

# **Mechanisms of Inbreeding Depression and Heterosis for Profitable Dairying**

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Genes in diploid organisms operate singly, in pairs, and in conjunction with genes at other locations throughout the nuclear DNA. Inbreeding depression and heterosis arise from the effects of gene combinations, that is, the effects of pairs of genes. Gene pairs are unique characteristics of individuals that are broken down and reformed each generation. This basic biological fact, introduced to many of us in high school biology, is the foundation of everything there is to say about this topic. Very few topics are so well rooted in a simple process. Simplicity suffers, however, under real-world challenges of combining breeds or selecting to improve within a pure breed under a multi-trait breeding objective. This paper attempts to explain in a rudimentary way the ways in which genes interact, transmit, and recombine and the implications of those processes to breeding options available to dairy farmers.

## **Mechanisms of inbreeding**

Inbreeding results from matings between related parents. Because breeding populations have finite size and long pedigree histories, mild inbreeding always exists by this definition. A more practical working definition of inbreeding is mating of parents more related than one would expect by chance alone. High levels of inbreeding are difficult to achieve in species where “selfing” is not possible. A 35-year project at the Beltsville Agriculture Research Center between 1912 and 1949 produced one dairy cow with an inbreeding coefficient of over 75%, the highest ever recorded for bovines under experimental conditions. A single generation of mating between this cow and an unrelated sire would break down all of the inbreeding in the dam. Extreme inbreeding is difficult to achieve and easy to eliminate – if you have access to an unrelated mate.

Selection toward a single breeding objective can increase inbreeding, even in large populations. U.S. Holsteins have been under effective selection pressure for higher production and improved type since mid-1960. From 1982 until 2004, average inbreeding in a pedigree-recorded population of over 1,000,000 Holsteins increased from 1% to 5%. These figures may well understate actual inbreeding, as estimates are relative to a 1960 pedigree base and some pedigree information is missing in this population grade and registered animals.

## **Consequences of inbreeding**

Inbreeding increases homozygosity. More gene pairs become identical because they are copies of the same ancestral genes. Consequences of inbreeding include an increase in uniformity of offspring of inbred individuals through reduced variation in genetic material between germ cells. Offspring face higher frequencies of deleterious recessive gene combinations, increased inbreeding depression, and greater variation in response to environmental stress. The last three effects of inbreeding are undesirable in commercial animals, while the first is of insufficient advantage to commercial producers to justify organized inbreeding programs.

While inbred animals are expected to express undesirable recessive characteristics more often than out bred animals, inbreeding does not cause “bad” alleles. Such alleles already exist in populations, almost exclusively as complete recessives, where dominant alleles suppress their expression and elimination through natural selection. Inbreeding increases probabilities that an individual will inherit two copies of such alleles from related parents who inherited the undesirable gene from one common ancestor. While

unfavorable under commercial production systems, this feature of inbreeding can be used to “purge” an inbred line of such alleles.

Inbreeding has been used to great advantage in plant species where generation intervals tend to be short, “selfing” allows rapid build-up of high levels of inbreeding, and many highly inbred lines can be developed and sustained simultaneously. Crosses of inbred lines produced hybrid corn – arguably one of the most successful advances in agriculture production in the last century. The role of inbreeding in animal breeding, however, is much more restricted and less successful.

Outbreeding – the mating of individuals less related than the average pair of animals in a population – produces opposite effects of inbreeding. Outbred individuals are less likely to express deleterious recessive alleles. Outbred animals may bear little resemblance to their parents due to breakdown of homozygous gene combinations and dominance. Outbred animals tend to be less subject to environmental stress than inbred animals. These characteristics have made outbred animals very useful under certain production systems, particularly those where reproductive efficiency is highly valued or environmental stress is not moderated by human intervention.

### **Two sources of homozygous gene pairs**

Homozygosity is common throughout animal genomes, particularly for genetic regions related to fitness and survival. Natural selection has driven unfavorable genes from breeding populations at many loci of genes. Random drift also contributes to homozygous combinations. A limited number of ancestors, perhaps survivors of a genetic bottleneck, may have, by chance, been homozygous at specific loci of genes where genetic variation once existed. A professor in my academic past, Dr. O. W. Robinson, called this a “founder effect”. [Bottlenecks also contribute to inbreeding and homozygosity at gene locations where genetic variation existed in founder animals.] If the possible ancestors are all homozygous for certain alleles, alleles passed to future generations will be alike, regardless of whether animals are closely related or not.

