H. Chantrenne 14 août 1963.

Proposal for a European Organization of Fundamental Biology

(This document is based on the discussions of a group of biologists held at Geneva on 28 March and 28 June 1963. With the exception of Section III it was drafted by Dr. J. C. Kendrew, who takes the sole responsibility for the details of the contents, since these have not been scrutinized by other members of the group. Section III, dealing with a proposal for a Federal Organization, was drafted by Professor C. H. Waddington who also contributed parts of Section I.)

I. PREAMBLE

1. The need to strengthen European fundamental biology

During the last two decades our understanding of the fundamental molecular processes by which the character of biological organisms is determined, maintained, and modified has been increasing in a spectacular manner. Biology is becoming perhaps the most intellectually exciting of the sciences, and it holds out hope of far-reaching practical applications.

The first steps leading to many of the recent advances were taken in Europe, but all European countries have now fallen far behind the United States in the provision of facilities for fundamental biology, and as a result there can be no doubt that the United States is leading not only in the volume but for the most part in the quality of the work being done in this field. The American success depends on six main factors:

(a) widespread provision of moderately expensive equipment (in the range from $5,000 to $50,000);

(b) general availability of attractive posts for able young workers, and the possibility for them to attain positions of independent responsibility at a relatively early age;

(c) easy communication between laboratories over a large area, so that facts and ideas are disseminated to a surprisingly great extent by word of mouth;

(d) frequent exchange of research workers between a large number of well-equipped centres, in consequence of an established tradition of inter-university mobility at all stages from research student onwards;

(e) the existence of many centres (e.g. Woods Hole, Cold Spring Harbor, Oak Ridge, various universities) at which high-level symposia and training courses are held, which enable workers from other fields (even as remote from biology as theoretical physics) to acquire the techniques and outlooks of the advancing areas of biology;

(f) rapid growth of the educational system as a whole, making it easier to create centres of research in fundamental biology outside the classical subdivisions of the subject.

In all these respects Europe lags behind. There is not enough money, either for building and equipping laboratories, or for creating the posts to fill them, or for travel. There is little mobility even within European countries, and practically none between them - biologists hardly ever move during their careers from one European country to another, as they do from one part of the U.S.A. to another, or from Europe to the U.S.A. European scientists do not talk to one another nearly as much as do American scientists. There are few large inter-disciplinary centres of research, to provide a focus for research in biology, a training ground

for new entrants to the field, and an incentive to the best young scientific talent of Europe to turn to fundamental biology. The traditional split of academic biology into zoology and botany, still widespread in Europe, makes it difficult to stimulate the development of borderline fields where most of the exciting advances take place; and the hierarchical organization of most university departments leaves little scope for creating good positions for outstanding young men.

The developments in America have made the transatlantic scene so attractive that it has tempted many of the most promising young European biologists to emigrate permanently to the United States. The drain of talent is already serious and may become calamitous, and something needs to be done to avoid a loss of intellectual capital which Europe cannot afford.

Even the temporary losses represented by young scientists going to America with post-doctoral fellowships are serious. Almost every able young European biologist wants to spend a couple of years in America, because he correctly judges that only there will he find the large inter-disciplinary laboratories and the intellectual ferment which will put him in touch with the latest advances and ideas in the field - ideas which he needs to absorb if he is to make correct decisions about his own future research program - and with the most recent techniques which he must master if he is to carry that program out. Each such temporary emigration represents the loss, which Europe can ill afford, of two productive years of a scientist's career, and it occurs on a large scale owing to the almost complete absence of comparable research centres in Europe.

2. Previous European initiatives

Some efforts have already been made, on a small scale, to remedy this state of affairs, e.g.

(a) An International Laboratory of Genetics and Biophysics has been organized by Dr. A. Buzzati-Traverso at Naples, and although at the present time only partly built it already functions in research and in the organization of advanced teaching courses. Its financial support is derived from Italian sources and from Euratom; up to now its staff has been for the most part Italian, but it is proposed for the future to recruit from all European countries.

