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ON A CLASS OF ELLIPTIC SINGULAR PERTURBATIONS WITH APPLICATIONS IN POPULATION GENETICS

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ABSTRACT

With the maximum principle for differential equations asymptotic estimates are made for a class of linear elliptic singular perturbation problems with resonant turning point behaviour in some of the independent variables. The method is applied to stationary solutions of the Kolmogorov backward equation from population genetics.

KEY WORDS & PHRASES: *maximum principle, elliptic singular perturbation, population genetics.*

*) This report will be submitted for publication elsewhere.

1. INTRODUCTION

In this paper we consider elliptic singular perturbations of first order differential operators vanishing at an interior surface of a domain. For Dirichlet problems of this type we construct asymptotic solutions and prove their validity by using the maximum principle.

DE JAGER [4] considered a similar class of problems in which a parabolic boundary layer occurs at the interior surface. We will investigate the case where the first order operator has the opposite sign giving arise to ordinary boundary layers along the boundaries of the domain. For this problem standard singular perturbation techniques do not lead to a uniquely determined outer solution. Similar to the method for elliptic singular perturbation problems with turning points of GRASMAN & MATKOWSKY [3], we pose an additional condition, so that a unique outer solution can be derived. Adding boundary layer corrections we obtain a uniform asymptotic approximation; its validity is proved by estimating asymptotically the remainder term. This proof, based on the maximum principle for elliptic differential equations, differs from the ones given by DE JAGER [4] and ECKHAUS & DE JAGER [1], as near the surface where the first order operator vanishes, the approximate solution varies in the normal direction in a way unsuitable for applying the maximum principle. In this paper we construct barrier functions that also take into account the behaviour of the asymptotic solution along the surface, so that the maximum principle will lead to meaningful results. This method requires a higher order accuracy in a neighbourhood of the surface.

The type of elliptic singular perturbations we deal with occur in problems from population genetics. The elliptic perturbation models the effect of random mating, while the parameter ε denotes the inverse of the population size. We will not attempt to give a complete description of the class of genetic problems to which our method applies, but confine ourselves to two examples: a one-locus model with migration and a two-locus model. Our asymptotic results hold for a subdomain of the continuous state space of possible genetic distributions; the elliptic equations for these problems degenerate at the boundaries of the full domain. In general existence of solutions of this last type of Dirichlet problems is not guaranteed; see FRIEDMAN [2,p.308].

2. FORMULATION OF THE MATHEMATICAL PROBLEM

We consider the Dirichlet problem for a function $\phi(x_1,\ldots,x_k,y_1,\ldots,y_m;\varepsilon)$ satisfying the linear uniformly elliptic differential equation

$$(2.1)\qquad L_\varepsilon\phi \equiv \varepsilon L_2 + L_1\phi = f(x,y;\varepsilon) \quad \text{in } \Omega$$

with boundary values

$$(2.2)\qquad \phi = h(x,y;\varepsilon) \quad \text{on } \partial\Omega,$$

where ε is a small positive parameter. The domain Ω is a bounded domain in $\mathbb{R}^n$, $n = k+m$, of a form such that

$$(2.3)\qquad (x,y) \in \Omega \quad \text{implies} \quad (x,0) \in \Omega.$$

The first and second order differential operators L_1 and L_2 have coefficients that are Hölder continuous in $\bar{\Omega}$,

$$(2.4)\qquad L_1 \equiv \sum_{j=1}^{m} b_j \frac{\partial}{\partial y_j},$$

$$(2.5)\qquad L_2 \equiv \sum_{i,j=1}^{k} \alpha_{ij} \frac{\partial^2}{\partial x_i \partial x_j} + \sum_{i=1}^{k}\sum_{j=1}^{m} 2\beta_{ij} \frac{\partial^2}{\partial x_i \partial y_j} + \sum_{i,j=1}^{m} \gamma_{ij} \frac{\partial^2}{\partial y_i \partial y_j}.$$

