SECTION 11 THEORETICAL BIOLOGY

Section Leader J.A.J. Metz

GENERAL INTRODUCTION

The section organises its activities around the grand unifying theory of biology: Darwinism. Organisms differ from the entities of physics and chemistry by the fact that they reproduce. That they do so only almost faithfully is the main cause of their present day diversity and complexity. Moreover, they are composed from parts in a hierarchical manner, leading to a combinatorial explosion of possibilities: the space of possible organisms is huge, and existing organisms occupy a nearly empty subset of this space. To understand its population, it is necessary to integrate studies of the principles by which organisms are built (development), their inner workings (function and so-called internal selection), the workings of the selective arena (population and community ecology), and the history of their descent (phylogeny). The section provides a single home for the IBL theoreticians active in these areas, thus creating a platform for the cross-fertilisation of disciplines, as well as of techniques, be they statistical, computational, or mathematical. Moreover, their independent affiliation allows the members of the section a great diversity of collaboration with the empirically oriented sections of the IBL, or outside the IBL if theoretical developments so demand. Historically, the section concentrated mainly on the phenotypic level, a strategy justified by the contorted and (in certain aspects) weak link between the genotypic and the phenotypic levels, and the apparent domination of the selective regime in determining many features of great biological interest, as corroborated by the predictive power of the theory. The theories of physiologically structured populations and of adaptive dynamics are internationally recognised successes. In more recent years the interface towards the genetic level is attracting more attention, with i.a. activities in the area of evo-devo and RNA function.

Research Projects:

1. *Bio-Informatics and Self-Organising Systems*

This project aims to contribute to the field of Bio-informatics by data-mining and the simulation of complex systems, and to the theory of self-organising complex systems. In the theme there is a distinct accent on intracellular processes, in particular those relating to the secondary and tertiary structure of RNA in relation to its function and evolution.

2. *Innovations and Constraints in Evolution*

This project focuses on innovations and mechanisms that facilitate evolutionary changes at the organismal level, in particular the constraining effects of internal selection, i.e., selection caused by characteristics of the developmental system. The main focus is on the conservation of the early organogenesis stage and on the conservation of adult traits that are determined during that stage, with the goal of understanding the interplay between genetic architecture, developmental mechanisms and stabilising selection.

3. *Ecological Dynamics and ESS Theory*

This project considers the population dynamics of single species as well as processes involving the interaction between several species on ecological time scales. In one direction novel mathematical tools are developed for the translation from complex individual level causes to population dynamical consequences. In the opposite direction the ESS route allows the prediction, based on their population dynamical consequences, of properties of individuals. In addition statistical methods are developed for analysing ecological data as well as data on individuals, in a manner useful for evolutionary theorising.

4. *Adaptive Dynamics*

This project considers evolutionary time-scales and the species level as well as between-species interaction. The aim here is the construction of an overarching theory of phenotypic evolution, as a direct dynamical extension of the evolutionary statics of ESS theory. This theory also deals with co-evolution and with the treelike structure of character evolution through adaptive speciation.

5 *Methodological Foundations of Phylogenetics*

This project aims to contribute to the development of conceptual and methodological issues in, as well as data analytical and computational techniques for, Phylogenetic Systematics. The project provides a home for the methodological and data analytical counterpart to projects 1, 2, and 4.

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RESEARCH

Project 1. *Bio-Informatics and Self-Organising Systems*

(Dr. A.P. Gultyaev, Dr. F.H.D. van Batenburg)

Possible chaperone-like effects of small RNAs on the folding of large RNA molecules have been studied by computer simulations. The simulations have been performed for the folding of ribosomal RNAs (rRNAs) of a number of organisms in the presence of small nucleolar RNAs (snoRNAs) in eukaryotes or snoRNA-like small RNAs (sRNAs) in Archaea. These computer experiments have been performed using genetic algorithm with a modification that incorporates a transient chaperone-like binding of small RNAs to specific sites on rRNAs. The chaperone effect was estimated by comparison of the final structure predictions with those produced by simulations in the absence of sRNAs and with the phylogenetically proven rRNA structures. The preliminary results show that sRNA molecules possessing two complementary sites at rRNAs guide the folding of rRNA, in particular, assisting in the formation of long-range interactions. Such a chaperone effect is more pronounced at higher temperatures and seems to be more significant in thermophylic Archaea. However, a similar influence can be also seen for eukaryotic snoRNAs with two binding sites. Some evolutionary comparisons between topologically similar snoRNA/rRNA complexes in various species may elucidate the features of coevolution and adaptation of rRNAs and sRNAs in various environments. (Sacha Gultyaev/Ruud Schoemaker).

