International Journal of Theoretical Physics, Vol. 31, No. 8, 1992

Solution Spectrum of Nonlinear Diffusion Equations

W. Ulmer[1]

Received September 28, 1991

The stationary version of the nonlinear diffusion equation $-\partial c/\partial t + D\,\Delta c = \lambda_1 c - \lambda_2 c^2$ can be solved with the ansatz $c = \sum_{p=1}^{\infty} A_p(\cosh kx)^{-p}$, inducing a band structure with regard to the ratio λ_1/λ_2. The resulting solution manifold can be related to an equilibrium of fluxes of nonequilibrium thermodynamics. The modification of this ansatz yielding the expansion $c = \sum_{p,q=1}^{\infty} A_{pq}(\cosh kx)^{-p}[(\cosh \alpha t)^{-q-1}\sinh \alpha t + b(\cosh \alpha t)^{-q}]$ represents a solution spectrum of the time-dependent nonlinear equation, and the stationary version can be found from the asymptotic behavior of the expansion. The solutions can be associated with reactive processes propagating along molecular chains, and their applicability to biophysical processes such as active transport phenomena and control circuit problems is discussed. There are also applications to cellular kinetics of clonogenic cell assays and spheroids.

1. INTRODUCTION

Many problems of many-particle physics and related disciplines (e.g., physical chemistry, molecular biophysics, and technical sciences such as control theory) give rise to a need for an extended analysis of diffusion processes. Fick's law of diffusion

$$-\partial c/\partial t + D\,\Delta c = 0 \tag{1}$$

which is a special case of the Fokker–Planck–Kolmogorov equation, is only partially applicable to the above-mentioned areas because reactive processes are not included in equation (1). In particular, dissipative structures and the equilibrium of fluxes in nonequilibrium thermodynamics (NTD) are becoming of increasing importance (Prigogine, 1967; Trzesowski, 1989; Turing, 1952). Active transport and the biophysical mechanisms responsible for the permeation of biomolecules through cell membranes in opposite direction to the diffusion current $\mathbf{j}_D = D\,\nabla c$ (Austin *et al.*, 1983; Panda,

[1] FB Radiotherapy, Department Medizinphysik/Biophysik, Klinikum Amberg, Mariahilfbergweg D-8450 Amberg, Germany.

1981; Vaz and Criado, 1985; Vaz *et al.*, 1985*a,b*) are of particular importance in neurobiophysics.

Nonlinear generalizations of equation (1), e.g.,

$$-\partial c/\partial t + D\,\Delta c = \lambda_1 c - \lambda_2 c^2 \tag{2}$$

are promising starting points for many problems of NTD (Das and Sihi, 1979; Flannery, 1982; Kramer and Riecke, 1985; Mishin, 1982*a,b*) and molecular biophysics (Talekar, 1981; Ulmer, 1983, 1985; Vaz *et al.*, 1985*b*). Soliton solutions result from equation (2) (Satsuma, 1981; Stix, 1979), and these solutions may be considered for the propagation of reactive processes in molecular chains and fluids.

Equation (2) contains a nonlinear rate equation besides the diffusion term. By either assuming a spatial equilibrium concentration or formally putting $D=0$, we obtain a pure kinetic equation

$$-\partial c/\partial t = \lambda_1 c - \lambda_2 c^2 \tag{3}$$

Particular solutions of equation (3) have been considered following the extension of this equation to two mutually coupled constituents of matter (Phillipson and Schuster, 1983). Such solutions are very informative as models of regulatory processes, but some shortcomings with regard to dissipative structures are evident. Equation (3) requires spatial equilibrium, whereas in NTD and molecular biophysics spatial inequilibrium is an essential feature of dissipative structures.

Many starting points for generalizations have been taken into account to adjust equation (1) to the complexity of dissipative structures (e.g., biological systems) by the consideration of diffusion and kinetics in curvilinear spaces (Trzesowski, 1989), but it appears that the most essential extension of equation (1) is the nonlinear term $\lambda_2 c^2$ introduced in equation (2). As shown in Ulmer (1985), equation (2) may be made invariant under Galilei transformations by the introduction of an additional term $-\mathbf{v}\,\nabla c$

$$-\partial c/\partial t - \mathbf{v}\,\nabla c + D\,\Delta c = \lambda_1 c - \lambda_2 c^2 \tag{4}$$

because this term can take account of a convection current due to a pressure gradient besides the diffusion current $\mathbf{j}_D$. If $c(\mathbf{x}, t)$ is a solution function of equation (2), then by the substitution $\mathbf{x} \Rightarrow \mathbf{x}' = \mathbf{x} - \mathbf{v}t$, $c(\mathbf{x} - \mathbf{v}t, t)$ becomes a solution function of equation (4). Equation (4) agrees with equation (2) only in the reference system $x' = x - vt$, $t' = t$ (one space coordinate),

$$-\partial c/\partial t + D\,\partial^2 c/\partial x'^2 = \lambda_1 c - \lambda_2 c^2 \tag{4a}$$

Thus equation (4) contains, besides the diffusion term $D\,\Delta c$ according to equation (1), the transport term $\mathbf{v}\,\nabla c$, which represents an essential part of the Boltzmann equation. In particular, the nonlinear term $\lambda_2 c^2$ can also be related to the collision interaction term of this equation because $c(x, t)$ represents a statistical distribution function of identical particles at the position x. In the following, we regard equation (4) as a reference equation for similar problems, because equations (1)-(3) result as special cases from (4).

The relationship between Fick's law (1) and the linear Schrödinger equation has been pointed out in many textbooks of quantum theory, and a similar connection is obvious between the nonlinear diffusion equations (2), (4), and (4a) and the nonlinear Schrödinger equation

$$i\hbar \frac{\partial \Psi}{\partial t} + \frac{\hbar^2}{2m} \frac{\partial^2 \Psi}{\partial x^2} = \lambda |\Psi|^2 \Psi \tag{5}$$

Ulmer (1988, 1989) presented solution spectra of equation (5) obtained, e.g., by the expansion

$$\Psi = \sum_{p=1}^{\infty} A_p [\cosh(kx - vt)]^{-p} \tag{6}$$

In this communication we consider the applicability of the ansatz (6) to the above-mentioned nonlinear diffusion equations. In a further step, it is shown that the presented starting point (6) is also adequate for more complex problems of coupled constituents.

