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In de verdediging

Onder de kop 'In de verdediging' kunnen net of bijna gepromoveerden zichzelf en hun werk onder de aandacht van wiskundig Nederland brengen.

If you'd be visiting Dublin and see someone on a Dutch granny bike, it may very well be Maciej Dobrzyński. He was a Ph.D. student in Amsterdam until about half a year ago. In his own words, his strong addiction to biking is one of the positive outcomes of his Amsterdam episode. He is still resisting the four-wheel lifestyle; instead, he owns three bikes. Dobrzyński: "One of the numerous advantages of having a bike is that it's immediately ready to ride in both right- and left-hand traffic. Very handy indeed since I currently live in Ireland."

1. Gene expression and cell signalling

On January 13, Dobrzyński successfully defended his Ph. D. thesis *Molecules in Motion: a theoretical study of noise in gene expression and cell signaling*, written under guidance of Jan Verwer (CWI and UvA) and Hans Westerhoff (VU).

In order to develop certain mathematical tools he analysed two important parts of the biological cellular machinery: (i) gene expression – a process of synthesis of a protein (an essential building block of every organism) from its genetic code; and (ii) cell signalling – a set of biochemical processes that allow organisms to sense, among others, the presence of nutrients or toxins in the environment.

2. Randomness

The background of his analysis is biomedical. Designing personalised medicine, using microorganisms to neutralise toxic waste or to produce human insulin requires understanding of complex biochemical processes in living organisms. Until recently, such understanding could only be obtained by experiments. However, nowadays large quantities of high quality data are available, while computing power has exploded, making sufficiently realistic models possible: Codification of biological knowledge into mathematical equations can help to predict organism's behaviour using computers rather than experiments. The task is not easy though. Even a single minuscule biological cell contains millions of molecules interacting in thousands of chemical reactions.

The biochemistry that is crammed in tiny cells must be well coordinated in both time and space in order for an organism to develop and to function. A mistake in recognising a food source or the presence of a toxic chemical may be catastrophic for an organism. Some of the errors or inaccuracies stem from random effects that are inevitable for a system that small.

It is this randomness in a biological cell that is the focus of Dobrzyński's thesis. He used his analysis of gene expression and cell signalling to developed mathematical tools to study problems like the mistakes described above. His aim was to assess under what circumstances random effects can be avoided, and when organisms can benefit from them. It is for instance biochemical randomness that allows bacteria to resist antibiotics or cancer cells to survive chemotherapy. Being able to affect and disrupt these processes requires theories like the one presented in the thesis.

3. Analytical model and simulations fitted exactly

The last project for his thesis was the theoretical analysis of a simple biological system giving microbes a way to sense the physicochemical conditions outside of the cell, a so called two-component signaling system. Together with his co-workers and friends Frank Bruggeman and Jordi Vidal Rodríguez, Dobrzyński did some computer simulations to get an idea of how the system performs in the presence of molecular fluctuations. The simulations were quite long: they involved explicit simulations for random walk of individual molecules in the cell. Then he set out to derive analytical expressions starting from (biological) first principles. The equations were quite complex but matched the

simulations exactly! Looking back at this now, it was not that surprising but at that time they were extremely happy to see that a lengthy mathematical expression could reproduce their painstakingly long simulations. Not a very common situation in life-science, Dobrzyński supposes. With that result in hand they could draw many interesting conclusions about the system.

4. Best and hardest moments coincided

Dobrzyński thinks that for every scientist understanding is always a very satisfying state of mind. Not surprisingly, that moment of understanding came at the end of his Ph.D. programme. At some point, he had two accepted papers, two more in preparation, and he was making plans for the next step. Things he was working on suddenly became much clearer: a great period. Ironically, the hardest period coincided with the best. The last mile turned out to be the hardest for him. Even though the content was there he found it difficult to wrap things up in an elegant manner and to produce a booklet. Nonetheless, the process of writing was very didactic. It proved that having something almost done is very far from actually having it done.

5. Java Eiland and Rembrandt

Originally from Poland, Dobrzyński didn't have any specific expectations regarding working in the Netherlands. Overall, he found living in the Netherlands really great. In fact it was a fulfillment of one of his earlier dreams. Back in the late nineties he was sightseeing the Eastern Docklands (Oostelijk Havengebied) in Amsterdam; a project partly still under development at the time. He literally fell in love with the architecture of Java Eiland. Only a few years later he was enjoying the surroundings as a resident (!). The sight of water from his window and the laid-back atmosphere at the cafes is something to remember for a long time.

Moreover, Dobrzyński has been a hobbyist photographer since long, but got really inspired in Amsterdam[1]. Especially the modern architecture and the lighting conditions that change almost every hour were really stimulating for him. He guesses this is exactly why Rembrandt really 'saw the light of day'.

6. Stochastic models and laboratory experiments

A couple of months ago, Dobrzyński started as a postdoc at Systems Biology Ireland in Dublin. The institute is headed by two renowned scientists, Walter Kolch and Boris Kholodenko and it is located on the premises of University College Dublin. The lab was founded about a year ago and is developing into a very dynamic centre for research on the interface between biology, mathematics, physics, chemistry and computing.

In his project he is continuing stochastic modelling of cell biology. At the same time he is taking advantage of the proximity of experimental labs. His colleagues have patiently introduced him to some of the basic experimental techniques. Dobrzyński hopes to be a much more frequent visitor of the laboratory part of the institute soon. He is certainly not a standard mathematician!

[1] See www.macdobry.net