Mathematical Modeling of Rhesus Agglutinogen Dynamics in the Human Population

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Abstract
The work is devoted to the development of a research methodology for one class of degenerate biological models. The work examines the critical states of systems consisting of several subpopulations, as well as the conditions under which bifurcations (catastrophes) are possible in the system.

Keywords
Mathematical modeling, Rhesus factor, bifurcation, human population

1. Introduction

The Rhesus factor, aF one of the quality indicators of blood, was first identified during the study of the body of the Rhesus monkey. Rhesus factor is an antigen (protein) located on the surface of red blood cells (erythrocytes). Scientists Landsteiner (Nobel prize winner for the discovery of the blood group) and Wiener found it about 55 years ago. Their discovery helped establish that about 85% of people have the Rh factor and are therefore Rh-positive, while the other 15% who do not have it are Rh-negative. For the most part, neither a positive nor a negative Rh factor poses any threat to a person.

To understand the reasons for the phenomenon discussed above, consider a separate couple of a man and a woman, in which the man is Rh-positive and the woman is Rh-negative. In this case, theoretically, a Rhesus conflict between the organism of the mother and the child is possible. It begins when the child imitates the Rh factor of the father, which happens in most cases, because this genetic information is contained directly in the sperm shell. If the Rhesus gene is inherited from the father, the baby's blood in the mother's womb will become incompatible with her blood.

The essence of the conflict is that the Rh factor of the fetus, passing through the placental barrier, enters the blood of the mother, her body, perceiving the fetus as a foreign body, produces protective antibodies (bilirubin). Bilirubin can affect the brain of the unborn child and cause hearing and vision defects in it. At the same time, since the number of fetal erythrocytes continuously increases, the liver and spleen, trying to quickly produce red blood cells, increase significantly in size. Over time, the content of erythrocytes and hemoglobin in the child's blood decreases and their level becomes dangerously low. Rh-conflict can sometimes cause dropsy in children or a tumor of the fetus, lead to a fatal case in an infant.

During the first pregnancy, Rhesus conflict develops quite rarely, because the mother's immune system encounters foreign erythrocytes (red blood cells) for the first time, and, accordingly, the mother's body produces few antibodies that are unfavorable for her baby. With the next pregnancy, the probability of a threat during the conflict increases significantly. Since the antibodies are still in the woman's blood, they break through the placental barrier and begin to destroy the red blood cells of the unborn baby.

The mass share of people with a positive Rh factor is approximately 85% of the total population of the planet, respectively, 15% of representatives of the $Rh-$ race. It is clear that if $Rh+$ representatives were determined only by a combination of dominant alleles YY, the frequency of

ProfIT AI 2023: 3rd International Workshop of IT-professionals on Artificial Intelligence (ProfIT AI 2023), November 20–22, 2023, Waterloo, Canada
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birth of babies with $Rh-$ would be $(0{,}15)^2 = 0{,}0225$ an order of magnitude less than known statistical data. And therefore, among the representatives there are individuals represented by a mixed genotype Yy, but at the same time have phenotypic features of the subpopulation $Rh+$.

Applied problems, for which the mathematical model of intergroup interactions [3], [5-6] is applicable, take place in various fields of science, such as genetics [4], biology, demographic studies [7], ecology, etc.

2. Problem statement

Consider an Rh-positive person as two possible combinations:

- two dominant genes YY and a combination of a dominant and a recessive gene Yy, the subgroups corresponding to them will acquire the values x1, x2, respectively;
- Rh-negative people represented by a set of two recessive genes yy and subgroup x3.

From now on, we will consider the system of interaction of two genomes - positive and negative Rh. Suppose that we have 100 people in a certain spatial area, 85 of whom are Rh+, and 15 are Rh-. In the corresponding system, there are 200 genes, 30 of which are recessive and are represented by the x3 subpopulation. And the total number N of the recessive gene y must satisfy the condition (N/200)^2=0.15. It is easy to show that the number of recessive genes will be N=77.5, 30 of which are represented by Rh-negative people with the yy gene combination. Therefore, in order to maintain the ratio (Rh+)/(Rh-)=85/15, there must be 15% Rh-negative people with the yy genome, 47.5% Rh+ people with a mixed Yy genotype, and 37.5% Rh+ and combination of the YY genome.