2. THE SOLUTION SPECTRUM OF THE EXPANSION $c = \sum_{p=1}^{\infty} A_p (\cosh kx)^{-p}$

To illustrate the method, we first consider the solution spectrum of the equation (in one space coordinate)

$$D\, \partial^2 c / \partial x^2 = \lambda_1 c - \lambda_2 c^2 \tag{7}$$

which can be solved by the above expansion corresponding to equation (6). Straightforward generalizations (time dependence of nonstationary solutions, extension to three space coordinates) are possible. Each solution function of equation (7) represents either a stationary solution of equation (2) with $\partial c/\partial t = 0$ or a concentration profile $c(x')$ propagating with velocity v $(x' = x - vt)$ according to equation (4). A solitary wave solution of equation (7) is obtained by the ansatz

$$c = A(\cosh kx)^{-2} + B \tag{8}$$

Thus, equation (7) is satisfied if the relations

$$B \equiv 0, \qquad A = +3\lambda_1/2\lambda_2, \qquad k^2 = \lambda_1/4D \qquad (\lambda_1 > 0, \lambda_2 > 0) \tag{8a}$$

or

$$B = +\lambda_1/\lambda_2, \qquad -A = 3\lambda_1/2\lambda_2, \qquad k^2 = -\lambda_1/4D \qquad (\lambda_1 < 0,\ \lambda_2 > 0) \tag{8b}$$

hold. However, only the soliton solution (8a) can be normalized

$$\int_{-\infty}^{+\infty} c(x)\, dx = 1 \rightarrow A = k/2 \tag{8c}$$

Although solitary solutions are valuable in many applications, the increasing importance of nonlinear problems is a rationale for finding systematic solution methods. With the help of the expansion

$$c = \sum_{p=1}^{\infty} A_p (\cosh kx)^{-p} \tag{9}$$

equation (7) becomes

$$Dk^2 \left\{ \sum_{p=1}^{\infty} A_p [p^2 (\cosh kx)^{-p} - p(p+1)(\cosh kx)^{-p-2}] \right\}$$

$$= \lambda_1 \sum_{p=1}^{\infty} A_p (\cosh kx)^{-p} - \lambda_2 \sum_{p,q=1}^{\infty} A_p A_q (\cosh kx)^{-p-q} \tag{9a}$$

Because equation (9a) must be satisfied for arbitrary values of the argument x, the coefficients of each power of cosh kx resulting from equation (9a) have to satisfy this equation, and similar conclusions have been made with regard to the nonlinear Schrödinger equation (5) (Ulmer, 1988, 1989). The condition $\rho = 1 \rightarrow (\cosh kx)^{-1}$ implies the relation

$$A_1 (Dk^2 - \lambda_1) = 0 \tag{9b}$$

Because A_1 is arbitrary [and will be defined later by the normalization condition $\int_{-\infty}^{+\infty} c(x)\, dx = 1$], the relation $\lambda_1 = Dk^2$ must hold. The continuation to higher-order powers $[(\cosh kx)^{-\beta}, \beta > 1]$ is straightforward, e.g., $\rho = 2, 3$ imply

$$A_2 = -\lambda_2 A_1^2 / 3\lambda_1$$

$$A_3 = A_1/4 + \lambda_2^2 A_1^3 / 12\lambda_1^2$$

With the help of equations (9a) and (9b) the expansion coefficients $A_2, A_3, \ldots$ of equation (9) are determined recursively in terms of $A_1 : A_1 \rightarrow A_2 \rightarrow A_3 \rightarrow A_4 \cdots \rightarrow A_p$, and Table I presents the expansion coefficients up to the order $p = 10$.

Table I. The A_1 Dependence of the Expansion Coefficients A_p $(p=1,2,\ldots,10)^a$

p	A_p	A_1u^0	$A_1^2u^1$	$A_1^3u^2$	$A_1^4u^3$	$A_1^5u^4$	$A_1^6u^5$	$A_1^7u^6$	$A_1^8u^7$	$A_1^9u^8$	$A_1^{10}u^9$
1	A_1	1	0	0	0	0	0	0	0	0	0
2	A_2	0	$1/3$	0	0	0	0	0	0	0	0
3	A_3	$1/2^2$	0	$1/2^2\cdot 3$	0	0	0	0	0	0	0
4	A_4	0	$1/2^1\cdot 3$	0	$1/2^1\cdot 3^3$	0	0	0	0	0	0
5	A_5	$1/2^3$	0	$1/2^4$	0	$5/2^4\cdot 3^4$	0	0	0	0	0
6	A_6	0	$5/2^4\cdot 3$	0	$8/2^4\cdot 3^3$	0	$1/2^4\cdot 3^4$	0	0	0	0
7	A_7	$5/2^3$	0	$9/2^6\cdot 3$	0	$25/2^6\cdot 3^4$	0	$7/2^6\cdot 3^6$	0	0	0
8	A_8	0	$7/2^5\cdot 3$	0	$14/2^5\cdot 3^3$	0	$9/2^5\cdot 3^5$	0	$2/2^5\cdot 3^7$	0	0
9	A_9	$7/2^7$	0	$14/2^7\cdot 3$	0	$50/2^7\cdot 3^4$	0	$49/2^8\cdot 3^6$	0	$1/2^8\cdot 3^6$	0
10	A_{10}	0	$7/2^7$	0	$96/2^8\cdot 3^3$	0	$81/2^8\cdot 3^5$	0	$32/2^8\cdot 3^7$	0	$5/2^8\cdot 3^9$

[a] $u=-(\lambda_2/\lambda_1)$. According to this table, A_{10} is given by $A_{10}=7\cdot 2^{-7}uA_1^2+96\cdot 2^{-8}\cdot 3^{-3}u^3A_1^4+81\cdot 2^{-8}3^{-5}u^5A_1^6+32\cdot 2^{-8}3^{-7}u^7A_1^8+5\cdot 2^{-8}3^{-9}u^9A_1^{10}$.

