European Communications in Mathematical and Theoretical Biology
2017, No. 20

Communications

European Society for Mathematical and Theoretical Biology

A European Forum for Information, Presentation and Exchange
Official Communication Bulletin of ESMTB

Letter from the President

Dear colleagues and members of the ESMTB,

One hundred years ago, in 1917, D'Arcy Thompson published his classic *On Growth and Form*. Explaining biological morphology based on physical analogy and mathematical transformations, he was among the first to argue that mathematical theory should have a prominent role in biological explanation. In D'Arcy Thompson's opinion, mathematics described and explained biological morphology more elegantly and efficiently than 'mere words' [1].

D'Arcy Thompson would have been pleased to see that next year, 2018, will be dedicated to the interface of mathematics and biology. The Year of Mathematical Biology 2018 will start already in December 2017 with a Simons semester at the Banach Center in Warsaw, Poland. The official 'kick-off' will follow in Joensuu, Finland in January 2018 with a Mathematical Weekend co-organized by the Finnish Mathematical Society, the European Mathematical Society (EMS) and ESMTB. From page 4 Torbjörn Lundh describes all the events announced so far in the context of the Year of Mathematical Biology. He will also introduce the annual Day of Mathematical Biology, on October 10. A full overview will be maintained at https://www.esmtb.org/news/141-year-of-mathematical-biology-2018.

The main event of the Year of Mathematical Biology 2018 will be the European Conference for Mathematical and Theoretical Biology 2018 in Lisbon, Portugal. It will be exceptionally organized jointly with the EMS and the Portuguese Mathematical Society. The conference chairs, Maíra Aguiar, Carlos Braumann and Nico Stollenwerk, together with the local organizing committee and the scientific committee have already secured a great line-up of plenary speakers. The deadline for minisymposia will be 15 November 2017 and contributed talks can be submitted until February 20th. ECMTB 2018 promises to become again an inspiring event, bringing together scientists from the whole width of our field: some seeking mathematical solutions for their biological questions, others looking for new mathematical challenges and approaches in biology.

At ECMTB 2018 you will also be able to attend the talk of the winner of the 2016 Reinhard Heinrich Doctoral Thesis Award. This year the submissions were of exceptionally high quality: therefore no less than three runner-ups were selected: Dr. Yuval Zelnik, CNRS, France, for his thesis *Regime Shifts in Spatially Extended Ecosystems,* Dr. Kayin Leung, Utrecht University, The Netherlands, for her thesis *Dangerous Connections – the Spread of Infectious Diseases on Dynamic Networks* and Robert Ross, University of Oxford, for his thesis *Modelling Cell Migration, Proliferation and Interactions on Growing Domains*.

However, one applicant clearly stood out for his work on the dynamics of microbial metabolic pathways at ecosystem scales: Dr. Stilianos Louca of the University of British Columbia, with his thesis *The Ecology of Microbial Metabolic Pathways*. His thesis work led to seven publications, including papers in *Science*, *PNAS,* and *Nature Ecology & Evolution*. I congratulate him on behalf of the award committee and the ESMTB. Please read the summary of his thesis, followed by those of the runner-ups, from page 7 onwards.

With that, I will leave you to read the rest of his issue of *Communications*, but not without saying goodbye. Together with Barbara Boldin, Reinhart Bürger, Ryszard Rudnicki and Vitaly Volpert I will be leaving the board in 2018; I would like to thank all four of them for our pleasant board meetings and good collaboration, Barbara in particular for being the society's secretary for the last six years, and Vitaly for preparing the *Communications.* This also means that we will have new elections; all members will have received an e-mail to invite them to vote.

Enjoy the rest of 2017. After all, *every* year is a year of mathematical biology!

Roeland Merks, merks@cwi.nl

[1] W. Arthur, D'Arcy Thompson and the theory of transformations, Nat Rev Genet, vol. 7, no. 5, pp. 401–406, Apr. 2006.

2018: The year of Mathematical Biology

Torbjörn Lundh

I'm a bit curious, what do you answer when people ask you what you're working on? I use to answer, mathematical biology. What is that, they say. Well, it's like you know how physicists use mathematics all the time in their science, but here we take biological problems and use, and even sometimes develop new, mathematics to solve these problems. Can you do that, they then ask. I didn't know that was possible. Yes you can, I say, but it's still rather new, at least compared to physics. And biology is so much more complicated and complex than physics, so the mathematical problems are in general much harder. After that, the conversation can take different routes like: Go away nerd, or, That is so interesting (without visible irony), please tell me more.

We as a community need to be more "visible". That's why the suggestion from the European Math Society came as a godsend gift. The suggestion was to make 2018 a theme year for Mathematical Biology. And now, we are only half a year away from that. The year will kick off up in north east at Juensuu in Finland in January.

Then there will be different conferences, summer schools and workshops the whole year. One could actually just travel around to visit these meetings the whole year, that is, if one is a highly financially independent scholar. The announced meetings are currently the following:

- EMS-Finnish Mathematical Society-ESMTB joint Mathematical Weekend, A kick-off event for the Year of Mathematical Biology, 4th-5th January 2018, Joensuu, Finland.
- Simons Semester on Mathematical Biology, December 2017-March 2018, Banach Center, Warsaw, Poland.
- Intensive Research Program in Mathematical Biology, April-June 2018, Centre de Recerca Matemàtica, Spain.
- Mathematical perspectives in the biology and therapeutics of cancer, 9-13 July 2018, CIRM, France.
- 11th European Conference on Mathematical and Theoretical Biology (ECMTB 2018), a joint conference of the European Society for Mathematical and Theoretical Biology and the European Mathematical Society, 23-27 July 2018, Lisbon (Portugal).
- CEMRACS 2018, Numerical and mathematical modeling for biological and medical applications: deterministic, probabilistic and statistical descriptions, 16 July - 24 August 2018, CIRM, Marseille, France.
- The Helsinki Summer School on Mathematical Ecology and Evolution, August 2018, Helsinki (Finland).
- Thematic Program in Mathematical Biology, September-December 2018, Institut Mittag-Leffler, Sweden.
- Differential Equations arising from Organising Principles in Biology, 23-29 September 2018, Mathematisches Forschungsinstitut Oberwolfach, Germany.

For more details please see http://euro-math-soc.eu/year-mathematical-biology-2018, which will be continuously updated.

There is now a logo thanks to the artistic Arturo Araujo who otherwise works on bone cancer models.

But, and this is important, the year is much more than lining up meetings all over Europe. So think about what you could do? Arrange a special lunch or tell your scientific journalist friend about this hot emerging field that even has a special year, or why not set up a flash mob interpreting mathematical biology? Or maybe a special day at your department? (If you arrange something, please contact me so we can add it on the official list. It does not have to be huge, but it would be great to have a long and highly varied list.)
For the last suggestion, there is a special date that should be picked: October 10.
That date was decided in our common ESMTB-SMB-board meeting in Nottingham last summer to be the yearly "day of mathematical biology" with start in 2018. The reasons to pick that specific date was that we wanted a day that both we and the Americans could write in the same manner (i.e. not as the pi-day 3/14) which left us with dates such as n/n. Then it was suggested that the concrete interface between our decimal system and our anatomy is our ten digits. Luckily we also have ten toes. Furthermore, as our president Merks pointed out, if we prefer to use base 2, ten is written as 1010.

This is a photo of my class in Gothenburg, October 10, 2016, performing a pilot test.

So dear Math Biologists, jump on this theme year and arrange something, anything, and let us celebrate our good fortune to work in this intriguing scientific field in its exciting stage of development.

The Reinhart Heinrich thesis award

The ecology of microbial metabolic pathways
Extended PhD thesis summary

Stilianos Louca, University of British Columbia, Department of Mathematics and Biodiversity Research Centre
Thesis supervisor: Prof. Dr. Michael Doebeli

Nominated by: Eva Kisdi, University of Helsinki

I. Introduction

Microorganisms are the most ancient, the most abundant and the most diverse life form on Earth. Yet, our understanding of microbial ecology and its role in ecosystem biochemistry remains extremely limited, partly because the enormous microbial diversity poses a challenge to the mathematical modeling of microbial communities. The bulk of biogeochemical fluxes is driven by a core set of metabolic pathways, such as photosynthesis or nitrification, which through time have spread across microbial clades that can co-occupy or replace each other within metabolic niches (1). Hence, the question arises whether the distribution and activity of these pathways - regardless of the associated organisms - can be predicted purely based on energetic and stoichiometric constraints, such as the availability of light or specific terminal electron acceptors for respiration. Under such a "pathway-centric" paradigm, physicochemical environmental conditions would be strongly coupled to the bulk metabolic functioning of microbial communities, but would only weakly affect which species happen to perform a particular metabolic function. This paradigm, if accurate, would greatly simplify the modeling of microbially mediated processes in the environment. As I describe below, during my PhD I developed and tested the applicability of pathway-centric theories for microbial ecology using a combination of mathematical modeling, statistics, bioinformatics and field surveys.

II. Decoupling function and taxonomy in microbial communities

A key prediction of pathway-centric paradigms is that microbial metabolic pathways should display similar dynamics when compared between similar environments, even if the actual taxa associated with each pathway (i.e., belonging to a specific "functional group") changed. To test this prediction, I performed shotgun environmental DNA sequencing (a.k.a. metagenomics) of aquatic microbial communities hosted within the foliage of several bromeliad plants (a popular model system for community ecology). In metagenomics, the entire genetic content of a community is sequenced in order to estimate the overall abundances of genes associated with specific pathways. Using this technique, I was able to assess the functional structure of the microbial communities and the taxonomic diversity within each of several functional groups, such as photoautotrophs, methanogens or fermenters (3). I showed that microbial communities in all bromeliads exhibited similar functional structure, despite highly variable taxonomic composition within individual functional groups (Figure 2), consistent with a pathway-centric paradigm.

