Journal of the Nigerian Association of Mathematical Physics
Volume **12 (May, 2008), 431 - 434**

Mathematical model of human genetics with overlapping generations.

Simeon Chioma Inyama,
Department of Mathematics and Computer Science
Federal University of Technology, Owerri, Imo State, Nigeria

Abstract:

In this paper are present a mathematical model of human genetics with overlapping generations. The model which is a system of ordinary differential equations is analyzed using techniques from dynamical systems theory. It is shown that the system is always unstable. It is also shown that if x(t), y(t) = z(t) are the genotype frequencies, then x(t), y(t), and z(t) respectively tend to constants as t increases.

***Keywords*:** mathematical model, Human genetics, Overlapping generations, steady, state, dynamical system theory.

1.0 Introduction

Some human cells have single chromosomes (sperm or eggs), but most have chromosomes occurring in matched sets. When a single chromosome occurs, the cell is called a *haploid* cell. It is a *diploid* cell if the chromosomes occur in matched homologous pairs. Human beings are diploid organisms having 23 chromosome pairs, and many plants are polyploids.

Attention is directed first at one gene locus having two alleles. These are denoted by *A* and *a*. If the organism is haploid, then it can be either of type *A* or type *a* at that locus. Therefore, a population of these organisms is partitioned by this locus into those of type *A* and those of type *a*. If the organism is diploid, then the possible types at the locus are *AA*, *Aa*, and *aa*. Note that *Aa* and *aA* and *aA* are indistinguishable in the organism, and so are lumped together in the single notation *Aa*. These genetic types in a population are called the *genotypes.*

Cell reproduction occurs either through asexual reproduction (mitosis) or sexual reproduction (meiosis). In sexual reproduction, diploid parents each form haploid cells called *gametes.* These are the sperm (male) and the ova (female). The gametes combine to form a fertile cell called the *zygote*. The zygote is a diploid cell that goes on to reproduce by mitosis. The gametes can be thought of as having chromosomes being one strand each from each parent, although the actual situation is more complicated. For example, if the parents have genotypes AA and aa, respectively, then the gametes are A and a, respectively, so the offspring must have genotype Aa.

Cells having genotypes *AA* and *aa* are called *homozygotes* and the *Aa*'s are *heterozygotes*. So mating of homozygotes results in homozygous or heterozygous progeny, depending on whether or not the homozygotes are identical. The type of matings and resulting frequencies of progeny genotypes were observed in 1850 by G. Mendel [14].

Many models and methods have been devised for studying human genetics. Many of these models used discrete models. Some of such early models include those of Ewens [5], Crow and Kimura [4], Moran [15], Cavalli-Sforza and Bodmer [2], Ludwig [12] and Feller [8].

Fisher and Wright [9, 16] presented a discrete time model. They assumed the population to mate at random and be synchronized with non-overlapping generations. They further assumed the population size to remain constant (= μ) through the generations. The model was then analyzed.

e-mail: scinyama2003@yahoo.com

Galton, Watson and Fisher [10] used the approach of branching process and focused on the fate of a small number of A genes. They determined the probability distribution of offspring and its generating function which they assumed did not depend on the parents' history. They also calculated the extinction probabilities. Fisher, Wright and Haldane [10] used the method of averaging to formulate their own model. They modeled the gene pool from generation to generation by the sequence $\{g_n\}$. They assumed that the fitnesses are almost constant but periodic and finally showed that the mean values of the fitnesses determined the gene pool's evolution. Calabrese, P[1] developed a new model to estimulate the evolution of so-called recombination hotspots in the genome. The mathematical model and its associated software has brought much-needed rigor to evolutionary investigation of how natural selection acts on individual genes. The model is also believed to aid the search for disease-associated genes within the human genoms.

Kendal, J.R. and Laland, K.N. [11] presented a mathematical model for Memetics. The goal of this article was to point out the similarities between memetics and cultural evolution and gene-culture co-evolutionary theory and to illustrate the potential utility of the models to memetics. They illustrated how the theory can be applied by developing a simple illustrative model to test a hypothesis from the memetics literature. For other mathematical models on human genetics see [3, 6, 7, 13].

2.0 The model formulation

One way to handle overlapping generations in the mathematical mode of human genetics is to use continous functions to describe the genotype frequencies. Before we go into the model we first define the symbols and parameters that will be used here.

2.1 Symbols and parameters

$D(t)$ = number of AA genotypes at time t
$2H(t)$ = number of Aa genotypes at time t
$R(t)$ = number of aa genotypes at time t
$P(t)$ = total population size at time t
b = common birth rate of $D(t)$, $H(t)$ and $R(t)$
d_1 = death rate of genotype AA
d_2 = death rate of genotype Aa
d_3 = death rate of genotype aa

2.2 Assumptions

(i) $D(t)$, $H(t)$, $R(t)$ are smooth functions of t.
(ii) The subpopulations $D(t)$, $H(t)$, $R(t)$ reproduce according to Malthus rule, with common birth rates b.
(iii) The different types of genotypes have different death rates.

