Polymerized Surfactant Aggregates: Characterization and Utilization

JANOS H. FENDLER*

Department of Chemistry and Institute of Colloid and Surface Science, Clarkson College of Technology, Potsdam, New York 13676

PIETRO TUNDO

Istituto di Chimica Organica della Universita di Torino, Torino, Italy

Received February 7, 1983 (Revised Manuscript Received July 5, 1983)

Organized surfactant aggregates—micelles, microemulsions, monolayers, bilayers, and vesicles—have been extensively exploited for developing chemistry based on membrane-mediated processes.[1-4] Advantage is taken of surfactant aggregates in membrane mimetic chemistry to compartmentalize reactive substrates. This, in turn, leads to altered reaction rates, reaction paths, and stereochemistries.[1] Systems are also available for mediating molecular transport,[1,5] recognition,[6-8] artificial photosynthesis[1,9-12] and target-directed drug deliveries.[1,13,14] Lastly, but not leastly, organized surfactant assemblies, as the term membrane mimetic implies, can be considered to model structures and interactions in real membranes.[15]

Although thousands of research pulbications have documented the utilization of micelles, microemulsions, monolayers, bilayers, and vesicles (Figure 1),[1-4] their full potential have hardly been exploited. Is there a need for introducing a new type of system—polymerized surfactant aggregates?[17] The affirmative answer to this question is shared by ever increasing groups around the world.[18] Enhanced stabilities, controllable sizes, rigidities, and permeabilities have prompted the development of polymerized surfactant aggregates. Ideally, polymerized surfactant assemblies should combine the beneficial properties of stable and uniform polymer particles with the fluidities of micelles, microemulsions, and vesicles. Considerable data exist on the polymerization of monolayers and organized multilayers.[19-22] In contrast, there are only few publications on the polymerization of microemulsions[23,24] and bilayers.[25] Polymerization of aqueous micelles is, at best, ambiguous.[26-29] Attention will be focused in the present Account on polymerized vesicles.[30]

Synthetic Strategies

The synthetic approach is necessarily targeted to surfactants that (i) are known to form vesicles with optimal morphologies, (ii) contain appropriately placed polymerizable double bonds that can be cross-linked to a desired degree, and (iii) are amenable to postvesicle functionalization. Additionally, the synthetic routes should be general enough to lead to surfactants with variable chain lengths and headgroups. Surfactants initially synthesized in our laboratories using these strategies are listed in Chart I.[39] Each surfactant is

Janos H. Fendler has been Professor of Chemistry at Clarkson College since January 1982. Previously he was Professor at Texas A&M University. His current interest is the development of chemistry based on membrane-mediated processes. In addition, he studies excited-state stereochemistry, enantiomeric recognition, and circularly polarized laser-initiated processes. The present Account is based on his Award address at the Kendall Award Symposium at the 185th National Meeting of the American Chemical Society.

Pietro Tundo is Associate Professor of Organic Chemistry at the University of Turin, Italy. Born in 1945, he obtained his doctoral degree at the University of Bologna in 1969. His research interest includes phase-transfer catalysis and innovative organic synthesis.

(1) Fendler, J. H. "Membrane Mimetic Chemistry"; Wiley-Interscience: New York, 1982.

(2) Fendler, J. H.; Fendler, E. J. "Catalysis in Micellar and Macromolecular Systems"; Academic Press: New York, 1975.

(3) Fendler, J. H. *Acc. Chem. Res.* **1976**, *9*, 153–161.

(4) Fendler, J. H. *Acc. Chem. Res.* **1980**, *13*, 7–13.

(5) Tien, T. H. "Bilayer Lipid Membranes (BLM) Theory and Practice"; Marcel Dekker: New York, 1974.

(6) Tabushi, I.; Kobuke, Y.; Imuta, J. *Nucleic Acid Res.* **1979**, *6*, 175–179.

(7) Hirata, F.; Axelrod, J. *Science* **1980**, *209*, 1082–1090.

(8) Shimomura, M.; Kunitake, T. *J. Am. Chem. Soc.* **1982**, *104*, 1757–1759.

(9) Calvin, M. *Acc. Chem. Res.* **1978**, *11*, 369–374.

(10) Fendler, J. H. *J. Phys. Chem.* **1980**, *84*, 1485–1491.

(11) Porter, G. *Proc. R. Soc. London, Ser. A* **1978**, *362*, 281–303.

(12) Gratzel, M. *Acc. Chem. Res.* **1981**, *14*, 376–384.

(13) Gregoriadis, G. "Drug Carriers in Biology and Medicine"; Academic Press: London, 1979.

(14) Kimeberg, H. K.; Mayhew, E. G. *CRC Crit. Rev. Toxicol.* **1978**, *6*, 25–79.

(15) Radhakrisnan, R.; Gupta, C. M.; Erni, B.; Robson, R. J.; Curatolo, W.; Majumdar, A.; Ross, A. H.; Takagaki, Y.; Khorana, H. G. *Ann. NY Acad. Sci.* **1980**, *346*, 165–198.

(16) Gierash, L. M.; Lacy, J. E.; Thompson, K. F.; Rockwell, A. L.; Watnick, P. I. *Biophys. J.* **1982**, *37*, 275–280.

