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744 Detection of quantitative trait loci affecting conformation traits in Holstein cattle. M. S. Ashwell*[1,3], D. W. Heyen[2], T. S. Sonstegard[3], C. P Van Tassell[3], and H. A Lewin[2], [1]*North Carolina State University, Raleigh* [2]*University of Illinois, Urbana* [3]*USDA-ARS, Beltsville*.

Putative quantitative trait loci (QTL) affecting conformation traits in Holsteins have been detected using genotypic data generated by two research groups. Each research group conducted an independent genome scan in a select group of Holstein grandsire families. Six families were used by both groups and genotyped for 367 microsatellite markers in order to identify QTL affecting milk production and health traits. The same merged dataset has now been reanalyzed to identify putative QTL affecting conformation traits. Seventeen linear traits and four composite index traits were included in the analysis. The phenotypes were obtained from the Holstein Association USA (http://www.holsteinusa.com) and included standardized transmitting abilities for body type, feet and legs, and udder traits. Data were analyzed using QTL Express (http://qtl.cap.ed.ac.uk), a web-based regression interval mapping method. Preliminary analysis had identified 34 putative QTL affecting the conformation traits within the grandsire families. These QTL were significant at the chromosome-wise level (F-statistic > 15) and were located on 15 bovine autosomes. Additional analysis is underway to determine which of these QTL, if any, are significant at the genome-wise level.

Key Words: Conformation Trait, Quantitative Trait Loci, Dairy Cattle

745 Statistical power for detecting epistasis QTL effects under the F2 design. Y. Mao* and Y. Da, *Department of Animal Science, University of Minnesota, St. Paul*.

Epistasis refers to gene interaction effect involving two or more genes. Statistical methods for mapping quantitative trait loci (QTL) with epistasis effects have become available recently. However, little is known about the statistical power and sample size requirements for mapping epistatic QTL using genetic markers. In this study, we developed analytical formulae to calculate the statistical power and sample requirement for detecting each epistasis effect. The genetic modeling of QTL genotypic values and variance used the linear partition of Kempthorne (1954), and Bulmers presentation of this linear partition (1980) was used for efficient derivation of variances and covariances. To achieve succinct mathematical expressions and intuitive interpretations, epistasis heritability is defined to denote the ratio of the epistasis variance to the phenotypic variance. Assuming two interactive QTL without linkage and all epistasis effects have the same absolute value, the heritability of additive x additive (a x a) effect is about twice as large as that of additive x dominance (a x d) or dominance x additive (d x a) effect, and is about four times as large as that of dominance x dominance (d x d) effect. Consequently, among the four types of epistasis effects involving two loci, a x a effect is the easiest to detect whereas d x d effect is the most difficult to detect. The statistical power for detecting a x a effect is similar to that for detecting dominance effect of a single QTL. The power is poor for detecting a x d or d x a effect and is extremely poor for detecting d x d effect. The sample size requirements for detecting a x d, d x a and d x d are highly sensitive to increased distances between the markers and the interacting QTLs. Therefore, using dense marker coverage is critical to detecting those effects.

Key Words: Epistasis, QTL, Statistical power

746 Including genetic groups for QTL effects in marker assisted selection. K. J. Hanford*[1], R. M. Thallman[2], S. D. Kachman[3], and L. D. Van Vleck[1], [1]*USDA-ARS, Roman L. Hruska U.S. Meat Animal Research Center, University of Nebraska, Lincoln,* [2]*USDA-ARS, Roman L. Hruska U.S. Meat Animal Research Center, Clay Center, NE,* [3]*Department of Statistics, University of Nebraska, Lincoln*.

Genetic group effects provide a means of accounting for the effect of selection that cannot be accounted for by records of relatives. In a polygenic animal model, genetic group effects are incorporated into the mixed model equations (MME) by adding one equation for each genetic group corresponding to foundation (phantom) animals. With minor modifications the rules for the inverse of the relationship matrix without genetic groups can be used to obtain the inverse of the coefficient matrix after absorption of the equations for the phantom animals needed for solving the MME. With identification of quantitative trait loci (QTL), information from closely linked genetic markers can be included in prediction of breeding values with mixed model equations to implement marker assisted selection (MAS), where effects of QTL alleles are considered random. As with the polygenic animal model, the distribution of the QTL alleles can be different within different subpopulations. Genetic group effects for the QTL may also arise from QTL effects that depend on the genetic background of the different subpopulations. Current methods for MAS with solutions from mixed model equations do not allow for incorporating genetic group effects for QTL. An extension has been developed which allows genetic group effects to be incorporated in the MME to obtain genetic evaluations for MAS by augmenting the MME by the number of genetic groups used in models without marker information. Rules for constructing the inverse of the QTL coefficient matrix after absorption of the equations for the phantom animals and augmenting the MME with this matrix have been derived and will be presented.

