Mathematical Models and Methods in Applied Sciences

The Langevin or Kramers Approach to Biological Modeling

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In the Langevin or Ornstein-Uhlenbeck approach to diffusion, stochastic increments are applied to the velocity rather than to the space variable. The density of this process satisfies a linear partial differential equation of the general form of a transport equation which is hyperbolic with respect to the space variable but parabolic with respect to the velocity variable, the Klein-Kramers or simply Kramers equation. This modeling approach allows for a more detailed description of individual movement and orientation dependent interaction than the frequently used reaction diffusion framework.

For the Kramers equation, moments are computed, the infinite system of moment equations is closed at several levels, and telegraph and diffusion equations are derived as approximations. Then nonlinearities are introduced such that the semi-linear reaction Kramers equation describes particles which move and interact on the same time-scale. Also for these non-linear problems a moment approach is feasible and yields non-linear damped wave equations as limiting cases.

We apply the moment method to the Kramers equation for chemotactic movement and obtain the classical Patlak-Keller-Segel model. We discuss similarities between chemotactic movement of bacteria and gravitational movement of pyhsical particles.

Keywords: Langevin equation, moment closure, biological modeling

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1. Introduction

Spread in space is an important feature for most biological species. In many cases, moving in space and interaction among individuals and with the environment occur on the same time scale. If motion is modeled by diffusion then reaction diffusion equations for population densities are the standard deterministic models. These models have been successfully applied to many problems, e.g. to minimal habitat size, invasion speed, chemotaxis, or pattern formation. Ample reference is given in the monographs ([2,5,11,33,35]).

In diffusion models (i.e., in Brownian motion) the state of the particle is its position in space, the particle has no defined velocity, not even a direction. If velocity or direction is an essential feature of the process to be modeled, reaction transport equations are better suited to describe simultaneous interaction and spread. Typical examples are the formation of schools or flocks ([26]), aggregation of algae and other microorganisms ([50,6]), and alignment of actin filaments ([30,13]). Reaction transport equations explicitly include the velocity of an individual ([16,37]). The space of possible velocities typically is a bounded set such as a ball or a sphere, the change of velocity is given by a transition kernel. These models avoid infinite propagation speeds and allow for interaction terms which depend on the velocity ([14,26]). Analytically, these equations are rather different from reaction diffusion equations, nevertheless, under certain scalings of parameters, their long-time behavior can be approximated by reaction diffusion equations ([18,32,45]).

Solutions of linear diffusion and transport equations describe probability densities for single particle processes. On the other hand, the solutions can be interpreted as population densities, see e.g. Othmer *et al.*,[37] where position jump and velocity jump processes are used to derive equations for the densities of moving populations. In general it is difficult to relate a given semi-linear reaction transport or reaction diffusion equation to a stochastic process ([7,23]). For the Fisher equation and related hyperbolic systems there are even different stochastic interpretations ([28,37]).

Another approach by, e.g. Okubo[35] is to describe position and velocity of a particle by stochastic differential equations. Typically, these models are called *Langevin equations*. Langevin equations are based on Newton's law for movement in a force field, from which a Fokker-Planck equation for the velocity distribution is derived. In biological modeling, Langevin equations for velocity distributions have been used to describe cell motility ([1,42,44,43]) and later also position in space. The resulting equations for densities depending on space and velocity, e.g. Kramers' equation, are models for populations moving in space ([44,47,43,10]).

Schweitzer and Schimansky-Geier[44] study an ensemble of finitely many discrete random-walkers which interact with their environment. The movement of the walkers is described by a Langevin equation. The authors discuss cell aggregation and chemotaxis and they investigate numerical pattern formation and pattern coarsening, also known as *Ostwald ripening*.

Schimansky-Geier *et al.*[43] introduce the notion of *active Brownian particles*.

These are random walkers which generate a self-consistent external field and respond to it. An example is the secretion of an attracting chemical signal in chemotaxis. The authors survey for systems of active Brownian particles various dynamic effects, which have been found numerically using Monte-Carlo simulations. Among these patterns are aggregations, spikes, spotted rings, traveling waves, spiral waves, and moving spots. Many of these patterns are also known for reaction-advection-diffusion equations ([33,19,6,14]). Schimansky-Geier *et al.* emphasize the advantage of modeling with Langevin equations: *"Our model considers fluctuations which are always present, and is applicable also to problems where only small particle numbers govern the process of structure formation."* (p.101).

Erdmann *et al.*[10] study active Brownian particles in a given potential with velocity dependent friction function. Numerical simulations reveal interesting pattern formations. Recently, Mantzaris *et al.*[27] modeled angiogenesis and tumor growth using Langevin equations.

