# RECOMMENDATIONS FOR THE UNDERGRADUATE MATHEMATICS PROGRAM FOR STUDENTS IN THE LIFE SCIENCES

An Interim Report of

The Panel on Mathematics for the Life Sciences

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#### 1. Introduction

The Panel on Mathematics for the Biological, Management, and Social Sciences was primarily concerned with the mathematics curriculum for prospective graduate students in those fields. Their recommendations, which were published in the 1964 CUPM report Tentative Recommendations for the Undergraduate Mathematics Program of Students in the Biological, Management, and Social Sciences (BMSS), were meant to serve as a basis for discussion and experimentation. From these discussions it became apparent that (1) some of the recommendations would be very difficult for mathematics departments to implement, (2) a different program was needed for the terminal bachelor's degree, (3) the single program presented would not seem to be ideally suited to the diverse fields included in the BMSS disciplines, especially at the advanced level. In response to these findings, CUPM decided to concentrate on individual disciplines and, as a first step, appointed the present Panel on Mathematics for the Life Sciences, charged with making recommendations for the mathematical training of all undergraduate life science students, not only pregraduate stu-(Here, life sciences are taken to mean agriculture and renewable resources, all branches of biology, and medicine.)

The Panel on Mathematics for the Life Sciences has undertaken, through conferences and extensive consultation with leaders in the biological field, to learn from them what mathematics they consider to be necessary for their students. In particular, the Panel held several meetings with representatives of the Commission on Undergraduate Education in the Biological Sciences (CUEBS). After the biologists had specified the mathematics needed by students of biology, the Panel proceeded to describe mathematics courses that contain this mathematics. This report is the outcome of these consultations and studies. Finally, the Panel held a special conference in which a preliminary draft of this report was submitted to a group of biologists for comment and criticism. The discussions and conferences with the biologists have emphasized a serious fourth problem: (4) heavy requirements in chemistry, physics, and biology make it difficult for a major in the life sciences to add mathematics courses to his program.

In preparing this report, the Panel considered all four of the problems mentioned above, and it presents herewith its recommendations for a basic mathematics core for life science undergraduate majors (see Part I) and for certain more specialized studies (see Part II).

Part I describes a basic core of mathematics for all undergraduate majors in the life sciences. In Section 2 we describe the level of mathematical preparation on which this core is based. In Section 3 the recommendations for the mathematical core are stated and justified, and in Section 4 we treat some of the principles and details of implementation of this core.

The Panel feels strongly that every life science major should gain substantial experience with computers (digital, analogue, and hybrid). We feel that the time is ripe now for a detailed treatment of the role of the computer in the undergraduate program, especially as it relates to the life science student. This accounts for the detail found in Section 5.

Part II outlines certain more specialized studies which this Panel believes will be important for some students in mathematics as well as for students in the life sciences. Section 6 describes a program for undergraduate preparation for the study of biomathematics at the graduate level. A description of an upper-division course focusing on the building of mathematical models in the life sciences and some suggestions for its implementation appear in Section 7.

Certain of the courses in <u>A General Curriculum in Mathematics</u> for <u>Colleges</u> are cited frequently; their descriptions appear elsewhere in this COMPENDIUM.

#### I. MATHEMATICS FOR UNDERGRADUATE BIOLOGY MAJORS

# 2. Background of the Students

In recent years much effort has been expended to improve mathematics education in the elementary and secondary schools. Several programs of improvement in secondary schools have already had considerable effect and we hope that they will have a great deal more. In particular, we hope that mathematics courses in the secondary school will contain a judicious mixture of motivation, theory, and applications. For the purposes of our discussion it is assumed that the student is acquainted with both the algebraic and geometric aspects of elementary functions (see the description of Mathematics 0 in Commentary on A General Curriculum in Mathematics for Colleges, page 75 ); moreover, we assume that the student has been exposed to the idea of a set, mathematical induction, binomial coefficients, and the summation notation. Thus, our discussion applies to students in the life sciences who are prepared to begin their collegiate mathematics with a calculus course, although departments of mathematics may have to offer precalculus courses in order to prepare some students adequately for this program.

Historically, mathematics has been closely allied to the physical sciences, especially to physics. In secondary schools and in elementary undergraduate courses, applications of mathematics have traditionally been limited to the physical sciences. Therefore, it is not uncommon for students whose interests lie in other fields to enroll in a bare minimum of mathematics courses. If students are to possess the prerequisites stated above, proper counseling both in

high school and in college is imperative. Students must be made aware of the doors that are closed to them in fields of the life sciences, as well as in the physical sciences and engineering, when they terminate their study of mathematics prematurely. We hope that this message will be transmitted to guidance and counseling personnel, and we urge all concerned to give attention to ways by which counseling of potential life science students can be improved in their locality.

