Fractional populations of blood groups

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We rederive the Castle-Hardy-Weinberg law on the fractional populations of blood groups using a renormalization group approach. The result shows that the ratios between the four fractional populations of blood groups A, B, AB, and O are fixed and do not change from generation to generation. We also consider a simple case of mutation, where the blood group A is divided into A_1 and A_2, and there exists a mutual transformation between the two. It is shown that detailed information about the fractional ratio between the populations can be obtained using the existing data. [S1063-651X(97)02907-3]

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I. INTRODUCTION

Many concepts in the physical sciences can be applied to problems in the biological sciences. One of the remarkable examples would be the isomorphism between cluster distributions in physics and genetic diversity in biology [1]. In this paper, another well-known concept in physics is used in order to understand a problem in biology, namely, the fractional populations of blood types. This concept in physics is introduced in the theory of renormalization, especially the renormalization group equations and fixed points. Using this concept, we will consider the problems of the ratios between fractional populations of blood groups.

In genetics, there are rules by which hereditary blood type is determined. The key fact is that there are three factors A, B, and O, among which each human has two factors. A child receives two factors, one from the mother and the other from the father. Factors A and B are dominant over O, in other words, populations of blood type A are composed of those of AA and AO, and similarly for blood type B. For instance, if the blood type of the parents are AB and O, the blood types of their children should be A and B. With these genetic rules for blood types, we raise the following question. Will the fractional population for each blood group change from generation to generation? One of the purposes of this paper is to answer this question. To this end, we have to find equations which govern the fractional populations of blood groups for each generation. The derivation of the equations is presented in the next section. The equations show that all fractional populations of blood groups are fixed among successive generations. This result is already known as the Castle-Hardy-Weinberg law [2], which states that there is a particular equilibrium condition under random mating.

More detailed investigations on blood types show that several subgroups of A exist and the most important are A_1 and A_2 [3,4]. Accordingly subgroups A_1, A_2, A_1B, and A_2B are recognized. The subgroup A_1 represents the majority, and another subgroup A_2 the minority. The populations of the minority are generally so small that there are not many data related to A_1 and A_2 populations. However, it is remarkable that, for the white population only, the minority blood type A_2 is quite common. The reported data are given by $A_1{:}A_2 = 80{:}20$, and $A_1B{:}A_2B = 60{:}40$ [4,5]. Therefore, for the white population, it is reasonable to argue that there are four blood factors A_1, A_2, B, and O, and that the race is composed of the six blood groups A_1, A_2, A_1B, A_2B, B, and O, instead of the conventional four blood groups.

The second topic of this paper is to consider the case where a simple mutation is involved. Here, we assume that a mutual transformation between A_1 and A_2 is allowed with a small probability. The equations governing populations will be modified accordingly. Using the renormalization equations and the existing population data, we can determine the ratio between the mutation probabilities. Furthermore, we show that A_1 is superior to A_2; in other words, A_1A_2 belongs to the blood group A_1. The final theoretical result of this paper is that the blood group A of the white race is divided as $A_1A_1{:}A_1A_2{:}A_2A_2{:}A_1O{:}A_2O = 9{:}12{:}4{:}3{:}2$.

II. BLOOD GROUP EQUATIONS

The purpose of this section is to find the equations which govern the fractional populations of the blood groups in successive generations. These ''blood group equations'' correspond to the ''renormalization group equations'' in physics. Here, the generation in this case corresponds to the scaling in renormalization group equations. Let $AA(n)$, $AO(n)$, $BB(n)$, $BO(n)$, $AB(n)$, and $OO(n)$ denote the ratios of fractional populations for the nth generation. The sum of the six fractions should be 1.

Consider the factors $A(n)$, $B(n)$, and $O(n)$ for the nth generation, which represent the fractional populations giving

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the corresponding genetic factors,

$$A(n)=AA(n)+\frac{1}{2}AO(n)+\frac{1}{2}AB(n),$$
$$B(n)=BB(n)+\frac{1}{2}BO(n)+\frac{1}{2}AB(n), \quad (1)$$
$$O(n)=OO(n)+\frac{1}{2}AO(n)+\frac{1}{2}BO(n).$$

The coefficient $\frac{1}{2}$ is used under the condition that there is no preference for any blood factor during the meiosis. It is easy to note $A(n)+B(n)+O(n)=1$.

Assuming that the blood types are not correlated with sex, in other words, that the population ratios for female are the same as those for male, each population ratio for the $(n+1)$th generation is determined by the blood group equations written as

$$AA(n+1)=A(n)\times A(n),$$
$$AO(n+1)=2A(n)\times O(n),$$
$$BB(n+1)=B(n)\times B(n),$$
$$BO(n+1)=2B(n)\times O(n), \quad (2)$$
$$AB(n+1)=2A(n)\times B(n),$$
$$OO(n+1)=O(n)\times O(n).$$

Here, the coefficient 2 represents that a blood type AB child can receive the blood factor A or B from the mother or from the father. These equations have the same mathematical structure as the renormalization group equations, which are used widely in the theory of critical phenomena.