(17) The term polymerized surfactant aggregates is preferred over polymeric surfactant aggregates since the former is thought to convey that polymerization is subsequent to aggregate formation.

(18) Fendler, J. H. In "Surfactants in Solution"; Mittal, K. L.; Lindman, B., Ed.; Plenum Press: New York, 1983; in press.

(19) Ackerman, R.; Inacker, O.; Ringsdorf, H. *Kolloid Z. Z. Polym.* **1971**, *249*, 1118–1126.

(20) Puterman, M.; Fort, T., Jr.; Lando, J. B. *J. Colloid Interface Sci.* **1974**, *47*, 705–718.

(21) Barraud, A.; Raudel-Teixier, A.; Rosilio, C. *Semin. Chim. Etal. Solide* **1975**, *9*, 21–16.

(22) Day, D.; Hub, H. H.; Ringsdorf, H. *Isr. J. Chem.* **1979**, *18*, 325–329.

(23) Atik, S. S.; Thomas, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 4279–4280.

(24) Lianas, P. *J. Phys. Chem.* **1982**, *86*, 1935–1937.

(25) Benz, R.; Prass, W.; Ringsdorf, H. *Angew. Chem. Int. Ed., Engl.* **1982**, *21*, 368–369.

(26) Kammer, V.; Elias, H. G. *Kolloid Z. Z. Polym.* **1972**, *250*, 344–351.

(27) Mielke, I.; Ringsdorf, H. *Makromol. Chem.* **1972**, *153*, 307–322.

(28) Ringsdorf, H.; Thuning, D. *Makromol. Chem.* **1977**, *178*, 2205–2210.

(29) Paleous, C. M.; Dias, P. *J. Polym. Sci., Polym. Chem. Ed.* **1978**, *16*, 1495–1503.

(30) Related researches by other groups are given in ref 22, 31–37.

(31) Regen, s. C.; Czech, B.; Singh, A. *J. Am. Chem. Soc.* **1980**, *102*, 6638–6640.

0001-4842/84/0117-0003$01.50/0

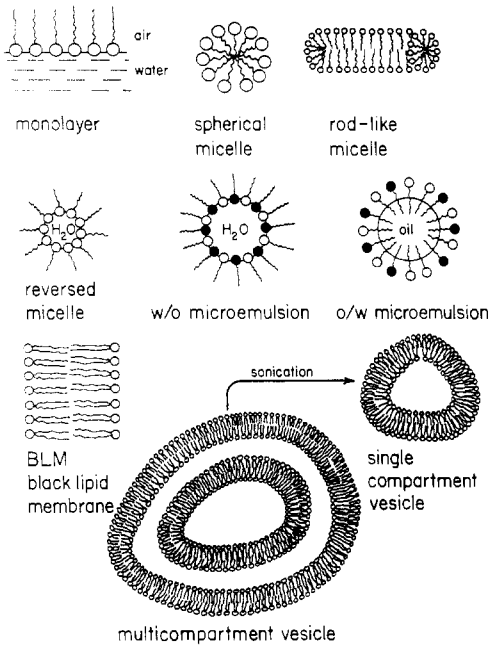


Figure 1. An oversimplified representation of organized structures formed from surfactants.

seen to contain two long alkyl chains (C_{13}–C_{18}), attached typically to a quarternary nitrogen, and a polar headgroup. These structural features are recognized to be favorable for forming stable bilayer vesicles.[44] The surfactants are seen to contain alkyl, alkene, hydroxy, phosphate, sulfate, carboxylate, and viologen moieties. Viologen-containing surfactants allow the investigation of redox active aggregates.[41] The types of polymerizable groups on the surfactants vary from alkenes to styrene. Styrene, of course, readily polymerizes, and its polymerization can very conveniently be followed by absorption spectroscopy. Polymerizable groups are located either at the end of the hydrocarbon tail of the surfactants (**1–5**) or at (**7**, **9**, **10**, **12**, **14**, **15**, and **16**) or near to (**13** and **17**) their headgroups. In surfacant **6** there are double bonds both at the end of alkyl chains and at the headgroup. Consideration has been given to introducing labile ester linkages in **13** and **17**. Taking advantage of the general methodologies developed[41-43] many additional functionalized vesicle-forming surfactants can be readily synthesized.

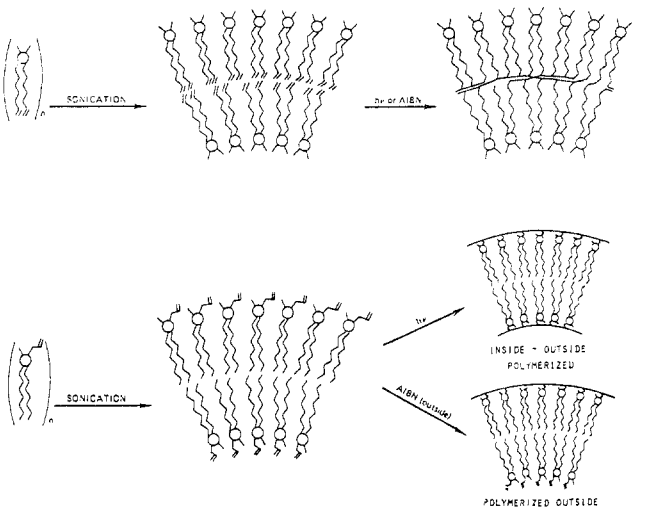


Figure 2. Schematics of polymerization of surfactant vesicles.

