

ABSTRACT

WACKEL, HANNA. Evidence of Genetic Variation for Recombination Rate in Purebred Swine Populations. (Under the direction of Dr. Christian Maltecca)

Recombination can affect the genetic gain of a trait in different ways. A high recombination rate can cause instability of genomic predictions as a result of the linkage disequilibrium breaking between markers and QTL. Conversely, recombination rate can maintain and increase the ability to recruit genetic variability by virtue of the same process.

The objectives of this study were to understand the differences in recombination rate between male and female populations; find the differences in recombination rate in breeds; and to estimate heritabilities of recombination for each population. Within this research, we investigated the potential effects of sex and breed as well as the genetic variation of recombination events in swine. Differences in recombination rate between ambient temperatures and relative humidity were also estimated.

Data originated from four breed/sex commercial nucleus populations of Smithfield Premium Genetics: Large White sires (LWS, n=270), Large White dams (LWD, n=1755), Landrace sires (LRS, n=281) and Landrace dams (LRD, n=1356). Individuals in the analysis were genotyped at 10k, 60k or 80k Illumina SNP chips then all imputed to 80k using the Fimpute software. The software FindhapV4 was used to obtain the total number of recombination events for each between each parent and progeny (n=20,712 total progeny records).

The R package MCMCglmm was employed to fit a model with the total number of recombination events in the genome as the predicted variable. Animal and contemporary group (herd, year, and season of observed recombination event) were random predictors, while sex, parity, male age class (based on four quantiles) and breed were fixed effects.

To estimate differences in recombination rate in environments the package MCMCglmm was used again in R. The fixed effects were either ambient temperature or relative humidity were classified into 10 classes based on quantiles. Other effects in the model include the random animal and contemporary group effects.

Heritability estimates of recombination were obtained within each breed/sex combination using THRGIBBS1F90. The model included the number of recombination events as a predictor variable and a random sire or dam effect for each population. The sire/dam effects were assumed $N(0, \mathbf{A}\sigma_a^2)$ and $N(0, \mathbf{H}\sigma_a^2)$ where \mathbf{A} and \mathbf{H} were a pedigree or a blended pedigree/genomic relationship matrix, respectively. Two fixed effects were included: a contemporary group and a covariate for age at recombination event.

Least squares mean estimates (LSME) of total number of recombination events for sex were 16.25(± 0.15) in dams and 12.09(± 0.18) in sires. LSME for breed were 14.32(± 0.23) in LW and 14.05(± 0.23) in LR. Sex and breed were both significant at $p < 0.0001$ and $p = 0.0312$ respectively. The LSME for parity in females was 16.04(± 0.20), 16.23(± 0.22), 16.72(± 0.29) for the 1st, 2nd and 3rd parity respectively. The significant differences in age in females were between the 3rd and 1st parity ($p = 0.0131$), where the 3rd parity had a significant increase of 0.68(± 0.25). The differences between temperature classes, humidity classes, or male age classes did not have a significant effect on recombination rate in this study.

Heritabilities of recombination across the whole genome were 0.04(± 0.03) for LRS, 0.07(± 0.03) for LRD, 0.09(± 0.06) for LWS, and 0.11(± 0.03) for LWD. Heritabilities, when genomic data was included, were 0.05(± 0.04) for LRS, 0.23(± 0.03) for LRD, 0.08(± 0.05) for LWS, and 0.26(± 0.03) in LWD.

Heritabilities per chromosome for recombination rate were also estimated in two separate models, one using only the pedigree to estimate the relationship matrix and the other using the pedigree and SNP chip information to estimate the relationship matrix. Estimates of heritability in the pedigree only model did not exceed $0.16(\pm 0.06)$ and were as low as $0.02(\pm 0.02)$ for all sex/breed combinations. Estimates in the blended pedigree and SNP chip model did not exceed $0.07(\pm 0.03)$ and were as low as $0.01(\pm 0.01)$ for all sex/breed combinations. On average, the estimates for heritability were lower in the blended model.

Results of this research indicate that both sex and breed affect recombination rate, with females as well as the LW showing a significant larger number of recombination events. The increase in number of recombination events in females is in line with what has been observed in other species including humans, mice and cattle. Environmental variables did not have a significant effect on recombination rate in our current analysis. Variance components estimates also show that recombination is under genetic control with heritabilities ranging from low to moderate with the use of pedigree or genomic information, respectively. These findings could contribute to a better understanding of recombination rate in swine populations and indicate that it might be possible to modify this trait through selection, although the direction in which the trait should be moved will need to be further investigated.

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Evidence of Genetic Variation for Recombination Rate in Purebred Swine Populations.

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BIOGRAPHY

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CHAPTER 1
LITERATURE REVIEW

VARIATION IN RECOMBINATION RATE IN LIVESTOCK POPULATIONS

INTRODUCTION

Recombination events in sexually reproducing organisms are important for creating new variation in the next generation. The act of recombination is advantageous because it can break linkage disequilibrium (LD) during double stranded breaks (DSB) in meiosis which can separate possible advantageous from disadvantageous alleles (Feldmant et al., 1980).

Without new variation in the genome introduced by recombination, the majority of current populations would not be able to adapt to the environment around them (Charlesworth, 1976). Understanding how the environment influences recombination is important for understanding how populations adapt to new environments. A large number of factors, including environmental pressure, influence recombination rate in livestock populations whether it is by increasing or decreasing recombination rate. Recombination in livestock populations has not been extensively researched but differences in recombination rate in sex (Lynn et al., 2005), breed (Thomsen et al., 2001), and age (Wang et al., 2016) have been identified. Recombination can be advantageous or disadvantageous in selected populations in livestock because it may introduce variation into the population which can influence the genetic gain of a trait in a positive or negative way (Myers et al., 2008). In most animals, a sizable body of literature exists pointing to a genetic control of recombination rate. In livestock only recently has the interest in the genetic architecture of this trait gained momentum as a result of the large amount of genotyped individuals created by genomic selection programs. Estimates of the genetic component of recombination rate in livestock species may be helpful in selecting for high or low rates of recombination in future populations (Gonen et al., 2017).

RECOMBINATION MECHANISMS

Recombination is the act of DNA swapping between homologous chromosomes during meiosis where the chromosomes line up before they divide to create gametes. During this alignment in meiosis, genetic material can be exchanged between chromosomes by the act of “crossing over”. The physical act of crossing over occurs when there is a double stranded break in the DNA. During this break, the genetic material of the two homologous chromosomes can be shared and create new variations within the genetic code (Reich et al., 2002). The two chromosomes are then repaired and are split into gametes. This “crossing over” is known as homologous recombination and is common in all sexually reproducing populations (Van Vleck et al., 1987).

Non-homologous recombination events can happen as well. In some cases, non-homologous chromosomes can recombine due to many double stranded breaks in the genome. This process is called translocation (Frank et al., 2007). There are different types of translocation within the act of breakage and relocation. Nonreciprocal translocation can introduce deletions or duplications within the genome and can be fatal. If the DNA between each chromosome is equally transferred, then the exchange of DNA can be called a reciprocal translocation. This is a less dramatic form of translocation, but can still result in lower fertility rates in the offspring due to difficulty of homologous chromosomes pairing up during meiosis (Van Vleck et al., 1987).

The last type of breakage and reattachment that can occur on a chromosome is called an inversion. An inversion can occur when there are multiple breaks on one chromosome at the same time. This may result in one chromosome flipping DNA around and some genes located at the “top” of the chromosome may be switched with those located at the “bottom”. This

translocation of DNA can result in lowered fertility rates as well due to the same complications that occur in reciprocal translocation (Van Vleck et al., 1987).

CAUSES OF VARIATION IN RECOMBINATION RATE IN POPULATIONS

Variation in the phenotype in the next generation can be due to many different things, one of them being recombination. Recombination is only a feature of sexual reproduction which is prominent in many higher eukaryotes. Muller's ratchet (Muller, 1964) explains why it is advantageous for an organism to reproduce sexually. He gives this credit to recombination. Recombination introduces new variation within a sexually reproducing population by shuffling the genetic code that is already available. In asexual species, the organism is self-sexing, which will only result in offspring that are an exact genetic copy of the parent. In populations that use sexual reproduction, the parent's genes within a population can recombine to introduce new combinations to correct for previously disadvantageous genes (Peabody et al., 2017). This new set of recombined genes can allow for the offspring to have a better chance at survival than the parents. Recombination controls the rate at which new haplotypes are introduced into a population. These new haplotypes can contain more or less recombination hotspots within the next generation (Coop and Przeworski, 2007).

Since about half of a parent's genetic material is inherited by the offspring, we can assume that some genetic traits of the parent may not be inherited. The differences in siblings can be due to how the gametes are formed (Fisher, 1919). As stated before, in meiosis, recombination can determine what genetic material will be passed onto the offspring of an animal. Different recombination rates may be influenced by population structure. Small population numbers are synonymous with an increasing threat of extinction which is

synonymous with decreased genetic variation, inbreeding, and fixation throughout these small populations (Shaffer, 1981).

When there is an absence of recombination within regions of the genome, linkage disequilibrium (LD) blocks can appear. Since these alleles are close together on the genome and there is a low frequency of recombination within these blocks, then we can assume that the block will be inherited and are very unlikely to recombine (Reich et al., 2001). This behavior does not obey Mendel's second law, the law that genes are sorted independently from other genes into gametes (Bateson, 1913). If this LD block is inherited throughout generations without any recombination then it can be assumed that this LD block is tightly linked and will persist without interruption of recombination (De Roos et al., 2008).

Recombination rate is also positively correlated with age in females. The older an animal is, the larger the number of offspring will be and the more recombination events will occur to try to sufficiently diversify between their offspring (Burt and Bell, 1987). It was also seen in pigs, that the number of aneuploidies, or an abnormal number of chromosomes in a cell due to lack of recombination, was seen to decrease with age. Specifically, the rate of recombination was seen to increase with age in pig populations (Hornak et al., 2011).