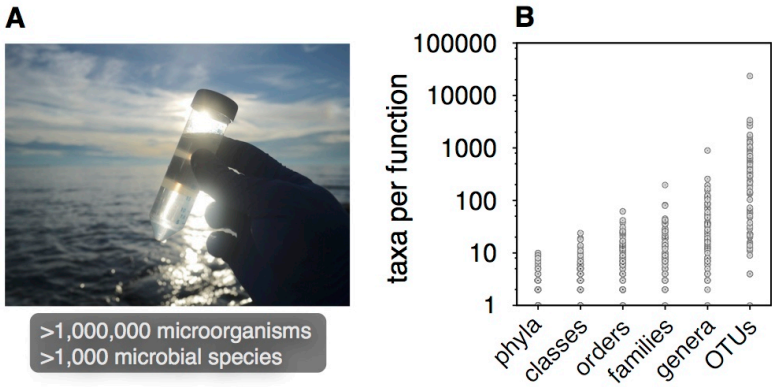

Figure 1. Microbial diversity in the global ocean microbiome. (A) A single teaspoon of seawater can contain millions of microorganisms and thousands of microbial species. (B) Many different taxa contain genes enabling them to perform the same metabolic functions (e.g. photosynthesis or methane oxidation). The figure shows the number of taxa associated with each function (one dot per function), for various taxonomic resolutions (e.g., phyla, classes, orders etc.). At the finest taxonomic resolution (operational taxonomic units, or OTUs), some of these functions may be performed by thousands of OTUs. Hence, the question arises whether we can model biogeochemical processes based on the population dynamics of the genes responsible for various functions, rather than of the organisms hosting them. Fig. B adapted from (2).

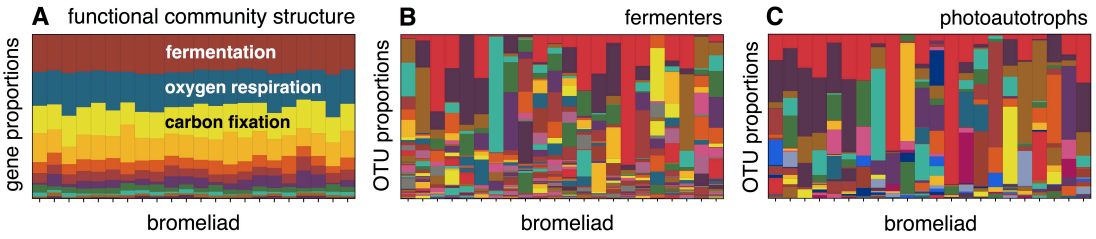

Figure 2. Functional stability despite taxonomic variability in microbial communities across bromeliads. (A) Functional structure of microbial communities, in terms of the relative abundances of genes associated with various metabolic pathways (one color per gene group, one column per bromeliad). (B,C) Taxonomic composition within individual functional groups (B: fermenters; C: photoautotrophs), in terms of the proportions of operational taxonomic units (OTUs, a prokaryote species analog; one color per OTU, one column per bromeliad). Adapted from (3).

To further explore the generality of these findings at a larger scale, I analyzed DNA sequencing data from the recent Tara Oceans global microbiome survey (4), in combination with oceanographic data from satellite imaging and cruises. By classifying >30,000 marine microorganisms into various metabolic functional groups (Figure 3), I was able to disentangle functional from taxonomic community variation across space and time (2). Using multivariate non-linear regression, I showed that physical and chemical environmental conditions strongly explained the distribution of microbial functional groups across the world's oceans, but only poorly explained the taxonomic composition within individual functional groups, consistent with my previous observations in bromeliads. Hence, microbial

community assembly appears to exhibit two roughly independent "axes of variation": Functional composition, which is mainly determined by the environment, and taxonomic composition within functional groups, which can vary widely despite functional constancy.

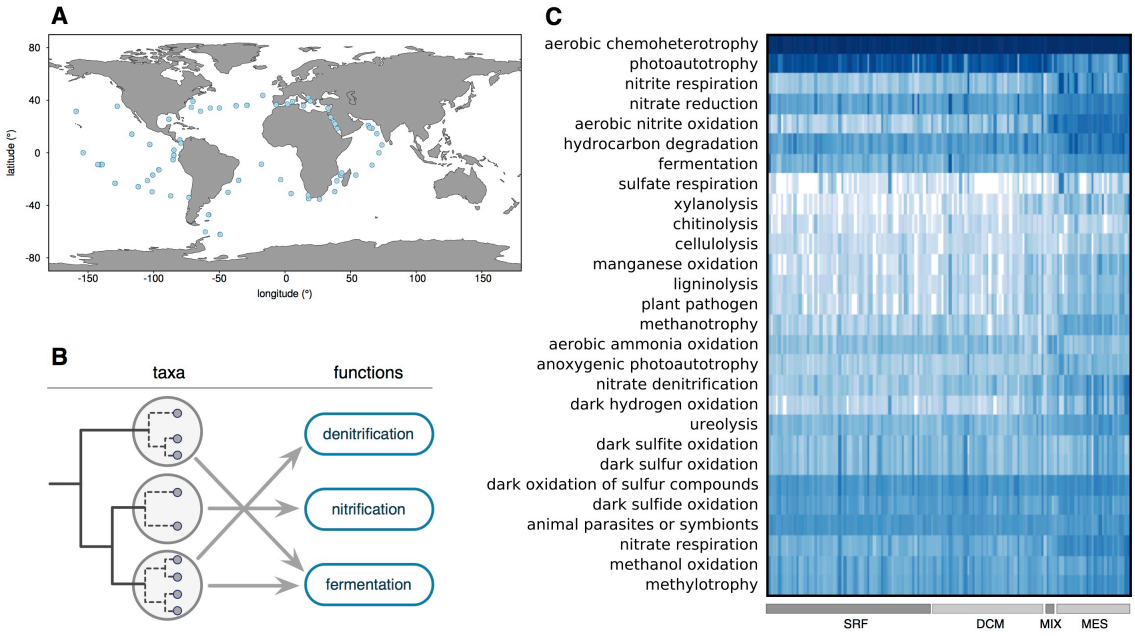

Figure 3. Decoupling function and taxonomy in the global ocean microbiome. (A) Geographical locations of samples used to examine the relationship between taxonomic and functional composition of ocean microbial communities (2). Data from (4). (B) Schematic of method used to estimate the functional composition of microbial communities, in terms of the abundance of metabolic functional groups: Microbial taxa detected using DNA sequencing were mapped to functional groups, such as denitrification or nitrification, based on experimental evidence from the literature. (C) Estimated profiles of microbial communities in terms of various metabolic functional groups (rows) across the ocean (one column per sample). Darker colors correspond to higher relative abundances of functional groups. Samples are grouped according to water column zone (SRF: surface water; DCM: deep chlorophyll maximum; MIX: mixed layer; MES: mesopelagic). Profiles reveal that in terms of metabolic functions, microbial communities exhibit a highly predictable structure across depth, with anaerobic processes (such as nitrate respiration and fermentation) becoming particularly important in the mesopelagic zone. Adapted from (2).

III. Explaining the Decoupling Between Function and Taxonomy

If environmental conditions are strongly coupled to the metabolic function of microbial communities, but exert less influence on who gets to perform each function, then this means that other mechanisms cause taxonomic variation over space or time while potentially maintaining stable (or predictable) metabolic functioning. To better understand what these mechanisms may be, I used statistical techniques from community ecology, including null model testing and variation partitioning. Both in bromeliads (3) and across the global ocean (2), I found that the taxonomic variation within functional groups could not be explained by neutral stochastic drift nor by spatial dispersal processes, and that this variation was potentially driven by deterministic biotic interactions. Such biotic interactions could potentially include phage-host interactions, whereby specialist phages induce the temporary collapse of their host populations whenever these reach high densities, thus allowing competing populations with similar nutritional requirements to invade. Using simulation models (Figure 4), I demonstrated that such and other biotic interactions could indeed

promote intense taxonomic turnover within functional groups, while maintaining relatively stable bulk metabolic process rates (5,6). A key prediction of my models was that this decoupling between function and taxonomic composition becomes stronger as the local microbial diversity within each functional group (i.e., the "functional redundancy") becomes larger.

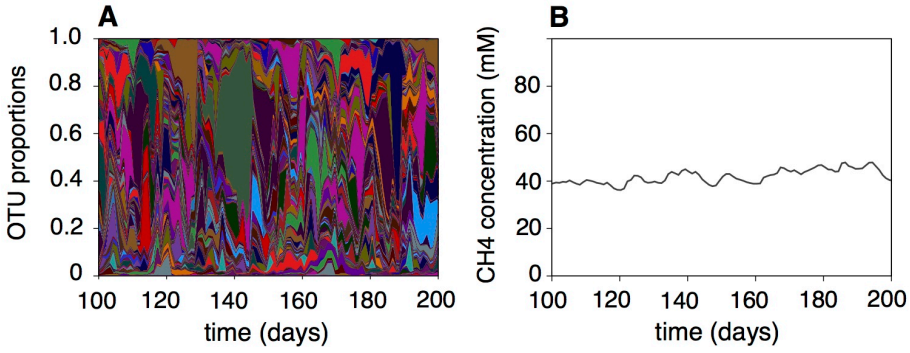

Figure 4. Example simulation of a model for a flow-through methanogenic bioreactor, where input glucose is transformed into methane by a microbial community. (A) Taxonomic community composition over time (in terms of proportions of operational taxonomic units, or OTUs; one color per OTU). (B) Methane ($\mathbf{CH_4}$) concentration in the bioreactor's effluent over time. The model is able to explain how microbial communities can maintain constant metabolic performance (in this case methane production) while being highly variable in terms of their taxonomic composition. Adapted from (6).

