

Genetic Analysis of Breeds Versus Natural Populations Reveal Different Objectives of Selection

Jerold S Bell DVM, Dept. of Clinical Sciences, Cummings School of Veterinary Medicine at Tufts University

Several published papers on pure-bred dogs and pedigreed cats document the loss of genetic diversity, increased average inbreeding coefficients, and small effective population size. Some papers attempt to either label these changes as minor and inconsequential, or conversely make breeding recommendations to reverse the process.

There is a different view, and that is to accept that these changes occur due to selection as a prerequisite to breed formation. They are not inherently correlated to impaired genetic health nor do these population parameters need to be artificially controlled.

Examples from individual breeds are used to demonstrate these findings, however similar results are found in all breeds.

INBREEDING COEFFICIENTS

- Pure-bred dog and pedigreed cat breeds developed through targeted artificial selection for conformational, behavioral, and/or working standards.
- Regardless of the background of the founders, high inbreeding coefficients and low effective population size are a natural consequence of breed development.
- Inbreeding coefficients show the genetic relatedness of the parents of individuals.
- The “background inbreeding” on the founders establishes the basis for the breed, and it’s positive and negative genetic contributions.

Population expansion and purging of unhealthy lines characterizes the formation of breeds.

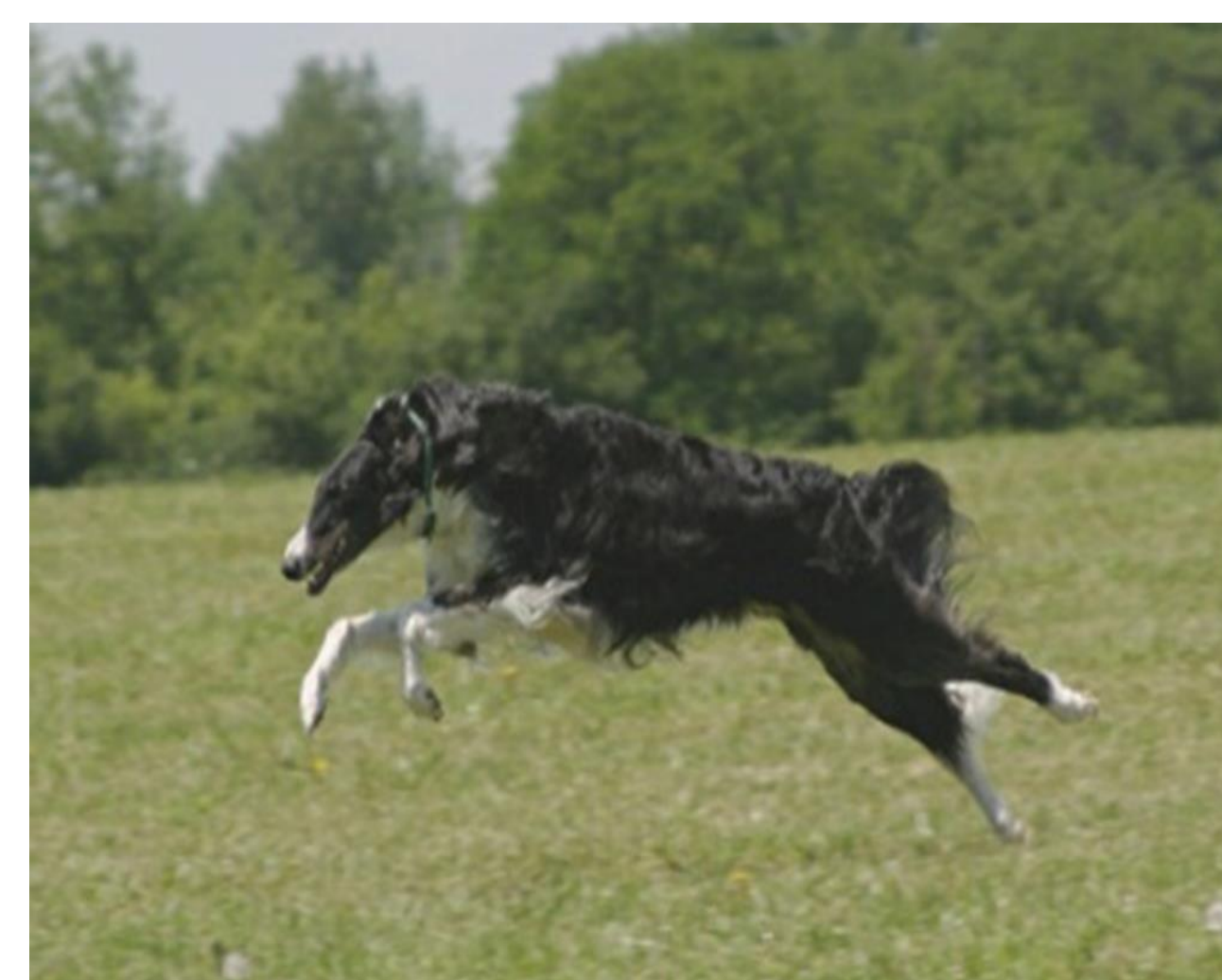
- With a closed studbook, total generational inbreeding coefficients can only go up over time.
- The total generational inbreeding coefficient decreases when either new dogs are entered into the studbook, or new dogs with incomplete pedigrees are added to the database that therefore appear to be “unrelated”.
- A mean 10 generation inbreeding coefficient calculated from generation to generation will decrease in an **expanding population** where the average relatedness of breeding pairs is less than the previous generation.
- When the mean 10 Gen IC increases, it is usually because breeders are concentrating on **popular sires**.
- As a breed population expands, a progressively smaller percentage of the population reproduces in a non-random manner to produce the next generation. This results in linkage disequilibrium, genetic drift, significant rapid changes in allele frequencies, and within-breed stratification.

