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MATHEMATICAL MODEL OF ARTIFICIAL SELECTION IN FAVOUR OF HOMOZYGOT DOMINANT GENE IN INBREEDING

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Abstract

The concept of inbreeding in human beings and its effect have been discussed in this research. Inbred unions are characterized by greater fertility, although they also result in higher levels of post-natal morbidity and mortality due to the expression of detrimental recessive genes inherited from a common ancestor(s). Artificial selection of the parents was used to determine the frequencies of the offspring and a five state Markov Chain model was used to determine the pattern of gene distribution. The paper is meant to reduce homozygote recessive gene which can be a carrier of any particular trait in a given population. The same model can also be applied to reduce homozygote dominant gene. The result from table 8 shows that, when genetic counseling is carried out with the various mating pattern as shown in the first column of table 5, the gene of the homozygote recessive will be eradicated within a given period of time from the population, irrespective of the Initial Probability State Vector (IPSV). This selection model will not only reduce the gene of the homozygote recessive, but also that of the heterozygote as we can see from table 8.

Keywords: Markov Chain, Inbreeding, Natural Selection, Artificial Selection.

Introduction.

Theory of Inbreeding: The word “consanguinity”, carries unsound and confusing connotations. Its etymology from the Latin word con (with) and sand (blood) harks back to the pre-mendelian days when the blood was thought to be the vehicle of genetic transmission from one generation to the next. Such popular expression such as “ he stems from bad blood”, “ blood is thicker than water”, “blood brother”, “blood ties” and my own flesh and blood” demonstrate the inroads of this false theory on our everyday speech. Unfortunately, the common synonym “inbreeding” (as opposed to “out crossing”) also carries odious connotation for man. (Choji & Garba, 2004).

Generally, the fundamental topic in the study of inbreeding is the concept of genetic relatedness. It is common to notice two individuals possess the same gene as one another because of common ancestor for example brother and sister must share even more genes because they have same parents, but they might conceivably share even more gene because their grand parents might also be related to one another. Hence, the theory of genetic relatedness will help solve the problem of how similar genetically, two individuals are to each other on the basis of non-ancestry. It also provides an important tool for answering other questions relating to the role of different mating systems in organizing the genotype variation and the analysis of phenotype resemblance between relatives. and (Clarke, 1981).

Natural Selection: This is the mechanism by which new species are formed from pre-existing species. This hypothesis is based on three observations and two deductions which may be summarized as follows. Observation 1. Individuals within a population produces on average more offspring than are needed to replace themselves (Fred,1976). Observation 2. The numbers of individuals in a population remains approximately constant. Deduction 1. Many individual fails to survive or reproduce. There is a struggle for existence within a population. Observation 3. Variation exists within all population. Deduction 2. In the struggle for existence, those individuals showing variations best adapted to their environment have a reproductive advantage and produce more offspring than less well-adapted organisms. Deduction 2 offers a hypothesis called natural selection which provide a mechanism accounting for evaluation (Choji & Garba, 2004).

Artificial Selection: The basis of artificial selection is the isolation of natural population and the selection breeding of organisms showing characteristics or traits which have some usefulness to humans (James & Clarke, 1981). The importance of genetic diversity in Livestock is directly related to the need for genetic improvement of economic traits as well as facilitates rapid adaptation to potential changes in breeding goals. Several goat breeds have been evaluated for genetic variation based on morphological, physiological, pathological, productive, reproductive and behavioral feature, (Awobajo, 2018). Sun et al., (2017) were able to established that inbreeding mating does decrease the mean fitness of polygenic population in general, but does not decrease the mean fitness with mixed dominant-recessive genotype.

Brother-Sister Mating: Brother-sister mating are the most extreme form of inbreeding that can occur in most animals. Even hermaphroditic forms like many snails and worms cannot self fertilize. Selfing is a process reserved principally for plants. Brother-sister mating is not nearly as common among animals in nature as in selfing among plants. The main use of the theory of brother-sister mating is with experimental breeding programs. (Choji & Edemenana, 2001). It is necessary to estimate the likely effects of inbreeding on the fundamental economic traits and physiological health (Tiaji et al., 2020).

Markov Chain Model

A markov chain Model is one of the vital tools used in stochastic process. The construction of Markov Chain require two basic ingredients, namely a transition matrix and an initial distribution. So by definition of transition matrix we assume a finite set S ,where $S = \{1,...,m\}$ states. Assign to each pair $(i, j) \in S^2$ of states a real number P_{ij} such that the properties.