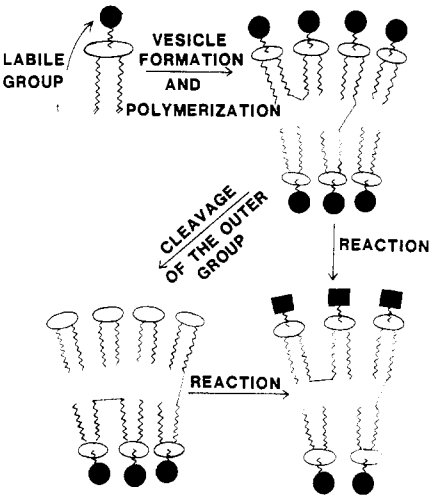


Figure 3. Schematics of dissymmetrical polymerized vesicle formation.

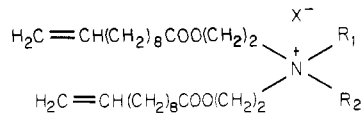
Vesicle Formation and Polymerization

Stable vesicles have been formed either by slow injection of a surfactant solution in alcohol or ether into thermostated water or by the ultrasonic dispersal of the surfactant in water, kept above the gel to liquid transition (the phase transition) temperature of the vesicle.[1] This latter method has been routinely used in our laboratories since it reproducibly leads to vesicles in the desired concentration range ($(1–5) \times 10^{-3}$ M stoichiometric surfactant). Increasing the sonication time results in an exponential decrease of the turbidity of the solution and of the radius and polydispersity of the vesicles. Hydrodynamic radii of well-sonicated charged surfactant vesicles are in the 200–800-Å range.[43] Typically, size distribution of a given surfactant vesicle deviates ±10% from the mean. Smaller and more monodispersed surfactant vesicles can be obtained by gel filtration and/or ultracentrifugation.

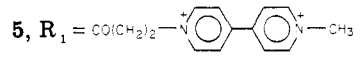
Irradiation by ultraviolet light or exposure to an initiator (azoisobutyronitrile, AIBN, or potassium persulfate) of surfactant vesicles results in the loss of the polymerizable double bonds. This can be monitored by magnetic resonance or absorption spectroscopy. Depending on the position of the double bonds, vesicles can be linked either across their bilayers or across their

(32) Hub, H.; Hupfer, B.; Koch, H.; Ringsdorf, H. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 938–940.
(33) Johnson, D. S.; Sanghera, J.; Pons, M.; Chapman, D. *Biochim. Biophys. Acta* **1980**, *602*, 57–69. Pons, M.; Johnson, D. S.; Chapman, D. *Ibid.* **1982**, 461–465.
(34) Regen, S. L.; Singh, A.; Oehme, G.; Singh, M. *Biochem. Biophys. Res. Commun.* **1981**, *101*, 131–136; *J. Am. Chem. Soc.* **1982**, *104*, 791–795.
(35) Akimoto, A.; Dorn, K.; Gros, L.; Ringsdorf, H.; Schupp, H. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 90–91.
(36) O'Brien, D. F.; Whitesides, T. H.; Klingbiel, R. T. *J. Polym. Sci., Polym. Lett. Ed.* **1981**, *19*, 95–101.
(37) Lopez, E.; O'Brien, D. F.; Whitesides, T. H. *J. Am. Chem. Soc.* **1982**, *104*, 305–307; *Biochem. Biophys. Acta* **1982**, *693*, 437–443.
(38) Paleos, C. M.; Christias, C.; Evangelatos, G. P.; Dais, P. *J. Polym. Sci., Polym. Chem. Ed.* **1982**, *20*, 2565–2573.
(39) Experimental details have been provided in primary publications (ref 40–43).
(40) Tundo, P.; Kippenberger, D. J.; Klahn, P. L.; Prieto, N. E.; Jao, T. C.; Fendler, J. H. *J. Am. Chem. Soc.* **1982**, *104*, 456–461.
(41) Tundo, P.; Kippenberger, D. J.; Politi, M. J.; Klahn, P.; Fendler, J. H. *J. Am. Chem. Soc.* **1982**, *104*, 5352–5358.
(42) Tundo, P.; Kurihara, K.; Kippenberger, D. J.; Politi, M.; Fendler, J. H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 81–82.
(43) Kippenberger, D.; Rosenquist, K.; Odberg, L.; Tundo, P.; Fendler, J. H. *J. Am. Chem. Soc.* **1983**, *105*, 1129–1135.
(44) Kunitake, T.; Okahata, Y.; Shimomura, M.; Yasunami, S.; Takarabe, K. *J. Am. Chem. Soc.* **1981**, *103*, 5401–5413.

