Artificial Lipid Membranes as Model Systems in Membrane Chemistry

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ABSTRACT

Artificial lipid membranes have become indispensable model systems for understanding the structural and functional properties of biological membranes. By replicating the essential features of natural lipid bilayers under controlled experimental conditions, these biomimetic platforms enable detailed investigations of membrane organization, transport processes, protein–lipid interactions, and cellular communication. This article provides an overview of the major classes of artificial lipid membrane systems, including black lipid membranes, solid-supported lipid bilayers, tethered bilayer lipid membranes, and synthetic vesicles, highlighting their structural characteristics, fabrication approaches, advantages, and limitations. It further discusses their diverse applications in membrane chemistry, including

biosensor development, drug discovery and permeability testing, electrophysiological studies, and synthetic biology. Recent advances in artificial cell research and membrane engineering demonstrate the growing potential of these systems for developing responsive biomimetic platforms capable of mimicking complex cellular functions. Although challenges remain in recreating the dynamic complexity of living cell membranes, continued progress in membrane engineering, nanotechnology, and synthetic biology is expected to expand the practical applications of artificial lipid membranes in biomedical research, diagnostics, personalized medicine, environmental monitoring, and sustainable biotechnology. As increasingly sophisticated model systems emerge, artificial lipid membranes will continue to serve as powerful tools for advancing both fundamental membrane science and innovative technological applications.

INTRODUCTION

The lipid bilayer is one of the most remarkable self-assembled structures found in nature. It not only serves as a protective barrier for cells and intracellular compartments but also provides a platform for communication and transport processes across biological membranes. The intricate nature of cell membranes has inspired the development of simplified model membrane systems, whose size, composition, and architecture can be precisely controlled to investigate membrane components and their interactions with biological molecules. (Nancy *et al* 2023; Chan *et al* 2007). And the diverse functions of biological membranes inspired the early development of artificial lipid-based models aimed at recreating membrane behavior in vitro, thereby enabling the study and application of chemoreception in sensor development. (Siontorou *et al* 2017).

Artificial membranes are synthetic amphipathic lipid bilayers, typically consisting of phospholipids and cholesterol, designed to emulate the structural features of biological membranes. Owing to their simplicity and experimental controllability, these systems provide effective platforms for investigating membrane chemistry and elucidating the roles of membrane lipids and proteins.

Types of Artificial membranes

1. **Black lipid membranes (BLMs)-** It was introduced nearly six decades ago as model systems for studying the structure and function of biological membranes. They consist of planar phospholipid bilayers formed across small apertures measuring approximately 50–500 µm in diameter. Early BLMs were prepared using synthetic phosphatidylcholine lipids with different fatty acid compositions. However, because these membranes were relatively unstable, supported and tethered lipid bilayer systems were later developed to improve membrane stability. (Nisticò *et al* 2023).

Black lipid membranes, also known as free-standing or suspended bilayers, are lipid membranes formed across micro- or nanoscale pores. Typically, a lipid film is spread over an aperture in a Teflon sheet or polymer support, creating a membrane suspended between two aqueous compartments. These membranes can be accessed from both sides, making them particularly useful for studying membrane transport and ion channel activity, including the measurement of currents passing through individual ion channels. Although suspended bilayers offer high fluidity and accessibility, they are relatively fragile. Early black lipid

membranes suffered from poor stability; however, advances in nanofabrication have enabled the creation of nanoscale pores in metal substrates, improving membrane stability while maintaining access to both sides of the bilayer and preserving the natural orientation of membrane proteins (Köper *et al* 2007; (Rebaud *et al* 2014).

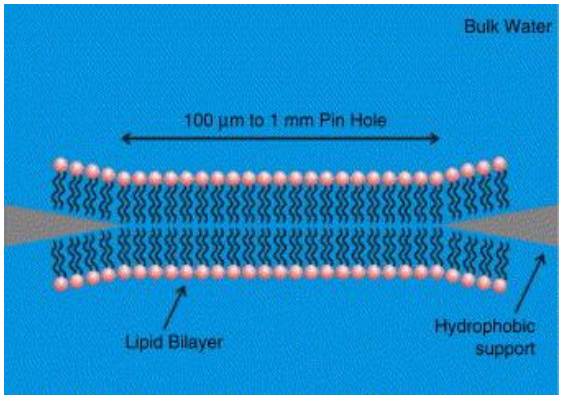

Fig1. Showing Black Lipid mmbrane.

