

4.2. CRYSTALLIZATION OF MEMBRANE PROTEINS

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 C₆ to C₁₆.

Detergent	Molecular weight	CMC (mM)	Detergent	Molecular weight	CMC (mM)
Alkyl dihydroxypropyl sulfoxide			cyclohexyl-C ₅	494	2.4
C ₈	238	20.6	cyclohexyl-C ₆	508	0.56
<i>N,N</i> -Dimethylalkylamine- <i>N</i> -oxides			cyclohexyl-C ₇	522	0.19
C ₈	173	162	<i>n</i> -Alkanoyl- <i>N</i> -methylglucamides ('MEGA- <i>n</i> ')		
C ₉	187	50	C ₈	321	79
C ₁₀	201	20	C ₉	335	25
C ₁₂	229	1–2	C ₁₀	349	6
<i>n</i> -Dodecyl- <i>N,N</i> -dimethylglycine (zwitterionic)	271	1.5	Methyl-6- <i>O</i> -(<i>N</i> -heptylcarbonyl)- α -D-glucopyranoside ('HECAMEG')	335	19.5
<i>N</i> -Alkyl- β -D-glucopyranosides			<i>n</i> -Alkylphosphocholines (zwitterionic)		
C ₆	264	250	C ₈	295	114
C ₇	278	79	C ₉	309	39.5
C ₈	292	30	C ₁₀	323	11
C ₉	306	6.5	C ₁₂	315	1.5
C ₁₀	320	2.6	C ₁₄	379	0.12
<i>n</i> -Alkanoyl- <i>N</i> -hydroxyethylglucamides ('HEGA- <i>n</i> ')			C ₁₆	407	0.013
C ₈	351	109	Polyoxyethylene monoalkylethers (C _{<i>n</i>} E _{<i>m</i>})		
C ₉	365	39	C ₈ E ₄	306	7.9
C ₁₀	379	7.0	C ₈ E ₅	350	7.1
C ₁₁	393	1.4	C ₁₀ E ₆	422	0.9
Alkyl hydroxyethyl sulfoxide			C ₁₂ E ₈	538	0.071
C ₈	222	15.8	<i>n</i> -Alkanoylsucrose		
<i>n</i> -Alkyl- β -D-maltosides			C ₁₀	497	2.5
C ₆	426	210	C ₁₂	525	0.3
C ₈	454	19.5	<i>n</i> -Alkyl- β -D-thioglucopyranosides		
C ₉	468	6	C ₇	294	29
C ₁₀	483	1.8	C ₈	308	9
C ₁₁	497	0.6	C ₉	322	2.9
C ₁₂	511	0.17	C ₁₀	336	0.9
C ₁₃	525	0.033	<i>n</i> -Alkyl- β -D-thiomaltopyranosides		
C ₁₄	539	0.01	C ₈	471	8.5
C ₁₆	567	0.006	C ₉	485	3.2
cyclohexyl-C ₁	438	340	C ₁₀	499	0.9
cyclohexyl-C ₂	452	120	C ₁₁	513	0.21
cyclohexyl-C ₃	466	34.5	C ₁₂	527	0.05
cyclohexyl-C ₄	480	7.6			

aqueous phase. The membrane proteins are found exclusively in the viscous phase and crystals – if formed – are difficult to handle. Some detergents, *e.g.* those with polyoxyethylene head groups, undergo a phase separation at higher temperatures. This phenomenon has been used to separate solubilized membrane proteins, which are found in the detergent-rich phase, from the water-soluble proteins. The latter are concentrated in the detergent-depleted phase (Bordier, 1981). Other detergents, *e.g.* octyl- β -D-glucopyranoside, show this phase separation at lower temperatures. Therefore, if phase separation causes problems, a change of the crystallization temperature may help.

The polar head groups of the detergents influence their usage in many ways. One would like to have a small polar head group, because the head group 'covers' the part of the protein's polar surface that is adjacent to the hydrophobic surface belt. The bigger the head group the more of the polar surface is covered and unavailable for the polar interactions needed to form the crystal lattice. Unfortunately, detergents with small polar head groups are

rather denaturing. Detergents with charged head groups cannot be used, but detergents with zwitterionic head groups, *e.g.* sulfo-betaines, can be tried with more stable proteins. The head group of a very successful detergent, *N,N*-dimethyldodecylamine-*N*-oxide, is of zwitterionic nature. I estimate that it can only be used with about 20% of all membrane proteins. Detergents with sugar residues as head groups have been used successfully. Octyl- β -D-glucopyranoside also tends to be denaturing. The lifetime of many membrane proteins can be prolonged by a factor of three by the use of nonyl- β -D-glucopyranoside instead of the shorter homologue. Such behaviour is observed within each series of homologous detergents; an increase in the alkyl chain by one methylene group leads to an increase in stability by a factor of three, an increase by two methylene groups leads to an increase in stability by a factor of about ten. Unfortunately, decyl- β -D-glucopyranoside is too insoluble to be used as detergent. For less stable membrane proteins, alkylmaltoside detergents or alkanoylsucrose detergents have to be tried. There is one special problem when using alkyl- β -D-