



**DEPARTEMENT OF SCIENTIFIC COMPUTING
FACULTY OF COMPUTER & INFORMATION SCIENCES
AIN SHAMS UNIVERSITY**

NANOROBOTICS CONTROL FOR BIOMEDICAL APPLICATIONS

A Thesis Submitted to the Department of Scientific Computing,
Faculty of Computer & Information Sciences Ain Shams University,
In the Partial Fulfillment of the Requirements for Ph.D. Degree of Computer and
Information Sciences

BY

SARA YOUSEF SERRY ELSAYED AHMED

*MSc. Degree in Scientific Computing Department
Faculty of Computer & Information sciences
Ain Shams University*

SUPERVISED BY

Prof. Dr. TAHA EL-ARIF

*Professor in Computer Science Department
Faculty of Computer & Information sciences
Ain Shams University*

Dr. SAFAA AMIN

*Associative Professor in Scientific Computing Department
Faculty of Computer & Information sciences
Ain Shams University*

(2015)

ABSTRACT

Early successes in nanomedicine have created a growing demand for the development and application of advanced nanorobotic techniques with medical applications. This thesis presents the results of a proposed cooperative control strategy for a swarm nanorobot system in a human body environment in which the developed control schemes were applied in a nanorobot drug delivery scenario.

Part 1 of the study tested a proposed algorithm to solve the problem of communication between nanorobots and their movements in a swarm to a predefined target area. The nanorobots' communication and movement problems were solved in a self-organized way by modifying (1+1) Evolution Strategy (ES) with a 1/5th success rule, a method is herein referred to as the MES algorithm, which enables nanorobots to make decisions toward a predefined goal. The algorithm employs correspondence-based organization between nanorobots to allow them to find and reach the target area. A simulation of the performance and behavior of nanorobots was conducted to demonstrate the potential of the proposed algorithm. The simulator employed three mutation strategies applied randomly (straight strategy, swap strategy and high strategy) when a nanorobot optimized a movement plan.

The study applied the results of comparative study of these strategies to determine the most productive of the three, defined as the one requiring the least time on average to reach the target area. Simulation analyses indicated that the high mutation strategy is the most efficient mutation strategy for swarm nanorobots, resulting in optimum results in reaching predefined target sites. Part 1 of the proposed study tests this finding and demonstrated the benefits of high mutation strategy in action.

In Part 2 of the study, a proposed technique was tested to solve the path-planning problem of swarm nanorobots' navigation within the human environment. Blood

elements were treated as obstacles to nanorobot movement. Blood flow was also factored into the movement problem, as was the environment's physical properties, including blood viscosity and density, both of which can potentially affect nanorobot behavior. To account for all these considerations in a human body environment, two algorithms were combined, yielding a single algorithm responsible for the self-organized control of nanorobots to avoid obstacles during their movement trajectory. The technique is based on modification of the Particle Swarm Optimization algorithm, referred to as the MPSO algorithm, and modification of the Obstacle Avoidance Algorithm, referred to as the MOA algorithm. The proposed MPSO algorithm generated the best locations in a given operational area enabling nanorobots to detect the target areas. The proposed MOA algorithm allowed nanorobots to efficiently avoid collision with blood elements. The simulation results show that the combined MPSO-MOA algorithm safely routes all nanorobots past blood elements while navigating within the human body. The communication between nanorobots in a swarm was implemented as reported in this thesis through MES and MPSO algorithms.

Part 3 of the thesis incorporates a comparative study among these two algorithms. Comparisons show that communication using MPSO is more effective in determining the global optimal solution with significantly better computational efficiency (less function evaluations) by implementing statistical analysis and formal hypothesis testing.

In Part 4 of the study, a movement control algorithm was developed for nanorobots sensitive to the environmental acidity value (pH) of human cells, to deliver drugs in a tumor area while navigating in the bloodstream environment. The nanorobots were able to communicate with their neighbors using the proposed MPSO algorithm. Additionally, the proposed MOA algorithm allowed nanorobots to avoid collision with blood cells. Each nanorobot was able to measure the pH value at its current position using biosensors. Through

cooperation, nanorobots were able to drive the swarm to a tumor area defined by a pre-determined pH value (less than 7.0). Upon locating tumor cells, nanorobots released a drug that raised the pH value of the cell until it was destroyed. Graphical interface simulations have shown the effectiveness of the proposed algorithm. Validation of the designed system with simulated conditions proved that the drug delivery of nanorobots was robust during navigation, diagnosis, and curing of the tumor cells.

