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CONFÉRENCES
JACQUES-MONOD

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# Analyses moléculaires de l'organisation et du remodelage des membranes

## *Molecular basis for membrane remodelling and organisation*


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**Rapport sur la Conférence**
*Conference Report*

**French summary / Résumé en français**

La conférence Jacques Monod “Analyses moléculaires de l’organisation et du remodelage des membranes”, s’est tenue à Roscoff du 16 au 20 mai 2022. Cette conférence organisée par Ludger Johannes (Président) et Anne-Claude Gavin (Vice-Présidente) a réuni un total de 103 participants du monde entier (incluant entre autre : France, Allemagne, Suisse, UK, Europe, Israël, USA, Inde,), dont les 2 organisateurs, 27 conférenciers invités, 71 participants (étudiants en thèse, post-doctorants et chefs d’équipes), 2 éditeurs de journaux scientifiques (Journal of Cell Science, Nature Reviews Molecular and Cell Biology) et 1 représentant de l’industrie (Lipotype GmbH).

Au cours de cette conférence les participants ont discuté des avancées les plus récentes concernant l’organisation et du remodelage des membranes, et en particulier 1) l’organisation membranaire, 2) la déformation de la membrane et la mécanosignalisation, 3) l’endocytose et trafic intracellulaire, 4) la biogenèse des membranes et le métabolisme, 5) reconnaissance cellulaire et 6) la chemobiologie des membranes.

Grâce à l’implication des participants, des orateurs invités (27 présentations), des orateurs sélectionnés sur la base de leurs résumés (16 présentations) et des organisateurs (2 présentations), la conférence a été un véritable succès et une occasion unique d’échanger autour de ce champ de recherche qui se situe au cœur de l’interaction des cellules avec leur environnement.

The Jacques Monod conference "Molecular analysis of membrane organization and remodeling" was held in Roscoff from May 16 to 20, 2022. This conference, organized by Ludger Johannes (Chairman) and Anne-Claude Gavin (Vice-Chairman), brought together a total of 103 participants from all over the world (including among other: France, Germany, Switzerland, UK, Europe, Israel, USA, India), including the 2 organizers, 27 invited speakers, 71 participants (PhD students, post-docs and team leaders), 2 scientific journal editors (Journal of Cell Science, Nature Reviews Molecular and Cell Biology) and 1 company (Lipotype GmbH). The conference was a real success, and a unique opportunity to exchange ideas on this field of research, which lies at the heart of the interaction between cells and their environment.

**Aim of the conference**. Biological membranes provide tight barriers that allow to isolate cells from their environment, and to delineate the cells' interior into intracellular compartments with defined functions. As such, these membranes must be constantly remodelled to allow for selective exchanges and to support and accompany shape transitions that cells undergo during normal development and in specific disease states. The 2022 conference has highlighted developments that have occurred since the previous meeting in 2017, which itself followed up on initial conferences on this theme in 2011 and 2014. Specifically, the 2022 conference has broken new grounds when compared to the previous ones by putting an emphasis on 3 areas that have lately been particularly dynamic: The resolution revolution in cryo-electron microscopy (cryo-EM), which opens unprecedented possibilities for near-atomistic structure determination on model membrane substrates and in cells; the rise of chemical biology as a source for tailor-made tools and ground-breaking concepts in the life sciences; and the integration of membrane biogenesis with metabolism based on ever more performant mass spectroscopy equipment that allows to work with ever smaller quantities of materials. While related topics are covered in other meetings (e.g., the Molecular Membrane Biology Gordon conference or the EMBO Endocytosis conference), in none of these cases are membrane shape changes the uniquely underlying theme, which makes the "Molecular analysis of membrane organization and remodeling" conference truly stand out. This is also reflected by the fact that interdisciplinary has become second to none to this conference. Indeed, also for the 2022 meeting biophysics, computational biology, and systems biology have played key roles as providers of novel conceptual perspectives and methodological innovation. The program included a number of physicist speakers whose capacity to engage productively with the membrane biology community was one of the highlights of the meeting.

**Conference overview**. The conference started on Monday, May 16, 2022, with welcome drinks and a dinner at the Gulf Stream Hotel, followed by 2 introductory lectures. All lectures were given in the beautiful auditorium of the Station Biologique CNRS. Part of Wednesday afternoon, May 18, 2023, was devoted to a visit of the Batz Island. The scientific program of the conference ended in the early evening of Thursday, May 19, 2023, followed by a banquet. People departed early in the morning of Friday, May 20, 2023.