1. $P_{ij} \geq 0 \forall (i, j) \in S^2$ (1)

2. $\sum_{j \in s} P_{ij} = 1 \forall i \in S$ (2)

are satisfied and define the transition matrix P by

$$P = \begin{bmatrix} P_{11}, P_{12}, ..., P_{im} \\ P_{21}, P_{22}, ..., P_{2m} \\ . \\ . \\ . \\ P_{m1}, P_{m2}, ..., P_{mm} \end{bmatrix} \quad (3)$$

Let $(X_n)_{n \in N_0}$ be a sequence of random variable with values in S . Here, n denotes the time at which the state X_n occurs. So far, we have only specified the ingredients for the evolvement of probabilities throughout the time. To complete the construction of Markov Chain, we need to specify an initial distribution. Hence, we denote $D_s$as the set of discrete distributions on S , such that

$$D_s = \left\{ P = (P_i)_{i \in s} : P_i \geq 0, \sum_{i \in} P_i = 1 \right\} \quad (4)$$

where we represent distributions as row vectors. We call $P_0 = (P_{0i})_{i \in s} :\in D_s$ the initial distribution of the chain $(X_n)_{n \in N_0}$ if $P[X_0 = 1] = P_{0i}$ for all states $i \in S$ .A discrete time Markov process is completely described by its square transition matrix P . P_{ij} means the probability of transition from state i to state j . $P_i(0)$ implies the probability of the system being in state 1, at time $t = 0$. The probability that the system in state 1 at $t = t_1$ is given by

$$P_1(t = t_1) = [P_{11}, P_{12}, ..., P_{n1}] \begin{bmatrix} P_1(0) \\ P_2(0) \\ . \\ . \\ . \\ P_n(0) \end{bmatrix} \quad (5)$$

In general, we can write

$$P(t = t_1) = \begin{bmatrix} P_1(t = t_1) \\ P_2(t = t_1) \\ . \\ . \\ . \\ Pn(t = t_1) \end{bmatrix} = \begin{bmatrix} P_{11}, P_{12}, ..., P_{1n} \\ P_{21}, P_{22}, ..., P_{2n} \\ . \\ . \\ . \\ P_{n1}, P_{n2}, ..., P_{nn} \end{bmatrix}^T \begin{bmatrix} P_1(0) \\ P_2(0) \\ . \\ . \\ . \\ P_n(0) \end{bmatrix} \quad (6)$$

T indicates the transpose of the matrix or vector as the case may be

(Choji & Edemenang, 2001). Probability state vector is a vector composed of state probabilities, which sum up to 1. A state is a situation that a process can assume at any given time and are mutually exclusive and exhaustive. If for instance $P_i(0)=1$ then $P_j(0)=0$ for $i, j=1,2,3,$ and for $i \neq j$

Transition matrix, is a matrix of conditional probabilities of moving from one state to another. Subsequent, probability state vectors can be obtained as follows

$$P(0)=[P_1=(0)]=\begin{bmatrix} P_1(0) \\ P_2(0) \\ . \\ . \\ . \\ P_3(0) \end{bmatrix} \quad (7)$$

$$P(1)=P(0)^T P, P^T(2)=P(1)^T P,...,P^T(n)=P(n-1)^T P$$

Derivation of The Transition Matrix for Brother-Sister Mating

Brother –Sister matings are the most extreme form of inbreeding that can occur in most animals. Even hermaphroditic forms like many snails and worms cannot self-fertilize. Selfing is a process reserved principally for plants. But today we see many nations passing law for different types of marriage without considering the associated danger. This research will therefore review the work of Jonathan Roughgarden on the danger of Brother-Sister mating and also, proffer solution if at all Sib mating must take place.

According to Roughgarden (1997) there are six possible combination in Brother- Sister mating for a trait that is either homozygote dominant or homozygote recessive. These are the six combinations $AA*AA$ $AA*Aa$ $AA*aa$ $Aa*Aa$ $Aa*aa$ $aa*aa$. If we let P_t, Q_t, R_t, S_t, T_t denote the fraction of all mating that are of type $AA*AA$ $AA*Aa\ldots$, respectively, we can develop simple formulas to predict $P_{t+1}, Q_{t+1}\ldots$ *from* $P_t, Q_t, \ldots$ based on the assumption that all mating occurs between brother and sister.

This combination could be seen in the table 1below.

Table 1 Fraction of all mating types

	Kind of	**Offspring**	**Crossing**			
Parental Mating	AA*AA	AA*Aa	AA*aa	Aa*Aa	Aa*aa	aa*aa
AA*AA	1	0	0	0	0	0
AA*Aa	1/4	½	0	¼	0	0
AA*aa	0	0	0	1	0	0
Aa*Aa	1/16	¼	1/8	¼	¼	1/16
Aa*aa	0	0	0	¼	½	¼
aa*aa	0	0	0	0	0	1

From table 1 above, we can write down the equations for the variables $P, Q, R, S \text{ and } T$ by summing down the column as defined in equation 8 bellow.

$$\begin{aligned} P_{t+1} &= P_t + \tfrac{1}{4}Q_t + \tfrac{1}{4}S_t \\ Q_{t+1} &= \tfrac{1}{2}Q_t + \tfrac{1}{2}S_t \\ R_{t+1} &= \tfrac{1}{8}S_t \\ S_{t+1} &= \tfrac{1}{4}Q_t + R_t + \tfrac{1}{4}S_t + \tfrac{1}{4}T_t \\ T_{t+1} &= \tfrac{1}{4}S_t + \tfrac{1}{2}T_t \\ U_{t+1} &= \tfrac{1}{16}S_t + \tfrac{1}{4}T_t + U_t \end{aligned} \tag{8}$$

Equations 8 are the fractions of the different mating combinations at t+1, given the fraction at time t.