The main tasks of the study are:

- development of a mathematical model of Rhesus agglutinogen dynamics among the human population;
- identification of parameters and initial conditions of the mathematical model
- resolution of the numerical experiment
- analysis of the obtained results

3. Mathematical modeling

The research is based on the idea of a population as a set of individuals, which can be conditionally divided into n subpopulations that are genetically more or less homogeneous, but differ significantly from each other. They are not reproductively isolated, and there is a certain probability of the offspring of an individual from the i-th subpopulation entering the j-th subpopulation. The differential model of the system can be written in a general form as follows [1]:

$$\frac{dx_j}{dt} = \sum_{i=1}^{n} A_{ji} \cdot f_i(x), \qquad j = \overline{1,n}\ , \tag{1}$$

where xj is the size of the j-th subpopulation, and fi(x) is a function describing the total reproductive capabilities of the i-th subpopulation, and Aji is the proportion of the offspring of the i-th subpopulation that goes to the j-th.

We assume that for any i

$$\sum_j A_{ij} = 1.$$

The function fi(x) reflects the well-known logistic law

$$f_i(x) = a_i \cdot \left(1 - \frac{1}{K}\sum_{l=1}^{n} x_l\right) x_i\,. \tag{2}$$

where a_i reflects the reproductive capabilities of the subpopulation with the index i and K is the capacity of the habitat of the population.

According to (1), (2), the growth of a subpopulation approaches zero in the case when its number approaches zero or when the total number of all subpopulations approaches the maximum possible ecological capacity of the environment K.

The system (1), (2) is not Voltaire in the sense that its trajectories can cross the coordinate axes and, for example, the local behavior of the system in the vicinity of the coordinate origin is determined by its properties not only in the first quarter.

To study the equilibrium points [2] of the system (1), (2), we use the standard Lyapunov analysis. It is easy to see that one of the equilibrium points is the zero point (origin of coordinates).

In addition, there is an infinite number of equilibrium points that lie on the plane

$$\sum_i x_i = K. \qquad (3)$$

The nature of the location of the equilibrium points is quite natural from an ecological point of view. Of course, in the case of a complete absence of individuals of this species, they cannot arise from nothing. If the subpopulations occupy the same ecological niche and do not differ in the resources they consume, their arbitrary distribution of numbers in this niche is balanced.

Theorem 1. The system (1), (2) is degenerate in the neighborhood of singular points of the stationary hyperplane (3).

Proof. The general form of the i-th component of the Jacobian matrix of systems (1), (2) is as follows:

$$J_{ij} = A_{ij} a_j \left(1 - \frac{\sum_{k=1}^{n} X_k}{K} \right) - \frac{\sum_{p=1}^{n} A_{ip} a_p x_p}{K}.$$

According to (3), the general form of the ith component of the Jacobi (J) matrix of the system (1), (2) at the points of the stationary hyperplane will take the form:

$$J_{ij} = -\frac{1}{K} \sum_{k=1}^{n} A_{ik} \cdot a_k \cdot X_k .$$

Since J_{ij} does not directly depend on j , is valid

$$J_{pi} = J_{hi}, \ p,h = \overline{1,n} ,$$

from which it follows that the column vectors of the Jacobian matrix are linearly dependent,

$$Det(J) = 0,$$

and therefore the system is degenerate at singular points of the stationary hyperplane

$$\sum_{i=1}^{n} x_i = K .$$

The theorem is proved.

We consider the model of Rhesus agglutinogen dynamics in the form of a system of intergroup dynamics (1) with a logistic function (2) in basic quality, which in the case will take the form

$$\begin{cases} \dot{x}_1 = (a_1 A_{11} x_1 + a_2 A_{12} x_2 + a_3 A_{13} x_3)\left(1 - \frac{x_1 + x_2 + x_3}{K}\right) \\ \dot{x}_2 = (a_1 A_{21} x_1 + a_2 A_{22} x_2 + a_3 A_{23} x_3)\left(1 - \frac{x_1 + x_2 + x_3}{K}\right) \\ \dot{x}_3 = (a_1 A_{31} x_1 + a_2 A_{32} x_2 + a_3 A_{33} x_3)\left(1 - \frac{x_1 + x_2 + x_3}{K}\right) \end{cases}. \qquad (4)$$

4. Solving of the problem

When determining the coefficients A_{ij} of system (4), we will be guided by known data on the equilibrium distribution of subpopulations of people with different indicators of the Rh factor. The coefficient A_{ij} should be proportional to the mass fraction of the j-th subpopulation in the equilibrium distribution $x_1 : x_2 : x_3 = 37{,}5 : 47{,}5 : 15$ and the mass fraction of the increase of the subpopulation with the index i during interaction with other subpopulations. The structure of the corresponding interaction is presented in Table 1.

