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DIFFUSION IN FISHER'S POPULATION MODEL

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ABSTRACT. We consider Fisher's selection model for a single locus with n alleles. The population is distributed in a spatial domain, migration is represented by a diffusion term. For the resulting parabolic system with zero flux boundary conditions we show that if the selection model has a stable polymorphism, then every solution of the parabolic system converges to a spatially homogeneous stationary solution. If initially all genes are present in the population, then this solution is the polymorphism. The results carry over to some types of convolution equations.

Diffusion in Fisher's population model. We consider the well-known Fisher-Wright-Haldane model of population genetics for n alleles a_1, a_2, $\ldots$, a_n, where p_j is the frequency of the j-th allele, and $f_{jk} = f_{kj} > 0$ is the fitness (viability, malthusian parameter) of the genotype $a_j a_k$. We assume continuous time, i.e., overlapping generations. The differential equations read

$$(1) \qquad \dot{p}_j = \sum_{k=1}^{n} f_{jk} p_k p_j - \sum_{r,s=1}^{n} f_{rs} p_r p_s p_j, \quad j = 1, 2, \ldots, n.$$

For the derivation of the model and for results on the ordinary differential equation we refer to [1], [2], [4], or [3]. The last reference contains an account of the earlier literature and more detailed results.

We prefer to use a condensed notation. Let $F = (f_{jk})$ be the matrix of viabilities and $p = (p_j)$ the column vector of frequencies. Furthermore define the diagonal matrix $P = (p_j \delta_{jk})$. Always a^* (transpose) is the row vector corresponding to the column vector a, in particular $e^* = (1, \ldots, 1)$. Then a^*b is a scalar product, ba^* is a dyad, and a^*Fa is a quadratic form. With this notation equations (1) read

$$(2) \qquad \dot{p} = PFp - p^*Fp \cdot p.$$

We consider the population distributed in a bounded spatial domain Ω of $\mathbf{R}^m$ with smooth (say C^3) boundary and describe migration and reproductive interaction of neighboring individuals by a diffusion term

$$(3) \qquad p_t = PFp - p^*Fp \cdot p + \Delta p.$$

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in Ω. Of course the diffusion rate must be the same for all alleles, therefore we can normalize it to one by rescaling the space variables. On the boundary $\partial\Omega$ we assume a no flux condition (**n** outer normal)

$$\partial p/\partial n = 0. \tag{4}$$

Our first result is the following theorem.

THEOREM 1. *Let the ordinary differential equation* (2) *have an exponentially stable stationary state with all components positive* (*stable polymorphism*). *Then for every initial function* $p(\cdot, 0)$ *the solution converges uniformly in* Ω *towards a spatially homogeneous* (*i.e., constant*) *function, which is a stationary state of the ordinary differential equation.*

If initially all types are present, i.e., $p_j(x, t) \not\equiv 0$ for $j = 1, \dots, n$, then this stationary solution is the polymorphism.
The proof proceeds in several steps.

1. **Stationary solutions.** The state space of (2) is the simplex

$$S = \{p \in \mathbf{R}^n : p \geqq 0, e^*p = 1\}. \tag{5}$$

If p is a stationary solution of (2), then

$$PFp = p^*Fp \cdot p. \tag{6}$$

If $p > 0$ (componentwise), then

$$Fp = ce \tag{7}$$

with $c = p^*Fp$. On the other hand if (7) has a positive solution, then it can be normalized to give $e^*p = 1, p^*Fp = c$.

We observe that to any of the faces of S corresponds a model of the form (2) with lower dimension, which is obtained by setting some components equal to zero. These reduced models describe populations in which some of alleles are not present. If p is a stationary point on one of the faces, then we can reorder the components to obtain $p^* = (q^*, \ 0)$. Then we choose corresponding partitions

$$p = \begin{bmatrix} q \\ 0 \end{bmatrix}, \quad e = \begin{bmatrix} e_1 \\ e_2 \end{bmatrix}, \quad F = \begin{bmatrix} F_{11} & F_{12} \\ F_{21} & F_{22} \end{bmatrix}. \tag{8}$$

For such a stationary state we find

$$F_{11}q = q^*F_{11}q \cdot e_1. \tag{9}$$

The pure states of the form $(0, \dots, 0, 1, 0, \dots, 0)$ are always stationary. In general there may be $2^n - 1$ stationary solutions. A polymorphism exists if (7) has a positive solution p. It is well known that p is exponentially stable if and only if the matrix F has $n - 1$ negative eigenvalues. Of course the spectral radius is a positive eigenvalue.

