senting vote of House members—the number necessary to suspend House committee rules. Right now, the bill's supporters are confident of support from less than one-third of the House.

In the Senate, backers of the bill are still awaiting a response by Richard Russell (D–Ga.), chairman of the Senate Armed Services Committee. Though support of the bill seems to be slightly stronger in the Senate, Kennedy aides say they have no real strategy on where to go if the Armed Services Committee refuses to hold hearings.

—FRANK CLIFFORD

Sweden: New Institute to Focus on Applied Microbiology

Stockholm. In mid-April an industrially oriented interloper, the Project for Applied Microbiology, will occupy a new temporary building among the celebrated medical research departments of Stockholm's Karolinska Institutet. There a team under C.-G. Hedén will prepare for the creation of an Institute of Applied Microbiology, hopefully in 2 years. It will examine the opportunities for research in nonmedical bioengineering, for contract work for industry, and for applied microbiology relevant to international needs, especially those of the developing countries. This new venture is supported by the Swedish government's Council for Applied Research. It is a natural outcome of Hedén's interests in novel microbiological techniques, cultivated during two decades. Eight years ago, a bioengineering unit was created for him in the Karolinska's bacteriological department. He will continue to direct that unit, and its recent achievements and interests provide an indication of what may be expected from the new venture.

With the risks of biological warfare in mind, the Swedish Medical Research Council, which deals with military as well as civilian matters, established the bacteriological bioengineering unit. In addition to acting as adviser to the government, Hedén was to study and develop techniques for the large-scale handling of pathogenic microorganisms, particularly in connection with the preparation of vaccines. The work was not secret and remained compatible with the unit's status as a university department; Hedén had a free hand in selecting research projects.

The attraction for the Medical Research Council was the big pilot-scale fermentation plant, completed by the Karolinska in 1958 for its own purposes. As a facility for culture of both pathogenic and nonpathogenic species, it is still unusually large for university biological work. Indeed, with the present trend to continuous culture it begins to look cumbersome. Hedén had played a leading part in the planning and design of the pilot plant; already-existing industrial techniques were inadequate. The plant features extensive automation and remote control, and adaptation to reduced-pressure operation for the handling of pathogens. Much of its versatility is due to the steam-sterilized "stericonnectors" invented by Hedén, which allow vessels to be quickly and safely linked by flexible tubing.

Defense requirements have influenced the pattern of research. The gonococcus provided, at the outset, a test case for concentrated culture of notoriously fastidious pathogens. P. Gerhardt successfully applied a two-phase technique, consisting of a medium solidified with agar and overlaid with a liquid medium. More recently, R. Brooks has preserved gonococcus by freezing and storage in liquid nitrogen. A two-phase liquid culture technique, pioneered by P. A. Albertsson, was adapted to the preparation of tetanus toxin and anthrax antigen by M. Puziss, an American microbiologist working with Hedén. In such a culture, two immiscible aqueous polymers are stirred together; the microorganisms grow in dextran from nutrients transferred from the polyethylene glycol phase, while metabolites cross the interface into the polyethylene glycol. This system can be described as "dialysis without a membrane." The titer of tetanus toxin obtained by this method was a thousandfold greater than that obtained from conventional cultures.

Two interests of the bacteriological bioengineering group have wide implications. Current work on methods for large-scale tissue culture was originally prompted by the probable need for rapid virus-vaccine production in the event of biological warfare. Fundamental research on the physical properties of DNA may prove relevant to identification of unknown nucleic acids. The group's interests have broadened continuously. As expected, the Karolinska pilot plant proved useful for purposes other than experiments related to vaccine production. Its scale made possible the preparation of sparse metabolites and enzymes in quantities useful for fundamental research in Sweden and abroad; its flexibility permitted wide-ranging experimental work on the culture of microorganisms. The Swedish Defense Research Institute (FOA) now has its own group concerned with biological warfare, and the Institute for Applied Microbiology, using the same Karolinska pilot plant, will eventually take over the residual defense activities from the bioengineering group. Hedén remains concerned with the international control of biological warfare and has been prominent in the Pugwash movement's study of the possibilities; he headed the inspection team in the four-nation trial (1966) of safeguards against diversion of microbiological facilities to weapons production.

"The study of artificial environments in which living cells or labile biological substances are produced, preserved, destroyed or modified as desired." That is how Hedén defines his brand of bioengineering. He sees it as a link between basic and applied research; and the work of his group during the past 8 years on the effects of high pressure on microbial cultures illustrates this interplay.

It began with the practical problem of extracting labile toxins at subzero temperature from the bacterium *Bordetella pertussis.* To disrupt the cells, L. Edebo exploited the phase change from ice I to ice III which occurs below

−20°C at about 2000 atmospheres. Repeated phase transitions produced by pressure changes, combined with strong shear obtained by forcing the frozen bacterial paste through a narrow channel, empties the cells satisfactorily. This technique was then applied to isolation of bacterial cell walls; currently, cell-wall preparations of staphylococcus are of interest as possible antigens for vaccines against antibiotic-resistant strains.

