

The Effect of Inbreeding on Linkage Disequilibrium

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ABSTRACT: The aim of this work was to study the linkage disequilibrium (LD) in simulated populations with different levels of inbreeding. Historical populations based on the genome of White Leghorn hens were simulated along 1023 generations allowing different historical and genetic events as bottleneck, changes on rates of females per males and mutation for SNPs and QTLs. Three different scenarios were simulated in recent populations, varying the mating type (random mating, less related or more related individuals) and heritability of traits (0.15 and 0.37) along 10 generations. The last four generations were genotyped and the LD was calculated. The heritability of the traits had no difference on the values of LD, but the inbreeding affected the effective population size (N_e) leading to different levels of LD between the populations.

Keywords: Hens; Inbreeding; Linkage disequilibrium; Simulation

Introduction

Inbreed populations generally have small N_e , and the genetic drift is one consequence of it causing loss of genetic diversity (Lacy, 1989). Thus, the inbreeding is a factor that must be controlled in animal breeding programs not to threaten the reproduction ability and survival of the animals (Sorensen et al., 2005). The population structure and the N_e affect directly the linkage disequilibrium. The LD is a non-random association of alleles at two or more loci (Qanbari et al., 2010). Thus, the aim of this work was to study the impact of different levels of inbreeding on linkage disequilibrium.

Materials and Methods

Historical population. The data set was simulated based on the genome of White Leghorn hens. All simulations were done using the QMSim program (Sargolzaei and Schenkel, 2009). The historical populations were simulated with an N_e of 1100 breeding animals with random mating with 50% of males and 50% of females along 1000 generations of constant size. After 1000 generations, it was simulated a bottleneck along 20 generations (generation 1001 to 1020) decreasing the N_e gradually from 1000 to 640 breeding animals. The bottleneck was important to generate the linkage disequilibrium and random drift, and it mimics the process of domestication in which occurs the decrease of the N_e (Henson, 1992). After this step, the historical populations were expanded for three generations (1021 to 1023)

under random mating of 80 males with 560 females of the generation 1020. The proportions of males to females were 1:7 with four progenies for each female, totaling 2240 animals at generation 1023. The genetic drift and recurrent mutation occurred until generation 1020, and the mutation rate was $2,5 \times 10^{-5}$ for SNP markers and QTL.

Recent population. After the historical populations, three different scenarios with different mating systems were simulated in each recent population. The recent populations REC1, REC2, and REC3 were simulated with maximizing or minimizing the inbreeding and random mating, respectively. Two traits were simulated, one with heritability equal to 0.15 and other equal to 0.37. These traits were simulated based on the heritabilities and phenotypic variances for total egg production and egg weight reported by Savegnago et al. (2011). The phenotypic variances for these traits were 130.32 and 16.11kg², respectively.

Genome. The genome was simulated for REC1, REC2, and REC3 based on the genome of the *Gallus gallus* 4.0 (NCBI, 2013), with eight macrochromosomes and 19 microchromosomes totaling 958Mb (10^6 base pairs). Only the autosomes were simulated and the microchromosomes 16 and 32 were omitted because QMSim cannot simulate chromosomes with less than 1Mb. The number of simulated QTL was 3747, which were all QTL reported for *Gallus gallus* (Hu et al., 2013), and 49978 SNPs equally spaced along the genome with 52.17Mb between adjacent SNPs.

Linkage disequilibrium. The linkage disequilibrium (LD) measured by the r^2 was calculated according to Hill and Robertson (1968) as the correlation between the allelic frequencies in two or more loci:

$$r^2 = \frac{D^2}{f(A)f(a)f(B)f(b)}$$

in which $D = f(AB) - f(A)f(B)$, and $f(AB)$, $f(A)$, $f(a)$, $f(B)$, $f(b)$ are observed frequencies of alleles of the markers A, a, B, b. Bohmanova et al., (2010) showed that r^2 is more appropriate to estimate the LD of biallelic markers because it is less sensitive to the allelic frequency. The DL can be resulted from migration, mutation, selection, the effective size of the population, and other events (Wright, 1931; Lander and Schork, 1994).

Results and Discussion

The mating systems had only effect on the magnitude of the LD (Figure 1). Brito et al. (2011) showed that the decreasing of the LD was due to the recombination rate between markers. The selection of the animals does not influence the LD.

Qanbari et al. (2010) studied commercial stocks of White Leghorn laying hens and GmbH (brown hens), reporting DL of 0.67 ± 0.38 to 0.28 ± 0.30 for the White Leghorns and for GmbH, respectively, at distances 0-0.05Mb between adjacent SNPs. The differences were explained due to the small historical population of White Leghorn line compared to the GmbH.

The DL was 0.29 ± 0.28 at distance 0 to 0.05 Mb between adjacent SNPs in the first recent generation in all scenarios. After 10 generations under selection, the highest value of DL was 0.52 ± 0.37 at a distance between 0 to 0.05 Mb between adjacent SNPs in REC1 to the trait with heritability equal to 0.15. The populations REC1 had inbreeding values higher than the others, ranging from 0.22 (trait with heritability 0.15) to 0.22 (trait with heritability 0.37), leading to decrease the Ne and increase the LD. The REC2 and REC3 populations had small differences about inbreeding rates and their Ne were similar between them but higher compared to REC1, leading lower LD compared to REC1.

Conclusion

The heritability of the traits had no difference on the values of LD, but the inbreeding affected the Ne leading to different levels of LD between the populations.

Literature Cited

- J. Bohmanova, M. Sargolzaei, and F.S. Schenkel. 2010. *BMC Genomics*, 11:421.
- F.V. Brito, J.B. Neto, M. Sargolzaei, et al. 2011. *BMC Genetics*, 12:80.
- E.L. Henson. 1992. *In situ Conservation of Livestock and Poultry*. FAO Anim. Prod. Health.
- W.G. Hill, A. Robertson. 1968. *Theor. Appl. Genet.*, 38:226-231.
- Z.L. Hu, C.A. Park, X.L. Wu, et al. 2013. *Nucleic Acids Res.* 41:D871-D879.
- R.C. Lacy. 1989. *Zoo Biol.*, 8:111-123.
- E.S. Lander, N.J. Schork. 1994. *Genetic dissection of complex traits*. *Sci. Washington*, 265:2037-2048.
- NCBI. 2013 National Center for Biotechnology Information. EUA. http://www.ncbi.nlm.nih.gov/genome/111?project_id=10808. (accessed 14 December 2013.)
- S. Qanbari, E.C.G. Pimentel, J. Tetens, et al. 2010. *Anim. Genet.*, 41:346-356.
- M. Sargolzaei, and F. S. Schenkel. 2009. *Bioinformatics*, 25:680-681.
- R.P. Savegnago, S.L. Caetano, S.B. Ramos, et al. 2011. *Poult Sci.*, 90:2174-2188.
- A.C. Sorensen, M.K. Sorensen, P. J. Berg. 2005. *J. Dairy Sci.* 88: 1865-1872.
- S. Wright. 1931. *Genetics*. 16:97-159.

Figure 1: Linkage disequilibrium (LD) of the recent populations for the two traits with different heritability estimates. REC1, REC2, and REC3 populations were simulated with maximizing or minimizing the inbreeding and random mating, respectively.