It appears that the Langevin formulation for a number of random walkers is well accessible to Monte-Carlo simulations. Many of the results mentioned above use simulation techniques to show pattern formation. It is of great interest to try to understand the various forms of pattern formation also analytically. Okubo and Grünbaum[34] briefly discuss the use of Langevin equations and corresponding Kramers equations in the context of biological applications. On page 151, they write *"... the complicated biodiffusion problems of this chapter* [i.e., Langevin, Kramers' and Patlak's equations] *impede an analytical development ..."*

One aim of the present paper is to face the challenge of analysis of non-linear Kramers equations and to provide some (novel) approaches to their analytical treatment.

In the Physics literature, Langevin equations for individual particles together with the corresponding partial differential equations for the probability density function are used widely, in particular in statistical mechanics to describe the motion of a particle in a potential ([40,41]). The terminology can sometimes be confusing as some authors refer to one particular partial differential equation as the *Fokker-Planck equation*, whereas others use that name for the general evolution equation derived from a (system of) stochastic differential equations.

The Langevin equation for a particle with mass m moving under the influence of an external force F with friction constant γ is given by

$$dx = v\,dt, \tag{1.1}$$

$$dv = (-\gamma v + F(x)/m)\,dt + q\xi(t)\,dt, \tag{1.2}$$

where $q = \sqrt{\gamma kT/m}$, with temperature T, Boltzmann constant k, and Gaussian white noise $\xi(t)$, see e.g. Risken [41]. In the one-dimensional case, the corresponding distribution function $u(t, x, v)$ satisfies the *Kramers equation* (sometimes also *Klein-*

Kramers equation)

$$u_t + vu_x = \frac{\partial}{\partial v}\left[\gamma v - \frac{F(x)}{m} + \frac{\gamma kT}{m}\frac{\partial}{\partial v}\right] u. \tag{1.3}$$

The steady states of this equation are given by the *Boltzmann distributions* ([10])

$$\bar{u}(x,v) = c\exp\left(-\frac{W(x)}{kT}\right)\exp\left(-\frac{m}{2kT}v^2\right), \qquad W(x) = \int F(x)dx.$$

For large friction constant γ, the Langevin system (1.1) yields the *Smoluchowski equation* or *Fokker-Planck equation*

$$u_t = \frac{1}{m\gamma}\frac{\partial}{\partial x}\left[-F(x) + kT\frac{\partial}{\partial x}\right] u \tag{1.4}$$

which has the equilibrium distributions:

$$\bar{u}(x,v) = c\exp\left(-\frac{W(x)}{kT}\right).$$

As an important equation in Theoretical Physics, equation (1.3) and its generalizations have been analyzed in great detail. For example, fundamental solutions were constructed and existence and smoothness results have been proved by Bouchut[4] and Victory and O'Dwyer[49], approximation theorems have been derived (Poupaud and Soler[39]) and variational principles for unbounded external forces have been studied by Huang[20].

If the external force comes from a potential which is generated by the particles themselves (e.g. self-gravitation), then the equation is also known as the *Vlasov-Poisson-Fokker-Planck equation*. As we show later, the Vlasov-Poisson-Fokker-Planck equation is closely related to chemotaxis models of the form of the Patlak-Keller-Segel equations.

The purpose of this paper is twofold. First, we want to make the Kramers equation available as a biological modeling tool for the detailed description of movement and interaction of individuals. Second, we use the moment approach to derive the telegraph equation and the diffusion equation (Smoluchowski's equation) from the Kramers equation and discuss approximation properties.

The paper is organized as follows. In Section 2, we discuss the underlying stochastic models for the diffusion equation and for the Kramers equation, introduce scalings and formulate the *reaction Kramers equation*. In Section 3, we prove existence of solutions to the reaction Kramers equation. Then in Section 4, we apply the moment approach to the linear Kramers equation and we state approximation results for the telegraph and the diffusion equation. In Section 5, we apply the theory developed thus far to derive the classical chemotaxis equations from the Kramers equation and exhibit the relationship with gravitation physics.

2. Modeling Background

2.1. *Reaction Diffusion Equations*

The solution $u(t, x)$ of the linear scalar diffusion equation

$$u_t = D\Delta u \tag{2.5}$$

is the density at the space position x at time t. The function u can be interpreted as a probability or, in the present context, as a population density. The positive number D is the diffusion coefficient, with dimension length^2/time.

If particles interact (e.g. are born and die) and move on the same time scale and if interaction is governed by the ordinary differential equation $\dot{u} = f(u)$, then the compounded process of migration and interaction is usually described by a reaction diffusion equation

$$u_t = D\Delta u + f(u). \tag{2.6}$$

In the case of a "simple hump", i.e., a function of the form $f(u) = au(1 - u)$, the equation is called the Fisher or Fisher-KPP equation. It is not completely trivial that the two "actions" $D\Delta$ and f should be joined by a "plus" sign. In fact, for more general models like transport equations things get more complicated. The early authors Fisher[12] and in particular Kolmogorov *et al.*[23] have taken great care to justify the approach, see Hadeler[16] and Hillen[17] for a detailed exposition. We mention in passing that there exists also an interpretation of (2.6) in terms of Brownian motion with branching, originally found by McKean[28] ([16]).

