Molecular view on protein sorting into liquid-ordered membrane domains mediated by gangliosides and lipid anchors

de Jong, Djurre H.; Lopez, Cesar A.; Marrink, Siewert J.

Published in:
Faraday Discussions

DOI:
10.1039/c2fd20086d

Publication date:
2013

Supplementary material for:

Molecular view on protein sorting into liquid-ordered membrane domains mediated by gangliosides and lipid anchors

Djurre H. de Jong, Cesar A. Lopez, and Siewert J. Marrink
DOI: 10.1039/b000000x [DO NOT ALTER/DELETE THIS TEXT]

Coarse grain parametrization of the GM1 ganglioside

Here we give a short description of the parameterization of the GM1 ganglioside. A more detailed account will be published elsewhere[1]. The complete topology files can be downloaded from http://cgmartini.nl

The glycosphingolipid GM1 is characterized by the presence of an oligosaccharide head group consisting of a chain of glucose and galactosyl monosaccharides, as depicted in figure S1. These rings are consecutively connected through 1-4 and 1-3 glycosidic bonds. The glucose unit, in turn, is linked to a ceramide backbone. The second sugar monomer of the sugar chain has a sialic acid residue, n-acetylneuraminic acid, linked to it making the overall lipid anionic. Due to the high branching, we find that the most suitable CG representation is provided by the mapping approach used for monosaccharides in the Martini force field[2], in particular glucose. In the Martini representation, glucose consists of three particles of polar nature, one of type 'P1', and two 'P4'. For the CG particles in the GM1 head group representing a branching point the polarity is reduced from 'P4' to 'P1'. In the second galactose ring a double branching point is present and the polarity of the respective CG particle is further reduced to the level of an 'Nda' particle. The *n*-acetylneuraminic acid group was represented by five particles, with the acetyl group represented by a 'P4' particle, the carboxylic acid by 'Qa' (carrying a negative charge), the glycerol unit as 'P5', and the remaining parts of the sugar ring by two 'P1' particles. A close up of the CG representation of GM1 is given in figure S1.

Optimization of the bonded interactions of the GM1 head group was performed by comparison to distributions obtained from mapped AA simulations using an atomistic forcefield based on the Gromos carbohydrate force field[3]. Consecutive CG beads are connected through a series of tight harmonic bonds with force constants ranging from f_c = 20,000-30,000 kJ mol^{-1} nm^{-2}. A number of angle and dihedral potentials were used to control the flexibility and preferred orientation of the individual sugar units. In practice, this set of bonded interactions did not prove sufficient to match the global conformation of the GM1 head. To match the structural conformation observed in AA simulations, an additional elastic network was added to the system. This network, depicted in figure S1, consists of long range bonds (0.5-0.9 nm) with a weak force constant f_c = 100 kJ mol^{-1} nm^{-2}.

Similar to the glycerol backbone of glycerolipids, the sphingosine backbone of GM1 is represented by two CG particles. The amide group is represented by a 'P5'

particle like the peptide bond in proteins, and the di-hydroxyl group by a 'P4' bead. The trans-bond connecting the di-hydroxyl group with the rest of the aliphatic tail is represented by a 'C3' particle, as suggested for unsaturated bonds in the Martini lipid model[4].. Compared to glycerol, the bond between the two backbone beads required a shorter distance and a higher force constant in order to reproduce the AA distance distributions. Whereas the bond between the glycerol backbone beads has an equilibrium distance of 0.37 nm and a force constant of f_c = 1,250 kJ mol^{-1} nm^{-2}, for the sphingosine backbone bond we obtained 0.27 nm and f_c = 30,000 kJ mol^{-1} nm^{-2}. In practice this bond is replaced by a constraint. Three angle potentials were added to model the bending of the ceramide linkage properly. Interestingly, the trans unsaturated bond of the sphingosine does not affect the alignment of the lipid tail very much in comparison to glycerolipids; at the CG level it is represented by the same angle potential with equilibrium angle ϕ_0 = 180 degrees and f_c = 25 kJ mol^{-1}.

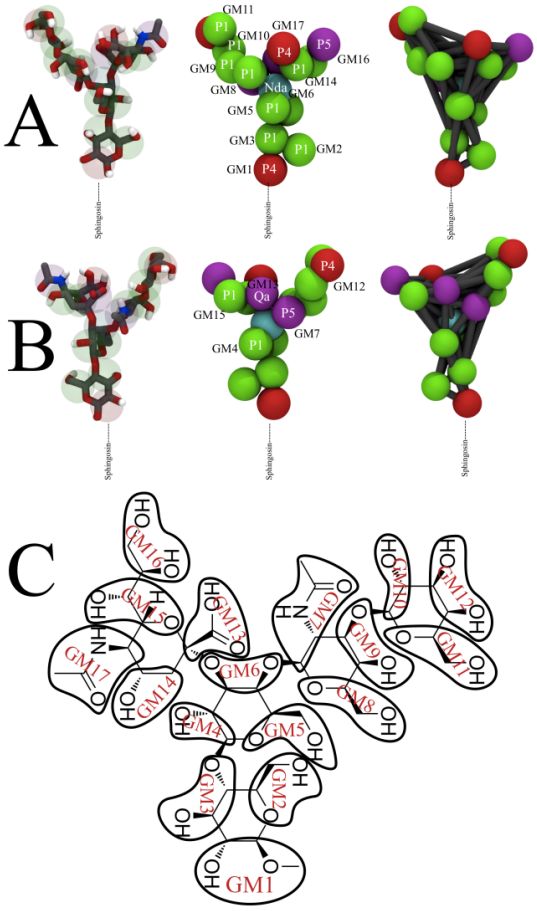

Fig. S1. Choice of beads and mapping scheme for the GM1 head group. A) Atomistic (left) and CG (midde) representation, and elastic network (right). B) Same representations viewed from the other side. C) Mapping scheme of the GM1 head group.

References

1 C.A. Lopez, A.H. de Vries, S.J. Marrink, in preparation, 2012.
2 C.A. López, A.J. Rzepiela, A.H. de Vries, L. Dijkhuizen, P.H. Hünenberger, and S.J. Marrink, *J. Chem. Theory Comput.,* 2009, **5**, 3195-3210
3 R.D. Lins, and P.H. Hünenberger, *J. Comput. Chem.*, 2005, **26**, 1400-1412