

APPROXIMATE TRAVELING WAVES IN LINEAR REACTION-HYPERBOLIC EQUATIONS*

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Abstract. Linear reaction-hyperbolic equations arise in the transport of neurofilaments and membrane-bound organelles in axons. The profile of the solution was shown by simulations to be approximately that of a traveling wave; this was also suggested by formal calculations [M. C. Reed, S. Venakides, and J. J. Blum, *SIAM J. Appl. Math.*, 50 (1990), pp. 167–180]. In this paper we prove such a result rigorously.

Key words. axonal transport, hyperbolic equations, asymptotic approximations, traveling waves

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1. Introduction. This paper is concerned with the mathematical analysis of reaction-hyperbolic equations which describe transport of materials along a straight ray $l_0 = \{x : 0 < x < \infty\}$. The model is motivated from biology; it describes the transport of proteins and other molecules along the axon of a neuron. The proteins are formed near the nucleus of the cell, that is, at $x = 0$, and are transported to various locations along the axon, moving towards the synaptic end. Some material is also transported back, in retrograde motion. The transported materials include, for example, vesicles, membrane-bound organelles, and neurofilaments. Motor proteins attached to a vesicle (or a neurofilament) carry this cargo as they pace along a microtubule, step by step, energized by adenosine triphosphate (ATP) molecules. While some of the motors may be moving along a microtubule, others may be “resting” on-track, or even off-track, for a while. Thus the model has to deal with several populations of vesicles, depending in what state of motion they are. Earlier models of axonal transport were developed by Reed and Blum [10, 1, 2]. Using mass reaction laws and conservation of mass, they derived a system of hyperbolic equations and studied (mostly numerically) the particle concentration profile along the axon. The numerical results show that the transport of the particle concentrations has the profile of “approximate traveling waves”; experimentally, they arise from radiolabeling proteins in the soma and then observing the progress of the wave of label as it goes down the axon. The wave goes at constant velocity, but the front spreads so it is only approximately a traveling wave. Reed, Venakides, and Blum [11] considered a mathematical problem derived from such a transport model, in the biologically relevant case when the transition between the various populations is fast relative to the transport. Recent experimental results and computational models [4, 6, 8, 12, 13] also describe the dynamics of such transport.

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Consider, for example, two populations p and q , with transition rates

$$p \xrightleftharpoons[k_2]{k_1} q,$$

where q is moving and p is resting. Then the corresponding reaction-hyperbolic system describing their transport is given by

$$(1.1) \quad \begin{aligned} \varepsilon p_t &= -k_1 p + k_2 q, \\ \varepsilon (q_t + v_2 q_x) &= k_1 p - k_2 q, \end{aligned}$$

where ε is a small positive constant. The general transport problem for n species may be written in the form

$$(1.2) \quad \varepsilon (\partial_t + v_i \partial_x) p_i = \sum_{j=1}^n k_{ij} p_j \text{ for } 0 < x < \infty, t > 0, 1 \leq i \leq n,$$

where $k_{ij} \geq 0$ if $i \neq j$, the velocities v_i may be positive, negative, or zero, and

$$(1.3) \quad \sum_{i=1}^n k_{ij} = 0$$

by conservation of mass; thus,

$$k_{jj} = - \sum_{\substack{i=1 \\ i \neq j}}^n k_{ij}.$$

We need to complement (1.2) with initial conditions, and with boundary conditions at $x = 0$ for each p_i for which $v_i > 0$.

The special case

$$(1.4) \quad \begin{aligned} v_i &= 0, \quad 1 \leq i \leq n-1, \\ v_n &> 0, \\ p_i(x, 0) &= 0, \quad 1 \leq i \leq n, \quad 0 < x < \infty \\ p_n(0, t) &= 1, \quad t > 0, \end{aligned}$$

was studied by Reed, Venakides, and Blum [11]. They derived formulas which suggest that if we write p_n in the form

$$(1.5) \quad p_n(x, t) = Q_\varepsilon \left(\frac{x - vt}{\sqrt{\varepsilon}}, t \right),$$

then

$$(1.6) \quad Q_\varepsilon(s, t) \rightarrow Q_0(s, t) \text{ as } \varepsilon \rightarrow \infty,$$

where Q_0 is a solution of the heat equation

$$(1.7) \quad \begin{aligned} \partial_t Q_0 - \sigma^2 \partial_s^2 Q_0 &= 0, \quad -\infty < s < \infty, t > 0, \\ Q_0(s, 0) &= 1 \text{ if } s < 0, \\ Q_0(s, 0) &= 0 \text{ if } s > 0; \end{aligned}$$

the parameters v, σ^2 are computed from the v_j and k_{ij} . Formula (1.5), together with (1.6), (1.7), shows the approximate traveling wave profile for the transport of the concentration $p_n(x, t)$. The assertion (1.5) in [11] was only formal, but Brooks [3] developed a probabilistic model which enabled her to prove (1.5), in some sense, in the special case of (1.1).

One of the aims of the present paper is to give a rigorous proof of (1.6) for the case (1.4), or more generally for the case when all $v_j \geq 0$, and

$$p_i(x, 0) = \lambda_i q_0 \left(\frac{x}{\sqrt{\varepsilon}} \right), \quad 1 \leq i \leq n,$$

$$p_j(0, t) = \lambda_j \text{ if } v_j > 0,$$

where either $q_0 \equiv 0$ or $q_0(s)$ has compact support and $q_0(0) = 1$; here $(\lambda_1, \dots, \lambda_n)$ is a vector with positive components and, at the same time, a generator of the null space of the matrix (k_{ij}) .

The proof, given in section 3, is by PDE methods. Since, in the case $q_0 \equiv 0$, the function Q_0 is discontinuous only at the point $(0, 0)$ while Q_ε is discontinuous along the half-line $x = vt, t \geq 0$, we don't expect the convergence in (1.6) to be in the uniform sense, at least not near the origin $(0, 0)$; we shall prove the convergence in the weak L^r -sense for any $1 < r < \infty$.

In the case of (1.1) we shall prove, in section 2, in case q_0 is not identically zero, a "strong" convergence in (1.6), namely,

$$(1.8) \int_{-\frac{vT}{\sqrt{\varepsilon}}}^{\infty} (Q_\varepsilon(s, t) - Q_0(s, t))^2 ds + \int_0^T \int_{-\frac{vT}{\sqrt{\varepsilon}}}^{\infty} (\partial_s Q_\varepsilon(s, t) - \partial_s Q_0(s, t))^2 ds dt \leq C\sqrt{\varepsilon}.$$

This estimate also holds for the case (1.2) if $n = 2$, i.e., for $v_2 > 0$ and $v_1 \geq 0$.

In [9] Pinsky considered the system (1.2) for $-\infty < x < \infty, t > 0$, with initial data

$$p_i(x, 0) = f \left(\frac{x}{\sqrt{\varepsilon}} \right) \text{ for all } i, \quad -\infty < x < \infty,$$

and proved that

$$|Q_\varepsilon(s, t) - Q_0(s, t)| \leq C\sqrt{\varepsilon},$$

where $Q_0(s, t)$ is a solution of a heat equation as in (1.7) for $-\infty < s < \infty, t > 0$, with $Q_0(s, 0) = f(s), -\infty < s < \infty$. Pinsky's dynamical system is derived from a different (stochastic) model and, in particular, he assumes that $\sum_{j=1}^n k_{ij} = 0$ instead of (1.3). His proof is based on the construction of boundary layers and estimates via the Fourier transform in x ; that proof does not extend to the system (1.2), (1.4), not even in the case $n = 2$.

