DIFFUSION MEDIATED TRANSPORT IN MULTIPLE STATE SYSTEMS

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Abstract. Intracellular transport in eukarya is attributed to motor proteins that transduce chemical energy into directed mechanical motion. Nanoscale motors like kinesins tow organelles and other cargo on microtubules or filaments, have a role separating the mitotic spindle during the cell cycle, and perform many other functions. The simplest description gives rise to a weakly coupled system of evolution equations. The transport process, to the mind's eye, is analogous to a biased coin toss. We describe how this intuition may be confirmed by a careful analysis of the cooperative effect among the conformational changes and the potentials.

1. Introduction. Motion in small live systems has many challenges, as famously discussed in Purcell [25]. Prominent environmental conditions are high viscosity and warmth. Not only is it difficult to move, but maintaining a course is rendered difficult by immersion in a highly fluctuating bath. Intracellular transport in eukarya is attributed to motor proteins that transduce chemical energy into directed mechanical motion. Nanoscale motors like kinesins tow organelles and other cargo on microtubules or filaments, have a role separating the mitotic spindle during the cell cycle, and perform many other functions. Because of the presence of significant diffusion, they are sometimes referred to as Brownian motors. Since a specific type tends to move in a single direction, for example, anterograde or retrograde to the cell periphery, these proteins are sometimes referred to as molecular rachets. How do they overcome the issues posed by Purcell to provide the transport necessary for the activities of the cell?

Many models have been proposed to describe the functions of these proteins, or aspects of their thermodynamical behavior, beginning with Ajdari and Prost [1], Astumian and Bier, cf. eg. [2], and Doering, Ermentrout, and Oster [6], Peskin, Ermentrout, and Oster [23]. They consist either in discussions of distribution functions directly or of stochastic differential equations, which give rise to the distribution functions via the Chapman-Kolmogorov Equation. We have also suggested an approach for motor proteins like conventional kinesin where a dissipation principle is derived based on viewing an ensemble of motors as independent conformation changing nonlinear spring mass dashpots, [5], as motivated by Howard [11]. The dissipation principle, which involves a Kantorovich-Wasserstein metric, identifies the environment of the system and gives rise to an implicit scheme from which evolution equations follow, [3], [13], [15]. All of these descriptions consist, in the end, of Fokker-Planck type equations coupled via conformational change factors, typically known as weakly coupled

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parabolic systems. Our own is also distinguished because it has natural boundary conditions. Here our attention is directed towards the stationary solution of such a system to understand its transport properties.

A special collaboration among the potentials and the conformational changes in the system must be present for transport to occur. Here we investigate this for a system of n states. In Chipot, Hastings, and Kinderlehrer [4], the two component system was analyzed. As well as being valid for an arbitrary number of active components, our proof here is based on a completely different approach.

Let us introduce the equations we shall study. Suppose that $\rho_1, ..., \rho_n$ are partial probability densities defined on the unit interval $\Omega = (0,1)$ satisfying

$$\begin{aligned} &\frac{d}{dx}(\sigma\frac{d\rho_i}{dx} + \psi_i'\rho_i) + \sum_{j=1,...,n} a_{ij}\rho_j = 0 \ in\ \Omega \\ &\qquad\qquad \sigma\frac{d\rho_i}{dx} + \psi_i'\rho_i = 0 \ on\ \partial\Omega,\ i = 1, ...n, \\ &\rho_i \geqq 0 \ in\ \Omega,\ \int_\Omega (\rho_1 + \cdots + \rho_n)dx = 1. \end{aligned} \tag{1.1}$$

Here $\sigma > 0$, $\psi_1, ..., \psi_n$ are smooth non-negative functions of period $1/N$, and $A = (a_{ij})$ is a smooth rate matrix of period $1/N$, that is

$$\begin{aligned} &a_{ii} \leqq 0,\ a_{ij} \geqq 0\ for\ i \neq j\ and \\ &\sum_{i=1,..,n} a_{ij} = 0,\ j = 1, ..., n. \end{aligned} \tag{1.2}$$

We shall also have occasion to enforce a nondegeneracy condition

$$a_{ij} \not\equiv 0\ in\ \Omega,\ i, j = 1, ..., n. \tag{1.3}$$

The conditions (1.2) mean that $P = \mathbf{1} + \tau A$, for $\tau > 0$ small enough, is a probability matrix. The condition (1.3), we shall see, ensures that none of the components of ρ are identically zero passive placeholders in the system. The system (1.1) are the stationary equations of the evolution system

$$\frac{\partial \rho_i}{\partial t} = \frac{\partial}{\partial x}(\sigma \frac{\partial \rho_i}{\partial x} + \psi_i' \rho_i) + \sum_{j=1,\dots,n} a_{ij}\rho_j = 0 \ in \ \Omega, \ t > 0,$$
$$\sigma \frac{\partial \rho_i}{\partial x} + \psi_i' \rho_i = 0 \ on \ \partial\Omega, \ t > 0, \ i = 1, ...n, \tag{1.4}$$
$$\rho_i \geqq 0 \ in \ \Omega, \ \int_\Omega (\rho_1 + \cdots + \rho_n) dx = 1, \ t > 0.$$

Evidence of transport, to the left for example, would be some property of the form: $\rho_1 + \cdots + \rho_n$ is decreasing on Ω. This particular property does not hold. We shall prove that under appropriate geometric conditions on the ψ_i and the a_{ij}, this sum is bounded above by a decreasing exponential, that is,

$$\rho_1(x) + \cdots + \rho_n(x) \leqq C_0 e^{-\frac{C}{\sigma}x}, \quad x \in \Omega, \tag{1.5}$$

for σ sufficiently small. We would like to offer a preview of the features of the ψ_i and the a_{ij} and their cooperation that promotes this behavior.

To be avoided for transport are circumstances that lead to decoupling in (1.1), for example,

$$A\rho = 0, \ where \ \rho = (\rho_1, ..., \rho_n),$$

since in this case the solution vector is periodic. Such circumstances may be related to various types of detailed balance conditions. For example, if it is possible to find a solution ρ that minimizes the free energy of the system

$$F(\eta) = \sum_{i=1\cdots n} \int_\Omega \{\psi_i \eta_i + \sigma \eta_i \log \eta_i\} dx,$$

then $A\rho = 0$.

But avoiding this is not nearly sufficient. First we require that the potentials ψ_i have some asymmetry property. Roughly speaking, to favor transport to the left, towards $x = 0$, a period interval must have some subinterval where all the potentials ψ_j are increasing and in addition every point must have a neighborhood where at least one ψ_i is increasing. Some interchange among the n states must take place. To explain more clearly, suppose we are considering an ensemble of motors where each motor may occupy one of n states. The density of motors in state i at time (x,t) is given by $\rho_i(x,t)$, a solution of (1.4), whose stationary equations are (1.1). Then in the subinterval where all ψ_j are increasing, we may sum the equations of (1.1) and employ a Gronwall argument to obtain some exponential decrease, as suggested in (1.5).

Now we explain what is necessary to control the solution in the balance of a period interval. As mentioned, in any neighborhood in Ω, at least one ψ_i should be increasing to promote transport toward $x=0$. States tend to accumulate near the minima of the potentials, which correspond to attachment sites of the motor to the microtubule and its availability for conformational change. This typically would be where the matrix A is supported. In a neighbohood of such a minimum, states which are not favored for left transport should have the opportunity to switch to state i, so we impose $a_{ij}>0$ for all of these states. The weaker assumption, insisting only that the state associated with potential achieving the minimum have this switching opportunity, is insufficient because other states, perhaps not associated to increasing potentials, may also be available. This is a type of ergodic hypothesis saying that there must be mixing between at least one potential which transports left and all the ones which may not. Our hypothesis is not optimal, but some condition is necessary. One may consider, for example, simply adding new states to the system which are uncoupled to the original states. In fact, it is possible to construct situations where there is actually transport to the right by inauspicious choice of the supports of the a_{ij} as we show in section 4.

Here we only consider (1.1) although many other and more complex situations are possible. One example is a system where there are many conformational changes, not all related to movement. For example, one may consider the system whose stationary state is

$$\begin{aligned} \frac{d}{dx}(\sigma\frac{d\rho_i}{dx}+\psi_i'\rho_i)+\sum_{j=1,\dots,n}a_{ij}\rho_j&=0 \ in\ \Omega \quad i=1,...m,\\ \sum_{j=1,\dots,n}a_{ij}\rho_j&=0 \ in\ \Omega \quad i=m+1,...n,\\ \sigma\frac{d\rho_i}{dx}+\psi_i'\rho_i&=0 \ on\ \partial\Omega,\ \ i=1,...m,\\ \rho_i\geqq 0 \ in\ \Omega,\ \int_\Omega(\rho_1+\cdots+\rho_n)dx&=1. \end{aligned} \tag{1.6}$$

We leave such explorations to the interested reader.

