

DESIGN OF QFT CONTROLLER FOR GLUCOSE INSULIN REGULATION

A thesis submitted in partial fulfillment of the requirements for

the award of the degree of

Bachelor of Technology

in

Electrical and Electronics Engineering

By

MOHAMED SHA S (EE12B1006)

RAJAKUMAR R (EE12B1013)



DEPARTMENT OF ELECTRICAL AND ELECTRONICS ENGINEERING

NATIONAL INSTITUTE OF TECHNOLOGY PUDUCHERRY

KARAIKAL – 609605.

MAY 2016

BONAFIDE CERTIFICATE

This is to certify that the project titled **DESIGN OF QFT CONTROLLER FOR GLUCOSE INSULIN REGULATION** is a bonafide record of the work done by

MOHAMED SHA S (EE12B1006)

RAJAKUMAR R (EE12B1013)

in partial fulfillment of the requirements for the award of the degree of **Bachelor of Technology in Electrical And Electronics Engineering** of the **NATIONAL INSTITUTE OF TECHNOLOGY PUDUCHERRY**, during the year 2015-2016.

Dr.T.Vinopraba

Project Guide

Dr. K Chandrasekaran

Head of the Department

Project viva-voice held on _____

Internal Examiner

External Examiner

ABSTRACT

Diabetes is a widespread disease in the western world today. Many researchers are working on methods for diagnosing and treating diabetes. A tool used for this is mathematical models of the blood glucose and insulin kinetics.

In this thesis one of the models, Bergman's minimal model is analyzed through derivation and simulations. It is a model consisting of glucose and an insulin kinetics part. The part, describing glucose kinetics has the problem that it overestimates glucose effectiveness and underestimates insulin sensitivity, which is interpretation parameter of a test called the IVGTT (Intravenous Glucose Tolerance Test).

Modifications and additions which could be done in order to describe the glucose and insulin kinetics more thoroughly are described. Based on Bergman's minimal model, two coupled models are proposed. A coupling between the two basic parts of Bergman minimal model and a coupling between the two modified parts of Bergman's minimal model. The basic coupling is called the original model. It can be used to describe the IVGTT for a healthy and a glucose resistant subject. Through calculation and simulation it is shown that the original model has an equilibrium problem, when a parameter p_3 is less than the basal concentration G_b .

The modified coupling, which is able to describe the glucose-insulin system for a Type 1 diabetic on treatment, is tested for reactions to insulin injections and change in basal insulin production. A QFT controller, controlling insulin delivery is implemented and it is shown how it can be used with the modified model, in order to test it for meal disturbance.

QFT is an engineering design theory devoted to the practical design of feedback control systems. Comparatively, QFT can take uncertainty's scopes and performance requirements into account, analyze and design robust controller on Nichols Chart (NC) quantitatively in order to make the open loop frequency curve comply with boundary conditions and have robust stability and performance robustness.

In this project work, an attempt has to be made to design robust QFT controller to overcome the uncertainties and nonlinearities in the human body for maintaining the glucose level at the nominal rate.

Keywords: QFT, Nichols Chart, IVGTT, Human Blood, Robust controller

ACKNOWLEDGEMENT

This project consumed huge amount of work, research and dedication. Still, implementation would not have been possible if we did not have the support of many individuals. Therefore we would like to extend our sincere gratitude to all of them.

First and foremost we are thankful to respected Director Madam, **Dr. S. K. Pandey** for permitting us to undertake this project work.

We are grateful to **Dr. K. Chandrasekaran**, Head of the Department, Electrical and Electronics Engineering for provision of expertise, and technical support in the implementation. The success of this project wouldn't have been possible without his support.

We would like to express our deep and sincere gratitude to our supervisor **Dr. T. Vinopraba**, Assistant Professor, Department of Electrical and Electronics Engineering for her continual effort in this thesis work. Her guidance, encouragement, suggestion and very constructive criticism have contributed immensely to the evolution of our idea on the topic and without her this work would not have been possible.

Nevertheless, we express our gratitude towards our families and colleagues who kept us on track and provided hours of entertainment and stimulating conversation.

CONTENTS

CHAPTER NO.	TITLE	PAGE NO
	ABSTRACT	i
	ACKNOWLEDGEMENT	ii
	TABLE OF CONTENTS	iii
	LIST OF SYMBOLS	vi
	LIST OF ACRONYMS	vii
	LIST OF FIGURES	viii
	LIST OF TABLES	ix
1	INTRODUCTION	
	1.1 General Introduction	1
	1.2 Objectives of the thesis	2
	1.3 Scope	2
	1.4 Approach and Methodology	3
	1.5 Materials and Equipments	3
	1.6 Contribution of the thesis	3
	1.7 Organization of the thesis	4
2	LITERATURE REVIEW	
	2.1 Quantitative Feedback Methodology	5
	2.1.1 Template Generation	5
	2.1.2 Bound Generation	7
	2.1.3 Loop Shaping	9
	2.2 QFT Controller and its Applications	9
	2.2.1 Glucose insulin regulation using QFT	10
	2.3 Summary	13

3	MATHEMATICAL MODEL OF GLUCOSE INSULIN REGULATION	
	3.1 General Introduction	14
	3.2 IVGTT	15
	3.3 Bergman's minimal model	16
	3.3.1 The glucose minimal model	16
	3.3.2 The insulin minimal model	17
	3.3.3 The original model	17
	3.4 Summary	18
4	QUANTITATIVE FEEDBACK THEORY DESIGN AND ANALYSIS	
	4.1 General Introduction	20
	4.1.1 Uncertainty	20
	4.1.1.1 Structured Uncertainty	21
	4.1.1.2 Unstructured Uncertainty	22
	4.1.2 Robust Stability and Robust Performance	22
	4.1.3 2 DOF Closed Loop Formulation	23
	4.2 QFT Design Procedure	25
	4.2.1 Objective of QFT	26
	4.2.2 Methodology of QFT	26
	4.2.2.1 Templates	27
	4.2.2.2 Choice of Frequency Array	29
	4.2.2.3 Choics of Nominal Plant	30
	4.2.2.4 Computation of Bounds	30
	4.2.2.5 Loop Shaping	33
	4.3 Features and Characteristics of QFT	34
	4.4 Shortcomings of QFT	34
	4.5 Summary	35

5	QFT CONTROLLER DESIGN FOR GLUCOSE INSULIN REGULATION	
	5.1 General Introduction	36
	5.2 Description of Problem	36
	5.3 Performance Specifications	38
	5.3.1 Robust Stability Specifications	38
	5.3.2 Robust Tracking Specifications	39
	5.4 QFT Design for UAV	41
	5.4.1 Template Generation and Nominal plant selection	41
	5.4.2 Bound Computation	43
	5.4.2.1 Robust Stability Bounds	43
	5.4.2.2 Robust Tracking Bounds	44
	5.4.2.3 Composite Bounds	44
	5.4.3 Loop shaping	45
	5.4.4 Prefilter shaping	47
	5.5 Design analysis and closed loop validation	49
	5.6 Results and Discussion	50
6	SUMMARY AND CONCLUSION	
	6.1 Summary and Conclusion	51
	6.2 Future prospects	52
	REFERENCES	53
	APPENDIX A	56
	APPENDIX B	64
	APPENDIX C	69

LIST OF SYMBOLS

P-Plant

L_0 -Nominal loop transmission function

G_c -Controller/compensator

F-Prefilter

K- Process gain

ω -Frequency

ω_n -Natural frequency

δ -Damping ratio

a-Parameter value

y-Output

u-Input

LIST OF ACRONYMS

QFT-Quantitative Feedback Theory

SISO-Single Input Single Output

MIMO-Multi Input Multi Output

DOF-Degree Of Freedom

NC-Nichols Chart

6 DOF-Six Degree Of Freedom

3 DOF –Three Degree OF Freedom

MISO-Multi Input Single Output

GM-Gain Margin

PM-Phase Margin

IVGTT- Intravenous Glucose Tolerance Test

LIST OF FIGURES

Figure No.	Title	Page No
3.1	An IVGTT for a Normal subject Model	15
4.1	2DOF control system	24
4.2	Bode plot of Uncertain plant family	28
4.3	Template for uncertain plant family	29
4.4	Robust Stability Bound for an uncertain plant	31
4.5	Robust Tracking Bound for an uncertain plant	31
4.6	Group Bounds for an uncertain plant	32
4.7	Intersection Bounds for an uncertain plant	32
4.8	Nominal Open Loop Shaping	33
5.1	Bode diagram of the uncompensated system	37
5.2	Time response of the uncompensated system	38
5.3	Time response of the tracking specifications	40
5.4	Frequency response of the Tracking specifications	40
5.5	MATLAB QFT controller design	41
5.6	Open Loop response of the Nominal plant	42
5.7	Templates for glucose insulin regulation model	43
5.8	Robust Stability Bounds of glucose insulin regulation model	44
5.9	Robust Tracking Specification of glucose insulin regulation model	45
5.10	Open Loop Frequency Response of the glucose insulin model without controller	46
5.11	Final loop shaped frequency response	47
5.12	Closed Loop Bode without Prefilter	48
5.13	Closed loop frequency response with proposed Controller & Prefilter	48
5.14	Closed Loop Time domain tracking response with proposed Controller	49

LIST OF TABLES

Table No	Title	Page No
2.1	Literature on glucose insulin regulation control systems	10
2.2	Case studies on QFT controller employed industrially	12
3.1	Parameters of bergman's minimal model	17

CHAPTER 1

INTRODUCTION

1.1 GENERAL INTRODUCTION

The formulation of control problems, based on the mathematical model of physical systems, is intrinsically complex. Uncertainty arises when some aspects of the system model is not completely known at the time of analysis and design. In real time platform any control system is susceptible to disturbances and noises, the effect of these signals would adversely affect the performance of the system. The design objectives are best realized via the feedback control mechanism which may reduce the influence generated by uncertainties and achieve desirable performance although it introduces the issues of high cost (the use of sensors), system complexity (implementation and safety) and application of inadequate/inappropriate feedback controller may lead to an unstable closed loop system though the original open-loop system is stable.

The need and importance of robustness in control systems design has been particularly brought into the limelight during the last four decades. When multivariable design techniques were first developed in the 1960s, the emphasis was placed on achieving good performance, and not on robustness. These multivariable techniques were based on linear quadratic performance criteria and Gaussian disturbances, and proved to be successful in many aerospace applications. However, Linear Quadratic Gaussian (LQG) methods show poor robustness properties to other industrial problems. This led to a substantial research effort to develop other control theory that could explicitly address the robustness issue in feedback design.

Many earlier works on robust control algorithms to practical problem has been failed due to inability of the implementation of the designed controller. Either it has too high order or very high gain that it is impractical to realize .One of the robust control technique that can overcome the aforesaid problems is the Quantitative Feedback Theory (QFT). Quantitative Feedback Theory is a phrase, coined by Professor Isaac Horowitz in 1960, used to identify the method he developed for designing robust control systems.

QFT is useful for practical design of feedback system which is needed due to the presence of uncertainty in the plant model and disturbances acting on the plant. Feedback is used to obtain plant's stability by reducing the sensitivity to parameter variation and attenuate the effect of disturbances. QFT provides robust control and performance regardless to any change in plant. It is a methodology to design robust controllers based on frequency domain. This technique allows designing robust controllers which fulfil some minimum quantitative specifications considering the presence of uncertainty in the plant model and the existence of perturbations. With this theory, Horowitz showed that the final aim of any control design must be to obtain an open-loop transfer function with the suitable bandwidth (cost of feedback) in order to reduce the perturbations. The Nichols plane is used to achieve a desired robust design over the specified region of plant uncertainty where the aim is to design a compensator $G_c(s)$ and a prefilter $F(s)$ (if it is necessary), so that performance and stability specifications are achieved for the family of plants.

QFT works well in both Single Input Single Output (SISO) and Multiple Input Multiple Output (MIMO) system and has been proven as the robust control and performance in the area of communication, agricultural, marine and aerospace engineering.

1.2 OBJECTIVE OF THESIS

The main objectives of this project are evident from its title, i.e.

1. The mathematical modeling of glucose insulin regulation of human body.
2. Detailed study of control strategy of QFT.
3. To design and implement the QFT controller for blood glucose controlling model with structured parametric uncertainty that satisfies the desired performance specifications.

1.3 SCOPE

This thesis discusses QFT controller design methodology and implements it on the glucose insulin regulation in human model.

1.4 APPROACH AND METHODOLOGY

This work begins with the mathematical description of blood glucose regulation of human body model with the parametric uncertainty, followed by the description of QFT robust control method and design of QFT controller for the blood glucose level in human body.

The steps used for design QFT controller for blood glucose control are:

- Determine the plant transfer functions, $P_i(s)$
- Obtain the parametric uncertainty range
- Determine the frequency response data
- Extract the template data from the frequency response data
- Plot the templates
- Choose of nominal plant
- Use the templates to form the stability and performance bounds
- Shape the Nominal Loop, $L_o(s)$
- Extract the controller $G_c(s)$, from $L_o(s)$
- Synthesize the prefilter, $F(s)$
- Simulate using $G_c(s)$, $F(s)$ and $P_i(s)$

1.5 MATERIALS AND EQUIPMENTS

The design and analysis is performed using MATLAB QFT Tool box. The QFT tool box has an Interactive design Environment (IDE) in which the entire QFT design procedure is done.

1.6 CONTRIBUTION OF THE THESIS

The main contribution of the thesis can be summarized as follows

- The QFT control methodology is studied and implemented in glucose insulin regulation model.

- The QFT controller for the case study is validated through simulation and is found to be satisfactory according to the design specifications. The same can be used for the robust control of glucose insulin regulation.

1.7 ORGANIZATION OF THE THESIS

This thesis is organized in the following way:

Introduction to the research work along with problem statement, scope, approach and methodology, materials and equipment and organization of the thesis are presented in this **Chapter 1**.

Chapter 2 of this document summarizes a literature review of scholarly researches in the blood glucose insulin regulation model and QFT controller design.

Chapter 3 presents the mathematical modelling of glucose insulin regulation model.

Chapter 4 deals with the control design methodology which is one of the main topics approached in this work. First the Quantitative Feedback Theory is discussed and then the control architecture using QFT for SISO system is presented with all its features, characteristics and shortcomings.

Chapter 5 shows the results of QFT controller applied for the glucose insulin regulation model through simulation.

Chapter 6 summarizes the thesis work and concludes along with the future direction of work.

CHAPTER 2

LITERATURE SURVEY

There is a large body of literature extent on QFT and glucose insulin control system. For the purpose of this dissertation which is really focused on the QFT controller design for the glucose insulin regulation model, the previous works are surveyed predominantly in the QFT design domain and controller design of glucose level in human body. Attempts to design the QFT controller for many uncertain plants which require robustness is also discussed. Subsequently the previous works on the mathematical modelling and control of glucose level will be shown.

2.1 QUANTITATIVE FEEDBACK THEORY METHODOLOGY

QFT, one of the pioneering robust control theory developed by I. Horowitz (1963, 1991, 1992). The QFT approach is based on classical ideas of frequency domain loop-shaping of the open-loop transfer function. There have been so many researches done in its theoretical and application field which are briefly discussed in this chapter. To begin with the discussions of researches that have been already done in its development area, the topic is divided into the procedural steps of QFT (i.e. template generation, bound generation, loop shaping) for clarity of understanding.

2.1.1 Template generation

First and foremost step in QFT is to generate the templates of the plant at the trial frequencies. Due to presence of uncertainty in the plant the frequency response of the plant also give rise to a region of uncertainty or so called Template in NC for a fixed frequency. Several approaches have been proposed to take care of template generation problem. The parameter gridding method may be the simplest way to generate plant templates. However, this method has several disadvantages. A brief survey on template generation methods is discussed by D. J. Balance and G. Hughes [3]. In this paper the following types of template generation techniques with their merits & demerits are reviewed viz parameter gridding, modified parameter gridding, boundary calculation and circular approximation, parametric methods, Kharitonov polynomial approach &

boundary following approach. If the numerator and denominator of the plant transfer function are dependent and affine Barlett claim the boundary of the template can only be generated by the edges of parameter box. In the paper by I. J. Fialho, V.Pande, P.S.V.Nataraj (1992), Bhattacharyya et.al. Explain the template generation method by using Kharitonov polynomials & Kharitonov segments. The paper by W. Chen and Donald J. Balance (1998), presents a general procedure for template generation of structured uncertain plant including nonlinear & multilinear perturbation. In the recent work by Shih-Feng Yang (2009) an improved algorithm is presented for affinely dependent parametric uncertain system where first identifying the set of points on an edge of the parameter domain box whose image lies in the interior of the plant template and then eliminating the identified sets of points in the plant template generation procedure. Yang claims that the computational burden for generating the plant template thus obviously reduces in this way.

2.1.2 Bound generation

Plant template points were used in most of the earlier QFT bound generation algorithms. There are some kinds of bound in QFT depending upon the different control specification viz. robust stability bound, tracking bound, plant sensitivity reduction bound, plant input and output disturbance rejection bound, noise rejection, control effort minimization bound. The algorithms developed by Chait and Yaniv (1993), Chait, Borghesani, and Zheng (1995), and Rodrigues, Chai, and Hollot (1997), solve quadratic inequalities generated from plant template points to compute this bounds at a fixed frequency and controller phase. Then, the whole QFT bound at the frequency is computed by a controller phase sweeping procedure.

Gutman et.al., (2007) developed a recursive grid algorithm to compute QFT bounds where the NC is gridded with a coarse grid size & a coarse boundary of the QFT bound is generated by computing, at the grid points, the values of a function associated with the controller, the desired frequency specification and the plant template points. The algorithm developed by Moreno, Bonos, and Berenguel (2006) computes QFT bounds by first constructing a specification surface in the three dimensional space with axes of the phase and magnitude of the nominal loop transmission and the value of a function

associated with the plant template points and specification. Then, the QFT bounds are generated by computing the level curves of the specification surface at heights corresponding to the specifications. Compared with the quadratic inequality based approaches, the algorithms developed by Gutman et. al., (2007) and Moreno et. al., (2006), can compute QFT bounds with multi valued boundaries.

QFT bounds computed from plant template points can lead to an unfavorable trade-off between the computational burden and the accuracy of the computed QFT bounds. To overcome the problem, Nataraj and Sardar (2000), and Nataraj (2002) have developed algorithms which can generate inner and outer enclosures of exact QFT bounds from interval plant templates. Although the given robustness specifications are guaranteed in these two algorithms but the application of these two algorithms has the limitation of generating templates for plants with parametric uncertainties varying in a box domain & unable to compute QFT bounds with multi-valued boundaries.

The envelope algorithm proposed by J. J Martin Romero, Montserrat Gil-Martinez and Mario Garcia Sanz (2009), is also widely adopted. Their approach is based on envelope curves and shows that a QFT control specification can be expressed as a family of circumferences. Then, the controller bound is defined by the envelope curve of this family and can be obtained as an analytical function. This offers the possibility of studying the QFT bounds in an analytical way with several useful properties. Gridding methods are avoided, resulting in a lower computational effort procedure. The new formulation improves the accuracy of previous methods and allows the designer to calculate multi valued bounds.

The work by Shih-Feng Yang (2010) an efficient algorithm for computing QFT bounds from plant template points is discussed in which sufficient condition has been established for checking whether a plant template point lies in the QFT bound or not along with a pivoting procedure to trace out the boundary of the QFT bound with a prescribed accuracy.

