

1. The origin Plans

(1+1)

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2. The Present Position

The laboratory has now been in operation for about 1 1/2 years. All three Divisions ~~have settled down~~ ~~have settled~~ down are now well set up, with substantial programmes of work in progress. There has been considerable informal collaboration between the Divisions, and much facilitated by the centre. There has also been a fair amount of sharing of apparatus. Joint <sup>research programmes</sup> ~~work~~ between the Divisions has only recently started but may be expected to develop further.

We note, with <sup>some</sup> regret, that no collaboration has yet sprung up between Prof. Mitchell's departments and our own.

## The Present Position

Since 1958 Molecular Biology has made great progress.

The major developments have been the ~~solid state~~ the structure

we can ~~must~~ first <sup>ask</sup> whether the space and facilities

provided were adequate for this program and for the staff

As to facilities, it engaged ~~It~~ is fair to say that the ~~space and equipment~~ for the

four senior ~~work~~ workers the space and equipment <sup>provided</sup> was

~~most~~ very good. It has, however, proved inadequate in two

respects

(1) ~~The~~ Insufficient space was allowed for Huxley

and Klug to build up groups <sup>within the laboratory.</sup> ~~consequently~~

~~these~~ ~~groups~~ ~~of~~ ~~these~~

<sup>to</sup> Huxley and Klug have international reputations and on any assessment should have more space. The same would have been decided to stay

true of Tassieres if he had ~~stayed~~ stayed with us.

② the space required for biochemistry was <sup>somewhat</sup> underestimated.

~~The second floor~~

~~However, Parkeover state that if~~

~~There is a~~ The total extra space needed to cover these requirements is not very ~~far~~ great. Probably an extra 2,000 ft<sup>2</sup> would have been enough.

However since then ~~the~~ Molecular Biology has advanced ~~very~~ rapidly. ~~The structure~~ ~~the structure~~ The X-ray

analysis of myoglobin and haemoglobin ~~has~~ <sup>has</sup> made great strides. ~~The genetic~~ The mechanism of protein synthesis and

the genetic code are now partly understood. It is broadly true

~~to say~~ to say that all the <sup>in outline</sup> classical problems of Molecular Biology are either solved or well on the

way to solution. The time has come, therefore, to

make a reassessment of ~~the whole of~~ our work.

Insert over

The case

It may seem surprising that there should be  
necessity so soon after the laboratory has been  
built, but this is because the rate of advance  
of scientific research is ~~now~~ becoming almost as  
fast as the rate of erecting buildings.

### 3. Immediate Developments

#### A. Structural Studies and Protein Synthesis

The major problem here is to relate structure to function, not only for the two oxygen carriers but for ~~the~~ some enzymes as well. ~~but~~ we feel that ~~the~~ <sup>the</sup> ~~great~~ <sup>great</sup> effort expended on the problem of enzyme structure should be balanced by studies on enzyme function. ~~This would~~

~~be developed as~~ ~~and~~ ~~the~~ ~~Hardley~~ ~~In~~ ~~addition~~ ~~we~~

We also feel that our strength in x-ray analysis and electron microscopy should be matched by an ability to apply optical and other physical methods to the study of biological macromolecules.

The studies on enzyme function could be more easily ~~expanded~~ ~~and~~ be directed by Hardley ~~also~~. ~~The~~ ~~to~~ ~~be~~

For the physical chemistry, we should need to recruit someone from outside. The total floor space needed for these purposes is about 2000 ft<sup>2</sup>.

## B. Molecular Genetics

The next major problem in this field is the genetics and biochemistry and genetics of control mechanisms. We feel that in the first place this can ~~more~~ for technical reasons, be and this <sup>work</sup> has already been started most easily & studied in micro-organisms. ~~However~~ <sup>however</sup> ~~the~~

~~It is~~ <sup>nevertheless</sup> very desirable to continue the present studies on protein synthesis <sup>and</sup> the genetic code ~~to~~ to provide a proper background to the attack on the control problem.

