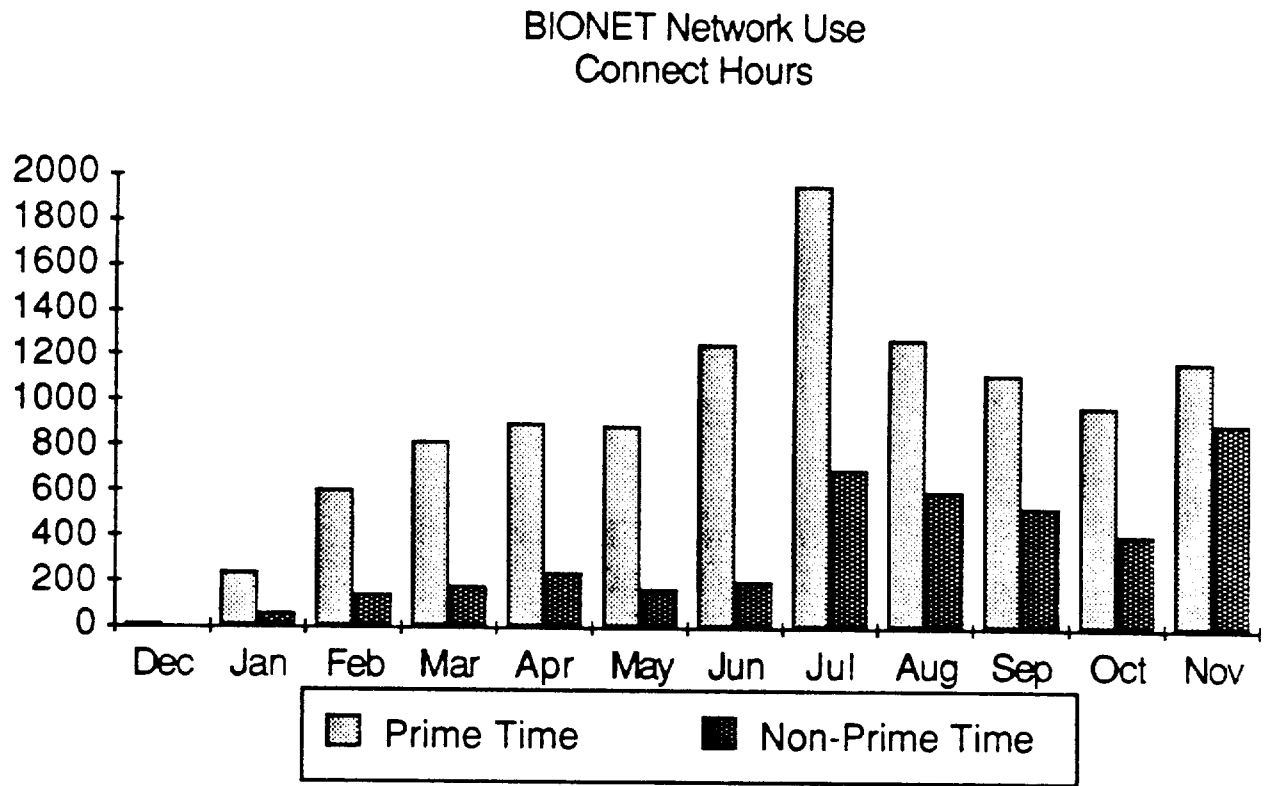


Figure III-7: Total Telenet and UNINET Network Use, 12/84 - 11/85

File Search.

FIND, DFIND--These utilities were added. They permit a concise display of matching text in a file, displaying respectively either a whole paragraph or a single line containing the match. Complicated search keys may be specified and the output can be directed to a file.

System utilities.

Several of these were added: TTYINI (sets terminal parameters more accurately by default), CALC (numeric calculations), RTTY (terminal display of a file in reverse order), DIREDD and CLEAN (display and hard copy directory management), MPW (suggest good random passwords to users), LASTN (displays last N lines of a file).

Programming Languages.

C--We installed the KCC compiler for the C programming language from Stanford University together with a new version of the FAIL assembler.

III.A.5.e. Computer Software - Contributed Library

We have set up a special directory on BIONET, the <CONTRIBUTED> directory, as a repository for contributed software and databases from the outside community. This directory is protected so that staff and BIONET investigators have access, but other users of the DEC-2060, for example customers of IntelliGenetics, do not. This was done so that persons who wish their software to be accessible only for not-for-profit research have a mechanism to do so.

The software and databases that have been contributed are summarized in Subsection III.A.2, above.

III.A.5.f. Database Library

We maintain all major collections of biological sequence data on BIONET, including the GenBank and European Molecular Biology Laboratory (EMBL) nucleic acid sequences, and the Protein Identification Resource database of protein sequences. We also maintain the Cold Spring Harbor database of restriction enzymes (contributed by Dr. Roberts, see Subsection III.A.2). We provide VectorBanktm, from IntelliGenetics, for use in programs designed to model cloning experiments. These databases are updated immediately on receipt from the suppliers.

Where necessary for use in Core Library programs, we reformat these databases; the original databases are also maintained in separate directories for programs designed to access those formats.

III.B. Highlights

The following are highlights of the BIONET Resource's second year of operation.

- 560 PI's have been granted access to the BIONET Resource, substantially exceeding our early estimates of the size and interest of the community. These scientists have already published over 50 scientific papers in which the Resource played an important role in obtaining the results of their investigations.
- Collaborative research projects have brought to the Resource both new computer software to complement what was available already, and new databases, bibliographies, and computer-readable textbooks. These augmentations of the Resource are widely used by BIONET scientists.
- Our investigations of special computer hardware for rapid searches of nucleic acid and protein sequence databases have led to identification of and writing of specifications for a machine to be used in conjunction with existing facilities. Such a device would dramatically improve such searches, thereby increasing the amount of computer time available to other investigators.
- Our BIONET Satellite program for establishing a loosely-linked network of computers has gotten off to a promising start. The communications and networking facilities of BIONET will be used to maintain electronic mail and bulletin boards accessible by all Satellite resources.

