niques and in biochemical screening techniques are planned for the 1972 course. Also, some of the free time is used by conscientious students for visits to investigators, to the library at the Jackson Laboratory, or to the neighboring Mount Desert Island Biological Laboratory, which specializes in marine biology. The final session of the course is customarily either a summing up by one of the lecturers or a panel discussion by several of the senior faculty, representing both human and mouse aspects of the problems.

Through the 12 years of its existence the course has encountered most of the problems that were pointed out by Francis Crick (*3*) in his perceptive essay "On running a summer school"—for example, too many lectures, inadequate briefing of lecturers on the level appropriate to the audience, and so on. However, most of the defects have been remedied in recent years. Achievement of the proper level has presented no serious problems because a number of the guest lecturers are alumni of the course and the group of lecturers from Hopkins and the Jackson Laboratory has undergone little change. Some of Crick's considerations—legible name tags, distributed lists of home addresses, opportunities to get together in a social setting for informal discussions—have from the beginning been standard operating procedure at Bar Harbor. For example, at a party each night after the evening lecture all the lecturers of that day and usually many of the others are available for discussions.

It is likely that the Bar Harbor course has had a significant and beneficial influence on the progress of research and teaching in human genetics in this country and elsewhere. There is no sign of decline in the usefulness of or demand for the Bar Harbor course—either the medical genetics or the mammalian genetics course.

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Order in an Anarchic Field

Problems in cellular and multicellular differentiation and morphogenesis in a wide range of organisms including *Saccharomyces, Paramecium, Naegleria, Neurospora, Blastocladiella, Physarum, Polysphondylium,* and *Dictyostelium* were discussed at a workshop meeting on Differentiation in Eukaryotic Microorganisms held on 18 to 21 February 1972 at La Jolla, California.

These discussions proved useful, not because of new factual information presented, but because all participants made very strong efforts to define real questions that must be answered to understand cell differentiation, whether in one-cell or multicellular organisms. Two central problems emerged. (i) How are the hundreds of enzymes that change during development coordinated in a temporally and quantitatively regulated sequence? This is the problem of complexity. (ii) How are the products of enzymatic reactions laid down so as to form a structure of definite shape and size? This is the morphogenetic problem. Many of the presentations were approaches to one or the other of these questions.

The meeting was opened by T. Sonneborn (Indiana) who talked on morphogenesis in ciliates. A major question concerns the source of information for controlling the developmental behavior of the unit territory which belongs to each kinety on the cortex of *Paramecium.* Evidence from natural "microsurgical" experiments in which rows of cilia are inverted suggests that certain aspects are controlled by the pattern of the surrounding cortex, while others are determined by information from within the unit. Sonneborn concluded that further analysis would probably have to utilize specific conditional mutants, which he is now attempting to isolate.

S. Brody (La Jolla) reported on a series of mutants that affect the pattern of mycelial branching in *Neurospora* and his efforts to identify the responsible biochemical lesions. The difficulties encountered are instructive. One set of mutants is deficient in reduced nicotinamide adenine dinucleotide phosphate, but it is not clear how this compound affects cell wall biosynthesis. Second, genetically distinct mutants were found which affect the same enzyme (glucose-6-phosphate dehydrogenase), but all have visibly different patterns of mycelial branching. Although biochemical events must determine the branching pattern, it is clear that the relation is not one-to-one.

Somewhat related is work on *Blastocladiella* presented by D. Sonneborn (Wisconsin). His starting point is the hypothesis that some of the changes that occur in cell development may occur by rearrangement of structural material already present in the cell, without new gene activity or synthesis of new enzymes. One specific instance is the sudden increase in cell wall glucosamine compounds and the simultaneous sudden decrease in stored glycogen which occurs over a 20-minute period when germinating zoospores form hyphal outgrowths.

In contrast with these biochemical or genetic analyses, P. Green (Stanford) presented a physical interpretation of morphogenesis in the growing cell of the alga *Nitella.* The attempt was to express the shape changes in terms of a distribution of rates of expansion of the cell wall, and to determine the physical factors (like orientation of microfibrils) which modulate the rate. Green suggested that the gap between morphogenesis and biochemical genetics must be bridged from the phenotypic end.