In the probabilistic view the solution u of the diffusion equation is seen as the density for a particle governed by the Wiener process

$$dx = \sqrt{D}\xi(t)dt. \tag{2.7}$$

The path of the particle (in the (t, x) continuum) is (almost surely) continuous but nowhere differentiable. If the process is seen as a limiting case of a walk on a discrete grid, then the assumed particle can make any number of turns in a finite time interval. From this feature of Brownian motion (criticized by Einstein[8]), the parabolic nature of the diffusion equation derives as well as the phenomenon of infinitely fast propagation. They are consequences of the assumption that the particle is characterized only by its position in space and has no assigned velocity, inertia, or memory. These deficiencies of the diffusion equation are inherited by the reaction diffusion equation.

2.2. *The Kramers Equation*

The Kramers equation can be directly derived from the Langevin equation (1.1). The idea behind the Langevin approach is that the stochastic increments are applied to the velocity of the particle rather than to its position in space. If we denote the

velocity variable by v then the equations for an individual particle read

$$dx = v\,dt, \tag{2.8}$$

$$dv = -\gamma v\,dt + \sqrt{d}\xi(t)\,dt. \tag{2.9}$$

The constant $\gamma > 0$ measures the strength of a feedback that pulls the velocity back to zero; it plays the role of a damping coefficient. The constant $d > 0$ is the diffusion rate for the velocity, not to be confused with the diffusion rate D in the diffusion equation (2.5). The stochastic process described in (2.9) is a simple form of an *Ornstein-Uhlenbeck process* [36].

The general mechanism to derive second order partial differential equations from particle-based processes is to expand the distribution function in an appropriate basis of some function space. Applied to (2.8,2.9) the mechanism is known as the Kramers[24]-Moyal[31] expansion. It leads to the following linear partial differential equation for the density $u(t, x, v)$ of the particle with respect to position x and velocity v at time t

$$u_t + v \cdot \nabla_x u - \gamma\,\mathrm{div}_v(vu) = d\Delta_v u, \tag{2.10}$$

which can also be written in more extended form as

$$u_t + v \cdot \nabla_x u - \gamma v \cdot \nabla_v u - \gamma u = d\Delta_v u. \tag{2.11}$$

For convenience, we explicitly present (2.10) for a one-dimensional space variable,

$$u_t + vu_x - \gamma(vu)_v = du_{vv}. \tag{2.12}$$

The form (2.11) clearly shows the structure of the problem. With respect to space the equation is hyperbolic. Particles have a well-defined velocity v. If $d = 0$ then the problem is hyperbolic also with respect to v. The characteristic differential equations are $\dot{t} = 1$, $\dot{x} = v$, $\dot{v} = -\gamma v$. If $d > 0$ then the problem is parabolic with respect to v, and equations (2.8,2.9) can be seen as generalized characteristic equations.

Equation (2.10) is usually written with $\gamma = 1$. We keep $\gamma > 0$ for future scaling purposes. Equation (2.10) is known as the *Kramers* or the *Klein-Kramers equation,* and also as the linear *Vlasov-Poisson-Fokker-Planck equation* without potential.

Equation (2.11) may be more suitable as a biological model than the diffusion equation, because when particles, say algae or amoebae, move then it is not their position but their motion which is subject to stochastic effects. Equation (2.11) might also be beneficial for small population sizes, where stochastic variations between individuals cannot be neglected.

If the velocity space is compact then one does not need the negative feedback term in (2.9) and one can put $\gamma = 0$. For instance, in two dimensions one can assume that the particle speed is constant and that the stochastic increments apply to particle orientation. Then Langevin's equations (2.8,2.9) become

$$dx = |v|\begin{pmatrix}\cos\varphi\\ \sin\varphi\end{pmatrix}dt, \quad d\varphi = \sqrt{d}\xi(t)\,dt,$$

which, on the macroscopic level, yields the two dimensional *Bartlett*[3] *equation* ,

$$u_t + \cos\varphi\, u_x + \sin\varphi\, u_y = d u_{\varphi\varphi}.$$

The quantity $1/\sqrt{d}$ is a measure of persistence of movement direction. In Bartlett's model the speed is constant, the velocity diffuses on the unit sphere, in the Kramers equation the velocity diffuses in the whole space.