Furthermore, it is assumed that

$$(2.6)\qquad b(x,y) = 0 \quad \text{iff} \quad |y| = 0,$$

$$(2.7)\qquad \theta(x,y)\cdot b(x,y) \le 0 \quad \text{on } \partial\Omega,$$

$$(2.8)\qquad \sum_{j=1}^{m} b_j(x,y)y_j \le -L|y|^2 \quad \text{in } \bar{\Omega},$$

where $\theta(x,y)$ is the outward normal to $\partial\Omega$, L a positive constant independent of ε and $|y|$ the Euclidean length of y. The behaviour of the solution depends strongly upon the first term of L_2 near the surface $|y| = 0$. We define the bounded domain $\Gamma \subset \mathbb{R}^k$ by

$$(2.9) \qquad \Gamma = \{x \mid (x,0) \in \Omega\}$$

and state the following lemma, which is easily proved from the definition of ellipticity; see for example [9,p.56].

LEMMA 2.1. *Let the differential operator* L_2 *be uniformly elliptic in* Ω*; then the operator*

$$(2.10) \qquad \sum_{i,j=1}^{k} \alpha_{ij}(x,0) \frac{\partial^2}{\partial x_i \partial x_j}$$

is uniformly elliptic in Γ.

3. THE MAXIMUM PRINCIPLE

For the elliptic operator L_ε given by (2.1) we formulate the maximum principle as follows: a twice continuously differentiable function ϕ satisfying $L_\varepsilon \phi > 0$ in a domain Ω cannot have a maximum in Ω; see PROTTER & WEINBERGER [9,p.61]. The following lemma is a direct consequence of the maximum principle.

LEMMA 3.1. *If the twice continuously differentiable functions* ϕ *and* ψ *satisfy*

$$(3.1) \qquad |L_\varepsilon \phi| < -L_\varepsilon \psi \quad \text{in } \Omega$$

and if $|\phi| \le \psi$ *on* $\partial\Omega$*, then* $|\phi| \le \psi$ *in* $\bar{\Omega}$.

PROOF. From the maximum principle and (3.1) we deduce that $\phi-\psi$ cannot have a maximum in Ω and since $\phi-\psi \le 0$ on $\partial\Omega$, we conclude that $\phi-\psi \le 0$ in $\bar{\Omega}$. Similarly, $-\phi-\psi$ does not have a maximum in Ω and $-\phi-\psi \le 0$ at $\partial\Omega$, so that $-\phi-\psi \le 0$ in $\bar{\Omega}$. Combining these results we obtain $|\phi| \le \psi$ in $\bar{\Omega}$. □

In the next step we give an asymptotic estimate for the solution of (2.1), (2.2). For that purpose use will be made of so-called barrier functions: Lemma 3.1 is applied with a given function ψ as barrier function.

THEOREM 3.1. *Let the twice continuously differentiable function* ϕ *satisfy*

$$(3.2)\qquad |L_\varepsilon \phi| \le M\{|y|^2 + \varepsilon\} \quad \textit{in } \Omega$$

and $|\phi| \le N$ *on* $\partial\Omega$ *with* M *and* N *positive constants independent of* ε. *Then a constant* K *independent of* ε *exists such that*

$$(3.3)\qquad |\phi| \le K \quad \textit{in } \bar{\Omega}.$$

PROOF. We introduce the barrier function

$$(3.4)\qquad \psi(x,y) = -U(x) + R|y|^2 + S,$$

in which we choose $R > M/L$ with L given by (2.8) and U(x) such that

$$(3.5)\qquad \sum_{i,j=1}^{k} \alpha_{ij}(x,0)\frac{\partial^2 U}{\partial x_i \partial x_j} = 2M + 2R \sum_{i,j=1}^{k} \gamma_{ij}(x,0) \quad \text{in } \Gamma.$$

Since the coefficients α_{ij} and γ_{ij} are Hölder continuous, there exists a positive constant F, such that

$$(3.6)\qquad \sum_{i,j=1}^{k} \alpha_{ij}(x,y)\frac{\partial^2 U}{\partial x_i \partial x_j} - 2R \sum_{i,j=1}^{k} \gamma_{ij}(x,y) > -F \quad \text{in } \Omega.$$