What effect does pressure have on bacteria at a higher temperature? Having begun high-pressure work, members of the group turned their attention to this question. Other workers had reported that high pressure protected enzymes against effects of heat. T. Lindahl found that pressure had a similar beneficial effect on DNA from bacteria (*Bacillus subtilis*); a pressure of 10,000 atmospheres did not denature the DNA, while a pressure of 2700 atmospheres shifted the heat-denaturation curve upward by about 6°C.

More unexpectedly, L. Rutberg discovered that pressure can induce attack on bacteria by latent bacteriophage—an effect normally associated with mutagenic agents. Rutberg confirmed an earlier result that high pressure accelerated the rate of inactivation of *Escherichia coli* B. In the course of these experiments an unknown phage sometimes appeared in the culture. Rutberg was confident that no spurious infection had occurred; he was subsequently able to confirm that pressure indeed activated latent phage. A pressure of only 150 atmospheres sustained for 2 minutes could induce phage activity in some strains of *E. coli*. The mechanism of induction is still obscure; the discovery is of direct technical significance, because ordinary microbiological operations frequently generate substantial pressures and may therefore inadvertently cause phage induction.

Culture of diploid tissue cells (including human diploid cells) is, in Hedén's view, a most promising current development in medical biology. He believes that within a very few years human diploid tissue cells may replace other material, such as monkey kidney, for virus-vaccine production, in view of extraneous effects associated with the use of animal tissue. Human diploid cell cultures should serve many experimental purposes and, as a goal for perhaps a decade hence, Hedén cites the preparation of gamma globulin by culture technique.

Fears about the subsequent appearance of cancer cells in a diploid cell culture have been a brake on the development of this technique. Some individuals are now confident that, if the culture is maintained for not more than a few dozen generations and if a watch is kept for possible neoplastic cells, a diploid culture should be quite acceptable for medical purposes. Technical means of handling the material on a large scale are plainly critical. The principal advance in the Karolinska group has been in the choice of a surface for supporting the diploid cells. O. Molin has shown that titanium discs are very suitable—better than glass; and it is quite easy to provide some thousands of square centimeters of titanium surface in a one-liter bottle. Synchronous growth may be obtained by spinning the titanium discs, washing off newly divided cells which can then be used to start a synchronous culture. In another procedure to achieve partial harvesting, the medium is replaced with a weak solution of trypsin. In this way, a culture could be maintained for a month, with half the population being harvested every 24 to 48 hours.

The invention in 1963 of a technique for preparing films of oriented DNA opened up an important area of research for the bacteriological bioengineering group and for others anxious to study this material. A. Rupprecht developed a wet-spinning method, in which a thread of DNA is continuously stretched during precipitation and then wound on a slowly advancing cylinder so that the molecular strands lie parallel to one another. From the time of the x-ray diffraction work on DNA by M. F. H. Wilkins and his colleagues in London (1951), various means of obtaining oriented DNA have been tried but none provided solid or gelatinous

IDA Mathematician Dismissed

Princeton, N.J. Mathematician James Simons was fired by the Institute for Defense Analyses (IDA) on 29 March because of his refusal to engage in military-related research—a refusal which grew out of his opposition to the Vietnam war. In an interview with *Science*, Simons said that he had been advised of the decision by Richard Leibler, head of the Princeton division of IDA, who told him that his refusal to engage in military work made it impossible for IDA to justify his salary to IDA's sponsor. Simons said he had indicated his willingness to work on IDA's nonmilitary projects.

According to Simons, the decision on dismissal was made by Gordon J. F. MacDonald, IDA's vice president for research, in consultation with General Maxwell Taylor, IDA's president. Simons, a Berkeley Ph.D. who came to Princeton in 1964 after a year at Harvard as an assistant professor of mathematics, said MacDonald had told him at a meeting in Washington on 26 March that Simon's "unwillingness to work on defense material would have to be resolved very quickly."

Simons said that his refusal to work on military matters had been known to IDA officials for the last 6 months. In November of last year Simons had a letter published in the New York *Times* stating his desire for quick withdrawal from Vietnam and saying that, despite IDA president Maxwell Taylor's support for the war, "some of us at that institution have a different view."

Simons said he believed that the IDA leadership regarded him as a "ringleader." And, he said, "there is probably some truth in that. There is no question that I was getting some people here to move away from the philosophy that IDA ought to remain restricted to defense research."

Simons' dismissal will draw further attention to IDA's delicate relationships with its university members. Last month a special Princeton faculty committee recommended that Princeton reconsider its relationship with IDA and renegotiate its arrangements, in conjunction with other university members, so that universities cannot be said to be responsible for IDA's activities. In February a University of Chicago faculty committee said that Chicago should sever its membership in IDA.—THOMAS PLATE samples large enough for most physical measurements. By means of Rupprecht's technique, films of arbitrary size and thickness can be formed; adjacent threads agglomerate while dyring and form a homogeneous material.

Rupprecht has since refined his method, and samples of oriented DNA have served in a range of studies of potential importance for a better understanding of the genetic material and for verification of quantum chemical theories. Rupprecht's preoccupation has been with the orientation technique; most of the physicochemical studies are being made in cooperation with other specialists.