Chart I.
Vesicle-Forming Polymerizable Surfactants

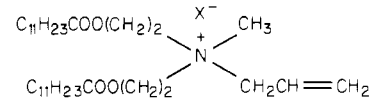


1, $R_1 = R_2 = CH_3$
2, $R_1 = CH_3$; $R_2 = (CH_2)_2OH$
3, $R_1 = OP(OH)_2$, no charge on N
4, $R_1 = H$; $R_2 = (CH_2)_2SO_3^-$

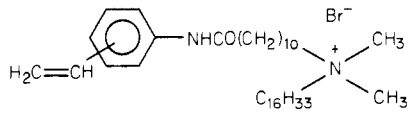


5, R_1 =

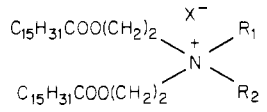
Br^-, I^-, no charge on N
6, $R_1 = CH_3$; $R_2 = CH_2CH{=}CH_2$

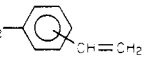
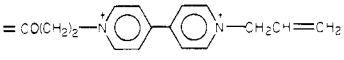


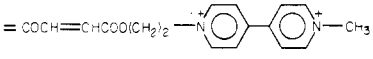
7



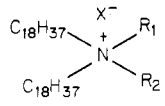
8

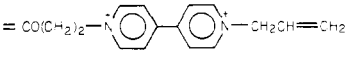


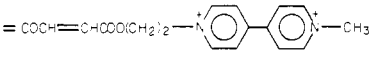
9, $R_1 = CH_3$; $R_2 = CH_2CH{=}CH_2$
10, $R_1 = CH_3$; R_2 = 
11, R_1 = COCH=CHCOOH, no charge on N
12, R_1 = 

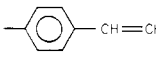
$2Br^-$, no charge on N
13, R_1 = 

Br^-, I^-, no charge on N



14, $R_1 = CH_3$, $R_2 = CH_2CH{=}CH_2$
15, R_1 = COCH=CHCOOH no charge on N
16, R_1 = 

Br^-, no charge on N
17, R_1 = 

Br^-, I^-, no charge on N
18, $R_1 = CH_3$; $R_2 = CH_2CH_2SH$
19, $R_1 = R_2 = CH_2CH_2SH$
20, $R_1 = CH_3$; R_2 = 

headgroups. The artist's rendering of linkings in Figure 2 admits our ignorance as to the topology of this process. At present, we do not know whether surfactants are separately linked in each half of the bilayers or cross-linked across them. Vesicles having double bonds in their headgroups (**6**, **7**, **10**) can be "zipped up" either at their inner or their outer surfaces or alternatively be polymerized both at their outer and inner surfaces (Figure 2). Irradiation by light results in the complete loss of vinyl protons (monitored by FT ^1H NMR). Conversely, polymerization by external addition of an initiator to already sonicated vesicles causes only 60% loss of the vinyl protons. This corresponds to cross-linking only the external surface of the vesicles.[40]

Chemical dissymmetry can be generated by limiting reactions to the outer surfaces of polymerized surfactant vesicles (Figure 3). Polymerization is necessary for the stabilization of dissymmetrical vesicles. Chemical dissymmetry has been created in polymerized vesicles prepared from **13** and **17**.[42] Cleavage of the labile ester groups on the outer surfaces lead to vesicles with viologen moieties in their inner and carboxylate groups in their outer surfaces.[42] Stable chemically dissymmetrical vesicles open the door to numerous applications.

Vesicles prepared from mixtures of judiciously selected polymerizable surfactants offer interesting opportunities for investigating stable copolymerized systems. Polymerization of controlled concentrations of surface active monomers can also be examined in the matrix of vesicles prepared by cosonicating polymerizable and nonpolymerizable surfactants. What is the lowest concentration of monomer that leads to cross-linking? How fast is the lateral mobility of the polymerizable surfactant? How many and what types of polymer domains are formed? How are these domains affected by external parameters? Can polymeric domains in surfactant vesicles be utilized in molecular recognition? Answers to these questions are highly relevant to our understanding of membrane phenomena and are also related to solid-state polymerizations.

The correct alignment of surfactants in some, but not all, vesicles is an essential requirement for polymerization. Vesicles prepared from surfactants containing polymerizable double bonds and viologen functionalities in their headgroups (**12** and **16**) could not be polymerized under any experimental conditions.[41] Apparently, intermolecular double bonds cannot be brought sufficiently close together in the vesicles for cross-linking. Even the addition of spacers (acrylonitrile, for example) did not induce polymerization.[41] In the absence of bulky, and presumably rigid, viologen groups, polymerization across the headgroups of surfactant vesicles is quite feasible (compounds **6**, **7**, and **9**).

Irradiation of vesicles prepared from **10** by a 450-W Xenon lamp or by 15-ns bursts of 266-nm laser pulses led to the decrease of styrene absorbance by a first-order process (Figure 4).[45] The calculated rate constants were independent of the vesicle concentrations (vesicles, unlike micelles, do not break down on dilution)[1-4] but increased linearly with increasing intensity of the laser pulses. These data were rationalized in terms of intravesicular surface photopolymerizations, at an apparent reduced reaction dimensionality,[46] and analyzed on a per vesicle rather than on a volume basis. As a first approximation, the vesicle surface has been assumed to be hexagonally packed, each monomer being surrounded by six neighbors. The photoinitiated free radical could react with any one of its neighbors to initiate polymerization, to disproportionate, or to form nonpolymeric photoproducts. Alternatively, the free

(45) Reed, W.; Guterman, L.; Tundo, P.; Fendler, J. H. *J. Am. Chem. Soc.*, in press.
(46) Richter, P. H.; Eigen, M., *Biophys. Chem.* 1974, 2, 225–234.