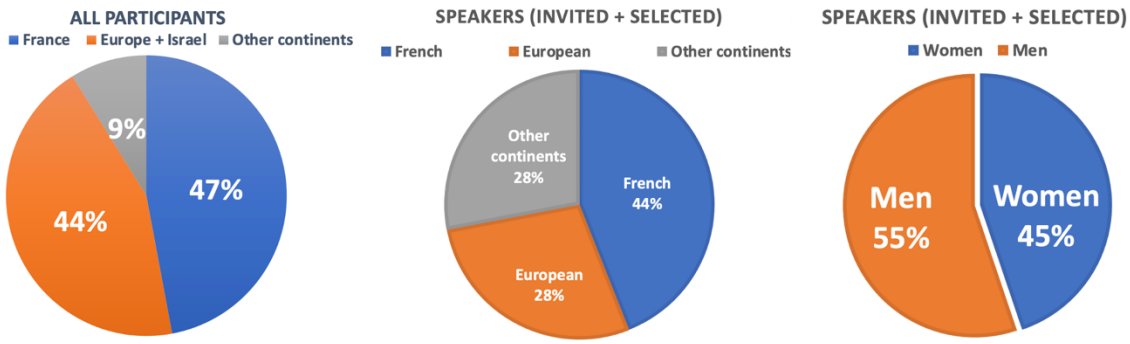
- 2 introductory lectures (30 min)
- 6 sessions with dedicated chairs chosen amongst the conference participants:
    - Session 1 — Membrane organization
    - Session 2 — Membrane deformation-mechanosignaling
    - Session 3 — Endocytosis and intracellular trafficking
    - Session 4 — Membrane biogenesis-metabolism

Session 5 — Cellular recognition
Session 6 — Chemical biology of membranes

- 29 presentations by invited speakers and organizers in sessions (20 min + 10 min for questions)
- 16 presentations selected from abstracts (15 min + 5 min for questions)
- 2 poster sessions (2 hours each)

All aspects of management of the conference and the food were more than satisfactory, thanks to the expert care of Nathalie Babic and her colleagues. Overall, the conference was a big success, with a highly positive and even enthusiastic feedback of participants at both scientific and organizational levels.

## Conference statistics = placeholder, to be replaced by our figures




## Scientific program

Selective transport across membranes is in some cases assured by channels. In other cases, however, biomolecules are englobed in vesicular or tubular carriers that detach from donor compartments and then fuse with acceptor compartments. The biogenesis of these carriers by bud formation and membrane scission, and their fusion with acceptor membranes are tightly regulated processes for which the membranes must undergo narrow curvature changes. These cannot occur spontaneously and need to be driven by protein machinery, in interaction with membrane lipids. Protein-lipid assemblies are very dynamic, often involving multiple bond interactions that are individually of low affinity. The field of membrane remodeling and organization therefore remains a fruitful ground of conceptual and methodological innovation.

## Introductory lectures

**Petra Schwille** from the Max Planck Institut of Biochemistry, Munich, Germany, reported on experimental biophysics approaches to study active mechanisms of lateral protein organization on membranes. Using reconstitution approaches, she documented the swiping movement of bacterial MinD/E proteins and Ftz filaments that as a force inducing system. **Elina Ikonen** from the University of Helsinki, Finland, exemplified the mechanisms that govern the distribution, trafficking, and storage of major lipid species, such as cholesterol and related lipids. She exposed new tools to visualize the distribution and trafficking of these lipids in cells.

**Session 1 — Membrane organization** (Chairs: Dimitrios Stamou, Alison Forrester, Vadim Frolov, Larissa Van Ek, Patricia Bassereau, Ranjit Gulvady)