Another important factor that affects recombination rate is sex. In many species it has been seen that females have a larger recombination rate than males (Burt et al., 1991). The Haldane-Huxley rule (Dunn and Bennett, 1967) explains that the increase of recombination in females is due to the female being a homogametic sex, or the sex that contains the two same sex chromosomes (XX) (Haldane, 1922). The difference between males and females has been proposed to be due to synaptonemal complexes which assemble homologous chromosomes

during meiosis (Hayashi et al., 2010). These differences are due to how the SC are built in males and females with females having more initiation sites for crossovers (Lynn et al., 2005).

Differences in breed can also contribute to why there are differences in recombination rate. In cattle, differences in recombination rate have been discovered between German Angus and German Simmental breeds. The differences arose on chromosome 23 specifically, with the German Simmental cattle having more recombination events than the German Angus (Weimann et al., 2003). In pigs, it has been seen that recombination rate seems to favor the white breeds, in that, pig breeds that have been classified as a white breed have been seen to have a higher number of recombination events (Cassady et al., 2002).

There is a difference in recombination rate between domestic species and wild type species. Domestic species have a larger number of recombination events. The intensity of selection in domestic species is increasing recombination events in animals. Differences in recombination rate between domestic pig populations are also present. The differences between domestic and wild pigs were first explained by Burt et al. (1987) and the higher rate of recombination was found to be a consequence of indirect selection of higher crossover rate (Ollivier, 1995).

RECOMBINATION AND THE ENVIRONMENT

The result of a fluctuating environment may give way to an increase in recombination (Charlesworth, 1976). When environmental pressure forces changes within a population, recombination is an adaptation to try to survive in a changing environment. This is best seen in bacteria, as they change and evolve extremely rapidly. The changes within this population are due to horizontal transfer between bacterial species by way of recombination. This has allowed bacteria to survive and evolve in many extreme environments (Claverys et al., 2000).

In the model organism, *Drosophila*, evolutionary rates have been studied to understand the changes that a genome can undergo to combat environmental stressors. It is true that the more stressful the environment, the lower the chance of survival. It can be assumed that the more stressful the environment, the higher the recombination rate which increases the genetic variability available in a population. The opposite goes for a stable environment, the more constant the environment, the lower the recombination rate which lowers the genetic variability (Parsons, 1988).

Recombination is only advantageous in an environment when LD is broken, for example alleles *bc*, is of greater fitness than the previous alleles that were in LD *Bc* and *bC*. Without recombination a population will become fixed on those alleles that are most fit for the environment they persist in. With new gene combinations by recombination, the population is able to advance in a changing environment. This is only if these recombinants are rare. This is because if the population is constantly recombining, then there will be no stability within the genome and a population may acquire lethal combinations of alleles (Eshel and Feldman, 1970).

As discussed before, it has been seen that recombination can increase due to age of the female. It has been proposed that the reason for this increase in recombination could be due to not only the age of the oocyte itself, but environmental stressors as well (Lamb et al., 2005). In mice, the age of the female was seen to have an effect on recombination rate, increasing recombination rate to compensate for environmental change (Speed and Chandley, 1983). This effect of the environment on recombination could be influencing the rate of recombination and the genetic architecture of the trait as well.

GENETIC ARCHITECTURE OF RECOMBINATION RATE

Recombination can happen across the entire genome, but it has been seen that recombination events most likely happen in clusters called hotspots. Recombination hotspots are regions in the genome where recombination occurs more frequently than other regions (Lichten and Goldman, 1995). Recombination events within these hotspots are higher than compared to other parts of the genome. There have been studies in humans on recombination hotspots to try to define how increased recombination at these areas effects functions in the organism. Some important hotspot functions have been identified and are found to be deleterious and disease-causing which contributes to the instability of the genome (S. Myers, Freeman, Auton, Donnelly, & Mcvean, 2008).

Variation in recombination across the genome is therefore for the most part, related to variation in the number and location of hotspots. Consequently a large part of the genetic architecture of recombination has been linked to recombination hot spots. Around 50% of all recombination events fall within recombination hotspots along the genome (Crawford et al., 2004). These areas on the chromosome that contain the most recombination events are in the telomeric region which is located at the end of the chromosome (Coop et al., 2008).

Recombination has also been seen to lengthen the telomeric region in embryos which is why most recombination events are found in telomeric regions during meiosis (Liu et al., 2007).

Hotspot regulation within the human and mouse genome has been found to be controlled by a zinc-finger motif, PRDM9. PRDM9 zinc-finger motif is found to bind to these specific hotspots and determine their location within the genome. PRDM9 positions these hotspots during meiosis before they are split into gametes (Myers et al., 2010). Not only does PRDM9 bind to

these recombination clusters, but it is also seen to initiate recombination in some areas of the genome as well (Baudat et al., 2010).

PRDM9 has been seen to evolve rapidly. Many theories to the quick evolution include selection for specific binding to some hotspots (Oliver et al., 2009), selection for degradation of hotspots (Boulton et al., 1997), or a resolution to an insufficient number of recombination events in the genome (Coop and Przeworski, 2007). The importance of the PRDM9 motif to bind to these hotspots can be seen when it is knocked out. When PRDM9 is lost in mice populations, infertility and trouble repairing double stranded breaks occurs which can both be detrimental to a population (Hayashi et al., 2005).

Other binding regulators have been seen to have an impact on recombination rate as well. Recently, trans-regulation of these hotspots has been discovered in mice. On chromosome 15 in mice, there is a single trans-regulation locus that was named *Rcr1* and was seen to control the sites of double stranded breaks and repairs within the DNA (Parvanov et al., 2009). Another locus located in mice on chromosome 15 and 18 was discovered to have trans-regulating activity is called *Dsbc1*. This locus has been seen to specify the activity for a specific hotspot, *Psmb9*, in the genome (Grey et al., 2009).

Other important sequence variants in humans that are correlated to recombination include the RNF212 gene. It is responsible for chiasma formation and needed for recombination in the cell. SNPs associated with this region are seen to be significant in both males and females. Even though the expression is seen in both sexes, the effect is not the same. This haplotype in males is associated with high recombination rate, but in females, the exact haplotype is associated with low recombination rate. The two extreme differences in sex will average the recombination rate for the whole population. If one haplotype is over expressed in a population, the differences in

recombination rate in the two sexes will even out the overall mean of recombination rate. These findings can conclude that the genetic architecture for males and females for recombination rate may be similar, but the expression of these genes can have totally different outcomes (Kong et al., 2008).

Recombination rate can vary between different species and within species between different breeds as well (Thomsen et al., 2001). The genetic architecture of recombination rate can even vary between individuals in the same breed. Within mice, males were seen to vary greatly in the rate of recombination through multiple generations due to loci located on the X chromosome. The female population did not differ greatly in recombination rate compared to the male population. It was seen that males evolve their recombination rate quicker than females and there was a larger divergence between breeds in male populations. This may be due to the X chromosome QTL controlling initiation and placement of recombination hotspots (Dumont et al., 2011).

Several genetic determinants of recombination have been found to be shared among humans, model organisms and livestock. In Soay sheep, recombination rate in females was found to be significantly impacted by genomic regions containing *RNF212* and *CPLX1*. The *PRDM9* motif was not seen to have a strong impact, but homolog copies were present on many Soay Sheep chromosomes (Johnston et al., 2016).

Similarly, genetic variants identified in humans have been found to be significant in cattle as well. The genes *REC8* (10) and *RNF212* were seen to influence overall recombination rate within the genome (Sandor et al., 2012). *PRDM9* (chromosome 1) was also seen to influence the position and usage of hotspots. Specifically, one allelic change in the locus for *PRDM9* in cattle was seen to decrease recombination events in both males and females (Ma et al., 2015). The

persistence of the PRDM9 motif through many species shows the importance of this motif for recombination rate regulation and is an integral part of the genetic architecture of recombination rate.

GC rich areas or areas on the genome that have a large number of G and C nucleotide pairs, within the genome are more prone to recombination. This phenomenon has been seen in many species (Tortereau et al., 2012; Clément and Arndt, 2013; Weng et al., 2014) and was seen in yeast to be correlated with more local recombination rate rather than total genome recombination rate that would be regulated by hotspot motifs such as PRMD9 (Birdsell, 2002). The local genetic architecture of recombination rate has also been seen in pigs where higher recombination in pigs was found in GC-rich areas (Mary et al., 2014). These GC-rich areas may explain the recombination events that are found outside of recombination hotspots as GC bonds are seen to be less stable (Yakovchuk et al., 2006), which may lead to an increase in double-stranded breaks in the genome outside of recombination hotspots.

Unlike GC rich areas, RNF212 (chromosome 4) and PRDM9 (chromosome 5) regulate genome wide recombination rate in humans. These motifs found in a study by Kong et al. (2014) were not seen to have a large effect in hotspot recombination occurrence locally, but were seen to have significant effects on recombination event occurrence throughout the whole genome. Defining GC-rich areas and hotspot regulating motifs can explain the genetic architecture of local and global recombination rate in livestock populations.

ESTIMATES OF RECOMBINATION RATE IN LIVESTOCK

Previously, before genotyping was available, the number of recombination events was determined by counting the number of chiasmata (crossing over events) under a microscope (Nachman, 2002). Nowadays, estimation of recombination rate can be obtained most accurately

with genomic data in the form of SNP panels. This estimation of the number recombination events is based on how much SNP information is shared between parent and offspring. Previous generations beyond the parents of the offspring are also helpful to the estimation of recombination events between generations (Ma et al., 2015).

Estimating recombination in a livestock population can rely heavily on genomic data, but pedigree information is also important. With the pedigree relationship matrix (A-matrix), the ancestry of an animal can be estimated and described in a numeric matter. Recombination between parent and offspring can first be detected in the pedigree by detecting inconsistencies between full siblings. True inconsistencies between siblings can be attributed to Mendelian sampling which can be in the form of a crossover event. If differences occur, a test for a recombination event can be done by genotyping to get the most precise result (Pl Calus et al., 2011).