Identical alleles are referred to as “alike in state” when they were inherited from unrelated parents. Alleles that are alike because they were inherited from related parents, both of whom received a copy of the same allele from their common ancestor, are “identical by descent”. Formulas for calculation of inbreeding coefficients rely on probabilities of genes being identical by descent. Genes that are “alike in state” are ignored. Genetic effects of homozygous gene combinations are the same, regardless of whether genes are alike in state or identical by descent.

### **How does inbreeding happen in dairy cattle?**

Most dairy farmers, given an economically acceptable choice, would avoid close inbreeding. Acceptable choices aren’t always readily available. Dairy cattle in U.S. herds are either direct descendants of bulls widely used in AI service or a generation removed through use of sons of A.I. bulls in natural service. Bulls in A.I. service are used in many herds, which increases relationships between females that may be separated by time and distance. Prior to widespread use of A.I., relationships between females within a herd were likely higher than today, because many females were half sibs sired by the same bull. However, half sibs seldom existed in different herds. Such relationships are common today. Furthermore, selection toward a generally similar and stable breeding objective by A.I. studs caused the same animals to appear as parents of bulls in A.I.

Two sires in the U.S. Holstein population from the 1960’s, Round Oak Rag Apple Elevation and Pawnee Farm Arlinda Chief, became highly influential through extensive use as sires of sons, sires of bull mothers, and through heavy use of successful progeny tested descendants. The February 2007 Holstein Red Book reported that Elevation and Chief were responsible for 15.2% and 14.7% of all the genes

carried by Holstein bulls likely to be used as A.I. sires this year. Matings of these current A.I. bulls to cows and heifers in the current Holstein population (daughters of these bulls themselves or of their sires) will certainly produce many gene combinations that are homozygous by reason of “identity by descent” from Elevation and Chief. It would be very difficult to construct a mating between truly unrelated animals in U.S. Holsteins provided remote generations were probed for relationships. Elevation and Chief appear very rarely in the first four generations of today’s A.I. bulls, but appear again and again in generations seven through ten.

### **Options to avoid inbreeding**

Avoiding inbreeding entirely is highly restrictive, if it is possible at all. Dairy cattle of pure breed origin must serve a functional purpose in production of dairy products. Profit oriented herd managers want productive cattle, have the tools (progeny testing, sire evaluations, etc) to differentiate between more and less productive choices, and will logically favor a subset of the purebred population for breeding purposes. Rather than “avoiding” inbreeding, a more workable option would be to reduce and/or control major undesirable effects of inbreeding. Relationship between pairs of prospective parents in a breeding population should be constrained to a target compatible with reasonable genetic progress.

Several steps can be taken to reduce relationships without unduly compromising genetic progress toward economically justifiable goals. The key concept would be to recognize that maximum genetic progress comes at a high price in inbreeding depression and in restriction of future options to maintain some genetic diversity. The most important decisions to control inbreeding and obtain most (but not all) benefits of selection are made by managers of A.I. young sire sampling programs. These managers respond to demands from semen purchasers, so the family of important decision makers to moderate effects of inbreeding is inclusive. I suggest that the following approaches be considered:

- Limit the number of sons of the “top” sire of sons in any given time period. Use an expanded list of sires of sons, with particular interest in bulls with divergent pedigrees.
- Limit the use of the most popular bull mothers or bull-mother families. This objective parallels the expanded list of sires of sons above. E.T. and other reproductive technologies give us the power to use the best females too much.
- Diversity of breeding objectives stimulates diversity of genetic background. Separate selection indices for intensive management conditions and grazing herds are an example of such diversity and should be pursued by dairy producers.
- The industry, and in particular, individual dairy farmers through semen purchases, should embrace with enthusiasm inclusive selection indices directed towards improvement of lifetime economic merit. Such indices offer opportunity for prospective parents with divergent pedigrees to find a role in genetic improvement programs.

Success begets success (and increases relationships) through use of pedigree information in genetic evaluations. Yet, Mendelian segregation remains a powerful tool for genetic improvement. Sampling divergent pedigrees (with the unavoidable reduction in genetic merit) must be rewarded in the marketplace. Ultimately, dairy producers will demand, and pay for, pedigree diversity. Payment may be through higher semen prices for bulls with unique pedigrees (but potentially lower genetic merit than “mainstream” genetics) or through use of unrelated parents from another breed in a crossbreeding program. Independence of dairy producers in the U.S. will lead to a variety of approaches in the years to come. I am optimistic that the trend will be away from the small and restrictive set of bull mothers and sires of sons that has dominated the breeding industry until very recently.

