ABSTRACT: The past century has seen animal breeding and genetics evolve and expand from definition and validation of basic population genetics theory to development of selection index theory to today's relatively sophisticated genetic prediction systems enabling industry genetic improvement. The end of the first century of the American Society of Animal Science coincides with the rapid movement of the field into the era of genome-enabled genetic improvement and precision management systems. Led by recent research infrastructure investments by the United States and international partners to develop chicken, bovine, swine, ovine, and equine “genomic toolboxes,” the animal breeding community is poised to play a crucial role in the century to come. These genomic toolboxes provide the needed platforms for developing whole-genome selection programs based on linkage disequilibrium for a wide spectrum of traits; allow the opportunity to redefine genetic prediction based on allele sharing as opposed to traditional pedigree relationships; and provide for the first time simultaneous information upon which to practice genetic selection and plan precision management of specific genotypes, all early in the life of the animal. An area of major focus will be mining of the genomes through systems biology approaches to better understand gene and metabolic networks—what has previously been lumped into poorly understood genotype by environment and genotype by genotype interactions. Perhaps the greatest obstacle to the successful merger of genomic and quantitative approaches will be the lack of necessary animal resource populations to appropriately define and measure phenotypes (i.e., the so-called phenomic gap) for difficult-to-measure traits such as resistance to disease and stress, adaptability, longevity, and efficiency of nutrient utilization. Additionally, because of de-emphasis of quantitative genetics and animal breeding programs in academia over the past quarter century, a dearth of qualified young scientists to effectively mine the genomes must immediately be addressed. Although the motivating factors may have changed, the need for high-quality animal breeding and genetics research and education has never been greater.

Key words: animal breeding, genomics, whole-genome selection

INTRODUCTION

Genetic improvement in livestock has a truly amazing history, with the Journal of Animal Science having been the world’s premier publication venue for many of the major scientific innovations that have occurred since 1908 (Hohenboken, 2009). Although the majority of advancements in the past 100 yr have been made using quantitative genetics approaches, in recent years it has been nearly impossible to miss seemingly daily news reports about exciting discoveries in the relatively new field of molecular genetics and genomics. While most of these reports have focused on the unraveling of the human genome and its implications for human health, there has been significant spillover into plant and animal agriculture as well. At times over the past 15 yr, it has seemed that this new and exciting field would hold all of the immediate answers to breeding improved beef and dairy cattle, swine, sheep, and horses. Today we have draft genome sequence assemblies of the bovine and equine genomes completed and made publicly available along with a host of rapidly developing diagnostic tools, with the same now underway for the porcine and ovine species. Such transformational technological developments, coupled with several major societal shifts that are predicted to result in changes of epic proportions for the livestock industry and its producers, make the centennial anniversary of American Society of Animal Science (ASAS) an ideal time to consider needs in the field of animal breeding and genetics to fully address these challenges.
HISTORICAL PERSPECTIVE—GENETIC THEORY TO SELECTION AND MATING SYSTEM TOOLS

The first half of the 20th century was an immensely prolific time in agricultural science. Arguably, the most dramatic discoveries were actually in the fields of genetics and statistics. During the 1920s and 1930s, the field of population genetics came of age, primarily as a means of quantifying and describing the writings of Darwin from the late 1800s. The emerging leaders of this field helped to describe the concepts of genes, gene loci, chromosomes, and cellular reproduction. They were also instrumental in establishing the field of biometrics—statistics as applied to biological phenomena. These early statisticians developed much of the underlying theory used broadly in science today. At the same time there were pioneering scientists who had the foresight to develop populations of livestock upon which they began to practice long-term selection and inbreeding.

Scientists also made what seemed to be an unrelated but extremely valuable discovery in plant genetics during this same period with the observation that when 2 unrelated lines of germplasm were crossed (hybridized), the resulting crossbred progeny had better performance than the expected average of the parents. The concept of heterosis between mildly inbred lines was born—and with it the seed industry and crop agriculture was revolutionized. At the time, livestock breeders did not see any great benefit from this phenomenon, but that would dramatically change later (Cundiff, 1970; Dickerson, 1973).

