



Sciences biologiques,  
Écologie et Environnement  
**CONFÉRENCES  
JACQUES-MONOD**



## **Virus evolution: the mutualism-antagonism continuum of virus-virus interactions**

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Report for the Conference Jacques Monod held in Roscoff on Oct 14-18 2024

### **Abstract**

The conference gathered experts from many fields working on various aspects of virus-virus interactions, ranging from mutualistic to parasitic, and harnessing different approaches to studying virus evolution (e.g., molecular biology, theory, mathematical modelling, genomics, phylogenetics, clinical studies, laboratory experiments). Altogether, this allowed the common theme of virus-virus interactions to be addressed from myriad perspectives, by researchers representing the breadth of career stages in academia, including graduate students, postdocs, beginning faculty and established experts. Moreover, some participants represented industry and government agency labs studying translational goals, creating a vibrant conference that spanned basic and applied research on virus-virus interactions, where virus evolution featured prominently.

# **1 General report**

## **1.1 Attendance & practical aspects**

The conference was an amazing success with 112 participants with 27 invited speakers and 85 contributing participants. At the end of registration, the conference had exceeded room capacity such that we had to make a waiting list. Of the 112 attending individuals, 46 were based in France (41 %), 38 elsewhere in Europe (34 %), and the remaining 28 in countries in North America and elsewhere (25%), with a total of 13 different countries represented in the conference. This combination made the conference a truly international one. Of our participants, 54 were women, and it is notable that 11 of the 27 invited speakers were women. Fifty-eight participants were PhD students, MSc or postdocs.

## **1.2 Conference final program**

One female invited speaker could not participate because of personal reasons. The approved program was otherwise fully followed. The presenters and session chairs did an excellent job of keeping the talks on time, which facilitated all of the practical aspects (coffee breaks, lunch breaks and dinners).

In total, we incorporated 43 oral presentations, including 27 invited speaker talks and 16 contributed talks. Because of the inherent bias towards experienced researchers among invited speakers, we biased the selection of contributed talks towards young researchers (PhD students or postdocs) to yield a total of 11 contributed talks were given by young researchers (~70% of contributed talks). Of the oral contributions, 21 (49%) were given by women.

# **2 Scientific presentations and discussion**

## **2.1 Social interactions among viruses, host immunity and context dependence in virus interactions I**

Brooke explored how defective interfering particles (DIPs) compete with wild-type influenza virus genomes, modulating viral pathogenicity and driving evolutionary dynamics. Specific nucleotide variants were identified that influence competition dynamics between wild-type and deletion-containing viral genomes.

Diaz Munoz showed how strain identity determines reassortment frequencies and how host cell metabolism influences defective viral genome production. Their findings highlight how virus-virus interactions are strain-specific and host-dependent.

Farjo demonstrated that superinfection exclusion limits viral replication in already infected cells, irrespective of genetic distance between coinfecting influenza strains, providing insights into the stages at which this exclusion mechanism impacts viral infection.

Lowen discussed how spatially structured viral populations compete for susceptible cells, creating antagonistic interactions despite coinfection boosting viral productivity, emphasizing the importance of spatial and biological scale in influenza virus interactions.

Willemsen explored interactions between giant viruses and unicellular hosts, highlighting mutualistic and antagonistic relationships. Her research delved into how these interactions impact viral competition, gene transfer, and viral replication at cellular and community levels.

Iranzo explored the relationship between horizontally transmitted mobile genetic elements (MGE) and antiphage defense systems. His phylogenetically aware analyses of >20000 prokaryotic genomes annotated for MGEs revealed that overall there is no association, though whenever associations exist they are very strong. The taxon specificity of associations could be explained by the linkage

hypothesis: when a defense system is lost an MGE is lost as well, and conversely, such that there is a concerted gain and loss of MGEs and defenses.

Etienne discussed the evolutionary arms race between viruses and hosts, focusing on ancestral immunity mechanisms conserved across life forms and how they shape modern immune responses and viral adaptation.

Maurin tracked the evolution of a virulent phage, showing host-range expansion and increased virulence through parallel mutations. Her work emphasized the genetic mechanisms behind phage adaptation in variable environments.

García-Arenal demonstrated that plant viruses can act as mutualists under stress conditions, improving plant survival. However, the outcome of these interactions is highly context-dependent, influenced by environmental factors and plant life history traits.

## **2.2 Social interactions among viruses, host immunity and context dependence in virus interactions II**

Noris revealed that geminiviruses can facilitate horizontal gene transfer by integrating host DNA into viral genomes, producing extrachromosomal circular DNA (hv-eccDNA) that can be transmitted to other hosts, advancing understanding of plant-virus gene exchange mechanisms.

