

Modelling pathways that control endothelial cell apoptosis

Introduction

- Field of the project: Apoptosis of endothelial cells: a complex process consisting of several events.
- Combining different data types: time course microarray data, phenotype data.
- Cell Illustrator : a petri net-based application we have used to model the apoptosis pathway from our data.

Contents

I) Apoptosis

I.1) Mecanism of apoptosis

I.2) Experimental procedure in endothelial cells

II) Cell Illustrator

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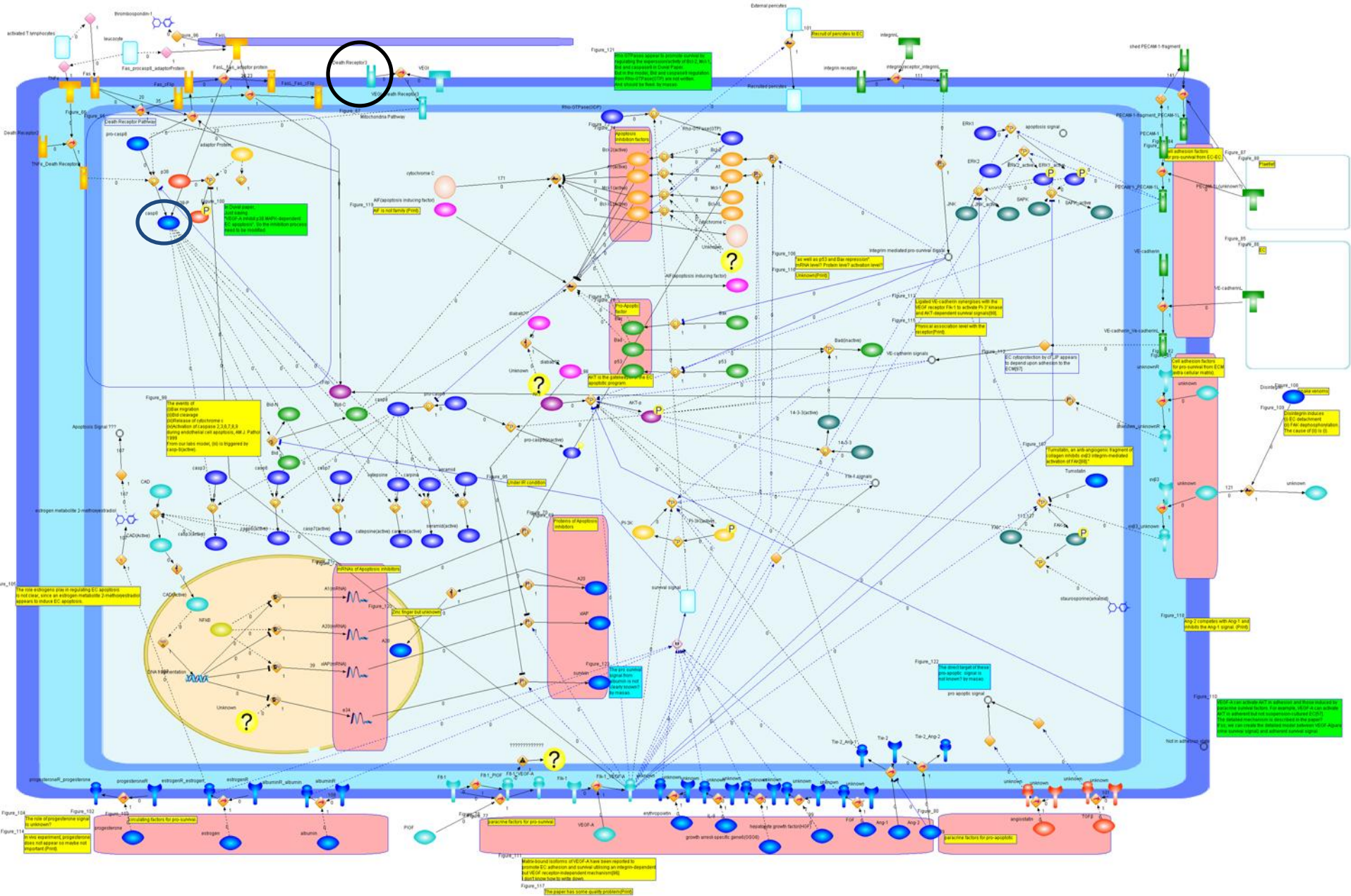
III) Project