Using these equations, we find that

$$AA(n+1)+AO(n+1)+BB(n+1)+BO(n+1)+AB(n+1)+OO(n+1)$$
$$=\{A(n)+B(n)+O(n)\}\{A(n)+B(n)+O(n)\}=1, \quad (3)$$

which is consistent with the fact that the sum of the six population ratios should be preserved along succeeding generations.

Furthermore, we notice that

$$A(n+1)=AA(n+1)+\frac{1}{2}AO(n+1)+\frac{1}{2}AB(n+1)$$
$$=A(n)\times\{A(n)+B(n)+O(n)\}=A(n). \quad (4)$$

This shows that $A(n)$ is conserved. Similarly we can show that $B(n)$ and $O(n)$ are also conserved. This fact states that there is no change in genotypic proportions in a population from generation to generation. When there is no mutation, this conservation of blood types is hardly surprising. We intuitively expect that fractional population does not change under random mating conditions and this fact was named the Castle-Hardy-Weinberg law [2].

This result can be applied in understanding relationships between consanguinities. Suppose that one consanguinity shows a quite different fractional population ratio from the other; this means that the origins of the two are different from each other. For instance, the American Indians have a predominant population of blood type O, about 70–100 % [6]. Therefore, we may be able to trace the origin of the American Indians by identifying another consanguinity with a dominant O blood type.

III. MUTATION

In order to understand the effect of mutation on the blood populations, it is necessary to allow mutations between the blood groups. However, mutations between A, B, and O are so rare that there are no decent data on this matter. Therefore we will here consider only a special case of mutation. The generalization of the following discussion for mutations between A, B, and O would be straightforward.

The blood group A is known to be divided into two types, A_1 and A_2. Especially, for the white race, the A_2 fraction is substantial, while it is quite rare for other races. It is reported that, for the white race, the ratios of the blood groups A_1, A_2, A_1B, A_2B are found to be $A_1B:A_2B=60:40$ and $A_1:A_2=80:20$ [4,5].

Here we consider a situation where the mutation between A_1 and A_2 is allowed. We let the probability of changing the blood factor A_1 to A_2 be x, and denote by y the probability of changing the blood factor A_2 to A_1

$$A_1 \overset{x}{\Rightarrow} A_2, \quad A_1 \overset{y}{\Leftarrow} A_2. \quad (5)$$

Then the new fractional populations which deliver factors to their children are modified as

$$[A_1A_1(n)]_{\text{new}}=(1-x)^2A_1A_1(n)+(1-x)yA_1A_2(n)+y^2A_2A_2(n),$$
$$[A_1A_2(n)]_{\text{new}}=2x(1-x)A_1A_1(n)+\{(1-x)(1-y)+xy\}A_1A_2(n)+2y(1-y)A_2A_2(n), \quad (6)$$

$$[A_2A_2(n)]_{\text{new}}=x^2A_1A_1(n)+x(1-y)A_1A_2(n)+(1-y)^2A_2A_2(n),$$

$$[A_1O(n)]_{\text{new}}=(1-x)A_1O(n)+yA_2O(n),$$

$$[A_2O(n)]_{\text{new}}=xA_1O(n)+(1-y)A_2O(n),$$

$$[A_1B(n)]_{\text{new}}=(1-x)A_1B(n)+yA_2B(n),$$

$$[A_2B(n)]_{\text{new}}=xA_1B(n)+(1-y)A_2B(n),$$

$$[BB(n)]_{\text{new}}=BB(n),$$

$$[BO(n)]_{\text{new}}=BO(n),$$

$$[OO(n)]_{\text{new}}=OO(n).$$

The factors introduced for the blood group equations should also be modified with the new fractional populations. In fact, we write

$$\begin{aligned}
\widetilde{A}_1(n)&=[A_1A_1(n)]_{\text{new}}+\frac{1}{2}[A_1A_2(n)]_{\text{new}}+\frac{1}{2}[A_1O(n)]_{\text{new}}+\frac{1}{2}[A_1B(n)]_{\text{new}},\\
\widetilde{A}_2(n)&=[A_2A_2(n)]_{\text{new}}+\frac{1}{2}[A_1A_2(n)]_{\text{new}}+\frac{1}{2}[A_2O(n)]_{\text{new}}+\frac{1}{2}[A_2B(n)]_{\text{new}},\\
\widetilde{B}(n)&=[BB(n)]_{\text{new}}+\frac{1}{2}[BO(n)]_{\text{new}}+\frac{1}{2}[A_1B(n)]_{\text{new}}+\frac{1}{2}[A_2B(n)]_{\text{new}},\\
\widetilde{O}(n)&=[OO(n)]_{\text{new}}+\frac{1}{2}[A_1O(n)]_{\text{new}}+\frac{1}{2}[A_2O(n)]_{\text{new}}+\frac{1}{2}[BO(n)]_{\text{new}}.
\end{aligned}\tag{7}$$