IMPACT OF RECOMBINATION EVENTS IN LIVESTOCK SPECIES

The homozygous alleles in livestock populations that are due to relatedness can be coined as identical by descent (IBD). Those alleles that are IBD can be traced back to one parent haplotype. Inbreeding can be calculated as the probability that two alleles at a locus are the same due to those alleles being IBD. This estimate of inbreeding is important to animal breeding because it can give insight to the regions of homozygosity that may have undesirable recessive traits (Lander and Botstein, 1987). Without keeping inbreeding in check, it can quickly become a problem within a population. Inbreeding depression can cause reduced fitness in an animal which decreases fertility as well (Charlesworth and Willis, 2009). This is due to the obvious lack of genetic variation (Keller and Waller, 2002). In these populations, selection is nonexistent which leads to increased homozygosity and can lead to the accumulation of unfavorable mutations

(Lynch et al., 1995). An increase in recombination rate could be a helpful tool to try to account for these problems in small populations by adding genetic variation (Burt and Bell, 1987).

Recombination rate has been seen to influence reproductive traits in swine. An experiment done by Cassady, Young, and Leymaster (2002) tried to understand how influencing recombination rate would change reproductive traits including total number born and litter birth weight. Recombination increased the number of fully formed pigs and increased litter birth weight as well. Recombination was also seen to decrease age at puberty as well. By influencing recombination rate within pig populations, Cassady et al. were able to influence important industry traits. These significant findings could influence how recombination rate is utilized in the industry.

SELECTION FOR RECOMBINATION RATE

Selection experiments on recombination rate in *Drosophila* trying to measure the effect of suppressing crossing over has showed that by selecting against crossover events, the advancements of traits in the population in a positive or negative direction were reduced by 22-28%. These findings quantify just how important recombination is to advance a population. Without recombination in a population, selection advances would not have as strong of an effect if the population did have recombination (McPhee and Robertson, 1970).

It has also been shown in *Drosophila* that increased recombination can be achieved via directional selection and can be inherited with increased allele frequencies. The selection for a stable optimum may have some drawbacks, as the population may start to fix allele frequencies and the rate of recombination will decrease. This will lead to lower genetic variability and may decrease the chance of survival if the environment were to change (Flexon and Rodell, 1982).

In simulations of livestock breeding programs to manipulate recombination rates, it was found that increasing recombination rate increased the response to selection for other traits in the population. Selection for increased recombination rate also decreased the amount of genetic variation lost. These simulations have shown that an increase in recombination rate helps the response to selection, but only if the recombination rate is increased by 10 or 20 fold. This large increase in the rate in a real life livestock program seems almost infeasible, but may be possible with the help of new genomic technologies (Battagin et al., 2016).

Simulations have been run to see how manipulating recombination hotspots using genomic technologies would affect the genome (Gonen et al., 2017). If a hotspot was shifted towards a QTL that is not usually subject to any recombination then a large jump in genetic gain was seen. This is because the recombination events around this QTL are introducing new allelic combinations into the population. This in turn introduces variation and can increase genetic gain. If this was to be put into practice in livestock programs today, the manipulation of certain areas along the genome can increase genetic gain within a population. The feasibility of this practice lies in the properties of the PRDM9 motif. This motif, as explained before, has properties that allow it to control the location of recombination hotspots through the genome during meiosis. If this protein, along with new CRISPR-CAS9 technologies were put into place (Ran et al., 2013), new allelic combinations can be manipulated by breeding programs.

CONCLUSION

Recombination rate is important to understand in current livestock populations. It affects the amount of genetic variation that is introduced randomly into the population by crossing over during meiosis. An increase in the variation within the genome can introduce new combinations of genes that may be advantageous to the next generation. While increasing recombination rate

may have positive effects, there is also the possibility that linkage disequilibrium between markers and important QTL could be broken by recombination (Feldmant et al., 1980).

Recombination has an important role in livestock species and is affected by many factors that can include sex (Lynn et al., 2005), age (Hornak et al., 2011), and breed (Cassady et al., 2002) as well as the environment (Burt and Bell, 1987).

Recombination rate has been shown to influence livestock populations by manipulating the structure of the genome by way of PRMD9 (Myers et al., 2010). This influence on the genome has been seen to increase or decrease the rate of recombination and has been seen to have strong influences on specific regions called recombination hotspots. These hotspots are irregular areas in the genome that have a higher recombination rate than those spots on the genome that do not contain a hotspot region (Lichten and Goldman, 1995). Further research into the action of the PRMD9 motif can help better understand the genetic architecture behind recombination rate in populations.

There can be a significant change in pig reproductive traits by influencing recombination rate in livestock populations (Cassady et al., 2002). Significant changes in litter weight and full pigs born alive can be attributed to a change in recombination rate. Simulations in selecting for recombination rate (Battagin et al., 2016) have also shown by increasing recombination rate, the genetic gain in a phenotypic trait will increase as well.

Recombination rate is important to understand because it influences the genetic variation in livestock populations. The genetic architecture of recombination rate, specifically the function of PRMD9, could affect the regulation of hotspots and where hotspots are placed within the genome. The estimation of recombination rate and the heritability of recombination rate is

important for selecting for recombination rate in livestock populations. Selection for recombination rate in an industry setting could possibly change the genetic gain of a trait as well.

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CHAPTER 2
EVIDENCE OF GENETIC VARIATION FOR RECOMBINATION RATE IN
PUREBRED SWINE POPULAITONS

ABSTRACT

Recombination can affect the genetic gain of a trait in different ways. A high recombination rate can cause instability of genomic predictions as a result of the linkage disequilibrium breaking between markers and QTL. Conversely, recombination rate can maintain and increase the ability to recruit genetic variability by virtue of the same process. Within this research, we investigated the potential effects of sex and breed as well as the genetic variation of recombination events in swine. Data originated from four breed/sex commercial nucleus populations of Smithfield Premium Genetics: Large White sires (LWS, n=270), Large White dams (LWD, n=1755), Landrace sires (LRS, n=281) and Landrace dams (LRD, n=1356). Individuals in the analysis were genotyped at 10k, 60k or 80k Illumina SNP chips and then all imputed to 80k using the Fimpute software. The software FindhapV4 was used to obtain the total number of recombination events for each individual's progeny (n=20,712 total progeny records). The R package MCMCglmm was employed to fit a model with the total number of recombination events in the genome as the predicted variable. Animal and contemporary group (herd, year, and season of observed recombination event) were random predictors, while sex, breed, parity and male age class were fixed effects. Heritability estimates of recombination were obtained within each breed/sex combination using THRGIBBS1F90. The model included the number of recombination events as a predictor variable and a random sire or dam effect for each population. The sire/dam effects was assumed $N(0, \mathbf{H}/\mathbf{A}\sigma_{s/d}^2)$ where \mathbf{A} and \mathbf{H} were a pedigree or blended relationship matrix, respectively. Two fixed effects were included, a contemporary group and a covariate for age at recombination event. Least squares mean estimates (LSME) of total number of recombination events for sex were 16.25(\pm 0.152) in dams and 12.09(\pm 0.181) in sires. LSME for breed were 14.32(\pm 0.229) in LW and 14.05(\pm 0.231) in LR. Sex and breed were

both significant ($p < 0.05$). The differences between ambient temperature classes, humidity classes, or male age classes did not have a significant effect on recombination rate in this study. Heritabilities of recombination across the whole genome were $0.039(\pm 0.036)$ for LRS, $0.074(\pm 0.030)$ for LRD, $0.090(\pm 0.062)$ for LWS, and $0.107(\pm 0.034)$ for LWD. Heritabilities, when genomic data was included, were $0.050(\pm 0.036)$ for LRS, $0.232(\pm 0.028)$ for LRD, $0.084(\pm 0.045)$ for LWS, and $0.257(\pm 0.029)$ in LWD. Heritabilities for recombination on each chromosome were also estimated. These results show that recombination is heritable and that both sex and breed are significant contributors, with females and LW having a significantly larger number of recombination events. Further research should focus on defining genetic architecture that may be contributing to variation in recombination rate.

INTRODUCTION

Recombination is the act of transferring DNA between homologous chromosomes during meiosis. Recombination can alter significantly genetic variation in a population. An increase in recombination rate can increase genomic variance by breaking linkage blocks and allowing new haplotypes to form in a population (Feldmant et al., 1980). Conversely, a decrease in recombination rate can increase the uniformity of a population. The effects of recombination on both genetic and phenotypic variability can be seen in all species that use sexual reproduction (Muller, 1964). Recombination rate, measured as the number of recombination events in the genome in this study, has therefore long been recognized as an important parameter to understand the genetic makeup of animal populations, although its effects have been historically studied mostly in humans, mice and other model organisms. Nonetheless, recent studies in domestic species have shed light on the effect of recombination rate in different livestock populations (Cassady et al., 2002; Weng et al., 2014; Johnston et al., 2016). Particularly, in

swine, previous work has been done to characterize recombination rate in modern hog populations. Ollivier (1995), found that recombination rate differs between domesticated and wild pigs, with domestic populations showing a higher crossover frequency. The Haldane-Huxley rule (Dunn and Bennett, 1967) states that the heterogametic sex or the sex that has two different sex chromosomes (ex. XY in humans, cattle, pigs etc.) is known to have less recombination events than the homogametic sex. The heterogametic sex is usually the male sex, but in some species like chickens (females are ZW), this is not the case (Haldane, 1922). In this regard, Tortereau (2012) found higher recombination rates in female pigs, compared to males. These results are in line with findings in other species (Lynn et al., 2005).

Cassady et al., (2002) analyzed recombination rate in many swine breed populations including Landrace, Large White, Yorkshire and Chester White. His study found that recombination rate tended to increase in the white breeds and these new genetic combinations had little to no impact on reproductive traits.

Age is another factor that influences recombination rate. Specifically, it has been seen in pig populations that age in females is positively correlated with recombination rate with older females showing higher recombination rate (Hornak et al., 2011). The increase in recombination rate with age could be an important factor when selecting for dams, keeping in mind that older dams could have a larger number of recombination events.

Furthermore it is known that meiotic recombination rates can vary considerably among environmental conditions (Stevison et al., 2017). It has been previously shown that ambient temperature and humidity can affect recombination rate (Hunter et al., 2016).