We conclude the introduction by pointing out several open problems:

- (i) Extend the strong convergence result to $n > 2$.
- (ii) Extend the results of this paper to the case of forward *and* backward velocities (i.e., anterograde and retrograde transport).
- (iii) Study the case where the kinetics is nonlinear.

2. The case $n = 2$. Throughout this paper we shall use the notation

$$D = \{(x, t) : 0 < x < \infty, t > 0\}.$$

Consider the process $p \xrightleftharpoons[k_2]{k_1} q$, where k_1, k_2 are positive constants, with dynamics

$$(2.1) \quad \varepsilon(p_t + v_1 p_x) = -k_1 p + k_2 q,$$

$$(2.2) \quad \varepsilon(q_t + v_2 q_x) = k_1 p - k_2 q$$

in D , where v_1, v_2 are given constant velocities, and ε is a small positive number. We intend to prove that, as $\varepsilon \rightarrow 0$, $q(x, t)$ will behave like $Q(\frac{x-v_2 t}{\sqrt{\varepsilon}}, t)$, where $Q(s, t)$ is a solution of a parabolic equation. Such a result requires, of course, that the initial values for q should be of the form $q_0(\frac{x}{\sqrt{\varepsilon}})$. We also choose initial data which are in equilibrium with respect to the process $p \xrightleftharpoons[k_2]{k_1} q$. Thus, we assume that

$$(2.3) \quad p(x, 0) = \frac{k_1}{k_2} q_0\left(\frac{x}{\sqrt{\varepsilon}}\right), \quad q(x, 0) = q_0\left(\frac{x}{\sqrt{\varepsilon}}\right) \quad \text{for } 0 \leq x < \infty.$$

We further assume that $v_1 \geq 0$, $v_2 > 0$, $v_1 \neq v_2$ and prescribe the boundary condition

$$(2.4) \quad q(0, t) = 1 \quad \text{for } t > 0.$$

If $v_1 = 0$, then no boundary conditions are imposed on p ; however, if $v_1 > 0$, then we prescribe the boundary condition $p(0, t) = \frac{k_2}{k_1}$ for $t > 0$.

We shall require that $q_0(s)$ is in C^4 ($0 \leq s < \infty$) and that

$$(2.5) \quad \begin{aligned} 0 \leq q_0(s) \leq 1 \text{ if } s > 0, \quad q_0(s) = 0 \text{ if } s > A_0 \text{ for some } A_0 < \infty, \\ q_0(0) = 1, \quad \partial_s^j q_0(s)|_{s=0} = 0 \text{ if } 1 \leq j \leq 4. \end{aligned}$$

The last two conditions ensure that the initial and boundary data fit at $(0, 0)$ up to order 4. Note that (2.5) implies that $0 \leq q_0(s) \leq 1$.

It will be convenient to first deal with the case

$$(2.6) \quad v_1 = 0.$$

However, in order not to repeat some of the calculations, we shall perform these calculations for general v_1 .

By standard ODE arguments we deduce that the solution (p, q) is continuously differentiable in \bar{D} , that $(\partial_x p, \partial_x q)$ satisfy the same system as (p, q) , and that

$$k_1 \partial_x p(x, 0) = k_2 \partial_x q(x, 0) = k_2 \partial_x q_0\left(\frac{x}{\sqrt{\varepsilon}}\right), \quad 0 < x < \infty;$$

furthermore, if $v_1 = 0$, then

$$\varepsilon v_2 \partial_x q(0, t) = k_1 p(0, t) - k_2 q(0, t) \rightarrow 0 \text{ if } t \rightarrow 0.$$

Since $\partial_x q(x, 0) \rightarrow 0$ as $x \rightarrow 0$, the initial-boundary data are continuous at $(0, 0)$. It follows, as before, that the second order derivatives of p, q are continuous in \bar{D} , and similarly one can prove that also the third order derivatives of p, q are continuous in \bar{D} .

LEMMA 2.1 (maximum principle). *The following inequalities hold:*

$$0 \leq p \leq \frac{k_2}{k_1}, \quad 0 \leq q \leq 1.$$

Proof. Let us first consider the system (2.1)–(2.4) in $D_L = D \cap \{x < L\}$, for $0 < L < \infty$. We modify (2.1), (2.2) by subtracting a small positive number μ from the right-hand sides, and we denote the corresponding solution by (p_μ, q_μ) . We claim that

$$(2.7) \quad p_\mu < \frac{k_2}{k_1}(1 + \mu), \quad q_\mu < 1 + \mu.$$

Indeed, if this is not true, then consider a point (x_0, t_0) with the smallest t_0 for which equality occurs in (2.7) either for p_μ or for q_μ . Suppose, for definiteness, that $q_\mu(x_0, t_0) = 1 + \mu$. Because of the boundary and initial conditions, $x_0 \neq 0$ and $t_0 \neq 0$. At (x_0, t_0) we have

$$\varepsilon(\partial_t + v_2\partial_x)q_\mu = k_1p_\mu - k_2q_\mu - \mu \leq -\mu < 0.$$

Thus, there would be an earlier time at which $q_\mu \geq 1 + \mu$, which is a contradiction. Taking $\mu \rightarrow 0$ and then $L \rightarrow \infty$ we obtain the inequalities $p \leq \frac{k_2}{k_1}$, $q \leq 1$. Similarly one can prove, by taking $\mu < 0$, that $p \geq 0$, $q \geq 0$. \square

We now proceed to derive the asymptotic behavior for $q(x, t)$ as $\varepsilon \rightarrow 0$. We begin by deriving a second order PDE for q . From (2.1), (2.2) we obtain

$$(2.8) \quad \varepsilon(\partial_t + v_1\partial_x)(\partial_t + v_2\partial_x)q + (k_1 + k_2)\partial_t q - (k_1v_2 + k_2v_1)\partial_x q = 0.$$

Introduce a change of variables

$$s = \frac{x - vt}{\sqrt{\varepsilon}}, \quad Q_\varepsilon(s, t) = q(x, t),$$

where v will be determined later on. The domain D is transformed into the domain

$$\Omega = \left\{ (s, t) : -\frac{vt}{\sqrt{\varepsilon}} < s < \infty, t > 0 \right\}.$$

Later on we shall use the notation

$$\begin{aligned} \Omega_T &= \Omega \cap \{t < T\}, \\ \Gamma_T &\equiv \Gamma_{T,\varepsilon} = \left\{ (s, t) : s = -\frac{vt}{\sqrt{\varepsilon}}, 0 < t < T \right\}, \text{ where } 0 < T \leq \infty, \\ L_0 &= \{(s, 0) : 0 < s < \infty\}, \\ s_t &\equiv s_{t,\varepsilon} = -\frac{vt}{\sqrt{\varepsilon}}. \end{aligned}$$

Note that

$$(2.9) \quad \begin{aligned} \partial_t q &= \partial_t Q_\varepsilon - \frac{v}{\sqrt{\varepsilon}}\partial_s Q_\varepsilon, \quad \partial_x q = \frac{1}{\sqrt{\varepsilon}}\partial_s Q_\varepsilon, \text{ and} \\ \partial_t Q_\varepsilon &= \partial_t q + v\partial_x q, \quad \partial_s Q_\varepsilon = \sqrt{\varepsilon}\partial_x q. \end{aligned}$$

It is easily seen that if we choose

$$(2.10) \quad v = \frac{k_1 v_2 + k_2 v_1}{k}, \text{ where } k = k_1 + k_2,$$

then we obtain the following equation for Q_ε :

$$(2.11) \quad \partial_t Q_\varepsilon - \sigma^2 \partial_s^2 Q_\varepsilon + \partial_{ts} K \sqrt{\varepsilon} Q_\varepsilon + \frac{\varepsilon}{k} \partial_t^2 Q_\varepsilon = 0 \text{ in } \Omega,$$

where

$$(2.12) \quad \sigma^2 = \frac{k_1 k_2}{k^3} (v_2 - v_1)^2, \quad K = \frac{k_2 - k_1}{k^2} (v_2 - v_1).$$