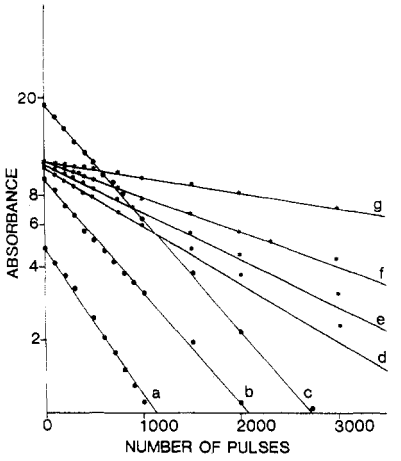


Figure 4. Pulsed laser induced polymerization of surfactant vesicles prepared from **10** (R_H = 700 Å). Plotted are the absorbances at 250 nm taken subsequent to exposure to repetetive laser pulses vs. the number of total laser pulses. At constant laser power (1 mJ/pulse) changes in the concentration of **10** ($a = 7.0 \times 10^{-6}$ M, $b = 1.5 \times 10^{-5}$ M, $c = 1.4 \times 10^{-4}$ M) are seen not to affect the polymerization rate. Conversely, at constant concentration of **10** (1.4×10^{-4} M), increasing laser power caused faster polymerizations (d = 0.6 mJ/pulse, e = 0.50 mJ/pulse, f = 0.35 mJ/pulse, g = 0.15 mJ/pulse).

radical may return to the ground state or react with oxygen, impurity, or the wall of the vessel. Differential equations have been derived for these processes, linearized, solved, and scaled. The scaled equations described well the observed kinetics of vesicle photopolymerizations and allowed the assessment of the degree of polymerization. Monomer chain lengths have been approximated to be in the range of 3.5–23. Significantly, polymerization rates of **10** in alcohol were found to be very much slower than those in vesicles and showed a multiorder concentration dependence.[45]

Characterization of Polymerized Vesicles

Hydrodynamic parameters obtained for surfactant vesicles are best accommodated in terms of closed prolate ellipsoidal structures.[4] Polymerized vesicles retain the sizes of their nonpolymerized counterparts. For example, polymerization of vesicles prepared from **10** by 20-s sonication only alters the hydrodynamic radius, R_H, from 2500 to 2750 Å.[45] Similarly, polymerization of vesicles with R_H = 277 Å, prepared by a minute sonication of **9**, leads to vesicles with R_H = 286 Å.[43] Electron microscopy and glucose entrapments provide evidence for maintaining the vesicle structure intact during polymerization. Due attention should be given, however, to interpreting electron micrograms.[47]

Polymeric vesicles in the absence of additives do not undergo morphological changes for several months. This property can advantageously be utilized for stabilizing very small single compartment liposomes (SUV). While dipalmitoylphasphatidylcholine, DPPC, liposomes of $R_H \simeq 150$ Å remain stable above their phase-transition temperature, they undergo slow spontaneous aggregation and fusion to vesicles of $R_H \geq 700$ Å at lower temperatures.[48,49] The estimated half-lifetime of the growth of SUV liposomes at 23 °C is ca. 67 h.[48] Similar growth has been observed in vesicles pre-

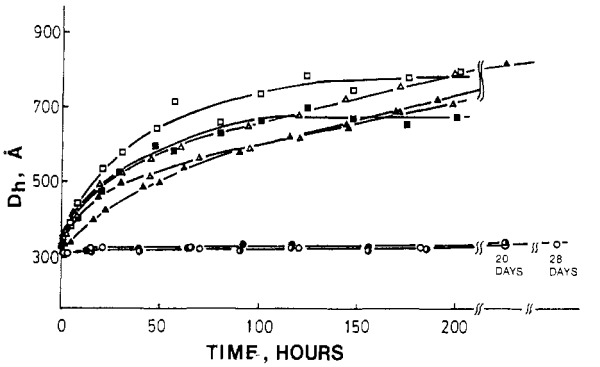


Figure 5. Spontaneous growth of DPPC (10.2×10^{-4} mol dm^{-3} (□), 5.0×10^{-4} mol dm^{-3} (■)) and nonpolymerized DPPC/8 ([DPPC] = 7.4×10^{-4} mol dm^{-3} + [8] = 4.4×10^{-4} mol dm^{-3} (△), [DPPC] = 4.7×10^{-4} mol dm^{-3} + [8] = 2.8×10^{-4} mol dm^{-3} (▲), [DPPC] = 3.4×10^{-4} mol dm^{-3} + [8] = 2.3×10^{-4} mol dm^{-3} (▲)) vesicles as a function of incubation time. Polymerized DPPC/8 vesicles ([DPPC] = 5.3×10^{-4} mol dm^{-3} + [8] = 3.5×10^{-4} mol dm^{-3} (◑), [DPPC] = 3.6×10^{-4} mol dm^{-3} + [8] = 2.5×10^{-4} mol dm^{-3} (●), [DPPC] = 2.6×10^{-4} mol dm^{-3} + [8] = 1.6×10^{-4} mol dm^{-3} (○)) are seen to retain their sizes for extended periods. Plotted are the hydrodynamic diameters (D_h) of the vesicles, determined by dynamic light scattering, against incubation time at 23 °C.

