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Ab Initio Studies of Rotation and Solvent Effects for two important membrane molecules: DPPC and DMPC

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ABSTRACT

DPPC (dipalmitoylphosphatidylcholine) and DMPC (dimyristoylphosphatidylcholine) are taken as phospholipids with an equal polar heads and with the difference in the length of hydrocarbon chains. Results obtain from the structural optimization of the isolated DPPC and DMPC in the gas phase, at the Hartree-Fock level of theory by means of STO-3g,3-21G, 6-31G and 6-31G* basis sets. the most important dihedral angle of these molecules (DPPC and DMPC) is chosen and the energy of 14 important atoms were scanned within 180 degrees rotation and sites that have most changes are determined and any rotated molecule separately placed in the 19 solvents (The method is HF/6-31G* model) and then dielectric effect of surrounding were analyzed. The solvent effect on the stability of DPPC & DMPC molecules were discussed using Onsager model.

Keywords: Membrane; DPPC; DMPC; Onsager model

INTRODUCTION

Transfer of ions through membranes and the function of enzymes attached to membranes provide two examples of these situations [1] .

Biological membranes are an essential part of life processes in living organisms. Membrane function goes beyond its obvious role as a physical barrier to contribute to important life processes. Membranes are semipermeable, highly selective barriers containing ion channels and pumps to modulate and maintain balance as required. Consequently, a fundamental understanding of bilayers and membrane proteins from the atomic point of view is of great biochemical , biophysical, and medical interest [2] .

Membrane proteins function within a complex heterogeneous environment differs markedly from the aqueous medium of globular proteins. Significant progress has been made toward understanding some of the key characteristics of both lipids and membrane proteins which determine the favorable energetics of this environment [3] .

Many physical and biochemical properties of lipid bilayers are important to the bilayer's fundamental role as the basisof biological membranes. These properties are now commonly investigated by atomistic molecular dynamics (MD) simulation and Quantum Mechanics(QM) [4] .

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Membranes are asymmetric structures. The choline-containing phospholipids are localed mainly in the outer molecular layer[7].This asymmetric distribution is maintained by an ATP-dependent protein which specifically translocates Phosphatidylethanolamine (and phosphatidyl serine) to the inside of the plasma membrane [5].

All major lipids in membranes contain both hydrophobic and hydrophilic regions and are therefore termed amphipathic. Dipalmitoylphosphatidylcholine (DPPC) and dimyristoylphosphatidylcholine (DMPC) are studied. DPPC and DMPC are taken as phospholipids with an equal polar heads and with the difference in the length of hydrocarbon chains[6,7].These two molecules have saturated fatty acid tail groups[8].On a molecular level it has been of interest to explore to what extent PC head groups differ with respect to molecular conformation, lateral interactions,
and dipole arrangements and how these features affect the properties and topology of the membrane surface [9,10].

DPPC and DMPC are important phospholipids in cell bilayer, then investigation of interaction between peptides and bilayer of these molecules is very important [11]. The main component that is responsible for considerable lowering of the interfacial tension is DPPC which accounts for 50%-70% of the PC[12]. DPPC has gel to liquid crystalline transition temperature(Tm) of 41.5 degree of centigrade and at a physiological temperature of 37 degree of centigrade it is in an ordered gel state [13].

These two molecules are zwitterionic having a negative charge on the phosphate group and a positive charge on the amin. The hydrocarbon chain of DPPC is 16 and DMPC is 14 carbons long .Then the Solvent effects on This molecules is important[2,14].

In this work, we made to use of the Ab-initio calculations to determine minimum energy conformations of the dimyristoyl phsphatidylchline and Dipalmitoylphosphatidylcholine and have performed calculations according to the continuum solvating model by Onsager [15].

2. COMPUTATIONAL METHODS

2.1. Geometries

All calculations were done with the Gaussian 98[18] ab initio packages at the Hartree-Fock (HF) level of theory. Four basis sets were used, namely the STO-3G 3-21G, 6-31G and 6-31G*.
First, the geometry of DPPC, DMPC were full optimized at the RHF/ 6-31G*, 6-31G, 3-21G and STO-3G levels of the theory in the gas phase.

2.2. Rotation

The most important dihedral angle of these molecules (DPPC and DMPC) is chosen and the energy was scanned within 180 degrees rotation. In this manner, the optimization of total molecules, important dihedral angles of these molecules were rotated every time 15 degrees and every time The volume of DPPC and DMPC molecules were obtained using the “volume” keyword.