The conserved RNA structures of translational enhancers in a group of plant viruses have been predicted. The functioning of these enhancers is validated in experiments. Interestingly, strong conformational requirements in the structures result in the possibility of synergistic cooperation of enhancers from different viruses in stimulating RNA translation. (Sacha Gultyaev, in collaboration with the groups of Prof. C. Pleij, LIC and of Dr. F. Meulewaeter, Bayer Crop Science NV, Gent, Belgium).

Project 2. ***Innovations and Constraints in Evolution***
(Dr. F. Galis, Prof. Dr. J.A.J. Metz)

A first subproject on Evo-Devo largely concentrates on the role of internal selection as a conserving evolutionary force. A collaborative experimental program is going on with the Pathology department of the VUMC (Free University Medical Center). A central question in understanding biological diversity is how developmental pathways constrain evolution: the fundamental constancy of gene networks and developmental mechanisms underlying body plans is poorly understood. Such understanding is essential i.a. to determine how data obtained from model organisms generalize. Because many adult traits are determined during early organogenesis, early developmental events have a persisting influence. In this project we focus on how such projected effects constrain the power of natural selection in shaping adaptive evolution. Our working hypothesis is that strong integration between the patterning of the embryonic axes is the root cause of the conservation of body plans. Due to this integration, positive mutational changes of some character cause that many negative pleiotropic effects (abnormalities) elsewhere that they are nearly excluded (so-called internal selection). We have studied as an example of extreme conservation the number of cervical vertebrae in mammals, which is virtually always seven. This number has not changed despite millions of years of evolution with drastic changes in external selection pressures. The number of vertebrae of adjacent thoracic and other vertebrae is far more variable among mammals. The cause of this evolutionary constraint is unknown. We have investigated in humans whether internal selection constrains changes of the number of cervical vertebrae. To this end, we have determined the incidence of variations on the number of cervical, thoracic and lumbar vertebrae in radiographs of human foetuses and infants that died and analysed several existing datasets on the incidence in infants and adults. We found that individuals with a change in the number of cervical vertebrae have an extremely high chance to die before reproduction. Furthermore, we found that cervical ribs are associated with the presence of multiple and major congenital anomalies. Changes in the number of thoracic vertebrae appear to experience considerably weaker internal selection. This is in agreement with the weaker evolutionary constraint on these variations. In a meta-analysis of the literature we have identified specific couplings between the A-P patterning of the mesoderm determining the number of cervical vertebrae and the A-P patterning of other germ layers and/or patterning along other embryonic axes. Such couplings include patterning of the lateral plate mesoderm, the neural tissues, the left/right axis and midline. The multiple, correlated defects that we found in human foetuses can be understood as resulting from such couplings. We intend to further test the predicted couplings by statistically analysing for the incidence of specific combinations of abnormalities in our dataset. This work is done in collaboration with Dr. Liliane Wijnaendts (pathologist), VUMC, Dr. Hans Feuth (internal diseases) and Dr. F.M. Helmerhorst (gynaecologist), LUMC)