2.1.3 Loop shaping

Horowitz et al. (1980) had first described in his paper the optimization of the loop transfer function. An automatic loop shaping technique of QFT Controllers using linear programming has been presented in the paper by Y. Chait (1997) .Another approach is proposed by Min-Soo Kim and Chan-Soo Chung (2005) of automatic Loop-Shaping of QFT Controllers using genetic algorithms and evolutionary computation. Since the loop shaping is performed on the NC the papers by W. Chen and D. J. Balance (1997, 2001), analyses the stability criterion of open as well as closed loop system on Nichols Chart and also stability of the new nominal closed loop system arising in QFT controller design for Non Minimum Phase (NMP) and unstable plants. Here it has been discussed that for NMP and unstable plant, not only the robust bounds but also the robust stability line must be shifted with frequency. Cutting throat researches are going on in rectifying the required experience in shaping the loop in order to find the initial and final controller and prefilter, various automatic loop shaping techniques have been proposed for the same. H. Mansor and S. B. Mohd Noor have developed a self-tuning QFT based deadbeat controller which gives the combined performance of a robust and adaptive controller. Using a grain dryer plant model as a pilot case-study, the performance of the self-tuning deadbeat QFT controller was evaluated and analysed.

2.2 QFT CONTROLLER AND ITS APPLICATIONS

A simple technique to deal with the MIMO problems is to reduce it to a sequence of SISO problems. In the book of Houpis et al., presents a detailed analysis on both the methods with illustrative examples. Some other works considering sequential QFT are references [13] and [14].

In the book, QFT Fundamentals and Applications by Constantine H. Houpis et al. represent the theory & application of QFT in lucid manner with simple examples. It deals with the basics of QFT for the MISO analog & the MIMO plants with structured plant parameter uncertainties. It has also discussed discrete QFT with proper example.

The current intense interest in QFT is partly due to the availability of good software tools. Various CAD packages for QFT bound computation and the loop shaping process are available viz. QFT MATLAB Toolbox (1994), the U.S. Air-force QFT

package developed by Houpis and Sating (1997), and the Qsyn Toolbox by Gutman (1996).

The main application area of QFT includes the Flight Control System, Robotics, Power system stabilizers, Wastewater Treatment system, Distillation Columns, different process control system & Power Electronics. In reference [1], [12], [14], [15], [18] numerous applications of QFT can be found.

2.2.1 Glucose insulin regulation using QFT

Table 2.1 Literature on glucose insulin regulation control systems

SL. NO.	REFERENCE	AUTHORS	COMMENTS
1.	Mathematical models and software tools for the glucose-insulin regulatory system and diabetes	Athena Makroglou (2005)	The models are in the form of ordinary differential, partial differential, delay differential and integro-differential equations. Some Computational results are also presented.
2.	A Bayesian Approach to Bergman's Minimal Model	Kim E. Andersen (1979)	The classical minimal model of glucose disposal was proposed as a powerful modeling approach to estimating the insulin sensitivity and the glucose effectiveness, which are very useful in the study of diabetes.

SL.NO.	REFERENCE	AUTHORS	COMMENTS
3.	Glucose-Insulin System based on Minimal Model: a Realistic Approach	Mohamed Darouach (2015)	. New approach to represent the glucose and insulin levels on patients with diabetes type 1 based on the well-known minimal model.
5.	Minimal Model	Richard N. Bergman. (2005)	An approach to understanding the composite effects of insulin secretion and insulin sensitivity on glucose tolerance and risk for Type 2 diabetes mellitus.
6.	Modeling and Simulation of Glucose-Insulin Metabolism	Kongens Lyngby (2007)	Bergman's minimal model is described through derivation and simulations.

QFT controllers have also been used to control a variety of cases other than glucose insulin regulation control system like in various process control applications as given below in the Table 2.2.

Table 2.2 Case studies on QFT controller employed industrially

SL .NO	TITLE	AUTHOR	WORK DONE
1.	Robust Control Design for Nonlinear Magnetic Levitation System using QFT	P. S. V. Nataraj and Mukesh D. Patil (2006)	Presents a methodology for design of robust control of nonlinear magnetic levitation system
2.	Multivariable QFT controller for heat exchangers	Barreras et. al.(2003)	A MIMO model of heat exchangers of a solar plant and a robust controller is designed despite the external disturbances
3.	Application of Robust QFT Linear controller in civil engineering	Amini et. al. (2003)	Adaptive linear robust control has been applied in civil engineering
4.	Automated Linear Controller Design For Mildly Nonlinear Systems Using QFT	Roozbeh Kianfar (2009)	Classical local linearization is carried out and QFT controller is designed to meet the specifications
5.	Robust Controller Design for Load Frequency Control Based on QFT	Asha Rani G.S and Beena .N (2014)	Presents a robust controller design for Load Frequency Controller based on QFT and uses in power system control.

SL .NO	TITLE	AUTHOR	WORK DONE
6.	Applications of QFT robust control techniques to marine systems	Mansilla et.al. (2011)	An analysis of the application of the QFT technique to different marine system is presented
7.	Design Of QFT Controller for A Bench-Top Helicopter System Model	Mansor et. al.(2007)	QFT controller is designed for the system and compared with PID
8.	Boiler drum-level control using QFT	Nataraj et. al. (2013)	QFT based robust control design approach for industry relevant boiler drum control problem
9.	Application of Robust QFT Linear controller in civil engineering	Amini et. al. (2003)	Adaptive linear robust control has been applied in civil engineering

2.5 SUMMARY

The chapter reviews the literature in QFT and Glucose insulin regulation control with an objective to study the important existing works in QFT design and Glucose insulin regulation control. The major share of literature reviewed is on the design steps of QFT and its application to practical dynamically uncertain plants.

CHAPTER 3

MATHEMATICAL MODEL OF GLUCOSE INSULIN REGULATION

3.1 GENERAL INTRODUCTION

Diabetes is associated with a large number of abnormalities in insulin metabolism, ranging from an absolute deficiency to a combination of deficiency and resistance, causing an inability to dispose glucose from the blood stream. Following three factors, referred to as The Metabolic Portrait (Pacini and Bergman, 1986), play an important role for glucose disposal.

- i) *Insulin sensitivity* is the capability of insulin to increase glucose disposal to muscles, liver and adipose tissue.
- ii) *Glucose effectiveness* is the ability of glucose to enhance its own disposal at basal insulin level.
- iii) *Pancreatic responsiveness* is the ability of the pancreatic β -cells to secrete insulin in response to glucose stimuli.

Failure in any of these may lead to impaired glucose tolerance, or, if severe, diabetes. Quantitative assessment is possible by the **The Minimal Model** (Bergman et al., 1979), and may improve classification, prognosis and therapy of the disease (Martin et al., 1992). The minimal model is based on an **Intravenous Glucose Tolerance Test (IVGTT)**, where glucose and insulin concentrations in plasma are sampled after an intravenous glucose injection. In the minimal model the glucose and insulin kinetics are described by two components, where the parameters traditionally have been estimated separately within each component. The glucose-insulin system is an integrated system and coupling of the components to obtain a unified model seems appropriate. However, this leads to a highly ill-posed inverse problem and it can easily be show that, for even commonly observed combinations of parameter values the system may not admit a well-defined equilibrium.

3.2 IVGTT

Another test is the Intravenous Glucose Tolerance Test (IVGTT). Together with a mathematical model, this test can be used to estimate insulin sensitivity, glucose effectiveness, and the pancreatic responsiveness parameters. One of the mathematical models used to interpret the IVGTT is Bergman's minimal model, which is introduced in the next section. The IVGTT test procedure begins with an injection of a glucose bolus intravenously, containing 0.30 g glucose pr. kg. body weight. Then the blood samples are taken frequently for a 3 hour period. These blood samples are analyzed and glucose and insulin levels are measured. A typical IVGTT for a normal subject,

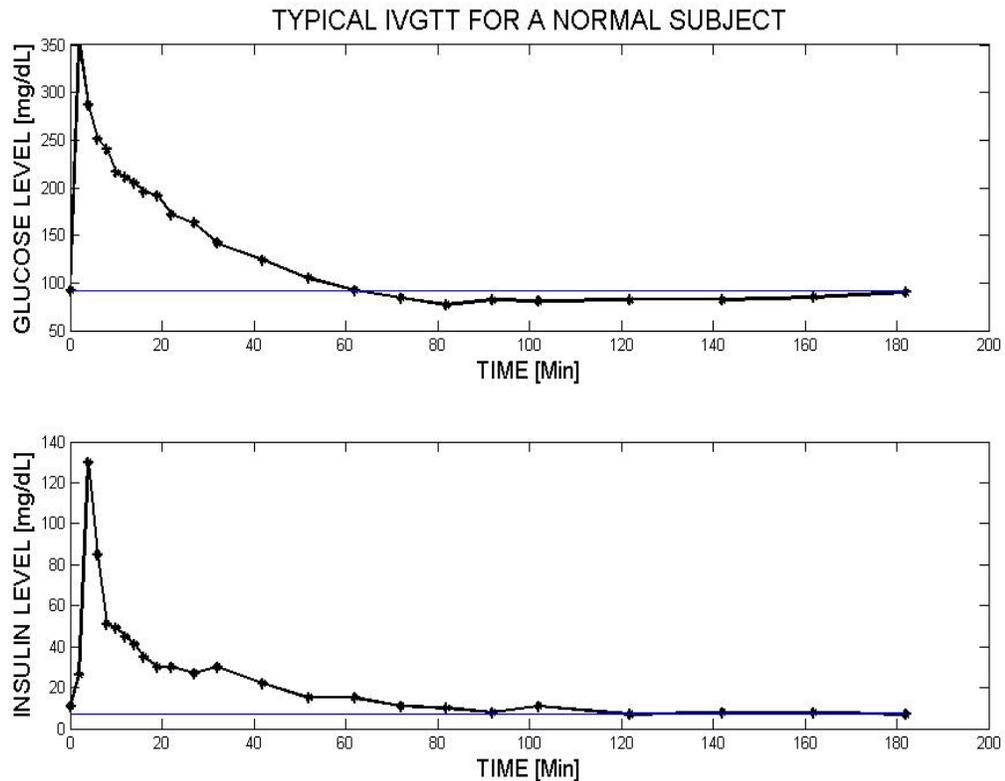


Figure 3.1: An IVGTT for a Normal subject

from studies by Bergman et al. is shown in Figure 3.1. From Figure 3.1, the glucose level decays slowly to a minimum level below the basal value and then slowly reaches the basal value. The insulin peaks just after the injection, and then decays to a level above the baseline and then peaks a little again. Finally it decays to the basal value. This is just a typical pattern and the glucose and insulin level may not behave exactly like this.

3.3 BERGMAN'S MINIMAL MODEL

Bergman's minimal model is a one compartment model, meaning that the body is described as a compartment/tank with a basal concentration of glucose and insulin. The minimal model actually contains two minimal models. One describing glucose kinetics, how blood glucose concentration reacts to blood insulin concentration and one describing the insulin kinetics, how blood insulin concentration reacts to blood glucose concentration. The two models respectively take insulin and glucose data as an input. The two models have mostly been used to interpret the kinetics during the IVGTT test, and in their original form they cannot be used to much else, but with small additions or modifications they can also be used to describe meals and exogenous insulin infusion. In this section a description of the two kinetics are done and finally two couplings are proposed, which could be used as simulators of the entire blood glucose-insulin system.

3.3.1 THE GLUCOSE MINIMAL MODEL

The original glucose minimal model describes how the glucose level behaves according to measured insulin data during an IVGTT. The model is a one compartment model divided into two parts. The first part is the main part describing the glucose clearance and uptake. The second part describes the delay in the active insulin $I(t)$ which is a remote interactor which level affects the uptake of glucose by the tissues and the uptake and production by the liver. These two parts are described mathematically by two differential equations:

$$\frac{dG(t)}{dt} = -(p1 + X(t) * G(t) + p1 * Gb) \quad (3.1)$$

$$\frac{dX(t)}{dt} = -p2 * X(t) + p3(I(t) - Ib) \quad (3.2)$$

3.3.2 THE INSULIN MINIMAL MODEL

Now the model describing glucose kinetics as a product of insulin data input has been described. But a description of the insulin kinetics is missing. Bergman presented the following minimal model of insulin kinetics, represented here by the differential equation:

$$\frac{dI(t)}{dt} = p6[G(t) - p5] * t - p4[I(t) - Ib] \quad (3.3)$$

3.3.3 THE ORIGINAL MODEL

The first coupling proposed is a coupling between the original minimal models, without additions and/or modifications. From now on this coupled model, will be called the original model. The model is represented by the following differential equations:

$$\frac{dG(t)}{dt} = -(p1 + X(t) * G(t) + p1 * Gb) \quad (3.4)$$

$$\frac{dX(t)}{dt} = -p2 * X(t) + p3(I(t) - Ib) \quad (3.5)$$

$$\frac{dI(t)}{dt} = p6[G(t) - p5] * t - p4[I(t) - Ib] \quad (3.6)$$

Table 3.1 Parameters of Bergman's minimal model

PARAMETER	UNIT	DESCRIPTION
G(t)	[mg/dL]	Blood glucose concentration
X(t)	[1/min]	The effect of active insulin
I(t)	[mU/L] [mg/dL]	Blood insulin concentration
Gb	[mg/dL]	Basal blood glucose concentration

I _b	[mU/L]	Basal blood insulin concentration
P1	[1/min]	Glucose clearance rate independent of insulin
P2	[1/min]	Rate of clearance of active insulin(decrease of uptake)
P3	[L/(min ² mU)]	Increase in uptake ability caused by insulin.
P4	[1/min]	Decay rate of blood insulin.
P5	[mg/dL]	The target glucose level
P6	[mUdL/ Lmgmin]	Rate of pancreatic release after glucose bolus

3.4 SUMMARY

The glucose insulin regulation model is mathematically analyzed and transfer function model is obtained. The uncertainty range is obtained. The model obtained was of second order and have parametric uncertainties in gain, natural frequency and damping ratio.

CHAPTER 4

QFT DESIGN AND ANALYSIS

In the 1960's, as a continuation of the pioneering work of Bode, Isaac Horowitz introduced a frequency domain design methodology [14] that was refined in the 1970's to its present form, commonly referred to as the QFT [13][14]. QFT technique is a robust control design based on frequency domain methodology. It is useful for practical design of feedback system in ensuring plant's stability by reducing the sensitivity to parameter variation and attenuates the effect of disturbances. Parameter variation or physical changes to the plant is taken into account in the QFT controller's design.

The QFT design is performed in the frequency domain instead of the time domain. By using the frequency domain, the mathematics of the problem are greatly simplified (algebraic multiplication in the frequency domain versus convolution in the time domain). QFT was originally introduced to design robust controllers for highly uncertain, LTI, SISO systems. Recent research has extended the technique to handle MIMO [8], [13], [16], nonlinear and time varying plants [13]. MIMO systems are mathematically decomposed into their Multi Input Single Output (MISO) counterparts, where the coupling between the channels is treated as a disturbance that needs to be rejected. A beneficial byproduct of MIMO QFT design is the approximate decoupling of the resulted closed loop robust control system [8], [14].

QFT is different from other methods of controller design in the transparency of its techniques. An important element is the creation of templates at various frequencies. The size of the templates indicates whether or not a robust design is achievable. If a robust design is not achievable, then the templates can be used as a metric in the reformation of the control design problem. Another element of the design process is the ability to concurrently analyze frequency responses of the LTI plants that represent the nonlinear dynamical system throughout its operating environment. This gives the designer insight into the behavior of the system. The designer can use this insight for such things as picking out key frequencies to use during the design process, as an indicator of potential problems such as NMP behavior, and as a tool to compare the

nonlinear system with the desired performance boundaries. The next element of QFT consists of the design boundaries. During the actual loop shaping process, the designer uses boundaries plotted on the NC. These boundaries are only guidelines and the designer can exercise engineering judgment to determine if all the boundaries are critical or if some of the boundaries are not important. This transparency allows the engineer to determine if a control solution is possible early in, and during, the design process. If no solution exists, changes must be made to ease the design specifications. In most modern control techniques, the designer would realize that specifications could not be met only after repeated trial and error. The designer clearly understands the cost of such iterations made while designing the controller.

The remainder of this chapter discusses the different steps involved in the QFT design process with respect to flight control system design, giving some of the theory behind the steps. However, it is assumed that the reader has some general knowledge of QFT and for the most part results are given without proof. In section 4.1 Introduction to QFT control theory has been discussed, while in section 4.2 QFT design procedure has been reviewed. In 4.4 different features and advantages offered by QFT algorithm has been discussed. Finally in section 4.5 some shortcomings of QFT have been highlighted.

4.1 GENERAL INTRODUCTION

QFT is a very powerful robust control design algorithm for the achievement of assigned performance tolerances over specified ranges of structured plant parameter uncertainties. This section deals with the basic aspects of QFT. In 4.1.1 it describes different types of uncertainties that may present in a practical environment. 4.1.2 deals with the notion of robust performance of a control system. Section 4.1.4 discusses the basic concepts of 2DOF system.

4.1.1 Uncertainty

A control system is said to be robust if it is insensitive to differences or errors between the actual system and the model of system. These differences or errors are referred to the model uncertainty. It is an impossible modeling task to formulate an exact

mathematical model of a physical system which is valid for every operating condition. The uncertainties are unavoidable in a real time environment. Uncertainties present in the system model often lead to some undesirable phenomenon in the control system. Unmodeled system dynamics or models order reduction, unknown or unpredictable inputs (input output disturbances, sensor noise), changes of operating point etc. are the main source of uncertainty in the system. Uncertainties are dealt in two environments namely static and dynamic. In static category there is perfect knowledge of the range of the uncertainty whereas in dynamic the knowledge of environment is imperfect.

Based on their origination uncertainties can be classified in two categories: disturbance signals and dynamic perturbations. The former includes input and output disturbance (such as a gust on an aircraft), sensor noise and actuator noise, etc. The later represents the discrepancy between the mathematical model and the actual dynamics of the system in operation. A mathematical model of any real system is always just an approximation of the true, physical reality of the system dynamics. Typical sources of the discrepancy include unmodeled (usually high frequency) dynamics, neglected nonlinearities in the modeling, effects of deliberate reduced order models, and system parameter variations due to environmental changes and torn and worn factors. Parametric uncertainties are an important subset of dynamic perturbation class. These complex uncertainties typically occur in the high frequency range of operation and may include unmodeled lags (time delay), parasitic coupling, hysteresis and other nonlinearities. However, dynamic perturbations in many industrial control systems may also be originated from an inaccurate description of component characteristics, torn and worn effects on plant components, or shifting of trim points, etc. Such perturbations may be represented by variations of certain system parameters over some possible value ranges (complex or real). They may adversely affect the low-frequency range performance and are called “parametric uncertainties”. Parametric uncertainties can be classified in following two subcategories of uncertainty

4.1.1.1 Structured Uncertainty

Parametric uncertainty implies specific knowledge of variations in parameters of the transfer function. Specific knowledge about the variations in plant

parameters is known. An example of structured uncertainty is demonstrated to clear the idea. An Open loop transfer function of a system is described by $\frac{k}{(s+m)(s+5)}$ where $m \in [1, 10]$ and $k \in [1, 10]$. A general procedure to represent the parametric uncertainty is given e.g. in [50, 51]. The parametric uncertainty can be quantified by assuming that each uncertain parameter is bounded within region $[a_{\min}, a_{\max}]$. That is, the parameter sets which may be expressed as

$$a = a_0(1 + \sigma\Delta), \quad -1 \leq \Delta \leq 1 \quad (4.1)$$

Where a_0 is the nominal parameter value, σ is the relative magnitude of the gain uncertainty and Δ is a real scalar.