Quang demonstrated that defective viral genomes (DVGs) can contribute to viral adaptation by acting as viral mutators, accumulating mutations and recombining with standard viral genomes.

McKellar explored novel deltaviruses, which hijack glycoproteins from helper viruses to produce infectious particles. His research revealed that these viruses might physically attach to helper viruses, enhancing their ability to cross species barriers.

Jouvenet's team investigated how RNA viruses overcome the innate immune response, identifying novel interferon-stimulated genes that modulate viral replication. The study also examined viral strategies to evade interferon defenses, contributing to our understanding of viral evolution and host specificity.

Sanjuán's team revealed that most animal RNA viruses can enter human cells, suggesting that viral entry represents a weak barrier to zoonotic transmission, with factors like receptor binding proteins playing a secondary role in cross-species infection.

Piganeau presented genomic and metagenomic approaches to study virus-host interactions in marine picoplankton. Her lab isolated and sequenced microalgae and Prasinoviruses, exploring mechanisms of transitions from resistance to susceptibility, often accompanied by chromosome size changes, through omics data.

Wendling examined how integrative viruses compete for chromosomal insertion sites in bacteria. Her study revealed that competition drives viral diversification, with ecological competition playing a key role in the evolution of integrative viruses and host-virus coevolution.

## **2.3 Evolutionary ecology of virus interactions in natural environments.**

Sullivan discussed the ecological roles of ocean viruses, which influence microbial populations and global biogeochemical cycles. He explored virus evolution, focusing on co-evolutionary metabolic exchanges, resistance costs, and the impact of viruses on early life on Earth.

Baudoux highlighted the impact of viral lysis on marine food-web dynamics and biogeochemical cycles. Her research focused on how viral infections of marine diatoms alter cellular metabolism and carbon fixation, with significant implications for marine ecosystems.

De Almeida presented a small RNA-based metagenomics approach to analyze mosquito viromes, revealing interactions between insect-specific viruses and arboviruses. His findings suggest that co-infection with certain viruses can enhance the transmission of dengue and Zika viruses.

Roumagnac used metagenomics to investigate how plant diversity influences viral richness in grassland ecosystems. His study found that plant richness, biomass, and geography significantly impact viral diversity, supporting the host-diversity-begets-parasite-diversity hypothesis.

Manley's research focused on how temperate phages use peptide-based communication systems to decide between lytic and lysogenic cycles. She demonstrated that phages can recognize non-cognate signals from unrelated phages, suggesting cross-phage communication could be adaptive.

Wilfert showed, among other things, that the deformed wing virus acquired transmission by the honeybee parasite *Varroa destructor*, which drastically altered honeybee virome, with deformed wing virus becoming dominant, while other viruses decreased in prevalence, impacting the wider bee community over time.

Boots examined how mass migration of honeybee colonies for almond pollination influences viral dynamics. Longitudinal data revealed that co-infections and viral dynamics are significantly shaped by environmental perturbations, with no sign of significant interactions among viruses and with changes in the virome observed throughout the almond bloom.

Alizon studied the HPV infection kinetics in a cohort of young women, revealing patterns of viral load growth, plateau, and clearance. The results indicate that rapid infection clearance may be associated with immune responses, especially cytokines and TCR-Gamma-Delta cells, while HPV genomes exhibited unexpected evolutionary lability.

After briefly discussing differences and similarities between viruses and plasmids, Bonhoeffer presented theoretical predictions on the conditions which would favor that a given gene is borne by a plasmid vs. the bacterial chromosome. The outcome depends on the cost of plasmid carriage, the fitness of the plasmid, the selection acting on the gene under consideration, the relative rates of gene loss on the plasmid vs. the chromosome.

## **2.4 Effects of virus interactions on adaptability and evolvability.**

Elena explored how RNA viruses exhibit social traits, such as cooperation and defection, due to high mutation rates. He highlighted how viral quasispecies can evolve through public goods games, leading to diverse strategies like ultra-defection and cooperation. More generally he showed that quasispecies models can be expressed in terms of social evolution models.

Gandon discussed how viruses evolve plastic virulence strategies based on environmental conditions and coinfection frequency. He modeled how viruses modulate host exploitation to maximize transmission, predicting that sensing infection density leads to lower virulence in frequent coinfections.

Romero explored how population size impacts HIV recombination and resistance to broadly neutralizing antibodies (bNAbs). Her models suggest that recombination before treatment disperses escape mutations, while reduced recombination during bottlenecks limits new resistant haplotypes. Long-read sequence analysis of experimental HIV populations submitted to treatment revealed that single lineages are often rescued by multiple escape mutations, while the same escape mutation can rescue different lineages through recombination or recurrent mutation. Thus, extremely parallel evolution permits HIV to persist through population contractions.