III.1) Discovers

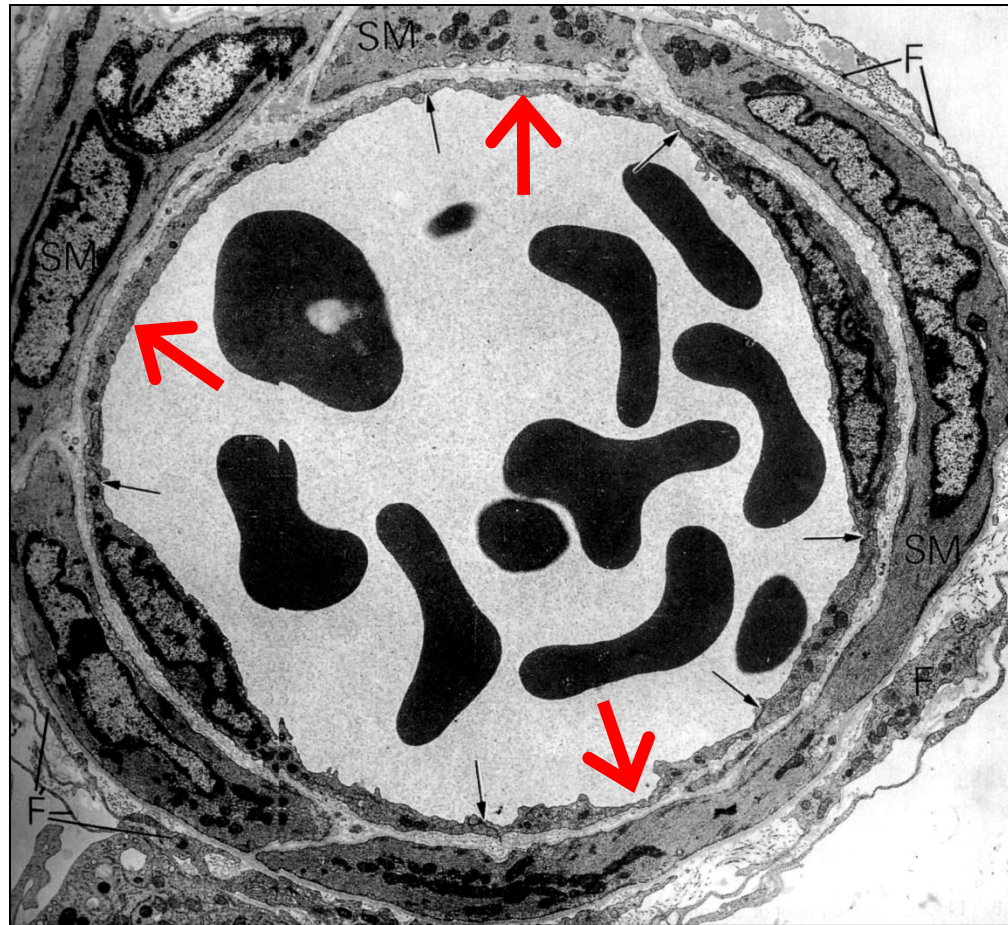
I) Apoptosis

- Apoptosis = programmed cell death = cell suicide
- An important event in biology, apoptosis removes cells that are no longer required, and removes cells that have become cancerous or infected with viruses.
- Altered apoptosis is part of many diseases.
- Phenomenon is still poorly understood, complex.