For $|y|^2 \ge (1 + F/M)\varepsilon$ we have

$$(3.7)\qquad -L_\varepsilon\psi = \varepsilon\left\{\sum_{i,j=1}^{k} \alpha_{ij}\frac{\partial^2 U}{\partial x_i \partial x_j} - 2R\sum_{i,j=1}^{m}\gamma_{ij}\right\} - 2R\sum_{j=1}^{m} b_j y_j >$$

$$> -\varepsilon F + 2RL|y|^2 \ge M(|y|^2 + \varepsilon).$$

Because of the Hölder continuity of α_{ij} and γ_{ij} at $|y| = 0$ the following estimate can be made for $|y|^2 < \varepsilon(1 + F/M)$ and ε sufficiently small; see (3.5).

$$(3.8)\qquad \sum_{i,j=1}^{k} \alpha_{ij}(x,y)\frac{\partial^2 U}{\partial x_i \partial x_j} - 2R \sum_{i,j=1}^{m} \gamma_{ij}(x,y) > M.$$

Thus, for $|y|^2 < \varepsilon(1 + F/M)$ we have

$$(3.9)\qquad -L_\varepsilon\psi > \varepsilon M + 2RL|y|^2 > M(|y|^2 + \varepsilon).$$

Finally S of (3.4) is taken sufficiently large such that

(3.10) $\psi \geq N$ on $\partial\Omega$.

From (3.7) and (3.9) we conclude $|L_\varepsilon\phi| \leq -L_\varepsilon\psi$ in Ω, while from (3.10) it follows that $|\phi| \leq \psi$ on $\partial\Omega$. Using Lemma 3.1 we obtain the estimate $|\phi| \leq \psi$ in $\bar{\Omega}$. Since the function U(x) as well as the domain Ω is bounded, a positive constant K can be found such that $\phi \leq K$ in $\bar{\Omega}$, which completes the proof of the theorem. □

COROLLARY 3.1. *Let the twice continuously differentiable function* $\phi(x,y;\varepsilon)$ *satisfy*

(3.11) $$|L_\varepsilon\phi| \leq M(|y|^2 + \varepsilon)\delta_f(\varepsilon) \quad \textit{in } \Omega$$

and $|\phi| \leq N\delta_h(\varepsilon)$ *on* $\partial\Omega$ *with* δ_f *and* δ_h *continuous positive functions for* $0 < \varepsilon < \varepsilon_0$ *(*ε_0 *sufficiently small) and with* M *and* N *independent of* ε. *Then a constant* K *independent of* ε *exists such that in* $\bar{\Omega}$

(3.12a) $$|\phi| \leq K\delta_f(\varepsilon) \quad \textit{if} \quad \delta_h/\delta_f \textit{ is bounded for } \varepsilon \to 0,$$

or

(3.12b) $$|\phi| \leq K\delta_h(\varepsilon) \quad \textit{if} \quad \delta_f/\delta_h \textit{ is bounded for } \varepsilon \to 0.$$

PROOF. As a barrier function we take

$$\psi(x,y;\varepsilon) = \{-U(x) + R|y|^2 + S\}\delta_f(\varepsilon) + S\delta_h(\varepsilon)$$

and proceed as in the proof of Theorem 3.1. □

Thus, Corollary 3.1 produces an asymptotic estimate for the solution of (2.1), (2.2) from the asymptotic estimates of the data f and h.

4. ASYMPTOTIC APPROXIMATION

Let us assume that by some matched asymptotic expansion procedure we have found a formal uniformly valid asymptotic approximation, say ϕ_{as}, of ϕ satisfying (1.1) and (1.2). Its validity is proved as follows. Substitution of $\phi = \phi_{as} + R$ into (1.1) and (1.2) yields

(4.1a) $\quad L_\varepsilon R = f - L_\varepsilon \phi_{as} \quad$ in Ω,

(4.1b) $\quad R = h - \phi_{as} \quad$ on $\partial\Omega$.