Regoes presented long-term experiments with HIV-1 and bacteriophage phiX174, showcasing strong parallel evolution. These experiments aim to evaluate the capacity of phylodynamic methods to uncover evolutionary and population history through genomic and epidemiological data in cases

where these histories and propagation parameters are known. The results show that migration rates are wrongly inferred.

## 2.5 Importance of virus interactions in disease.

Turner explored how lytic phages interact within microbial communities, affecting ecological dynamics and phage therapy outcomes. His studies focused on co-infection strategies and interactions with satellite phages, revealing novel insights into phage evolution and applications in combating antibiotic resistance.

Domingo-Calap studied phage-phage interactions in *Klebsiella pneumoniae* phage cocktails, identifying synergistic and antagonistic effects that influence phage infectivity and resistance. Her research supports optimizing phage combinations to enhance therapeutic outcomes in bacterial infections.

Ferriol-González investigated how *Klebsiella* phages adapt to diverse host environments. Phages evolved through Receptor Binding Protein (RBP) modifications, exhibiting variable levels of parallel evolution and recombination depending on their specialization degree, offering insights into phage adaptation and host range expansion.

Koskella emphasized the importance of understanding bacteria-phage coevolution in complex communities, where historical contingency, cross-resistance, and prophage interactions shape future bacterial and viral evolutionary trajectories. Similarly to plasmids in Bonhoeffer's talk, she showed prophages may protect their hosts against superinfection leading to an interesting interplay between genes carried by phages or the bacterial chromosome. She also presented a meta-analysis addressing whether a healthy ecosystem is one rich in parasites, showing that the current results are inconclusive: in most cases there is no correlation between parasite alpha-diversity and dysbiosis.

Chevallereau explored how spatial structure affects the spread of anti-CRISPR phages in *Pseudomonas aeruginosa*. Her experimental and theoretical work revealed that spatial structure can either promote or inhibit viral spread depending on the properties of the anti-CRISPR proteins.

Sofonea considered how viral polymorphism and interactions at the within-host level influence transmission and evolution, demonstrating a selection bias towards higher virulence driven by small phenotypic mutations, confirmed through mathematical modeling and stochastic simulations.

Elie's simulations show that individual heterogeneity in transmission rates and infection durations significantly affects outbreak dynamics, with realistic infection duration distributions leading to faster outbreaks and adaptive mutations influencing parasite emergence.

Lythgoe explored how within-host viral replication impacts evolution at the population level, using deep-sequencing data from HIV, hepatitis C, and SARS-CoV-2, revealing the role of within-host processes on viral spread and evolution between hosts.

Metcalf discussed how viral interactions and cross-immunity shape immune escape evolution, using coronaviruses and influenza as case studies, and emphasized the complexities of natural systems and host immune heterogeneity, in particular with respect to host gender, in predicting immune escape dynamics.

## 2.6 Social interactions among viruses, host immunity and context dependence in virus interactions III.

Shepherd described the "dirty mouse" model for studying cross-species virus transmission. Using next-generation sequencing, her team tracked transmission of viruses sampled in pet shop mice *Mus musculus* to wild mice *Peromyscus maniculatus*, documenting cases of dead-end transmission and

strong transmission bottlenecks and calling for more work identifying viral genetic changes facilitating cross-species transmission.

Irby's study of *Pseudomonas aeruginosa* genomes revealed how prophages engage in social dilemmas, with some being domesticated by hosts, offering mutual benefits like antibiotic resistance, while others retain horizontal gene transfer potential, shaping bacterial evolution. Her analysis showed in particular that antiphage defense genes are carried by domesticated prophages which lost the capacity to be horizontally transmitted.

Zwart presented theoretical results showing that the capacity of multipartite viruses to modulate the relative frequency distribution of their segments, termed genome formula, can be adaptive. He then showed results on the tripartite cucumber mosaic virus (CMV) segment frequency variation, discovering high genome formula variability within hosts. His research suggested that multipartite virus evolution is driven by within-host selection, with field studies showing genome formula adaptation based on environmental conditions.

Blanc revisited results on the multipartite faba bean necrotic stunt virus (FBNSV) showing that its segments can collectively function in different host cells and more separately between hosts. He then showcased the monopartite segmented tomato spotted wilt virus (TSWV), where experimental findings suggest that individual virions often carry only one genomic segment, to challenge assumptions about monopartite segmented virus particle packaging, and to suggest that such viruses may function in a way reminiscent of the multipartite viruses.