## Options to utilize heterosis through crossbreeding

Heterosis arises from favorable gene combinations. Gene combinations are not equally important to all traits in dairy cattle or other species. Furthermore, more genetically divergent breeds are more likely to generate more heterosis than breeds with more similar genetic backgrounds. Traits subject to small amounts of inbreeding depression (perhaps somatic cell score is one such example) are expected to show less heterosis, as inbreeding depression results from the breakdown of favorable gene combinations. Producers should be realistic about the benefits of heterosis for any trait and for specific pairs of breeds before finalizing expectations for crossbreeding. We know very little about heterosis for specific breed combinations for most traits in dairy cattle. For some important traits such as productive life and fertility, even general heterosis is not well established.

Dairy producers should anticipate that benefits of additive genetic merit of individual breeds are more important to performance of a particular cross than is heterosis. This is not to discount the benefits of heterosis. However, heterosis alone should not be expected to overcome breed weaknesses in individual traits. The best rule for planning crossbreeding programs is to choose breeds carefully. Producers who don't like one of the breeds they use in a cross probably won't like the crossbred, either.

Breed additive merit for different traits in dairy cattle is better established than heterosis for specific crosses, but we have few breed comparisons in the scientific literature where cows of different breeds performed at the same time in the same herds. The table that follows is one comparison of breeds for mature body size and production characteristics, two performance areas that will affect breeder approval of crosses. The averages shown are certainly subject to adjustment, but were selected to represent breeds realistically rather than to favor any breed. Changes may affect conclusions regarding breeding plans in important ways and should always be made based on better information.

<b>Breed</b>	<b>Mature body wt</b>	<b>Milk yield</b>	<b>Fat yield</b>	<b>Protein yield</b>	<b>Fat %</b>	<b>Protein %</b>
Holstein	1600	23,300	840	700	3.6	3.0
Jersey	1100	17,600	810	640	4.6	3.6
Brown Swiss	1600	20,700	830	680	4.0	3.3
Swedish Red	1300	20,000	840	700	4.2	3.5
Normande	1100	16,000	700	580	4.4	3.6
Montbeliarde	1450	18,000	680	610	3.8	3.4

The choice of breeds to include in such a table is problematic in itself, as the listing omits choices that may appeal to others. The six breeds in the table either have long histories of performance as dairy breeds under U.S. conditions or are from European breeding programs with considerable recent success in genetic improvement towards dairy breeding objectives. The list does not include other viable populations such as New Zealand Jersey and Friesian strains or numerous dairy breeds/strains in Europe that may ultimately play important roles in U.S. crossbreeding programs.

## Predicting performance of breed crosses

The "merit" of any combination of two or more breeds is the average of breed means, weighted by the percent of that breed in a cross, plus the benefits of heterosis for the trait, adjusted for any recombination loss generated by the breeding program that produced the cross. For instance, the expected performance for a 3-breed cross where Holstein-Jersey cows were mated to Brown Swiss sires would include 25% of the Jersey and Holstein breed average, plus 50% of the Brown Swiss average. This particular cross includes no loss of heterosis from recombination, because breeds represented in the female line are not

represented in the sire line. All gene combinations produced arise from different breed origins. Expected milk yield, then, with 5% heterosis would be

$$(1 + \text{retained heterosis}) \times [(\text{Holstein contribution}) + (\text{Jersey contribution}) + (\text{Brown Swiss contribution})]$$

or

$$(1.05) [(.25)(23,200) + (.25)(17,600) + (.50)(20,700)] = 21,604 \text{ lbs}$$

A Jersey bull could be used as a backcross on the same Holstein-Jersey dam, creating quite different results. Heterosis would be reduced. Half of the genes contributed by the dam would be of Jersey origin, and would combine with Jersey genes of the sire to eliminate 50% of the heterosis in the Holstein-Jersey dam. Additive breed merit would also be affected. In this case, expected milk yield with 5% heterosis would be

$$(1.025) [(.25)(23,200) + (.75)(17,600)] = 19,501 \text{ lbs}$$

The 3-breed crossbred exceeds the 75% Jersey backcross for milk yield by over 2,000 lbs per lactation because of more heterosis, but more importantly because of replacement of genes from a Jersey sire with a Brown Swiss sire. Brown Swiss exceed Jerseys by 3,100 lbs of milk. Loss of heterosis cost the backcross 475 lbs of milk yield but the replacement of Brown Swiss genes with an additional 50% Jersey genes reduced yield by 1,550 lbs. An additional advantage to the 3-breed cross, in this case, is that full heterosis is applied to higher breed additive merit.

