



A MATTER OF SCALE: WITHIN-HOST AND BETWEEN-HOST PROCESSES DRIVING COEVOLUTION WITH PARASITES

Les processus intra- et inter-hote influençant la coevolution hote-parasite : une question d'echelle

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Résumé du rapport

La 6e édition de la Conférence Monod sur l'écologie évolutive des relations hôte-parasite s'est tenue à Roscoff en octobre 2023. Elle était organisée par Andrea GRAHAM (Princeton, US) et Oliver KALTZ (Montpellier), et a accueilli 90 participants. L'objectif central de la conférence était d'examiner comment la dynamique au sein de l'hôte (e.g., la compétition ou l'immunité) est liée à la dynamique de la transmission et de la dispersion des parasites à travers les populations d'hôtes. La compréhension de ces échelles d'organisation biologique peut révéler comment l'évolution façonne les phénotypes de l'hôte et du parasite. Nous avons pu réunir des scientifiques de premier plan dans ce domaine, adoptant des approches diverses, utilisant des innovations techniques variées, des modèles expérimentaux ainsi que des modèles mathématiques.

Le programme était divisé en quatre sessions de communications orales sur des thèmes généraux, accompagnées de deux sessions de posters. Les communications orales ont consisté en un mélange de 22 exposés de conférenciers invités (30 minutes) et de 20 exposés de participants (15 minutes). Les orateurs invités venaient de France (9), d'Europe (8) et des États-Unis (5), tandis que les 68 autres participants venaient de 16 pays différents (Europe, Inde, Brésil et États-Unis). Nous avons veillé à bien respecter la parité femme-homme (57 % des orateurs étaient des femmes) et la diversité d'avancement de carrière des orateurs. Environ un tiers des participants étaient des doctorants.

Session 1 : Signatures génétiques et génomiques de la coévolution hôte-parasite : De fortes signatures génétiques et génomiques de la sélection naturelle devraient être observées dans les relations coévolutives étroites entre les hôtes et les parasites. Neuf exposés ont exploré les lignes de preuves les plus récentes pour de tels patterns à travers différents systèmes.

Session 2 : Dynamique évolutive de l'attaque et de la défense : Les signatures génétiques de l'évolution antagoniste doivent être accompagnées de patterns correspondants dans les phénotypes. Cette question a été étudiée dans 16 exposés sur la dynamique phénotypique des stratégies d'attaque et de défense, et qui apportent de l'évidence de l'adaptation réciproque entre les parasites et les hôtes.

Session 3 : Évolution des hôtes et des parasites au sein de la Tangled Bank : Les divers aspects fascinants de la coévolution hôte-parasite se déroulent dans le contexte de la "Tangled Bank" (Darwin), en présence d'autres espèces symbiotiques. Neuf exposés ont traité de ces aspects multi-espèces, comprenant des interactions compétitives et facilitatrices dans l'environnement externe, ainsi qu'à l'intérieur des hôtes (par exemple, le microbiome).

Session 4 : Patterns spatio-temporels des hôtes et des parasites : La planète Terre offre des environnements spatio-temporellement très variés, ce qui a également un impact sur les trajectoires de coévolution hôte-parasite. Durant cette dernière session, 8 exposés ont abordé la variation spatio-temporelle des interactions hôte-parasite à travers une diversité d'approches, des études mathématiques ou d'observation sur le terrain aux études expérimentales en laboratoire. De plus, les deux sessions de posters très animées (d'une durée de 2h chacune) ont accueilli 48 contributions, représentant un mélange varié de nos quatre grands thèmes.

Les maladies infectieuses représentent un problème intrinsèquement multi-échelle pour les biologistes évolutionnistes, nécessitant l'intégration des processus intra et inter-hôtes, ainsi que l'hétérogénéité spatiale et temporelle des paysages dans lesquels les hôtes et les parasites vivent et se dispersent/transmettent. Nous avons été ravis de constater que les quatre sessions de la conférence n'ont pas seulement abordé ces thèmes, mais qu'elles les ont aussi véritablement intégrés. La discussion générale a également mis en évidence une caractéristique unique de cette

conférence, à savoir la remarquable diversité des approches et des systèmes, qui favorise les échanges entre les disciplines. Les participants ont souligné l'atmosphère extrêmement amicale et non compétitive de la conférence, les sessions de posters exceptionnelles et productives, et la forte représentation des jeunes scientifiques. Ces conditions sont idéales pour favoriser de nouvelles collaborations et s'informer sur les possibilités d'emploi. Le maintien d'un tel environnement productif et collaboratif sera l'un des principaux objectifs de toute nouvelle conférence. Un soutien unanime et enthousiaste s'est exprimé en faveur du renouvellement de cette conférence et de la nomination d'Oliver KALTZ et de Britt KOSKELLA (Californie-Berkeley, États-Unis) aux postes de président et de vice-président, respectivement.