Continuing with the assumption (2.6), we also have

$$(2.13) \quad Q_\varepsilon(s, 0) = q_0(s), \quad s > 0,$$

and, by (2.2), (2.3), (2.9), and (2.10),

$$(2.14) \quad \partial_t Q_\varepsilon(s, 0) = -\frac{k_2(v_2 - v_1)}{k} \frac{1}{\sqrt{\varepsilon}} \partial_s q_0(s), \quad s > 0.$$

Since $q(0, t) = 1$ the function $p(0, t) \equiv k_2/k_1$ is the solution of (2.1) at $x = 0$, so that also

$$\varepsilon \partial_x q(0, t) = \frac{\varepsilon}{v_2} (\partial_t q + v_2 \partial_x q) = \frac{1}{v_2} (k_1 p - k_2 q) = 0 \text{ at } (0, t).$$

Hence

$$(2.15) \quad Q_\varepsilon = 1, \partial_s Q_\varepsilon = \partial_t Q_\varepsilon = 0 \text{ on } \Gamma_T \text{ for any } T > 0.$$

If W, ϕ are bounded continuously differentiable functions in $\bar{\Omega}_T, T < \infty$, and $\phi(s, T) \equiv 0$, then, by integration by parts,

$$\iint_{\Omega_T} \partial_t W \cdot \phi ds dt = - \int_{\Gamma_T \cup L_0} W \phi ds - \iint_{\Omega_T} W \cdot \partial_t \phi ds dt,$$

where in the integrals along Γ_T and L_0 the variable s is increasing from left to right. Similarly, if $\phi(s, t)$ or $W(s, t)$ converges to zero as $s \rightarrow \infty, 0 < t < T$, then

$$\iint_{\Omega_T} \partial_s W \cdot \phi ds dt = - \int_{\Gamma_T} W \phi dt - \iint_{\Omega_T} W \cdot \partial_s \phi ds dt,$$

where in the integral along Γ_T the variable t is increasing from $t = 0$ to $t = T$. With the above understanding of the integrals along Γ_T , we have

$$(2.16) \quad \int_{\Gamma_T} W \phi dt = \int_{\Gamma_T} \frac{\sqrt{\varepsilon}}{v} W \phi ds.$$

Let \tilde{Q}_ε denote the unique bounded solution of the parabolic equation

$$(2.17) \quad \partial_t \tilde{Q}_\varepsilon - \sigma^2 \partial_s^2 \tilde{Q}_\varepsilon = 0 \text{ in } \Omega,$$

with the initial and boundary conditions

$$(2.18) \quad \begin{aligned} \tilde{Q}_\varepsilon(s, 0) &= q_0(s) \text{ on } L_0, \\ \tilde{Q}_\varepsilon &\equiv 1 \text{ on } \Gamma_\infty. \end{aligned}$$

Recalling that $\partial^j q_0(s) = 0$ at $s = 0$ for $1 \leq j \leq 4$, one can easily verify that \tilde{Q}_ε satisfies the consistency conditions of order 2 at $(s, t) = (0, 0)$. Hence all the derivatives

$$(2.19) \quad \partial_t^k \partial_s^l \tilde{Q}_\varepsilon \quad (0 \leq 2k + l \leq 4) \quad \text{are continuous at } (0, 0).$$

In the next two lemmas we prove that these functions are uniformly bounded in Ω , and that they converge uniformly to zero as $s \rightarrow \infty$, the uniformity being with respect to ε .

LEMMA 2.2. *The following inequalities hold:*

$$(2.20) \quad |\partial_t^k \partial_s^l \tilde{Q}_\varepsilon(s, t)| \leq C \text{ in } \Omega \quad (0 \leq 2k + l \leq 4),$$

where C is a constant independent of ε .

Proof. Consider the function

$$U(x, t) = \tilde{Q}_\varepsilon(s, t), \text{ where } s = \frac{x - vt}{\sqrt{\varepsilon}}.$$

Since $\partial_t \tilde{Q}_\varepsilon = \partial_t U + v \partial_x U$, there holds

$$(2.21) \quad \partial_t U = \alpha \varepsilon \partial_x^2 U - \beta \partial_x U \text{ in } D,$$

where α, β are positive numbers depending only on k_i, v_i , and

$$(2.22) \quad U(x, 0) = q_0\left(\frac{x}{\sqrt{\varepsilon}}\right), \quad x > 0,$$

$$(2.23) \quad U(0, t) = 1, \quad t > 0.$$

The function $V = \partial_x U$ satisfies the heat equation (2.21) and, since $\partial_t U(0, t) = 0$,

$$\partial_x V - \frac{\gamma}{\varepsilon} V = 0 \text{ at } x = 0, t > 0, \quad \text{where } \gamma = \frac{\beta}{\alpha}.$$

Hence V cannot take positive maximum or negative minimum at $(0, t)$, $t > 0$. By the maximum principle we then deduce that

$$|\partial_x U| \leq \frac{1}{\sqrt{\varepsilon}} \sup_{x>0} \left| q_0' \left(\frac{x}{\sqrt{\varepsilon}} \right) \right| \leq \frac{C}{\sqrt{\varepsilon}}$$

on the set $\{(x, t) : x > 0, t > 0\}$.

We proceed to apply the above argument to the function $V_1 = \partial_t \partial_x U$, which is again a solution of the heat equation (2.21), with

$$\partial_x V_1 - \frac{\gamma}{\varepsilon} V_1 = \frac{1}{\alpha \varepsilon} \partial_t^2 U = 0 \text{ at } x = 0, t > 0.$$

By the maximum principle we then get

$$\begin{aligned} |\partial_x V_1|_{L^\infty(\mathbb{R}_2^+)} &\leq \sup_{x>0} |V_1(x, 0)| \\ &= \sup_{x>0} \left| \alpha \varepsilon \partial_x^3 q_0 \left(\frac{x}{\sqrt{\varepsilon}} \right) - \beta \partial_x^2 q_0 \left(\frac{x}{\sqrt{\varepsilon}} \right) \right| \\ &\leq \frac{C}{\varepsilon}. \end{aligned}$$

Hence

$$\left| \partial_x(\partial_x^2 U) - \frac{\gamma}{\varepsilon}(\partial_x^2 U) \right| = \frac{|V_1|}{\alpha\varepsilon} \leq \frac{C}{\varepsilon^2}.$$

Multiplying by $e^{-\gamma x/\varepsilon}$ and integrating in x over (x, ∞) we get

$$|e^{-\gamma x/\varepsilon} \partial_x^2 U(x, t)| \leq \frac{C}{\varepsilon} e^{-\gamma x/\varepsilon}.$$

Hence

$$|\partial_x^2 U(x, t)|_{L^\infty(\mathbb{R}_2^+)} \leq \frac{C}{\varepsilon}.$$

Similarly, working with the function $V_2 = \partial_t^2 \partial_x U$, we deduce, by the maximum principle, that

$$|V_2|_{L^\infty(\mathbb{R}_2^+)} \leq \frac{C}{\varepsilon^{3/2}}.$$

Hence

$$\left| \partial_x(\partial_t \partial_x^2 U) - \frac{\gamma}{\varepsilon}(\partial_t \partial_x^2 U) \right| \leq \frac{C}{\varepsilon^{5/2}}.$$

As before, we deduce by integration that

$$|\partial_t \partial_x^2 U(x, t)|_{L^\infty(\mathbb{R}_2^+)} \leq \frac{C}{\varepsilon^{3/2}}.$$