2. **Solid-supported lipid bilayers** –It was first introduced by McConnell and co-workers and are typically formed by the adsorption and rupture of small unilamellar vesicles on hydrophilic solid surfaces. Compared with black lipid membranes, these bilayers exhibit greater mechanical stability and robustness. Their fluidity is preserved by a thin layer of water, approximately 10–20 Å thick, trapped between the solid support and the lipid bilayer. (Tamm *et al* 1985; Johnson *et al* 1991). A schematic diagram of a supported lipid bilayer is shown in Fig2. The range of materials suitable for supporting phospholipid bilayers is relatively limited. To achieve high-quality membranes with minimal defects and excellent lipid mobility, the supporting surface must be smooth, clean, and hydrophilic. Commonly used substrates include fused silica, borosilicate glass, mica, and oxidized silicon.

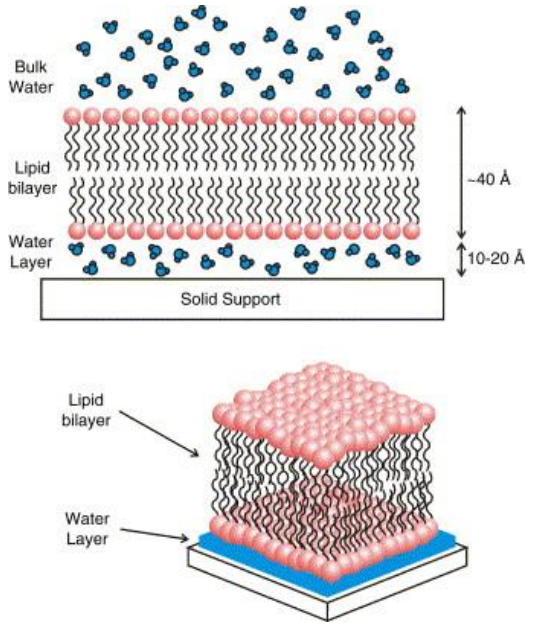

Fig2. **Solid-supported lipid bilayers**

Three main approaches are commonly used to fabricate supported phospholipid bilayers for sensor applications. The first involves sequential transfer of two lipid monolayers, where the lower leaflet is deposited using the Langmuir–Blodgett technique and the upper leaflet is added through the Langmuir–Schaefer method by horizontally contacting the substrate with the lipid film Fig3a. The second approach relies on the adsorption and fusion of lipid vesicles from an aqueous suspension onto the substrate surface (Brian *et al* 1984; McConnell *et al* 1986) Fig3b. A third strategy combines these methods, with the initial monolayer deposited by the Langmuir–Blodgett technique followed by vesicle fusion to generate the second leaflet (Kalb *et al* 1992) Fig3c.

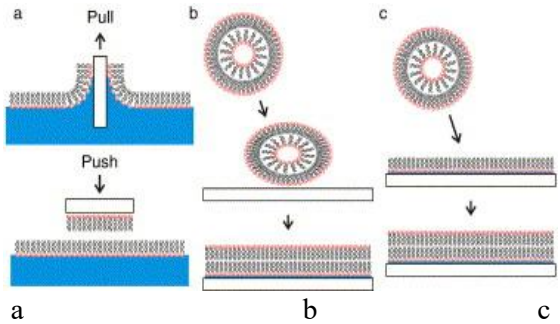

Fig 3 Methods to fabricate supported phospholipid bilayers

The primary advantage of solid-supported phospholipid bilayers is their enhanced mechanical stability and robustness compared with unsupported membranes. Another important benefit is their compatibility with a range of surface-sensitive analytical techniques, including atomic force microscopy, quartz crystal microbalance, surface plasmon resonance, and vibrational sum-frequency spectroscopy. However, these systems are limited by the fact that the lipid bilayer remains closely associated with the underlying substrate. As a result, transmembrane proteins may interact with the support surface, potentially restricting their mobility and impairing their biological function (Castellana *et al* 2006).

3. **Tethered Bilayer Lipid Membranes-** **Tethered** bilayer lipid membranes (tBLMs) represent an alternative type of solid-supported membrane in which a reservoir is created between the substrate and the lipid bilayer. Compared with polymer-supported membranes, tBLMs generally exhibit higher electrical resistance and superior long-term stability. In these systems, the inner lipid leaflet is separated from the support by a spacer molecule that simultaneously anchors the membrane covalently to the surface. Although gold substrates functionalized with thiol-based anchors are most commonly used (Schiller *et al* 2003), tBLMs have also been prepared on silicon, aluminium, and mercury surfaces using various surface chemistries (Atanasov *et al* 2005). The outer leaflet is typically formed either by rapid solvent exchange or through the fusion of lipid vesicles with the anchored monolayer.

