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 potentials present in the equations.

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. Proteins like kinesin function as nanoscale motors, towing 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?

There are many descriptions of the function 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]. For more recent work, note the review paper [26] and [27] Chapter 8. The descriptions consist either in discussions of stochastic differential equations, which give rise to the distribution functions via the Chapman-Kolmogorov Equation, or of distribution functions directly. In [5], we have suggested a dissipation principle approach for motor proteins like conventional kinesin, motivated by Howard [12]. 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], [14], [16], [19], [20]. and more generally [29]. Most of these formulations consist, in the end, of Fokker-Planck type equations coupled via conformational change factors,
typically known as weakly coupled parabolic systems. Our own is also distinguished because it has natural boundary conditions. To investigate transport properties, our attention is directed towards the stationary solution of such a system, as we explain below.

A special collaboration among the potentials and the conformational changes in the system must be present for transport to occur. To investigate this, we introduce the $n$–state system we shall study. Suppose that $\rho_1, ..., \rho_n$ are partial probability densities defined on the unit interval $\Omega = (0, 1)$ satisfying

$$
\frac{d}{dx} (\sigma \frac{d\rho_i}{dx} + \psi'_i \rho_i) + \sum_{j=1, \ldots, n} a_{ij} \rho_j = 0 \text{ in } \Omega
$$

$$
\sigma \frac{d\rho_i}{dx} + \psi'_i \rho_i = 0 \text{ on } \partial \Omega, \ i = 1, \ldots, n,
$$

$$
\rho_i \geq 0 \text{ in } \Omega, \ \int_{\Omega} (\rho_1 + \cdots + \rho_n) dx = 1.
$$

(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

$$
a_{ii} \leq 0, \ a_{ij} \geq 0 \text{ for } i \neq j \text{ and } \sum_{i=1, \ldots, n} a_{ij} = 0, \ j = 1, \ldots, n.
$$

(1.2)

We shall also have occasion to enforce a nondegeneracy condition

$$
a_{ij} \neq 0 \text{ in } \Omega, \ i, j = 1, \ldots, n.
$$

(1.3)

The conditions (1.2) mean that $P = 1 + \tau A$, for $\tau > 0$ small enough, is a probability matrix. The condition (1.3), we shall see, ensures that none of the components of $\rho$ are identically zero passive placeholders in the system. In this context, the potentials $\psi_1, ..., \psi_n$ describe interactions among the states, the elements of the protein’s structure, and the microtuble track and the matrix $A$ describes interchange of activity among the states. The system (1.1) are the stationary equations of the evolution system

$$
\frac{\partial \rho_i}{\partial t} = \frac{\partial}{\partial x} (\sigma \frac{\partial \rho_i}{\partial x} + \psi'_i \rho_i) + \sum_{j=1, \ldots, n} a_{ij} \rho_j = 0 \text{ in } \Omega, \ t > 0,
$$

$$
\sigma \frac{\partial \rho_i}{\partial x} + \psi'_i \rho_i = 0 \text{ on } \partial \Omega, \ t > 0, \ i = 1, \ldots, n,
$$

$$
\rho_i \geq 0 \text{ in } \Omega, \ \int_{\Omega} (\rho_1 + \cdots + \rho_n) dx = 1, \ t > 0.
$$

(1.4)

Before proceeding further, let us discuss what we intend by transport. In a chemical or conformational change process, a reaction coordinate (or coordinates) must be
specified. This is the independent variable. In a mechanical system, it is usually evident what this coordinate must be. In our situation, even though both conformational change and mechanical effects are present, it is natural to specify the distance along the motor track, the microtubule, here the interval \( \Omega \), as the independent variable. We interpret the migration of density to one end of the track during the evolution as evidence of transport.

We shall show in Section 4 that the stationary solution of the system (1.1), which we denote by \( \rho^\sharp \), is globally stable: given any solution \( \rho(x,t) \) of (1.4),

\[
\rho(x,t) \to \rho^\sharp(x) \text{ as } t \to \infty
\]

(1.5)

So the migration of density we referred to previously may be ascertained by inspection of \( \rho^\sharp \). In the sequel, we simply set \( \rho = \rho^\sharp \).

If the preponderance of mass of \( \rho \) is distributed at one end of the track, our domain \( \Omega \), then transport is present. Our main result, stated precisely later in Section 3, is that with suitable potentials \( \psi_1, \ldots, \psi_n \) and with favorable coupling between them and the rate matrix \( A \), there are constants \( K \) and \( M \), independent of \( \sigma \), such that

\[
\sum_{i=1}^{n} \rho_i(x + \frac{1}{N}) \leq Ke^{-\frac{M}{N} \sum_{i=1}^{n} \rho_i(x)}, \quad x \in \Omega, \quad x < 1 - \frac{1}{N}
\]

(1.6)

for sufficiently small \( \sigma > 0 \). So from one period to the next, total mass decays exponentially as in Bernoulli trials with a biased coin.

In summary, transport results from functional relationships in the system (1.1) or (1.4). The actual proof is technical, as most proofs are these days, and a detailed explanation of the conditions we impose is given after Theorem 3.2, when the notations have been introduced. Here we briefly consider the main elements of our thinking. We also refer to [10] for a more extended discussion.

To favor transport, we wish to avoid circumstances that permit decoupling in (1.1), for example,

\[
A\rho = 0, \quad \text{where } \rho = (\rho_1, \ldots, \rho_n),
\]

since in this case the solution vector is periodic. Such circumstances may be related to various types of detailed balance conditions. In detailed balance, we would find that

\[
a_{ij} \rho_j = a_{ji} \rho_i \quad \text{for all } i, j = 1, \ldots, n,
\]

implying that \( A\rho = 0 \). For example, if it is possible to find a solution \( \rho \) of (1.1) that minimizes the free energy of the system

\[
F(\eta) = \sum_{i=1}^{n} \int_{\Omega} \left\{ \psi_i \eta_i + \sigma \eta_i \log \eta_i \right\} dx,
\]

then \( A\rho = 0 \).
But avoiding these situations is not nearly sufficient. First we require that the potentials $\psi_i$ 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 $\psi_j$ are increasing. In addition every point must have a neighborhood where at least one $\psi_i$ is increasing. Some coupling among the $n$ states must take place.

Now we explain the nature of the coupling we impose, the properties of the matrix $A$. As mentioned above, in any neighborhood in $\Omega$, at least one $\psi_i$ should be increasing to promote transport toward $x = 0$. Density tends 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 neighborhood 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. 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 5.