This implies, by (2.21), that

$$\left| \partial_x(\partial_x^3 U) - \frac{\gamma}{\varepsilon}(\partial_x^3 U) \right| \leq \frac{C}{\varepsilon^{5/2}}.$$

and, by integration, as before,

$$|\partial_x^3 U(x, t)|_{L^\infty(\mathbb{R}_2^+)} \leq \frac{C}{\varepsilon^{3/2}}.$$

Similarly we can estimate $\partial_x^4 U$ by working with the function $V_3 = \partial_t^3 \partial_x U$. We conclude that

$$|\partial_x^j U(x, t)|_{L^\infty(\mathbb{R}_2^+)} \leq \frac{C}{\varepsilon^{j/2}} \text{ for } j = 0, 1, 2, 3, 4.$$

It follows that

$$|\partial_s^j \tilde{Q}_\varepsilon(s, t)| \leq C \text{ in } \Omega.$$

The remaining inequalities in (2.20) follow from the differential equation (2.17). \square

LEMMA 2.3. *For any $0 < T < \infty$, the following inequalities hold for some $\gamma > 0$:*

$$(2.24) \quad |\partial_t^k \partial_s^l \tilde{Q}_\varepsilon(s, t)| \leq C e^{-\gamma s^2} \text{ in } \Omega_T \cap \{s > 0\} \quad (0 \leq 2k + l \leq 4),$$

where C is a constant independent of ε .

Proof. Recall that $\tilde{Q}_\varepsilon(s, 0) = 0$ if $s > A_0$, so that also $\partial_s^l \tilde{Q}_\varepsilon(s, 0) = 0$ if $s > A_0$. We can then compare $\partial_s^l \tilde{Q}_\varepsilon$ with a solution of (2.17) of the form

$$\frac{C}{\sqrt{t}} e^{-\delta s^2/t} \text{ in } G \equiv \{s > A_0, t > 0\} \left(\text{where } \delta = \frac{1}{4\sigma^2} \right).$$

The difference

$$V = \frac{C}{\sqrt{t}} e^{-\delta s^2/t} - \partial_s^l \tilde{Q}_\varepsilon(s, t)$$

is a bounded solution of (2.17) in G , with $V(s, 0) = 0$ if $s > A_0$ and $V(A_0, t) > 0$ (< 0) if C is positive and large (negative and large in absolute value). By the maximum principle for parabolic equations in an unbounded domain (see, e.g., [7, Chap. 2, Thm. 9]), we conclude that $V > 0$ ($V < 0$) in G in the case where C was positive (negative), so that the inequality (2.24) with $k = 0$ follows. The remaining estimates follow from (2.17). \square

Consider the function

$$W = Q_\varepsilon - \tilde{Q}_\varepsilon \text{ in } \Omega_T, \quad 0 < T < \infty.$$

It satisfies the equation

$$(2.25) \quad \partial_t W - \sigma^2 \partial_s^2 W + K\sqrt{\varepsilon} \partial_{ts}^2 W + \frac{\varepsilon}{k} \partial_s^2 W = F_\varepsilon,$$

where

$$(2.26) \quad F_\varepsilon = -K\sqrt{\varepsilon} \partial_{ts}^2 \tilde{Q}_\varepsilon - \frac{\varepsilon}{k} \partial_t^2 \tilde{Q}_\varepsilon.$$

Clearly

$$(2.27) \quad W \equiv 0 \text{ on } L_0 \cup \Gamma_T$$

and, by (2.9), (2.15),

$$(2.28) \quad \partial_t W = -\partial_t \tilde{Q}_\varepsilon, \quad \partial_s W = -\partial_s \tilde{Q}_\varepsilon = -\frac{\sqrt{\varepsilon}}{v} \partial_t \tilde{Q}_\varepsilon \text{ on } \Gamma_T.$$

Also, by (2.14),

$$\partial_t Q_\varepsilon = \partial_t q + v \partial_x q = \frac{v - v_2}{\sqrt{\varepsilon}} q'_0(s) \text{ on } L_0,$$

so that

$$(2.29) \quad \partial_t W = -\frac{k_2(v_2 - v_1)}{k\sqrt{\varepsilon}} q'_0(s) \text{ on } L_0.$$

From Lemmas 2.2 and 2.3 we deduce that

$$\iint_{\Omega_T} F_\varepsilon^2 \leq \iint_{\Omega_T \cap \{s < 0\}} C_0 \varepsilon + \iint_{\Omega_T \cap \{s > 0\}} C_0 \varepsilon e^{-2\gamma s^2} \leq C\sqrt{\varepsilon},$$

where C_0, C are constants (independent of ε). Hence, for any function $Z \in L^2(\Omega_T)$ and any small $\eta > 0$,

$$(2.30) \quad \left| \iint_{\Omega_T} F_\varepsilon Z \right| \leq \eta \iint_{\Omega_T} Z^2 + C\sqrt{\varepsilon},$$

where C is a constant which depends on η and T .

LEMMA 2.4. *For any $0 < T < \infty$, there exists a constant $C = C(T)$ such that*

$$(2.31) \quad \iint_{\Omega_T} W_t^2 dsdt + \sup_{0 \leq t \leq T} \int_{s_t}^\infty W_s^2(s, t) ds \leq C,$$

$$(2.32) \quad \iint_{\Omega_T} (W^2 + W_s^2) dsdt \leq C\sqrt{\varepsilon}.$$

Proof. If we multiply (2.25) by W_t and integrate over Ω_T , we get

$$(2.33) \quad \iint_{\Omega_T} W_t^2 - \sigma^2 \iint_{\Omega_T} W_t W_{ss} + K\sqrt{\varepsilon} \iint_{\Omega_T} W_t W_{ts} + \frac{\varepsilon}{k} \iint_{\Omega_T} W_t W_{tt} \\ = - \iint_{\Omega_T} W_t F_\varepsilon.$$

We proceed to evaluate terms on the left-hand side of (2.33). By integration by parts we obtain

$$- \iint_{\Omega_T} W_t W_{ss} = - \iint_{\Omega_T} [\partial_s(W_t W_s) - W_{ts} W_s] \\ = \int_{\Gamma_T} W_t W_s dt + \frac{1}{2} \int_{s_T}^\infty W_s^2(s, T) ds - \frac{1}{2} \int_{L_0 \cup \Gamma_T} W_s^2 ds,$$

and, by (2.28),

$$\int_{\Gamma_T} W_t W_s dt = \frac{\sqrt{\varepsilon}}{v} \int_{\Gamma_T} \tilde{Q}_{\varepsilon, t}^2 dt$$

and

$$\int_{L_0 \cup \Gamma_T} W_s^2 ds = \int_{\Gamma_T} W_s^2 ds = \int_{\Gamma_T} \tilde{Q}_{\varepsilon, s}^2 ds = \frac{\sqrt{\varepsilon}}{v} \int_{\Gamma_T} \tilde{Q}_{\varepsilon, t}^2 dt,$$

where in the last equation we used also (2.16). Hence,

$$(2.34) \quad -\sigma^2 \iint_{\Omega_T} W_t W_{ss} = \frac{1}{2} \sigma^2 \int_{s_T}^\infty W_s^2(s, T) ds - \frac{1}{2} \sigma^2 \frac{\sqrt{\varepsilon}}{v} \int_{\Gamma_T} \tilde{Q}_{\varepsilon, t}^2 dt.$$

Next,

$$(2.35) \quad K\sqrt{\varepsilon} \iint_{\Omega_T} W_t W_{ts} = \frac{1}{2} K\sqrt{\varepsilon} \iint_{\Omega_T} \partial_s(W_t^2) \\ = -\frac{1}{2} K\sqrt{\varepsilon} \int_{\Gamma_T} W_t^2 dt = -\frac{1}{2} K\sqrt{\varepsilon} \int_{\Gamma_T} \tilde{Q}_{\varepsilon, t}^2 dt.$$