If we are able to show that the right-hand sides of (4.1) and (4.2) have the appropriate asymptotic behaviour, then by application of Corollary 3.1 the smallness of the remainder term R is established. It is to be expected that the solution of (1.1), (1.2) has a boundary layer structure, which may complicate the construction of a suitable function ϕ_{as} as its derivatives may be of a larger order of magnitude in the boundary layer. This difficulty is surmounted by including (small) boundary layer corrections to the asymptotic approximation. Depending on the shape of the domain different types of boundary layers may arise.

In the sequel we restrict ourselves to the case $m = 1$ for convex domains with nowhere characteristic boundaries, so that inequality (2.7) is strictly satisfied. These domains have the form

(4.3) $\quad \Omega = \{(x,y) \mid -p^-(x) < y < p^+(x),\ x \in \Gamma\}$

with $p^\pm(x) > 0$ in Γ, $p^\pm(x) = 0$ on $\partial\Gamma$ and because of our method of approximation $p^\pm \in C^3(\bar{\Gamma})$. We consider the Dirichlet problem for the function $\phi(x_1,\ldots,x_k,y;\varepsilon)$ satisfying

(4.4) $$\varepsilon\left[\sum_{i,j=1}^{k} \alpha_{ij} \frac{\partial^2\phi}{\partial x_i \partial x_j} + \sum_{i=1}^{k} 2\beta_i \frac{\partial^2\phi}{\partial x_i \partial y} + \gamma \frac{\partial^2\phi}{\partial y^2}\right] - y\frac{\partial\phi}{\partial y} = 0$$

with $\alpha_{ij},\beta_i,\gamma \in C^\infty(\bar{\Omega})$. This problem is assumed to have continuous boundary values

(4.5) $\quad \phi(x,\pm p^\pm(x);\varepsilon) = h^\pm(x) \quad$ for $x \in \bar{\Gamma}$

with $h^\pm \in C^2(\bar{\Gamma})$. The asymptotic approximation of ϕ has the form

(4.6) $\quad \phi_{as}(x,y;\varepsilon) = U_0(x) + V_0^+(x,y;\varepsilon) + V_0^-(x,y;\varepsilon)$

with $U_0(x)$ satisfying

(4.7a) $$\sum_{i,j=1}^{k} \alpha_{ij}(x,0) \frac{\partial^2 U_0}{\partial x_i \partial x_j} = 0 \qquad \text{in } \Gamma$$

(4.7b) $$U_0(x) = h(x) \qquad \text{on } \partial\Gamma,$$

and with

(4.8a) $$V_0^{\pm}(x,y;\varepsilon) = \tilde{h}^{\pm}(x)\exp\left[\frac{p^{\pm}(x)\{p^{\pm}(x)\mp y\}}{\varepsilon q^{\pm}(x)}\right],$$

(4.8b) $$q^{\pm} = \sum_{i,j=1}^{k} \frac{\partial p^{\pm}}{\partial x_i}\frac{\partial p^{\pm}}{\partial x_j}\alpha_{ij}^{\pm} \mp \sum_{i=1}^{k}\frac{\partial p^{\pm}}{\partial x_i}\beta_i^{\pm} + \gamma^{\pm}, \qquad \tilde{h}^{\pm} = h^{\pm} - U_0,$$

where $\alpha_{ij}^{\pm},\beta_i^{\pm},\gamma^{\pm} = \alpha_{ij},\beta_i,\gamma(x,\pm p^{\pm}(x))$.

<u>THEOREM 4.1</u>. *Let the function* $\phi(x_1,\ldots,x_k,y;\varepsilon)$ *satisfy* (4.4) *in the domain* Ω *defined by* (4.3) *with boundary values* (4.5). *Then there exists a positive constant* K *independent of* ε *such that*

(4.9) $$|\phi-\phi_{as}| \le K\varepsilon \qquad \text{in } \bar{\Omega}$$

with ϕ_{as} *given by* (4.6)-(4.8).