The general formation law $A_p = A_p(A_1)$ is given by the recurrence formula

$$A_p = \frac{pA_1^p u^{p-1}}{3^{p-1}2^{p-1}} + \sum_{r=1}^{M} \frac{f_r(p) A_1^{p-2r} u^{p-1-2r}}{3^{p-1-2r} 2^{p-1}} \tag{10}$$

where

$$f_r(p) = \frac{(p-2r)^2}{r!} \prod_{j=1}^{r-1} (p-j) \tag{10a}$$

and

$$u = -\lambda_2/\lambda_1$$
$$M = (p-1)/2 \quad \text{if } p \text{ is odd}; \qquad M = p/2 - 1 \quad \text{if } p \text{ is even} \tag{10b}$$

Formula (10) can be obtained by the following relations resulting from equation (9a): Assume a coefficient A_p with odd p, where A_p is given by

$$A_p = \frac{p-2}{p+1} A_{p-2} - \frac{2\lambda_2}{(p+1)(p-1)\lambda_1} \times (A_1 A_{p-1} + A_2 A_{p-2} + \cdots + A_{(p-1)/2} A_{(p+1)/2}) \tag{10c}$$

then the preceding coefficient A_{p-1} being of even order is given by the expression

$$A_{p-1} = \frac{p-3}{p} A_{p-3} - \frac{\lambda_2}{\lambda_1 p(p-2)} \times (A_{(p-1)/2}^2 + 2A_1 A_{p-2} + \cdots + 2A_{p'-1} A_{p'+1}) \qquad p' = (p-1)/2 \tag{10d}$$

Thus we can substitute A_{p-1} occurring in (10c) by the expression (10d) and repeat the procedure successively to eliminate $A_{p-2}, A_{p-3}, \ldots,$ until A_1.

However, we have not yet defined A_1, because formula (10) only expressed the A_1 dependence of A_p ($p > 1$), and A_1 can be defined by a norm implying the consideration of the convergence properties of the expansion (9) related to (9a).

The subsequent convergence analysis follows partially the corresponding analysis related to the nonlinear Schrödinger equation (5) and the expansion (6) (Ulmer, 1988, 1989), but because $c(x)$ may either be regarded as a concentration function or a probability distribution, the assumption of the L_1 norm $\to \int_{-\infty}^{+\infty} c(x)\,dx = 1$ is adequate, whereas with regard to equation (5) we have assumed the L_2 norm $\to \|\Psi\|_2 = 1$. Using formula (10), we consider now the pointwise convergence of equation (9a); the existence of the L_1 norm can be readily derived by the pointwise convergence. Thus, the convergence problems arising from the nonlinear term of equation (7) can be clarified by considering the linear version of equation (7) by taking $\lambda_2 = 0$; using the substitution $\rho = (\cosh kx)^{-1}$, we find for equation (9) the simple form

$$\frac{A_{2p+1}}{A_{2p-1}} = \frac{4p^2 - 2p}{4p^2 + 4p}\rho^2 \tag{11}$$

where $\lambda_1 = k^2/D$. The relation (11) is absolutely convergent for $\rho < 1$ ($\Rightarrow x \neq 0$), whereas for $\rho = 1$ ($\Rightarrow x = 0$) the ratio A_{2p+1}/A_{2p-1} becomes 1 by taking $\lim p \to \infty$, implying that the condition for absolute convergence does not hold independent of the k value of $(\cosh kx)^{-p}$, and there is no restriction with regard to the k value. Due to the nonlinear contributions of equation (9a) with $\lambda_2 \neq 0$, we show that this equation exhibits pointwise convergence for $-\infty \leq x \leq +\infty$, but the expansion (9) is only conditionally convergent. It should be noted that we may restrict our analysis to the zero point $\rho = 1$, because the convergence of $c = \sum_{p=1}^{\infty} A_p \rho^p$ is satisfied for $\rho < 1$ if it holds for $\rho = 1$.

With regard to equation (9a) and formula (10), the Leibniz criterion of conditionally convergent series is applicable:

$$\text{(i)} \qquad \sum_{p=1}^{\infty} A_p = \sum_{p=1}^{\infty} |A_p|(-1)^p \tag{12}$$

$$\text{(ii)} \qquad \lim_{p\to\infty} A_p \to 0 \tag{12a}$$

$$\text{(iii)} \qquad |A_1| > |A_2| > |A_3| > \cdots > |A_p| \tag{12b}$$

Thus, condition (i), equation (12), immediately follows from formula (10) (see also Table I) because for those A_p with odd p the powers of A_1, according to $A_p = A_p(A_1)$, are also odd and the powers of u ($u = -\lambda_2/\lambda_1$) are of even order. Therefore, sign A_p ($p > 1$) agrees with sign A_1 for odd p, whereas with regard to even p we have the reverse situation: the powers $A_p(A_1)$ are of even order and the powers of u are odd throughout, yielding sign $A_p = -$sign A_1 for even p.

The conditions (12a) and (12b) imply a recursive function with regard to the formation law (10): As a first step, the inequalities $|A_1| > |A_2| > |A_3| > |A_4|$ must be fulfilled for suitable upper and lower bounds of u. In a second step, it has to be examined whether the bounds satisfy the subsequent inequalities for $p > 4$. If they are not generally suitable, the procedure must be continued by taking into account coefficients A_p with $p > 4$. With respect to equations (9a) and (10) the relations

$$
\begin{aligned}
|u_{\max}| &< 3/A_1 \\
|u_{\min}| &> 2/A_1 - \delta/A_1, \qquad \delta < 11/108
\end{aligned}
\tag{13}
$$

turn out to be sufficient for the Leibniz conditions (12a) and (12b).

