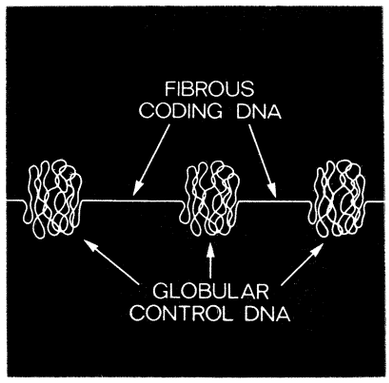
A speculative model for cell biology

In the early 1950's Francis H. Crick and James D. Watson opened up the field of molecular biology by collecting and synthesizing all of the known information and solving the problem of the structure of DNA. Now, using ideas and data from many sources, Crick is attempting to do the same in the field of cell biology. In the Nov. 5 NATURE he proposes a general model for the structure of chromosomes.

His model assumes that the DNA in a chromatid (one of two spiral filaments making up a chromosome) is a very long molecule that probably runs from one end of the chromatid to the other. Along this molecule chromosomal DNA falls into two classes. A small fraction is fibrous DNA that codes for proteins and a much greater amount is globular DNA, necessary for control purposes. The fibrous and globular DNA alternate along the length of the molecule. This uneven distribution and classification of DNA would account for the fact that, in higher organisms, there is always much more DNA in



Nature

genetic material than can be accounted for by the number of genes needed to code for proteins. The function of most of the DNA (globular) is therefore to regulate the activity of the rest.

The fibrous DNA is made up of the conventional double-stranded, double-helical DNA, and reproduces according to the original Watson-Crick model. The globular portion, Crick proposes, contains areas of single-stranded, unwound DNA that act as recognition sites for regulator molecules. Being single stranded they more easily attract regulators and, being unwound they are more accessible to these molecules. This, says Crick, "may be expensive to arrange but in the long run it will provide a much greater abundance of versatility."

Because there are a relatively small number of genes to produce a great many traits, this versatility of regulators is necessary. One regulator or control element, for example, might be needed for each type of cell in which a gene is to function. Another reason may be that a very precise quantitative control is required.

To make this model work, forces and energy are needed to unpair the recognition stretches of the DNA. Chromosomal proteins—probably the histones—will achieve this.

Crick, now at the MRC Laboratory of Molecular Biology in Cambridge, England, only summarizes his conclusions in NATURE (a much fuller account is in preparation). He terms his model speculative and not fully detailed and admits it raises at least as many questions as it attempts to answer. But, he concludes, "I hope it may serve as a focus for discussions and for the design of experiments."

Plasticizers: New entry on list of suspected contaminants

The difficult-to-answer questions about environmental contaminants are almost always those having to do with toxicity. For some substances, there is only a presumption of guilt; the time and research necessary to prove low-level toxicity is prohibitive.

Many widely used substances fall into this category. During the past year, yet another has been added to the growing list of suspect substances: phthalate esters, compounds used as plasticizers in polyvinyl chloride plastics. Polyvinyl chloride plastics are built into hundreds of common manufactured objects from new car interiors to medical equipment.

The latest piece of evidence about these phthalate ester compounds, reported in the Nov. 9 BIOCHEMISTRY, is of the presence of one of them in the heart muscles of cattle, dogs, rabbits and rats. The discovery was made by Darius J. Nazir, Aurora P. Alcaraz and Padmanabhan P. Nair of Sinai Hospital in Baltimore and Barbara A. Bierl and Morton Beroza of the U.S. Department of Agriculture. The material, di-2-ethylhexyl phthalate, constituted as much as 60 percent of the fat in the mitochondria in the heart cells of the animals, report the researchers.

The unanswered questions in connection with the discovery are numerous. There is no certainty that the chemical comes from the environment and no firm evidence that it is not produced by the bodies of the animals. The effects are still unclear, but there is a possibility of alteration of the permeability of cell membranes and consequent alteration of body processes. It is not known why the substance was found only in heart cells.

Somewhat more definite was a report by Foster L. Mayer of the Interior Department's Fish Pesticide Laboratory in Columbia, Mo., at an Oct. 28 American Chemical Society meeting. Mayer reported that growth and reproduction of an aquatic invertebrate, *Daphnia magna,* was inhibited as much as 60 percent by only three parts per billion of one of the most common phthalate esters. But he admitted that the toxicological evidence is still slim, as is evidence about the fate of the esters in aquatic ecosystems. There is no doubt, however, that the compounds are entering aquatic ecosystems, sometimes in large amounts, especially near industrial areas. " . . . A more detailed study of toxicological effects of phthalate esters is essential to elucidate their impact on these systems," Mayer said.

The October issue of ENVIRONMENT surveys earlier available literature on the plasticizers and concludes there is little doubt the plasticizers "migrate" from the plastics—to which they are added for flexibility—either through leaching by liquids or through vaporization into the atmosphere. The article adds that evidence points to the stability, and thus persistence, of the compounds in nature. But again the toxicological evidence is slim; for instance, although it has been clearly proven, at the Johns Hopkins School of Hygiene and Public Health and elsewhere, that the esters enter the human body from blood and other saline liquids stored in plastic containers or administered through plastic tubing, toxic effects have not been definitely proven. But the correlation between the presence of diethyl phthalate and changes in liver function, for instance, clearly points to the need for further study.

There is evidence, continues the article, that the plasticizers have teratogenic effects in chickens and rats.

A consortium of plastics companies is discussing with Nazir and other scientists the possibility of a detailed study of di-2-ethylhexyl phthalate in human tissues. This would be an important beginning. □