The blood group equations are now written in the same fashion as in the preceding section,

$$\begin{aligned}
A_1A_1(n+1)&=\widetilde{A}_1(n)\times\widetilde{A}_1(n),\\
A_1A_2(n+1)&=2\widetilde{A}_1(n)\times\widetilde{A}_2(n),\\
A_2A_2(n+1)&=\widetilde{A}_2(n)\times\widetilde{A}_2(n),\\
A_1O(n+1)&=2\widetilde{A}_1(n)\times\widetilde{O}(n),\\
A_2O(n+1)&=2\widetilde{A}_2(n)\times\widetilde{O}(n),\\
BB(n+1)&=\widetilde{B}(n)\times\widetilde{B}(n),\\
BO(n+1)&=2\widetilde{B}(n)\times\widetilde{O}(n),\\
A_1B(n+1)&=2\widetilde{A}_1(n)\times\widetilde{B}(n),\\
A_2B(n+1)&=2\widetilde{A}_2(n)\times\widetilde{B}(n),\\
OO(n+1)&=\widetilde{O}(n)\times\widetilde{O}(n).
\end{aligned}\tag{8}$$

Using these equations, we first notice that $\widetilde{A}_1(n)+\widetilde{A}_2(n)+\widetilde{B}(n)+\widetilde{O}(n)=1$ for any generation n. Furthermore, we find that for the factor $\widetilde{O}(n)$,

$$\begin{aligned}
\widetilde{O}(n+1)&=OO(n+1)+\frac{1}{2}A_1O(n+1)+\frac{1}{2}A_2O(n+1)+\frac{1}{2}BO(n+1)=\widetilde{O}(n)\times\widetilde{O}(n)+\widetilde{A}_1(n)\times\widetilde{O}(n)+\widetilde{A}_2(n)\times\widetilde{O}(n)+\widetilde{B}(n)\\
&\times\widetilde{O}(n)=\widetilde{O}(n)\times\{\widetilde{O}(n)+\widetilde{A}_1(n)+\widetilde{A}_2(n)+\widetilde{B}(n)\}=\widetilde{O}(n).
\end{aligned}\tag{9}$$

$\widetilde{O}(n)$ is conserved as expected. Similarly we can show that $\widetilde{B}(n)$ is also conserved. However, the factors $\widetilde{A}_1(n)$ and $\widetilde{A}_2(n)$ are not conserved separately, but $\widetilde{A}_1(n)+\widetilde{A}_2(n)$ is conserved,

$$\widetilde{A}_1(n+1)+\widetilde{A}_2(n+1)=A_1A_1(n+1)+A_1A_2(n+1)+A_2A_2(n+1)+\frac{1}{2}A_1B(n+1)+\frac{1}{2}A_2B(n+1)+\frac{1}{2}A_1O(n+1)$$

$$+\frac{1}{2}A_2O(n+1)=\{\widetilde{A}_1(n)+\widetilde{A}_2(n)\}\times\{\widetilde{O}(n)+\widetilde{A}_1(n)+\widetilde{A}_2(n)+\widetilde{B}(n)\}=\widetilde{A}_1(n)+\widetilde{A}_2(n). \tag{10}$$

Using Eqs. (6)–(8) and $\widetilde{O}(n)+\widetilde{B}(n)=1-\widetilde{A}_1(n)-\widetilde{A}_2(n)$, $\widetilde{A}_1(n+1)$ and $\widetilde{A}_2(n+1)$ are written in terms of $\widetilde{A}_1(n)$ and $\widetilde{A}_2(n)$ as

$$\begin{aligned}\widetilde{A}_1(n+1)&=(1-x)\widetilde{A}_1(n)+y\widetilde{A}_2(n),\\ \widetilde{A}_2(n+1)&=x\widetilde{A}_1(n)+(1-y)\widetilde{A}_2(n).\end{aligned} \tag{11}$$

Here, we assume that the current fractional population distribution has reached an equilibrium, which corresponds to a fixed point. At a fixed point, $(\widetilde{A}_1^*,\widetilde{A}_2^*)$, the above equations become

$$0=-x\widetilde{A}_1^*+y\widetilde{A}_2^*. \tag{12}$$

Thus we find that $\widetilde{A}_1^*:\widetilde{A}_2^*=y:x$. Using the information on $A_1B:A_2B$, we can determine the ratio of x to y.

$$\frac{A_1B}{A_2B}=\frac{\widetilde{A}_1^*\times\widetilde{B}^*}{\widetilde{A}_2^*\times\widetilde{B}^*}=\frac{\widetilde{A}_1^*}{\widetilde{A}_2^*}=\frac{y}{x}. \tag{13}$$

For the specific case of $A_1B:A_2B=60:40$, we conclude that $x:y=2:3$.