Consider finally

$$\varepsilon \iint_{\Omega_T} W_t W_{tt} = \frac{\varepsilon}{2} \int_{s_T}^\infty W_t^2(s, T) ds - \frac{\varepsilon}{2} \int_{L_0 \cup \Gamma_T} W_t^2 ds.$$

Since

$$-\frac{\varepsilon}{2} \int_{\Gamma_T} W_t^2 ds = -\frac{\varepsilon}{2} \int_{\Gamma_T} \tilde{Q}_{\varepsilon, t}^2 ds = -\frac{\sqrt{\varepsilon}}{2v} \int_{\Gamma_T} \tilde{Q}_{\varepsilon, t}^2 dt,$$

and

$$-\frac{\varepsilon}{2} \int_{L_0} W_t^2 ds = \mathcal{O}(1)$$

by (2.29) and the fact that (by (2.17), (2.18)) $\tilde{Q}_{\varepsilon,t} = 0$ on $L_0 \cap \{s > A_0\}$, we obtain

$$(2.36) \quad \varepsilon \iint_{\Omega_T} W_t W_{tt} = \frac{\varepsilon}{2} \int_{s_T}^\infty W_t^2(s, T) ds - \frac{\sqrt{\varepsilon}}{2v} \int_{\Gamma_T} \tilde{Q}_{\varepsilon,t}^2 dt + \mathcal{O}(1).$$

Substituting (2.34)–(2.36) into (2.33) and using also (2.30) with $Z = W_t$, $\eta = \frac{1}{2}$, and the inequality $|\tilde{Q}_{\varepsilon,t}| < C$ on Γ_T , we obtain

$$\iint_{\Omega_T} W_t^2 + \frac{1}{2} \sigma^2 \int_{s_T}^\infty W_s^2(s, T) ds + \frac{\varepsilon}{k} \int_{s_T}^\infty W_t^2(s, T) ds \leq C \sqrt{\varepsilon} \int_{\Gamma_T} dt + \mathcal{O}(1).$$

This implies $\iint_{\Omega_T} W_t^2 < C_1(T)$, and $\int_{s_t}^\infty W_s^2(s, t) ds < C_2(t)$ for $t \in [0, T]$ and some continuous function C_2 , and (2.31) follows, with $C(T) = C_1(T) + \sup_{0 \leq t \leq T} C_2(t)$.

To prove (2.32) we multiply (2.25) by W and integrate over Ω_T . By integration by parts we obtain

$$(2.37) \quad \begin{aligned} & \frac{1}{2} \int_{s_T}^\infty W^2(s, T) ds + \sigma^2 \iint_{\Omega_T} W_s^2 - K \sqrt{\varepsilon} \iint_{\Omega_T} W_s W_t \\ & + \frac{\varepsilon}{k} \int_{s_T}^\infty (W W_t)(s, T) ds - \frac{\varepsilon}{k} \iint_{\Omega_T} W_t^2 = \iint_{\Omega_T} W F_\varepsilon. \end{aligned}$$

By Lemma 2.3 and (2.31),

$$\left| K \sqrt{\varepsilon} \iint_{\Omega_T} W_s W_t \right| \leq \frac{1}{2} \sigma^2 \iint_{\Omega_T} W_s^2 + \frac{K^2 \varepsilon}{2 \sigma^2} \iint_{\Omega_T} W_t^2 \leq \frac{1}{2} \sigma^2 \iint_{\Omega_T} W_s^2 + C \varepsilon.$$

Also, by (2.30),

$$\left| \iint_{\Omega_T} W F_\varepsilon \right| \leq \eta \iint_{\Omega_T} W^2 + C \sqrt{\varepsilon}, \quad C = C(\eta).$$

Hence

$$(2.38) \quad \begin{aligned} & \frac{1}{2} \int_{s_T}^\infty W^2(s, T) ds + \frac{1}{2} \sigma^2 \iint_{\Omega_T} W_s^2 + \frac{\varepsilon}{2k} \int_{s_T}^\infty (W^2)_t(s, T) ds \\ & \leq \eta \iint_{\Omega_T} W^2 + C \sqrt{\varepsilon}. \end{aligned}$$

Integrating both sides with respect to T , $0 < T < T_0$, and choosing $\eta = \frac{1}{4T_0}$, we obtain

$$(2.39) \quad \iint_{\Omega_{T_0}} W^2 + \int_0^{T_0} \left(\iint_{\Omega_T} W_s^2 \right) dT + \varepsilon \int_{s_{T_0}}^\infty W^2(s, T_0) ds \leq C \sqrt{\varepsilon},$$

where C depends on T_0 . Finally, if we use the inequality

$$\int_0^{T_0} \left(\int_0^T f(t) dt \right) dT = \int_0^{T_0} (T_0 - t) f(t) dt \geq \delta_0 \int_0^{T_0 - \delta_0} f(t) dt$$

with $f(t) = \int_{s_t}^\infty W_s^2(s, t) ds$ in (2.39), we obtain the estimate (2.32). \square

We extend the function $\tilde{Q}_\varepsilon(s, t)$ by 1 into the domain $\{s < -vt/\sqrt{\varepsilon}, t > 0\}$, and wish to estimate $\tilde{Q}_\varepsilon - Q_0$, where Q_0 is the bounded solution of

$$(2.40) \quad \partial_t Q_0 - \sigma^2 \partial_s^2 Q_0 = 0 \text{ in } \mathbb{R}_+^2,$$

$$(2.41) \quad Q_0(s, 0) = q_0(s) \text{ if } s > 0, \quad Q_0(s, 0) = 1 \text{ if } s < 0.$$

LEMMA 2.5. *The following inequality holds:*

$$(2.42) \quad \int_{-\infty}^\infty (\tilde{Q}_\varepsilon - Q_0)^2(s, T) ds + \int_0^T \int_{-\infty}^\infty (\partial_s \tilde{Q}_\varepsilon - \partial_s Q_0)^2 ds dt \leq C\sqrt{\varepsilon},$$

where $0 < T < \infty$ and C is a constant independent of T and ε .

Proof. We first estimate $\tilde{Q}_\varepsilon - Q_0$ on Γ_T . For this purpose we represent the function $V \equiv 1 - Q_0$ in the form

$$V(s, t) = \int_0^\infty \frac{e^{-\frac{(s-\zeta)^2}{4\sigma^2 t}}}{\sigma\sqrt{4\pi t}} \phi(\zeta) d\zeta, \quad \phi(\zeta) = 1 - q_0(\zeta)$$

and compute

$$V\left(-\frac{vt}{\sqrt{\varepsilon}}, t\right) = \int_0^\infty \frac{e^{-\frac{(-\frac{vt}{\sqrt{\varepsilon}} - \zeta)^2}{4\sigma^2 t}}}{\sigma\sqrt{4\pi t}} \phi(\zeta) d\zeta.$$

Substituting

$$\xi = \left(\frac{vt}{\sqrt{\varepsilon}} + \zeta\right) \frac{1}{\sqrt{t}}$$

we obtain

$$\left|V\left(-\frac{vt}{\sqrt{\varepsilon}}, t\right)\right| \leq C \int_{v\sqrt{t/\varepsilon}}^\infty e^{-\frac{\xi^2}{4\sigma^2}} d\xi \leq C e^{-\frac{\alpha t}{\varepsilon}} \quad (\text{for some } \alpha > 0).$$

