Genetic Modification: Natural selection, artificial selection and genetic engineering

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ABSTRACT

Genetic modification goes on in nature through the effects of a variety of natural factors - physical and biological - which modify gene frequencies and genotypic frequencies among individuals of each generation. It also goes on artificially since man started improvement of plants and animals through conscious domestication, selection and crossbreeding in various ways for food and other desired ends. Genetic modification under these circumstances has positive and negative effects. The consumer public has accepted the products without hitches. While conventional genetic modification under sexual reproduction within species, apart from beneficial effects, produces negative effects which have management systems in place, modern genetic modification (transgenesis: inter-specific exchange of genes using engineering techniques) has similar effects at varying degrees depending on species involved, the negative ones needing more careful studies particularly as far as animals are concerned. The real problem today is therefore not genetic modification *per se* but how to manage the unintended consequences of modern genetic modification while benefiting from its positive effects. Adequate risk management arrangements for negative effects should handle public concerns.

Key words: selection, crossbreeding, mutation, fitness, migration, transgenesis, gene frequency

RESUME

La modification génétique est opérée en nature par les effets d'une variété de facteurs - physiques et biologiques - qui modifient des fréquences de gène et des fréquences de génotype parmi des individus de chaque génération. Elle est opérée également artificiellement, puisque l'homme a commencé l'amélioration des plantes et des animaux par la domestication, la sélection et le croisement planifiés par diverses manières pour l'alimentation et d'autres buts désirées. La modification génétique dans ces circonstances a des effets positifs et négatifs. Le public consommateur a accepté les produits sans soucis. Tandis que la modification génétique conventionnelle sous la reproduction sexuelle dans l'espèce, hors des effets bénéfiques, produit les effets négatifs qui ont des systèmes de gestion en place, la modification génétique moderne (transgénèse: l'échange interspécifique des gènes employant des techniques de génie génétique) a les effets semblables aux degrés variables selon des espèces impliquées, les négatives qui nécessitent des études plus soigneuses en particulier en ce qui concerne des animaux. Donc, le problème réel d'aujourd'hui n'est pas la modification génétique *per se* mais comment gérer les conséquences inattendus de la modification génétique moderne tout en tirant les bénéfices de ses effets positifs. Les mesures adéquates de gestion des risques pour des effets négatifs devraient calmés des soucis publics.

Mots clés : sélection, croisement, mutation, survivance, migration, transgénèse, fréquences de gène

Introduction

The appellation "genetically modified organism" or GMO to most people today seems to refer to some exotic monster not only by its looks but also by its direct and indirect effects on man. This results from the way it has been presented to the public. Hence, the objective of this paper is to put genetic modification in context and hopefully improve public understanding of/decision-making on the subject.

To appreciate what a GMO is, given the diversity of our audience, let us start with some basic definitions:

- Chromosome : a coloured threadlike body composed of Deoxyribonucleic Acid (DNA) (genetic material in the nucleus of the cell). Chromosomes contain sequences of genes arranged in pairs (a member of a pair is on either of two strands of the chromosome). There is a constant number of chromosomes per species.

- Meiosis: formation of male or female reproduction cells (eggs or sperms). The chromosome number of the species is halved (but reconstituted when the egg meets the sperm at fertilization).

- Gene : basic hereditary unit (made up of DeoxyriboNucleic Acid -DNA) which determines protein structure or RiboNucleic Acid (RNA). It is located at a point (locus) on a chromosome. Each member of the pair of genes at the locus is called an allele.

- Genotype: genetic identity of an individual (e.g. AA, Aa where "A" and "a" are alleles.)

- Phenotype: outward manifestation of genetic identity, often in interaction with environment.

- Transgene: a gene construct introduced (from another species) into an organism by human intervention, using modern genetic modification techniques.

Normal Situation

- The genetic structure of a population (plant or animal) is determined by the proportions of different genotypes in the population (Falconer, 1989) (e.g. for locus "A", number of AA, Aa, and aa individuals in a population of 100 ?)

- Proportions in the current generation determine proportions in the next generation.

- For the locus A in the entire population, assume: - frequency of A = p
  - frequency of a = q
  - p + q = 1

  and that for the next generation, gametes produced are as follows at meiosis:
  AA => A gametes (1 type)
  Aa => A, a gametes (2 types)
  Aa => a gametes (1 type)

  The result is the matings in Table 1.