4.1.1.2 Unstructured Uncertainty

The main source of unparametric uncertainty is error in the model because of missing dynamics, usually at high frequencies, due to a lack of understanding of the physical process. Only the case of parametric uncertainty is considered in this thesis.

4.1.2 Robust Stability and Robust Performance:

When all possible loops of an uncertain plant family P with a single controller G_c are internally stable, then one can conclude that the controller G_c provides robust stability for the plant family P .

The two conditions for robust stability are

- Stability of the nominal system (corresponding to the nominal plant P_0)
- The Nichols envelope does not intersect the critical point (which is the $(-180^\circ, 0\text{dB})$ point in a Nichols chart or the $(-1, 0)$ point in the complex plane).

The second condition is equivalent to placing a magnitude constraint on the complementary sensitivity function.

$$\left| \frac{L_c(j\omega)}{1 + L_c(j\omega)} \right| < \infty, \quad \forall P_i \in P, \omega \in [0, \infty). \quad (4.2)$$

It corresponds to a minimum Gain Margin (GM) and Phase Margin (PM), [46] as follows:

$$GM \geq 20 \log \left\{ \frac{\gamma + 1}{\gamma} \right\} \quad [\text{dB}] \quad (4.3)$$

$$PM \geq 2 \sin^{-1} \left\{ \frac{1}{2\gamma} \right\} \quad [\text{deg}] \quad (4.4)$$

where $\mathbf{L}_c(j\omega)$ denotes the set of the loop gains frequency responses.

The general concern of robust performances that the internal stability and a specified performance should hold for all the plant. General performance specifications are sensitivity reduction, disturbance rejection at input, controller effort minimization and noise rejection. But it is a very difficult to obtain those above mentioned specification by means of an open loop controller. Herein lays the justification of feedback control systems. Whenever the white model of the plant is not available to the designer, one must employ feedback mechanism to ensure the desired control performance and stability of the overall system (plant together with the controller). In next section brief discussion is made on the importance of feedback and 2DOF.

4.1.3 Closed Loop Formulation

The typical 2DOF feedback system configuration in QFT is shown in Fig. 4.1. $P(s)$ is the plant transfer function, $H(s)$ is feedback sensor transfer function and the transfer functions G_c and F denote the controller and prefilter to be synthesized. The general closed loop specifications of the system in Figure 4.1 are typically described in of terms inequalities on the systems transfer functions from some inputs to some outputs, as follows:

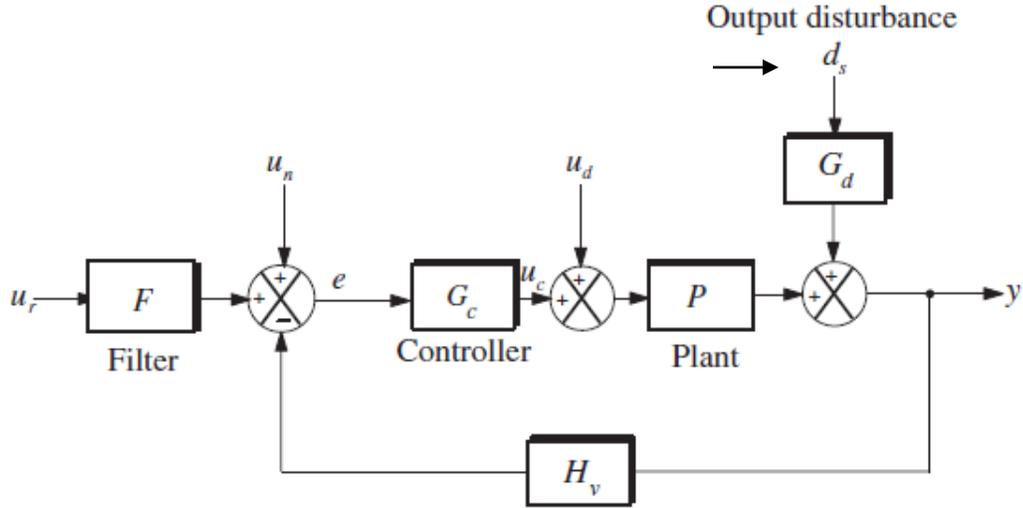


Fig 4.1 2DOF control system

(i) Disturbance rejection at plant output: for a given uncertain set of LTI $\forall P_i \in \{P\}$ the transfer function from the disturbance at the plant output d_s , the plant output y is bounded by

$$\left| \frac{y}{d_s} \right| = |T_D(j\omega)| \leq \gamma_s(\omega) \quad (4.5)$$

where

$$T_D(j\omega) = \frac{G_D(j\omega)}{1 + L_G(j\omega)} \quad (4.6)$$

$G_D(j\omega)$ is the disturbance frequency response and $L_G(j\omega) = PH_V G_c(j\omega)$ is the loop frequency response.

- Disturbance rejection at plant input: for $\forall P \in \{P\}$ the transfer function from the disturbance at the plant input u_d to the plant output y is bounded by

$$\left| \frac{y}{u_d} \right| = \left| \frac{P(j\omega)}{1 + L_g(j\omega)} \right| \leq \gamma_p(\omega) \quad (4.7)$$

- Noise rejection: For $\forall P \in \{P\}$ the transfer function from the sensor output u_N to the plant output y is bounded by

$$\left| \frac{y}{u_N} \right| = \left| \frac{PG_c(j\omega)}{1 + L_g(j\omega)} \right| \leq \gamma_N(\omega) \quad (4.8)$$

- Tracking specification: The tracking specification defines the acceptable range of variations in the closed loop tracking responses of the system due to uncertainty and disturbances. It is generally defined in the time domain, but normally transformed into the frequency domain. For $\forall P \in \{P\}$ the transfer function from the reference u_r to the plant output y is bounded by

$$T_L(j\omega) \leq |T(j\omega)| \leq T_U(j\omega) \quad (4.9)$$

Where

$$T_d(j\omega) = \frac{P(j\omega)G_c(j\omega)}{1 + L_g(j\omega)} \quad (4.10)$$

Denotes the closed loop frequency response without the prefilter, $T_L(j\omega)$ and $T_U(j\omega)$ are the equivalent frequency responses of the lower and upper tracking bounds. These transfer functions are systematically derived from the desired step response of the system.

4.2 QFT DESIGN PROCEDURE

One approach to robust control is QFT which is actually an extension of classical frequency domain idea. (This section is mainly adopted from Yaniv O., *Quantitative Feedback Design of Linear and Non Linear Control Systems* [18] and Houpis C.H., Rasmussen S.J, *Quantitative Feedback Theory Fundamentals and Applications*, Marcel Dekker Inc. [19]).

4.2.1 Objective of QFT:

- To design a low order controller for systems with significant parameter uncertainty.
- QFT highlights the trade off (*quantification*) among
 - i. The simplicity of the controller structure.
 - ii. The minimization of the ‘cost of feedback’ (*bandwidth*).
 - iii. The model uncertainty (*parametric and non-parametric*).
 - iv. The achievement of the desired performance specifications at every frequency of interest.

4.2.2 QFT Design Methodology

The QFT design procedure outline can be summarized in the following way

1. Synthesize the desired tracking model, disturbance model and stability specifications.
2. Specify the boundary of the region of the plant parameter uncertainty.
3. Select a frequency array prior to the design process.
4. Obtain the plant templates that describe the parametric uncertainty on NC.
5. Select the nominal plant transfer function $P_0(s)$.
6. Determine the stability contour on the NC.
7. Determine the disturbance contour on NC.
8. Determine the tracking bound on NC.
9. Synthesize the nominal loop transmission function $L_0(s) = G_c(s)P(s)$
That satisfies all the bounds and stability contour (Loop shaping).
10. Synthesize the pre filter.
11. Simulate the system in order to obtain the time response data for each of the plants.

The project considers two robust performance specifications, robust stability and tracking respectively. The disturbance rejection is not taken into consideration in this design and hence is not discussed in this chapter.

4.2.2.1 Template

The key issue with robust control systems is uncertainty and how the control system can deal with this problem. In QFT, all plant uncertainties are represented in terms of plant templates on the NC. The term plant template is used to denote the collection of frequency responses of an uncertain system at a fixed frequency for all possible uncertainties. The algorithms for computing bounds require input data in terms of frequency responses (templates) rather than in terms of transfer functions. The magnitude and phase of the plants at each frequency yields a set of points on the NC instead of a single point thus at each selected frequency a connected region is constructed which encloses this set of points. Large number of templates indicates large uncertainty. There are various methods available to solve the template generation problem. The most commonly used methods are:

- **Parameter gridding method:** The simplest and most commonly used method of template generation where each uncertain parameter interval is divided into a number of discrete values. Then the system transfer function is calculated for each of the possible combinations of the parameters and the template is calculated by taking an outer bound of the values calculated. If an appropriate set of grid has been chosen to capture sensitivity of the transfer function to the parameter variation the obtained template is usually accurate and that it is not conservative.
- **Kharitonov segments method:**
Another approach to generate and determine an outer bound on template is use of Kharitonov Polynomials. This is made by determining the Kharitonov line segments which capture the magnitude of the parameter uncertainty. The external vertices of the template are identified from these segments and the actual template is then known to lie within the convex polygon joining these points.

Suppose a plant $P(s) = \frac{k}{(s+a)(s+b)}$ where the parameters range as given below:

$$k \in [1,10]$$

$$a \in [1,5]$$

$$b \in [20,30]$$

To give the clear idea on template, the Bode plot is given in Figure 4.2 for the given range of parameters. As can be seen from the figure, the variation of the plants is frequency dependent. In the high and low frequency range there is no difference in phase. Also in the high frequency band there is less variation in magnitude than anywhere else.

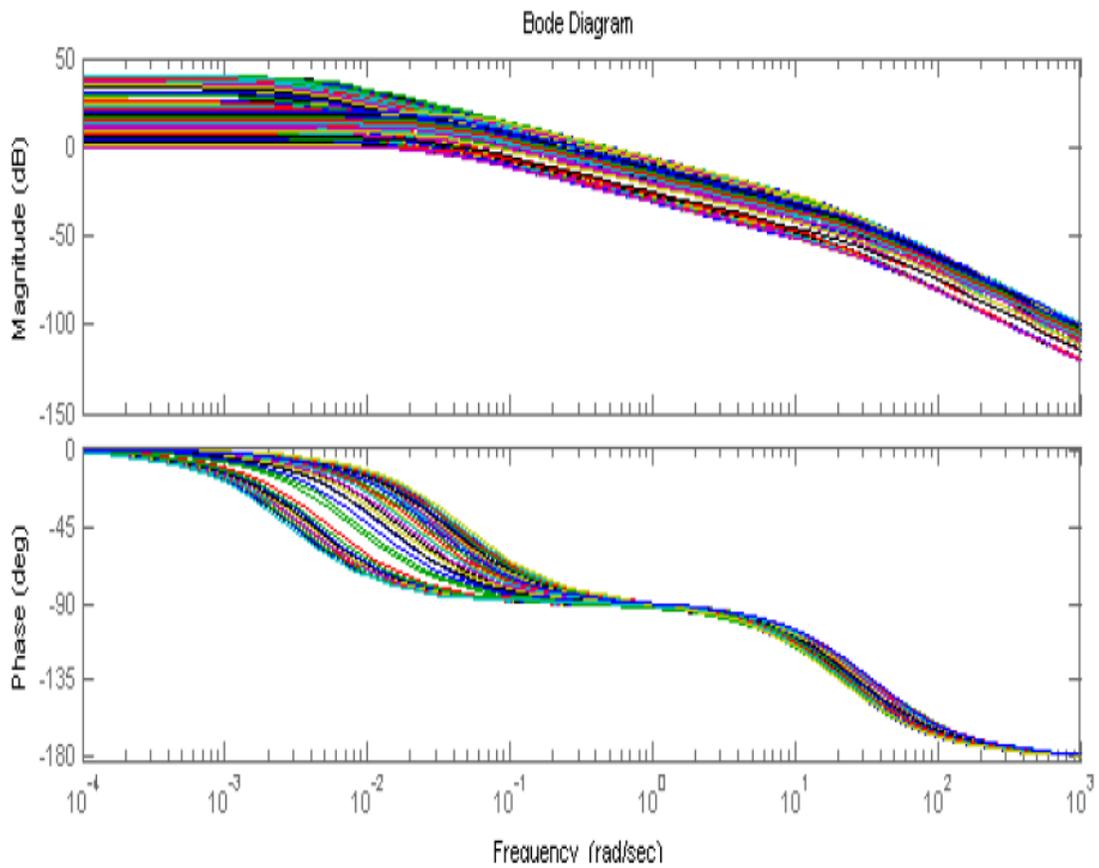


Figure 4.2 Bode plot of uncertain plant family

For simply connected templates, it is necessary and sufficient to work with the boundary of these templates [4]. Figure 4.3 shows the sample template generated for a family of uncertain plants where the star represents the nominal plant.

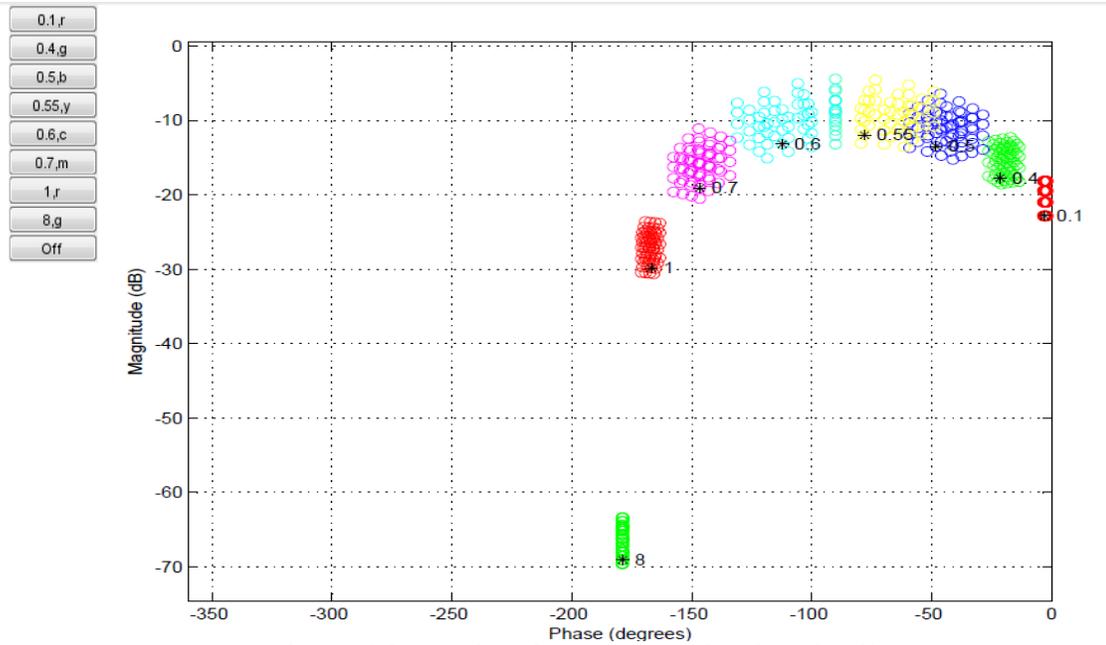


Figure 4.3 Template for an uncertain plant family

4.2.2.2 Choice of frequency array

In QFT design process, an appropriate frequency band for a computing templates and bounds has to be selected. An important question arises, for which there is no definite global answer, is how to select this array from the possible range between zero and infinity. Fortunately, for engineering design we need only a small set that can be found with, at the most, a few repetitions. The basic rule is that for the same specification, the bounds will change only with changes in the shape of the template. Therefore, a guideline for selecting the frequency range is to search frequencies where the shape of the template shows significant variations compared to those at other frequencies [4][5].

4.2.2.3 Choice of Nominal plant

In order to compute bounds, it is necessary to choose a plant from the uncertainty set as the nominal plant. If there is no uncertainty the fixed plant is the nominal one. This is required in order to perform QFT design with a single nominal loop. In parametric uncertainty model any plant in P can be chosen as the nominal plant. Normally the most stable minimum phase plant is chosen as the nominal plant (a plant whose NC point is always at the lower left corner of the template for all frequencies for which the templates are obtained). It is due to the fact that it is more convenient to work with a minimum phase function because the bode integrals can be used and optimal loop shaping can be derived easily. However it is common practice to select a nominal plant which we think is most convenient for design with condition that the selected nominal plant must be the same for the rest of the frequencies for which templates are to be obtained.

4.2.2.4 Computation of Bounds

Given the plant templates, QFT converts closed loop magnitude specifications into magnitude and phase constraints on a nominal open-loop function. These constraints are called QFT bounds. The preferred bound calculation algorithm is proposed in [14][4] (also used by the QFT MATLAB toolbox, [6]). The computed bounds are combined and their intersection is taken to form the composite bounds of the system. Figure 4.4, 4.5, 4.6, 4.7 represents various types of bounds generated.