(b) A series of meetings called by UNESCO led to the foundation of the International Cell Research Organization (ICRO). This body, which is at present dependent on UNESCO finances, has a world-wide scope, but one of its activities takes the form of a federation of a small number of European laboratories, aimed at a certain degree of pooling of resources (both material and intellectual) for mutual assistance

3. The origins of the present proposals

During the last six months a small group of senior European biologists has twice met at CERN in Geneva to try to make more comprehensive proposals, which are to be presented for discussion at a wider meeting in Ravello in September 1963 at the invitation of the Italian Physical Society. In brief, this group believes that the condition of fundamental biology in Europe is a serious one, and that the steps needed to improve it should include the provision of:

(a) better laboratory facilities,

(b) more posts, especially for younger workers,

(c) facilities for greater mobility.

The proposed scheme consists of two parts, which might be considered separately but which would certainly be mutually reinforcing. One part of the scheme takes the form of the foundation of a new central laboratory to act as a focus of the highest grade of biological research; the other, of a federal organization of existing laboratories.

II THE INTERNATIONAL LABORATORY

(for convenience referred to as CERB, by analogy with CERN)

4. The case for an international laboratory

Modern fundamental biology is an ill-defined field, most active at the borderlines between established disciplines. Experience has shown that advances are most likely to occur if a number of workers using diverse approaches and techniques can be located together in a single laboratory or in a group of laboratories. Such groupings fall outside the traditional pattern of biological departments; in some places the not altogether satisfactory name 'molecular biology' has been used to indicate the kind of inter-disciplinary approach which is needed.

There are good reasons for establishing large laboratories in fundamental biology, in the interests both of good research and of good training. In this field everyone is a specialist in some particular area or technique; the real advances come from cross-fertilization, from understanding other peoples' ideas and techniques and from day-to-day exchange of ideas - in fact from the collision of existing attitudes and methods - and all of these are best achieved by propinquity, by being able to talk to experts in fields other than one's own working down the corridor. As to training in research, it may well be argued that at the pre-doctoral stage a scientist should concentrate rather narrowly on the acquisition of a particular set of skills; but after the Ph.D., when he should be getting his own ideas and developing an independent research program, the young post-doctoral fellow needs to be in a large laboratory where work is going on in all aspects of the field. He will not be so well served by working in a small laboratory active in only a few areas - and in Europe today with very few exceptions such a laboratory is all he can hope to find; hence the almost universal demand for American post-doctoral fellowships which has already been mentioned. The argument for large institutes in this field is not the same as that in high-energy physics, where the need (now satisfied by CERN) was for a very powerful and expensive machine which could only be provided in a central institute; in biology the essential "plant" is rather an interacting group of differing techniques and talents, each only moderately expensive, but in sum costing so much as to be beyond most national resources, either financial or human. Quite apart from financial considerations there is not a single country in Europe, with the possible exception of the United Kingdom, which could muster the human resources and skills needed for such an inter-disciplinary institute even if existing laboratories could be totally deprived of staff. As things stand today, there is no laboratory, or group of laboratories, in Europe which covers more than about a third of the

field. In America, on the other hand, there are several excellent examples; for only in America is it possible to muster the necessary resources of money and of talent on a national basis.

The present proposal is for the establishment of an International Laboratory of Fundamental Biology (or Molecular Biology) in Europe, large enough to satisfy the criteria just outlined, and with possibilities of expansion into new areas as they develop. The arguments in favour of the proposal are the following:

(a) as already indicated, even if the larger European countries were prepared to devote the financial resources to establishing such laboratories on a national scale, it is very doubtful whether, having regard to existing commitments, any of them could muster the necessary human resources within their own boundaries; the smaller countries could certainly find neither. In any case it seems probable that national enterprises cannot be sufficient in sum to redress the balance between Europe and America. A pooling of European national resources might, however, achieve this.