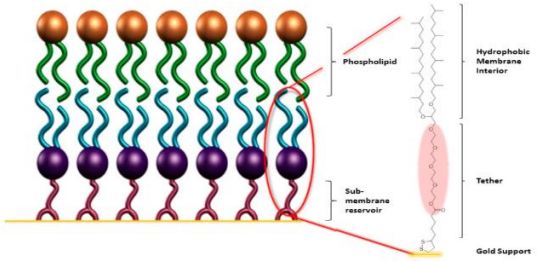

Fig 4. Tethered bilayer lipid membranes (tBLMs)

Ideally, tethered bilayer lipid membranes (tBLMs) are designed to overcome the limitations of polymer-supported bilayers, including their complex fabrication procedures and relatively high defect levels. At the same time, they should preserve membrane fluidity and provide a well-hydrated space beneath the bilayer that supports the incorporation and function of membrane proteins.

Tethered bilayer lipid membranes (tBLMs) have been widely employed in studies examining membrane structure, membrane function, protein–membrane interactions, and the behavior of membrane proteins incorporated within lipid bilayers. Variations among tBLM systems are primarily determined by the density of the tethering molecules and the chemical nature of the tethering lipids. These characteristics strongly affect the physical and functional properties of the membrane. In addition, the composition of the outer leaflet can be modified as required, enabling the design of customized biomimetic membrane interfaces.

Tethered membranes have also been fabricated on nanostructured substrates designed for surface-enhanced infrared absorption spectroscopy (SEIRAS). Although SEIRAS requires a relatively rough surface, stable and well-sealed lipid bilayers can still be formed, making them suitable for ion channel investigations. This technique provides detailed structural information about membrane proteins in their native environment, offering an important alternative to crystallographic methods that rely on dried protein crystals and may not accurately reflect the proteins' natural conformations. (Andersson *et al* 2016).

4. **Vesicles**- Membrane-bound vesicles are vital cellular structures involved in the uptake, transport, and secretion of substances. Their lipid bilayer membranes contain diverse lipids and proteins that

contribute to their biological functions. Advances in synthetic biology have stimulated the development of artificial vesicles designed to imitate the characteristics of natural cell membranes.

Synthetic vesicles containing a single lipid bilayer are categorized based on their size into small unilamellar vesicles (SUVs, <200 nm), large unilamellar vesicles (LUVs, 200 nm–1 μm), and giant unilamellar vesicles (GUVs, >1 μm). Vesicles containing multiple bilayers are known as multilamellar vesicles (MLVs) or multivesicular vesicles (MVVs). Among these, GUVs are widely used in artificial cell research because their large size allows direct microscopic observation and easier manipulation of membrane properties, resembling the dimensions of many prokaryotic cells. Furthermore, artificial vesicles may possess either symmetric or asymmetric lipid distributions between their inner and outer membrane leaflets, while the incorporation of diverse functional molecules can enhance their complexity and functionality. (Shin *et al* 2022).

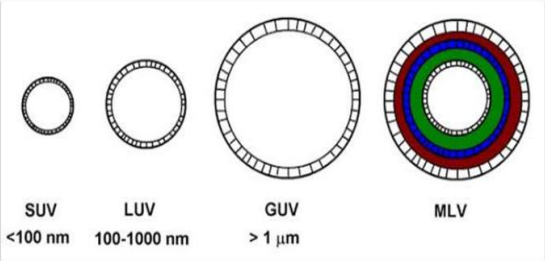

Fig 5. Various types of Vesicles

Applications of Lipid Artificial Membrane

1. **Biosensors**- A biosensor is a device that identifies an analyte through a biochemical recognition event and converts the resulting response into an electrical signal. Lipid bilayer-based biosensors offer a unique advantage by utilizing membrane dynamics for signal transduction. Recognition of the analyte induces changes in membrane properties, including charge distribution, dipole potential, membrane fluidity, and transmembrane potential, which enhance ion transport across the bilayer. Consequently, the membrane acts as both a transducer and a natural signal amplifier.