Table 1
Scheme of reproduction of the Rhesus factor dynamics model

Father / mother	x_1	x_2	x_3
x_1	x_1	$0{,}5x_1 + 0{,}5x_2$	x_2
x_2	$0{,}5x_1 + 0{,}5x_2$	$0{,}25x_1 + 0{,}5x_2 + 0{,}25x_3$	$0{,}5x_2 + 0{,}5x_3$
x_3	x_2	$0{,}5x_2 + 0{,}5x_3$	x_3

According to the closed system condition ($\sum_{i=1}^{3} A_{ij} = 1$, $j = \overline{1,2,3}$), the transition coefficients will acquire the values given in the Table 2.

Table 2
Coefficients A_{ij} of system (4)

i / j	1	2	3
1	0.67	0.14	0
2	0.33	0.43	0.14
3	0	0.43	0.86

Taking into account the peculiarities of the interaction of Rhesus-agglutinogen among the human population and the stationary distribution $x_1 : x_2 : x_3 = 0{,}375 : 0{,}475 : 0{,}15$, the parameters of the growth rate will be presented in the following form:

$$a_i = 1 - F_i ,$$

$$F_i = \sum_{j=1}^{n} A_{ij} - \sum_{k=1}^{n} Q_k ,$$

where a_i is the reproductive potential of the i-th subpopulation;

$F_i \in [0;1]$ - probability of Rhesus conflict;

Q_i - compatibility of the i-th subpopulation in the equilibrium distribution.

The values of parameters F_i, a_i, $i = \overline{1,2,3}$ are as follows:

$$F_1 = 0{,}34 ,\quad F_2 = 0{,}17 ,\quad F_3 = 0 ,\qquad a_1 = 0{,}66 ,\quad a_2 = 0{,}83 ,\quad a_3 = 1 .$$

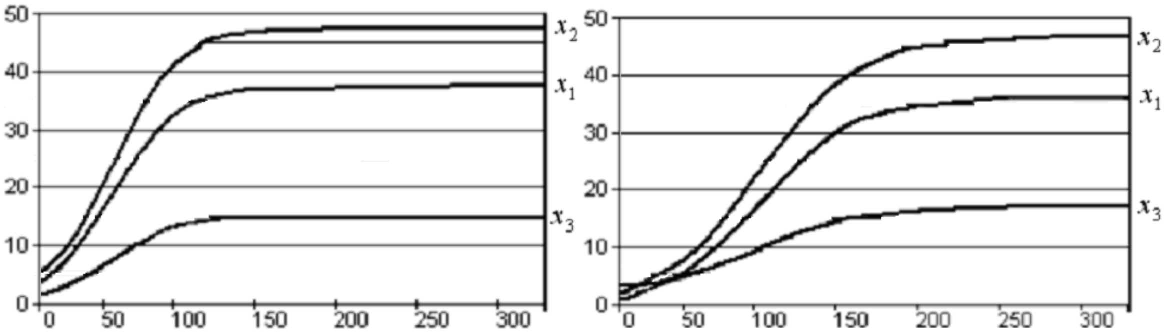
Proceeding from the provisions set out above, as well as from the assumption that the capacity of the area of human existence is limited to some finite value (this value is in most cases sufficiently large compared to the value of the initial conditions).

The range capacity value was conditionally chosen equal to 100. We have a differential model of the dynamics of the Rhesus factor among the human population in the following form:

$$
\begin{cases}
\dfrac{dx_1}{dt} = (0{,}67x_1 + 0{,}18x_2) \cdot \left(1 - \dfrac{x_1 + x_2 + x_3}{100}\right) \\
\dfrac{dx_2}{dt} = (0{,}33x_1 + 0{,}54x_2 + 0{,}14x_3) \cdot \left(1 - \dfrac{x_1 + x_2 + x_3}{100}\right). \\
\dfrac{dx_3}{dt} = (0{,}28x_2 + 0{,}86x_3) \cdot \left(1 - \dfrac{x_1 + x_2 + x_3}{100}\right)
\end{cases}
\tag{5}
$$

5. Numerical results

In Figure 1 presents the dynamics of the system with rather small compared to the parameter K and different initial conditions. As we can see, with the passage of time, not only is the numerical priority of the respective subpopulations established, but also the final ratios are almost indistinguishable from each other.

