



Multivariate Linkage Continued

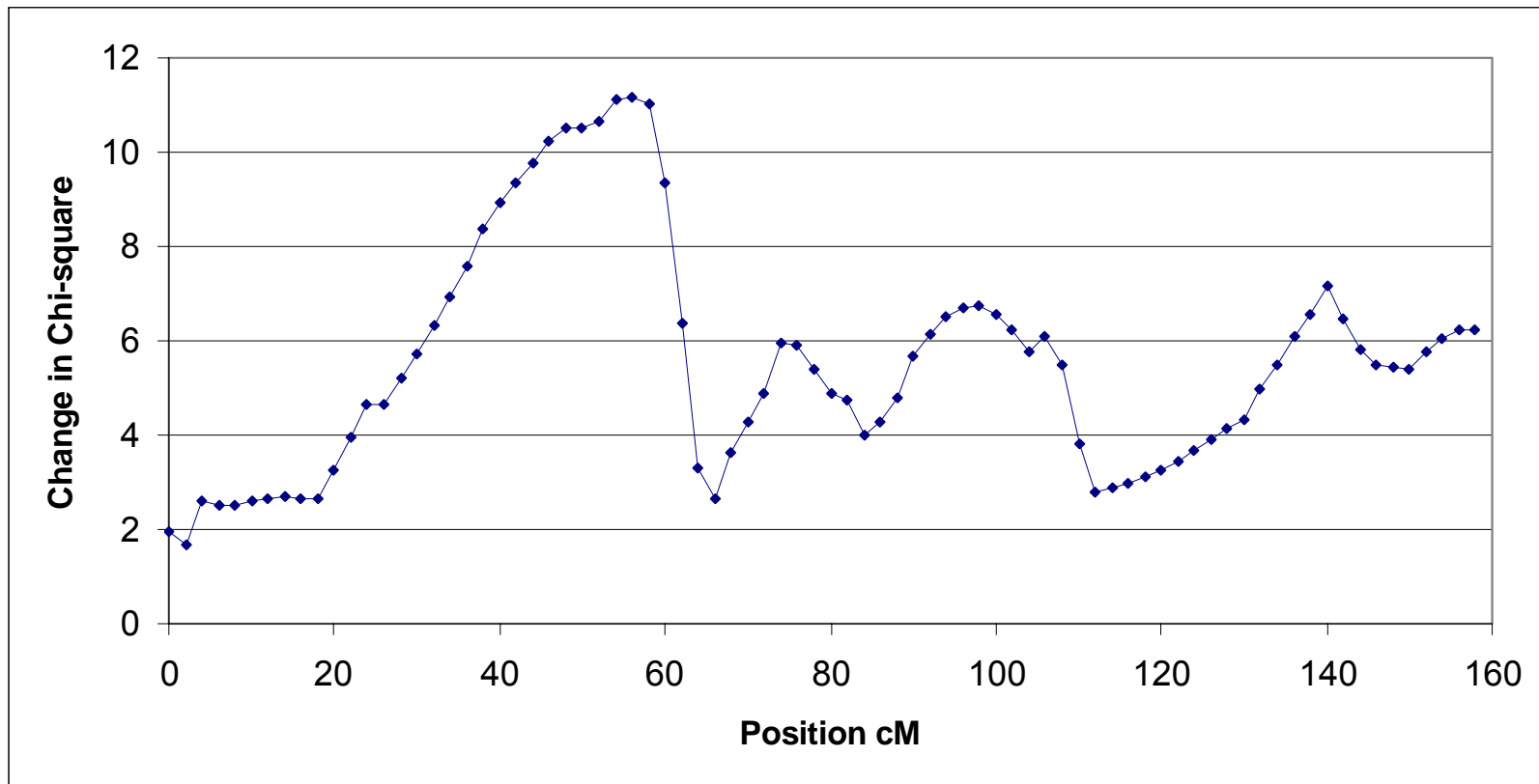
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[Running a loop]