<u>PROOF</u>. We introduce the local coordinate $\eta = (p^{\pm}(x)\mp y)/\varepsilon$ and expand L_ε with respect to ε,

$$L_\varepsilon \equiv \varepsilon^{-1}M_0^{\pm} + M_1^{\pm} + M_2^{\pm} + \ldots ,$$

$$M_0^{\pm} \equiv q^{\pm}(x)\frac{\partial^2}{\partial\eta^2} - p^{\pm}(x)\frac{\partial}{\partial\eta},$$

while $M_m^{\pm}$, $m > 0$, is of the form

$$M_m^{\pm} \equiv \sum_{i,j=1}^{k} r_{ijm}^{\pm}(x)\frac{\partial^2}{\partial x_i\partial x_j} + \sum_{i=1}^{k} s_{im}^{\pm}(x)\frac{\partial^2}{\partial x_i\partial\eta} + t_m^{\pm}(x)\frac{\partial^2}{\partial\eta^2} + u_m^{\pm}(x)\frac{\partial}{\partial\eta} \qquad (r_{ij1} = 0).$$

We introduce additional boundary layer terms

(4.10) $$\tilde{\phi}_{as}(x,y;\varepsilon) = U(x) + V_0^{+}(x,\eta) + V_0^{-}(x,\eta) + \varepsilon\{V_1^{+}(x,\eta) + V_1^{-}(x,\eta)\} + \varepsilon^2\{V_2^{+}(x,\eta) + V_2^{-}(x,\eta)\}$$

with V_i satisfying

(4.11a) $M_0^{\pm}V_0^{\pm} = 0,$ $V_0^{\pm}(x,0) = \tilde{h}^{\pm}(x),$

(4.11b) $M_0^{\pm}V_1^{\pm} = -M_1^{\pm}V_0^{\pm},$ $V_1^{\pm}(x,0) = 0,$

(4.11c) $M_0^{\pm}V_2^{\pm} = -M_1^{\pm}V_1^{\pm} - M_2^{\pm}V_0^{\pm},$ $V_2^{\pm}(x,0) = 0,$

(4.11d) $V_i^{\pm}(x,\eta) \to 0$ as $\eta \to \infty,$ $i = 0,1,2.$

The expression for $V_0^{\pm}$ we gave in (4.8); $V_i^{\pm}$ with $i > 0$ is of the type

(4.12) $$V_i^{\pm}(x,\eta) = \sum_{j=1}^{2i} A_{ij}(x)\eta^j \exp\left\{-\frac{p^{\pm}(x)\eta}{q^{\pm}(x)}\right\}.$$

Let $\tilde{R} = \phi-\tilde{\phi}_{as}$. By straightforward calculation one finds that a constant $\tilde{M}$ exists such that $|L_\varepsilon\tilde{R}| \le M\varepsilon^2$ in Ω, while also $|\tilde{R}| \le \tilde{N}\varepsilon$ on $\partial\Omega$ for some $\tilde{N} > 0$. From Corollary 3.1 we conclude that $|\tilde{R}| \le \tilde{K}\varepsilon$ in $\bar{\Omega}$ for some $\tilde{K}$. Finally, the proof is completed by checking the additional boundary layer terms $\varepsilon^i V_i^{\pm}$, $i = 1,2$ which are $O(\varepsilon)$ in $\bar{\Omega}$. □

REMARKS. When making higher order approximations, one has to take into account corner layer contributions in an ε-neighbourhood of $(x,0)$, $x \in \partial\Gamma$. The higher order terms for the outer- and boundary layer expansions follow from the fundamental iteration process (see [1]) with an additional equation of the type (4.7a) for the terms of the outer expansion.

5. APPLICATION TO PROBLEMS IN POPULATION GENETICS

A population consisting of different genotypes with random mating can be described by stochastic as well as by deterministic mathematical models. We will deal with a deterministic model, a diffusion equation known as the Kolmogorov backward equation, being the limit of a stochastic model as the population size increases indefinitely; see MARUYAMA [6,p.221]. Our asymptotic analysis applies to the stationary solution of the Kolmogorov backward equation of a certain class of genetic problems. We will give two illustrating examples.