2.3 The model

With the above symbols/parameters and assumptions, we now formulate the model as a system of ordinary differential equations.

Let
$$p = (H+R)/P \tag{2.1}$$

And
$$q = (H+R)/P \tag{2.2}$$

where p is the proportion of the gene pool which are of type A and q is the proportion of the gene pool which are of type a. An AA fertilized by an A gene produces an AA offspring and so on. Therefore,

$$\frac{dD}{dt} = bDP + 2Hb(P/2) - d_1 D = bPp^2 - d_1 D$$

$$\frac{d2H}{dt} = 2bPpq - d_2 2H$$

$$\frac{dR}{dt} = bPq^2 - d_3R$$
$$\frac{dP}{dt} = bP - (d_1D + 2d_2H + d_3R)$$

Hence the model is

$$\left.\begin{aligned} \frac{dD}{dt} &= bPp^2 - d_1D \\ \frac{dH'}{dt} &= bPpq - d_2H' \\ \frac{dR}{dt} &= bPq^2 - d_3R \\ \frac{dP}{dt} &= bP - (d_1D + d_2H' + d_3R) \end{aligned}\right\} \qquad (2.3)$$

where $H' = 2H$

3.0 Steady state analysis

The steady state occurs at the point where $\frac{dD}{dt} = \frac{dH'}{dt} = \frac{dR}{dt} = \frac{dP}{dt} = 0$. Solving this gives the steady state as $(D_0, \mathrm{H}_0', \mathrm{R}_0, \mathrm{P}_0) = (\psi_1 p^2, \psi_2 pq, \psi_3 bq^2)P_0$, where $D_0, \mathrm{H}_0', \mathrm{R}_0, \mathrm{P}_0$ are the steady state values of *D, H′, R, P* and $\psi_i = b/d_i$, $\mathrm{i} = 1,2,3$. From these values we obtain $p^2 + pq + bq^2 = 1/b$ at steady state. Linearizing (2.3) we obtain the Jacobian as

$$J = \begin{pmatrix} -d_1 & 0 & 0 & bp^2 \\ 0 & -d_2 & 0 & bpq_2 \\ 0 & 0 & -d_3 & bq^2 \\ -d_1 & -d_2 & -d_3 & b \end{pmatrix}$$

Hence $$|J - \lambda \mathrm{I}| = \begin{vmatrix} -d_1 - \lambda & 0 & 0 & bp^2 \\ 0 & -d_2 - \lambda & 0 & bpq \\ -0 & 0 & -d_3 - \lambda & bq^2 \\ -d_1 & -d_2 & -d_3 & b - \lambda \end{vmatrix} = 0$$

The eigenvalues are $\lambda_1 = -\mathrm{d}_1, \lambda_2 = -\mathrm{d}_2, \lambda_3 = -\mathrm{d}_3, \lambda_4 = b$

$\lambda_1, \lambda_2, \lambda_3$ are negative while λ_4 is positive. Since b can not take a negative value, it means that (2.3) can not be stable. Hence it always remains unstable. For (2.3) to be stable b must be negative which is not possible.

***Theorem* 3.1**

If the genotype frequencies are defined as $x(t) = D(t)/P(t), 2\mathrm{y}(t) = 2\mathrm{H}(t)/P(t), Z(\mathrm{t}) = \mathrm{R}(t)/P(t)$ *and the A-gene frequency p(t) = x(t) + y(t), also if there is a slow selection by death:* $d_i = d + \varepsilon\Delta_i$, $\mathrm{i} = 1, 2, 3$ *then when* $\varepsilon = 0, \mathrm{dP}/dt = 0$ *and* $x \to p^2, \mathrm{y} \to \mathrm{pq}, z \to \mathrm{q}^2$ *as t increases*

Proof:

Since $x(t) = D(t)/P(t)$, $\frac{dx}{dt} = \frac{PdD/dt - DdP/dt}{P^2} = b\left(p^2 - x\right) + x\left(\bar{d} - d_1\right)$

Similarly $\frac{dy}{dt} = b(pq - y) + y(\bar{d} - d_2),\ \frac{dz}{dt} = b(q^2 - z) + Z(\bar{d} - d_3),\ \frac{dp}{dt} = \frac{d}{dt}(x + y) = p\bar{d} - (d_1 x + d_2 y)$

where $\bar{d} = d_1 x + 2d_2 y + d_3 Z$. Setting $d_i = d + \varepsilon\Delta_i$ for i = 1, 2, 3 and using method of matched asymptotic expansions we get $\bar{d} - d_i = \varepsilon(\Delta_1 x + 2\Delta_2 y + \Delta_3 z - \Delta_i) = \varepsilon(\bar{\Delta} - \Delta_i)$

$$\therefore \frac{\mathrm{dx}}{\mathrm{dt}} = b(p^2 - x) + \varepsilon x(\bar{\Delta} - \Delta_1),\ \frac{\mathrm{dy}}{\mathrm{dt}} = b(pq - y) + \varepsilon y(\bar{\Delta} - \Delta_2),\ \frac{\mathrm{dz}}{\mathrm{dt}} = b(q^2 - z) + \varepsilon z(\bar{\Delta} - \Delta_3)$$

