Linkage Newsletter

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LINKAGE COURSES

The third linkage course at Columbia University is an *Advanced Course* and will be held *November 8-10, 1990* (Thursday 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.* Unfortunately, there is presently no possibility for travel stipends or for reduced admission fees.

BUG REPORT

I am grateful to Drs. Bertram Müller and Tiemo Grimm (Würzburg, F.R. Germany) for making me aware of the following bugs in the LINKAGE programs. The bugs have an effect only when one works with different mutation rates in the two sexes. In PREPLINK, the order of male and female mutation rates is reversed, and in the LINKAGE analysis programs, the likelihood is calculated incorrectly when male and female mutation rates are different. In the versions currently being mailed out, these errors have provisionally been corrected by Dr. L. Sandkuyl and Joseph Terwilliger.

SOFTWARE NOTES

Version 5.1 of the LINKAGE programs is still in preparation. It should be available in September or October. A test version of it runs about 10% faster than version 5.03, and the release version should be somewhat faster still. Version 5.1 will also be available under OS/2 (see below).

A serious **potential pitfall** in the LINKAGE programs was recently uncovered by one of my collaborators, Dr. Chantal Mérette. She analyzed a pedigree for linkage between a dominant disease and a marker with 8 alleles. The data clearly showed a recombination, but the MLINK program (version 5.04) did not report a lod score of minus infinity at $\theta=0$. The explanation was as follows. The marker was coded as an *allele numbers* locus type with 8 alleles. In LINKAGEC.PAS, there is a program constant, MAXFACT, which gives the maximum number of

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binary codes at a single locus. MAXFACT was left at its former value of 5 since no *binary factors* loci were to be analyzed. As it turns out, MAXFACT is also relevant for *allele numbers* loci and must be at least as large as the number of alleles, MAXALL. In future versions, a check will be incorporated to verify that this is indeed the case. For now, users should verify manually that MAXFACT≥MAXALL in LINKAGEC.PAS.

Conversion of the LINKAGE programs to the **Macintosh** (Dr. D. Weeks) is still in progress but has been relatively slow due to time constraints. These programs should become available towards the end of 1990. They will be announced in this newsletter. It should be noted, however, that presently there are no plans to also have LCP (Linkage Control Program) running on the Macintosh, since converting LCP by us would be too much of a time commitment.

Adapting the LINKAGE programs to **OS/2** is going smoothly. The problems with the Prospero Pascal compiler reported in the previous issue of this newsletter have been resolved. The current version of the compiler, version iio 5.202, is free from the bugs seen in previous versions. It is available from Prospero Software, 100 Commercial Street Suite 306, Portland, Maine 04101, and is highly recommended. The purchase price ($253 after educational discount, plus $5 handling charge) includes both the MS-DOS and OS/2 versions. It has several advantages over Turbo Pascal. For example, programs need not be broken into smaller units for compilation; file buffers can be set for any files, not just text files as in Turbo Pascal; up to 4 MB of memory can be addressed dynamically under OS/2 so that larger problems can be run (Turbo Pascal is not available under OS/2). ProPascal shares with Turbo Pascal the restriction that no Pascal procedure can be larger than 64KB in code (none of the procedures in the LINKAGE programs exceeds that limit). On the other hand, our test problem runs 34% faster when compiled with Turbo Pascal than with ProPascal (for DOS). We may be able to increase speed under ProPascal somewhat but probably not up to the level of Turbo Pascal. More details will be given in the next issue of the newsletter.

Several of the **HOMOG** programs have been updated. The HOMOG2 program has been changed to report likelihood ratios instead of p-values for the test of homogeneity versus heterogeneity. Since even the asymptotic distribution of the test statistic is unknown for the case addressed by the HOMOG2 program (when going from two to one component, this single restriction automatically eliminates two parameters), the formal p-values seem unreliable. Also, a specialized version of the HOMOG3 program has been added: HOMOG3R assumes that a locus is linked to either of two markers on different chromosomes, or is unlinked with the two markers. As usual, new program versions are obtained by requesting from us a list of programs with ordering instructions.

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Advanced Linkage Course

Thursday through Saturday, November 8-10, 1990

Course Description and Prerequisites

This course is intended for researchers who already have experience with linkage analysis and would like to become more proficient in analyzing linkage data and handling unusual problems. A working knowledge of IBM PC's is assumed. The course will begin with a brief introduction to theory and techniques. Its main part will consist of problem-solving sessions with use of computer programs (LINKAGE version 5.04 or, hopefully, version 5.1; MENDEL; HOMOG; Linkage Utility Programs) and general question-and-answer sessions. The topics to be covered comprise heterogeneity, pseudoautosomal linkage, inbreeding loops, risk calculations, sex-specific recombination fractions, etc. Computer programs can be copied (on 3½" or 5¼" diskettes) and taken home. A manual will be mailed before the start of the course.

The course will be taught by myself and my collaborators. It will take place in the classroom of the Health Sciences Library (701 West 168th Street) which is equipped with 20 microcomputers of type IBM PS/2 (3½" diskette drives). Due to space limitations, course attendance is *limited to 30 participants*. Participants should plan on arriving in New York in the evening of Wednesday, November 7, 1990.

Course Fee

The fee for the 3-day-course is *$400* for researchers at an academic institution, and *$500* for individuals from private (for profit) companies. It may be paid by a check drawn on a U.S. bank, made payable to Columbia University Dept. of Psychiatry, by Government pay order, or by Travellers checks, 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, 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? Wed Thu Fri Sat

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: _____