- Alternate method for running all markers is to run a 'repeat' script
 - multi_repeat.mx
 - #repeat n – where n is number of times the loop will run
 - Use 'exit' at the end of your last group
 - End the script with #end repeat
 - Can refer to i using \$repeat_number – where i is the number of the current repeat

Results change in chi-square



Probability

- Calculating the p-value can be problematic for MV linkage
- Univariate Linkage (1 QTL estimate)

Univariate Linkage: (1 QTL estimate)

Under standard conditions, twice the difference in natural log-likelihood between models is distributed asymptotically as a χ^2 distribution with degrees of freedom equal to the difference in the number of parameters between the models

BUT

In linkage analysis, the likelihood ratio test is conducted under *non-standard* conditions

That is, the true value of some of the parameters under the null hypothesis (i.e. $\sigma_q^2 = 0$) are located on the boundary of the parameter space defined by the alternative hypothesis.

Under these conditions, the likelihood ratio statistic is distributed as a mixture of χ^2 distributions, with the mixing proportions determined by the geometry of the parameter space. For example, in the case of a univariate VC linkage analysis, the test is asymptotically distributed as a 50:50 mixture of χ_1^2 and a point mass at zero (Self & Liang, 1987).

[In practical terms...]

- Univariate linkage
 - 50:50 mixture 0, χ_1^2
 - Calculate p-value for χ_1^2 and divide by 2
- LOD score = $\Delta\chi^2/4.6$

[In practical terms...]

- Bivariate linkage

- 25:50:25 mixture 0, χ_1^2 , χ_2^2
- Calculate:
$$p = \frac{\chi_1^2}{2} + \frac{\chi_2^2}{4}$$

[3+]

- The mixture starts becoming very complex
- Begins to approach χ_q^2 - where q is the number of QTL parameters estimated
(Marlow et al., 2003)
- Simulation is the best approach
- Alt. can use χ_q^2 but this will be a conservative test

Graphical representation

- $-\text{LOG}_{10}p$
- Back convert the p-value to a chi-square on 1 df and compute the LOD score as $\Delta\chi^2/4.6$
- Graph the p values

Viewpoint



Harry Beeby

- Graph the linkage results using viewpoint
 - Open by double clicking
 - Go to file and open the file uni-graph.txt
 - Chose a univariate plot
 - Go to Edit - select plotted columns and select $-\log(10)p$ & backconvert
 - Go to Edit - line attributes change colours

Viewpoint

- Nested model in which proportion of QTL variance was equated at each time point
- Result called 'LOD1_parameter' add it back into the graph

```
G4:Constraint Group
Constrant
Begin Matrices;
U Computed nvar nvar =U1
P Full 1 nvar free
End Matrices;
Begin Algebra;
D=\d2v(U) ;
End Algebra ;
Constraint D=P ;
END
```

Does the equated model 'perform' better than the full model?

Why?/Why not?

[Check the path coefficients]

- Explore the linkage results using veiwpoint
 - Go to file and open the file multi-graph.txt
 - Chose a multivariate plot
 - Explore the path coefficients
- Compare to the multivariate graph of demo-prints.txt

More information about viewpoint in viewpoint.ppt

[Viewdist]

- Find the families that contribute the most & the least to the LOD score using viewdist
 - Input data will be %p files from the null and linkage models – marker 58
 - Open by double clicking
 - Go to file and open difference file
 - The first file to read in is null.p
 - The second is marker58.p

[Viewdist]

- Chose an 'internal plot'
- Define column mappings
 - Graph column 2
 - Do not change other defaults
- Find the 3 'highest' families and look to see if they are outliers at marker58
 - Open file maker58.p
 - Chose a 'normal plot'
 - Graph column 4

[Viewdist]

- Conclusion are they outliers?
 - If so what would this mean
 - If so may want to rerun the linkage in this region excluding these families

More information about viewdist in viewdist.ppt