III.C. Administrative Changes

III.C.1. Facilities

In July, 1985, IntelliGenetics acquired control of the DEC-2060 and related facilities from IntelliCorp. Thus, all facilities used by BIONET are now totally under the management of IntelliGenetics. 50% of the machine is still devoted to BIONET as part of the Cooperative Agreement under which we are funded. As discussed previously in Paragraph III.A.5.b, BIONET actually consumes substantially more than 50% of the computer (cpu) time.

As part of these changes, the Knowledge Systems Division (KSD) of IntelliCorp separately purchased several DEC-VAX systems and over the period of September and October, 1985, reduced its share of the 2060 from 20% to 4%. The pie chart describing the current percentage allocations of the system to each category was presented previously in Figure III-1.

III.C.2. Personnel

As part of the reorganization of the computer facility, several changes in personnel have taken place. R. David Roode joined IntelliGenetics in the role of Biotechnology Computer Facilities Manager. Mary Yardley became Operations Supervisor and Lauri Kanerva continues as Senior Computer Operator. Andrea Gorman and John Shelton assumed other roles in IntelliCorp. Other major changes in personnel

were brought about by budget cuts as discussed at the beginning of this report. We are currently engaged in a search for a BIONET Scientist to assume the role of Ms. Ari Azhir, who has recently left the company.

On November 15, Marcia Allen was added as a second Scientific Consultant to the BIONET staff. This was made possible by the improved financial condition of the Resource. This addition was chosen specifically to improve our user consultation services and to enable us to revitalize our training program.

III.D. Resource Advisory Committee and Allocation of Resources

Our methods of allocating resources (staff and computer time) are relatively simple. The DEC-2060 computer uses its windfall scheduler to allocate cpu time to the various categories of users and overhead, as described in detail in Subsection III.A.5. These cpu cycles are distributed on a first-come, first-served basis. Because of the limited number of communication ports into the 2060 (currently 18, see Paragraph III.A.5.a), we have asked the community not to have more than one person per PI group using BIONET at the same time during prime time. The community has done an excellent job in complying with this policy.

In October, 1985, we doubled the disk space available to each PI's group. This has eased substantially the problems several groups encountered in managing large sequencing projects or individual databases of sequences.

We have devoted most of our staff time to the Collaborative Research and Service components of the Resource. In the next year we will devote additional staff time to foster collaborations and to our Core Research activities. This will be possible because the community is becoming more sophisticated in its use of BIONET and we have already augmented our staff in support of the Service component.

On August 21, 1985, we held a meeting with "local" members of the National Advisory Committee (see below) Tom Rindfleisch, Joshua Lederberg and Charles Yanofsky, to take advantage of Joshua Lederberg's visit to the Bay Area. One question which was posed at that meeting was how fairly the Resource, in terms of computer cycles, was being distributed to the community. One answer to this has been obtained by summary statistics on the top 20 users of BIONET over the past twelve months. Our data indicate that 38% of the total cpu cycles were delivered to the top 20 users. This statistic must be interpreted in the light of two important facts. One, the top 20 users on a month-by-month basis show substantial differences, reflecting the nature of computing in the area (significant use of the computer is often followed by additional laboratory studies suggested in part by the computational results). Second, the needs of different PI's differ substantially. Those who require frequent access to the databases will use substantially more cpu time than other PI's who may be doing restriction mapping or assembly of

consensus sequences. The former group will use a disproportionate share of the Resource, and this fact is what has prompted us to seek an alternative solution by applying new hardware to serial search, as described previously under our Core Research program (Subsection III.A.3).

The last meeting of our full National Advisory Committee was held March 23, 1985. The next scheduled meeting is February 24, 1986. The current membership of the Committee is as follows:

- Professor Joshua Lederberg, MD, PhD. (Chair), President, The Rockefeller University.
- Dr. Saul Amarel, PhD., Director, Information Processing Techniques Office, Defense Advanced Research Projects Agency, Department of Defense.
- Professor Alan Maxam, PhD., Dana Farber Cancer Institute, Harvard Medical School, Harvard University.
- Dr. Richard J. Roberts, PhD., Senior Staff Investigator, Molecular Biology, Cold Spring Harbor Laboratory
- Thomas Rindfleisch, MS, Director, Knowledge Systems Laboratory, Department of Computer Science, Stanford University.
- Professor Charles Yanofsky, PhD., Department of Biological Sciences, Stanford University.
- Professor Fotis Kafatos, PhD., Department of Cellular and Developmental Biology, Harvard University.

III.E. Dissemination of Information on Resource's Capabilities

We discuss two areas related to dissemination of information about the Resource that we have pursued this grant year. The first is interactions with the scientific community through participation at conferences, advertising the availability of BIONET, and mailing information about the Resource to NIH grantees. The second is use of the electronic mail and bulletin board facilities of the Resource itself to keep the BIONET community aware of changes and improvements.

III.E.1. Community Interactions and Awareness

We have used three methods this year to inform the community about BIONET and to solicit applications for access to the Resource. The first method has been participation at major conferences, where we have presented papers and/or have had booths at exhibitions. These efforts were summarized previously under Training, Subsection III.A.4. At these conferences, we have distributed the standard application packets to scientists, after demonstrating to them the capabilities of the Resource.

The second method is advertising. Due to our limited budget, we have placed only one advertisement this year, in the special computer issue of *Nucleic Acids Research*, which appears in January, 1986. The text of the ad is provided in Appendix VII.

The third method is a mass mailing to NIH grantees whose research areas were characterizable as related to molecular biology, biological chemistry, and so forth. This list was provided to us by Dr. Charles Coulter, BRTP/DRR/NIH, who obtained the list and associated mailing labels by searching the NIH database of information on research areas of its grantees. The keywords chosen for the search were purposefully general to capture as many potential investigators as possible. Thus, there were some investigators chosen who are working in tangential areas, for example, classical genetics.