#### 3. The Basic Core: Recommendation and Justification

The Panel on Mathematics for the Life Sciences has considered the problem of recommending a basic core of mathematics courses for students in the life sciences. The prospective life science major, whatever his specialty or career goal, now needs more mathematics than was recognized to be the case a few years ago. As a result of its study, the Panel concludes that the mathematical core for the undergraduate life science major should include one year of calculus, some linear algebra, and some probability and statistics.

More specifically, the Panel believes that this core can be provided by the following courses: Mathematics 1 (Calculus I), Mathematics 2 (Calculus II), Mathematics 3 (Elementary Linear Algebra), and Mathematics 2P (Probability). Outlines for all of these courses can be found in Commentary on A General Curriculum in Mathematics for Colleges. In addition, we recommend that each student gain some experience in the use of an automatic computer in the first two years of study. This might come in the form of a sequence of laboratory exercises (see Section 5) in which algebraic language problems are developed and run. Institutions which do not have computation centers may be able to provide service via remote terminals or through the courtesy of nearby organizations. This permits the use of computing algorithms, lecture demonstrations, or problem assignments in biology and mathematics courses at appropriate times.

The recommendations are consistent with the findings of the two life science commissions sponsored by the National Science Foundation. In Publication No. 18 of the Commission on Undergraduate Education in the Biological Sciences, "Content of Core Curricula in Biology" (June, 1967), pp. 30-31, we find: "Fourth, we recommend that careful attention be given to relating biology courses to the background of the student in mathematics, physics, and chemistry...in mathematics, at least through the level now generally taught as calculus, ...some background in physical and organic chemistry." This recommendation clearly indicates that a full-year sequence of calculus (including multivariable calculus) should be taken by a biology major. In this same publication the curricula for biology majors at Purdue University, Stanford University, North Carolina State University, and Dartmouth College are presented. At three of these institutions, one year of calculus is required in addition to some probability and linear algebra. In the remaining institution,

additional calculus is required instead of "finite mathematics" (here taken to mean basic linear algebra with applications--such as Markov chains--and combinatorial probability).

In 1967 the Commission on Education in Agriculture and Natural Resources (CEANAR) charged a committee "to recommend mathematics requirements to be met ten to fifteen years hence in undergraduate curricula for Agriculture and Natural Resources." In its report\* this committee chose to state its recommended requirements almost entirely in terms of courses described in the CUPM report A General Curriculum in Mathematics for Colleges. Mathematics 1, 2P, and some computer instruction are recommended for majors in all areas covered by CEANAR. Moreover, for students majoring in technology programs, Mathematics 2 and Mathematics 7 (Probability and Statistics) are recommended; to this students majoring in science programs should add Mathematics 3 and Mathematics 4 (a third course in calculus).

There are other good reasons for recommending this core of four mathematics courses: 1, 2, 3, and 2P. First of all, these are standard mathematics courses whose broad availability should facilitate implementation. Secondly, this curriculum is flexible enough to accommodate a student who may decide to change his major. For example, if in the first year or two he enters a discipline that involves more mathematics, he will not have lost any time. Thirdly, compressing this material into a shorter three-course sequence is unwise from a pedagogical point of view. Very few students are capable of gaining even a minimal mastery of calculus in a one-semester course, and at least one semester is needed to cover a significant amount of linear algebra or of probability. Moreover, if a student eventually decides to take more advanced mathematics and still continue in the branch of life sciences he originally chose, he will have the appropriate prerequisites. In this connection we discuss in Section 7 the role of a course in the applications of mathematics to the life sciences for the research-bound student. Since such a course involves relatively advanced mathematics, it will carry certain further mathematical prerequisites beyond the core itself.

Preparation for research in certain areas of biology will demand competence in mathematics equivalent to the Master's degree level. Some biologists have even asserted that a student who has a Bachelor's degree with a major in mathematics and appropriate courses in chemistry and physics would be welcomed as a graduate student in biology, even though he had had no courses in biology. Further development of this line of thought is found below in Section 6 on biomathematics.

<sup>\*</sup> See "Undergraduate Education in the Physical Sciences and Mathematics for Students in Agriculture and Natural Sciences," pp. 32-35. This report is available from the Division of Biology and Agriculture, the National Research Council, 2101 Constitution Avenue, Washington, D. C. 20418.