Cell Illustrator : An apoptosis model

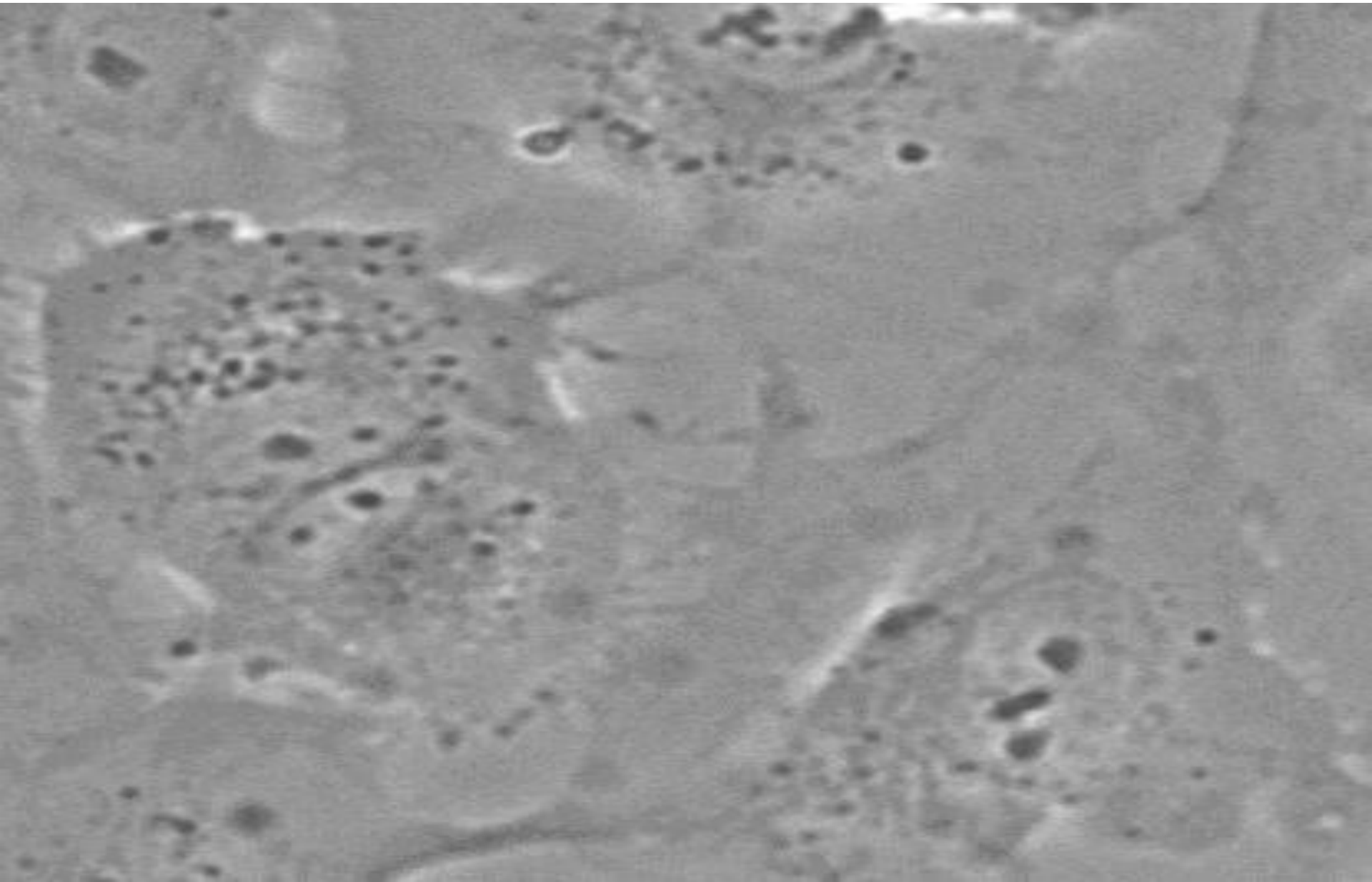


Endothelial cells line blood vessels



apoptosis of endothelial cells is a common part of many diseases

The process of apoptosis



We have caused endothelial cells to commit suicide by apoptosis in the lab

- To do this, we removed growth factors from endothelial cells. This activates their in-built apoptosis suicide program.
- We recorded several features the death of 75 cells using a time lapse microscope (255 images, each 4 minutes over 17 hours)
 - loss of attachment
 - membrane blebbing
 - nuclear condensation
 - Anexin V binding
 - Caspase 3 activation
- We also performed microarray analysis of the cells as they died

II) Cell Illustrator

- Cell Illustrator : software tool.
- Cell Illustrator : allow to model.
- Cell Illustrator : use to visualize.

Cell Illustrator

Cell Illustrator 4.0

Functionality

Key Features

Simulation Engines

Release Notes

Case Studies

Lineup

CI Project

Related Projects

Scientific Publications

System Requirements

Documentation/Support

Forum

Trial License - CI Pro

Previous Version

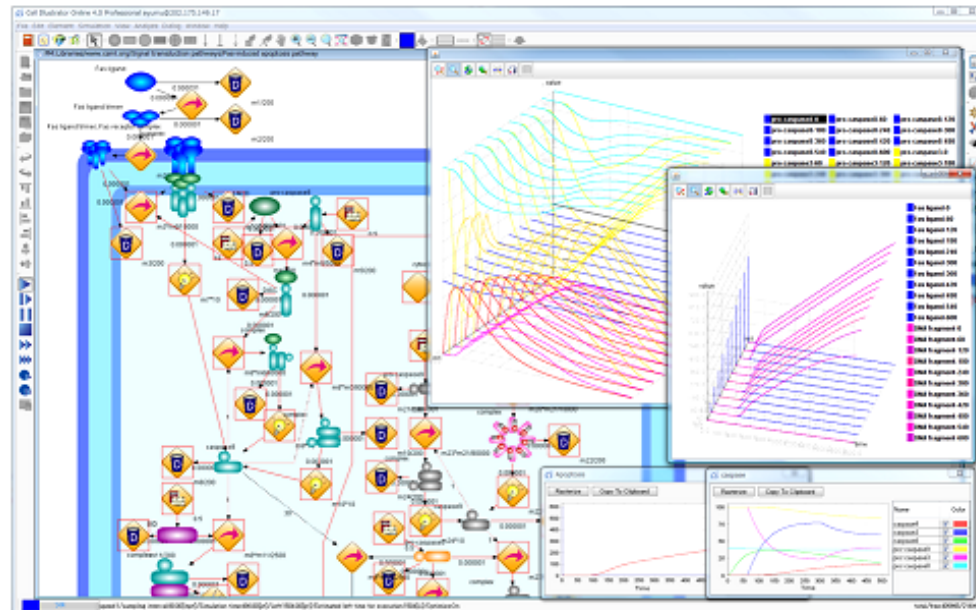
Contact

Cell Illustrator 4.0

Cell Illustrator 4.0 is a software tool that enables biologists to draw, model, elucidate and simulate complex biological processes and systems. It has outstanding drawing capabilities, moreover it allows researchers to model metabolic pathways, signal transduction cascades, gene regulatory pathways as well as dynamic interactions of various biological entities such as genomic DNA, mRNA and proteins.



Cell Illustrator 4.0 models are used to visualize biological pathways, interpret experimental data and test hypotheses. In addition, it provides researchers with model diagrams of publication quality and simulation result charts.



Cell Illustrator 4.0 has new lineup that launches from Browser with Java web start technology, the trial version is available for two weeks from the following websites,

II) Cell Illustrator

II.1) Function

Modeling and simulation engine of Cell Illustrator™ is based on an extension of the *Petri-net methodology*.

Three types of abstractions:

- entities.
- processes.
- connectors.

II) Cell Illustrator

II.1) Function

Three types of entities.

-Discrete Entity : 

-Continuous Entity : 

-Generic Entity : 

II) Cell Illustrator

II.1) Function

Three types of process.

-Discrete Process : 

-Continuous Process : 

-Generic Process : 

II) Cell Illustrator

II.1) Function

Three types of connectors.

-Process Connector : 

-Inhibitory Connector : 

-Association Connector : 

II) Cell Illustrator

II.2) Possibilities

Possibility of modeling many biological processes.