EXAMPLE 5.1. We consider a diploid population with two alleles a and A at one locus divided into two colonies of each N individuals. Let p_i denote the fraction of allele A at colony i. Assuming random mating without selection or mutation and with nett migration proportional to the difference in p_i, we obtain the Kolmogorov backward equation

$$\frac{\partial\phi}{\partial t} = \frac{p_1(1-p_1)}{2N}\frac{\partial^2\phi}{\partial p_1^2} + \frac{p_2(1-p_2)}{2N}\frac{\partial^2\phi}{\partial p_2^2} - \mu(p_1-p_2)\frac{\partial\phi}{\partial p_1} + \mu(p_1-p_2)\frac{\partial\phi}{\partial p_2}, \tag{5.1}$$

where $\phi(p_1,p_2,t)$ denotes the probability density of the fractions p_i at time t. This equation holds in the square $S = \{(p_1,p_2) \mid 0 < p_1,\ p_2 < 1\}$. Substitution of

$$x = p_1 + p_2 - 1, \qquad y = p_1 - p_2 \tag{5.2}$$

transforms the stationary equation of (5.1) into

$$\varepsilon\left[(1-x^2-y^2)\left(\frac{\partial^2\phi}{\partial x^2} + \frac{\partial^2\phi}{\partial y^2}\right) - 8xy\,\frac{\partial^2\phi}{\partial x\partial y}\right] - y\,\frac{\partial\phi}{\partial y} = 0, \qquad \varepsilon = 1/(4\mu N), \tag{5.3}$$

in a domain $\Omega = \{(x,y) \mid |x\pm y| < 1\}$. We consider the Dirichlet problem of (5.3) with $0 < \varepsilon << 1$ for a subdomain $\Omega_\delta \subset \Omega$ of the form

$$\Omega_\delta = \{(x,y) \mid |y| < 1 - \sqrt{x^2-\delta^2+2\delta},\ |x| < 1-\delta\} \tag{5.4}$$

with boundary values h on $\partial\Omega_\delta$. Equation (5.2) relates a point $(x,y) \in \bar{\Omega}$ to the distribution of alleles at some time. Let $p_{\delta,\varepsilon}(x,y;x_0,y_0)$ denote the probability density of leaving Ω_δ the first time at $(x,y) \in \partial\Omega_\delta$ if starting at $(x_0,y_0) \in \Omega_\delta$. The following relation between $p_{\delta,\varepsilon}$ and ϕ, is known to be valid

$$\int_{\partial\Omega_\delta} p_{\delta,\varepsilon}(x,y;x_0,y_0)h(x,y;\varepsilon)d\sigma = \phi(x_0,y_0;\varepsilon) \tag{5.5}$$

where $d\sigma$ denotes a positive measure on $\partial\Omega_\delta$; see MATKOWSKY & SCHUSS [7]. If (x_0,y_0) is chosen in the outer region of Ω_δ the system leaves Ω_δ at either a point of $\partial\Omega_\delta$ with $x < -1+2\delta$ or with $x > 1-2\delta$ with probabilities that tend to

$$\text{(5.6ab)} \qquad \text{pr(left exit)} = \frac{1-\delta-x_0}{2-2\delta}, \qquad \text{pr(right exit)} = \frac{1-\delta+x_0}{2-2\delta}$$

as $\varepsilon \to 0$. This result is derived from (5.5) by choosing appropriate boundary values h. As $\delta \to 0$ this asymptotic result tends to the exact solution of the problem for the full domain with arbitrary $\varepsilon > 0$.

EXAMPLE 5.2. A population of N diploid individuals, each characterized by its genotype with respect to two loci and with two alleles at each locus, is described by the fractions of gametes of types AB, Ab, aB and ab. Let these fractions be denoted by p_i, $i = 1,2,3,4$. In case of random mating such system is modeled by the Kolmogorov backward equation

$$\text{(5.7)} \qquad \frac{\partial\phi}{\partial t} = \sum_{i=1}^{3} \frac{p_i(1-p_i)}{4N} \frac{\partial^2\phi}{\partial p_i^2} - \sum_{i=1}^{2} \sum_{j=i+1}^{3} \frac{p_i p_j}{2N} \frac{\partial^2\phi}{\partial p_i \partial p_j} +$$

$$- \mu\{p_1(1-p_1-p_2-p_3) - p_2p_3\}\left(\frac{\partial\phi}{\partial p_1} - \frac{\partial\phi}{\partial p_2} - \frac{\partial\phi}{\partial p_3}\right)$$

