New and Notable

Chiral Discrimination in Two Dimensions

Jay T. Groves and
Harden M. McConnell
Department of Chemistry, Stanford University, Stanford, California 94305-5080
USA

A connection between chirality of crystal shape and molecular shape was first made by Pasteur nearly 150 years ago when he isolated enantiomers from a racemic mixture of sodium ammonium tartrate. Even though this general subject is now familiar to scientists, recent works, including an article in this issue of the *Biophysical Journal*, present a number of surprises in monolayer systems at the air-water interface.

In a recent paper, Nassoy et al. (1995) observed a spontaneous chiral segregation of a racemic mixture of R and S myristoylalanine in a Langmuir monolayer. Using epifluorescence microscopy, these authors observed a chiral discrimination, which occurs following compression of the film into its condensed phase. The resulting domains, which are initially plastic, roughly circular, and easily deformable under a shear flow, evolved over the course of an hour into a collage of "curved needles." These needle-like domains showed significant resemblance to the brittle, sharp-edged domains that are observed when monolayers of either enantiomer are compressed into the condensed phase (Akamatsu et al., 1992). This evolution was paralleled by a drop in the surface pressure at fixed area to the pressure expected for monolayers of the pure enantiomer. Further structural information on these monolayers was obtained from grazing incidence x-ray diffraction. Diffraction scans for the equilibrated racemic mixture indicated an oblique unit cell identical to that observed for the pure R and S two-dimensional crystals. Thus the authors argue convincingly that the combination of pressure-area data, microscopic imaging, and x-ray diffraction provide conclusive evidence that they have achieved the two-dimensional analog of the Pasteur experiment.

In this issue of the *Biophysical Journal*, Bringezu et al. present experimental evidence for chiral discrimination in a different monolayer system. Focusing on triple-chain phosphatidylcholine (PC) molecules these researchers observe a "rich polymorphism" for the shorter chain PC, whereas PC monolayers with chains just two carbon atoms longer were found to be monophasic. In this work, chiral discrimination was used to study the sensitive dependence of tail ordering on slight variations in the chemical structure at the hydrophobic/hydrophilic interface. The tail hydrocarbons of the triple chain PC have a larger area than the head groups and were thus expected to dominate the packing structure. The persistence of chiral effects from the head groups comes as a surprise especially in light of theoretical calculations.

Andelman and de Gennes have studied the problem of chiral discrimination in monolayers from a theoretical point of view (Andelman and Gennes, 1988; Andelman and Orland, 1993). Their overall result is that heterochiral interactions should be generally favored, in contrast to recent experimental observations; it is interesting to look at the origins of this discrepancy. These theoretical results were obtained by analyzing a quantity, Δ, which has been defined as the chiral discrimination factor. This parameter can be computed from the pair free energy and internal energy, and entropy for the two enantiomeric pairs R-R and R-S, as a function of intermolecular distance. In particular, Δ is calculated from the difference between the second virial coefficients in the two cases. One possible source of discrepancy between these theoretical predictions and the experimental observations is that using only the second virial coefficient is probably not sufficient to characterize the solidification of racemic mixtures as the authors have noted. The authors also suggest that, although their calculation of the two-body effect implies that it is small, it may be sufficient to "trigger strongly collective effects such as a phase transition."

In 1982 Arnett and Stewart conjectured that chiral discrimination may be enhanced in two-dimensional systems (Stewart and Arnett, 1982). We suggest that there may be a fundamental reason for this. Monolayers at the air-water interface are unique in that there are long-range electrostatic forces that can cause domains to change shape and sometimes break apart (McConnell and Moy, 1988; see also Andelman et al., 1987). The physical separation of a solid solution into its two enantiomers would be driven by these forces if the lowering of the electrostatic energy exceeded the increase of the line tension energy. Thus, although the forces responsible for chiral discrimination between molecular shapes are doubtless of short range, the physical separation of macroscopic crystals or domains of the enantiomers may be driven by these long range forces. Experimental evidence consistent with this idea can be found in the early work of McConnell and collaborators as discussed below.

Weis and McConnell (1984) used epifluorescence microscopy to observe lipid domains of a phospholipid, dipalmitoylphosphatidylcholine (DPPC), at the air-water interface. The R and S enantiomers of this lipid produced domains with obvious chiral shapes. The racemic mixtures showed no chirality and thus no chiral discrimination in the solid solution of the two enantiomers. In this system, however, the effective line tension between the solid and liquid phases can be reduced by the inclusion of a low concentration of cholesterol (Weis and McConnell, 1985), resulting in the appearance of domain structures consistent with an intradomain fission into two enantiomers. This segregation, illustrated schemati-

---

Received for publication 14 February 1996 and in final form 14 February 1996.

0006-3495/96/04/1573/02 $2.00

cally in Fig. 1, could be facilitated by the long range dipolar forces mentioned above. It may be noted that there is a subtle effect of line tension that can oppose intradomain fission. Consider a long rectangular-strip domain of racemic mixture in which there is long range orientational tilt order in the direction of the long axis. The line tension energy can be reduced if molecules of one chirality concentrate on the left-hand boundary and vice versa. This can, in principle, stabilize nonchiral domain shapes.

There are a number of other reasons that chiral segregation may fail to be observed in systems even though the segregated state may have lower free energy. The kinetics of the separation may be too slow, which might account for the failure of Bringezu et al. to observe segregation in the case of the longer chain lipids. Also, it has been suggested that tilt ordering in monolayers may be similar to incommensurate or frustrated phases in three-dimensional systems because of the different packing requirements of the head and tail groups (Charvolin, 1989; see also McConnell, 1991). This can lead to modulated phases with alternating tilt angles (Scheringer et al., 1992), thus affecting and even eliminating the chiral shapes of domains. Apparent reversal of tilt direction is seen in the monolayer domains of R-DPPC, as in Fig. 1 *A*, and at point T in Fig. 7 in Weis and McConnell (1985).