The era following World War II was a particularly exciting time for livestock genetic improvement, as it was in many fields. The 1940s saw some of the greatest minds to ever grace the study of livestock genetic improvement at their prime. J. L. Lush, who many refer to as the modern-day father of animal breeding (Dickerson, 1973; Dickerson and Willham, 1983), was busy defining, with coworkers Hazel and Dickerson, the concept of the “selection index” and “breeding value” (Hazel, 1943; Lush, 1947). The field of biometrics had matured to the point where it was now possible to determine from experimental populations that performance for traits affecting production could be measured, and that many of these traits appeared to be heritable.

In 1953, Watson and Crick presented for the first time in the scientific literature the molecular structure of the genetic code—DNA (Watson and Crick, 1953). Combined with the theories of genes and heritable variation of traits, it was now possible to visualize how these genetic differences at the gene level might one day be exploited for genetic improvement.

Also, in the 1950s, 2 significant events occurred that would permanently change the nature of livestock breeding. The first was that AI techniques matured to an adoptable level for cattle breeders, especially dairy producers. Coupled with the earlier institution of the Dairy Herd Improvement programs of USDA, volumes of data began to accumulate matching pedigrees to milk production records. At the same time, computing technology was beginning to surface as a usable tool, even though it was rudimentary to what we now have today. Dairy cattle breeders had enough foresight, however, to understand the power of coupling quantitative genetics theory to AI; as a result, genetic evaluation as an applied science was born. Furthermore, the plans of the dairy industry did not go unnoticed by other livestock breeding communities, and performance data recording quickly became mainstream practice in all of the species under various models, often at the level of breed registries and societies. Several organizations were also established in the industries to develop uniform guidelines for performance recording, including the Beef Improvement Federation, National Swine Improvement Federation, and the National Association of Animal Breeders. These organizations were provided critical leadership by animal breeders who were leaders in the field and in ASAS.

The late 1960s and early 1970s was the next period of great change in livestock breeding and genetics. Two things occurred somewhat simultaneously: the importation of germplasm from several lines and breeds and the next generation of computing technology coming of age. As a result of their faster growth rates, size, and altered body composition, several of these breeds quickly took a strong foothold in the seedstock industry. Breed associations and initial breeding companies took advantage of developing computer technology in the 1970s to deploy the first across-herd genetic evaluations using sire-maternal grandsire models, and the initial era of breeding value estimation across large-scale populations was born. These efforts built upon selection index theory and its applications employing mixed-model equations, first suggested by Henderson (1959, 1973, 1975) and further deployed by Willham (1979) among many others.

Additionally, producers discovered that hybrid vigor was indeed possible—and very economically beneficial—when many of the new breed lines were used in systematic crossbreeding programs (Dickerson, 1970, 1973). One of the most widely noted efforts in this area was developed and carried out at the USDA-ARS US Meat Animal Research Center (MARC) through programs like the Germ Plasm Evaluation program led by Larry Cundiff and the Germ Plasm Utilization program led by Keith Gregory. Since 1968, this collective effort has produced the fundamental body of knowledge now used worldwide to understand genetic variation within and between breeds, and how to effectively use it in beef cattle production (Gregory and Cundiff, 1980). Similar programs and results have also been produced and published in the Journal of Animal Science for sheep and swine through the US MARC efforts (Young, 1995; Freking et al., 2000).

The 1980s was a true time of transition for livestock breeding. Computing technology had matured to the
level where statistical methodology could be applied to large pedigreed performance databases—so-called BLUP methodology. Scientists successfully worked out the reduced animal model, allowing the inverse of the numerator relationship to be solved (Quaas and Pol- lak, 1980) and were successful in using these methods to compute for the first time what we now know as EPD and predicted transmitting ability within breeds. These new genetic evaluation tools were significantly more powerful than the previously used breeding value estimates from the sire/maternal grandsire model approach. In the time since, we have become the ben- efticiaries of continual refinement in genetic prediction methodology, including more accurate predictions as well as a plethora of new traits exhibiting useful levels of genetic variation (Koots et al., 1994a,b) added to the evaluation pipeline.