The application of lipid membranes and liposomes in biosensor technology has emerged as a promising area of research. Their appeal lies in the ability to replicate natural chemoreceptive processes within a simple laboratory system while providing high detection sensitivity. Furthermore, lipid bilayers offer a biomimetic environment that supports the activity of enzymes, antibodies, receptors, and other biological molecules. These components may be integrated into the membrane through either non-specific physical adsorption or more precise chemical immobilization strategies (Siontorou *et al* 2017).

2. **Drug Discovery, Delivery, and Testing**- Drug–membrane interactions are critical because most therapeutic agents must cross cellular membranes to reach intracellular targets. These interactions can influence drug distribution, transport, accumulation, and overall efficacy. For example, structurally similar quinolones have been shown to exhibit different intracellular accumulation profiles. Investigations using Langmuir–Blodgett lipid membrane models revealed that the drugs induced varying degrees of membrane condensation, reflecting differences in their lipophilic characteristics caused by minor structural modifications (Bensikaddour *et al* 2008).

Modern drug delivery systems often employ polymer-based coatings such as chitosan and dextrans. These materials can influence the interactions between drugs and lipid membranes to varying extents. Studies using Langmuir–Blodgett membrane models have shown that chitosan can bind electrostatically to lipid head groups, potentially hindering

drug entry into cells. Additionally, the delivery of reactive plasma species into cancer cells remains an active area of research. Membrane model studies suggest that the combined effects of electric field fluctuations and lipid oxidation promote pore formation in the membrane, facilitating the transport of reactive species into the cell (Pavinatto *et al* 2007).

Also, the assessment of drug permeability remains a fundamental component of pharmaceutical development, despite ongoing discussions regarding the limitations of existing methods. Variability among assays often arises from differences in experimental design and tissue selection. In this context, membrane model-based systems have gained attention as potential standardized platforms for permeability evaluation. The parallel artificial membrane permeability assay (PAMPA) employs a freely suspended lipid bilayer within a 96-well microtiter plate to investigate passive transport processes. Alternative approaches utilizing liposomes distributed across porous multiwell plates have also been explored and validated through extensive studies (Siontorou *et al* 2017).

2. **Tools in Research-** The application of membrane models in electrophysiological and biochemical studies expanded significantly following the first successful recording of a single ion channel. Since the pioneering work carried out in the mid-1970s, well-established methods have enabled detailed investigations of ion channel kinetics. More recently, scanning electrochemical microscopy has been employed to examine channel activity in lipid bilayers supported on glassy carbon electrodes. In these studies, perchlorate ions acted as stimuli, while ruthenium (II) complex cations served as probe ions. The channel remained closed in the absence of stimulation, and kinetic rate constants were determined by comparing measured ion currents with theoretical predictions under varying experimental conditions (Zhang *et al* 2015).

Current Trends and Future Perspectives- Recent research has focused on designing artificial systems capable of intercellular communication. For example, Gardner *et al*. (2019) developed signaling liposomes that produce sugars in response to an increase in the surrounding pH. These sugars were released into the medium and detected by *Vibrio harveyi*, triggering a quorum-sensing response that led to the production of bioluminescent proteins. In another study, Lentini *et al*. created a hybrid natural–synthetic system in which liposomes sensed environmental changes that could not be detected by *Escherichia coli*. The liposomes then released signaling molecules that activated a cellular response in the bacterium, effectively providing *E. coli* with an artificial sensing mechanism.

Despite considerable advances in synthetic cell research, the construction of a multi-responsive artificial cell remains an unmet goal. Such a system would require the in-situ generation and precise localization of numerous membrane-associated transporters and sensing proteins to enable complex interactions with the external environment. While the synthesis of sensor peptoids within liposomes presents relatively few challenges, their controlled incorporation into the membrane is considerably more demanding. Existing evidence suggests that physically driven self-organization may be more effective than conventional engineering strategies, which have thus far achieved limited success (Lentini *et al* 2016).

CONCLUSIONS

Artificial lipid membranes can be designed and modified in many different ways, making them versatile tools for research and practical applications. They are widely used in areas

such as biosensor development, drug testing, drug discovery, and the study of biological systems. As researchers gain better control over membrane structures, more advanced platforms containing complex protein networks are being created. Although these systems are still mostly developed in research laboratories, continued progress in science and technology is likely to make them suitable for routine commercial use.

And the artificial cells are one of the newest and most exciting applications of artificial membranes. Even though modern technology cannot yet fully reproduce living cells, these systems have already opened new possibilities for understanding biological processes. They provide a unique opportunity to explore how life may have evolved from simple molecular assemblies into complex cellular organisms. Beyond fundamental research, artificial cells could have important applications in environmental protection, personalized medicine, chemical manufacturing, crop improvement, and sustainable agriculture.

