Biochimica et Biophysica Acta xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Biochimica et Biophysica Acta

journal homepage: www.elsevier.com/locate/bbamem

Review

Functional role of water in membranes updated: A tribute to Träuble

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ARTICLE INFO

Article history:
Received 8 July 2014
Received in revised form 20 March 2015
Accepted 26 March 2015
Available online xxxx

Keywords:
Lipid membrane
Permeability
Water diffusion
Kinks-water pocket

ABSTRACT

The classical view of a cell membrane is as a hydrophobic slab in which only nonpolar solutes can dissolve and permeate. However, water-soluble non-electrolytes such as glycerol, erythritol, urea and others can permeate lipid membranes in the liquid crystalline state. Moreover, recently polar amino acid's penetration has been explained by means of molecular dynamics in which appearance of water pockets is postulated. According to Träuble (1971), water diffuses across the lipid membranes by occupying holes formed in the lipid matrix due to fluctuations of the acyl chain trans–gauche isomers. These holes, named "kinks" have the molecular dimension of CH_2 vacancies. The condensation of kinks may form aqueous spaces into which molecular species of the size of low molecular weight can dissolve. This molecular view can explain permeability properties considering that water may be distributed along the hydrocarbon chains in the lipid matrix. The purpose of this review is to consolidate the mechanism anticipated by Träuble by discussing recent data in literature that directly correlates the molecular state of methylene groups of the lipids with the state of water in each of them. In addition, the structural properties of water near the lipid residues can be related with the water activity triggering kink formation by changes in the head group conformation that induces the propagation along the acyl chains and hence to the diffusion of water.

Contents

1. Introduction

1.1. The selective barrier of the lipid membrane

The classical picture of a cell is a compartmentalized system in which the membrane is the selective barrier of contention of the cellular material [1,2]. In this view, the core of the membrane is the lipid bilayer

Abbreviations: Arg, arginine; Asp, aspartic acid; Glu, glutamic acid; Lys, lysine; Phe, phenylalanine; Trp, tryptophan; Tyr, tyrosine.

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http://dx.doi.org/10.1016/j.bbamem.2015.03.031
0005-2736/

described as an autonomous rigid phase in which partition rules the thermodynamics of transport processes. In addition, from the electrical standpoint, the bilayer is considered as a slab of low dielectric permittivity that should be impermeable to ions and polar solutes.

Water transport through biological membranes has been thoroughly revised by different authors [3–5]. Briefly, water transport can occur in three ways: 1) by diffusion through the lipid matrix; 2) through transport proteins such as channels and some occlusion transport proteins such as glucose transporters, and 3) through water channel proteins specifically expressed by cells for such purpose. A common feature in all these ways is that water transport is passive, i.e. driven by a gradient of water chemical potential between the inner and the outer compartment.

Biological membranes appear to be composed of a complex mixture of lipids varying in head group size and chain length. The isolation and characterization of lipids from cell membranes allowed preparation of experimental model systems, which mimic several properties of biological membranes. Lipids swollen in an excess of water above the transition temperature form closed particles trapping an aqueous solution. These multilamellar liposomes are able to swell and shrink according to if they are dispersed in hypotonic or hypertonic solutions, respectively in comparison to the solution in its interior. This osmometer behavior is due to the selectivity of the bilayer to solutes according to size and charge and to the high rate of diffusion of water across the lipid matrix [6].

The lipid barrier is selective but not an ideal semipermeable one. This is to say that for some solutes it is completely impermeable while for others it displays a wide range of permeability properties. This partial permeation denotes that water can flow through the lipid bilayer provided that a gradient of water chemical potential is present and that aqueous soluble solutes can also go through the membrane. In terms of the thermodynamics of irreversible processes, these two fluxes are coupled, i.e. they interfere and connect to each other, contrary to the primitive view that solutes flow through some region and water across other. The assumption that solute and water permeations take place as independent processes is opposed by the findings of Hill and Cohen and van Zoelen [7,8], who demonstrated a strong solute–solvent interaction in the membrane phase. Kedem and Katchalsky [9] described by means of the formalism of thermodynamics of irreversible processes the simultaneous non-independent permeation of non-electrolytes and water. This approach clearly demonstrates that both fluxes are not independent i.e. water permeation affects the permeation of the nonelectrolytes and vice versa.

The formalism of the irreversible thermodynamics defines a reflection coefficient which is equal to one when the solute is completely reflected and only water can flow through the membrane, i.e. in this case, the membrane is ideally selective or semipermeable. Large solutes such as sucrose, dextran or ions fit into this classification. Other solutes such as glycerol, urea, ethylenglycol, erythritol permeate the bilayer at different rates, i.e. they are described by different values of reflection coefficients, all of them lower than one [10].