Overview

In 2004, Thierry RIGAUD (Dijon) and Dieter EBERT (Basel, Switzerland) organised a Jacques Monod Conference (JMC) on the Evolutionary Ecology of Host-Parasite Relationships. This conference was so successful, and sparked such enthusiasm and growth in the research community, that additional JMCs on various aspects of host-parasite coevolution then took place in 2007, 2011, 2014, and 2017. The following is the final report for the most recent JMC on the evolutionary ecology of host-parasite interactions, which took place in Roscoff in October 2023 and was hosted by Andrea GRAHAM (Princeton, US) and Oliver KALTZ (Montpellier).

These JMCs are special because they bring together a uniquely multidisciplinary and interactive community of disease ecologists, ecological immunologists, and evolutionary biologists who work on a wide range of host-parasite systems (including prokaryote, protist, invertebrate, and vertebrate hosts, infected by parasites ranging from viruses to metazoa) and who use diverse approaches (experimental, phenotypic, genomic, and/or theoretical). Arguably, no other conference in the world brings together such a diverse spectrum of researchers focused on host-parasite coevolution.

As a result, we were able to attract the most prominent researchers in the field, many of whom leapt at the opportunity to catch up on the latest breakthroughs in this large, and compartmentalized, field, while also meeting the new talent – i.e., the junior scientists who will shape the future of the field. Indeed, every invited speaker in our initial "wish list" enthusiastically accepted the invitation, and many other prominent researchers in the field applied to come as participants. When, over the course of pandemic lockdowns, we had to postpone the conference twice, several researchers had to withdraw due to professional or personal conflicts that did not permit them to switch from 2021 to first 2022 and then 2023. We were able to replace those speakers by issuing invitations to equally senior leaders who all accepted, again with great enthusiasm.

The program was divided into 4 broad-themed sessions for oral communications (see below). Oral communications consisted of a mix of invited speaker talks (30 min) and contributed participant talks (15 min) chosen from the abstracts. As in previous years, the quality of the contributed abstracts was extremely high (many coming from established scientists), making the choice of short talks an extremely difficult one. In the end, we balanced the sex ratio, geographical diversity, and career stages of the final list of speakers. We also took care to make the poster sessions highly dynamic.

The conference demographics were as follows.

22 invited speakers

France:

Richard CORDAUX (Paris-Saclay), Laurent DEBARBIEUX (Institut Pasteur), Alison DUNCAN (Montpellier), Tatiana GIRAUD (Paris-Saclay), Oliver KALTZ (Montpellier), Yannick MORET (Bourgogne), Thierry RIGAUD (Dijon), Ana RIVERO (Montpellier), Gabriele SORCI (Dijon)

Europe:

Becca ASQUITH (Imperial, UK), Sylvia CREMER (IST, AT), Dieter EBERT (Basel, CH), Isabel GORDO (Gulbenkian, PT), Manfred MILINSKI (Plön, DE), Jens ROLFF (Berlin, DE), Olivia ROTH (Kiel, DE), Stineke VAN HOUTE (Exeter, UK) Rest of the world:

Michael BOOTS (Berkeley, US), Andrea GRAHAM (Princeton, US), Katia KOELLE (Emory, US), Britt KOSKELLA (Berkeley, US), Micaela MARTINEZ (Columbia, US)

The 68 non-invited participants came **from 16 different countries** (France, Austria, Belgium, Denmark, Germany, Poland, Portugal, Spain, Sweden, Switzerland, The Netherlands, UK, Israel, India, Brazil, and the US). Approximately one-third (n=24) of these participants were PhD students. Here, we note that in addition to the generous support of CNRS for this conference, we had some US government support (from the National Science Foundation as well as the National Institutes of Health) that allowed us to offer travel bursaries for US-based Ph.D. students and postdoctoral scholars.

