early stages of this work and Mr. J. Kucera and Mrs. Nelda Smith for assistance in carrying out the transformation assays. We also appreciate the marked strains sent by Drs. L. Lerman and A. W. Ravin. This work was supported by Public Health Service Grant C-2170 from the National Cancer Institute, National Institutes of Health.

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$$W_x = xq^2(1 - q)^{x-1},$$

where q is the probability of a bond having been broken.

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*OBSERVATIONS IN MYELIN STRUCTURE: INCISURES AND NODAL REGIONS**

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Biophysical studies employing polarization optics, X-ray diffraction, and electron microscopy have provided valuable information concerning the layered structure of nerve myelin at the molecular level.[1–4] Electron microscope studies of the myelination process by Geren[5] led to the concept that the lipid-protein layered structure, which repeats very regularly in the radial direction, is produced by the wrapping about the axon of many folds of the surface membrane of the Schwann cells, which come to surround the outgrowing axon. Geren's findings have been confirmed by a number of investigators (see particularly Robertson[6]), so that the general concept has now been well established. However, the structure of the myelin at the Schmidt-Lanterman incisures and at the nodes of Ranvier remains to be determined, and it is with this problem that the author's investigation deals. A

full understanding of the structural relations at incisures and at the nodes would be of significance not only in evaluating the Geren hypothesis but also because of its bearing on physiological processes, such as impulse propagation. In the present paper we shall be concerned primarily with the structure of the incisures. The nodal structure has also been dealt with,[7, 8] but the results obtained at that time were not definitive. In more recent work Robertson[9–11] has furnished important new evidence on nodal structure.

Methods and Materials.—The peroneal and cubital branches of frog sciatic nerves were used in all experiments. Fixation was in Palade's fixative made isotonic with frog blood, pH 7.4, and containing potassium ions (6 mM) and calcium ions (4.2 mM). After imbedding in methacrylate, thin sections were cut with a modified Minot microtome. Glass knives were usually used, but in some cases a diamond knife, kindly provided by Dr. H. Fernandez-Moran, was employed. The observations were made with an RCA type EMU-2B electron microscope provided with a compensated pole piece and a 50-μ aperture.

Results.—Incisures are readily recognized in thin transverse sections of myelinated fibers because at these levels the myelin appears as two concentric ribbons separated by a relatively empty space (Fig. 1). Mitochondria and other cytoplasmic organelles, including granules of the type described by Gasser,[12] were not observed in this space. However, in fortunate sections it is seen that the lumen of the incisure is traversed by thin ribbons which may be seen to be continuous with the spiral wrapping of the myelin on either side of the incisure. Within the incisure the ribbons disappear from sight because of the thinness (*ca.* 200–400 A) of the section.

To test the idea that the layers do in fact traverse the incisures, longitudinal sections were studied. Only when traction was applied to the fiber, did the incisures appear as distinct clefts or channels. The surface membrane of the axon (axolemma) was continuous under the incisure; hence there is no continuity between axoplasm and incisural space.

In fibers which had been protected as much as possible from traction, the continuity of the myelin layers across the cleft was manifest. In Figure 2, which is fairly typical of such preparations, it may be seen that layers peel off tangentially and, sometimes after changing direction several times, are incorporated into the layered structure on the other side of the cleft.

Thus it is seen that the so-called incisures do not constitute channels[12–14] through which materials may be exchanged between the axon interior and its environment (see Stoeckenius and Zeiger[15]) or through which ions may flow (unless this could occur in the extremely thin space, unresolved in these electron micrographs, between pairs of apposed membranes). Rather, the incisural space is traversed by as many membranes as occur in the compact myelin. The resistance to diffusion or ion flow is therefore similar in both regions.

This structure is consistent with Geren's membrane theory of myelin formation. With rotation of Schwann cell with respect to axon, Schwann cell protoplasm is squeezed out from between the membrane pairs. If protoplasm is squeezed out in the axial direction, as the spiral is tightened and layer condensation occurs, protoplasmic constituents might be expected to accumulate in the regions of the incisures and at the nodes.

