

About biomathematics and other contemporary mathematical issues

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On the occasion of the 150th anniversary of the publication of “On the Origins of Species by Means of Natural Selection”, a landmark in Biology, CIM has organised an international conference on “The Mathematics of Darwin’s Legacy”, in collaboration with the European Society for Mathematical and Theoretical Biology. This conference brought to Lisbon Mats Gyllenberg, professor of applied mathematics (biomathematics) and chairman of the Department of Mathematics of the University of Helsinki. This article is an edited conversation held during the conference with one of the conference organisers and currently director of CIM.

Gyllenberg is currently the president of the Finnish Mathematical Society, one of the two editors-in-chief of the Journal of Mathematical Biology and has been appointed Chairman of the permanent PESC (Physical and Engineering Sciences) standing committee of the European Science Foundation (ESF) for the three-year period 2009-2011. This ESF Committee is one of the five science units of the ESF, and its fields of interest include physics, chemistry, mathematics, technical sciences, computer sciences and material sciences and introduces new programmes and networks, and through its opinions, it also has a more extensive influence in the ESF’s research policies, being the current Forward Look on “Mathematics in Industry”, proposed by the applied mathematics committee of the European Mathematical Society, a recent example.

Working in Biomathematics

You made your PhD already in mathematical biology. What was your training as a mathematician?

Indeed I took my undergraduate studies at the University of Technology in Helsinki. So my main topic was mathematics, abstract mathematics. Functional analysis was my favorite topic and I wrote a master thesis on von Neumann algebras. But already during my university studies I took microbiology and biochemistry as a minor. So I have really done the some laboratory work. I have grown bacteria and I have done a lot of real experiments. From the very beginning I knew that I would become a mathematician but I was very interested in biology and then I realized that I can combine these two. My PhD thesis was already on “Dynamics of Structured Populations”

In the “Mathematics Genealogy” I found that you are a “descendent” of the Finnish mathematician Lindelöf, because Lehti was your adviser and he was advised by Järnefelt that was a student of Lindelöf, which by the

way had a Swedish name. At the time he became professor at the University of Helsinki, Finland was still a Grand-Duchy of the Russian empire.

Yes! That is true. It is a pity that Lindelöf’s adviser is not known. He probably didn’t have one. Most Finnish mathematicians have a common ancestor and that is Lindelöf. In fact, still today we have a Swedish speaking minority. I belong myself to this minority, as well as Lars Ahlfors, probably the great Finnish mathematician of all time.

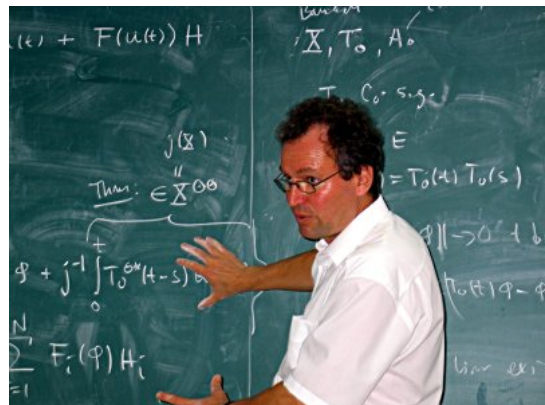


Figure 1: *Matts Gyllenberg.*

In fact, there exists a strong mathematical tradition in Finland, that started before Finland became an independent country. But even if Ahlfors started in Europe he spent most of his career in the United States.

Indeed, he moved to the United States, quite early. He was the first Fields medalist in 1936, if I remember correctly. Ahlfors was also a student of Lindelöf. I would say that it was really Lindelöf who started the Finnish school of analysis and complex function theory, which after Nevanlinna and Ahlfors have become quite famous.

After your PhD, that was already towards biomathematics you stayed in Finland or you did your career

elsewhere?

In fact, during my PhD work I spent a year in Amsterdam working together with Odo Diekmann who had influence on my work. I mean, I wouldn't be the mathematician I am today without the collaboration with Odo, which started then and is still going. We still write papers together and so on. Then I was a visiting professor at Vanderbilt University, Nashville, Tennessee and in 1989 I got my first chair of mathematics. That was in the Luleå University, Sweden. I stayed in Sweden for three and a half years and then I came back to Finland, working in the University of Turku. I spent also some time as a Visiting Professor in Santa Barbara, Gothenburg and Utrecht and now I have been for five and a half years in the University of Helsinki.