The 20 participants selected to contribute short talks were:

Wieslaw BABIK (Jagiellonian, PO), Frida BEN-AMI (Tel Aviv, IS), Dan BOLNICK (Connecticut, US), Camille BONNEAUD (Exeter, UK), Vania DE ASSIS (Florida, US), Josie ELLIOTT (Bath, UK), Martin GUILLEMET (Montpellier, FR), Maija JOKINEN (Zurich, CH), Imroze KHAN (Ashoka, India), Chris LANE (Rhode Island, US), Eva LIEVENS (Konstanz, DE), Reese MARTIN (Vanderbilt, US), Yannis MICHALAKIS (Montpellier, FR), Gemma PALOMAR (Alcala, ES), Romain PIGEAULT (Poitiers, FR), Melanie SAUBIN (Lorraine, FR), Ana SANTACRUZ (Stowers, US), Nathalie STEINEL (Lowell, US), Helena WESTERDAHL (Lund, SE), and Marie-Anne VAN SLUYS (São Paulo, Brasil).

In addition, we hosted **two lively poster sessions**, each lasting 2h, on the Tuesday and the Thursday afternoons. The quality of the poster presentations was extremely high, generating great interest and extended discussions between the attendees and the poster-contributors. Many of the poster presenters commented afterwards that they had never received so much constructive feedback on their work in any other forum.

The conference had a relatively **balanced sex ratio**: 53% of the attendees and 57% of the speakers (i.e., 12 invited speakers, including the Chair, and 12 short talk contributions) were women. This continues the promising trend of increased visibility of female scientists, including senior scientists, in the field that we noted at the 2017 JMC on host-parasite coevolution.

We also made sure to offer plenty of time for **informal discussions**: long (2h) lunch/walk breaks, regular 30m coffee breaks, an afternoon walk in the rain on Batz Island, and a post-banquet drink in town that allowed the participants to mingle and continue discussions for a few hours after the scientific sessions had ended but before departure from lovely Roscoff.

Scientific program

Our primary aim was to foster the interdisciplinary exchanges that are essential to understanding the coevolution of hosts and parasites. Critically, we aimed to examine **within-host dynamics** (e.g., of competition or immunity) alongside the **dynamics of parasite transmission and dispersal across host populations**, because insights across these scales of biological organization reveal how evolution shapes host and parasite phenotypes. Such insights are fostered by amazing technical innovations, clever experimental designs, and mathematical models that innovatively collapse empirical complexities into tractable yet testable equations. We therefore brought together scientists taking diverse approaches to the evolutionary ecology of hosts and parasites.

The conference program closely followed the structure proposed in the original application and was divided into four integrative Sessions (see program in **Annex I**)

- Session 1: Genetic & Genomic Signatures of Host-Parasite Coevolution
- Session 2: Evolutionary Dynamics of Attack & Defence
- Session 3: Evolution of Hosts & Parasites Within the Tangled Bank
- Session 4: Spatiotemporal Patterns of Hosts & Parasites

Session 1: Genetic & Genomic Signatures of Host-Parasite Coevolution

The strongest genetic and genomic signatures of natural selection are predicted to be observed in the tight coevolutionary relationships between hosts and parasites. This session explored the most recent lines of evidence for such patterns across a wide array of systems. The session started with a captivating talk by Tatiana GIRAUD (Paris-Saclay, France) on the genomics of host shifts and local adaptation in plant-fungus interactions. She described startlingly frequent host shifts and long-distance dispersal by the fungi, counterbalanced by defensive adaptations in the plants. The next speaker was Richard CORDAUX (Paris-Saclay, France), whose talk dealt with the infectious sex-determining mechanisms of pillbugs. He described an impressive diversity of gametic and Wolbachia-altered determinants of host sex and elicited interesting questions about why feminization of hosts is apparently so favorable for parasite transmission. The next talk by Dieter EBERT (Basel, Switzerland) focused on a very tractable system for coevolutionary studies: water fleas infected by microsporidia. He drew upon decades of research in that system to show how genetic variation in hosts and parasites reveals rapid coevolutionary processes such as Red Queen dynamics and results in tremendous heterogeneity in host resistance across large geographical areas. Eva LIEVENS (Konstanz, Germany) explored another interesting experimental system in which algae and viruses exhibit arms race coevolutionary dynamics. She showed compelling evidence for fluctuating selection on host resistance in the face of rich viral diversity. Next, Imroze KHAN (Ashoka, India) offered intriguing experimental evidence of costs of resistance in flour beetles fighting bacteria. He speculated that the costs of resistance were potentially mediated by cytotoxic intermediates that increase the mutational load borne by hosts.