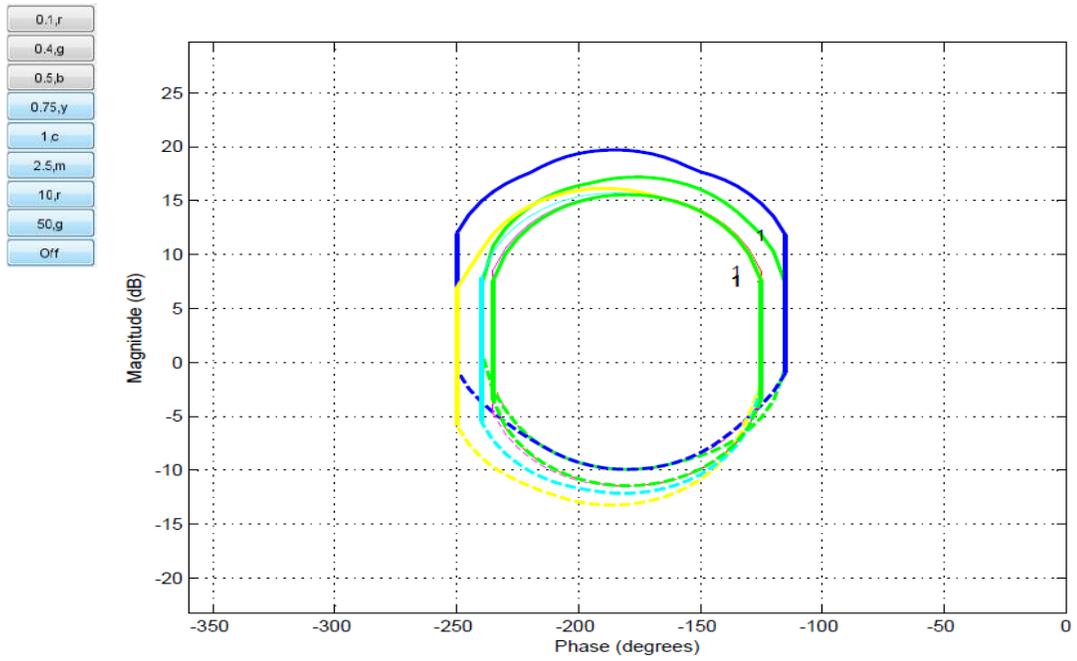


Figure 4.4 Robust Stability Bound for an Uncertain Plant

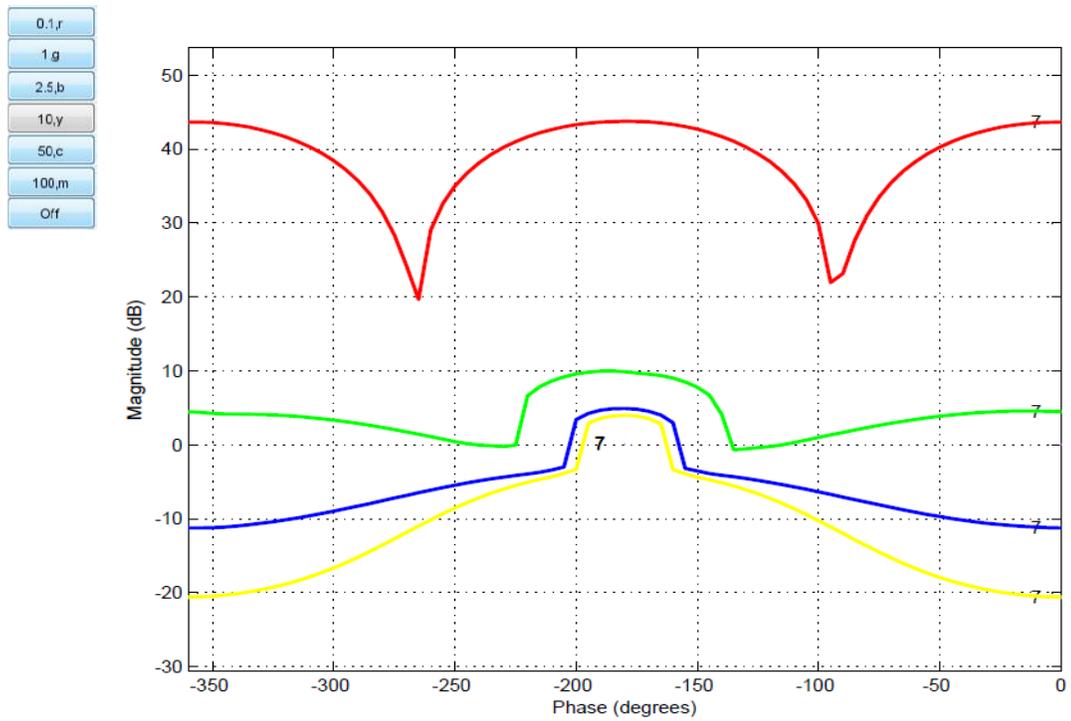


Figure 4.5 Robust Tracking Bounds for an Uncertain plant.

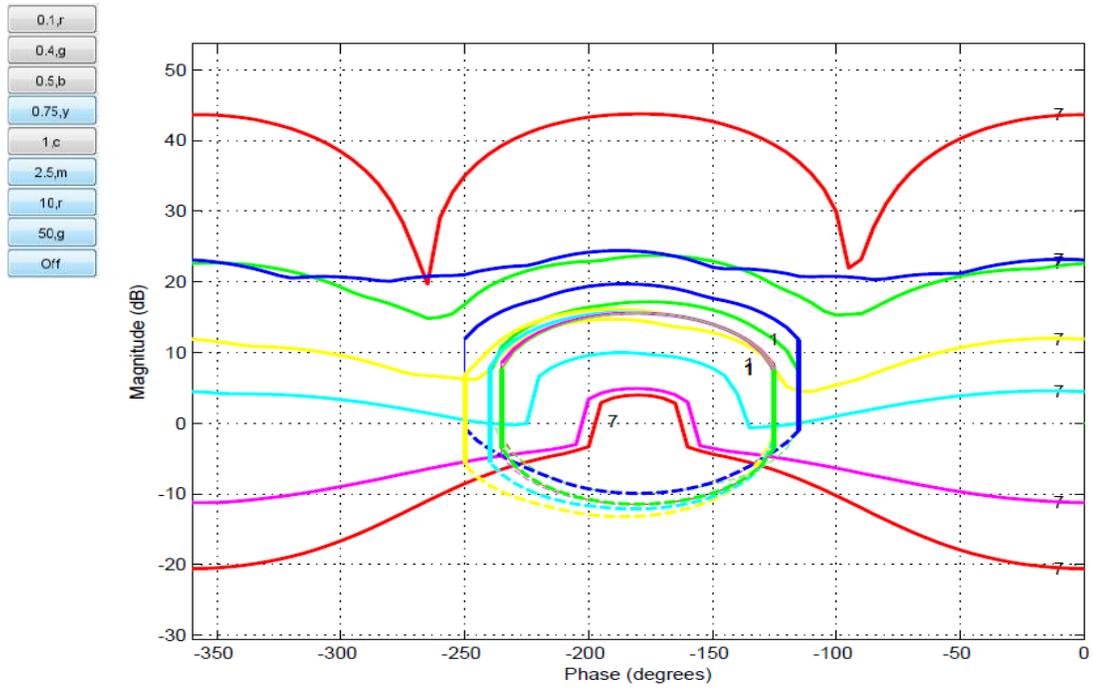


Figure 4.6 Group Bounds of an Uncertain plant family

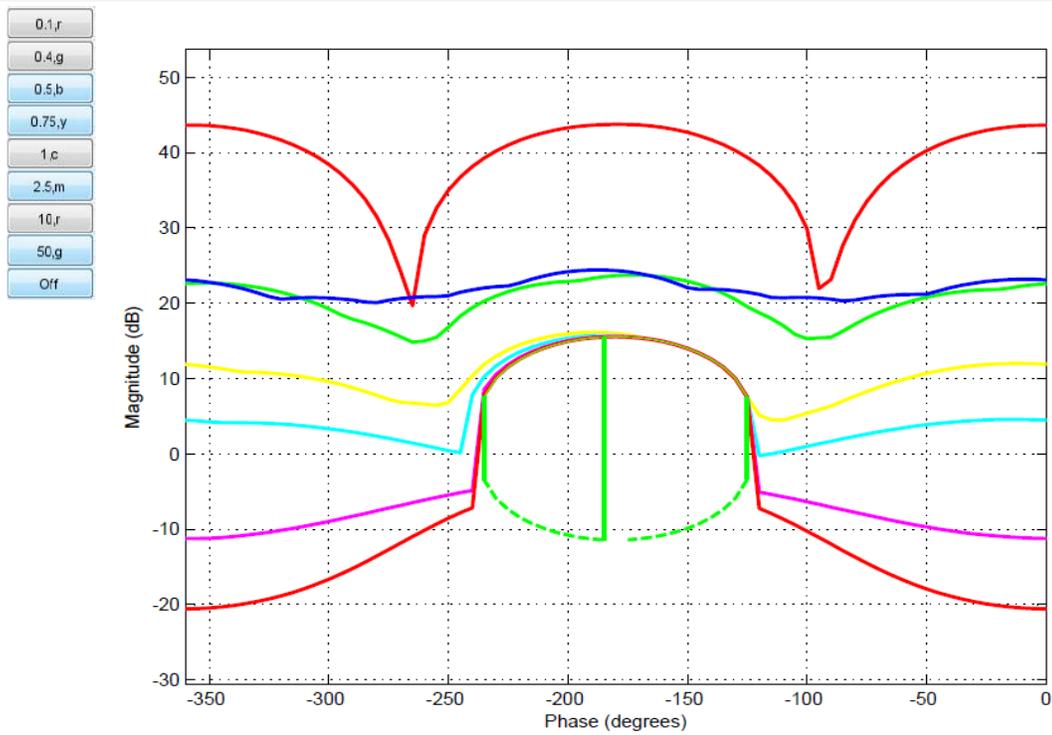


Figure 4.7 Intersection of Bounds for an uncertain plant family

4.2.2.5 QFT Loop-shaping

The final step in a QFT design involves the design (loop shaping) of a nominal loop function that meets its bounds. The controller design then proceeds using the NC and classical loop-shaping ideas. The objective is to synthesize a controller, $G_c(s)$, which meets the design specifications and maximizes the controller bandwidth. Generally speaking, loop shaping involves adding poles and zeros until the nominal loop lies near its bounds and results in nominal closed-loop stability. The beauty of QFT lies in loop-shaping it provides the user with the power to consider different controller complexity and values and weighs possible tradeoffs almost instantly. An excellent exposition of loop shaping can be found in [2]. Loop-shaping depends upon the experience of the loop shaper. Fig 4.5 shows the open loop nominal transfer function along with the bounds.

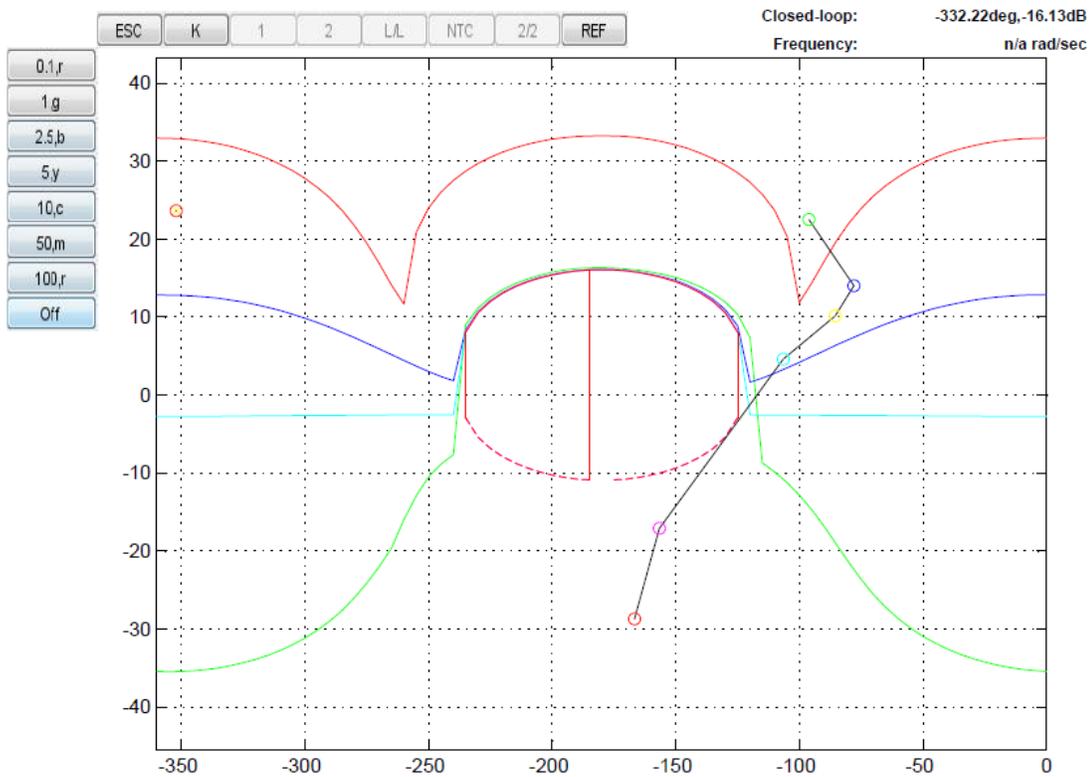


Figure 4.8 Nominal Open Loop Shaping

4.3 FEATURES AND CHARACTERISTICS OF QFT

The QFT characteristics can be summarized as follows [19].

- The method extends classical frequency-domain loop shaping concepts to cope with simultaneous performance specifications and uncertainty descriptions.
- The amount of feedback is tuned to the amount of plant and disturbance uncertainty the performance specifications.
- Design trade-offs at each frequency are transparent between stability, performance, plant uncertainty, disturbance level, controller complexity and bandwidth.
- The development time for robust control systems can be shortened, and controllers can be designed quickly to accommodate changes in specifications, uncertainties and disturbances.

4.4 SHORT COMINGS OF QFT

The short comings are listed below:

- QFT cannot work on NMP system directly. It is extended for this system.
- The controller and pre filter obtained in QFT are not unique.
- The choice of optimum controller and pre filter are dependent on many factors viz. the stability and other performance criteria, hardware constraints, operating frequency range restriction, situation of working environment.
- Phase tracking problem is not considered in classical QFT.
- In order to get a satisfactory tracking characteristics for a typical input signal, a prefilter has been used at the expense of degradation of tracking performance of others input signal , for example ,ramp signal.
- In order to design a robust controller, there should be stability specifications or tracking specifications or other necessary specifications in addition to plant structured uncertainties.

4.5 SUMMARY

The basic idea in QFT is to convert design specifications at closed loop and plant uncertainties into robust stability and performance bounds on open loop transmission of nominal system and then design controller by using loop shaping [4]. This deals with all the important steps of QFT controller design and does not contain any material.

CHAPTER 5

QFT CONTROLLER DESIGN FOR GLUCOSE INSULIN REGULATION

5.1 GENERAL INTRODUCTION

Glucose insulin regulation plays a vital role for diabetes patients. QFT will control glucose insulin level. QFT can take uncertainty's scopes and performance requirements into account, analyze and design robust controller on NC quantitatively in order to make the open loop frequency curve comply with boundary conditions and have robust stability and performance robustness.

QFT has been widely used in aerospace field and is mature for robust controller design of LTI SISO system. In this chapter, QFT designs for LTI glucose insulin regulation system are presented. Consequently, the main contribution of this chapter is to show how the QFT controller methodology can be successfully employed for robust control design of blood glucose subject to system uncertainties due to parameter variations with the help of MATLAB QFT toolbox. The effectiveness and robustness of the proposed control system is confirmed by simulation results, where the MATLAB TM QFT Frequency Domain Control Design Toolbox [6] and MATLAB TM, Simulink control systems block set [11] are used as a setup platform for design and validation.

5.2 DESCRIPTION OF PROBLEM

The overall mathematical model of glucose insulin regulation control can be represented as a second order transfer function and input control signal given below:

$$P(s) = \frac{G(s)}{I(s)} = \frac{K}{s^2 + as + b} \quad (5.1)$$

Using system identification techniques from experimental data the parameter variations obtained [19] are:

$$K \in [-33.26, -12.03];$$

$$A \in [16, 47];$$

$$b \in [24,57].$$

This uncertainty in parameters produces a family of plants $P(s)$, a family of sixty four plants have been used for this project work.

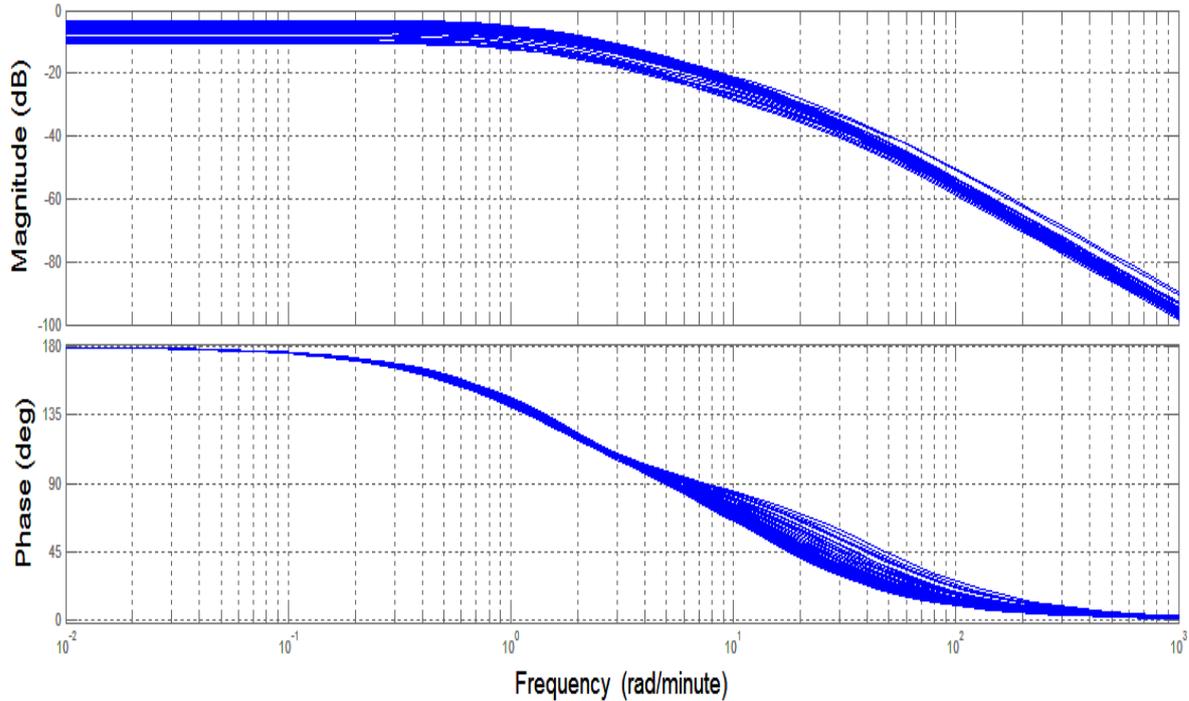


Figure 5.1 Bode diagram of uncompensated system

5.3 PERFORMANCE SPECIFICATIONS

The parameter uncertainty given in equation (5.1) produces a set of plant transfer functions $P(s)$. It is desired that $\forall P \in P(s)$, the closed loop system satisfy the following specifications. Since the design objective focuses on robust stability and robust tracking other design specifications are not deal in this chapter

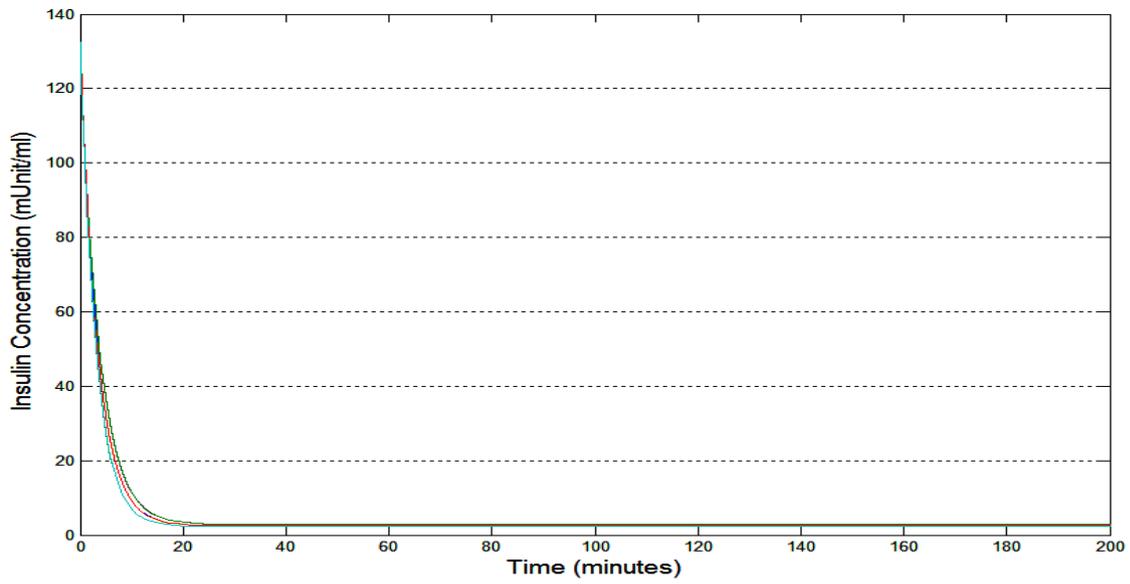
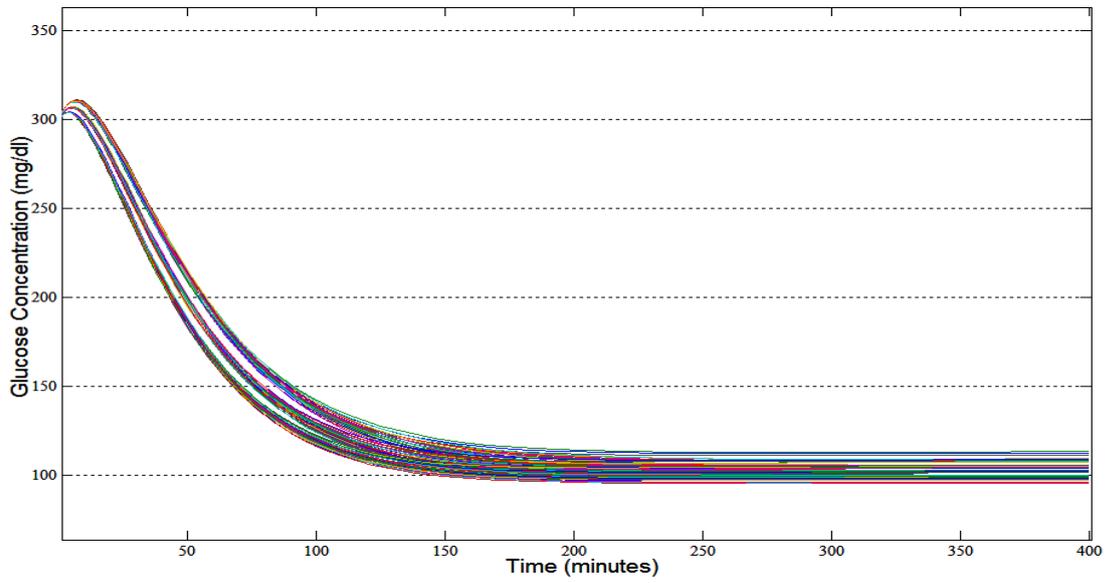


Figure 5.2 Time response of the uncompensated system.