Using the information on $A_1:A_2$, we can answer the question of whether the blood type A_2 belongs to A_1 or A_2 and also obtain detailed information on the populations of blood group A.

For these purposes, suppose that A_1A_2 belongs to A_1; then we find

$$\frac{A_1}{A_2}=\frac{A_1A_1+A_1A_2+A_1O}{A_2A_2+A_2O}=\frac{\widetilde{A}_1^*\times\widetilde{A}_1^*+2\widetilde{A}_1^*\times\widetilde{A}_2^*+2\widetilde{A}_1^*\times\widetilde{O}^*}{\widetilde{A}_2^*\times\widetilde{A}_2^*+2\widetilde{A}_2^*\times\widetilde{O}^*}. \tag{14}$$

Using $x\widetilde{A}_1^*=y\widetilde{A}_2^*$, we obtain the ratio of $\widetilde{O}^*$ to $\widetilde{A}_2^*$ in terms of the ratio of A_1 to A_2:

$$\frac{\widetilde{O}^*}{\widetilde{A}_2^*}=\frac{(y^2+2xy)/x^2-A_1/A_2}{2(A_1/A_2-y/x)}. \tag{15}$$

Since $\widetilde{O}^*$ and $\widetilde{A}_2^*$ must be positive, we have the following condition for a meaningful result:

$$\frac{y}{x}<\frac{A_1}{A_2}<\frac{y^2+2xy}{x^2}. \tag{16}$$

Now, consider the other case where A_1A_2 belongs to A_2; we find

$$\frac{A_1}{A_2}=\frac{A_1A_1+A_1O}{A_2A_2+A_1A_2+A_2O}=\frac{\widetilde{A}_1^*\times\widetilde{A}_1^*+2\widetilde{A}_1^*\times\widetilde{O}^*}{\widetilde{A}_2^*\times\widetilde{A}_2^*+2\widetilde{A}_1^*\times\widetilde{A}_2^*+2\widetilde{A}_2^*\times\widetilde{O}^*}. \tag{17}$$

In this case, the ratio of $\widetilde{O}^*$ to $\widetilde{A}_2^*$ becomes

$$\frac{\widetilde{O}^*}{\widetilde{A}_2^*}=\frac{y^2/x^2-(2y/x+1)A_1/A_2}{2(A_1/A_2-y/x)}. \tag{18}$$

We have a condition similar to the above case using the positiveness of $\widetilde{O}^*$ and $\widetilde{A}_2^*$:

$$\frac{y^2}{x^2+2xy}<\frac{A_1}{A_2}<\frac{y}{x}. \tag{19}$$

Using the existing data $y/x=\frac{3}{2}$, Eq. (16) and Eq. (19) are written as

$$\begin{aligned}\frac{3}{2}<\frac{A_1}{A_2}<\frac{21}{4}\quad&\text{for } A_1A_2\in A_1,\\ \frac{9}{16}<\frac{A_1}{A_2}<\frac{3}{2}\quad&\text{for } A_1A_2\in A_2.\end{aligned} \tag{20}$$

By using the information of $A_1:A_2=80:20$, we conclude that A_1A_2 belongs to A_1. Furthermore, from Eq. (15), we find the ratio of $\widetilde{O}^*$ to $\widetilde{A}_2^*$,

$$\frac{\widetilde{O}^*}{\widetilde{A}_2^*}=\frac{1}{4}. \tag{21}$$

Using $\widetilde{O}^*:\widetilde{A}_2^*$, $\widetilde{A}_1^*:\widetilde{A}_2^*$ and Eq. (8), we find that $A_1A_1:A_1A_2:A_2A_2:A_1O:A_2O=9:12:4:3:2$.

IV. CONCLUSION

The motivation of this paper is to find how the fractional populations for four blood groups A, B, AB, O are changing from generation to generation. We present the governing equations, which are similar to the discretized renormalization group equations. The equations show that the fractional population for each blood group does not change.

We also consider the case where blood group A is divided into two groups A_1 and A_2 and mutual mutations are allowed. Using the governing equations and the existing statistical data, we find the following three results. First, $x:y=2:3$, where x and y are the genotypic mutation probability from A_1 to A_2 and vice versa, respectively. Second, the blood group of A_1A_2 belongs to A_1. Third, the detailed population fractions of blood type A are given by $A_1A_1:A_1A_2:A_2A_2:A_1O:A_2O=9:12:4:3:2$. We believe that the above theoretical model calculation can be improved and refined with more detailed experimental data.

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