Strikingly, while the studies discussed in the previous section highlight how recombination is a complex and important parameter, little is still known about the possible genetic control of

recombination in swine populations. The advent of genomic selection (Fernando and Grossman, 1989) has made available large cohorts of individual pigs genotyped with dense panel markers (Jiao et al., 2014; Lu et al., 2017). This, in turn, provides the unique opportunity to investigate recombination rate more in depth. Particularly, it has been shown in other livestock species (Myers et al., 2010; Weng et al., 2014; Groenen et al., 2009) that recombination rate is under direct genetic control and has a specific genetic architecture that is relatively conserved (Johnston et al., 2016) across species. Currently this information is for the large part lacking in swine.

The objectives of this study were, therefore, to analyze differences in recombination rate between two of the major breeds employed in commercial swine breeding in the United States: Landrace and Large White. Along with breed differences, the effect of sex and sex by breed interaction on recombination rate also was estimated. We further investigated the existence of a direct genetic control of recombination in swine by estimating variance components and heritabilities of whole genome recombination rate. Finally, the environmental effect of temperature and humidity on recombination events in swine was investigated.

MATERIALS AND METHODS

Animal Population Structure

Recombination events were recorded in 281 Landrace sires (LRS), 1,356 Landrace dams (LRD), 270 Large White sires (LWS), 1,755 Large White dams (LWD) originated from Smithfield Premium Genetics (SPG) nucleus lines. The Large White population was born between 2007 and 2016 and the Landrace population was born between 2009 to 2016. A total of 20,712 progeny observations were used for analysis. A descriptive summary of the data used can be found in Table 1.

Recombination Event Estimation

The original data included individuals genotyped with Illumina porcine chips of various densities, namely, 10K (19,452 individuals), 60K (6,574 individuals) and 80K (25,347 individuals). Family trios were created, consisting of sire, dam and their respective progeny. In order to minimize the effect of imputation for low density panels on the estimation of recombination rate (Weng et al., 2014), only trios consisting of individuals genotyped for either 80K or 60K SNP were retained for further analyses. All, individuals were imputed to 80K, using FImpute (Sargolzaei et al., 2014). FindhapV4 (VanRaden et al., 2011) was subsequently employed to obtain cross over events for all trios. Each trio data consisted of the total number of crossovers for each progeny/chromosome/parent combination. A recombination event was detected as a new haplotype(s) appearing in the offspring of the family trio: phased genotype recombinations were then traced back to either the sire or the dam, so that for each progeny of the family trio maternal and paternal recombinations were measured. A summary of the data used in the analysis can be found in Table 1. Recombination events were further aggregated into whole genome's recombination events.

In order to investigate potential environmental effects on recombination, age at meiosis (time of recombination) was obtained for dams and sires for each trio progeny data. For females, this was calculated by taking the progeny date of birth and subtracting the number of days for gestation, yet because of possible confoundings between parity and age at meiosis only parity was employed in subsequent analyses. For males, the age at meiosis was calculated starting from progeny birth date by subtracting 113 days for gestation and another 35 days to account for the time to spermatogenesis (Zeng et al., 2006). Age at meiosis in males was further classified into 4 groups based on the quartiles of the distribution for ease of interpretation of results.

Contemporary groups that had 5 or less records were excluded from the analysis because having that few records could not represent of that contemporary group and could create unwanted variation within the model.

Statistical Analysis

We first obtained differences in recombination between breeds, sex and age groups. For this analysis four separate analyses were run, for each of the parameters investigated.

The R (version 3.3.1) package MCMCglmm (Hadfield, 2010) was used with the following model:

$$(1) \mathbf{y} = \boldsymbol{\mu} + \mathbf{Factor} + \mathbf{Parent} + \mathbf{CG} + \mathbf{e}$$

where \mathbf{y} is the overall number of recombination events in the genome from parent to offspring; $\boldsymbol{\mu}$ is the population mean; **Factor** is the fixed effect of either breed, sex, female parity, or male age at meiosis. Male age at meiosis was categorized into four classes using four quantiles of the whole male population in which $\frac{1}{4}$ of the population is in each quantile, average age of each class can be seen in Table (6). **Parent** is the random effect of the parent who has repeated records of each of its progeny's recombination recorded. Parent are in this case assumed $N(0, \mathbf{I}\sigma^2_P)$; **CG** is the random effect of the contemporary group calculated as the concatenation of year, season and farm of when and where the crossovers occurred and assumed $N(0, \mathbf{I}\sigma^2_{CG})$; and \mathbf{e} is the residual effect assumed $N(0, \mathbf{I}\sigma^2_E)$. The package 'lsmeans' (Lenth, 2016) was used to estimate the least square means as well as the contrasts of each sex, breed or age effect in the model. A summary of the individuals present in each analysis can be found in Table 2.

Temperature and Humidity Effects

Differences in recombination rate between different temperature and humidity classes were investigated. The MCMCglmm package in R was again utilized along with ‘lsmeans’ to calculate contrasts between temperature and humidity classes. The model used included:

$$(2) \mathbf{y} = \boldsymbol{\mu} + \mathbf{T} + \mathbf{Parent} + \mathbf{CG} + \mathbf{e}$$

where \mathbf{T} was the fixed effect of either temperature or humidity classes and everything else was as in (1).

The temperature and humidity information was obtained from the National Climatic Data Center Quality Controlled Local Climatological Data (<https://www.ncdc.noaa.gov/qclcd/QCLCD?prior=N>) database at the National Oceanic and Atmospheric Administration. The data used in this analysis originated from weather stations that were closest to the zip codes of the farms of data collection (no more than 100 km away) in this study. The assignment of zip codes to weather stations was done using the R packages ‘zipcode’(Breen, 2012) and ‘geosphere’(Hijmans, 2017). The weather parameters used in this study were the average temperature and the relative humidity of the day of recombination event (defined above). The data from all farms was classified into 10 separate classes for ease of analysis. This classification was done by using 10 quantiles from coldest to hottest (or less humid to most humid) to create 10 separate classes, where each class is 1/10 of the overall population. Average temperature and average humidity for each class can be seen in Tables 7 and 8.

Variance Components and Heritability Estimates

Variance components and heritability estimates for genome wide as well as for chromosomal recombinations were estimated using the THRGIBBS1F90 software (Tsuruta and Misztal, 2006). The model used for this analysis had form:

$$(3) \mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{Z}\mathbf{a} + \mathbf{W}\mathbf{pe} + \mathbf{e}$$

Where \mathbf{y} is the number of recombination events between parent and offspring, \mathbf{b} is a vector of fixed effects comprised of a contemporary group (defined as before) as well as the covariate for either male age group or parity for male and female, respectively, \mathbf{a} is a vector of repeated parent records, \mathbf{pe} = vector of permanent environmental effects and \mathbf{e} = vector of residual effects . The \mathbf{X} , \mathbf{Z} and \mathbf{W} are design matrices that are associated with the fixed effects, the additive genetic and the permanent environmental effect, respectively. The random additive genetic and permanent environmental effects were assumed $N(0, \mathbf{A}\sigma_a^2)$ and $N(0, \mathbf{I}\sigma_{pe}^2)$ respectively, where \mathbf{A} is the pedigree numerator relationship matrix and \mathbf{I} an identity matrix. A blended pedigree and genomic relationship matrix, \mathbf{H} , was also fitted $N(0, \mathbf{H}\sigma_a^2)$ (Misztal et al., 2009). Residuals are assumed $N(0, \mathbf{I}\sigma_e^2)$.

While total recombination was modeled as counts, Chromosomal recombination estimates were obtained from categorical trait with $y = 1$ if the chromosome did not have any recombination and 2 otherwise. A descriptive summary of the number of unique animals and their progeny records used in these analyses can be found in Table 3.

All analyses in THRGIBBS1F90 were run at 240,000 cycles with a burn-in of 40,000 and every 20th sample was stored for subsequent inference. Convergence was assessed by visual inspection of the trace plots. Posterior means, standard deviations and highest posterior densities were obtained for all the parameters of interest. Heritabilities were calculated using the variance estimates for the additive genetic variance σ_a^2 , the permanent environmental variance σ_{pe}^2 , and the residual σ_e^2 . Heritability, h^2 , was calculated as follow:

$$(4) h^2 = \frac{\sigma_a^2}{\sigma_a^2 + \sigma_{pe}^2 + \sigma_e^2}$$

RESULTS AND DISCUSSION

The genome wide average phenotypic number of recombination per breed/sex can be found in Figure 1.

Least square means from model (1) can be found in Tables 4, 5 and 6. Breed had a significant effect ($P < 0.05$) on recombination rate. LW (14.32 ± 0.23) had 0.27 ± 0.13 more recombination events compared to LR (14.05 ± 0.23).

Differences in recombination rate among livestock breeds have not been extensively researched. In pigs, significant differences have been found between the wild and domestic populations with domestic populations having higher recombination events than their wild counterparts (Davies et al., 1995). It has also been seen that there are differences within the domestic population. A study done by Ollivier (1995) has shown that differences between linkage maps among American, Swedish and European breeds. Our study confirms and expands these findings.

Unsurprisingly, there were significant differences ($P < 0.0001$) between sexes. This significant difference between males and females has been seen in different species such as e.g. cattle and pigs (Tortereau et al., 2012). In most species females have a higher number of recombination events than males. This was confirmed by this study: males had 12.09 ± 0.18 recombinations while females had 16.25 ± 0.15 recombinations, a difference of 4.16 recombinations. This large difference in recombination rate has been seen in mice and may be due to the way in which the synaptonemal complex forms during meiosis in females (Lynn et al., 2005). This finding in mice could be extended to other mammalian species as well, such as pigs but further studies would be necessary.

The LSME for the dam parity were 16.04 ± 0.20 , 16.23 ± 0.22 and 16.72 ± 0.29 for parity 1, 2, or 3+, respectively. There was a significant difference ($p < 0.05$) between parity 1 and 3. With an increase in age comes and increase in about half of a recombination event, 0.48 ± 0.25 . This is in line with other studies in swine stating that an older oocyte has more recombination events on average than a younger oocyte (Campbell et al., 2015). LSME for the age classes in males, found in Table 6, were 12.10 ± 0.12 , 12.18 ± 0.12 , 12.13 ± 0.13 , and 12.28 ± 0.15 for the 1st, 2nd, 3rd and 4th age classes, respectively. There were no significant differences between any of the male age classes. This could be due to the fact that the data presented contained less male than female records which may have not been a large enough sample to distinguish differences in male's ages.