(b) A first-class international laboratory in Europe would provide both short-term and long-term appointments for bright young biologists who would otherwise emigrate to America, where alone full-time post-doctoral research appointments are available in any numbers. It would bring more of the most able young scientists of Europe into the field; at present talent is recruited into fundamental biology on a much greater scale in America, largely owing to the presence there of many flourishing inter-disciplinary centres which have a powerfully attractive effect. It would offer post-doctoral training facilities at present unavailable in Europe; and it would also by its example stimulate the universities of Europe to establish positions and departments in which all these men could find permanent employment. It has been the experience of CERN that European physics has been stimulated in many ways, direct and indirect, by the presence of an international laboratory at Geneva; some pessimists predicted that it would starve the universities of good men, but in fact the reverse has occurred.

(c) The laboratory would have a rapid turnover of staff, and would do much to improve the mobility of scientists from one European country to another; it would be a source of the best candidates for professorial positions in all the European countries.

(d) Politically and economically the countries of Europe are drawing more closely together. The creation of international research institutes helps this process of unification, perhaps more than the creation of international organizations, since an institute means working together while an organization means only talking together.

5. Program of the laboratory

The new outlook on biology has emerged largely in consequence of our increased ability to investigate fine structure - macromolecular (protein and nucleic acid structures), topological (genetic material) and organizational (viruses, muscle, ribosomes). Many new techniques have contributed - X-ray diffraction, electron microscopy, spectroscopy, chemistry, fine-structure genetics. In consequence we can now discuss function in molecular terms, at least in principle. But in

most areas the new techniques have only been deployed in a fragmentary way - we know the structure of one kind of nucleic acid, of one or two proteins; the general principles of virus architecture have been elucidated; the broad outlines of parts of the genetic map of one or two organisms have been established. Today, the general character of biological organizations can be grasped; we can begin to apprehend the total behaviour of a simple organism such as E. coli in the broadest outline, with no details anywhere and with large areas of total ignorance (how do cells divide? how does the cell membrane work?). In principle there seems no good reason why, by the application of techniques which are already in our hands, we should not achieve a virtually complete understanding of such an organism - but to do this will demand an exploitation of these techniques on a very large scale.

The relation between function and structure in macromolecules like proteins is in no single instance understood in detail; we do not yet comprehend the action of a single enzyme in structural terms. Genetic maps need detailed plotting, in many kinds of organisms. In the fields of biosynthesis, of replication and of energy transfer only the main lines have been established. A major part of the activity of any laboratory of fundamental biology must be devoted for years to come to consolidation of the new territory, in other words to topics like the following, already flourishing but due for a long period of fruitful activity -

(a) Biological structure : proteins, nucleic acids, viruses, the genetic apparatus, mitochondria, ribosomes, membranes.

(b) Structure and function : protein - especially enzyme - function interpreted in structural terms; selective permeability of membranes; mechanism of action of ribosomes and mitochondria.

(c) Biosynthesis and replication : mechanism of protein synthesis, nucleic acid replication.

(d) Control systems : control of protein synthesis, nucleic acid replication etc.

(e) Energy paths in living organisms : photosynthesis, mechanism of energy transfer etc.

(f) The immune response and problems of molecular recognition.

Beyond these topics there are others clearly ripe for investigation in fundamental molecular terms, e.g.

(g) Differentiation and embryology : hitherto attention has been concentrated mechanisms common to different cells; we are now in a position to study ways in which cells of common origin come to differ. The process of differentiation has of course been studied extensively in the past, but for the most part only at the morphological level.

(h) Recognition : how does one cell recognise another? The recognition mechanism is quite obscure, but of fundamental importance in many fields - embryology, immunology, the central nervous system.

(i) Central nervous system : in spite of the extended classical studies of the neurophysiologists, our knowledge of the mechanism of the central nervous system of even very simple animals is exceedingly small; even so fundamental a question as the nature of memory (electric circuits, protein molecules, nucleic acid molecules?) remains without a definitive solution. Macromolecular structure, cybernetics, computer technology, the mechanism of selective permeability in membranes - all these are approaches to the problem which should begin to converge during the next decade.

(j) Cancer : increased understanding of the processes of differentiation and the mechanisms of control will make possible a new and fundamental approach to this apparently irreversible loss of control in cell proliferation.

