globulin synthesis should clarify the relationship of various classical types of lymphoid cells.

The synthesis of immunoglobulins by cultured lymphoblastoid cells derived from the buffy coats of patients with myeloid leukemias, lymphosarcomas, and Hodgkin's disease has been demonstrated in our laboratories (*2*). Over 50 cell lines originated from 26 patients are available for study. In contrast, no immunoglobulins have been detected in cell lines derived from malignancies of nonhemopoietic tissues.

We would appreciate the opportunity of obtaining blood samples from patients with multiple myeloma who have plasma cells in their peripheral blood.

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Protein Conformations in Biological Membranes

The conclusions of Maddy and Malcolm (*1*), based upon infrared spectroscopy of dried erythrocyte membranes and optical rotatory dispersion of solutions of membrane proteins, are unwarranted for the conformations in vivo of proteins in biological membranes. Their quotation from my book (*2*) and their added remarks do not convey the points that I propose an extended β-type conformation only for the primarily structural proteins of hydrated membranes in vivo (decidedly not for all the proteins, nor in dried membranes), and that this conformation is stabilized by interactions with both the lipid phase and the aqueous phase of the membrane (involving hydrophobic interactions as a major component). According to this treatment, one may expect a large decrease in the amount of extended conformation upon either dehydrating the membrane or greatly reducing its lipid content. In fact I discuss in detail (*2*) the total conversion of the extended conformation of the structural proteins to a globular conformation as a result of reduction or loss of the lipid phase under certain conditions, and the reversible partial conversion to the globular conformation during membrane transformations.

In the present state of our knowledge it is a step backward to conclude that findings regarding the conformations of proteins in dried membranes set guidelines for future studies and for theorizing concerning the conformations in vivo of membrane proteins. It would be interesting to know the basis for the authors' statement that air drying of a membrane should not be expected to reduce the amount of β-conformation present. For such an assertion to carry weight it should be based on detailed knowledge of either the structure of the membrane or the variation in β-conformation with drying in some pertinent lipid-protein model.

Maddy and Malcolm remark that many workers seem to have overlooked the possibility that cholesterol molecules may form hydrogen bonds with one another and dissolve in the hydrocarbon chains of the lipid phase; references are desirable to some of the treatments of membrane structure in which this possibility was not overlooked. The presence of proteins in extended conformations in biological membranes, far from being an "intractable element" relative to micellar transformations of the lipid phase, as Maddy and Malcolm assert, is an essential element of the only detailed theoretical treatment of such membrane transformations (*2*).

If the relevance of the highly indirect experimental approach of Maddy and Malcolm could be demonstrated first in some model system, say by elucidating the structure of the simple aqueous gelatin gel from structural studies of dried gelatin films, one might have a precedent for drawing conclusions regarding the structure of biological membranes in vivo from structural studies of dried membranes.

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It should be clear from our paper that we do not exclude extended conformations, only the β-conformation, as an important structural feature of cell-membrane proteins. The term β-conformation refers to structures with extended or nearly extended polypeptide chains, each with a twofold screw axis and peptide hydrogen bonds between the chains (for example see *1*). The presence of this structure in silk and β-keratin, or in other proteins as a result of thermal or other denaturation processes, leads to a cross-linked structure insoluble in water; there has been no previous suggestion that it needed additional stabilizing forces. We showed that the proteins of the erythrocyte ghost are not exceptional in this respect, in that the β-form can be observed in dry denatured films. As to Kavanau's proposed stabilization by hydrophobic interactions, it is difficult to see how these occur between protein and lipid. Haydon and Taylor have pointed out the steric problems (*2*); if the protein were in the β-form these would be particularly severe, since the nonpolar side chains would not be long enough to penetrate beyond the polar lipid head-groups. This is a fundamental probem that Kavanau does not answer in his detailed theoretical treatment.

During further work we have obtained infrared spectra of fresh erythrocyte ghosts suspended in D_2O and of a solution of ghost protein in D_2O; both spectra show an amide I band which is symmetrical about 1648 cm^{-1} and which is unaffected by drying. Thermal denaturation, followed by drying of the protein, leads to a broader asymmetrical band with peaks at 1648 and 1632 cm^{-1}. We attribute the latter peak to formation of denatured β-protein: this peak is not detected in the unheated preparations.

These observations support our conclusion that there is no experimental foundation for the supposition of an extensive array of protein in the β-conformation adjacent to the lipid; they meet Kavanau's criticisms more directly than would experiments on gelatin. Since gelatin, with its high proline content, does not form the β-conformation it is difficult to see how it could settle the point at issue.

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