Ability to change elements properties

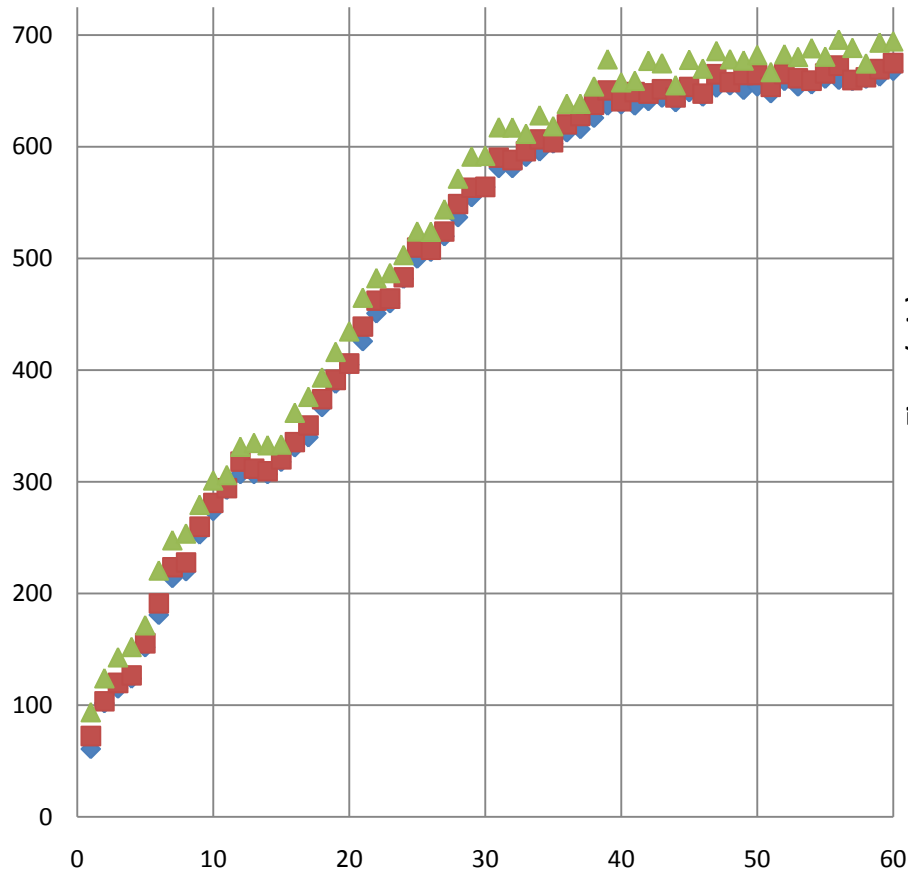
Ability to edit a model at each moment.

Ability to simulate the model.