The LSME for recombination rate for classes of ambient temperature and humidity are shown in Tables 7 and 8. No significant contrasts were found in the current analysis for both parameters. It should be noted that even though farms in the current analysis varied in location from Virginia, North Carolina, and Texas (Figure 6), differences in ambient temperature and humidity were probably not sufficient to elicit a significant effect on recombination rate in this study.

Variance estimates for additive genetic effect, permanent genetic effect and the residual effect for total number of recombinations for both the pedigree based model and the blended pedigree and genomic model, model (3), are reported in Table 9 along with heritability estimates and standard errors. Heritabilities differed for breed/sex combination ranging from 4% to 11% with pedigree data and from 5% to 26% with the **H** matrix analysis. Heritabilities in Landrace were lower than in Large White across sexes, both in pedigree and blended analyses. Conversely

dams had higher h^2 estimates across breeds. In most cases the use of the blended **H** matrix increased heritability estimates with the exception of LWS.

Lower heritabilities for males could be explained by a different genetic architecture between male and female (Lynn et al., 2005). Nonetheless caution should be employed in the interpretation of these results given that the distribution of phenotypes was different between males and females due to population structure and this might have played a significant role in the estimates of variance.

The differences between heritability estimates within sexes between models employing **A** vs. **H** can largely be attributed to genomic information added by the genomic component. This information helps better discern the realized relationships among animals.

Heritability estimates for each chromosome are reported in Table 10 and Table 11, for **A** and **H** models, respectively. Pedigree-based estimates ranged from essentially 0 to moderate, depending on the combination of chromosome/breed/sex. Heritability estimates were similar between breeds with sex but different across sexes, suggesting as for the genome wide analysis a possibly different genetic architecture across males and females, in accordance to what already has been found in other species (Lynn et al., 2005; Hedrick, 2007; Wang et al., 2016).

Heritability estimates using blended pedigree/genomic information are found in Table 11. The estimates for heritability ranged from 0.01 (± 0.01) to 0.07 (± 0.03) across all breed sex combination. Heritability estimates in this case were significantly lower than the ones obtained through the pedigree model as shown in Figures 2-5. Since genomic information is better at accounting for possible pedigree mistakes (Wang et al., 2014) it is possible that differences in heritabilities between the two models reflect parentage mistakes accounted for in the analysis by **H**.

CONCLUSION

In the current work we have highlighted differences in recombination rate between sex and breeds in swine populations. Females showed higher recombinations rates compared to males and Large White compared to Landrace. Furthermore we have shown the existence of a sizable genetic component for recombination rate across the four different populations. Recombination rate is currently not considered as a possible target of selection in swine populations yet its use could prove beneficial for the swine industry. The rate of change in the genome due to recombination could be selected for higher or lower variation by including EBV for recombination rates in the selection index. By selecting for a higher recombination, more variation would be introduced into nucleus populations due to the faster breakdown of existing LD created by the inbreeding of the populations due to selection. This could potentially increase the genetic variation within a given population and the creation of new favorable haplotypes for selection. Furthermore, the shortening of regions of low diversity would release some of the inbreeding depression accumulated in the population. The first consequence of this has been investigated with the use of simulation by Battagin et al. (2016). Increasing recombination rate would increase the overall response to selection and decrease the loss of genetic variance. The second has been shown by Howard et al. (2017a, b). Conversely, by selecting for lower recombination, uniformity in a population could increase. This could, in turn, be exploited, for example, in terminal lines in swine. Recombination rate was also different by breed, sex and age. These differences should be accounted for if selection were to take place. It should be noted that these differences in recombination rate are in consistent with other studies and show the same trends. By studying recombination rate in these populations, the random variation introduced by recombination into these livestock populations can be better understood,

accounted for, and in some case exploited in selection programs. Further studies should investigate the genetic architecture of recombination in order to identify key determinants, possibly opening the possibility of gene editing for recombination rate

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Table 1. Summary statistics of animals included in the analysis.

	Landrace*		Large White*	
	Sires	Dams	Sires	Dams
Total Animals	281	1356	270	1755
Recorded Progeny	4660	4628	5718	5706
Years Spanned	2009-2016	2009-2016	2007-2016	2007-2016
Average Number of Recombination Events in Total Genome	12.06	16.37	12.63	16.80

* Swine nucleus population from Smithfield Premium Genetics

Table 2. Number of unique individuals and the number of progeny from those individuals in each separate analysis using parity, male age, breed or sex as fixed effects

	Large White	Landrace	Males	Females	# Progeny
Parity	1755	1356	-	3111	10334
Male Age	270	281	551	-	10378
Breed/Sex	2025	1637	551	3111	20712

Table 3. Descriptive summary of animal SNP chip and pedigree records used for estimating heritabilities, Model (3), by population.

	Landrace Sire	Landrace Dam	Large White Sire	Large White Dam
Animals Genotyped	281	1356	270	1755
Total Animals in Pedigree	291137	291137	391159	391159
Number of Parents of Animals Genotyped with No Genotypic Information	2019	3533	1519	3005
Total Number of Animals used	2300	4889	1789	4760

Table 4. Least Squares Mean Estimates (LSME) and standard error (SE) for recombination events for breed (Landrace (LR) or Large White (LW)) and sex using model (1). Contrasts for significant differences in each category are also reported.

		LSME	SE	Contrast	Estimate	SE	p-value
Breed	LR	14.05	±0.23	LW-LR	0.27	±0.13	0.0312*
	LW	14.32	±0.23	-	-	-	-
Sex	Male	12.09	±0.18	M-F	-4.16	±0.23	<0.0001*
	Female	16.25	±0.15	-	-	-	-

Table 5. Least Squares Mean Estimates (LSME) and standard error (SE) for recombination events for parity using only female parent information in model (1). Contrasts for significant differences in each category are also reported.

Parity		LSME	SE	Contrast	Estimate	SE	p-value
	1	16.04	±0.20	2-1	0.20	±0.14	0.2908
	2	16.23	±0.22	3-1	0.68	±0.25	0.0131*
	≥3	16.72	±0.29	2-3	0.48	±0.25	0.0525

Table 6. Least Squares Mean Estimates (LSME) and standard error (SE) for recombination events for male age class using only male parent information in model (1). Contrasts between age classes were all not significant (NS).

	Class	Average Age (days)	LSME	SE	Contrast
Male Age	1	209.5	12.10	±0.12	NS
	2	267.5	12.18	±0.12	NS
	3	340.5	12.13	±0.13	NS
	4	710	12.28	±0.15	NS

Table 7. Temperature class averages as well as least squares means estimates for recombination events for each class. Contrasts between classes are all found to be not significant (NS).

Class	Avg. Temp. (C)	LSME	SE	Contrasts
1	2.78°	15.75	±0.32	NS
2	6.46°	16.22	±0.30	NS
3	9.51°	16.07	±0.29	NS
4	11.25°	16.49	±0.28	NS
5	13.54°	16.28	±0.28	NS
6	14.65°	16.21	±0.28	NS
7	17.99°	16.54	±0.28	NS
8	23.68°	16.47	±0.27	NS
9	26.74°	16.13	±0.29	NS
10	28.33°	15.52	±0.32	NS

Table 8. Relative humidity class averages as well as least squares means estimates for recombination events for each class. Contrasts between classes are all found to be not significant (NS).

Class	RH	LSME	SE	Contrast
1	35.52	16.20	±0.30	NS
2	43.13	15.95	±0.29	NS
3	47.44	16.04	±0.29	NS
4	53.27	16.23	±0.28	NS
5	56.43	16.28	±0.29	NS
6	60.46	16.19	±0.27	NS
7	65.06	16.23	±0.27	NS
8	68.13	16.32	±0.27	NS
9	74.54	16.17	±0.27	NS
10	80.75	16.05	±0.31	NS

Table 9. Variance and heritability estimates (SE in parenthesis) for total genome recombination rate using a pedigree based relationship matrix and using a blended pedigree and genomic based relationship matrix.

	Pedigree				Pedigree + Genomic			
	σ^2_A	σ^2_{PE}	σ^2_e	h^2	σ^2_H	σ^2_{PE}	σ^2_e	h^2
LRS	0.52 (±0.49)	3.24 (±0.58)	9.66 (±0.21)	0.04 (±0.03)	0.67 (±0.50)	3.10 (±0.57)	9.66 (±0.21)	0.05 (±0.04)
LRD	1.61 (±0.67)	7.02 (±0.72)	13.20 (±0.33)	0.07 (±0.03)	5.02 (±0.69)	3.42 (±0.50)	13.21 (±0.33)	0.23 (±0.03)
LWS	1.22 (±0.86)	2.49 (±0.81)	9.83 (±0.19)	0.09 (±0.06)	1.13 (±0.63)	2.58 (±0.61)	9.83 (±0.19)	0.08 (±0.05)
LWD	2.30 (±0.74)	6.40 (±0.71)	12.83 (±0.29)	0.11 (±0.03)	5.64 (±0.75)	3.53 (±0.47)	12.81 (±0.29)	0.26 (±0.03)

Table 10. Heritability estimates of occurrence of recombination per chromosome in 4 sex/breed populations using pedigree information only.

