the clinical significance of product inhibition and of the type of drug interaction described here.

(1) N. Gerber and K. Arnold, *J. Pharmacol. Exp. Ther.*, **167**, 77(1969).

(2) N. Gerber, W. L. Weller, R. Lynn, R. E. Rangno, B. J. Sweetman, and M. T. Bush, *ibid.*, **178**, 567(1971).

(3) P. G. Dayton, S. A. Cucinell, M. Weiss, and J. M. Perel, *ibid.*, **158**, 305(1967).

(4) K. Arnold and N. Gerber, *Clin. Pharmacol. Ther.*, **11**, 121 (1970).

(5) J. J. Ashley and G. Levy, *J. Pharmacokinetics Biopharm.*, in press.

(6) P. Borondy, T. Chang, and A. J. Glazko, *Fed. Proc.*, **31**, 582 Abstr. (1972).

(7) J. J. Ashley and G. Levy, *Res. Commun. Chem. Pathol. Pharmacol.*, **4**, 297(1972).

(8) T. Chang and A. J. Glazko, in "Antiepileptic Drugs," D. M. Woodbury, J. K. Penry, and R. P. Schmidt, Eds., Raven, New York, N. Y., 1972, p. 154.

(9) G. Levy and J. A. Procknal, *J. Pharm. Sci.*, **57**, 1330(1968).

(10) E. Jähnchen and G. Levy, *Proc. Soc. Exp. Biol. Med.*, in press.

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Further Comments on the Existence of Spherical Micelles

Sir:

A study of the shape of micelles (1), based on the combination of their measured size with geometric considerations of the extended length of the normal paraffin moiety, indicated that few surfactants having a single normal alkyl chain form spherical micelles. In Fig. 1 of a recent communication (2), Zografi and Yalkowsky superimposed the results of their calculations, based on similar geometric considerations, on Fig. 1 of *Reference 1*. The figure is a plot of z, the aggregation number or the number of surfactant molecules per micelle, *versus* the number, n, of carbon atoms in the linear hydrocarbon chain of the single-chain surfactants. Micelles with (z, n) coordinates above the curves are unlikely to be spherical. Of the 32 surfactants considered and plotted in Fig. 1, only one fulfilled the geometric prerequisites for spherical shape

according to the solid line embodying the results of our original computations (1). Only 26 separate points were shown in Fig. 1 because the coordinates of another six surfactants overlapped points already plotted.

The values of z calculated according to Eq. 5 and listed in the last column of Table I of *Reference 2*[1] have the largest differences from our maximum z values consistent with spherical shape. They are represented by the uppermost of the three curves of Fig. 1. There are 18 surfactants with coordinates above that curve and 14 with coordinates below or on it, which shows that even according to the more divergent of the two analyses of Zografi and Yalkowsky (2), the majority of the surfactants under consideration are still unlikely to form spherical micelles. Moreover, the vertical axis was compressed by using a logarithmic scale for z, so that even points apparently lying close to the curve correspond to distinctly higher aggregation numbers than are consistent with spherical shape.

Of the two simplifications introduced in the original geometric considerations, the first is expressed in Eq. 4 of *Reference 1*, which correlates the molecular weight, m, of the normal alkyl chain of a single surfactant molecule with the number, n, of carbon atoms in that chain:

$$m = 14.03n + 1.01 \cong 14.03n \qquad \text{(Eq. 1)}$$

This is equivalent to neglecting the length of the carbon–hydrogen bond and the van der Waals radius of the farthest hydrogen atom of the terminal methyl group. The second approximation, designed to compensate for the previous one, is to consider n carbon–carbon bond lengths in the hydrocarbon chain instead of the actual number $n - 1$.

With the aid of Fig. 1, the length of the n-paraffin chain is now calculated rigorously and without approximations. The chain is fully extended and in the all-*trans* conformation. Segment a, representing the contribution of the farthest hydrogen atom of the terminal methyl group, consists of two parts. The first is the van der Waals radius of this hydrogen atom, 1.2 Å (3). The second part is the length of the corresponding hydrogen–carbon bond projected in the direction of the longitudinal axis of the extended chain, namely, 1.09 Å times the sine of one-half of the hydrogen–carbon–hydrogen bond angle of 111.5° (3–5), or 1.09 Å sin (111.5°/2) = 1.09 Å × 0.8266 = 0.90 Å. Adding the two parts gives a = 2.10 Å.

