GENETIC SELECTION AND EQUILIBRIUM STABILITY

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The problem of the equilibrium stability of a phenotypic selection process, with a single pair of autosomal alleles, has been numerically studied, on the basis of previously established reproduction differential equations.

INTRODUCTION

B. de Finetti (1927) studied the phenotypic selection process with a single pair of autosomal alleles, A and a, with genotypes AA, aa, Aa, and phenotypes D = AA + Aa and R = aa, considering an identical fertility rate for every individual in our population.
B. de Finetti and C. Rossi (1976) studied the same process with regard to differential fertility, caused by different ages of the individuals (males and females) that generate the process. The following integral reproduction equations were found to represent such a process:

$$N_i(t) = \sum_{j=k=1}^{3} \sum^{3} \nu_{jk}{}^{(1)} \lambda_{jk} \int_{\alpha}^{\beta}\int_{\gamma}^{\delta} N_j(t-\zeta)\, N_k(t-\eta) P(\zeta, \eta)\, d\zeta\, d\eta \qquad (1)$$

$$i = 1, 2, 3$$

where:

1) $N_i(t)$ is the number of children, born during the year t, of genotype i (1 = AA, 2 = aa, 3 = Aa);

2) $\nu_{jk}(i)$ is the probability to get a child of genotype i from parents of genotypes j and k;

3) $[\alpha, \beta]$ is the woman fertility interval;

4) $[\gamma, \delta]$ is the man fertility interval;

5) $P(\zeta, \eta)\, \lambda_{jk}$ is a weight function of living, mating and fertility, of individuals of genotypes j and k, aged ζ and η.

The function $P(\zeta, \eta)$ could be completely calculated on the basis of demographic tables, while the constants λ_{jk} were used as selection parameters to investigate the process (de Finetti and Rossi 1976).
On the basis of the functions $N_i(t)$ we could calculate every other interesting function, in particular the function $Z_i(t)$ ($i = 1, 2, 3$), which represents the proportion of individuals, whose genotype is i, living during the year t. An analytic solution of the integral equations would be quite difficult, and would not give a useful contribution to the study of the process. So, we decided to investigate the problem numerically, in several situations, to get an idea of the process, while varying the initial composition of our population and the selection parameters.

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We got a geometrical representation of the results, using de Finetti diagrams, for the instantaneous percentage composition of the population. We also got a practical demonstration of the equivalence between the integral and differential equations to investigate special problems. For instance, they are equivalent to study asymptotic behaviour, without events which disturb the fertility of some particularly aged individuals, but not others.

In the present paper the equilibrium stability of the process will be studied, while varying selection parameters, on the basis of previous results, using differential reproduction equations and selection parameter tables (de Finetti 1927).

Table. Z_1, Z_2, Z_3: *genotypic percentage divided by 10; (B, — A), (D, — C): coordinates of the eigenvectors;* α_1, α_2: *eigenvalues.*

