Linkage Newsletter

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EDITORIAL

The description of the new PC version of the LINKAGE programs in the last Newsletter has apparently caused some confusion, and I would like to set the record straight. The changes made by Dr. Sandkuyl were soon also implemented by Dr. Lathrop and, due to an unfortunate lack of coordination between Paris and New York, we independently started mailing out upgraded program versions. This is to let users know that Dr. Lathrop's version 4.9 and our version 5.03 are essentially the same. We will jointly issue a new version, 5.1, which will be slightly different from the present versions.

I sometimes get letters from readers who are concerned that they might not have received all issues of the Newsletter. The proper explanation is usually that the Newsletter has not appeared as regularly as one might wish. The following volumes/issues have so far been sent out: 1/1, 1/2 (1987); 2/1 (1988); 3/1, 3/2 (1989).

LINKAGE COURSES

The second linkage course at Columbia University is a *Beginner's Course* and will be held *March 21-24, 1990* (Wednesday through Saturday). Registration is now open until the course is full. An application form is attached to this newsletter. *Please pass on copies of the attached announcement to anyone interested.* In the fall of 1990, an advanced course will be offered (3 days) but the date has not been set yet.

COMPARISON OF COMPUTERS FOR LINKAGE ANALYSES

While various benchmark programs are used to compare computers, the most useful criterion for a linkage analyst is how quickly a computer can run a typical linkage analysis. Dan Weeks and I have, therefore, used the same benchmark problem as the one discussed in the 2/1 Newsletter and had MLINK calculate 10 likelihoods for the first 4 loci in the family published by Lathrop and Lalouel, Am J Hum Genet 42/3, 1988, p. 502 (in individual 32, the third marker phenotype was changed from 11 to 12).

For the present runs, the program constant maxcensor was set equal to 30,000 which generally improved computing speed by approximately 20% as compared with maxcensor=1000. The times indicated in the table, below, are the number of seconds required to calculate the ten likelihoods. On multiuser systems, the CPU time is given rather than elapsed time, which gives these systems an advantage of perhaps 10% over single user systems. The computers are identified by manufacturer, model, processor (clock speed in MHz given after hyphen), numeric coprocessor if present, operating system in parentheses, and compiler. On the machines running under MS-DOS/PC-DOS ("DOS"), the compiler used was Turbo Pascal version 5.0.

The times shown below not only measure machine performance but also, for example, some aspects of the efficiency of the compiler used. Other compiler characteristics are not given. For example, the Pascal compiler on the Silicon Graphics machine took less than 30 seconds to compile the MLINK program yet carried out some checks not done by other compilers.

Computer	Seconds
DEC DECstation 3100 RISC (Unix)	17
Silicon Graphics Personal Iris 4D/25, RISC-20 (Unix)	20
Sun SPARCstation 1 (Unix)	37
DEC VAXstation 3100 (VMS)	62*
Proteus, 80386-25, 80387-25 (DOS 4.0)	96
Dell System 310, 80386-20, 80387-20 (DOS 4.0)	116
IBM 4381-11 mainframe (CMS), Pascal/VS	119
Compaq Deskpro, 80386-20, 80387-16 (DOS 3.3)	147
Mac SE/30, 68030-16, 68882, MPW Pascal	162
IBM PS/2 Model 70, 80386-20, 80387-20 (DOS 3.3)	178
DEC Microvax II	191
Compaq Deskpro, 80386-16, 80287 (DOS 3.3)	374
PC Designs, 80386-16, 80287-10 (DOS 3.3)	459
Toshiba 3100e, 80286-12, 80287-10 (DOS 3.3)	486
IBM AT, 80286-8, 80287-5 (DOS 3.3)	658
Compaq Deskpro, 80286-8, 80287-5 (DOS 3.3)	658

*Compiled with VMS Pascal with the /NOCHECK/OPTIMIZE=ALL option and linked with the /NOTRACEBACK option.

SOFTWARE NOTES

Dr. Kenneth Lange announced at the Baltimore meeting of the American Society of Human Genetics November 11-15 that the full source code of the *Programs for Pedigree Analysis (MENDEL, FISHER, SEARCH, and dGENE)* is now available effective immediately. Interested researchers should contact Dr. Lange (Tel. 213-825-5018) and will have to sign a user agreement.

Dr. Daniel Weeks is working on implementing the *LINKAGE programs on the Macintosh*. Test versions of the programs run fine; see computer comparison chart, above. Generally available versions should be ready in a few months. These programs will run best on a Macintosh with a math coprocessor. The Macintosh programs will have an advantage over the MS-DOS programs since they can use all available memory.

I started adapting the *LINKAGE programs to OS/2* using the Prospero OS/2 Pascal compiler. Potentially, using the linkage programs under OS/2 could be an attractive solution (low cost, multitasking) for researchers who need to run more than the relatively small maximum number of loci under MS-DOS but do not want to purchase a workstation running Unix or VMS. OS/2 has virtually the same command set as DOS, so a minimal adaptation is required when changing from DOS to OS/2.