Homozygosity is a natural consequence of breed formation.

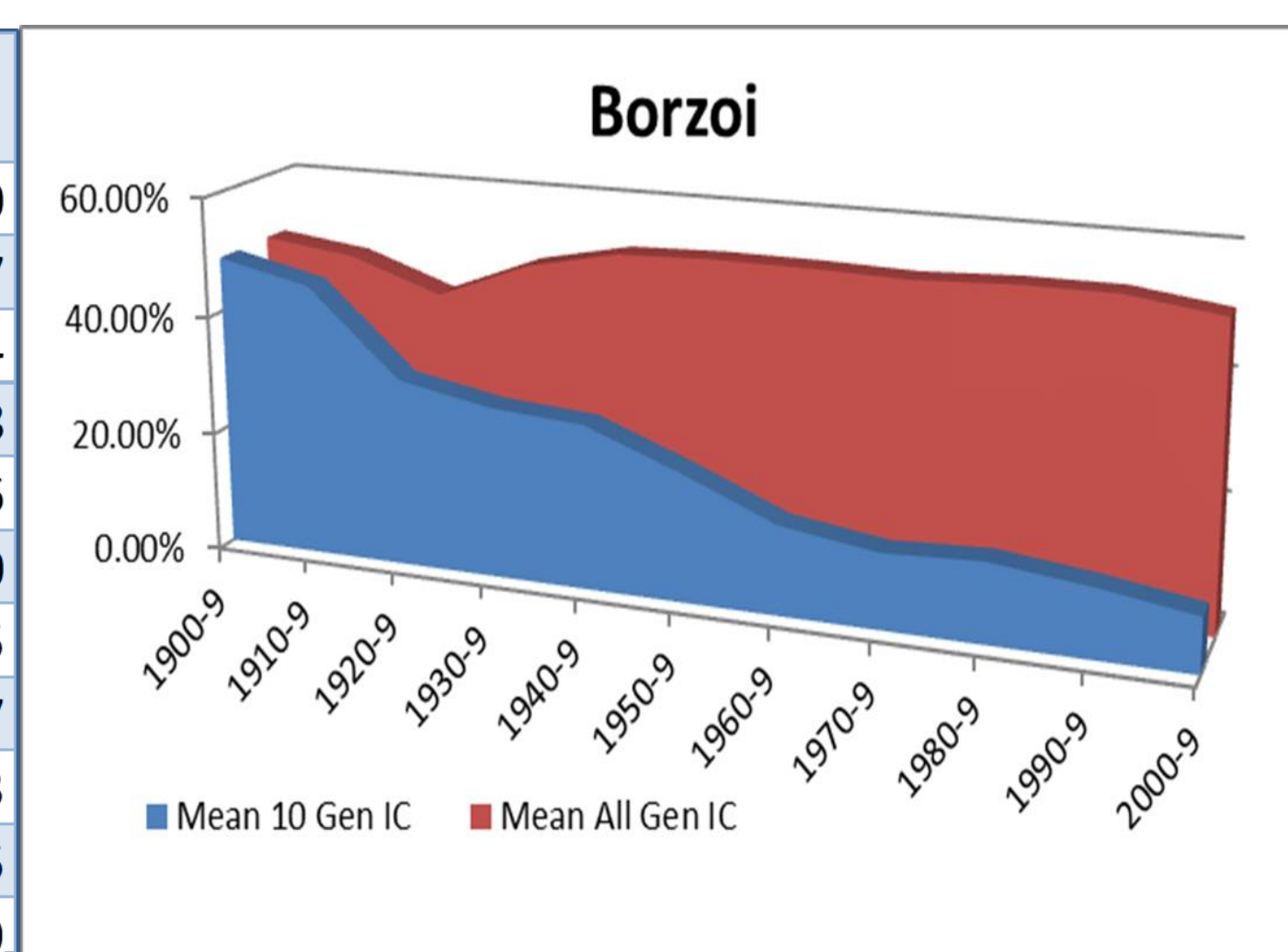
Within-breed stratification (different family lines) are required to provide breeding choices and selective pressure for breed and health improvement.