2. Existence. There are several ways to approach the existence question for (1.1). In [4], we gave existence results based on the Schauder Fixed Point Theorem and a second proof based on an ordinary differential equations shooting method. The Schauder proof extends to the current situation, and higher dimension if that is of interest, but the shooting method was limited to the two state case. Here we offer a new ordinary differential equations method proof which is of interest because it separates existence from uniqueness and positivity, showing that existence is a purely algebraic property depending only on the second line in (1.2),

$$\sum_{i=1,..,n} a_{ij} = 0, \;\; j = 1, ..., n, \tag{2.1}$$

while positivity and uniqueness rely on the more geometric nature of the inequalities. We shall prove Theorem 2.1 below, followed by a brief discussion of a stronger result whose proof is essentially the same. Recall that $\Omega = (0, 1)$.

THEOREM 2.1. *Assume that $\psi_i, a_{ij} \in C^2(\overline{\Omega}), i, j = 1, ..., n$ and that (2.1) holds. Then there exists a solution $\rho = (\rho_1, ..., \rho_n)$ to (1.1). Assume furthermore that (1.2) and (1.3) hold. Then ρ is unique and*

$$\rho_i(x) > 0 \text{ in } \Omega \quad \text{and} \quad \rho_i \in C^2(\overline{\Omega}), \;\; i = 1, ..., n.$$

Proof. Introduce

$$\phi_i = \sigma \frac{d\rho_i}{dx} + \psi_i' \rho_i \;\; \text{in } \Omega, i = 1, ..., n$$

Our system may be written as the system of $2n$ ordinary differential equations, where (2.1) holds,

$$\begin{aligned} \sigma \frac{d\rho_i}{dx} &= \qquad \phi_i - \psi_i' \rho_i, \quad i = 1, ..., n \\ \frac{d\phi_i}{dx} &= \; - \sum_{j=1,...,n} a_{ij} \rho_j, \quad i = 1..., n. \end{aligned} \tag{2.2}$$

Let Φ denote the $2n \times 2n$ fundamental solution matrix of (2.2) with $\Phi(0) = \mathbf{1}$. Let Ψ be the $2n \times n$ matrix consisting of the first n columns of Φ. Then

$$\Psi = \begin{pmatrix} R \\ S \end{pmatrix},$$

where R and S are $n \times n$ matrix functions with $R(0) = \mathbf{1}$ and $S(0) = 0$. We wish to obtain a solution

$$\begin{pmatrix} \rho \\ \phi \end{pmatrix} = \Phi c$$

such that $\phi(0) = \phi(1) = 0$. To have $\phi(0) = 0$, we need the last n components of c to be zero, so

$$\begin{pmatrix} \rho \\ \phi \end{pmatrix} = \Psi d$$

where d is the vector consisting of the first n components of c. We then need the last n components of $\Psi(1)d$ to be zero, namely

$$S(1)d = 0. \tag{2.3}$$

Now in this setup, we have $\phi_i(0) = 0,\ i = 1, ..., n$ and from (2.1),

$$\sum_{i=1,\ldots,n} \frac{d\phi_i}{dx}(x) = 0,\ x \in \Omega,$$

whence

$$\sum_{i=1,\ldots,n} \phi_i(x) = 0,\ x \in \Omega.$$

But this simply means that

$$\sum_{i,j=1,\ldots,n} S_{ij}(x)d_j = 0\ for\ any\ d \in R^n$$

so the sum of the rows of S is zero for every $x \in \Omega$, i.e., $det\ S(x) = 0$, and so S is singular. Hence we can find a solution to (2.3).

Now we assume (1.2) and (1.3). If the solution is positive, it is the unique solution. This follows a standard argument. Suppose that ρ is a positive solution and that ρ^* is a second solution. Then $\rho + \mu\rho^*$ is a solution for any constant μ and $\rho + \mu\rho^* > 0$ in Ω for sufficiently small $|\mu|$. Increase $|\mu|$ until we reach the first value for which some ρ_i has a zero, say at $x_0 \in \Omega$. For this value of i we have that for $f = \rho + \mu\rho^*$, f_i has a minimum at x_0 and

$$-\frac{d}{dx}(\sigma\frac{df_i}{dx}+\psi_i' f_i)-a_{ii}f_i=\sum_{\substack{j=1,\dots,n\\ j\neq i}} a_{ij}f_j \geqq 0 \tag{2.4}$$

$$\sigma\frac{df_i}{dx}+\psi_i' f_i=0 \tag{2.5}$$

By an elementary maximum principle, [24], cf. also [4], we have that $f_i \equiv 0$.

We now claim that $f \equiv 0$. Choose any f_j and assume that it does not vanish identically. Using the maximum principle as before, $f_j > 0$. Now choose a point x_0 such that $a_{ij}(x_0) > 0$. Substituting onto (2.4) we now have a contradiction because $f_i \equiv 0$. Thus there is at most one solution satisfying (1.1).

It now remains to show that there is a positive solution. We employ a continuation argument. Note that there is a particular case where $\psi_i'(x) \equiv 0$ for all i and $a_{ii}(x) = 1-n$, and $a_{ij}(x) = 1$ for $j \neq i$. The solution in this case is $\rho_i(x) = \frac{1}{n}$, with our normalization in (1.1). For the moment, it is convenient to use a different normalization in terms of the vector d found above: choose the unique $d = (d_1, ..., d_n)^T$ satisfying $\max_i d_i = 1$.

For the special case above with

$$\psi_i' = 0, \quad a_{ii} = 1-n, \quad and \quad a_{ij} = 1, \; i \neq j,$$

we find that $d = (1, ..., 1)^T$. To abbreviate the system in vector notation, let ψ_0' and ψ' be the diagonal matrices of potentials $\psi_i' = 0$ and ψ_i', respectively, and let A_0 and A denote the matrices of lower order coefficients. For each λ, $0 \leqq \lambda \leqq 1$, we solve the problem

$$\begin{aligned}\sigma\frac{d^2\rho}{dx^2}+\frac{d}{dx}((\lambda\psi'+(1-\lambda)\psi_0')\rho)+(\lambda A+(1-\lambda)A_0)\rho=0 \; in \; \Omega\\ \sigma\frac{d\rho}{dx}+(\lambda\psi'+(1-\lambda)\psi_0'))\rho=0 \; at \; x=0,1.\end{aligned} \tag{2.6}$$

For $\lambda = 0$, (2.6) has a unique solution satisfying $\max_i \rho_i(0) = 1$ and this solution is positive. As long as the solution is positive, the argument given above shows that is its unique. As we increase λ from 0, the solution is continuous as a function of λ, since the vector d will be continuous as long as it is unique.

Let Λ denote the subset of $\lambda \in [0, 1]$ for which there is a positive solution of (2.6). To show that $\Lambda \subset [0, 1]$ is open, consider $\lambda_0 \in \Lambda$ and a sequence of points in Λ^c, the complement of Λ, convergent to λ_0. For each of these there is a non-positive solution of (2.6), and we may assume that the initial conditions d are bounded. Hence a subsequence converges to the initial condition for a non -positive solution with $\lambda = \lambda_0$, which contradicts the uniqueness of the positive solution.

To show Λ is closed, again suppose the contrary and that $\hat{\lambda}$ is a limit point of Λ not in Λ. Now some component $\hat{\rho}_i$ must have a zero, and $\hat{\rho}_i \geqq 0$ in Ω. Then by the maximum principle used above, $\hat{\rho}_i \equiv 0$. We now repeat the argument above to conclude that $\hat{\rho}_j \equiv 0$ in Ω for all $j = 1, ..., n$. But this is impossible because we have imposed the condition that $\max_i \hat{\rho}_i(0) = 1$. This implies that Λ is open, so $\Lambda = [0, 1]$.

Renormalizing to obtain total mass one completes the proof.

