COMPUTER MODELING FOR DENDRITIC CONSTRUCTION AND CONNECTIVITY OF NEURAL CELLS

By

Samar Ahmed Mahmoud Abbass

A Thesis Submitted to the
Faculty of Engineering at Cairo University
in Partial Fulfillment of the
Requirements for the Degree of
MASTER OF SCIENCE
in
Biomedical Engineering and Systems

FACULTY OF ENGINEERING, CAIRO UNIVERSITY
GIZA, EGYPT
2019

COMPUTER MODELING OF DENDRITIC CONSTRUCTION AND CONNECTIVITY OF NEURAL CELLS

By

Samar Ahmed Mahmoud Abbass

A Thesis Submitted to the
Faculty of Engineering at Cairo University
in Partial Fulfillment of the
Requirements for the Degree of
MASTER OF SCIENCE
in
Biomedical Engineering and Systems

Under the Supervision of

Dr. Amr A. R. Sharawi

Associate Professor of
Biomedical Engineering and Systems
Faculty of Engineering, Cairo University

Prof. Dr. Medhat A. El-Messiery

Professor of
Engineering Physics
Faculty of Engineering, Cairo University

Prof. Dr. Noha Mohamed Salem

Professor of
Engineering Physics
Faculty of Engineering, Cairo University

FACULTY OF ENGINEERING, CAIRO UNIVERSITY
GIZA, EGYPT
2019

COMPUTER MODELING FOR DENDRITIC CONSTRUCTION AND CONNECTIVITY OF NEURAL CELLS

By

Samar Ahmed Mahmoud Abbass

A Thesis Submitted to the
Faculty of Engineering at Cairo University
in Partial Fulfillment of the
Requirements for the Degree of
MASTER OF SCIENCE
in
Biomedical Engineering and Systems

Approved by the Examining Committee

_____
Dr. Amr A. Sharawi, Thesis Main Advisor

_____
Prof. Dr. Medhat A. El-Messiery, Advisor

_____
Prof. Dr. Noha M. Salem, Advisor

_____
Prof. Dr. Ahmed M. Badawi, Internal Examiner

_____
Prof. Dr. Samir Youssef M. Marzouk, External Examiner
- Dean of Productivity and Quality Institute, Arab Academy for Science, Technology and Maritime Transport

FACULTY OF ENGINEERING, CAIRO UNIVERSITY
GIZA, EGYPT
2019

Engineer's Name: Samar Ahmed Mahmoud Abbass
Date of Birth: 13/5/1991
Nationality: Egyptian
E-mail: Samar.abbass.m@eng-st.cu.edu.eg
Phone: 01226745322
Address: 17 Mokarar, Omr Ibn El Khattab, Omranya Gharbia, Giza

Registration Date: 1/3/2014
Awarding Date: …./…./2019
Degree: Master of Science
Department: Biomedical Engineering and Systems

Supervisors:

Dr. Amr A. R. Sharawi
Prof. Dr. Medhat A. El-Messiery
Prof. Dr. Noha Mohamed Salem

Examiners:

Prof. Dr. Samir Y. M. Marzouk (External examiner)
- Dean of Productivity and Quality Institute, Arab Academy for Science, Technology and Maritime Transport

Prof. Ahmed M. Badawi (Internal examiner)
Dr. Amr A. Sharawi (Thesis main advisor)
Prof. Dr. Medhat A. El-Messiery (Advisor)
Prof. Dr. Noha M. Salem (Advisor)

Title of Thesis:

Computer Modeling for Dendritic Construction and Connectivity of Neural Cells

Keywords:
Dendritic morphology; Neuron growth; Neural Network connectivity

Summary:

A computational stochastic model that describes the growth of neuronal dendrites in a single nerve cell and within neural network; the model supplies the ability to study different growth factors like randomized growth, position of stimulus directing dendrites and boarders of spanning dendritic tree, as well as a full understanding of network connectivity. Quantitative metrics are calculated to verify the model outputs to realistic constructions like dimensional and electrical metrics. The outputs show that the model is considered to be reliable for discipline types of nerve cells.

Disclaimer

I hereby declare that this thesis is my own original work and that no part of it has been submitted for a degree qualification at any other university or institute.

I further declare that I have appropriately acknowledged all sources used and have cited them in the references section.

Name: Samar Ahmed Mahmoud Abbass Date:

Signature:

Dedication

This first-fruit work is dedicated to my father, Prof. Dr. Ahmed Mahmoud Abbass (RIP), the great man who planted in me the passion of love to science and exploration. He taught me how to discover my way in the right field. He also taught me the scientific ethics as he used to be hard working, very helpful and humble to his students.