IV. PATHWAY-CENTRIC MODELING OF ECOSYSTEM BIOGEOCHEMISTRY

The above findings motivated me to develop pathway-centric mathematical models for specific natural and engineered ecosystems (7,8). These models explicitly consider the dynamics of microbial metabolic pathways at ecosystem scales, regardless of the taxonomic diversity associated with each pathway. Notably, I constructed a biogeochemical model for the oxygen-depleted water column in Saanich Inlet, a heavily studied fjord off the coast of Vancouver Island (8). Oxygen-depleted zones are widespread regions of the ocean in which microbial anaerobic processes exert a disproportionate influence on global nitrogen and sulfur budgets, with resulting feedbacks on marine primary productivity and climate. My model describes the growth dynamics and activity of metabolic pathways involved in carbon, nitrogen and sulfur cycling in Saanich Inlet (Figure 5A), using a system of reaction-advection-diffusion equations of the following structure:

$$\frac{\partial E}{\partial t} = \frac{\partial}{\partial z}\left(D\frac{\partial E}{\partial z}\right) - v\frac{\partial E}{\partial z} - qE + \frac{\beta}{m}R \cdot \Delta G.$$

Here, E is the pathway (or gene) density as a function of depth and time, R is the reaction rate and ΔG is the Gibbs free energy of the reaction. The first two terms correspond to turbulent transport across the water column, the 3rd term corresponds to enzyme degradation and the last term to the conversion of energy into biomass. This model was calibrated using chemical concentration measurements (Figure 5B), and was able to largely explain independent DNA, mRNA and protein sequence data provided by collaborating labs (Figure 5C). The model yielded detailed insight into the microbial processes in oxygen-depleted water columns, with important implications for marine nitrogen cycling. More generally, this work revealed that gene abundances and geochemical conditions largely determine gene expression patterns and biogeochemical process rates, demonstrating the predictive potential of pathway-centric

mathematical models for microbial ecology.

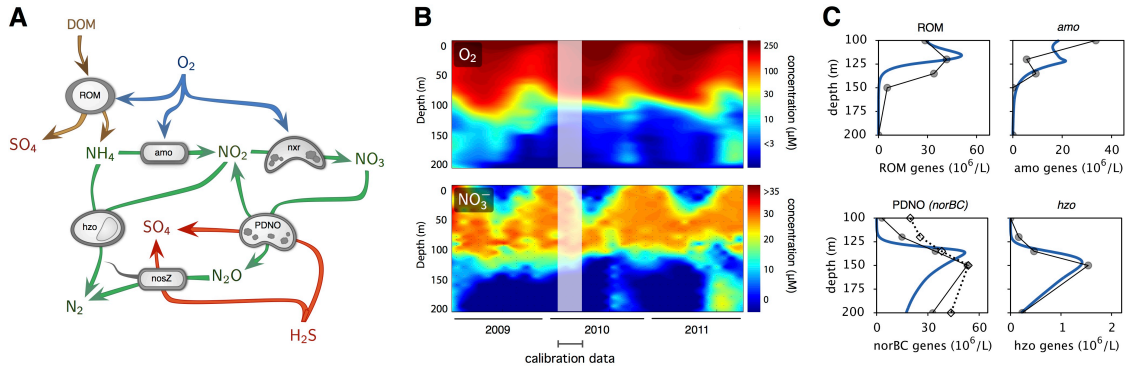

Figure 5. Pathway-centric modeling of carbon, nitrogen and sulfur cycling in Saanich Inlet. (A) Structure of the modeled metabolic network. Arrows represent chemical fluxes catalyzed by various microbial metabolic pathways. (B) Oxygen ($\mathbf{O_2}$) and nitrate ($\mathbf{NO_3^-}$) depth profiles in Saanich Inlet, over the course of 3 years (2009-2011). The shaded interval marks the chemical data used to calibrate the model. (C) DNA concentration profiles for a subset of modeled pathways (ROM: remineralization of organic matter; *amo*: aerobic ammonia oxidation; PDNO: partial denitrification to nitrous oxide; *hzo*: anaerobic ammonia oxidation), as predicted by the model (blue curves) and compared to metagenomic sequence data taken in February, 2010 (grey dots). Adapted from (8).

V. Conclusions

My work has shown that, to a certain approximation, environmental conditions and the induced metabolic functioning of microbial communities can become decoupled from the taxonomic composition within individual functional groups. On the one hand, this decoupling between function and taxonomy allows for the formulation of elegant pathway-centric ecosystem models. Pathway-centric theories for microbial ecology also directly profit from metagenomic sequencing, which provides information on the genetic content of a community regardless of the taxa present. On the other hand, the decoupling between function (or environmental conditions) and taxonomy challenges conventional approaches to modeling the distribution of microbial taxa based on environmental variables alone. Indeed, building accurate microbial taxon distribution models may turn out to be a Sisyphean struggle. Disentangling the variation in "function space" from the variation in the "residual taxon space" (i.e. within functional groups), as demonstrated in my thesis (2,3), will be an important step in future microbial ecological studies.

VI. Acknowledgements

I would like to express my deep appreciation to my PhD supervisor, Michael Doebeli. I would like to thank all of my collaborators, from whom I've learned a lot and with whom I was able to accomplish much of the work presented here: Laura Parfrey, Steven Hallam, Vinicius Farjalla, Mellisa Chen, Alyse Hawley, Sean Crowe, Aria Hahn, Sergei Katsev, Captain Monica Torres-Beltran, Maya Bhatia, Celine Michiels, David Capelle, Gaute Lavik, Sam Kheirandish, Saulo Jacques, Aliny Pires, Juliana Leal and Diane Srivastava. I am grateful to the Department of Mathematics, University of British Columbia (UBC), to the Pacific Institute for the Mathematical Sciences (PIMS) and to the Natural Sciences and Engineering Research Council of Canada (NSERC) for funding. Thanks to the Biodiversity Research Centre for hosting me during my PhD. I sincerely thank the ESMTB awarding committee for choosing my thesis for the Reinhart Heinrich Doctoral Thesis Award 2016, and for the opportunity to publish my thesis summary in this issue of ECMTB. I thank Eva Kisdi

for nominating me for this award.

VII. References

1. Falkowski PG, Fenchel T, Delong EF. The microbial engines that drive earth's biogeochemical cycles. Science. 2008;320(5879):1034–9.
2. Louca S, Parfrey LW, Doebeli M. Decoupling function and taxonomy in the global ocean microbiome. Science. 2016;353(6305):1272–7.
3. Louca S, Jacques SMS, Pires APF, Leal JS, Srivastava DS, Parfrey LW, et al. High taxonomic variability despite stable functional structure across microbial communities. Nat Ecol Evol. 2016;1:15.
4. Sunagawa S, Coelho LP, Chaffron S, Kultima JR, Labadie K, Salazar G, et al. Structure and function of the global ocean microbiome. Science. 2015;348(6237).
5. Louca S, Doebeli M. Transient dynamics of competitive exclusion in microbial communities. Environ Microbiol. 2015;18(6):1863–74.
6. Louca S, Doebeli M. Taxonomic variability and functional stability in microbial communities infected by phages. Environ Microbiol [Internet]. 2017;in press. Available from: http://dx.doi.org/10.1111/1462-2920.13743
7. Louca S, Doebeli M. Reaction-centric modeling of microbial ecosystems. Ecol Modell. 2016;335:74–86.
8. Louca S, Hawley AK, Katsev S, Torres-Beltran M, Bhatia MP, Kheirandish S, et al. Integrating biogeochemistry with multiomic sequence information in a model oxygen minimum zone. Proc Natl Acad Sci. 2016;113(40):E5925--E5933.

Thesis abstract for the ESMTB Communications

Dangerous connections: the spread of infectious diseases on dynamic networks

KaYin Leung, kayin.leung@math.su.se
Supervisors: Odo Diekmann and Mirjam Kretzschmar

Do concurrent partnerships (partnerships overlapping in time) drive HIV epidemics in sub-Saharan Africa? More than a decade ago, this hypothesis was put forward as an explanation for the HIV epidemics among heterosexual populations in this region. The concurrency hypothesis has been widely debated, and that motivated my PhD research. We set out to study the concurrency question from a mathematical modeling perspective.

Dynamic networks models: understanding concurrency and HIV

Mathematical models have proven to be very useful in understanding infectious disease dynamics. Traditionally, mass action contacts are assumed. This means that, in the large population limit, two individuals meet no more than once. While this assumption may be reasonable for e.g. host-vector diseases such as malaria, for sexually transmitted infections such as HIV (and the role of concurrent *partnerships*) it no longer suffices. It becomes essential to take the underlying sexual network of the population into account. In case of HIV, the time scale of the infection necessitates the incorporation of partnership dynamics due to individuals forming and breaking partnerships over time as well as demographic turnover due to individuals becoming sexually (in)active. We set out to develop and analyze an analytically tractable modeling framework for the spread of infection on dynamic networks incorporating demography.

The development of the framework enabled us to study epidemiological questions related to concurrency and HIV. We showed that concurrency could drive an HIV epidemic by moving the basic reproduction ratio R_0 across the epidemic threshold. We also showed that gender asymmetry in concurrency is related to lower disease prevalence. These studies yielded better qualitative understanding of the role that concurrency could have in HIV epidemics. Moreover, the strength of the two studies lies on the methodological side. We carefully defined scenarios that enabled us to study the effect of a specific property on the disease dynamics.

Model formulation and analysis

The modeling framework itself turned out to be the main focus of my PhD research. The general idea of the framework is as follows. In the tradition of physiologically structured population models, we start by modeling individual-level behavior. We keep track of individuals and their partners, but not of partners of these partners. The latter are dealt with through the mean field at distance one assumption. The key feature is that each individual can be decomposed into a number of conditionally independent *binding sites*. While we model individual-level behavior (via the binding sites), our interest lies in the population-level dynamics. (Can an epidemic outbreak occur? What would be the endemic prevalence? Etcetera.) A systematic procedure relates the three levels of binding sites, individuals, and the population to each other. At the binding-site and individual level we deal with Markov chain descriptions. Population-level influences are captured through environmental variables, e.g. the propensity of an individual to form a new partnership depends, among others, on the

overall ‘availability’ of partners in the population (we have only three environmental variables in the simplest setting). By relating the binding sites – via individuals – to the population we obtain a deterministic description at the population level. This allows us to close the feedback loop: we end up with only a few equations for the environmental variables. These equations capture the dynamics at all three levels. Moreover, they enable us to characterize important epidemiological quantities such as R_0.

