Table 4.2.2.1
Potentially useful detergents for membrane-protein crystallizations with molecular weights and CMCs [in water, from Michel (1991) or as provided by the vendor]

The lengths of the alkyl or alkanoyl side chains are given as C_6 to C_{16}.

Detergent	Molecular weight	CMC (m*M*)
Alkyl dihydroxypropyl sulfoxide		
C_8	238	20.6
N,*N*-Dimethylalkylamine-*N*-oxides		
C_8	173	162
C_9	187	50
C_{10}	201	20
C_{12}	229	1–2
n-Dodecyl-*N*,*N*-dimethylglycine (zwitterionic)	271	1.5
N-Alkyl-β-D-glucopyranosides		
C_6	264	250
C_7	278	79
C_8	292	30
C_9	306	6.5
C_{10}	320	2.6
n-Alkanoyl-*N*-hydroxyethylglucamides ('HEGA-*n*')		
C_8	351	109
C_9	365	39
C_{10}	379	7.0
C_{11}	393	1.4
Alkyl hydroxyethyl sulfoxide		
C_8	222	15.8
n-Alkyl-β-D-maltosides		
C_6	426	210
C_8	454	19.5
C_9	468	6
C_{10}	483	1.8
C_{11}	497	0.6
C_{12}	511	0.17
C_{13}	525	0.033
C_{14}	539	0.01
C_{16}	567	0.006
cyclohexyl-C_1	438	340
cyclohexyl-C_2	452	120
cyclohexyl-C_3	466	34.5
cyclohexyl-C_4	480	7.6
cyclohexyl-C_5	494	2.4
cyclohexyl-C_6	508	0.56
cyclohexyl-C_7	522	0.19
n-Alkanoyl-*N*-methylglucamides ('MEGA-*n*')		
C_8	321	79
C_9	335	25
C_{10}	349	6
Methyl-6-*O*-(*N*-heptylcarbamoyl)-α-D-glucopyranoside ('HECAMEG')	335	19.5
n-Alkylphosphocholines (zwitterionic)		
C_8	295	114
C_9	309	39.5
C_{10}	323	11
C_{12}	315	1.5
C_{14}	379	0.12
C_{16}	407	0.013
Polyoxyethylene monoalkylethers (C_nE_m)		
C_8E_4	306	7.9
C_8E_5	350	7.1
$C_{10}E_6$	422	0.9
$C_{12}E_8$	538	0.071
n-Alkanoylsucrose		
C_{10}	497	2.5
C_{12}	525	0.3
n-Alkyl-β-D-thioglucopyranosides		
C_7	294	29
C_8	308	9
C_9	322	2.9
C_{10}	336	0.9
n-Alkyl-β-D-thiomaltopyranosides		
C_8	471	8.5
C_9	485	3.2
C_{10}	499	0.9
C_{11}	513	0.21
C_{12}	527	0.05

gents have to be tried. There is one special problem when using alkyl-β-D-glucopyranosides or alkyl-β-D-maltosides as detergents: the commercially available detergents are often 'contaminated' with the α-anomers in varying, sometimes substantial, concentrations. The α-anomers are much less soluble, and appear to prevent crystallization. In the case of photosystem I from a thermophilic cyanobacterium, it has been reported that for a 2% α-anomer content in dodecyl-β-D-maltoside preparations no crystals can be obtained, with a 0.5–2% content the diffraction of the crystals is anisotropic with a reduction in resolution to 5–6 Å, whereas diffraction to better than 3.5 Å resolution in all directions is observed when the content of the α-anomer is below 0.1% (Fromme & Witt, 1998). The percentage of α-anomer can be determined using NMR spectroscopy or high-performance liquid chromatography. During ageing of detergent solutions, a conversion from the β-anomer to the α-anomer is expected. Therefore, ageing of detergent solutions has to be prevented.

The detergents that have been successfully used to crystallize membrane proteins can also be found in Table 4.2.1.1. The possibilities for developing new detergents for membrane-protein crystallization have not been exhausted. There is a need for new detergents, *e.g.* detergents with head groups with sizes between glucose and maltose are still missing!

It has been observed that crystals of the photosynthetic reaction centre from the purple bacterium *Rhodopseudomonas viridis* could be obtained when *N*,*N*-dimethyldodecylamine-*N*-oxide is used as detergent, but not when *N*,*N*-dimethyldecylamine-*N*-oxide is used. Even crystals formed with the dodecyl homologue lost their order when soaked in a buffer containing the decyl homologue. These observations were found to have an obvious explanation when the location of the detergent molecules bound to the protein was determined using neutron crystallography (Roth *et al.*, 1989); the detergent molecules surrounding neighbouring photosynthetic reaction centres in the crystal lattice are in contact. It is likely that attractive interactions between neighbouring protein-bound detergent micelles contribute to the stability of the crystal lattice. Particularly striking (see Table 4.2.3.1) is the dependence of the crystal quality on the alkyl-chain length in the case of the two-subunit cytochrome *c* oxidase from the soil bacterium *Paracoccus denitrificans*. Well ordered crystals were obtained with undecyl-β-D-maltoside, but not with the decyl and dodecyl homologues. Table 4.2.3.1 also lists the names of important vendors of detergents.

4.2.4. The 'small amphiphile concept'

From the arguments and observations presented above, it is evident that the size and shape of the detergent micelle are very important in membrane-protein crystallization. Detergent micelles can be made smaller (and their curvatures changed) when small amphiphilic molecules like heptane-1,2,3-triol are

Copyright © 2012 International Union of Crystallography