Finally -

(k) Some of the fields which will be of the greatest importance in 10 years' time cannot be listed because they have not yet been thought of. Any plans for CERB should include provision for substantial extension, not of existing groups but by the creation of totally new ones.

In addition to its research facilities, CERB should be able to perform two other functions.

(a) To carry out advanced teaching and to organize symposia, summer schools etc The major part of such activities would be better undertaken in Naples (see para. 8c. below), nevertheless on particular occasions there might be special reasons why they should take place at CERB.

(b) To act as a focus for the proposed Federal Organization (see III below) and perhaps to provide a home for its central administration.

6. Staffing problems

(a) The scientific staff of CERB would fall into the following main categories:

(i) Senior long-term staff, generally heads of groups

(ii) Senior short-term staff and visitors (6 months to 2 years)

(iii) Junior staff and post-doctoral fellows.

The work of the laboratory could only be maintained at a high level if a substantial flow of short-term staff and visitors of very good quality were available. These would be attracted if the senior long-term staff were of the highest calibre.

(b) It follows that the first and crucial operation would be to secure the appointment of from six to ten senior staff of very high quality. It may be assumed that facilities, conditions of work, and equipment would be of the best standards; but to secure these key appointments it would be necessary to offer terms of service and salaries comparable in real purchasing power to those available anywhere in the world including America. Given a salary structure comparable to that of CERN, together wit tax and other concessions of the kind normally made available to international

organizations by the Swiss government, the question of remuneration should be soluble; but it would also be necessary to offer permanent tenure to the key men.

(c) Though the selection of a few key men for the senior positions would be of critical importance, and though the laboratory would certainly attract many senior visitors of very high quality from all over the world, CERB would essentially be a place for the young. It would be a training ground for post-doctoral fellows, and it would provide short-term appointments for young men awaiting permanent positions in the universities. The majority of the staff positions would last from three to six years, and this limited tenure would encourage a flow back to the universities.

(d) It would be fatal to impose any kind of geographical quota system in selecting staff. Quality should be the over-riding consideration, especially for the top-level appointments a few of whom might, for example, be recent emigrants to America who would welcome an opportunity of returning to Europe, or even American-born scientists.

7. Location

A number of possible sites has been discussed, but the general consensus is that Geneva offers a combination of advantages which cannot be equalled elsewhere. In Geneva CERB would be alongside CERN, a closely analogous organization, and there could be fertile interchange of ideas between physicists and biologists; the Swiss are used to the idea of international institutes and organizations and give them special facilities and privileges; it might be easier to secure the support of all European nations if the laboratory were built on neutral territory; the climate is good; language problems are minimal; many types of school are available; Geneva is near the centre of gravity of Europe and there are excellent communications.

8. Relationship to the International Laboratory of Genetics and Biophysics at Naples

(a) The Naples laboratory might be held to be, in embryo, an international institute on the lines envisaged. Many people think, however, that it cannot perform all the functions of such an institute, mainly for geographical reasons: Naples is too far from the centre of Europe, and may be inconvenient for many Europeans as a place to settle for a period of years owing to difficulties in language, schooling and climate. On the other hand, it already exists as an international group of scientists, internationally financed and active in several parts of the field; its location on the shores of the Mediterranean is ideal for obtaining much important biological material; and as a summer resort it is extremely attactive to visiting workers.

(b) The ideal would seem to be a very close association between CERB and the Naples laboratory; the latter might fulfil some of the functions of Woods Hole and Cold Spring Harbor in the United States. The association would be fostered by interchange of scientists, and perhaps by a few joint appointments and by the provision of fellowships tenable in either institute at will.

(c) Naples seems especially suitable for the organizing of summer schools and advanced courses. The most appropriate plan would appear to be that for the most part such activities should be concentrated at Naples, and they would be undertaken by CERB only if there were special reasons, such as availability of equipment etc., which made Geneva more convenient in particular cases. Special funds should be made available at the Naples laboratory to enable it to carry out the major part of these activities.

