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GENETICS OF X-LINKED DISEASES AND HOW TO GET THE BEST POPULATION

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Abstract:
We want to discuss the genetics of X-linked diseases for the population existing in reality, remembering that the states of abnormal sex-chromosomes are not considered in S.Roy1.From these equations of heredity conditions of getting best population are discussed. Considering genetic drift,mutation etc. mathematical genetics of main sex-linked diseases when all the main Y-linked diseases and all the main X-linked are considered and in this connection mathematical genetics of all characters are discussed in S. Roy2. From these equations of heredity also conditions of getting best population can be obtained.

INTRODUCTION AND SOLUTION OF THE PROBLEM:

If one gene in X-chromosome is defective, we can classify a population into five possible states: XY, XY, XX, XX, XX where $\overline{X}$ denotes X-chromosome containing defective gene. Let the frequency ratios of these states be $p_1(0)$, $p_2(0)$, $p_3'(0)$, $p_3''(0)$ and $p_4(0)$ respectively.

Assuming that in the time of selection one normal male will not select an abnormal female or normal female carrying the X-linked disease if the normal male gets a normal female. Similarly a normal female will not select an abnormal male if she gets a normal male in the time of selection. Then the frequency of the above five states depends upon the following five cases:

1). $P_1(0) < P_3'(0) + P_3''(0)$, $P_1(0) = P_3'(0)$

2). $P_1(0) < P_3'(0) + P_3''(0)$, $P_1(0) > P_3'(0)$

3). $P_1(0) < P_3'(0) + P_3''(0)$, $P_1(0) < P_3'(0)$

4). $P_1(0) = P_3'(0) + P_3''(0)$

5). $P_1(0) > P_3'(0) + P_3''(0)$

We shall consider only the first two cases. The other cases will convert to case 1 often 1 or 2 generations.

Case I: When $p1(0) < p3'(0) + p3''(0)$, $p1(0) = p3'(0)$

We have seen from S.Roy1 that

$$\therefore \quad p1(2n) = p1(0) + \frac{1}{3}\left(1 - \frac{1}{2^{2n}}\right)p3''(0)$$

$$p2(2n) = p4(0) + p3''(0)\,\frac{2}{3}\left(1 + \frac{1}{2^{2n+1}}\right) \text{ Here } p1(0) = p3'(0)$$

$$p3'(2n) = p1(0) + \frac{1}{3}\left(1 - \frac{1}{2^{2n}}\right)p3''(0)$$

$$p3''(2n) = \frac{1}{2^{2n}}\,p3''(0)$$

$$p4(2n) = p4(0) + p3''(0)\,\frac{2}{3}\left(1 - \frac{1}{2^{2n}}\right)$$

Similarly proceeding, we can show that for the odd generations

$$p1(2n+1) = p1(0) + p3''(0)\,\frac{1}{3}\left(1 + \frac{1}{2^{2n+1}}\right)$$

$$p2(2n+1) = p4(0) + p3''(0)\,\frac{2}{3}\left(1 - \frac{1}{2^{2n+2}}\right) \text{ Here } p1(0) = p3'(0)$$

$$p3'(2n + 1) = p1(0) + p3''(0)\ \frac{1}{3}\left(1-\frac{1}{2^{2n}}\right)$$

$$p3''(2n + 1) = \frac{1}{2^{2n+1}}\ p3''(0)$$

$$p4(2n + 1) = p4(0) + p3''(0)\ \frac{2}{3}\left(1-\frac{1}{2^{2n+2}}\right)$$

Remark of case 1:

From the above data, we can say that p1(2n) continuously increases to p1(0) + $\frac{1}{3}$ p3′′(0) and p1(2n + 1) continuously decreases to p1(0) + $\frac{1}{3}$ p3′′(0).

maximum value of p1(2n) is p1(0) + $\frac{1}{3}$ p3′′(0)

and minimum value of p1(2n) is p1(0),

minimum value of p1(2n + 1) is p1(0) + $\frac{1}{3}$ p3′′(0)

and maximum value of p1(2n + 1) is p1(0) + $\frac{1}{2}$ p3′′(0).