Chromosome	$h^2(\text{SE})$			
	LRS	LRD	LWS	LWD
1	0.09 (± 0.05)	0.04 (± 0.04)	0.10 (± 0.05)	0.08 (± 0.04)
2	0.12 (± 0.06)	0.02 (± 0.02)	0.12 (± 0.06)	0.03 (± 0.02)
3	0.08 (± 0.05)	0.05 (± 0.03)	0.06 (± 0.04)	0.07 (± 0.03)
4	0.07 (± 0.05)	0.06 (± 0.04)	0.06 (± 0.04)	0.04 (± 0.03)
5	0.09 (± 0.05)	0.06 (± 0.03)	0.08 (± 0.05)	0.05 (± 0.03)
6	0.06 (± 0.04)	0.04 (± 0.03)	0.04 (± 0.04)	0.06 (± 0.03)
7	0.08 (± 0.04)	0.11 (± 0.05)	0.04 (± 0.03)	0.01 (± 0.01)
8	0.11 (± 0.05)	0.06 (± 0.03)	0.03 (± 0.03)	0.11 (± 0.04)
9	0.08 (± 0.05)	0.02 (± 0.02)	0.07 (± 0.05)	0.04 (± 0.02)
10	0.14 (± 0.06)	0.05 (± 0.04)	0.14 (± 0.04)	0.03 (± 0.02)
11	0.12 (± 0.05)	0.03 (± 0.03)	0.09 (± 0.05)	0.07 (± 0.04)
12	0.11 (± 0.06)	0.02 (± 0.02)	0.06 (± 0.05)	0.09 (± 0.04)
13	0.04 (± 0.03)	0.02 (± 0.02)	0.05 (± 0.04)	0.04 (± 0.02)
14	0.09 (± 0.06)	0.07 (± 0.04)	0.12 (± 0.05)	0.12 (± 0.04)
15	0.06 (± 0.04)	0.06 (± 0.03)	0.15 (± 0.06)	0.03 (± 0.02)
16	0.10 (± 0.05)	0.03 (± 0.03)	0.16 (± 0.06)	0.04 (± 0.02)
17	0.09 (± 0.05)	0.08 (± 0.04)	0.08 (± 0.05)	0.06 (± 0.03)
18	0.09 (± 0.05)	0.07 (± 0.04)	0.12 (± 0.06)	0.06 (± 0.03)

Table 11. Heritability estimates of occurrence of recombination per chromosome in 4 sex/breed populations using blended pedigree/genomic relationship matrix information.

Chromosome	$h^2(\text{SE})$			
	LRS	LRD	LWS	LWD
1	0.04 (± 0.03)	0.02 (± 0.01)	0.04 (± 0.03)	0.02 (± 0.01)
2	0.02 (± 0.02)	0.02 (± 0.01)	0.04 (± 0.03)	0.01 (± 0.01)
3	0.02 (± 0.02)	0.04 (± 0.01)	0.02 (± 0.02)	0.03 (± 0.01)
4	0.01 (± 0.01)	0.04 (± 0.02)	0.02 (± 0.02)	0.02 (± 0.01)
5	0.03 (± 0.02)	0.04 (± 0.01)	0.04 (± 0.03)	0.03 (± 0.01)
6	0.02 (± 0.02)	0.04 (± 0.02)	0.02 (± 0.02)	0.02 (± 0.01)
7	0.02 (± 0.02)	0.05 (± 0.02)	0.02 (± 0.02)	0.01 (± 0.01)
8	0.04 (± 0.03)	0.03 (± 0.01)	0.01 (± 0.01)	0.05 (± 0.01)
9	0.02 (± 0.02)	0.03 (± 0.01)	0.02 (± 0.02)	0.02 (± 0.01)
10	0.07 (± 0.04)	0.02 (± 0.01)	0.06 (± 0.03)	0.03 (± 0.01)
11	0.06 (± 0.03)	0.05 (± 0.02)	0.03 (± 0.02)	0.04 (± 0.01)
12	0.02 (± 0.02)	0.02 (± 0.01)	0.04 (± 0.03)	0.03 (± 0.01)
13	0.02 (± 0.02)	0.02 (± 0.01)	0.02 (± 0.02)	0.02 (± 0.01)
14	0.04 (± 0.03)	0.04 (± 0.02)	0.07 (± 0.03)	0.03 (± 0.01)
15	0.02 (± 0.02)	0.03 (± 0.02)	0.03 (± 0.03)	0.01 (± 0.01)
16	0.03 (± 0.03)	0.05 (± 0.02)	0.05 (± 0.03)	0.03 (± 0.01)
17	0.02 (± 0.02)	0.04 (± 0.01)	0.06 (± 0.03)	0.02 (± 0.01)
18	0.05 (± 0.03)	0.04 (± 0.01)	0.03 (± 0.02)	0.02 (± 0.01)

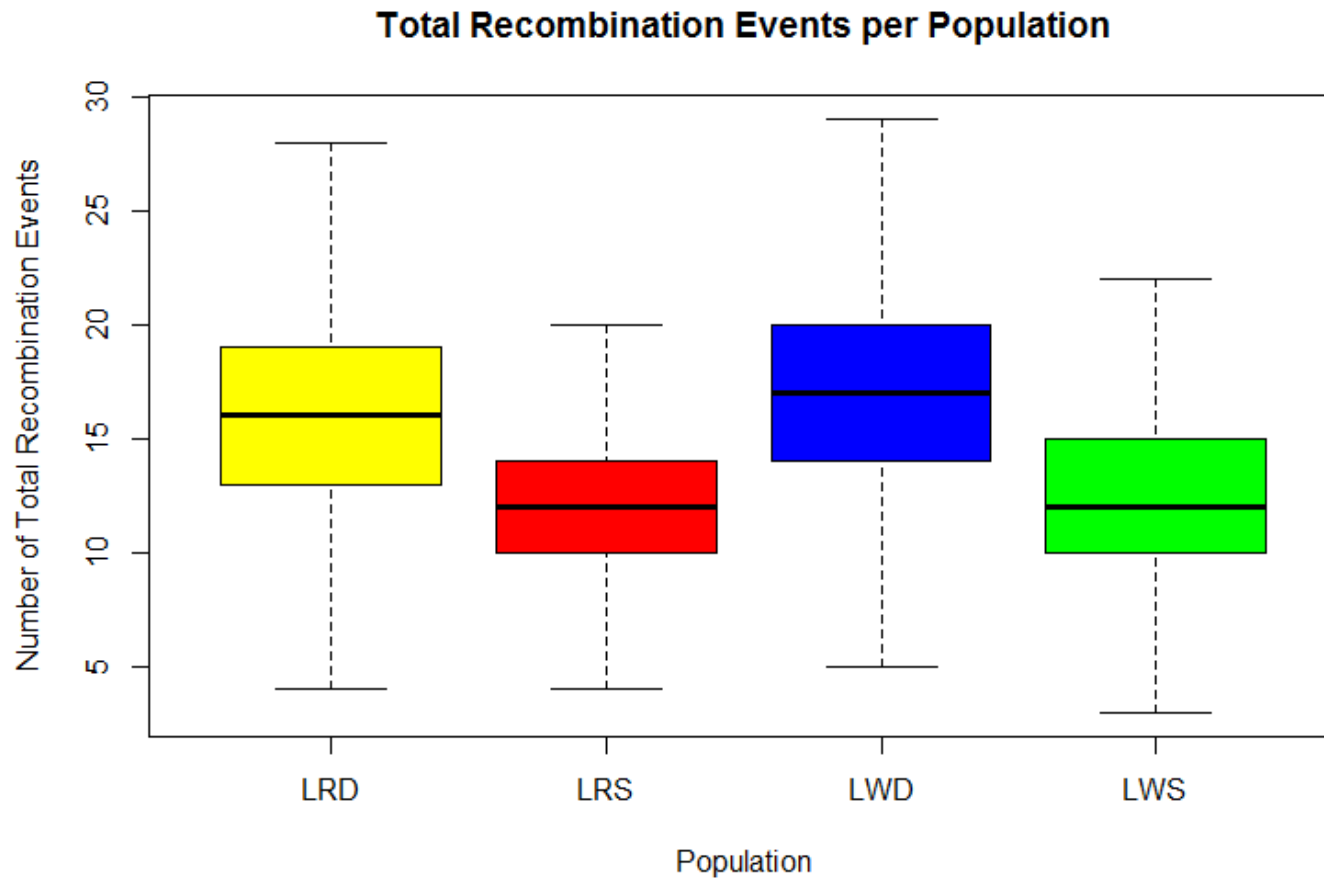


Figure 1. Boxplot of genome-wide recombination events in the genome by each breed/sex population.