This long session covered theoretical and computer-based modelling of membranes, their dynamic or high-resolution imaging, their lateral compartmentalization in 2D, or their bending in 3D. **Patricia Bassereau** from Institut Curie, Paris, France, reported on experimental biophysics approaches to study membrane deformation and curvature-dependent protein sorting, notably in the IRSp53 and actin-dependent formation of filopodia. **Agata Nawrotek** from École normale supérieure Paris-Saclay, France, presented her research on the functional cycle of the Rac1 GTPase and the fact that membranes are an integral part of this cycle. **William Prinz** from the National Institutes of Health, Bethesda, USA, presented a novel reconstitution system to study the formation of lipid droplets and started to dissect the role of seipins in the process. **Daniel Levy** from Institut Curie, Paris, France, described his cryo-electron tomography studies on VAP proteins and their role in the generation of membrane contact sites. **Roberto Weigert** from the National Cancer Institute, Bethesda, USA, took the conference participants on a ride by intravital subcellular microscopy to explore how action/myosin-II cages drive secretory granule exocytosis in salivary gland cells. **Anaïs Vlieghe** from the Center of Psychiatry and Neuroscience, Paris, France, has investigated the function of cardiolipin and other lipids in mitochondrial membrane fission driven by mitofusins and has discovered a function of actin and spectrins as diffusion barriers. **Corinne Albigès-Rizo** from the Institute for Advanced Biosciences, Grenoble, France, has dissected the role of integrins in SMAD signaling and their interaction with the BMP pathway. **Daniel Roderer** from the Leibniz-Institute for Molecular Pharmacology, Berlin, Germany, has started to use cryo-electron microscopy to understand how the intestinal fusobacterium interacts with E-cadherin on intestinal cells. **Dimitrios Stamou** from the University of Copenhagen, Denmark, explored shallow curvature and their existence at steady state at the plasma membrane outside specialized areas such as endocytic pits. **Doris Höglinger** from Heidelberg University, Germany, has presented chemical tools and sensors to study the mechanisms involved in lipid-mediated signaling events, notably sphingosine transport by NPC-1 and the role of STARD3 in cholesterol transport from the endoplasmic reticulum to lysosomes.

**Session 2 — Membrane deformation-mechanosignaling** (Chairs: Bruno Antonny, Ranjit Gulvady, Feng-Ching Tsai, Alison Forrester)

In relation to membrane bending, **Tom A. Rapoport** from Harvard Medical School, Boston, USA, presented his recent investigations into the REEP family of ER proteins and their role in autophagy. **Delphine Muriaux** from the Institut de Recherche en Infectiologie de Montpellier, France, has identified cellular factors that help the Gag protein from HIV to bend membranes, notably IRSp53. **Ilpo Vattulainen** from the University of Helsinki, Finland, presented computational and theoretical biophysics approaches to the study of membranes in the dry eye syndrome and lung surfactant. **Christophe Lamaze** from Institut Curie, Paris, France, explained how highly bent caveolar membrane invaginations function in mechanoprotection and mechanosignaling. **Anne Kenworthy** from the University of Virginia, Charlottesville, USA, presented groundbreaking data on the ultrastructural organization of caveolae. **Guillaume Montagnac** from Institut Gustaf Roussy, Villejuif, France, presented mechanisms by which clathrin contributes in an endocytosis-independent manner to cell adhesion and migration, notably also in interplay with caveolae. **Oliver Daumke** from the Max Delbrück Center, Berlin, Germany, shared cryo-electron microscopy data on the interaction between Mic60 and Mic19 and their possible function as a diffusion barrier on inner mitochondrial membranes. **Bruno Antonny** from the Institut de Pharmacologie Moléculaire et Cellulaire, Valbonne, France, has

studied the biochemistry of very small TPD54 vesicles and their localization to Golgi and other small structures.

**Session 3 — Endocytosis and intracellular trafficking** (Chairs: Bart M. H. Bruininks, Kevin Titeca, Giovanni D'Angelo, Larissa Van Ek, Alison Forrester, Kevin Titeca)

In this session, trafficking processes to and from the plasma membrane were discussed from mechanistic and functional perspectives. **Harvey McMahon** from the Medical Research Council Laboratory of Molecular Biology, Cambridge, England, presented evidence for aggregation-dependent endocytosis for the clearance of aggregates from the plasma membrane. **Stéphanie Miserey-Lenkei** from Institut Curie, Paris, France, discussed mechanisms of membrane trafficking between Golgi at fusion hot spots near focal adhesions at the plasma membrane. **Markku Hakala** from the University of Geneva (Switzerland) described the reconstitution of endosomal ESCRT-0/clathrin lattices in model membrane systems. **Volker Haucke** from the Leibniz Institut für Molekulare Pharmakologie, Berlin, Germany, illustrated the links between early endosomes, the ER and mitochondria and suggested that ER shape changes transmit early endosomal signals to mitochondria. **Yael Elbaz-Alon** from the Weizmann Institute of Science, Rehovot, Israel, also pointed out a tripartite interaction between ER, endosomes and mitochondria, via the ER protein PDZD8, Rab7 on endosomes and unknown determinants on mitochondria. **Jennifer Hinshaw** from the National Institutes of Health, Bethesda, USA, described how she uses high resolution cryo-EM to dissect the molecular mechanisms by which the pinchase dynamin severs membranes, and notably a novel link to actin. **Henri-François Renard** from Namur University, Belgium, discussed the link between the galectin-driven endocytosis of CD166 and the formation of immune synapses between melanoma cells and cytotoxic T lymphocytes. **Stéphane Frémont** from Institut Pasteur, Paris, France, evaluated the role of MICAL in actin dynamics linked to the budding of HIV at the plasma membrane. **Cécile Gauthier-Rouvière** from the Centre de Recherche de Biochimie Macromoléculaire, Montpellier, France, presented new evidence for the role of flotillins in clathrin-independent endocytosis, notably via the oligomerization of these proteins. **Raya Sorkin** from Tel Aviv University, Israel, has provided evidence for migrasomes, which are extracellular vesicles that are left behind when cells have moved on, and the possible rome of TSPN4 on these structures. **Felix Campelo** from the Institute of Photonic Sciences, Barcelona, Spain, talked about TANGO1 and its role in the formation of transport carriers at the ERGIC.