Condition (1.3) is more restrictive than necessary for uniqueness and positivity of the solution. For an improved result, recall that $P_\tau = \mathbf{1} + \tau A,\ \tau > 0$ small is a probability matrix when (1.2) is assumed. A probability matrix P is ergodic if some power P^k has all positive entries. In this case it has an eigenvector with eigenvalue 1 whose entries are positive, corresponding to a unique stationary state of the Markov chain it determines, and other well known properties from the Perron-Frobenius theory. Such matrices are often called irreducible and sometimes even "regular". We may now state an improvement of Theorem 2.1

Theorem 2.2. *In Theorem 2.1 replace condition (1.3) with*

$$\int_0^1 P_\tau(x)dx$$

is ergodic. Then the conclusions of Theorem 2.1 hold.

We outline the changes which must be made to prove this result. The previous proof relied on showing that if for some $i,\ \rho_i \equiv 0$, then $\rho_j \equiv 0$ for every j. This followed from the maximum principle and the feature of the equations that each consituent was nontrivially represented near at least one point $x_0 \in \Omega$. But suppose that $a_{ij} \equiv 0$ for some j. In this case we could have $\rho_j > 0$ and this has no effect on ρ_i.

Under the assumption that $\int_0^1 P_\tau(x)dx$ is ergodic, some nondiagonal element in the i^{th} row of A is not identically zero. This means that there is a $\pi(i) \neq i$ such that $\rho_i \equiv 0$ implies that $\rho_{\pi(i)} \equiv 0$. We may repeat this argument since ergodicity implies that the permuation π can be chosen so that $\pi^m(i)$ cycles atound the entire set of integers $1, ..., n$.

3. Transport. As we observed in the existence proof of the last section, the condition (1.1) implies that

$$\sum_{i=1,\dots,n} \frac{d}{dx}(\sigma \frac{d\rho_i}{dx} + \psi_i' \rho_i) = 0$$

so that

$$\sum_{i=1,\dots,n} (\sigma \frac{d\rho_i}{dx} + \psi_i' \rho_i) = \gamma = const.$$

In the case of interest of kinesin-type models, the boundary condition of (1.1) implies that $\gamma = 0$. In other words,

$$\sum_{i=1,\ldots,n} (\sigma \frac{d\rho_i}{dx} + \psi_i' \rho_i) = 0 \tag{3.1}$$

A simulation of typical behavior in a two species system is given in Figure 3.1.

THEOREM 3.1.

Suppose that ρ is a positive solution of (1.1)*, where the coefficients $a_{ij},\ i,j = 1,...,n$ and the $\psi_i,\ i = 1,...,n$ are smooth and 1/N-periodic in $\overline{\Omega}$. Suppose that (1.2) holds and also that the following conditions are satisfied.*

(i) Each ψ_i' has only a finite number of zeros in $\overline{\Omega}$.
(ii) In any interval in which no ψ_i' vanishes, $\psi_j' > 0$ in this interval for at least one j.
(iii) There is some interval in which $\psi_i' > 0$ for all $i = 1,...,n$.
(iv) If $I, |I| < 1/N$, is an interval in which $\psi_i' > 0$ for $i = 1,..,p$ and $\psi_i' < 0$ for $i = p+1,..,n$, and a is a zero of at least one of the ψ_k' which lies within ϵ of the right-hand end of I, then for ϵ sufficiently small, there is at least one index i, $i = 1,...,p$, with $a_{ij} > 0$ in $(a-\eta, a)$ for some $\eta > 0$, all $j = p+1,..,n$.

Then, there exist positive constants K_1, K_2 independent of σ such that

$$\sum_{i=1}^{n} \rho_i(x + \frac{1}{N}) \le K_1 e^{-\frac{K_2}{\sigma}} \sum_{i=1}^{n} \rho_i(x),\ x \in \Omega,\ x < 1 - \frac{1}{N} \tag{3.2}$$

for sufficiently small σ.

Note that (3.1) holds under the hypotheses of the theorem. Also note that from (*iv*), where $a_{ij} > 0, j = p+1,...,n$, necessarily, $a_{ii} < 0$ according to (1.2).

We shall prove Theorem 3.2 below. For this, it is convenient to consider a single period interval rescaled to be $[0,1]$. Theorem 3 then follows by rescaling and applying Theorem 3.2 to period intervals.

THEOREM 3.2. *Suppose that ρ is a positive solution of* (1.1)*, where the coefficients $a_{ij},\ i,j = 1,...,n$ and the $\psi_i,\ i = 1,...,n$ are smooth in* $[0,1]$*. Suppose that (1.2) holds and also that the following conditions are satisfied.*

(i) Each ψ_i' has only a finite number of zeros in $[0,1]$*.*
(ii) In any interval in which no ψ_i' vanishes, $\psi_j' > 0$ in this interval for at least one j.
(iii) There is some interval in which $\psi_i' > 0$ for all $i = 1,...,n$.
(iv) If I is an interval in which $\psi_i' > 0$ for $i = 1,..,p$ and $\psi_i' < 0$ for $i = p+1,..,n$, and a is a zero of at least one of the ψ_k' which lies within ϵ of the right-hand

end of I, then for ϵ sufficiently small, there is at least one i, $i = 1, ..., p$, we have $a_{ij} > 0$ in $(a - \eta, a)$ for some $\eta > 0$, $j = p + 1, .., n$.

Then, there exist positive constants K_1, K_2 independent of σ such that

$$\sum_{i=1}^{n} \rho_i(0) \leq K_1 e^{-\frac{K_2}{\sigma}} \sum_{i=1}^{n} \rho_i(1), \tag{3.3}$$

for sufficiently small σ.

The conclusion of the Theorem 3 is that the magnitude of the solution ρ, $\sum_{i=1}^{n} \rho_i$, is much smaller at $x = 1$ than at $x = 0$, or in terms of the Theorem 2, that it is bounded above by an exponentially decreasing function for small σ. There is no suggestion that $\sum_{i=1}^{n} \rho_i$ is itself exponentially decreasing and it is not. Indeed, the core of the mathematical argument is that $\sum \rho_i$ is exponentially decreasing on intervals where all ψ_i' are positive, while not significantly increasing in the remainder of [0,1]. The $\sum \rho_i$ may increase, even exponentially, in regions within δ of a zero of a ψ_i', but because the total length of these intervals is very small, the increase is outweighed by the decrease elsewhere. The argument in intervals where the signs of the ψ_i' are mixed is more delicate and relies on the coupling, as spelled out in (*iv*), the nonvanishing of some a_{ij} near the minima of ψ_i.

Proof of Theorem 3.1.

Since each ψ_i' has only finitely many zeros, we can enclose these zeros with intervals of length 2δ, where $\delta > 0$ and small will be chosen later. The remainder of [0,1] consists of a finite number of closed intervals $J_m, m = 1, ..., M$, in which no ψ_i' vanishes and so we have that $\psi_i' \geqq k(\delta) > 0$ or $\psi_i' \leqq -k(\delta) < 0$ for each i and some positive $k(\delta)$. From (*iii*), $k(\delta)$ may be chosen so that in at least one J_m, $\psi_i' \geqq k(\delta)$ for all i.

First we establish the exponential decay which governs the behavior of the solution. This will be a simple application of Gronwall's Lemma. Consider an interval $I_0 = J_m$ for one of the $m's$ where $\psi_i' \geq k(\delta)$ for all i. Suppose that

$$\sup_{I_0} \big\{ \inf_i \psi_i'(x) \big\} = K_0,$$

where, of course, K_0 is independent of δ for small δ. So there is a point $x_0 \in I_0$ where

$$\psi_i'(x_0) \geqq K_0, \quad i = 1, ..., n.$$

and

$$\psi_i'(x) \geqq \frac{1}{2} K_0, \quad |x - x_0| < L_0, \quad i = 1, ..., n.$$

for

$$L_0 = \frac{1}{2} \frac{K_0}{\max_{i=1...n} \{\sup_{[0,1]} |\psi_i''|\}}$$

Hence, from (3.1),

$$\frac{d}{dx} \sum_{i=1}^{n} \rho_i \leqq -\frac{K_0}{2\sigma} \sum_{i=1}^{n} \rho_i \quad in\ |x - x_0| < L_0,$$

so that

$$\sum_{i=1}^{n} \rho_i(x_0 + L_0) \leqq e^{-\frac{1}{\sigma}K_0 L_0} \sum_{i=1}^{n} \rho_i(x_0 - L_0).$$

Since $\sum_{i=1}^{n} \rho_i' \leqq 0$ in I_0, we have that

$$(\sum_{i=1}^{n} \rho_i)(\xi^*) \leqq e^{-\frac{1}{\sigma}K_0 L_0} (\sum_{i=1}^{n} \rho_i)(\xi) \quad where\ I_0 = [\xi, \xi^*] \tag{3.4}$$

Indeed, we could extend I_0 to an interval in which we demand only that all $\psi_i' \geqq 0$.