There were approximately 4030 mailing labels from this list. A brochure describing BIONET was sent to each of these investigators on November 10, 1985. The brochure itself is shown in Appendix VIII. The brochure is two-sided, and folded in half along perforations. Persons wishing an application packet need only fill out the requested information, tear off the return half and send it back to us. So far we have received 315 requests back for application forms. Many of these returns also have requested information on the BIONET Satellite program.

III.E.2. Electronic Communications

The electronic communication facilities of BIONET provide another important way to disseminate information about the Resource. In addition, electronic mail and bulletin boards provide a mechanism for scientific and technical interchanges among members of the community. Information on the types of electronic mail communications with BIONET was summarized previously in discussion of the Service component of the Resource (see Subsection III.A.1). We have also established a second mechanism for sharing information electronically, on-line bibliographies. Bulletin boards and bibliographies are discussed in the next sections.

III.E.2.a. Bulletin Boards

The electronic bulletin boards are an important component of the BIONET Resource. They provide BIONET users with a facility for the exchange of data, laboratory techniques and ideas with others of like mind. For example, a laboratory just beginning a study of the conservation of DNA sequences might experience some frustrating technical problems. A message to the MOLECULAR-EVOLUTION bulletin board, describing the problem, will probably reach and be read by more than 1000 BIONET users, some of whom will have experienced similar problems and can offer solutions. Obviously, the users represent a wealth of knowledge. Communication is the key to accessing and disseminating that knowledge.

BIONET's bulletin board system consists currently of 20 bulletin boards of varied topics. The topics were selected from user requests and from a survey of the most frequently asked questions. We have designed the system so that each BIONET user automatically receives messages that are of concern to all users, but can decide independently which other bulletin boards he or she would like to subscribe to. Subscribing to a bulletin board is an automated procedure which results in the automatic presentation of new messages

upon logging onto the system. However, all users have access to all bulletin boards, whether or not they are subscribers, through the electronic mail facility.

The bulletin board topics are as follows:

BIBLIOGRAPHIES	Instructions for using BIONET's online bibliographies that have been contributed by members of the BIONET community.
BIONET-NEWS	Information relevant to all BIONET users. All BIONET users automatically subscribe.
CONTRIBUTED-SOFTWARE	Reviews/instructions for using the software that has been contributed to BIONET by BIONET users.
EMPLOYMENT	Postings of job opportunities by BIONET users.
IMMUNOLOGY	Information/inquiries relating to immunology.
LIBRARIES	Requests/postings of availability for/of cDNA libraries or codon usage tables.
MOLECULAR-BIOLOGY-LAB-METHODS	Information/inquiries relating to laboratory techniques.
MOLECULAR-EVOLUTION	Information/inquiries relating to the study of evolutionary relationships of genes or proteins.
ONCOGENES	Information/inquiries relating to oncogenes.
PC-COMMUNICATIONS	Instructions/inquiries relating to using a PC to communicate and to transfer files to and from the BIONET computer.
PC-SOFTWARE	Reviews/inquiries of software packages for any type of personal computer.
PLANT-MOLECULAR-BIOLOGY	Information/inquiries relating to the study of plant genetics.
POLITICS	Concerns/opinions which may or may not be related to research in molecular biology.
PROGRAM-APPLICATIONS	Instructions/suggestions for using the BIONET programs for special applications or research projects.
PROTEIN-ENGINEERING	Information/inquiries relating to protein engineering.
RESTRICTION-ENZYMES	Information/inquiries relating to restriction

enzymes.

STARTUP	For new users, a quick introduction to BIONET including the most frequently asked questions from new users and their solutions.
TOPS20-HINTS	Instructions/suggestions for managing your directories, copying files, running batch jobs or any other system facilities/commands.
VECTORS	Information/inquiries relating to vectors and vector construction.
YEAST-GENETICS	Information/inquiries relating to yeast genetics.

There are about 170 different messages on the bulletin boards, 18 are suggestions for lab techniques, 17 which involve the trading of libraries, and 21 reviews of software used for molecular biology research. Surprisingly enough, the most popular bulletin boards are the PC topics, and the least used bulletin board is ONCOGENES. The number of messages reflects an under-utilization of this resource, which we will address with our more aggressive plan described below. But interviews with BIONET users and feedback from the reapplication forms indicates that the number of messages on the bulletin boards does not entirely reflect the level of interaction among members of the BIONET community. In many instances, the bulletin boards have served as a catalyst for the dissemination of information across the community.

With limited staff, it was impossible to actively promote the bulletin board communities. However, with the implementation of subscription fees and the hiring of additional personnel, we have begun to select active members of the BIONET community to serve as bulletin board leaders. These scientists will submit and solicit articles, reviews and information from the community and post them on a bulletin board. They will receive special access privileges, and will monitor and update the messages. The bulletin board leaders will also post monthly updates on BIONET-NEWS describing the new messages sent to their bulletin board. This way, every member of the community will have the opportunity to remain informed about collaborations or new developments in molecular biology without having to read messages that may not be in his or her field. It will also eliminate the problem of having messages on multiple bulletin boards. We feel that with the implementation of our more aggressive plan for bulletin board community leaders, the bulletin boards on BIONET will prove to be an even more important component for the dissemination of information among the molecular biology research community.

III.E.2.b. Bibliographies

In response to a suggestion from the National Advisory Committee, Bionet set up a procedure whereby Bionet users could contribute their personal bibliography files for the use of others. The various format-independent text searching programs available on Bionet makes this feasible. The program FIND allows users to search for particular text words or other character patterns in single files and to print out specified amounts of text around the patterns. The program XSEARCH allows users to search many files for patterns, and the program QUEST permits the combined flexibility of both FIND and XSEARCH. The most important aspect of these tools is that they are general, context-independent searching methods so that bibliographic data in almost any format could be searched.