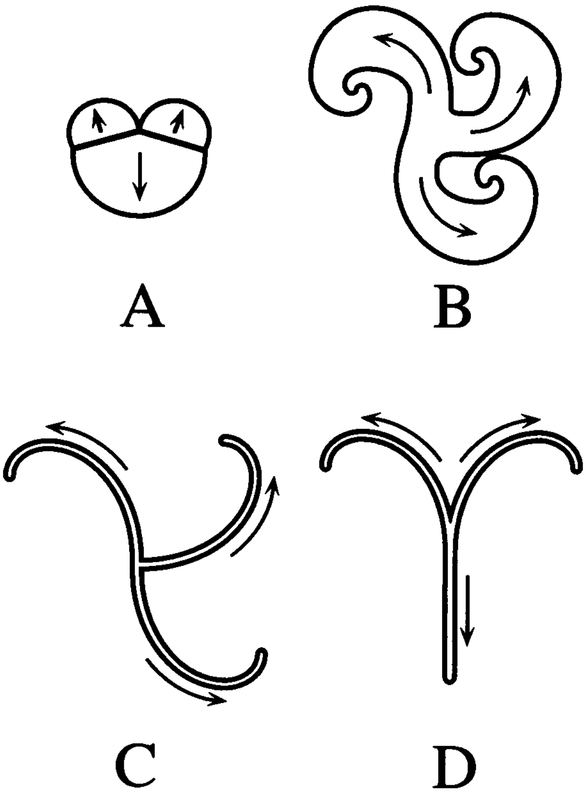

FIGURE 1 Sketches of solid (plastic) lipid monolayer domains of DPPC in equilibrium with the surrounding liquid lipid. The arrows represent directions of long-range orientational order as revealed by fluorescence anisotropy. Many of the observed solid domains appear to arise from a primitive triplet such as that sketched in *A* (McConnell, 1991; Moy et al., 1986). A large chiral domain of R-DPPC, as depicted in *B*, has three thick arms that twist in the same direction and appear to emanate from a center with the structure shown in *A* (Weis and McConnell, 1984). A low concentration (2 mol %) of cholesterol in the monolayer greatly reduces the line tension allowing the enantiomeric domains to form long, thin chiral arms as illustrated in *C* for R-DPPC (Gaub et al., 1986; Weis and McConnell, 1985). In the racemic DPPC mixture, the three subdomains join as illustrated in *D*, suggesting that one of the curving arms is enriched in R-DPPC while the other is enriched in S-DPPC. See Fig. 6 *C* in Weis and McConnell (1985).

The use of chiral molecules in studies of monolayers at the air-water interface is a powerful approach to the understanding of intermolecular forces in systems of biological interest. It is to be anticipated that further studies of the relation between chiral discrimination and molecular structure will continue to bear fruit.

REFERENCES

Akamatsu, S., O. Bouloussa, K. To, and F. Rondelez. 1992. Two-dimensional dendritic growth in Langmuir monolayers of D-myristoyl alanine. *Phys. Rev. A.* 46:4504.

Andelman, D., F. Brochard, and J.-F. Joanny. 1987. Phase transitions in Langmuir monolayers of polar molecules. *J. Chem. Phys.* 86:3673–3681.

Andelman, D., and P. G. de Gennes. 1988. Chiral discrimination in a Langmuir monolayer. *C. R. Acad. Sci.* 307:233.

Andelman, D., and H. Orland. 1993. Chiral discrimination in solutions and in Langmuir monolayers. *J. Am. Chem. Soc.* 115:12322–12329.

Charvolin, J. 1989. Lyotropic liquid crystals, structures and phase transitions. *In* Phase Transitions in Soft Condensed Matter. T. Riste and D. Sherrington, editors. Plenum Press, New York and London. 211:95–111.

Gaub, H. E., V. T. Moy, and H. M. McConnell. 1986. Reversible formation of plastic two-dimensional lipid crystals. *J. Phys. Chem.* 90:1721–1725.

McConnell, H. M. 1991. Structures and transitions in lipid monolayers at the air-water interface. *Annu. Rev. Phys. Chem.* 42:171–195.

McConnell, H. M., and V. T. Moy. 1988. Shapes of finite two-dimensional lipid domains. *J. Phys. Chem.* 92:4520–4525.

McConnell, J. D. C. 1991. Incomensurate structures. *Phil. Trans. R. Soc. Lond. A.* 334:425–437.

Moy, V. T., D. J. Keller, H. Gaub, and H. M. McConnell. 1986. Long-range molecular orientational order in monolayer domains of phospholipid. *J. Phys. Chem.* 90:3198–3202.

Nassoy, P., M. Goldmann, O. Bouloussa, and F. Rondelez. 1995. Spontaneous chiral segregation in bidimensional films. *Phys. Rev. Lett.* 75:457–460.

Scheringer, M., K. Hilfer, and K. Binder. 1992. Orientational ordering in lipid monolayers: a two-dimensional model of rigid rods grafted to a lattice. *J. Chem. Phys.* 96:2269–2277.

Stewart, M. V., and E. M. Arnett. 1982. Chiral monolayers at the air-water interface. *In* Topics in Stereochemistry. N Allinger, E. L. Eliel, and S. H. Wilen, editors. Wiley, New York. 13:195–262.

Weis, R. M., and H. M. McConnell. 1984. Two-dimensional chiral crystals of phospholipid. *Nature.* 310:47–49.

Weis, R. J., and H. M. McConnell. 1985. Cholesterol stabilizes the crystal-liquid interface in phospholipid monolayers. *J. Phys. Chem.* 89:4453–4459.