2.3. Solvent Model

For the simulation of a polar environment the Onsager self-consistent reaction field (SCRF) model [17] was used as implemented in Gaussian 98. In the Onsager method, the solute molecule is placed in a spherical cavity of radius A0 surrounded by a continuum with constant dielectric properties.[9] A dipole in the molecule will induce a dipole in the medium, and the electric field applied by the solvent dipole will in turn in interact with the molecular dipole leading to net stabilization.

The salvation calculations were performed using Onsager [17] method at HF/6-31G*. For Onsager model, it requires values of volume (A0) of the molecule and the dielectric constant (ε) of solvent. The volume of DPPC and DMPC molecules was obtained using the “volume” keyword.

The molecular geometry obtained by HF/6-31G* level optimization in the gas phase, rotated and then any one separately placed in 19 solvents and the results were compared with another (keyword, scrf=dipole).

3. RESULTS AND DISCUSSION

3.1. Geometry optimization of DPPC and DMPC

Dipalmitoylphosphatidylcholine (DPPC) and dimyristoylphosphatidylcholine (DMPC) molecules were chosen as starting structures for gas phase (Fig.1).

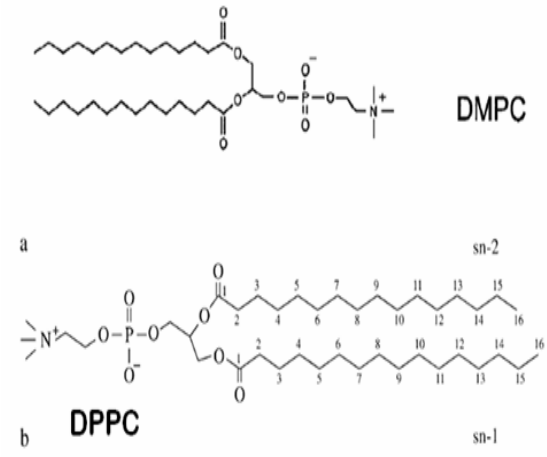


Fig.1. DPPC and DMPC molecule.

The DPPC and DMPC zwitterionic are found to be unstable in the optimized gas phase at HF/3-21G, 6-31G and 6-31G* level [16].the obtained result from optimization and stabilization is in table1.

Table 1. Conformational energy of DPPC and DMPC obtained by geometry optimization at basis set 6-31G*, 6-31G, 3-21G, STO-3G levels

basis set	E(kcal/mol)	
	DPPC	DMPC
STO-3G	-1583811.262	-148406.112
3-21G	-1594584.634	-149458.505
6-31G	-1602682.003	-1505418.2
6-31G*	-1603386.341	-1505422.1

According to observed result, is obtained minimum energies are related the basis set 6-31G* level. Therefore we have selected basis set 6-31G* for other calculation in this work.

3.2. Rotation

There is relation between energy and rotation angle. First, the most important dihedral angle that is 60 degree, every time increases 15 degree (Table2). The minimized energy about DMPC and DPPC is in the 60 degree and other minimized energy is in the 150 degree.

There is relation between energy and rotation angle. First, the most important dihedral angle that is 60 degree, every time increases 15 degree (Table2). The minimized energy about DMPC and DPPC is in the 60 degree and other minimized energy is in the 150 degree.

3.3. Solvent effects

Most chemical reactions and biological process take place in solutions. We present a Quantum-mechanical analysis of the solvent effect on stability DPPC and DMPC molecules. (Table 3)

Table 2. Different rotations in most dihedral angle of DPPC and DMPC

DPPC													
Rotation	0	15	30	45	60	75	90	105	120	145	160	175	180
Angle	60	75	90	105	120	135	150	165	179.9264	-165.0748	150.0753	-135.0739	-120.076
DMPC													
Rotation	0	15	30	45	60	75	90	105	120	145	160	175	180
Angle	60	75	90	105	120	135	150	165	179.9345	-165.0669	-150.0664	-135.0664	-120.0655

Table 3. The solvent effect on stability energy in different rotations by HF/6-31G* method: **(a)** DPPC **(b)** DMPC

(a)