Key Words: BLUP, Genetic Groups, MAS

747 Computational analysis of putative imprinting signatures of bovine IGF-II and IGF-II receptor genes. I. G. Imumorin*[1], J.J. Kim[2], O. O. Mgbere[3], and D. O. Umesiobi[4], [1]*Valdosta State University, Valdosta, GA,* [2]*Iowa State University, Ames,* [3]*Rivers State Univesity of Science & Technology, Port Harcourt, Nigeria,* [4]*University of Natal, Pietermaritzburg, South Africa*.

The IGF-II gene and its receptor (IGF-IIR) are members of the insulin family of polypeptide growth factors and also represent two of the earliest imprinted genes identified in mice and later in humans. The IGF-II gene has been shown to be paternally expressed in sheep and pig, but yet to be tested experimentally for genomic imprinting in cattle, whereas maternal expression of IGF-IIR has been reported in a single uncorroborated study in cattle. We conducted preliminary computational analysis of five concatenated cDNA sequences of bovine IGF-II and a full length cDNA sequence of bovine IGF-IIR downloaded from GenBank to gain some insight into putative imprinting signatures of both genes. A total of 2,451 nucleotides of the IGF-II gene and 9,061 nucleotides of IGF-IIR were analyzed. These cDNA sequences were searched for motifs that may be common with genomic sequences of human and mouse IGF-II and IGF-IIR genes using MEME analysis and the motif weight matrix outputs from MEME analyses were subjected to analysis by the MAST program. The MAST analysis identified highest scoring motif sequences of 200 bases for IGF-II and 166 bases for IGF-IIR, which were analyzed by EMBOSS-CpG Plot program respectively. IGF-II contained a 61-base CpG island, with a GC content of 67% and an observed/expected CpG ratio of 0.78. No CpG island in the IGF-IIR motif sequence was identified. This might indicate a differentially methylated region (DMR) in the bovine IGF-II promoter, which is a common signature of imprinted genes. However, a more accurate and robust analysis of these genes awaits the full bovine genomic sequences for comparison with conserved non-coding but regulatory sequences of the mouse and human orthologs of IGF-II and IGF-IIR genes, which in turn require experimental validation of imprinting status.

Key Words: Imprinting, Bovine IGF-II, Bovine IGF-II Receptor

748 Evaluation of microsatellite markers on bovine chromosomes 1 and 5 for potential allelic associations with meat charcteristics and growth traits in beef cattle. K. S. Kim*[1], S. Costello[2], G. J. M. Rosa[1], A. M. Mullen[2], N. E. Raney[1], and C. W. Ernst[1], [1]*Michigan State University, East Lansing,* [2]*National Food Centre, Dublin, Ireland*.

Association between molecular marker and phenotypic data is an important tool to expedite genetic improvement of livestock species. Several bovine chromosomal regions (QTL) have been reported to have significant associations with growth and performance traits in cattle. In this study, potential effects of previously identified QTL regions on growth

and beef quality traits were investigated in commercial beef cattle populations. Eight microsatellite markers spanning QTL regions on bovine chromosomes (BTA) 1 and 5 were genotyped in beef cattle populations from Michigan and the Republic of Ireland. Haplotypes of these markers were constructed using the PHAGE program (www.gmap.net). Analyses of allelic associations with phenotypes were performed with chi-square tests to compare allelic frequencies between groups with high and low phenotypic values. Initial analyses have been performed with the Michigan (n=85) and Irish (n=75) data sets. In the Michigan data, the BTA1 markers exhibiting significant allelic frequency differences were BM1312 for slaughter weight (P<0.06), BMS6506 for birth weight (P< 0.06), and BMS4048 for hot carcass weight (P<0.05). Significant associations of these markers with meat quality traits from the Irish cattle were also found with BM1312 for firmness (P<0.003), BMS4001 for flavor (P<0.005) and texture (P<0.05), and BMS4048 for pH (P<0.05). A haplotype of BM1312-BMS4001 markers also revealed a significant allelic difference for firmness (P<0.01) and texture (P<0.05) traits. Significant differences in allelic frequency from BTA5 markers were found with BL4 for flavor (P<0.05), and ETH10 for intramuscular fat % (P< 0.05). Our results suggest that QTL reported on BTA 1 and 5 may be segregating in commercial beef cattle populations and their effects may extend to economically important meat quality traits. Thus, further study is warranted to define beneficial haplotypes for potential use in marker assisted selection to improve these traits in beef cattle.

