HARDWARE IMPLEMENTATION FOR CARDIAC ELECTRICAL EXCITATION AND CONDUCTION USING AN FPGA

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For my beloved husband Zainul Idlan Bin Komar,

my adorable son Zainul Zafran and my beautiful daughter Zainur Zafrah,

all my family and to everyone who supports me, it just begins…

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ABSTRACT

Contraction of the heart is controlled by electrical excitations of cardiac cell membranes. The electrical excitations of the cells and their propagation in the heart tissue provide a basis of the physiological function of the heart through the cardiac excitation-conduction mechanism. One way to understand normal and abnormal dynamics of the heart is to simulate a comprehensive mathematical model of the cardiac excitation in order to study underlying mechanisms of the heart electrical system. However, simulating the dynamics of large numbers of a cellular model to form a tissue model requires an immense amount of computational time. In order to reduce the computational time required for the simulation, a hardware implementation of cardiac electrical excitation-conduction analysis system has been developed based on FitzHugh-Nagumo (FHN) model for a mammalian cardiac ventricular cell. In this research, one dimensional (1D) ring-shaped cable model with 80 compartments of the cell model designed using MATLAB Simulink blocks is able to be converted into synthesizable VHSIC (Very High Speed Integrated Circuit) of Hardware Description Language (VHDL) code by using an FPGA-based rapid-prototyping approach of MATLAB HDL Coder in order to simulate an action potential signal and its conduction through a hardware-implemented Field Programmable Gate Array (FPGA). Then, the VHDL design is functionally verified on an FPGA Xilinx Virtex-6 board using MATLAB HDL Verifier through FPGA-in-the-Loop (FIL) simulation approach. Simulations of cardiac cellular processes and reentrant arrhythmia are successfully conducted on Xilinx Chipscope Pro. High accuracy results have been obtained from the FPGA-on-board simulation compared to a software-based computer simulation with Percentage Error (PE) of 1.28% and 1.56% in performing the simulations of reentrant initiation and annihilation, respectively. The simulations are also capable to run in real time.

ABSTRAK

Kontraksi jantung dikawal oleh eksitasi elektrik pada membran sel jantung. Pengujaan elektrik pada sel dan perambakan sel-sel dalam tisu jantung memberikan asas fungsi fisiologi jantung melalui mekanisme eksitasi-kontraksi. Salah satu cara memahami dinamik normal dan tidak normal pada jantung adalah mensimulasikan satu model matematik yang komprehensif untuk mengkaji mekanisme sistem jantung. Walaubagaimanapun, simulasi dinamik model sel dengan jumlah yang banyak bagi membentuk tisu memerlukan tempoh masa pengiraan yang lama. Dalam usaha mengurangkan masa pengiraan simulasi, pelaksanaan perkakasan jantung elektrik bagi sistem analisis eksitasi-kontraksi telah dihasilkan berdasarkan model Fitzhugh-Nagumo (FHN) untuk sel ventrikel jantung pada mamalia. Dalam kajian ini, kabel bentuk cecincin satu dimensi (1D) dengan 80 sel direka menggunakan blok MATLAB Simulink seterusnya ditukar secara automatik kepada bahasa perihal peralatan litar bersepadu berkelajuan tinggi (VHDL) boleh sintesis menggunakan kaedah protataip-pantas MATLAB HDL Coder untuk mensimulasikan isyarat keupayaan tindakan dan konduksinya melalui pelaksanaan peranti tatasusunan get boleh aturcara (FPGA). Kemudian, fungsi reka bentuk VHDL itu disahkan pada satu papan tunggal FPGA Xilinx Virtex-6 menggunakan Pengesah HDL melalui simulasi gelung dalam FPGA (FIL). Simulasi proses sel jantung dan aritmia berjaya dikendalikan pada penganalisis logik terbenam Xilinx Chipscope Pro. Keputusan dengan ketepatan yang tinggi telah diperolehi daripada simulasi atas papan FPGA berbanding dengan simulasi komputer berasaskan perisian dengan peratus ralat (PE) 1.28% dan 1.56%, masing-masing dalam melaksanakan simulasi penghasilan dan penghapusan masuk-semula. Simulasi ini juga mampu beroperasi dalam masa nyata.