More on R_0

Let’s discuss R_0 in some more detail. R_0 is often considered *the* most important quantity in infectious disease dynamics. We can interpret it as the expected number of secondary transmissions caused by one typical newly infected individual at the beginning of an epidemic. Part of the attraction of R_0 is due to the clear individual-level interpretation while at the same time informing us about population-level dynamics: R_0 is a threshold parameter for an epidemic outbreak to occur if infection is introduced in a fully susceptible population.

Sometimes, it can be beneficial to take a different perspective on things. This was very much true for R_0 in my PhD research. In the context of the binding site formalism, if we consider transmission ‘opportunities’ rather than *actual* transmissions, deriving R_0 becomes a piece of cake, while maintaining the biological interpretation. All we need is the linearization in the trivial steady state of two equations for the environmental variables. This yields a 2x2 next-generation matrix of which R_0 is the dominant eigenvalue. In particular, we obtain an explicit expression for R_0. In contrast, the classical perspective on R_0 would start with the linearization of a rather high dimensional system of ordinary differential equations that, after much work, can be reduced to obtain the same expression for R_0. Clearly, the first approach with little work is preferred (we took the laborious route first, see chapters 3 and 4 of my thesis).

To conclude

This abstract has hopefully aroused interest in the binding site formalism for infectious disease spread on dynamic networks incorporating demography (and you will continue to read the actual thesis). The binding site formalism is, hopefully, a useful addition to the mathematical toolbox for infectious disease dynamics. The simplicity of the formalism allows for better qualitative understanding into transmission dynamics on networks such as understanding questions related to concurrency and HIV. Even if reality is simplified in many ways, the formalism is flexible and easily allows for several meaningful generalizations. Furthermore, it could serve as the foundation for more complex models. Finally, part of the beauty of research is that no model is ever the end of the story. In particular, after the completion of my thesis, we gained better understanding of the subtleties involved with the mean field at distance one assumption (or: how does one deal with partners of partners).

Thesis

KY Leung (2016). Dangerous connections: the spread of infectious diseases on dynamic networks. PhD thesis. Utrecht University. http://dspace.library.uu.nl/handle/1874/334192

Abstract of "Modelling cell migration, proliferation and interactions on growing domains"

Robert J. H. Ross
Wolfson Centre for Mathematical Biology, Mathematical Institute, University of Oxford, Radcli_e Observatory Quarter, Woodstock Road, Oxford, OX2 6GG
Supervisors:
Professor Ruth E. Baker, Wolfson Centre for Mathematical Biology, Mathematical Institute, University of Oxford
Dr Christian A. Yates, Centre for Mathematical Biology, Department of Mathematical Sciences, University of Bath

My doctoral thesis focusses on developing mathematical tools to model many-body processes on growing domains. The motivation for this focus was to develop methods to more accurately describe the behaviour of migratory cell populations found during embryonic development. This is important as domain growth is often implemented in an overly simplistic manner in mathematical models of developmental processes. To accurately model migratory cell populations on growing domains it was necessary to develop a novel mathematical framework [1]. This framework was required so that I could model the evolution of spatial correlations between cells on growing domains. Consequently, I was able to generate new hypotheses about the behavior of migratory cell populations on growing domains, such as how domain growth can generate cell patterning [2, 3]. My doctoral work also included a successful collaboration with developmental biologists from the University of Edinburgh, in which I modelled the migration of melanoblasts in murine embryonic development [4]. By means of this collaboration I proposed a novel mechanism for the colonisation of the epidermis by melanoblasts in the embryonic mouse [4]. This novel mechanism was a departure from the predominant thinking at the time that colonisation of the epidermis by melanoblasts required complex cell-cell interactions or extracellular signals. In a separate project, also with my experimental collaborators, I suggested time and cost-saving alterations to a commonly performed experiment for identifying cell motility parameters [5]. This work on parameter estimation used approximate Bayesian computation, and could have very important experimental implications for parameter identification in cell migratory processes.

The research component of my thesis begins in Chapter 2 with a study of how a type of neural crest stem cell (melanoblasts) colonises the epidermis during murine development [4]. The failure of neural crest stem cells to correctly develop is associated with many human birth defects. In addition, it has been shown that children with neurofibromatosis type 1 have an elevated risk of developing certain cancers. Therefore, studying melanoblast colonisation of the epidermis during embryonic development has significant clinical relevance. I have shown, through the use of an individual-based model (IBM) parameterised by experimental data, that a simple mechanism consisting of undirected cell migration and proliferation, in tandem with domain growth, can account for the colonisation of the epidermis by melanoblasts in the embryonic mouse.

The IBM, in conjunction with experimental data, also suggests that impaired proliferation in melanoblasts is the cause of piebaldism in mice rather than impaired migration. This result challenged a long-held perspective that piebaldism is caused by a defect in melanoblast

motility, and received a significant amount of press coverage[1]. Importantly, my work demonstrates that colonisation of the epidermis by melanoblasts is achieved without the need for complex cell-cell interactions or extracellular signals. This result has broader implications for cell behaviour in other neural crest stem cell lineages and their associated neurocristopathies.

The central topic of Chapters 4, 5 and 6 of my thesis is deriving accurate continuum approximations of IBMs that include agent proliferation and domain growth. In Chapter 4 I present methods to include the effects of domain growth on the evolution of spatial correlations between agents in a continuum approximation of a one-dimensional exclusion process model of cell motility and proliferation [1]. To model the effect of domain growth on spatial correlations it was necessary to develop a novel mathematical framework. I include the effect of spatial correlations by deriving a system of ordinary differential equations (ODEs) that describe the expected evolution of individual and pairwise density functions for agents on a growing domain. I then demonstrate how to simplify this system of ODEs using an appropriate approximation. This simplification allows domain growth to be included in models describing the evolution of spatial correlations between agents in a tractable manner.

In order to describe cell migratory processes more realistically it is necessary to extend the methods presented in Chapter 4 to higher dimensions. Therefore, in Chapters 5 and 6 I present methods to include the effects of domain growth on the evolution of spatial correlations between agents in a continuum deterministic approximation of a two-dimensional model of cell motility and proliferation [2]. In Chapter 5 I show that, depending on the way in which domain growth is implemented, different steady state densities are predicted for otherwise identical agent populations. Furthermore, I demonstrate that depending on the specific implementation of domain growth, the initial size of the IBM domain may impact upon the evolution of the agent density. In Chapter 6 I extend the results presented in Chapter 5 to show that, depending on the way in which domain growth is implemented, different species dominate in multi-species simulations [3]. Continuum approximations of the IBM that ignore spatial correlations cannot capture any of the aforementioned behaviour, while those that account for spatial correlations can. The results in Chapters 5 and 6 show that the mechanism used to implement domain growth can determine the long term behaviour of agent populations, and in certain circumstances, establish patterning.

In order to employ the modelling approaches developed in Chapters 3 to 6 to represent biological systems of interest and generate experimentally testable hypotheses, it is necessary to accurately parameterise them. Therefore, in Chapter 7 I develop methods to identify parameters for cell motility and adhesion in a simple wound-healing experiment [5]. Building on the results of Chapter 3 I implement different cell-cell interactions in an IBM simulating a wound-healing experiment, and address issues of parameter identifiability and experimental design. I show that, given an unrealistic experimental design, cell motility and adhesion parameters can be successfully retrieved from synthetic data using approximate Bayesian computation. However, this unrealistic experiment lies beyond current experimental limits. As such, using my IBM I then improve the design of a practically realisable experiment, and show that estimation of model parameters is more accurate if the domain upon which the

[1] Piebald mystery solved: scientists discover how animals develop patches (The Guardian), Black and white cats `owe distinctive colouring to faulty genes' (The Independent).

experiment is performed is expanded, as opposed to increasing the number of experimental replicates. This means an experimentalist interested in parameterising a cell migratory process is better served by simply increasing the field of view of the microscope used in the experiment, rather than increasing the number of experimental replicates. The findings presented in this chapter of the thesis will be of particular interest to those concerned with performing experiments that enable the effective parameterisation of cell migratory processes. More generally, I also suggest time and cost-saving alterations to a commonly performed experiment for identifying cell motility parameters.

To conclude, in my doctoral thesis I present methods to describe the behaviour of motile, proliferative and interactive cells on growing domains. My thesis demonstrates many novel results. These include the mechanisms by which melanoblasts colonise the epidermis during murine embryonic development, the effects of domain growth on cell patterning, and potential time and cost-saving alterations to a commonly performed experiment for identifying cell motility parameters. The mathematical and scientific developments presented in my doctoral thesis means it is of interest to both theoretical and experimental researchers alike.

References

[1] R. J. H. Ross, C. A. Yates, and R. E. Baker. The effect of domain growth on spatial correlations. Physica A, 466:334{345, 2017.
[2] R. J. H. Ross, R. E. Baker, and C.A. Yates. How domain growth is implemented determines the long term behaviour of a cell population through its effect on spatial correlations. Physical Review E, 94(1):012408, 2016.
[3] R. J. H. Ross, C. A. Yates, and R. E. Baker. Variable species densities are induced by volume exclusion interactions upon domain growth. Physical Review E, 95(3):032416, 2017.
[4] R. L. Mort, R. J. H. Ross, K. J. Hainey, O. Harrison, M. A. Keighren, G. Landini, R. E. Baker, K. J. Painter, I. J. Jackson, and C. A. Yates. Reconciling diverse mammalian pigmentation patterns with a fundamental mathematical model. Nature Communications, 7 (10288), 2016.
[5] R. J. H. Ross, R. E. Baker, M. Parker, A. Ford, R. L. Mort, and C. A. Yates. Using approximate Bayesian computation to quantify cell-cell adhesion parameters in a cell migratory process. npj Systems Biology and Applications, 3(9), 2016.