Although the Panel feels that an offering to life science students of fewer than four semesters of mathematics course work will not meet the objectives laid out by the life scientists whom we have consulted, we must recognize that this amount of mathematics is more than will be accepted by some of them as a requirement for all undergraduate life science majors. We have been urged to consider what can be done with three courses. Any three-course program will lose some of the desirable features described in the last paragraphs. We present several options of three courses and point out some of the advantages and shortcomings of each:

- (1) Mathematics 1, 2, 3;
- (2) Mathematics 1, 3, and 2P;
- (3) Mathematics 1, some appropriate interweaving of 2 and 3, and 2P;
- (4) Mathematics 1, 2, and one semester of finite mathematics;
- (5) An integrated three-semester sequence, specifically designed for life science students and built around finite mathematics, calculus through multivariable calculus, probability, and statistical inference.

It may be well to observe that each of the above options could lead to completion of the core in graduate school, if this were desired. This could be done with standard courses in the case of options 1 or 2 or with one or more special courses in the case of other options.

Some features of the options are highlighted in the following

	Number of special mathe-matics courses required	Number of core subjects omitted entirely	Full year of calculus included
Core	0	0	Yes
Option 1	0	1	Yes
Option 2	0	1	No
Option 3	1	0	No
Option 4	1	0	Yes
Option 5	3	0	No

The first column measures to some extent the extra load placed on the mathematics department by each option. The offering of each special course involves planning and coordination activities and in a small institution may have a high cost per student because of limited enrollment.

Any option involving special courses inevitably raises the possibility of requiring additional course work (or equivalent thereof) to provide the proper prerequisites for further study in mathematics. The severity of this effect can be assessed only in the context of a

given institution, a given spectrum of courses, and some designated group of students at a given skill level.

Column 3 relates to the remark that offering less than a full year of experience in calculus seems to be insufficient.

The Panel feels that option 1 is the least undesirable, since 1) probability can be added by many students as an elective, 2) this sequence is easier for most mathematics departments to staff than one involving probability, and 3) many schools now offer linear algebra as an integral part of the calculus sequence. Option 2 is considerably less desirable than option 1, since it omits multivariable calculus, a topic that the Panel feels is vital to modern biology (see the previous reference to CUEBS Publication No. 18).

Options 3, 4, and 5 share the disadvantage of having no efficient continuing mathematics course which can be used to complete the core material.

Options 3 and 4 may be desirable for larger institutions in which the mathematics and biology departments can work out arrangements for an additional elective special course which would complete the core. If many departments were to adopt one of these options, graduate departments might choose to require that the core be completed in graduate school. Care must be exercised in implementing option 3 to include topics in calculus that are needed in physics and chemistry prerequisites to biology courses.

The essential feature of option 5 is to construct a threesemester sequence, illustrated by life science examples and containing essential material from the calculus, while interweaving some probability, statistics, and linear algebra in an integrated format. However, in situations where there are substantial numbers of students who have not had appropriate mathematics courses by the time they begin graduate work in biology, the departments of biology and mathematics may wish to collaborate in designing special programs. It is more important for a graduate biology student to understand the basic concepts of the mathematics he uses than to develop the computational skills needed by a physical scientist or engineer. By taking advantage of the maturity, strong motivation, and established field of interest of these students, satisfactory programs (such as option 5 above) stressing the understanding of these mathematical concepts could be designed in such a way as to require less time than the standard undergraduate courses.

Such cooperation involving another department with the mathematics department has proved successful in the past. This was particularly true in some areas of the social sciences, where the demand for such programs eventually diminished when the great majority of entering graduate students came with a sufficient mathematical background. The research needs of some biology departments have motivated them to hire biomathematicians, who could participate in teaching the graduate programs envisioned here.

#### 4. The Basic Core: Implementation

The Panel recommends that all life science majors be required to complete two semesters of calculus and one semester each of linear algebra and probability (including some statistics). These courses, Mathematics 1 and 2, Mathematics 3, and Mathematics 2P, are discussed in detail in Commentary on A General Curriculum in Mathematics for Colleges, page 33. In many undergraduate curricula these courses must serve many needs: prospective biology majors find themselves in the same classes with students from a wide variety of disciplines (such as engineering, economics, business administration, one of the physical sciences, or even mathematics). When this is the case, it is unlikely that special emphasis on biological applications will be featured in any part of this four-course program. A few institutions, however, can afford to present all, or some part, of this core program exclusively for students whose main interests lie in the life sciences. We do not address ourselves to the task of making detailed recommendations to this group since we feel that an institution offering a special mathematics core for life scientists will wish to take advantage of local features and design a hand-tailored program. Between these extremes, we find institutions able to give varying amounts of special attention to life science orientation in the mathematics core. Our suggestions below are directed primarily to this group. We expect that there will be considerable latitude in the extent and manner that these recommendations are utilized.

