A Methodology for Simulating Biological Cell Systems With Cellular Automata: The Case of the Human Heart

Project report

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1 Introduction

This thesis is a final B.Sc. project with research emphasis in the School of Computer Science at Reykjavik University. The project was done by Guðrún Fema Ólafsdóttir during the spring semester of 2011.

Biological systems are very complex system. Researches that increase our understanding in e.g. development and growth of organs, are a very important factor to enhance the biology and for better understanding on various diseases. In this project the main goal is to develop a new methodology to study the development of the heart that is based on simulation with computer models. The standard way to do such research is to use partial differential equations. They require knowlegde of all physical terms for the system that is being looked at. These terms are not known for the development of the heart. Here we use cellular automata, but they have given good results when simulating other biological systems.

This report is arranged as follows. It start with project progress summary. The next section discusses risk factors and risk anlysis. After that we have the post mortem evaluation and finally we have conclusion.

2 Progress summary

In this chapter we will discuss the project plan and the progress summary. We start by giving a detailed plan for the project, where we list the parts of the project, when we work on that part and how many days and hours we plan to spend on it.

Nr.	Name of the project	Days	Beginning	End	Hours
	Multi-level model of the heart		12.1.2011	16.5.2011	530
1	Preparation	11	12.1.2011	23.01.2011	50
Analysis		**12**	**24.01.2011**	**06.02.2011**	**60**
2	Develop project schedule	4	24.01.2011	28.01.2011	20
3	Risk analysis	1	29.01.2011	30.01.2011	5
4	Develop risk plans	1	29.01.2011	30.01.2011	5
5	Introduction	1	01.02.2011	01.02.2011	5
6	Background - summarize	1	02.02.2011	02.02.2011	5
7	Goals	0.5	05.04.2011	05.04.2011	2
8	Presentation of research questions	1	06.02.2011	06.02.2011	5
9	Project progress summary	2	03.04.2011	04.02.2011	10
10	Project description – finished	0.5	05.04.2011	05.02.2011	3
Preparation for the simulation					
		18	**07.02.2011**	**27.02.2011**	**90**
11	Heart	2	07.02.2011	09.02.2011	10
12	Write about heart	1	07.02.2011	09.02.2011	5
13	Cell signaling in the heart	4	10.02.2011	16.02.2011	20
14	Write about cell signaling	1.5	10.02.2011	16.02.2011	8
15	Finish writing about background	1.5	16.02.2011	17.02.2011	8
16	Prepare Vélaldin	1.5	18.02.2011	19.02.2011	8
17	Evaluating results	4	19.02.2011	25.02.2011	20
18	Write about evaluating results	1.5	19.02.2011	25.02.2011	8
19	Presentation for 2nd meeting	1	26.02.2011	26.02.2011	5
Prototype of the model - Deriving the rules					
1st iteration		**6**	**28.02.2011**	**06.03.2011**	**30**

20	Deriving the first rules	2	28.02.2011	01.03.2011	10
21	Implementation of the model	1	02.03.2011	02.03.2011	5
22	Studies of the model	1	03.03.2011	03.03.2011	5
23	Results	1	04.03.2011	04.03.2011	5
24	Evaluation for the next phase	1	05.03.2011	05.03.2011	5
2nd iteration		**12**	**07.03.2011**	**20.03.2011**	**60**
25	Implementation of the model	3	07.03.2011	09.03.2011	15
26	Studies of the model	3	10.03.2011	12.03.2011	15
27	Results	3	14.03.2011	16.03.2011	15
28	Evaluation for the next phase	3	17.03.2011	19.03.2011	15
3rd iteration		**12**	**21.03.2011**	**03.04.2011**	**60**
29	Implementation of the model	3	21.03.2011	23.03.2011	15
30	Studies of the model	3	24.03.2011	26.03.2011	15
31	Results	3	28.03.2011	30.01.2011	15
32	Evaluation for the next phase	3	31.03.2011	02.04.2011	15
Interpretation of the simulation - Answering questions					
5th iteration		**18**	**04.04.2011**	**24.04.2011**	**90**
33	Different rule sets for the stage	5	04.04.2011	08.04.2011	25
34	Little changes in rule sets	3	09.04.2011	12.04.2011	15
35	The size of rule sets.	2	13.04.2011	14.04.2011	10
36	The main principles	4	15.04.2011	19.04.2011	20
37	Cell's neighborhood size	2	20.04.2011	21.04.2011	10
38	The best way to evaluate results	2	22.04.2011	23.04.2011	10
6th iteration		**6**	**25.04.2011**	**01.05.2011**	**30**
39	Finish introduction.	0.5	25.04.2011	25.04.2011	3
40	Finish writing research report	3.5	25.04.2011.	30.04.2011	17
41	Start writing project report	2	26.04.2011	30.04.2011	10
7th iteration		**12**	**02.05.2011**	**16.05.2011**	**60**
42	Finish writing project report	8	02.05.2011	10.05.2011	40
43	Update research report	4	11.05.2011	15.05.2011	20

This is the project plan that was made at the beginning of the semester. It was divided into four main phases: preparation and analysis, preparation of the simulation, prototype of the model – deriving the rules and interpretation of the simulation – answering questions.

Researches are hard to plan, because we don't know the outcome and possible obsticles that we need to overcome during the research. Therefore, the plan changed in the third phase, that is, the modeling phase.