2.3. *Scaling and Approximation*

Using an appropriate scaling, the Kramers equation reduces to the diffusion equation. At the level of the "characteristic system" (2.8,2.9) the transition is formally simple. With the scaling

$$\gamma \to \gamma/\varepsilon, \qquad d \to d/\varepsilon^2, \tag{2.13}$$

system (2.8,2.9) becomes

$$\begin{aligned} dx &= v\, dt, \\ \varepsilon dv &= -\gamma v\, dt + \sqrt{d}\xi(t) dt. \end{aligned}$$

and for $\varepsilon \to 0$, we get formally

$$dx = v\, dt = \frac{\sqrt{d}}{\gamma}\xi(t)\, dt,$$

which is a diffusion process (2.7) with $D = d/\gamma^2$.

On the level of the partial differential equations the same transition, i.e., going directly form the Kramers equation (2.10) to the diffusion equation (2.5) without using stochastic tools, seems more difficult. In simple terms the question is how one can approximate the operator $\gamma\nabla_v \cdot (vu) + d\Delta_v u$ in (2.10) with $D\Delta_x u$ in (2.5).

In the standard physics literature ([41]) this transition is performed by conjugation with an exponential function (implying the introduction of a small parameter) and an expansion into Hermite polynomials, an approach already known to Laplace ([21]). Setting the higher order terms in this expansion to zero, one formally obtains the telegraph equation and also the diffusion equation, which is usually known as Smoluchowski's equation in this context. We propose a simpler approach using moments for which we show an approximation property in Section 4.

2.4. *Kramers Equation with Reaction*

Here we supply the linear Kramers equation with reaction terms to make it a refined version of a reaction diffusion equation. We assume that particles are born with a rate $m(\bar{u})$ and die with a rate $g(\bar{u})$, where $\bar{u}$ is the total number of particles at a given location,

$$\bar{u}(t,x) = \int u(t,x,v)\, dv. \tag{2.14}$$

Newborn particles start their motion at the position of their parent and choose their velocity according to some given probability distribution with density $H(v)$. We assume that the function H is continuous, non-negative, normalized to $\int H(v)dv = 1$ and rotationally symmetric.

As in reaction transport equations and in correlated random walks ([14,16]), we observe that a newborn particle can choose a velocity at random while a vanishing particle can only disappear with the velocity it has. Hence, in contrast to reaction diffusion equations, birth and death enter the equation in different ways,

$$u_t + v \cdot \nabla_x u - \gamma \mathrm{div}_v(vu) = d\Delta_v u + H(v)m(\bar{u})\bar{u} - g(\bar{u})u. \tag{2.15}$$

We shall call (2.15) the *reaction Kramers equation*. With the kinetic reaction term f being defined as

$$f(u) = m(u)u - g(u)u, \tag{2.16}$$

equation (2.15) can be seen as a refined version of the reaction diffusion equation (2.6).

3. Existence of Solutions

In this section we first collect and review known results and estimates on solutions of the linear Kramers equation (2.10), formulate them in terms of operator semigroups and finally show existence of solutions to the Kramers equation with reaction (2.15).

3.1. *The Linear Case*

The linear Kramers equation (2.10) is a special case of what is referred to as the Vlasov-Poisson-Fokker-Planck equation in the literature. We collect some results from Bouchut[4] and Victory and O'Dwyer[49]. Since we think of applications in biological modeling we choose to work in the space $\mathcal{L}^1 = L^1(\mathbb{R}^{2n})$, such that the norm of a nonnegative function represents the total number of individuals.

There is an explicit representation of the Green's function G of equation (2.10) Appendix A. Using G, one can write the solution for given initial data $u_0 \in \mathcal{L}^1$ as

$$u(t,x,v) = \int\int G(t,x,v,y,\nu)u_0(y,\nu)dyd\nu. \tag{3.17}$$

From (3.17) and the fact that $\int\int G(t,x,v,y,\nu)dxdv = 1$ ([49]), the following results have been derived.

Proposition 3.1 (Bouchut[4], Lemma 1). *For initial data $u_0 \in \mathcal{L}^1$ there is a unique solution $u \in \mathcal{C}([0,\infty), \mathcal{L}^1)$ to equation (2.10) which has the additional smoothness properties*

$$\partial^\alpha_{x,v} u \in \mathcal{C}((0,\infty), \mathcal{L}^1) \cap \mathcal{C}((0,\infty), \mathcal{C}_0(\mathbb{R}^{2n}))$$

for any multi-index α. Furthermore the estimate

$$\|u(t)\|_{\mathcal{L}^1} \leq \|u_0\|_{\mathcal{L}^1} \qquad \text{for all} \qquad t \geq 0.$$

holds. For nonnegative initial data the solution is nonnegative for all times and the total mass is preserved.