The life science major should be given more consideration than has been the custom in the past, even by the first group of institutions that cannot afford to provide special courses or sections of courses. Traditionally, the applications given in calculus, for example, are almost exclusively chosen from the physical sciences. With the rapid growth of the life sciences, it is only reasonable that increased emphasis be given to illustrative examples from this field, even in a calculus course in which the interests of most of the students lie elsewhere.

We now proceed to our comments on the modifications necessary to make the core courses more suitable to the needs of the life science students.

[Editor's note: In the case of Mathematics 1 and 2, the Panel's suggestions relative to the original course outlines in the 1965 General Curriculum in Mathematics for Colleges have been incorporated into the revised outlines in Commentary on A General Curriculum in Mathematics for Colleges (1972). Thus, we refer the reader to the new outlines.]

Mathematics 1. Calculus I.

See Commentary on A General Curriculum in Mathematics for Colleges, page 44.

Mathematics 2. Calculus II.

See Commentary on A General Curriculum in Mathematics for Colleges, page 51.

#### Mathematics 2P. Probability.

Relative to this course, an outline of which is given in Commentary on A General Curriculum in Mathematics for Colleges, page 76, we make the following comments:

- a. With respect to (1) of the GCMC description, the introduction of the probability axioms should be properly motivated by the frequency interpretation (see Hodges, J. L. and Lehmann, E. L. Basic Concepts of Probability and Statistics. San Francisco, California, Holden-Day, Inc., 1964) in order to connect these concepts with the empirical traditions of the life sciences.
- b. With respect to sections (2) and (3), some time could be saved by merging the sections so that the Poisson and normal distributions would be introduced as limits of the binomial distribution. For the normal approximation, we feel that the most efficient presentation—in consideration of both time spent and student understanding—would be to discover numerically that a sequence of binomial cumulative distribution functions, after the usual normalization, tends to the normal distribution (see Mosteller, F. R., et al. Probability with Statistical Applications, 2nd ed. Reading, Massachusetts, Addison-Wesley Publishing Company, Inc., 1970).
- c. We feel that two-state Markov chains, as a generalization of sequences of Bernoulli trials, should be included in the course. The presentation of these could begin in the discussion of conditional probability in section (1). A solution for the limiting distribution of the process and a numerical demonstration of convergence to this limit should then follow the other limit theorem discussions, taking up one or two lessons.
- d. If Mathematics 3 is included as a prerequisite for Mathematics 2P, topics such as the Markov process in (c) can be presented more efficiently and in greater depth in matrix form.

A modified course description of 2P appropriate for students in the life sciences can then be given as follows:

1. Probability as a mathematical system. (11 lessons) Variability of experimental results, sample spaces, events as subsets, probability axioms and immediate consequences, finite sample spaces and equiprobable measure as a special case, random variables (discrete and continuous), conditional probability and stochastic independence, Bayes' formula. Sequences of independent Bernoulli trials, two-state Markov chains.

- 2. Probability distributions. (15 lessons) Characterization of probability distributions by density and distribution functions, illustrated by the binomial and uniform distributions. Expected values, mean and variance. Chebychev inequality, Poisson distribution introduced as approximation to the binomial, normal approximation to the binomial, Central Limit Theorem, stationary distribution of a simple Markov chain, Law of Large Numbers, discussion of special distributions motivated by relevant problems in the life sciences.
- 3. <u>Statistical inference</u>. (13 lessons) Concept of random sample, point and interval estimates, hypothesis-testing, power of a test, regression, examples of nonparametric methods, illustrations of correct and of incorrect statistical inference.

#### Mathematics 3. Elementary Linear Algebra.

[Editor's note: Here the Panel on Mathematics for the Life Sciences referred the reader to Mathematics 3 (Linear Algebra) in the 1965 General Curriculum in Mathematics for Colleges and made several suggestions for modifying this course in order that it be more appropriate for students in the life sciences. Some of the Panel's suggestions were incorporated into the revised version of Mathematics 3 (Elementary Linear Algebra) which appears in Commentary on A General Curriculum in Mathematics for Colleges, page 55.

Another appropriate course, featuring many of the Panel's suggested modifications, is Mathematics L (Linear Algebra) of A Transfer Curriculum in Mathematics for Two-Year Colleges, page 231.

# 5. Recommendations for Computing

#### Automatic Computing

We recommend that every undergraduate in the life sciences have some contact with an automatic digital computer, and that this contact begin as early as possible in his program of study. Among the many bases for this recommendation are: that many mathematical models in the life sciences, as witnessed by the current technical literature, are procedural in nature and are best studied with the computer; that many analytic techniques of experimental biology are of practical value only when applied with an automatic computer; and that the automatic computer could play an important role in undergraduate biology lectures and laboratory if the students were prepared to make use of it.