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

$$\frac{d}{dx} (\sigma \frac{d\rho_i}{dx} + \psi_i' \rho_i) + \sum_{j=1,\ldots,n} a_{ij} \rho_j = 0 \text{ in } \Omega, \ i = 1,\ldots,m,$$

$$\sum_{j=1,\ldots,n} a_{ij} \rho_j = 0 \text{ in } \Omega, \ i = m + 1,\ldots,n,$$

$$\sigma \frac{d\rho_i}{dx} + \psi_i' \rho_i = 0 \text{ on } \partial \Omega, \ i = 1,\ldots,m,$$

$$\rho_i \geq 0 \text{ in } \Omega, \int_\Omega (\rho_1 + \cdots + \rho_n) dx = 1.$$ (1.7)

One such example is in [10]. We leave additional such explorations to the interested reader. 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.

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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 to higher dimensions, 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),

\[ \sum_{i=1}^{n} a_{ij} = 0, \quad j = 1, \ldots, n, \quad (2.1) \]

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 \( \psi_i, a_{ij} \in C^2(\bar{\Omega}), i, j = 1, \ldots, n \) and that (2.1) holds. Then there exists a (nontrivial) solution \( \rho = (\rho_1, \ldots, \rho_n) \) to the equations and boundary conditions in (1.1). Assume furthermore that (1.2) and (1.3) hold. Then \( \rho \) is unique and

\[ \rho_i(x) > 0 \text{ in } \Omega \text{ and } \rho_i \in C^2(\bar{\Omega}), \quad i = 1, \ldots, n. \]

Proof. Introduce

\[ \phi_i = \sigma \frac{d\rho_i}{dx} + \psi_i' \rho_i \text{ in } \Omega, i = 1, \ldots, n \]

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

\[ \sigma \frac{d\rho_i}{dx} = \phi_i - \psi_i' \rho_i, \quad i = 1, \ldots, n \]
\[ \frac{d\phi_i}{dx} = - \sum_{j=1}^{n} a_{ij} \rho_j, \quad i = 1, \ldots, n. \quad (2.2) \]

Let \( \Phi \) denote the \( 2n \times 2n \) fundamental solution matrix of (2.2) with \( \Phi(0) = 1 \). Let \( \Psi \) be the \( 2n \times n \) matrix consisting of the first \( n \) columns of \( \Phi \). Then

\[ \Psi = \begin{pmatrix} R \\ S \end{pmatrix}, \]

where \( R \) and \( S \) are \( n \times n \) matrix functions with \( R(0) = 1 \) 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 \( \phi_i(0) = 0 \), \( i = 1, \ldots, n \), for each column of \( S \) and from (2.1),

\[
\sum_{i=1,\ldots,n} d\phi_i(x) = 0, \quad x \in \Omega,
\]

whence

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

But this simply means that for each \( j \)

\[
\sum_{i=1,\ldots,n} S_{ij}(x) = 0
\]

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 (nontrivial) 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 $\rho$ is a positive solution and that $\rho^*$ is a second solution. Then $\rho + \mu \rho^*$ is a solution for any constant $\mu$ and $\rho + \mu \rho^* > 0$ in $\Omega$ for sufficiently small $|\mu|$. Increase $|\mu|$ until we reach the first value for which some $\rho_i$ 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

$$-\frac{d}{dx} (\sigma \frac{df_i}{dx} + \psi_i' f_i) - a_{ii} f_i = \sum_{j=1,\ldots,n} a_{ij} f_j \geq 0$$  \hspace{1cm} (2.4)$$

$$\sigma \frac{df_i}{dx} + \psi_i' f_i = 0$$  \hspace{1cm} (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 $d = (d_1, \ldots, d_n)^T$ satisfying $\max_i d_i = 1$.

For the special case above with

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

we find that $d = (1, \ldots, 1)^T$. To abbreviate the system in vector notation, let $\psi'_0$ and $\psi'$ be the diagonal matrices of potentials $\psi'_i = 0$ and $\psi'_i$, respectively, and let $A_0$ and $A$ denote the matrices of lower order coefficients. For each $\lambda$, $0 \leq \lambda \leq 1$, we solve the problem

$$\sigma \frac{d^2 \rho}{dx^2} + \frac{d}{dx}((\lambda \psi' + (1 - \lambda) \psi'_0)\rho) + (\lambda A + (1 - \lambda) A_0)\rho = 0 \text{ in } \Omega$$

$$\sigma \frac{d \rho}{dx} + (\lambda \psi' + (1 - \lambda) \psi'_0)\rho = 0 \text{ at } x = 0, 1.$$  \hspace{1cm} (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 it
is unique. As we increase $\lambda$ from 0, the solution is continuous as a function of $\lambda$, since the vector $d$ will be continuous as long as it is unique.

Let $\Lambda$ 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 $\Lambda^c$, the complement of $\Lambda$, convergent to $\lambda_0$. 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 $\Lambda$ is closed, again suppose the contrary and that $\hat{\lambda}$ is a limit point of $\Lambda$ not in $\Lambda$. Now some component $\hat{\rho}_i$ must have a zero, and $\hat{\rho}_i \geq 0$ in $\Omega$. 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 $\Omega$ for all $j = 1, \ldots, n$. But this is impossible because we have imposed the condition that $\max_i \hat{\rho}_i(0) = 1$. This implies that $\Lambda$ 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 $P_\tau = 1 + \tau A$, $\tau > 0$ 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 constituent 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 $\rho_i$.

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 permutation $\pi$ can be chosen so that $\pi^m(i)$ cycles around the entire set of integers $1, \ldots, n$.

This completes the proof of existence of a unique solution of the stationary system with $\max_i d_i = 1$. This solution is also positive. Renormalizing to obtain total mass 1 completes the proof.
3. Transport. As we observed in the existence proof of the last section, the condition (1.1) implies that
\[ \sum_{i=1,\ldots,n} \frac{d}{dx} \left( \sigma \frac{d\rho_i}{dx} + \psi'_i \rho_i \right) = 0 \]
so that
\[ \sum_{i=1,\ldots,n} \left( \sigma \frac{d\rho_i}{dx} + \psi'_i \rho_i \right) = \gamma = \text{const.} \]
In the case of interest of kinesin-type models, the boundary condition of (1.1) implies that \( \gamma = 0 \). In other words,
\[ \sum_{i=1,\ldots,n} \left( \sigma \frac{d\rho_i}{dx} + \psi'_i \rho_i \right) = 0 \] (3.1)
A simulation of typical behavior in a two species system is given in Figure 3.1.

**Theorem 3.1.** Suppose that \( \rho \) is a positive solution of (1.1), where the coefficients \( a_{ij}, i,j = 1,\ldots,n \) and the \( \psi_i, i = 1,\ldots,n \) are smooth and \( 1/N \)-periodic in \( \Omega \). Suppose that (1.2) holds and also that the following conditions are satisfied.