Note that even though equation (2.10) is hyperbolic with respect to x and parabolic only with respect to v, solutions are smooth with respect to both variables for $t > 0$.

Solutions of (2.10) show an additional smoothing effect. Recall that $\bar{u}(t,x)$ denotes the total number of particles at (t,x). Since this function appears in the nonlinearity, we are interested in some estimates. It is true, of course, that $u \in \mathcal{L}^1$ implies that $\bar{u} \in L^1(\mathbb{R}^n)$. However, $u \in (\mathcal{C}_b \cap L^1)(\mathbb{R}^{2n})$ does not imply $\bar{u} \in \mathcal{C}_b(\mathbb{R}^n)$. For a counterexample, see Appendix B. (This phenomenon does not occur if the velocity space is bounded.) Hence, the next result comes as a surprise.

Proposition 3.2 (Bouchut[4], (21–23)). *Let $u_0 \in \mathcal{L}^1$ and let u be the solution of (2.10). Then the function $\bar{u}$, defined by (2.14), is given as a convolution*

$$\bar{u}(t,x) = \frac{1}{(4\pi d\chi(t))^{N/2}} \int_{\mathbb{R}^n} e^{-\frac{|x-y|^2}{4d\chi(t)}} \int_{\mathbb{R}^n} u_0 \left(y - \frac{1-e^{-\gamma t}}{\gamma} v, v \right) dv\, dy, \tag{3.18}$$

where

$$\chi(t) = \frac{1}{\gamma^2}(\gamma t - (1 - e^{-\gamma t})).$$

In particular, $\bar{u}(t,x) \in \mathcal{C}^\infty(\mathbb{R}^n)$ for all $t > 0$.

From (3.18) we can conclude that

$$\|\bar{u}(t)\|_\infty \leq \frac{1}{(4\pi d\chi(t))^{N/2}} \|u_0\|_{\mathcal{L}^1} \to 0$$

as $t \to 0$.

In terms of semigroup theory for linear evolution equations, the statement of Proposition 3.2 can be expressed as follows.

Proposition 3.3. *The operator*

$$Ku = -v \cdot \nabla_x u + \gamma \mathrm{div}_v(vu) + d\Delta_v u \tag{3.19}$$

generates a strongly continuous semigroup of contractions on $\mathcal{L}^1$. The open right half plane is contained in the resolvent set of K.

Proof. We use the above estimates and apply Theorem II.6.7 and formula II.1.14 in Engel and Nagel[9]. □

3.2. *The Nonlinear Case*

We write the Kramers equation with reaction (2.15) in the form

$$u_t = Ku + F[u], \tag{3.20}$$

with K as in (3.19) and

$$F[u] = H(v)m(\bar{u})\bar{u} - g(\bar{u})u. \tag{3.21}$$

In general, equations of the form (3.20) can be treated by applying the variation of constants formula and a contraction argument. This argument requires that F be Lipschitz in the space considered. In the present case, if m and g are bounded by constants, the operator $F : \mathcal{L}^1 \to \mathcal{L}^1$ is well-defined and linearly bounded but, similar to the Nemytskij operator, not Lipschitz.

To remedy this situation, we define local averages of $\bar{u}$ (2.14) by

$$\bar{u}^\delta(t,x) = \frac{1}{\Omega_n \delta^n} \int_{|x-y|\le\delta} \bar{u}(t,y)dy \tag{3.22}$$

for fixed $\delta > 0$, where Ω_n denotes the volume of the unit ball in $\mathbb{R}^n$, and introduce the modified nonlinearity

$$\hat{F}[u] = H(v)m(\bar{u}^\delta)\bar{u} - g(\bar{u}^\delta)u. \tag{3.23}$$

In this case, production and mortality depend on the local averages. The number δ can be interpreted as a radius of interaction of individuals. We show the following result.

Theorem 3.1. *Let $\delta > 0$. Suppose that the functions m and g are bounded and locally Lipschitz. Then the modified reaction Kramers equation*

$$u_t = Ku + \hat{F}[u], \qquad u(0) = u_0$$

has a unique nonnegative global solution $u \in \mathcal{C}([0,\infty), \mathcal{L}^1)$ for all nonnegative initial data $u_0 \in \mathcal{L}^1$.