We can determine D, H, and R, the genotype frequencies, given the mating type frequencies P, Q, and R,…,Then D, H, and R, are found as follows:

$$D_{t+1} = P_t + \tfrac{1}{2}Q_t + \tfrac{1}{4}S_t \tag{9}$$

The frequency of AA at t+1 equals all the offspring from $AA * AA$ mating plus half the offspring of $AA * Aa$ mating, plus one quarter of the offspring from $Aa * Aa$ mating. Similarly,

$$\begin{aligned} H_{t+1} &= \tfrac{1}{2}Q_t + R_t + \tfrac{1}{2}S_t + \tfrac{1}{2}T_t \\ R_{t+1} &= \tfrac{1}{4}S_t + \tfrac{1}{2}T + U_t \end{aligned} \tag{10}$$

As we iterate the equation 9 and 10, we discovered that there is loss of heterozygosity with corresponding increase in the proportion of homozygotes. This gene movement shows that inbreeding will increase the risk for any trait that either homozygote dominant or recessive in any given population.

In order overcome such risk, we can apply artificial selection which at the long run will wipe away trait from the population and that is major focus of this research.

Artificial Selection in Favour of Homozygote Dominanat Gene

In order to eradicate the trait which is homozygote recessive from the population, the following type of mating among Brother-Sister was adopted

Table 2 Parental Crossing of AA * Aa

	AA * AA	AA*Aa	AA*aa	Aa * Aa	Aa * aa
PC AA * AA	1	0	0	0	0

From the figure above, the offspring of AA * AA mating are AA so these offspring can obviously only form AA * AA among themselves. The second row is

Table 3 Parental Crossing of AA * Aa

	AA * AA	AA * Aa	AA * aa	Aa * Aa	Aa * aa
P C AA * Aa	1/4	1/2	0	1/4	0

This row is simple. The offspring of an AA * Aa parental cross are half AA and half Aa. Therefore, when these offspring mate among themselves (remember they must mate among themselves because there is brother-sister mating), they will form AA * AA, AA * Aa and AA * Aa combinations in the ratio of $\frac{1}{4}, \frac{1}{2}, and\ \frac{1}{4}$. The most complicated row is for crosses among the offspring of Aa *Aa parents. The offspring themselves are $\frac{1}{4}AA, \frac{1}{2}Aa, and\ \frac{1}{4}aa.$ Thus they will form with one another all possible combinations in the following ratios:

Table 4 Parental Crossing of Aa * Aa

	AA *AA	AA *Aa	AA *aa	Aa *Aa	Aa *aa
P C Aa *Aa	1/16	1/4	1/8	1/4	1/4

Other parental crossing and their corresponding offspring were derived in the same way. And the various frequencies of the offspring can be represented in a matrix as shown below.

Table 5 fraction of all mating types

	Kind of	**Offspring**	**Crossing**		
Parental Mating	AA *AA	AA *Aa	AA *aa	Aa *Aa	Aa *aa
AA *AA	1	0	0	0	0
AA *Aa	1/4	½	0	¼	0
AA *aa	0	0	0	1	0
Aa *Aa	1/16	¼	1/8	¼	¼
Aa *aa	0	0	0	¼	1/2

Since we are making selection against any trait that is homozygote recessive, we therefore exclude the parental crossing of affected male mating with affected female that is aa *aa and also, the offspring crossing of affected male and female that emanated from the parental crossing of affected male and a female who is a carrier. Hence the last row and the last column in table 1 was deliberately omitted, thereby giving us a 5 by 5 matrix.

