J. At. Mol. Sci.
doi: 10.4208/jams.012711.021511a

Vol. **2**, No. 4, pp. 281-288
November 2011

The properties of glycophorin A transmembrane helices in erythrocyte asymmetric membrane: a molecular dynamics study

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Received 27 January 2011; Accepted (in revised version) 15 February 2011
Published Online 28 June 2011

Abstract. We have performed an 80ns molecular dynamics (MD) simulation of human red blood erythrocyte asymmetric membrane model. The NAMD code and CHARMM27 force field were used. We have estimated some features of embedded glycophorin A (GpA) protein and have discussed some important problems concerning the interaction between the protein and surrounding media. It is stated that the lipid environment and protein immediate neighboring lead to the changes in helix-helix association, as well as to the protein orientation. The interaction nature between protein and neighboring phospholipid chains are dominant forces governing to helix-helix association.

PACS: 87.14.ep, 87.15.ap, 87.15.kt

Key words: glycophorin A (GpA) protein, erythrocyte membrane, molecular dynamics simulation, helix-helix association

1 Introduction

The glycophorin A (GpA) is the major intrinsic membrane protein of the erythrocyte, which is largely composed of hydrophobic amino acids and spans the membrane once, presenting its amino-terminal end at the extra-cellular surface of the human red blood cell. The GpA system has been studied by a variety of biochemical and biophysical techniques aimed at understanding the basis of this self-association.

The molecular dynamics simulation (MD) method, which is intensively used for bio-systems study, is a great tool to well understand the intra- and intermolecular structure of biological systems [1–5]. During last decade a lot of works were done using MD study for investigation of structure and behavior of biological membranes [4–7].

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It is known, that the transmembrane part of human GpA is responsible for dimerization [8]. NMR study provides us to measure and better understand the so called helix-helix contacts [9]. In parallel to real experiment, the MD study of GpA feature have been done by Braun and coworkers [9]. They have studied GpA transmembrane helices embedded in sodium dodecyl sulfate (SDS) micelles to reveal the dimerization contacts. The native structure of transmembrane domain of GpA was examined by Soumana and coworkers [10] and they claimed that GxxxG-like helix motif at the dimer interface is presumed to drive receptor oligomerization. The GxxxG sequence motif mediates the association of transmembrane helices by providing a site of close contacts between them and therefore outside the contact interface can exert a significant influence on transmembrane helix association affinity [11]. Some studies have shown that small and/or polar residues are more occur in helical interface of GpA than other amino acids [12]. Smith and coauthors report that the direct packing contacts of the GpA occur between glycire residues at position of 79 and 83 in the transmembrane sequence. The estimated distance between the above mentioned residues is about 4.9 Åbased on MAS NMR distance measurements [13, 14].

The main purpose of this work is to investigate the structure and dynamical properties of GpA in human red blood erythrocyte asymmetric membrane. We are going to explain the influence of lipid environment and protein immediate neighborhood on helix-helix contracts and protein orientation. The effect of boundary neighboring lipids on protein is still debated issues, and to the best of our knowledge, there is no computer simulation study of multicomponent complex systems with embedded protein. A few works were done on DPPC and DMPC with embedded GpA pure systems and as well GpA has been intensively studied with presence of SDS micelle [13] and in vacuum [15].

The asymmetry and more accuracy model of human red blood erythrocyte membrane lead to the real mimic of biological membrane and will help us to understand the behavior of protein and surrounding phospholipids.

According to the real experimental finding [16], the phospholipid composition is the following. 24:0 SM lingoceroyl sphingomyelin (LSM), 16:0 SM hexadecanoyl sphingomyelin (HSM), 1-stearoyl-2-arachidonoyl-sn-glycero-3-phosphatidylserine (SAPS), 1-stearoyl-2-docosahexaenoyl-sn-glycero-3-phosphatidylserine (SDPS), 1-stearoyl-2-oleoyl-sn-glycero-3-phosphatidylethanolamine (SOPE), 1-stearoyl-2-arachidonoyl-sn-glycero-3-phosphatidylethanolamine (SAPE), 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphatidylcholine (POPC), 1-stearoyl-2-oleoyl-sn-glycero-3-phosphatidylcholine (SOPC) and cholesterol.

2 Construction and simulation details

The construction of model membrane was implemented by using of Hyperchem (Hypercube Inc.) software and MDesigner [17, 18]. First the molecules of POPE, POPC, SAPE, SOPC, SAPS, SDPS, LSM, HSM, and Cholesterol were created and we have received a system consisting of 252 molecules of phospholipids, cholesterol, and 27 Sodium counterions by random replication making allowance for asymmetry of model membrane and final concentration of