Proof. The solution is given by the variation of constants formula

$$u(t) = T(t)u_0 + \int_0^t T(t-s)\hat{F}[u(s)]ds, \tag{3.24}$$

where $T(t)$ is the semigroup generated by K. A priori, the norm of the solution can be bounded as

$$\|u(t)\|_{\mathcal{L}^1} \le \|u_0\|_{\mathcal{L}^1} + (\|m\|_\infty + \|g\|_\infty) \int_0^t \|u(s)\|_{\mathcal{L}^1} ds \tag{3.25}$$

since $\|T(t)\| \le 1$. Hence, by Gronwall's Lemma, the solution grows at most exponentially in t. It remains to show that $\hat{F}$ is locally Lipschitz on $\mathcal{L}^1$. Let $u, w \in \mathcal{L}^1$

with $\|u\|, \|w\| \leq M$. Then

$$\begin{aligned}
&2\|g(\bar{u}^\delta)u - g(\bar{w}^\delta)w\|_{\mathcal{L}^1} \\
&\leq \|(g(\bar{u}^\delta) + g(\bar{w}^\delta))(u-w)\|_{\mathcal{L}^1} + \|(g(\bar{u}^\delta) - g(\bar{w}^\delta))(u+w)\|_{\mathcal{L}^1} \\
&\leq 2\|g\|_\infty \|u-w\|_{\mathcal{L}^1} + \mathrm{Lip}(g,M)\|\bar{u}^\delta - \bar{w}^\delta\|_\infty \|u+w\|_{\mathcal{L}^1} \\
&\leq 2\left(\|g\|_\infty + \frac{1}{2\delta} M \mathrm{Lip}(g,M)\right) \|u-w\|_{\mathcal{L}^1},
\end{aligned}$$

where $\mathrm{Lip}(g,M)$ is the Lipschitz constant of g on $[0,M]$. The case of the function $u \mapsto H(v)m(\bar{u}^\delta)\bar{u}$ is treated similarly. □

4. The Moment Equations

4.1. *The Linear Case*

For convenience, we use the one-dimensional notation to derive the moment equations. The argument, however, carries over to several space-dimensions. For the solution $u(t,x,v)$ of (2.12) we form moments

$$m_i(t,x) = \int v^i u(t,x,v) dv \tag{4.26}$$

for $i = 0, 1, 2, \ldots$ where the integral is taken over the velocity space $\mathbb{R}$. The zero moment equals the total density introduced in (2.14), $\bar{u}(t,x) = m_0(t,x)$. Multiplying (2.12) by v^i and integrating over v we get a countable sequence of moment equations. Here we present the first four equations

$$m_{0t} + m_{1x} = 0, \tag{4.27}$$

$$m_{1t} + m_{2x} = -\gamma m_1, \tag{4.28}$$

$$m_{2t} + m_{3x} = -2\gamma m_2 + 2d m_0, \tag{4.29}$$

$$m_{3t} + m_{4x} = -3\gamma m_3 + 6d m_1. \tag{4.30}$$

Of course, no finite subsystem is closed, and we do not even expect that the solutions of an increasing sequence of moment systems will converge to a solution of (2.12). But we can expect that suitably chosen closed finite sub-systems represent good approximations to solutions of (2.12).

We proceed as follows. We differentiate (4.27) with respect to t, differentiate (4.28) with respect to x and multiply by -1, and we multiply (4.27) by γ,

$$m_{0tt} + m_{1tx} = 0, \tag{4.31}$$

$$-m_{1tx} - m_{2xx} - \gamma m_{1x} = 0, \tag{4.32}$$

$$\gamma m_{0t} + \gamma m_{1x} = 0.$$

Then we add the three equations and get

$$m_{0tt} + \gamma m_{0t} = m_{2xx}. \tag{4.33}$$

We multiply (4.33) by 2γ and differentiate (4.29) twice with respect to x,

$$2\gamma m_{0tt} + 2\gamma^2 m_{0t} = 2\gamma m_{2xx},$$
$$m_{2txx} + m_{3xxx} + 2\gamma m_{2xx} = 2d m_{0xx}. \tag{4.34}$$

Adding these two equations, we get

$$2\gamma m_{0tt} + 2\gamma^2 m_{0t} + m_{2txx} + m_{3xxx} = 2d m_{0xx}. \tag{4.35}$$

Now we apply the scaling (2.13) and arrive at

$$\frac{\varepsilon}{\gamma} m_{0tt} + m_{0t} + \frac{\varepsilon^2}{2\gamma^2}(m_{2txx} + m_{3xxx}) = \frac{d}{\gamma^2} m_{0xx}. \tag{4.36}$$

Omitting the term with ε^2 and writing again $\bar{u}$ instead of m_0, we get a telegraph equation or damped wave equation

$$\frac{\varepsilon}{\gamma}\bar{u}_{tt} + \bar{u}_t = D\bar{u}_{xx}, \tag{4.37}$$

with

$$D = \frac{d}{\gamma^2}. \tag{4.38}$$

Omitting also the first order term we get the diffusion equation

$$\bar{u}_t = D\bar{u}_{xx}. \tag{4.39}$$

Repeating the same argument for several space variables, we find that with the same scaling (2.13) the Kramers equation (2.10) is first reduced to a damped wave equation

$$\frac{\varepsilon}{\gamma}\bar{u}_{tt} + \bar{u}_t = D\Delta_x u,$$

and then, for $\varepsilon \to 0$, to the diffusion equation

$$\bar{u}_t = D\Delta_x \bar{u}.$$

Hence the diffusion equation can be seen as the diffusion limit of the Kramers equation for rapid diffusion in the velocity space and strong feedback.

