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Chiral discrimination and recognition in Langmuir monolayers

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Abstract

Chiral discrimination is a phenomenon where one chiral molecule can distinguish the identical molecule, the molecule which is its mirror image or a different chiral molecule. This is one of the most subtle aspects of molecular recognition. The present review discusses recent molecular studies of chiral discrimination as recognition phenomena. The focus is at the molecules in Langmuir monolayers at air/water interface. Recent detailed experiments and molecular theoretical developments show that it is possible to correlate the chiral discrimination starting from molecular structure concerned.

Keywords: Chiral discrimination; Molecular recognition; Langmuir monolayer; Chiral recognition; Air–water interface; Odorant

1. Introduction

Langmuir monolayers have been successfully used as simple model systems to understand biological membranes. The principal driving factor of membrane structure is a balance between the hydrophobic effect and the head group repulsion and the same factor controls the self-aggregation of monolayers. The interest in these biomimetic models arise primarily from the important biological role of membranes as cell constituent that is absolutely essential for all live being on earth. The easy compressibility and possibility of tuning the intermolecular interaction by variation of the external pressure added further interest in the monolayer. Recently subtle aspects of the molecular structure and intermolecular interaction in amphiphiles at monolayers and bilayers are revealed which might shed new light on biological recognition processes in membranes. Membranes are present in organs where a biological recognition process is initiated, for example, in nose, eye, ear, skin etc. The external stimulation reaches the membrane and then, signals are sent to the brain through various biochemical steps. Major focus of research was directed so far towards receptor proteins. However, little is known whether the amphiphile act as an inert matrix holding the receptors or they also play an important role in recognition processes. The question is not irrelevant considering the fact that all guest/ligand molecules cannot interact with receptor protein and a substantial number of molecules may be transported via the membrane to the receptor (particularly, when the receptor is buried in the membrane). The recognition by the lipid plays an important role in the latter case. Recognition processes in monolayers and bilayers represent interesting model systems due to the possibility of designing recognition sites at the air–water interface [1•,2••,3].

Recent experimental observation and molecular theoretical understanding of the chirality-dependent intermolecular interaction, principally focused on studies on the basis of Langmuir monolayers, showed that amphiphilic molecules can preferentially interact with identical molecules or its enantiomers or different chiral molecules, and can discriminate them. This is an extremely subtle phenomena since the two enantiomers differ only in the properties that depends on their chirality and nothing else. This process is also a recognition where the preferential interaction of a homo-pair or hetero-pair depends on the nature of intermolecular energy profile. The manifestation of self-recognition due to discrimination is consequently difficult to

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observe and to explain [4••]. Understanding this recognition is intimately related with the problem of homochiral evolution. The discrimination and concomitant recognition is an indication that amphiphilic molecules in the condensed state of monolayers have the capability to act as recognition systems which depend on their molecular chirality. The molecular chiral structure drives the intermolecular separation and orientation in the condensed phase in such a way that the interaction between identical molecules, enantiomeric molecules or other chiral molecules becomes non-identical. Consequently, discrimination and recognition are manifested. Thus, chirality plays a dominant role in such recognition processes. The omnipresence of chirality in biological systems are well known. Whether the chirality in biological systems plays a role in recognition is an open question and little work is done in this direction [5]. With this end in view, we discuss chiral discrimination and recognition of amphiphiles in monolayers in the following sections.

2. Chiral discrimination and self-recognition in monolayers

Different experimental techniques such as, surface pressure versus area per molecule (π–A) isotherm measurements, optical techniques like Brewster angle microscopy (BAM) as well as fluorescence microscopy studies and lattice structural information based on grazing incidence X-ray diffraction (GIXD) studies have shown that chiral amphiphiles can discriminate and recognize the same type of enantiomers or their mirror images depending on the molecular structure of the amphiphile concerned. Previous studies on how a chiral amphiphile can distinguish the same or enantiomeric molecules via homochiral or heterochiral interaction have been reviewed [4••,6•,7•]. Early studies of chiral discrimination principally relied on measurements of π–A isotherms, and on this basis it is difficult to obtain unambiguous molecular level interpretation. A number of studies have been made which deal with chiral amphiphilic peptides, amphiphilic nucleotides containing a chiral sugar ring or other chiral amphiphilic molecules [4••], but unfortunately, little focus is directed towards the chiral discrimination aspect of the problem. To be explicit, little attempt has been made to observe the discrimination phenomena. Another related event is the formation of chiral mesoscopic or macroscopic structures from achiral compounds. These topics will be partly discussed in an accompanying article [7•]. Here we focus on recent molecular understanding of the phenomena that is primarily focused on chiral discrimination as self-recognition.