Table 1: Matings at a single locus,(A) under Hardy-Weinberg equilibrium conditions

Male/Female	p(A)	q(a)
p(A)	p^2 (AA)	pq (Aa)
q(a)	qp (aA)	q^2 (aa)

The ratio of resulting progeny genotypes is:

$$p^2_{(AA)} : 2pq_{(Aa)} : q^2_{(aa)}.$$

When p and q :
a) remain unchanged, and
b) there is random mating,

the expression:

$$P^2(AA) : 2pq(Aa) : q^2(aa)$$

is known as the Hardy -Weinberg law/equilibrium*. *The equilibrium is maintained from generation to generation as long as there is random mating and no selective forces of any type.*

Disturbed situation: Genetic modification

i) Natural forces that modify genotypes of individuals and population structure:

- A change in a gene leads to :

a) change in gene frequency and
b) change in genotype (zygotic) frequency.

*Hardy was a mathematician and Weinberg a physician

Forces involved include :

1. *Mutation*
   - This is heritable (i.e. in gametes) change from one *allele* to *another*:

$$A \xrightarrow[v]{u} a$$

- If u = v, mutation has no effect
- If u # v, that is mutation is directional and effective

the gene frequencies (p, q) will be modified (increased or decreased).

Hence, genetic structure of the next generation will depend not only on the gene frequencies in the preceding generation but also on the mutation rate.

. Mutant alleles may be :

a) eliminated by elimination of carriers (through some pre-disposing susceptibility to physical or biological factors).

(b) genetic drift: Mutant alleles may be fixed/spread in the population through favourable (physical and biological) forces acting on the carriers. The fixation/spread (modified frequency) is at the elimination of the other allele(s) at the locus. The result is modification of genotype frequency of the next generation.

2. *Survival forces*

Fitness : some alleles may affect the ability to survive to reproductive age and produce viable offspring. A frequency distribution of reproductive success for a population of sexually matured adults, may be such that:

affected genotypes may

i) die early or

ii) be handicapped in one way or another with respect to mating chances.

• The result is that the *"fitter" individuals (genotypes) determine the genotypes and gene frequency for the next generation.* Such a generation has fewer or no "defective" genes. It is therefore genetically different from the preceding one.

3. *Migration*

A population of plants/animals may be composed of "natives" and "immigrants". The "immigrants" may modify the genetic structure of the population by increasing a given gene frequency:

For a given locus,

q_o = gene frequency among natives
q_m = gene frequency among immigrants
q_1 = gene frequency among mixed popula tion (i.e. natives and immigrants)

$q_1 = mq_m + (1 - m)q_o = m(q_m - q_o) + q_o$
where m = proportion of new immigrants/ genereation

Äq due to one generation of immigrants:

$$Äq = q_1 - q_o$$
$$= m\,(q_m - q_o)$$

Thus the rate of change in gene frequency in a population undergoing immigration (introgression) depends on :

(a) immigration rate (m), and

(b) difference in gene frequency between "immigrants" (q_m) and "natives" (q_o).

ii) Artificial forces that modify genotypes of individuals and population structure

Matings are based on particular genotype(s) or traits/characteristics {Assortative mating} :

(i) in human (and some animal) populations: choice of spouses/mating partners.

(ii) in plant and animal breeding :

(a) selection is based on defined criteria to determine individuals for mating to produce individuals with given traits in the next generation, and

(b) crossbreeding to combine variety/breed characteristics or differences in chosen traits for desired results.

Whether in selection or in crossbreeding, it is based on the "breeding value" (i.e. value associated with genes carried by individuals and transmitted to their progeny). The measure of the breeding value is the "average effect" (Falconer, 1989). The average effect may be assigned to

(a) a gene in the population or

(b) the difference between one gene and

another of an allelic pair.

The "*average effect of a gene*" then is the "*mean deviation from the population mean of individuals which received that gene from one parent, the gene from the other parent having come randomly from the population*" (e.g. 20 calves receiving a gene, A, from 1 bull mating 40 cows which donate the other allele, a).

This is easier seen as "average effect of gene substitution" at one locus of 2 alleles, e.g.:

. changing "A" to "a" in a population (Aa ⟶ aa).

. This is equal to the difference between average effects of "A" and "a" genes involved in the substitution.

. The average effect of gene substitution depends on

. the gene and

. population.

. The average effect is high when gene frequency is high and low when gene frequency is low.