This recommendation is stated separately from our recommendation of a CORE mathematics program for the life sciences student because we feel that experience in automatic computing will become part of a general liberal arts requirement rather than part of a major in either biology or mathematics. In many colleges a first course in computing is not the responsibility of the mathematics

department but of a computer science department or a department in which computer applications are already numerous. As applications in subject-area courses increase, the need for an introduction to computing separate from the courses in biology, chemistry, mathematics, and physics may disappear.

CUPM has established a panel to consider instruction in computer science and the use of computers for instruction in mathematics. Our recommendations may be used to select options from their recommendations when they become available and to set an amount of experience appropriate for the biology major. [See Recommendations for an Undergraduate Program in Computational Mathematics (1971) and Recommendations on Undergraduate Mathematics Courses Involving Computing (1972).]

It should be noted that our basic recommendation in automatic computing is minimal. For example, the recommended experience does not include the introduction to analog or to hybrid analog-digital computing, and it includes only the briefest view of the complex problems of numerical analysis. We hope that some analog experience could be gained in advanced biology laboratory work. We also urge that the student be cautioned against the misuse of computing techniques, to avoid any tendency toward confusing the mastery of a programming language with an adequate knowledge of mathematics.

We suggest two alternatives for a one-semester course by which this computing experience can be gained. These are described in detail in Section 9. [See also the course C1 in Recommendations for an Undergraduate Program in Computational Mathematics, page 563.] The first alternative is an informal program of weekly lectures and discussions of one hour extending through the freshman year, supplemented by a large number of assigned programming exercises to be developed and run at the student's convenience. It would amount to about one half a semester course for which credit might or might not be given. The second is a formal 3-semester-hour course with five or six assigned programming exercises, to be taken normally in the sophomore year. These suggestions will be stated more completely, but first it seems proper to point out the advantages and problems of the two approaches.

Basic computer programming skills have commonly been acquired through programs of self-instruction. Many computer scientists feel that it is best to provide the student with a computing facility, some reference manuals as to its use, an introductory lesson or two, and then to stay out of his way as he practices by developing programs which are of particular interest to him or are relevant to his other studies. They would not give formal academic credit for this work. We would temper this plan by continuing the lessons or discussion periods beyond the most basic introduction and assigning some specific programs to insure that the student is exposed to various classical and valuable computing techniques. Even with this modification, the plan has the obvious advantage of not making significant demands on either faculty or student time, an important factor

considering the already heavy required curriculum in the life sciences. It reasonably could, in fact, be carried out without academic credit. Unfortunately, the student freedom which permits this implies a lack of control over facility usage, so this alternative can prove expensive in machine charges.

The second alternative, a formal semester course introducing the student to computing, has the disadvantage of adding to an already exacting schedule. A most troublesome additional problem is that we do not feel that the introductory course in many computer science programs is appropriate to students in the life sciences. In that they are planned to set the foundation for further work in mathematics or computer science, they often do not cover computing applications adequately. The course we propose may, therefore, add an additional load on the mathematics faculty, particularly distasteful because of its partial redundancy. A formal course has two powerful advantages, however. The students will be brought to a higher level of competency and machine charges per student can be kept relatively low. This applied computing course could be relevant to fields beyond the life sciences, of course, and could be planned to serve all undergraduates not intending to specialize in computer science.

#### Continuing the Computing Experience

Given the contact with computers which we recommend, the student will be able to use the computer to extend his studies both in mathematics and in the life sciences. Experience has shown that he will, in fact, do so. It is important, therefore, that facilities be available to support this use. While accurate estimates of potential use are impossible, many students will continue computing at about the rate begun in the introductory course if given a chance.

Of importance in taking proper advantage of the student's computing experience is the use of computing exercises and demonstrations whenever relevant in the regular biology curriculum. We point out that the relevance is striking in many areas. For example, a course in population genetics could use a computing facility as a regular laboratory instrument, and some topics such as genetic drift are difficult to present without the computer. Too often, the student will recognize this value before the instructor. It is essential that every effort be made to introduce the potential of applied computing, as well as all other mathematical techniques, to the life science faculty. Among the possible means for this faculty education are: the involvement of the life science faculty in the program of computer instruction, the preparation and distribution of materials and understandable manuals on local computing facilities, the preparation and distribution of computer demonstration and laboratory materials for specific courses, and, most important, a demonstration of interest by the mathematics or computing faculty in biological research along with patient collaborative effort with life scientists.