HISTORICAL PERSPECTIVE—SHIFTING TO THE ERA OF THE GENOMES

The other monumental event in the 1980s was the unleashing of a new field of science called genomics. This term was first used in 1986 to collectively describe the scientific discipline of mapping, sequencing, and analyzing genomic level DNA information. A technology called polymerase chain reaction (Mullis and Falouona, 1987) unleashed the forces of research into the genetic code of plants and animals. It had only taken 34 yr to go from understanding the structure of DNA to being able to start mining information from the genome!

As molecular genetics tools became available to lab scientists in the late 1980s, researchers began the arduous process of genetic mapping. Because they were unable at that time to know the base sequence of the DNA code, they had to use a somewhat “black-box” approach to identify locations on the chromosomes that might contain genes affecting these traits. This process, called linkage mapping, took advantage of DNA polymorphisms called microsatellite markers, a type of variation found readily throughout the genome. In 1994, the first genetic linkage maps of cattle detailing a few hundred markers were published by USDA-ARS scientists from US MARC (Bishop et al., 1994) and Australian Commonwealth Scientific and Industrial Research Organization (CSIRO) scientists (Barendse et al., 1994). Similar efforts have culminated in linkage maps for swine (Rohrer et al., 1994), sheep (Maddox et al., 2001), and horses (Swinburne et al., 2000). Today, these linkage maps combined with radiation hybrid and bacterial artificial chromosome maps are much better defined (e.g., the recent “composite bovine map” where a total of over 21,000 individual markers are included; Snelling et al., 2007).

The availability of the first linkage maps allowed researchers to begin the search for regions of the genome harboring genes containing polymorphisms causing differences in performance for economically impor- tant traits—what have become known as QTL. Several livestock resource populations were formed to identify QTL affecting a wide variety of traits. The results of these projects were exciting and stimulated a consider- able amount of attention in the livestock industry in the mid to late 1990s, promising that the application of marker-assisted selection was just around the corner and would soon revolutionize livestock breeding (An- dersson et al., 1994; Soller, 1994). Unfortunately, as is too often the case, the immediate promise of genomics was clearly oversold, as it has since become clear that the identification of QTL was only a first “baby step” in the process to bringing these results to a practicable technology (Dekkers, 2004).

Fortunately for the livestock genomics community, the US government had placed a high priority, through the National Institutes of Health, on better understand- ing the human genome, motivated by the possibility of developing new ways to combat human disease and improve human health. Initially, many of the same ap- proaches of linkage mapping were used in human ge- nomics, with the additional twist that model organ- isms, principally the laboratory mouse and rat, were studied as proxies for man, leveraging the remarkably high genomic similarity of 90% or greater between related mammalian species. Scientists also observed that although the arrangement of the pieces of the genetic puzzle was not the same across species, large regions of the genome had been conserved throughout evolution. This now allowed the opportunity to take information from species being studied with very large research budgets to infer what might be the case in livestock spe- cies using “comparative mapping.” While this approach did yield results, including the identification of the cal- lipyge condition in sheep (Cockett et al., 1994) and the myostatin gene causing double-muscling in cattle (Casas et al., 2000), only a handful of genes have been mapped to date through the “QTL-search followed by comparative mapping or fine mapping” approach.

The human genetics community quickly recognized that if progress in delivering new tools through genom- ics for human health applications was to occur expe- ditionously, building of genome sequence infrastructure was required. Linkage maps, QTL searches, compara- tive mapping, and some fine mapping were useful, but extremely inefficient, timely, and high in cost. Thus, in the last half of the 1990s, the National Institutes of Health, through its National Human Genome Research Institute (NHGRI), built a plan for sequencing the human genome, along with the highly used lab spe- cies of the mouse and rat. The project became broadly known as the Human Genome Project and involved a network of sequencing centers contracted to do high- throughput whole-genome sequencing. An initial rough draft of the human genome sequence was completed in 2001, followed by a complete, finished sequence in April 2003, and a detailed haplotype map in 2005, 50 yr after Watson and Crick’s initial elucidation of the double-stranded helical nature of DNA (Collins et al., 2003; International HapMap Consortium, 2005). The
cattle, poultry, and swine industries, however, were placed in a position to reap huge rewards from the infrastructure built by NHGRI to sequence the human genome (National Academy of Sciences, 2002; NSTC, 2003). To build the most comprehensive infrastructure to capitalize on the human genome for discoveries in human health, NHGRI launched down a path in 2002 of supporting the sequencing of several other genomes (http://64.225.252.6/nstc/html/IWGGAD2004.pdf). These were chosen to most highly leverage the investment in human genomics, as based on comparative mapping and medical model species use. Over the past 5 yr, the 6-fold or greater draft sequence assemblies have been placed in the public domain through the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/), for the chicken (International Chicken Genome Consortium, 2004), bovine (Gibbs et al., 2002; Kappes et al., 2006), and equine species. The swine genome is currently being sequenced and is expected to be completed to the same level in 2009, and plans are underway for the same to occur for the sheep genome. All of these “big science” sequencing projects have required a new form of funding and international collaboration, involving multiple governments and agencies, industry, and academia partners (Green et al., 2007).