Results from Wakwa Agricultural Research Centre (Ebangi et al, 2001; Ebangi et al, 2002) show how selection during a 17 year period modified the genetic structure of 2 cattle populations with long generation intervals (7-8 years) (Tawah et al, 1993) for 12 month weight (Fig. 1 and 2):

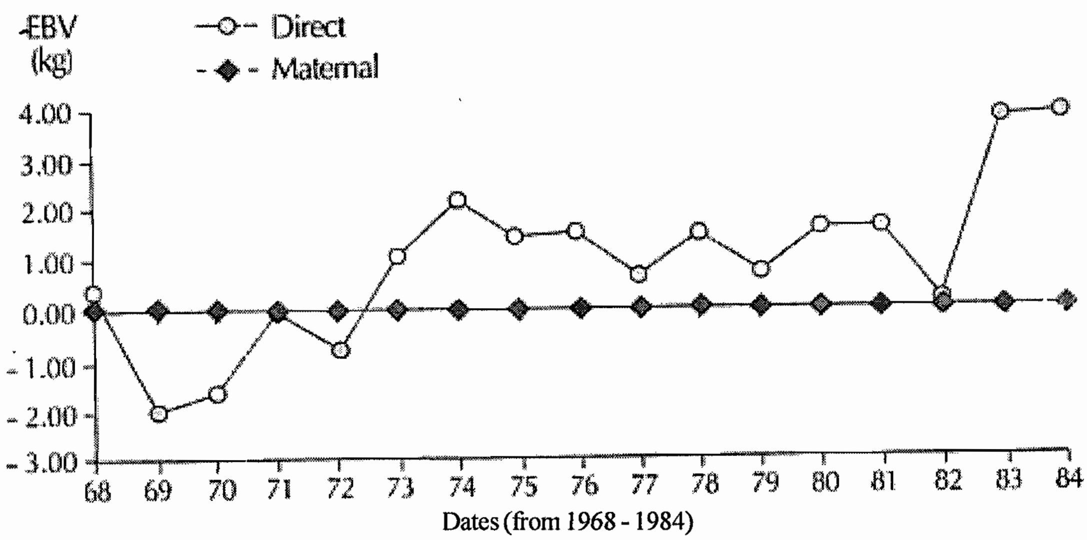

Fig. 1: Direct and maternal genetic trends for yearling weight in Wakwa beef Cattle. EBV = estimated breeding value.

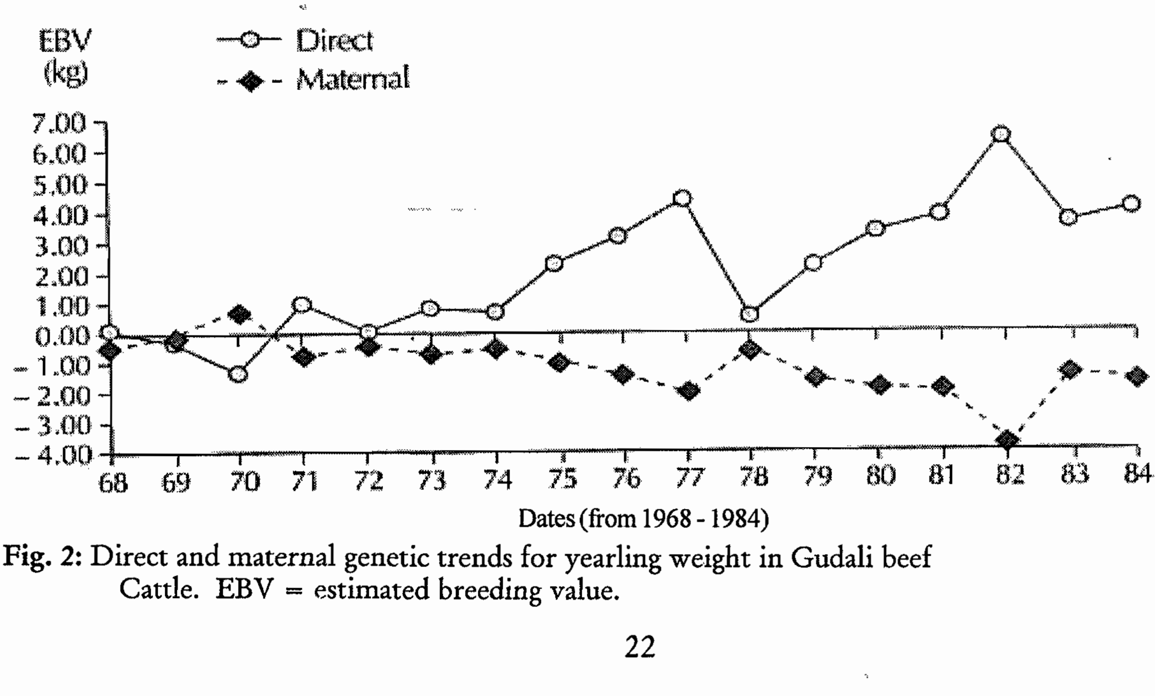

Fig. 2: Direct and maternal genetic trends for yearling weight in Gudali beef Cattle. EBV = estimated breeding value.