Similarly we obtain

$$\left|\partial_s V\left(-\frac{vt}{\sqrt{\varepsilon}}, t\right)\right| \leq (C/\sqrt{t}) e^{-\frac{\alpha t}{\varepsilon}}.$$

Consider the function $R = \tilde{Q}_\varepsilon - Q_0\varepsilon$. It satisfies the equation

$$(2.43) \quad \partial_t R - \sigma^2 \partial_s^2 R = 0 \text{ in } \Omega_T,$$

and, by the last two estimates,

$$(2.44) \quad |R|_{\Gamma_T} \leq C e^{-\frac{\alpha t}{\varepsilon}}, \quad |\partial_s R|_{\Gamma_T} \leq \frac{C}{\sqrt{t}} e^{-\frac{\alpha t}{\varepsilon}}.$$

If we multiply (2.43) by R and integrate over Ω_T , we obtain, after integration by parts,

$$\frac{1}{2} \int_{s_T}^\infty R^2(s, T) ds - \sigma^2 \iint_{\Omega_T} (\partial_s R)^2 = \frac{1}{2} \int_{\Gamma_T} R^2 ds - \sigma^2 \int_{\Gamma_T} R \cdot \partial_s R dt.$$

Using (2.44) we find that each of the two integrals on the right-hand side is bounded by $C\sqrt{\varepsilon}$, and thus we derive the estimate (2.42). \square

Combining the estimates (2.32), (2.42) we obtain the following theorem.

THEOREM 2.6. *Consider the system (2.1)–(2.4) under the assumptions (2.5) and (2.6). Then we can write q in the form*

$$(2.45) \quad q(x, t) = Q_\varepsilon \left(\frac{x - vt}{\sqrt{\varepsilon}}, t \right),$$

where $Q_\varepsilon(s, t)$ (extended by 1 for $s < -vt/\sqrt{\varepsilon}$) converges to the solution $Q_0(s, t)$ of (2.40), (2.41) as $\varepsilon \rightarrow 0$ in the following sense:

$$(2.46) \quad \sup_{0 \leq t \leq T} \int_{-\infty}^{\infty} (Q_\varepsilon - Q_0)^2(s, t) ds + \int_0^T \int_{-\infty}^{\infty} (\partial_s Q_\varepsilon - \partial_s Q_0)^2 ds dt \leq C\sqrt{\varepsilon}$$

for any $0 < T < \infty$, where C is a constant which may depend on T .

Remark 2.1. The proof of Theorem 2.6 extends to the case where the first two conditions on $q_0(s)$ are replaced by the weaker condition that $\partial_s^j q_0(s)$ are continuous functions for $s \geq 0$ and they belong to $L^2(\mathbb{R})$ for $0 \leq j \leq 4$.

Remark 2.2. Theorem 2.6 extends, with essentially the same proof, to the case where $v_1 > 0$, provided $v_1 \neq v_2$ and we prescribe the boundary condition $p(x, t) \equiv \frac{k_2}{k_1}$ at $x = 0$.

Remark 2.3. Consider the case where $q_0 \equiv 0$, and take for simplicity $v_1 = 0$. Then the initial and boundary data form a function which is discontinuous at $(0, 0)$, so that the proof of Theorem 2.6 cannot be extended to this case. If we introduce an approximating system by changing the initial data,

$$(2.47) \quad q(x, 0) = q_{0\delta} \left(\frac{x}{\sqrt{\varepsilon}} \right), \quad q_{0\delta}(0) = 1, \quad q'_{0\delta} \leq 0, \quad q_{0\delta}(s) = 0 \text{ if } s \geq \delta,$$

then for the corresponding solution (p_δ, q_δ) we have the following result.

THEOREM 2.7. *The following inequality holds:*

$$(2.48) \quad \sup_{T > 0} \int_0^\infty [(p_\delta(x, T) - p(x, T))^2 + (q_\delta(x, T) - q(x, T))^2] dx \leq C\delta,$$

where C is a constant independent of the function $q_{0\delta}$.

Proof. Set $\tilde{p} = p_\delta - p$, $\tilde{q} = q_\delta - q$. Then

$$\partial_t \tilde{p} = -k_1 \tilde{p} + k_2 \tilde{q}, \quad (\partial_t + v_1 \partial_x) \tilde{q} = k_1 \tilde{p} - k_2 \tilde{q}.$$

Multiplying the first equation by $k_2 \tilde{p}$ and the second equation by $k_1 \tilde{q}$ and adding, we obtain the inequality

$$k_2 \partial_t \tilde{p}^2 + k_1 ((\partial_t + v_1 \partial_x) \tilde{q})^2 \leq 0.$$

Integrating over $0 < x < \infty$, $0 < t < T$, the inequality (2.48) easily follows. \square

Theorem 2.7 combined with Theorem 2.6 suggests that, if $q_0(s) \equiv 0$, then $q(x, t) - Q_0(\frac{x-vt}{\sqrt{\varepsilon}}, t)$ converges to zero in some sense when Q_0 is the solution of (2.40), (2.41) with $q_0(s) \equiv 0$. This situation will be considered, for more general dynamical systems, in section 3.

3. The case $n > 2$. Let $K = (k_{ij})$ be an $n \times n$ matrix satisfying the following conditions:

$$(3.1) \quad k_{ij} \geq 0 \text{ if } i \neq j.$$

$$(3.2) \quad \sum_{i=1}^n k_{ij} = 0 \left(\text{so that } k_{jj} = - \sum_{\substack{i=1 \\ i \neq j}}^n k_{ij} \right).$$

$$(3.3) \quad \text{For any indices } i_0 \neq i_1 \text{ there are } j_1, j_2, \dots, j_m \text{ such that } \\ j_1 = i_0, j_m = i_1, \text{ and } k_{j_l j_{l+1}} > 0 \text{ for } l = 1, \dots, m - 1.$$

As proved in [11], under conditions (3.1)–(3.3), the null space of the matrix (k_{ij}) is one-dimensional, and it is generated by a vector $(\lambda_1, \dots, \lambda_n)$ with positive components. For simplicity we take $\sum_{j=1}^n \lambda_j = 1$. For later reference we write

$$(3.4) \quad \sum_{j=1}^n k_{ij} \lambda_j = 0 \text{ for } 1 \leq i \leq n.$$

In this section we consider a collection of populations undergoing transitions

$$p_i \xrightleftharpoons[k_{ji}]{k_{ij}} p_j \text{ for } i, j = 1, \dots, n$$

with the dynamics given by (1.2), in the special case (1.4), or, more generally, for the case when $v_j \geq 0$ for all j , and

$$(3.5) \quad p_i(x, 0) = \lambda_i q_0 \left(\frac{x}{\sqrt{\varepsilon}} \right), \quad 1 \leq i \leq n, \\ p_j(0, t) = \lambda_j \text{ if } v_j > 0.$$

Here we have the following:

$$(3.6) \quad \text{either } q_0 \equiv 0, \text{ or } q_0(s) \text{ is of class } C^n, \text{ has compact support, } q_0(0) = 1, \text{ and } q_0^{(k)}(0) = 0 \text{ for all } k = 1, \dots, n.$$

THEOREM 3.1. *Let the matrix (k_{ij}) satisfy conditions (3.1)–(3.3), and consider the system (1.2) with $v_j \geq 0$ for all $1 \leq j \leq n$, $v_n > 0$, and with the initial and boundary conditions (3.5), where q_0 is a function satisfying (3.6). Then, for some constants $v > 0$ and $\sigma^2 > 0$, the following holds:*

$$(3.7) \quad p_j(x, t) = Q_{\varepsilon, j} \left(\frac{x - vt}{\sqrt{\varepsilon}}, t \right) \quad (1 \leq j \leq n),$$

where, as $\varepsilon \rightarrow 0$,

$$(3.8) \quad Q_{\varepsilon, j} \rightarrow \lambda_j Q_0 \text{ weakly in } L^r(\mathbb{R}_+^2)$$

for any $1 < r < \infty$, and $Q_0(s, t)$ is the bounded solution of (2.40), (2.41).