The existence of the L_1 norm $\int_{-\infty}^{+\infty} c(x)\,dx = 1$ can be derived from the pointwise convergence. Using the relations

$$S_p = \int_{-\infty}^{+\infty} dx\,(\cosh kx)^{-p} = S_1 \frac{1\cdot 3\cdot 5\cdots(p-2)}{2\cdot 4\cdot 6\cdots(p-1)} \qquad (p > 1 \text{ and odd})$$

and

$$S_p = \int_{-\infty}^{+\infty} dx\,(\cosh kx)^{-p} = S_2 \frac{2\cdot 4\cdot 6\cdots(p-2)}{3\cdot 5\cdot 7\cdots(p-1)} \qquad (p > 2 \text{ and even})$$

where $S_1 = \pi/k$ and $S_2 = 2/k$, we obtain

$$\int_{-\infty}^{+\infty} c(x)\,dx = A_1S_1 + A_2S_2 + \cdots + \sum_m A_mS_m = L_1(c) = 1 \tag{14}$$

because $S_1 > S_2 > S_3 > \cdots > S_p$ ($\lim_{p\to\infty} S_p \to 0$) and

$$L(c) = S_1\left|A_1 + \left(A_2S_2 + \cdots + \sum_p S_pA_p\right)S_1^{-1}\right| \leq S_1 \sum_{p=1}^{\infty} A_p$$

hold. With regard to the relation $A_p = A_p(A_1)$, according to equation (10), the L_1 norm (14) implies a polynomial equation in terms of powers of A_1 of infinite order, yielding for each permitted value $u = -\lambda_2/\lambda_1$ with $|u_{\min}| < |u| < |u_{\max}|$ a denumerably infinite set of solutions $c^M(x)$, where $M = 1, 2, 3, \ldots, \infty$.

It should be pointed out that the expansion (9) provides further solutions and their convergence properties are rather equivalent because we only have to perform proper substitutions. Thus, on putting $A_1 \equiv 0$, the expansion (9) reads

$$c_2(x) = \sum_{p=2}^{\infty} A_p(\cosh kx)^{-p} \tag{15}$$

and k is determined by $k^2 = \lambda_1 D/4$. Now the coefficients A_p $(p > 2)$ are given by the relation $A_2 \to A_4 \to A_6 \to A_{2p}$, and A_2 assumes the role of the norm amplitude. Thus in this case all coefficients with odd p $(A_3, A_5, \ldots)$ vanish identically. With the same justification we can put all $A_p \equiv 0$ $(p < \beta)$ and take only the sum

$$
\begin{gathered}
c_\beta^M = \sum_{p=\beta}^{\infty} A_p^M(\cosh kx)^{-p} \\
\beta = 1, 2, 3, 4, \ldots, \qquad M = 1, 2, 3, 4, \ldots
\end{gathered}
\tag{16}
$$

Then the determination of all coefficients A_p $(p > \beta)$ is expressed in terms of A_β: $A_p = A_p(A_\beta)$. Thus for each eigenfunction (16) of equation (7) with $\beta = 1, 2, 3, \ldots$, there exists a denumerably infinite set of functions ($M = 1, 2, \ldots$) for each permitted k value (or ratio $u = -\lambda_2/\lambda_1$). Between k^2 and λ_1 the relation

$$k^2 = \lambda_1/\beta^2 D \qquad (\beta = 1, 2, 3, \ldots) \tag{16a}$$

holds. Because the Leibniz criterion for conditionally convergent series has to be applied to each eigenfunction, we obtain a "band structure" of a permitted spectrum of the ratio $u = -\lambda_2/\lambda_1$:

$$|u_{\min}(\beta)| < |u(\beta)| < |u_{\max}(\beta)| \tag{16b}$$

This "band structure" with regard to the ratio u holds because it is impossible to form absolutely convergent expansions of equation (9) with regard to the nonlinear equation (7) or (9a).

The solution manifold given by the expansion (9) is symmetric because of the property $[\cosh(kx)]^{-p} = [\cosh(-kx)]^{-p}$ for each p. By regarding the solution manifold of the nonlinear Schrödinger equation (5), which also shows solutions of the form $\Psi = \sum_p A_p(\cosh kx)^{-p-1} \sin kx$, the question arises of whether equation (7) can also be solved by the antisymmetric expansion

$$c = \sum_{p=1}^{\infty} A_p(\cosh kx)^{-p-1} \sinh kx \tag{17}$$

However, this is not possible because equation (7) exhibits only a nonlinear term of second order $(\lambda_2 c^2)$, implying the square of antisymmetric contributions $[(\cosh kx)^2 - 1 = (\sinh kx)^2]$, in contrast to the cubic nonlinearity $\sim|\Psi|^2\Psi$ of equation (5). On the other hand, the linear combination of expansions (9) and (17),

$$c = \sum_{p=1}^{\infty} [A_p(\cosh kx)^{-p} + B_p(\cosh kx)^{-p-1} \sinh kx] \tag{18}$$

can satisfy equation (7). The coefficients A_p and B_p are determined recursively by collecting all terms related to the powers $(\cosh kx)^{-p}$ and $(\cosh kx)^{-p-1} \sinh kx$. We also note that the Galilei-transformed solution of the expansion (9) $(x \to x' = x - vt)$,

$$c_\beta^M(x - vt) = \sum_{p=\beta}^{\infty} A_p^M[\cosh(kx - v't)]^{-p} v' = kv \tag{19}$$

satisfies equation (4) with regard to one space coordinate, but the expansion (19) does not represent the time dependence according to equation (2), because by taking $v = 0$ it turns out we obtain the stationary version $\partial c/\partial t = 0$, whereas the complete time dependence requires solutions of the form $c(x-vt, t)$ to satisfy both equation (2) and equation (4). Solutions of this property can be found with some modifications of the ansatz (18). In spite of this lack of the manifold (19) or (9), it is valuable to know the solution spectrum of stationary concentration distributions (stable wave packets) propagating with the velocity v in one space dimension.