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

Then, there exist positive constants \( K,M \) independent of \( \sigma \) and depending on the potentials \( \psi_i, i = 1,\ldots,n \) and the coefficients \( a_{ij}, i,j = 1,\ldots,n \) such that
\[ \sum_{i=1}^{n} \rho_i(x + \frac{1}{N}) \leq Ke^{-\frac{N}{4}} \sum_{i=1}^{n} \rho_i(x), \quad x \in \Omega, \quad x < 1 - \frac{1}{N} \] (3.2)
for sufficiently small \( \sigma \).

Note that (3.1) holds under the hypotheses of the theorem. Also note that from (iv), where \( a_{ij} > 0, j = p+1,\ldots,n, \) 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 3.1 then follows by rescaling and applying Theorem 3.2 to period intervals.

**Theorem 3.2.** Suppose that \( \rho \) is a positive solution of (1.1), where the coefficients \( a_{ij}, i,j = 1,\ldots,n \) and the \( \psi_i, i = 1,\ldots,n \) are smooth in \([0,1]\). Suppose that (1.2) holds and also that the following conditions are satisfied.
(i) Each $\psi_i'$ has only a finite number of zeros in $[0,1]$.
(ii) There is some interval in which $\psi_i' > 0$ for all $i = 1, \ldots, n$.
(iii) In any interval in which no $\psi_i'$ vanishes, $\psi_j' > 0$ in this interval for at least one $j$.
(iv) If $I$ is an interval in which $\psi_i' > 0$ for $i = 1, \ldots, p$ and $\psi_i' < 0$ for $i = p + 1, \ldots, n$, and $a$ is a zero of at least one of the $\psi_k'$ which lies within $\epsilon$ of the right-hand end of $I$, then for $\epsilon$ sufficiently small, there is at least one $i$, $i = 1, \ldots, p$, for which $a_{ij} > 0$ in $(a - \eta, a)$ for some $\eta > 0$, $j = p + 1, \ldots, n$.

Then, there exist positive constants $K, M$ independent of $\sigma$ and depending on the potentials $\psi_i, i = 1, \ldots, n$ and the coefficients $a_{ij}, i, j = i, \ldots, n$ such that

$$\sum_{i=1}^{n} \rho_i(1) \leq Ke^{-M} \sum_{i=1}^{n} \rho_i(0),$$

for sufficiently small $\sigma$.

The conclusion of the Theorem 3.2 is that the magnitude of the solution $\rho$, $\sum_{i=1}^{n} \rho_i$, is much smaller at $x = 1$ than at $x = 0$, or in terms of the Theorem 3.1, that it is bounded above by an exponentially decreasing function for small $\sigma$. 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 $\psi_i'$ are positive, while not significantly increasing in the remainder of $[0,1]$. The $\sum \rho_i$ may increase, even exponentially, in regions within $\delta$ of a zero of a $\psi_i'$, 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 $\psi_i'$ 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 $\psi_i$, and we briefly describe it below.

First let us assess how, essentially, the constants $K, M$ depend on the parameters, especially the potentials $\psi_i$, by examining an interval where $\psi_i' > 0$ for all $i$. Such an interval exists by condition (ii) of the theorem. Let $[a, b]$ be such an interval and set

$$q(x) = \min_{i=1,\ldots,n} \psi_i'(x).$$

From (3.1),

$$\frac{d}{dx} (\rho_1 + \cdots + \rho_n)(x) \leq -\frac{1}{\sigma} q(x)(\rho_1 + \cdots + \rho_n)(x)$$

so that by integrating,

$$(\rho_1 + \cdots + \rho_n)(b) \leq e^{-\frac{1}{\sigma} \int_a^b q(x)dx} (\rho_1 + \cdots + \rho_n)(a)$$

If there are several such intervals, we just combine the effects and this is the essence of how $K, M$ (particularly $M$) depend on the $\psi_i'$. In other words, a Gronwall type argument is successful here.

Now let us try to explain the role of the coupling. This comes into play when condition (iv) of the hypotheses hold. Suppose that $\nu \in \{1, \ldots, p\}$ is a favorable index in the
interval $I$ and consider the $\nu^{th}$ equation

$$
\sigma \rho''_\nu + \psi'_\nu \rho_{\nu} + \psi''_\nu \rho_{\nu} + \sum_{j \neq \nu}^n a_{\nu j} \rho_j = 0, \tag{3.4}
$$

Equation (3.4) represents a balance between $\rho_{\nu}$ and the other $\rho_j$. As seen in the sequel, since the items in the $\Sigma$ are nonnegative, they may be discarded and (3.4) can be employed to find an upper bound for $\rho_{\nu}$ on $I$, because $\psi_{\nu}$ is increasing. We can then exploit (3.4) to impede the growth of the unfavorable $\rho_j, j = p+1, \ldots, n$. Namely $\{\rho_j\}$ cannot be too large without forcing $\rho_{\nu}$ negative. But this can only be assured if the coupling is really there, namely if $a_{\nu j} > 0$. This is the motivation for the ergodic type hypothesis in (iv).

**Proof of Theorem 3.2.**

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

$$
\sup_{I_0} \left\{ \inf_i \psi'_i(x) \right\} = K_0,
$$

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

$$
\psi'_i(x_0) \geq K_0, \quad i = 1, \ldots, n,
$$

and

$$
\psi'_i(x) \geq \frac{1}{2} K_0, \quad |x - x_0| < L_0, \quad i = 1, \ldots, n,
$$

for

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

Hence, from (3.1),

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

so that

$$
\sum_{i=1}^n \rho_i(x_0 + L_0) \leq e^{-\frac{1}{2} K_0 L_0} \sum_{i=1}^n \rho_i(x_0 - L_0).
$$
Since \( \sum_{i=1}^{n} \rho_i' \leq 0 \) in \( I_0 \), we have that

\[
(\sum_{i=1}^{n} \rho_i)(\xi^*) \leq e^{-\frac{1}{2}K_0L_0} (\sum_{i=1}^{n} \rho_i)(\xi)
\]

where \( I_0 = [\xi, \xi^*] \) (3.5)

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

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

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

where

\[
K_1 = \max_{i=1...n} \sup_{0 \leq x \leq 1} |\psi_i'|,
\]

so that

\[
\left( \sum_{i=1}^{n} \rho_i \right) (a + \delta) \leq e^{\frac{1}{2}2K_1\delta} \left( \sum_{i=1}^{n} \rho_i \right) (a - \delta)
\]

(3.6)

There may be \( N \) such intervals, but over them all the exponential growth is only \( \frac{2}{\delta}NK_1\delta \), and we can choose \( \delta \) sufficiently small, which does not affect \( K_0, L_0 \) so that

\[
2NK_1\delta < K_0L_0
\]

Finally, with \( \delta \) so chosen, we consider an interval \( I_2 = [\alpha, \beta] \) where, say,

\[
\psi_i' \geq k(\delta), \ i = 1, ..., p, \ \text{and} \quad \psi_i' \leq -k(\delta), \ i = p+1, ..., n.
\]

(3.7)

We may assume that there is some overlap, that the endpoints \( \alpha, \beta \) of \( I_2 \) are in \( 2\delta \) intervals considered above. In the interval \( I_2 \), we shall bound \( \rho_1, \ldots, \rho_p \) on the basis of (3.7) above. We shall then argue that \( \rho_{p+1}, \ldots, \rho_n \) are necessarily bounded or, owing to the coupling of the equations, the positivity of \( \rho_1, \ldots, \rho_p \) would fail.