Conductivity (d-c) measurements on dried oriented DNA have shown semiconductor characteristics of the DNA helix, such as were postulated by A. Szent-Györgyi, and, in agreement with results from unoriented DNA, reported by several other investigators. However, there is no marked anisotropy in the conductivity of the oriented DNA; Rupprecht attributes this negative result to structural changes that occur in the DNA during drying.

Using moist films for studies of hydration of DNA, Rupprecht has found a dependence of the proton magnetic resonance signal on the orientation of the DNA helices in relation to the magnetic field. The result is strikingly similar to that obtained for collagen by H. J. C. Berendsen of Gröningen, who explained the effect by postulating chains of water molecules in parallel alignment with the collagen fibers. Rupprecht and Berendsen's group plan to cooperate in further work in the oriented DNA. At the Medicinska Nobelinstitutet in Stockholm, A. Ehrenberg has begun studying electron spin resonance in moist oriented DNA samples that have been frozen, and afterward irradiated with gamma rays from a cobalt-60 source. He, too, has found marked dependence of amplitude on the orientation of the DNA helices in the magnetic field. So far, identification of thymine radicals has been reported, and the work is continuing with DNA moistened with heavy water (D_2O), in the expectation that other radicals will be identifiable and that the mechanism of their formation by irradiation may be elucidated.

Measurements of the mechanical properties of the oriented DNA threads and films, and their dependence on spinning conditions, provide Rupprecht with a basis for systematic development of his technique. He has found that the tensile strength of the fibers are markedly dependent on temperature. At present he is engaged in developing thin fibers for high-resolution x-ray diffraction studies, and thin films for use in research on the optical properties of oriented DNA.

A final example of the techniques originating in Hedén's group is E. A. Falch's "one-dimensional" culture for automatic screening of microorganisms. He uses a strip of newly solidified agar containing various nutrients and inoculated along its length with bacteria. The agar is carried into an incubator on a moving surface—a polypropylene belt in the original tests. Zones of growth or inhibition can be detected optically when the agar emerges from the incubator. The uses envisaged range from labor-saving selection of microbial strains that synthesize a particular compound, to automatic identification of microorganisms. The technique was first demonstrated in 1965, but it still awaits full development.

Requests from other laboratories for various items of equipment developed by the Karolinska bioengineering group overtaxed their workshop. In 1966, a company, Biotec, was created to manufacture some of the specialized equipment developed by Hedén and his group. The company has been successful and has established branches in the United States, Britain, and Japan. Biotec, is, incidentally, one of the companies sponsored by Incentive AB, a new Swedish financial enterprise dedicated to encouragement of new industry, with emphasis on science-based activities.

The Project for Applied Microbiology, within the scope indicated at the outset, will be concerned with trouble-shooting and *ad hoc* research for industrial clients, and also with long-term research on its initiative. As an example of a long-term project, it will take over work, already in progress in the bioengineering group, on culture of methane-fermenting bacteria as a potential source of protein-rich food. Fast-growing strains and appropriate media have been found, but the principal bioengineering problem is one of gas transfer—of oxygen as well as of methane—to the culture. Algal species may have earlier application, if problems of harvesting and food technology can be solved. Hedén is particularly interested in *Spirulina*, "discovered" by Belgian and French microbiologists as an algal species that Africans in Chad have eaten for centuries. *Spirulina* is particularly easy to harvest because the helical form of the alga tangles the crop into strong mats. One of the first activities of the project will be to convene a meeting on *Spirulina* cultivation to help establish a coordinated research program in this area.

Hedén was the instigator of two conferences on Global Impacts of Applied Microbiology, the first in Stockholm in 1963 and the second in Addis Ababa in 1967. The conferences were convened to draw attention to microbiological needs of the developing countries. The international outlook of the Project for Applied Microbiology is best illustrated by the so-called BIORED scheme (biological resources development teams), which will become its responsibility. This scheme was first proposed by the bioengineering group in 1965 as a contribution to the International Biological Program. A feasibility study, in Ethiopia last year, indicated the form which the first of such operations might take (a base laboratory and a mobile unit in a 2-ton truck) and disclosed a range of local studies of practical importance in Ethiopia. At present the scheme is waiting for the necessary arrangement between the Swedish and Ethiopian governments.—NIGEL CALDER

RECENT DEATHS

Louis G. Austin, 54; professor of biology, Virginia State College, Norfolk; 29 February.

John M. Boutwell, 93; former president of Society of Economic Geologists; 2 March.

George E. Boxer, 53; executive director of the Merck Institute for Therapeutic Research; 14 March.

L. Beverley Chaney, 77; retired clinical professor of neurology, Columbia University College of Physicians and Surgeons; 12 March.

Herbert G. Deignan, 61; ornithologist emeritus and honorary research associate of the vertebrate zoology section, Smithsonian Institution; 15 March.

McKay Donkin, 63; vice president for finance and treasurer of Pennsylvania State University; 17 March.

Rudolph E. Langer, 74; chairman emeritus of the mathematics department, University of Wisconsin, and former director of the U.S. Army Mathematics Research Center; 12 March.