Users were informed of these text searching tools by a BBOARD message and two sample bibliographic files were announced by the Bionet co-investigators. They included the following files:

```

PS : <BRUTLAG.BIB>
CHROMOSOME.BIB.25      ; References on chromosome structure
COMPUTER.BIB.30        ; Computer algorithms and methods
DNA.BIB.5              ; DNA structure and topology
DROSOPHILA.BIB.16     ; Drosophila molecular genetics
GENETICS.BIB.17       ; Molecular and classical genetics
METHODS.BIB.29        ; General laboratory methods
RESTRICTION.BIB.16    ; Rich Roberts restriction enzyme refs
TOPOISOMERASE.BIB.48  ; DNA topoisomerase references

PS : <KEDES>
MUSCLE.BIB.1          ; References on muscle proteins and genes

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These files were not greatly referenced nor was there a lot of feedback from the community. One other user, (Tom Broker) volunteered a complete bibliography of work performed on papovaviruses and we are helping him mount this extensive bibliographic database.

The primary problem with this approach is that personal databases are just that, very personal, limited in scope and generally not kept up to date. When scientists want to access bibliographic information online, they usually go to more complete collections such as MEDLINE or DIALOG.

What would be much more useful to the BIONET community would be to provide access to full text copies of well known reference works, such as the bibliographies of *Drosophila* by Herskowitz, Genetic Maps by O'Brien, Genetic variations of *Drosophila melanogaster* etc. Most of these works are not prepared in computer readable form.

Genetic Variations of Drosophila melanogaster

Fortunately, Dr. Dan Lindsley did prepare this extensively used reference work in a computer readable

form. It is fondly known as the Redbook and it has been the bible of *Drosophila* genetics and a primary research resource for 17 years. Recently Dr. Lindsley has undertaken to produce a new edition of this work. Moreover, both he and his publisher have agreed to make both editions of the Redbook available on BIONET for online access. The advantages of having the book available online is that one can effectively cross index the entire book for any word that appears in the book. For example, using the text searching tools mentioned above, one can find all mutations that affect bristles as well as all suppressors of bristle mutants. This kind of cross indexing is not possible in any other way. Methods for finding all known mutants at any genetic map position or in any region of the polytene chromosome are also possible. While there are Appendices in the back of the Redbook to allow the location of the genes by location, online access allows one to have descriptions of all genes that are similar in 1) location, 2) function or 3) which interact with each other.

We have made the Redbook available in both chapter form, identical with the chapters as they appear in the book itself, and in two large sections of the books including all the point mutations (in the file <REDBOOK>MUTANTS) and all the chromosome rearrangements (in the file <REDBOOK>OTHERS). These latter files aide in finding mutants using the FIND program. We have just received a tape containing initial chapters of the new version of the Redbook and we intend to make this available in the same way, with updates as the work is completed. Currently the new version is about 60% complete.

Cloned Segments of the Drosophila Genome

In addition to *Genetic Variations of Drosophila melanogaster*, Dr. John Merriam (UCLA) has compiled a list of all the molecular markers on the *Drosophila* chromosomes. This compilation includes all cloned segments of *Drosophila* DNA that have been mapped to specific genetic positions as well as all rearrangements whose break points have been cloned. These cloned segments are extremely useful to molecular biologists who wish to isolate specific genes from *Drosophila* using the walking procedure. Moreover, this compilation will eventually develop into a complete molecular map of the *Drosophila* genome to complement the genetic one. We are working with Dr. Merriam to provide this useful resource on Bionet.

Once both the new edition of the *Genetic Variations of Drosophila melanogaster* and the *Cloned Segments of the Drosophila Genome* are available, this will be written up for publication as letters to the editors of various molecular and genetic journals. A description of the databases will be submitted to *Drosophila* Information Services, where most geneticists currently go for this kind of information.

Once these works are made available and properly announced we will evaluate their usefulness to the community as judged by the number of read accesses and how many individuals access these databases.

We will also determine how many new users apply for BIONET use primarily to access these genetic databases. Currently WHOIS reports that there are 14 laboratories who mention the word *Drosophila* in their research title. There are probably many other laboratories that are concerned with *Drosophila* as a research organism but who do not have *Drosophila* in their research title (i.e. HOGNESS).

We can also consider recruiting other genetic databases which currently exist or will shortly in a computer readable form. Some examples would be the *E. coli* genetic map (BLATTNER) and the human genetic maps (RUDDLE and WHITE). These extensive genetic and restriction maps are a natural complement to the DNA and protein sequence information that BIONET now provides and we hope that these higher order rearrangements of genetic function will be as useful in the future as are the sequence databases at the present.

III.F. Suggestions and Comments

We have two suggestions that would dramatically improve the productivity of the BIONET Resource, and would increase its availability and utility to the scientific community.

The first suggestion we have relates to the relationship between the Resource and the NIH staff. We have, in general, received a great deal of support from staff at the Office of Grants Management and BRTP itself. However, we simply must have more warning regarding decisions at the federal level that affect our budget. The dislocations we experienced in the first months of this grant year were substantial, and much time was wasted on administrative, as opposed to scientific, problems. The NIH is in a delicate position, in that it cannot afford to alarm its awardees about potential budget cuts that might not take place. But the down side risks of this approach, in our opinion, are more dangerous. We know that there may be additional NIH budget problems in fiscal 1986. We request that we be kept informed, even if information is tentative and subject to change, about any decisions that could affect our Year 3, and subsequent awards.