Acknowledgments

In the name of Allah, the most merciful, the most gracious; all thanks to Allah the Lord of the Heavens and Earth and peace be upon Prophet Muhammed and his companions.

First and foremost, I would like to express my deepest gratitude and indebtedness to my academic supervisors: Prof. Dr. Medhat El-Messiery, Dr. Amr Sharawi and Prof. Dr. Noha Salem. It has been a pleasure to work with them and learn from such extraordinary advisors. They were always very helpful and never hesitated to lend me their time and knowledge.

I am indebted to Prof. Medhat El-Messiery for his guidance and mentoring. He constantly provided me with new research ideas and helped me to gather a lot of information about neuroscience. He was always pushing me forward and his insight and invaluable advises - not only in scientific research, but also in other aspects of life - have great impacts on me.

I owe Dr. Amr Sharawi valuable supervision, continuous encouragement, useful suggestions and active help during this work. He was never late to help, and he made my research possible. I learned from Dr. Amr a lot from all courses he taught me (under- and post-graduate courses), I was able to build strong knowledge of modeling and use this science conveniently in this research.

I am very thankful to Prof. Noha for her invaluable experience and knowledge that I have gained from her. Her enthusiasm and passion to our work have always motivated me to work harder. I benefited from her valuable comments, constructive criticism, support, effort and patience with me. She had high influence on me, personally.

Thanks to all academic professors who helped me with their precious advice and support, from Biomedical Engineering dept.: Dr. Inas Yassine, Dr. Tamer Basha and Dr. Muhammed Rushdi, Dr. Mona Taher, Dr. Sherif El Gohary and Dr. Ayman El Deeb. And from Engineering Physics dept.: Dr. Mohamed Hesham, Dr. Mona El Naggar, Dr. Samia Ibrahim, Dr. Nihal Yassin, Dr. Fayza Gamal and Dr. Nadia Ra'fat.

I would like to thank IBRO-Imbizo organizations for providing me a full scholarship in the computational neuroscience summer school 2018 through my master pursuit and giving me a chance to learn discipline neuroscience studies and researches. I would like to thank my abroad neuroscience family: Tim vogels, Joseph Raimondo, Yiota, Larry Abbott, Adrienne Fairhall, Byron Yu, Srikanth Ramaswamy, Michael Hausser, Timothy Lillicrap, Blacke Richard, Misha Tsodysk, Mate Lengyl, Friedimann, William, Alex, Katharina, Agostina and Emma.

Special Thanks to Athanasia Papoutsi and Peter Latham for lending me their precious time and continuous help and support through the summer school and later.

Big Thanks to all my neuroscience friends. And special thanks to those fellows who helped me through fruitful discussions: Gonul Uludag, Mohamed Gomaa, Muhammed Aburidi, Khedr, Jasmine Poirier and Ana Claudia.

Sincerely, I would like to thank my close friends who supported me with technical and incorporeal help and advice: Manar Nasser, Ghaidaa Walaa El-Din, Ola Sarhan, Asmaa Mohamed and Shaimaa Ahmed.

Thanks to Noha Mohamed Fouad for being my supporting friend and also my psychologist in the hard time. Thanks for her radiating energy.

Many thanks to Wafaa Saber -a professor to be- for being my ideal consultant and giving me her precious advice.

Special thanks to Mina Elias for passing me his experience and getting me in his interesting valuable chats.

Uncountable thanks to my friends Tasneem Salah and Sarah Hamdy for every joyful moment they gifted me and their wonderful companionship through my study, my work and my life.

Special thanks to my dearest friend Kariman Mahmoud for our unbroken bond and for never giving up in me, and continuous support and encouragement. Thanks for her tolerance and being the first key of success and happiness. Thanks for all good and bad times we passed and will pass.

And unlimited thanks to my life-long companion Amany Amr for living with me every scene in the master experience from start to end. Thanks for sharing me every career and my personal life through the master degree period. And thanks for every given joy and every wiped tear.

Last but not the least, I would like to share my success with my beloved family. Without them, the dream would never have come true, they always encouraged me to do my best. I am most grateful to my mother "Magy" for unconditional love and all patience, sacrifices and for always putting me in the first priority. I also feel blessed for having my sister "Sara" who surrounded me with all love, care and advice. And glad deeply with the wonderful gift, my grandmother "Kadria", for her existence and her prayers to me every single moment.