5.3.1 Robust Stability Specifications

$$\left| \frac{L_G(j\omega)}{1 + L_G(j\omega)} \right| \leq 2, \omega \geq 0 \quad (5.2)$$

Implies at least 28° lower PM and at least 1.66 lower GM (not simultaneously). To compute in general these margins, use the following formulae (5.2) and (5.3)

The lower gain margin and lower phase margin are given as below:

$$GM = 1 + 1/\gamma \quad (5.3)$$

$$PM = 180 - \theta, \quad (5.4)$$

$$\theta = \cos^{-1}(0.5/\gamma^2 - 1) \in [0, 180] \quad (5.5)$$

5.3.2 Tracking Specifications

Overshoot : < 2%

Steady State Error : Nil

It is proposed that the initial form of Upper Tracking model that captures the tracking specification can be defined by a standard second order system.

$$T_{U(i)}(s) = \frac{1.07}{s^2 + 2.58s + 4.622} \quad (5.4)$$

The initial tracking bound can be modified to enhance the robust tracking performance of the system. An additional zero is added at $s = -4.622$ to the model $T_{U(i)}(s)$ to flare up the tracking bounds in the high frequency range. The resulting model becomes faster than previous one, but the peak gain becomes more than desired. Then shifting the pole to the left and simultaneously checking the time-domain specifications the accepted tracking bound is represented by following transfer function:

$$T_{U(f)}(s) = \frac{-(1.07 + 8)}{s^2 + 9.817s + 20.48} \quad (5.5)$$

In case of the lower tracking bound, initial model set as

$$T_L(s) = \frac{-20.4}{(s + 9.33)(s + 6.213)} \quad (5.6)$$

Then an addition of a pole at $s = -2.803$ with this $T_{L(in)}(s)$ is carried out to lower down its bode magnitude curve without affecting its time domain characteristics. The acceptable tracking bound range defined by these two bound transfer function is depicted in Figure 5.3 and 5.4 in both time domain and frequency domain.

$$T_{U(f)}(s) = \frac{-20.4}{s^3 + 17.32s^2 + 89.74s + 137.5} \quad (5.7)$$

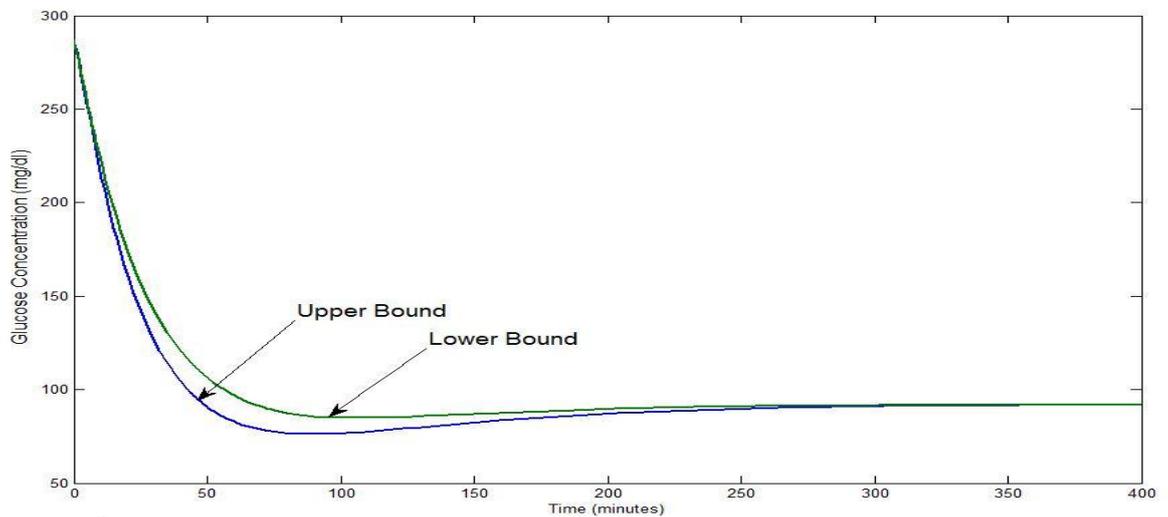


Figure 5.3 Time response of tracking specifications

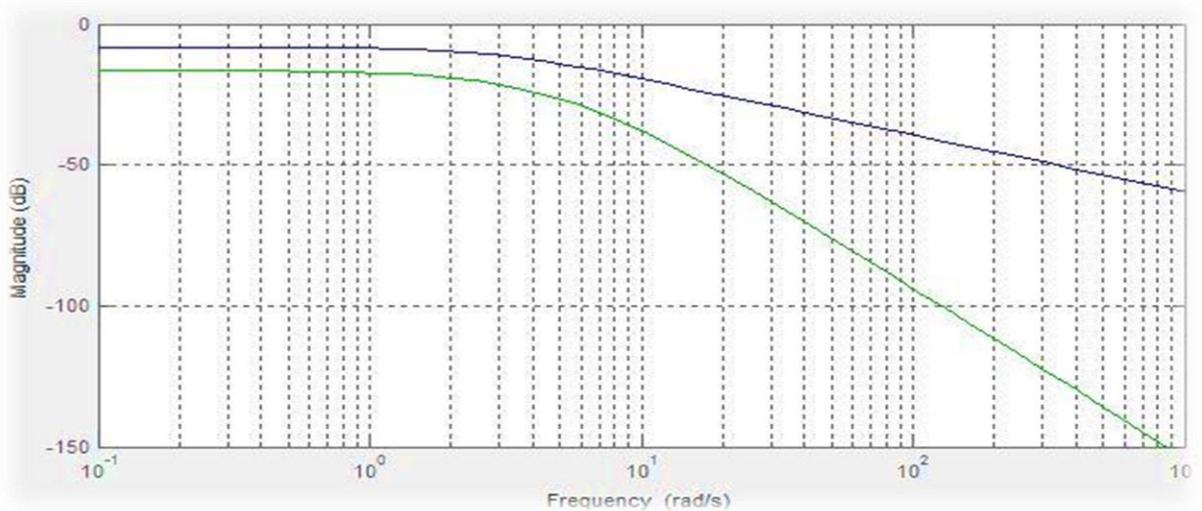
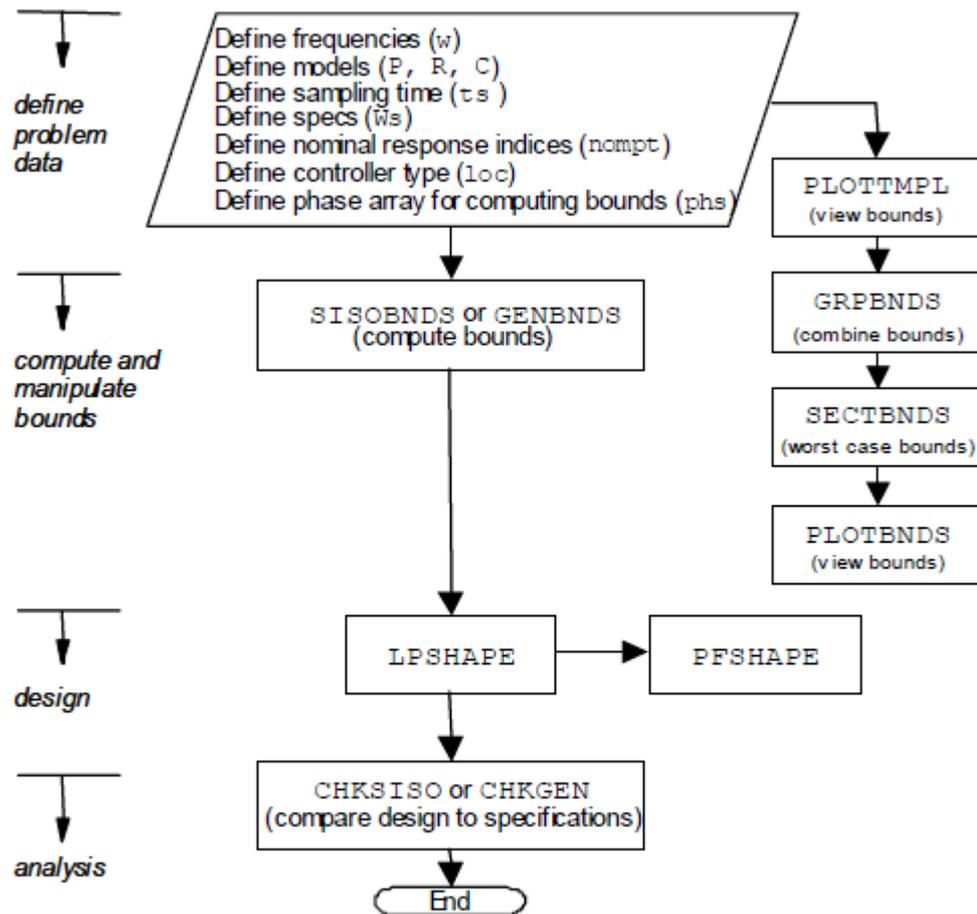


Figure 5.4 Frequency response of tracking specifications

5.4 QFT DESIGN STEPS

The schematic diagram given below shows the QFT controller design using MATLAB QFT Toolbox.



Flow chart showing basic steps in a QFT design

Figure 5.5 MATLAB QFT controller design

5.4.1 Template generation and nominal plant selection

The trial frequency array is given as follows [3] :

$$w = [0.1, 0.5, 1, 5, 10, 50, 100, 200] \text{ (rad/s).}$$

The first plant in the set of 64 uncertain plants is selected as the nominal. Here the random selection of the nominal plant is carried out with the surety that the selected nominal plant is stable [3] [5].

The nominal plant is as given below:

$$T_n(s) = \frac{-12.03}{s^2 + 47s + 57} \quad (5.8)$$

The time domain characteristic of the nominal plant - Peak Amplitude- 0.117,

SettlingTime-200,overshoot-2%

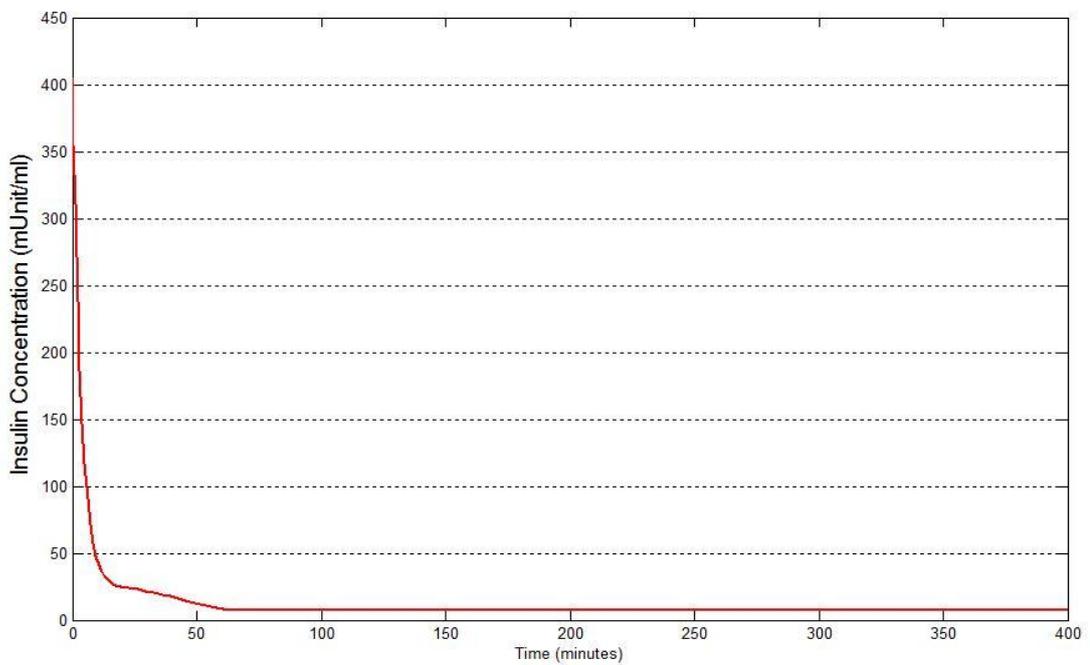
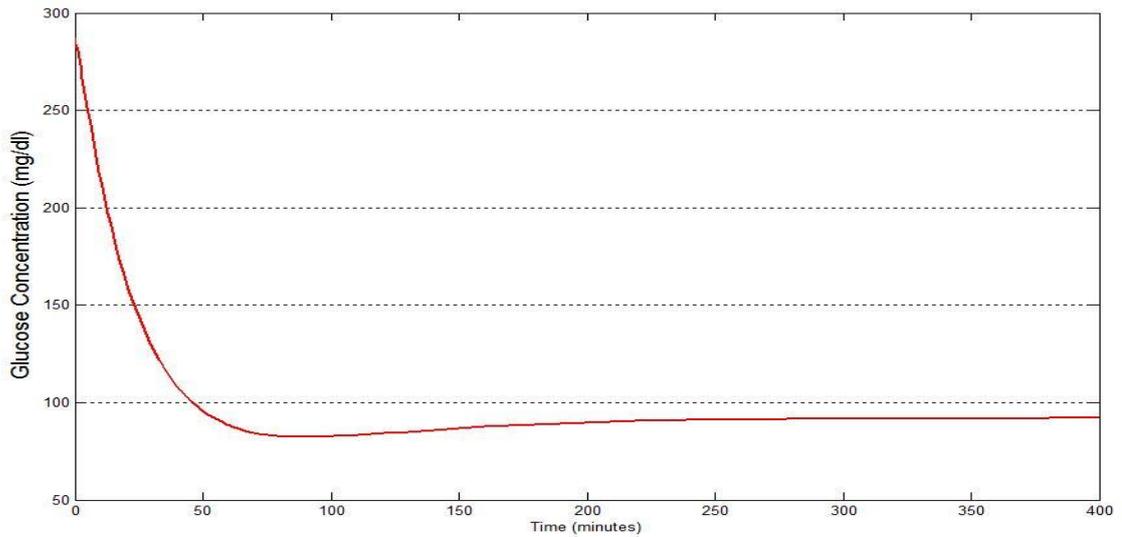


Figure 5.6 Open loop response of the nominal plant

From the time response (Figure 5.6) it can be clearly observed that the nominal plant response is far away to that of the desired response of the system due to the presence of uncertainty. The compensator $G_c(s)$ is to be designed so that this variation to the uncertainty in the plant is within allowable tolerances. Also, the Prefilter $F(s)$ must be designed to track the input by the plant response satisfactorily.

The plot templates at these trial frequency points are computed. Figure (5.7) shows the plant template using Kharitonov segment method obtain for the family of plants given in Appendix A using MATLAB QFT toolbox. The nominal plant is represented by a star mark.

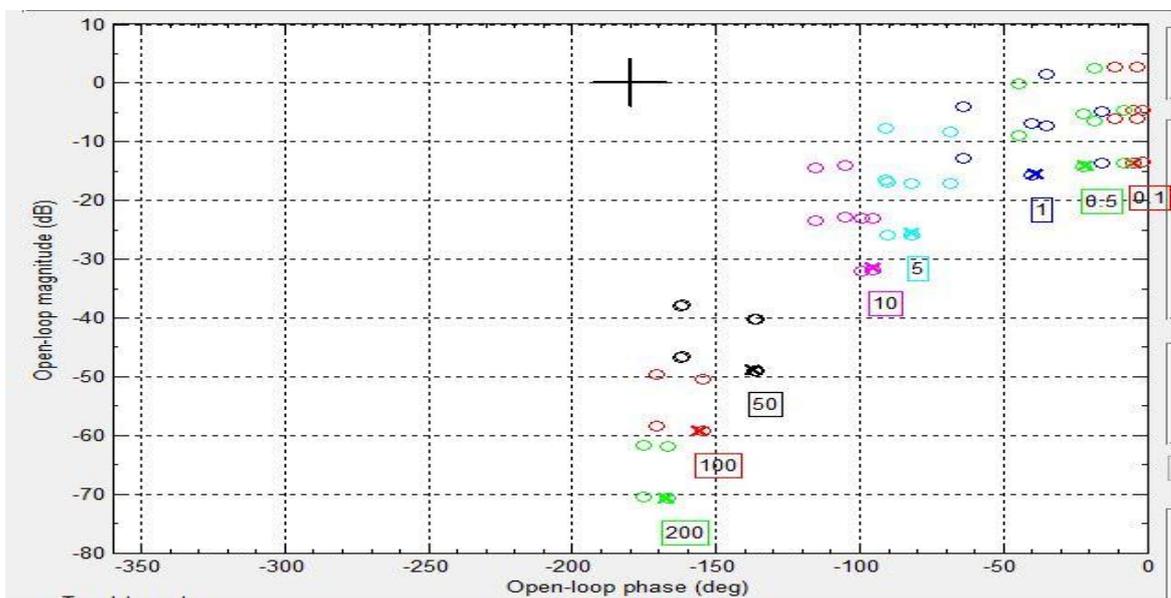


Fig 5.7 Templates for the glucose insulin regulation plant

5.4.2 Bound Computation

To compute the performance bounds performance specifications & the plant templates are used. The robust stability margin bounds on the NC generated by Horowitz - Sidi method [11] using QFT toolbox is shown in the Figure 5.8- 5.11.