If incisures are not diffusion pathways, one may perhaps venture the suggestion

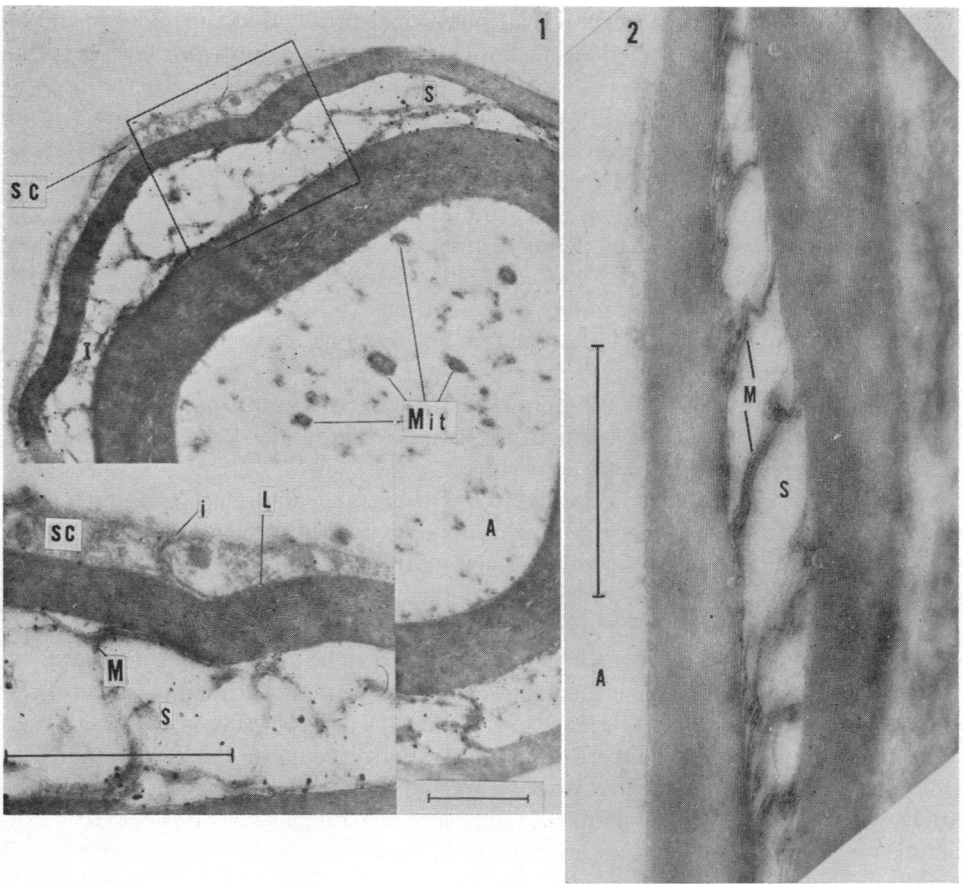

FIG. 1.—Transverse section of a myelinated nerve fiber at the level of an incisure. *SC*, Schwann cell; *S*, incisural space; *i*, infolding of Schwann cell surface membrane which fuses with compact myelin at *L*; *M*, myelin layer projecting into incisural space; *Mit*, mitochondria; *A*, axoplasm. Magnification, 22,000. Blocked-out region shown in insert at higher magnification (51,000).

FIG. 2.—Longitudinal section at the level of an incisure. The continuity of myelin layers on both sides of the incisure is clearly shown. Legend as before. Magnification 56,000.

that, somewhat along the lines suggested by Glees,[16] they may play a role in mechanical adaptation to distorting influences by a kind of telescopic distension of the cylindroconic internodal segments.

Another interesting feature of myelin structure, which is also clearly consistent with Geren's membrane hypothesis, is the peeling-off of the myelin layers near the node, with a change of direction varying from 45° to as much as 135°, to reach the axolemma upon which they are inserted. In Figure 3 this peeling-off of layers is clearly shown, although the axolemma is not evident. Between the detached layers which have already changed direction, empty spaces occur; these had already been observed by histologists and may well correspond to the "spiny bracelets" of Nageotte (see Gasser[12]).