After a coffee break full of lively discussion, the session resumed with a talk by Alison DUNCAN (Montpellier, France) who generated inbred lines of spider mites and competed them on bean plant hosts. She reported no impacts of competition on virulence but found a surprising enhancement of dispersal when disparate mite genotypes shared a host. The session then shifted gears away from experimental systems and towards characterization of immunogenetics and parasite evolution in natural populations. First up in this series was Katia KOELLE (Emory, US), who delivered her talk virtually due to a severe last-minute travel disruption. She described the evolution of influenza and coronaviruses across biological scales, with a particular focus on genetic bottlenecks that arise when these viruses are transmitted to new human hosts, no matter the diversity and abundance of virions in the original host. Her mathematical tools combined with rich sequencing data provided an inspiring example of the inferential power and applied importance of phylodynamics. Next up was Helena WESTERDAHL (Lund, Sweden) who offered startling evidence of allelic diversity of Major Histocompatibility Complex (MHC) Class I genes in passerines in general and reed warblers in particular. For instance, whereas mammals are thought to express up to 6 MHC Class I allelic variants per individual, reed warblers come in at nearly 30 variants per bird. Her talk sparked many questions about the evolutionary drivers of such diversity. Yannis MICHALAKIS (Montpellier, France) then concluded the session by describing other natural systems of outstanding yet puzzling genetic diversity: multipartite viruses of plants such as fava beans. He described tremendous diversity in the rates of transmission of different segments of viral genomes that offer the potential for broad host range, yet elicited questions about why such viruses appear restricted to plant hosts. The session therefore shed new light on the genetics and genomics of mutual adaptation between microparasites and their coevolutionary partners (algal to human).

Session 2: Evolutionary Dynamics of Attack & Defence

With or without genetic evidence of antagonistic evolution between hosts and parasites, the phenotypic dynamics of strategies for attack and defense can offer compelling evidence of reciprocal adaptation between parasites and hosts. This session began with Stineke VAN HOUTE (Exeter, UK), whose excellent talk dealt with the evolution of attack strategies among bacteriophage. She showed evidence for viral countermoves (primarily the production of anti-CRISPR particles) that disable the famously powerful and specific CRISPR-Cas defences of bacterial hosts. Ana RIVERO (Montpellier, France) then spoke about potential drivers of malaria parasite aggregation within mosquito hosts. She described intriguing data from avian malaria experiments that indicate individual mosquitoes don't differ much in susceptibility, but instead that parasites somehow aggregate in the last mosquitos to bite a given bird. This observation inspired lively discussion but for now, the mechanism enabling this attack strategy remains mysterious. Next, Mike BOOTS (Berkeley, US) used mathematical analysis of gigantic metaanalytic datasets on wildlife to argue why bats (and platypuses, for that matter) might be special hosts for viruses. A key finding was that those taxa, due to their life histories and ecologies, select for the highest within-host replication rates, favoring the evolution of virulence especially when antigenic escape evolution is also favored. This was followed by an excellent talk by Natalie STEINEL (Lowell, US) who considered the costs and benefits of immunomodulation of stickleback hosts by tapeworm parasites. Her data revealed that melanomacrophages (a cell type that bridges between innate and adaptive immune function in fish) were suppressed by certain parasite genotypes. Wieslaw BABIK (Jagiellonian, Poland) then offered a thought-provoking talk at the intersection of MHC immunogenetics with host life history trade-offs. Specifically, he used a mathematical model to demonstrate that Red Queen coevolution, but not heterozygote advantage, helps to predict increased host body size at maturation. His talk prompted questions about the mysteries of anglerfish who get on with life in the absence of functional MHC, and there was great interest in future work to test his integrative predictions. At the last moment, Marie-Anne VAN SLUYS (São Paulo, Brazil) had to cancel her talk due to illness, unfortunately.