Rotation	15	30	45	60	75	90	105	120	135	150	165	180
ε	E(kcal/mol)											
78.39	-1603388.5	-1556580.3	-1603384.6	-1603382.8	-1603382.1	-1603382.3	-1603384	-1603383.3	-1603383.8	-1603380	-1603378.5	-1603380.3
46.8	-1603388.3	-1556580.3	-1603384.5	-1603382.8	-1603382.1	-1603382.3	-1603384	-1603383.2	-1603383.6	-1603380	-1603378.4	-1603380.2
38.2	-1603388.3	-1556580.2	-1603384.5	-1603382.8	-1603382.1	-1603382.3	-1603383.9	-1603383.2	-1603383.6	-1603380	-1603378.4	-1603380.1
36.64	-1603388.3	-1556580.2	-1603381.9	-1603382.8	-1603382.1	-1603382.3	-1603383.9	-1603383.2	-1603383.6	-1603380.5	-1603378.4	-1603380.1
32.63	-1603388.3	-1556580.2	-1603384.5	-1603382.7	-1603382.1	-1603382.3	-1603383.9	-1603383.1	-1603383.6	-1603380	-1603378.4	-1603380.1
24.55	-1603388.2	-1556580.1	-1603384.4	-1603382.6	-1603382	-1603382.2	-1603383.5	-1603383.1	-1603383.5	-1603380	-1603378.2	-1603379.9
20.7	-1603388.2	-1556580.1	-1603384.3	-1603382.6	-1603381.9	-1603382.3	-1603383.8	-1603383	-1603383.4	-1603380	-1603378.2	-1603379.8
10.36	-1603387.9	-1556579.8	-1603383.9	-1603382.3	-1603381.8	-1603381.9	-1603383.5	-1603382.7	-1603382.9	-1603379.9	-1603377.3	-1603379.3
8.93	-1603387.8	-1556579.8	-1603383.9	-1603382.3	-1603381.6	-1603381.9	-1603383.4	-1603382.6	-1603382.8	-1603379.8	-1603377.7	-1603379.3
7.58	-1603387.7	-1556579.6	-1603383.8	-1603382.2	-1603381.6	-1603381.8	-1603383.3	-1603382.5	-1603382.6	-1603379.6	-1603377.6	-1603378.9
6.89	-1603387.6	-1556579.6	-1603383.7	-1603382.1	-1603381.5	-1603381.8	-1603383.2	-1603382.4	-1603382.4	-1603379.6	-1603377.6	-1603378.7
5.621	-1603387.5	-1556579.4	-1603383.5	-1603381.9	-1603381.4	-1603381.6	-1603383	-1603382.3	-1603382.2	-1603379.3	-1603377.3	-1603378.4
4.9	-1603387.3	-1556579.3	-1603383.3	-1603381.8	-1603381.3	-1603381.5	-1603382.9	-1603382.1	-1603381.9	-1603379.1	-1603377.1	-1603378.2
4.335	-1603387.2	-1556579.2	-1603383.2	-1603381.7	-1603381.1	-1603381.4	-1603382.8	-1603381.9	-1603381.8	-1603378.9	-1603377	-1603377.9
2.379	-1603386.4	-1556578.4	-1603382.3	-1603381	-1603380.4	-1603380.8	-1603381.9	-1603381.1	-1603380.4	-1603377.8	-1603375.9	-1603376.4
2.247	-1603386.3	-1556578.4	-1603382.2	-1603380.9	-1603380.4	-1603380.7	-1603381.8	-1603380.9	-1603382.3	-1603377.7	-1603375.9	-1603376.3
2.228	-1603386.3	-1556578.4	-1603382.2	-1603380.9	-1603380.4	-1603380.7	-1603381.8	-1603380.9	-1603382.3	-1603377.7	-1603375.8	-1603376.2
2.023	-1603386.1	-1556578.2	-1603382	-1603382.3	-1603380.3	-1603380.6	-1603381.6	-1603380.8	-1603380	-1603377.5	-1603375.6	-1603375.9
1.99	-1603386.1	-1556578.1	-1603381.9	-1603380.7	-1603380.2	-1603380.5	-1603381.5	-1603380.7	-1603379.8	-1603375.7	-1603375.5	-1603375.8

