INDOLE DERIVATIVES INTERACT WITH DOPC IN LANGMUIR MONOLAYERS

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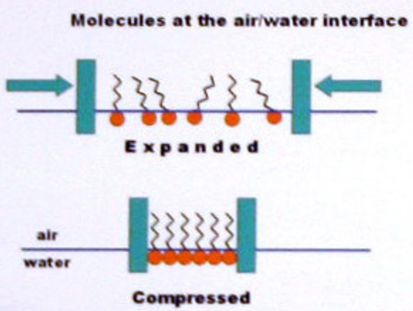
Introduction

The fundamental unit of every living organism is a cell. The lipid bilayer of the cell membrane maintains the integrity of the cell. It serves as a barrier to protect the cell's contents as well as regulate the transport of materials into and out of the cell. In addition to these physiological functions, the lipid bilayer has wider applications in drug delivery and gene therapy. It is difficult to study and perform experiments on lipid bilayers. When the bilayers are surrounded by water, they float freely making the layers hard to observe. It is easier to study a single layer of cells, called a monolayer, as they are present on the surface of water. The monolayers are present at the surface of water due to amphiphiles. A lipid consist of a hydrophilic, water loving, head and a hydrophobic, fearing water, tail. Due to these affinities, the hydrophilic heads are closest to the water subphase while the hydrophobic tails are orientated upward, away from the water. The lipid is therefore located at the air-water interface.

A Nima Film Balance may be used to detect the changes in surface pressure at the air-water or oil-water interface. In addition to phospholipid monolayers, fatty acids may also be studied with the Nima Film Balance as each are insoluble in water and surface active. The balance consists of a shallow Teflon trough with a moveable barrier that compresses the monolayer.

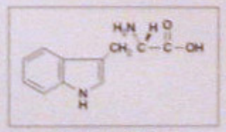
The trough is shallow because the interactions that are of interest occur at the surface of the water. It is composed of Teflon as the material does not allow molecules to attach to the trough and distort the results. Surface tension decreases as particles are added. Pure water has a surface tension of approximately 72 mN/m, but a monolayer can cause this to drop nearly to zero. (Nima, 2004).

The change in surface tension caused by the presence of a monolayer on a water surface is called its surface pressure. The changes in surface pressure are detected by a sensor. As the barrier of the trough compresses the monolayer, an isotherm is produced. This isotherm shows the change in surface pressure compared the area per molecule at a constant temperature. It can be used to identify types of molecules and their characteristics due to the behaviors produced at certain areas. As seen in the figure below, when the monolayer is expanded, the molecules are disorderly and random. As the monolayer compresses the molecules are forced closer together and become more organized. The barrier further compresses the monolayer which causes the molecules to stand vertically.



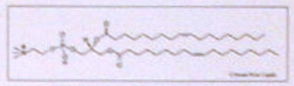
This is represented on the graph when the slope of the isotherm increases and almost becomes vertical. The molecules are so close that they are unable to take up any less space per molecule. The start of the isotherm is called the take-off point. The earlier a monolayer changes the surface tension indicates that more area per molecule is occupied by the lipid.

Literature states that tryptophan, an indole derivative, prefers membrane surfaces and may participate in interface interactions. It is suggested that this preference is due to tryptohphan's aromatic structure and affinity for the electrostatic complexes in the interface environment. Tryptophan may stabilize the interface and thus serve as a membrane anchor protein. To further investigate these interactions, a model system was created.



L-Tryptophan

DOPC, a Langmuir monolayer, served as the lipid in the model system. A 0.25 M Phosphate buffer at physiological pH was used as the substrate in the system.



1,2-Dioleoyl-*sn*-Glycero-3-Phosphocholine (DOPC)

Results & Discussion

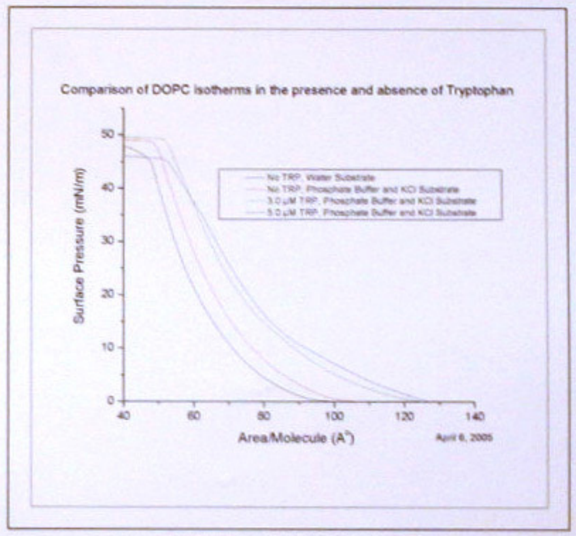


Figure 1: Comparison of DOPC isotherms in the presence and absence of Tryptophan

As shown in Figure 1, there is not a drastically significant difference between the isotherm of DOPC with a water substrate and the isotherm of DOPC with a phosphate buffer-KCl substrate at physiological pH. The DOPC present on the interface reacts similarly when using these two substrates. The use of 0.1 M KCl proves that the mere addition of ions does not measurably affect the surface tension. The introduction of minute quantities, 3.0 µM and 5.0 µM, of tryptophan significantly shifts the isotherm to the right. The shift indicates the expansion of the monolayer as modeled by DOPC. At higher concentrations of tryptophan, there is greater expansion. The lack of inflection points in the isotherms indicates that there are no phase changes.

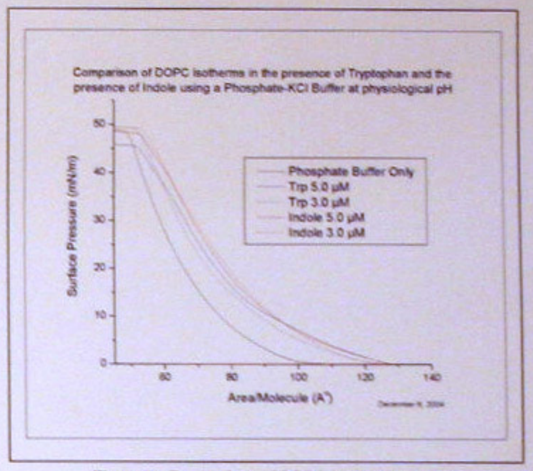
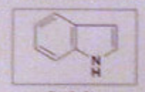


Figure 2: Comparison of DOPC isotherms in the presence of Tryptophan and the presence of Indole

In order to analyze which portion of the tryptophan molecule causes the expansion, indole was tested. As indicated in Figure 2, indole, a tryptophan analogue, exhibits a similar aromatic structure, but lacks the characteristic side chain. At respective concentrations, both tryptophan and indole share comparable starting points. Upon compression, the molecular behavior differs. The indole isotherm, displays a steeper result, indicating more area per molecule occupied by DOPC. The tryptophan isotherm exhibits tighter compression when compared to indole. Given the results, subsequent tryptophan analogues will be examined (i.e. tryptamine, 3-indole acetic acid), so as to further investigate the influential portion(s) of tryptophan.



Indole

References:

NIMA Technology, http://www.nima.co.uk, 2005; Abel, E., et al, 2000.; Yau, W., et al, 1998.

Acknowledgements:

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