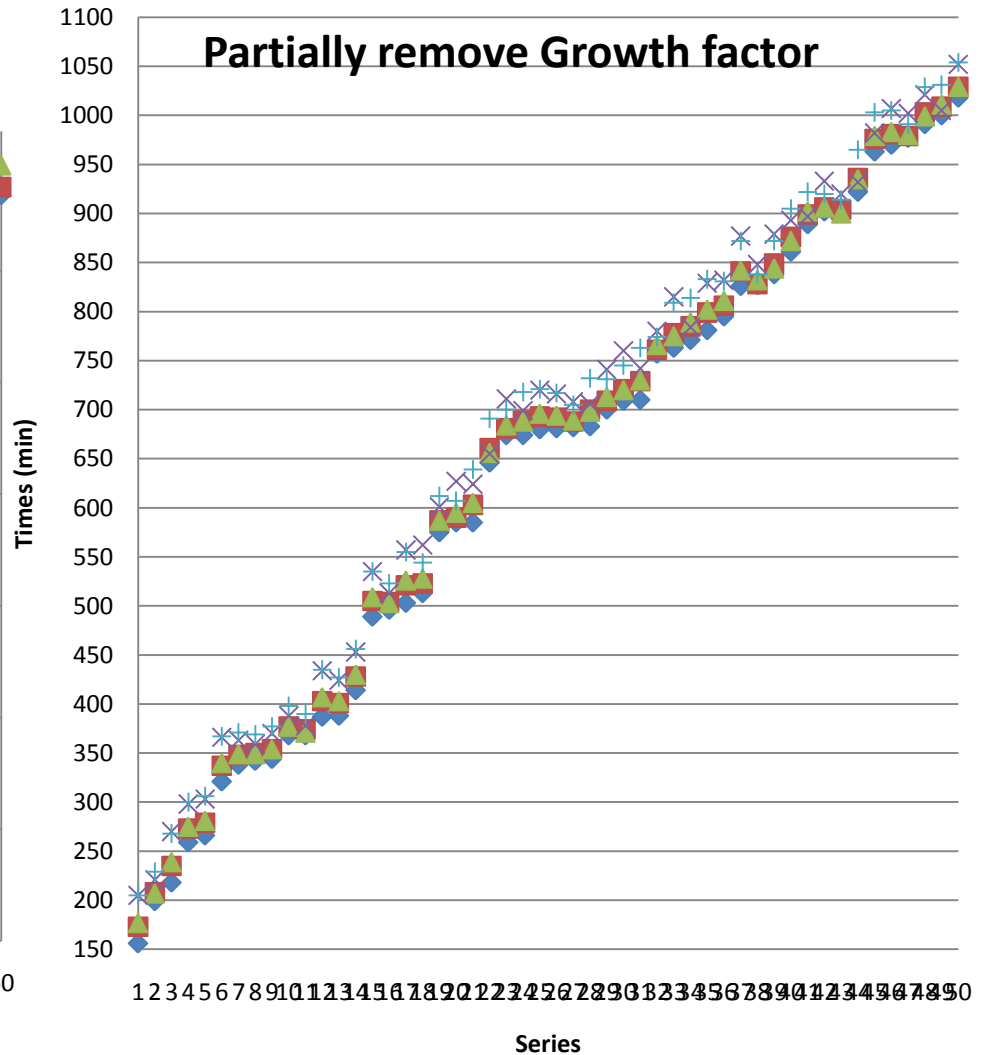
III) Project

III.1) Discoveries from image data

Completely remove growth factor

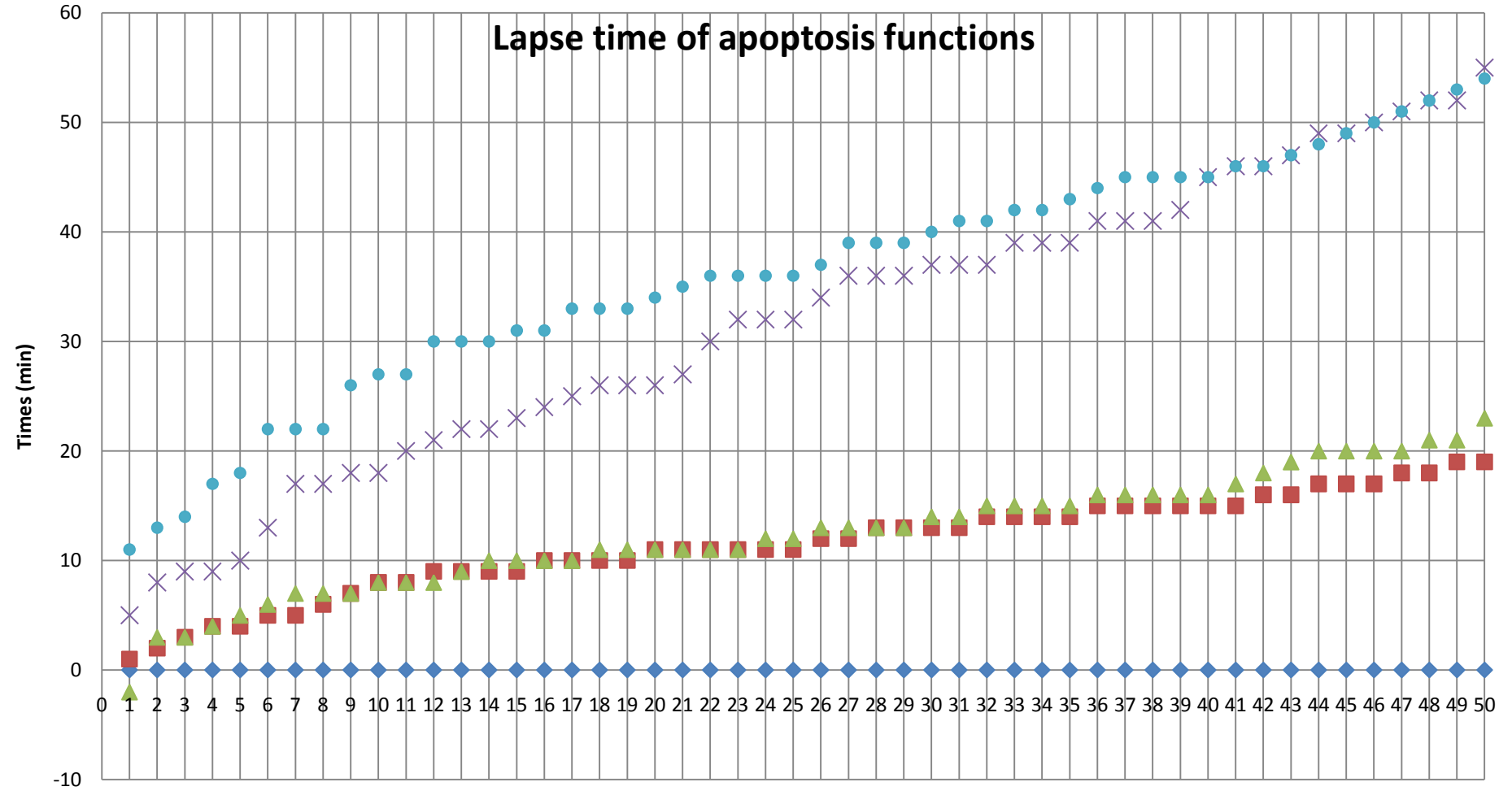


◆ retraction ■ blebbing ▲ PI entry



III) Project