Key Words: Beef Cattle, Microsatellite Markers, Beef QTL

749 A combined line-cross and halfsib model to detect and characterize QTL in an F2 outbred cross population. J.-J. Kim* and J. C. M. Dekkers, *Iowa State University, Ames*.

Data from an F2 outbred cross is typically analyzed by a least squares line-cross (LC) model to detect QTL that differ between breeds. Alternatively, data can be analyzed by a half-sib (HS) model for F1 sires to allow for QTL segregating within breeds. The LC and HS models can also be combined (CB model). Objectives of this study were to evaluate the power to detect QTL and to characterize QTL into LC, HS, or CB QTL, i.e. QTL that are fixed, segregating at similar or different frequencies in the parental breeds, using model lack-of-fit tests. Phenotypic and marker data for a 100 cM chromosome with 11 equidistant markers were simulated on 512 F2 progeny for two mating designs: I (II): 2 (20) F0 sires, 10 (80) F0 dams, 8 (19) F1 sires. A biallelic QTL was simulated at 75 cM with additive values of 0.8, 0.5 or 0.32 phenotypic SD. A total of 6000 replicates were generated with the actual difference in QTL allele frequencies (FD) between the alternate F0 parents ranging from 0 to 1. Significance thresholds were from 3000 simulations without QTL. The LC model was most powerful for any size fixed QTL (FD=1) in both designs, followed by the CB model. For FD =0.5, the CB model was more powerful than the HS and LC models (99, 97 and 97% for the large QTL for CB, HS, LC; 84, 76 and 68% for the medium QTL; 44, 40 and 35% for the small QTL, in design I). For FD=0, the HS model had more power than the CB and LC models (74, 70 and 10% for the medium QTL for HS, CB, LC; 30, 22 and 7% for the small QTL in design I). For FD=1, most detected QTL were defined as LC QTL in both designs. This proportion decreased with FD. The opposite was observed for HS QTL. The proportion CB QTL among detected QTL was greatest for FD=0.5 and decreased as FD moved away from 0.5. The latter was more pronounced for the large than the small QTL, for which the proportion of CB QTL was nearly constant across FD. Our results show that the CB model can increase power to detect QTL and enables characterization of QTL detected in F2 crosses that segregate within breeds.

Key Words: QTL Mapping, Line-Cross Halfsib Analysis, Combined Model

750 Identification of an ovulation rate QTL in cattle on BTA14 using selective DNA pooling and interval mapping. M. G. Gonda*[1], J. A. Arias[2], G. E. Shook[1], and B. W. Kirkpatrick[2], [1]*Dairy Science Department, University of Wisconsin-Madison,* [2]*Animal Sciences Department, University of Wisconsin-Madison*.

Increased twinning incidence in beef cattle has the potential to improve production efficiency. However, phenotypic selection for twinning rate is difficult because of the traits low heritability and the long time interval necessary to collect phenotypic records. Therefore this trait and the correlated trait of ovulation rate are ideal candidates for marker-assisted selection. The objective of this study was to identify ovulation rate quantitative trait loci (QTL) in two related sire families. The families (paternal halfsib sires 839802 and 839803) were from a population of cattle selected for ovulation rate at the USDA Meat Animal Research Center, Clay Center, Nebraska. Putative ovulation rate quantitative trait loci have previously been identified in the 839802 family on chromosomes 7 and 19; however, marker coverage in the original scan was not complete. This study fills the gaps in marker coverage of the earlier study by adding approximately 60 informative microsatellites to each sire family. Each family was genotyped using selective DNA pooling. Sons and daughters were included in either the high or low pool based on their estimated breeding value deviations from the midparent average (EBVMD) for ovulation rate. Approximately 40% (839802) and 26% (839803) of available progeny comprised the high and low pools combined. Pooled typing revealed possible associations (nominal P<0.05) between ovulation rate and marker genotype for eleven and fifteen microsatellites in the 839802 and 839803 families, respectively. Subsequent interval mapping provided additional support for the presence of an ovulation rate quantitative trait locus on BTA 14 (chromosome-wise P <0.02).

Key Words: Ovuation Rate, Quantitative Trait Locus, Selective DNA Pooling

751 Power and sample size calculations for two color microarray experiments with biological and technical replication. J. P. Steibel*[1], R. J. Tempelman[1], and G. J. M. Rosa[1,2], [1]*Department of Animal Science, Michigan State University, East Lansing,* [2]*Department of Fisheries and Wildlife, Michigan State University, East Lansing*.

