BBA - Biomembranes 1863 (2021) 183609

Contents lists available at ScienceDirect

BBA - Biomembranes

journal homepage: www.elsevier.com/locate/bbamem

Foreword to: Biophysical studies of membrane systems and interactions - Commemorative issue in honour of Professor Michèle Auger

Dror E. Warschawski [a], K.V. Lakshmi [b], Isabelle Marcotte [c,*]

[a] Laboratoire des Biomolécules, LBM, CNRS UMR 7203, Sorbonne Université, École normale supérieure, PSL University, 75005 Paris, France
[b] Department of Chemistry and Chemical Biology and The Baruch '60 Center for Biochemical Solar Energy Research, Rensselaer Polytechnic Institute, Troy, NY 12180, USA
[c] Department of Chemistry, Université du Québec à Montréal, P.O. Box 8888, Downtown Station, H3C 3P8 Montreal, Canada

ARTICLE INFO

Keywords:
Membrane interactions
Membrane peptides and proteins
Solid-state NMR
Spectroscopy
Membrane structure
Membrane lipids

1. Foreword

Professor Michele Auger (1963–2018) pioneered NMR methods to study membrane interactions, and membrane proteins by solid-state NMR, and other spectroscopic techniques. She was passionate about nurturing the next generation of chemists and biophysicists through teaching, training and mentoring students and junior colleagues. She is deeply missed.

Professor Michèle Auger passed away in October 2018, after a long, fruitful and highly rewarding career in the field of membrane biophysics. Michèle was mostly interested in the importance of membranes as key biological interfaces, and in her research she deployed a wide range of experimental approaches to study them. She has contributed immensely to our knowledge on the physical chemistry of membranes, membrane interactions, and membrane-bound proteins and peptides through the application of solid-state nuclear magnetic resonance (SS-NMR), as well as infrared and Raman spectroscopy, and various other complementary techniques. This special issue, which is dedicated to these topics, is a tribute to her career, with contributions by numerous collaborators and friends.

In consideration of Michèle's extensive contributions to the investigation of lipid bilayers, the enormous complexity of lipid systems and their role in peptide interactions are covered in this issue. In his review article, Hideo Akutsu nicely presents how complementary spectroscopic approaches can allow one to better study the miscibility of various phospholipids in a bilayer [1]. The role of the phospholipid headgroups in creating interactions with membrane-active molecules is also illustrated in this review using antimicrobial peptides (AMPs), notably studied by Michèle together with her collaborators and students [2–4]. In their paper, Ramos et al. revisit the lamellar to hexagonal phase transition in membranes as studied by ^{31}P and ^{2}H SS-NMR, calculating the partitioning constant of alkanes between, but also within, the different phases [5].

Membranes that are oriented in the magnetic field, either magnetically or mechanically, can bring valuable information on the position

* Corresponding author.
E-mail address: marcotte.isabelle@uqam.ca (I. Marcotte).

https://doi.org/10.1016/j.bbamem.2021.183609
Received 1 March 2021; Accepted 17 March 2021
Available online 29 March 2021

and interactions of proteins and peptides through SS-NMR studies. The development and application of such approaches have been amongst Michèle's many scientific contributions (for example [6–9]). This special issue presents the characterization of new orientable systems and the application of oriented membranes to gather information on AMPs and lipids. A review of two widely used lipid nano-objects - bicelles and nanodiscs – is presented by Erick Dufourc [10]. Moreover, in their paper, Park et al. explore the use of phospholipid polymer macrodiscs that align in the magnetic field as a new alternative to bicelles for studying membrane proteins by SS-NMR [11]. Di Mauro et al. show that the insertion of paramagnetic tags in the outer polymer belt of lipid nanodiscs can reduce NMR acquisition times [12]. Gravel et al. propose new oriented membranes composed of phospholipids and Tween 80 - a detergent that is often used to isolate and stabilize membrane proteins, thereby conveniently avoiding the detergent removal step prior to SS-NMR investigations [13]. They show that the orientation of these elongated vesicles can be flipped in the magnetic field when lanthanide ions are added, and they determine the orientation of a model peptide. Michèle actively participated in this research together with her student Matthieu Fillion, and her former students Alexandre Arnold and Isabelle Marcotte.