In addition to the development of the draft sequence, each of the genome projects has also sought to develop tools that will move livestock genomics research forward quickly (Wong et al., 2004; Kappes et al., 2006). In each case, additional light sequencing of animals representing additional breeds has allowed detection of large pools of new SNP. Additionally, full-length complementary DNA sequences have been developed for multiple tissue systems from the sequencing animals for the study of gene expression and further extension to expression-QTL approaches. Currently these genome sequences are being annotated through a worldwide community effort to provide a full picture of the “gene atlas” of the species.

As the genomic toolboxes were being built over the past few years, the development and release of commercial DNA tests has begun to escalate. With several companies now in the market space for this group of technologies, most with quite different business models, a variety of tests and platforms have come of age. The initial products released in the market over the past several years have generally involved small numbers of markers that have been shown to be associated with small but growing amounts of the genetic and phenotypic variation in traits of economic importance (Van Eenennaam et al., 2007).

Since 2005, the landscape in this field has been changing at a dramatic rate. This is largely because of the rapid growth in high-throughput genotyping platforms that have suddenly made it cost effective to genotype large numbers of markers in a single run. Recent efforts have culminated in the development of a panel of 56,000 bovine SNP markers (Van Tassell et al., 2008) with similar tools being developed for the chicken, swine, and sheep research communities that are expected within the next year. These developments have vastly accelerated the research and development pipeline in both public and private sectors and are poised to radically transform genomic diagnostics in the coming decade or sooner for these species. We can expect to see large panels of SNP assays made available (thousands as opposed to <100 available today) that will simultaneously provide diagnostics of multiple traits of economic interest, parentage and individual animal identification and traceability, and genetic defects of importance—all in one assay platform. Furthermore, the deployment of whole-genome selection approaches (Meuwissen et al., 2001) to livestock improvement appears to be on the threshold of reality, with recent reports for dairy cattle clearly pointing to significant enhancements in accuracy of breeding value estimates on young bulls from addition of “50K” whole-genome prediction above pedigree estimates (VanRaden et al., 2000).

Collectively, the developments of the past 2 decades have brought the field of animal breeding and genetics to a new launching point. Coming to the edge of this new universe brings into clear focus the fact that the needs in the coming century are great if the field is to be able to effectively mine this new wealth of genomic information to 1) improve livestock productivity and well-being; 2) enhance natural resource stewardship while reducing the environmental footprint of production; and 3) ultimately improve the quality of human life.

MEETING FUTURE CHALLENGES IN THE GENOME-ENABLED ERA

Several key societal and industry shifts are currently changing the landscape of animal agriculture, including the following:

1) By 2020 to 2030, world demand for meat and dairy products is expected to increase 40 to 50% (Rosegrant et al., 2001; FAO, 2002), which will stimulate the competitiveness of food animal products.

2) An increased call from the general public for decreasing the environmental footprint of livestock and poultry production, including range, water, and air quality.

3) Competition for energy sources and feedstuffs for alternative energy production, heightening the emphasis on improved energy utilization and animal adaptability to production environments.

4) Increased attention to animal well-being and welfare, pointing out the need for robust scientific criteria to actually assess animal well-being in our production systems.
5) Increased brand differentiation, including process and historical identity of products being called for in the marketplace by retailers and their consumers.

6) Increased interest and purchasing power of consumers for products from nonconventional production systems (i.e., “natural” and “organic”).