3. SOME EXTENSIONS

The consideration of concentration profiles in one space dimension as given by equations (9) and (19) is mainly justified by the clarity of the underlying procedure. A possible generalization to three space coordinates of the expansion (9) solving equation (7) that is just as straightforward as in one space coordinate is given by the substitution $kx \to k_1x + k_2y + k_3z$. Then equation (9) becomes

$$c(x, y, z) = \sum_{p=1}^{\infty} A_p[\cosh(k_1x + k_2y + k_3z)]^{-p} \tag{20}$$

and formula (10) remains valid if the substitution $k^2 = k_1^2 + k_2^2 + k_3^2$ is performed, yielding $\lambda_1 = Dk^2$. The convergence analysis referring to pointwise convergence also remains unchanged, but the L_1 norm does not exist if $c(x, y, z)$ is given by equation (20). By the substitutions $u = k_1x + k_2y + k_3z$, $v = k_2y$, and $w = k_3z$ we obtain

$$\iiint_{-\infty}^{+\infty} c(x, y, z)\, dx\, dy\, dz \to \iiint_{-\infty}^{+\infty} c(u)\, du\, dv\, dw \tag{20a}$$

which is divergent with respect to v and w. The expansion (20) only permits the introduction of the maximum norm, which also results from the property of pointwise convergence,

$$M(c) = \max_{x,y,z=0} c(x, y, z) = 1 \to \sum_{p=1}^{\infty} A_p = 1 \tag{20b}$$

On the other hand, the introduction of a product function

$$c(x, y, z) = \sum_{p=1}^{\infty} A_p(\cosh k_1x)^{-p}(\cosh k_2y)^{-p}(\cosh k_3z)^{-p} \tag{20c}$$

would be compatible with the L_1 norm, but the nonlinear equation (7) cannot be satisfied.

However, the extension of equation (7) to three space coordinates ($D\,\Delta c = \lambda_1 c - \lambda_2 c^2$) can be solved rigorously by the following modification of the expansion (9):

$$c_\beta^M = \sum_{p,q,r=\beta}^{\infty} A_{p,q,r}^M (\cosh k_1 x)^{-p} (\cosh k_2 y)^{-q} (\cosh k_3 z)^{-r} \tag{21}$$

where β and M run over $1, 2, 3, \ldots, \infty$.

It is apparent that the effort to determine the coefficients $A_{p,q,r}$ for $p, q, r > \beta$ in terms of $A_{\beta,\beta,\beta}$ increases significantly. On the other hand, the convergence analysis for the consideration of pointwise convergence is equivalent to that given by the relations (12), (12a), and (12b), and the expansion (21) can be subjected to the L_1 norm

$$\iiint_{-\infty}^{+\infty} c(x, y, z)\, dx\, dy\, dz = 1$$

because the norm amplitude $A_{\beta,\beta,\beta}$ can be fixed by the L_1 norm. With regard to equation (7), the following relation holds:

$$k^2 = \lambda_1 / D\beta^2 \qquad (k^2 = k_1^2 + k_2^2 + k_3^2) \qquad (\beta = 1, 2, 3, \ldots) \tag{22}$$

We also point out that the parameter M ($M = 1, 2, \ldots$) has the same meaning as in equation (16). Although the expansion (21) represents an extension to the three-dimensional case, the determination of the coefficients $A_{p,q,r}$, where $p, q, r > \beta$, in terms of $A_{\beta,\beta,\beta}$ is an enormous combinatorical task, and only the diagonal elements $A_{p,p,p}$ are identical with the one-dimensional case. The off-diagonal elements $A_{p,q,r}$, where $p \neq q \neq r \neq p$, are responsible for the failure of the product ansatz (20c). We have performed some test calculations with regard to the case $\beta = 1$ and have verified that *almost* all off-diagonal elements $A_{p,q,r}$ vanish identically, but the nonvanishing elements are the very reason that the expansion (20c) cannot satisfy the stationary version of equations (2) and (4). We also note that with regard to three dimensions it is not necessary to restrict the diffusion coefficient D to the isotropic case, because in the anisotropic case (consideration of the principal axes) the relation (22) has to be modified slightly

$$\lambda_1 = (D_1 k_1^2 + D_2 k_2^2 + D_3 k_3^2)\beta^2 \qquad (\beta = 1, 2, \ldots) \tag{22a}$$

In view of the increased combinatorical task resulting from the ansatz (21), it appears that for practical applications computer programs are needed for the calculation of the elements $A_{p,q,r}$, where p, q, and r are restricted to, e.g., $M_0 = 100$ instead of taking $M_0 \to \infty$.

At the present stage, our main interest lies in the treatment of the time dependence of equation (2) or equation (4) by the restriction to one space coordinate. This can be done with the help of the expansion (18) and the consideration of the ansatz (21). From the ansatz (21) it follows that if $c(x)$ is a stationary solution of equation (2) in one space coordinate, then by the substitution $x \to x - vt$ we do not obtain the general time-dependent solution of equation (2) representing an extension to two variables, but only a particular solution of equation (4), because we have not yet treated the time as an independent variable. Thus equation (2) or equation (4) is of second order with regard to the spatial derivatives, but of first order with regard to the time derivative. Therefore we can maintain the ansatz (9) with respect to the x coordinate, whereas for the time we have to take into account the ansatz (18), and because we consider now two independent variables, the simplest ansatz reads

$$c(x, t) = \sum_{p,q=1}^{\infty} A_{p,q}[(\cosh \alpha t)^{-q-1} \sinh \alpha t + b(\cosh \alpha t)^{-q}] (\cosh kx)^{-p} \tag{23}$$