Samar Ahmed Mahmoud Abbass

Table of Contents

DISCLAIMER ..... **I**

DEDICATION ..... **II**

ACKNOWLEDGMENTS ..... **III**

TABLE OF CONTENTS ..... **V**

LIST OF TABLES ..... **VII**

LIST OF FIGURES ..... **VIII**

LIST OF ACRONYMS ..... **XI**

LIST OF ACRONYMS ..... **XII**

ABSTRACT ..... **XIII**

CHAPTER 1 : INTRODUCTION **1**

1.1. NEURONS 1
1.2. NEURO-SIMULATION 8
1.3. NEURON GROWTH 9
1.4. EXPERIMENTAL NEUROSCIENCE AND LABS 11
1.5. THE AIM OF THE PRESENT WORK 13

CHAPTER 2 : LITERATURE REVIEW AND THEORETICAL APPROACHES **14**

2.1. BASIC PRINCIPLES OF CHARGES ACROSS THE CELL MEMBRANE 14
2.2. THEORETICAL MODELS 15
2.2.1. Hodgkin-Huxley Model 15
2.2.2. The Cable Equation 16
2.2.3. McCulloch-Pitts Model 19
2.3. ACTION POTENTIAL 20
2.4. PREVIOUS PROGRAMMING SIMULATION TECHNIQUES 21
2.5. PREVIOUS NEURON GROWTH MODELS 23

CHAPTER 3 : THE PROPOSED MODEL OF NEURON GROWTH AND INTERACTION **32**

3.1. COMPUTATIONAL METHODOLOGY 32
3.2. INITIATION OF NEURON RANDOM GROWTH 33
3.3. INTERACTION OF NEURON GROWTH WITH STIMULUS 34
3.4. SIMULATION OF ELECTRIC CONDUCTION THROUGH NEURON 35
3.5. DIMENSIONAL PROPERTIES OF A NEURON 36
3.6. INTERACTION OF NEURON RANDOM GROWTH WITH NEURAL NETWORK… 40

CHAPTER 4 : RESULTS **43**

4.1. SINGLE NEURON OUTPUT 43
4.1.1. Random Growth 43
4.1.2. Directed Growth 48
4.1.3. Semi-directed Growth 50
4.2. NEURAL NETWORK OUTPUT 53
4.2.1. Random Growth 53
4.2.2. Directed Growth 55
4.2.3. Synapses 55
CHAPTER 5 : DISCUSSION 63
CHAPTER 6 : CONCLUSION AND FUTURE WORK 68
REFERENCES 69
APPENDIX A: DIFFERENT FREE SOFTWARE TOOLS FOR NEURAL REGENERATIONS 74
APPENDIX B: RUNNING CODE DEMO 76

List of Tables

Table 1.1: Freeware tools for the various tasks in neuroinformatics 74

List of Figures

Figure 1.1: The neuron structure consists of the soma, the axon, and dendrites [5] 2
Figure 1.2: Different types of neuron: 1) Unipolar 2) Bipolar 3) Multipolar 4) Pseudo-unipolar [5] 2
Figure 1.3: Different morphologies of neuron according to dendritic characteristics and radiation patterns [8].....4
Figure 1.4: dendrites different arborizations based on existence of target in certain growth stage.....5
Figure 1.5: Brain parts and lobes.....7
Figure 1.6: Full diagram of total nervous system.....8
Figure 1.7: Growth phases of neurons [17].....9
Figure 2.1: Equivalent circuit of cell membrane [31] 15
Figure 2.2: Simplified circuit of cell membrane [31].....16
Figure 2.3: Propagation of current through dendrite [29] 17
Figure 2.4: The net current entering a region must equal zero [33] 18
Figure 2.5: McCulloch-Pitts simplified model for neuron [35] 19
Figure 2.6: Process of action potential on cell membrane [37].....20
Figure 2.7: Synapse that connects axon terminal of presynaptic neuron and dendrite of postsynaptic neuron [38] 21
Figure 2.8: Growth of single neural cell [43].....23
Figure 2.9: GUI of L-neuron software package [44].....24
Figure 2.10: Two identical cells built by the critical percolation method in different orientations (A) 0-degree (B) 30-degree (C) 60- degree [50] 26
Figure 2.11: Development of axons and dendrites with time. [52].....27
Figure 2.12: TREES toolbox coding and output neuron structure [54] 28
Figure 2.13: Axial resistance in non-uniform and uniform branching models [56].....28
Figure 2.14: Output network of NETMORPH program [57].....29
Figure 2.15: Varying bf and bw for optimal correlation between synthetic and real constructions [48].....30
Figure 2.16: Representation of a network by an ensemble of barcode pairs (SYNSeq). (A) An example of small network. In SYNSeq, each neuron is represented by a short unique nucleotide sequence called a barcode. (B) The connectivity matrix corresponding to the network in A. (C) Network connections are encoded by pairs of barcodes with a spacer (black arrow) representing the connections' direction. (D) We represent barcodes by uniqueletters of an alphabet for brevity.....31
Figure 3.1: Simplified geometrical shape of simulated branching dendrite [30]. 34
Figure 3.2: Voltage membrane of semi-finite cable as a function of distance [30] 36
Figure 3.3: Voltage decay curve when signal is transferred through branching point in the dendrite with abrupt change in axial resistance Ra [30].....36
Figure 3.4: The average segment length in each level for a 10-level dendritic tree neuron.....37
Figure 3.5: The average segment length in each level for a 20-level dendritic tree neuron.....38
Figure 3.6: Average area in each growth level vs growth level in 10-level grown dendritic tree neuron.....38