G. Gerisch (Max-Planck-Institut, Tübingen) reported on his studies of the mechanism of aggregation and adhesion in the cellular slime mold *Dictyostelium.* He has been able to distinguish two adhesive components, one inhibited by ethylenediaminetetraacetate (EDTA) and another that is present only in developing cells and is insensitive to EDTA. Studies with univalent antibodies suggest that the second adhesive site is distinct from the first and may be involved in end-to-end cellular adhesion seen in aggregating cells. H. Aldrich (Gainesville) presented electron microscopic evidence from freeze-etched preparations for an increase in intramembrane 153-Å diameter particles during aggregation. These particles may be involved in morphogenetic adhesions.

Other offerings dealt in one way or another with the problem of the biochemical complexity of cell differentiation. B. Wright (Boston Biomedical Research Institute) reviewed her position that control of formation of the end product, such as cell wall, is in

most cases mediated by regulators acting near the terminal step rather than on earlier gene expression. A computer model containing relevant biochemical data has been built to identify the critical variable, or bottleneck, that limits the metabolism of trehalose and uridine diphosphoglucose during development of *Dictyostelium*. This method has suggested that substrate supply rather than enzyme synthesis may be the factor relevant to rate of end product synthesis.

Another approach was presented by W. Loomis (La Jolla). During development of *Dictyostelium*, a variety of enzymes of amino acid and carbohydrate metabolism have been found to appear in orderly sequence. The effects of each enzyme on morphogenesis and accumulation of later enzymes could be determined if appropriate temperature-sensitive mutants were available. Loomis described a series of temperature-sensitive mutants affected in one of these enzymes (acetylglucosaminidase). The loss of the enzyme in each of the mutant strains resulted in aberrant pseudoplasmodial function at the nonpermissive temperature.

Related to this work are electrophoresis studies very similar in outlook by D. Francis (Delaware), who described multiprotein changes during development of cellular slime molds and by R. Siegel who applied electrophoresis and other techniques to the study of conidiation in *Neurospora*. Siegel asked whether there are genes that must be turned off for development to occur, in addition to those that must be turned on. In a parallel study in *Saccharomyces*, L. Hartwell (Washington) described a series of temperature-sensitive mutants that arrest at different stages of the cell cycle. He concluded that each event depends on the completion of a preceding event, and asked what controls are necessary for starting the cycle and whether there is a unique event that acts as a trigger.

A. Jacobson (M.I.T.) and J. Haber (Brandeis) presented evidence that ribosomal RNA may change during development of *Dictyostelium* and sporulation of *Saccharomyces*, respectively. The implication of these findings to transcriptional and translational controls was discussed.

These several studies have the strength of dealing with the regulation of a series of genes or a series of proteins and, hence, truly approach the complexity of reality. Likewise, they all suffer from being nonspecific to a

greater or lesser degree, in that the physiological role of the gene or protein is not identified.

The study of cell differentiation has long been the anarchic field par excellence. Perhaps now we are coming out of the era of technique-oriented research on cell problems, in which newly popular techniques have been applied to every available system with little regard to whether they provide significant insight. It appears that many members of the La Jolla group have set their sights on the large biological problems, toward whose solution any relevant technique can be brought to bear.

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Bryozoology II

The second international conference on bryozoology was held in Durham, England, from 6 to 16 September 1971. It was attended by 68 scientists from 14 countries, about a third of the membership of the International Bryozoology Association (IBA). The IBA includes those chiefly concerned with any aspect of the biology and paleobiology of the approximately 3,500 extant and 15,000 extinct species of bryozoa (ectoprocts and endoprocts). The conference had as its dominant theme the necessity of first understanding the life processes of living forms before trying to unravel the significance of fossil forms.

The old question of why does species A live in place X rather than in place Y is still being asked, but with a new frame of reference. Although much of the evidence remains anecdotal, some facts useful for a deductive theory are beginning to emerge. The rate of budding of new individuals appears to differ widely from one species to the next. New discoveries of larvae that initially become three to nine individuals—rather than the single individual commonly assumed—show that certain species obtain a flying start on preempting space on which to grow (F. J. S. Maturo, University of Florida; P. L. Cook, British Museum; G. Eitan, Hebrew University). In some forms, the capacity for retaining space is aug-