Yuval Zelnik

Regime Shifts in Spatially Extended Ecosystems

Ben-Gurion University of the Negev, Beer-Sheva, Israel
Advisors: Prof. Ehud Meron and Prof. Golan Bel

The research of regime shifts revolves around the notion that many systems are bistable or multistable, so that more than one possible state of the system is stable for the same set of parameters. In these conditions, abrupt (catastrophic) regime shift may occur, where the system transitions quickly and irreversibly between qualitatively different states due to a small change in external conditions or a small perturbation of the system's state itself. The aim of my thesis was to investigate the validity of such results for explicitly spatial systems, and develop an understanding of transitions that are unique to spatially extended systems. In many ecosystems, and in particular in dryland vegetation systems, the spatial structure of the system is heterogenous due to internal processes that lead to emergent patchiness. Periodic patterns are often observed in such dryland ecosystems, and several model studies have explained their properties and mechanisms. I thus focused on using models for dryland vegetation to explore the dynamics of ecosystems where a bistability between periodic vegetation patches and either bare-soil or uniform-vegetation exists. In particular, specific attention was given to the phenomena of localized states, a spatial mix between a periodic state and a uniform one. Localized states have been recently found in many models with bistability of periodic patterns and uniform states, and have been shown to have significant effects on the properties and possibility of regime shifts in these systems. My thesis focused on four research projects that were later published as individual papers in different journals. I present each of these below in their chronological order, briefly describing the main results and conclusions drawn from them. The common thread in all of these was using theoretical models of dryland vegetation to understand the variety of patterns observed, and explore the dynamics that occur in such systems.

In the first study we used different models of dryland vegetation to explore the dynamics of regime shifts, and desertification in particular, in dryland ecosystems. All the models considered predict the same basic vegetation states and stability properties along a rainfall gradient, including a bistability range of bare soil and periodic spot patterns. In particular, a multitude of patterns with different wavelength exist within the same parameter range. Our study found that different transitions can occur in these systems, the first and simplest is a global abrupt transition from the spot-pattern state to the bare-soil state, due to a small change in conditions or a global disturbance. Local disturbances, on the other hand, can lead to shift to a different periodic pattern with a different length-scale. Most strikingly, in all models the bare-soil state never grows at the expense of the periodic-pattern state throughout the entire bistability range; bare-soil domains either stay fixed in size or contract and disappear. This implies that desertification cannot occur as a gradual process by front propagation, but only as an abrupt shift. These results raise several open questions, such as whether bare-soil expansion can be explained by water-biomass interactions alone, or additional processes must be considered. From the perspective of pattern formation theory the finding that the bare-soil state never expands into patterned states questions the utility of the Maxwell-point concept in this context and calls for further mathematical analysis.

Our second study focused on the interplay between different mechanisms for pattern formation. Vegetation pattern formation is driven by positive feedbacks between local vegetation growth and water transport towards the growing vegetation. The depletion of water in the vicinity of the growing vegetation inhibits the growth there and promote nonuniform vegetation growth. At least three mechanisms of water transport can be distinguished: Overland water flow due to higher infiltration rates in dense vegetation (``infiltration feedback''), fast soil-water diffusion coupled to strong water uptake (``uptake-diffusion feedback''), and water conduction by laterally extended root zones (``root-augmentation feedback''). We focuses on the first two mechanisms, that lead to spatial distributions of biomass and water which are in-phase and anti-phase respectively. Surprisingly, we found that the

combination of these two mechanisms leads to the growth of a single mode that is neither in-phase nor anti-phase. Nevertheless, the instability does contain information about the two distinct modes - beyond the instability point there is a family of periodic patterns ranging continuously from in-phase to anti-phase patterns. This behavior is unlike the more typical case of combining two distinct pattern-forming mechanisms, which only show the distinct modes and combinations thereof. This predicted multiplicity of biomass-water spatial distribution bears on the biodiversity of water-limited ecosystems, as different patterns of biomass and water density imply different niches for various plans and animals.

In the third study we have focused more concretely on asking wether a gradual regime shift may be occurring in a given ecosystem. We chose as a case-study the fairy circles in Namibia, a well studied ecosystem exhibiting patterned vegetation of a uniform matrix of perennial grass, punctured by circular gaps of bare soil some 4-8 m across, that form a semi-regular pattern. Various explanations for the formation of fairy circles were suggested, ranging from poisonous gas to the feeding habits of ants. Different studies have shown a strong correlation between certain termite species and of fairy circles, suggesting that termites are the cause of their formation. On the other hand, fairy circles have been suggested to be an emergent phenomenon in the context of pattern formation, explaining the spatial structure, but lacking a specific physical mechanism. Finally, a recent study reported observations of the formation of fairy circles and the disappearance of others. Using a simple mechanistic pattern-forming model, we showed how the formation of fairy circles can result from interactions between water and vegetation. We compared the dynamics seen in satellite images to model simulations to show that both transitions may be the consequence of short periods of droughts or heavy-rains. We also showed that both changes in fairy circle number and in their size are correlated to rain events. Our study shows how a spatial analysis of ecosystem transitions highlights the complex dynamics of these systems. It give credence to pattern-formation as the underlying mechanism of fairy circles, as well as highlight the possible regime shift that may be occurring in this system. In particular it suggests that dryland ecosystems may undergo gradual transitions due to their spatial heterogeneity. Of practical interest is that these transitions can occur when the system is still within the bistability range, and far form the critical point.

In the fourth study we focused on how changing conditions and repeated disturbances can induce different regime shifts in dryland ecosystems. We focused on two bistability ranges, between patchy vegetation and either uniform-vegetation or bare-soil, and compared the system response to perturbations in these two parameter ranges. We found that oscillations in precipitation, can lead to markedly different results in the two bistability ranges. For the bistability with uniform-vegetation, large enough perturbations always lead the system to the same preferred patterned state, but the speed of the transition depends on the amplitude of the oscillations. For the other bistability, the amplitude determined which final state the system will reach, but in all cases the shift was fast – within a few periods. The model therefore suggests that the process of desertification may be gradual for higher precipitation rates, but tends to be more abrupt as the system gets close to the bare-soil state. We also considered at the effect of repeated local disturbances, by removing vegetation spots at random locations. We found that at the low precipitation range the system always crashes to a bare-soil state, while for intermediate precipitation the system responds quickly so that the effect of disturbances is negligible. Interestingly, for high precipitation the system is highly plastic due to the existence of localized states, so that the system response is very local. This also means that if the initial conditions are of (stable) low overall vegetation, then the local disturbances actually increase the overall vegetation over time.

Minutes of the ESMTB Board meeting

Minutes of the ESMTB Board meetings during ECMTB 2016
Nottingham, 10th-15th July 2016

During the ECMTB 2016 in Nottingham the Board of ESMTB convened on several occasions, including a joint meeting with the Board of the Society for Mathematical Biology (SMB).

Present (at at least one of the meetings): Barbara Boldin (BB, Minutes), Reinhard Bürger (RB), Andrea de Gaetano (AdG), Susanne Ditlevsen (SD), Torbjörn Lundh (TL), Anna Marciniak-Czochra (AMC), Roeland Merks (RM, Chair), Ryszard Rudnicki (RR), Vitaly Volpert (VV)
Absent with apology: Frank Hilker

1. Minutes of the previous ESMTB Board meeting

Minutes of the previous ESMTB Board meeting are approved. They can be found in the 2016 edition of ESMTB Communications.

2. 2018 is The Year of Mathematical Biology

The Year of Mathematical Biology is a joint venture of the European Mathematical Society (EMS) and ESMTB. The main objectives are to celebrate the huge increase and importance of applications of mathematics to biology and life sciences in the last years and to foster the feedback-loop between life sciences and mathematics for years to come (see http://www.euro-math-soc.eu/year-mathematical-biology-2018 for more information).

Among the activities that are already planned in the Year of Mathematical Biology are:

- the 11th ECMTB in Lisbon (Portugal), organised jointly by ESMTB and EMS (see below),
- a thematic program in Mathematical biology at the Mittag-Leffler Institute in Sweden (september – december 2018). Torbjörn Lundh, who is a member of the organising committee briefly introduces the preliminary program,
- an intensive Research program in Mathematical biology at the Centre de Recerca Mathematica, Spain (april – june 2018),
- a workshop on Mathematical perspectives in the biology and therapeutics of cancer at CIRM Luminy, France (july 2018),
- activities at the Banach Center in Bedlewo and in Warsaw, Poland. Ryszard Rudnicki announces planned activities, including a school on Modern mathematical techniques for biological sciences, workshops on Structured population models, Information transmission in biological systems, Recent progress in chemotaxis, From individual based models to structured populations and the Simons semester on Mathematical Biology.

Three ESMTB Board members who are also members of the organisation committee for the Year of Mathematical Biology (AMC, TL and RM) will keep an up-to-date list of planned activities. The list will available on http://www.euro-math-soc.eu/year-mathematical-biology-2018 and on the ESMTB website www.esmtb.org.

In addition to The Year of Mathematical Biology, it is proposed that from 2018 on, the 10th of October is declared the annual global Day of Mathematical Biology. ESMTB should encourage its members to act as national coordinators and organise events in mathematical biology in their countries.

3. Joint meeting with the Board of SMB
During ECMTB 2016 in Nottingham, the Board of ESMTB met with the Board of the Society for Mathematical Biology. The president of SMB, Santiago Schnell (SS), expresses his gratitude regarding joint ESMTB-SMB conferences. Among the discussed themes are:

- The Year of Mathematical Biology: SS informs the Board that in addition to the events mentioned above, activities in Mathematical biology are planned at the Fields Institute in Toronto. Additional events are in preparation.
- SS puts forward an idea that, in addition to conferences, workshops and summer schools, the Year of Mathematical Biology would be celebrated with special issues in the Journal of Mathemat-ical Biology and the Bulletin of Mathematical Biology (the official journals of ESMTB and SMB, re-spectively) that will reprint classics in mathematical biology, annotated or discussed by today's leading experts. The idea will be discussed with the editors-in-chief of the two journals.
- Future joint ESMTB-SMB conferences: ESMTB has a serious offer for the organisation of ECMTB in 2020, which may also be the opportunity for the next joint conference with SMB. The offer is met with SMB Board's approval and potential dates are discussed.