~~However~~ ~~the~~ ~~is~~ ~~the~~ ~~way~~ ~~we~~ ~~can~~ ~~now~~ ~~achieve~~

It is obvious that the problem of control mechanism will lead us to <sup>higher organisms and to</sup> embryology, and while it is not easy at this stage to see the most fruitful line of development.

~~It is~~ ~~considered~~ two points ~~can~~ should be made:

- ① it would be sensible to start exploratory work <sup>now</sup> on

one or two "model systems". ~~to pick up a~~

(4)

(3)

~~from small metazoan~~ we have in mind a small

7

200

metazoan, ~~on which we can apply~~ the choice to be

1400

suitable for <sup>rapid</sup> genetic and biochemical techniques, but

work on higher organization is not excluded.

(2) This area ~~is~~, of all those discussed here, is likely to expand steadily as time goes on.

To develop this work we have the ideal person in Brenner. It will be recalled that Brenner was

originally recruited to in order to build up the genetic biochemical and genetical work of his

position in the present laboratory is indispensable,

not only because of his obvious ability and his detailed

technical knowledge, but because he is <sup>practically</sup> the only  
 senior worker in the laboratory with a ~~long~~ biological  
 and medical  
 background.

We estimate that for the first phase of this  
 work ~~the~~ about 2000 fr<sup>c</sup> would be required.

Optimum fr<sup>c</sup>

~~Longer Term Plan.~~

#### 4. Longer Term Plans

In the long run it is inevitable that molecular biology will merge towards and become part of cell biology. Insert A It is our strong conviction that

the proper direction for our work to take is towards more biological studies. Insert B ~~work has~~ We are

extremely fortunate in having in Brewer the Insert C that it is doubtful if he could take on these <sup>ungraded</sup> additional problems ~~with~~ ideal person to direct this work, ~~As far as assistance~~ ~~from senior~~ ~~person.~~

A possible arrangement ~~we can see the~~ ~~most~~ ~~likely~~ ~~development~~

would be to find a new senior person to look after ~~the~~ the biochemical part of the Molecular

(A)

We do not wish to spend our time  
~~studies~~ ~~and~~ solving problems which although both  
molecular and biological are of trivial biological  
interest.

(B)

We shall then be in a position to  
approach central ~~biological~~ biological problems  
from our molecular view-point.

(it will be recalled that we originally had T. Miller in mind for this role)  
Secretary of Division, and to ~~cost~~ create a new

Division for Control Mechanisms under Bremer.

~~It will be recalled that we originally~~

However wherever ~~is~~ eventually proposed it will

entail space for Bremer's expansion, and it

would be sensible to ~~allow for~~ start to

build this space now, even if ~~it were not~~ <sup>is</sup>

fully equipped immediately. The ~~cost~~ we have in

mind for this is 4,000 ~~6,000~~ <sup>for</sup>.

5 Optimum size of laboratory

It has been said - - -

together.

We should point out that it is quite easier to find  
such a constellation of senior workers who get along so  
well together than they would to stay together!

The position of Dr. Leslie Orgel is a rather special one and has to be considered apart from the development of the laboratory.

In the first place it should be realized that ~~the~~  
~~many~~ ~~ways~~ ~~Dr. Orgel~~ ~~has~~ ~~been~~ ~~for~~ ~~many~~ ~~years~~  
 is ~~not~~ ~~a~~ ~~member~~ ~~of~~ ~~our~~ ~~laboratory~~ in fact it  
 very closely associated with us ever since he came to  
 Cambridge in 1956. ~~has~~ ~~discussed~~ ~~some~~ ~~of~~ ~~our~~ ~~work~~ ~~with~~  
 him, ~~she~~ ~~meeting~~ ~~not~~ ~~only~~ ~~has~~ ~~he~~ ~~followed~~ ~~all~~  
 our work in considerable detail, ~~but~~ ~~he~~ ~~has~~ ~~been~~ ~~co-author~~  
 of ~~two~~ ~~theoretical~~ ~~papers~~ and <sup>in the process</sup> has acquired a wide  
 and deep knowledge of molecular biology. ~~He~~ ~~is~~ ~~the~~ ~~co-author~~  
 He has written (either

alone or in collaboration will in) ~~see~~ several theoretical  
~~or molecular biology~~  
 papers, and is at present engaged in a critical review  
 It is universally recognized that he  
 on the difficult subject of mutagenesis. He has one of  
 the keenest intellects in ~~the~~ molecular biology, ~~combined~~