Michalakis studied reassortment in multipartite viruses, recalling that these viruses *a priori* have a much higher capacity to reassort than other viruses, since genomic segments can exchange between viral isolates without coinfection in the same host cell. He presented a systematic analysis of single segment reassortments between FBNSV isolates to show that phenotypic traits of this virus, like viral load, transmission and symptom development, are overall robust to reassortment while the genome formula is very labile, suggesting that trait robustness may be achieved by segment frequency distribution modulations.

### 3 Conclusion and recommendations

As evident in the scientific report, the contents presented were rich and of the highest quality, generally representing leading edge work in the field of virus evolution. Many participants were clearly interested in advancing the basic understanding of virus-virus interactions via a focus on virus evolution, and very many described how their basic research related to applied goals, or were conducting translational studies that directly addressed problems of societal concern in conservation biology, agriculture, and medicine.

Participants engaged in lively discussions at the end of the talks, during the poster sessions, coffee breaks, meals and for many, after meals. All participants remarked how much they appreciated the very engaging friendly and productive atmosphere allowing debates and exchanges of scientific points of view in a highly welcoming and inclusive setting.

The recommendation we can provide for INEE, INSB and INSERM is that virus evolution is a perfect topic to achieve truly interdisciplinary research on a clearly important topic, as the COVID-19 pandemic and disease importance of viruses reminds us. Moreover, the very many exciting talks on virus interactions in natural ecosystems and the ongoing discoveries of viruses new to science similarly reminds that virus biodiversity, and the direct and indirect ecological interactions among viruses are fundamental for understanding past, present and future of virus evolution across all levels of biology on Earth.

The conference ended with two important votes. The first was unanimously in favor of applying for a renewal of a conference on virus evolution, focusing on a subtopic different than in

prior years. The second was also strongly in favor of the team that would lead this effort in applying for a renewal. Dr. Yannis Michalakis (CNRS, Montpellier) moves from vice-chairperson to chairperson of the conference. He will be assisted by Dr. Anice Lowen (Emory University) as vice-chairperson.

We would like to acknowledge the extremely useful and competent assistance by Nathalie Babic. We would also like to thank the restaurant personnel for the quality of their service. On a practical note one thing that could be improved is the acoustic quality of the poster room. The current room's acoustics, combined to the large affluence inherent to these conferences, makes discussions difficult to follow, which is counter productive and against the spirit of these conferences. We do not know what can be done, either to ameliorate the acoustics of the currently used room or perhaps find another room for poster sessions, but we think the issue deserves thorough consideration as poster sessions are an important asset for Jacques Monod Conferences.

## Résumé en français

La conférence a rassemblé des experts de nombreux domaines travaillant sur divers aspects des interactions entre virus, allant du mutualisme au parasitisme, et utilisant différentes approches pour étudier l'évolution des virus (p. ex. biologie moléculaire, théorie, modélisation mathématique, génomique, phylogénétique, études cliniques, expériences en laboratoire). Dans l'ensemble, cela a permis d'aborder le thème commun des interactions entre virus à partir d'une myriade de perspectives, par des chercheurs représentant l'étendue des étapes de la carrière dans le milieu universitaire, y compris des étudiants des cycles supérieurs, des postdocs, des professeurs débutants et des experts établis. De plus, certains participants représentaient des laboratoires de l'industrie et d'organismes gouvernementaux, créant ainsi une conférence dynamique qui couvrait la recherche fondamentale et appliquée sur les interactions entre virus, où l'évolution des virus occupait une place centrale.

La conférence a connu un grand succès avec 112 participants, soit 27 conférenciers invités et 85 participants inscrits. À la fin de l'inscription, la conférence avait dépassé la capacité d'accueil et nous avons dû établir une liste d'attente. Sur les 112 personnes présentes, 46 étaient basées en France (41%), 38 ailleurs en Europe (34%) et les 28 autres dans des pays d'Amérique du Nord et d'ailleurs (25%), avec un total de 13 pays différents représentés à la conférence. Cette combinaison a fait de la conférence un événement véritablement international. Parmi nos 112 participants, 54 étaient des femmes, alors que 11 des 27 personnes invitées étaient des femmes. Cinquante-huit participants étaient des étudiants en thèse, master ou postdocs. Au total, nous avons eu 43 exposés oraux, 27 donnés par les conférenciers invités et 16 exposés contribués. Parmi ces derniers 11 ont été présentés par de personnes en début de carrière (~70% des exposés contribués).

Les participants ont eu des discussions animées à la fin des exposés, pendant les séances posters, les pauses café, les repas et pour plusieurs, après les repas. Les participants ont apprécié l'atmosphère amicale permettant des échanges productifs dans un cadre accueillant et inclusif.