Another subproject is on the intra-specific relationship between size and longevity in dogs in collaboration with Tom van Dooren and Inke van der Sluijs of the Animal Ecology section and with Marc Nussbaumer of the Natural History Museum in Berne. We found that the widespread notion that lifespan decreases with size intraspecifically, which is mainly based on dog data, does not hold true for dogs. This notion is based on a misinterpretation of the data. This conclusion is not only important to dogs, since the negative intraspecific relationship in dogs is usually assumed to be representative for the situation in mammals and, in particular, humans, i.e., large humans die younger than small ones. Although large dogs indeed die surprisingly young, this is only true when different breeds are compared, but not within breeds. We have shown that within breeds the relationship is not negative and even slightly (but significantly) positive in the larger of our two datasets. Furthermore, we have shown, using results from the literature, that the very early deaths in dogs from large breeds (St. Bernard, Newfoundland, Irish Wolfhound, Great Dane etc.) are to an important extent the result of diseases associated with the extremely high growth rates that have been co-selected with size. The earlier found negative intraspecific relationship is considered as puzzling as it contrasts with the positive relationship found across species. It is also in disagreement with the predictions of the free radical theory of aging. Laying bare the intrinsic relationship between size and longevity by accounting for the confounding effects of differences between breeds, removes both problems to a considerable extent. We expect the dog pattern to be exemplary for aging patterns of animals bred in captivity, such as laboratory rats.

Project 3. ***Ecological Dynamics and ESS Theory***

(Dr. P. Haccou, Prof. Dr. J.A.J.Metz)

The section collaborates in an international collective of mathematical researchers (in particular Odo Diekmann, Utrecht, and Mats Gyllenberg, Helsinki) to extend the integral equation approach to physiologically structured population dynamics. In 2004 we finally have gotten close to producing the last of the standard ingredients of a general nonlinear theory: a proof of a general linearised stability principle is nearing completion.

The idea of environmental feedback loop, basic to the technical developments in the theory of structured populations, also underlies the idea of feedback dimension: the number of essential variables occurring in this loop. Starting from a sufficiently abstract and therefore general characterisation of this idea we have derived a general extension of Levin’s idea that there can be no more species than resources, applicable to fluctuating environments, as well as a more quantitative variant, relating the options for coexistence in dependence on additional niche variables to the “bandwidth” of the feedback loop (collaboration with Géza Meszéna, Budapest).

A second group of population dynamically oriented subprojects concerns population dynamics in randomly fluctuating environments. The theoretical predictions on invasion success in fluctuating environments were compared with empirical results from laboratory experiments (collaboration with Nathan Pike, Regis Ferriere, and Thomas Tully, Paris, publ Proc Roy Soc. 2004). In addition we developed conservation guidelines to protect populations from going extinct when there is environmental uncertainty. We examined effects of the presence and reliability of cues about the current population size on such strategies, and optimal monitoring effort to improve cue reliability for multiple year situations (collaboration with Hiroyuki Yokomizo and Yoh Iwasa, Kyushu, Publ JTB 2004).

At the ESS end of the spectrum we have shown that in a structured population with multiple birth states it is possible to use the characteristic polynomial of the next generation operator evaluated at 1 as a fitness proxy for ESS calculations, even when the goal is to prove global uninvadability, provided the demographic parameters are continuous in the traits and the set of feasible trait values is connected.

A second project at the ESS end concerns the merger of population genetics with the theory of physiologically structured populations. Almost the whole of population genetics is based on the Hardy-Weinberg assumption. Yet, this assumption only holds when there is no difference whatsoever in the life history parameters of the sexes, a situation almost never realised in nature. Using the fitness proxy referred to above, we have derived general global uninvadability criteria for simple genetic polymorphisms without making the Hardy-Weinberg assumption. Luckily, ideal free ESSes (where all male fitnesses are equalised and so are the female fitnesses) can be calculated in the classical way, as for them the general uninvadability criteria reduce to those for the Hardy-Weinberg case. So here the classical results are all right, even though the textbook derivations are wrong.

Project 4. ***Adaptive Dynamics***

(Prof. Dr. J.A.J. Metz, Dr. P. Haccou, Dr. C. de Kovel, drs. J. Beltman, drs. M. Durinx, drs. C. Rüffler)

As a step towards the extension of AD to Mendelian populations we have (1) shown how the Canonical Equation generalises, with but a meaning change of one coefficient, to monomorphic two-sex populations, (2) derived CEs describing the evolution of simple genetic polymorphisms, either through the introduction of new (pseudo-)alleles or through modifier evolution.

