Effects of inbreeding in animals and humans

Genetics is the branch in biology which studies the origin, transmission and expression of genetic information, and the variation it causes amongst species. In this essay I will talk particularly about inbreeding in animals and humans, and the effect of this on their population.

As described by the famous naturalist Charles Darwin, natural selection works by selecting those individuals amongst species with the traits and characteristics that will make them more likely to survive in the environment in which they live, compared to other members of the same species. This gives those individuals a reproductive advantage. Therefore these individuals will pass on their genes to the following generations. This process hence eliminates alleles of traits from the gene pool that cause an individual to be less fit to live compared to the other members of their species population.

Inbreeding occurs when two individuals from the same species mate, which are more closely related than if you had selected them randomly from the whole population. In simple terms it means mating between individuals that are related to one another. Within animals this can mean mating between brothers and sisters, father and daughter or mother and son, although this degree of inbreeding is rarely seen in humans, it can also observed and is usually seen as mating between cousins etc.

Naturally animals do not voluntarily inbreed with their close relatives, and we can see some mechanisms in animal behaviour which prevents this from happening. For instance animals which live in a pack for example prairie dogs usually kick out their young males to prevent them from inbreeding

with their female relatives. Additionally the reluctance of females to copulate with closely related males prevents this further (Hoogland 1982). Nevertheless natural inbreeding can be observed in some mammals. These include the meadow vole and the American pika, where inbreeding has become their normal reproductive path.

However in humans inbreeding is a voluntary action of the individuals itself, which can be influenced by environmental pressures and mental isolation (individual chooses mate from a certain culture, background etc). A prominent example is where the pharaoh frequently married his sisters to carry on the family name and keep the royalty to one family. As I will discuss, this brings an explanation to the large numbers of infant mummies, at the burial places.

Humans frequently and deliberately inbreed animals to fix traits into a breed and for many other reasons this is called ‘ selective inbreeding’ and the purposes of this include; scientific research, food supply, and as pets.

A common example of this is the selective inbreeding of mice, used for scientific research purposes. Repeated inbreeding produces mice that are completely uniform, as their genome becomes homozygous (identical alleles at a given gene loci) at virtually all of their gene loci. This property offers numerous advantages over outbred mice, which are mice that have been bred from parents that are not closely related.

The uniformity of the inbred strains reduces the number of mice needed for experiments, because the experimental variability in the phenotype is limited to variations to epigenetic, extra genetic and/or varying uncontrolled

environmental factors.(Hedrich 2004) The use of inbreeding in this way has indirect beneficial effects to both the animal and human population, as the results obtained from such experiments contribute to our understanding of health, which will further be inflicted onto the population for a better living.

Figure 1 shows the cross between mice. It illustrates the pairing of a gene allele annotated ‘ D’ for the dominant allele, and ‘ d’ for the recessive allele during inbreeding between brothers and sisters. We can see that over time the chromosome locus for the gene becomes homologous. Considering this happens for the rest of the gene loci, a pure inbreed line is produced. Although not shown or mentioned in the diagram, many mice die during the inbreeding process due to the allele rearrangement bringing together defective alleles, which leads to the mice dying. This hence leaves behind healthy inbred mice, which are said to have shed their genetic load (the number of deleterious alleles in a heterozygous condition present in an individuals genome).

Therefore the first evident consequence of inbreeding on a population is the reduction in genetic diversity due to loss of alleles from mortality, and as a result there is increased homozygosity.

Reduction in genetic diversity also referred to as genetic erosion explains the fact that as you inbreed animals and humans the alleles at corresponding chromosomal loci become identical and therefore reducing the diversity within the genome and hence within the population. But how would genetic erosion effect the population? The first reason is that it can result in a loss of potentially valuable and useful alleles from the gene pool, thus reducing the

capability of the population to adapt to varying environmental conditions e. g. climate change, new pathogens etc, which increases their risk of extinction. This is particularly important especially in the animal populations.

Genetic diversity is measured by using a technique that analyses short tandem repeats (STR) also known as microsatellites in the genome. The STR consists of short DNA sequences repeated a variable number of times, the number of repeats of this sequence vary within individuals, and so measuring the length of these variable sequences represents the variation within individuals which therefore reflects the genetic diversity.

We can further work out the association of genetic diversity to a particular ancestor. The inbreeding coefficient is used to estimate probability that two alleles at a locus in an individual are identical by descent from a common ancestor (Klug 2010). For example inbreeding coefficient for second cousins is 1/64 and for third cousins is 1/256. The inbreeding coefficient is inversely related to the frequency of heterozygotes in the population. It can be calculated by the following equation:

In the equation N is the number of loops seen in a pedigree, whilst n is the number of ancestors in each loop. Using the example in figure 2 which shows the inbreeding between first cousins;

N = 2

n = 5

F = 2 (½)^5

Therefore the inbreeding coefficient between first cousins is;

F = 1/16,

Genetic drift is the random variation in allele frequency from generation to generation. Inbreeding has very similar effects to genetic drift in small populations. In both cases heterozygosity decreases and homozygosity increases. In the case of inbreeding in large populations however, allele frequency stays relatively the same as homozygosity increases. Genetic drift causes only small departures from the Hardy-Weinberg; where as those caused by inbreeding can be extreme.