Introducing the ansatz (23) into equation (2), we obtain

$$\begin{aligned}
&\sum_{p,q=1}^{\infty} A_{p,q}[(\cosh kx)^{-p} q\alpha(\cosh \alpha t)^{-q} - \alpha(q+1)(\cosh \alpha t)^{-q-2} \\
&\quad + q\alpha b(\cosh \alpha t)^{-q-1} \sinh \alpha t] \\
&\quad + Dk^2 \sum_{p,q=1}^{\infty} A_{p,q}[(\cosh \alpha t)^{-q-1} \sinh \alpha t + b(\cosh \alpha t)^{-q} \\
&\quad \times [p^2(\cosh kx)^{-p} - p(p+1)(\cosh kx)^{-p-2}] \\
&= \lambda_1 \sum_{p,q=1}^{\infty} A_{p,q}(\cosh kx)^{-p}[(\cosh \alpha t)^{-q-1} \sinh \alpha t + b(\cosh \alpha t)^{-q}] \\
&\quad - \lambda_2 \sum_{p_1,p_2,q_1,q_2=1}^{\infty} A_{p_1,q_1} A_{p_2,q_2}(\cosh kx)^{-p_1-p_2} \\
&\quad \times [(\cosh \alpha t)^{-q_1-q_2} - (\cosh \alpha t)^{-q_1-q_2-2} + b^2(\cosh \alpha t)^{-q_1-q_2} \\
&\quad + 2b(\cosh \alpha t)^{-q_1-q_2-1} \sinh \alpha t]
\end{aligned} \tag{23a}$$

A comparison of the expression (23a) with the simplified version (9a) shows that many terms of the computation procedure referring to $A_{p,q}$ can be used. If p and q run from 1 to infinity, then all coefficients $A_{p,q}$ are determined in terms of $A_{1,1}$. This results from (23a) using conclusions we have previously made: Thus all contributions referring to each power of the form

$(\cosh kx)^{-\beta}(\cosh \alpha t)^{-\beta'}$ and $(\cosh kx)^{-\beta}(\cosh \alpha t)^{-\beta'-1}\sinh \alpha t$ according to equation (23a) must satisfy this equation. For $p = q = 1$ we obtain

$$\begin{aligned} A_{1,1}\alpha + Dk^2 A_{1,1} b &= \lambda_1 A_{1,1} b \\ A_{1,1}\alpha b + Dk^2 A_{1,1} &= \lambda_1 A_{1,1} \end{aligned} \tag{23b}$$

It follows from the relation (23b) that the further relations

$$\begin{aligned} b = 1 &\rightarrow \alpha = \lambda_1 - Dk^2 \\ b = -1 &\rightarrow \alpha = Dk^2 - \lambda_1 \end{aligned} \tag{23c}$$

must be valid.

The convergence analysis completely follows the relations (10)-(14), and it is satisfying that the computational procedure for the determination of the coefficients $A_{p,q}$ in terms of $A_{1,1}$ can be reduced to the previously discussed one by proper substitutions. The norm amplitude is now defined by $A_{1,1}$. However, the case discussed above according to the ansatz (23) requires only the L_1 norm with reference to the space variable $\int_{-\infty}^{+\infty} c(x)\, dx = 1$, whereas with regard to the time variable we can make use of the initial condition $c(x, t=0) = c_0(x)$. This initial condition is consistent with the ansatz (23), as $(\cosh \alpha t)^{-q} \rightarrow 1$ and $\sinh \alpha t \rightarrow 0$ for $t \rightarrow 0$ (q arbitrary). The ansatz (23) is also compatible with the stationary restrictions given by equations (7), (9b), or (22), as by taking $\alpha \rightarrow 0$, equation (9) results from (23) and the relation (23c) implies the relation (9b).

In principle, it is possible to regard the ansatz (23) in three space dimensions according to the expansion (21), but the increasing effort is evident, and therefore essential properties such as convergence conditions and the exact computation of the expansion coefficients should be performed with the help of simplified versions. With regard to the expansion (23) it is also true that we do not have to take the sum from $p, q = 1, \ldots,$ to infinity, because we may also start from $p, q = \beta, \ldots,$ to infinity and put all terms of $A_{p,q} \equiv 0$ if p or q is less than β. Then the relation (23c) must be slightly modified:

$$\begin{aligned} b = 1 &\rightarrow \alpha\beta = \lambda_1 - Dk^2\beta^2 \\ b = -1 &\rightarrow \alpha\beta = Dk^2\beta^2 - \lambda_1 \end{aligned} \qquad (\beta = 1, 2, \ldots) \tag{23d}$$

Therefore we are able to summarize this by the expansion

$$\begin{aligned} c_\beta^M(x - vt, t) = \sum_{p,q=\beta}^{\infty} & A_{p,q}^M [\cosh(kx - v't)]^{-p} \\ & \times [(\cosh \alpha t)^{-q-1}\sinh \alpha t + b(\cosh \alpha t)^{-q}] \\ & \qquad (\beta, M = 1, 2, \ldots) \end{aligned} \tag{24}$$

We obtain the solution spectrum of equation (4), and by taking $v=0$, we see that the expansion (24) represents the solution spectrum of equation (2), because for simplicity we have only considered one space coordinate. With the help of the expansion (21) we may modify equation (24) to obtain the solution manifold of equation (2) in three space dimensions,

$$\begin{aligned} c_\beta^M(x, y, z, t) &\\ = \sum_{p_1,p_2,p_3,q=\beta}^{\infty} & A^M_{p_1,p_2,p_3,q}(\cosh k_1x)^{-p_1}(\cosh k_2y)^{-p_2}(\cosh k_3z)^{-p_3}\\ &\times[(\cosh \alpha t)^{-q-1}\sinh \alpha t + b(\cosh \alpha t)^{-q}] \end{aligned}$$

$$(\beta, M=1,2,\ldots) \qquad (24a)$$

but the recursive procedure for the determination of the coefficients $A^M_{p_1,p_2,p_3,q}$ increases considerably and therefore we prefer model considerations in one space coordinate.