ACKNOWLEDGMENTS

First, I would like to express a special thank you to my **Professor. Taha Elarif** , who was always willing to assist me in the elaboration of this thesis. His suggestions and comments were valuable for a more in-depth analysis of this fascinating and complex topic.

I also would like to sincerely thank my Ph.D. advisor, **Dr. Safaa Amin**, for her tremendous advice and support over the past four years. Her intuitive insights always enlighten me on where the research work should go and what is necessary to get there. Her passion and strictness is exactly what works for my future career exploration.

Finally, I wish to thank my family members, my father **Yousef Serry**, my mother **Taiseer Abdelfatah**, my sister, my brother, and special thanks to my husband **Ahmed**. Without their constant love and support, none of this would be possible.

TABLE OF CONTENTS

LIST OF FIGURES.....	x
LIST OF TABLES.....	xiii
LIST OF ABBREVIATIONS.....	xiv
LIST OF PUBLICATIONS	xv
CHAPTER 1. INTRODUCTION.....	1
1.1 Problem Definition.....	2
1.2 Motivations and Objective.....	2
1.2.1 Cooperative Control for Swarm Nanorobots Target Detection.....	4
1.2.2 Navigation and Control Design of Swarm Nanorobots in the Human Environment	5
1.2.3 Cooperative Control Design for Nanorobots in Drug Delivery	6
1.3 Main Contributions.....	7
1.4 Thesis Organization.....	9
CHAPTER 2. LITERATURE REVIEW.....	11
2.1 Introduction.....	11
2.2 Nanotechnology Framework for Medical Applications.....	12
2.3 Nanomedicine Applications.....	14
2.4 Nanorobotics.....	21
2.4.1 Bio-Nanorobotics Architecture and NEMS.....	23
2.4.2 Swarm Nanorobot System.....	27
2.4.3 Optimization and Learning Algorithms for Swarm Nanorobots.....	30
2.5 Swarm Nanorobots in Nanomedicine	33
2.6 Summary and Conclusions.....	39