p1(2n) gets it's minimum value at the starting point and gets it's maximum value when *n* tends to infinity. p1(2n + 1) gets it's minimum value when *n* tends to infinity and p1(2n + 1) gets it's maximum value at the generation. Also we can say that frequency ratio of the first state in any odd generation is always greater than that of the 1st state in any even generation. When *n* tends to infinity, then both p1(2n) and p1(2n + 1) reach to stable equilibrium. p2(2n) continuously decreases and p2(2n + 1) continuously increases. p2(2n) gets maximum value p4(0) + $\frac{4}{3}$ p3′′(0) when $n = 0$ i.e. at the starting point and gets its minimum value p4(0) + $\frac{2}{3}$ p_3′′(0), when *n* tends to infinity. When *n* tends to infinity it reaches a stable equilibrium. p2(2n + 1) gets its minimum value p4(0) + $\frac{p3''(0)}{2}$, when $n = 0$ i.e. at the first generation and gets its maximum value p4(0) + $\frac{2}{3}$ p3′′(0), when *n* tends to infinity. When tends to infinity, it reaches a stable equilibrium. Also, we can say that the frequency ratio of the 2nd state in any odd generation is always less than that of the 2nd state in any even generation.

p3′(2n) and p3′(2n + 1) continuously increases from p1(0) i.e. p3′(0) to p3′(0) + $\frac{1}{3}$ p3′′(0). The frequency ratio of this state in any even generation is greater than that in the previous odd generation and equal to that in the next odd generation. When *n* tends to infinity, p3′(2n) and p3′(2n + 1) reaches a stable equilibrium.

p3′′(*n*) continuously decreases from p3′′(0) to 0.

p4(2n) and p4(2n + 1) continuously increases from p4(0) to p4(0) + $\frac{2}{3}$ p3′′(0).

The frequency ratio of this state in any even generation is equal to that in the previous odd generation and is less than that in the next odd generation. When *n* tends to infinity, p4(2n) and p4(2n + 1) reaches a stable equilibrium.

when p1(0) < p3′(0) + p3′′(0), p1(0) > p3′(0)

In this case, We have seen from S.Roy1 that

$$\text{p1(n)}= \left\{\frac{(-1)^{n+2}}{3}\frac{1}{2^{n-2}} + \frac{(-1)^{n+1}}{3}\frac{1}{2^{-1}} + \frac{1}{3}\right\}p1(0) + \left\{\frac{(-1)^{n+1}}{3}\frac{1}{2^{n-1}} + \frac{(-1)^{n+2}}{3}\frac{1}{2^{n-1}}\right\}p2(0) +$$

$$\left\{\frac{(-1)^{n+1}}{3}\frac{1}{2^{n-2}} - \frac{(-1)^{n-1}}{3}\frac{1}{2^{n-1}} + \frac{2}{3}\right\}p3'(0) + \left\{\frac{(-1)^{n-1}}{6}\frac{1}{2^{n-1}} + \frac{1}{3}\right\}p3''(0) +$$

$$\left\{\frac{(-1)^{n+2}}{3}\frac{1}{2^{n-1}} + \frac{(-1)^{n+1}}{3}\frac{1}{2^{n-1}}\right\}p4(0)$$

p2(n) =

$$\left\{\frac{(-1)^{n+2}}{3}\frac{1}{2^{n-2}} + \frac{(-1)^{+1}}{3}\frac{1}{2^{n-2}}\right\}p1(0) + \left\{\frac{(-1)^{n+1}}{3}\frac{1}{2^{n-1}} + \frac{(-1)^{n+2}}{3}\frac{1}{2^{n-2}} + \frac{1}{3}\right\}p2(0)$$

$$+\left\{\frac{(-1)^{n+1}}{3}\frac{1}{2^{n-2}} + \frac{(-1)^{n+2}}{3}\frac{1}{2^{n-2}}\right\}p3'(0)$$

$$+\left\{\frac{(-1)^{n+1}}{6}\frac{1}{2^{n-1}} + \frac{1}{3}\right\}p3''(0) + \left\{\frac{(-1)^{+2}}{3}\frac{1}{2^{n-1}} + \frac{(-1)^{n+1}}{3}\frac{1}{2^{n-2}} + \frac{2}{3}\right\}p4(0)$$

p3′(n) =

$$\left\{\frac{(-1)^{n+1}}{3}\frac{1}{2^{n-2}} + \frac{(-1)^{n}}{3}\frac{1}{2^{n}} + \frac{1}{3}\right\}p1(0) +$$

$$\left\{\frac{(-1)^{n}}{3}\frac{1}{2^{n}} + \frac{(-1)^{n+1}}{3}\frac{1}{2^{n}}\right\}p2(0) + \left\{\frac{(-1)^{n}}{3}\frac{1}{2^{n-1}} + \frac{(-1)^{+1}}{3}\frac{1}{2^{n}} + \frac{2}{3}\right\}$$

$$p3'(0) + \left\{\frac{(-1)^{n}}{6}\frac{1}{2^{n}}\frac{1}{2^{+1}} + \frac{1}{3}\right\}p3''(0) + \left\{\frac{(-1)^{n+1}}{3}\frac{1}{2^{n}} + \frac{(-1)^{n}}{3}\frac{1}{2^{n}}\right\}p4(0)$$