CONTENTS

LIST OF PUBLICATIONS

1. **N.A. Adon**, F. Mahmud, M.H. Jabbar & N. Othman. (2015). Optimization in MATLAB for Cardiac Excitation Modeling Towards FPGA Standalone Simulation Tools. *Applied Mechanics and Materials Trans Tech Publications, Switzerland*, Vol. 773-774, pp. 761-765. ISSN: 1662-7482.

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8. N. Othman, **N.A. Adon** & F. Mahmud. (2017). FPGA in-the-loop Simulations of Cardiac Excitation Model under Voltage Clamp Conditions. *International Conference on Engineering, Science and Nanotechnology (ICESNANO) 2016*, Vol. 1788, pp. 030105-(1-7). American Institute of Physics (AIP) Conference Proceeding. ISBN: 978-0-7354-1452-5.

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LIST OF ABBREVIATIONS

1D	One Dimensional
2D	Two Dimensional
3D	Three Dimensional
AIDS	Acquired Immune Deficiency Syndrome
ASIC	Application Specific Integrated Circuit
BER	Bit Error Rate
CAB	Configurable Analog Blocks
CLB	Configurable Logic Blocks
CoreGen	Core Generator
DDR	Double Data Rate
DEPE	Differential Equation Processing Element
DSP	Digital Signal Processing
FHN	FitzHugh-Nagumo
FIL	FPGA-In-the-Loop
FL	Fraction-Length
FMC	FPGA Mezzanine Cards
FPAA	Field Programmable Analog Array
FPGA	Field Programmable Gate Array
GPU	Graphics Processing Unit
HDL	Hardware Description Language
HIV	Human Immunodeficiency Virus
ICON	Integrated Controller
ILA	Integrated Logic Analyzer
IOB	Input Output Blocks
ISE	Integrated Software Environment
ISim	ISE Simulator

JTAG	Joint Test Action Group
LUT	Lookup Table
MAC	Multiply Accumulate Operations
MMCM	Mixed Mode Clock Managers
MSE	Mean Squared Error
NCD	Native Circuit Description
NGD	Native Generic Database
ODE	Ordinary Differential Equation
PAR	Place And Route
PC	Personal Computer
PCI	Payment Card Industry
PCR	Polymerase Chain Reaction
PDSP	Programmable Digital Signal Processors
PE	Percentage Error
PRC	Phase Resetting Curve
RAM	Random Access Memory
RTL	Register Transfer Language
SNR	Signal to Noise Ratio
SOC	System On Chip
SVPWM	Space Vector Pulse Width Modulation
VHDL	VHSIC Hardware Description Language
VHM	Virtual Heart Model
VHSIC	Very High Speed Integrated Circuit
VLSI	Very Large Scale Integration
VSI	Voltage Source Inverter
WHO	World Health Organization
WL	Word-Length
XSG	Xilinx System Generator

CHAPTER 1

INTRODUCTION

1.1 Background of the research

Since a decade ago, cardiovascular disease has remained the top major killer cause of death in the world issued by the World Health Organization (WHO). Referring to Figure 1.1, the ten leading causes of death in the world are ischemic heart disease, stroke, chronic obstructive pulmonary disease, lower respiratory infection, lung cancer, Human Immunodeficiency Virus (HIV) or Acquired Immune Deficiency Syndrome (AIDS), diarrhoeal disease, diabetes mellitus, road injury and hypertensive heart disease. According to the WHO, cardiovascular diseases killed 17.5 million people in 2012 that was 3 in every 10 deaths [1]. It was reported that 7.4 million people died of ischemic heart disease, 6.7 million from stroke and 1.1 million from hypertensive heart disease.