#### II. SPECIALIZED STUDIES

## 6. Undergraduate Preparation for Biomathematics

The present state of biomathematics is such that one cannot expect to study this subject as an undergraduate. The best that can be expected of an undergraduate curriculum is to provide the student with a strong background in mathematics, physics, chemistry, and biology as preparation for graduate study. Indeed, because of its dependence upon the other sciences, biology may be emphasized the least in the undergraduate program and then, presumably, the most in the graduate program. In most colleges the undergraduate who is enrolled in such a program will be regarded as a major in mathematics.

Before going into details concerning the mathematics component, we consider some general principles on which a biomathematics program should be based.

- (1) About one third of the student's undergraduate curriculum will be devoted to the mathematical sciences, including statistics and computing. A second third will be devoted to physics, chemistry, and biology, and the remainder to the humanities and social sciences to fulfill degree requirements. Since the student will normally be a major in mathematics, it is important that departments of mathematics allow their majors to choose electives freely in the biological sciences.
- (2) Many institutions give several different versions of basic courses in the sciences. The crucial difference is usually the extent to which mathematics is used. It is vital, therefore, that the student plan his program so as to take the most sophisticated version of each course that is available. This injunction applies especially to courses in physics and in physical chemistry.
- (3) Very few universities have a department of biomathematics. Most graduate students who study this subject will be enrolled in some life science department. It is essential, therefore, that the undergraduate program of such a student include enough courses in biology for him to gain admission to a graduate program in a life science area. This need not imply that the undergraduate program must contain very many courses in biology. Many leading life science departments will admit a person with as strong a background in mathematics and chemistry as is contemplated here if he has had as few as four semester courses of undergraduate biology and some may even require no undergraduate biology.
- (4) It is neither practical nor desirable for a student to make an irrevocable commitment to a particular specialty early in his college career. As was stated in the preceding paragraph, a student who elects the program that is being presented here should be qualified for admission to a graduate life science program. He may then choose to specialize in some area of biology other than

biomathematics. On the other hand, he may decide to do graduate work in mathematics only. By adding a substantial course in abstract algebra to the program described below, he should become eligible for admission to most graduate departments of mathematics.

(5) Of the natural sciences, chemistry will receive the greatest emphasis. Courses in organic chemistry and the strongest possible course in physical chemistry will certainly be included in the program; biochemistry may also be included, although some schools prefer to introduce this topic at the graduate level.

With these considerations in mind, we now turn to the mathematics in this program. The computer experience and the core of four mathematics courses discussed in Sections 4 and 5, as well as in the GCMC report, form the foundation of this preparation. To this we add semester courses in Calculus, Advanced Multivariable Calculus, Statistics and Probability, and a two-semester sequence of Real Variable Theory, as described in Mathematics 4, 5, 7, 11, and 12 in Commentary on A General Curriculum in Mathematics for Colleges, page 33 The GCMC Mathematics 10, preferably in the version described in Section 7 below, and a Numerical Analysis course (see Mathematics 8, page 83) should be included.

A biomathematician will need to know more mathematics than is presented in this program. For example, he will have only a touch of differential equations in Mathematics 2 and 4, and will ordinarily need considerably more probability and statistics than is covered in Mathematics 2P and 7. Thus, his graduate program will include additional work in mathematics, although it will consist predominantly of biology. A biomathematics student (as well as other biology graduate students) may wish to follow a plan that is currently used in many other graduate fields: electing one mathematics course each term until the Master's degree requirements in mathematics are met. A few biomathematicians may wish to include course preparation for the Ph.D. degree both in mathematics and in the life sciences.

#### 7. A Course in Applications of Mathematics in the Life Sciences

A course in applied mathematics (Mathematics 10) is briefly described in Commentary on a General Curriculum in Mathematics for Colleges. The essential feature of this course is "model building and analysis" coupled with appropriate interpretation and theoretical prediction. The philosophy of this approach to applied mathematics is well stated on page 92, and we recommend the reader's careful attention to that material in order to establish the necessary point of view for consideration of a course entitled Introduction to Applied Mathematics: Life Sciences Option. [See also the 1972 report Applied Mathematics in the Undergraduate Curriculum, page 705.

Three versions of a model-building course are developed in detail in <u>Applied Mathematics in the Undergraduate Curriculum</u>, page 705. We consider here another version designed for students with a particular interest in the life sciences.

Applications of mathematics in the life sciences may be classified basically into two broad categories, <u>deterministic</u> and <u>stochastic</u>. Moreover, a third category should also be added, that of <u>mixed</u> models, wherein the particular phenomenon under consideration may be modeled in either deterministic or stochastic fashion.

Specific prerequisites for a life sciences version of Mathematics 10 will vary according to which topics are studied, but in any case they include the basic core, supplemented suitably--usually with additional work in calculus and differential equations (Mathematics 4 and 5) and perhaps with additional work in probability and statistics (Mathematics 7).