Proof. For clarity we first prove the theorem for $j = n$, $q_0(0) = 1$, $q_0 \in C^n$, and set $Q_{\varepsilon, j} = Q_\varepsilon$. As in section 2 one can prove that the functions $p_j(x, t)$ belong to

$C^n(\bar{D})$. Then, by algebraic elimination, as in [5, p. 14], it follows that each of the functions p_j satisfies the equation

$$(3.9) \quad \det \left(\lambda_{ij} - \delta_{ij}\varepsilon(\partial_t + v_j\partial_x) \right) w = 0.$$

We shall henceforth use this equation for the function $p_n(x, t)$. Introducing the function Q_ε as in (3.7), the calculations in [9], [11] show that

$$(3.10) \quad \partial_t Q_\varepsilon - \sigma^2 \partial_s^2 Q_\varepsilon = P(\partial_s, \partial_t) Q_\varepsilon,$$

where $v = \sum_{j=1}^n \lambda_j v_j$, $-\sigma^2 = \frac{a_{02}}{a_{10}}$, where a_{kl} are defined by $\det(k_{ij} - \gamma\delta_{ij} - \lambda(v_i - v)\delta_{ij}) = \sum_{0 \leq k+l \leq n} a_{kl} \gamma^k \lambda^l$, and

$$(3.11) \quad P(\partial_s, \partial_t) = \sum_{l+k \leq n} \beta_{lk} \varepsilon^{l+\frac{k}{2}-1} \partial_t^l \partial_s^k,$$

where the β_{lk} are constants depending only on k_{ij} and v_j .

Set $p_i(x, t) = P_i(\frac{x-vt}{\sqrt{\varepsilon}}, t)$. Then

$$(3.12) \quad \varepsilon \left(\partial_t + \frac{v}{\sqrt{\varepsilon}} \partial_s \right) P_i + \frac{v_i}{\sqrt{\varepsilon}} \partial_s P_i = \sum_{j=1}^n k_{ij} P_j.$$

LEMMA 3.2. *There holds*

$$\partial_t^l \partial_x^k p_j(0, t) = 0 \text{ for all } 0 \leq k+l \leq n, t > 0,$$

or, equivalently,

$$\partial_t^l \partial_s^k P_{j,\varepsilon} \left(\frac{-vt}{\sqrt{\varepsilon}}, t \right) = 0 \text{ for all } 0 \leq k+l \leq n, t > 0.$$

Proof. Let $A = \{i : v_i = 0\}$, $B = \{i : v_i > 0\}$. We break (1.2) at $x = 0$ into two subsystems:

$$(3.13) \quad \partial_t p_i(0, t) = \sum_{j \in A} k_{ij} p_j(0, t) + \sum_{j \in B} k_{ij} p_j(0, t) \text{ for } i \in A,$$

$$(3.14) \quad \partial_t p_i(0, t) + v_i \partial_x p_i(0, t) = \sum_{j=1}^n k_{ij} p_j(0, t) \text{ for } i \in B.$$

Since $p_j(0, t) \equiv \lambda_j$ if $j \in B$, and $p_i(0, 0) = \lambda_i$ if $i \in A$, using (3.4) we deduce that the unique solution of the ODE system (3.13) is $p_i(0, t) \equiv \lambda_i$ for all $i \in A$. Then $p_j(0, t) \equiv \lambda_j$ for all $j = 1, \dots, n$ and (3.14) gives

$$(3.15) \quad \partial_x p_i(0, t) = 0 \text{ for } i \in B.$$

We now apply ∂_x to (1.2) and deduce analogously to (3.13), (3.14) that

$$(3.16) \quad \partial_t \partial_x p_i(0, t) = \sum_{j \in A} k_{ij} \partial_x p_j(0, t) + \sum_{j \in B} k_{ij} \partial_x p_j(0, t) \text{ for } i \in A,$$

$$(3.17) \quad \partial_t \partial_x p_i(0, t) + v_i \partial_x \partial_x p_i(0, t) = \sum_{j=1}^n k_{ij} \partial_x p_j(0, t) \text{ for } i \in B.$$

Note that, by (3.15), we have $\sum_{j \in B} k_{ij} \partial_x p_j(0, t) = 0$; also, $\partial_x p_i(0, 0) = 0$ for all $i \in A$. Then the unique solution of the ODE system (3.16) is $\partial_x p_i(0, 0) \equiv 0$ for all $i \in A$, so that, upon recalling (3.15), $\partial_x p_i(0, 0) \equiv 0$ for all $i = 1, \dots, n$. By differentiating (3.15) in t we obtain $\partial_t \partial_x p_i(0, t) \equiv 0$, and using (3.17) we conclude that $\partial_x^2 p_i(0, t) \equiv 0$ for all $i \in B$.

In the same way, if we differentiate (1.2) twice in x , we can conclude that $\partial_x^2 p_j(0, t) \equiv 0$ for all $1 \leq j \leq n$, and similarly $\partial_x^k p_j(0, t) \equiv 0$ for all $1 \leq k \leq n, 1 \leq j \leq n$. This implies the statement of the lemma. \square

LEMMA 3.3. *There holds*

$$\partial_t^l \partial_s^k P_{j,\varepsilon}(s, 0) = O(\varepsilon^{\frac{1}{2}-l}) \text{ for all } l \geq 1, k + l \leq n, s > 0.$$

Proof. By (3.12), at $t = 0$,

$$\partial_t P_m(s, 0) = \frac{v - v_m}{\sqrt{\varepsilon}} \partial_s P_m(s, 0) + \frac{1}{\varepsilon} \sum_{j=1}^n k_{mj} P_j(s, 0) = \frac{v - v_m}{\sqrt{\varepsilon}} \lambda_m q'_0(s),$$

i.e., $\partial_t P_m(s, 0) = C_1^1 \varepsilon^{-\frac{1}{2}} q'_0(s)$ for some constant C_1^1 . Next, applying ∂_t to (3.12), we obtain

$$\begin{aligned} \partial_t^2 P_m(s, 0) &= \partial_t \left(\frac{v - v_m}{\sqrt{\varepsilon}} \partial_s P_m(s, 0) + \frac{1}{\varepsilon} \sum_{j=1}^n k_{mj} P_j \right) (s, 0) \\ &= C_1^2 \varepsilon^{-\frac{3}{2}} q'_0(s) + C_2^2 \varepsilon^{-1} q''_0(s) \end{aligned}$$

for some constants C_1^2 and C_2^2 . Similarly, for any $l \leq n$ we obtain

$$\partial_t^l P_m(s, 0) = \sum_{j=1}^l C_j^l \varepsilon^{l-\frac{j}{2}} q_0^{(j)}(s)$$

for some constants C_j^l , which implies the statement of the lemma. \square

We return to the proof of Theorem 3.1 for p_n , in the case $q_0(0) = 1, q_0 \in C^n$. As in the proof of the maximum principle (Lemma 2.1) one can prove that

$$(3.18) \quad 0 \leq p_j(x, t) \leq \lambda_j.$$

We extend the function $Q_\varepsilon(s, t)$ by 1 into $\{-\infty < s < -\frac{vt}{\sqrt{\varepsilon}}, t > 0\}$. By (3.18) with $j = n$, any sequence $\varepsilon' \rightarrow 0$ has a subsequence $\varepsilon'' \rightarrow 0$ such that $Q_{\varepsilon''} \rightarrow \bar{Q}$ in $L^r(\mathbb{R}_2^+)$ for any $0 < r < \infty$, where $\mathbb{R}_2^+ = \{(s, t) \in \mathbb{R}_2 : t > 0\}$