Segment b in Fig. 1 represents the contribution of a single carbon–carbon bond to the length of the extended chain. It equals the length of the carbon–carbon bond, namely, 1.541 Å (4, 5), multiplied by the sine of one-half of the tetrahedral angle of 109.5° (3–5), or 1.541 Å sin (109.5°/2) = 1.541 Å × 0.8166 = 1.258 Å. Alternatively, it can be calculated as 1.541 Å cos 35.25° = 1.258 Å. There are $n - 1$ such carbon–carbon bonds in a hydrocarbon chain of n carbon atoms, contributing $(n - 1)$ 1.258 Å to the length of the extended chain.

Table I—Maximum Values for the Aggregation Number of Micelles of n-Alkyl Surfactants Consistent with Spherical Shape

n	Extended Chain Length[a], Å	$d_{25}°/_{25}°{}^b$	m^c, Å	$z_{max}{}^d$
10	14.05	0.791	141.31	39.2
12	16.57	0.802	169.37	54.3
14	19.08	0.811	197.43	72.0
16	21.60	0.818	225.49	92.2
18	24.12	0.823	253.55	114.9

[a] From Eq. 2. [b] Specific gravity of the hydrocarbon moiety. [c] From Eq. 5. [d] From Eq. 4.

The contribution e of the bond between the α-carbon atom and the oxygen or nitrogen heteroatom is calculated as the covalent radius of the carbon atom, 0.77 Å (3), multiplied by the sine of one-half of the tetrahedral bond angle. The presence of a heteroatom does not significantly distort that angle (4, 5). Therefore, $e = 0.77$ Å sin $(109.5°/2) = 0.63$ Å. The heteroatom may be an ether or an ester oxygen belonging to a polyoxyethylated nonionic surfactant or an alkyl sulfate, respectively. Either oxygen atom has two pairs of unshared electrons with which it binds two water molecules by hydrogen bonds (6). If the heteroatom is a nitrogen cation, it is also hydrated. Therefore, the boundary between the hydrocarbon core and the shell of hydrated headgroups of the micelle lies between the α-carbon and the heteroatom. It could even be argued that the α-carbon atom bound to an ether or ester oxygen, being at the positive end of a permanent dipole of medium strength, attracts the oxygen atom of a water molecule through dipole–dipole interaction.

The extended chain length of the hydrocarbon moiety, L, is thus represented by the equation:

$$L = 2.10 + (n - 1)1.258 + 0.63 =$$
$$2.73 + (n - 1)1.258 \quad \text{(Eq. 2)}$$

This is the maximum value for the radius of the hydrocarbon core of a spherical micelle that does not have a hole in its center. The approximate Eq. 6 of the original calculations (1) is now replaced by the exact expressions:

$$0.7346 (zm/d)^{1/3} \leqslant L \quad \text{(Eq. 3)}$$

and:

$$z \leqslant \left(\frac{L}{0.7346}\right)^3 \frac{d}{m} \quad \text{(Eq. 4)}$$

where d is the specific gravity of the hydrocarbon core. Use of the true values for m given by:

$$m = 14.03n + 1.01 \quad \text{(Eq. 5)}$$

results in the exact values for z_{max}, the highest aggregation number consistent with spherical shape, listed in the last column of Table I. According to these values, of the 32 surfactants considered, 23, or 72%, have aggregation numbers in excess of z_{max} and are, therefore, unlikely to form spherical micelles. Only nine surfactants have aggregation numbers equal to or below z_{max} and may form spherical micelles.

The geometric considerations of Zografi and Yalkowsky (2) have two shortcomings. First, the contribution of
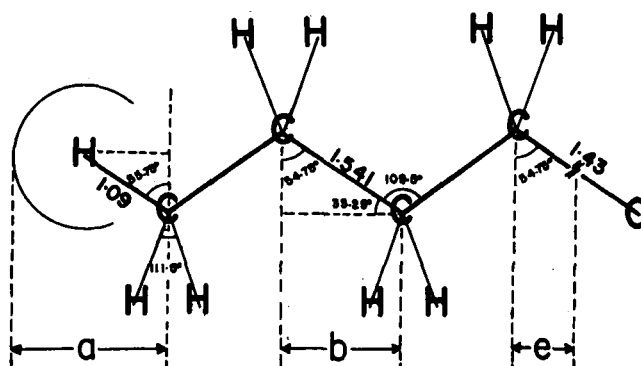