Example: Borzoi Breed

- Computerized pedigree databases can only be as informative as the completeness of the pedigrees. This database goes back 50+ generations to breed founders.
- The mean 10 generation inbreeding coefficient for Borzois in the 2000s is 9.1%, but the total generational inbreeding coefficient is 50.3%.



Period	Count	Mean # Gen	Mean 10 Gen IC	Mean All Gen IC	Mean # Unique Anc
1900-9	587	14.6	49.10%	49.30%	83.0
1910-9	764	18.6	45.70%	47.40%	144.7
1920-9	2749	24.9	31.40%	42.10%	226.4
1930-9	1952	26.1	28.50%	48.40%	200.8
1940-9	2225	32.3	27.40%	51.70%	229.6
1950-9	1207	36.6	21.40%	52.20%	305.0
1960-9	3323	41.7	14.80%	52.10%	377.5
1970-9	8031	45.7	12.50%	51.70%	420.7
1980-9	8824	48.8	13.30%	52.40%	424.3
1990-9	5884	52.3	11.50%	52.40%	463.5
2000-9	668	53.8	9.10%	50.30%	491.9



RELATIONSHIP COEFFICIENTS

- Individuals within a breed all share approximately the same percentage of genes with specific influential ancestors; usually beyond the 10th generation.
- These are the pivotal ancestors that were considered to most accurately represent the breed standard and be able to reproduce it, as well as to not produce detrimental genetic traits and disorders.
- They became influential because their offspring also epitomized the breed and reproduced it, as well as their offspring and so forth down the generations.
- If individuals do not produce healthy quality individuals to the standard, then they are not used for breeding, and their ancestral influence diminishes.
- These influential ancestors are different than **popular sires**, whose influence on the breed is immediate without generational data on what genes for positive and negative traits or disorders are being passed on.

Example: Burmese Breed

The Burmese cat breed originated in the early 1930s based on inbreeding on a single female of unknown origin (Wong Mau).