REFERENCES

A.A. Brian, H.M. McConnell, Proc. Natl Acad. Sci. USA 81 (1984) 6159.

Andersson, J., & Köper, I. (2016). Tethered and polymer supported bilayer lipid membranes: structure and function. *Membranes*, *6*(2), 30.

Atanasov, V., Knorr, N., Duran, R. S., Ingebrandt, S., Offenhäusser, A., Knoll, W., & Köper, I. (2005). Membrane on a chip: A functional tethered lipid bilayer membrane on silicon oxide surfaces. *Biophysical journal*, *89*(3), 1780-1788.

Bensikaddour, H.; Snoussi, K.; Lins, L.; Van Bambeke, F.; Tulkens, P.M.; Brasseur, R.; Goormaghtigh, E.; Mingeot-Leclercq, M.-P. Interactions of ciprofloxacin with DPPC and DPPG: Fluorescence anisotropy; ATR-FTIR and ^{31}P NMR spectroscopies and conformational analysis. *Biochim. Biophys. Acta* 2008, *1778*, 2535–2543.

Castellana, E. T., & Cremer, P. S. (2006). Solid supported lipid bilayers: From biophysical studies to sensor design. *Surface science reports*, *61*(10), 429-444.

Chan, Y. H. M., & Boxer, S. G. (2007). Model membrane systems and their applications. *Current opinion in chemical biology*, *11*(6), 581-587.

E. Kalb, S. Frey, L.K. Tamm, Biochim. Biophys. Acta 1103 (1992) 307

Gardner, P.M.; Winzer, K.; Davis, B.G. Sugar synthesis in a protocellular model leads to a cell signalling response in bacteria. *Nat. Chem.* 2009, *1*, 377–383.

H.M.McConnell,T.H.Watts,R.M.Weis,A.A.Brian,Biochim.Biophys. Acta 864 (1986) 95.

Köper, I., 2007. Insulating tethered bilayer lipid membranes to study membrane proteins. Molecular BioSystems, 3(10), pp.651-657.

L.K. Tamm, H.M. McConnell, Biophys. J. 47 (1985) 105

Lentini, R.; Martín, N.Y.; Mansy, S.S. Communicating artificial cells. *Curr. Opin. Chem. Biol.* 2016, *34*, 53–61

Nancy Nisticò, Maria Greco, Maria Chiara Bruno, Elena Giuliano, Paolo Sinopoli, Donato Cosco, Biomimetic lipid membranes: An overview on their properties and applications, Applied Materials Today, Volume 35, 2023, 101998, ISSN 2352-9407.

Pavinatto, F.J.; Caseli, L.; Pavinatto, A.; dos Santos, D.S., Jr.; Nobre, T.M.; Zaniquelli, M.E.D.; Silva, H.S.; Miranda, P.B.; de Oliveira, O.N., Jr. Probing chitosan and phospholipid interactions using Langmuir and Langmuir-Blodgett films as cell membrane models. *Langmuir* 2007, *23*, 7666–7671.

Rebaud, S. *et al*., 2014. Tethered bilayer lipid membranes (tBLMs): Interest and applications for biological membrane investigations. Biochimie, 107, pp.135-142.

S.J. Johnson, T.M. Bayerl, D.C. McDermott, G.W. Adam, A.R. Rennie, R.K. Thomas, E. Sackmann, Biophys. J. 59 (1991) 289.

Schiller, S.M.; Naumann, R.; Lovejoy, K.; Kunz, H.; Knoll, W. Archaea analogue thiolipids for tethered bilayer lipid membranes on ultrasmooth gold surfaces. *Angew. Chem. Int. Ed.* 2003, *42*, 208–211.

Shin, J., Cole, B. D., Shan, T., & Jang, Y. (2022). Heterogeneous synthetic vesicles toward artificial cells: engineering structure and composition of membranes for multimodal functionalities. *Biomacromolecules*, *23*(4), 1505-1518

Siontorou, C. G., Nikoleli, G. P., Nikolelis, D. P., & Karapetis, S. K. (2017). Artificial lipid membranes: Past, present, and future. *Membranes*, *7*(3), 38.

Zhang, Z.; Shi, J.; Huang, W. Study of the ion-channel behavior on glassy carbon electrode supported bilayer lipid membranes stimulated by perchlorate anion. *Mater. Sci. Eng. C* 2015, *55*, 431–435.