1Foreword to biophysical studies of membrane systems and interactions -

2 Commemorative issue in honour of Professor Michèle Auger

3 *Dror E. Warschawski¹, K.V. Lakshmi² and Isabelle Marcotte^{3*}*

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5¹ Laboratoire des Biomolécules, LBM, CNRS UMR 7203, Sorbonne Université, École
6normale supérieure, PSL University, 75005 Paris, France

7

8² Department of Chemistry and Chemical Biology and The Baruch '60 Center for
9Biochemical Solar Energy Research, Rensselaer Polytechnic Institute, Troy, NY 12180,
10USA

11

12³ Department of Chemistry, Université du Québec à Montréal, P.O. Box 8888, Downtown
13Station, H3C 3P8, Montreal, Canada

14

15

16*Corresponding author

17Tel: 1-514-987-3000 #5015

18Fax: 1-514-987-4054

19E-mail: marcotte.isabelle@uqam.ca

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23FOREWORD

24 Professor Michèle Auger passed away in October 2018, after a long, fruitful and
25highly rewarding career in the field of membrane biophysics. Michèle was mostly
26interested in the importance of membranes as key biological interfaces, and in her
27research she deployed a wide range of experimental approaches to study them. She has
28contributed immensely to our knowledge on the physical chemistry of membranes,
29membrane interactions, and membrane-bound proteins and peptides through the
30application of solid-state nuclear magnetic resonance (SS-NMR), as well as infrared and
31Raman spectroscopy, and various other complementary techniques. This special issue,
32which is dedicated to these topics, is a tribute to her career, with contributions by
33numerous collaborators and friends.

34 In consideration of Michèle's extensive contributions to the investigation of lipid
35bilayers, the enormous complexity of lipid systems and their role in peptide interactions
36are covered in this issue. In his review article, Hideo Akutsu nicely presents how
37complementary spectroscopic approaches can allow one to better study the miscibility of
38various phospholipids in a bilayer [1]. The role of the phospholipid headgroups in
39creating interactions with membrane-active molecules is also illustrated in this review
40using antimicrobial peptides (AMPs), notably studied by Michèle together with her
41collaborators and students [2-4]. In their paper, Ramos *et al.* revisit the lamellar to
42hexagonal phase transition in membranes as studied by ^{31}P and ^2H SS-NMR, calculating
43the partitioning constant of alkanes between, but also within, the different phases [5].

44 Membranes that are oriented in the magnetic field, either magnetically or
45mechanically, can bring valuable information on the position and interactions of proteins
46and peptides through SS-NMR studies. The development and application of such
47approaches have been amongst Michèle's many scientific contributions (for example [6-
489]). This special issue presents the characterization of new orientable systems and the
49application of oriented membranes to gather information on AMPs and lipids. A review
50of two widely used lipid nano-objects - bicelles and nanodiscs – is presented by Erick
51Dufourc [10]. Moreover, in their paper, Park *et al.* explore the use of phospholipid
52polymer macrodiscs that align in the magnetic field as a new alternative to bicelles for

53 studying membrane proteins by SS-NMR [11]. Di Mauro *et al.* show that the insertion of
54 paramagnetic tags in the outer polymer belt of lipid nanodiscs can reduce NMR
55 acquisition times [12]. Gravel *et al.* propose new oriented membranes composed of
56 phospholipids and Tween 80 - a detergent that is often used to isolate and stabilize
57 membrane proteins, thereby conveniently avoiding the detergent removal step prior to
58 SS-NMR investigations [13]. They show that the orientation of these elongated vesicles
59 can be flipped in the magnetic field when lanthanide ions are added, and they determine
60 the orientation of a model peptide. Michèle actively participated in this research together
61 with her student Matthieu Fillion, and her former students Alexandre Arnold and Isabelle
62 Marcotte.

63 In their paper, Jeong *et al.* tackle the structures of three promising AMPs by solution
64 NMR, and their position relative to the membrane was studied by SS-NMR in bicelles
65 [14]. While bicelles have originally been developed mostly for SS-NMR applications,
66 Evans *et al.* expand on their use by performing electron paramagnetic resonance (EPR),
67 and circular dichroism (CD) spectroscopy studies, focusing on the transmembrane
68 peptide fukutin-I [15]. The paper from Schmidt and Davis investigates liquid ordered–
69 liquid disordered fluid phase coexistence in lipid mixtures [16]. Using two types of
70 oriented membranes, *i.e.*, magnetically (bicelles) and mechanically oriented bilayers, they
71 study the interaction of a synthetic peptide, and look at the lipid phase behavior as well as
72 the orientation and dynamics of the peptide. Furthermore, Strandberg *et al.* explore the
73 role of the positively charged residue at the N-terminus in the pore forming activity of
74 AMP-analogs using mechanically oriented bilayers and ^{15}N SS-NMR, as well as CD
75 spectroscopy [17]. Piscidin 1, a biologically active host defense peptide originally
76 obtained from fish, contains an unexpected amino terminal copper and nickel-binding
77 motif. Using a variety of biophysical methods, including ^{15}N SS-NMR with oriented
78 membranes, Paredes *et al.* show that metalation and oxidized-lipid incorporation
79 improves its activity and that this peptide is more specific to anionic lipids [18].