5.4.2.1 Robust Stability Margin

Robust stability margin for the glucose insulin regulation plant model is generated in MATLAB using QFT Toolbox based on the specification given in the section. The toolbox functions have been given in the Appendix C. The robust

stability contours for the model is shown in the Figure 5.8. For the system to be robust stable the open loop transmission function should not pass through the stability bound.

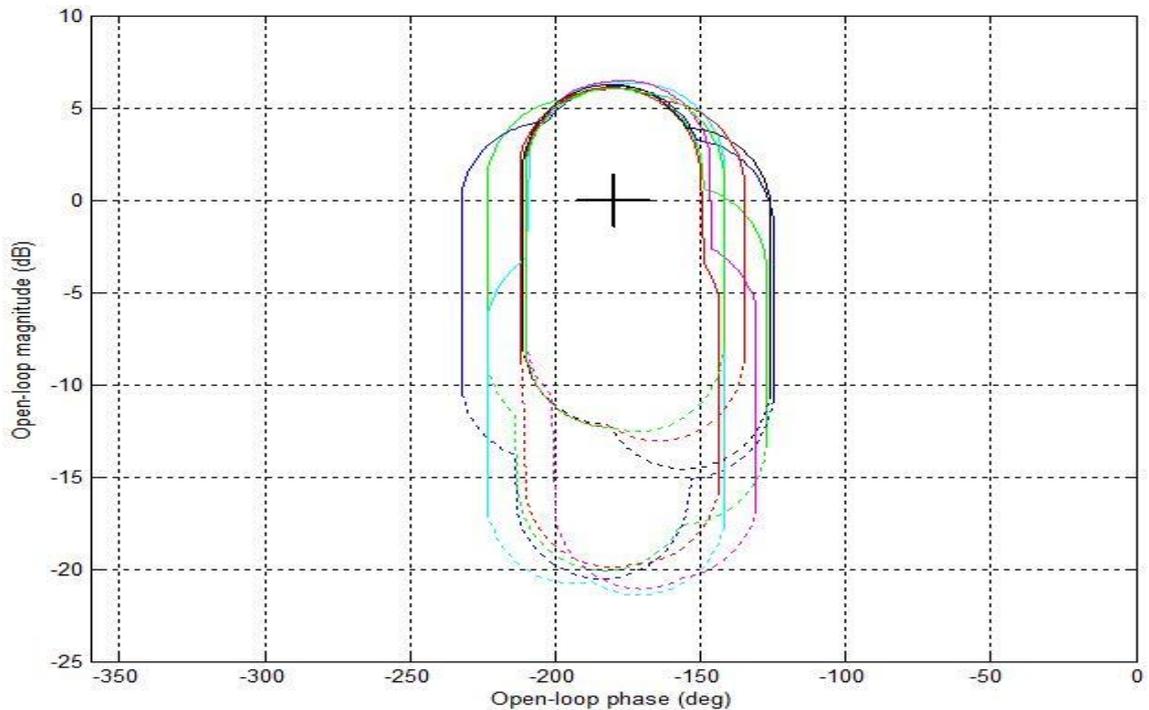


Figure 5.8 Robust Stability Bounds of glucose insulin regulation model

5.4.2.2 Robust Tracking bounds

Robust tracking bounds according to upper and lower tracking specifications for the glucose insulin regulation model specified in the section 5.2.2 is shown here in Figure 5.9. The tracking bound specifications are first generated in time domain and then converted into frequency domain. The bound and plot are given in Appendix C.

5.4.2.3 Composite bounds

The grouping of both the robust and tracking bounds gives the composite bounds of the glucose insulin regulation model and is as shown in Figure 5.10 and respective Matlab QFT Toolbox function has been mentioned in Appendix C.

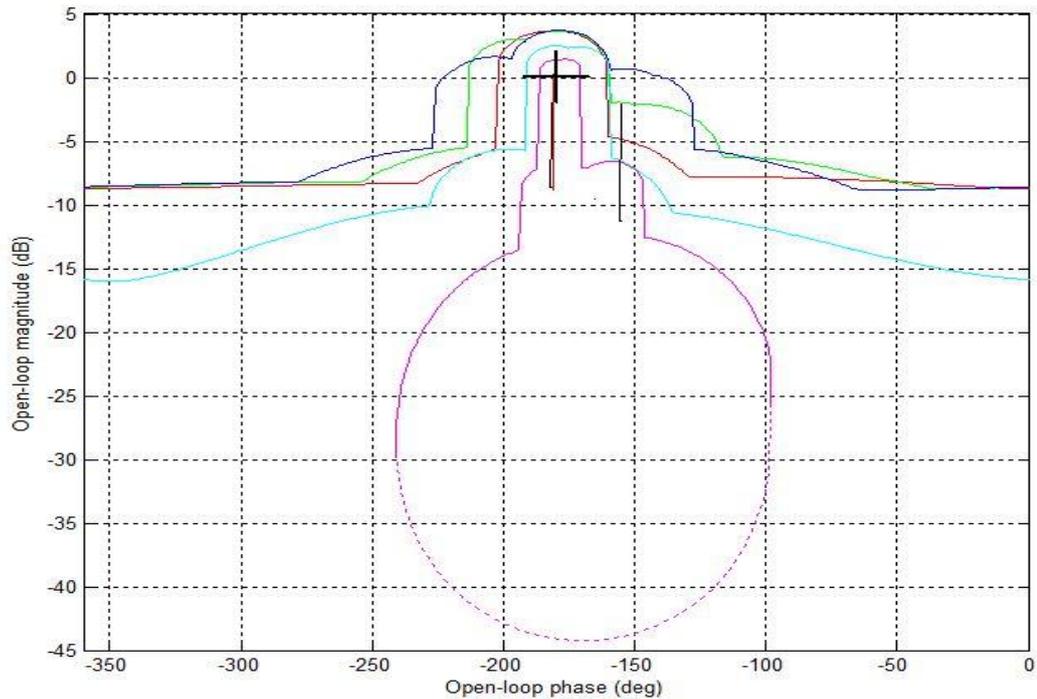


Figure 5.9 Robust tracking Bound for glucose insulin regulation model

5.4.3 Loop shaping (Controller design)

Having computed stability and performance bounds, the next step in a QFT design involves the design (loop shaping) of a nominal loop function that meets its bounds. This part of the design process is not automatic but depends on the skill of the designer. It involves adding poles and zeros until the nominal loop lies near its bounds and results in nominal closed loop stability. The adjustments in gain and lead or lag are also done to shape the loop. The design can be iterated and the order of the controller designed can be reduced using the Matlab QFT Toolbox Interactive Design Environment (IDE). The nominal loop has to satisfy the worst case of all bounds.

In Figure (5.12), it is observed that without applying any controller or compensator the open loop frequency response is too far from the robust stability bound and also it is located below the appropriate tracking performance bounds at most of trial frequencies. Hence the loop has to be shaped such that the open loop transmission function lies considerably nearer to robust bounds and above or on the tracking at most of the trial frequencies. Since the loop stays below the appropriate tracking bounds at each trial frequency a suitable control gain has to be introduced to push the loop upwards. The pole at the origin provides a very high gain at low frequencies as an integral control and the pole zero pairs are added in such a way that

the performance bounds are satisfied. The adjustment of gain plays a very important role in shaping the loop. The initial loop shaped transmission is shown in Figure 5.13 and the final loop shaped controller after certain iterations is shown in Figure 5.14

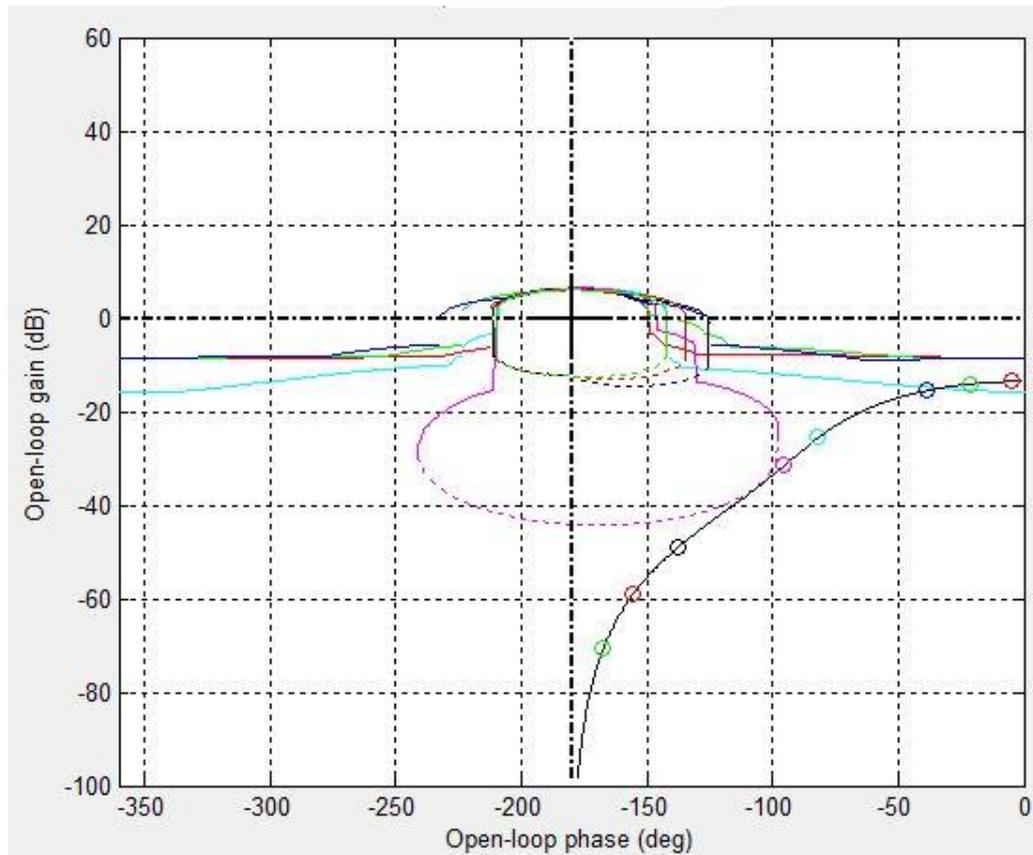


Figure 5.10 Open Loop Frequency Response of the glucose insulin model without controller

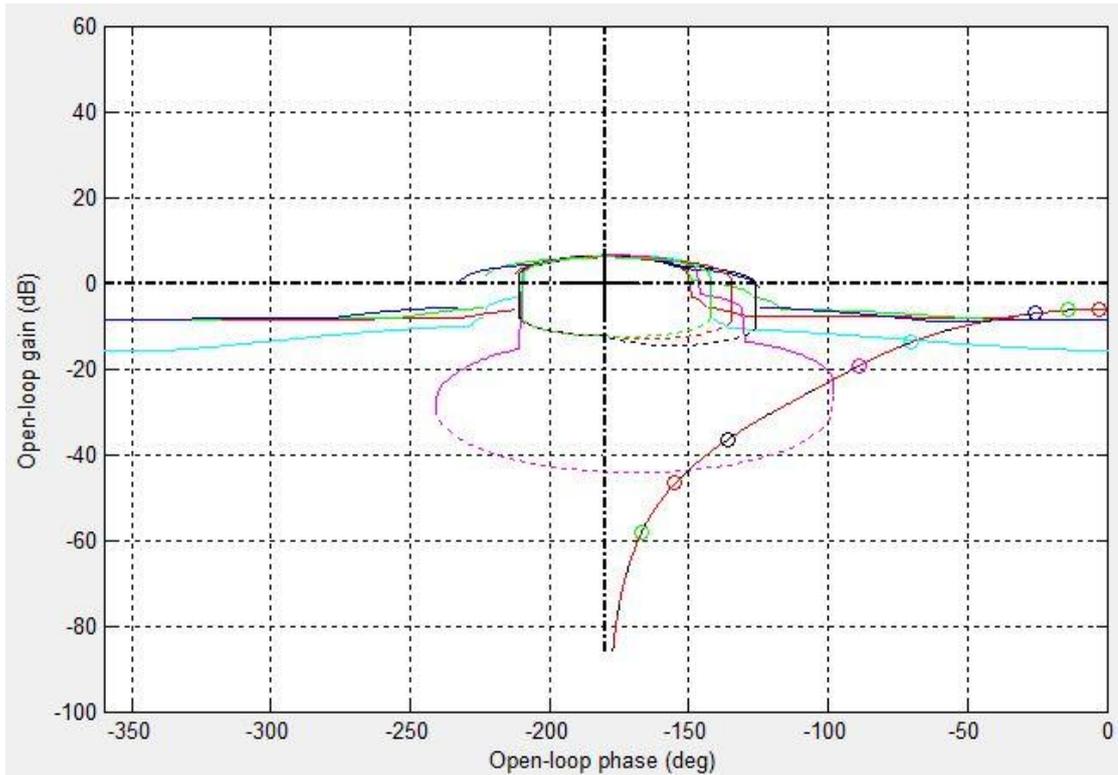


Figure 5.11 Final loop shaped frequency response

After completing the loop shaping the resultant controller that are obtained as

$$G_c(s) = \frac{20.161 (s + 8.627)}{(s + 36.63)(s + 21)} \quad (5.9)$$

5.4.4 Prefilter Design

From the Figure 5.15 it is clearly evident that nominal plant together with controller $G_c(s)$ is outside the specified upper and tracking boundaries. Here nominal open loop without $F(s)$ is plotted in blue and yellow line and blue-green lines give the performance tracking specification boundaries. The designed controller has reduced the variations in the closed loop frequency response to the desired range with ensuring closed loop stability. Now, a prefilter is required to position the required shape of closed loop frequency response.

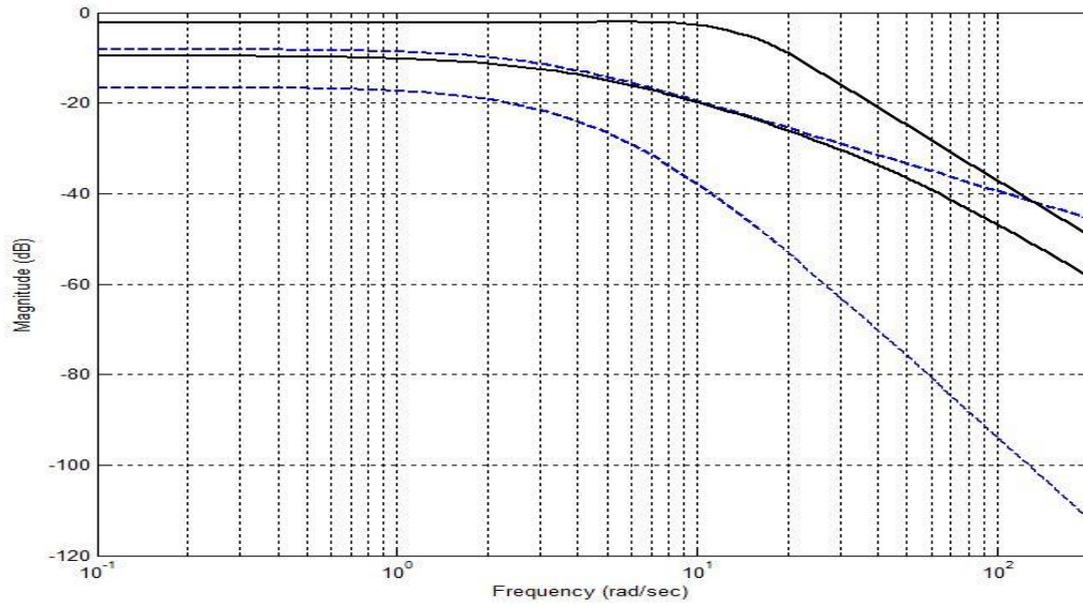


Figure 5.12 Closed Loop Bode without Prefilter

Obviously a dynamic prefilter is required to shape the frequency response to be within the desired range.

The prefilter is finally designed as

$$G_F(s) = \frac{0.0225 (s + 580.4)(s + 68860)}{(s + 23.7)(s + 380.1)} \quad (5.10)$$

The resulting closed loop frequency response with this Prefilter is shown in Figure 5.16.

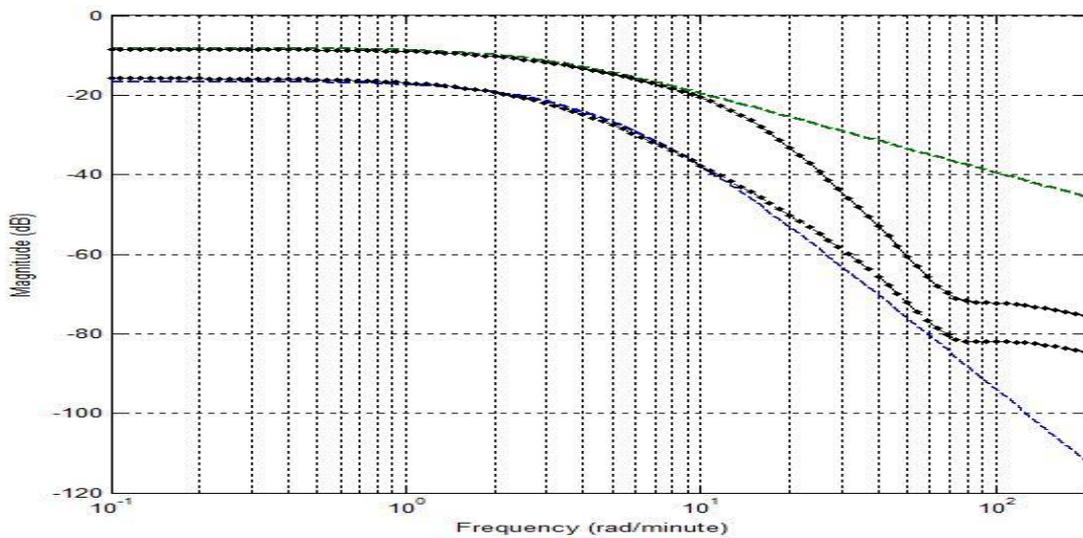


Figure 5.13 Closed loop frequency response with proposed Controller & Prefilter

5.5 Design analysis and closed loop validation

The final step in the QFT design procedure is to analyze the closed loop system performance with designed Controller $G_c(s)$ and $F(s)$ to check if the closed loop system satisfies all the performance specifications defined by the equation (5.2), (5.5) and (5.7).

Figure 5.17 gives the whole response with both controller and prefilter respectively together with the tracking requirement.