A variety of chiral amphiphiles exhibit discrimination, for example, *N*-tetradecyl γ,δ-dihydroxypentanoic acid, *N*-dodecyl mannonamide and gluconamide, *N*-stearoylvaline and alanine, *N*-octadecanoyl alanine, *N*-myristoyl alanine, hexadecylthiophospho-2-phenylglycinol, dipalmitoyl phosphatidyl choline and glycerolic head group amphiphiles [8•,9–16••,17••,18–20•,21]. We discuss the cases where the underlying molecular mechanism of the discriminating effect and recognition is studied on a molecular basis. Amphiphiles such as, dipalmitoyl phosphatidyl choline (DPPC), dipalmitoyl phosphatidyl ethanolamine (DPPE), *N*-tetradecyl-γ,δ-dihydroxypentanoic acid amide (TDHPAA), *N*-stearoyl serine methyl ester (SSME), and *N*-palmitoyl aspartic acid monolayers (PAA) exhibit generally preference for interaction with molecules of the same chirality (L with L and D- with D) while such amphiphiles as stearoyl amine glycerol (SAG) show preferential interaction with their mirror image isomer (Fig. 1). The recognition can be concluded on the basis of differences in the characteristic features of the π–A isotherms, different shapes of the condensed-phase domains or differences in the lattice structures of the enantiomer (or its mirror image) and the racemic mixture. Two types of interactions can take place. If D–D or L–L interaction is favored over the D–L interaction, it is designated as “homochiral interaction”. On the other hand, if the interaction of the two different enantiomers (D–L) is more favored compared to the interaction between a pair of the same type of enantiomers (D–D or L–L) it is called “heterochiral interaction”. However, a typical molecule can show both homochiral and heterochiral preference depending on the intermolecular distance and orientation, for example, in amino acid head group and glycerolic head group monolayers [16••,17••]. This point should be discussed shortly. If homochiral interaction is sufficiently strong, then it is possible that D-rich or L-rich domains would separate out from a racemic mixture. Such phase separation is an example of “chiral symmetry breaking” and indicates that the same type of isomers recognizes each other stronger than their enantiomers. This phenomenon is a two dimensional analogue of *prebiotic chiral segregation with homochiral preference*. Interestingly, various experimental observations indicated that both homo- and heterochiral recognition is possible depending on the chiral molecular structure.

Different chiral features of domains composed of enantiomeric and racemic amphiphiles of TDHPAA, SSME and PAA are shown in Figs. 2, 3 and 4. The discriminating features are clearly seen from the differences in the structural features of the domains composed of D-, L-, and DL (racemic) amphiphiles. The bifurcation of a small arm from the *S*-enantiomer of TDHPAA develops in an exactly opposite direction to the development of the bifurcation of a similar smaller arm from the *R*-enantiomer (Fig. 2). The racemate seems to grow rather symmetrically from a common center. In racemates, the chiral symmetry breaking takes place with enantiomeric excess by the two sides of a common center. In SSME and PAA (Figs. 3 and 4), the directions of curvature of the enantiomeric domains are of specific handedness and the racemates show the development of both forms of handedness. The development of arms of both handedness from the racemate could possibly be a signature of chiral symmetry breaking in SSME monolayers. The features shows that in the case of TDHPAA, SSME and PAA the same type of enantiomers can recognize themselves more effectively than their mirror images. Theoretical studies of the chiral discrimination energies have shown that the enantiomeric pairs are closely packed and have a lower minimum pair potential compared to the racemic pairs. Consequently, recognition of the same type of enantiomers is favored compared to the racemic pairs [17••]. The difference in the pair potential is $\Delta U=(U(\text{enantiomeric})-U(\text{racemic}))/k_BT$, where U(enantiomeric) and