To compile the LINKAGE programs with Prospero Pascal requires splitting them into separately compilable so-called segments. A test version of the MLINK program runs fine, but the following compiler error was encountered. The R compiler switch controls whether the floating-point coprocessor will be used (R1) or not (R0). With R0, compiling is no problem but with R1, the Likelihood procedure cannot be compiled due to an 'internal compiler error'. The Prospero company cannot duplicate the error on an IBM clone, but the error definitely occurs under IBM OS/2 on an IBM PS/2 model 70 with 80387 coprocessor. Progress in this matter will be reported in the next Newsletter. Prospero OS/2 Pascal might be quite useful as its present implementation allows dynamically addressing up to 4MB of memory compared to approximately ½MB with Turbo Pascal under DOS.

The standard Pascal version of the LINKAGE programs is available from Dr. Mark Lathrop in Paris. It may easily be adapted to Pascal/VS on *IBM mainframes running under VM/CMS*. The following considerations apply.

-       All Pascal file names, eg, DATAFILE, will be connected to disk files with the same name preceded by 'file', eg, FILE DATAFILE.

- To assign the standard output file to the terminal, the statement TERMOUT(OUTPUT) should be added at the beginning of the main program body.

- In Pascal/VS, real variables cannot be smaller than $10^{**}(-78)$ in absolute value, or else an underflow occurs which will be indicated on the screen. If this happens, the results calculated after the underflow occurred are not reliable and should not be used. The possibility of underflows occurring limits the size of the problem you may analyze.

- Each occurrence of the up arrow sign, $\wedge$, has to be replaced by the @ sign.

I am sometimes asked to send source code of the LINKAGE programs by *Bitnet*. While this might be an attractive way of distributing source code, it is presently too complicated for my collaborators in that it requires special attention to each such request. I am sorry that I cannot at this time provide this service, but it may become available at a later date. We will explore the possibility of using a server so that interested researchers can request programs or other text by Bitnet without us having to upload and send them.

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Beginners' Linkage Course

Wednesday through Saturday, March 21-24, 1990

Course Description and Prerequisites

This course is for researchers with little or no experience in using linkage progr-ams. A basic knowledge of linkage analysis is, however, required. *Topics:* Introduction to linkage analysis; practical aspects of data collection; strategies and methods of linkage analysis; reduced penetrance; application of computer programs (LINKAGE version 5.1; Programs for Pedigree Analysis [MENDEL]; Linkage Utility Programs); affecteds-only analyses; inbreeding loops; simple risk calculations. Computer programs can be taken home (on 3½" or 5¼" diskettes). A copyrighted course manual will be mailed for study before the course begins. Please distribute copies of this course announcement to any interested persons.

The course will be held in the microcomputer classroom of the Health Sciences Library (Columbia-Presbyterian Medical Center, 701 West 168th Street) which is equipped with 20 IBM PS/2 machines. The number of participants is *limited to 25*. People should plan on arriving in New York in the evening of Tuesday, March 20, 1990. For telephone information, please call Katherine Montague at (212) 960-2504 Mon/Tue/Thu or Fri, between 8:30 am and 12:30 pm New York time.

An advanced course will be held in the autumn of 1990 (date not yet fixed). The topics will comprise linkage with pseudoautosomal loci; estimating and testing for heterogeneity; linkage disequilibrium; risk calculations, also under linkage disequilibrium and locus heterogeneity.

Course Fee

The fee for the 4-day-course is *$400* for researchers at an academic institution, and *$500* for individuals from private (for profit) companies. It may be paid by check made payable to Columbia University Dept. of Psychiatry, or by Government pay order, but send no money now -- applicants will receive a bill and information regarding cancellation policy. As there is presently no support for this course from sources other than the course fee (a grant application is under review), no reduction of the cost to applicants is possible. This fee covers tuition and course related expenses (handouts, diskettes, etc.) but not room, board or meals. Course participants will receive a list of good and moderately priced hotels in New York and will have to make their own arrangements (except foreign participants). A small number of guest rooms are available in Bard Hall next to the Health Sciences Library (double rooms at $60 per room per night, single rooms at $55).

Application for Linkage Course by Dr. Jurg Ott

Please fill out this page and send it by mail or, preferably, by FAX. People interested in staying in a double room at Bard Hall should indicate a preferred roommate, or else we will match applicants.

Your name: _____

Affiliation: _____

Address: _____

_____

_____

Tel. number: _____

FAX number: _____ Bitnet:_____

Interested in staying at Bard Hall?   YES / NO   DOUBLE / SINGLE

If yes, which nights?   Tue Wed Thu Fri Sat Sun

What size diskettes do you use?   3½" 3½"HD 5¼"HD (please circle)
  (we prefer 3½"; we have no easy way of writing to low-density 5¼" disks)

For applicants from abroad: Do you want us to make hotel reservations?   What accommodations?

Below, please describe which linkage programs you have used if any, how many families you have analyzed, and other experience in linkage analysis you might have:

Signature: _____   Date: _____