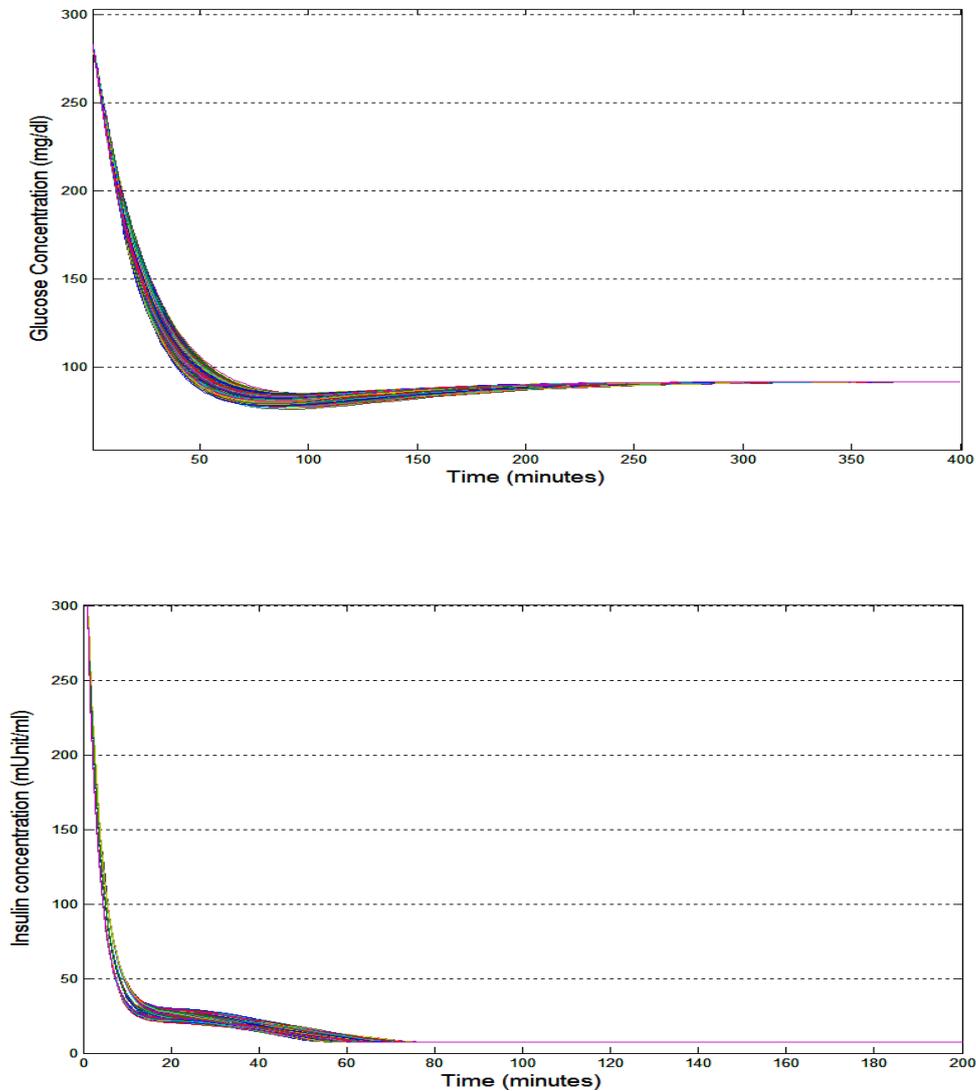


Figure 5.14 Closed Loop Time domain tracking response with proposed Controller

5.6 RESULTS AND DISCUSSION

In this chapter a glucose insulin regulation system is taken and QFT based robust controller is designed for this plant. At first the upper and lower tracking models are designed and they are compared with set tracking models [13]. Plant templates are analytically formed by analysis of open loop Bode of the uncertain plant family. Gridding of the template is done with outmost care. Robust stability bounds tracking bounds are generated using QFT Matlab toolbox which uses Horowitz-Sidi bound calculation method [11].

Finally Loop shaping is done on NC using the CAD environment of QFT Toolbox using MATLAB. Plant response is checked with this obtained controller. To meet the satisfactory tracking performance for the final output of the plant Prefilter is designed. Then the time response and frequency response of the plant response together with controller and prefilter is verified which shows that with this proposed controller and prefilter the plant ultimately satisfy all the given stability and performance criteria.

CHAPTER 6

CONCLUSION AND FUTURE SCOPE

6.1 SUMMARY AND CONCLUSION

Control systems have long been used to control various items such as power systems, robotics, motors and many other items. However, using control systems technologies and applying them to a biological situation helps to gain understanding of both the biology and the engineering. Truly there is no longer a separating of disciplines, but rather a melding of ideas in which everyone can learn from one another.

Diabetes is a disease itself stems from the pancreas not being able to fully control the release and regulation of insulin, and in turn, glucose. The common treatment to this is insulin shots to counteract the glucose in the body. Some new technologies to help control diabetes include insulin pumps, pancreas transplants, and stem cell injections.

A transfer function of the way the pancreas is supposed to work is attainable using some simple equations that model the way the system works. Combining this equations and simplifying to create less terms and make for an easier simulation can lead to a final equation that encompasses most of what controls the relationship between glucose and insulin. With this equation, a time domain equation, a Laplace transform can be used to convert to the s-domain to help with simulation and make for easier math than the differential equations of the time domain. This transfer function in the s-domain is what is generally used in control systems analysis.

Using the QFTCT control system tools, an accurate model of the pancreas and its function can be viewed. These simulations can also be expanded to include a view of what a potential pseudo pancreas could add to the system. When dealing with the such complex biological functions, safety is a very important concern. Any item added to the way the system is to function must be fully tested to insure that the system does not oscillate out of control, or even go off to infinity causing many problems. The work involved familiarization with Matlab and extensive reading on QFT theory, software design and design examples. The frequency responses and the

simulation results have shown that the design of a SISO system (including external disturbance inputs) proved to be successful for all controllers obtained. Thus, the least complex controller can be chosen as it satisfies the given specifications.

In general the thesis work can be concluded in such a way that robust control design procedure based on the QFT method has been applied successfully to design a robust controller for Blood Glucose Insulin regulation in order to achieve robust output in spite of different uncertainties.

6.2 FUTURE SCOPE

Biotechnology is a vast and opening field. Each day it seems new and exciting technologies are being applied to the biological field. It really is an exciting thing that we can cure some of these diseases. With each new advancement, a greater sense of our responsibility should be acknowledged. When using new technologies to mimic biological functions, care should be taken to make sure that these items are safe.

Future research (among which the possible implementation of other input variables like delivered farmaca) is required to further increase the model performance. Also the validity of the model on patients belonging to the medical (instead of surgical) ICU needs to be investigated.

REFERENCES

- [1] Ali H.I., “Robust QFT controller design for positioning a Permanent Magnet Stepper Motors” International Journal of Computer and Electrical Engineering, vol. 1, no. 1, pp : 9-14, 2009.
- [2] Bailey F. N. and Hui C. H., “Cascaded tools for loop gain phase shaping design of SISO robust controllers” Proceedings of IEEE Control System Society Workshop on Computer Aided Control System, pp. 151–167, Cincinnati, Ohio, USA, 1989.
- [3] Balance D.J, Chen W, “Plant template generation in Quantitative Feedback Theory” Technical report, Centre for Systems and Control, University of Glasgow, UK, 1998.
- [4] Balance D.J, Chen W, “QFT Design for uncertain non minimum phase and unstable plants” Technical report, Centre for Systems and Control, University of Glasgow, UK, 1997.
- [5] Balance D.J, Chen W, “Stability analysis on Nichols Chart & its application in QFT” Technical Report, Centre for Systems and Control, University of Glasgow, UK, 1997.
- [6] Borghesani C., Chait Y., Yaniv O., “Quantitative Feedback Theory Toolbox user’s Guide”, The Math Works Inc., Massachusetts, USA, 2001.
- [7] Cervera, J., Banios A., Monje C.A., Vinagre B. M., “Tuning of fractional PID controllers by using QFT”, 32nd Annual Conference of the IEEE Industrial Electronics Society, 2006.
- [8] Duncan G.A., “Digital control system design for a unique non MIMO process using QFT technique”, IEEE Proceedings on Control Theory Application, vol. 142, no. 5. 1995.
- [9] GarciaSanz M., Gil Mart´inez., Mart´in Romero J.J “Analytical formulation of robust performance or stability bounds for QFT controller design ”, European Control Conference, Kos, Greece, July 2007.
- [10] GarciaSanz M., Ostolaza J.X., “QFT robust control of a wastewater treatment plant”, Proceedings of the IEEE Int. Conference on Control Applications, vol.1, no.1 pp: 21-25, 1998.
- [11] Horowitz I., “Quantitative Feedback Theory”, IEEE Proceedings, vol.129, Pt.D, no.6, November, 1982.
- [12] Gu D.W., Petkov P.Hr., Konstantinov M.M., “Robust Control Design with MATLAB”, Springer Verlag, London,2005.
- [13] Houpis C.H., Rasmussen S.J, “Quantitative Feedback Theory Fundamentals & Applications”, Marcel Dekker Inc., New York, 1999.

- [14] Hamilton, Steven W. "QFT Digital Controller For An Unmanned Research Vehicle With An Improved Method For Choosing The Control Weightings", MS thesis, Air Force Institute of Technology, Wright-Patterson AFB, OH , December 1987.
- [15] GarciaSanz M., Ostolaza J.X., "QFT robust control of a wastewater treatment plant", Proceedings of the IEEE Int. Conference on Control Applications, vol.1, no.1 pp: 21-25, 1998.
- [16] Kerr M., Jayasuriya, Asokanthan S., "Robust stability in sequential MIMO QFT", American Control Conference, 2003, vol.6, no.2, pp:4834, 4839 vol.6, 4-6 June 2003.
- [17] Kianfar R., Wik T., "Automated controller design using linear Quantitative Feedback Theory for nonlinear systems", Control and Automation, 2009. ICCA 2009. IEEE International Conference on Control Applications, vol. 87, no. 7, pp:1955, 1961, 9-11 Dec. 2009.
- [18] Yaniv O., "Quantitative feedback design of linear and nonlinear control systems", Kluwer Academic Publishers, Boston, 1999.
- [19] Bergman, R. N., Ider, Y. Z., Bowden, C. R. and Cobelli, C. (1979). Quantitative estimation of insulin sensitivity, *American Journal of Physiology* **236**(6): E667 – E677.
- [20] Chee F, Fernando T. Closed Loop Control of Blood Glucose. Springer: Berlin, 2007.
- [21] Drewry, H. H., A study of sugar tolerance tests in two hundred patients with convulsions. *Bull. Neurol. Inst. N. Y.*, 1937, 6, 62.
- [22] Bergman, R. N., and C. Cobelli. 1980. Minimal modeling, partition analysis, and the estimation of insulin sensitivity. *Fed. Proc.* 39: 110-115.
- [23] Bergman, R. N., C. R. Bowden, and C. Cobelli. 1981. The minimal model approach to quantification of factors controlling glucose disposal in man. In *Carbohydrate Metabolism: Quantitative Physiology and Mathematical Modeling*. C. Cobelli, and R. Bergman, editors. John Wiley & Sons, Inc., London. 269-296.
- [24] Kaveh P, Shtessel Y. Blood glucose regulation using higher order sliding mode control. *International Journal of Robust and Nonlinear Control* 2008; **18**:557–569.

APPENDIX A

Pitch Domain Uncertain Transfer Function

Following are the family of uncertain plants generated using MATLAB.

A.1 Nominal s-domain transfer function of the uncertain plant

$$P_1 = \frac{-12.03}{s^2 + 47s + 57}$$

A.2 Off nominal s-domain transfer function of the uncertain plant

$$P_2 = \frac{-33.26}{s^2 + 16s + 24}$$

$$P_3 = \frac{-33.26}{s^2 + 16s + 32.25}$$

$$P_4 = \frac{-33.26}{s^2 + 16s + 40.5}$$

$$P_5 = \frac{-33.26}{s^2 + 16s + 48.75}$$

$$P_6 = \frac{-33.26}{s^2 + 16s + 57}$$

$$P_7 = \frac{-33.26}{s^2 + 23.75s + 24}$$

$$P_8 = \frac{-33.26}{s^2 + 23.75s + 32.25}$$

$$P_9 = \frac{-33.26}{s^2 + 23.75s + 40.5}$$

$$P_{10} = \frac{-33.26}{s^2 + 23.75s + 48.75}$$

$$P_{11} = \frac{-33.26}{s^2 + 23.75s + 57}$$

$$P_{12} = \frac{-33.26}{s^2 + 31.5s + 24}$$

$$P_{13} = \frac{-33.26}{s^2 + 31.5s + 32.25}$$

$$P_{14} = \frac{-33.26}{s^2 + 31.5s + 40.5}$$

$$P_{15} = \frac{-33.26}{s^2 + 31.5s + 48.75}$$

$$P_{16} = \frac{-33.26}{s^2 + 31.5s + 57}$$

$$P_{17} = \frac{-33.26}{s^2 + 39.25s + 24}$$

$$P_{18} = \frac{-33.26}{s^2 + 39.25s + 32.25}$$

$$P_{19} = \frac{-33.26}{s^2 + 39.25s + 40.5}$$

$$P_{20} = \frac{-33.26}{s^2 + 39.25s + 48.75}$$

$$P_{21} = \frac{-33.26}{s^2 + 39.25s + 57}$$

$$P_{22} = \frac{-33.26}{s^2 + 47s + 24}$$

$$P_{23} = \frac{-33.26}{s^2 + 47s + 32.25}$$

$$P_{24} = \frac{-33.26}{s^2 + 47s + 40.5}$$

$$P_{25} = \frac{-33.26}{s^2 + 47s + 48.75}$$

$$P_{26} = \frac{-33.26}{s^2 + 47s + 57}$$

$$P_{27} = \frac{-27.95}{s^2 + 16s + 24}$$

$$P_{28} = \frac{-27.95}{s^2 + 16s + 32.25}$$

$$P_{29} = \frac{-27.95}{s^2 + 16s + 40.5}$$

$$P_{30} = \frac{-27.95}{s^2 + 16s + 48.75}$$

$$P_{31} = \frac{-27.95}{s^2 + 16s + 57}$$

$$P_{32} = \frac{-27.95}{s^2 + 23.75s + 24}$$

$$P_{33} = \frac{-27.95}{s^2 + 23.75s + 32.25}$$

$$P_{34} = \frac{-27.95}{s^2 + 23.75s + 40.5}$$

$$P_{35} = \frac{-27.95}{s^2 + 23.75s + 48.75}$$

$$P_{36} = \frac{-27.95}{s^2 + 23.75s + 57}$$

$$P_{37} = \frac{-27.95}{s^2 + 31.5s + 24}$$

$$P_{38} = \frac{-27.95}{s^2 + 31.5s + 32.25}$$

$$P_{39} = \frac{-27.95}{s^2 + 31.5s + 40.5}$$

$$P_{40} = \frac{-27.95}{s^2 + 31.5s + 48.75}$$

$$P_{41} = \frac{-27.95}{s^2 + 39.25s + 57}$$

$$P_{42} = \frac{-27.95}{s^2 + 39.25s + 24}$$

$$P_{43} = \frac{-27.95}{s^2 + 39.25s + 32.25}$$

$$P_{44} = \frac{-27.95}{s^2 + 39.25s + 40.5}$$

$$P_{45} = \frac{-27.95}{s^2 + 39.25s + 48.75}$$

$$P_{46} = \frac{-27.95}{s^2 + 39.25s + 57}$$

$$P_{47} = \frac{-27.95}{s^2 + 47s + 24}$$

$$P_{48} = \frac{-27.95}{s^2 + 47s + 32.25}$$

$$P_{49} = \frac{-27.95}{s^2 + 47s + 40.5}$$

$$P_{50} = \frac{-27.95}{s^2 + 47s + 48.75}$$

$$P_{51} = \frac{-27.95}{s^2 + 47s + 57}$$

$$P_{52} = \frac{-22.65}{s^2 + 16s + 24}$$

$$P_{53} = \frac{-22.65}{s^2 + 16s + 32.25}$$

$$P_{54} = \frac{-22.65}{s^2 + 16s + 40.5}$$

$$P_{55} = \frac{-22.65}{s^2 + 16s + 48.75}$$

$$P_{56} = \frac{-22.65}{s^2 + 16s + 57}$$

$$P_{57} = \frac{-22.65}{s^2 + 23.75s + 24}$$

$$P_{58} = \frac{-22.65}{s^2 + 23.75s + 32.25}$$

$$P_{59} = \frac{-22.65}{s^2 + 23.75s + 40.5}$$

$$P_{60} = \frac{-22.65}{s^2 + 23.75s + 48.75}$$

$$P_{61} = \frac{-22.65}{s^2 + 23.75s + 57}$$

$$P_{62} = \frac{-22.65}{s^2 + 31.5s + 24}$$

$$P_{63} = \frac{-22.65}{s^2 + 31.5s + 32.25}$$

$$P_{64} = \frac{-22.65}{s^2 + 31.5s + 40.5}$$

$$P_{65} = \frac{-22.65}{s^2 + 31.5s + 48.75}$$

$$P_{66} = \frac{-22.65}{s^2 + 31.5s + 57}$$

$$P_{67} = \frac{-22.65}{s^2 + 39.25s + 24}$$

$$P_{68} = \frac{-22.65}{s^2 + 39.25s + 32.25}$$

$$P_{69} = \frac{-22.65}{s^2 + 39.25s + 40.5}$$

$$P_{70} = \frac{-22.65}{s^2 + 39.25s + 48.75}$$

$$P_{71} = \frac{-22.65}{s^2 + 39.25s + 57}$$

$$P_{72} = \frac{-22.65}{s^2 + 47s + 24}$$

$$P_{73} = \frac{-22.65}{s^2 + 47s + 32.25}$$

$$P_{74} = \frac{-22.65}{s^2 + 47s + 40.5}$$

$$P_{75} = \frac{-22.65}{s^2 + 47s + 48.75}$$

$$P_{76} = \frac{-22.65}{s^2 + 47s + 57}$$

$$P_{77} = \frac{-12.03}{s^2 + 47s + 24}$$

$$P_{78} = \frac{-12.03}{s^2 + 47s + 32.25}$$

$$P_{79} = \frac{-12.03}{s^2 + 47s + 40.5}$$

$$P_{80} = \frac{-12.03}{s^2 + 47s + 57}$$

APPENDIX B

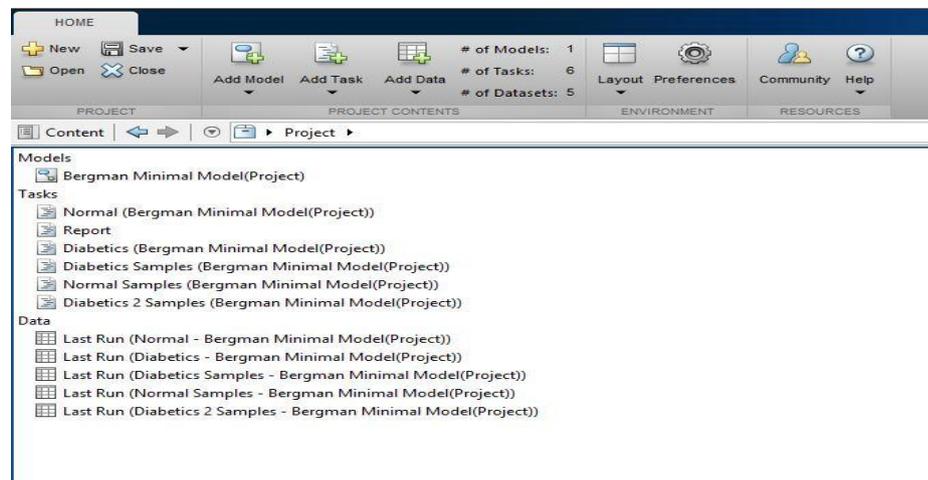
SIMBIOLOGY - A SIMULATOR

B.1 INTRODUCTION

Simbiology is the user interface making the modified model easier to use. Simbiology is a Matlab program. Simbiology software provides an integrated environment for modeling biological processes, simulating the dynamic behavior of these processes, and analyzing the model with simulation and experimental data. Biological processes include metabolic, genetic and signaling pathways with transform, binding, and transport reactions.