Z_1	Z_2	Z_3	A	B	C	D	α_1	α_2
0	5	5	—0.207	0.289	—0.866	0.207	—0.293	—1.707
0	6	4	—0.133	0.162	—0.926	0.133	—0.201	—1.670
0	7	3	—0.088	0.123	—1.065	0.088	—0.127	—1.704
0	8	2	—0.055	0.072	—1.256	0.055	—0.072	—1.780
0	9	1	—0.032	0.041	—1.640	0.032	—0.045	—2.086
1	4	5	—0.049	0.093	—0.439	0.049	—0.112	—0.986
1	5	4	0.018	—0.038	—0.462	—0.018	0.048	—0.900
1	6	3	0.067	—0.145	—0.509	—0.067	0.183	—0.851
1	7	2	0.104	—0.246	—0.522	—0.104	0.326	—0.807
1	8	1	0.109	—0.373	—0.412	—0.109	0.534	—0.766
1	9	0	0.000	—0.577	—0.000	—0.000	1.001	—0.900
2	3	5	—0.003	0.011	—0.132	0.003	—0.017	—0.616
2	4	4	—0.031	—0.145	—0.173	—0.031	0.221	—0.566
2	5	3	0.057	—0.255	—0.223	—0.057	0.384	—0.560
2	6	2	0.071	—0.323	—0.234	—0.071	0.538	—0.562
2	7	1	0.057	—0.445	—0.179	—0.057	0.713	—0.620
2	8	0	0.000	—0.577	—0.000	—0.000	1.000	—0.800
3	2	5	0.004	0.013	0.132	—0.004	—0.026	—0.407
3	3	4	—0.010	—0.191	0.037	0.010	0.340	—0.405
3	4	3	0.014	—0.312	—0.043	—0.014	0.526	—0.407
3	5	2	0.030	—0.404	—0.036	—0.030	0.670	—0.436
3	6	1	0.027	—0.488	—0.076	—0.027	0.820	—0.523
3	7	0	0.000	—0.577	0.000	0.000	0.999	—0.699
4	2	4	—0.069	—0.193	0.232	0.069	0.403	—0.316
4	3	3	—0.035	—0.348	0.091	0.035	0.626	—0.306
4	4	2	—0.004	—0.433	0.010	0.004	0.754	—0.342
4	5	1	0.007	—0.512	—0.019	—0.007	0.879	—0.431
4	6	0	0.000	—0.576	—0.000	0.000	0.999	—0.600
5	1	4	—0.103	—0.033	0.539	0.103	0.246	—0.294
5	2	3	—0.089	—0.345	0.218	0.089	0.685	—0.245
5	3	2	—0.036	—0.448	0.082	0.036	0.812	—0.254
5	4	1	—0.008	—0.519	0.019	0.008	0.906	—0.341
5	5	0	0.000	—0.577	0.000	0.000	1.000	—0.500
6	1	3	—0.162	—0.288	0.423	0.162	0.660	—0.253
6	2	2	—0.070	—0.454	0.150	0.070	0.857	—0.185
6	3	1	—0.022	—0.526	0.048	0.022	0.933	—0.252
6	4	0	0.000	—0.577	0.000	—0.000	1.000	—0.401
7	1	2	—0.125	—0.441	0.265	0.125	0.888	—0.168
7	2	1	—0.035	—0.530	0.071	0.035	0.952	—0.163
7	3	0	0.000	—0.576	—0.000	0.000	0.999	—0.300
8	1	1	—0.059	—0.521	0.114	0.059	0.962	—0.102
8	2	0	0.000	—0.577	0.000	0.000	1.000	—0.200
9	1	0	0.000	—0.578	0.000	—0.000	1.001	—0.100

MATHEMATICAL MODEL

The differential reproduction equations are the following:

$$\begin{cases} \frac{dx_1}{dt} = \frac{1}{x}\left(\lambda_{11}\, x_1^2 + \lambda_{13}\, x_1 x_3 + \frac{1}{4}\lambda_{33}\, x_3^2 \right) - \mu_1 x_1 \\ \frac{dx_2}{dt} = \frac{1}{x}\left(\lambda_{22}\, x_2^2 + \lambda_{23}\, x_2 x_3 + \frac{1}{4}\lambda_{33}\, x_3^2 \right) - \mu_2 x_2 \\ \frac{dx_3}{dt} = \frac{1}{x}\left(2\lambda_{12}\, x_1 x_2 + \lambda_{13}\, x_1 x_3 + \lambda_{23}\, x_2 x_3 + \frac{1}{2}\lambda_{33}\, x_3^2 \right) - \mu_3 x_3 \end{cases} \qquad (2)$$

λ_{jk} are called assortative mating parameters between genotypes j and k; μ_j is the mortality rate of individuals of genotype j; x_i is the number of individuals of genotype i, $x = x_1 + x_2 + x_3$.

For the phenotypic diffusion process we can write:

$\lambda_{11} = \lambda_{13} = \lambda_{31} = \lambda_{33} = \lambda_D$
$\lambda_{22} = \lambda_R$
$\lambda_{12} = \lambda_{21} = \lambda_{23} = \lambda_{32} = \lambda_M$

There are only three different selection parameters. We shall call $Z_i = \frac{x_i}{x}$ the proportion of individuals of genotype i $(Z_1 + Z_2 + Z_3 = 1)$.