7) Recognition that we are concerned about the loss of genetic diversity, while recognizing the need to increase product uniformity and consistency. Considerable debate and disagreement in the industry regarding the value and usefulness of heterosis in the commercial sector exists for some of the livestock species.

8) The need for information continues to accelerate, with the cry for emphasis on economically relevant traits to the commercial industry, yet we have done little to put in to place evaluation for animal health, functionality, and adaptability traits (i.e., remaining heavy emphasis on output traits with not much to work with on the input side of the profit equation even though it was called for in work over 30 yr ago; Cartwright, 1970; Dickerson, 1970).

9) Structural changes in the livestock industries including consolidation, integration, and vertical coordination continue to change at a rapid rate.

10) New genomic technologies are rapidly moving the field into a brave new world of genome-enabled improvement and precision animal management. The widespread availability of genomic technologies offers the potential to invert the genetic improvement pyramid and will likely change the delivery and structure of the breeding sector in the marketplace.

11) Mining the genome in the post-genome-sequence world is here to stay, yet we are woefully inadequate in being ready to handle all of the information that is upon us in a practically meaningful way.

The issues above, coupled with the fact that we are quickly entering the age where we have more data than we know how to effectively handle in an era where technology is outpacing our abilities to utilize it, quickly lead to the conclusion that the field of animal breeding and genetics is now entering in to a second Renaissance Age.

Although the ushering in of the genomics era has been immensely exciting scientifically, it has not come without significant and tangible costs. This research is expensive to conduct, requires large project teams, is lab intensive, and has brought to the table a host of issues associated with intellectual property rights. As research and education programs around the world geared up to make progress in this arena, other programs were often redirected to the newer arenas of molecular genetics and genomics. As a result, over the past 20 yr, the majority of traditional animal breeding positions and research herds and flocks in the public sector were eliminated or redirected into genomics and molecular biology. This has resulted in a gradual increase in the average age of animal breeding and genetics researchers and educators. Additionally, a shift has occurred in the funding for research and development with an increasingly greater percentage in this area being found in the private as compared with the public sector.

These concerns lead the USDA to recently develop a Blueprint for USDA Efforts in Agricultural Animal Genomics (USDA, 2007). This strategic plan was developed after an extensive period of information gathering and synthesis from comprehensive stakeholder groups and communities in the United States and abroad (Burfening et al., 2006; Green et al., 2007). The plan was built on the foundation that quantitative genetics has been used for many years in selecting animals for improved production (e.g., growth, yield, efficiency) and has achieved remarkable results, while pointing to the fact that addition of animal genomic technology to quantitative genetics programs has the potential to lead to more accurate and rapid animal improvement, especially for phenotypic traits that are difficult to measure (e.g., disease resistance, animal well-being, feed efficiency, product quality). Additionally, animal genomics offers new opportunities to develop precision management systems to optimize the production environment based on the genotype of the animal. The USDA Blueprint lays out a plan for how research, education, and extension efforts in animal genomics are expected to deliver the following genome-based technologies, “science to practice,” to animal producers: 1) whole-genome-enabled animal selection; 2) prediction of genetic merit of individual animals from genome-based data combined with phenotypes; 3) integration of genomic data into large-scale genetic evaluation programs and the use of genomic information to design precision mating systems; 4) precision management systems to optimize animal production, health, and well-being; and 5) genomic capabilities that enable parentage and identity verification (traceability).

To deliver these outcomes, the field of traditional animal breeding and genetics will play a crucial role in addressing key priorities in the genome-enabled era. In fact, as pointed out in the USDA Blueprint, the most critical challenges in delivering value to the livestock industries from the cumulative significant investments in animal genomics are in the 2 high-need priority areas of large, highly resourced, and deeply phenotyped populations (i.e., phenomics) and in bioinformatics and computational biology. This is particularly true for the difficult-to-measure traits that have long been out of reach for genetic improvement. This includes phenotypes to genomically address the economically relevant trait areas of reproductive success and longevity in varied environments, efficiency of nutrient utilization, animal temperament, stress susceptibility, and either
innate resistance or susceptibility to disease. New opportunities to alter the nutrient profile and consumer desirability of animal products also are a target in the phenomics arena. Metagenomics approaches offer the opportunity to better understand the microbial environment of the rumen and digestive environments, and, better understanding of the interaction between host and pathogen should lead to improved animal health and productivity. Opportunities for customized animal health management are now considered possible through the application of genomic profiling of animals for enhanced precision of pharmaceutical use, and pharmacogenomic approaches offer potential for development of a new generation of improved biologicals and therapeutics (Gay et al., 2007).