Next consider an interval, say I_1 of length 2δ centered on a zero a of one of the ψ_i'. From (3.1) we have that

$$\left| \frac{d}{dx} \left(\sum_{i=1}^{n} \rho_i \right) \right| \leq \frac{K_1}{\sigma} \sum_{i=1}^{n} \rho_i \quad in\ I_1$$

where

$$K_1 = \max_{i=1..n} \sup_{0 \leqq x \leqq 1} |\psi_i'|,$$

so that

$$\left(\sum_{i=1}^{n} \rho_i \right)(a + \delta) \leqq e^{\frac{1}{\sigma} 2K_1 \delta} \left(\sum_{i=1}^{n} \rho_i \right)(a - \delta) \tag{3.5}$$

There may be N such intervals, but over them all the exponential growth is only $\frac{2}{\sigma} N K_1 \delta$, and we can choose δ sufficiently small, which does not affect K_0, L_0 so that

$$2NK_1\delta < K_0 L_0$$

Finally, with δ so chosen, we consider an interval $I_2 = [\alpha, \beta]$ where, say,

$$\begin{aligned} \psi_i' &\geqq k(\delta), i = 1, ..., p,\ and \\ \psi_i' &\leqq -k(\delta), i = p+1, ..., n. \end{aligned} \tag{3.6}$$

We may assume that there is some overlap, that the endpoints α, β of I_2 are in 2δ intervals considered above. In the interval I_2, we shall bound $\rho_1, ...\rho_p$ on the basis of (3.6) above. We shall then argue that $\rho_{p+1}, ..., \rho_n$ are necessarily bounded or, owing to the coupling of the equations, the positivity of $\rho_1, ..., \rho_p$ would fail.

Write the equation for ρ_1 in the form

$$\sigma \rho_1'' + \psi_1' \rho_1' + \psi_1'' \rho_1 + a_{11} \rho_1 + \sum_{j=2}^{n} a_{1j} \rho_j = 0, \tag{3.7}$$

so that

$$\frac{d}{dx}\left(\rho_1' e^{\frac{1}{\sigma}(\psi_1(x)-\psi_1(\alpha)}\right) = -\frac{1}{\sigma}\Big\{(a_{11}+\psi_1'')\rho_1 + \sum_{j=2}^{n} a_{1j}\rho_j\Big\} e^{\frac{1}{\sigma}(\psi_1(x)-\psi_1(\alpha))},$$

and carrying out the integration,

$$\rho_1'(x) = \rho_1'(\alpha)e^{\frac{1}{\sigma}(\psi_1(\alpha)-\psi_1(x)} - \frac{1}{\sigma}\int_\alpha^x \Big\{(a_{11}+\psi_1'')\rho_1 + \sum_{j=2}^{n} a_{1j}\rho_j\Big\} e^{\frac{1}{\sigma}(\psi_1(s)-\psi_1(x))} ds \tag{3.8}$$

Now the $a_{1j}, j \geqq 2$, and the ρ_i are all non negative, so we may neglect the large sum and find a constant K_2 for which

$$\rho_1'(x) \leqq \rho_1'(\alpha)e^{\frac{1}{\sigma}(\psi_1(\alpha)-\psi_1(x))} + \frac{K_2}{\sigma}\int_\alpha^x \rho_1(s) e^{\frac{1}{\sigma}(\psi_1(s)-\psi_1(x))} ds \tag{3.9}$$

Note that for small σ,

$$\int_\alpha^x e^{\frac{1}{\sigma}(\psi_1(s)-\psi_1(x))} ds \leqq \int_\alpha^x e^{\frac{k(\delta)}{\sigma}(s-x)} ds \leqq \frac{\sigma}{k(\delta)} \tag{3.10}$$

Integrating (3.9),

$$\begin{aligned}\rho_1(x) - \rho_1(\alpha) &\leqq \rho_1'(\alpha)\int_\alpha^x e^{\frac{1}{\sigma}(\psi_1(s)-\psi_1(x))} ds + \frac{K_2}{\sigma}\int_\alpha^x \int_\alpha^t \rho_1(s) e^{\frac{1}{\sigma}(\psi_1(s)-\psi_1(t))} ds dt \\ &\leqq K(\delta)\sigma|\rho_1'(\alpha)| + K(\delta)\int_\alpha^x \max_{[\alpha,t]} \rho_1 dt,\end{aligned}$$

so,

$$\max_{[\alpha,x]} \rho_1 \leqq \rho_1(\alpha) + K(\delta)\sigma|\rho_1'(\alpha)| + K(\delta)\int_\alpha^x \max_{[\alpha,t]} \rho_1 dt.$$

We may now use Gronwall's Lemma to obtain

$$\rho_1(x) \leqq K(\delta)\big\{\rho_1(\alpha) + \sigma|\rho_1'(\alpha)|\big\}, \quad \alpha \leqq x \leqq \beta \tag{3.11}$$

Similar estimates hold for $\rho_2, ..., \rho_p$.

Our attention is directed to $\rho_{p+1}, ..., \rho_n$. Our first step is lower bounds for $\rho_1', ..., \rho_p'$, for which it suffices to carry out the details for ρ_1'. We can use (3.11) to modify our formula (3.8). Using (3.10),

$$\begin{aligned}\rho_1'(x) \geqq \rho_1'(\alpha)e^{\frac{1}{\sigma}(\psi_1(\alpha)-\psi_1(x))} &- \frac{1}{\sigma}\max_{I_2}\rho_1 \max_{I_2}(a_{11}+\psi_1'')\int_\alpha^x e^{\frac{1}{\sigma}(\psi_1(s)-\psi_1(x))} ds \\ &- \max_{[\alpha,x]}(\rho_{p+1}+\cdots+\rho_n)\max_{1\leqq i\leqq n}\max_{I_2} a_{ij}\int_\alpha^x e^{\frac{1}{\sigma}(\psi_1(s)-\psi_1(x))} ds\end{aligned}$$

So,

$$\rho_1'(x) \geqq \rho_1'(\alpha)e^{\frac{1}{\sigma}(\psi_1(\alpha)-\psi_1(x))} - K(\delta)\big\{\rho_1(\alpha)+\sigma|\rho_1'(\alpha)|\big\} - K(\delta)\max_{[\alpha,x]}(\rho_{p+1}+\cdots+\rho_n), \quad \alpha \leqq x \leqq \beta \tag{3.12}$$

Similarly for $\rho'_2, ..., \rho'_p$.

With our technique we can handle only the sum $\rho_{p+1} + \cdots + \rho_n$ and not individual $\rho_i, p+1 \leqq i \leqq n$. From (3.1), and taking into account (3.11), (3.12), and the signs of the ψ'_i,

$$\begin{aligned}\frac{d}{dx}(\rho_{p+1} + \cdots + \rho_n) &= -\frac{d}{dx}(\rho_1 + \cdots + \rho_p) - \frac{1}{\sigma}(\psi'_1\rho_1 + \cdots + \psi'_p\rho_p) - \frac{1}{\sigma}(\psi'_{p+1}\rho_{p+1} + \cdots + \psi'_n\rho_n) \\ &\geqq -\frac{K_1(\delta)}{\sigma}\sum_{i=1}^{p}(\rho_i(\alpha) + |\frac{d\rho_i}{dx}(\alpha)|) + \frac{K_2(\delta)}{\sigma}\sum_{i=p+1}^{n}\rho_i \quad in\ I_2 \qquad (3.13)\end{aligned}$$

Let

$$C(\alpha) = \sum_{i=1}^{p}(\rho_i(\alpha) + |\frac{d\rho_i}{dx}(\alpha)|),$$

which means (3.13) assumes the form

$$\frac{d}{dx}(\rho_{p+1} + \cdots + \rho_n) \geqq -\frac{K_1(\delta)}{\sigma}C(\alpha) + \frac{K_2(\delta)}{\sigma}(\rho_{p+1} + \cdots + \rho_n). \qquad (3.14)$$

We assert that

$$\rho_{p+1} + \cdots + \rho_n \leqq \frac{K_1(\delta)}{K_2(\delta)}C(\alpha) \quad \alpha \leqq x \leqq \beta - \delta. \qquad (3.15)$$