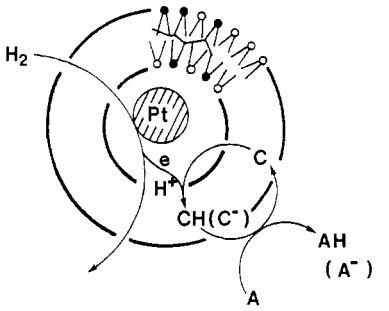


Figure 6. Use of polymerized vesicle entrapped colloidal platinum in catalysis. Electron and/or hydrogen carriers distributed in vesicle bilayers mediate the colloidal platinum catalyzed reduction of extravesicular molecules by hydrogen bubbling. C and CH (or C$^-$) are the oxidized and reduced forms of the electron and/or hydrogen carrier; A and AH (or A$^-$) are the oxidized and reduced electron and/or hydrogen acceptor; Pt is the polymerized vesicle entrapped colloidal platinum catalyst.

pared from mixtures of 8 and DPPC (DPPC/*8* = 2:1, w/w). Polymerization has completely stabilized these mixed vesicles; their hydrodynamic radius remained ≃150 Å for weeks at any temperature (Figure 5).[50] Unlike their nonpolymerized counterparts, polymerized vesicles do not break down in the presence of up to 25% alcohol or detergents.[31,32,40]

Substrate entrapment, retainment, and ion permeabilities are important properties of polymerized vesicles. Polymerized vesicles, prepared from phospholipids, have been shown to be completely sealed and to have retained entrapped carbon-14 labeled glucose better than their nonpolymerized counterparts.[34] Proton and hydroxide ion permeabilities across the bilayers of polymerized vesicles have been determined by incorporating pH-sensitive dyes (bromophenol red and bromocresol green, for example) into the interior of vesicles.[51] Dyes external to the vesicles had been removed by gel filtration and passages through ion-exchange

(47) Talmon, Y. *J. Colloid Interface Sci.* **1983**, *93*, 366–382.
(48) Chang, E. L.; Gaber, B. P.; Sheridan, M. *Biophys. J.* **1982**, *39*, 197–201.
(49) Wong, M.; Thompson, T. E. *Biochemistry* **1982**, *21*, 4233–4139.
(50) Kurihara, K.; Fendler, J. H. *J. Chem. Soc., Chem. Commun.*, in press.
(51) Guterman, L.; Politi, M.; Kurihara, K.; Ishiwatari, T.; Fendler, J. H., unpublished results, 1983.

resins. Absorption changes of the vesicle-entrapped dyes subsequent to injecting small volumes of NaOH provided information on hydroxide ion transfer rates across the vesicle bilayers. Both the initial absorbance and its rate of change could be reproduced by adding equal moles of HCl. These titrations could be repeated several times with identical results. Half-lifetimes for proton transfer across vesicles are in the 6–12-min range. Polymerization markedly increased these half-lifetimes. Addition of an ionophore decreased the half-lifetimes for proton transfer of 20–60 s.[51]

Polymerized vesicles prepared from surfactants containing styrene, phosphate, and vinyl moieties underwent temperature-dependent phase transitions.[43] These transitions correspond, presumably, to changes from "gel" to "liquid crystalline" phases. Below the phase-transition temperature, surfactants in the bilayers are in their highly ordered "gel" states, with their alkyl chains in all trans conformations. Above the phase-transition temperature, the surfactants become "fluid" as the consequence of gauche rotations and kink formation. Fluidities of polymerized vesicles also manifest in their KCl-mediated growth. Addition of 3×10^{-2} M KCl to unpolymerized and polymerized vesicles, prepared from **9**, resulted in the increase of their hydrodynamic radii from 213 to 511 Å (nonpolymerized) and from 206 to 485 Å (polymerized).[43]

An important implication of the observed fluidities, permeabilities, and osmotic activities of polymerized vesicles is that polymerization does not lead to complete three-dimensional cross-linking. At present, only indirect information is available on the degree of polymerization. Thin-layer and gel-permeation chromatography[51] as well as kinetic analysis (vide supra)[45] indicated relatively short chain lengths in photopolymerized vesicles prepared from **8** to **10**. Vesicles prepared from other surfactants and/or polymerized by other means are unlikely to have similar degrees of polymerizations. Precise determination of the degree of polymerization is hampered by the very nature of the species involved. Destruction of polymerized vesicles (freeze-drying, followed by dissolution in organic solvents) leads to polyelectrolytes that undergo solvent-, temperature-, and electrolyte-induced association and coiling.