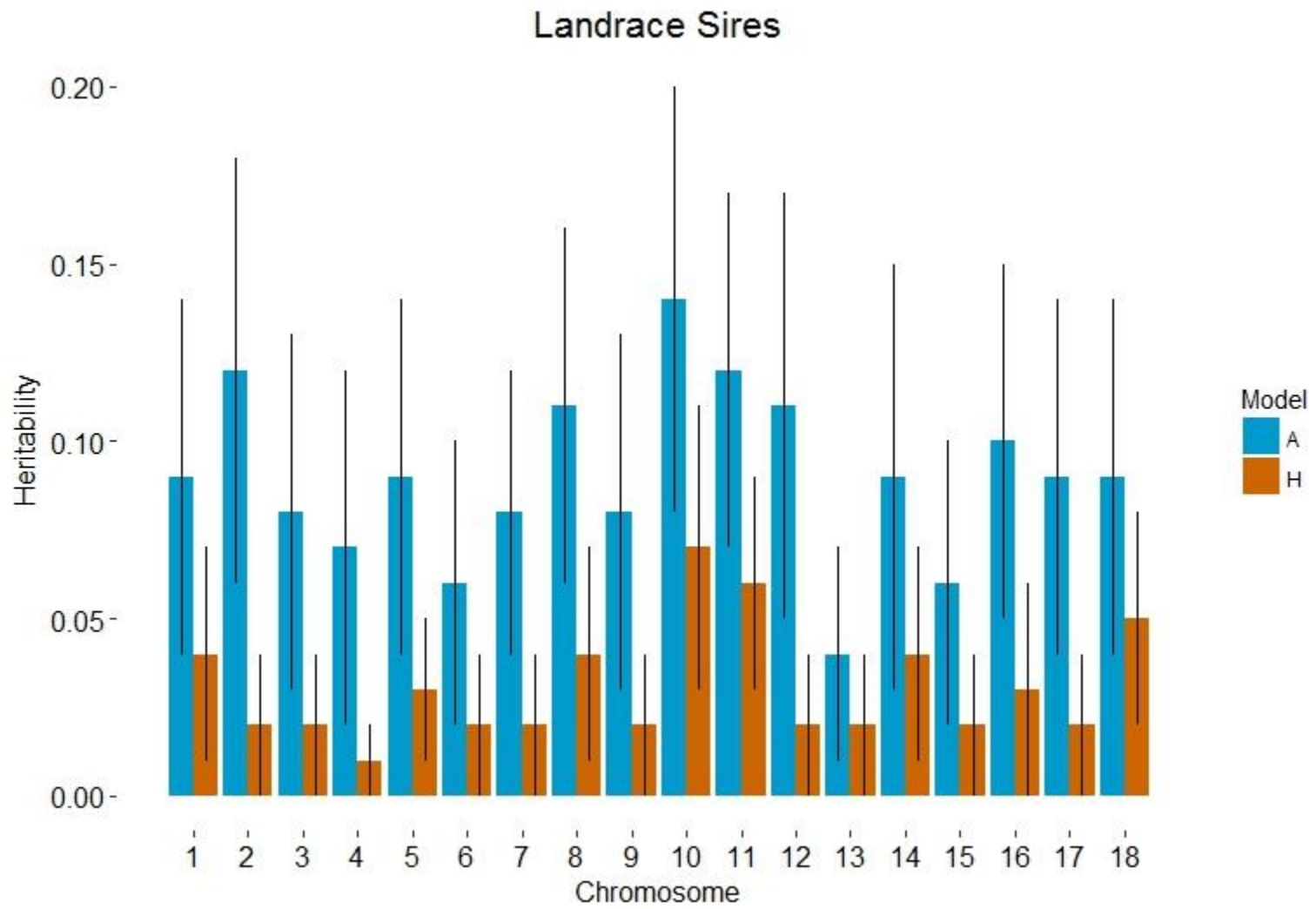


Figure 2. Heritability estimates for Landrace Sires (LRS) for each chromosome using an **A** or **H** matrix.

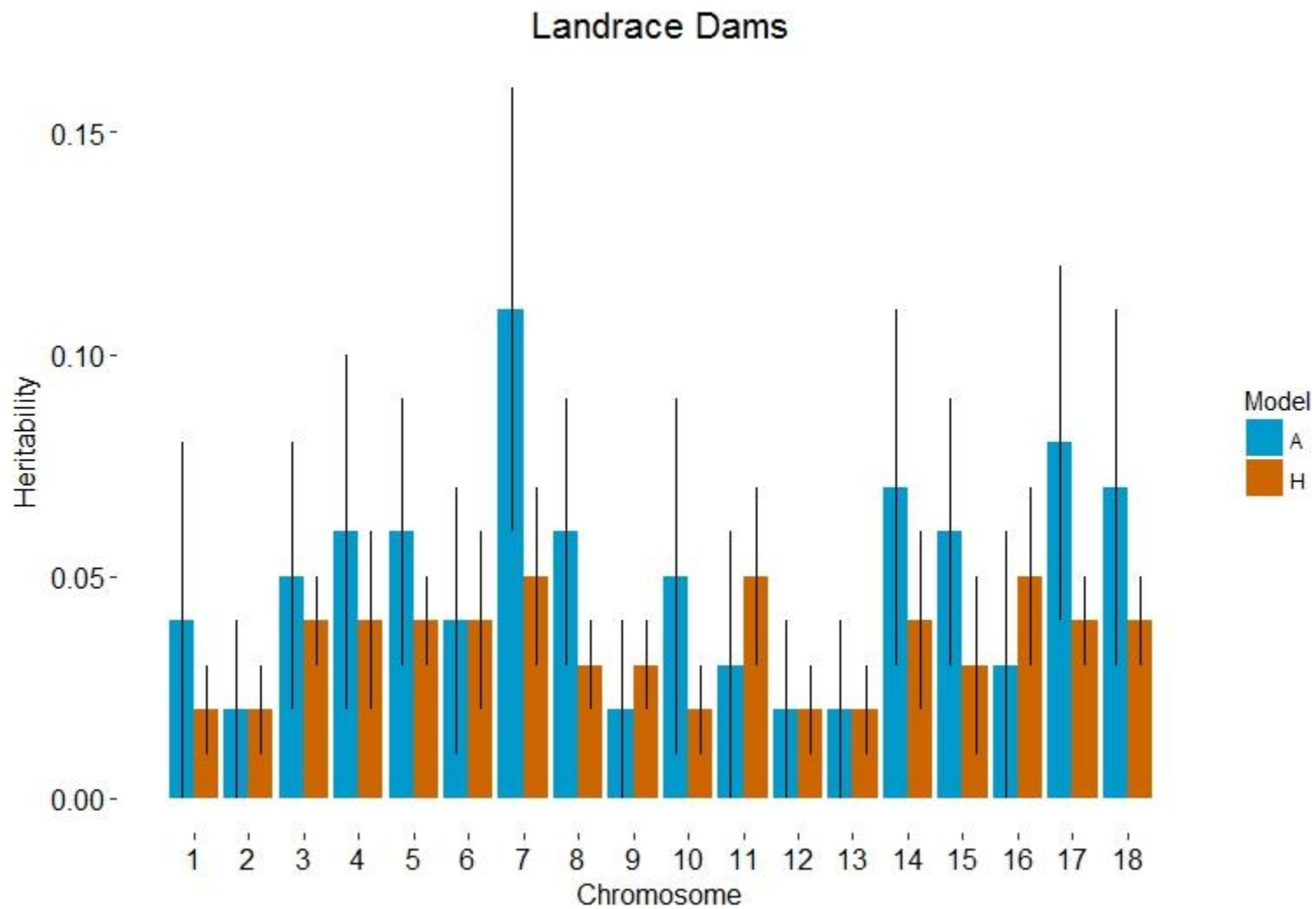


Figure 3. Heritability estimates for Landrace Dams (LRD) for each chromosome using an **A** or **H** matrix.

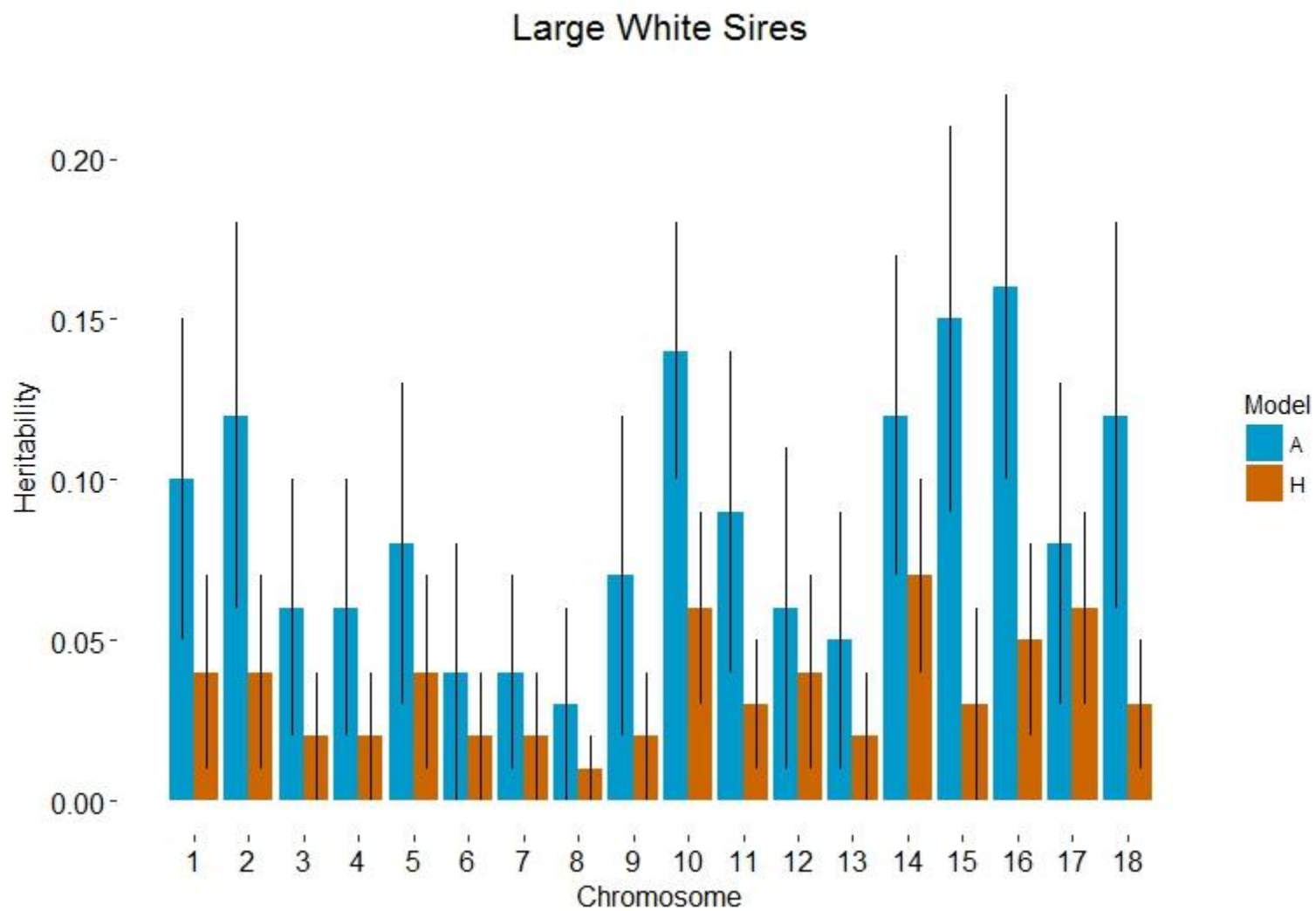


Figure 4. Heritability estimates for Large White Sires (LWS) for each chromosome using an **A** or **H** matrix.