Suppose the contrary and that

$$\begin{gathered} A > 1 \quad and \\ (\rho_{p+1} + \cdots + \rho_n)(x^*) > \frac{AK_1(\delta)C(\alpha)}{K_2(\delta)} \ for\ some\ x^* \in [\alpha, \beta - \delta]. \end{gathered} \qquad (3.16)$$

This continues to hold in $[x^*, \beta]$, since at a first $x \in I_2$ where it fails, (3.14) would imply that $\rho_{p+1} + \cdots + \rho_n$ were increasing, which is not possible. Indeed, integrating (3.14) between points $x^*, x \in I_2$ with $x^* < x$, we have that

$$\begin{aligned}(\rho_{p+1} + \cdots + \rho_n)(x) &\geqq (\rho_{p+1} + \cdots + \rho_n)(x^*)e^{\frac{K_2(\delta)}{\sigma}(x-x^*)} + \frac{K_1(\delta)}{K_2(\delta)}C(\alpha)(1 - e^{\frac{K_2(\delta)}{\sigma}(x-x^*)}) \\ &\geqq \frac{AK_1(\delta)}{K_2(\delta)}C(\alpha)e^{\frac{K_2(\delta)}{\sigma}(x-x^*)} + \frac{K_1(\delta)}{K_2(\delta)}C(\alpha)(1 - e^{\frac{K_2(\delta)}{\sigma}(x-x^*)}) \\ &= (A-1)\frac{K_1(\delta)}{K_2(\delta)}C(\alpha)e^{\frac{K_2(\delta)}{\sigma}(x-x^*)} + \frac{K_1(\delta)}{K_2(\delta)}C(\alpha), \quad x^*, x \in I_2 \quad (3.17)\end{aligned}$$

Now let us suppose, without loss of generality, that (iv) holds for $i = 1$, that is, we can find a $K_3(\delta) > 0$ such that

$$\sum_{i=p+1}^{n} a_{1j}\rho_j \geqq K_3(\delta)(\rho_{p+1} + \cdots + \rho_n) \quad in\ [\beta - \delta, \beta] \qquad (3.18)$$

Keep in mind that

$$e^{\frac{K_2(\delta)}{\sigma}(x-x^*)} \geqq e^{\frac{K_2(\delta)}{\sigma}\frac{1}{4}\delta} = e^{\frac{K_4(\delta)}{\sigma}} \quad for\ \beta - \frac{1}{4}\delta \leqq x \leqq \beta.$$

Then we have from (3.8)

$$\begin{aligned}\frac{d\rho_1}{dx}(x) \leqq& \frac{d\rho_1}{dx}(\alpha)e^{-\frac{1}{\sigma}(\psi_1(x)-\psi_1(\alpha))} + \frac{K(\delta)}{\sigma}C(\alpha)\int_\alpha^x e^{\frac{1}{\sigma}(\psi_1(s)-\psi_1(x))}ds \\ &- \frac{(A-1)K_1(\delta)K_3(\delta)C(\alpha)}{K_2(\delta)}e^{\frac{1}{\sigma}K_4(\delta)} \\ \leqq& \frac{d\rho_1}{dx}(\alpha)e^{-\frac{1}{\sigma}(\psi_1(x)-\psi_1(\alpha))} + K(\delta)C(\alpha) \\ &- \frac{(A-1)K_1(\delta)K_3(\delta)C(\alpha)}{K_2(\delta)}e^{\frac{1}{\sigma}K_4(\delta)},\ for\ \beta - \frac{1}{4}\delta \leqq x \leqq \beta\end{aligned}$$

Above, $\psi_1(x) > \psi_1(\alpha)$, so the exponential in the first term on the right may be neglected. From the trivial inequality

$$\begin{aligned}0 \leqq \rho_1(x) &= \rho_1(\alpha) + \int_\alpha^x \rho_1'(s)ds \\ &\leqq C(\alpha) + \int_\alpha^x \rho_1'(s)ds,\end{aligned}$$

we have that

$$\begin{aligned}0 \leqq \frac{\rho_1(x)}{C(\alpha)} &\leqq 1 + \int_\alpha^x (1+K(\delta))ds - \int_{\beta-\frac{1}{4}\delta}^{\beta-\frac{1}{8}\delta}(A-1)\frac{K_1(\delta)}{K_2(\delta)}K_3(\delta)e^{\frac{K_4(\delta)}{\sigma}})ds \\ &\leqq 1 + (1+K(\delta))(\beta-\alpha) - (A-1)\frac{K_1(\delta)}{K_2(\delta)}K_3(\delta)e^{\frac{K_4(\delta)}{\sigma}}\frac{1}{8}\delta \qquad (3.19) \\ &for\ \beta - \frac{1}{8}\delta \leqq x \leqq \beta\end{aligned}$$

Since $A > 1$, the above cannot hold for small σ depending only on δ because the extreme right hand side of (3.19) is 0. This proves (3.15). Note that the size of σ determined by (3.19) depends on the geometrical features of the potentials $\psi_i, i = 1, ..., n$, but not on $C(\alpha)$, that is, the magnitude of the solution ρ.

The theorem now follows by concatenating the three cases.

4. Stability of the stationary solution. In this section we discuss the trend to stationarity of solutions of the time dependent system (1.4). We have the stability theorem

THEOREM 4.1. *Let $\rho(x,t)$ denote a solution of (1.4) with initial data*

$$\rho(x,0) = f(x) \qquad (4.1)$$

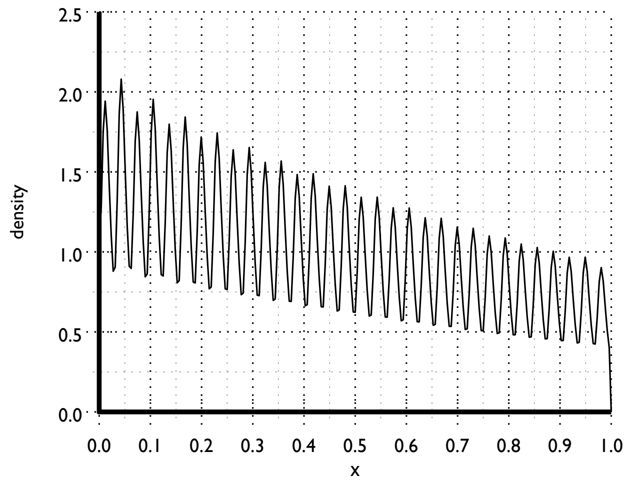

FIG. 3.1. *Transport in a two species system with period sixteen. The abcissa shows the total density $\rho_1 + \rho_2$. In this computation, ψ_2 is a one-half period translate of ψ_1 and the support of the $a_{ij}, i, j = 1, 2$ is a neighborhood of the minima of the $\psi_i, i = 1, 2$. The simulation was executed with a semi-implicit scheme.*

satisfiying

$$f_i(x) \geqq 0, \; i = 1, ..., n, \; and \sum_{i=1,...,n} \int_\Omega f_i dx = 1.$$

Then

$$\rho(x,t) - \rho_0(x) = O(e^{-\omega t}) \; ast \to \infty, \tag{4.2}$$

for some positive constant ω, where ρ_0 is the steady positive solution obtained in Theorem 1.

Thus the steady positive solution is globally stable. One proof of this was given in [4] for n = 2, and this proof may be extended to general n. A proof based on monotonisity of an entropy function is given in [22]. A different type of monotonicity result showing that the solution operator is an L^1-contraction is given in [10]. Here we outline a different way of viewing the problem based on inspection of the semigroup generated by the operator, written in vector form,

$$S\rho = \sigma \frac{\partial^2 \rho}{\partial x^2} + \frac{\partial}{\partial x}(\psi' \rho) + A\rho \tag{4.3}$$

with natural boundary conditions. All of the methods are based on ideas from positive operators via Perron-Frobenius-Krein-Rutman generalizations or on closely related monotonicity methods.

We need the result that (4.3) has a real eigenvalue λ_0, which is simple and has an associated positive eigenfunction, and that all other eigenvalues λ satisfy $\mathrm{Re}\lambda < \lambda_0$.