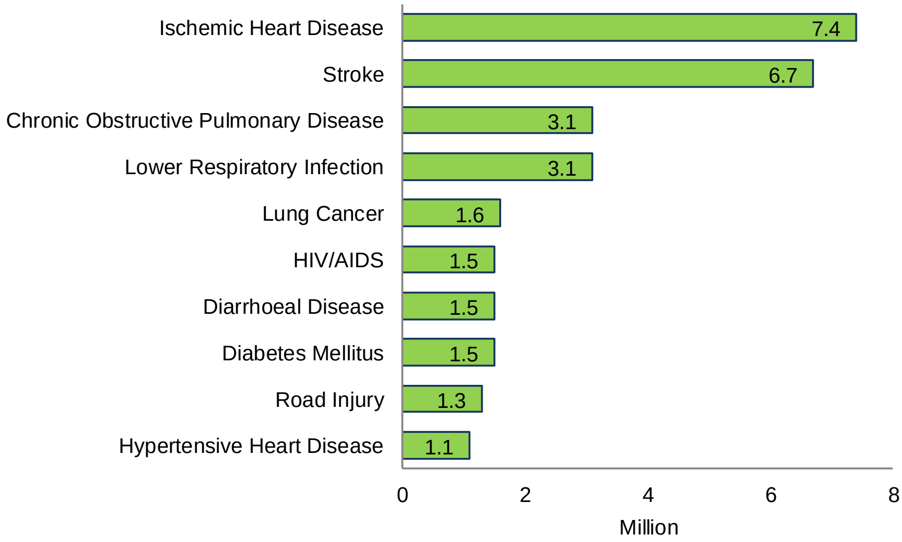

Figure 1.1: The ten leading causes of death in the world [1].

Ischemic heart disease caused by decreased blood flow and reduced oxygen supply to the heart muscle [2]. The disease can interrupt the electrophysiology function of the ion channels responsible for the cellular electrical activity of the heart. Changes in the intracellular and extracellular occur during ischemic and can alter the electrophysiology of several species of ionic channels are in fact related to disturbances in the cellular activity of cardiac myocytes [3]. Thus, until now, many studies have been done to elucidate the causes and interpret the underlying mechanisms in cardiac electrophysiological which are through experimental [4], [5] clinical measurement [6], [7] and computational model simulation [8], [9], [10] studies.

Although, experimental study is generally preferable, but it has several restrictions such as requires high variables quantity for monitoring, expensive and high-resolution data in investigating larger preparations [11], [12]. Meanwhile, clinical tools have become widely used in cardiac electrophysiological studies, often indispensable in evaluating patients with specific cardiac electrical activity [13]. Clinical data are used to validate computational modeling which allow integration of previous findings, quantitative assessments of the models and the projection across relevant spatial and temporal scales [14]. However, clinical tools have several drawbacks which are risk assessment tools, potential harms to patients and the effectiveness or difficulty in comparing results across studies [15], [16]. In contrast, a model simulation technique is not associated with such problems and also has the capability to increase study parameters through mathematical representations and decreasing the time responsible for investigating cardiac dynamics [17], [18].

There are numerous mathematical model had been represented in excitable media for the simulation studies such as Hodgkin–Huxley [19], FitzHugh-Nagumo (FHN) model [20], [21], continued with the Noble model [22], [23], Beeler and Reuter model [24], [25], Luo-Rudy model [26], [27] and details models in order to show different regions of the heart. However, advancement of the computational technique has initiated cardiac cell models to become more complicated as variable parameters in the mathematical descriptions are increased in order to present the cellular process in more details [28], [29]. Thus, a large number of the cell models in forming a tissue model cause drawback in the amount of computational processing which would increase a time required to run the model simulations [30].