You have a large number of publications within mathematical biology and applied mathematics but you have also many publications in dynamical systems. In fact, we can see your interest by bio-mathematics, in particular structured population dynamics and in the mathematical theory of evolution. But you have also works in differential equations. How do you relate this to analysis and differential equations?

It is a little different. Of course it is analysis, for sure, but actually my interest in differential equations or integral equations came from the population dynamics because the basic thing in population is reproduction. So the birth rate is something which you should determine in order to know how the population evolves and those who are born today are born from parents that were born in the past. So it's very easy to understand that we get some sort of functional delay equation or Volterra integral equation. So it was really from biological problems that I got my interest in integral and differential equations and, of course, I have also done work in this area without direct applications to biology.

Biomathematics, Euler and Darwin

I remember our conversation last February in Barcelona when I met you during a CRM meeting in biomathematics. You mentioned then the 1760 Euler model of human population with an integral operator and, later, you sent me your article on "Mathematical aspects of physiologically structured populations", where you referred to Euler's description of an exponentially growing population with a steady age distribution (balanced exponential growth) done more in the spirit of an actuary than a biologist. That means that you also have some interest in the history of mathematics or it is just a side interest?

It is a side interest. But I really think that most mathematicians are too lazy. We know that many results are rediscovered over and over again because it is easier to

prove a lemma then go to the library and try to find the original or previous results. But Euler was absolutely fantastic! He knew a lot of things, from an intuitive point of view, and only later on his results have been made rigorous mathematics. But it is often the case, when we go back to the old masters, we learn a lot by reading Euler or Riemann.



Figure 2: Poster of the International Conference “The Mathematics of Darwin’s Legacy”, November 23-24, 2009.

I should mention that the exponential growth in population is basically due to Euler. In fact we can find already in his book “Introductio in analysin infinitorum”, from 1748 where he lays the foundations of infinitesimal analysis, four interesting examples about geometrical growth of populations in the chapter about logarithms and the exponential. And that was not the first time that mathematicians had interest in quantifying population. It is also quite well-known the pioneer 1760 memoir of Daniel Bernoulli on “Essai d’une nouvelle analyse de la mortalité causée par la petite vérole et des avantages de l’inoculation pour la prévenir”, and its role in understanding the benefit of vaccination in the diminishing smallpox mortality. So, there was already biomathematics in some special examples before Darwin. What do you think about the conference on “The Mathematics of Darwin’s Legacy”, that brought you this time to Portugal?

As a matter of fact, I think this was a wonderful conference. I like this small workshop type of conference more than the big ones. It was also good that there were only a small number of speakers, and we had one full hour to our lectures. I think that this is much better than to have 20 minutes communications. I think that we really heard during these two days very good lectures and I learnt a lot from them. On the other

hand, the subject of the conference is absolutely central in biomathematics today. Now, my main interest in mathematical biology, aside from structured population is the mathematical theory of evolution, in particular, adapted dynamics, the interaction between ecology and evolution by natural selection. As we have heard during this conference also evolution by natural selection is something inherently mathematical, although Darwin did not formulate it at all the mathematical relations.

He could not because he had no genetics in his theory. But soon afterwards, the English biometric tradition started with Dalton and Pearson with the development of the statistical theory, in particular, for the scientific treatment of biological data...



Figure 3: An aspect of the International Conference on “The Mathematics of Darwin legacy” at the University of Lisbon.

In the very first lecture of this conference it was pointed out by Warren Ewens that there is an obvious problem, a contradiction, because at Darwin’s time it was thought that the inheritance of the mother and the father were blended at conception. It is so evident that the future generations would all look alike and there would be no variation upon which natural selection could operate. And this somehow shows the great genius of Darwin, that although he was not mathematically trained, he saw that there was some sort of contradiction that he could not really resolve it, but he just stepped aside to continue to develop his theory. That was great. Darwin took from Malthus the idea of exponential growth, although Malthus has called it geometrical growth, but that’s the same thing, and he also had this wealth of examples from breeding domestic animals. So Darwin knew artificial selection, and, combining the exponential growth with the selection principles known from animal breeding, he could arrive at his theory of evolution by natural selection. Usually, when big leaps are made in science, they are usually done by somebody combining ideas from two completely different theories and then make a synthesis. And the success of Darwin is also one of those examples, and, of course, there was a strong mathematical element in Darwin’s syntheses.

