

Third semester report

Botond Kalocsai (kalocsaibotond@gmail.com)

Ph. D. Program: **Statistical Physics, Biological Physics and Physics of
Quantum systems**

Supervisor: **Tibor Vellai**

Ph. D. Thesis title: **Reverse-engineering of molecular biological processes of
ageing**

Contents

1	Introduction	1
2	Research work	1
3	Studies	3

1 Introduction

This semester, we tried establishing an analytical model from our computational population dynamics model for cellular ageing. So far, our numerical simulations seem to capture the properties of ageing. Nevertheless, their scientific value is limited compared to analytical models.

2 Research work

Just like we did with the numerical model of cell ageing, we formulated rules of time evolution in our analytical model attempts. We describe the state of a cell with genetic redundancies, i.e. the number of copies of transcription available genetic elements on the genome.

For the continuous case, these rules take the form of a system of first-order differential equations of the genetic redundancies. The problem with these differential equations is that they describe a purely deterministic time evolution. Ageing is a stochastic process with a asymptotic deterministic outcome (death). Hence, we need to embed our analytical model into a probabilistic framework.

One way to go is to formulate ageing as a stochastic differential equation, as a form of diffusion upon the phase space of genetic redundancies, to arrive at a Fokker-Planck equation. In this formulation, the system of ordinary differential equations is interpreted as a drift vector. The main problem with this approach is that we do not know anything about the diffusion coefficient. Also, diffusion behaviour does not show the asymptotic deterministic behaviour of ageing. The main problem with this approach is that we do not know about the diffusion coefficient. Also, diffusion behaviour does not show the asymptotic deterministic of ageing.

A more parsimonious approach would be to embed our deterministic differential equations into a probabilistic framework analogously to the Lieuville equation (in Hamiltonian formalism). On the phase space of genetic redundancies, cells are conserved quantities. Consequently, a continuity equation for the finding probability density will be valid in this phase space. The phase space velocity field uniquely determines the continuity equation. In this formulation, the first-order ordinary system directly defines the phase space velocity field.

A more parsimonious approach would be to embed our deterministic differential equations into a probabilistic framework analogously to the Lieuville equation (in Hamiltonian formalism). On the phase space of genetic redundancies, cells are conserved quantities. Consequently, a continuity equation for the finding probability density will be valid in this phase space. The phase space velocity field uniquely determines the continuity equation. The first-order ordinary differential equation system explicitly defines the phase space velocity field.

It is important to note that our ordinary differential equations also encode some stochastic behaviour. The retrotransposon copying process is inherently random. However, it is describable with a copy time-rate-like quantity. Moreover, the destructive and non-destructive retrotransposon insertions are also inherently stochastic but describable with destruction time-rate-like quantities in the deterministic equations.

On the other hand, the difficulty of precise measurements in the internals of biological systems and the asymptotic deterministic behaviour of ageing, i.e. assured senescence and death, might preempt the need for analytical models of such sophistication. If we do not have many observables, then we have to make do

with simple phenomenological models of the few observables we have that only aim to describe the asymptotic deterministic behaviour of assured senescence and death. It seems that we can describe the asymptotic behaviour with the somatic and cancer cell division potential and retrotransposon proliferation rates because we presume the beneficial role retrotransposons play as antagonistic agents against cancer proliferation.

3 Studies

In this semester, I completed the “Research Trends in Biology (progressive level)” (BIO/0/1) course. This course was a lightweight one I took to gain a more encompassing outlook on modern research trends. As an extracurricular activity, I heavily invested in learning GPU programming (OpenCL, PyOpenCL) because of its usefulness in bioinformatics and science in general.