Very recent work on sample size and power calculations for microarray experiments have simply considered arrays or spots as the experimental units. Nevertheless, biological replicates should be considered to be the fundamental experimental units when broad inferences are of interest. In other words, dye-swap arrays on the same two samples and or multiple spots per gene on a slide should be treated as subsamples. We address sample size calculation and analysis of microarray experiments using linear mixed effects models, with special attention directed towards the distinction between biological replication and technical replication within a broad inference context. Three experimental designs were considered: 1) the Loop design, 2) the Dye swap design, 3) and the Reference design. Power was determined for three levels of differential expression (1.25, 1.5 and 2.0 fold-change), and for several different levels of biological replication (n = 2,,10) and technical replication (r = 1,,4) based on five different sets of variance components. Results for the loop and the dye swap experiments were virtually identical with slight differences depending on, whether or not Satterthwaites approximation to degrees of freedom was used. The reference design, however, provided the lowest power of test in almost all situations, particularly when the residual variance was large. Increasing technical replication yielded very marginal improvements in power except in situation with high residual variance. Our power analysis indicates that in situations of relatively high biological variability, as many as 40 individuals per treatment are necessary to have at least an 80% probability of concluding differential expression on a gene with 1.25 fold change. This result is particularly relevant for experiments involving livestock species, in which the biological variance (animal-to-animal variability) is generally considerably larger than the technical variance (variability among arrays and among spots). In this situation, the only meaningful way to improve experimental power is by increasing the number of animals in the trial.

Key Words: Microarray, Power Analysis, Biological Replication

752 A new method to fine map a quantitative trait locus using linkage disequilibrium. H. Gilbert*[1,2], M. Z. Firat[2], L. R. Totir[2], J. C. M. Dekkers[2], and R. L. Fernando[2], [1]*Institut National de la Recherche Agronomique, Cedex, France,* [2]*Animal Science, Iowa State University, Ames*.

A new approach was developed to fine map a biallelic QTL using linkage disequilibrium (LD). It uses the probability that a maternal (paternal) QTL allele of each individual is the mutant QTL allele, conditional on the pedigree and marker information. These probabilities were derived recursively from the haplotype-specific mutant QTL allele frequencies in the founders. As the haplotypes of founders are not known, their

probabilities were estimated by MCMC methods. This model has fewer parameters than the usual model, because it relates the means and covariances of the QTL gametic values to the QTL allele effect and their frequencies. Consequently, this approach is expected to be more accurate. To overcome the computing difficulties in exact calculation of IBD probabilities, an MCMC method was used to derive approximate conditional probabilities of inheriting maternal and paternal QTL alleles. A residual maximum likelihood method (REML) was implemented to map the QTL, using a Newton-Raphson algorithm. The QTL position, QTL effect, haplotype-specific mutant QTL allele frequencies and polygenic and residual variance components were jointly estimated for each interval. The derivatives of the residual likelihood were obtained by automated differentiation. A simulated population was analyzed to compare the ability of this technique to fine map a QTL with two others methods. In the first method, identity by descent QTL covariances are used to model LD and cosegregation of the alleles at linked loci. In the second, identity by descent QTL covariances are used only to model the cosegregation of the alleles, and LD is modeled by including the marker haplotypes as fixed effects in the model. LD was simulated by introducing a mutation at the QTL followed by 100 generations of random mating. Different genetic designs were simulated, under linkage and linkage disequilibrium and with various QTL effects, to obtain power and accuracy of the parameter estimates.

Key Words: QTL, Linkage Disequilibrium, Simulation

753 Assessment of respiratory chain complex activities and electron transport chain protein expression in muscle mitochondria in Angus steers with low and high feed efficiency. B. A. Sandelin*[1], A. H. Brown Jr[1], C. Ojano-Dirain[1], M. Iqbal[1], M. A. Brown[2], W. O. Herring[3], M. Akin[4], Z. B. Johnson[1], and R. T. Baublits[1], [1]*University of Arkansas, Fayetteville,* [2]*USDA-ARS Grazinglands Research Laboratory, El Reno, OK,* [3]*Smithfield Premium Genetics Group, Roanoke Rapids, NC,* [4]*Circle A Angus Ranch, Iberia, MO.*