The session continued with Sylvia CREMER (IST, Austria) who wowed the audience with incredible tales of ants undertaking "social immunity" to purge infection from their colonies. Analogies with public health measures and vertebrate immune function were inescapable: for example, ants groom the most heavily-infected nestmates first, and prior experience of grooming makes ants faster at removing parasites from nestmates. The tour de force talk concluded with evidence that individual ants' own immune systems are boosted by exposure to the parasites that they remove! Next, Andrea GRAHAM (Princeton, US) outlined how cytokine feedback loops among competing types of immune responses in mammals can generate bifurcation in the duration of infection that hosts experience. Her mathematical model predicted critical importance of the earliest phases of the induced cytokine response in the eventual outcome, and she described ongoing work to test that prediction in rewilded mice experimentally exposed to gastrointestinal nematodes. Yannick

MORET (Dijon, France) then spoke about transgenerational immune priming in flour beetles. His data on specificity in the induced responses were impressive, as was his ability to distinguish between the costs of initial versus sustained upregulation of antimicrobial peptides. The next speaker was Josie ELLIOTT (Bath, UK) who spoke about horizontal gene transfer as a way for microbes to improve their immune function. She reported that receptor mutation better foiled bacteriophage except upon low nutrient or high temperature conditions, when the evolution of CRISPR-Cas defence was favored. Resource-dependence of optimal defence was also a theme of the next talk, by Reese MARTIN (Vanderbilt, US). He described a mathematical model of pleiotropy between immunity and development that generated interesting resource-dependent bifurcations between alternative states of resistance and tolerance.

Another discussion-rich coffee break was followed by the final suite of talks of the session. Becca ASQUITH (Imperial, UK) gave a fascinating talk about immune regulatory mechanisms that shape associations of disease outcomes with variants of the Human Leukocyte Antigen (i.e., human MHC). In particular, she described how receptors on Natural Killer cells enhance effects of HLA variants, with previously undetected yet strong effects on human susceptibility to viruses and autoimmune diseases. Olivia ROTH (Kiel, Germany) was up next to return our focus to fish. She outlined the incredible biology of seahorses and pipefishes, including the evolution of male pregnancy that was paralleled by immunological adaptations analogous to those exhibited by pregnant female mammals. Her talk therefore reinforced the emerging theme that immunogenetics are intertwined with host life history evolution. Daniel BOLNICK (Connecticut, US) then presented evidence of immunogenetic "evolution in action" in stickleback fish across a suite of lakes formed during the last ice age. He explained how fibrotic immune responses against tapeworm infections are costly yet evolve rapidly in exposed populations of fish. The session concluded with two excellent short talks. Camille BONNEAUD (Exeter, UK) spoke about the evolution of virulence of mycoplasmas in wild finches over the past 25 years and the concomitant escape of mycoplasma from bacteriophage when they invaded the new host species. Vania DE ASSIS (Florida, US) then rounded off the session with an interesting talk about the immunological predictors of Lyme disease competence of rodent reservoirs across a latitudinal gradient. The session therefore spanned host taxa from prokaryotes to insects, fish, birds, and mammals, and infectious disease agents from viruses to worms. Covering such a breadth of systems highlighted conceptual similarities and general predictors of the evolution of strategies for parasite attack and host defence.

Session 3: Evolution of Hosts & Parasites Within The Tangled Bank

All of the fascinating intricacies of host-parasite coevolution play out in the context of a "tangled bank" (in Darwin's words) of other symbiotic species. This multi-species aspect comprises competitive and facilitative interactions in the external environment, as well as within hosts. This session aimed to elucidate the ways in which microbial symbionts alter trajectories of host-parasite intereactions. Britt KOSKELLA (Berkeley, US) launched the session with a fantastic talk about tomato plants fighting experimental bacterial infections. She reported that competition from microbial symbionts on/in leaves protects the host against pathogenic microbes, and that these effects were enhanced when bacteriophages were present. She also described puzzling dose-dependence, with more dilute symbiont treatments bringing maximal benefits to the plant. Manfred MILINSKI (Plön, Germany) next took the floor, with an exposition of why he doesn't actually believe that microbes serve as cues for MHC-associated mate choice in sticklebacks. We were then treated to an excellent talk by Gemma PALOMAR (Alcala, Spain) in which she reported

astonishing diversity of mite-transmitted malaria parasites in the lizards of Tenerife. Her talk elicited many probing questions about the mobility of mites. Unfortunately, Melanie SAUBIN (Lorraine, France) had to cancel her talk at the last minute due to illness.