In the beginning the plan was to spend 5 hours a day for the research, 6 days a week. In the whole, the plan was to spend 530 hours on the research. What we could not anticipate was the time spent on being sick, which really took a lot of time. I ended up with spending about 470 hours on the project.

2.1 Preparation and Analysis

This phase started with preparation. Vélaldin was downloaded and installed and simple graphical view for it was made, to view the simulation. Then reading material about the heart and cellular automata was found. Next the analysis for the project was made, that is, the project plan and the risk analysis. Then I wrote the introduction and the background section, finished forming the research questions and finished the project description. This phase went as planned and I spent about 110 hours on it.

2.2 Preparation for the simulation

This phase started with studying the heart development and the cell signals in the heart development. After that cellular automata were studied and how we could use them doing the model. The phase ended with some final adjustments of Vélaldin for the model. This phase spanned about 120 hours, but that is 30 more hours than initially was planned for this phase. The main

reason is the time consumption of reading biological litterature.

2.3 Prototype of the model – Deriving the rules

Initially this phase was supposed to contain three iterations, where each iteration consisted of: implementation of the model, studying the model, results and evaluation for the next phase. This is where the project plan changed. After doing the first iteration and getting no results, I figured that I needed another approach for finding the rules, so that I could answer my research questions. The rest of the phase I spent on finding a good way to derive the rules. In total I spent 110 hours on this phase. The plan was to spend 150 hours on this phase but because of personal reasons I spent 40 hours less.

2.4 Interpretation of the simulation – Answering questions

Since the previous phase didn't go according to plans, the plan for this phase was different then we intended to at the beginning of the semester. No useful model that could be used to answer some questions about the model existed, but the new approach made us able to answer the research questions. The rest of the phase was spent on writing the reports and finishing the presentation. About 130 hours were spent on this phase. The plan was to spend 180 hours on this phase, so I spent 60 hours less then was planned on this phase.

3 Risk Analysis Summary

In order to follow the project plan and to be on schedule a risk analysis was made with the risk factors that could affect the project. First the risk factors were found. All risk factors that could in anyway harm or interupt the research were listed. Each risk factor was then evaluted, the probability of its occurrence and how it would affect the project. Following is a table with the risk factors and the solutions.

Nr.	Risk event	Probability of A lot					Magnitude of Impact					Risk Response	Solution Date
	Name	1	2	3	4	5	1	2	3	4	5	Type of action	Date
	Related to the Project												
1	Too extensive project			x					x			Change my research questions, so that I know I can find answers to them in 3 months.	07.02.2011
2	Simulation phases take too long			x					x			I need to write a lot during the simulation phases about the results of the simulation.	04.04.2011
3	Too big simulation for Vélaldin	x								x		If it happens we need to make some changes or adjustments to Vélaldin, or find a new a CA software system, that has similar properties as Vélaldin.	07.03.2011
4	Too few related works					x		x				New way of thinking and new ideas need to be brought to the table.	28.02.2011
5	Too little known about cell signaling			x					x			Talk to heart specialists, biologists and other researchers studying cell signals.	28.02.2011
6	Losing data	x									x	Take back-up every day.	07.02.2011
	Personal												
7	Skin disease		x				x					Work at home. If it gets serious, i have many extra hours in April.	-

8	My new disease				x				x			Being treated right now. If it gets serious i have many extra hours in April.	-
	Other												
9	Another courses					x	x					Plan everything few weeks ahead. The last assignment is due 29th of March.	15.03.2011

The probabilities can be on the scale 1-5, where 1 means that there is almost no chance that it will happen and 5 means that it is very likely that it will happen.

The magnitude of impact can be on the scale 1-5, where 1 is almost no impact and 5 means very much impact.

4 Post Mortem Evaluation

In all research there are things that go well and things that don't go as well, but we never know what those things are before we start the research. In this section we will discuss what went well and what didn't go as well.

4.1 What went well?

Simulating the heart development is a very extensive project and has never been done before. What I was most worried about was to find good research questions that I could answer, while doing this project. Before hand, these were the questions that I needed to answer, when I had no good way or approach to generate the rules, so I could know that they would represent the model. I think that I found a very good approach to derive the rules, in a way that I know that they actually represent the heart development and not some random rules. Although I don't have any model that can answer my research questions, the new approach for deriving the rules answers all the research questions we wanted to answer and eliminates problems we had.

I also think that planning the project went very well, eventhough everything didn't go like I planned. The plan was realistic, when it came to deciding how much time needed to be spent on each part of the reseach, and I was very happy that I could follow my plan most of the time ,except in phase 3.

4.2 What didn't go well?

Initially the plan was to create a model, but since we didn't have any proper way to derive the rules, the model gave no significant results. All researches are hard to plan, and because we didn't get any proper results, we needed to change the plan.

The things that required more time than I planned, was reading biological literature, especially reading about cell signaling. The material is very complicated and the processes hard to understand. It is very time consuming to read these articles and sometimes they are not useful for the project.

Initially I wanted to spend 530 hours doing this research. In the middle of the semester I got ill and therefore I spent less time studying. Nevertheless, I was able to spend 470 hours and answering all the research questions.

5 Conclusion

Planning researches is hard, but nevertheless necessary. Learning how to plan researches is therefore important and I think that my plan went well. Planning was a thing that I needed to improve and I think I improved a lot during this project.

Simulating the heart development is a subject that has been on my mind for a long time – but I always learn new things about the heart and how I could be able to simulate its development using cellular automata. By duing this thesis I have solved few of the problems concerning this subject and I am few steps closer to simulating the heart development then I was before I started this research.