In the nodal region one may observe the ending of double layers of the myelin. It will be recalled that in the Geren model the dark lines represent two primitive membranes which have fused. As the fusion of spiral wrappings proceeds, Schwann

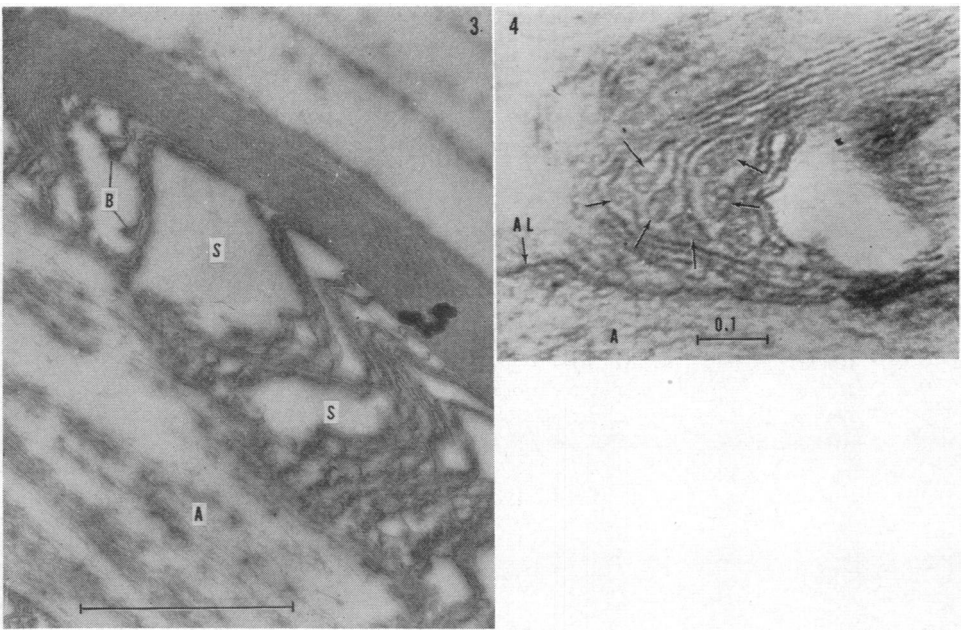

FIG. 3.—Longitudinal section showing termination of myelin layers near the node of Ranvier. *B*, loop profiles at end of myelin layers; other lengends as before. Magnification 56,000.

FIG. 4.—Pear-shaped profiles of endings of myelin layers near node of Ranvier depicted with arrows. *AL*, axolemma; other legends as before. Magnification 180,000.

cell protoplasm is squeezed tangentially and axially, accumulating in cylindrical sacks at the nodal end of each membrane doublet. Loops or pear-shaped endings, *ca.* 300 A in diameter and corresponding to the profiles of such sacks, were seen very frequently in our sections. Examples are shown in Figure 4. In other cases the loops have opened up, suggesting that, because of pressure generated during development, the sacklike endings may have ruptured.

Summary.—The layered structure of the myelin sheath of frog nerves is discussed, with particular reference to the region of the Schmidt-Lantermann incisures. It is shown, in the incisure, that the membrane doublets peel off from one side of the compact myelin, traverse the open space, and join the compact myelin on the other side. The incisure is thus not a diffusion channel from axolemma to extracellular space and is unlikely to be involved in current flow during impulse propagation. The structure of the myelin near the node is also briefly described. These structures are consistent with Geren's membrane theory of the origin of nerve myelin.

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*THE INACTIVATION OF GROWTH-PROMOTING DISLOCATIONS WITH TEMPERATURE, PRESSURE, AND POISONS**

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INTRODUCTION

Crystal growth involves catalytic structures usually lumped together as "nucleation." Such structures may be screw dislocations or some other bridge between phases. In any case this bridge structure will have thermodynamic properties different from those of the crystal in bulk. Such catalytic structures are, in particular, to be expected for the growth of ice crystals on crystals of silver iodide. In our theory we assume that there are δ possible sites per square centimeter, of which β are active as catalysts and the number γ are deactivated. We suppose further that β and γ are in dynamic equilibrium.

THEORY

The data to be explained are given as delay time for ice formation in a supercooled liquid-vapor mixture, in which vapor is therefore supersaturated with respect to ice, seeded with a standard amount of silver iodide crystals. The reciprocal of this delay time should be proportional to the velocity of ice formation.

At low temperatures the apparent activation energy is 13.8 kcal. This represents the heat of vaporization of supercooled water droplets plus a small activation energy. At high temperatures, above $-17°$ C., one obtains an apparent activation energy of -40.4 kcal. In this case we suggest that a rapidly established equilibrium exists between surface active sites (dislocations) at which ice formation can