The second suggestion relates to the fact that there is increasing number of computer resources for molecular biology and related areas funded through DRR, alone. These resources make up a significant fraction of the BRTP/DRR budget, yet each has been funded through the traditional grant proposal and review process. What has resulted is a number of resources with complementary goals and facilities that have no means of communication with one another to easily exchange their stock in trade, electronic mail, new software and updated databases. Our program for BIONET Satellites is designed to take some steps toward network interconnections, but we do not have the budget nor the mandate to solve this problem alone. Obviously, a proposal can be generated for the necessary funds to build such a network, but it is not clear whether there would be sufficient new science to be successful. The networking problem has already been solved by others, so any proposal would be primarily technological. We suggest that DRR

Staff and Council, who must already be cognizant of the situation, investigate and propose some future programmatic goals. We would be pleased to participate in this effort.

I. Letter to BIONET Scientists

BIONET™ National Computer Resource
for Molecular Biology
c/o IntelliGenetics
124 University Avenue
Palo Alto, CA 94301
14 June 1985

***** IMPORTANT ANNOUNCEMENTS ABOUT BIONET *****

SUBSCRIPTION FEE

SWITCH to UNINET

BULLETIN BOARDS

BATCH JOBS

Dear BIONET Scientist:

I am writing this letter to bring you up to date on a number of changes that will be occurring in the near future on the BIONET Resource. By most measures, our first year of operation has been very successful. We currently have more than 450 Principal Investigators, representing over 1400 individual scientists, who have received approval for access to BIONET. In late March, our National Advisory Committee met with us to review progress and set directions for the next year (we are on a March 1 to February 27 funding cycle). Some of the changes that will be occurring are an outgrowth of that meeting, especially with regards to funding problems, communications and the use of bulletin boards and electronic mail.

As most of you know from a bulletin on BIONET (you can review the bulletin by issuing the MM command BBOARD BIONET-NEWS and reading the bulletin entitled "Budget cuts for BIONET") budget cuts at the NIH have led to substantial reductions in our budget for this grant year. For the past three months, with the help of consultants and our Advisory Committee, we have been studying solutions to the problems posed by these cuts. To reiterate, we have had to reduce staff from 8.5 full time equivalents to about 5.5, and we project that our telecommunications budget will be consumed late this fall unless some prompt action is taken. The following sections on Subscription Fee and Switch to UNINET represent our best solutions to these problems, solutions that will enable us to continue to provide you with high quality service and to build the Collaborative and Core Research aspects of BIONET. Most importantly, the changes mean that you will not have to pay the full cost of your telecommunications. This was crucial to us in order that those laboratories that are suffering

from funding problems still be able to access BIONET.

Subscription Fee

There are several possible solutions to the problems of staff reductions and a substantial projected deficit in our telecommunication budget. We have initially focused our attention on the latter problem, because without telecommunications access, there would be no Resource! Many solutions to this problem would have the effect of making access prohibitively expensive for those laboratories with limited resources; such laboratories are often those that need access to BIONET the most. Fortunately, we have found what seems to be a good compromise. With the concurrence of our National Advisory Committee, we are instituting a nominal subscription fee to BIONET, which, when combined with available funds, will make up the deficit. The fee will also allow us to expand our telecommunication services as the BIONET community grows, by increasing the number of network lines to the computer.

We regret to have to impose a fee on such short notice. Our long range plans indicated that some type of access charge would have to be leveled eventually, but we had not anticipated it happening this quickly. We received notice of our budget cuts on February 26, three days before the beginning of our second year. Since that time we have tried unsuccessfully to have the cuts rescinded, but the NIH, Congress and the OMB are still at odds over the 1985 NIH budget and no rapid solution appears to be forthcoming. We are also exploring other funding sources, but have no assurances at this time that any additional money will be available.

To cover our costs, the fee we must request is \$400 per year per Class I Principal Investigator (PI). We hope that virtually every PI on BIONET will be able to afford this nominal expense. This fee should be received by us on or before August 1, 1985. Checks should be made payable to IntelliGenetics, marked clearly as BIONET Subscription Fee, and attached to the enclosed Subscription Fee form. Class I PI's in Alaska, Hawaii, Canada and Mexico must pay the subscription fee because their telecommunications costs will be billed to BIONET by UNINET. *PI's in other foreign countries, who will be billed separately by their network vendors, will NOT have to pay a subscription fee.*

Switch to UNINET

We will soon be moving over to a new vendor for telecommunications services, UNINET. The primary reason for this change is that UNINET has offered very attractive pricing for use of BIONET. They will be charging us a fixed rate per month per communications line, independent of use. This charging scheme means that we can do much more precise planning for our current and future budgets. In addition, other organizations that have recently switched from Telenet, our current vendor, to UNINET report better network response and reliability, plus more rapid action on problems with the network. We will still pay careful attention to minimizing your need for long periods of connection to BIONET. In particular, we are working on simplifying BATCH submissions (see below) so that you can logout from BIONET, leaving the line available for another person to use. We have also implemented a procedure that will detach your job after a period of time of non-use (currently two hours) should you accidentally forget to logout your job.

This switch will take place on or about July 1; after that time Telenet will no longer be available for access to BIONET. You will receive a mailing from UNINET with complete instructions on use of the network prior to that time. You will be reminded by bulletins on the BIONET-NEWS bulletin board when you login about precise schedules. Use of UNINET is even less complicated than Telenet. The primary difference will be in the telephone number that is dialed plus slightly different recognition characters to "wake up" the network. Depending on location, and because UNINET's distribution of local nodes is different from Telenet's, you may have to call a longer distance for access, or you may

