

ARE THIRD OR HIGHER ORDER LINKAGE DISEQUILIBRIUM RELEVANT?

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Introduction

In population genetics linkage disequilibrium (LD) is the non-random association of alleles at different loci. The level of linkage disequilibrium between two loci (A,a) and (B,b) can be quantified by the coefficient of linkage disequilibrium D_{AB} , which is defined as $D_{AB} = p_{AB} - p_A p_B$. There exists an ample literature on the extension of LD in livestock species and its relevance. However, the LD among three or more loci has been frequently overlooked in livestock species from both the point of view of its estimation and its relevance. For three loci ($A, B,$ and C) the third-order coefficient is $D_{ABC} = p_{ABC} - p_A D_{BC} - p_B D_{AC} - p_C D_{AB} - p_A p_B p_C$ where D_{AB} , D_{BC} and D_{AC} are the pairwise disequilibrium coefficients (Bennet, 1954). It can be interpreted as the non-independence among these alleles that is not accounted for by the pairwise coefficients. Here, we consider the relevance of this parameter in some contexts interesting in animal breeding.

Main results

Third order disequilibrium and the partition of genetic variance

In a three loci ($A,a / B,b / C,c$) quantitative trait, the variance components will be $V_A, V_D, V_{AA}, V_{AD}, V_{DD}, V_{AAA}, V_{AAD}, V_{DAA}$ and V_{DDD} . If all the three loci are in linkage equilibrium the partition of variance will be orthogonal. If now we assume that only a third order LD exists, only the variance of triple epistatic interactions will be affected. But, because the partition is not orthogonal the covariance between the genetic effects will be affected in such a way that only the additive and dominance variance will remain invariant. The same happens if we add a third order LD in a model where second order LD exists.

Third order disequilibrium and the variance explained by the markers

It is well known that in the simplest situation of one QTL (Q,q) and one linked marker (M,m) the proportion of additive and dominance variance explained by the marker is always lower than the true values (the missing heritability problem, Maer(2008)). If now we consider one QTL (Q,q) and two markers (M,m and N,n) and only D_{MNQ} is present among an additive QTL and two markers, an apparent additive x additive variance would appear. And if the QTL shows dominance both an apparent additive x additive and dominance x dominance variance would appear.

Let's now consider the situation of two QTLs (Q,q and R,r) and one marker (M,m). If there is not epistasis the inclusion of a three order linkage disequilibrium does not affect the apparent variance explained by the markers but if we include epistasis the apparent variance explained by the markers is affected.

Third order LD and the genetic vs genomic correlation

Gianola et al. (2015) demonstrate that correlation parameters inferred using markers can give a distorted picture of the genetic correlation between traits. They show that genomic correlation could be higher, lower or even of opposite sign that the genetic correlation. Here we show that in an additive setting the third or higher order LD do not affect the genomic correlation between two traits.

References

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- Gianola et al., 2015. Genetics: 201: 23–29.
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