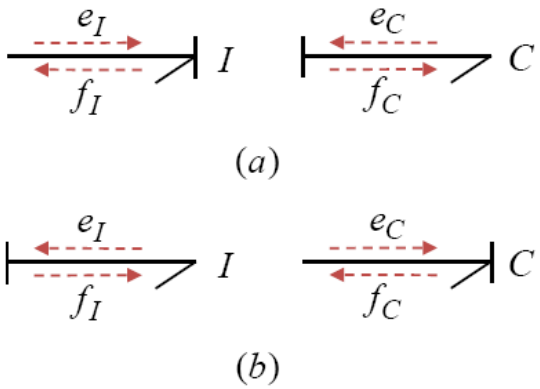
Description of the Bond Graph Elements.

BG element	Element with integral causality	Constitutive relation
Se (source of effort)		$Se = e$
Sf (source of flow)		$Sf = f$
R (resistance)		$f = \frac{1}{R}\, e$
		$e = R\, f$
C (capacitance)		$e = \frac{1}{C}\int f\, dt$
I (inductance)		$f = \frac{1}{I}\int e\, dt$
$0 - junction$ (common effort junction)		$e_1 = e_2 = e_3$ $f_1 = f_2 + f_3$
$1 - junction$ (common flow junction)		$f_1 = f_2 = f_3$ $e_1 = e_2 + e_3$
TF (transformer)		$e_2 = r\, e_1\,;\quad f_1 = r\, f_2$
		$f_2 = r\, f_1\,;\quad e_1 = r\, e_2$
GY (gyrator)		$e_2 = r\, f_1\,;\quad e_1 = r\, f_2$
		$f_2 = r\, e_1\,;\quad f_1 = r\, e_2$
De (effort measurement)		$De = e$
Df (flow measurement)		$Df = f$

If a derivative causality is assigned, the I elements accepts a flow as input and produces an effort as output, while the C element accepts effort as input and produces flow as output (*Figure (b)*).

$$\begin{cases} e_I = I\frac{df_I}{dt}, \\ f_C = C\frac{de_C}{dt} \end{cases}$$

Causal propagation is useful to analyze Bond Graph model. Indeed the causal



Storage elements I and C in (a) integral causality and (b) derivative causality.

strokes give information about causal conflict (incompatibility of equations), derivative causalities (loss of states), algebraic and causal loops (solvability and complication level of the numerical model), and control and monitoring properties.

State-space equations from Bond Graph

The system state-space equations can be derived from a Bond Graph model by introducing the constitutive equations for each subsystem (behavioral equations) and the constraints imposed by the junctions (conservation law equations). The dimension of the state vector is equal to the number of I and C elements in integral causality. Moreover, the state vector of a system (x) is composed of energy variables p and q associated to the I and C elements, respectively.

$$x = \begin{bmatrix} p_I \\ q_c \end{bmatrix} = \begin{bmatrix} \int e_I \\ \int f_C \end{bmatrix}$$

The state variables are not presented in a Bond Graph model, only their derivative.

$$\dot{x} = \begin{bmatrix} \dot{p}_I \\ \dot{q}_c \end{bmatrix} = \begin{bmatrix} e_I \\ f_C \end{bmatrix}$$

In general, for a Bond Graph model with no derivative, causalities, the state-space equations can be deduced through following steps:

1. Write constitutive equations of each element (*R, C, I*),

2. write structural or constraint laws associated with junction structure (0, 1, *TF, GY*),

3. and finally combine these different laws to obtain equation through sequential ordering and substitutions.

Structural analysis

In the context of modeling, control synthesis and fault diagnosis, most results are usually dependent on the systems parameters. This fact prevents from obtaining valid information about the system at an early design stage. In addition, once a parameter is modified, a new analysis phase must be conducted in order to verify if the results on systems performance remain valid. This is where the role of structural analysis is introduced. Indeed, structural analysis enables results to be obtained by analyzing the structure of the system information, and therefore being valid for most values of numerical parameters.

A Bond Graph model allows to perform structural analysis, and enables to deduce a variety of structural properties, such as: system controllability, observability, diagnosability, etc. This analysis only depends on the types of elements (Bond Graph) composing the system, and on the way that they connect between each other regardless of their numerical value.

Structural controllability and observability can be directly concluded from a Bond Graph model without the use of any calculations, as proposed in.

Definition A.1: The system is structurally controllable if and only if two conditions are satisfied:

- There is a causal path connecting a source to each I, and C element in integral causality;
- All I and C elements accept a derivative causality. If this is not completely respected, a dualization of the sources is required to put all I and C elements in derivative causality.

Definition A.2: The system is structurally observable if and only if two conditions are satisfied:

- There is a causal path connecting a detector to each I, and C element in integral causality;
- All I, and C elements accept a derivative causality. If this is not completely respected, a dualization of the detectors is required to put all I, and C elements in derivative causality.

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