Two structural views of the membrane have been proposed to interpret these results. One of them considers a solubility model in which a ternary mixture of water, lipid and solute is formed in some degree during the transport process.

Another model suggests that water and solute diffuse through pores formed in a rigid matrix. This proposal disregards lipids as influencing the solvent properties of water i.e. solute is dissolved in water pools enclosed by the lipid matrix. However, these descriptions are quite extreme and membrane responses are a complex combination of the two proposals due to its unique physicochemical properties. One of these properties is that the lipid walls (hydrophilic and hydrophobic groups) organize water in a different structure than in bulk phase, which, in consequence, has different thermodynamic (surface tension) properties. Thus, the lipid membrane is able to admit different amounts of water according to the presence of different solutes and to the different type of lipids. This makes that the membrane has a notable versatility to act as a non-polar solubility barrier or a polar sieve, which implicitly demands a dynamics of water in the lipid matrix. Therefore, a clarification of the organization of water molecules in different regions of the bilayer and its thermodynamic properties in comparison to bulk water is required.

From a molecular point of view, according to Träuble (1971), the movement of water molecules across membranes can be produced as a consequence of the thermal fluctuations of the conformational isomers in the hydrocarbon chains of the membrane lipids resulting in the formation of so-called "kinks" [11].

"Kinks" are described as mobile structural defects of free volumes in the hydrocarbon phase of the membrane (Fig. 1A). Kink diffusion is a fast process with a diffusion coefficient of kinks of c.a. 10^{-5} cm^2/s. Low molecular weight molecules such as urea, glycerol and some aminoacids can fit in the free volume of the kinks and migrate together with the kinks across the membrane. Thus, kinks are intrinsic polar carriers in the lipid membranes.

Träuble noted that water molecules can fit neatly in g–t–g kinks between two chains calculated by Flory as low energy motion for chain polymers [12]. Water molecules filling the vacancies may jump from vacancy to vacancy, randomly according to its formation by thermal agitation. In this case, water would be molecularly dispersed in the hydrocarbon matrix. This picture suitably applies to the diffusion of water molecules in a liquid crystalline state of saturated phospholipids.

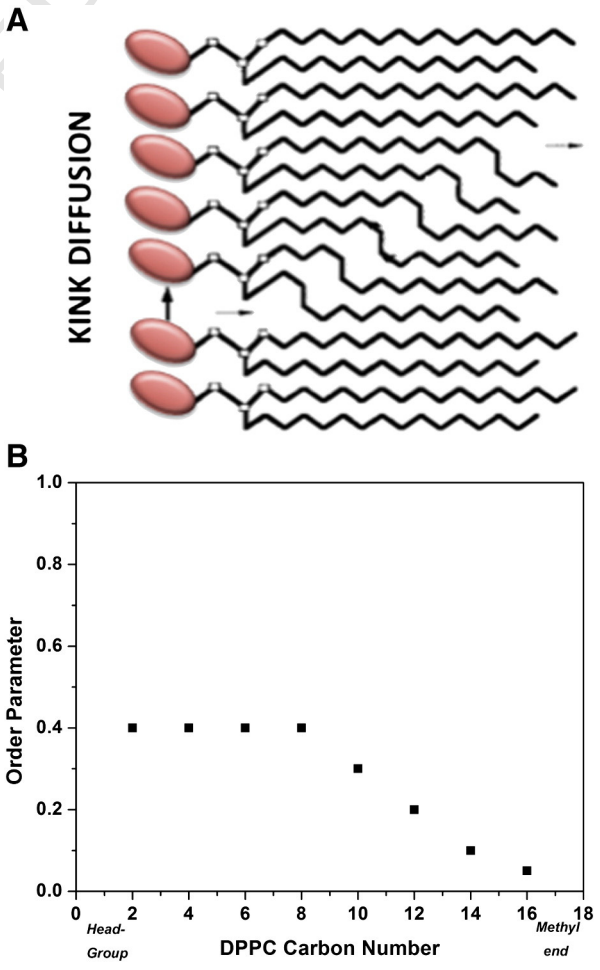

Fig. 1. A. Schematic representation of "kinks" in the lipid bilayer pictured as mobile structural defects. This picture is only a partial view and should be extended to the whole membrane in the liquid crystalline state. B. Order parameter in relation to kink formation.

Please cite this article as: E.A. Disalvo, et al., Functional role of water in membranes updated: A tribute to Träuble, Biochim. Biophys. Acta (2015), http://dx.doi.org/10.1016/j.bbamem.2015.03.031