Molecular modelling insight into membrane-detergent interactions.

Bouffioux, O., Lacapere, J.J.*, Thomas-Soumarmon, A.**, Brasseur R.
Centre de Biophysique Moléculaire Numérique, Faculté Universitaire des Sciences Agronomiques, Passage des Déportés 2, 5030 Gembloux, Belgium. * Section de Recherche, UMR 168 CNRS, Institut Curie Paris, France. **INSERM U10, Hopital X. Bichat, 170 Bd. Ney, 75018 Paris, France.

Choosing a detergent is a key step in membrane protein solubilization and cristallization. It is based on some 'A Posteriori' experimental observations principles[1].
Here, we present a theoretical study of interactions of some widely used detergents (C8E4, Triton X-100, LDAO, and Octyl-β-D-glucopyranoside) with a lipidic bilayer model and with a membrane protein : MSCL[2,3].
The aim is to understand more precisely the mechanism of detergent action in the course of solubilization.

We modelised the detergent molecules and computed their MHP to visualise their hydrophobic and hydrophilic domains. The depth of insertion in a model membrane has been analysed with IMPALA[4]. The mode of the detergent – membrane protein interactions have been analysed with TAMMO[5].

Results show that those detergents can be seperated in two classes:
- In the first one, detergents have a hydrophobic alkyl chain longer than the lipid bilayer (minimum of 38 Å) and thus, the detergent is tilted with respect to the acyl chains of lipids. They insert in such a way that their mass centre is at the centre of the bilayer. As a consequence, this kind of detergent should be particularly indicated for lipid solubilization.
- In the second class, detergents have shorter alkyl chains and a more important hydrophilic part. Their mass centre is near the interface of lipids polar headgroups and apolar tails. Therefore they do not cross the bilayer. Due to their potential capacity to have interactions with polar groups, they should be more indicated for protein solubilization.

References

1. Hartmut, M., Cristallization of Membrane Proteins, CRC PRESS (1991).
2. Saint, N., Lacapère, J-J., Gu, L-Q., Ghazi, A., Martinac, B., Rigaud J-L., (1998) JBC 273 (24), 14667-14670.
3. Chang, G., Spencer, R. H., Lee, A. T., Barclay, M. T., Douglas C. R., (1998) Science 282, 2220.
4. Ducarme, Ph., Rahman, M., Brasseur, R., (1998) Proteins 30, 357-371.
5. Brasseur, R., Molecular Description of Biological Membranes by Computer Aided Conformational Analysis, Vol I, CRC PRESS (1990).