be lucky, and find a UNINET node nearer to you!

Bulletin Boards

The primary use for bulletin boards is the sending of messages to a group of people interested in specific topics. It is often much simpler to send a bulletin than to send electronic mail because for the latter you must maintain an accurate mailing list. The BIONET system keeps track of who wants to read which bulletin boards, thereby saving you considerable effort.

Our current system is based on the bulletin board topics you selected as part of your application to BIONET. These topics are automatically added to your LOGIN.CMD file as part of setup of your account on BIONET. Everyone has BIONET-NEWS in this file. You are notified automatically when you login that you have bulletins to read, and are given their titles and a choice to read them or to ignore them.

We have had some successful use of the bulletin boards, but also several disappointments. On the positive side, there have been several valuable exchanges among members of the community, and several of you have expressed an interest in being a community leader, albeit on topics more specific than the current, generic ones. On the negative side, many people are ignoring important bulletins by skipping over the reading of them on login to BIONET. Also, the current topics are too limited to inspire use of the bulletin boards.

For these reasons, we are going to change our approach somewhat, to include the following steps:

- We will use a new list of topics, selected from your suggestions and current patterns of use of the bulletin boards. Periodically, we will add new topics to the list based on your suggestions. This will make the set of topics more useful to you and your colleagues.
- We will revise your existing LOGIN.CMD file to contain only the BIONET-NEWS bulletin board, and make it simple for you to add other topics at your discretion.
- We would like BIONET-NEWS to be read by *EVERYONE*, all the time. We will continue to encourage you to post bulletins that are of wide community interest on BIONET-NEWS. To prevent the occasional user of BIONET from being overwhelmed by bulletins on this bulletin board, we will periodically move outdated bulletins to topical bulletin boards, or delete them, so that only a few important and timely bulletins remain to be read.

Attached to this letter you will find a revised list of bulletin boards that represents a start to meeting some of our goals, together with instructions on how to add one of the new topics to your LOGIN.CMD file so that you are notified about interesting subjects when you login.

BATCH Jobs

Many members of the community have asked how they can submit lengthy computations to the system and logout and go away, to return at some later time to review the results. That capability is available through the BATCH system on the BIONET computer. Attached to this letter are some simple instructions on how to SUBMIT such computations to run in BATCH overnight. We hope they are useful to you.

In conclusion, I want to thank you for your participation in what has been a successful experiment in making powerful computational facilities available to a very large number of scientists. Your enthusiastic contributions to this success are appreciated, and we at BIONET hope they will continue unabated despite the budgetary problems discussed previously.

Sincerely,

Dennis H. Smith
Resource Manager, BIONET

II. Justification of \$400 Fee

The following message was sent by electronic mail to Dr. Rich Roberts, a member of BIONET's National Advisory Committee, in response to questions from him on the justification for setting the fee at \$400.

7-Aug-85 12:17:13-PDT,3352;000000000001
 Mail-From: SMITH created at 7-Aug-85 12:16:59
 Date: Wed 7 Aug 85 12:16:58-PDT
 From: Dennis Smith <SMITH>
 Subject: Re: charges
 To: ROBERTS
 cc: AMAREL, KAFATOS, LEDERBERG, MAXAM,
 RINDFLEISCH, YANOFKY, SMITH
 In-Reply-To: Message from "Richard J. Roberts <ROBERTS>" of
 Wed 7 Aug 85 06:34:44-PDT

Rich,

The figure was determined by taking a hard look at our budget to see what was needed and then to estimate, based on the profile of accepted PI vs. those who actually used the system, how many would sign up.

In brief - we need about \$50,000 to meet telecommunications costs, i.e., to avoid going into the red. We desperately need another consultant and a scientist, the latter for core research, and that would cost 50-60K depending on obvious factors. Given a target of roughly \$100K, we'd need 250 PI's signed up at \$400 each. Our estimates out of a group of 450 PI's was that 175 - 200 was a good guess. The first 125 would pay our projected deficit and the remainder MIGHT allow us to hire another user consultant, our highest priority.

The message to the community soliciting comments yielded only a few comments, almost all of which were essentially, "Siggghh, but it's worth it" and two complaints.

Since the fee was announced, we have received nearly the 125 target of checks or requests for invoices, and 8 refusals. None of the eight was a significant previous user of the system.

I have made it clear that we would not turn anyone away for lack of funds. There are two people in this situation, and I will not cut them off if they can't raise the full amount. One was the type of person you described, who was mainly interested in communication.

We give people at least 30 days after subscription is due, and a much longer period if they let us know about their problems, so they have at least 60 days and more if they need it.

So, those are the current facts. An issue remaining from your message is treatment of those who wish only access to communication facilities, and that should certainly receive some discussion. There are several mechanical problems with this, but, more importantly, I have been discouraged by the community's response to the communication facilities. We have excellent use of electronic mail, but only sporadic use of bulletin boards. The reality of the last 8 months of reasonable use of the system is that lots of people are banging away at it to solve their problems, and use mail and links, and advising, and phone calls to generally very good purposes - they have some really interesting problems that involve sophisticated use of the programs, i.e., little chaff or nonsense. But it seems to be a cottage industry out there, and despite our efforts to simplify further the bulletin boards and our letter and messages to demonstrate their use and make it easy to add and promote new topics, only that segment of the community with previous "electronic" experience is making any use of those facilities.

Comments and suggestions welcomed.

Dennis

PS - I am trying to get in touch with Lederberg, who is now in CA to schedule at least a local meeting of NAC members and the next full meeting. Do you have any constraints over the next few months? -----

III. Letter on Class IV Access