One feature of life science models is that the mathematics used tends to be either almost trivial or relatively advanced; good "junior-level" models seem hard to find. Thus, for the present, successful offering of a life science version of Mathematics 10 would seem to call for an instructor who is well qualified both in mathematics and in the life sciences. Moreover, this instructor should be broadly interested and knowledgeable in applied mathematics and, in particular, in model building. Earlier CUPM reports have recommended that, in the absence of such a member of the mathematics faculty, Mathematics 10 should not be offered. It has been found in a number of institutions, however, that a viable alternative may be obtained through a joint effort of an interested member of the mathematics faculty and specialists in various other disciplines. Both mathematics and biology can thus be adequately represented and the essential feature of strong motivation is present. An undergraduate seminar led jointly by such a faculty team, with models being proposed by the members of the class, has been found to work well in practice. A format suitable for this purpose has been described by S. A. Altman ("A Graduate Seminar on Mathematics in Biology." CUEBS News, Vol. V, No. 1, October, 1968, pp. 9-10).

An institution with a strong, modern biological sciences department should be able to offer a course such as that suggested above. This is especially true if the members of the life sciences faculty are interested in bringing in mathematical ideas and there is also present at the institution a mathematics cadre interested in the applied mathematical sciences. Several members of the Panel have had some experience in offering courses based on model building in both physical and life sciences. Such an approach revolves around an artful use of the case study method, with the class thereafter pursuing the mathematical structure, detective story fashion, wherever it may lead. Usually the mathematical structure itself is developed en route only to the extent that is demanded by the model, although appropriate avenues are of course indicated to the students for following up any particular portions of the mathematics that may especially interest them.

We conclude this section with a few general comments concerning mathematical models in the life sciences.

Model construction consists, for the mathematician at least, of laying down an appropriate axiom system, either as a formal set of axioms or by means of a system of defining equations. Equations of motion in physiology and biophysics, linear algebra formulations of protein sequences or of population state vectors, dynamical systems describing population interactions, combinatorial models of genetic phenomena or of macromolecule configurations are all instances of such axiom systems. Once an appropriate mathematical structure (i.e., a set or sets with operations) has been specified, the further analysis proceeds within the mathematical structure, emerging at certain strategic times with interpretations or theoretical predictions drawn from the mathematical deductions themselves. To the extent that these conclusions are in accord with those aspects of the actual phenomenon that are regarded as significant in that context, so, too, may the original mathematical model be regarded as a good one. One of the virtues of such a procedure, as noted in the GCMC report, is that "the attempt to build a satisfactory mathematical model (often) forces the right question about the original situation to come to the surface." It is clear, therefore, that the modeling process is often one of successive approximations, hopefully convergent to a sound theory at some stage. An essential part of the instructor's responsibility would seem to be conveying to the life sciences student the realization that once an appropriate mathematical structure has been determined via axiomatization, he can work strictly within this mathematical structure, to come back in the end with certain interpretations and theoretical predictions relevant to the particular life science phenomenon under consideration. All too often there seems to be what amounts to almost a mental block in many biologists' thinking that precludes their leaving the realm of empirical laws and statistical description (mathematics as curve fitting) to work within the mathematical structure itself. The great significance of this latter mode of procedure for the astonishing growth of the physical sciences during the past half century has been well described by Mostow, Sampson, and Meyer (Fundamental Structures of Algebra. New York, McGraw-Hill Book Company, 1963. Preface) in the following terms:

"The great evolution of the physical, engineering and social sciences during the past half century has cast mathematics in a role quite different from its familiar one of a powerful but essentially passive instrument for computing answers. In fact that view of mathematics was never a correct one.... Its inadequacy is becoming increasingly apparent with the growing recognition that mathematics is at the very heart of many modern scientific theories—not merely as a calculating device, but much more fundamentally as the sole language in which the theories can be expressed. Thus mathematics plays an organic and creative part in science, as a limitless source of concepts which provide fruitful new ways of representing natural phenomena."

The objective of the proposed course in applications of mathematics in the life sciences is to develop in students the capability to utilize these powerful mathematical methods in the fashion indicated above.

#### III. APPENDICES

# 8. Course Outlines for Mathematics 0, 1, 2, 3, 2P

See Commentary on A General Curriculum in Mathematics for Colleges, page 33.

#### 9. Course Outlines for an Introduction to Computing

Following are outlines of programs for the two alternatives suggested in Section 5. [See also the course C1 in Recommendations for an Undergraduate Program in Computational Mathematics, page 563.]