Write the equation for \( \rho_1 \) in the form

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

(3.8)

so that

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

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and carrying out the integration,

$$\rho_1'(x) = \rho_1'(\alpha) e^{\frac{1}{\sigma}(\psi_1(\alpha) - \psi_1(x))} - \frac{1}{\sigma} \int_{\alpha}^{x} \left( (a_{11} + \psi_1''(s)) \rho_1 + \sum_{j=2}^{n} a_{1j} \rho_j \right) e^{\frac{1}{\sigma}(\psi_1(s) - \psi_1(x))} ds$$  \hspace{1cm} (3.9)

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

$$\rho_1'(x) \leq \rho_1'(\alpha) e^{\frac{1}{\sigma}(\psi_1(\alpha) - \psi_1(x))} + \frac{K_2}{\sigma} \int_{\alpha}^{x} \rho_1(s) e^{\frac{1}{\sigma}(\psi_1(s) - \psi_1(x))} ds$$  \hspace{1cm} (3.10)

Note that for small $\sigma$,

$$\int_{\alpha}^{x} e^{\frac{1}{\sigma}(\psi_1(s) - \psi_1(x))} ds \leq \int_{\alpha}^{x} e^{\frac{k}{\sigma}(s-x)} ds \leq \frac{\sigma}{k(\delta)}$$  \hspace{1cm} (3.11)

Integrating (3.10),

$$\rho_1(x) - \rho_1(\alpha) \leq \rho_1'(\alpha) \int_{\alpha}^{x} e^{\frac{1}{\sigma}(\psi_1(\alpha) - \psi_1(s))} ds + \frac{K_2}{\sigma} \int_{\alpha}^{x} \int_{\alpha}^{s} \rho_1(t) e^{\frac{1}{\sigma}(\psi_1(s) - \psi_1(t))} dt ds$$

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

so,

$$\max_{[\alpha,x]} \rho_1 \leq \rho_1(\alpha) + K(\delta) \sigma |\rho_1'(\alpha)| + K(\delta) \int_{\alpha}^{x} \max_{[\alpha,t]} \rho_1 dt.$$ $$\leq \rho_1(\alpha) + K(\delta) \sigma |\rho_1'(\alpha)| + K(\delta) \int_{\alpha}^{x} \max_{[\alpha,t]} \rho_1 dt.$$  \hspace{1cm} (3.12)

We may now use Gronwall’s Lemma to obtain

$$\rho_1(x) \leq K(\delta) \{ \rho_1(\alpha) + \sigma |\rho_1'(\alpha)| \}, \quad \alpha \leq x \leq \beta$$  \hspace{1cm} (3.12)

If we insert this into (3.10), we obtain

$$\rho_1'(x) \leq |\rho_1'(\alpha)| + K(\delta) \{ \rho_1(\alpha) + \sigma |\rho_1'(\alpha)| \}, \quad \alpha \leq x \leq \beta$$  \hspace{1cm} (3.13)

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

Our attention is directed to $\rho_{p+1}, \ldots, \rho_n$. Our first step is lower bounds for $\rho_1', \ldots, \rho_p'$, for which it suffices to carry out the details for $\rho_1'$. We can use (3.12) to modify our formula (3.9). Using (3.11),

$$\rho_1'(x) \geq \rho_1'(\alpha) e^{\frac{1}{\sigma}(\psi_1(\alpha) - \psi_1(x))} - \frac{1}{\sigma} \max_{[\alpha,x]} \rho_1(\max_{l_2} |a_{11} + \psi_1''(\alpha)|) \int_{\alpha}^{x} e^{\frac{1}{\sigma}(\psi_1(s) - \psi_1(x))} ds$$

$$- \frac{1}{\sigma} \max_{[\alpha,x]} (\rho_2 + \cdots + \rho_p + \rho_{p+1} + \cdots + \rho_n) \max_{l_2} \max_{1 \leq i \neq \alpha} a_{1i} \int_{\alpha}^{x} e^{\frac{1}{\sigma}(\psi_1(s) - \psi_1(x))} ds$$

So, since by (3.12) we have bounds for $\rho_2, \ldots, \rho_p$, we can write

$$\rho_1'(x) \geq \rho_1'(\alpha) e^{\frac{1}{\sigma}(\psi_1(\alpha) - \psi_1(x))} - K(\delta) \{ \rho_1(\alpha) + \sigma |\rho_1'(\alpha)| \} - K(\delta) \max_{[\alpha,x]} (\rho_{p+1} + \cdots + \rho_n), \quad \alpha \leq x \leq \beta$$  \hspace{1cm} (3.14)
Similarly for $\rho'_2, \ldots, \rho'_p$.

With our technique we can handle only the sum $\rho_{p+1} + \cdots + \rho_n$ and not individual $\rho_i, p+1 \leq i \leq n$. From (3.1), and taking into account (3.12), (3.14), and the signs of the $\psi'_i$,

\[
\frac{d}{dx}(\rho_{p+1} + \cdots + \rho_n) = -\frac{d}{dx}(\rho_1 + \cdots + \rho_p) - \frac{1}{\sigma} (\psi'_1 \rho_1 \cdots + \psi'_p \rho_p) \\
- \frac{1}{\sigma} (\psi'_{p+1} \rho_{p+1} + \cdots + \psi'_n \rho_n) \\
\geq -\frac{K_1(\delta)}{\sigma} \sum_{i=1}^{p} (\rho_i(\alpha) + \sigma|\frac{d\rho_i}{dx}(\alpha)|) \\
+ \frac{K_2(\delta)}{\sigma} \sum_{i=p+1}^{n} \rho_i \text{ in } I_2 
\]

(3.15)

Let

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

which means (3.15) assumes a fortiori the form

\[
\frac{d}{dx}(\rho_{p+1} + \cdots + \rho_n) \geq -\frac{K_1(\delta)}{\sigma} C(\alpha) + \frac{K_2(\delta)}{\sigma} (\rho_{p+1} + \cdots + \rho_n). 
\]