2. **The mean viability**. The function $W: S \to \mathbf{R}_+$ given by

$$W(p) = p^*Fp \tag{10}$$

is called the mean viability. It serves as a Lyapunov function for the system (2) since

$$\frac{dW(p(t))}{dt} = G(p) \geqq 0 \tag{11}$$

where

$$G(p) = 2(p^*FPFp - (p^*Fp)^2). \tag{12}$$

The quantity $G(p)$ is in fact non-negative and vanishes if and only if p is stationary (see [3], [4]). We show that W is a negative definite form on S if an exponentiable stable polymorphism $\bar{p}$ exists. With $\bar{p} = (\bar{p}_j)$ define $q_j = (q_j)$, $q_j = \bar{p}_j^{1/2}$, and $Q = (q_j\delta_{jk})$. From $F\bar{p} = ce$, $c = \bar{p}^*F\bar{p}$, follows $QFQq = cq$, $(QFQ - \alpha qq^*)q = (c - \alpha)q$.

Since F has $n - 1$ negative eigenvalues, so has QFQ (by Sylvester's inertia theorem), and $QFQ - \alpha qq^*$ has n negative eigenvalues if we choose $\alpha > c$. Again by Sylvester's theorem, $F = F - \alpha ee^*$ has n negative eigenvalues. For variations in S, i.e., for vectors u with $e^*u = 0$, we have

$$u^*Fu = u^*(F - \alpha ee^*)u = u^*Fu. \tag{13}$$

If F has one positive and $n - 1$ negative eigenvalues, then every symmetric submatrix of order k has one positive and $k - 1$ negative eigenvalues. This fact follows easily from the Weyl inequalities and the positivity of F.

Define a function $V: \mathbf{R}_+^n - \{0\} \to \mathbf{R}_+$,

$$V(p) = \frac{p^*Fp}{(e^*p)^2}. \tag{14}$$

On S we have $V(p) = W(p)$. The derivative is

$$V'(p) = \frac{2}{e^*p}\left[\frac{p^*F}{e^*p} - V(p)e^*\right]. \tag{15}$$

At an equilibrium $\bar{p} \in S$, $\bar{p}^* = (q^*, 0)$

$$(V'(\bar{p}))^* = \begin{bmatrix} F_{11}q - q^*F_{11}q \cdot e_1 \\ F_{21}q - q^*F_{11}q \cdot e_2 \end{bmatrix}. \tag{16}$$

In view of (9) the first component vanishes, the vector q is stationary with respect to the face of S in which it is contained.

We know that $V = W$ is a uniformly concave function on S, since the corresponding $(n - 1)$-dimensional form has all negative eigenvalues. Furthermore the maximum is assumed at the polymorphism which is an interior point of S. Thus the derivatives with respect to those components vanishing in p are positive, thus

$$F_{21}q - q^*F_{11}q \cdot e_2 > 0. \tag{17}$$

We linearize the differential equation at p to obtain

$$\dot{y} = PFy + YFp - 2p^*Fy \cdot p - p^*Fp \cdot y.$$

Decompose $y = (y_1, y_2)$, then

$$\dot{y}_1 = Q(F_{11}y_1 + F_{12}y_2) + Y_1F_{11}q - 2qq^*F_{11}y_1 - q^*F_{11}q \cdot y_1 \tag{18}$$

$$\dot{y}_2 = Y_2F_{21}q - q^*F_{11}q \cdot y_2. \tag{19}$$

Thus y_2 satisfies a linear equation, where the matrix is a diagonal matrix with positive entries.