80 Over the years, Michèle's work has been targeting important health issues such as
81 antimicrobial resistance and amyloid-based diseases [19-21]. Recent work on the
82 structure and membrane interactions of AMPs is presented in this special issue. Arias *et*

83 *al.* were able to identify the preferred location of individual fluorinated aromatic residues
84 in various analogs of tetracycline, either membrane-embedded or solvent-exposed, by
85 solution ^{19}F NMR methods [22]. Using an approach combining CD spectroscopy, with
86 solution and SS-NMR, Sani *et al.* reveal that maculatin 1.1 adopts a transmembrane
87 orientation in bilayers [23]. Raheem *et al.* study the mechanism of action of two aurein
88 2.2 analogs. Aurein has a strong antimicrobial effect against the human pathogen
89 *Staphylococcus aureus*, and more active analogs can be generated from this peptide [24].
90 A paper from Paquet-Côté *et al.* involving both Michèle and her long-term collaborator
91 and colleague Normand Voyer, studies the antimicrobial activity of crown-ether peptide
92 analogs. It shows that increasing length improves the permeabilization activity of these
93 crown peptides, and that peptides with larger crown ethers have increased
94 permeabilization activity [25]. Using a novel in-cell approach, Santisteban *et al.* probe
95 the interaction of two AMPs (MSI-78 and BP100) with the membranes of Gram(+)
96 bacteria by ^2H SS-NMR [26].

97 Michèle also worked on a variety of proteins over the years, such as amyloid-forming
98 peptides involved in Alzheimer's disease, the islet amyloid peptide from diabetes, a
99 transglutaminase-inhibitor adduct, the photointermediates of bacteriorhodopsin and α -
100 synuclein. Together with Robert Griffin, Ann McDermott, K.V. Lakshmi and others, she
101 was part of the revolution that brought SS-NMR to the fore as a major player for protein
102 structure determination [27,28]. This special issue also presents investigations of other
103 biologically-relevant peptides and proteins, such as ion channels, receptors and fiber-
104 forming proteins. In their paper, Aisenbrey and Bechinger approach the membrane
105 interaction and topology, oligomerization and dynamics of the HIV gp41 protein, both
106 from a lipid and from a protein perspective, through a variety of biophysical techniques
107 including CD and fluorescence spectroscopy, as well as SS-NMR [29]. Ghosh and
108 Welicky investigate the interaction of HIV gp41 and influenza HA fusion peptide by ^2H
109 SS-NMR and reveal its insertion into the hydrophobic part of the bilayer [30]. Zhang and
110 McDermott study the effects of the membrane lipid composition on the functional states
111 of KcsA. Using SS-NMR, they show that anionic lipids would promote channel
112 inactivation [31]. De Vlugt *et al.* employ through-bond SS-NMR spectroscopy to identify
113 the flexible portions of the non-annular lipids that co-purify with the Anabaena Sensory

114Rhodopsin (ASR) and find the presence of phosphatidyl ethanolamine lipids that are
115tightly bound to ASR [32]. Thompson and Baenziger review the effects of lipids on the
116function of pentameric ligand-gated ion channels [33]. Malik *et al.* investigate the
117differences in dynamics between the methylated and unmethylated states of a bacterial
118chemoreceptor using SS-NMR [34]. In their paper, Mark *et al.* use a sophisticated EPR
119experiment, called 2D HYSORE, to determine the electronic structure of two redox-
120active tyrosine residues of photosystem II, which play an important role in water
121oxidation driven by light energy [35]. Finally, Haya *et al.* investigate the effect of the
122pancreatic hormone glucagon on the lipid bilayer, and report morphological changes in
123DMPC bilayers as a function of the aggregation state of glucagon [36].

124 Michèle's spirit will continue to live within us when we get together to talk about our
125science and in the scientific questions that we pursue in our laboratories. And, in
126acknowledging this, we can still feel her positive energy and her passion for science that
127she communicated to all of her students and scientific colleagues. We lost a wonderful
128and inspiring colleague and a dear friend far too early, but her memory will certainly stay
129with us for a long time to come.

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