The objectives of this study were to determine the relationships between feed efficiency (FE, gain/feed) and respiratory chain complex activity and mitochondrial protein expression in cattle. Feed efficiency was determined on 92 head of contemporary Angus steers fed over a 130 d period. Individual animal intake was measured by a Calan Broadbent Feeding system. Animals were fed five finishing rations (stepwise) throughout the feeding period. Animals were harvested at a commercial packing plant and muscle (Sternohyoideus) samples were obtained from steers with Low (0.154 $\pm$ 0.02, n=7, L) and High (0.252 $\pm$ 0.02, n=7, H) FE. Muscle homogenate and mitochondria were isolated using differential centrifugation. Activities of respiratory chain complexes were measured using spectrophotometric methods. The protein bands were separated in 10% SDS-PAGE, stained with Coomassie blue and intensities were quantified using Scion software. Mitochondrial protein expressions were assessed with Western blot analysis with a chemiluminescence detection system. Activities of respiratory chain Complexes (I and II) were higher ($P < 0.02$) in L compared to H steers. While the expression of four immunoreactive mitochondrial proteins, NAD4 (Complex I), core I (Complex II), Cox II (Complex IV), ANT1 (ADP/ATP channels), were higher ($P < 0.05$) in N compared to L steers, there were no differences in the expression of several other proteins. SDS-PAGE revealed that the intensities of seven protein bands were higher in H compared to L steers. It appears that differences in complex activities and protein expressions may be involved in the phenotypic expression of feed efficiency in cattle.

Key Words: Feed Efficiency, Angus, Muscle Mitochondria

754 Samples classification using microarray data: Dealing with potential diagnostics misclassification. R. Rekaya*, *Department of Animal and Dairy Science, University of Georgia, Athens.*

While microarray was successfully applied in gene expression profiling of tissues/cells, and methods for selecting a subset of discriminative genes for samples classification have been proposed, the robustness of those procedures to potential misclassification was never investigated. For complex and heterogeneous responses such as disease traits, several subclasses with varying phenotypes exist. Using typical diagnostics tools, different types of a specific disease/trait can be difficult to tell apart. As a result, such similarity can lead to misdiagnosis. It is recognized that an accurate diagnostic is crucial for a successful use of gene profiling as a classification tool. Unfortunately, the accurate assignment of a subject to a specific disease/trait type is a difficult and expensive process. Although, the results obtained using microarray seem to indicate a more accurate prediction, the problem of misclassification is not yet resolved. This type of ambiguity is not rare, and it is either too difficult to detect, or economically unfeasible. In gene expression experiments involving animals, and even human, the present cost of the technology precludes extensive testing. In this study, a method for dealing with this problem or at least to attenuate its effects using a statistical model capable of accounting for potential misclassification was implemented. A simulation was conducted where 30 arrays with 10,000 genes each were generated. In the first case, a binary response was assumed. In the second case, a multinomial response with 5 classes was assumed. In both cases, the status for every sample was assigned as a function of the gene expression intensities in each array. Artificially, some samples status was changed randomly to introduce a misclassification rate of 5% and 10%. When the miscoded data was analyzed without consideration of misclassification, a change of 20-35% of discriminative genes was observed depending on the type of trait and the percentages of miscoding. When the miscoded data was analyzed with a model that contemplated misclassification, the change in the set of discriminative genes ranged from 2 8% depending primarily on the miscoding rate.

Key Words: Microarray, Misclassification, Gene Expression

755 Statistical methods to detect imprinted QTL with gender-specific recombination frequencies. Nicole R. London* and Yang Da, *Department of Animal Science, University of Minnesota, St. Paul.*

Imprinting is characterized by differential expression of alleles due a parent-of-origin effect. In this study, we developed statistical methods to detect and map imprinted quantitative trait loci (QTL) accounting for gender-specific recombination frequencies under the F2 and reciprocal backcross (RBC) designs. Multi-allelic markers were assumed for both designs. Under the F2 design with gender-specific recombination frequencies, additive and imprinting effects are confounded using currently available contrasts for testing additive and imprinting effects. Alternative contrasts were developed to independently estimate these effects. These contrasts are functions of gender-specific recombination frequencies, and reduce to the currently available contrasts when the two genders have equal recombination frequency. The RBC design requires a reciprocal mating system in terms of parental gender to detect imprinting effect. Contrasts for use with the RBC design were developed to independently test for additive and imprinting effects. These models were used to analyze a simulated population of animals. Monte Carlo simulation studies were conducted to evaluate the theoretical results on statistical power for detecting additive, dominance, and imprinting effects under the F2 and RBC designs. Marker and QTL genotypes were generated such that the true recombination frequency and each QTL effect used to generate these genotypes could be obtained reversely from the data. The analysis of the data showed the methods are accurate and computationally feasible to use with large data sets. Statistical powers observed from the simulated data agreed weel with predicted powers. The power depends on the effect size, heritability of the trait, and the marker QTL recombination frequency. An F2 design has higher power than a RBC design to detect imprinting effects. The sample size necessary to detect imprinting effects is similar to the requirements to detect additive effects.

Key Words: Imprinting, QTL, Recombination frequency