$p3''(n) = \frac{1}{2^n} p3''(0)$

$p4(n) =$

$$\left\{\frac{(-1)^{n+1}}{3}\frac{1}{2^{n-1}}+\frac{(-1)^{n}}{3}\frac{1}{2^{n-1}}\right\}p1(0)+\left\{\frac{(-1)^{n}}{3}\frac{1}{2^{n}}+\frac{(-1)^{n+1}}{3}\frac{1}{2^{n-1}}+\frac{1}{3}\right\}p2(0)+$$
$$\left\{\frac{(-1)^{n}}{3}\frac{1}{2^{n-1}}+\frac{(-1)^{n+1}}{3}\frac{1}{2^{n-1}}\right\}p3'(0)+\left\{\frac{(-1)^{n}}{6}\frac{1}{2^{n}}\frac{1}{2^{n+1}}\frac{1}{3}\right\}p3''(0)$$
$$\left\{\frac{(-1)^{n+1}}{3}\frac{1}{2^{n}}+\frac{(-1)^{n}}{3}\frac{1}{2^{n-1}}\frac{2}{3}\right\}p4(0)$$

Remarks :-

When $p1(0) < p3'(0) + p3''(0)$, $p1(0) > p3''(0)$, $p1(n)$ tends to $\frac{1}{3}p1(0) + \frac{2}{3}p3'(0) + \frac{1}{3}p3''(0)$.

$p2(n) \to \frac{1}{3}p2(0) + \frac{1}{3}p3''(0) + \frac{2}{3}p4(0)$

$p3'(n) \to \frac{1}{3}p1(0) + \frac{2}{3}p3'(0) + \frac{1}{3}p3''(0)$ as n tends to infinity

$p3''(n) \to 0$

$p4(n) \to \frac{1}{3}p2(0) + \frac{1}{3}p3''(0) + \frac{2}{3}p4(0)$

$\therefore$ for all cases $p1(n)$, $p2(n)$, $p3'(n)$, $p3''(n)$, $p4(n)$ reach a stable equilibrium, when n tends to infinity.

If $\{ -\frac{1}{2}p1(0) + \frac{1}{2}p3'(0) + \frac{1}{4}p3''(0) \} > 0$,

then $p1(2n + 1)$ i.e. odd generations strictly monotone decrease from

$p3'(0) + \frac{1}{2}p3''(0)$ to $\frac{1}{3}p1(0) + \frac{2}{3}p3'(0) + \frac{1}{3}p3''(0)$

and $p1(2n + 2)$ i.e., even generations strictly monotone increase from

$\frac{1}{2}p1(0) + \frac{1}{2}p3'(0) - \frac{5}{12}p3''(0)$ to $\frac{1}{3}p1(0) + \frac{2}{3}p3'(0) + \frac{1}{3}p3''(0)$.

Also, the frequency ratio of this state in any even generation is less than that in any odd generation.

If $\{ -\frac{1}{2}p1(0) + \frac{1}{2}p3'(0) + \frac{1}{4}p3''(0) \} < 0$

then $p1(2n + 1)$ i.e., odd generations, strictly monotone, increase from

$p3'(0) + \frac{1}{2} p3''(0)$ to $\frac{1}{3} p1(0) + \frac{2}{3} p3'(0) + \frac{1}{3} p3''(0)$

and p1(2n + 2) i.e., even generation strictly monotone decrease from

$$\frac{1}{2} p1(0) + \frac{1}{2} p3'(0) + \frac{1}{4} p3''(0) \text{ to } \frac{1}{3} p1(0) + \frac{2}{3} p3'(0) + \frac{1}{3} p3''(0)$$

Also the frequency ratio of the first state in any odd generation is less than that in any even generation.

If $\{ -\frac{1}{2} p2(0) + \frac{1}{4} p3''(0) + \frac{1}{2} p4(0) \} > 0$ then p2(2n + 1) i.e., odd generation strictly monotone decrease from

$$\frac{1}{3} p3''(0) + p4(0) \text{ to } \frac{1}{3} p2(0) + \frac{1}{3} p3''(0) + \frac{2}{3} p4(0)$$

Maximum value of p2(2n + 1) is $\frac{1}{2} p3''(0) + p4(0)$ and minimum value is $\frac{1}{3} p2(0) + \frac{1}{3} p3''(0) + \frac{2}{3} p4(0)$.

p2(2n + 2) i.e., even generation strictly monotone increase from $\frac{1}{2} p2(0) + \frac{1}{4} p3''(0) + \frac{1}{2} p4(0)$ to $\frac{1}{3} p2(0) + \frac{1}{3} p3''(0) + \frac{2}{3} p4(0)$.