We can change variables to get only two independent coordinates:

$$\frac{Z_1\text{-}Z_2}{\sqrt{3}} = \zeta;\ Z_3 = \eta$$

is the most expressive change we can make. Using such variables we can get the coordinates of the velocity vector as functions of composition of population and selection parameters. With some calculation on the basis of differential reproduction equations, we get the following formulas:

$$\begin{cases} \dot{\zeta} = \frac{1}{4\sqrt{3}}\left(1 - \eta + \zeta\sqrt{3}\right)\left(1 - \zeta\sqrt{3}\right)\left[\left(\lambda_M - \lambda_D\right)\left(1 + \eta - \zeta\sqrt{3}\right) + \left(\lambda_R - \lambda_M\right)\left(1 - \eta + \zeta\sqrt{3}\right)\right] = f_{\wedge}\left(\zeta, \eta\right) \\ \dot{\eta} = 2\lambda_M\left(1 - \eta\right)\left[\left(1 - \eta\right)^2 - 3\zeta^2\right] + \left[\lambda_M\left(1 - 2\eta\right) - \frac{1}{2}\lambda_R\left(1 - \eta + \zeta\sqrt{3}\right) + \right. \\ \qquad \left. + \frac{1}{2}\lambda_D\eta + \lambda_D\left(1 - \eta - \zeta\sqrt{3}\right)\right]\eta\left(1 - \eta + \zeta\sqrt{3}\right) = g_{\wedge}\left(\zeta, \eta\right) \end{cases} \qquad (3)$$

When selection parameters are specified, we get a cubic relation between the velocity vector and the composition of population:

$$\begin{cases} \dot{\zeta} = f(\zeta, \eta) \\ \dot{\eta} = g(\zeta, \eta) \end{cases} \qquad (4)$$

If we get the Taylor expansion with origin in an equilibrium point $(\bar{\zeta}, \bar{\eta})$, we can write:

$$\begin{cases} \dot{\zeta} = f_\zeta(\bar{\zeta}, \bar{\eta})\,\Delta\zeta + f_\eta(\bar{\zeta}, \bar{\eta})\,\Delta\eta + O(\Delta\zeta\text{-}\Delta\eta) \\ \dot{\eta} = g_\zeta(\bar{\zeta}, \bar{\eta})\,\Delta\zeta + g_\eta(\bar{\zeta}, \bar{\eta})\,\Delta\eta + O(\Delta\zeta\text{-}\Delta\eta) \end{cases} \qquad (5)$$

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If we consider a little neighborhood of the equilibrium point, we can neglect $O(\Delta\zeta, \Delta\eta)$:

$$\begin{cases} \dot{\zeta} = f_\zeta(\bar{\zeta}, \bar{\eta})\,\Delta\zeta + f_\eta(\bar{\zeta}, \bar{\eta})\,\Delta\eta \\ \dot{\eta} = g_\zeta(\bar{\zeta}, \bar{\eta})\,\Delta\zeta + g_\eta(\bar{\zeta}, \bar{\eta})\,\Delta\eta \end{cases} \tag{6}$$

Where $\Delta\zeta, \Delta\eta$ are the coordinates of the infinitesimal shifting vector from the equilibrium point. We get now a linear relation between the coordinates of the velocity vector in a neighborhood of an equilibrium point and the coordinates of the infinitesimal shifting vector from the same equilibrium point.

To get information about equilibrium stability we can study such linear vectorial relation and, in particular, the eigenvectors. Such a problem has been numerically analyzed for the points of the lattice represented in the Figure.

The eigenvectors and the eigenvalues of the linear relation have been calculated for such points, which are the equilibrium points corresponding to particular values of selection parameters, as stated by B. de Finetti (1927).