BIONET™

Important Notice on

Reduced Subscription Fee for Communication

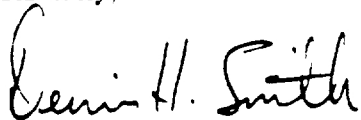
Dear BIONET Scientist:

I am writing to you because our records indicate that you either have not logged in to BIONET or that you have used the system but have not chosen to pay the subscription fee we had to implement late this summer. Your account still exists on the system and will remain there temporarily. It is not currently accessible by you pending further information about your intentions to remain a participating member of the BIONET community.

We know that the current funding situation is as serious for many of you as it has been for BIONET. Many scientists have made special arrangements with us to maintain access to the system pending availability of new grant funding, institutional support and so forth. We want to be sure that you understand that we will not prevent access to BIONET simply due to lack of funding. If you have special circumstances and need access to BIONET to support your research, I encourage you to contact Mary Warner or myself ((415) 965-5576,77).

One of the goals of BIONET is to foster active communication and collaboration among molecular biologists. Therefore, we would like everyone to be able to access at least the electronic mail and bulletin board facilities, even if access to analysis programs is not desired. Therefore, we have instituted a new class of BIONET membership, Class IV, which offers access to electronic mail, electronic bulletin boards and file transfer programs. These facilities will allow you to interact and exchange information with your colleagues on BIONET. Because such interaction does make use of our telecommunications facilities, we must also charge a subscription fee for access, but at the reduced rate of \$100 per Principal Investigator per year. We have included a Subscription Fee Form which lists this option. We very much hope that you will choose at least this method for participating in the BIONET community.

Sincerely,



Dennis H. Smith

Resource Manager, BIONET

IV. Reapplication Form for BIONET Access

BIONET™

26 September 1985

Dear BIONET Principal Investigator:

The National Institute of Health requires, as part of our Annual Report, that we review the status of all BIONET subscribers each year. Thus, we need information from you on any changes, from your original application, with respect to institutional affiliation, address, funding status, sub-investigators, etc. Most importantly, we need a list of all publications in which BIONET played a role. We also ask that at this time you reaffirm your original agreement for access to BIONET.


Use the enclosed forms to:

- Update your title, affiliation, mailing address and/or phone number
- Update the list of your sub-investigators
- Note change in status of funding
- Provide a list of current publications resulting, in part, from the use of the BIONET Resource (Remember to cite the BIONET Grant # 1 U41 RR-01685-02 in all such publications.)
- Provide a brief description on how BIONET was used in your research.

We would also like to give you this opportunity to comment on the BIONET resource - what role it is playing in your research and any suggestions/requests for improvement.

Because we must prepare our Annual Report in December, we need you to return this re-application to us no later than November 1, 1985. Thank you for your cooperation.

Sincerely,



Mary Lou Warner
BIONET Administrator

BIONET RESOURCE**Reapplication****Fiscal 1986**

Principal Investigator (full name and title):

Affiliation: Department, School and Institution (Changes Only):

Mailing Address (Changes Only):

Area code and phone number(Changes Only):

BIONET Agreement

As Principal Investigator of this grant to use the BIONET Resources, I agree to adhere to all conditions and restrictions for use of the BIONET Resource, as described in the document "The BIONETtm Resource, Description and Applications Form" and such further regulations as may be issued from time to time by the NIH or the NAC.

The BIONET Resource will not be used for any commercial purpose which is not specifically identified to and approved by the NAC. Any pertinent change in sponsorship, continuity of grant support, or use made of BIONET will be reported promptly to the BIONET Resource Manager.

I have also furnished a copy of this re-application to the responsible officer of my institution, whose signature appears below.

I also assume full responsibility for all users listed on this applications form and will monitor their compliance to the conditions and restrictions for access to the BIONET Resource. I will inform the BIONET Consultant, (electronic mail address: BIONET), by electronic mail, immediately about any changes in this group of users, i.e., departure of existing user or addition of new staff qualified to use the resource. I will inform new users of the above mentioned conditions and restrictions.

Date: _____

Name of official: _____

Signature of Principle Investigator_____
Signature of Official

BIONET re-application page 2**Current Sub-investigators**

If your group of sub-investigators has changed since your last correspondence, please note the changes below:

<u>NAME</u>	<u>Title</u>	<u>Phone number</u>	<u>Change</u>
-------------	--------------	---------------------	---------------

Funding Status

Please note any change in status of your funding, including Institution, Grant Number, title of grant, and duration of grant.

Current Publications

Please list current publications resulting, in part, from the use of the BIONET Resource (use standard bibliographic format). Remember to cite the BIONET Grant # 1 U41 RR-01685-02 in all such publications. A sample citation would be: *Computer resources used to carry out our studies were provided by the BIONET^{4m} National Computer Resource for Molecular Biology, whose funding is provided by the Biomedical Research Technology Program, Division of Research Resources, National Institutes of Health, Grant # 1 U41 RR-01685-02.*

BIONET Re-application Page 3**Use of BIONET**

Briefly describe how BIONET has been used in conjunction with your research:

COMMENTS

We invite your comments, suggestions and requests about the BIONET Resource. Which programs are the most useful to you - the least? Should the bulletin boards be broader in scope - more specific? Would you like more interaction with other users? What else would you like to see included in the BIONET Resource, for example, other computer programs. Would you like more information about the BIONET Satellite Resources?

V. Program for the Rutgers/Waksman Workshop

If you receive more than one copy of this brochure, please pass extra copies on to a friend or co-worker.

One-Day or Three-Day Workshop
 Introduction to *BIONET*™:
 A National Computer Resource for Molecular Biology

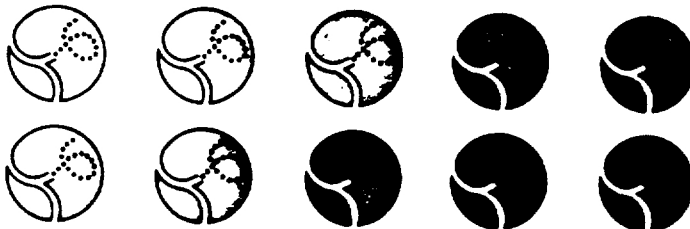
THE STATE UNIVERSITY OF NEW JERSEY
RUTGERS
 Waksman Institute of Microbiology
 P O Box 759
 Piscataway, New Jersey 08854-0759