4. GENERAL DISCUSSION

There are many applications where diffusion processes play an essential role with respect to the requirement of stationary conditions [equation (2) or equation (4)], referred to as equilibrium of fluxes by NTD. According to Prigogine (1967), the formation of dissipative structures induced by diffusion can be realized by nonequilibrium stationary states that are stable for small disturbances. Thus, the existence of dissipative structures is closely related to the so-called local thermodynamic equilibrium states. Therefore we point out that the stationary equation (7) is useful if it is founded by a general time dependence, e.g., equation (2). By taking formally $\alpha\to 0$, we obtain in fact the condition (16a) from the relation (23d), and the expansion (23) is converted to the ansatz (9). However, if the condition

$$\frac{\lambda_1}{Dk^2\beta^2} = 1+\eta \qquad (|\eta| \ll 1) \qquad (25)$$

holds for some values of β or (and) proper D, then those concentration distribution functions $c_\beta^M(x, t)$ satisfying relation (25) for some β values realize nonequilibrium stationary states in the sense of NTD, as long as the associated time interval $T(\eta)$ does not exceed α^{-1}. But by taking $t\to\infty$ (or by consideration of a sufficiently long, finite time t) the time behavior of the solution manifold $c_\beta^M(x, t)$ of equation (23) does not provide stable nonequilibrium states, because these solutions vanish for $t\to\infty$, and therefore the following interpretation holds: If $c_\beta^M(x)$ is the initial concentration distribution at $t=0$, then for long time intervals ($t\to\infty$) the time-dependent parts of equation (23) behave as damping functions with vanishing concentrations for $c_\beta^M(x, t \to \infty)$. The same behavior is also true for the Gaussian distribution function

$$c(x, t) = \frac{1}{2(D\pi t)^{1/2}} \exp\left(\frac{-x^2}{4Dt}\right)$$

of the pure diffusion equation (1).

Although the solution spectrum (23) is consistent with the nonlinear diffusion equation (2) [or (4), if the modification (24) is considered] there exists a slight modification of the expansion (23) satisfying also equation (2). With regard to the expansion (23), we have assumed the normalization condition

$$\int_{-\infty}^{+\infty} c(x, t=0)\, dx = 1$$

but the expansion (23) would also permit an additional integration

$$\iint_{-\infty}^{+\infty} c(x, t)\, dx\, dt < \infty$$

which we do not require. Thus, for the normalization condition

$$\int_{-\infty}^{+\infty} c(x, t=0)\, dx = 1$$

it is sufficient to permit a time dependence with nonvanishing contributions by taking $t \to \infty$, e.g., a $\tanh(\alpha t)$ contribution, and the modified version of equation (23) reads

$$c_\beta^M(x, t) = \sum_{p,q=\beta}^{\infty} A_{p,q}^M (\cosh kx)^{-p} \times [(\cosh \alpha t)^{-q} (\sinh \alpha t)^\beta + b(\cosh \alpha t)^{-q}] \tag{26}$$

implying also a term $(\tanh \alpha t)^\beta$ for $q = \beta$. The behavior of this expansion satisfying equation (2) is interesting, because the initial states $c_\beta^M(x, t=0)$ agree with the final states $c_\beta^M(x, t \to \infty)$, and only for $0 < t < \infty$ may the states vary in dependence on the time parameter. Thus, equation (2) is consistent with two rather similar solution manifolds given by the expansions (23) and (26), but they differ considerably with regard to their asymptotic behavior $t \to \infty$.

Studies have also been made of solitary solutions of equation (2) closely related to the expansion (26) (Hirota, 1981; Kramer and Riecke, 1985; Satsuma, 1981; Ulmer, 1983, 1985), which may be constructed on the basis of the solitary solutions (8) of the stationary nonlinear equation (7) and of the solitary solutions

$$c(t) = \lambda_1/2\lambda_2 - (\lambda_1/2\lambda_2)\tanh(\lambda_1 t/2) \tag{27}$$

and

$$c(t) = \lambda_1/2\lambda_2 + (\lambda_1/2\lambda_2)\tanh(-\lambda_1 t/2) \tag{27a}$$

of the nonlinear kinetic equation (3). Equation (2) is referred to as the Fisher equation (Mishin, 1982*a*,*b*; Stix, 1979) and Kolmogorov early supposed the existence of wavefront solutions (Das, 1984). Steeb (1985) analyzed the group-theoretic properties of equations (1) and (2) using generators of the Lie groups.

Solitary solutions of equations (2) and (4) have been considered in statistical physics [e.g., many-particle physics and biophysics (Das and Sihi, 1979; Flannery, 1982; Hirota, 1981; Kramer and Riecke, 1985; Mishin, 1982*a*,*b*; Satsuma, 1981; Stix, 1979; Ulmer, 1983, 1985], and the extension of the pure diffusion equation (1) by the kinetic terms $\lambda_1 c - \lambda_2 c^2$ makes it possible to describe the stationary states of an equilibrium of fluxes. The characterization of such stable nonequilibrium states is of great relevance in molecular biophysics [e.g., chromosome band structure analysis (Ulmer, 1983, 1985) and the active transport of K^+ and Na^+ ions through cell membranes ($Na^+ \rightarrow$ outside and $K^+ \rightarrow$ inside the cell) as supported by hydrolytic ATP decay]. It has been shown (Panda, 1981) that this transport phenomenon is not satisfactorily understood by the Onsager relations. Soliton mechanisms have been playing an increasing role in biophysics since Davydov (1979) successfully elucidated the release of free energy by ATP decay in α-helix proteins and the energy transport mechanism of muscle contraction. The solution manifold (19) of the nonlinear equation (4) can also be interpreted as stable soliton solutions associated with the propagation of a reactive process described by the concentration distribution $c(x - vt)$ in molecular chains or fluids.

