

Corrections and Updates to *Handbook of Human Genetic Linkage*

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Below, the currently known corrections to this book are listed. Copyright has been transferred from the Johns Hopkins University Press, Baltimore, to the authors, Joseph Terwilliger and Jurg Ott. The book will soon be available online with errors corrected.

Most example and exercise data are available as [computer files](#). Many thanks to Harald Göring for corrections he has pointed out in the text.

Please note that most exercises were calculated on a Vaxstation. Therefore, results and presentation may differ slightly from what you'll see in your Windows or Linux output.

Page 8: Replace the text in section 1.4 by the online document, <http://www.jurgott.org/linkage/LinkagePC.html>

Page 8, line 12 from the bottom: ... type PKUNZIP *.ZIP ... (no space in pkunzip).

Page 14/15: The company that produced the PC-WRITE text editor no longer exists. We recommend the use of the Windows programs *EDIT* or *Notepad*.

Page 15, last line in example data: in *EDIT*, the [EOF] character is produced with Ctrl-P Ctrl-Z (hold down Control key and press P, then Z, and release the Control key). Instead of inserting an [EOF] character in column 1 after the last pedigree data line, you may proceed as follows to ensure that your input file does not contain any empty trailing lines: Press Ctrl-End, which will position the cursor at the end of the file. If this position is not in column 1 of the line immediately following the last pedigree data line, press the Backspace key repeatedly until the cursor is all the way to the right on the last pedigree data line.

Page 20, Exercise 2: The user is advised to watch out for a built-in 'mistake' -- please find it yourself. Enter the data completely as directed including the mistake - error trapping procedures are described in Exercise 3, so it is prudent to leave things as they are to fully appreciate the kind of error trapping explained with this example.

Page 31, line 9 from the bottom: lod score should read 0.124929, instead of 0.129429.

Page 35, line 21 from the bottom reads clearer as follows: "... exit the program, and LCP will write the PEDIN.BAT file.

Page 37, line 10 from the bottom: There is a constant multiplier, $\log(e)$, which has been left out of the equation for the first derivative of the lod score. Since it is a constant, it has no effect on the conclusions when the first derivative is set equal to zero.

Page 39, Table 5-2: At $\theta = 0.5$, the \log_{10} likelihood should be 16.395399 instead of 16.195199.

Page 48, Table 6-2: At $\theta = 0.45$, the lod score should be 0.008472, instead of 0.025347.

Page 57, line 7 from the bottom: chapter 12, not chapter 10. Be aware that the values given in table 12-7 are incorrect (see comments to page 96).

Page 68, line 9 from the bottom and table 9-3: where pedigree file EX3.PED is referred to, it should be changed to EX3A.PED. Also, the results in table 9-3 were obtained with a constant penetrance of 0.50. With age-dependent penetrance classes as in the dominant case above, the following six lod scores should be obtained: 0.699815, 0.523004, 0.344353, 0.177339, 0.049606, and 0 (thanks to Alda Ambrosio for pointing this out).

Page 71: line 5 from the bottom: The formula for prevalence in sex-linked recessive diseases where only males are allowed to be affected as given in the text assumes that the prevalence, ϕ , refers to the prevalence among males. The total population prevalence would be half of this value, since males are half the population.

Page 72, figure 9-2: The first individual in the 4th generation (marker genotype 2/4) should be 9 years old, not 10.

Page 74 - (in chapter 10): the numbering of loci is off by one - on page 74, line 3, it should say add a SIXTH locus, not a FIFTH locus. From this point on, the loci are undernumbered by 1.

Page 75, table 10-1: Under the heading 'Penetrances for Genotypes', the genotypes should be 11 12 22, not 12 12 22.

Page 76, line 20 from the bottom: Use pedigree file EX3A.PED where EX3.* is referred to in the text.

Page 76, line 18 from the bottom: "mgrandpa, dau1", not "mgrandma, dau1."

Page 77, line 5 from the bottom: Note that the allele frequencies given here for ABO are different than what was used in exercise 8. Use the frequencies indicated in the text on page 77.

Page 80, top line: When it says to recode the disease as a recessive trait, what is meant is that you should think of the "normal" trait as the trait of interest, which should be coded as "2" in the pedigree file. It is not intended that you falsely assume the disease is inherited as a recessive, but rather that if the disease is dominant over normalcy, then normalcy is recessive to the disease.

Page 80, Line 7: Should say EX12.* not EX9.*

Page 83, figure 11-1: Individual 1.2 should be drawn as affected in both pedigrees.