Which confirmation came afterward with the help of mathematics, because the “synthesis” of Mendelism and Darwinism was done basically using mathematical ideas and models, such as the Hardy-Weinberg law in population genetics. On one hand, the evolution theory was very important in the development of mathematical statistics. For instance, the new methods and concepts that Fisher invented in statistics were done in the beginning of the 20th century and were strongly motivated by biology and by the evolution theory. Their application in his 1930 book on “The Genetical Theory of Natural Selection” lead to conclusions that were confirmed by the works of biologists such as Haldane, Wright and Dobzhansky, among others. On the other hand, those decades were also crucial for the mathematisation of biology using differential equations. So, Lotka-Volterra models, for instance, that appeared in 1925-1926 are very well-known and still have a tremendous influence in population dynamics. It’s very interesting the comparison between these two independent contributions, the one by Lotka, with a statistical-physics approach to biology, and the other by Volterra with its mechanical approach. The evolution theory in the second half of the 20th century raised other aspects that Darwin did not really foresee. Besides the reproduction, the mutation and the selection there is the cooperation between live entities and, of course, its mathematical models, like evolutionary game theory for instance, that are current research topics. What do you think about this?

It’s extremely important. I would say about Lotka-Volterra system that these models have been extremely productive because they are sufficiently simple as equations. Of course, a lot of idealization is made, but that’s always the case in the mathematical models of biology. They are simple, but at the same time they have sufficiently rich behaviour that you can really get biological insight and, on other hand, they have been a wonderful inspiration for mathematicians. Of course, for two dimensional systems almost everything is known, but already in three dimensions there are a lot of very interesting mathematical questions. For instance, the whole theory of monotone dynamical systems really has got its source in the Lotka-Volterra system. When we have cooperation or competition then you can have this ordering depending whether is cooperation or competition, you have to change the direction. They have some sort of monotonicity. That has been a wonderful source of inspiration for mathematicians. I like very much this two way interaction. Mathematics is needed to get biological insight; biological questions are useful to give inspiration to create new mathematics. In my work I collaborate quite a lot with biologists and their intuition often helps me to find the right way of proving my terms. One should always bear in mind that this dialogue between mathematicians and biologists is extremely important.

Editing Mathematical Biology

You are now one of the Editors-in-Chief of the Journal of Mathematical Biology. Is there a difference between mathematical biology, biology or mathematics papers? How do you cope with this interaction?

Originally, the Journal of Mathematical Biology was founded about 30 years ago. The name of the journal was, I think, analog with mathematical physics, which is mathematics. Mathematical biology was also viewed as being really mathematics and not biology. But now this has changed a lot and we really require for a paper to be published in the Journal of Mathematical Biology that there is real biology in it. So, there must be some new biological insight that you get from mathematics. Of course, mathematics should not be elementary or trivial. So, the ideal papers are when new mathematical methods are developed, some new mathematics created in order to get insight into some biological questions.

You mean Interdisciplinary? But this is a very difficult issue. I'm also an editor myself of a European Mathematical Society journal, Interfaces and Free Boundaries, aiming the combination of Mathematical Modelling, Analysis and Computation. Those ideal interdisciplinary papers are very rare.

Yes! Of course, we also publish some quite mathematical papers, which get the inspiration from biology, and are potentially, at some later time, applicable to some real biological system. So, I think that my predecessor as Editor-in-Chief, Odo Diekmann, made a wonderful work making this journal the best one in mathematical biology or biomathematics, whatever you want to call it, and really in quality is of course the number one. I think we have been able to keep this high quality.

I think it is essential in a mathematical journal, in any scientific journal, to have a good referee system. So, in a journal, like Journal of Mathematical Biology, do you have a referee for mathematics and another for biology? When you have a conflict with the two points of view, how do you solve it? Do you act as an Editor-in-Chief or ask a third opinion?

This is quite often the case. It depends on the submitted manuscript, but, as I said, we require that there must contain real biology. There must be interpretation and insight in biology. This actually often requires that we have referees from both biology and mathematics. The other question concerning conflict is quite difficult. It is impossible to give a general answer, because every paper is different. Of course there are two completely opposing views. I have to make up my mind myself. As an Editor-in-Chief I have the last word. There are basically two options. Either I reject the paper or I ask the author to make major revisions in order to be able to publish it within the scope of the journal. I mean, it depends from case to case. It's very difficult to give a general opinion.