3. **A spatial Lyapunov function.** Consider a particular solution $p(x, t)$ of the initial value problem and define $w: \Omega \times (0, \infty) \to (0, \max W]$ by

$$w(x, t) = W(p(x, t)). \tag{20}$$

Then

$$\begin{aligned} w_{x_i} &= 2p^*Fp_{x_i} \\ w_{x_ix_i} &= 2p^*_{x_i}Fp_{x_i} + 2p^*Fp_{x_ix_i} \\ \Delta w &= 2\sum_{i=1}^{m} p^*_{x_i}Fp_{x_i} + 2p^*F\Delta p \\ w_t &= 2p^*Fp_t, \end{aligned}$$

and thus in Ω

$$w_t - \Delta w = G(p) - 2\sum_{i=1}^{m} p^*_{x_i}Fp_{x_i}, \tag{21}$$

and on $\partial\Omega$

$$\partial w/\partial n\mathbf{n} = 0. \tag{22}$$

The solution $p(x, t)$ of (3) (4) is globally bounded, the nonlinearity is analytic. Therefore the path $\{p(\cdot, t), t \geqq t_0 > 0\}$ is compact in $C^2(\Omega \to \mathbf{R}^n)$. Since w is a quadratic form, evaluated along the solution, also the path $\{w(\cdot, t): t \geqq t_0 > 0\}$ is compact in $C(\Omega \to \mathbf{R})$.

We define the spatial integral

$$M(t) = \int_\Omega w(x, t)\,dx\,/\,|\Omega|. \tag{23}$$

Integrating (21) we find

$$M(t) \geqq 0. \tag{24}$$

$M(t)$ is bounded above by max W, therefore it converges from below towards some $\bar{M}$.

For every $t \geqq 0, \tau \geqq 0$ the function $w(x, t + \tau)$ is bounded below by the solution $v(x, t, \tau)$ of

$$v_\tau = \Delta v \quad \text{in } \Omega, \qquad v_{\mathbf{n}} = 0 \qquad \text{on } \partial\Omega \tag{25}$$
$$v(x, t, 0) = w(x, t).$$

The function v approaches a constant,

$$v(x, t, \tau) \to M(t) \tag{26}$$

thus

$$\liminf_{\tau \to \infty} w(x, t + \tau) \geqq M(t)$$
$$\bar{w}(x) = \liminf_{t \to \infty} w(x, t) \geqq \bar{M}. \tag{27}$$

A simple argument shows

$$\lim_{t \to \infty} w(x, t) = \bar{M} \quad \text{for } x \in \Omega. \tag{28}$$

(Let $x = x_0 \in \Omega$ and a sequence $t_j \to \infty$ be such that $w(x, t_j) \to \chi > \bar{M}$. Then choose a subsequence t_{jk} such that $w(x, t_{jk}) \to \tilde{w}(x)$ uniformly in Ω. Then $\tilde{w}(x_0) = \chi > \bar{M}$, $\tilde{w}(x) \geqq \bar{M}$, $\int_\Omega \tilde{w}(x) dx = \bar{M}$, which cannot be.) Thus $w(\cdot, t)$ converges pointwise to a constant. Since the path is compact in C^2, we can choose any sequence $t_j \to \infty$ and find a subsequence t_{jk} such that $w(\cdot, t_{jk}) \to \tilde{w}(x)$. But then follows $\tilde{w}(x) \equiv \bar{M}$. Thus $w(\cdot, t) \to \bar{M}$ in $C^2(\Omega \to \mathbf{R})$. Then it follows from (21) and $\Delta w \to 0$, that

$$G(p) \to 0 \tag{29}$$

$$\sum_{i=1}^{n} p_{x_i}^* F p_{x_i} \to 0. \tag{30}$$

Again, consider any sequence $t_j \to \infty$. Then there is a subsequence t_{jk} such that $p(\cdot, t_{jk})$ converges in C^2. By (30) all first derivatives go to zero, thus $p(\cdot, t_{jk})$ approximates a constant. By (29) this constant is a stationary solution of (2).

Thus the limit points of $p(\cdot, t)$ are spatially homogeneous stationary points. Convergence follows from the fact that all stationary points of (2) are isolated (see §2).