Figure 3.7: Average area in each growth level vs growth level in 20-level grown dendritic tree neuron....39
Figure 3.8: Cumulative resistance vs cumulative segments lengths in 10-segment branch....39
Figure 3.9: Cumulative resistance vs cumulative segments lengths in 20-segment branch....40
Figure 3.10: (a) Positions of distributed 7 cells (b) Position od distributed 50 cells....41
Figure 4.1.a: Random grown neuron with 10 levels....43
Figure 4.1.b: Random grown neuron with 10 levels without axon....44
Figure 4.1.c: Growth rate of a 10 level grown neuron....45
Figure 4.2.a: Random grown neuron with 15 levels with axon....45
Figure 4.2.b: Random grown neuron with 15 levels without axon....46
Figure 4.2.c: Growth rate of 15 level grown neuron....46
Figure 4.3.a: Random grown neuron in 20 levels of growth....47
Figure 4.3.b: Random grown neuron in 20 levels of growth without axon....47
Figure 4.3.c: Growth rate of 20 level grown neuron....48
Figure 4.4: neuron growth directed by stimulus existence at position (1,1) with 10 levels grown up....49
Figure 4.5: Directed neuron growth to stimulus at position (1,1) and 15 levels of growth....49
Figure 4.6: directed neuron growth with 20 levels towards the stimulus at position (1,1)....50
Figure 4.7.a: Semi-directed neuron growth with 5 random levels and 15 directed levels towards stimulus at position (1,1)....50
Figure 4.7.b: Semi-directed neuron growth with 5 random levels and 15 directed levels towards stimulus at position (1,1) without axon....51
Figure 4.8.a: Semi-directed neuron growth with 10 random levels and 10 directed levels towards stimulus at position (1,1)....51
Figure 4.8.b: Semi-directed neuron growth with 10 random levels and 10 directed levels towards stimulus at position (1,1) without axon....52
Figure 4.9.a: Semi-directed neuron growth with 15 random levels and 5 directed levels towards stimulus at position (1,1)....52
Figure 4.9.b: Semi-directed neuron growth with 15 random levels and 5 directed levels towards stimulus at position (1,1) without axon....53
Figure 4.10.a: Random grown neural network with 10 growth levels....54
Figure 4.10.b: Random grown neural network with 10 growth levels without axons....54
Figure 4.11.a: Directed grown network with 15 growth levels....55
Figure 4.11.b: Directed grown network with 15 growth levels....56
Figure 4.12: Network of 7 nerve cells....56
Figure 4.13: First sequence [2-3]....57
Figure 4.14: Second sequence [4-5-1]....57
Figure 4.15: Network of 20 nerve cells....58
Figure 4.16: Voltage in mV at soma surface of each excited cell in the 20-cells network....58
Figure 4.17: Signal transfers through sequence [1-4]....59
Figure 4.18: Signal transfer through sequence [12-9-2-3-4-1]....59
Figure 4.19: Signal transfers through sequence [11-3-4-1]....60
Figure 4.20: Signal transfers through sequence [6-7-8-10]....60
Figure 4.21: Signal transfers through sequence [18-7-8-10]....61
Figure 4.22: Signal transfers through sequence [19-7-8-10]....61

Figure 4.23: 130-cell Network in hexagonal structure 62
Figure 5.1: Voltage attenuation with distance on dendritic branch consisting of 4 segments 63
Figure 5.2: Voltage attenuation with distance on dendritic branch consisting of 10 segments 64
Figure 5.3: Voltage at soma vs total branch length of dendrite considering initial voltage 70 mV 65
Figure 5.4: Voltage attenuation vs dendrite length for dendrites of variable total lengths of equal segment lengths 66
Figure 5.5: Voltage attenuation vs dendrite length for dendrites of variable total lengths for unequal segment lengths 67

List of Acronyms

α	Arbitrary Constants
β	Arbitrary Constant
C_j	Membrane Capacitance
D	Diffusivity coefficient / Rate of growth
λ	Constant length decay
ΔE	Energy
Δt	Time step
P_c	Critical Probability
R_a	Axial resistance
R_m	Membrane resistance
V_o	Initial Voltage
V_m	Voltage Membrane
Θ_r	Angle of subtree root
Θ_s	Direct angle from the growing dendrite to the position of stimulus