Take any smooth function ϕ with compact support $K \subset \mathbb{R}_2^+$. If we multiply ϕ by the left-hand side of (3.10) and perform integration by parts, we obtain

$$(3.19) \quad \iint_K \phi(\partial_t Q_\varepsilon - \sigma^2 \partial_s^2 Q_\varepsilon) = \iint_K Q_\varepsilon(-\partial_t - \sigma^2 \partial_s^2) \phi,$$

provided ε is sufficiently small so that K stays to the right of Γ_∞ . Similarly, from the right-hand side of (3.10) we get

$$(3.20) \quad \iint_K \phi P(\partial_s, \partial_t) Q_\varepsilon = \iint_K Q_\varepsilon P^*(\partial_s, \partial_t) \phi,$$

where P^* is the adjoint of the differential operator P defined in (3.11). As $\varepsilon = \varepsilon'' \rightarrow 0$ the right-hand side of (3.20) converges to zero. Hence, by (3.10), the same is true of each of the two sides of (3.19), so that

$$\iint_K \bar{Q}(-\partial_t - \sigma^2 \partial_s^2) \phi = 0.$$

It follows that \bar{Q} is a weak solution of the heat equation

$$(3.21) \quad \partial_t \bar{Q} - \sigma^2 \partial_s^2 \bar{Q} = 0 \text{ in } \mathbb{R}_2^+.$$

By regularity of weak solutions we conclude that \bar{Q} is a smooth solution of (3.21).

Next let ϕ be a smooth function with compact support K in $\{(s, t) : s > 0, -1 < t < \infty\}$. If we multiply the right-hand side of (3.10) by ϕ and integrate by parts, we obtain

$$\iint_K Q_\varepsilon P^*(\partial_s, \partial_t) \phi - \int_{K \cap \{t=0\}} \phi \left(\sum_{l+k \leq n} \beta_{lk} \varepsilon^{l+\frac{k}{2}-1} \partial_t^{l-1} \partial_s^k \right) Q_\varepsilon,$$

and by Lemma 3.3 the last integral converges to zero as $\varepsilon \rightarrow 0$; the first integral also converges to zero, as in the previous case. We conclude from (3.10) that

$$\iint_K \phi(\partial_t Q_\varepsilon - \sigma^2 \partial_s^2 Q_\varepsilon) \rightarrow 0 \text{ as } \varepsilon \rightarrow 0.$$

By integration by parts, the left-hand side is equal to

$$\iint_K Q_\varepsilon(-\partial_t - \sigma^2 \partial_s^2) \phi - \int_{K \cap \{t=0\}} \lambda_n q_0 \phi.$$

Hence, as $\varepsilon = \varepsilon'' \rightarrow 0$, we get

$$\iint_K \bar{Q}(-\partial_t - \sigma^2 \partial_s^2) \phi - \int_{K \cap \{t=0\}} \lambda_n q_0 \phi = 0.$$

This means that \bar{Q} takes the initial data $\lambda_n q_0(s)$ in a weak sense and, by regularity results, also in the classical sense.

Finally, take a smooth function ϕ with compact support K in $\{(s, t) : s < 0, -1 < t < \infty\}$. We proceed as in the previous case, but with the function $R_\varepsilon = Q_\varepsilon - \lambda_n$. By Lemma 3.3, when integrating by parts, we do not get any boundary integrals on Γ_∞ . Hence, after going to the limit with $\varepsilon = \varepsilon'' \rightarrow 0$, we find that $\bar{Q} - \lambda_n$ takes the initial value 0 on $\{(s, t) : s < 0, t = 0\}$. We have thus proved that $\bar{Q} = Q_0$, and this completes the proof of the theorem for p_n in the case $q_0(0) = 1, q_0 \in C^m$.

Consider next the case $q_0 \equiv 0$. Since the solution is not continuous, the preceding proof cannot be applied directly. Instead, we approximate the problem by introducing initial data as in Theorem 1, but with

$$q'_0(s) \leq 0, \quad q_0(s) \equiv 0 \text{ if } s > \delta.$$

We denote the corresponding solutions by $p_{j,\delta}$ and set $q_{\delta,\varepsilon} = p_{j,\delta}$. We introduce a function $Q_{\delta,\varepsilon}(s, t)$ by

$$q_{\delta,\varepsilon}(x, t) = Q_{\delta,\varepsilon}(s, t), \quad s = \frac{x - vt}{\sqrt{\varepsilon}}.$$

Then any sequence $(\delta', \varepsilon') \rightarrow 0$ has a subsequence $(\delta'', \varepsilon'') \rightarrow 0$ such that $Q_{\delta'', \varepsilon''} \rightarrow \bar{Q}$ weakly in $L^r(\mathbb{R}_2^+)$, and, as before, \bar{Q} coincides with the solution of the heat equation (1.7).

The proof of Theorem 3.1 for any p_j is the same as for p_n , since Lemmas 3.2 and 3.3 hold for any $1 \leq j \leq n$. \square

REFERENCES

- [1] J. J. BLUM AND M. C. REED, *The transport of organelles in axons*, Math. Biosci., 90 (1988), pp. 233–245.
- [2] J. J. BLUM AND M. C. REED, *A model for slow axonal transport and its application to neurofilamentous neuropathies*, Cell Motility Cytoskeleton, 12 (1989), pp. 53–65.
- [3] E. A. BROOKS, *Probabilistic methods for a linear reaction-hyperbolic system with constant coefficients*, Ann. Appl. Probab., 9 (1999), pp. 719–731.
- [4] A. BROWN, L. WANG, AND P. JUNG, *Stochastic simulation of neurofilament transport in axons: The “stop and go” hypothesis*, Mol. Biol. Cell, 16 (2005), pp. 4243–4255.
- [5] R. COURANT AND D. HILBERT, *Methods of Mathematical Physics*, Vol. 2, John Wiley and Sons, 1962.
- [6] G. CRACIUN, A. BROWN, AND A. FRIEDMAN, *A dynamical system model of neurofilament transport in axons*, J. Theoret. Biol., 237 (2005), pp. 316–322.
- [7] A. FRIEDMAN, *Partial Differential Equations of Parabolic Type*, Prentice-Hall, Englewood Hills, NJ, 1964.
- [8] A. FRIEDMAN AND G. CRACIUN, *A model of intracellular transport of particles in an axon*, J. Math. Biol., 51 (2005), pp. 217–246.
- [9] M. PINSKY, *Differential equations with a small parameter and the central limit theorem for functions defined on a finite Markov chain*, Z. Wahrsch. Verw. Gebiete, 9 (1967), pp. 101–111.
- [10] M. C. REED AND J. J. BLUM, *Theoretical Analysis of radioactivity profiles during fast axonal transport: Effects of deposition and turnover*, Cell Motility Cytoskeleton, 6 (1986), pp. 620–627.
- [11] M. C. REED, S. VENAKIDES, AND J. J. BLUM, *Approximate traveling waves in linear reaction-hyperbolic equations*, SIAM J. Appl. Math., 50 (1990), pp. 167–180.
- [12] L. WANG AND A. BROWN, *Rapid intermittent movement of axonal neurofilaments observed by fluorescence photobleaching*, Mol. Biol. Cell, 12 (2001), pp. 3257–3267.
- [13] L. WANG, C.-L. HO, D. SUN, R. K. H. LIEM, AND A. BROWN, *Rapid movement of axonal neurofilaments interrupted by prolonged pauses*, Nat. Cell Biol., 2 (2000), pp. 137–141.