in a domain $S = \{(p_1,p_2,p_3) \mid p_i > 0,\ p_1+p_2+p_3 < 1\}$. Substitution of

$$\text{(5.8)} \qquad p_1 = x_1x_2 + y, \quad p_2 = x_1(1-x_2) - y, \quad p_3 = (1-x_1)x_2 - y$$

transforms the equation for the stationary problem into

$$\text{(5.9)} \qquad \varepsilon\left[\sum_{i=1}^{2}\left\{x_i(1-x_i)\frac{\partial^2\phi}{\partial x_i^2} + 2y(1-2x_i)\frac{\partial^2\phi}{\partial x_i \partial y}\right\} + 2y\,\frac{\partial^2\phi}{\partial x_1 \partial x_2} + \right.$$

$$\left. + \{x_1x_2(1-x_1)(1-x_2) + y(1-2x_1)(1-2x_2) - y^2\}\frac{\partial^2\phi}{\partial y^2}\right] - y\,\frac{\partial\phi}{\partial y} = 0,$$

$$\varepsilon = 1/(2+4N\mu),$$

while the domain S transforms into a domain Ω satisfying (2.3), (2.7) and (2.8). Again we consider the Dirichlet problem of (5.9) with $0 < \varepsilon \ll 1$ for a subdomain $\Omega_\delta \subset \Omega$ with $\partial\Omega_\delta$ bounded away from $\partial\Omega$ and with $\partial\Omega_\delta \to \partial\Omega$ as $\delta \to 0$. In the limit $\varepsilon \to 0$ the probability of leaving Ω_δ at some point of $\partial\Omega_\delta$, if starting at the outer region of Ω_δ, depends according to formula (5.5) entirely on the function $U(x_1,x_2)$ satisfying

$$(5.10a)\qquad x_1(1-x_1)\frac{\partial^2 U}{\partial x_1^2} + x_2(1-x_2)\frac{\partial^2 U}{\partial x_2^2} = 0 \quad \text{in} \quad \Gamma_\delta = \{(x_1,x_2) \mid (x_1,x_2,0) \in \Omega_\delta\}$$

$$(5.10b)\qquad U = h \quad \text{on} \quad \partial\Gamma_\delta,$$

where h is some appropriately chosen boundary value. Using this result one can prove that for $\varepsilon \to 0$ the two-locus system, if starting in the outer region of Ω, tends to linkage equilibrium ($y = 0$) along the subcharacteristic of L_1 by choosing an appropriate domain Ω_η with η arbitrary small but independent of ε; see Figure 1. For a more extensive discussion of this problem we refer to LITTLER [5].

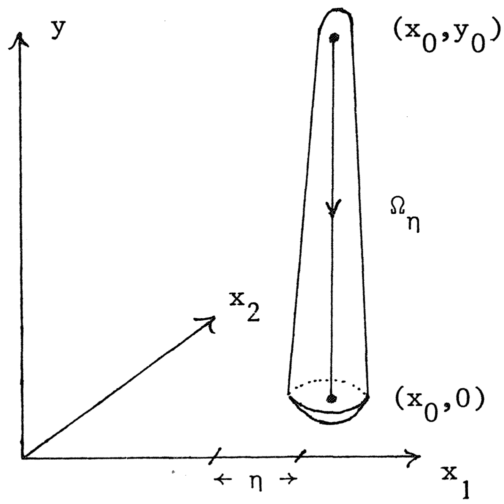

Fig. 1 The path towards linkage equilibrium as $\varepsilon \to 0$.

REMARKS. The asymptotic solution (5.10) for the outer region tends to a regular limit as $\delta \to 0$. From this limit expression one may derive the probability of first fixation of a specified allele in a same manner as we find the probability of loosing either one of the two alleles in Example 5.1 from (5.6) by letting $\delta \to 0$. Finally it is mentioned that for both examples more accurate approximations can be obtained by computing the next terms of the asymptotic expansion in ε as we remarked in Section 4. In Example 5.2 this would lead to new quantitative results for linkage disequilibrium when ε is small; see also OHTA & KIMURA [8].

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