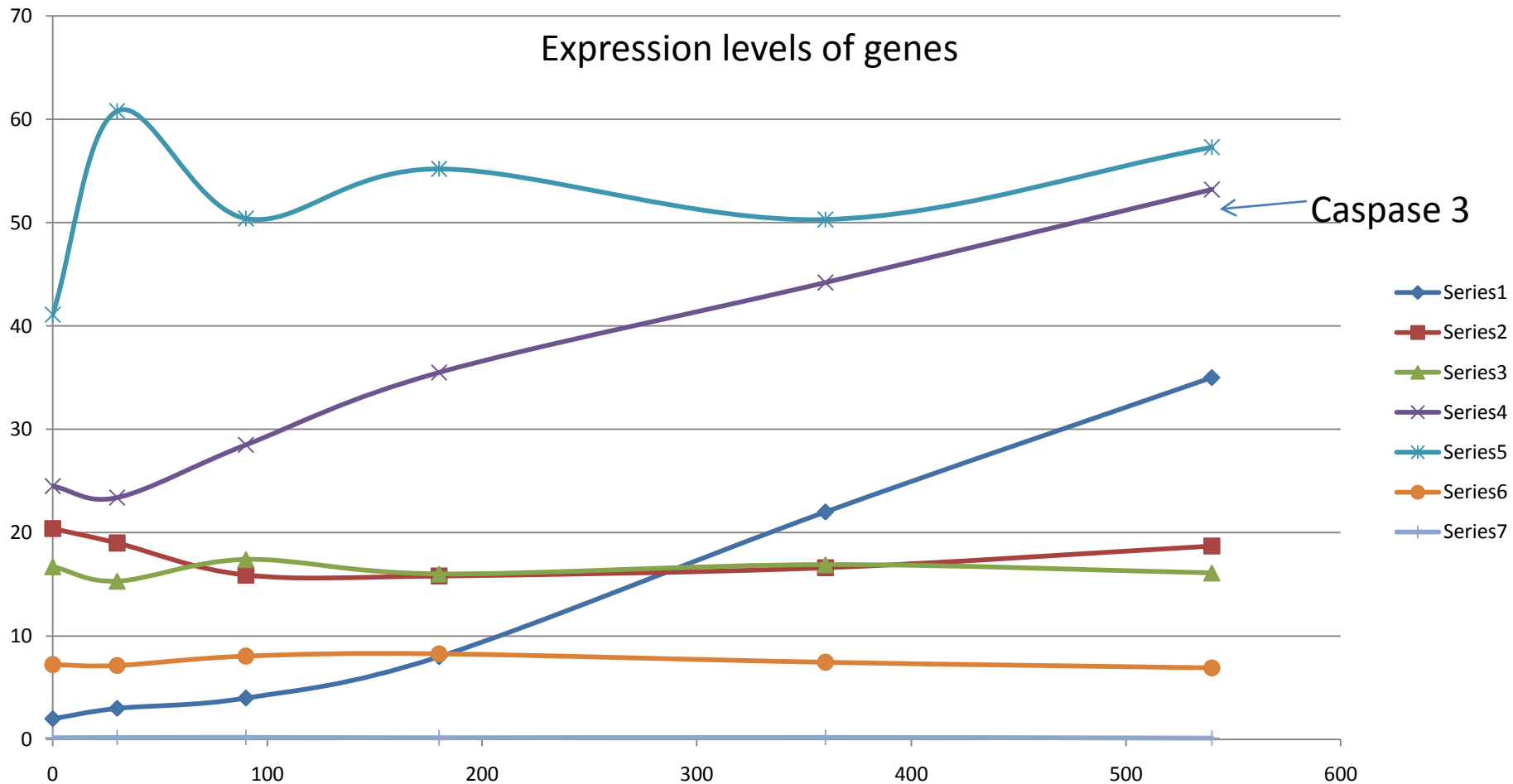
Lapse time of apoptosis functions



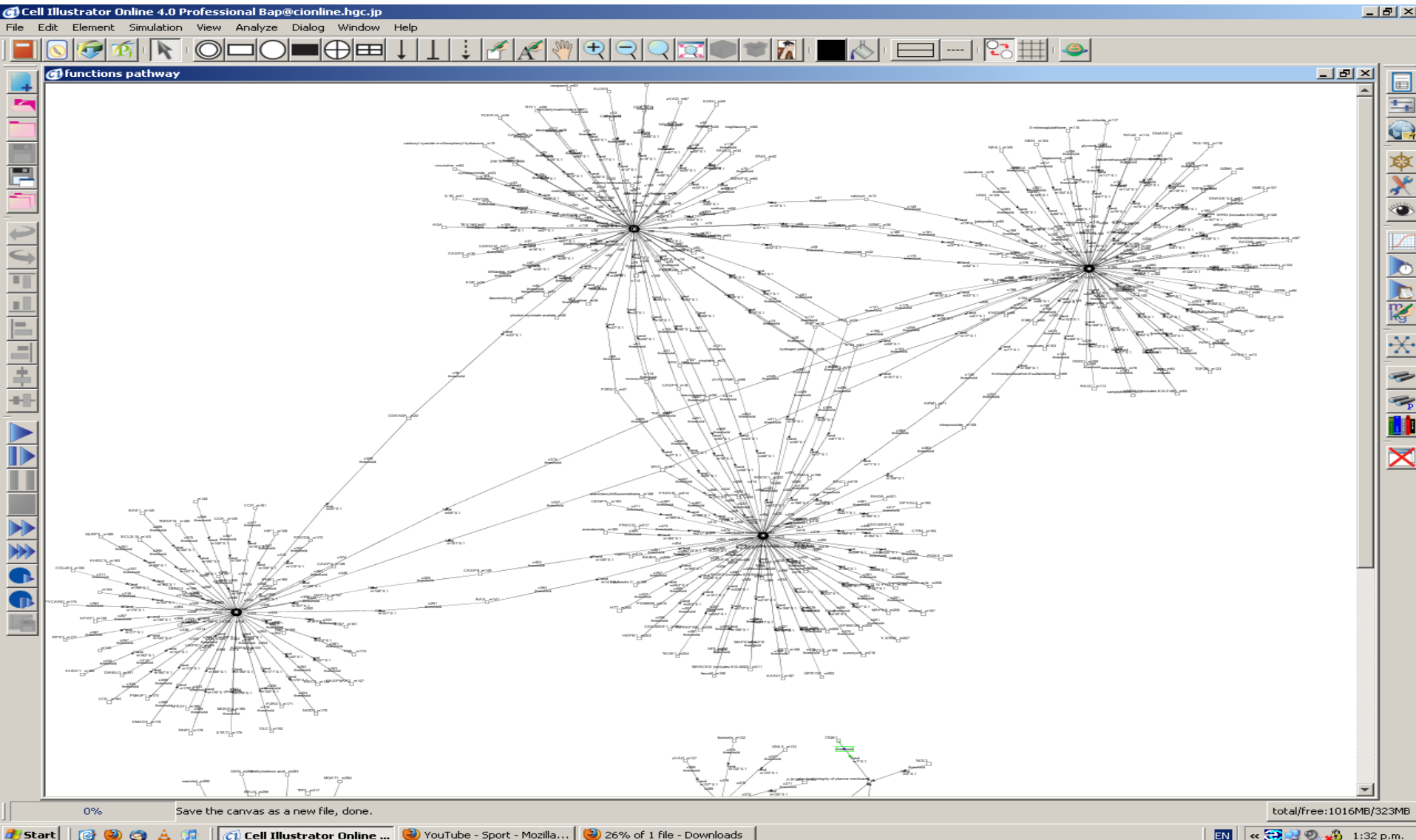
◆ cell detachment ■ retraction to blebbing ▲ retraction to AnV binding ✕ retraction to nuclear condensation ● retraction to PI entry