According to Prof. Yoshihiko Nakamura (2012), two second motion according of the neuromusculoskeletal model of human takes one hour to compute reduction of computation cost. These situations can be concluded that a real-time model simulation technique has been difficult to achieve especially in the electrophysiological that involves high level dimensional models and simulation conditions [31], [32]. However, a real-time model simulation system is very important in order to diagnose cardiac abnormalities due to heart failure since it simulate more realistically cardiac work and it would be a very useful and convenient system to be applied in medical education and training in cardiac surgical planning such as permanent pacemaker insertion, catheter-based intervention and invasive cardiovascular surgeries [33], [34], [35].

In order to overcome this computational challenge, high performance and low power consumption hardware-based implementation can provide valuable tools for real-time simulation analysis in electrophysiological studies applications such as in the medical and educational field [36], [37]. Currently, researchers have moved forward to use hardware-implemented of analysis tool for cardiac electrophysiology considering their several advantages of extremely fast and parallel mode execution, low power usage, reconfigurable, development ease and low cost [38], [39], [40]. Hence, various types of hardware had been used to simulate the electrical potentials exist across the membrane of cells using hardware such as analog-digital circuit [41], microcontroller [42], Graphic Processing Unit (GPU) [30], [43] and Field Programmable Analog Array (FPAA) [44], [45]. However, these previous studies have shown limitations due to their power consumption and inefficient regarding rapid calculations in performing the real-time operation [46].

Therefore, reconfigurable hardware in the form of Field Programmable Gate Array (FPGA) has appeared as a viable system solution with complex chips in the construction of high performance systems at an economical price [47], [48]. FPGA technology is now considered very useful by an increasing number of designers in various fields of application as it offers reconfigurable hardware, programmable circuit architecture, execute in parallel mode with million gate counts and a low power consumption [47], [49]. Moreover, it is also capable of solving higher orders of Ordinary Differential Equations (ODEs) describing the electrical behavior of the cell membrane [38].

In recent literature, a large number of studies using FPGA for biomedical application are reported [50], [51], [52]. As regards, these have given motivation to implement the FPGA to perform real-time simulations, primarily responsible for the cardiac abnormal activity. This research will emphasise the simulation of reentrant excitation-conduction of cardiac cells realised by coupling 80 active circuits in one dimensional (1D) ring-shaped based on FHN [53] model. In this research, the 1D ring-shaped cable model is constructed using MATLAB Simulink based FPGA rapid-prototyping method towards a real-time simulation in producing an analysis tool to study the underlying mechanism of the heart through understandings of non-linear dynamics in cardiac excitation.

The FPGA configuration is generally specified using a Hardware Description Language (HDL), therefore for rapid design and faster development, the HDL code is generated using MATLAB HDL Coder that is capable to convert the designed MATLAB Simulink model to Very High Speed Integrated Circuit (VHSIC) Hardware Description Language (VHDL) code. Furthermore, the FPGA-based model simulation system which is designed through MATLAB HDL Coder is verified using an FPGA-in-the-Loop (FIL) approach. Towards the hardware implementation in real-time model simulation analysis tool, the design system is then implemented on Xilinx Virtex-6 XC6VLX240T FPGA development board and simulated through embedded logic analyser Xilinx Chipscope Pro. The dynamics of the FHN model simulation using FPGA board are compared to those obtained from the conventional software-based computer simulation technique to evaluate the accuracy and performance of the simulation-based analysis system in order to demonstrate that the FPGA model can be utilised for simulating large scale cellular network in real-time as an alternative to the software-based computer simulation technique in the future.