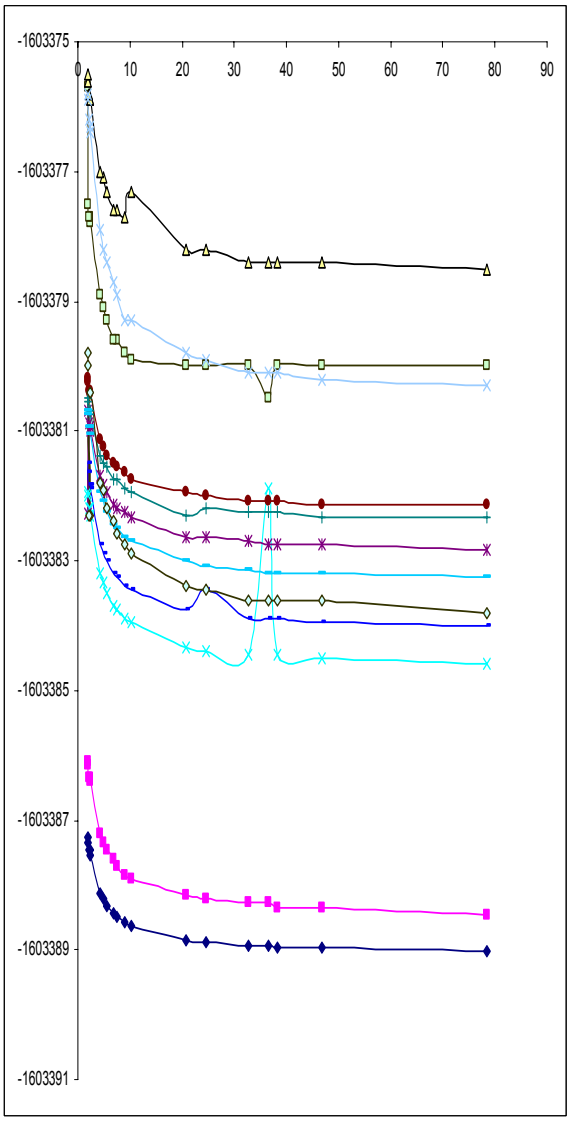
Table3. Continue

(b)

Rotation	15	30	45	60	75	90	105	120	135	150	165	180
ε	E(kcal/mol)											
78.39	-1505424.1	-1505421.5	-1505419.7	-1505418.5	-1505418.4	-1505419.8	-1505419.6	-1505419.4	-1505418.7	-1505417.3	-1505416.2	-1505415
46.8	-1505424	-1505421.4	-1505419.7	-1505418.4	-1505418.3	-1505419.8	-1505419.5	-1505419.4	-1505418.6	-1505417.2	-1505416.1	-1505414
38.2	-1505424	-1505421.4	-1505419.7	-1505418.4	-1505418.3	-1505419.7	-1505419.5	-1505419.3	-1505418.5	-1505417.1	-1505416.1	-1505414
36.64	-1505424	-1505421.4	-1505419.6	-1505418.4	-1505418.3	-1505419.7	-1505419.5	-1505419.3	-1505418.4	-1505417.1	-1505416.1	-1505414
32.63	-1505424	-1505421.4	-1505419.6	-1505418.4	-1505418.3	-1505419.7	-1505419.5	-1505419.3	-1505418.4	-1505417.1	-1505416	-1505414
24.55	-1505423.9	-1505421.3	-1505419.5	-1505418.3	-1505418.2	-1505419.7	-1505419.4	-1505419.2	-1505418.3	-1505417	-1505415.9	-1505414
20.7	-1505423.9	-1505421.3	-1505419.3	-1505418.3	-1505418.2	-1505419.6	-1505419.4	-1505419.2	-1505418.3	-1505416.9	-1505415.8	-1505414
10.36	-1505423.6	-1505421	-1505419.2	-1505418	-1505417.9	-1505419.3	-1505419.1	-1505418.8	-1505417.9	-1505416.4	-1505415.3	-1505414
8.93	-1505423.5	-1505420.9	-1505419.1	-1505417.9	-1505417.8	-1505419.2	-1505419	-1505418.7	-1505417.8	-1505416.3	-1505415.3	-1505414
7.58	-1505423.4	-1505420.8	-1505419	-1505417.8	-1505417.7	-1505419.1	-1505418.9	-1505418.6	-1505417.6	-1505416.1	-1505414.9	-1505413
6.89	-1505423.3	-1505420.8	-1505418.8	-1505417.8	-1505417.6	-1505419.1	-1505418.8	-1505418.5	-1505417.5	-1505416	-1505414.8	-1505413
5.621	-1505423.2	-1505420.6	-1505418.7	-1505417.6	-1505417.5	-1505418.9	-1505418.7	-1505418.3	-1505417.3	-1505415.7	-1505414.5	-1505413
4.9	-1505423	-1505420.5	-1505418.6	-1505417.5	-1505417.3	-1505418.8	-1505418.5	-1505418.1	-1505417.1	-1505415.5	-1505414.2	-1505413
4.335	-1505422.9	-1505420.4	-1505417.9	-1505417.4	-1505417.2	-1505418.6	-1505418.4	-1505418	-1505416.9	-1505415.3	-1505414	-1505413
2.379	-1505422.2	-1505419.7	-1505417.8	-1505416.7	-1505416.4	-1505417.8	-1505417.6	-1505417	-1505415.8	-1505414	-1505412.5	-1505412
2.247	-1505422.1	-1505419.6	-1505417.8	-1505416.6	-1505416.3	-1505417.8	-1505417.5	-1505416.9	-1505415.7	-1505413.8	-1505412.4	-1505411
2.228	-1505422.1	-1505419.6	-1505417.6	-1505416.6	-1505416.3	-1505417.7	-1505417.5	-1505416.9	-1505415.7	-1505413.8	-1505412.3	-1505411
2.023	-1505421.9	-1505419.5	-1505417.5	-1505416.5	-1505416.2	-1505417.6	-1505417.3	-1505416.7	-1505415.5	-1505413.5	-1505412.1	-1505411
1.99	-1505421.8	-1505419.4	-1505419.6	-1505416.4	-1505416.7	-1505417.5	-1505417.3	-1505416.6	-1505415.3	-1505413.4	-1505412.1	-1505411

