UNIVERSITI TEKNOLOGI MARA

IMPROVED MODEL FOR BLOOD GLUCOSE CONTROL USING MULTI-PARAMETRIC MODEL PREDICTIVE CONTROL (MP-MPC)

NUR FARHANA BINTI MOHD YUSOF

Thesis submitted in fulfillment of the requirements for the degree of **Doctor of Philosophy** (Chemical Engineering)

Faculty of Chemical Engineering

May 2019

AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

Name of Student	:	Nur Farhana Binti Mohd Yusof
Student I.D. No.	:	2011212052
Programme	:	Doctor of Philosophy (Chemical Engineering) – EH990
Faculty	;	Chemical Engineering
Thesis Title	:	Improved Model for Blood Glucose Control using Multi-parametric Model Predictive Control (mp-MPC)

Sumparn, Signature of Student :

Date : May 2019

ABSTRACT

Keeping pace with emerging technologies, artificial pancreas is highly recommended to be used as an alternate way to solve blood glucose level, BGL problem for type 1 diabetes and non-diabetes patients as well. However, due to the lack of effectiveness in algorithm, the blood glucose level in patient's body is still not achieving the optimum level. This study was undertaken to improve medical treatment for type 1 diabetes and critically ill patients with stress-hyperglycaemia by ensuring all parameters involved in glucose-insulin interaction physically are included in the model's equations. Mathematical models which describe insulin delivery mechanism for type 1 diabetes (Hovorka model 2004) was reviewed referring to the reference model. The research work continued with system identification technique with the objective to study the interrelation among all parameters and variables in the diabetic model. As a consequence, the results derived from the method, give us better comprehension in determining which parameters give higher effects on the glucose and insulin systems. Due to these changes, the equations in Hovorka model 2004 have been modified in glucose subsystem, plasma insulin concentration and insulin subsystem while the other equations remain unchanged. It is understood that time-tomaximum insulin absorption, $T_{\text{max,I}}$ is the most important parameter since it had effect on all variables and gave highest effect percentage, 66.89% at plasma insulin concentration, I(t). Parameter addition in diabetic equation showed increment in the sensitivity behaviour of variables and improved the reaction rate through the simulation. Simulation with 16.7 mU/min and 100 mU/min of insulin administration. u(t) were compared. Fluctuation of BGL with u(t) equals to 100 mU/min illustrates safer range (4.4 to 6.6 mmol/L) in contrast to the other amount of u(t). Clinical data of critically ill patients were selected for validation since the data for type 1 diabetes patients were difficult to obtain in Malaysia. The existence of control in simulation of patient 5 indicated better and safer blood glucose regulation, while in without control condition, the patient was easily in hypoglycaemia state (0.2 mmol/L at 519 minutes). The effect of blood glucose fluctuation with different amount of enteral and parenteral glucose were also studied and it showed that 10 g/hr of enteral glucose was the best option, while there was no significant difference in BGL with three types of parenteral glucose amounts. The effect of glucose and insulin against time for both clinical and simulation studies to the types of gender were investigated. From the results, it is clear that male has more frequency to be in safe BGL compared to the female for both scenarios. The graph clearly indicated that the simulation studies took less than 100 minutes, while the clinical studies needed approximately 120 minutes to reach safe BGL boundary. Employing the modified Hovorka equations, simulation work on BGL were examined with 16.7, 20.0, 50.0, 75.0 and 100 mU/min of u(t). 16.7 and 20.0 mU/min were found the most appropriate amounts of u(t) to regulate BGL in safe range. As a result, we managed to have a good correlation on interactions between the parameters in glucose-insulin intervention. For model validation purpose, actual patient data which refers to data of critically ill patients in this research are used due to scarcity of data available for type 1 diabetes patient in Malaysia. Critically ill patient data are referred as case study as these patients behave in the same manner as type 1 diabetes when they are subjected to hypoglycaemia or hyperglysemia due to meal disturbances.

TABLE OF CONTENT

			Page	
CON	FIRMA	TION BY PANEL OF EXAMINERS	ii	
AUT	HOR'S	DECLARATION	iii	
ABS	TRACT		iv	
ACK	NOWL	EDGEMENT	v	
ТАВ	LE OF (CONTENT	vi	
LIST	OF TA	BLES	x	
LIST	OF FIG	GURES	xiii	
LIST	OF AB	BREVIATIONS	xvi	
LIST	r of no	MENCLATURE	xvii	
CHA	PTER (DNE : INTRODUCTION	1	
1.1	Resear	ch Background	1	
1.2	Proble	m Statement	4	
1.3	Object	ives	5	
1.4	Scope	and Limitation of Study	5	
1.5	Hypot	hesis	6	
1.6	Signif	icance of Study	7	
1.7	Outlin	e of the Thesis	8	
CHA	APTER 7	TWO: LITERATURE REVIEW	9	
2.1	Introd	uction	9	
2.2	Diabe	tes History	10	
2.3	Types	of Diabetes	13	
2.4	Revol	Revolution of Diabetes Treatment		
2.5	Histor	History of Artificial Pancreas		
	2.5.1	Function of An Artificial Pancreas	30	
	2.5.2	System of Artificial Pancreas	31	
	2.5.3	Control Algorithm	31	
	2.5.4	Multi-parametric Model-based Predictive Control (mp-MPC)	32	

2.6	Clinic	Clinical Studies			
	2.6.1	Comparison Between Artificial Pancreas and Insulin Pump			
		Therapy	34		
	2.6.2	Comparison Between Artificial Pancreas and State-of-The-Art			
		Open-Loop Therapy	36		
	2.6.3	Studies on Insulin and Glucagon	38		
	2.6.4	Wireless Artificial Pancreas	39		
2.7	Agenc	ties and Associations	39		
СНА	PTER	THREE : RESEARCH METHODOLOGY	41		
3.1	Introd	uction	41		
3.2	Refere	ence Diabetic Equation	42		
	3.2.1	Type 1 Diabetic Equations	44		
	3.2.2	Improvement of Type 1 Diabetic Equations	48		
	3.2.3	Equations for Critically Ill Patients	51		
3.3	Syster	n Identification	57		
	3.3.1	Constants and Parameters	57		
3.4	Matla	b	58		
	3.4.1	Simulation with Hovorka model	59		
	3.4.2	Simulation with improved Hovorka model	59		
CHA	PTER	FOUR : RESULTS AND DISCUSSION	60		
4.1	Introd	luction	60		
4.2	Impro	ovement of Existing Hovorka Diabetic Model Using System			
	Identi	fication Technique To Enhance The Interrelation Between			
	Relat	ed Parameters.	60		
	4.2.1	Percentage Effects of All Variables	61		
4.3	Simu	ation of The Modified Diabetic Model Equations Resulted from			
	Employing The System Identification Technique and Comparison with				
	The H	Existing Model	63		
	4.3.1	Simulation with The Existing Model	63		
	4.3.2	Improvement on Hovorka Equations	68		
	4.3.3	Simulation Result Comparison Between Hovorka Model 2004			