Figure 1—Normal alkyl chain in the fully extended all-trans conformation.

a single bond to L does not equal the length of that bond because the bond is not parallel to the chain axis but follows a zigzag course conforming with the tetrahedral angle. The contribution is the projected length of that bond onto the chain axis, or the bond length times the sine of one-half the tetrahedral bond angle. The second point, already discussed, is that the heteroatom, which is either an oxygen atom or a nitrogen cation, is associated with water and cannot be considered part of the hydrocarbon core of the micelle. As Zografi and Yalkowsky pointed out, Tartar (7) solved this point by taking one-half of the carbon–oxygen bond[2] distance as contribution to the hydrocarbon core. Therefore, one C—C bond length in their Eq. 4 should be replaced by one-half of a C—O bond length multiplied by the sine of one-half of the tetrahedral bond angle. Applying these considerations to Eq. 4 of Reference 2 changes it to:

$$R \leqslant 1.27 (n - 1) + 2 + (1.42/2) \sin (109.5°/2) \quad \text{(Eq. 6)}$$

which brings it into agreement with Eq. 2 in this article.

When assuming a spherical shape for micelles, the radii of their hydrocarbon cores cannot exceed the length of the extended alkyl chains as long as the cores have uniform density. Combining the values for L with those of the hydrocarbon density results in the revised values of z_{max}, the maximum aggregation number consistent with spherical micelles, listed in Table I. Comparison of z_{max} with the experimentally determined z values for 32 surfactants having a single n-alkyl chain shows that 23, or 72%, have higher z values and are unlikely to form spherical micelles.

The experimental data refer to surfactant solutions in water. The addition of electrolytes generally produces moderate increases in z of ionic surfactants in concentrations not exceeding 0.5 M for univalent counterions; higher electrolyte concentrations produce considerable increases (8), especially on approaching salting-out conditions. Therefore, the percentage of systems forming nonspherical micelles would have been even greater if aggregation numbers of ionic surfactants in dilute salt solutions had been included. Micelles in solu-

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[2] Zografi and Yalkowsky (2) referred to a C—S bond in the alkyl sulfate molecule but, since there is only a C—O—S bond, they evidently had the C—O bond in mind.

Table II—Areas at Saturation Adsorption of Single-Chain Surfactant Molecules at 20-25°

Surfactant	System	Method	Area/Molecule, Å²	Reference
Sodium lauryl sulfate	Air–water	Radiotracer	52.0	13
Sodium lauryl sulfate	Air–0.115 M NaCl	Radiotracer	38.4	14
Sodium lauryl sulfate	Air–water	Radiotracer	35	15
Sodium lauryl sulfate	Air–0.1 M Na⁺ᵃ	Radiotracer	33	15
Sodium lauryl sulfate	Air–water	Foaming	49.9	16
Sodium lauryl sulfate	Air–water	Surface tension	47	16
Sodium lauryl sulfate	Air–water	Foaming	34	17
Sodium lauryl sulfate	Air–water	Foaming	40	18
Sodium lauryl sulfate	Air–water	Surface tension	47	16
Sodium lauryl sulfate	Air–water	Surface tension	43.9	19
Sodium lauryl sulfate	Air–sodium chlorideᵇ	Surface tension	52	20
Sodium lauryl sulfate	Air–water	Surface tension	37.7	21
Sodium lauryl sulfate	n-Hexane–water	Interfacial tension	45.2	19
Sodium lauryl sulfate	n-Nonane–water	Interfacial tension	47.6	19
Sodium lauryl sulfate	n-Heptadecane–water	Interfacial tension	51.0	19
Sodium lauryl sulfate	n-Heptane–waterᶜ	Interfacial tension	49	22
Sodium lauryl sulfate	n-Heptane–sodium chlorideᵇ	Interfacial tension	53.4	20
Sodium lauryl sulfate	n-Heptane–water ± sodium chloride	Interfacial tension	50.0	23
Sodium lauryl sulfate	Petroleum ether–water ± sodium chloride	Interfacial tension	35.9	23
Sodium lauryl sulfate	Petroleum ether–0.05 M NaCl	Interfacial tension	43.0	24ᵈ
Sodium lauryl sulfate	Petroleum ether–0.10 M NaCl	Interfacial tension	45.0	24
Sodium lauryl sulfate	Petroleum ether–0.25 M NaCl	Interfacial tension	41.2	24
Sodium lauryl sulfate	Petroleum ether–0.50 M NaCl	Interfacial tension	41.0	24
Sodium decyl sulfate	n-Heptane–waterᶜ	Interfacial tension	50.0	22
Sodium tetradecyl sulfate	n-Heptane–waterᶜ	Interfacial tension	50.0	22
Sodium octadecyl sulfate	n-Heptane–water	Interfacial tension	45.6	23
Sodium undecanesulfonate	Air–sodium chlorideᵇ	Surface tension	53	20
Sodium undecanesulfonate	n-Heptane–sodium chlorideᵇ	Interfacial tension	54	20
Sodium dodecanesulfonate	Air–water	Foaming	50.7	16
Sodium dodecanesulfonate	Air–water	Suface tension	53	16
Sodium dodecanesulfonate	Air–water	Surface tension	48	25
Sodium pelargonate	Air–water	Surface tension	39.0	23
Sodium laurate	Air–water	Surface tension	39.0	23
Sodium laurate	Air–sodium chlorideᵇ	Surface tension	47	20
Potassium laurate	Air–potassium chlorideᵉ	Surface tension	43	20
Potassium laurate	Air–water	Surface tension	39.2	21
Potassium palmitate	Air–water	Surface tension	35.9	21
Potassium palmitate	Air–water	Radiotracer	37.7	21
Sodium laurate	n-Heptane–sodium chlorideᵇ	Interfacial tension	45	20
Potassium laurate	n-Heptane–potassium chlorideᵉ	Interfacial tension	44	20
Dodecylammonium chloride	Air–water	Interfacial tension	31.9	21
Dodecylammonium chloride	Air–water	Foaming	24	17