4.2. *The Moment Generating Function*

In the previous section we formally derived the telegraph and the diffusion equation. To prove that these approximations are indeed of order ε^2 or ε, repectively, we use the moment generating function

$$Q(t,x,s) = \int e^{v\cdot s}\, u(t,x,v)dv, \tag{4.40}$$

where $u(t,x,v)$ is solution of (2.12) and $s \geq 0$ is a dummy variable. As we expand $e^{v\cdot s}$ we find that

$$Q(t,x,s) = \sum_{j=0}^{\infty} \frac{m_j s^j}{j!}$$

and hence the moments are reproduced by

$$\frac{\partial^j}{\partial s^j} Q(t,x,0) = m_j(t,x). \tag{4.41}$$

We find that the moment generating function is the solution to an initial value problem.

Proposition 4.1. *The moment generating function (4.40) satisfies the equation*

$$Q_t + (\nabla_x \cdot \nabla_s)Q + \gamma(s \cdot \nabla_s)Q = ds^2 Q \tag{4.42}$$

with initial and boundary conditions

$$Q(0,x,s) = \int e^{v\cdot s} u(0,x,v)dv, \qquad Q(t,x,0) = \bar{u}(t,x). \tag{4.43}$$

Proof. Multiply equation (2.11) by $e^{v\cdot s}$, integrate over v and apply Green's formula. □

If we assume that u and hence Q are decaying fast enough as $|x| \to \infty$ then we can form the total population with respect to x and get the moment generating function $\bar{Q}(t,s)$ which keeps the information on the velocity distribution,

$$\bar{Q}(t,s) = \int Q(t,x,s)dx.$$

From (4.42), we get that $\bar{Q}$ satisfies a linear transport equation in the space of the dummy variable

$$\bar{Q}_t + \gamma s \cdot \nabla_s \bar{Q} = ds^2 \bar{Q}.$$

This equation can be solved explicitly by the method of characteristics. The characteristic differential equations are

$$\dot{t} = 1, \quad \dot{s} = \gamma s, \quad \dot{\bar{Q}} = ds^2 \bar{Q},$$

and the solution is given by

$$\bar{Q}(t,s) = \bar{Q}(0, e^{-\gamma t}s)\, \exp\left\{ \frac{ds^2}{\gamma} (\sinh(\gamma t)) \right\}.$$

Hence $\bar{Q}$ is bounded in $C^\infty([0,T], \mathbb{R}^n_+)$ for each $T > 0$. Since $Q(t,x,s) \geq 0$ this implies that Q is bounded in $L^1(\Omega, C^\infty([0,T], \mathbb{R}^n_+))$.

The goal is to find a C^∞ estimate for Q. The equation (4.42) for the moment generating function is weakly hyperbolic. The principal part of the symbol is $p_2(\xi,\sigma) = \xi\sigma$, where ξ, σ denote the dual variables of x, s w.r.t. Fourier transformation. We expect that results of Mizohata[29] on well-posedness of the Cauchy problem of weakly hyperbolic equations in Gevrey classes can be applied. Then the hypothesis (4.45) below can be reduced further.

4.3. *Approximation Property*

In the previous section, equation (4.36) has been derived for the moments m_0, m_2 and m_3. From this equation we formally obtained the diffusion equation (4.39) and the telegraph equation (4.37) as the order $O(1)$ and $O(\varepsilon)$ approximations, respectively. The aim of this section is to make these statements precise.

We require the following smoothness properties of the initial values,

$$u(0,x,v) = u_0(x,v) \in C_b^\infty(\mathbb{R}^2) \cap L^1(\mathbb{R}^2). \tag{4.44}$$

Furthermore, we require that there is some $\bar{s} > 0$ such that the moment generating function $Q(t,x,s)$ exists for $0 \le s < \bar{s}$ and satisfies

$$\sup_{0\le t\le T} \|Q(t,.,.)\|_{C^k(\mathbb{R}^2)} < C_Q(T), \tag{4.45}$$

for all $T > 0$, for $k \ge 6$, and some constant $C_Q(T)$.