In their paper, Jeong et al. tackle the structures of three promising AMPs by solution NMR, and their position relative to the membrane was studied by SS-NMR in bicelles [14]. While bicelles have originally been developed mostly for SS-NMR applications, Evans et al. expand on their use by performing electron paramagnetic resonance (EPR), and circular dichroism (CD) spectroscopy studies, focusing on the transmembrane peptide fukutin-1 [15]. The paper from Schmidt and Davis investigates liquid ordered–liquid disordered fluid phase coexistence in lipid mixtures [16]. Using two types of oriented membranes, i.e., magnetically (bicelles) and mechanically oriented bilayers, they study the interaction of a synthetic peptide, and look at the lipid phase behavior as well as the orientation and dynamics of the peptide. Furthermore, Strandberg et al. explore the role of the positively charged residue at the N-terminus in the pore forming activity of AMP-analogs using mechanically oriented bilayers and ^{15}N SS-NMR, as well as CD spectroscopy [17]. Piscidin 1, a biologically-active host defense peptide originally obtained from fish, contains an unexpected amino terminal copper and nickel-binding motif. Using a variety of biophysical methods, including ^{15}N SS-NMR with oriented membranes, Paredes et al. show that metalation and oxidized-lipid incorporation improves its activity and that this peptide is more specific to anionic lipids [18].

Over the years, Michèle's work has been targeting important health issues such as antimicrobial resistance and amyloid-based diseases [19–21]. Recent work on the structure and membrane interactions of AMPs is presented in this special issue. Arias et al. were able to identify the preferred location of individual fluorinated aromatic residues in various analogs of tritrpticin, either membrane-embedded or solvent-exposed, by solution ^{19}F NMR methods [22]. Using an approach combining CD spectroscopy, with solution and SS-NMR, Sani et al. reveal that maculatin 1.1 adopts a transmembrane orientation in bilayers [23]. Raheem et al. study the mechanism of action of two aurein 2.2 analogs. Aurein has a strong antimicrobial effect against the human pathogen *Staphylococcus aureus*, and more active analogs can be generated from this peptide [24]. A paper from Paquet-Côté et al. involving both Michèle and her long-term collaborator and colleague Normand Voyer, studies the antimicrobial activity of crown-ether peptide analogs. It shows that increasing length improves the permeabilization activity of these crown peptides, and that peptides with larger crown ethers have increased permeabilization activity [25]. Using a novel in-cell approach, Santisteban et al. probe the interaction of two AMPs (MSI-78 and BP100) with the membranes of Gram(+) bacteria by ^{2}H SS-NMR [26].

Michèle also worked on a variety of proteins over the years, such as amyloid-forming peptides involved in Alzheimer's disease, the islet amyloid peptide from diabetes, a transglutaminase-inhibitor adduct, the photointermediates of bacteriorhodopsin and α-synuclein. Together with Robert Griffin, Ann McDermott, K.V. Lakshmi and others, she was part of the revolution that brought SS-NMR to the fore as a major player for protein structure determination [27,28]. This special issue also presents investigations of other biologically-relevant peptides and proteins, such as ion channels, receptors and fiber-forming proteins. In their paper, Aisenbrey and Bechinger approach the membrane interaction and topology, oligomerization and dynamics of the HIV gp41 protein, both from a lipid and from a protein perspective, through a variety of biophysical techniques including CD and fluorescence spectroscopy, as well as SS-NMR [29]. Ghosh and Welicky investigate the interaction of HIV gp41 and influenza HA fusion peptide by ^{2}H SS-NMR and reveal its insertion into the hydrophobic part of the bilayer [30]. Zhang and McDermott study the effects of the membrane lipid composition on the functional states of KcsA. Using SS-NMR, they show that anionic lipids would promote channel inactivation [31]. De Vlugt et al. employ through-bond SS-NMR spectroscopy to identify the flexible portions of the non-annular lipids that co-purify with the Anabaena Sensory Rhodopsin (ASR) and find the presence of phosphatidylethanolamine lipids that are tightly bound to ASR [32]. Thompson and Baenziger review the effects of lipids on the function of pentameric ligand-gated ion channels [33]. Malik et al. investigate the differences in dynamics between the methylated and unmethylated states of a bacterial chemoreceptor using SS-NMR [34]. In their paper, Mark et al. use a sophisticated EPR experiment, called 2D HYSCORE, to determine the electronic structure of two redox-active tyrosine residues of photosystem II, which play an important role in water oxidation driven by light energy [35]. Finally, Haya et al. investigate the effect of the pancreatic hormone glucagon on the lipid bilayer, and report morphological changes in DMPC bilayers as a function of the aggregation state of glucagon [36].

Michèle's spirit will continue to live within us when we get together to talk about our science and in the scientific questions that we pursue in our laboratories. And, in acknowledging this, we can still feel her positive energy and her passion for science that she communicated to all of her students and scientific colleagues. We lost a wonderful and inspiring colleague and a dear friend far too early, but her memory will certainly stay with us for a long time to come.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We are indebted to Professor Hans Vogel for his constant help throughout the completion of this special issue of *BBA-Biomembranes*, in honour of Professor Michèle Auger. We also thank the authors for their contributions.

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