Average Relationship Coefficients for All Burmese Cats

Name	Date of Birth	Relationship Coefficient
Wong Mau	?	30.71%
Antonica Pamphula of Mizpah	1956	25.07%
Gerstdale Sealskin Jacket	1947	22.30%
Sabu Chin	1938	21.39%
Count Bruga	1950	21.31%
Gerstdale Brown Bomber of Forbidden City	1944	21.31%
Tai Mau	1930	16.90%
Yen Yen Mau	1932	16.63%

EFFECTIVE POPULATION SIZE

- Some studies of dog and cat breeds focus on the effective population size of breeds as a measurement of their genetic vitality and ability to maintain themselves as pure breeds (Calboli et al. 2008, *Genetics* 179:593-601).
- The nature of breed formation and development concentrates the genes of generationally proven superior producers. This is reflected in small computed effective population sizes.

Example: Nova Scotia Duck Tolling Retriever Breed

The Nova Scotia Duck Tolling Retriever breed developed based on a working phenotype from diverse founder breeds in the early 1900s.

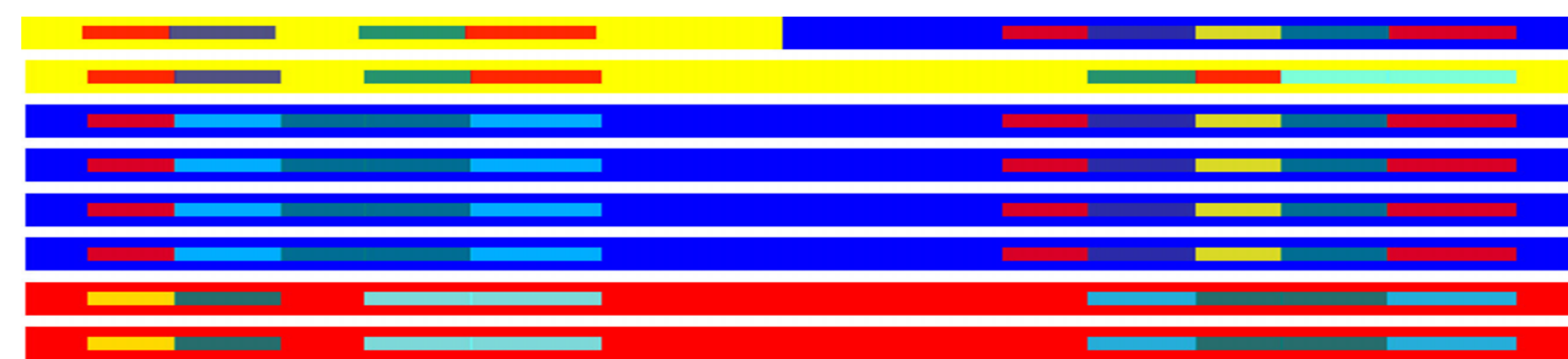


- Twenty-five ancestors contributed to the present day population
- Two founders explain 50% of the variation in the breed.
- Founder effective population size = 14.69 individuals.
- Breed effective population size = 71.89 individuals.

Population genetic indices do not differentiate between older, more populous breeds (who appear to have a more diverse population) and those still developing and expanding their gene pools. When earlier generations of established breeds are analyzed (prior to population expansion), they look just like developing breeds (with a less diverse population and lower effective population size).

Healthy breed gene pools require expanding, or large stable populations. Population contraction is detrimental to breed maintenance due to the loss of breeding lines and genetic diversity.

MOLECULAR GENETIC STUDIES



From Lindblad-Toh, et. al. *Nature* 2005

- Molecular genetic studies of dog breeds show large haplotype blocks (identical sections of chromosomes) and linkage disequilibrium (LD) representing the results of inbreeding and purging during breed development. (vonHoldt et al. *Genome Res.* 2011 Aug;21(8):1294-305.)
- Studies of dog breeds estimate that they lose on average 35% of their genetic diversity through breed formation. (Gray MM et. al. *Genetics* 2009; 181:1493-505)
- Breed formation creates “selective sweeps” where large chromosomal segments surrounding breed-defining genes become homozygous and fixed in the population. These include selected genes controlling phenotypes for size, coat color and texture, behavior, skeletal morphology, and other breed-specific characteristics. (DOGS: Akey et al. *Proc Natl Acad Sci U S A.* 2010 Jan 19;107(3):1160-5; CATS: Montague et al. *Proc Natl Acad Sci U S A.* 2014 Dec 2;111(48):17230-5.)