I have to ask one more question to you as an editor. Nowadays it is quite hard to find good referees who wish to give some constructive answer in time...

It is extremely difficult, terribly difficult. This has to do with the general hectic speed of life. Everybody is so busy. Many people don't answer at all, others say yes, and then promise, and then they forget, and you don't hear anything about it... I would say that the Journal of Mathematical Biology has such a good reputation, most referees who really take the job to review a paper, they do it quite well. They write detailed reports and produce rather long and constructive reviews. As an editor I'm quite happy with the referees we have.



Figure 4: Mats Gyllenberg, on the right, with José Francisco Rodrigues at University of Lisbon in November 24, 2009.

Mathematicians and scientific organisations

You are also the President of the Finnish Mathematical Society. How large is the Society? Does that function take much time from you?

It doesn't take so much time, no. The society is quite small. We have about 350 members, professional mathematicians, teachers, graduate students, some working in the industry... We have to accept every membership application in the Board of the Society, and the criteria being that they must be somehow connected to mathematics. For instance, they must have a master in mathematics, that's good, and if they work with mathematics in industry or, of course, if they are in the Academia and if mathematics is the main subject. Sometimes we reject applications when we think that they do not have anything to do with mathematics. The majority of members is working in the Academia or are PhD students. I don't know exactly the fraction, but it's not relevant the number of high-school teachers in our Society.

Is there a relation between the Finnish Mathematical Society and the National Committee of Mathematicians that represents Finland, now in Group III, at the International Mathematical Union?

No. Formally there is none. The National Committee is something separated from the Society and depends on the Finnish Academy of Science and Letters. Pertti Mattila is currently the Chairman of the Finnish National Committee of mathematicians.

You are now also the Head of the Department of Mathematics and Statistics of the largest university in Finland. In your department, what is the role of applied mathematics or other applied subjects as biomathematics, industrial mathematics ... ?

A few decades ago, it was really pure mathematics, classical functional theory, functional analysis... But recently we have been able to recruit new professors in applied mathematics, and very good ones. We have, besides the mathematical biology, which we have already discussed, we have a big group of mathematical biology, but there is also a very strong group in inverse problems. And this year we have appointed a professor in industrial mathematics. So, I think we have a very strong applied mathematics. We have a good bond between pure and applied. We have actually also two Centres of excellence at our department. One is on Inverse Problems Research, the other is in Analysis and Dynamics Research. I myself and the biomathematics group belong to this second one, because we deal with dynamical systems, modeling, biological phenomena. This is actually quite exceptional, because there are not so many of these national Centres of excellence in our country. Two are in mathematics and they are at our department. I'm quite proud of this.

That is the research component of the department. But there is also a teaching component, I presume. So, how are in Finland the mathematical courses with the Bologna degrees: 1st cycle, 2nd cycle and 3rd cycle? What is required to be a mathematical teacher in high-school?

To be honest we have not changed much in Finland. We had to introduce the bachelor degree after three years of university studies, and have two for the master. Mathematics teacher in high-school have to have a master in mathematics. And that is what is very good at the Finnish school system. We have highly educated teachers. They have also to take the pedagogical education, during the master. So, it means that they have slightly less courses in mathematics. But, still, they know the subject very well since they follow mathematical courses corresponding to at least four years.

And are you still accepting enough students in your mathematical courses at the University of Helsinki, or are you having problem as in many other European universities?

We get a lot of students, but we also have a drop out, which is rather high. I suppose that there are many young people who want to study medicine or law. But it's very difficult to get to the Medical and in the Law

Schools. And then they think: "OK! Let's go and study mathematics!", and then, they shift.

Interesting! So, these students to get into medicine or law school, some of them go through mathematics. That is not a bad idea...

Of course not! It's a very interesting idea. They gain them from us. So, we get about two hundred new students in mathematics, every year, and about 110 bachelors, for the master courses.

Do you also have technology or engineering courses in Helsinki University? And how is that going along with the others universities in the Finnish system?