Maximum value of p2(2n + 2) is $\frac{1}{3} p2(0) + \frac{1}{3} p3''(0) + \frac{2}{3} p4(0)$.

and minimum value is $\frac{1}{2} p2(0) + \frac{1}{4} p3''(0) + \frac{1}{2} p4(0)$.

Also the frequency ratio of second state in any even generation is less than that in any odd generation.

If $\{ -\frac{1}{2} p2(0) + \frac{1}{4} p3''(0) + \frac{1}{2} p4(0) \} < 0$, than the reverse process of the above takes place.

If $\{ -\frac{1}{2} p1(0) + \frac{1}{2} p3'(0) + \frac{1}{4} p3''(0) \} > 0$

then p3'(2n + 1) i.e. odd generations strictly increase from $\frac{1}{2} p1(0) + \frac{1}{2} p3'(0)$ to $\frac{1}{3} p1(0) + \frac{2}{3} p3'(0) + \frac{1}{3} p3''(0)$

Maximum value is $\frac{1}{3} p1(0) + \frac{2}{3} p3'(0) + \frac{1}{3} p3''(0)$.

and minimum value is $\frac{1}{2} p1(0) + \frac{1}{2} p3'(0)$.

If $\{ -\frac{1}{2} p1(0) + \frac{1}{2} p3'(0) + \frac{1}{4} p3''(0) \} < 0$.

then p3'(2n + 2) strictly increase from

$\frac{1}{4}$ p1(0) + $\frac{3}{4}$ p3′(0) + $\frac{1}{4}$ p3′′(0) to $\frac{1}{3}$ p1(0) + $\frac{2}{3}$ p3′(0) + $\frac{1}{3}$ p3′′(0).

Maximum value is $\frac{1}{3}$ p1(0) + $\frac{2}{3}$ p3′(0) + $\frac{1}{3}$ p3′′(0).

and minimum value is $\frac{1}{4}$ p1(0) + $\frac{3}{4}$ p3′(0) + $\frac{1}{4}$ p3′′(0).

P3′′(n) strictly decreases from p3′′(0) to 0

Maximum value of p3′′(n) is p3′′(0).

and minimum value is 0.

If { - $\frac{1}{2}$ p2(0) + $\frac{1}{4}$ p3′′(0) + $\frac{1}{2}$ p4(0) } > 0

then p4(2n + 1) strictly increases from $\frac{1}{2}$ p2(0) + $\frac{1}{2}$ p4(0) to $\frac{1}{3}$ p2(0) + $\frac{1}{3}$ p3′′(0) + $\frac{2}{3}$ p4(0)

Maximum value is $\frac{1}{3}$ p2(0) + $\frac{1}{3}$ p3′′(0) + $\frac{2}{3}$ p4(0)

and minimum value is $\frac{1}{2}$ p2(0) + $\frac{1}{2}$ p4(0).

If { - $\frac{1}{2}$ p2(0) + $\frac{1}{4}$ p3′′(0) + $\frac{1}{2}$ p4(0) } <0

Then p(2n + 2) strictly increases from

$\frac{1}{4}$ p2(0) + $\frac{1}{4}$ p3′′(0) to $\frac{1}{3}$ p2(0) + $\frac{1}{3}$ p3′′(0) + $\frac{2}{3}$ p4(0)

Maximum value is $\frac{1}{3}$ p2(0) + $\frac{1}{3}$ p3′′(0) + $\frac{2}{3}$ p4(0)

and minimum value is $\frac{1}{4}$ p2(0) + $\frac{1}{4}$ p3′′(0) + $\frac{3}{4}$ p4(0)

Therefore from previous discussions we can say that after a few generations we will face two types of populations, either p1(n) < p3′(n) + p3′′(n), p1(n) > p3′(n) ; or the population of the chain where the cases p1(n) = p3′(n) + p3′′(n) and p1(n) < p3′(n) + p3′′(n), p1(n) = p3′(n) arise one after another.Adjusting the frequency of the above five states we can remove bad characters from a population or we can minimise the bad characters. In this way we can make a population best. Similarly adjusting the frequency ratios of the above five states frequency of good states can be maximized.

Reference: 1.Roy,S. – "Mathematical Genetics of some sex-linked diseases" – Ind. journal of **Genetics** and Plant Breeding (1976) vol. 36(3), P-384-395.

2.Roy,S. - Some Contribution to Mathematical Bio-Science-Page 1-76,Usha Publishing House,College Street,West Bengal,India.