Animal breeders will need to lead the way on the integration of genomic and phenotypic data into a new era of genome-enabled animal improvement and management. Inclusion of molecular genetic information into breeding value prediction and mating system design will require new approaches, not the least of which is the ability to handle large volumes of data with efficient computing algorithms. The availability of dense marker panel information on individuals at the commercial as well as seedstock levels will require new and creative approaches to maximize the utilization of all of the potential genomic information that will be generated, from a wider sector of the gene pool. Development of customized genotyping platforms for traits within and across populations, and their continued calibration on well-phenotyped populations will be an ongoing challenge. And, it will be animal breeders working together with their colleagues in the disciplines of physiology, nutrition, muscle biology, growth and development, and immunology who will lead the way for genomic profiling to becoming a base mechanism to enable precision animal management.

As better understanding of the genomes of livestock species unfolds, animal breeders will need to determine how such current unknowns as copy number variants, rare alleles, and epigenetic effects are understood and incorporated into animal breeding programs. Genomic information will allow the field for the first time to truly estimate and understand epistatic and dominance effects and how to best utilize them in systematic programs. And, certainly it is now envisioned that full sequence of individual animals will be available long before ASAS celebrates another 50 yr of its history, driven heavily by the current emphasis of the human genetics research community on medical resequencing technologies. And last, much as predicted by leaders of the field in the past 100 yr such as Tom Cartwright, Dewey Harris, and Gordon Dickerson, it will be the new “systems biologists” who may be the legacy of quantitative genetics (Pomp et al., 2004)—who, instead of analyzing the individual components or aspects of the organism, will focus on all of the components and the interactions among them, all as part of one system. They will truly seek to understand how the interactions of numerous genes, proteins, mechanisms, and the external environment of the organism produce the phenotype of an animal. While the systems biology approach will be the basic science underpinning of the phenomics revolution, the real-world application will be animal breeders working together with their colleagues in the disciplines of physiology, nutrition, muscle biology, growth and development, immunology, microbiology, and economics to lead the way for genomic profiling to become a base mechanism to enable precision animal management.

Although the opportunities of this new Renaissance period of animal breeding and genetics are exciting, several daunting questions exist that must be addressed to ensure success. The reduction in number of academic animal breeding programs around the world, and particularly in North America, has resulted in a deficit of human talent and resources ready to take on these challenges. Not only are quantitative geneticists lacking, those few who are being produced in the remaining programs are entering a highly competitive job market where few are remaining in academia, with many of the trained animal breeding scientists being pulled into the plant and biomedical arenas. The need to rebuild infrastructure for developing scientists and expertise in the animal breeding area is critical and must be addressed through new strategies and models. More direct investment of private industry into the funding of these programs is beginning to occur and will need to increase in the near term. Increased reach of federal research programs into the education sector is also needed, principally through the increased availability of research funding in USDA-ARS for graduate student and postdoctoral training. The time may have come for US programs to break down past barriers that have prevented consortia-type funding so that large-scale, common sense interdependent partnerships can be instituted between federal and state agencies, universities, the private sector, and industry commodity organizations. This model has certainly had success in other areas of the world, and the area of animal breeding is one that would benefit greatly from such approaches. Finally, because of the rapid escalation in the development of genome- and phenome-based technologies, the need for public education and outreach efforts has never been greater. Again, creativity by the animal breeding community needs to be mustered to deliver this in an efficient, timely, and technologically proficient manner.

The next 100 yr of animal breeding and genetics in ASAS promises to be a truly exciting time. While the challenges are substantial, the potential and opportunities are much larger. The current and future generations of animal scientists who call themselves animal breeders will be standing on the shoulders of giants as we navigate our way forward. What we can say clearly is that we see a future that is very different from what we know today, but it will all be underpinned through diligent application and reliance on the principles of ba-
sical population and quantitative genetics coupled with the incorporation and understanding of genetic information. Opportunities abound.

**LITERATURE CITED**