To develop these formulas P_{t+1}, we need to summarize some information in the form of a table, in which the mating types that can occur among the offspring from a given parental combination are described. These are shown in tables below:

Table: 6 Table to determine the formula for P_{t+1}, Q_{t+1} , …

		AA *AA	AA *Aa	AA *aa	Aa *Aa	Aa *aa
		P_t	Q_t	R_t	S_t	T_t
AA *AA	P_t	1	0	0	0	0
AA *Aa	Q_t	¼	½	0	¼	0
AA *aa	R_t	0	0	0	1	0

Aa *Aa	St	1/16	1/4	1/8	1/4	¼
Aa *aa	T_t	0	0	0	1/4	½

From table 6 above, we can write down the equations for the variables $P, Q, R, S \text{ and } T$ by summing down the column as defined in equation 11 bellow.

$$\begin{aligned} P_{t+1} &= P_t + \tfrac{1}{4}Q_t + \tfrac{1}{16}S_t \\ Q_{t+1} &= \tfrac{1}{2}Q_t + \tfrac{1}{4}S_t \\ R_{t+1} &= \tfrac{1}{8}S_t \\ S_{t+1} &= \tfrac{1}{4}Q_t + R_t + \tfrac{1}{4}S_t + \tfrac{1}{4}T_t \\ T_{t+1} &= \tfrac{1}{4}S_t + \tfrac{1}{2}T_t \end{aligned} \qquad (11)$$

Equations 11 are the fractions of the different mating combinations at t+1, given the fraction at time t.

We can determine D, H, and R, the genotype frequencies, given the mating type frequencies P, Q, and R,…,Then D, H, and R, are found as follows:

$$D_{t+1} = P_t + \tfrac{1}{2}Q_t + \tfrac{1}{4}S_t \qquad (12)$$

That is, D_{t+1} the frequency of AA at t+1 which is equal all the offspring from $AA * AA$ mating plus half the offspring from $AA * Aa$ mating, plus one quarter of the offspring from $Aa * Aa$ mating. Similarly,

$$\begin{aligned} H_{t+1} &= \tfrac{1}{2}Q_t + R_t + \tfrac{1}{2}S_t + \tfrac{1}{2}T_t \\ R_{t+1} &= \tfrac{1}{4}S_t + \tfrac{1}{2}T_t \end{aligned} \qquad (13)$$

Table 7 Iterated fractions of the different mating combinations

	0	1	2	3	4	5
$P_{t+1} = P_t + \tfrac{1}{4}Q_t + \tfrac{1}{16}S_t$	1.31250	1.60938	1.87009	2.08396	2.25852	2.39982
$Q_{t+1} = \tfrac{1}{2}Q_t + \tfrac{1}{4}S_t$	0.75	0.8125	0.64063	0.53516	0.43066	0.34985
$R_{t+1} = \tfrac{1}{8}S_t$	0.125	0.21875	0.11719	0.10742	0.08154	0.06726
$S_{t+1} = \tfrac{1}{4}Q_t + R_t + \tfrac{1}{4}S_t + \tfrac{1}{4}T_t$	1.75	0.9375	0.85938	0.65234	0.53809	0.43139
$T_{t+1} = \tfrac{1}{4}S_t + \tfrac{1}{2}T_t$	0.75	0.8125	0.64063	0.53515	0.43066	0.34985

At time=0	At time=1	At time=2	At time=3	At time=4	At time=5
P_1=1.31250	P_2=1.60938	P_3=1.87009	P_4=2.08396	P_5=2.25852	P_6=2.39982
Q_1=0.75	Q_2=0.8125	Q_3=0.64063	Q_4=0.53516	Q_5=0.43066	Q_6=0.34985
R_1=0.125	R_2=0.21875	R_3=0.11719	R_4=0.10742	R_5=0.08154	R_6=0.06726
S_1=1.75	S_2=0.9375	S_3=0.85938	S_4=0.65234	S_5=0.53809	S_6=0.43139

T_1=0.75	T_2=0.8125	T_3=0.64063	T_4=0.53515	T_5=0.43066	T_6=0.34985

From equation 8, we can generate the frequency for the homozygote dominant gene, heterozygote and homozygote recessive gene.

Table 8 The frequency of the homozygote dominant, heterozygote and homozygote recessive gene

TIME	D	H	R
0	1.75000	2.50000	0.75000
1	2.12500	1.75000	0.81250
2	2.25000	1.50000	0.64063
3	2.40525	1.18750	0.53516
4	2.51463	0.96875	0.43066
5	2.60838	0.78125	0.34985
6	2.68259	0.63281	0.28278

Discussion

From table 7 above, it was observe that while the genotype frequency of the offspring of the homozygote gene is increasing, that of the heterozygote and homozygote recessive gene continue to decrease from generation to generation. As the process continues, the carrier and affected gene which in this case is the homozygote recessive gene will reduce until it is totally wiped out from the entire population and we will be left with the normal gene. Understanding different diseases and their mode of transmission from generation to generation will help in genetic counseling. Ignorant of genetic make up of the individual has made many people to marry the wrong partner and today they are suffering the consequences of their decision. A situation they would have been able to avoid at the initial stage. When the above selection is adopted for a trait that is either homozygote dominant or recessive, in a society where inbreeding is being practiced, within some period of time, the gene producing the trait will totally be eradicated from such society. So, counselors are to advice intending couples the danger of inbreeding and the right genetic combination that is safer, if at all they must marry.

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