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Polynomial dynamics of human blood genotypes frequencies ☆

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ABSTRACT

The frequencies of human blood genotypes in the ABO and Rh systems differ between populations. Moreover, in a given population, these frequencies typically evolve over time. The possible reasons for the existing and expected differences in these frequencies (such as disease, random genetic drift, founder effects, differences in fitness between the various blood groups etc.) are the focus of intensive research. To understand the effects of historical and evolutionary influences on the blood genotypes frequencies, it is important to know how these frequencies behave if no influences at all are present. Under this assumption the dynamics of the blood genotypes frequencies is described by a polynomial dynamical system defined by a family of quadratic forms on the 17-dimensional projective space. To describe the dynamics of such a polynomial map is a task of substantial computational complexity.

We give a complete analytic description of the evolutionary trajectory of an arbitrary distribution of human blood variations frequencies with respect to the clinically most important ABO and RhD antigens. We also show that the attracting algebraic manifold of the polynomial dynamical system in question is defined by a binomial ideal.

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1. Introduction

Since the discovery of human blood groups in 1900, their distributions in various countries and ethnicities have attracted the attention of researchers (Anstee, 2010). Such distributions vary a lot across the world (Kang et al., 1997; Ohashi et al., 2006; Sato et al., 2010) and, in general, evolve over time (Novitski, 1976). It is classically known that in the absence of evolutionary influences the allele frequency of a single trait achieves the Hardy–Weinberg equilibrium (Novitski, 1976) already in the second generation and then remains constant (Bernstein, 1923). Besides, blood groups frequencies satisfy an algebraic relation (Bernstein, 1930). The interplay between the frequencies of all possible genotypes or phenotypes combinations of a pair of genes (even though their frequencies are uncorrelated) is however much more complex (Lyubich, 1971). For a random initial population, the frequencies of all possible combinations of blood group and Rh factor phenotypes will only stabilize after an infinitely long evolution.

By computing the linkage disequilibria between alleles one can, in principle, find the frequency of any genotype in a given generation (Lyubich, 1971). However, finding explicit analytic formulas for the evolution of genotypes frequencies and invariant varieties of the polynomial dynamical system describing this evolution is a problem of great computational complexity. In the present paper we develop a symbolic solution technique which allows us to give a closed form description of the evolutionary trajectory. We show how the frequencies of human blood genotypes (distinguished by both blood group and Rh factor variations) with arbitrary initial distribution will evolve after any given number of generations in a population where no blood genotype is favored over another with respect to the ability to pass its genes to the next generation.

In demography and transfusiology, it is often important to know and predict the frequencies of blood genotypes or phenotypes with respect to *both* blood group and Rh factor (Anstee, 2010; Ohashi et al., 2006; Okada and Kamatani, 2012; Reilly and Szulkin, 2007). For instance, one would like to know the expected frequency of the Rh negative 4th blood group after a given number of years in a certain population. As we will see later, the convergence of the blood genotypes frequencies towards the limit distribution is rather slow (in the real time scale) for generic choice of their initial distribution. For instance, Table 1 shows that for $p = \frac{1}{2}$ the frequency of the OH phenotype in Example 1 below after two generations is 0.109 while its equilibrium value is 0.187. Moreover, the limit distribution might not be ever reached for a particular real population because of migration and evolutionary influences that affect the blood genotypes frequencies (Anstee, 2010; Lyubich, 1971). The Hardy–Weinberg result gives the equilibrium genotypes frequencies after an infinitely long evolution and the Bernstein equation (Bernstein, 1930; Novitski, 1976) relates these frequencies in a population that is already at the equilibrium.

The purpose of the present paper is to fill the gap between an initial distribution and the equilibrium state (that is in general only achieved after an infinitely long evolution) by giving an explicit closed form analytic formula for the frequencies distribution. We describe the evolution of the frequencies of all possible genotypes of human blood in the clinically most important ABO and Rh blood group systems for an arbitrary initial distribution of these frequencies and after any number of generations.

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2. Biological background

It is widely known that human individuals might have different blood. This difference is big enough to cause clinical or even lethal risks of blood transfusion from one person to another. Advances of transfusiology naturally led to classification of human blood. Despite the existence of numerous blood classification systems (Hoffman et al., 2012), the most important one is the widely known and used ABO and Rh blood system. In this system, human blood is classified with respect to the clinically most important ABO and RhD antigens.

Throughout the paper, we will be denoting the blood group traits by A, B, O, and the Rh factor traits by H (positive) and h (negative). Disregarding for the moment the Rh factor, we observe that a

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