Now assume $p_j(x, 0) \not\equiv 0$ for $j = 1, \ldots, n$. Then for small t and thus for all finite $t > 0$ we have $p(x, t) > 0$ for all $x \in \Omega$. Thus for every $t > 0$ the set $\{p(x, t) \colon x \in \Omega\}$ is a compact subset in the interior of S. Assume $p(\cdot, t)$ converges to a stationary state $\tilde{p} \in \partial S$. By uniform convergence we have that for every $\varepsilon > 0$ there is t_ε such that $|p(x, t) - \tilde{p}| < \varepsilon$ for all $x \in \Omega$

and $t \geqq t_\varepsilon$. But then for those components which vanish in $\bar{p}$ we have an equation (see §2).

$$v_t = \Delta v + Dv + o(\varepsilon).$$

Since $D > 0$ those components do not go to zero.

COROLLARY. *Instead of the boundary condition* (4) *assume the equilibrium Dirichlet condition on* $\partial\Omega$

$$p(x, t) = \bar{p} \tag{31}$$

where $\bar{p}$ *is the stable polymorphism. Then* $p(x, t) \to \bar{p}$ *uniformly.*

PROOF. The only necessary modification is the integration of (21),

$$\begin{aligned} \int_\Omega \Delta w(x, t)\, dx &= \int_{\partial\Omega} \frac{\partial w}{\partial \mathbf{n}}\, dx = 2 \int_{\partial\Omega} p^* F p_\mathbf{n} dx \\ &= 2\int_{\partial\Omega} \bar{p}^* F p_\mathbf{n} dx = 2 \int_{\partial\Omega} e^* p_\mathbf{n} dx \cdot \bar{p}^* F \bar{p} = 0. \end{aligned} \tag{32}$$

One observes that also in this case $\int w(x, t)\, dx$ is non-decreasing, reflecting the fact that max $W = W(\bar{p})$.

Integral equations. To a certain extent the results can be carried over to an equation where the diffusion term has been modified by a convolution or a more general integral term. Let Ω be bounded and open, let K: $\bar{\Omega} \times \bar{\Omega} \to \mathbf{R}_+$ be continuous, non-negative, and symmetric with

$$\int_\Omega K(x, y)\, dx = 1 \quad \text{for all } x \in \bar{\Omega}. \tag{33}$$

Then define D: $C(\bar{\Omega}) \to C(\bar{\Omega})$ by

$$\begin{aligned} (Du)(x) &= (Ku - u)(x) \\ &= \int_\Omega K(x, y.) u(y) dy - u(x). \end{aligned} \tag{34}$$

Then consider the equation (D acts componentwise)

$$p_t(x, t) = (Dp)(x, t) + \chi(\Delta p)(x, t) + PFp - p^* Fp \cdot p. \tag{35}$$

where $\chi > 0$ is a constant.

THEOREM 2. *The assertion of Theorem* 1 *remains valid also for equation* (35).

PROOF. We define again $w(x, t) = W(p(x, t))$. Then

$$w_t - Dw - \chi \Delta w = G(p) - \chi 2 \sum_{i=1}^{m} p_{x_i}^* F p_{x_i} + 2p^* FDp - Dw. \tag{36}$$

But (argument t omitted)

$$
\begin{aligned}
&2(p^*FDp)(x) - (Dw)(x) \\
&= 2p^*(x)F\int K(x, y)p(y)dy - 2p^*(x)Fp(x) \\
&\quad - \int K(x, y)p^*(y)Fp(y)dy + p^*(x)Fp(x) \\
&= - \int K(x, y)p^*(y)Fp(y)dy + 2\int K(x, y)p^*(x)Fp(y)dy \\
&\quad - \int K(x, y)p^*(x)Fp(x)dy \\
&= - \int K(x, y)(p^*(y) - p^*(x))F(p(y) - p(x))dy.
\end{aligned}
$$

We have used that K is symmetric. Thus each term on the right-hand side of (36) is non-negative. The first term vanishes for stationary solutions of the ordinary differential equation, the second and third term vanish for constant functions. Also we see $\int_\Omega (Du)(x)\, dx = 0$ for any $u \in C(\bar{\Omega})$. The rest of the proof is essentially the same as for Theorem 1. The limiting case $\chi = 0$, the pure integral equation, require some more detailed attention.

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