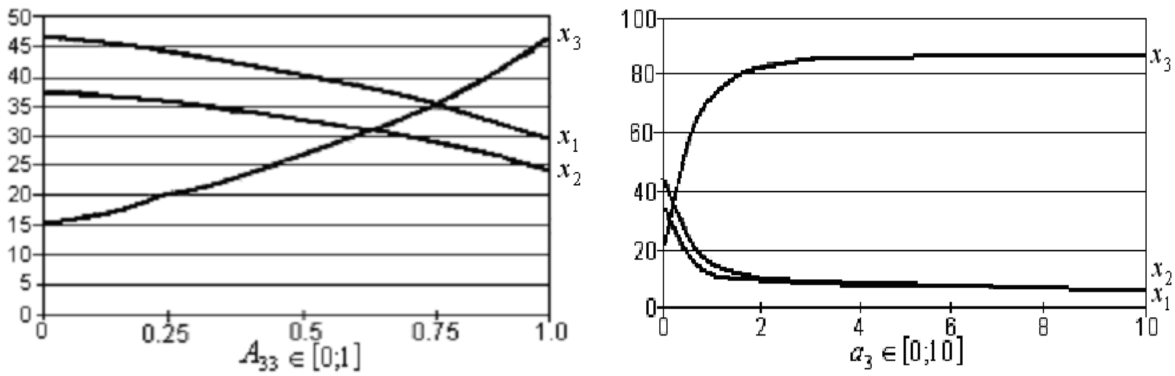


a) b)

Figure 1: The dynamics of the system (5) at a) $x_1^0 = 3{,}75; x_2^0 = 4{,}75; x_3^0 = 1{,}50$;
b) $x_1^0 = 1{,}00; x_2^0 = 2{,}00; x_3^0 = 3{,}00$

Note that in real ecological systems, the initial number of subpopulations can be arbitrary and even exceed the range's capacity.

Another factor of the system, on which the end point on the attractor significantly depends, are its parameters. Figure 2 shows the diagram of the dependence of the final equilibrium point on the coefficients A_{33} of the system and a_3 respectively.



a) b)

Figure 2: Graph of the dependence of the final equilibrium point on the coefficient a) A_{33}; b) a_3

When the coefficient A_{33} (Figure 2a) changes, the relative share of the third subpopulation increases exponentially. Moreover, not only the first, but also the second derivative of the corresponding curve reaches a positive value. The other two curves, gradually decreasing, maintain a proportional relationship between them. It can be concluded that the transition coefficients in general and in particular A_{33} are such parameters of the system that have a significant impact on its dynamics, therefore, by influencing them, it is possible to effectively control the system.

The graph (Figure 2b) illustrates the change in the end point of equilibrium when the parameter a_3 changes. The end point clearly depends on the propagation speed parameter a_i, but it varies only within certain limits. Despite the fact that the influence of the system coefficients is quite significant, the topology of the phase portraits does not undergo significant changes. Such changes occur only when parameters pass through bifurcation values, along with a qualitative change in the topological structure of the system's phase portrait.

6. Conclusions

Based on a mathematical model of subpopulation dynamics with a logistic function as a basic quality, the system of Rhesus agglutinogen dynamics among the human population was investigated. The applied part of the problem is studied in detail, as a result of which an applied interpretation of the equilibrium points of the model is given and a methodology for parameter identification is proposed. A number of model stability studies were conducted, the results of which showed that the mathematical model of Rhesus agglutinogen dynamics is sufficiently resistant to disturbances and external influences.

It was found that $t \to \infty$ the ratio of people with different indicators Rh does not significantly depend on the initial state of the system (initial ratio of numbers of subpopulations). The dependence of the final ratio of subpopulations of people with different indicators Rh on the reproduction rate coefficients and transition coefficients was investigated. According to the research results, it can be stated that the transition coefficients are decisive for the system, and when the growth rate coefficient changes, the dynamic changes, but the phase portrait of the system can undergo irreversible changes only when its sign changes.

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