ᵃ Na₂HPO₄ + NaH₂PO₄ buffer + enough NaCl to make the total Na⁺ concentration 0.1 M. ᵇ q.s. for constant Na⁺ concentration. ᶜ Measured at 50°. ᵈ Reference 24 is the same as Reference 6 of Zografi and Yalkowsky (2), who mistakenly quote the journal as Proc. Roy. Soc. ᵉ q.s. for constant K⁺ concentration.

tions of ionic surfactants of concentrations not far above the CMC and at moderate salt concentrations, up to about 0.5 M but well below salting-out concentrations, are believed to maintain their spherical shape (9, 10). The effect of 0.2 M NaCl on the micellar size of sodium lauryl sulfate is smaller than the difference between the micellar sizes measured by various methods at a given sodium chloride concentration (8, 11).

By assuming spherical shape and using the values for L, hydrocarbon density, and z_{max} of Table I, the surface area per hydrocarbon chain on the spherical boundary enclosing the hydrocarbon core ranges from 63.3 Å² for decyl derivatives to 63.6 Å² for octadecyl derivatives. This is twice the limiting area per molecule of sodium lauryl sulfate and three times that of dodecyl-amine hydrochloride and of fatty acid soaps at the air–water interface, indicating that an ionic headgroup shields its hydrocarbon chain only incompletely from contact with water in spherical micelles. An alternative model for small micelles, with a smaller external area per hydrocarbon chain, would be energetically more favorable (1).

It is argued that limiting surface areas are only attainable under the influence of significant external forces capable of overcoming the electrostatic repulsion and hydration of polar headgroups and that a more appropriate area for the purpose of comparison would be the area per molecule at the point of maximum adsorption at the air–water or oil–water interface (2). The first point does not apply to the 18 nonionic surfactants used in the study nor to ionic surfactants in solutions containing 1:1 electrolytes at concentrations below 0.5 M, where the area per hydrocarbon chain on the periphery of the core is still 63–64 Å² if they formed spherical micelles. For the 14 ionic surfactants in water, this argument was answered by Bury and Browning (12), who showed that the CMC value of a nonionic surfactant was lower by a factor of 10 than that of an ionic surfactant having the same hydrocarbon moiety. The difference results precisely from the need of the ionic surfactant to overcome the electrostatic repulsion of the polar headgroups to form micelles. Moreover, being water soluble, the surfactant molecules adsorbed at the interfaces will be de-

sorbed and enter the bulk aqueous solution to form micelles when the compression at the interface becomes excessive.