4. ECMTB 2016
Markus Owen, the chair of the organising committee of ECMTB 2016 in Nottingham offers some information about the conference. The conference hosts roughly 850 participants from 45 countries. A more detailed report will be available after the conference and printed in the next issue of ESMTB Communications. The Board thanks Markus Owen and his team for a most enjoyable and very well organised conference.

5. ECMTB 2018
The 11th European Conference on Mathematical and Theoretical Biology will take place at the The Faculty of Sciences of the University of Lisbon, Portugal during 23rd and 27th July 2018. This time round, ECMTB is a joint venture of ESMTB and EMS. More information will be available in due course on the conference website (in preparation).

6. ESMTB Board elections in 2017
At the end of 2017, five ESMTB Board members (BB, RB, RM, RR and VV) will end their six-year term on the Board on ESMTB. RM announces election of new Board members in 2017. The candidates will be announced and presented to ESMTB members in the first half of 2017 via EMSTB website (www.esmtb.org), ESMTB Newsletter, Twitter account (@ESMTBio) and Facebook page (facebook.com/ESMTB).

7. ESMTB Communications
The 2016 issue of ESMTB Communications was prepared, printed and disseminated in time for ECMTB in Nottingham, largely due to the efforts of VV and RM. VV describes the contents of the current issue and informs the Board that the 2017 edition will be his last. The next issue is to continue with the "History of mathematical biology" section (AdG offers to write another article) as well as the "European teams in mathematical biology". Since the conference in Nottingham is already the 10th ECMTB, the Board will also invite Mats Gyllenberg to write an article that will offer a look back at the history of ECMTB. The Board thanks VV for his efforts.

8. EMS-ESMTB Summer schools
In 2016, two EMS-ESMTB summer schools will take place: the 2016 Helsinki Summer school on Mathematical Ecology and Evolution will take place during August 21st and 28th (this year's theme is Structured populations) and the Lorenz Center in Leiden will host the (initially planned for 2015) Summer school on Mathematical Biology of Tissue mechanics during July 25th and July 29th.. A more detailed report on the program of the two summer schools can be found in the 2016 edition of ESMTB Communications.

The theme of the 2017 EMS-ESMTB summer school, organised in Denmark by Susanne Ditlevsen during June 26th and June 30th 2017 is Mathematical neuroscience. The plans for the 2018 EMS-ESMTB Helsinki Summer school on Mathematical Ecology and Evolution are also already in motion. More information on these two summer schools will be available in due course.

9. ESMTB travel support

ESMTB offers travel support to its members. The renewed travel support system is described by AdG, who is in charge of handling the travel award applications. The new system is running smoothly and the Board members thank AdG for his work.

10. The Reinhart Heinrich prize

ESMTB annually awards a PhD thesis prize in honour of prof. Reinhart Heinrich (1946-2006). In 2014 the award for the best PhD thesis in the field of mathematical and theoretical biology was giv-en jointly to Aurélie Carlier (University of Louvain, Belgium) and Juan Carlos López Alfonso (Complutense University of Madrid, Spain). The winner of the 2015 Reinhart Heinrich award is Linus Schumacher (Oxford University, UK).

The deadline for the 2016 Reinhart Heinrich award is 30th November 2016. More information about the award can be found in ESMTB Communications and on the ESMTB website www.esmtb.org.

11. ESMTB website and ESMTB Infoletter

ESMTB Infoletter is organised and sent by AMC, currently still via Dresden. In the near future, the system will be moved to Heidelberg and AMC will handle the Infoletter as well as the website.

12. Ties with other societies

ESMTB is a member of EMS and ICIAM. The ties with EMS are strong: the two societies organise annual joint summer schools and have a joint venture in the 2018 Year of Mathematical Biology (see above).

The temporarily weakened ties with ICIAM are now once again strong, thanks to the efforts of AdG. The Board thanks AdG for renewing the contacts with ICIAM.

13. ESMTB memberships

At the time of the ECMTB in Nottingham, ESMTB has only about 140 members. A concern is expressed about the decline in membership numbers and in apparent lack of interest in Society's activities. RM will send out personalised e-mail payment reminders and encourage people working in the field of mathematical and theoretical biology to play an active part in ESMTB. Only with strong membership can the Society continue to fulfil its mission. More should also be done to promote the Society and its activities, especially among the young people.

Barbara Boldin
Secretary of ESMTB

Minutes of the General Assembly of ESMTB
Wednesday, 13th July 2016

The meeting starts at 12.45
ESMTB president Roeland Merks (RM) starts the meeting by welcoming roughly 25 participants.

RM briefly describes Society's history, its mission and activities.

I. Summer schools and travel support
One of the main activities of ESMTB is support and organisation of summer schools, workshops and conferences. Among these are the now bi-annual ECMTB and the joint EMS-ESMTB summer schools.

In 2016, two EMS-ESMTB summer schools will take place: the 2016 Helsinki Summer school on Mathematical Ecology and Evolution will take place during August 21st and 28th (this year's theme is Structured populations) and the Lorenz Center in Leiden will host the (initially planned for 2015) Summer school on Mathematical Biology of Tissue mechanics during July 25th and July 29th.

The theme of the 2017 EMS-ESMTB summer school, organised in Denmark during June 26th and June 30th is Mathematical neuroscience. The plans for the 2018 EMS-ESMTB Helsinki Summer school on Mathematical Ecology and Evolution are also already in motion. More information on these two summer schools will be revealed in due course.

The Society offers travel support to its members. Currently, ESMTB has only about 140 paying members. RM emphasizes that, since ESMTB's sole source of income are membership fees, it is vital to encourage people working in the field of mathematical and theoretical biology to become members. Only with strong membership can the Society continue to fulfil its mission.

II. The Reinhart Heinrich PhD thesis prize
ESMTB annually awards a PhD thesis prize in honour of prof. Reinhart Heinrich (1946-2006). In 2014 the award for the best PhD thesis in the field of mathematical and theoretical biology was given jointly to Aurélie Carlier (University of Louvain, Belgium) and Juan Carlos López Alfonso (Complutense University of Madrid, Spain). The winner of the 2015 Reinhart Heinrich award is Linus Schumacher (Oxford University, UK). All three awardees presented their PhD work during ECMTB 2016. RM encourages nominations for the 2016 Reinhart Heinrich award and announces that the deadline is 30th November 2016. More information about the award can be found in ESMTB Communications and on the ESMTB website www.esmtb.org.

III. 2018 is The Year of Mathematical Biology

The Year of Mathematical Biology is a joint venture of the European Mathematical Society (EMS) and ESMTB. The main objectives are to celebrate the huge increase and importance of applications of mathematics to biology and life sciences in the last years and to foster the feedback -loop between life sciences and mathematics for years to come (see http://www.euro-math-soc.eu/year-mathematical-biology-2018 for more information).

Among the activities that are already planned in the Year of Mathematical Biology are:

- the 11th ECMTB in Lisbon (Portugal), organised jointly by ESMTB and EMS (see below),
- a thematic program in Mathematical biology at the Mittag-Leffler Institute in Sweden (september – december 2018). Torbjörn Lundh, who is a member of the organising committee briefly introduces the preliminary program,
- an intensive Research program in Mathematical biology at the Centre de Recerca Mathematica, Spain (april – june 2018),
- a workshop on Mathematical perspectives in the biology and therapeutics of cancer at CIRM Luminy, France (july 2018),

- activities at the Banach Center in Bedlewo and in Warsaw, Poland. Ryszard Rudnicki announces planned activities, including a school on Modern mathematical techniques for biological sciences, workshops on Structured population models, Information transmission in biological systems, Recent progress in chemotaxis, From individual based models to structured populations and the Simons semester on Mathematical Biology.

More information about the events in The Year of Mathematical Biology will be available in due course on http://www.euro-math-soc.eu/year-mathematical-biology-2018.

In addition to The Year of Mathematical Biology, it is proposed that from 2018 on, the 10th of October is declared an annual global Day of Mathematical Biology.

IV. ESMTB Board elections

At the end of 2017, five ESMTB Board members (Barbara Boldin, Reinhard Bürger, Roeland Merks, Ryszard Rudnicki and Vitaly Volpert) will end their six-year term on the Board on ESMTB. RM announces election of new Board members in 2017 and invites all interested ESMTB members to run in the coming elections.

The candidates will be announced and presented to ESMTB members in the first half of 2017 via EMSTB website (www.esmtb.org), ESMTB Newsletter, Twitter (@ESMTBio) and Facebook (facebook.com/ESMTB).

V. ECMTB 2018

The 11th European Conference on Mathematical and Theoretical Biology will take place at the The Faculty of Sciences of the University of Lisbon, Portugal during 23rd and 27th July 2018. This time round, ECMTB is a joint venture of ESMTB and EMS. Carlos Braumann, who chairs the local organising committee presents the preliminary plans for ECMTB 2018.

More information about the conference will be available on the conference website in due course.

VI. Conclusion

Roeland Merks thanks the organizers of ECMTB 2016 for a most enjoyable and very well organised conference. Once again, a concern is raised about the decline in ESMTB membership numbers and the apparent lack of interest in Society's activities. More should be done to promote activities of ESMTB and to encourage young people to play an active part in Society's life.

The meeting ends at 13.15.

Barbara Boldin
Secretary of ESMTB

Minutes of the ESMTB Board meeting

Amsterdam, the Netherlands
12th May 2017

Present: Barbara Boldin (BB; minutes), Reinhard Bürger (RB), Andrea de Gaetano (AdG), Susanne Ditlevsen (SD), Roeland Merks (RM; chair), Torbjörn Lundh (TL)
Guest: Mats Gyllenberg (MG; Editor-in-chief of the Journal of Mathematical Biology)
Absent: Frank Hilker, Anna Marciniak-Czochra, Ryszard Rudnicki, Vitaly Volpert

The meeting starts at 9:20.