(3.16)

We assert that

\[
\rho_{p+1} + \cdots + \rho_n \leq \frac{K_1(\delta)}{K_2(\delta)} C(\alpha), \quad \alpha \leq x \leq \beta - \delta.
\]

(3.17)

Suppose the contrary and that

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

(3.18)

This continues to hold in $[x^*, \beta]$, since at a first $x \in I_2$ where it fails, (3.16) would imply that $\rho_{p+1} + \cdots + \rho_n$ were increasing, which is not possible. Indeed, integrating (3.16) between points $x^*, x \in I_2$ with $x^* < x$, we have that

\[
(\rho_{p+1} + \cdots + \rho_n)(x) \geq (\rho_{p+1} + \cdots + \rho_n)(x^*)e^{\frac{K_2(\delta)}{\sigma}(x-x^*)} + \frac{K_1(\delta)}{K_2(\delta)} C(\alpha)(1 - e^{\frac{K_2(\delta)}{\sigma}(x-x^*)}) \\
\geq \frac{AK_1(\delta)}{K_2(\delta)} C(\alpha)e^{\frac{K_2(\delta)}{\sigma}(x-x^*)} + \frac{K_1(\delta)}{K_2(\delta)} C(\alpha)(1 - e^{\frac{K_2(\delta)}{\sigma}(x-x^*)}) \\
= (A - 1)\frac{K_1(\delta)}{K_2(\delta)} C(\alpha)e^{\frac{K_2(\delta)}{\sigma}(x-x^*)} + \frac{K_1(\delta)}{K_2(\delta)} C(\alpha), \quad x^*, x \in I_2
\]

(3.19)
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

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

(3.20)

Keep in mind that

\[
e^{-K_2(\delta)\frac{e^{-\frac{1}{2}(\psi_1(x)-\psi_1(\alpha))}}{\sigma} + \frac{K(\delta)}{\sigma}C(\alpha) - e^{-\frac{1}{2}(\psi_1(x)-\psi_1(\alpha))}}} \geq e^{-\frac{K_2(\delta)}{\sigma}K_4(\delta)} = e^{-\frac{K_2(\delta)}{\sigma}} = e^{-\frac{K_4(\delta)}{\sigma}} \quad \text{for } \beta - \frac{1}{4} \delta \leq x \leq \beta.
\]

Then we have from (3.9)

\[
\frac{d\rho_1}{dx}(x) \leq \frac{d\rho_1}{dx}(\alpha)e^{-\frac{1}{2}(\psi_1(x)-\psi_1(\alpha))} + \frac{K(\delta)}{\sigma}C(\alpha) \int_{\alpha}^{x} e^{-\frac{1}{2}(\psi_1(s)-\psi_1(\alpha))}ds
\]

\[
- \frac{(A-1)K_1(\delta)K_3(\delta)C(\alpha)}{K_2(\delta)e^{\frac{1}{2}K_4(\delta)}} \leq \frac{d\rho_1}{dx}(\alpha)e^{-\frac{1}{2}(\psi_1(x)-\psi_1(\alpha))} + K(\delta)C(\alpha)
\]

\[
- \frac{(A-1)K_1(\delta)K_3(\delta)C(\alpha)}{K_2(\delta)e^{\frac{1}{2}K_4(\delta)}} \leq \frac{d\rho_1}{dx}(\alpha)e^{-\frac{1}{2}(\psi_1(x)-\psi_1(\alpha))} + K(\delta)C(\alpha)
\]

\[
- \frac{(A-1)K_1(\delta)K_3(\delta)C(\alpha)}{K_2(\delta)e^{\frac{1}{2}K_4(\delta)}} \leq \frac{d\rho_1}{dx}(\alpha)e^{-\frac{1}{2}(\psi_1(x)-\psi_1(\alpha))} + K(\delta)C(\alpha)
\]

\[
- \frac{(A-1)K_1(\delta)K_3(\delta)C(\alpha)}{K_2(\delta)e^{\frac{1}{2}K_4(\delta)}} \leq \frac{d\rho_1}{dx}(\alpha)e^{-\frac{1}{2}(\psi_1(x)-\psi_1(\alpha))} + K(\delta)C(\alpha)
\]

(3.17).

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

\[
0 \leq \rho_1(x) = \rho_1(\alpha) + \int_{\alpha}^{x} \rho_1'(s)ds
\]

\[
\leq C(\alpha) + \int_{\alpha}^{x} \rho_1'(s)ds,
\]

we have that

\[
0 \leq \frac{\rho_1(x)}{C(\alpha)} \leq 1 + \int_{\alpha}^{x} (1 + K(\delta))ds - \int_{\beta - \frac{1}{4} \delta}^{\beta} (A-1) \frac{K_1(\delta)}{K_2(\delta)}K_3(\delta)e^{-\frac{1}{2}K_4(\delta)}ds
\]

\[
\leq 1 + (1 + K(\delta))(\beta - \alpha) - (A-1) \frac{K_1(\delta)}{K_2(\delta)}K_3(\delta)e^{-\frac{1}{2}K_4(\delta)} \frac{1}{8} \delta
\]

(3.21)

\[
\text{for } \beta - \frac{1}{8} \delta \leq x \leq \beta.
\]

Since \( A > 1 \), the above cannot hold for small \( \sigma \) depending only on \( \delta \) because the extreme right hand side of (3.21) becomes infinite as \( \sigma \to 0 \). This proves (3.17). Note that the size of \( \sigma \) determined by (3.21) depends on the geometrical features of the potentials \( \psi_i, i = 1, \ldots, n \), but not on \( C(\alpha) \), that is, the magnitude of the solution \( \rho \).

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

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

satisfying

$$f_i(x) \geq 0, \ i = 1, \ldots, n,$$

$$\sum_{i=1}^{n} \int_{\Omega} f_i \, dx = 1.$$ 

Then there are positive constants $K$ and $\omega$ such that

$$|\rho(x,t) - \rho_0(x)| \leq Ke^{-\omega t} \text{ as } t \to \infty,$$  

where $\rho_0$ is the stationary positive solution obtained in Theorem 2.1.

Thus the stationary 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 monotonicity 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 [11]. Here we outline a different way of viewing the problem based on inspection of the semigroup generated by the operator, written in vector form,
\[ S\rho = \sigma \frac{\partial^2 \rho}{\partial x^2} + \frac{\partial}{\partial x}(\psi\rho) + A\rho \]  

(4.3)

with natural boundary conditions. All the methods known to us 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 \( \lambda_0 \), which is simple and has an associated positive eigenfunction, and that all other eigenvalues \( \lambda \) satisfy \( \text{Re} \lambda < \lambda_0 \).