## **2-breed versus 3-breed crossbreeding systems with purebred sires**

The complexity of planning a crossbreeding program arises from

1. the breed choices available
2. several traits contribute to merit, with breed differences for each
3. heterosis for different traits (and breed combinations)
4. retained heterosis of the specific crossbreeding system

Each additional breed included in a system increases mating complications and increases the difficulty of managing a semen inventory. Dairy producers should be grateful, however, for the relative ease with which A.I. can be incorporate into a dairy breeding program. Beef breeders who use natural service need separate pens and perhaps even multiple pens for different breed groups! At some point, multiple pens will be required for bulls involved. Semen tanks are a most reasonable alternative.

Two-breed (and 3-breed) rotational systems using purebred bulls operate by mating each individual to a bull of the breed least represented in that individual's pedigree. The Jersey backcross in the example above would be mated to a Holstein bull, producing an individual that is 5/8 Holstein, 3/8 Jersey, with 75% retained heterosis. The next generation, sired by another Jersey bull, halves the Holstein proportion to 5/16, leaving 11/16 Jersey blood and 63% retained heterosis. At equilibrium, two breed rotational systems produce two groups of animals with 2/3 alleles from one breed and 1/3 from the other, with 67% retained heterosis.

The advantage of the 2-breed system is simplicity. The system also incorporates the two most favorable breeds for a particular producer's purpose. If a third breed is considered to be inferior for important traits, the 2-breed system can be quite attractive. The disadvantages of the 2-breed system are that one-third of heterosis is lost and that breed additive merit changes considerably between breed groups. For a Holstein-Jersey 2-breed system, mature body weights (using figures in the table) differ by almost 200 lbs for Jersey sired versus Holstein sired cattle.

The 3-breed system adds complexity, but also adds the opportunity to utilize a third breed in a rotational system. Heterosis is an advantage. At equilibrium, 86% of full crossbred heterosis is retained. The shift in percentages of genes from the breed of the sire is also reduced from 66% to 57%. However, for a trait like mature body size, a mixture of two large breeds like Holstein and Brown Swiss with one much smaller breed like Jersey still generates large size differences between Jersey-sired crosses and crosses sired by the other two breeds. From a management perspective, such issues should be resolved as much as possible by choice of pure breeds at the initiation of the project. Cow management is an alternative to a genetic approach, as large herds could solve most size problems by cow grouping.

### **Other systems**

Breeders have options to use systems other than those based on purebred sires. In dairy cattle breeding, however, availability of genetic evaluations from progeny tested and highly selected A.I. bulls is a tremendous impediment to any advantages arising from crossbred bulls. Other species have taken advantage of crossbred males, but those species, for the most part, have sought to improve traits expressed in both sexes relatively early in life. Milk production, fertility, and survival are not so kind to dairy producers. Selection of sires based on progeny-test results will remain an important consideration in dairy crossbreeding systems. This writer sees little advantage to use of crossbred bulls for the foreseeable future.

New “breeds” created as composites of existing breeds are another option that simplify mating systems and eliminate generation to generation variation in performance. Composites are subject to the same problems of inbreeding depression as pure breeds. Composites, however, can be “recreated” from the original pure breeds from time to time to take advantage of genetic progress within those pure breeds and to correct inbreeding buildup. Progeny testing programs would have to be developed for composites to allow for selection to operate. Limitations of time and expense of such programs may be prohibitive in light of potential benefits.

### **Conclusions**

Selection within pure breeds remains a viable option for producers wishing to improve traits that can also be modified through crossbreeding. Results, however, will be more slowly attained than for crossbreeding, and perhaps MUCH more slowly attained for traits where breed additive merit differs greatly and heterosis is substantial. Selection, however, imparts a permanent advantage that accumulates and builds over generations. Benefits from favorable gene combinations convey only to the individual and must be recreated each generation through mating plans.

Inbreeding in pure breeds motivates interest in crossbreeding but perhaps a more powerful force has been deterioration in health and fertility traits. Had breeding plans that included fitness traits been in effect (and effective) for the past 40 years, current interest in crossbreeding might have been greatly reduced, if existing at all. Under current conditions, however, breed differences in size, calving ease, fertility, and production traits encourages many producers to consider crossbreeding programs for commercial milk production.

Breeders devoted to their favorite pure breeds are encouraged to implement and to carefully follow selection plans that improve lifetime economic merit of the dairy cow. This effort requires selection pressure on the lowly-heritable, slow-to-change, difficult-to-measure fitness traits. Breeders opting to utilize crossbreeding programs should choose breed combinations carefully, use progeny-tested, purebred A.I. bulls and use the same selection for lifetime economic merit as purebred enthusiasts. Finally, crossbreeding programs should follow plans that maintain favorable combinations of breed additive merit and minimal recombination loss.