 Continuing Professional Education Program

INTRODUCTION TO *BIONET*™: A National Computer Resource for Molecular Biology

One-Day Workshop—June 17, 1985

Three-Day Workshop—June 17-19, 1985

The Waksman Institute
 of Microbiology



THE STATE UNIVERSITY OF NEW JERSEY
RUTGERS
 Campus of New Brunswick

ABOUT THE WORKSHOP LEADERS

Douglas Brutlag, Ph.D., Associate Professor of Biochemistry at Stanford University.

Dr. Brutlag, coinvestigator of *BIONET*, is an authority on nucleic acid enzymology. His work has focused on the evolution of nucleic acid sequences and the assembly of chromosomes. Dr. Brutlag has also had a long-term interest in computer systems and programming and was a coinvestigator of the MOLGEN project at Stanford.

Laurence Kedes, M.D., Professor of Medicine at Stanford University School of Medicine.

Dr. Kedes, coinvestigator of *BIONET*, was also a coinvestigator of the MOLGEN project and has been responsible for overseeing the development of several software projects in molecular biology. As a molecular and cellular geneticist, Dr. Kedes spends the majority of his research efforts investigating the nature of gene organization and regulation in animal cells.

Elaine Mansfield, Ph.D., Training Manager and Consulting Scientist for *BIONET*, IntelliGenetics, Inc.

Dr. Mansfield has worked for IntelliGenetics, Inc. for two years in Marketing and Customer Training and Support. She has conducted numerous on-site trainings and written user manuals for several of the IntelliGenetics programs. Dr. Mansfield currently oversees the training programs and collaborates user support services for *BIONET*. She holds a Ph.D. in human biochemical genetics from the University of California at Berkeley.

Introduction to **BIONET**[™]; A National Computer Resource for Molecular Biology

One-Day Workshop—June 17, 1985
Three-Day Workshop—June 17-19, 1985
The Waksman Institute of Microbiology

PURPOSE OF THIS WORKSHOP

BIONET is a national computer resource sponsored by the N.I.H. and established to provide academic scientists with an interactive timesharing computer, up-to-date sequence databases and analysis programs, and powerful communication tools for rapidly exchanging information with colleagues. This one- or three-day workshop will provide participants with an understanding of the programs, database organization, and advanced computer resources available on **BIONET**.

On the first day, the workshop leaders will use video projection systems to show actual on-line interaction of protein and DNA sequence analysis programs, electronic bulletin boards, and electronic mail facilities. A more in-depth presentation will be conducted as a two-day hands-on session for **BIONET** principal investigators or their representatives. Applications presented will include how to use the computer for efficiently managing DNA sequencing projects, sequence comparison methods, and optimal probe design. In addition, the procedure of transferring data from a personal computer to the **BIONET** computer will be demonstrated.

PROGRAM CONTENT

- An overview of **BIONET** and the computer system
 - Resource organization and goals
 - Core program library, sequence databases, and development library
 - Introduction to electronic mail and bulletin boards—communication tools for collaboration
 - System commands and directory organization
- Restriction mapping tools
 - Restriction fragment length calculation
 - Construction of restriction maps from enzyme digests
 - Strategies for generating large restriction maps
- Simulation and design of recombinant DNA experiments
- Sequence entry, verification and editing *The Genetic Editor*
- Managing large DNA sequencing projects
 - Methods for eliminating vector sequences from your gels
 - Customization to chemical- or dideoxy-sequencing methods
 - Strategies for assembling multiple gels and generating reliable consensus sequences
- Sequence database organization and searching methods
 - Comparing N.I.H. GenBank, EMBL, and NBRF databases
 - Rapid sequence alignment and similarity searches
 - Sequence retrieval using exact or ambiguous patterns
- Sequence analysis programs
 - Nucleic acid sequence analysis, comparison and manipulation
 - Amino acid sequence analysis, comparison and manipulation
- Sequence comparison methods
 - The algorithms, speed, precision and limitations
- Distributed processing—moving data to and from the **BIONET** computer

Schedule:

8:30 A.M.	Registration and coffee
9:00-noon	Morning session
1:30-4:30 P.M.	Afternoon session

LOCATION

Waksman Institute of Microbiology
Rutgers, The State University of New Jersey
Hoes Lane and Frelinghuysen Road
Piscataway, New Jersey 08854-0759

INTRODUCTION TO **BIONET**[™]; A National Computer Resource for Molecular Biology

June 17, 1985 Course Fee: One-Day Workshop: \$100
June 17-19, 1985 Three-Day Workshop: \$450

Check workshop desired One Day Three Day

Dr., Mr., Ms _____

Position/Title _____

Company/Institution _____

Address _____

City _____ State _____ ZIP _____

Telephone _____

Please make check payable to **Rutgers, The State University of New Jersey**. Return form with payment to the Continuing Professional Education Program, Waksman Institute of Microbiology, P.O. Box 759, Piscataway, New Jersey 08854-0759.

PLEASE POST

WHO SHOULD ATTEND

This session should be of interest to all **BIONET** recipients. In addition, principal investigators involved in molecular biology research would benefit from learning about the resource. IntelliGenetics commercial customers, and other molecular biologists are welcome to attend the one-day session. Attendance at the two-day hands-on session is designed primarily for **BIONET** recipients and may be limited to one representative per laboratory group.

WORKSHOP LEADERS

Douglas Brutlag, Ph.D., Department of Biochemistry, Stanford University.

Larry Kedes, M.D., Department of Medicine, Stanford University Medical Center

Elaine Mansfield, Ph.D., **BIONET** IntelliGenetics, Inc., Palo Alto, California

REGISTRATION AND FEE

The registration form and fee must be received in advance of the program date. This fee includes course admission, class materials, and beverage breaks.

For additional information or to reserve a space, contact Selma Gitterman, Director, Continuing Professional Education Program at 201/932-4258 between 1:00-4:00 P.M., E.S.T.

CONTINUING EDUCATION UNITS

CEUs are awarded to participants in this program. The CEU gives formal recognition to persons continuing their education and keeping up-to-date in their chosen field or profession.

ATTENDANCE

Attendance is limited for both workshops. The three-day session will be limited to 30 participants. Please register as early as possible.

How did you learn about this course?

Direct Mail Other _____

From Supervisor _____

From Posted Material _____

Other workshop topics I would be interested in _____

Please keep me on the mailing list

Yes No

Also add the following persons to the mailing list

Name _____

Company/Institution _____

Address _____

City _____ State _____ ZIP _____