As a more concrete project we have examined, in collaboration with the Behavioural Biology section, the effect of learning processes on speciation. It turns out that imprinting on habitat features can not only drive colonisation of new habitats but, furthermore, is an extremely effective mechanism in the formation of new species. This was examined with gene-culture coevolution models. We were able to prove analytically that under very general conditions there is selection toward an increased habitat preference, regardless of the amount in which different habitats are exploited initially. Furthermore, in a large class of models there is selection toward increased assortative mating as soon as habitat preferences are sufficiently high. These findings together imply that speciation will occur whenever a genetic polymorphism for viabilities in different habitats evolves at high habitat preferences. We examined the conditions under which this occurs for several models studied previously, We found that, even in cases where successful colonization and genetic divergence does not occur initially, speciation often takes place in the long run. Thus, speciation assisted by the learning of habitat features is an extremely effective mechanism (paper published in TPB 2005).

Using a suite of related models that occur in more phenomenological and more mechanistically based variants, we have shown how natural trade-off assumptions made for the various cases lead to radically different biological conclusions. This may serve as a warning against the use of less-than-well-argued trade-off assumptions (PhD project of Claus Rüffler, together with Martijn Egas from IBED, Amsterdam).

The book on Adaptive Speciation that took so much toil in the preceding years finally has appeared with Cambridge University Press.

Project 5 *Methodological Foundations of Phylogenetics*

(Dr. M. Zandee, Prof. Dr. D. Kornet, Dr. P. Haccou. drs. T.A.C. Reydon)

In the PhD project of Thomas Reydon the various ontologies of species interpretations have been worked out in detail. The interpretation of species as historical individuals is implied in the method of phylogenetic systematics, which aims to reconstruct the history of the earth's biodiversity; equally valid, but fundamentally different, is the conception of species as universal natural kinds, that is, sets of structurally similar organisms, as is required for understanding the ranges of their morphological viability. As spin-off for the general philosophy of science an explanation has been given for the structural variation in generalizations over natural kind members, up till then unjustifiably disqualified on the requirement of exceptionlessness, a requirement that has indeed to be met by generalizations over natural law governed events.

In collaboration with Russian researchers we have started the project "Information system 'Simulation and Analysis of Complex Histories of Evolution' (SACHE)", funded by a grant from NWO. The aim of this project is to develop methods for studying processes of speciation and extinction on the basis of DNA sequences, that allow for effects of environmental changes as well as species interactions. The methods will be implemented in a software package that can generate numerical simulations of DNA sequences for several evolutionary models. The results can for instance be analysed with the usual molecular-phylogenetic approaches. On the one hand, this will help to design criteria to distinguish between alternative scenarios for explaining current bio-diversity. Thus it can be used to examine the impact of different environmental factors. On the other hand this approach will be useful for testing different models of population processes (here there is a connection with projects 3 and 4).

PERSONNEL

Prof. Dr. J.A.J. (Hans) Metz	Professor UL
Prof. Dr. D.J. (Diedel) Kornet	Endowed Professor LUF
Dr. P. (Patsy) Haccou	Associate Professor UL
Dr. F.H.D. (Eke) van Batenburg	Assistant Professor UL
Dr. R. (Rino) Zandee	Assistant Professor UL
Drs. E. (Evert) Meelis	Assistant Professor UL
Dr. F. (Frietson) Galis	Assistant Professor UL
Dr. A.P. (Sacha) Gultyaev	Assistant Professor UL
Dr. C.G.F. (Carolien) de Kovel	Postdoc ALW (from 15/2/2004)
Dr. U. (Ulf) Dieckmann	Guest Researcher
Prof. Dr. P. (Piet) Dullemeijer	Guest Researcher (until 28/7/2004)
Dr. N. (Nelly) van der Hoeven	Guest Researcher
Drs. F.J.A. (Frans) Jacobs	Guest Researcher
Dr. Y.S.D.M. (Yde) de Jong	Guest Researcher
Dr. H.G.J. (Harald) van Mil	Guest Researcher (from 1/7/2004)
Dr. H. (Hubert) Turner	Guest Researcher
Dr. Ir. M.G.P. (Marco) van Veller	Guest Researcher (until 1/7/2004)
Dr. A.G. (Arno) Wouters	Guest researcher
Drs. L.E. (Lino) Paula	Lecturer UL
Drs. J.B. (Joost) Beltman	Grad. Student ALW (until 7/2004)