Photochemical Solar Energy Conversion in Polymerized Vesicles

Economically viable catalytic photosensitized water splitting is the ultimate aim of artificial photosynthesis.[9-12] One approach has involved the utilization of simple sensitizers (S) and relays (R) in surfactant vesicles.[4] The role of the vesicles is to bring about favorable energy deposition and transmission and, importantly, prevent back electron transfer between the reduced relay, R^-, and the oxidized sensitizer, S^+.

Ideally (i) the reduced relay (R^-) and the oxidized sensitizer (S^+) should be thermodynamically capable of generating hydrogen and oxygen from water (eq 1 and 2) and (ii) the process should be cyclic. In practice, the

$$2R^- + 2H_2O \rightarrow 2R + 2OH^- + H_2 \quad (1)$$

($2e^-$ reduction)

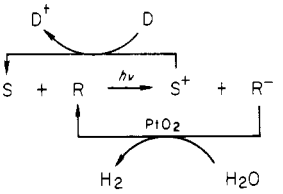
$$4S^+ + 2H_2O \rightarrow 4S + 4H^+ + O_2 \quad (2)$$

($4e^-$ oxidation)

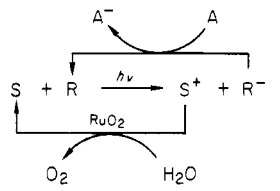
multielectron steps demand the use of catalysts and eq

(3)

3 is simplified to two half-cells (eq 4 and 5) that require



(4)



(5)

the use of sacrificial electron donors (D in eq 4) for H_2 production and sacrifical electron acceptors (A in eq 5) for O_2 production. Investigations of sacrificial H_2 generation provided valuable insight into the mechanism of this process. Efficient electron transfer had been demonstrated from a sacrificial donor, ethylenediaminetetraacetate, EDTA, to methyl viologen, MV^{2+}, via a sensitizer, tris(2,2-bipyridine)ruthenium chloride, $Ru(bpy)_3^{2+}$. $Ru(bpy)_3^{2+}$ was attached to the outer surfaces and MV^{2+} was placed on the inner surface of negatively charged dihexadecyl (DHP) vesicles, while EDTA was distributed in the bulk aqueous solution.[52] Initially, electron transfer was considered to occur across the vesicle bilayers.[52] Subsequently, electron transfer was shown to occur on the same outer surface of DHP vesicles, following photosensitized leakage of MV^{2+}.[53] These results as well as the relatively poor long-term stability of vesicles demanded alternative approaches. Functionally polymerized chemically dissymmetrical vesicles provide a means to efficient artificial photosynthesis without deleterious instabilities. $Ru(bpy)_3^{2+}$ photosensitized viologen reduction has been observed, for example, in dissymmetrical vesicles prepared from **13** and **17**.[42] Unfortunately, polymerization has destroyed substantial amounts of the redox activity. Entrapments of doped colloidal semiconductors in polymerized vesicles provided a promising alternative.[51]

Polymerized Vesicles as Drug Carriers

The intact and selective delivery to desired targets is an important aim of current pharmacological research. Although liposomes have been extensively explored as potential drug carriers,[13,14,54-57] their inherent instabilities and lack of discrimination have detracted somewhat from their potential. Polymeric vesicles may well overcome these difficulties. The enhanced activity of polymeric vesicle-incorporated ATP-synthetase is

(52) Tunuli, M. S.; Fendler, J. H. *J. Am. Chem. Soc.* **1981**, *103*, 2507–2513.
(53) Lee, L. Y. C.; Hurst, J. K.; Kurihara, K.; Politi, M. *J. Am. Chem. Soc.* **1983**, *10k*, 370–373.
(54) Gregoriadis, G.; Allison, C. "Liposomes in Biological Systems"; Wiley: New York, 1980.
(55) Fendler, J. H.; Romero, A. *Life Sci.* **1977**, *20*, 1109–1120.
(56) Tyrell, D. A.; Heath, T. D.; Colley, C. M.; Ryman, B. E. *Biochem. Biophys. Acta* **1976**, *457*, 259–302.
(57) Juliano, R. L. "Drug Delivery-Systems"; Oxford University Press: New York, 1980.

highly relevant.[58] ATP-synthetase consists of a hydrophobic and a hydrophilic portion; the former is incorporated into the bilayer and the latter is exposed into the aqueous environment. The isolated enzyme showed no activity, whereas phospholipids and polymeric surfactant vesicles reactivated the enzyme. Differential scanning calorimetry indicated the formation of "monomeric domains" that provided the site for AtP-synthetase incorporation.[58]

A considerably broader approach has been taken by Ringsdorf who had suggested potential applications of polymeric vesicles in cancer chemotherapy.[59] He envisaged cell-specific recognition and tumor-cell destruction by membrane-destroying agents (lysophospholipids, for example) incorporated into polymeric vesicles. Availability of polymeric vesicles capable of surviving the attack of membrane-destroying agents is an essential part of the proposal. Mechanism for the release of the agent would be provided by a trigger-mediated opening ("uncorking") of the polymeric vesicle. Alteration of pH, temperature, irradiation, and enzymes could trigger the release. Experimental realization of these bold propositions is only a question of time and our ingenuity.