1.2 Problem statement

As mentioned earlier in the introduction, due to a number of challenges in experimental and clinical investigations of the cardiac electrical behavior [54], mathematical models of cardiac tissue have been developed and analysed by simulating conduction of action potentials in a variety of conditions [18]. However, it is inevitable for those models to become large scale in the number of dynamical variables, requiring immense amounts of computational time for their dynamic simulations. This could cause difficulties in performing in-depth analysis on cardiac electrical functions since many hours of time is required to run dynamic simulations of electrical conduction in tissue or organ level on a conventional computer station. Although a high performance supercomputer is commonly used in conducting fast speed computations for the analysis, it usually requires high installation cost and high energy. Therefore, FPGA based hardware implementation of electrical excitation and conduction of a cardiac cell model simulation system is developed to overcome the challenges. The simulation of 1D ring-shaped cable model is conducted through this research work based on FHN model, a typical mathematical model of a cardiac cell.

1.3 Aim and research objectives

The aim of this research is to develop an analysis system in order to perform a real-time simulation of a cellular excitation reaction in tissue level based on a mathematical model by using FPGA hardware implementation. The proposed implementation can be deployed in a biomedical field for understanding and analysing the mechanism of abnormalities cardiac cycle and will function in the real FPGA-on-board application. To enable this, the thesis is presented in three objectives as follows:

Objective I: To construct a FHN model algorithm based on MATLAB HDL Coder for an FPGA implementation.

Objective II: To develop FPGA-based model simulation system for cardiac excitation and conduction towards real-time analysis tool implementation.

Objective III: To evaluate the technique with conventional simulation method in terms of its accuracy and performance based on simulation studies of the reentrant mechanism in a cardiac excitation-conduction.

1.4 Scope of the research

This research covers a study related to a mathematical model of the action potential conduction in a ventricular cardiac cell, which focuses on the FHN model for developing a new simulation-based analysis technique in cardiac excitation and conduction studies using FPGA. The FPGA-based hardware implemented real-time model simulation system will be developed by solving ODEs of the model based on a rapid-prototyping design flow through MATLAB HDL Coder. This technique accelerates the FPGA design process through automatic generation the VHDL code at a certain level in developing the system and faster optimisation. The rapid-prototyping method does not directly involve on a hardware architecture design of the FPGA by the developer which has more to do with an FPGA traditional design technique.

The reason for choosing the MATLAB HDL Coder as rapid-prototyping tool are because the MATLAB HDL Coder offers and keeps updating many advanced and latest functions for the FPGA design systems, and rapidly assembles system models usually using only existing blocks of MATLAB Simulink compare to other tools such as Xilinx System Generator (XSG), Digital Signal Processing (DSP) Builder and Labview. Besides, the MATLAB HDL Coder also provides FIL approach to verify the designed system based on various types of FPGA development boards from different manufacturers. Lastly, the generated code by MATLAB HDL Coder is modified, synthesised and implemented by using Xilinx ISE software on the FPGA. The results are displayed on the Xilinx Chipscope Pro as it is able to log data for further analysis.

The FHN model will be used to understand of reentrant mechanisms by performing 1D ring-shaped cable model in cardiac tissue. A 1D ring-topology-network of 80 compartments of the cell model is constructed through interconnection of gap junction resistances for exhibiting the reentrant action potential conduction. The number of the cell models presented is relied on the FPGA specification used and 80 cells is an appropriate number to perform the simulation of the cardiac excitation-conduction in FHN model-based 1D ring-topology-network. However based on the design and type of model, the number could be different. For example, the design of a two dimensional (2D) model might require more number of cells. The simulation results from the FPGA-based model will be compared to those obtained numerically MATLAB software-based computer simulations of the cardiac excitation-conduction activity using the FHN model to verify the accuracy according to an acceptable error simulation of not more than $\pm 1.5\%$ [55] and the timing performance of the simulation system.

1.5 Overall contributions

This project of developing a cardiac reentrant excitation-conduction simulation system has two significant contributions. Firstly, a new approach of FPGA system design based rapid-prototyping that can provide a high performance system and high accuracy result has demonstrated a significant contribution. Through this rapid-prototyping approach, various types of parameters are involved to analyse and optimise the system performances such as area, maximum frequency and power consumption in a much more convenient way. Secondly, the realisation of a real-time simulation of FHN model based cardiac action potential through FPGA

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