~~with~~ Moreover his judgement is good and his imagination is

~~fertile~~ fertile. If he wished to ~~be a member~~  
 (for which he would need very little space)

join <sup>us</sup> ~~as~~ as a theoretician / we should ~~support him~~

give ~~to~~ the proposal our whole-hearted support.

However he has made it completely clear that he

wishes to ~~be able to~~ direct experimental work. It

has been suggested that he take over <sup>direction of the</sup> the physical chemistry

in the laboratory. Reluctantly we have come to the

conclusion that this is not a good idea, since we feel

that although he wishes to do ~~a certain amount of~~  
 experiments on some aspects of the physical chemistry of biological

3

macromolecules

1 ~~that~~ his real interests lie elsewhere.

There seems little doubt that the problem that ~~most~~ attracts his attention above all others is that of the ~~origin~~ origin of life, and in particular the relatively simple chemical reactions which are presumed to have ~~not prepared the first~~ built up the concentration of <sup>small</sup> ~~simple~~ organic molecules needed before life could begin. He has thought about <sup>these</sup> ~~the~~ problems for several years, and has <sup>interesting</sup> ~~had~~ a novel idea ~~in~~ on what experiments should be done. ~~He~~ ~~is~~ His wide knowledge of molecular biology, combined with his ~~to~~ ~~any~~ grasp of theoretical chemistry make him ~~the~~ the ideal person for this work. It would be difficult to

match these qualifications ~~in any~~ <sup>anywhere</sup> ~~system~~ in the world, and impossible in Great Britain. We have no doubt that such work, discussed by him, would lead to very interesting results.

This problem - the origin of life - is not in the same state as the other ~~work~~ lines of work in the laboratory. Rather it recalls the state of ~~the~~ molecular biology at the time the Council first set up our Unit.

Many interesting things can be tried, but ~~the~~ definitive answers <sup>to the main questions</sup> are not likely to be obtained for some ~~time~~ <sup>time</sup>. ~~It is~~ Moreover the results ~~will~~ <sup>will be</sup> ~~very~~ <sup>will be</sup> mainly

of "pure" scientific interest, although we are confident that ~~the~~ <sup>they</sup> ~~scientific~~ <sup>will</sup> ~~work~~ <sup>also</sup> illuminate molecular biology, and thus, indirectly, ~~the~~ <sup>the</sup> medicine itself. ~~The~~ <sup>the</sup> ~~Fe~~

To support such work is therefore something of a gamble. We feel strongly, however, that this is ~~a~~ the sort of gamble which the Council (and other similar organisations) must take from time to time, ~~in~~ at least in a few well-chosen cases, if the ~~the~~ vitality of the ~~subject's~~ biological science is to be ~~the~~ preserved. ~~Moreover~~ Moreover ~~it is quite clear~~ that if Orsd ~~the~~ does not receive support he will go to the States, ~~and~~ ~~there~~ where he will have no difficulty at all in getting all the facilities he wants. The loss to British Molecular Biology would be very great. He is, after all, the youngest F.R.S. in the subject.

Although we cannot make a case that ~~Orgel's work~~  
~~is directly~~ this project of Orgel's is very closely linked ↓

to our other work, & we are naturally interested in it.

~~and we would welcome Orgel as a colleague. It is~~

clear that his work should be supported somewhere in

England. We would like him as a colleague and he

would like to work alongside us. <sup>obviously</sup> ~~through~~ the scramble

plan would be to provide space for him ~~in~~ &

as part of the extension of our laboratory. Failing that

we hope that a unit <sup>will</sup> ~~could~~ be created for him <sup>elsewhere in</sup> ~~in~~

Cambridge, so that we should not be able to remain in

close touch with him. The space he would require is

estimated as  $17^2$ .