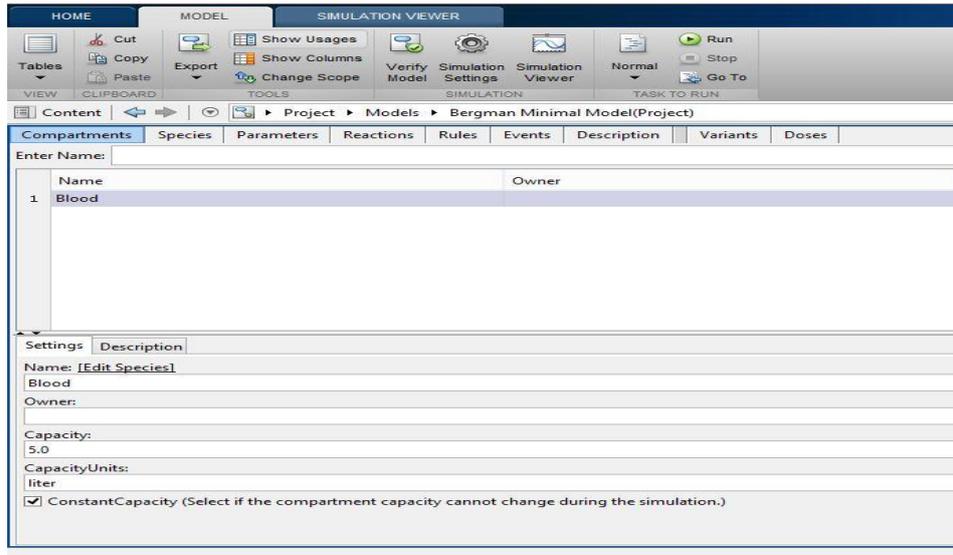
B.2 USING SIMBIOLOGY

The Simbiology desktop provides access to command-line functionality through a graphical user interface. The interface lets you model, simulate, and analyze biological pathways and reactions. Export your model to the MATLAB workspace and perform further analysis using the command line



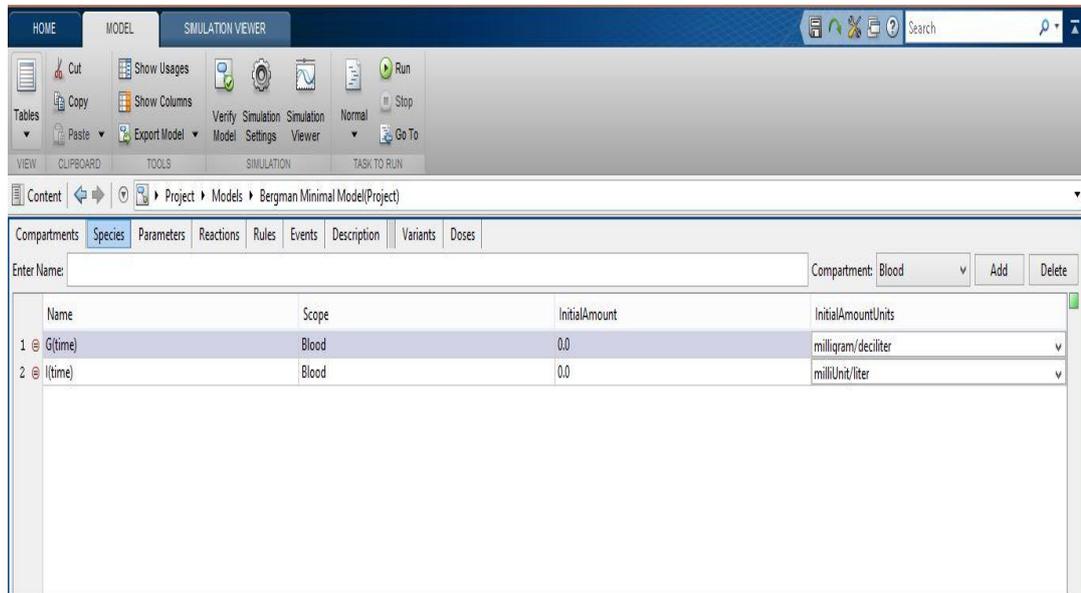
B.3 MODEL

A SimBiology[®] *model* is composed of a set of expressions (reactions, differential equations, discrete events), which together describe the dynamics of a biological system. You write expressions in terms of quantities (compartments, species, parameters), which are also enumerated in the model.



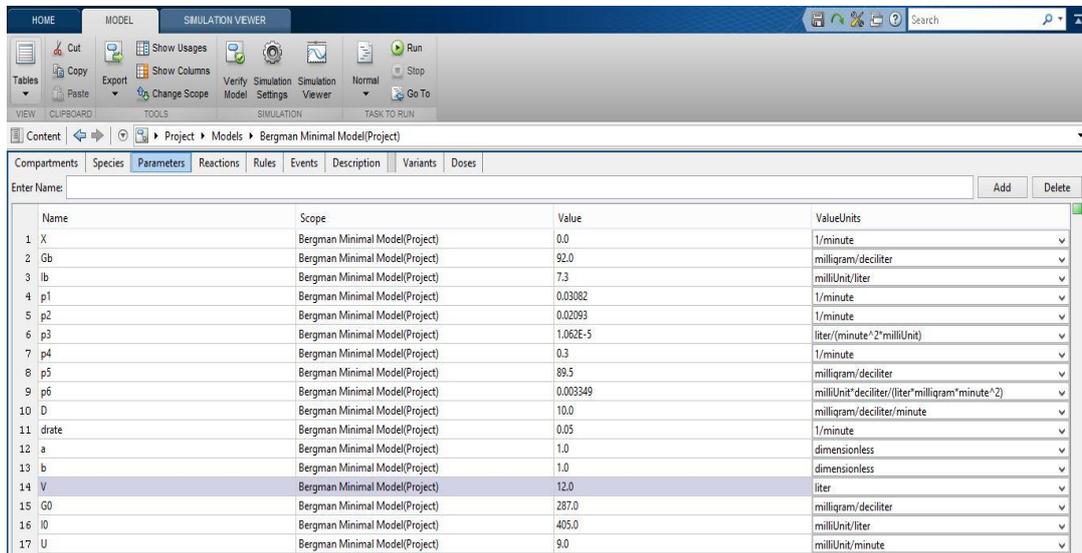
B.4 COMPARTMENTS

A compartment defines a physically bounded region that contains species. A compartment is characterized by a capacity expressed as volume, area, or length. A compartment can also contain other compartments, which adds hierarchy to a model. For example, a compartment named cytoplasm might contain a compartment named nucleus, thereby partitioning species based on their location.



B.5 SPECIES

A *species* characterizes the state of the biological system by representing the amount (or concentration) presents in the system for that entity. Examples of species are DNA, ATP and creatine. Species' amounts (or concentrations) vary during a

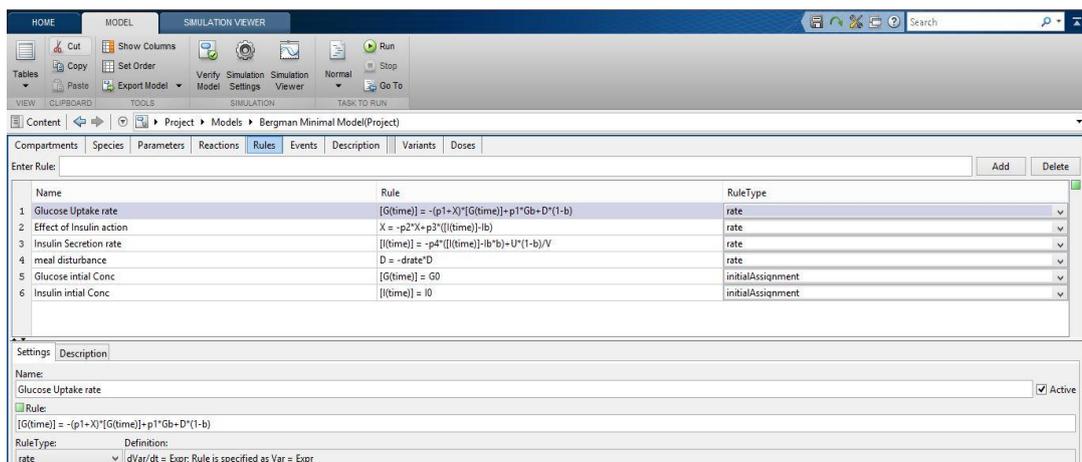


Name	Scope	Value	ValueUnits
1 X	Bergman Minimal Model(Project)	0.0	1/minute
2 Gb	Bergman Minimal Model(Project)	92.0	milligram/deciliter
3 lb	Bergman Minimal Model(Project)	7.3	milliUnit/liter
4 p1	Bergman Minimal Model(Project)	0.03082	1/minute
5 p2	Bergman Minimal Model(Project)	0.02093	1/minute
6 p3	Bergman Minimal Model(Project)	1.062E-5	liter/(minute^2*milliUnit)
7 p4	Bergman Minimal Model(Project)	0.3	1/minute
8 p5	Bergman Minimal Model(Project)	89.5	milligram/deciliter
9 p6	Bergman Minimal Model(Project)	0.003349	milliUnit*deciliter/(liter*milligram*minute^2)
10 D	Bergman Minimal Model(Project)	10.0	milligram/deciliter/minute
11 drate	Bergman Minimal Model(Project)	0.05	1/minute
12 a	Bergman Minimal Model(Project)	1.0	dimensionless
13 b	Bergman Minimal Model(Project)	1.0	dimensionless
14 V	Bergman Minimal Model(Project)	12.0	liter
15 G0	Bergman Minimal Model(Project)	287.0	milligram/deciliter
16 I0	Bergman Minimal Model(Project)	405.0	milliUnit/liter
17 U	Bergman Minimal Model(Project)	9.0	milliUnit/minute

simulation as a result of their participation in reactions, differential equations, and events. Therefore, species represent the dynamical state of a biological system.

B.6 PARAMETERS

A *parameter* is a quantity that is referred to by expressions. It typically remains constant during a simulation. For example, parameters are used as rate constants in reactions.

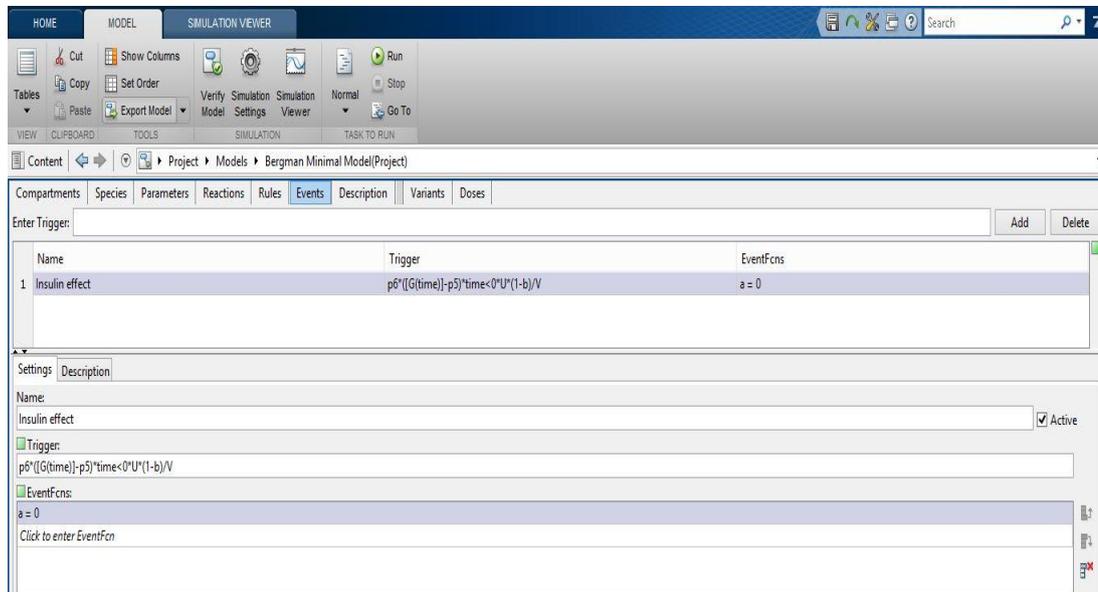


Name	Rule	RuleType
1 Glucose Uptake rate	$[G(\text{time})] = -(p1 \cdot X) \cdot [G(\text{time})] - p1 \cdot Gb \cdot D \cdot (1-b)$	rate
2 Effect of Insulin action	$X = -p2 \cdot X + p3 \cdot ([I(\text{time})] - lb)$	rate
3 Insulin Secretion rate	$[I(\text{time})] = -p4 \cdot ([I(\text{time})] - lb \cdot b) - U \cdot (1-b) / V$	rate
4 meal disturbance	$D = -\text{drate} \cdot D$	rate
5 Glucose initial Conc	$[G(\text{time})] = G0$	initialAssignment
6 Insulin initial Conc	$[I(\text{time})] = I0$	initialAssignment

Settings	Description
Name:	Glucose Uptake rate <input checked="" type="checkbox"/> Active
Rule:	$[G(\text{time})] = -(p1 \cdot X) \cdot [G(\text{time})] - p1 \cdot Gb \cdot D \cdot (1-b)$
RuleType:	rate
Definition:	$dVar/dt = \text{Expr}; \text{Rule is specified as Var} = \text{Expr}$

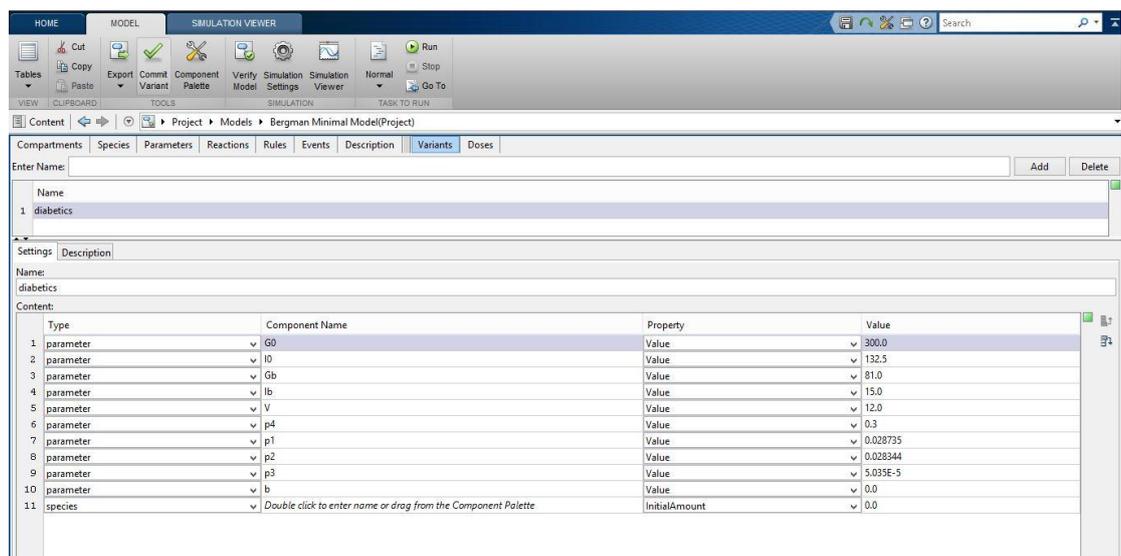
B.7 RULES

A *rule* is a class of mathematical expressions that include differential equations, initial assignments, repeated assignments, and algebraic constraints.



B.8 EVENTS

An *event* describes an instantaneous change in the value of a quantity (compartment, species, parameter). The discrete transition occurs when a user-specified condition becomes true. The condition can be a specific time or a specific time-independent condition.



B.9 VARIANT

A *variant* is a collection of quantities (compartments, species, and/or parameters) that you can use to alter a model's initial or base configuration, which is easier than individually modifying each quantity separately. For example, assuming that a different set of parameter values characterizes differences between wild type and mutant strains, you can use a variant to group parameter values indicative of these strains. You apply variants to a model to evaluate the model behavior under "variant" conditions.

APPENDIX C

Functions of QFT toolbox used

Some specific functions are used during this project:

1. To plot frequency response templates.
2. To compute QFT bounds as given in the control specifications.
3. To plot QFT bounds.
4. To group QFT bounds.
5. To compute the intersection of the concerned QFT bounds.
6. For Loop shaping in the Nichols Plot (NC) design environment.
7. To plot the Prefilter design environment.

These functions are described below:

1) Template Generation Function: `plottmpl (w,Wbd,P,nom)`

where the arguments are :

`w` : frequency array

`Wbd` : selected frequencies at which the templates are to be plotted and

it is subset of `w`

`P` : frequency response data

`nom`: nominal plant

2) QFT Bound Function : `sisobnds(ptype,w,wbd,ws,P,R,nom,G,loc,phs)`

General form of QFT bound computation function where the arguments are :

`ptype` : type of QFT bound

`ws` : performance specification

`R` : disk radius for nonparametric uncertainty

G : controller

Loc : location of unknown controller

Phs : phases at which bound is computed

3) QFT Bound Generation Function: plotbnds(bnds,ptype,phase)

where the arguments are :

bnds : the previously computed bound.

ptype : type of QFT bounds

phs : phases at which bound is computed

4) QFT Bound Grouping Function : grpdbnds(bd1,bd2,-----bd9)

where bd1, bd2 , -----bd9 : previously computed bounds respectively.

5) QFT Bound Intersection Function : sectbnds(bnds)

Where bnds is the QFT bounds array.

6) QFT Loopshaping Function

`>>lpshape(w,bdb,numpo,denpo,delay,numco,denco,phs)`

where the arguments are :

w : frequency array

bdb : computed QFT bounds.

numpo : represents the numerator of nominal plant

denpo : represents the denominator of nominal plant

numco : represents the numerator of initial controller

denco : represents the denominator of initial controller

phs : phase array

7) Prefilter Design Function : pfshape(p_{type},w,w_{bd},w_s,P,R,G,H,numfo,denfo)

where the arguments are :

w_s : performance specification

P : plant complex matrix

R : uncertainty disk radius

G : controller matrix

numfo : represents the numerator of initial filter

denfo : represents the denominator of initial filter

The robust specification and their problem type notation is given in the table C.1

Table C.1 List of Toolbox notation for Robust Specifications

Specification	Example of application	Toolbox notation (ptype)
$\left F \frac{PGH}{1 + PGH} \right \leq Ws_1$	Gain and phase margins (with sensor dynamics)	1
$\left F \frac{1}{1 + PGH} \right \leq Ws_2$	Sensitivity reduction	2
$\left F \frac{P}{1 + PGH} \right \leq Ws_3$	Disturbance rejection at plant input	3
$\left F \frac{G}{1 + PGH} \right \leq Ws_4$	Control effort minimization	4
$\left F \frac{GH}{1 + PGH} \right \leq Ws_5$	Control effort (with sensor dynamics)	5
$\left F \frac{PG}{1 + PGH} \right \leq Ws_6$	Tracking bandwidth (with sensor dynamics)	6
$Ws_{7a} \leq \left F \frac{PG}{1 + PGH} \right \leq Ws_{7b}$	Classical 2-DOF QFT tracking problem	7
$\left F \frac{H}{1 + PGH} \right \leq Ws_8$	Rejection of disturbances at plant output (with sensor dynamics)	8
$\left F \frac{PH}{1 + PGH} \right \leq Ws_9$	Rejection of plant disturbances (with sensor dynamics)	9