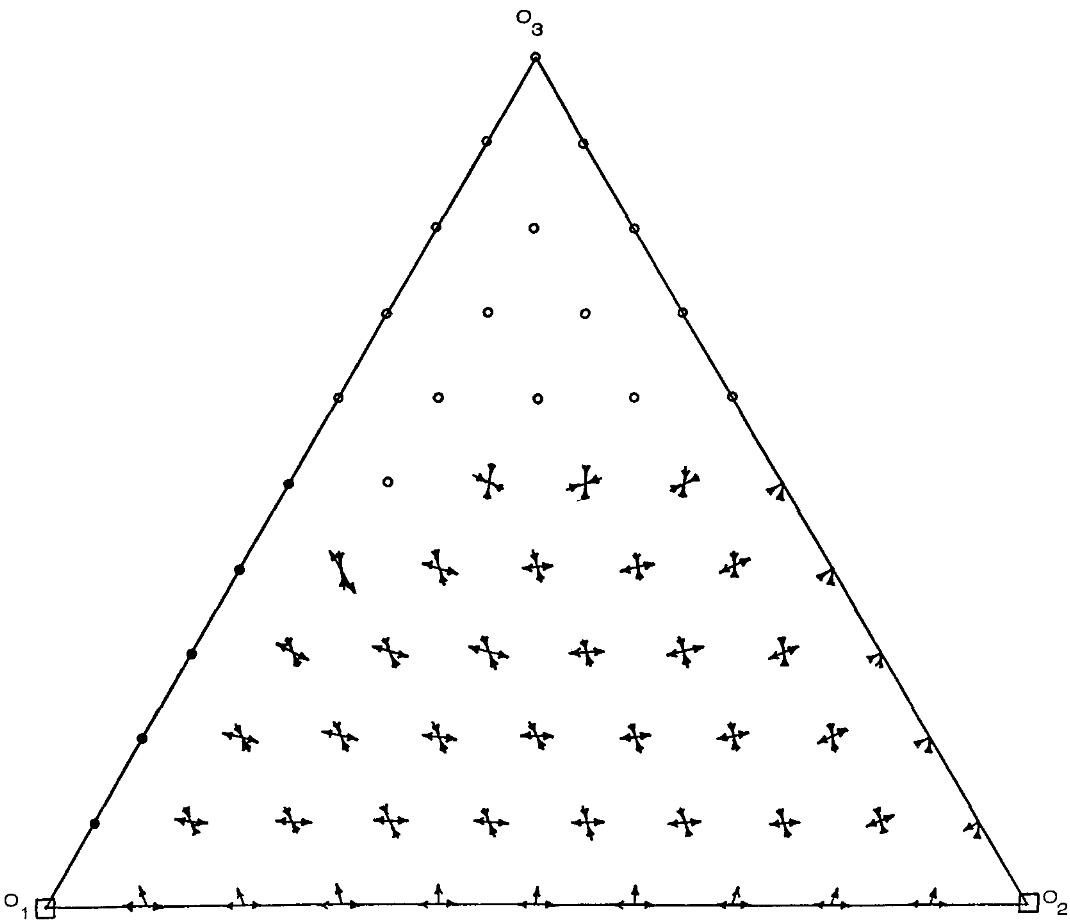

Figure. Representation of the eigenvectors of the linear correspondence between ζ, η and $\Delta\zeta$, $\Delta\eta$.
♀ impossibile equilibrium points; ○ undetermined equilibrium points; □ trivial equilibrium points.

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The results are shown in the Table and the eigenvectors are geometrically represented in the Figure.

All the conjectures made in previous papers are confirmed by such results. The points over the Hardy-Weinberg parabola are stable equilibrium points with two eigenvectors approaching the point: the paths in a neighborhood of such points are portions of parabolas tangent to one eigenvector.

The points under the Hardy-Weinberg parabola are unstable equilibrium points with one real eigenvector approaching the point and one real eigenvector departing from the point: the paths in a neighborhood of such points are portions of hyperbolas, whose asymptotes have the directions of the eigenvectors, on which the point which represents the instantaneous composition of population gets near to, and then gets far from, the equilibrium point.

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RIASSUNTO

Selezione Genetica e Stabilità dell'Equilibrio

Si studia numericamente il problema della stabilità dell'equilibrio in un processo di diffusione di caratteri derivanti da un paio di alleli di un locus autosomico in presenza di dominanza e in regime di accoppiamento assortativo basato sul genotipo.

RÉSUMÉ

Sélection Génétique et Stabilité de l'Equilibre

Le problème de la stabilité de l'équilibre est étudié numériquement dans un processus de diffusion des caractères dérivant d'un couple d'allèles d'un locus autosomique en présence de dominance et sous régime de croisement sélectif basé sur le génotype.

ZUSAMMENFASSUNG

Erbselektion und Gleichgewichtsstabilität

Das Problem der Gleichgewichtsstabilität wird zahlenmäßig in einem Diffusionsprozeß der Merkmale untersucht, die von einem Allelenpaar eines autosomen Locus herrühren bei Dominanz und unter dem Regime einer auf dem Genotyp basierenden Wahlkreuzung.

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