This is a standard result (see, for example, [33]) obtained using the ideas of positive operators. Very briefly, we define e^S by writing the solution of (4.3) as

$$\rho(x,t) = e^{tS} f(x). \tag{4.4}$$

Thus e^S is a positive operator, since $f \geqq 0$ implies $\rho \geq 0$, and clearly compact, and so has a real eigenvalue, e^{λ_0}, which is simple and has a positive eigenfunction, and all other eigenvalues e^{λ} have $\left|e^{\lambda}\right| < \left|e^{\lambda_0}\right|$. This leads to S having a real eigenvalue λ_0, simple and with a positive eigenfunction, and $\mathrm{Re}\,\lambda < \mathrm{Re}\,\lambda_0$ for any other eigenvalue. In fact, $\lambda_0 = 0$ because our problem has a positive steady state. Now form the

Laplace transform

$$\hat{\rho}(x,\lambda) = \int_0^\infty e^{-\lambda t} \rho(x,t)\, dt,$$

and (4.4) gives

$$\hat{\rho}(\cdot,\lambda) = (\lambda - S)^{-1} f, \tag{4.5}$$

and $\hat{\rho}$ is analytic in λ for $\mathrm{Re}\,\lambda \geq m - \delta$, say, except for an isolated singularity at $\lambda = 0$. Given the initial data f, we write

$$f = c\rho_0 + \rho^*,$$

where ρ^* is orthogonal to the positive eigenfunction, say ρ_0^*, of the adjoint operator of S. This determines c uniquely. Then, by the Fredholm alternative, we can solve

$$(S - \lambda I)\,\rho = \rho^*,$$

uniquely if we insist that the solution is orthogonal to ρ_0. Then $(S - \lambda I)^{-1} \rho^*$ is bounded, and

$$\begin{aligned} (S - \lambda I)^{-1} f &= c\,(S - \lambda I)^{-1} \rho_0 + O(1) \\ &= -\lambda^{-1} c\rho_0 + O(1) \end{aligned}$$

as $\lambda \to 0$, showing that the pole of $(S - \lambda I)^{-1}$ at $\lambda = 0$ has residue $-c\rho_0$. If we now

apply the inverse Laplace transform to (4.5), we get, integrating first up a vertical line $\mathrm{Re}\,\lambda = \gamma > 0$, and then moving it to $\mathrm{Re}\,\lambda = -\gamma$,

$$\rho(x,t) = c\rho_0 + O\left(e^{-\omega t}\right)$$

as required.

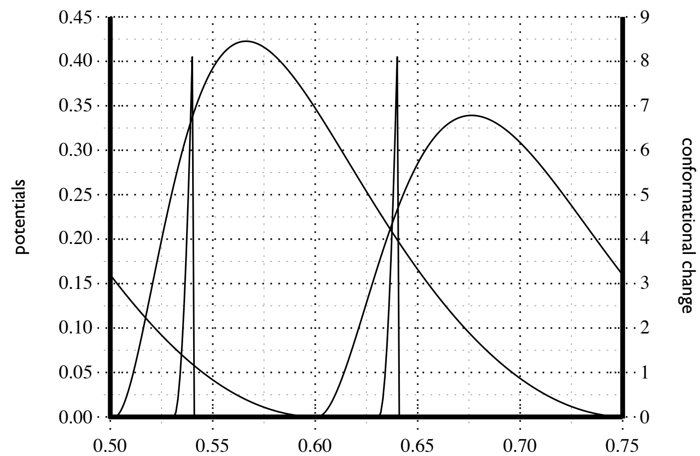

FIG. 5.1. *A period interval showing potentials and conformation coefficients which do not satisfy the hypothesis (iv) of Theorem 3.2.*

5. Discussion and some conditions for "reverse" transport. We now investigate what may happen if the conditions on the ψ_i in Theorem 3.1 are satisfied but those on the a_{ij} are not. In particular, we note that condition (iv) of Theorem 2 requires that if a is the minimum of one of the ψ_k, then some a_{ij} has support containing an interval $(a-\eta, a)$ to the left of a. We will show that without this condition, a_{ij} can be found such that the direction of transport is in the opposite direction from that described in Theorem 3.1. We remark that the necessity of some positivity condition on the a_{ij} to get transport is obvious, for if the a_{ij} are all identically zero, for example, or satisfy conditions that permit the functional F of the introduction to be minimized, then the solutions of (1.1) are periodic. What we look for in the following example is a situation in which there is transport, but in the opposite direction from that predictied by Theorem 2.2 even though the conditions on the ψ_i in that theorem are satisfied.

We now specialize to $n = 2$, a two state system. In constructing this example, we begin by considering functions ψ_i' and a_{ij} satisfying all of the hypotheses of Theorem 2.2, and reversing direction, with the transformation $x \to 1-x$. Thus, we set

$$\bar{\psi}_i(x) = \psi_i(1-x)$$
$$\bar{a}_{ij}(x) = a_{ij}(1-x).$$

From Theorem 3.2 we conclude that if $\bar{\rho}_1, \bar{\rho}_2$ is a solution of (1.1) but with $\bar{\psi}_i$ and $\bar{a}_{ij}$ replacing ψ_i and a_{ij}, then for small σ,

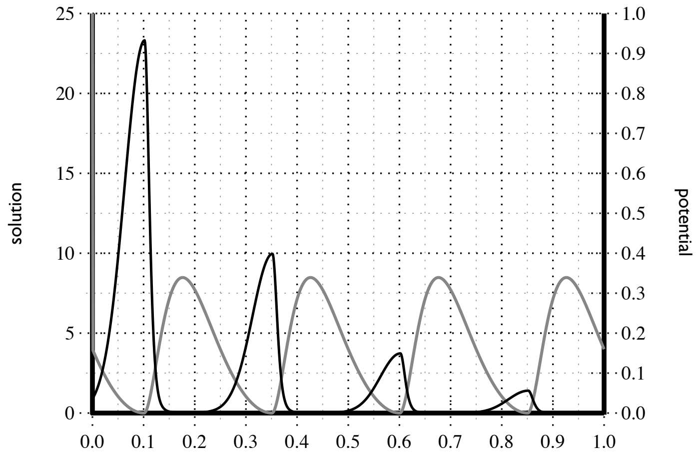

FIG. 5.2. *Reverse transport computed using the potentials and conformation coefficients shown in Figure 5.1. The simulation was done with XPP.*

$$\sum_{i=1}^{n} \bar{\rho}_i(0) \leq K_1 e^{-\frac{K_2}{\sigma}} \sum_{i=1}^{n} \bar{\rho}_i(1). \tag{5.1}$$

We then revert to the previous notation, dropping the bar's and letting ψ_i and a_{ij} denote data which give transport to the right in the sense of (5.1), as implied by Theorem 3.2. For example, we may assume that the following conditions are satisfied, cf. (1.2) and (1.3), for a two state system

$$a_{ii} < 0,\ i = 1,2 \tag{5.2}$$

$$a_{1i} + a_{2i} = 0 \text{ and } a_{ij} \not\equiv 0, \quad i = 1,2 \tag{5.3}$$

$$\text{If } \psi_1'(x) \geq 0 \text{ then } \psi_2'(x) < 0, \text{ while if } \psi_2'(x) \geq 0, \text{ then } \psi_1'(x) < 0 \tag{5.4}$$

$$\text{There is an interval in which } \psi_1' < 0 \text{ and } \psi_2' < 0. \tag{5.5}$$

Since our goal is simply a class of examples of reverse transport, we will impose further conditions on the ψ_i. Assume that ψ_1 has a minimum at $y_1 = 0$ followed by a maximum at $z_1 \in (0,1)$ and then a second minimum at 1, with $\psi_1(0) = \psi_1(1)$. Assume that ψ_2 has a minimum at $y_2 \in (z_1, 1)$ followed by a maximum at $z_2 \in (y_2, 1)$,and $\psi_2(0) = \psi_2(1)$. Assume that $\psi_i' \neq 0$ except at the minima and maxima specified above. We have $0 = y_1 < z_1 < y_2 < z_2 < 1$. There is no point where both $\psi_1' \geq 0$ and $\psi_2' \geq 0$ and so when the a_{ij} are all non-zero on $[0,1]$, we will have transport to the right as given in (5.1).

But we will now choose new a_{ij} to give transport to the left. For our existence we still need (1.2) and (1.3), in this case

$$a_{ii} \leqq 0,\ \ i = 1, 2 \tag{5.6}$$

$$a_{1i} + a_{2i} = 0 \ and \ a_{ij} \not\equiv 0, \quad i = 1, 2 \tag{5.7}$$

so the hypothesis (iv) of Theorem 3.2 about the relationship of the supports of the a_{ij} and the minima of the ψ_i will not be satisfied.