1. ESMTB Board elections 2017

The end of 2017 brings about the end of term for five members of the Board (Barbara Boldin, Reinhard Bürger, Roeland Merks, Ryszard Rudnicki and Vitaly Volpert). Elections for five new ESMTB Board members are planned for autumn 2017. The Board has put together a list of potential candidates for the coming elections. By the time of the meeting, six of them have accepted the invitation to run in the 2017 ESMTB Board elections (these are Maira Aguiar, Sandy Anderson, Ellen Baake, Ludek Berec, Bob Planque and Sander van Doorn). The Board agrees on a few additional potential candidates. When the list is finalised, the candidates will present themselves to ESMTB members via ESMTB Infoletter, ESMTB website and/or ESMTB Facebook account.

2. Report of the *ad interim* treasurer

In absence of treasurer Frank Hilker, the Society's previous treasurer Andreas Deutsch has kindly agreed to step in and help out with Society's finances. The Board is most grateful to Andreas Deutsch for all the help and expresses hope that the situation will be resolved in the near future.

RM presents a report on Society's membership and finances on behalf of the *ad interim* treasurer. At the end of 2016 ESMTB had 169 paying members. RM presents membership data categorised by members' country of affiliation, membership type and payment categories. Yet again, the need to promote the Society and its activities is emphasized.

In 2016 ESMTB issued travel support in the amount of 2.263,48 EUR and additional 910,00 EUR was granted to the awardees of the Reinhart Heinrich award. The ESMTB account balance at the time of the meeting is 27.688,59 EUR.

3. ESMTB member administration

The transfer of membership administration to Heidelberg has not been entirely successful and administration is still done with the help of Patrick Brösamle in Dresden, for which the Board is very grateful. A permanent solution is needed as soon as possible. It is decided that ESMTB start using a paid service to handle membership administration (e.g. Wild apricot, used by the Society for Mathematical Biology). The Society's next treasurer will be tasked to handle the transition.

4. 2018 - the Year of Mathematical Biology

The Year of Mathematical Biology 2018 is a joint venture of the European Mathematical Society (EMS) and ESMTB. The main objectives are to celebrate the huge increase and importance of applications of mathematics to biology and life sciences in the last years and to foster the feedback- loop between life sciences and mathematics for years to come (see http://euro-math-soc.eu/year-mathematical-biology-2018).

TL gives an update of the planned activities. The Year of Mathematical Biology kicks off with a mathematical weekend on the 4th and 5th of January 2018 in Joensuu, Finland, a joint effort of EMS, ESMTB and the Finnish Mathematical Society (for more details see http://www.uef.fi/web/matematiikanpaivat2018). Some of the other activities in the Year of Mathematical Biology are:

- 11th European Conference on Mathematical and Theoretical Biology (ECMTB 2018) in Lisbon (a joint conference of ESMTB and EMS),
- Simons semester on Mathematical biology at the Banach center in Poland,
- Thematic program in Mathematical biology at the Mittag-Leffler Institute in Sweden,
- Intensive research program in Mathematical biology at Centre de Recerca Matematica in Spain,
- Mathematical perspectives in the biology and therapeutics of cancer at CIRM, France
- Helsinki summer school on mathematical ecology and evolution in Finland
- Differential equations arising from organising principles in biology in Oberwolfach, Germany.

More information can be found on http://euro-math-soc.eu/year-mathematical-biology-2018.

In addition, the 10th of October is announced as the Day of Mathematical Biology, to be celebrated annually with events devoted to popularisation of Mathematical biology. The first Day of Mathematical biology in 2018 will occur during the Simons symposium at the Mittag-Leffler Institute in Sweden and will be celebrated with public lectures on mathematics in biology.

5. ESMTB travel grants

AdG reports on ESMTB travel grants system, the evaluation procedure and applications. The Board discusses ways to update the evaluation process and decides to drop the "economic hardship" criterion, which currently dominates in the evaluation. Moreover, only applicants that are ESMTB members at the time of the application will be considered. The Board debates on the possibility of different types of grants but decides not to introduce any new types at this moment.

In addition to awarding travel grants, ESMTB supports summer schools and workshops. Organisers of the events (co)supported by ESMTB will be encouraged to advertise on event websites the possibility of ESMTB travel support for participants who are members of ESMTB.

6. ESMTB website and Facebook account

It is vital to keep the ESMTB website up-to-date. This is currently done with the kind help of Bob Planque. Some suggestions to improve the website are to present interesting developments in the field, announce and introduce the Reinhart Heinrich award winners and to keep an up-to-date list of events and open positions.

The ESMTB Facebook account now has over 900 followers. Members are encouraged to post announcements and interesting developments or to send the material to one of the Board members.

7. ESMTB Communications

The 2017 issue of the ESMTB Communications is nearly completed, mostly thanks to the efforts of Vitaly Volpert. The Board expresses gratitude for Vitaly's work and discusses the final contributions to this year's issue: an overview of the activities (known thus far) in the Year of Mathematical Biology, a historical article about D'Arcy Wentworth Thompson and a contribution introducing selected groups working in mathematical biology in Europe.

8. Reinhart Heinrich prize

The Reinhart Heinrich award annually honours the best PhD Thesis in the field of Mathematical and Theoretical Biology. The awarding committee currently includes Reinhard Bürger, Carlos Braumann, Miguel Hererro, Philip Maini (chair) and Stefan Schuster. The 2016 Reinhart Heinrich prize was awarded to Stilianos Louca (Department of Mathematics and Biodiversity Research Center, University of British Columbia) for the PhD thesis entitled "The ecology of microbial metabolic pathways" (supervised by prof. dr. Michael Doebeli). A summary of the award winning thesis will be published in the 2017 issue of ESMTB Communications and the winner will be invited to present his work during the ECMTB 2018 in Lisbon.

9. Journal of Mathematical Biology

Mats Gyllenberg (editor-in-chief of the Journal of Mathematical Biology) reports on the current situation regarding the Journal of Mathematical Biology, the Society's official journal. There have

been a few changes to the editorial board. The number of submissions to the Journal of Mathematical Biology is increasing; currently this number is around 500 per year. Roughly 50% of the submissions are rejected without review and around 25% of submissions that are sent to reviewers are accepted. The number of pages per issue has increased to reduce the backlog. MG reports that the average quality of submissions has gone up in the last years.

A special issue of the Journal of Mathematical Biology in memory of Karl Hadeler is planned in 2018. MG invites ideas for further special issues, in particular issues on a specific topic in mathematical biology.

10. ECMTB 2018

The 11th European Conference on Mathematical and Theoretical Biology will take place at the The Faculty of Sciences of the University of Lisbon, Portugal during 23rd and 27th July 2018. This time round, ECMTB is a joint venture of ESMTB and EMS.

Maíra Aguiar and Carlos Braumann, the main organisers of ECMTB 2018, join the meeting via Skype to make an update on the progress. The venue is organised, lectures rooms have been booked and can host up to 699 participants. Nine plenary talks are planned and six of the invited speakers have already accepted the invitation. Between 12 and 14 rooms will be available for parallel talks. Mini-symposia talks and contributed talks are planned to have equal lengths in order to ease the transitions between talks. A call for mini-symposia is planned for November 2017. Arrangements have already been made for catering as well as the social program of the conference. The conference website will be completed soon and conference posters will be sent around to promote the event. The Board thanks Maira Aguiar and Carlos Braumann for their work.

ECMTB 2018 is the main event in the Year of Mathematical Biology. Since the Society's finances are in good health, the Board agrees to put aside additional funds for travel support for ECMTB 2018.

The meeting ends at 15:10.

Barbara Boldin
Secretary of ESMTB

European teams in mathematical biology

MathNeuro Team, Inria

The MathNeuro team is based at Inria Sophia Antipolis in the South-East of France, near Nice. The main focus of our research project is to address key questions in neuroscience using adapted mathematical tools while developing further some of these tools using both a theoretical and a computational approach. Our permanent members are Fabien Campillo, Pascal Chossat, Mathieu Desroches, Olivier Faugeras, Romain Veltz, together with our team assistant Marie-Cecile Lafont. We enjoy the presence of Elif Koksal Ersoz, who is a postdoctoral researcher, as well as that of Phd students Axel Dolcemascolo and Pascal Elson. We have three associate members with whom we have close collaborations: Daniele Avitabile (University of Nottingham, UK), Martin Krupa (University College Cork, Ireland) and Sera_m Rodrigues (Ikerbasque, BCAM, Bilbao, Spain).

The goal pursued in our team is to combine our different but complementary expertises in order to address new and challenging problems in theoretical neuroscience. Our team is strongly anchored in transdisciplinary work through several existing collaborations with groups, labs and individual researchers specialising in other disciplines. In particular, there is a close partnership between MathNeuro and the Institut de Pharmacologie Moleculaire et Cellulaire (IPMC) at Sophia Antipolis (labs of Massimo Mantegazza and Helene Marie), on the one hand, and with the University of Nice (Cedric Bernardin at the LJAD lab, Frederic Lavigne at the BCL lab), on the other hand. We also have a long-standing collaboration with the Unit of Neuroscience Information and Complexity (UNIC) lab at Gif-sur-Yvette (Alain Destexhe, CNRS).

Communication between neurons is organised around several pathways among which spikes emission and reception is very prominent; spikes are regarded as key information units. One key mechanism behind the spiking behaviour of neuron is that of excitability, the famous “all-or-none" property of such cells in response to stimuli. However, communication between neurons may

strengthen or weaken in time, either along the course of one stimulation or over longer time periods. This other key property of neurons in the way they communicate is called plasticity. Excitability and plasticity are two fundamental aspects of brain dynamics both in healthy and pathological states. These concepts are also of paramount importance in understanding how memories are formed and stored in the brain.

The brain is also remarkable for its capacity to properly function under strong perturbations. This can be seen at many levels as for example in our ability to see in dark/daylight conditions, or in poorly contrasted environments. It can also be seen at the level of the neural network which is constantly and strongly shaped by external inputs though the modification of its synapses, a form of plasticity called synaptic plasticity. It is also seen at the level of a single neuron submitted to drugs: it can adapt to (most of the time) properly function, i.e. have the same excitability despite huge changes in its molecular processes. This is usually explained by the theory of homeoplasticity. Learning and memory require all these di_erent mechanisms as they also involve many different time and space scales. The project underlying the MathNeuro team revolves around these pillars of neuronal behaviour in link with the initiation and propagation of pathological brain states in diseases such as migraine, epilepsy and Alzheimer.