This is a standard result (see, for example, Zeidler [30]) obtained using the ideas of positive operators, but to assist the reader and for completeness we give a sketch of the proof. We define \( e^S \) by writing the solution of (1.4) in terms of (4.3) as

\[ \rho(x, t) = e^{tS} f(x). \]  

(4.4)

This is consistent with the notions of exponent, since

\[ e^{(t+s)S} = e^{tS} e^{sS} \]

just expresses the fact that the solution at time \( t + s \) is just the solution after time \( s \) followed by a further time \( t \). We note that \( e^S \) is a positive operator, since \( f \geq 0 \) implies \( \rho \geq 0 \), making use of the maximum principle, [24], and it is compact, since it is essentially an integration. And so \( e^S \) has a real eigenvalue, \( e^{\lambda_0} \), which is simple and has a positive eigenfunction. Further, it is simple to see, for example by solving the equation explicitly, that if \( S \) has an eigenvalue \( \lambda \), then \( e^S \) has an eigenvalue \( e^\lambda \) and vice versa. Thus \( S \) has a real eigenvalue \( \lambda_0 \), which is simple and has a positive eigenfunction. Further, the fact that all the other eigenvalues \( e^\lambda \) of \( e^S \) have \( |e^\lambda| < e^{\lambda_0} \) implies that all other eigenvalues \( \lambda \) of \( S \) have \( \text{Re} \lambda < \lambda_0 \), as required.

We assume that the positive initial data \( f \) is normalized so that

\[ \sum_{i=1,...,n} \int_\Omega f_i dx = 1, \]  

(4.5)

as in (1.1).

Now form the Laplace transform

\[ \hat{\rho}(x, \lambda) = \int_0^\infty e^{-\lambda t} \rho(x, t) dt, \quad \text{Re} \lambda > 0 \]

and (4.4) gives

\[ \hat{\rho}(\cdot, \lambda) = (\lambda I - S)^{-1} f, \]  

(4.6)

and \( \hat{\rho} \) is analytic in \( \lambda \) for \( \text{Re} \lambda > 0 \), but (4.6) allows us to extend this into the left half plane except for an isolated singularity at \( \lambda = 0 \), for in our problem the fact that
we have a positive stationary solution implies that the real eigenvalue $\lambda_0$ is given by $\lambda_0 = 0$. The usual inversion formula gives

$$\rho(x, t) = \frac{1}{2\pi i} \int_{\gamma-i\infty}^{\gamma+i\infty} e^{\lambda t} \hat{\rho}(x, \lambda) d\lambda, \quad \gamma > 0 \quad (4.7)$$

Now for finite $\gamma$ and $\nu$, with $\nu$ large, and with $\lambda = \gamma + i\nu$,

$$||(\lambda I - S)^{-1}|| = O\left(\frac{1}{\nu}\right) \quad (4.8)$$

For we can write

$$-(T \rho)_i = \sigma \frac{d^2 \rho_i}{dx^2} + \frac{d}{dx}(\psi_i' \rho_i) + (A \rho)_i$$

$$= \sigma \frac{d}{dx}(e^{-\frac{1}{2}\psi_i} \phi'_i) - (a' \phi)_i$$

$$= -(M \phi)_i$$

where $\phi_i = e^{\frac{1}{2}\psi_i} \rho_i$ and $a'_{ij} = a_{ij} e^{-\frac{1}{2}\psi_i}$

The boundary conditions here are

$$\phi'_i(0) = \phi'_i(1) = 0, \quad i = 1, \ldots, n.$$

Now consider

$$\lambda I - S = \lambda I + T = \lambda I + M$$

and

$$((M + \lambda I) \phi, \phi) = \sum_{i=1, \ldots, n} \int_{\Omega} [(M + \lambda I) \phi_i] \tilde{\phi}_i dx. \quad (4.9)$$

The first term in $M$ is self adjoint, which gives a real contribution, and the second contribution in (4.9) is certainly

$$O\left\{ \sum_{i=1, \ldots, n} \int_{\Omega} |\phi_i|^2 dx \right\}.$$

Thus if $\nu$ is sufficiently large,

$$\text{im}((M + \lambda I) \phi, \phi) \geq \frac{1}{2} \nu \sum_{i=1, \ldots, n} \int_{\Omega} |\phi_i|^2 dx,$$

from which (4.8) follows easily.

Given the initial data $f$, we write

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

where $\rho^*$ is orthogonal to the positive eigenfunction, say $\rho^*_0$, of the adjoint operator of $S$. This determines $c$ uniquely, since

$$c(\rho_0, \rho^*_0) = (f, \rho^*_0),$$
and \((\rho_0, \rho'_0) \neq 0\) inasmuch as \(\rho_{0,i} > 0, \rho'_{0,i} > 0\). Then by the Fredholm alternative, we can solve, for any small \(\lambda\),

\[(S - \lambda I) \phi = \rho^*,\]

uniquely if we insist that the solution is orthogonal to \(\rho_0\). Then \((S - \lambda I)^{-1} \rho^*\) is bounded, and

\[(S - \lambda I)^{-1} f = c (S - \lambda I)^{-1} \rho_0 + O(1) = -\lambda^{-1} c \rho_0 + O(1)\]

as \(\lambda \to 0\), showing that the pole of \((S - \lambda I)^{-1}\) at \(\lambda = 0\) has residue \(-c \rho_0\) so we can now move the line of integration in (4.7) from \(\gamma > 0\) to \(\gamma < 0\). The contribution from the pole is \(c \rho_0\) and the contribution from large \(\lambda\) is small by (4.8). Further, once this move is made, the contribution from the vertical line is of the form \(O(e^{-\omega t})\). In all, therefore,

\[\rho(x,t) = c \rho_0 + O(e^{-\omega t}),\]

as required. Note that \(c = 1\) since

\[\sum_{i=1,\ldots,n} \int_{\Omega} \rho_i dx = \sum_{i=1,\ldots,n} \int_{\Omega} \rho_{0,i} dx.\]

5. **Discussion and some conditions for “reverse” transport.** We now investigate what may happen if the conditions on the \(\psi_i\) in Theorem 3.1 are satisfied but those on the \(a_{ij}\) are not. In particular, we note that condition \((iv)\) of Theorem 3.1 requires that if \(a\) is the minimum of one of the \(\psi_k\), 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 predicted by Theorem 3.1 even though the conditions on the \(\psi_i\) in that theorem are satisfied.

In constructing our example, we will specialize to \(n = 2\), a two state system. We also reverse direction. By this we mean that conditions (ii) and (iii) in Theorem 3.1, for \(n = 2\), will be replaced by

\[(ii') There is some interval in which \psi'_i < 0 for i = 1, 2.\]

\[(iii') In any interval in which neither \psi'_i vanishes, \psi'_j < 0 in this interval for at least one j.\]
Fig. 5.1. A period interval showing potentials and conformation coefficients which do not satisfy the hypothesis (iv') of Corollary 3.2.