9. The scale of the project

The figures below have been set down as a very tentative basis for discussion. They are proposals for the initial scale of the project; it has been suggested above that provision should be made for later expansion into new fields as they become important.

(a) Size

Gross: 75,000 sq. ft. (7000 sq. m.)

Net (research space): 50,000 sq. ft. (4,650 sq. m.)

- say 12 research groups with 4,000 sq. ft. (370 sq. m.) each.

(b) Cost

Building, services, benches	$3 x 10^6
Initial equipment	$2 x 10^6
Annual budget	$2 x 10^6

(c) Staff

Graduate scientists	-	120
Other grades	-	50

A laboratory on this scale would be very cheap by comparison with international institutes which might be contemplated in many other fields. It would employ as many research scientists as does CERN but on a budget only 15% as big. Thus if CERB were set up alongside CERN, which at present is the only European laboratory in the sense we have used the term, the result would be to double the size, as well as greatly to broaden the scope, of the international research effort of Europe, th the load on the budgets of contributing nations would increase by only 15%.

III THE FEDERAL ORGANIZATION

(for convenience referred to as EFBO, European Federal Biological Organization)

10. Purposes

The purposes of the Federal Organization would be:

(a) To facilitate communication between scientists working in different laboratories, by making possible personal visits for exchange of ideas, and visits to make temporary use of facilities available only in a few places. If, for instance (to quote an example which arose at the last CERN meeting) a scientist in Copenhagen found that he wished to fractionate a glycogen preparation according to its molecular weight but that no analytical centrifuge was available in his neighbourhood, he should be able to get in touch with a number of the federated labs and ask whether and when he could be given a week's run on their machine, and he should have money available for the trip without having to put a special application through a slow-moving administrative channel.

(b) To provide a fair number of fairly junior post-doctoral posts, for people in the first ten years after their doctorate. These post-doctoral fellows should be sent to the labs. most appropriate to their work, even if these were not in their country of origin; thus an Italian might be directed to Britain, a Swede to Germany, and so on in all possible combinations. Neither the number of fellowships awarded to citizens of any particular country, nor the number of fellows sent to work in that country, should be related to the financial contribution of that country, such questions being decided on scientific merits alone. The salaries of the fellows should be determined in relation to the salaries of the countries in which they would work, the Organization Fellowships being good and attractive jobs, but not paid at rates which would be disturbing to good relations within the laboratory concerned. (They would thus not usually be financially comparable with salaries obtainable in America, but would be better than most young people can find at present in their own countries.)

(c) To provide a smaller number of more senior posts, for people who could be regarded as independent research leaders. These posts might be "at Professorial level", but their exact relationship to official University Professorships would have to be adjusted with reference to the academic system in the various countries.

(d) To conduct training courses. Some of these would be in specialized techniques; others in one advancing field of biology for students of other aspects of biology; others again aimed at introducing certain aspects of biology to students of subjects such as physics, physical chemistry, mathematics etc. Several such courses have already been held or planned for the Naples laboratory, and it is desirable that most of them should be held there, so that a tradition and expertise in organizing them should be built up; but in special cases they might well be held at one or other of the federated labs, or at the central lab.

(e) To organize small informal discussion groups or seminars, usually on quite specialized topics, and at a very informal "working" level. The smallest such meetings, involving only four or five people, could be regarded as falling under the heading of "communications" under para (a) above. Somewhat larger meetings should probably be organized usually at the Central lab., which would thus become a general forum for European biology at the working level.

11. The form of the Federal Organization

(a) A rather small number of leading labs, scattered throughout Europe, would be designated by the EFBO Council as Members of the Laboratory Federation. There should probably not be more than 10-15 (though the number might later increase), and they should be selected because they possess a fairly extensive range of expensive equipment, are very active in research, and have facilities available to offer scientists from other labs.

(b) A number of leading biologists (say about 100) would be designated as Individual Members of EFBO. They would not necessarily be attached to one of the Federated labs. They would, at a later stage, elect the EFBO Council Their Membership would carry the right to certain financial resources for travel and telephone communication, which would be at their free disposal subject only to the condition that it was used for communication with another EFBO Member or Laboratory. The magnitude of the sum would be adjusted according to the distance of the Member's location from the centre of gravity of Europe (which can be taken as Geneva). Smaller sums for such purposes would be provided for the junior EFBO Research Fellows.