Tackling the aforementioned questions requires the development of new mathematical methods that we now list. Multi-scale analysis is essential in neuroscience, as in many other scientific disciplines, to come to grip with the complexity of the observed phenomena. The basic tools are dynamical systems (slow-fast ODEs, bifurcation theory) to study the dynamics of networks, their infinite dimensional analog to study the thermodynamic limit of large neural networks which leads to nonlinear PDEs. On the other hand, understanding small biochemical networks requires the use of (piecewise deterministic) Markov processes. Finally, we will develop theoretical and numerical bifurcation tools for the analysis of excitable models.

History of (bio)mathematics: algebra and infectious diseases

Andrea De Gaetano, CNR IASI BioMatLab Rome

Among the less-well known European biomathematicians of the past one notable example is that of Paolo Ruffini (Valentano 1765, Modena 1822). Italian high-school students associate automatically his name to Ruffini's Rule, a method for simplifying division of a polynomial by a first-degree binomial. What is however less universally known is that he was not only a mathematician, but also a medical doctor (and a degree-certified philosopher in the bargain), who actually actively cared for patients and described typhus in a seminal work (for the time) in 1820.

Ruffini is also known for the Abel-Ruffini theorem (which he proved, albeit imperfectly, in 1799, and which was then definitively proved by Abel in 1824). The theorem states that there exist fifth-degree algebraic equations whose solutions cannot be expressed by radicals (e.g. $x^5 - x + 1 = 0$).

A criterion to establish whether such an equation does admit closed-form explicit solutions was devised by Evariste Galois. It is of some interest to note that not only Galois was rejected two times upon attempting to enter the Ecole Polytechnique, but also that the work where he explained his results, and which is now the basis of Galois theory, was rejected in succession by Cauchy, Fourier (who indeed died while reading it) and Poisson. One of the most romantic mathematicians of all times, Evariste died aged 20 in a duel, allegedly defending the honor of a woman he loved, after having spent the night before the duel feverishly jotting down notes about his theory. Allegedly, because in fact Galois had been imprisoned for three years for revolutionary activity against the King of France, and it is suspected that the bullet that caused his death was shot by the gun of a secret police agent.

In any case, it was only Liouville that recognized, in 1842, that Galois' proof was correct and that it in fact preceded the work of Abel. Not that Abel could enjoy his temporary victory: born in Oslo under Swedish rule he suffered personal poverty in dire political times. Norway belonged to Denmark at the time when England destroyed the Danish fleet to make sure it could not help Napoleon, which of course prevented Norway from exporting timber to England and importing victuals, causing a general famine. In addition, Sweden took Norway from Denmark in 1814, Norway rebelled but was forcibly reduced to obedience. During these times, Abel asked and was assigned a small travel grant by Christina of Sweden to visit France and Germany. During his visit to France he submitted his work to Cauchy, who promptly misplaced and forgot it: it was found posthumously in Cauchy's papers and in it the famous Abel's Theorem was found.

In Germany Abel met August Leopold Creelle, not a great name himself but an influent and rich amateur mathematician, founder of the Journal of Pure and Applied Mathematics in Berlin. Creelle was impressed by Abel, probably fed him some good, hearty food, and started lobbying in his favor with his influential friends. Abel returned to Oslo, where the local University refused him a teaching position.

Creelle's letter announcing his appointment as Professor of Mathematics at the University in Berlin arrived two days after Abel's death of tuberculosis. Had Robert Koch started his study of bacteria in Germany earlier on, maybe Abel could have been cured and produced more mathematics: as it was, besides providing Abel with a scholarship, the reigning Swedish Caroleans endowed the Karolinska Institutet, who assigned to Koch the 1905 Nobel Prize for medicine for the discovery of the *bacterium tuberculosis*. This discovery was an epochal step in the improvement of the health of the working class and especially of charity children in nineteenth-century Europe, where unsanitary living conditions, sharing of bedding, eating and drinking implements were conducive to repeated epidemics of tuberculosis and typhus fever. Indeed, Ruffini might have definitely proved the impossibility of solving algebraically the quintic, had he not caught typhus himself when taking care of his patients in 1819.

EMS-ESMTB summer schools:
The Helsinki Summer School on Mathematical Ecology and Evolution 2016

For the fifth time, students and faculty met in the last week of August for an intense summer school on mathematical ecology in Finland. This time the focus theme was the dynamics of structured populations. Mats Gyllenberg gave a course on the formulation and analysis of structured population models, complemented with the lectures of André de Roos on models offering important and counter-intuitive insights into real-life systems. Hisashi Inaba lectured on infectious diseases in structured populations, connecting the present focus theme to epidemiology, a returning topic in our schools and focal interest of many young researchers. Two more courses focussed on evolution, again in a somewhat complementary fashion. Reinhard Bürger came back to teach in our school (he was also in our faculty of 2010), this time population genetics in spatially structured models. Hans Metz lectured on adaptive dynamics in structured populations - and much more! As before, we enjoyed the hospitality and excellent services of the Linnasmäki Congress Centre in Turku. And we much enjoyed working with 39 excellent and dedicated students, who made the school a wonderful experience! We thank EMS, the Magnus Ehrnrooth Foundation of The Finnish Society of Sciences and Letters, and the Finnish Centre of Excellence in Analysis and Dynamics Research for financial support, and our faculty as well as our students for their enthusiasm, effort, and excellence. And now we look forward to the next Helsinki Summer School on Mathematical Ecology and Evolution in 2018, the Year of Mathematical Biology.

Eva Kisdi (University of Helsinki), organizer

Reinhart-Heinrich Doctoral Thesis Award

ESMTB announces the annual Reinhart Heinrich Doctoral Thesis Award to be presented to the student submitting the best doctoral thesis within the current year 2017 in any area of Mathematical and Theoretical Biology.

Professor Reinhart Heinrich (1946 – 2006) started his research career in theoretical physics and then moved into biochemistry, becoming a full professor and head of theoretical biophysics at the Humboldt University, Berlin in 1990. He is considered a father of the field that is now named Systems Biology, since he investigated various topics such as modelling metabolic networks and metabolic control theory, modelling of signal transduction networks, nonlinear dynamics as applied to biological systems, protein translocation, lipid translocation, vesicular transport, and even DNA repair. Reinhart Heinrich was always searching for the principles that underlie observations, looking for different perspectives and connecting theoretical abstraction with biological evidence. In this way, he inspired numerous students, gave them insight and direction for future research in modern mathematical and theoretical biology, and organized a large number of memorable conferences. Gratefully acknowledging his stimulating support of our interdisciplinary field and, in particular, his way of guiding students and young scientists, the Board of ESMTB decided to offer a Doctoral Thesis Award annually to commemorate Reinhart Heinrich and his legacy in mathematical and theoretical biology.

Prize Awarding Committee includes:
Carlos Braumann
Andreas Deutsch
Philip Maini
David Rand
Stefan Schuster (former assistant to Reinhart Heinrich)

Award
A summary of the thesis receiving the award will be published as the lead article in the 2018 issue of the European Communications in Mathematical and Theoretical Biology. The ***award*** includes***:***

- an invitation to present a lecture at the forthcoming triennial ESMTB Conference or, alternatively, a limited travel grant by ESMTB for a scientific visit of the recipient's own choice;
- 1 year's free membership of ESMTB'
- A voucher for Springer books.

Application
Potential applicants may be nominated by any ESMTB member. To nominate a person for the **Reinhart Heinrich Doctoral Thesis Award**, the following information should be submitted to Andreas Deutsch (**andreas.deutsch@tu-dresden.de**):
1. Name, address, phone number, affiliation, and email address of the **nominator**.
2. Name, address, phone number, affiliation, and email address of the **nominee**.
3. A detailed **statement** describing why the nominee should be considered for the award.
4. An **extended summary** of the thesis (ca. 2-5 pages plus eventual pictures).
5. A **CV** of the nominee in some form.

Closing date for nominations is ***30th November 2017***, by which time the thesis should have received final acceptance by the institution granting the doctoral degree.
Shortlisted applicants will be asked to send their full thesis.

CALL FOR MEMBERSHIP FEES 2016/17

http://www.esmtb.org

ESMTB membership includes free electronic subscription of the official journal of the Society
Journal of Mathematical Biology
and reduced low subscription rates to the **print edition** (25 Euro) as well as for several other journals.

Please register at www.esmtb.org and send your payment of the required annual dues for 2017/18 by bank draft transfer or electronically (PayPal).

Membership Fees per year**:**

The **Individual Annual Membership Fee** is:

- 50 Euro (full member)
- 40 Euro (ISTMB, JSMB, NVTB, SFBT, SMB full member)
- 25 Euro (student, developing country or Eastern European member)
- 20 Euro (student SMB member)

The **Institutional Annual Membership Fee** is: 200 Euro

c. The Life Membership Fee is:

1. 750 EUR (age 40 or above)
2. 500 EUR (age 50 or above)
3. 250 EUR (age 60 or above)

Details for bank draft transfer:
Bank: Commerzbank
Account Name: ESMTB
Account Number: 04 076 801 01
Bank Code No.: 850 800 00
SWIFT-BIC: DRES DD FF
IBAN: DE 18 85080000 0407680101
Bank Address:
Commerzbank, Dr.Külz-Ring 10
D-01067 Dresden, Germany

Further information:
Prof. Frank Hilker, ESMTB treasurer
Institute of Environmental Systems Research
Osnabrück University
frank.hilker@uni-osnabrueck.de

ECMTB May 2017, No. 20: CONTENTS

LETTER FROM THE PRESIDENT 3
2018 THE YEAR OF MATHEMATICAL BIOLOGY 4
EXTENDED ABSTRACT OF THE AWARDED THESIS 7
MINUTES OF THE ESMTB BOARD MEETING 20
EUROPEAN TEAMS IN MATHEMATICAL BIOLOGY 28
HISTORY OF BIOMATHEMATICS 30
REINHART HEINRICH DOCTORAL THESIS AWARD 2016 33