Molecular genetic studies document homozygosity that mirrors the pedigree-based total inbreeding coefficients and common ancestral relationship coefficients.

- Dog breeds in Sweden show extensive loss of genetic variation and recent inbreeding, but no correlation of differences in these parameters to genetic health. (Jansson & Laikre. *J Anim Breed Genet.* 2014 Apr;131(2):153-62.)
- Inbreeding depression is not related to the rate or level of inbreeding, but the homozygosity of deleterious recessive alleles. (Pekkala et al. *Evol Appl.* 2014 Nov;7(9):1107-19.)

The genetic health of dog and cat breeds is not a direct function of homozygosity or heterozygosity; but of the accumulation and propagation of disease liability genes. These can only be assessed through health screening that monitors the frequency of inherited disorders, fertility and fecundity.

LESSONS FROM CATTLE



From Qanbar et al. *PLoS Genet.* 2014

- Analysis of mtDNA estimates approximately 80 female founders for the domestication of Taurine cattle. (Bollongino et al. *Mol Biol Evol.* 2012 Sep;29(9):2101-4.)
- Cattle have undergone a rapid recent decrease in effective population size associated with domestication, selection, and breed formation. (The Bovine HapMap Consortium. *Science.* 2009 Apr 24;324(5926):528-32.)
- Selective sweeps were found in 106 chromosomal regions related to domestication phenotypes such as; coat coloring pattern, neurobehavioral functioning, and sensory perception. (Qanbar et al. *PLoS Genet.* 2014 Feb 27;10(2):e1004148.)
- Inbreeding depression in cattle can be reduced by avoiding the production of offspring that are homozygous for deleterious alleles at specific genomic regions. (Pryce et al. *Genet Sel Evol.* 2014 Nov 18;46(1):71.)

NATURAL POPULATIONS

- Species and random-bred populations are propagated through natural selection working against traits and disorders that reduce the ability to survive, thrive, and reproduce.
- Natural selection does not select against detrimental recessive genes, but limits their expression through heterozygosity.
- Without selection against detrimental recessive genes, their frequency in the population will remain static, unless changed through genetic drift.
- Natural populations use random mating where every individual has an equal chance to reproduce.
- The resultant population is in **panmixia** where; 1) There is no selection for traits other than for survival and successful reproduction. 2) The genetic background is randomized for heterozygosity.
- Population genetic indices have been developed specifically to measure deviations from panmixia; which is considered detrimental to the survival of natural populations.
- When natural populations are endangered due to low effective population size, endangered species conservation plans call for **randomized outbreeding** that maximizes heterozygosity.

OUTBREEDING EFFECTS ON BREEDS

- Outbreeding homogenizes breeds and removes the genetic difference between individuals – thus decreasing within breed genetic diversity. It is a self-limiting process that eliminates unique lines.
- Outbreeding causes the dispersal of disease liability genes. The expression of genetic disease will occur at random – similar to what is seen in random-bred cats.

Randomization and homogenization are the opposite of what is appropriate for breeds under selection.

Genetic diversity involves breeding individuals from diverse areas of the gene pool, but not the types of matings (outbreeding versus linebreeding) that they are involved in.

GUIDELINES FOR BREED HEALTH IMPROVEMENT



- Healthy breed gene pools require expanding, or large stable populations with diverse lines.**
- Selection for breed characteristics should avoid disease related phenotypes.**
- Breed health should be measured based on regular surveys of health and reproduction.**
- Selection should be directed against specific disease liability genes and phenotypes.**
- Breeders should utilize quality carriers of testable disease-liability genes through breed and replace strategies.**
- Breeders should avoid the overuse of popular sires – the most significant factor in limiting breed genetic diversity.**