Concerning the second point, even the cross-sectional areas per surfactant molecules at the interfaces observed at saturation adsorption exceed the 63–64 Å² area per alkyl chain on the core periphery of spherical micelles by significant amounts. This is shown in Table II, where the area for sodium lauryl sulfate averaged from the 23 reported values is 44 Å² per molecule, 30% below the peripheral area calculated for a spherical micelle. Saturation adsorption was usually reached considerably below the CMC (20).

The agreement between the areas measured directly, using radiotagged surfactants or foam analysis, and the areas calculated from surface and interfacial tension data by means of the Gibbs adsorption equation is excellent. For sodium lauryl sulfate at the air–water interface, the average value was 42.2 Å² per molecule according to direct measurements and 43.9 Å² from the Gibbs adsorption equation. This vindicates the unit activity coefficient customarily used in that equation, as well as the factor "2" employed for ionic surfactants (16, 23).

Zografi and Yalkowsky (2) quoted a range of 50–70 Å² per molecule at saturation adsorption, which is considerably higher than the range of 24–54 Å² in Table II. Their high values stem from the inclusion of two series of surfactants which have more than one alkyl chain. The data of Boucher et al. (26) refer to α-sulfo fatty esters having Structure I. Each molecule

$$R—CH \diagup^{SO_3Na}_{\diagdown COOR_1}$$

I
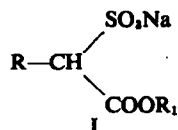
contains two hydrophilic groups and two alkyl chains, which obviously increase its cross-sectional area compared to surfactants containing a single alkyl chain and a single hydrophilic group. The interfacial orientation of the ester–sulfonate surfactants is also unusual (27). The data of Weiner and Zografi (28) refer to the chlorides of dodecylpyridinium, dodecyltrimethylammonium, and dodecylethyldimethylammonium which, at saturation adsorption, occupied an area of 69 Å² per molecule. The nitrogen cation of the first surfactant is part of a ring with five carbon atoms. In the other two, it is buried among four alkyl groups. The presence of these extra hydrocarbon moieties results in headgroups of large sizes in these and similar cationic surfactants, causing them to form micelles with more loosely packed hydrocarbon cores than surfactants containing single alkyl chains. This is shown by their superior solubilizing capacity when compared with micelles of anionic and cationic surfactants having a single alkyl chain (29, 30).

Since the micelles of tetraalkylammonium halides have hydrocarbon cores with comparatively low densities, the area of the long hydrocarbon chain on the envelope of the micellar core is higher than the 63–64 Å² value calculated for spherical micelles having the densities listed in Table I. These two classes of surfactants should not be included in a study (1, 2) on whether surfactants containing a single normal alkyl chain form spherical micelles. The interfacial area per molecule of a primary amine hydrochloride at saturation adsorption was less than one-half of the area per hydrocarbon chain on the periphery of the micellar hydrocarbon core if the micelle were spherical (17, 21). For mono-n-alkyl sulfates and alkali metal soaps, the interfacial areas per molecule were 30 and 35% below the micellar areas, respectively (Table II).

Another way of expressing the incomplete shielding of the hydrocarbon core from contact with water by the hydrophilic headgroups in spherical micelles is as follows (31). The cross-sectional area of the sulfate headgroup in an alkyl sulfate, measured on atomic models or estimated from atomic radii (3), is 25 Å², identical with the limiting area per molecule in an interface (24). This is the area actually occupied by the headgroup. The difference between 25 Å² and the interfacial area at saturation adsorption (44 Å²) or the peripheral area on a spherical micelle (63.3 Å²) per molecule of sodium lauryl sulfate is due chiefly to repulsion among the negatively charged headgroups. The void between the headgroups is filled with water. For an n-dodecyl surfactant forming spherical micelles, $z_{max} = 54$ Å and $L = R = 16.57$ Å. The area on the spherical envelope of the hydrocarbon core is $4\pi R^2 = 4\pi(16.57 \text{ Å})^2 = 3450$ Å². Of this peripheral area, 54×25 Å² = 1350 Å² or 39% is covered by sulfate headgroups, leaving 61% of the hydrocarbon surface exposed to water. Alkyl sulfates have comparatively bulky headgroups. Fatty acid soaps and primary amine hydrochlorides have considerably smaller headgroups, so that an even greater percentage of the periphery of their hydrocarbon core, approximately 75%, is in contact with water. A different model for micelles, exposing less of the hydrocarbon portion to water, would be energetically more favorable.