The molecular geometries are obtained by HF/6-31G* level optimization in the gas phase and then important dihedral angle of these molecules were rotated every time 15 degrees. The volume of DPPC and DMPC molecules were obtained using the "volume" keyword. Any one of rotated molecule separately placed in the 19 solvents (keyword, scrf=dipole). Regular alterations were observed concerning energy
versus dielectric constant. With increasing of dielectric constant of solvents, increases stability, for 13 A0 values of DPPC and DMPC (Fig.2).

(a)



(b)

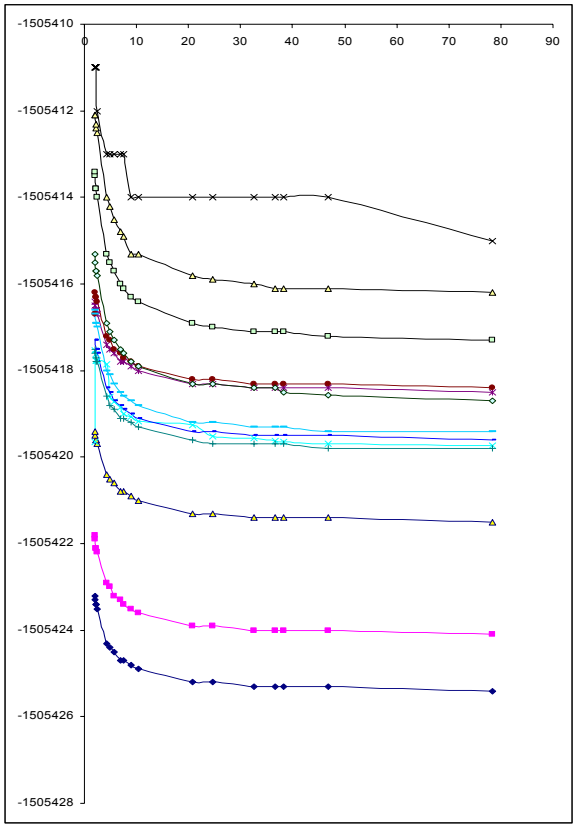


Fig.2. Energy (kcal/mol) versus Dielectric constant for 13 A0 values **(a)** DPPC and **(b)** DMPC.

CONCLUSIONS

The role of this ball is the same role of phosphorus in the membrane molecules and the hydrocarbons chaines have the same role of electroscope sheet. Hydrophobic and hydrophilic forces accruing on metal ions at the time that effect on membrane create one charge induction in the phosphorus atom. This effect on the hydrocarbons chains causes particular dynamic movement of phospholipids. This dynamic movement causes to enter and exit material to or of cytoplasm membrane.

Two regions of dielectric constant values are identified ($1<\varepsilon<10$) and ($10<\varepsilon<80$). As it was expected, with increasing of dielectric constant of solvents and stability of DPPC and DMPC were increased. With plot of the calculated energies and dielectric constant of DPPC and DMPC, we have good results. We propose for future is founding a empirical communicating between effect of solvent and membrane molecule.

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