CHAPTER 3. MODIFIED EVOLUTIONARY STRATEGY (MES) TO CONTROL THE COMMUNICATION BETWEEN A SWARM OF NANOROBOTS..... 41

3.1 Introduction..... 41

3.2 Evolutionary Algorithms in Global Optimization and Search..... 43

 3.2.1 Foundations of Evolutionary Algorithms..... 43

 3.2.2 Biological Background of Evolutionary Algorithms..... 45

 3.2.3 Classical Representations of Evolutionary Algorithms..... 47

 3.2.4 Implementation of Evolutionary Algorithms..... 52

3.3 Evolutionary Strategy (ES)..... 56

3.4 Evolutionary Strategy Approaches..... 58

 3.4.1 The ($\mu+\lambda$) Evolutionary Strategy 59

 3.4.2 The (1+1) Evolutionary Strategy..... 60

 3.4.3 The (1+1) Evolutionary strategy with -1/5th Success Rule... 61

3.5 Modified (1+1) ES with 1/5th Success Rule (MES) Algorithm for Nanorobots Swarm Communication..... 62

 3.5.1 Sensor and Coverage Model..... 63

 3.5.2 The Algorithm in Practice..... 64

 3.5.3 Nanorobots Mutation Strategies..... 65

3.6 Simulation Results..... 66

 3.6.1 Simulation Results Analysis..... 68

 3.6.2 Comparative Study among Random Mutation Strategies..... 75

3.7 Summary and Conclusions..... 78

CHAPTER 4. PATH PLANNING ALGORITHM FOR SWARM NANOROBOT IN A HUMAN BLOOD ENVIRONMENT..... 81

4.1 Introduction..... 81

4.2 Swarm Intelligence..... 82

 4.2.1 Swarm Intelligence Approaches..... 85

 4.2.2 Swarm Intelligence Optimization Distributed Algorithms.... 85

4.3 Physical Properties of Blood Stream Environment..... 90

4.4 The Structure of the Optimization Model..... 93

 4.4.1 Classical PSO Algorithm..... 94

 4.4.2 Modified PSO Algorithm (MPSO) for Nanorobot’s Movement Path Planning..... 99

 4.4.3 Polar Coordinate Based Obstacle Avoidance Algorithm..... 102

4.5 Movements Control Algorithm Enhancement Based on Local and Global Paths.....	104
4.5.1 Global Path Planning.....	105
4.5.2 Local Path Planning.....	106
4.5.3 Innovative Movement Control Algorithm.....	107
4.6 Simulation and Discussions.....	109
4.6.1 Simulation Scenario.....	110
4.6.2 Simulation Scheme.....	111
4.6.3 Simulation Results and Analysis.....	112
4.7 Comparison between MES and MPSO Algorithms for Target Detection	117
4.8 Summary and Conclusions.....	119
CHAPTER 5. MOVEMENT CONTROL COOPERATIVE SYSTEM FOR PH SENSITIVE NANOROBOTS IN DRUG DELIVERY.....	122
5.1 Introduction.....	122
5.2 Architecture of pH Sensitive Nanorobot.....	125
5.3 Existing Control Strategies.....	128
5.4 Environmental Acidity (pH) in Tumors.....	130
5.4.1 Tumor pH and its Measurement.....	131
5.4.2 The Tumor Microenvironment Modeling.....	133
5.5 Cooperative Control Strategy for Nanorobots in Drug Delivery.....	138
5.5.1 High pH Therapy Approach for Tumor Destruction.....	139
5.5.2 Control Problem Formulation.....	140
5.5.3 Control Algorithm for pH Sensitive Nanorobot in Drug Delivery.....	141
5.6 Simulation Results.....	143
5.7 Summary and Conclusions.....	147
CHAPTER 6. CONCLUSION.....	148
6.1 Conclusion.....	148
6.2 Future Work.....	151
REFERENCES.....	152
APPENDIX A: NANOROBOTS DRUG DELIVERY SIMULATOR.....	158

LIST OF FIGURES

2.1	Design of nanoscale robots.....	22
2.2	Timeline of various EAs.....	32
2.3	Schematic representation of a nanorobot.....	34
3.1	Search strategy of the classical Evolutionary Algorithm.....	51
3.2	General Evolutionary Strategy.....	56
3.3	High probability mutation strategy.....	67
3.4	Swap mutation strategy.....	68
3.5	Straight mutation strategy.....	68
3.6	Number of nanorobots that reach the final target using the straight strategy.....	69
3.7	Number of nanorobots in each target interval.....	69
3.8	Average time in initial optimization level using the straight strategy.....	70
3.9	Average time in partial optimization level using the straight strategy.....	70
3.10	Average time in full optimization level using the straight strategy.....	70
3.11	Comparison between optimization levels Using the straight strategy.....	71
3.12	Number of nanorobots that reach the final target.....	71
3.13	Number of nanorobots in each target interval.....	72
3.14	Average time in the initial optimization level using the swap strategy.....	72
3.15	Number of nanorobots that reached the final target.....	73
3.16	Number of nanorobots in each target interval.....	73
3.17	Average time in initial optimization level using the high strategy.....	73
3.18	Average time in partial optimization level using the high strategy.....	74

3.19	Average time in full optimization level using the high strategy.....	74
3.20	Comparison between optimization levels using the high strategy.....	74
3.21	Average time in the initial optimization level for the three strategies.....	75
3.22	Average time in the partial optimization level for the three strategies.....	76
3.23	Average time in the full optimization level for the three strategies.....	76
3.24	Number of nanorobots that reached the final target area for the three strategies.....	77
3.25	Number of nanorobots in each target interval for the three strategies.....	78
4.1	A classification scheme for swarm intelligence based on the structure of the underlying space.....	83
4.2	Obstacle in polar coordination	103
4.3	Graphical representation of the simulation for 10 nanorobots.....	113
4.4	Graphical representation of the simulation for 5 nanorobots.....	114
4.5	Percentage of coverage in each time interval.....	115
4.6	Time required for each nanorobot to generate the best value.....	116
4.7	Average time required for each nanorobot to avoid obstacles.....	116
4.8	Changing in velocity for 3 nanorobots over time.....	118
4.9	Comparison between communication algorithms using number of arrived nanorobots in each time interval.....	119
4.10	Comparison between communication algorithms using average time for full coverage.....	118

5.1	The region of $r < r_1$ is a necrotic core. The region of $r_1 < r < r_2$ is the layer of proliferating tumor cells.....	135
5.2	(a) The acid concentration profile.....	138
	(b) The pH value profile.....	138
5.3	(a) The tumor pH diffusion environment.....	138
	(b) The variance of tumor pH value in a 3D plot...	138
5.4	Representation of tumor pH environment in drug delivery system.....	145
5.5	Simulation for the process of a group of 25 pH sensitive nanorobots in drug delivery system.....	146