Choose a point $x_1 \in (y_1, z_1)$ and a point $x_2 \in (y_2, z_2)$. Our example is constructed initally using δ- functions, with a brief remark about the continuous case at the end. We consider the system

$$\begin{aligned} (\sigma\rho_1' + \psi_1'\rho_1)' &= (\delta(x - x_1) + \delta(x - x_2))(\rho_1 - \rho_2) \\ (\sigma\rho_2' + \psi_2'\rho_2)' &= (\delta(x - x_1) + \delta(x - x_2))(\rho_2 - \rho_1), \end{aligned} \tag{5.8}$$

with boundary conditions

$$\sigma\rho_i' + \psi_i'\rho_i = 0 \text{ at } x = 0, 1, \text{ for } i = 1, 2.$$

We wish to find further conditions which imply that there is a $c > 0$ independent of σ such that if (ρ_1, ρ_2) is a solution and $\rho_1 > 0$ and $\rho_2 > 0$ on $[0, 1]$, then

$$\rho_1(1) + \rho_2(1) < e^{-\frac{c}{\sigma}}(\rho_1(0) + \rho_2(0)). \tag{5.9}$$

We follow the technique in [4] , and let $\phi_i = \sigma\rho_i' + \psi_1'\rho_i$. Adding the equations in (5.8) shows that $\phi_1 + \phi_2$ is constant, and applying the boundary conditions shows that $\phi_1 + \phi_2 = 0$. This leads to the system

$$\begin{aligned} \sigma\rho_1' &= \hat{\phi} - \psi_1'\rho_1 \\ \sigma\rho_2' &= -\hat{\phi} - \psi_2'\rho_2 \\ \hat{\phi}' &= (\delta(x - x_1) + \delta(x - x_2))(\rho_1 - \rho_2), \end{aligned}$$

where $\hat{\phi} = \phi_1 = -\phi_2$. Observe that $\hat{\phi}$ takes a jump of amount $\rho_1(x_j) - \rho_2(x_j)$

at each x_j. Further, $\hat{\phi}$ is constant in the intervals $[0, x_1)$, (x_1, x_2), $(x_2, 1]$. Let $\hat{\phi}_j = \hat{\phi}(y_j)$. We then have

$$\rho_i(x_j) = \rho_i(y_j)\, e^{\frac{\psi_i(y_j) - \psi_i(x_j)}{\sigma}} + (-1)^{i-1}\hat{\phi}_j \int_{y_j}^{x_j} \frac{1}{\sigma} e^{\frac{\psi_i(s) - \psi_i(x_j)}{\sigma}} ds,$$

$i = 1, 2$. Hence,

$$\begin{aligned} \rho_1(x_j) - \rho_2(x_j) &= \rho_1(y_j)\, e^{\frac{\psi_1(y_j) - \psi_1(x_j)}{\sigma}} - \rho_2(y_j)\, e^{\frac{\psi_2(y_j) - \psi_2(x_j)}{\sigma}} \\ &\quad + \hat{\phi}_j \int_{y_j}^{x_j} \frac{1}{\sigma}\left(e^{\frac{\psi_1(s) - \psi_1(x_j)}{\sigma}} + e^{\frac{\psi_2(s) - \psi_2(x_j)}{\sigma}}\right) ds \end{aligned}$$

For $i = 1, 2$ let

$$
\begin{aligned}
a_i &= \frac{\psi_i(y_1)}{\sigma}\\
b_i &= \frac{\psi_i(x_1)}{\sigma}\\
c_i &= \frac{\psi_i(x_2)}{\sigma}\\
A_i &= \int_0^{x_1} \frac{1}{\sigma} e^{\frac{\psi_i(s)}{\sigma}} ds\\
B_i &= \int_{x_1}^{x_2} \frac{1}{\sigma} e^{\frac{\psi_i(s)}{\sigma}} ds\\
C_i &= \int_{x_2}^{1} \frac{1}{\sigma} e^{\frac{\psi_i(s)}{\sigma}} ds.
\end{aligned}
$$

Since $\psi_i(0) = \psi_i(1)$, we eventually obtain (computation facilitated by Maple)

$$
\begin{aligned}
\rho_1(1) &= k_{11}\rho_1(0) - k_{12}\rho_2(0) + k_{13}\hat{\phi}_1\\
\rho_2(1) &= -k_{21}\rho_1(0) + k_{22}\rho_2(0) - k_{23}\hat{\phi}_1
\end{aligned}
$$

where

$$
\begin{aligned}
k_{11} &= 1 + e^{-b_1}B_1 + e^{-b_1}C_1 + e^{-c_1}C_1 + e^{-b_1-c_1}B_1C_1 + e^{-b_1-c_2}B_2C_1\\
k_{12} &= e^{a_2-b_2-a_1}B_1 + C_1\left(e^{a_2-b_2-a_1} + e^{a_2-b_2-c_1-a_1}B_1 + e^{a_2-c_2-a_1} + e^{a_2-b_2-c_2-a_1}B_2\right)\\
k_{21} &= e^{a_1-b_1-a_2}B_2 + C_2(e^{-b_1} + e^{-c_1} + e^{-b_1-c_1}B_1 + e^{-b_1-c_2}B_2)\\
k_{13} &= e^{-a_1}(A_1 + B_1(1+v) + C_1(1+v) + e^{-c_1}C_1A_1 + e^{-c_1}C_1B_1(1+v)\\
&\quad + e^{-c_2}C_1A_2 + e^{-c_2}C_1B_2(1+v))\\
k_{22} &= 1 + e^{-b_2}B_2 + C_2(e^{-b_2} + e^{-b_2-c_1}B_1 + e^{-c_2} + e^{-b_2-c_2}B_2)\\
k_{23} &= e^{-a_2}A_2 + e^{-a_2}B_2(1+v) + e^{-a_2}C_2(1+v) + e^{-a_2-c_1}C_2A_1 + e^{-a_2-c_2}C_2A_2\\
&\quad + e^{-a_2-c_1}C_2B_1(1+v) + e^{-a_2-c_2}C_2B_2(1+v)
\end{aligned}
$$

with $v = e^{-b_1}A_1 + e^{-b_2}A_2$. As in [4], we solve each of the inequalities $\rho_1(1) > 0$,

$\rho_2(1) > 0$ for $\hat{\phi}_1$, and substitute the result into the other of these two relations. We find that

$$
\begin{aligned}
\rho_1(1) &\le \frac{k_{11}k_{23} - k_{21}k_{13}}{k_{23}}\rho_1(0) + \frac{k_{13}k_{22} - k_{12}k_{23}}{k_{23}}\rho_2(0),\\
\rho_2(1) &\le \frac{k_{11}k_{23} - k_{13}k_{21}}{k_{13}}\rho_1(0) + \frac{k_{13}k_{22} - k_{12}k_{23}}{k_{13}}\rho_2(0).
\end{aligned}
$$

To demonstrate exponential decay of $\frac{\rho_1(1)+\rho_2(1)}{\rho_1(0)+\rho_2(0)}$, we show that under certain additional conditions the four fractional coefficients $\frac{k_{11}k_{23}-k_{21}k_{13}}{k_{13}}$, $\frac{k_{11}k_{23}-k_{21}k_{13}}{k_{23}}$, $\frac{k_{13}k_{22}-k_{12}k_{23}}{k_{13}}$, $\frac{k_{13}k_{22}-k_{12}k_{23}}{k_{23}}$ tend to zero exponentially as $\sigma \to 0$. Further Maple computation (checked with Scientific Workplace) shows that

$$k_{11}k_{23}-k_{21}k_{13}=\frac{A_2}{e^{a_2}}+\frac{B_2}{e^{a_2}}+\frac{C_2}{e^{a_2}}+A_2\frac{B_1}{e^{a_2}e^{b_1}}+A_2\frac{C_1}{e^{a_2}e^{b_1}}+A_2\frac{B_2}{e^{a_2}e^{b_2}}+A_2\frac{C_1}{e^{a_2}e^{c_1}}$$
$$+A_2\frac{C_2}{e^{a_2}e^{b_2}}+B_2\frac{C_1}{e^{a_2}e^{c_1}}+A_2\frac{C_2}{e^{a_2}e^{c_2}}+B_2\frac{C_2}{e^{a_2}e^{c_2}}+A_2B_1\frac{C_1}{e^{a_2}e^{b_1}e^{c_1}}+A_2B_1\frac{C_2}{e^{a_2}e^{b_1}e^{c_2}}$$
$$+A_2B_2\frac{C_1}{e^{a_2}e^{b_2}e^{c_1}}+A_2B_2\frac{C_2}{e^{a_2}e^{b_2}e^{c_2}}$$