Reactivity Control in Polymerized Vesicles

There are four extreme sites of reactant localization in polymeric vesicles. Hydrophobic molecules can be distributed among the hydrocarbon bilayers of the vesicles. Alternatively, they can be anchored by a long chain terminating in a polar headgroup. Polar molecules, particularly those that are electrostatically repelled from the inner surface of the vesicles, may move about relatively freely in the vesicle-entrapped water pools or they may be associated with or bound to the inner and outer surfaces of vesicles. Polar molecules can also be anchored to the vesicle surface by a long hydrocarbon tail. A large variety of reactivity control can be realized in polymeric vesicles. Conceivably, the position of a reacting substrate will be different from that of the transition state and that from the product formed in the reaction. Such spacial relocation of molecules as they progress along their reaction coordinates can be exploited in catalyses and product separation. A type of functionally polymerized vesicle–reactant interaction can be visualized in which the reactant, an organic ester, for example, would enter the vesicle. Hydrolysis would then occur in the matrix of polymeric vesicles and the products would subsequently be expelled into the bulk solution. With use of nonpermeable reagents, reactions can be limited to sites located at outer vesicle surfaces. Alternatively, finely tuned processes can be realized by allowing reactions to occur consecutively (at controllable rates) in the separate halves of the bilayer in the vesicles. This type of flexibility is only feasible in polymerized vesicles.

Polymerization alters the extent of substrate vesicle binding. Consequently, reactivities are expected to be different in polymerized and nonpolymerized vesicles. This assumption has been experimentally realized in the hydrolysis and aminolysis of nitrophenyl esters.[51] Polymerization allows an unprecedented degree of reactivity control by localizing the substrate in different parts of the vesicles. Kinetics of reactivities in polymerized vesicles can be treated by equations developed for interactions in membrane mimetic systems.[60]

Polymerized vesicles are ideal media for the formation of small, uniform, catalytically active colloidal and subcolloidal particles.[51] Photolysis of K_2PtCl_4 entrapped in the interiors of vesicles prepared from mixtures of DPPC and **3** or **8** resulted in the formation of colloidal platinum and concomitant polymerization of **3** or **8** in the vesicle matrices.[61] Polymerized vesicle entrapped colloidal platinum showed extraordinary stability. It catalyzed the hydrogen gas mediated reduction of extravesicular compounds via vesicle-embedded electron and/or hydrogen carriers (Figure 6).[61] Generalization of these principles can lead to industrially important catalytic reductions.[51]

Concluding Remarks

The beneficial properties of polymerized vesicles justify the considerable current interest in their development and applications. In addition to the highlighted utilizations, studies of vesicle polymerization may well shed light on such diverse fields as biomembranes and emulsion polymerization. Liposomes, prepared from synthetic phospholipids containing covalently linked carbene or nitrene precursors at selected positions, have been photo-cross-linked in a series of elegant studies by Khorana and his co-workers.[62-64] This work had aimed at obtaining information on lipid–lipid and lipid–protein interactions in biological membranes.[15] Photolysis of liposomes prepared from ω-labeled surfactants, for example, resulted in exclusive cross-linking in the acyl chains of neighboring surfactants. Absence of cross-linking in the headgroup region is in accord with the known structures of liposomes, lack of migration of the terminal hydrophobic groups to the vesicle surface. Further refinements of this technique will provide an even greater insight into the microenvironment of bilayer vesicles.

Detailed investigations of rates and degrees of polymerization in vesicles prepared from appropriate polymerizable surfactants (and/or mixtures of surfactants)[45,51] will be related to complex emulsion polymerizations and to polymerization in droplets.[65,66] Polymerization of organized surfactant vesicles is fully expected to attract wide variety of researchers who will develop novel chemistries and applications.

Research in our laboratories could not have succeeded without the enthusiastic, dedicated, and skillful work of the co-workers whose names appear in the references listed. I am most grateful to them and to the agencies (National Science Foundation, Department of Energy and Army Research Office) who have provided financial support for different aspects of our researchers. We thank NATO for a travel grant.

(58) Wagner, N.; Dose, K.; Koch, H.; Ringsdorf, H. *FEBS Lett.* **1981**, *132*, 313–316.
(59) Gros, L.; Ringsdorf, H.; Schupp, H. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 305–325.
(60) Fendler, J. H. *Pure and Appl. Chem.* **1982**, *54*, 1809–1819.
(61) Kurihara, K.; Fendler, J. H. *J. Am. Chem. Soc.* **1983**, *105*, 6152.
(62) Gupta, C.; Radhakrishnan, R.; Gerber, G. E.; Olsen, W. L.; Quay, S.; Khorana, H. G. *Proc. Natl. Acad. Sci. U.S.A.* **1979**, *76*, 2595–2599.
(63) Curatolo, W.; Radhakrishnan, R.; Gupta, C. M.; Khorana, H. G. *Biochemistry* **1981**, *20*, 1374–1378.
(64) Radhakrishnan, R.; Costello, C. E.; Khorana, H. G. *J. Am. Chem. Soc.* **1982**, *104*, 3990–3997.
(65) Blackley, D. C. "Emulsion Polymerization"; Applied Science: London, 1975.
(66) Ugelstad, J.; Mork, P. C.; Kaggerud, K. H.; Ellingsen, T.; Berge, A. *Adv. Colloid Interface Sci.* **1976**, *24*, 1–64.