The session continued with Isabel GORDO's (Gulbenkian, Portugal) outstanding talk on the evolution of *E. coli* bacteria in mammalian guts. She aptly quoted Jacques Monod's statement that "what is true for *E. coli* is true for the elephant" and went on to indeed show, via statistical tools combined with elegant experiments, distinct trajectories of directional and diversifying selection on microbes in different contexts. Next, Jens ROLFF (Berlin, Germany) spoke eloquently about antimicrobial peptides (AMPs) as host defences and potentially valuable drugs in mixed-species communities. Especially impressive were his data suggesting that AMPs take minutes to kill microbes with high specificity, whereas antibiotics tend to take hours and are often broad-spectrum. He concluded with evidence that 7-AMP cocktails hold particular promise for host defence and confer robustness to the evolution of resistance in diverse symbiont communities.

Laurent DEBARBIEUX (Pasteur, France) was up next, with a return to considering lytic bacteriophage in the context of an intact microbiota. He described fine-scale spatial partitioning within the gut that enables populations of phage and microbes to coexist, as well as an example of a phage that requires an "intermediate host" microbe in order to adapt to its final host; such phage can only complete their life cycles in hosts with an intact, diverse microbiota. The session concluded with two short talks on new "model systems" for host-parasite coevolution in a symbiont-rich world. Ana SANTACRUZ (Stowers, US) gave an amazing talk on cavefish, which are blind, obese, starvation resistant, and long-lived if in a cave, but sighted, slim, and short-lived in rivers on the surface. She presented compelling evidence that cavefish do not escape parasites when underground and indeed exhibit greater symbiont community richness than do fish living on the surface. Finally, Chris LANE (Rhode Island, US) told us of a mysterious clade of Apicomplexa that contain bacterial endosymbionts and are apparently beneficial to their sea squirt host, in that the protozoan-prokaryote holobiont aids waste product detoxification in the renal sac of the ascidian. He framed his fascinating talk in light of the genome reductions often exhibited by parasites that can be reinstated in the Tangled Bank. The session therefore provided ample evidence that defensive and other physiological phenotypes of an array of plants and animals depend upon a diverse suite of symbionts, suggesting that host-parasite interactions are best understood, and clinical interventions are best honed, in a truly holistic context.

Session 4: Spatiotemporal Patterns of Hosts & Parasites

Planet Earth of course offers widely varied environments across both space and time that also impact trajectories of host-parasite coevolution. This final session therefore aimed to address spatiotemporal variation in host-parasite interactions through a variety of approaches, from mathematical or field-based observational to laboratory-based experimental studies. First, Oliver KALTZ (Montpellier, France) gave an intriguing talk on potential trade-offs between parasite virulence and host dispersal. He described an elegant series of experiments in protozoan hosts for whom he manipulated metapopulation structure while exposing them to bacteria. A key finding was that dispersing, highly connected hosts selected for relatively avirulent parasites and exhibited weak resistance against infection. Next, Thierry RIGAUD (Dijon, France) outlined the geographical distribution of diverse microsporidian parasites in amphipods while providing a very interesting history of Pasteur's work on the same clade of parasites, "cousins of fungi" with a host

range across insects and crustaceans. Maija JOKINEN (Zurich, Switzerland) then gave an excellent talk about complex viral communities in island plants. She reported results from ambitious reciprocal transplant experiments that revealed mixed evidence for local adaptation between plants and viruses as well as strong maternal effects on plant host health. Romain PIGEAULT thought-provoking (Poitiers, France) next presented evidence of anatomical compartmentalization of Wolbachia subpopulations within infected isopods (e.g., hemolymph, ovaries, or nerve chain of the host). Interestingly, he suggested that these anatomical compartments offer a structured fitness landscape and pose risk for short-sighted evolution for the parasites. In lieu of Frida BEN-AMI (Tel Aviv, Israel), who sadly cancelled at the last moment due to the onset of war, Ellen DECAESTECKER (Leuven, Belgium) then offered an impromptu talk in which she provided an interesting perspective on hierarchical interactions of water flea genotype with microbiota and environment (i.e., pond!) to determine tolerance of cyanobacteria. It's a complex world indeed.