It is argued that the determination of surface potentials of micelles by acid–base titration and electrophoresis gives charge densities and, hence, molecular areas that are similar to areas at saturation adsorption (2). Potentiometric titrations are applicable only to surfactants like trialkylamine oxides (32), which are nonionic but become cationic in the presence of strong acids, or to amphoteric surfactants like N-dodecyl-β-aminopropionic acid, N-dodecyl-β-iminodipropionic acid (33), and long-chain fatty acylcarnitines (34). The headgroups of these surfactants are bulky because they contain two to three hydrophilic moieties and/or multiple alkyl groups. This produces micelles with hydrocarbon cores of lower density than those formed by surfactants with single n-alkyl chains and with headgroups consisting of single ions, as already discussed. Therefore, even if the molecular areas in micelles of the complex, amphoteric surfactants approach or exceed 64 Å², this does not corroborate the existence of spherical micelles of single-chain surfactants.

Electrophoresis determines the ζ-potential from measurements of the electrophoretic mobility, U, according to the equation:

$$\zeta = \frac{f(\kappa R)\pi\eta U}{D} \qquad \text{(Eq. 7)}$$

where κ is the Debye–Hückel parameter, and η is the viscosity and D the dielectric constant of the water in the electric double layer. Lacking the exact values of η and D and their distribution across the double layer, it is common practice to use the corresponding values for bulk water, although D is somewhat lower and η considerably higher, especially in double layers associated with the high surface potentials of ionic micelles (35). The ζ-potentials are usually not corrected for surface conductance despite the pronounced effect of the latter on the mobility of particles with charge densities as high as those of ionic micelles in aqueous media of low ionic strength (36). These are the chief experimental difficulties in determining ζ-potentials. The main theoretical difficulties are to calculate the charge density at the micellar surface from the value of the ζ-potential measured at the plane of shear within the double layer and to correct for counterion binding. The exact solution to these complex problems remains to be found (35). Molecular surface areas in ionic micelles derived from electrokinetic measurements are subject to uncertainties of the same order of magnitude as the areas themselves and, therefore, do not lend themselves to distinguishing between spherical micelles and other models.

It is argued that independent evidence, obtained by light-scattering or hydrodynamic methods, is consistent with spherical shape (2). Light scattering only provides information on the shape of those particles whose largest dimension exceeds one-twentieth of the wavelength of light, or about 250 Å. In that case, dissymmetry develops, and it is possible to distinguish between a sphere, rod, random coil, ellipsoid, or cylinder from the angular intensity distribution of the scattered light (37, 38). A cylindrical micelle of sodium lauryl sulfate having an aggregation number of 200 (which is larger than that observed in 0.5 M NaCl solutions) would have a length of only 65 Å at a density of 1.14. It is too small by a factor of 4 to give measurable dissymmetry. Therefore, light scattering is not suitable for determining the shape of the small micelles formed at concentrations that are low multiples of the CMC.

To deduce the shape of a particle from hydrodynamic data requires a knowledge of the extent of its hydration. For instance, by assuming that the particle is ellipsoidal, the frictional ratio, f/f_o, the ratio of translational diffusion coefficients, D/D_o, or the intrinsic viscosity can be used to determine its asymmetry or axial ratio, provided its degree of hydration is known. The subscript o refers to the equivalent unhydrated sphere. An added complication is that the relationship between hydration, asymmetry, and frictional ratio or ratio of diffusion coefficients is different for micelles shaped like a sphere, a prolate ellipsoid, an oblate ellipsoid, a rod, and a lamella (38). Thus, hydrodynamic methods do not provide sufficient information to discern between the combined effects of micellar shape, asymmetry, and hydration on the data.

In conclusion, exact geometric considerations combined with experimentally determined aggregation numbers for surfactants containing a single normal alkyl chain are inconsistent with spherical shape for 72% of the micelles for which data are available. Spher-

ical shape would also result in incomplete shielding of the hydrocarbon portion of the surfactants from contact with water by the hydrophilic headgroups.

