Copy for Prof. Meselson's information

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DEPARTMENT OF MOLECULAR BIOLOGY

BERKELEY, CALIFORNIA 94720

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Dr. Rolf Björnerstedt
Research Institute of Nationa Defence
Forsvarets Forskningsanstalt
Avdelning 4,
Stockholm 80, Sweden

Dear Dr.Björnerstedt:

I am extremely enthusiastic about the decision of the Swedish PUGWASH group to focus its efforts on rapid detection methods for infectious agents. The second paragraph of your letter to me dated January 14th, 1966 states extremely well the happy circumstance that such research can be effective in discouraging secret development of biological weapons while at the same time producing results that could be of importance for public health and for clinical diagnostic procedures in hospitals. Unfortunately my commitments to teaching, research and other activities will prevent my attending the meeting in Stockholm on March 21-22, 1966. I will be glad to summarize below several thoughts that I have on the subject.

I know of only 2 methods which seem at the present time to have a reasonable chance of being successful in the rapid detection of air-borne bacteria and viruses. One is the automation of the well known fluorescent antibody staining technique and the other is the automation of methods of identifying bacteria via the morphology of their colonies growing on solid media. In the fluorescent antibody technique the main difficulty is a certain amount of lack of specificity and of cross reaction of antibodies which prevents positive identification and distinction between some of the species of bacteria. In particular pathogenic and non-pathogenic strains may often have the same reactions. As is well known this is a problem receiving a good deal of research effort in many countries and which is related to many important fundamental directions of biological investigation. On the other hand the automation of the fluorescent antibody technique seems to me quite simple and straightforward once the selectivity of the basic method is satisfactory. I would therefore not judge it worthwhile to worry at all about the automation and systems problems in developing a practical warning system but rather concentrate on fundamental immunological techniques of identification.

In contrast the problem of developing automatic methods for characterizing and recognizing colony morphology has not received much effort and the only currently active program I am aware of is going on in my own laboratory. We are building a flying spot scanner connected on-line with a fair size computer for the purpose of scanning petri dishes automatically, counting bacterial colonies and analyzing the appearance of these colonies by recording optical density profiles across a few typical diameters of the colony, looking at the characteristics of the edges of the colonies, their color, their surface roughness, etc. The identification of bacterial types by colony morphology has been used for a long time in a qualitative way and

there seem to be no deep fundamental problems associated with growing bacteria under well controlled conditions on a variety of media to see whether the combination of colony appearance under these several conditions will be sufficiently characteristic to allow identification of the parent organism. For success in this problem everything depends on accurate, reproducible data which can be obtained in large quantities only with some sort of automatic equipment that will allow us to gather enough information to judge which features of colony morphology are regular and genetically controlled and which are subject to large environmental fluctuations as to be useless for identification purposes. So far we have succeeded in demonstrating that our machine can distinguish among several bacterial species whose colonies are quite grossly different in appearance, including 2 E. coli K12 Hfrs (Hayes and Cavalli) Aerobacter aerogenes, Proteus mirabilis, E. coli strain B (Berkeley) and a few other commonly used experimental organisms. Within the next 6 months to a year I expect that we will have studied several hundred species and strains of bacteria and perhaps some fungi.

The colony morphology technique is not capable of the very fast reaction time that is possible with the fluorescent antibody technique but it may allow drug sensitivity measurements to be made on the same primary isolation plates in which the identification is done. That will be useful for protection of populations subjected to epidemics whether natural or the result of an aggressive act as well as useful in routine hospital clinical practice. Although the main motivation for our work on colony counting and automatic morphology recognition arises from basic problems in bacterial genetics and physiology we are aware of the important applications of this method to medical and public health problems should it prove successful. We will therefore be very happy to keep the Swedish Pugwash group informed on the progress in our work and will be glad to contribute to this collaboration whenever we have anything definite that may be of value.

With best wishes,

Sincerely yours,

Donald A. Glaser
Professor of Physics and
Molecular Biology

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