The rest of the talks tackled temporal aspects of host-parasite coevolution. Martin GUILLEMET (Montpellier, France) began by creatively framing an "imaginary parasite" in light of life history trade-offs. He was especially interested in the variance-covariance matrix of parasite life history traits, and discovered that positive covariance is predicted to accelerate the approach of a parasite lineage to the evolutionary limit, while negative covariance slows optimization. These broad insights were followed by a terrific talk by Micaela MARTINEZ (Columbia, US) on circadian and seasonal rhythms in immune function in human subjects. She reported results of a new clinical study suggesting circadian rhythms in immune cell trafficking but not production of inflammatory cytokines, with potential implications for optimal vaccine administration. The final talk on temporal dynamics was given by Gabriele SORCI (Bourgogne, France), who took experimental and meta-analytic approaches to investigate why host age is such a key predictor of the severity of infectious diseases. For instance, his experimental data suggested decreased resistance and tolerance of malaria with age in mice, due to the decline in both immune function and hematopoesis with increasing age. In parallel, case fatality rate that he compiled from the World Health Organization indicated that human mortality rates due to lower respiratory infections and fibrotic lung diseases increase with age more rapidly than all-cause mortality. The mouse-human parallels suggested many new avenues for future research on inflammaging and beyond. The session therefore addressed diverse ways in which host-parasite interactions unfold across space and time, on both ecological and evolutionary timescales.

General discussion and conclusion

Infectious diseases present an inherently multi-scale problem for evolutionary biologists: it is crucial that we understand both within-host processes (e.g., competition for resources or activation of immune defenses by parasites) and between-host processes (e.g., transmission-promoting strategies for replication or manipulation by parasites), including any fitness trade-offs posed by the transition between scales, to understand the evolution of parasite strategies of attack and host strategies for defense. For example, the evolutionary fitness of vector-borne parasites is shaped by immune selection and competition within the host, but also by transmission from host to vector, selective processes within the vector, and transmission from the vector to a new host. Likewise, the evolutionary fitness of hosts is shaped by the relative costs and benefits of immune defense in light of the risk and cost of parasitism for each host, and for the other hosts with which each host must compete for food and mates. Finally, these

interactions are impacted by spatial & temporal heterogeneity in the landscapes in which hosts and parasites live and disperse/transmit. We were delighted that the conferences sessions not only addressed but also integrated across these themes.

Every talk in the oral sessions elicited multiple questions from the audience. Ultimately, Vice-Chair Oliver KALTZ led a final General Discussion, which highlighted the following points:

- The strength of this conference and what renders it unique continues to be the remarkable **diversity of approaches and systems** thereby promoting exchanges across disciplines. Analogies and common patterns that emerged by comparing and contrasting disparate systems were a favorite aspect of the conference for many. The conference also allowed junior scientists to foster new collaborations and job opportunities.
- Participants also highlighted that the atmosphere of the conference was extremely friendly and uncompetitive with a diversity of voices and viewpoints represented. The strong representation of junior scientists among the speakers and the outstanding and productive poster sessions were considered especially conducive to opening the community to new members. Maintaining such a productive and collaborative environment will be a primary aim in any renewed conference.
- Considerable attention was also given to the issues of **continuity and change** in conference participants. The fact that several of 2023's senior participants (including the Chair and Vice-Chair) first attended as postdocs nearly 20 years ago was taken as a positive sign of community continuity. At the same time, to continue to foster growth and the inclusion of new scientists at any future conferences, consensus was that past Chairs might primarily be encouraged to give poster presentations from now on, or perhaps recent previous Chairs could speak on the first evening of any future versions.
- There was unanimous and enthusiastic support for this conference to be renewed, and for Oliver KALTZ (Montpellier http://www.eec.univ-montp2.fr/people/oliver-kaltz/) and Britt KOSKELLA (California-Berkeley, USA https://naturesmicrocosm.com/) to be the next Chair and Vice-Chair, respectively. The complementarity of their research topics (Oliver is an experimental evolutionary ecologist working on the role of environmental and dispersal heterogeneities in the epidemiology of infection in protozoan meta-populations, while Britt studies within-host ecological and evolutionary dynamics of microbes of wild and domesticated plants) will be a great asset for the organisation of the next conference.
- People expressed interest in circulation of the participant list a few weeks in advance of future conferences, if possible, to help people plan their experience more thoroughly. People also expressed interest in obtaining a pdf version of the abstract book, during the week of the conference or soon thereafter, to permit further reflection on conference themes if the JMC organization would permit that in future years.
- The Chair and Vice-Chair and all attendees deeply appreciated the fantastic organizational work carried out by Nathalie BABIC, whose efficiency and friendliness are second to none. We gave her a standing ovation. We were also very grateful for the work of the photographer who provided us with many souvenirs. And last but not least, we thank the CNRS whole-heartedly for their support of this inspiring and unique conference.