Drs. M. (Michel) Durinx	Grad. Student ALW (until 8/10/2004) UL (from 9/10/2004)
Drs. T.A.C. (Thomas) Reydon	Grad. Student ALW (until 7/2004)
Drs. C. (Claus) Rueffler	Grad. Student ALW (until 8/10/2004) UL (from 9/10/2004)
E. (Elizabeth) van Ast-Gray, M.Sc.	Secretary, UL (until 1/11/2004)
H. (Henny) Groenhuijzen	Secretary, UL

ALW	Netherlands Foundation for Life Sciences
LUF	Leiden University Fund
UL	Leiden University

COLLABORATIONS

National:

- Leiden Institute of Chemistry, Leiden University, Prof. dr. C. Pley, Dr. B. Kraal
- Leiden University Medical Centre, Leiden University Dr. W. Spaan, Dr. E. Snijder
- Leiden University Medical Centre, Leiden University, Prof. dr. F.M. Helmerhorst, Dr. H. Feuth
- Medical Pharmacology, Leiden University Dr. J. de Koning
- Free University Medical Centre, Amsterdam, Prof. dr. G. A. Meijer, Dr. L Wijnaends
- Mathematics, Agricultural University, Wageningen, Dr. L. Hemerik
- Agricultural University, Wageningen, Dr. P.A. Jansen
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- Mathematical Institute, Utrecht University, Prof. dr. O. Diekmann
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- Theoretical Biology, Free University, Amsterdam, Prof. dr. S.A.L.M. Kooijman, Dr. B. Kooi, drs. T. Troost
- Technical University Delft, Dr. H.G.J. van Mill
- University of Amsterdam, Prof. dr. J.M.J. Murre
- University of Maastricht, Prof. dr. E.O. Postma
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- Leiden University Medical Centre, Leiden University, Prof. dr. F.M. Helmerhorst, Dr. H. Feuth
- Medical Pharmacology, Leiden University, Dr. J. de Koning
- Free University Medical Centre, Amsterdam, Prof. dr. G. A. Meijer, Dr. L Wijnaends

International:

- University of Southern Denmark, Odense, Denmark, Dr. K. Gerdes
- Bayer Crop Science NV, Gent, Belgium, Dr. F. Meulewaeter

- McGill University, Montreal, Canada, Prof. dr. L. Chapman,
- Karlova University, Prague, Czech Republic, Dr. M. Kundrát
- University of Beireuth, Germany, drs. M. Steigenga
- Museum of Natural History, Bern, Switzerland, Dr. M. Nussbaumer
- University of California at Santa Cruz, USA, Prof. dr. B. Sinervo
- Wildlife & Fisheries Science, Texas A&M University, College Station, Texas, USA. Dr. T.J. DeWitt
- Yale University, Newhaven, Prof. dr. G.P. Wagner
- Mathematical Institute, University of Helsinki, Finland, Prof. dr. M. Gyllenberg
- Rothamsted Research Station, Harpenden, UK, Dr. F. van den Bosch, drs. I. Demon
- Laboratoire d'Ecologie, Ecole Normale Supérieure, Paris, France, Prof. dr. R. Ferrière, Dr. T. Tully, Dr. C. Cadet, Dr. M van Baalen
- Zoological Museum, Lausanne, Switzerland, Dr. O. Glaizot
- Division of Genomic Medicine, University of Sheffield, UK, Prof. dr. C. Cannings
- Kyushu University, Fukuoka, Japan, Prof. dr. Y. Iwasa, H. Yokomizo
- Chalmers University, Göthenbörg, Sweden, Prof. dr. P. Jagers
- Steklov Institute of Mathematical Sciences, Moscow, Russia, Prof. dr. V. Vatutin
- Eötvös University, Budapest, Hungary, Dr. G. Meszéna, Dr. L. Pasztor
- Universität Köln, Cologne, Duitsland, Prof. dr. D. Tautz
- Mathematical Institute, University of Helsinki, Finland, Prof. dr. M. Gyllenberg, Dr S.A.H. Geritz, Dr. É. Kisdi
- ADN-IIASA, Laxenburg, Austria, Dr. U. Dieckmann
- Université Pierre et Marie Curie et CNRS, Paris, France, Dr. S. Galam
- Stockholm University, Sweden, Prof. dr. O. Leimar
- Dept. Zoology Univ. Toronto, Canada, Prof. dr. P. Abrams
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- University of British Columbia, Vancouver, Canada, Dr. M. Doebeli
- Institut für Mathematik, Vienna, Austria, Prof. dr. K. Sigmund
- College of William and Mary, Williamsburg, USA, Dr. S.J.S. Schreiber
- Dept. Zoology Univ. Toronto, Canada, Prof. dr. D.R. Brooks
- Limnological Institute, Siberian branch of the Russian Academy of Sciences, Irkutsk, Russia, Prof. dr D.Y. Sherbakov, Dr. S.V. Semovski