An adverse effect in inbreeding can be observed if the chromosome locus which is becoming homozygous is actually defective or lethal. Within the population the alleles are randomly dispersed so that nearly everyone will carry at least one defective recessive allele for a given trait in their genome, and the expression of this allele is seen more frequently when you mate with someone that has a very similar genome to yours i. e. inbreeding. The severity of the situation depends on the trait being influenced by this inheritance.

This is what leads to inbreeding depression. Inbreeding itself doesn’t cause inbreeding depression; it is only when the increased homozygosity leads to an increase in the proportion of deleterious recessive alleles in a population compared to previous generation, and so leads to the more frequent occurrence of rare recessive alleles in a homozygous condition. This increases the occurrence of aberrant phenotypes which would have normally been masked in the heterozygous state. So there is a concomitant reduction

in the overall fitness in the population. Here fitness will be defined as the relative reproductive success and is estimated with the component of fitness such as viability or fecundity (Hartl and Clark 1989).

The second important consequence of genetic erosion is a reduction in the levels of heterozygosity and the consequences this leads to. As when mating with members of the population with a similar genome, will cause the individuals to become homozygous at many of there chromosome loci.

We can see the increase in homozygosity being represented by graph 1. This additionally demonstrates the closer the kinship within individuals then the more chance there is that their gene loci are going to end up being homozygous. This is because the closer they are related the more similar their genome will be therefore will reach homozygosity quicker than less related individuals.

Many studies have reported associations between individual heterozygosity for protein polymorphisms and viability, one of these studies was the theory of the heterozygote advantage.

Heterozygote advantage describes the situation in which an individual with a heterozygote genotype has a greater relative fitness than either the individuals with homozygote dominant or homozygote recessive genotype. This selection which prefers the heterozygote is one of the mechanisms that maintain polymorphism and helps to explain some kinds of genetic variability.

This theory has been demonstrated on many organisms but was initially experimented with the Drosophila melanogaster which is a classic model organism for research in genetics. It was demonstrated that a mutation was advantageous when in heterozygous state but is disadvantageous when in a homozygous state. This mutant allele was an autosomal gene that expressed an ebony body color. When the fruit fly inherited both copies of the allele, it expressed the dark ebony colour but was very weak which placed it in a reproductive disadvantage. When the organism was heterozygous for the allele it was healthy and had an improved viability.

Heterozygosity is also seen as advantageous in many situations within the human population as well. In particular an example which is well known is which in being heterozygote for the sickle cell anemia trait provides resistance for the infectious disease frequently seen in Africa; malaria. When an individual is affected by sickle cell anemia, their red blood cells lose their distinct round shape and become sickle-shaped when exposed to low-oxygen conditions. This deformation of the cells can cause them to become wedged in capillaries, which deprives other parts of the body of oxygen.

Those individuals who are heterozygote for this trait do not suffer from the adverse phenotypical symptoms but have some sickle shaped red blood cells mixed along side their healthy ones. For this reason they are genetically able to live healthily but also have an environmental advantage against malaria. This is because it is difficult for the malaria pathogen plasmodium to survive in the defective red blood cells due to its shape. As this is the plasmodiums main site of reproduction it can not lead to cause malaria. Therefore evolution plays its role by selecting those individuals with this heterozygous

genotype, who are better fit to survive in the malaria prone environment than others. They hence pass on their genes to the next generation. This process enables the sickle cell allele to remain in dynamic equilibrium within these populations.

By applying our knowledge of inbreeding, we can see how being homozygous at this loci would reduce this population’s fitness for survival especially in those parts of the world where malaria is persistent e. g. sub-Saharan Africa. As inbreeding will increase the chance that this allele will become heterozygous and the individuals will lose their environmental advantage.

Whilst studying the involvement of genes in cancer formation, it was noticed inbreeding also plays a part in the number of cancer cases observed. Island populations have higher number of inbreeding number compared to larger populations. This is due to the lower number of diverse mating partners. Anthropological research which lasted over three decades was carried out on island populations in Middle Dalmatia and Croatia. Using data taken from the Croatia Cancer registry as control data, the results of the experiment showed that there was a clear trend in the occurrence of cancer and inbreeding rate (Rudan I 1999). This therefore proved that genes too account for the reason cancerous cells occur, but more importantly to realise is that inbreeding increases this chance by bringing together these rare alleles of genes that would have normally remained on its own and hence disguised. Therefore inbreeding can be said to play a significant role in the occurrence cancer.

Inbreeding has many advantages in scientific research in controlled laboratory environments, but uncontrolled inbreeding in the population has many adverse effects. It can be therefore concluded that the effects of inbreeding leads to more disadvantageous situation that it does to advantageous considering the evidence seen from reduced fitness due to homozygosity and heterozygous advantage studies. Although this depends largely on the trait being inherited due to similar allele pairings. Nevertheless populations which have shed their genetic load can survive healthily by using inbreeding as their normal reproductive path, but then again it is suggested that where possible inbreeding should be avoided.