III) Project

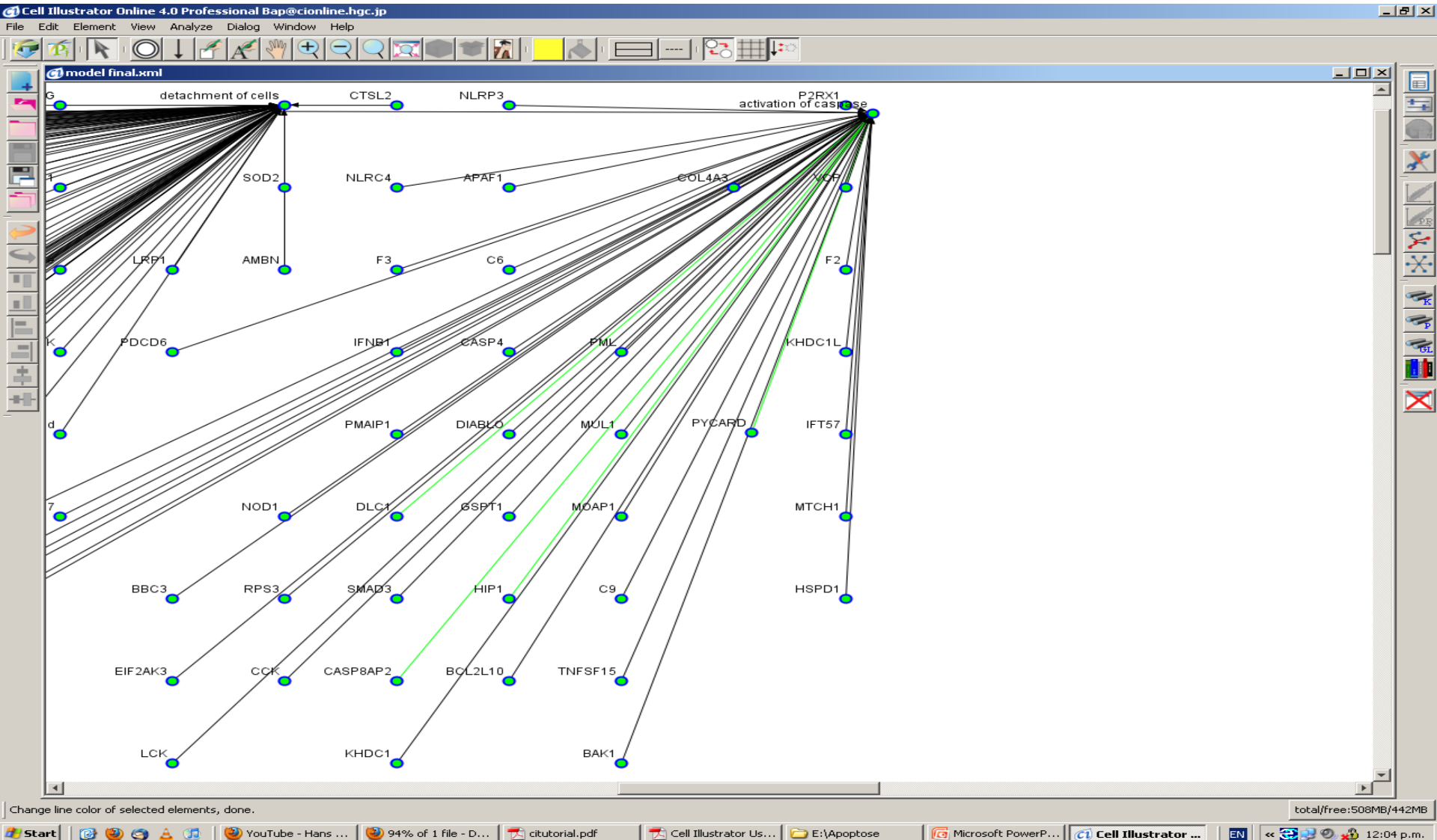
Use microarray data to identify gene expression changes that directly precede phenotype changes (t=x RNA data correlated with t=x+1 imaging data)