GRANTS

- ALW (809.34.002): Developing a bifurcation theory for Evolutionarily Stable Strategies. September 2000 to September 2004 (taken over by IBL until April 2005). Salary costs: ¤119,142, hardware: ¤3,403, travel: ¤2,269.
- ALW (810.34.001): Putting life history theory in a realistic ecological context. September 2000 to September 2004 (taken over by IBL until January 2005). Salary costs: ¤119,42, hardware: ¤3,063, travel: ¤11,345.
- ALW (810.34.008): Sexual imprinting, song learning and gene-culture co-evolution: modeling the evolution of brood parasitism in birds. August 2000 to February 2004. Salary costs: ¤90,756, hardware: ¤5,105, exploitation ¤908, travel: ¤8,622.
- ALW (813-04.001): Dimensions of speciation. February 2004 to February 2006. Salary costs: ¤104,501, hardware & travel: ¤10,000.
- NWO-OTKA: Netherlands-Hungarian exchange program on Adaptive Dynamics: the mathematical link between population dynamics and evolution. January 2001 to November 2004. Total amount: NLG 63,000.

- NWO: Simulation and Analysis of Complex Histories of Evolution (SACHE). Exchange program with the Limnological Institute, Siberian Branch of the Russian Academy of Sciences, Irkutsk, funded by the Russian Foundation for Basic Research, on speciation in Lake Baikal. 1/4/2004-1/4/2007. Total amount: ¤115,000.

PUBLICATIONS

Journal papers:

Beltman, J.B., **P. Haccou** and C. ten Cate (2004) Learning and colonisation of new niches: A first step towards speciation. Evolution 58: 35-46.

Born, E. van den, **A.P. Gultyaev** and E.J. Snijder (2004) Secondary structure and function of the 5'-proximal region of the equine arteritis virus RNA genome. RNA 10: 424-437.

Cadet, C., **J.A.J. Metz** & P. Klinkhamer (2004) Size and the Not-So-Single Sex: disentangling the effects of size on sex allocation. American Naturalist 164: 779-792

de Mazancourt, C. and **Dieckmann, U.** (2004). Trade-off geometries and frequency-dependent selection. American Naturalist 164: 765–778

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Haccou, P. and M.V. Schneider (2004) Modes of Reproduction and the Accumulation of Deleterious Mutations With Multiplicative Fitness Effects. Genetics 166: 1093-1104.

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Pike, N., T. Tully, **P. Haccou** and R. Ferrière (2004) The effect of autocorrelation in environmental variability on the estbalishment and persistence of populations: an experimental test. Proc Roy Soc B 271: 2143-2148.

Ravigné, V., Olivieri, I. and **Dieckmann, U**. (2004). Implications of habitat choice for protected polymorphisms. Evolutionary Ecology Research 6: 125–145

Reydon, T.A.C. (2004) Book review of Biological Complexity and Integrative Pluralism by Sandra D. Mitchell. Philosophy in Review / Comptes Rendus Philosophiques 24: 282-284.

Reydon, T.A.C. (2004) Book review of The Species Problem: Biological Species, Ontology, and the Metaphysics of Biology by David N. Stamos. Acta Biotheoretica 52: 229-232.