There are various processes such as DNA or RNA replication kinetics (Biebricher *et al.*, 1983; Eigen and Gardiner, 1984; Eigen, 1985; Poerschke, 1984) and lateral inhibition of diffusion at certain membrane regions (Austin *et al.*, 1983; Jovin, 1984; Vaz and Criado, 1985; Vaz *et al.*, 1985*a*,*b*), where diffusion processes and kinetics should be considered simultaneously. The restriction to solutions of equation (1) for chromosome band structure analysis (Talekar, 1981) is insufficient because pure diffusion lacks stationary nonequilibrium states. In view of the complexity of biological structures and processes, equations (2), (4), and (7) and the solution spectra represented by the expansions (9), (18), (19), (23), (24), and (26) represent simplified models because we have to consider synergistic interactions among the many constituents involved in biophysical processes. Equation (2) and its solution functions can be related to the autocatalytic process of the spatial distribution of a specific class of interacting molecules. The decay kinetics ($\sim\lambda_1 c$) and the formation of new molecules ($\sim -\lambda_2 c^2$) can be associated with a reservoir (similar to thermodynamics) consisting of an enormous concentration which remains unchanged by the admission and delivery of molecules according to the following scheme:

$$\text{reservoir} \xleftarrow[\lambda_1]{} c(x, t) \xleftarrow[\lambda_2]{} \text{reservoir}$$

In a previous investigation (Ulmer, 1990), we analyzed the kinetics and spatial distribution of the decay and renewal of cellular ATP (L 1210 cells) by ^{31}P-NMR spectroscopy after the cells were exposed to doses of γ-rays. It turned out that the concentration distributions of ATP before irradiation and at a long time after irradiation, where the recovery processes for renewal of ATP are completed, correspond rather precisely to the stationary conditions (initial and asymptotic) of the solution function (26) with $\beta = 1$, and the decay and repair kinetics observed by ^{31}P-NMR was in agreement with the time behavior of this function. Therefore the hydrolytic decay ATP$\rightarrow$ADP+inorganic phosphate in cells and the renewal ADP+ inorganic phosphates$\rightarrow$ATP via oxidative phosphorylation can be successfully compared with the above reservoir model, although for the latter reaction numerous steps and enzymes are involved.

A control circuit of two different classes of molecules [$c_1(x, t)$ and $c_2(x, t)$], which may also be considered as a cross-catalytic feedback mechanism, can be obtained through a two-component extension of equation (2),

$$-\partial c_1/\partial t + D_1\,\Delta c_1 = +\lambda_{12} c_2^2 c_1 - \lambda_{21} c_2 c_1^2 \tag{28}$$

and

$$-\partial c_2/\partial t + D_2\,\Delta c_2 = +\lambda'_{21} c_1^2 c_2 - \lambda'_{12} c_1 c_2^2 \tag{28a}$$

It is a particular feature of these equations that the decay of the concentration c_1 is connected to the formation of c_2 and conversely. The solution manifold of the coupled nonlinear equations (28), (28a) can be obtained (in one space coordinate) by the expansion

$$c^M_{k,\beta} = \sum_{p,q=\beta}^{\infty} A^M_{k,pq}(\cosh kx)^{-p} \times [(\cosh \alpha t)^q (\sinh \alpha t)^\beta + b_k(\cosh \alpha t)^{-q}] \tag{29}$$

$k = 1, 2$ and $M, \beta = 1, 2, 3, \ldots$. Now α and k^2 are functions of λ_{12}, λ_{21}, λ'_{21}, λ'_{12}, and D_k, and the parameters b_1 and b_2 are determined by the initial conditions $c_1(x, t=0)$, $c_2(x, t=0)$. The computational procedure is not significantly more intricate than that of the expansion (26), but we do not discuss here the solutions and their biophysical relevance. It should be mentioned that particular solutions referring solely to kinetic equations [D_1 and D_2 of equations (28), (28a) are assumed to be zero] have been considered in Phillipson and Schuster (1983). Turing (1952) very early pointed out that the solutions of such a class of coupled nonlinear equations can be used for structural assays.

With regard to equations (1) and (2), it should be mentioned that it is reasonable to also take into account a nonlinear transport equation of heat

$$-\partial T/\partial t + \kappa\, \Delta T = \lambda_1 T - \lambda_2 T^2 \tag{30}$$

which may be associated with a heat control circuit, because the term $\lambda_1 T$ can be related to the consumption of heat and the nonlinear term $\lambda_2 T^2$ to a source. The solution procedure is completely identical to the previously discussed methods, and it is possible to regard one component of equations (28), (28a) as a transport equation of heat according to equation (30). Then we obtain solutions where the decay and formation of molecules are connected to the local distribution of heat.

The biological applications of equation (2) have not yet been exhausted; according to Gierer (1980), we can replace molecules by "supermolecular" cells consisting of numerous interacting molecules, and the cells may also undergo decay by cellular death and renewal by cell division (mitosis). The interaction between cells is mediated via membranes, and therefore a nonlinear term is in fact justified. Since a cellular assay consists of ca. 10^6–10^8 cells (monolayers or spheroids of cell cultures), a cellular distribution function $N(x, t)$ related to the number of cells can replace the molecular concentration functions $c(x, t)$, and we obtain an analog of equation (2),

$$-\partial N/\partial t + D\, \Delta N = \lambda_1 N - \lambda_2 N^2 \tag{31}$$

The solution procedures can be transferred from the discussed methods. By doing so and making use of known results, we can explain how *in vitro* cultures can only grow up to a final extent. *In vivo*, one has to regard equation (31) as a system of interacting, highly differentiated cells (instead of clonogenic cultures) obeying also characteristic control circuits with respect to their growth and pattern arrays, and equations (28), (28a) only represent a starting point for more complex situations.

Thus, the study of nonlinear diffusion equations is justified for many disciplines. We finally mention that the simplified kinetic equation (3) has been subjected to computer studies on sequences of numbers (e.g., Feigenbaum set) without taking account of analytical solutions. The results are periodic alterations of regular structures and chaotic behavior, and this behavior corresponds to the band structure conditions following from conditional convergence, e.g., equations (12), (12a), (12b), and (16b). The so-called "chaotic behavior" of dynamical systems is related to nonintegrability, as shown by Prigogine *et al.* (1991).

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