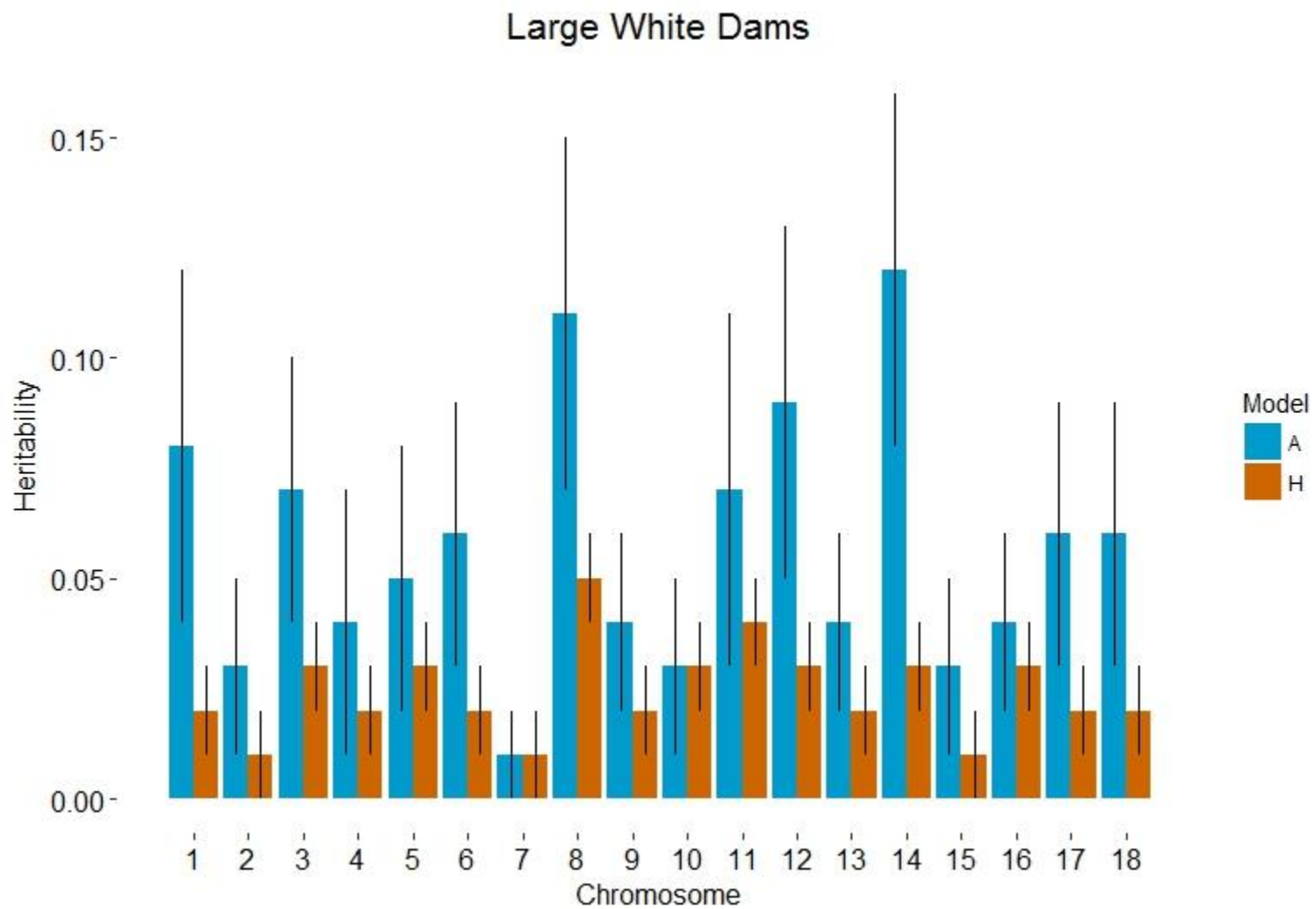
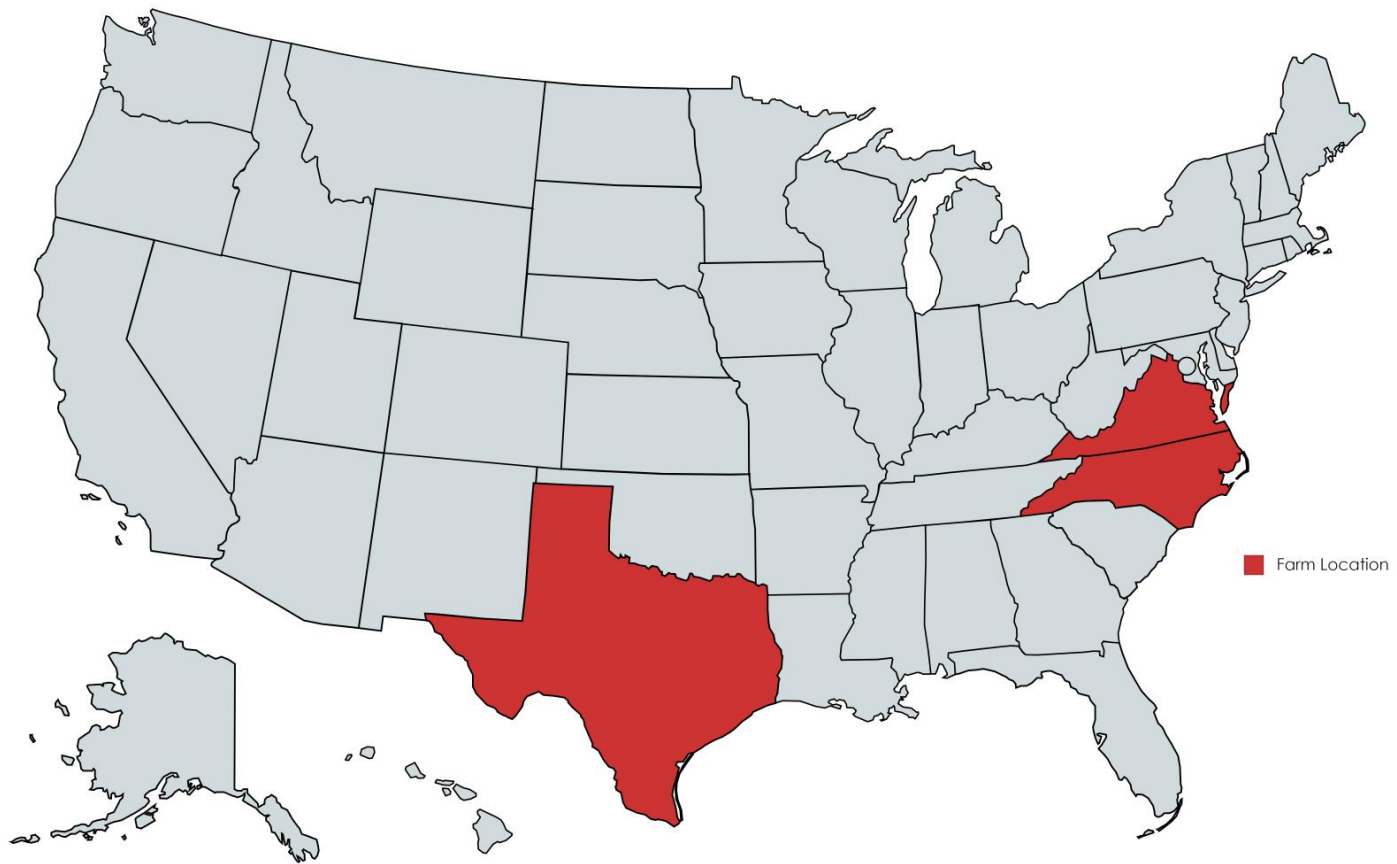


Figure 5. Heritability estimates for Large White Dams (LWD) for each chromosome using an **A** or **H** matrix.



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Figure 6. Locations of data collected for this study.

CHAPTER 3

CONCLUSION

Recombination rate in livestock populations, especially swine, has not been extensively researched and many characteristics of recombination rate have yet to be discovered.

Recombination rates in humans and mice have been explored and differences in some population parameters, age and sex, have been seen to have a strong effect on the rate of recombination. In other livestock species such as cattle, it has been shown that the rate of recombination differs between breeds as well. Other external factors, such as ambient temperature or relative humidity, have been shown to have impacts on recombination rate.

Heritability estimates for recombination rate are poorly understood with most estimates being around 0.10 and 0.15 using sheep. Heritabilities for the whole genome recombination rate is a more general heritability estimate for recombination, while heritabilities for each chromosome could give more information about which chromosomes may be contributing to the most variation through the genome.

In the current study differences in recombination rate in age, sex and breed in the population were estimated and the most significant differences ($p < 0.0001$) were between the male and female populations. This difference is the most consistent throughout most organisms, with the females having more recombination events on average than the males. Other significant differences included the difference between the first and third parity in females and a difference between the Landrace and Large White breeds. Differences in recombination rate due to age have been documented before in swine with a larger recombination rate connected to older female pigs. The difference between the two breeds discussed has never been recorded before,

but significant differences between larger populations (American, European, and Wild populations) have been documented.

Differences in recombination rate due to ambient temperature or relative humidity were not observed in this population of animals in contrast to the results of other studies.

Heritability estimates for each population were estimated using the blupf90 family of programs. Two models were used to estimate heritabilities for total genome recombination rate, one using only the pedigree to create the relationship matrix and one using the pedigree and the SNP chip information to create the relationship matrix. When SNP chip information was used, the estimates for heritability increased which could be due to a better relationship matrix. In both models, the female populations had a higher heritability than the males reaching 0.26 in the Large White dam population.

Heritability estimates for each chromosome in all populations were small and some heritabilities almost reaching zero. When SNP chip information was added into the model for each chromosome, the heritability estimates almost all decreased. The structure of the data could allude to differences between males and females in heritability estimates per chromosome. Sires, on average, had more progeny records than dams, which could increase the estimate of recombination because there is more variation within the sire populations than the dams.

The results of heritability estimates show that recombination rate is heritable within these swine populations. Selection on recombination can also drive the random variation introduced through recombination either up or down relative to either selecting for or against recombination rate. Variation introduced or taken out of the population could be helpful at many stages in production. For example, uniformity is desired at the terminal stage of swine production, so a decrease in recombination rate could be selected for. The differences in populations can also

affect the rate of recombination and should be taken into account before selection decisions on recombination rate can be made. Further research should look into the genetic architecture of recombination rate to see if there are any significant areas of the genome which may be contributing to variation within recombination rate.