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# The 40th anniversary of bilayer lipid membrane research

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**Abstract**

This paper presents a historic perspective on the origin of the lipid bilayer concept and its experimental realization. Additionally, current studies in close collaboration with our colleagues on the use of supported BLMs as biosensors and molecular devices are delineated. Further, recent research of others on BLMs (planar lipid bilayers) is referenced. © 2002 Elsevier Science B.V. All rights reserved.

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## 1. Introduction

In 1961 at the Symposium on the Plasma Membrane, when a group of unknown researchers reported the reconstitution of a bimolecular lipid membrane in vitro, the report was met with skepticism. Those present included some of the foremost proponents of the lipid bilayer concept, such as Davson, Danielli, Stoeckenius, Adrian, Mauro, Finean, and many others [1]. The research group began the report with a description of mundane soap bubbles, followed by 'black holes' in soap films, . . . ending with an invisible 'black' lipid membrane, made from lipid extracts of cow's brains. The reconstituted structure (60–90 Å thick) was created just like a cell membrane separating *two* aqueous solutions. The speaker then said ". . .upon adding one, as yet unidentified, heat-stable compound. . .from fermented egg white. . .to one side of the bathing solutions. . .lowers the resistance. . .by 5 orders of magnitude to a new steady state. . .which changes with applied potential. . .Recovery is prompt. . .the phenomenon is indistinguishable. . .from the excitable alga Valonia. . ., and similar to the frog nerve action potential" As one of the members of the amused audience remarked, ". . .the report sounded like. . . cooking in the kitchen, rather than a scientific experiment!" That was in 1961, and the first report was published a year later [1]. In reaction to that report, Bangham [2], the originator of liposomes, wrote in a 1996 article entitled 'Surrogate cells or Trojan horses': ". . .a preprint of a paper was lent to me by Richard Keynes, then Head of the Department of Physiology (Cambridge), and my boss. This paper was a bombshell. . .. They (Rudin, Mueller, Tien and Wescott) described methods for preparing a membrane. . .not too dissimilar to that of a node of Ranvier. . . The physiologists went mad over the model, referred to as a 'BLM', an acronym for Bilayer or by some for Black Lipid Membrane. They were as irresistible to play with as soap bubbles" [2].

Indeed, the group under the leadership of D.O. Rudin, then working in Philadelphia, PA, on the 9th floor, at Eastern Pennsylvania Psychiatric Institute (now defunct), was playing with soap bubbles with the 'equipment' purchased from the local toyshop! While nothing unusual for the researchers at work, it must have been a curious and mysterious sight for the occasional visitors who happened to pass through the laboratories there!

## 2. Results and discussion

The accompanying table below summarizes the results of the past four decades of investigation of bilayer lipid membranes (BLMs or planar lipid bilayers).

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| Decade | |
|---|---|
| First Decade (1961–1970) | Technique for BLM formation; excitability-inducing-material (EIM), discrete channel conductance; antigen–antibody, enzyme–substrate interactions photoelectric effects [14,15]. |
| Second Decade (1971–1980) | Models for the plasma membrane of cells, the nerve membrane, the cristae membrane of mitochondria [24,38], the thylakoid membrane of the chloroplast [8,14], the visual receptor membrane of the eye, and many others, last but not the least a model for the purple membrane of *H. halobium* [17]; ion channel reconstitution [35,36,38,39]. |
| Third Decade (1981–1990) | Molecular mechanisms of membrane processes. Supported BLMs on metal substrates (s-BLMs). Mechanisms of photosynthesis, membrane bioenergetics [21]. Solar energy utilization via semiconductor septum electrochemical photovoltaic cells [8,16], electroporation [19]. |
| Fourth Decade (1991–2001) | Supported BLMs on hydrogels (sb-BLMs), tethered (t-BLMs)[27]. Supported BLM-based sensors and devices. Molecular mechanisms of membrane processes [18,25,28,33–36,39] (apoptosis, [25], PDT [18]); BLM-based biotechnology and molecular electronics [9–13,22,23,26,30–32,37,40–48]; DNA–BLM interactions [29]. |

To mark the 40th anniversary of the discovery of the BLM, we have prepared an article for the occasion; it is titled "The Lipid Bilayer Concept and Its Experimental Realization: From Soap Bubbles, the Kitchen Sink, to Bilayer Lipid Membranes" [3]. This paper traces the inspiration for lipid bilayer research, which dates to Robert Hooke's and Newton's time (1672 and 1704, respectively). Today, after four decades of research and development, BLMs (also referred to nowadays as *planar lipid bilayers*), along with liposomes, have become established disciplines in certain areas of membrane biophysics and cell biology [4–8], and in biotechnology [9–12]. The lipid bilayer, existing in all cell membranes, is most unique in that it serves not merely as a physical barrier among cells, but functions as a two-dimensional matrix for all sorts of reactions. Also, the lipid bilayer, after suitable modification, acts as a conduit for ion transport, as a framework for antigen–antibody binding, as a bipolar electrode for redox reactions, and as a reactor for energy conversion (e.g. light to electric to chemical). Furthermore, a modified lipid bilayer performs as a transducer for signal transduction (i.e. sensing), and numerous other functions as well [13–20,48]. All these myriad activities require the ultrathin lipid bilayer of 5-nm thickness. To study BLMs in detail, the task has been a daunting one until a few years ago, since a 5-nm BLM is an extremely labile structure with limited lifetime. Planar BLMs can now be formed on various substrates with long-term stability, thereby opening the way for basic research and developments work in biotechnology [3,8,10–12].

## 3. Conclusion

As of today, black lipid membranes (BLMs or planar lipid bilayers) have been used in a number of applications ranging from fundamental membrane biophysics including photosynthesis, practical AIDS research, and 'microchips' study [3,48]. In reactions involving light, BLMs have provided insights to the conversion of solar energy via water photolysis, and to photobiology comprising apoptosis and photodynamic therapy [3,15,16]. Supported bilayer lipid membranes (s-BLMs) are being used in biosensor development [10–12]. In addition, the above-mentioned paper reviews the studies of our laboratory and recent research of others on the use of BLMs as models of certain biomembranes [7,16–21]. We also describe briefly our present work on s-BLMs as biosensors and molecular devices; as well as delineate the other experiments carried out in close collaboration with colleagues on s-BLMs [9,10,22–26,28–31,44].

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