Page 83, sample input file, line 5: m should be in column 16 as is F (in AF) five lines down. Line starting with S61: The word "symbols" should be all on this line; there is no blank line following this line. Line starting with 345: sex is f, not m. The first few lines of the input file are as follows:

```
1 0000
(20A4)
(2A4,21F4.0)
(20A4)
                                m
2 3
3 6
-1 0
2
Dis   D   +  AF  NA  MT
      0.001 0.999
      D   D   .9  .1  .01
      D   +   .9  .1  .01
```

+ + 0 1 1
 S61 1 2 3 1/1 1/2 1/3 2/2 2/3 3/3

Page 83, paragraph at bottom of page: This text is too brief for a full explanation of the input. Please consult section 5, "INPUT FILE," in the [LIPED manual](#). It will also explain the meaning of the four zero's on line 1 of the example input file.

Page 90, line 2: Should say 70% penetrance, not 75%.

Page 96, Table 12-7: The log likelihoods and lod scores are incorrect. The correct values are as follows:

Theta	log10(likelihood)	Lod score
0.00	-13.838789	4.210090
0.05	-14.282988	3.765890
0.10	-14.748045	3.300833
0.15	-15.235013	2.813866
0.20	-15.743824	2.305054
0.25	-16.270839	1.778040
0.30	-16.802341	1.246537
0.35	-17.301193	0.747686
0.40	-17.699404	0.349474
0.45	-17.943024	0.105854
0.50	-18.048878	0.000000

Page 96, line 8 of text: [1.21, 4.21], not [0.13, 3.13]. Also, in "support interval for theta", the theta symbol should be written without a hat.

Page 96, line 9 of text: [0, 0.30], not [0, 0.45).

Page 111, tables 14-3 and 14-4: "Interval 2" refers to rows while in columns, the different "Interval 1" recombination events are delineated.

Page 114, Tables 14-6 and 14-7: The odds under the order 1-3-2 should be 700,000, not 70,000.

Page 114, Table 14-7: The heading for column 2 should be "-2 ln(Like)", not "2 ln(Like)".

Page 131, lines 5, 4, and 2 from the bottom: Each case where it says "to the right of marker 3" should say "to the left of marker 3".

Page 137, line 13-15: numbers are slightly off - replace this section by the following:

"...region covering a 7cM range. The total exclusion region in this analysis is 23cM in an analysis with a positive lod score of 9. This is impossible with two-point analysis in this pedigree set. We saw that a 30-cM region..."

Page 141: R for interval 2 should be 0.811, not 0.0811.

Page 145, table 18-4: The column labeled "df" is more properly labeled "no. of parameters estimated". The number of degrees of freedom for testing a hypothesis versus another, listed above it, is given by the difference in numbers of parameters estimated.

Page 160, Exercise 16, line 3: change "the alternative locus order" to "different intermarker recombination fractions".

Page 162, Table 20-8: In sections 5===1===2---8---3 and 5---2===1===8---3, the lod scores listed are too small by a factor of 10. For example, -2.94 should be -29.4. To obtain accurate lod scores, divide the location scores by 4.6. The correct results for the first three sections are as follows:

Order/Theta's	Loc. Score	-2LN Like	Lod Score	Map loc.

1====5----2----8----3				
.500 .020 .020 .040	0.00	+4.288E+02	0	-inf
.400 .020 .020 .040	3.48	+4.253E+02	0.755	-0.8047
.300 .020 .020 .040	4.24	+4.246E+02	0.921	-0.4581
.200 .020 .020 .040	1.46	+4.273E+02	0.317	-0.2554
.100 .020 .020 .040	-8.37	+4.372E+02	-1.817	-0.1116
5====1====2----8----3				
.000 .020 .020 .040	-inf	infinity	-inf	0.0000
.004 .016 .020 .040	-135.63	+5.644E+02	-29.452	0.0040
.008 .012 .020 .040	-127.33	+5.561E+02	-27.650	0.0081
.012 .008 .020 .040	-128.22	+5.570E+02	-27.843	0.0121
.016 .004 .020 .040	-138.65	+5.675E+02	-30.107	0.0163
.020 .000 .020 .040	-inf	infinity	-inf	0.0204
5----2====1====8----3				
.020 .000 .020 .040	-inf	infinity	-inf	0.0204
.020 .004 .016 .040	-138.83	+5.676E+02	-30.146	0.0244
.020 .008 .012 .040	-127.46	+5.563E+02	-27.678	0.0285
.020 .012 .008 .040	-125.39	+5.542E+02	-27.228	0.0326
.020 .016 .004 .040	-131.93	+5.607E+02	-28.648	0.0367
.020 .020 .000 .040	-inf	infinity	-inf	0.0408

Page 163, Figure 20-1: This graph is based on the erroneous lod scores in Table 20-8. Therefore, the two humps immediately to the right of map location 0, with heights of about -3 each, should not be visible.