For (iv) we substitute a simpler condition which could be used in Theorem 3.1 as well, as it implies (iv).

(iv') There is a neighborhood of each local minimum of $\psi_1$ or $\psi_2$ in which $a_{ij} \neq 0$ for all $(i, j)$.

Figure 5.1 shows potentials satisfying (ii') and (iii').

We then have the following corollary of Theorem 3.1:

**Corollary 5.1.** If the hypotheses of Theorem 3.1 when $n = 2$ are satisfied, except that (ii'), (iii') and (iv') replace (i), (ii) and (iii), then there exist constants $K_1, K_2$ independent of $\sigma$ such that

$$\sum_{i=1}^{2} \rho_i (x) \leq K_1 e^{-\frac{K_2}{N}} \sum_{i=1}^{2} \rho_i \left( x + \frac{1}{N} \right), \text{ for } x \in \Omega, \ x \leq 1 - \frac{1}{N}.$$ 

We will now construct an example for the case $N = 1$ where conditions (i), (ii') and (iii') are satisfied, but not condition (iv'). Our example is constructed initially using $\delta$-functions for the $a_{ij}$, and with this class of rate coefficients we are able to show that there is a $c > 0$ such that for sufficiently small $\sigma$,

$$\rho_1 (1) + \rho_2 (1) < e^{-\frac{c}{2}} (\rho_1 (0) + \rho_2 (0)). \quad (5.1)$$
At the end we briefly discuss a slightly weaker form of reverse transport which we can then obtain for continuous coefficients.

Assume that $\psi_1$ 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 $\psi_1(0) = \psi_1(1)$. Further assume that $\psi_2$ has a minimum at $y_2 \in (z_1, 1)$ followed by a maximum at $z_2 \in (y_2, 1)$, and $\psi_2(0) = \psi_2(1)$. Finally assume that $\psi_i' \neq 0$ except at the minima and maxima specified above. Then $0 = y_1 < z_1 < y_2 < z_2 < 1$. 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 $[0, 1]$, transport will be to the right as given in Corollary 5.1.

But we will now choose new $a_{ij}$ to give transport to the left. Obviously, condition $(iv')$ must be violated. Choose a point $x_1 \in (y_1, z_1)$ and a point $x_2 \in (y_2, z_2)$. Then

$$0 = y_1 < x_1 < z_1 < y_2 < x_2 < z_2 < 1$$  \hspace{1cm} (5.2)

We consider the system

$$\begin{align*}
(\sigma \rho_1' + \psi_1' \rho_1)' &= (\delta(x - x_1) + \delta(x - x_2))(\rho_1 - \rho_2) \\
(\sigma \rho_2' + \psi_2' \rho_2)' &= (\delta(x - x_1) + \delta(x - x_2))(\rho_2 - \rho_1),
\end{align*}$$  \hspace{1cm} (5.3)

with boundary conditions

$$\sigma \rho_i' + \psi_i' \rho_i = 0 \text{ at } x = 0, 1, \text{ for } i = 1, 2.$$  \hspace{1cm} (5.4)
We wish to find further conditions which imply the inequality (5.1) for some \( c > 0 \) and sufficiently small \( \sigma \).

We follow the technique in [4], and let \( \phi_i = \sigma \rho'_i + \psi'_i \rho_i \). Adding the equations in (5.3) 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

\[
\begin{align*}
\sigma \rho'_1 &= \phi - \psi'_1 \rho_1 \\
\sigma \rho'_2 &= -\phi - \psi'_2 \rho_2 \\
\phi' &= (\delta (x - x_1) + \delta (x - x_2)) (\rho_1 - \rho_2), 
\end{align*}
\]

where \( \phi = \phi_1 = -\phi_2 \).

Having obtained (5.5) under the conditions \( \phi_i = 0 \) at \( x = 0, 1 \), we now weaken these conditions, assuming only that \( \phi_1 + \phi_2 = 0 \). In this way, the same analysis applies to any period interval of the functions \( \psi_i \), thus showing that if \( N > 1 \), decay occurs in each period interval. Therefore in (5.5) it is not assumed that \( \phi (0) \) or \( \phi (1) \) vanish. The only assumption made is that \( \rho_i > 0 \) on the entire interval, for \( i = 1, 2 \).

Observe that \( \phi \) takes a jump of amount \( \rho_1 (x_j) - \rho_2 (x_j) \) at each \( x_j \). Further, \( \phi \) is constant in the intervals \([0, x_1), (x_1, x_2), (x_2, 1] \). Let \( \phi_j = \phi (y_j) \). Then

\[
\rho_i (x_j) = \rho_i (y_j) e^\frac{\psi_i (y_j) - \psi_i (x_j)}{\sigma} + (-1)^{i-1} \phi_j \int_{y_j}^{x_j} \frac{1}{\sigma} e^\frac{\psi_i (s) - \psi_i (x_j)}{\sigma} ds,
\]

\( i = 1, 2 \). Hence,

\[
\rho_1 (x_j) - \rho_2 (x_j) = \rho_1 (y_j) e^\frac{\psi_1 (y_j) - \psi_1 (x_j)}{\sigma} - \rho_2 (y_j) e^\frac{\psi_2 (y_j) - \psi_2 (x_j)}{\sigma} + \phi_j \int_{y_j}^{x_j} \frac{1}{\sigma} \left( e^\frac{\psi_1 (s) - \psi_1 (y_j)}{\sigma} + e^\frac{\psi_2 (s) - \psi_2 (y_j)}{\sigma} \right) ds,
\]

For \( i = 1, 2 \) let

\[
a_i = \frac{\psi_i (y_1)}{\sigma}, b_i = \frac{\psi_i (x_1)}{\sigma}, c_i = \frac{\psi_i (x_2)}{\sigma},
\]

\[
A_i = \int_{x_1}^{x_1} \frac{1}{\sigma} e^\frac{\psi_i (s)}{\sigma} ds, B_i = \int_{x_1}^{x_2} \frac{1}{\sigma} e^\frac{\psi_i (s)}{\sigma} ds, C_i = \int_{x_2}^{1} \frac{1}{\sigma} e^\frac{\psi_i (s)}{\sigma} ds.
\]

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

\[
\rho_1 (1) = k_{11} \rho_1 (0) - k_{12} \rho_2 (0) + k_{13} \phi (0)
\]

\[
\rho_2 (1) = -k_{21} \rho_1 (0) + k_{22} \rho_2 (0) - k_{23} \phi (0)
\]
Further Maple computation (checked with Scientific Workplace) shows, for example,

tend to zero exponentially as

for some \( k \),

and \( k_{12}, \ldots, k_{23} \) are similar expressions in terms of the constants defined in \((5.6)\).

