

Understanding and managing inbreeding with runs of homozygosity in animal populations

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Inbreeding results from the mating of related individuals, and increases the probability that individuals from the population carry identical-by-descent (IBD) alleles, including deleterious variants that may contribute to inbreeding depression (ID) or associated with recessive genetic defects. Within individual genomes, IBD alleles are generally located in extended homozygous-by-descent (HBD) segments that appear as long stretches of homozygous genotypes called runs-of-homozygosity (ROH). Several approaches have been developed to identify such HBD segments, from rule-based approaches working with fixed-length windows to model-based approaches estimating HBD probabilities based on genotypes, allele frequencies, genotyping errors and the genetic map. These methods have also been extended to work with other technologies such as exome sequencing or low-fold sequencing.

In the field of animal genetics at large, including wild populations, livestock species, companion animals or species under conservation programs, many applications are nowadays relying on HBD segments. First, the proportion of the genome that is HBD is an estimator of the inbreeding coefficient, and allows consequently to study ID. Locus-specific HBD probabilities can also help to identify recessive deleterious variants associated with disease by homozygosity mapping approaches.

Since the length of HBD segments is inversely related to the number of generations to the common ancestor, the distribution of ROH in different length-based classes is informative about the past demographic history from a population and its mating structure. In particular, this information can be used to measure the impact of a bottleneck, whereas the absence of recent ROH (e.g., long) might suggest a recovered effective population size. Similarly, length of ROH can be used to study whether recent HBD contributes more to ID and whether short segments contain fewer deleterious variants as a result of purifying selection.

Based on these knowledge, conservation and breeding programs can be optimized to minimize the impact of deleterious variants and to avoid the mating between individuals that are expected to produce offspring carrying long ROH.