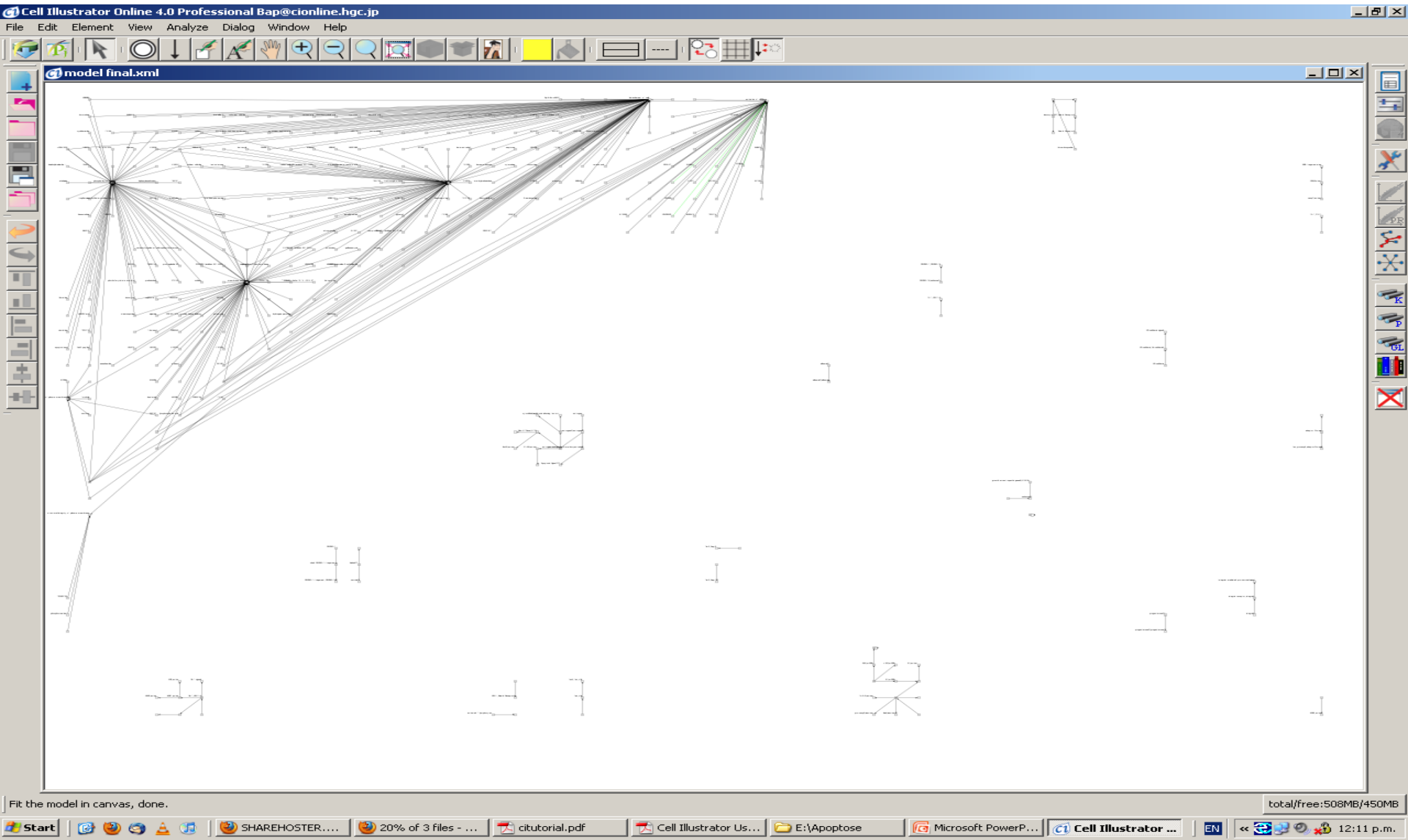
Combined cell Illustrator model



Cell Illustrator model with potential RNA-phenotype relationships highlighted in green



The final cell Illustrator model predicts hypotheses for testing in the lab, and will form the basis of a systems biology model of endothelial cell apoptosis



Conclusion

Completion of a primary model with possibility of simulation.

Establish hypotheses for testing in laboratory.

Following the modeling of apoptosis – add to our RNA and image data:

- proteomic data

- metabolomic data

Acknowledgements

I would like to thank for their help, advice and their generosity :

- Cristin Print
- Louis Ranjard
- Peter Tsai
- Masao Nagasaki