(1) H. Schott, *J. Pharm. Sci.*, **60**, 1594(1971).
(2) G. Zografi and S. H. Yalkowsky, *ibid.*, **61**, 651(1972).
(3) L. Pauling, "The Nature of the Chemical Bond," 3rd ed., Cornell University Press, Ithaca, N. Y., 1960, chap. 7.
(4) "Tables of Interatomic Distances and Configuration in Molecules and Ions," Special Publication No. 11, The Chemical Society, London, England, 1958, pp. S12–S19.
(5) "Tables of Interatomic Distances and Configuration in Molecules and Ions," Supplement 1956–1959, Special Publication No. 18, The Chemical Society, London, England, 1965, pp. S14s–S23s.
(6) H. Schott, *J. Chem. Eng. Data*, **11**, 417(1966).
(7) H. V. Tartar, *J. Phys. Chem.*, **59**, 1195(1955).
(8) E. W. Anacker, R. M. Rush, and J. S. Johnson, *ibid.*, **68**, 81 (1964).
(9) G. S. Hartley, *Kolloid-Z.*, **88**, 22(1939).
(10) J. Stauff, "Kolloidchemie," Springer-Verlag, Berlin, Germany, 1960, chap. 8.
(11) K. Shinoda, T. Nakagawa, B.-I. Tamamushi, and T. Isemura, "Colloidal Surfactants," Academic, New York, N. Y., 1963, chap. 1.
(12) C. R. Bury and J. Browning, *Trans. Faraday Soc.*, **49**, 209 (1953).
(13) K. Tajima, M. Muramatsu, and T. Sasaki, *Bull. Chem. Soc. Jap.*, **43**, 1991(1970).
(14) K. Tajima, *ibid.*, **43**, 3063(1970).
(15) G. Nilsson, *J. Phys. Chem.*, **61**, 1135(1957).
(16) J. E. Bujake and E. D. Goddard, *Trans. Faraday Soc.*, **61**, 190(1965).
(17) C. Walling, E. E. Ruff, and J. L. Thornton, *J. Phys. Chem.*, **56**, 989(1952).
(18) A. Wilson, M. B. Epstein, and J. Ross, *J. Colloid Sci.*, **12**, 345(1957).
(19) S. J. Rehfeld, *J. Phys. Chem.*, **71**, 738(1967).
(20) F. van V. Vaader, *Trans. Faraday Soc.*, **56**, 1067(1960).
(21) C. P. Roe and P. D. Brass, *J. Amer. Chem. Soc.*, **76**, 4703 (1954).
(22) W. Kling and H. Lange, *Proc. Int. Congr. Surface Activity*, 2nd, **1**, 295(1957).
(23) E. H. Lucassen-Reynders, *J. Phys. Chem.*, **70**, 1777(1966).
(24) D. A. Haydon and F. H. Taylor, *Phil. Trans. Roy. Soc. London, Ser. A*, **252**, 225(1960).
(25) L. Shedlovsky, J. Ross, and C. W. Jakob, *J. Colloid Sci.*, **4**, 25(1949).
(26) E. A. Boucher, T. M. Grinchuk, and A. C. Zettlemoyer, *J. Amer. Oil Chem. Soc.*, **45**, 49(1968).
(27) V. V. S. Rao, R. J. Fix, and A. C. Zettlemoyer, *ibid.*, **45**, 449(1968).
(28) N. D. Weiner and G. Zografi, *J. Pharm. Sci.*, **54**, 436(1965).
(29) R. L. Venable and R. V. Nauman, *J. Phys. Chem.*, **68**, 3498 (1964).
(30) H. Schott, *ibid.*, **71**, 3611(1967).
(31) A. F. H. Ward, *Proc. Roy. Soc., Ser. A*, **176**, 412(1940).
(32) F. Tokiwa and K. Ohki, *J. Phys. Chem.*, **70**, 3437(1966).
(33) *Ibid.*, **71**, 1824(1967).
(34) S. H. Yalkowsky and G. Zografi, *J. Colloid Interface Sci.*, **34**, 525(1970).
(35) J. T. Davies and E. K. Rideal, "Interfacial Phenomena," 2nd ed., Academic, New York, N. Y., 1963, chap. 3.
(36) C. W. Einolf and E. L. Carstensen, *Biochim. Biophys. Acta*, **148**, 506(1967).
(37) H. Benoit and P. Doty, *J. Phys. Chem.*, **57**, 958(1953).
(38) C. Tanford, "Physical Chemistry of Macromolecules," Wiley, New York, N. Y., 1963.

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