Reydon, T.A.C. (2004) Why does the species problem still persist? BioEssays 26: 300-305.

Rueffler, C., **T. J. M. van Dooren** and **J. A. J. Metz** (2004) Adaptive Walks on Changing Landscapes: Levins' Approach Extended. Theoretical Population Biology 65: 165-178.

Van Dooren, TJM, **Durinx M**, Demon I. (2004) Sexual dimorphism or evolutionary branching? Evol. Ecol. Res. 6: 857-971.

van Doorn, G.S., **Dieckmann, U.** and Weissing, F.J. (2004). Sympatric speciation by sexual selection: A critical re-evaluation. American Naturalist 163: 709–725

Yokomizo, H., **P. Haccou** and Y. Iwasa (2004) Multiple-year optimization of conservation effort and monitoring effort for a fluctuating population. Journal of Theoretical Biology 230: 157-171.

Book chapters and other publications:

Alphen, J.J.M. van, O. Seehausen, and **F. Galis** (2004) Speciation and species richness in African Haplochromine cichlids. Pp. 173-191 in: Metz, J.A.J. and U. Dieckman (Eds). Speciation. Cambridge University Press.

Bronstein, J.L., **Dieckmann, U**. and Ferrière, R. (2004). Coevolutionary dynamics and the conservation of mutualisms. Pp. 305–326 in: Ferrière, R, Dieckmann, U. and Couvet, D. (Eds). Evolutionary Conservation Biology Cambridge UP, Claessen, D. and **Dieckmann, U**. (2004). Adaptive speciation through ontogenetic niche shifts. Pp. 226–227 in: Dieckmann, U,, Metz, J.A.J., Doebeli, M. and Tautz, D, (Eds). Adaptive Speciation, Cambridge UP.

Dieckmann, U. (2004). Assortative mating and spatial coexistence. Pp. 306–307 in: Dieckmann, U,, Metz, J.A.J., Doebeli, M. and Tautz, D, (Eds). Adaptive Speciation, Cambridge UP.

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Dieckmann U & Ferrière R (2004). Adaptive dynamics and evolving biodiversity. Pp. 188–224 in: Ferrière, R, Dieckmann, U. and Couvet, D. (Eds). Evolutionary Conservation Biology Cambridge UP,

Dieckmann, U, **J.A.J. Metz**, M. Doebeli and D. Tautz (2004) Introuction. Pp. 1-16 in: Dieckmann, U., M. Doebeli, J.A.J. Metz and D. Tautz. Adaptive Speciation.. Cambridge UP.

Dieckmann, U, D. Tautz, M. Doebeli and **J.A.J. Metz** (2004) Epilogue. In: Dieckmann, U., M. Doebeli, J.A.J. Metz and D. Tautz. Adaptive Speciation. Pp. 380-394. Cambridge UP.

Doebeli, M. and **Dieckmann**, U. (2004). Adaptive dynamics of speciation: Spatial structure. Pp. 140–167 in: Dieckmann, U,, Metz, J.A.J., Doebeli, M. and Tautz, D, (Eds). Adaptive Speciation, Cambridge UP.

Ferrière R, **Dieckmann U** & Couvet D (2004). Epilogue. In: Evolutionary Conservation Biology, eds. Ferrière R, Dieckmann U & Couvet D, pp. 356–364. Cambridge University Press

Ferrière R, **Dieckmann U** & Couvet D (2004). Introduction. Pp. 1–14 in: Ferrière, R, Dieckmann, U. and Couvet, D. (Eds). Evolutionary Conservation Biology Cambridge UP,

Geritz, S.A.H., É Kisdi, G. Meszéna and **J.A.J. Metz** (2004) Adaptive Dynamics of Speciation: Ecological Underpinnings. Pp. 54-75 in: Dieckmann, U., M. Doebeli, J.A.J. Metz and D. Tautz. Adaptive Speciation. Cambridge UP.

Gyllenberg, M., I. Hanski and **J.A.J. Metz** (2004) Spatial Dimensions of Population Viability. Pp 59-79 in: Ferrière, R., U. Dieckmann and D. Couvet (Eds). Evolutionary Conservation Biology. Cambridge UP.

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