$\frac{dp}{dt} = \varepsilon[p\bar{\Delta} - (x\Delta_1 + y\Delta_2)]$, when $\varepsilon = 0$, $\frac{dp}{dt} = 0$ *and* $x \to p^2$, $y \to pq$ *and* $z \to q^2$ as t increases.

4.0 Summary and Conclusion

In this paper we have been able to formulate a mathematical model for human genetics with overlapping generations. The model is based on three assumptions:

a. The number of *AA* genotypes $D(t)$, the number of *Aa* genotypes $2H(t)$ and the number of aa genotypes $R(\mathbf{t})$ are smooth functions.

b. $D(t)$, $2H(t)$ and $R(t)$ reproduce according to malthus' rule with common birth rate, *b*.

c. The different genotypes have different death rates.

Based on these assumptions and the parameters defined, the model was formulated. The model was then analyzed. The steady state was determined as:

$$(D_0, \mathrm{H}_0', \mathrm{R}_0, \mathrm{P}_0) = (\Psi_1 p^2, \Psi_2 pq, \Psi_3 bq^2)P_0$$

and it was shown that this steady state is unstable. The conditions for the stability of the steady states is that the common birth rate of the different types of genotype is negative which is not possible.

It was later proved that if the genotype frequencies are defined as:

$$x(t) = D(t)/P(t),\ 2\mathrm{y}(\mathrm{t}) = 2H(t)/P(t),\ Z(\mathrm{t}) = R(t)/P(t)$$

and the A-gene frequency p(t) = x(t) + y(t), also if there is slow selection by death

$$d_i = d + \varepsilon\Delta_i,\ \mathrm{i} = 1, 2, 3$$

then when $\varepsilon = 0$, $\frac{\mathrm{dP}}{\mathrm{dt}} = 0$ and $\mathrm{x} \to \mathrm{p}^2$, $\mathrm{y} \to \mathrm{pq}$, $\mathrm{z} \to \mathrm{q}^2$ as t increases.

References

[1] Calabrese, P. (2007). New Mathematical Model to add rigor to studies of disease genetics and evolution. Proceedings of the National Academy of Science, California, U.S.A.

[2] Cavalla-Sforza, L.L and Bodmer, W.A. (1971). The Genetics of Human Populations. W.H. Freeman, San Francisco.

[3] Cavalla-Sforza, L.L.F (1981). Cultural transmission and evolution; a quantitative approach, Princeton: Princeton University press.

[4] Crow, J.F. and Kimura, M. (1970). An Introduction to Population Genetics Theory. Harper & Row, New York.

[5] Ewens, W.J. (1969). Population Genetics. Methuer, London.

[6] Feldman, M.W. and Laland, K.N. (1996). Cultural and Biological Evolutionary Processes, selection for a trait under complex transmission. Theoretical Population Biology. Vol. 9, 238 – 259.

[7] Feldman, M.W. and Laland, K.N. (1996). Gene-Culture Coevolutionary Theory. Tree Vol. 11, 453 – 457.

[8] Feller, W.J. (1969). Population Genetics. Methuer, London.

[9] Fisher, R.A. (1865). Versuche Uber Pflanzen-Hybriden.Verh.Naturforsch, ver. Brann, 10.

[10] Hoppensteadt, F.C. (1982). Mathematical Methods of Population Biology, Cambridge University Press, New York, 62 – 73, 75 – 82.

[11] Kendal, J.R. and Laland, K.N. (2000). Mathematical Models for Memetics, Journal of Memetics-Evolutionary Models of Information Transmission, Vol. 4.
[12] Ludwig, D.A. (1974). Stochastic Population Theories. Lecture Notes Biomath, Vol. 3, Springer-Verlag.
[13] Lumsden, C.J. and Wilson, E.O. (1981). Genes, Mind and Culture: the coevolutionary process, Harvard University Press.
[14] Mendel, G.J. (1865). Versuche Uber Pflanzen-Hybriden. Verh. Naturforsch, ver. Brann, 10.
[15] Moran, P.A.P. (1962). The Statistical Processes of Evolutionary Theory. Clarendon Press, Oxford.
[16] Wright, S. (1931). Evolution of Mendelian genetics. Genetics 16, 97 – 159.