Note that many cancellations have occurred, eliminating terms in which four or five integrals are multiplied. Also,

$$k_{13}k_{22}-k_{12}k_{23}=\frac{A_1}{e^{a_1}}+\frac{B_1}{e^{a_1}}+\frac{C_1}{e^{a_1}}+A_1\frac{B_1}{e^{a_1}e^{b_1}}+A_1\frac{C_1}{e^{a_1}e^{b_1}}+A_1\frac{B_2}{e^{a_1}e^{b_2}}+A_1\frac{C_1}{e^{a_1}e^{c_1}}$$
$$+A_1\frac{C_2}{e^{a_1}e^{b_2}}+B_1\frac{C_1}{e^{a_1}e^{c_1}}+A_1\frac{C_2}{e^{a_1}e^{c_2}}+B_1\frac{C_2}{e^{a_1}e^{c_2}}+A_1B_1\frac{C_1}{e^{a_1}e^{b_1}e^{c_1}}+A_1B_1\frac{C_2}{e^{a_1}e^{b_1}e^{c_2}}$$
$$+A_1B_2\frac{C_1}{e^{a_1}e^{b_2}e^{c_1}}+A_1B_2\frac{C_2}{e^{a_1}e^{b_2}e^{c_2}}$$

In estimating the integrals, first consider B_1. We will say that $f\propto g$ if there are positive numbers α and β such that for sufficiently small σ, $\alpha<\frac{f}{g}<\beta$. We then have

$$B_1=\int_{x_1}^{x_2}e^{\frac{\psi_1(s)}{\sigma}}ds\propto\sigma^k e^{\frac{\psi_{1,\max}}{\sigma}},$$

for some $k>0$ and with $\psi_{1,\max}=\psi_1(z_1)=\max_x\psi_1(x)$. Also, for possibly different values of k,

$$\begin{aligned}
A_1&\propto\sigma^k e^{b_1}\\
A_2&\propto\sigma^k e^{a_2}\\
B_2&\propto\sigma^k\left(e^{b_2}+e^{c_2}\right)\\
C_1&\propto\sigma^k\left(e^{c_1}+e^{a_1}\right)\\
C_2&\propto\sigma^k e^{\frac{\psi_{2,\max}}{\sigma}}.
\end{aligned}$$

Hence the two largest terms among A_1,A_2,B_1,B_2,C_1,C_2, $e^{a_1},e^{a_2},e^{b_1},e^{b_2},e^{c_1},e^{c_2}$, are B_1 and C_2, for small σ. For the moment we let $d_i=\frac{\psi_{i,\max}}{\sigma}$ and set

$$\begin{aligned}
A_1&=e^{b_1}\\
A_2&=e^{a_2}\\
B_1&=e^{d_1}\\
B_2&=e^{b_2}+e^{c_2}\\
C_1&=e^{c_1}+e^{a_1}\\
C_2&=e^{d_2}
\end{aligned}$$

We will find also that to get the desired backward transport, we need to take x_2 near to the maximum of ψ_2. Therefore for now we will set $x_2 = y_2$, so that $c_2 = d_2$. Finally, we can without loss of generality assume that $a_1 = 0$.

Remark: The additional conditions we will give for backwards transport for small σ are that the inequalities (5.10) and (5.11) below hold and that x_2 is sufficiently close to y_2.

We then have

$$k_{11}k_{23} - k_{21}k_{13} = \frac{1}{e^{b_1}} + \frac{2}{e^{c_1}} + \frac{3}{e^{a_2}}e^{b_2} + \frac{1}{e^{b_1}}e^{c_1} + \frac{3}{e^{b_1}}e^{d_1} + \frac{4}{e^{a_2}}e^{d_2} + \frac{4}{e^{b_2}}e^{d_2} + \frac{1}{e^{a_2}}\frac{e^{b_2}}{e^{c_1}} + \frac{1}{e^{b_1}e^{c_1}}e^{d_1} + \frac{1}{e^{a_2}e^{c_1}}e^{d_2} + \frac{1}{e^{b_2}e^{c_1}}e^{d_2} + 6$$

$$k_{22}k_{13} - k_{12}k_{23} = 6e^{b_1} + 2e^{c_1} + 6e^{d_1} + 2\frac{e^{b_1}}{e^{c_1}} + \frac{2}{e^{c_1}}e^{d_1} + 4\frac{e^{b_1}}{e^{b_2}}e^{d_2} + \frac{e^{b_1}}{e^{b_2}e^{c_1}}e^{d_2} + 2$$

$$k_{13} = 2e^{b_1} + 4e^{c_1} + 4e^{d_1} + 2\frac{e^{a_2}}{e^{b_2}} + \frac{e^{b_1}}{e^{c_1}} + 2\frac{e^{a_2}}{e^{d_2}} + \frac{2}{e^{c_1}}e^{d_1} + 2\frac{e^{b_2}}{e^{d_2}} + 2\frac{e^{a_2}}{e^{b_2}}e^{c_1} + 2\frac{e^{a_2}}{e^{b_2}}e^{d_1} + 2e^{a_2}\frac{e^{c_1}}{e^{d_2}} + 2e^{b_2}\frac{e^{c_1}}{e^{d_2}} + \frac{e^{a_2}}{e^{b_2}e^{c_1}}e^{d_1} + 4$$

$$k_{23} = \frac{4}{e^{a_2}}e^{b_2} + \frac{6}{e^{a_2}}e^{d_2} + \frac{3}{e^{b_2}}e^{d_2} + \frac{1}{e^{a_2}}\frac{e^{b_1}}{e^{c_1}}e^{d_2} + \frac{2}{e^{a_2}e^{c_1}}e^{d_1}e^{d_2} + \frac{1}{e^{b_2}e^{c_1}}e^{d_1}e^{d_2} + 4$$

We now assume that $d_1 > \max\{b_1, c_1\}$, $a_1 = 0 < \min\{b_1, c_1\}$, and $d_2 > \max\{a_2, b_2\}$. We compare terms pairwise wherever possible, eliminating the term which is necessarily smaller as $\sigma \to 0$. This results in the asymptotic relations

$$k_{11}k_{23} - k_{21}k_{13} \propto \frac{3}{e^{b_1}}e^{d_1} + \frac{4}{e^{a_2}}e^{d_2} + \frac{4}{e^{b_2}}e^{d_2}.$$

(This expression is unchanged if we drop the assumption that $a_1 = 0$.) Similarly,

$$k_{22}k_{13} - k_{12}k_{23} \propto 6e^{d_1} + 4\frac{e^{b_1}}{e^{b_2}}e^{d_2}.$$

(with a_1 included: $\frac{6}{e^{a_1}}e^{d_1} + \frac{4}{e^{a_1}}\frac{e^{b_1}}{e^{b_2}}e^{d_2}$),

$$k_{13} \propto 4e^{d_1} + 2\frac{e^{a_2}}{e^{b_2}}e^{d_1}.$$

(or with a_1 : $\frac{4}{e^{a_1}}e^{d_1} + \frac{2}{e^{a_1}}\frac{e^{a_2}}{e^{b_2}}e^{d_1}$), and

$$k_{23} \propto \frac{2}{e^{a_2}e^{c_1}}e^{d_1}e^{d_2} + \frac{1}{e^{b_2}e^{c_1}}e^{d_1}e^{d_2}.$$

(This is unchanged if $a_1 \neq 0$.) From these we conclude that the four fractions in question are exponentially small as $\sigma \to 0$ if in addition to the previous assumptions we have

$$d_2 - a_2 < d_1 - b_1 < d_2 - b_2. \tag{5.10}$$

and

$$d_1 > b_1 + c_1. \tag{5.11}$$

(If $a_1 \neq 0$ this becomes $d_1 + a_1 > b_1 + c_1$.) By continuity we see that these inequalities

will also suffice if c_2 is sufficiently close to d_2. The conclusions also hold with the factors σ^k included in the asymptotic expressions, since these don't affect the exponential limits. Finally we wish to obtain a result with continuous functions for the

a_{ij}. Here we don't have a limit result as $\sigma \to 0$. But suppose that $\varepsilon > 0$ is given, and in the equation (5.8) we choose σ so small that

$$\sum_{i=1}^{n} \rho_i (1) < \varepsilon \sum_{i=1}^{n} \rho_i (0).$$

Then for this σ the same inequality will hold for continuous functions α_{ij} sufficiently close in an appropriate sense to the δ-functions in (5.8).

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