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## Electric Biochemistry of Sphingomyelin

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### Structure and Biochemistry of Sphingomyelin Bilayer

Sphingomyelin is a major phospholipid in myelin sheaths, which play a pivotal role in saltatory conduction of myelinated axons [1]. Sphingomyelin consists of phosphorylcholine or phosphoryl ethanol amine and ceramide [2] to form lipid bilayer of cell membrane [3]. Under the physiological condition at neutral pH, choline is a positive residue, which associates with an anion such as a chloride ion. Phosphate forms diester bonds with choline and ceramide, and its hydroxy group is negatively ionized to form salt with a cation such as a sodium and potassium ion. Ceramide consists of sphingosine base and fatty acid, which are conjugated by a peptide bond. Consequently, sphingomyelin has a positive head group of choline, a negative phosphate diester bond, and two hydrophobic long tails connected with each other by a peptide bond.

When concentration of salts in solution is low, choline base could bind to phosphate residue intermolecularly within the lipid bilayer. When pH is high and low, choline base and phosphate residue are neutralized with hydroxyl anion and hydrogen cation, respectively. Choline residues, which are exposed at the very surface of sphingomyelin bilayer, could trap and release anions under chemical equilibrium. Thus, sphingomyelin bilayer could act as an anion exchanging resin in solution.

Under physiological condition, phosphate groups of sphingomyelins contact to one another and thus their cations could contact directly to the oxygen atom of the neighboring sphingomyelin molecules in a lipid bilayer (Figure 1). Consequently, the cation could transfer to adjacent oxygen atom, which had formed double bond with phosphorus in the next sphingomyelin, to form an ionic bond. In this case, the phosphorus should make a novel double bond to the other oxygen atom that had bound to another cation. Accordingly, all the phosphate groups participated in this reaction should transfer their cations from one to another through the chain of reaction. This cation transfer chain reaction occurs without any atomic translocation. It should be noted that the negative charge of oxygen flows in a direction opposite to that of cation transfer. The "flow of negative charge" causes ionic current along the surface of sphingomyelin lipid bilayer.

Within a sphingomyelin molecule, a hydrogen atom of hydroxyl group in sphingosine binds to an oxygen atom of phosphate group [2]. On the other hand, peptide bond of ceramide forms hydrogen bonds with another peptide bond of ceramide in neighboring sphingomyelins [2]. Thus, in lipid bilayer sphingomyelins associate with one another by hydrogen bond network. This nature of self-association of sphingomyelin molecules may cause an island of sphingomyelin to assemble a raft in bio-membrane of which sphingomyelin is a minor component.

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In a physiological condition, cytosolic solution contains 90mM potassium ion inside the lipid membrane while outer fluid contains 117mM sodium ion. Consequently, the phosphate group of sphingomyelin bilayer traps potassium and sodium ions inside and outside of the membrane, respectively. As discussed above, these cations could make an electric flow along the surface of the sphingomyelin bilayer.

As is shown in the Figure 1, sodium ion appears to fit in the membrane structure. Since diameter of potassium ion (276pm) is much larger than that of sodium ion (204pm), sodium-binding sphingomyelin may have lower thermal energy than potassium-binding one. Accordingly, there might be some ionic potential between sodium-binding outside and potassium-binding inside of the sphingomyelin bilayer under a physical condition, which should be taken account for calculation of membrane potential.

Since a long chains of alkyl hydrocarbons of fatty acid of the sphingomyelin is a perfect insulator, electric currents between outside and inside of the sphingomyelin membrane should pass through ion channels in the membrane but not through the lipid bilayer [3].

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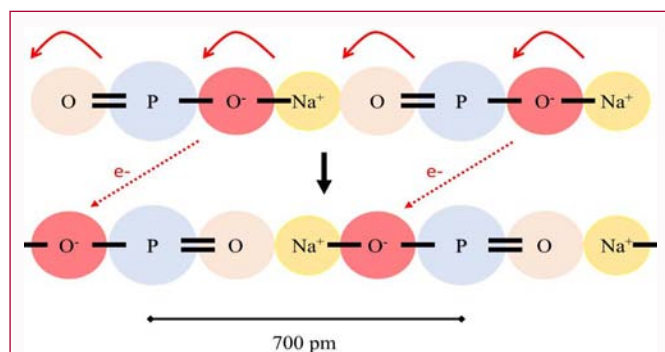
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**Figure 1: Atomic Model of current flow among phosphate residues of sphingomyelins at surface of lipid bilayer.** Atomic structure of phosphate residues of sphingomyelin is presented before (A) and after (B) the electric current flows. P, a phosphorus atom; O, an oxygen atom; O<sup>-</sup>, an oxygen anion; Na<sup>+</sup>, a sodium cation; e<sup>-</sup>, an electron; a red curved arrow, a flow of chemical bond; a red dotted arrow, a flow of electron; a rigid black line, a chemical bond.

Taken all together, sphingomyelin bilayer is considered as a sheet of insulator, whose surfaces are coated by electric conductance materials containing potassium- and sodium-binding phosphate groups inside and outside, respectively, to produce some membrane potential.

## Electrophysiological Aspects of Sphingomyelin

Sphingomyelin is a major component of myelin sheaths, which flow electric currents along their axon fibers for saltatory conductance, in the vertebrate white matter of nervous system. It is well known that

myelin sheaths act as a perfect insulator to prevent electric currents from leaking out of the axon fibers. Here, based on the structure of phospholipid, we would propose another important nature of myelin sheaths, which conduct electric currents all along the surface of the sphingomyelin sheaths for saltatory conductance of myelin. The phosphate groups could produce ionic current, after which each phosphate group could rotate randomly or thermodynamically on the surface of lipid bilayer. Consequently, they are ready to produce next electric current at any directions.

Sphingomyelin is a ubiquitous component of lipid bilayer in almost all the living things. In some cells, sphingomyelin forms rafts for some types of signal transduction of cells. Thus, sphingomyelin-dependent surface current is important not only for neural cells but also for any types of cells from prokaryotes to eukaryotes to maintain membrane potential and excitation.

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