(c) The day-to-day running of the Federation would be in the hands of a part-time Executive Secretary appointed by the Council (who would be a scientist assisted by full-time administrative secretary with a small clerical staff.

12. Financial implications

It is clearly impossible to make anything like firm estimates at this stage As a very rough guide to the orders of magnitude involved, one might make the following guesses:

(a) Communication expenses to Members and Fellows:

for each Member:	8 average return flights to Geneva	£240
	20 days subsistence at £4	80
	Telephone etc.	30
		£350

If this were provided for 100 Members and for 80 Research Fellows at half rate, this would amount to £49,000

(b) Research Fellows:

50 posts at £1,200 p.a.	£60,000	
30 posts at £1,800 p.a.	54,000	
10 posts at £3,000 p.a.	30,000	£144,000

(c)	Training courses	say	£35,000
(d)	Discussion Groups etc.	say	£10,000
(e)	Administration, secretariat etc.	say	£10,000
		Grand Total	£248,000

Thus the whole Federation would cost annually about a quarter of a million pounds, (say $700,000) when fully operating; presumably in the first few years this sum would be considerably reduced.

It might be shared between the nations roughly as follows:

Four "large" nations (Britain, France, Germany, Italy) 60%

Five (plus) "small" nations (Switzerland, Belgium, Holland, Denmark, Sweden, Norway?, Poland?, Czechoslovakia?, Hungary?, Jugoslavia?) 40%

Thus, even if the scheme was started by the four "large" nations alone, their share would not be more than £60,000 ($170,000) each for the full scheme, and perhaps two-thirds of that in the first two years. If all the nations enter, the contribution of the large nations would not be more than £40,000 ($105,000).

IV CONCLUSION

13. Proposals for action

If the ideas outlined above commend themselves, it will be necessary to translate them into action. A number of questions would require immediate discussion.

(a) Provisional form of organization. The affairs of the organization should be controlled by a Council consisting of scientists. Its eventual composition would depend on the national affiliations of the organization, which might be arranged either through some existing international body, or directly to governments, or (probably better) through National Academies or Research Councils. A provisional Council should be set up at once, perhaps composed for the most part of those scientists who have taken part in the initial discussions.

(b) Membership. It is envisaged that all the countries taking part would be European or in the areas bounding Europe; they would not be limited to any of the existing European groupings (such as NATO, the Common Market etc.)

(c) Raising funds . It is assumed that funds would be raised by direct approaches to governments or through National Academies. The sums involved would be, for CERB 5.10^6 initial expenditure, 2.10^6 annual budget; for EFBO an annual sum eventually rising to $0.7.10^6$. Consideration should perhaps be given to soliciting funds from international firms for the initial capital expenditure.

A small fund would be needed as soon as possible for initial administrative expenses, arranging discussions etc.

14 August, 1963

APPENDIX

The following is a (hopefully complete) list of those who took part in the Geneva meetings on 28 March and 28 June 1963:

Dr. T. Weis-Fogh (Denmark)
Dr. J. Monod (France)
Dr. R. Monier (France)
Prof. M. Delbrück (Germany)
Prof. H. Friedrich-Freksa (Germany)
Dr. A. Cavalli-Sforza (Italy)
Prof. A. Engström (Sweden)
Dr. A. Tissieres (Switzerland)
Prof. C. H. Waddington (United Kingdom)
Dr. J. C. Kendrew (United Kingdom)
Dr. R. B. Livingston (U.S.A.)
Prof. L. Szilard (U.S.A.)

Dr. V. F. Weisskopf (CERN)
Prof. G. Bernardini (CERN)
Dr. Baarli (CERN)
Mr. S. A. ff Dakin (CERN)

Dr. A. A. Buzzati-Traverso (International Laboratory of Genetics and Biophysics, Naples)

Dr. M. M. Kaplan (WHO)