Page 166, line 8: Should say $f(D/+) = f(D/D) = 0.25(1) + 0.75(0) = 0.25$

Page 170, line 13: Change "constant sex difference" to "no sex difference" at the beginning of this line.

Page 178, line 8 before section 21.3 : Change "section 3.4" to "section 3.1".

Page 178, line 4 before section 21.3: amend text as follows: "... to assume for μ ; however, because the mutation rate must fit with certain conditions regarding mutation-selection equilibrium, μ must be less than or equal to p , the frequency of the disease allele, as you will see in the following sections."

Page 180, paragraph 2, line 2: Should say make son3 unaffected, instead of son4.

Page 195, line 23 (in indented text from PREPLINK output), the last haplotype frequency line should read as follows (in the text it says ALLELES 1 1 ...):

ALLELES: 2 2 0.000000E+00
 ?
 0.146450

Page 196, line 10 from bottom: Should say "...indicated in the last column below..." instead of "above".

Page 200, paragraph 2: Many of the numbers are backwards. Throughout this paragraph, please interchange "allele 1" and "allele 2". Thus, in line 5, it should say $P(\text{allele 2} \mid \text{disease allele}) = 0.4$ and $P(\text{allele 1} \mid \text{disease allele}) = 0.4$. For the rest of this paragraph just interchange the marker alleles 1 and 2.

Page 209, 4th line from bottom: EX6A.DAT should be EX6.DAT

Page 223, first paragraph: In these models, the results given in the text assumed that $p_3 = 0.6$ under the dominant model, and $p_3 = 0.70$ in the recessive model. Making this change should give you the penetrance values given in table 25-11.

Page 223, third line from bottom: lod score with marker 2 should be 1.43, not 1.83.

Page 225, table 25-14: The header for the last column should say Table 25-13 penetrances, instead of 25-15.

Page 233, paragraph 2: You must run ESPA from the directory containing the ESPA program, unless it is installed to be accessible from elsewhere - merely putting it in the path is insufficient.

Page 236, last line: The right bracket should be moved to the left of the ~ sign.

Page 243, line line 4 from the bottom: "... full penetrance and two alleles, T (trait) and + (normal), such ..."

Page 244, line 10: "... carry allele 1." Line 19 from the bottom: "... with the T allele ..."

Page 250, line 4 should read: "...LCP (which calls LSP) to extract..."

Page 254, first equation on page: The P to the right of the equal sign should be part of the numerator (above the line).

Page 256, line 11 from the bottom should read: Line 1 - Three seeds for the random number generator (integers between 1 and 30323).

Page 262, Table 29-2: Results should be as follows:

Theta	Lod Score
0.0	4.210082
0.1	3.300826
0.2	2.305048
0.3	1.246533
0.4	0.349473

ILINK: theta hat = 0.0 Z(theta hat) = 4.210082

Page 265, paragraph 2: There are only two founders who were not typed at the marker locus, and not three as indicated in the text.

Page 272, line "H2: Linkage" (below line 3): replace 9.7123 by 9.7077.
Line "H2 vs H1": the two numbers on the right should be 19.415 16440
Line "H2 vs H0": the two numbers on the right should be 19.415 16440.

Page 277 middle, formula for PIC: replace all "n" by "a" (3 times).

Page 282, line 1: Mendelian, not Medelian.

Page 283, line 6: The correct email addresses are "Katherine.Montague@rockefeller.edu" for Katherine Montague and "ott@rockefeller.edu" for Jurg Ott. Programs are available from our websites <http://lab.rockefeller.edu/ott/programs> and <http://www.jurgott.org/linkage/>. The remainder of section B4 is obsolete.

Page 284, upper half: Programs developed by Dr. Daniel Weeks are available from his [web site](#).

Page 284, lines 21-26: The FASTLINK programs are available from <http://www.ncbi.nlm.nih.gov/CBBresearch/Schaffer/fastlink.html>

Questions should be directed to Dr. Alejandro Schaffer at email address schaffer@helix.nih.edu. This faster variant of LINKAGE runs on most systems with some minor modifications, though it performs better on larger machines.

Page 291, line 5 from the bottom: The Linksys program is no longer distributed by Dr. John Attwood.

Page 293, line 2: The CHROMLOOK program is no longer supported by Jonathan Haines.