# Introduction to Computing: Alternative 1

The course is comprised of weekly or biweekly one-hour lecture and discussion meetings and ten or more student programming exercises. It is set primarily for freshmen, although, if done with informality, it could involve the entire life science community, including the faculty. The prime goal is the development of basic applied programming skills in an algebraic language. There is little concern for the logical organization of the machine or detailed representation of information in the computer.

## <u>Materials</u>

- 1. An introduction to a common algebraic language, such as FORTRAN, PL/1, ALGOL, or the conversational languages BASIC, CAL, JOSS.
  - 2. A reference for elementary numerical methods.
  - 3. A reference for statistical methods.
- 4. A reference for simulation and other general problemsolving techniques.

# <u>Facilities</u>

Computing facilities will be required to handle the submittal

of approximately 60 batch process jobs of very short duration per student over the period of the course. If a time-shared facility is available, about 20 to 25 console hours will be required equivalently. The conversational use of a time-shared facility is to be preferred from the point of view of efficient use of student time.

#### Faculty

In order to assure relevance of the exercises to the life sciences, it would be desirable for an instructor from the life sciences faculty to handle the lectures and discussions for the life science students in this course, initially, with the advice and assistance of a member of the mathematics or computer science faculty. This would also serve as a logical entree to the education of the life science faculty to the potential of automatic computers and related models for their fields. We feel that many biologists will accept the challenge posed in this context, when assured adequate guidance.

There are a number of possible logistic problems related to running the programming exercises that will usually make teaching assistants at a very junior level valuable to this course.

#### Content

# Topics Suggested Problems (Approximate number of lecture hours in parentheses) (These may be presented in the context of a biological problem)

- Algorithms, flowchart representations. (1)
- First principles of an algebraic language. (6)
  - BASIC, FORTRAN, CAL, PL/I, or ALGOL. Organized so that students may begin programming as soon as possible.
- 2a. Mean and standard deviation of a sample.
- 2b. Selection sort.
- 2c. Table look-up.
- 2d. Linear interpolation in a table.

- 3. Very simple introduction to numerical calculus. (This <u>can</u> be carried out before the students have had any appreciable instruction in calculus.) (4)
  - Cautionary discussion of error in calculation, with examples.
- 4. Pseudo-random numbers. Simulation. (2)
- 5. Introduction to the literature of computer programs. (2)

- 3a. Area under a curve by Simpson's rule.
- 3b. Euler's method (point-slope).
- 3c. Root finding by method of false position.
- 4. Simulation of the rolling of a die.
- Use of a standard data analysis package such as the BIMD statistical programs.

Additional program or programs on topics of special interest to the student.

## Introduction to Computing: Alternative 2

This course is a one-semester 3-credit-hour introduction to applied computing. While the concern for representation of algorithms and data overlaps that of a first course in computer science, our suggestion differs in that the accent is always on application, on problem solving with a digital computer. There are three or four suggested programming exercises in an algebraic language and one or two in special-purpose languages suited for biological problems. The course is set primarily for sophomores.

#### Materials

- 1. An introductory text on computing.
- 2. References for elementary numerical methods and statistical methods.

## Faculty Paculty

The course must be handled by a specialist in computing, as opposed to Alternative 1, although the elective programming exercise could be directed by a teaching assistant from the life sciences.

#### Facilities

Computing facilities will be required to handle the submittal of approximately 30 batch process jobs of short duration per student.

About 15 console hours on a time-shared remote access computer would be required equivalently.

#### Content

#### Topics

(Approximate number of lecture hours in parentheses)

- The concept of an algorithm: discussion of its connotations. (2)
- Representation of algorithms: natural language, flowchart, algebraic language. (2)
- 3. Principles of an algebraic language: FORTRAN, PL/I, ALGOL, or a conversational language: BASIC, CAL, etc., as available. Illustrations from simple numerical and statistical methods. (10)
- 4. The evaluation of algorithms, logical organization of a computing machine. (5)
- 5. A sampling of computer applications and methods. Simple symbol manipulation, list structures, simulation examples, pseudo-random number generation, a simulation language such as SIMSCRIPT, and specific applications from the life sciences. (12)

6. Discussion or demonstration of special computing equipment involving graphical displays or real-time control of experiments. (3)

#### Suggested Problems

Problems listed under alternative 1 and others, such as

- 4. Test for well formation of string of parentheses.
- 5a. Generation of Markov chain from transition matrix (presented in behavioral terms) in algebraic language, or a flow simulation in SIMSCRIPT.
- 5b. Elective problem on a topic from the life sciences such as an epidemic simulation, or the analysis of data from an actual experiment.
- 5c. Numerical integration, or linear regression with printer plot of graphical output.