As in \([4]\), we solve each of the inequalities \( \rho_1 (1) > 0, \rho_2 (1) > 0 \) for \( \phi(0) \), and substitute the result into the other of these two relations. We find that

\[
\begin{align*}
\rho_1 (1) &\leq \frac{k_{11}k_{22} - k_{21}k_{13}}{k_{23}} \rho_1 (0) + \frac{k_{13}k_{22} - k_{12}k_{23}}{k_{13}} \rho_2 (0), \\
\rho_2 (1) &\leq \frac{k_{11}k_{23} - k_{21}k_{12}}{k_{13}} \rho_1 (0) + \frac{k_{13}k_{23} - k_{12}k_{22}}{k_{13}} \rho_2 (0).
\end{align*}
\]

The desired decay relation \((5.1)\) follows by showing that under certain additional conditions the four fractional coefficients

\[
\begin{align*}
\frac{k_{11}k_{23} - k_{21}k_{13}}{k_{13}}, \frac{k_{11}k_{23} - k_{21}k_{13}}{k_{23}}, \frac{k_{13}k_{22} - k_{12}k_{23}}{k_{13}}, \frac{k_{13}k_{22} - k_{12}k_{23}}{k_{23}}
\end{align*}
\]

\((5.7)\)
tend to zero exponentially as \( \sigma \to 0 \).

Further Maple computation (checked with Scientific Workplace) shows, for example, that

\[
\begin{align*}
k_{11}k_{23} - k_{21}k_{13} &= \frac{A_2}{e^{a_2}} + \frac{B_2}{e^{a_2}} + \frac{C_2}{e^{a_2}} + A_2 \frac{B_1}{e^{a_2}e^{b_2}} + A_2 \frac{C_1}{e^{a_2}e^{b_1}} + A_2 \frac{B_2}{e^{a_2}e^{b_2}} + A_2 \frac{C_1}{e^{a_2}e^{b_1}} \\
+ A_2 \frac{C_2}{e^{a_2}e^{b_2}} + B_2 \frac{C_1}{e^{a_2}e^{c_2}} + A_2 \frac{C_2}{e^{a_2}e^{c_2}} + B_2 \frac{C_2}{e^{a_2}e^{c_2}} + A_2 \frac{C_1}{e^{a_2}e^{c_1}} + A_2 \frac{B_1}{e^{a_2}e^{b_1}e^{c_2}} \\
+ A_2 B_2 \frac{C_2}{e^{a_2}e^{b_2}e^{c_1}} + A_2 B_2 \frac{C_2}{e^{a_2}e^{b_2}e^{c_2}}
\end{align*}
\]

Many cancellations have occurred, eliminating terms in which four or five integrals are multiplied. Similar formulas are obtained for the other expressions in \((5.7)\).

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

\[
B_1 = \int_{x_1}^{x_2} e^{-\frac{\psi_1(x)}{\sigma}} ds \propto \sigma^k e^{-\frac{\psi_{1\text{max}}}{\sigma}},
\]

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

\[
A_1 \propto \sigma^k e^{b_1}, \quad A_2 \propto \sigma^k e^{a_2}, \\
B_2 \propto \sigma^k (e^{b_2} + e^{c_2}), \quad C_1 \propto \sigma^k (e^{c_1} + e^{a_1}), \quad C_2 \propto \sigma^k e^{-\frac{\psi_{2\text{max}}}{\sigma}}
\]

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From (5.6) and (5.2), we see that the for small $\sigma$ 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 the moment we let $d_i = \psi_{i, \text{max}}/\sigma$ and set

$$A_1 = e^{b_1}, \quad A_2 = e^{a_2}$$
$$B_1 = e^{d_1}, \quad B_2 = e^{b_2} + e^{c_2}$$
$$C_1 = e^{c_1} + e^{a_1}, \quad C_2 = e^{d_2}$$

We will find also that to get the desired backward transport, we need to take $x_2$ near to the maximum of $\psi_2$. Therefore for now we will set $x_2 = z_2$, so that $c_2 = d_2$. Finally, we can without loss of generality assume that $a_1 = 0$. The additional conditions we will give for backwards transport for small $\sigma$ are that the inequalities (5.8) and (5.9) below hold and that $x_2$ is sufficiently close to $y_2$.

We then have

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

and similar expressions for $k_{22}k_{13} - k_{12}k_{23}$, $k_{13}$, and $k_{23}$.

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

$$k_{11}k_{23} - k_{21}k_{13} \propto \frac{3}{e^{b_1}}e^{d_1} + \frac{4}{e^{a_2}}e^{d_1} + \frac{4}{e^{b_2}}e^{d_2}$$
$$k_{22}k_{13} - k_{12}k_{23} \propto 6e^{d_1} + \frac{4}{e^{b_2}}e^{d_2}$$
$$k_{13} \propto 4e^{d_1} + \frac{2}{e^{b_2}}e^{d_1}$$
$$k_{23} \propto \frac{2}{e^{a_2}}e^{c_1}e^{d_1} + \frac{1}{e^{b_2}}e^{c_1}e^{d_1}e^{d_2}$$

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

$$d_2 - a_2 < d_1 - b_1 < d_2 - b_2.$$  \hspace{1cm} (5.8)

and

$$d_1 > b_1 + c_1.$$  \hspace{1cm} (5.9)
(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 $\sigma^2$ 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 for the equations (5.3) – (5.4), we choose $\sigma$ so small that for any positive solution,

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

Then for this $\sigma$, the same inequality will hold for continuous functions $a_{ij}$ sufficiently close in $L_1$ norm to the $\delta$-functions in (5.3) – (5.4).

In this paragraph we discuss the simulation parameters for Figure 3.1. Simulations, of which this is a sample, were executed with a semi-implicit scheme and run in Maple. In this case, for potentials we took $\psi_1(x) = \psi_0^1(2^4 x)$ and $\psi_2(x) = \psi_0^2(2^4 x)$ with $\psi_0^1(\xi) = \frac{1}{4} \left( \cos(\pi (\frac{\xi - 1}{4})) \right)^2$ and $\psi_0^2(\xi) = \frac{1}{4} \left( \cos(\pi (\frac{\xi - 1}{4})) \right)^2$. The matrix elements were $-a_{11} = a_{12} = a_{21} = -a_{22}$ with $a_{12}(x) = a_0^1(2^4 x)$ where $a_0^1(\xi) = \frac{1}{4} \left( \cos 2\pi (\xi - \frac{1}{4}) \right)^6$. The diffusion constant $\sigma = 2^{-7}$.

REFERENCES


[22] PERTHAME, B. The general relative entropy principle


