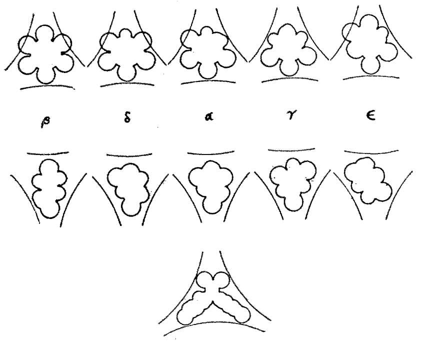

Fig. 1. Scale drawings from Stuart models showing the fit of various BHC isomers into a membrane interspace for plane (top) and one end-on (middle) orientation. The interspace (shown by curved lines) is formed by three cylindrical membrane molecules with a diameter of 40 A at a separation from each other of 2 A. All plane orientations, except that of γ-BHC, are excluded, although end-on orientations of all the isomers are permitted. At the bottom the only possible orientation of DDT is shown.

attracted to only one of the three surrounding membrane molecules, thus forming an interspace block but not a distortion.

If the foregoing model is to have any generality, it ought to be capable of accounting for the action of DDT and its various analogs. Diphenyltrichloroethane is capable of occupying the interspace in several orientations, one of which is with one benzene ring parallel to the surface, and another is with both benzene rings in an end-on orientation. The former orientation is not one in which the attractive forces of the halogen atoms can best be made effective, whereas the latter makes use of the attractive forces of not only the halogens but also the two benzene rings. To direct the orientation of diphenyltrichloroethane to end-on, *p,p′*, and, to a lesser extent, *m,m′* substitution with some group of the approximate size of chlorine is effective. If the *p,p′* substituent is made too large (for example, iodo or propoxy), penetration will be delayed or inhibited. By increasing the distance across the molecule (from the chlorine of trichloroethane to *p*-Cl), *p,p′* substitution makes it impossible for DDT to penetrate other than in an end-on orientation, as is shown at the bottom of Fig. 1.

Penetration in this orientation depends very much upon having the two benzene rings in an approximately end-on orientation. The free rotation of the benzene rings that is possible in *p,p′*-dichlordiphenylethane is constrained by 1,1,1-trichloro substitution in the ethane nucleus (*6*). This orientation of the two rings can be disturbed by a number of changes in the DDT molecule, such as by chlorination of the 2 position in ethane and by *ortho* chlorination of either of the benzene rings, changes that tend to rotate the benzene rings with respect to each other. These compounds are all much less active than DDT. Subtraction of halogen from the ethane nucleus is also capable of disorienting the rings, although this becomes important only when two or three halogen atoms have been removed. The change from DDT to dichlorodiphenyldichloroethylene increases markedly the distance between the chlorine atoms of dichloroethylene and their corresponding benzene rings (because of the change in bond angles), and hence makes the molecule nonpenetrating. The dichloroethylene compound is also relatively inactive. The steric situation responsible for the toxicity of DDT would thus appear to involve two factors: (i) a specific orientation of the two benzene rings with respect to each other, and (ii) a distance along the two axes of the molecule (ethane Cl to *p*-Cl) great enough to prevent a plane orientation of one of the rings in the interspace.

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References and Notes

1. This work was aided by a grant (B-139) from the National Institute for Neurological Diseases.
2. L. J. Mullins, *Chem. Rev.* 54, 289 (1954).
3. J. Ferguson, *Proc. Roy Soc.* (*London*) B127, 387 (1939).
4. J. H. Hildebrand and R. L. Scott, *The Solubility of Non-Electrolytes* (New York, 1950).
5. Space does not permit the derivation of this interspace size from experimental data on narcosis. In a more extensive paper it will be shown that the interspace size need not be set arbitrarily.
6. A somewhat contrary view is taken by R. Riemschneider [*Z. Naturforsch.* 9, 95 (1954)] who considers DDT analogs as most effective when free rotation of the benzene rings is possible. What has really been noted here is that ring substitution that tends to disturb the normal orientation of DDT results in less active compounds. This does not account for the usually diminished activity in dichlorodiphenylethane where free rotation is really possible.

25 April 1955

Improved Automatic Microtome

The automatic microtome I described in *Science* [**115**, 649 (1952)] that cuts and mounts serial sections of imbedded biological specimens on a 35mm strip of film base has been made more effective by two changes in the manner of its use: (i) specimens are mounted in tissuemat, and (ii) Mylar film is used so that it is possible to stain the sections after cutting.

Originally the instrument cut doubly imbedded specimens. It is preferable to use tissuemat, because it is routinely employed by many laboratories and because it saves imbedding time. The cutting of tissuemat sections works well under all conditions encountered, and they adhere well to the Mylar film without the use of an adhesive coating when the automatic microtome is carefully adjusted.

Staining previously was done on the tissue *in toto,* largely because of the damage suffered by acetate film in the various solvents. With Du Pont's Mylar film, which is not affected by solvents, we are now able to remove the tissuemat and stain the sections on the film in standard solutions.

Freshly cut sections are coated with a thin celloidin solution 0.5 percent and a thin coat of lacquer. Eastman film lacquer has been found to be excellent for the purpose. This treatment secures the sections to the film so that they do not become displaced in subsequent processing. A strip of 5 ft, or about 80 serial sections, can be wound on the reel of a 35mm developing tank such as the Nikor tank. The tissuemat is then extracted with Xylene, and the regular process is continued, using a series of solutions of alcohol. When the dyeing is completed, and the strip is again in Xylene, it is removed from the tank, and a second piece of Mylar film is placed on top of the strip, using a mounting medium. Longer strips can be used with automatic photographic developing equipment.

Projection or examination under the microscope is facilitated, since ordinary 35mm film-handling equipment can be used to bring successive sections into register. Copies may readily be made with ordinary motion-picture equipment.

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Elemental Sulfur Dust, a Nutrient for Lemon Leaves

Certain citrus growers in California have observed that they were able to pack more first-grade fruit from citrus trees that had been dusted with elemental sulfur dust than from nondusted trees. Losses due to injured peels of fruit unprotected from the sun's direct rays were to be expected, but these were considered negligible when they were compared with the increase in first-grade fruit obtained. It is not known how sulfur dust improved the grade of fruit or what unobserved physiological effects sulfur had. It became apparent to one of us, however, while he was assisting in the preparation of "Standard Values in Nutrition and Metabolism" (*1*), that elemental sulfur applied to foliage of higher plants has not been demonstrated to penetrate the foliage and to enter into the anabolic processes therein.