We have everything at the University of Helsinki, except for engineering, which is at the Technical University and is a separate university. In fact we have quite a number of universities in Finland, which is a big drawback in the Finnish system. We still have twenty universities and the population is five millions. Now, we are trying to decrease the universities by merging some of them, which I think is a good idea. For instance, the Helsinki University of Technology, the Business School, and then the School for Industrial Design, they have merged from the beginning of this year, for one bigger university.

In Finland, there is Nokia which is a world known leader in the telecommunications industry, that requires a lot of mathematics. Is there any particular role or cooperation between Nokia and the mathematical sciences in Finland?

In a sense, yes... I mean, the leaders of Nokia always emphasize the role of mathematics. It's extremely important. In this case we get moral support but we don't get any money from it. They hire mathematicians, they hire computer scientists...

You are also the first mathematician which is chairing of the Standing Committee for Physical and Engineering Sciences (PESC) of the ESF (European Science Foundation) since 1st January 2009. ESF has now a very good cooperation with the European Mathematical Society and had lunch the Forward Look in Mathematics and Industry. PESC has last June in Berlin the 12th Round Table Meeting of ESF Member Organisations exactly about Mathematics. If you allow me will I finish our conversation quoting some of your statements when you started your functions at the PESC/ESF enhancing the focus on interdisciplinary collaboration.

"During the past decade we have witnessed an unprecedented technological revolution. Progress in telecommunication, the world wide web and Google are only a few examples of technological advancements that have profoundly changed everyday life. These achievements are all based on fundamental research in disciplines like mathematics, physics and computer science - fields covered by PESC. This interaction between the pure and

the applied makes the PESC environment important and intriguing. (...) The traditional division of the natural sciences into “hard” sciences like mathematics, physics, chemistry and computer science and the “soft“ life sciences is old fashioned and in fact obsolete.

Modern (molecular) biology could not exist without collaboration with chemistry and physics. (...) The life sciences increasingly use mathematical and statistical modelling and are often dependent on heavy computing.”



Figure 5: *Group Picture*, International Conference “The Mathematics of Darwin’s Legacy”.

THE JORNADA MATEMÁTICA SPM/CIM ON MATHEMATICAL BIOLOGY

The *Jornadas SPM/CIM* are a joint initiative of the Sociedade Portuguesa de Matemática and the Centro Internacional de Matemática, with the purpose of enhancing collaboration between Portuguese mathematicians in all areas of research. This session took place on the 25th of November 2009, in the Complexo Interdisciplinar da Universidade de Lisboa, and was organised by Nico Stollenwerk, (CMAF/FCUL, University of Lisbon) and gathered both senior and junior researchers in Mathematical Biology, in a relaxed and lively atmosphere for discussions.

The opening lecture was given by Peter Jagers, from Chalmers University in Sweden, titled *Extinction versus persistence*.

The list of the other presentations given is as follows: *The hidden potential of recombination inhibitors: sidestepping the Darwinian inevitability of resistance?*, Philip Gerrish (Univ. de Lisboa/ Univ. of New Mexico), *Stability for Lotka-Volterra models with delays*, Teresa Faria (Univ. de Lisboa), *Evolutionary branching of a magic trait*, Tadeas Priklopil (Univ. of Helsinki), *Multi-scale models in tuberculosis: the case of drug resistance*, Paula Rodrigues (Univ. Nova de Lisboa), *Animal growth in random environments*, Carlos Braumann (Univ. de Évora), *Structured populations in the N-person snowdrift game*, Marta Santos, (Univ. de Lisboa), *Steady-state topologies of SIS dynamics on adaptive networks*, Stefan Wieland (Univ. de Lisboa), *Trimorphic generalist-specialist coexistence on two special resources*, Ilmari Karonen (Univ. of Helsinki), *Prediction of protein-protein interactions based on amino-acid sequences*, Valeria Manna (ICAR/CNR), *Hereditary maximum parsimony trees and not so hereditary ones*, by Mareike Fischer (Univ. of Vienna), *Stationary in moment closure and quasi-stationarity of the SIS model*, Alberto Pinto (Univ. do Minho).

The day closed with a round table discussion, chaired by José Francisco Rodrigues (CMAF/ Univ. de Lisboa) with the theme “Open questions and future prospects of mathematical biology”. Further details, including abstracts of the talks, can be seen at http://www.cim.pt/?q=spm_cim_jornada_mathematical_biology_2009