**Session 4 — Membrane biogenesis-metabolism** (Chairs: Kevin Titeca, Alison Forrester)

Cellular membranes are extremely complex, and consist of hundreds of different lipid species that can accumulate at specific locations and can form gradients that play important roles in defining organelles' identity and function. In this session, the organization of cellular membranes was discussed, which implies compartmentalized metabolism and involves enzymes often located in distinct organelles or even different cell types. **Giovanni D'Angelo** from the Ecole Polytechnique Fédérale de Lausanne (EPFL), Switzerland, presented data on how the glycosphingolipid make-up of a cell, termed the lipotype, contributes to establish and maintain cell identities during developmental processes. **Marie-Cécile Caillaud** from the Laboratoire de Reproduction et Développement des Plantes, Ecole Normale Superieure de Lyon, France, decorticated the mechanisms involved in the patterning of phosphoinositides in plant plasma membranes and how they contribute to cell division and the maintenance of a cellular memory of the division plane. **Cloé Feral** from the Institute for Research on Cancer

and Aging, Nice, France, analyzed the link between CD98hc, an amino acid transporter, and integrin in mechanosignaling. **Vanni Stefano** from the University of Fribourg, Switzerland, presented multi-scale molecular simulations on how structural properties of lipids determine their metabolic fate, from storage and catabolism to intracellular transport by lipid transport proteins. **Christian Klose** from Lipotype, Dresden, Germany, presented data on yeast lipidomics and how it improves our understanding of membrane remodeling processes.

**Session 5 — Cellular recognition** (Chairs: Cyril Hanus, Larissa Van Ek)
Pathogens have developed sophisticated systems that enable them to recognize, perturb, manipulate and highjack specific cellular membranes. The lectures in this session were dedicated to this and related emerging topics on cellular recognition. **Emmanuel Lemichez** from Institut Pasteur, Paris, France, presented the various roles and cellular targets of bacterial toxins in host–pathogen interactions, using genetic, cellular microbiology and animal model approaches. **Roland Knorr** from the Humboldt University, Berlin, Germany, investigated the interface between membranes and biomolecular condensates in model membrane systems and observed a spontaneous interaction. **Ludger Johannes** from Institut Curie, Paris, France, presented data on glycan-based construction of endocytic pits driven by glycan-binding lectins of cellular or pathogenic origin, and notably their capacity to bend membranes in interaction with glycolipids. **Emmanuelle M. Bayer** from Bordeaux University, France, presented results on the control of plant cell-to-cell communication through endoplasmic reticulum-plasma membrane contact sites at the level of plasmodesmata.

**Session 6 — Chemical biology of membranes** (Chairs: Luca Monticelli, Ranjit Gulvady)
Chemical biology is an area of research in which chemical and biological concepts and tools interact synergistically. This integrated approach is increasing applied to research on membranes. **Yamuna Krishnan** from the University of Chicago, USA, presented nucleic acid-based molecular devices for the study of ratiometric dosage of pH and $K^+$ in intracellular organelles. **Benoît Kornmann** from ETH, Zurich, Switzerland, presented data on lipid transport proteins and their redundancy at membrane contact sites. **Anne-Claude Gavin** from the University of Geneva, Switzerland, presented the liposome array system to measure protein-lipid interaction at large scale and its application to ApoE4 as an exceptionally efficient triacylglycerol binder. **Nir Gov** from the Weizmann Institute of Science, Rehovot, Israel, closed the meeting by providing a theoretical overview on membrane compartmentalization and deformation.

The conference was a scientific success, which certainly explains to a large extent the enthusiastic feedback from the participants. The fact that it was one of the first fully on site meetings after the confinement periods certainly has also added to the exceptionally vibrant atmosphere.

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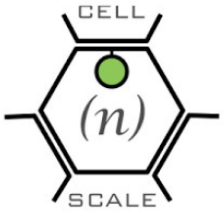
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