Note that:
For Gudali:

Total Direct gain : +5.5 kg EBV
Total Maternal gain: -2.5kg EBV
Total Genetic trend: +3.0 kg EBV
(resulting from negative genetic correlation of -0.81)

For Wakwa :

Total Direct gain : +4.0 kg EBV
Total maternal gain : -0.0kg EBV
Total Genetic gain : +4.0 kg EBV
(resulting from negative genetic correlation of -0.98)

Unintended effects of selection:

- Success in selected trait may lead to undesirable consequences:
  - . negative genetic correlation as in EBV above
  - . increase size = > increased pressure on the environment
  - . increase in fitness (reproductive) = > need for more space = > pressure on the environment and other species, etc.
  - . genetic erosion

Handling unintended eff.:cts

Unintended effects above have been handled by:

- involving more than one trait in selection,
- determining carrying capacities for given pasture lands, etc,
- off-take rate to allow "ecologically sound" stocking rate,
- conservation (*in situ* and/or *ex situ*) of displaced genes (varieties, breeds).

(iii) Transgenesis (Lando, 2004, for methods)
We have considered gene frequency, genotype frequency and average effect of gene action within species through *sexual reproduction*. Let us now consider transgenes (from the point of view of effects on the population) whose action is similar to that of dominant genes.

Transgene (tg) (Braig, H.R. and Yan, G; 2002):

$$q_{tg} = \frac{n_{tg}}{2N}, \text{ e.g. } \frac{100}{(2)(1000)} = \frac{1}{20} = 0.05$$

where:
n = 100 = number of alleles of tg in the population and

N = 1000 =0population size of the diploid population.

If q_{tg} increases, transgenic individuals have advantage over their wild types.
The transgene may :

(a) introduce a *novel* trait in the population where the trait did not exist:
(i.e. $q_{tgo} = 0$)

(b) increase the intensity (where trait exists $q_{tgo} > 0$)

$$\ddot{A}q_{tg} = q_{tg1} - q_{tgo} ;$$

where $q_{tgo} > 0$ in the population.

When the initial q_{tg} is "above the critical threshold density, the transgene can be spread and fixed within 60 – 100 generations" with the assistance of a ***driving mechanism*** (germ-line-based selfish genetic elements inherited" non-Mendelianly) [a driving mechanism introduces genetic characteristic into a given population directly/indirectly by eliminating individuals that do not carry the characteristic such as is the case with the sterile insect technique] (Turelli and Hoffman, 1991; cited by Braig and Yan, 2002).

(iv) Radiation/mechanical sheer/transposable elements (Braig and Yan, 2002)

(a) Chromosomal translocations: segment from one chromosome may be broken and attached to another (usually non-homologous) chromosome in exchange for another segment (i.e. reciprocal exchange of segments). Genes on the segments are consequently relocated resulting in:

(i) genetically altered organism (e.g. insects, etc),
(ii) .homologous translocations that are fertile (if viable),
. heterozygous translocations that are semi-fertile (i.e. semi-sterile).

(b) Polyploidy : replication of the entire set of chromosomes of an organism (plant) through radiation, chemical treatment or crossbreeding (Tomekpe et al, 1999).

The results include triploids, tetraploids among others and hence tripling, quadrupling, etc, of genes at given loci. This degree of genetic alteration leads to new varieties/species.

Conclusion

Genetic modification, change in the genetic make up of individuals and populations of which the individuals are elements, goes on in nature and artificially under the directional control of natural and man-made forces. Natural forces involved include mutation, fitness (survival) and migration. Artificial forces involved include domestication, selection, crossbreeding and radiation and other physical forces. Drastic changes resulting in multiplication of chromosome numbers lead to new varieties/species. All of these artificial forces have been used by man to improve plant and animal production. Genetic engineering(modern genetic modification simply called genetic modification) involves the introduction into one species a gene from another species using artificial methods. This confers on the recipient species ***novel trait(s)*** which before the introduction was/were unknown to the species. Both conventional and genetic engineering methods of genetic modification have positive and negative effects. While risk management methods for conventional genetic modification techniques are in place, risk management methods for genetic engineering techniques of genetic modification still need more input particularly for animals. Risk assessment and risk mangement for GMOs should follow the same regulations, because the end points of genetic modifications by both methods can be similar. Infact when such an approach is adopted, no adverse effects have so far been reported for GMOs obtained by modern biotechnology.

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