We consider a regular expansion of the 0-order moment m_0 in powers of ε:

$$m_0(t,x) = \sum_{j=0}^{N} m_0^{(j)} \varepsilon^j, \ N \ge 2.$$

If we compare orders of ε in (4.36), we get

$$\varepsilon^0: \quad m_{0t}^{(0)} = \frac{d}{\gamma^2} m_{0xx}^{(0)} \tag{4.46}$$

$$\varepsilon^1: \quad \frac{1}{\gamma} m_{0tt}^{(0)} + m_{0t}^{(1)} = \frac{d}{\gamma^2} m_{0xx}^{(1)} \tag{4.47}$$

with initial conditions

$$m_0^{(0)}(0,x) = m_0(0,x), \qquad m_0^{(1)}(0,x) = 0. \tag{4.48}$$

Equations (4.46), (4.48) define a parabolic initial value problem for $m_0^{(0)}(t,x)$. Once $m_0^{(0)}$ is known equations (4.47), (4.48) define a parabolic initial value problem for $m_0^{(1)}$. With these solutions $m_0^{(0)}$ and $m_0^{(1)}$ we define

$$w(t,x) := m_0^{(0)}(t,x), \tag{4.49}$$

$$W(t,x) := m_0^{(0)}(t,x) + \varepsilon m_0^{(1)}(t,x). \tag{4.50}$$

We see that $w(t,x)$ satisfies a diffusion equation

$$w_t = \frac{d}{\gamma^2} w_{xx},$$

while $W(t,x)$ satisfies a telegraph equation up to second order

$$\frac{\varepsilon}{\gamma} W_{tt} + W_t = \frac{d}{\gamma^2} W_{xx} - \frac{\varepsilon^2}{\gamma} m_{0tt}^{(1)}.$$

The main result of this section is the following approximation property.

Theorem 4.1. *Let (4.44) and (4.45) be satisfied, and let w and W be defined by (4.49), (4.50). Then for all $T > 0$ there are constants $C_1, C_2 > 0$ which depend on T, γ, d, C_Q such that*

$$\|m_0(t,.) - w(t,.)\|_\infty \leq C_1 \varepsilon, \tag{4.51}$$

$$\|m_0(t,.) - W(t,.)\|_\infty \leq C_2 \varepsilon^2. \tag{4.52}$$

To prove the above Theorem, we first show the following estimate:

Lemma 4.1.

$$\left\| \frac{1}{\gamma} m_{0tt}(t,.) + \frac{\varepsilon}{2\gamma^2} \left(m_{2txx}(t,.) + m_{3xxx}(t,.) \right) \right\|_\infty \leq \left(\frac{1+\gamma}{\gamma} + \frac{\varepsilon}{\gamma^2}(1+\gamma+d) \right) C_Q(T).$$

Proof. Since all derivatives of the moment generating function up to sixth order are bounded we can estimate the spatial derivatives of the moments for $k + j \leq 6$

$$\frac{\partial^k}{\partial x^k} m_j(t,x) = \frac{\partial^{k+j}}{\partial x^k \partial s^j} Q(t,x,0)$$

and obtain

$$\left\| \frac{\partial^k}{\partial x^k} m_j(t,x) \right\|_\infty \leq C_Q(T).$$

Then we write (4.34) as

$$m_{2txx} = -m_{3xxx} - 2\gamma m_{2xx} + 2d m_{0xx}$$

and estimate

$$\|m_{2txx}(t,.)\|_\infty \leq (1 + 2\gamma + 2d)\, C_Q(T).$$

From (4.31) and (4.32) it follows that $m_{0tt} = m_{2xx} + \gamma m_{1x}$, and hence we can apply the above to get

$$\|m_{0tt}\|_\infty \leq (1+\gamma)\, C_Q(T). \qquad \square$$

Proof of Theorem 4.1.

1. The diffusion approximation. We define $z := m_0(t,x) - w(t,x)$. Then $z(t,x)$ satisfies

$$z_t - \frac{d}{\gamma^2} z_{xx} = \varepsilon \left(-\frac{1}{\gamma} m_{0tt} - \frac{\varepsilon}{2\gamma^2}(m_{2txx} + m_{3xxx}) \right), \tag{4.53}$$

with initial condition $z(0,x) = 0$. We denote by $S(t)$ the semigroup generated by the operator $\frac{d}{\gamma^2}\Delta$ on $C_0(\mathbb{R})$ to write the solution of (4.53) as

$$z(t,x) = \varepsilon \int_0^t S(t-\tau) \left[-\frac{1}{\gamma} m_{0tt} - \frac{\varepsilon}{2\gamma^2}(m_{2txx} + m_{3xxx}) \right] d\tau.$$

Then the estimate in Lemma 4.1 yields the desired approximation result

$$\|z(t,.)\|_\infty \leq \varepsilon T \left(\frac{1+\gamma}{\gamma} + \frac{\varepsilon}{\gamma^2}(1+\gamma+d) \right) C_Q(T).$$

2. The telegraph approximation. We now let $Z(t,x) := m_0(t,x) - W(t,x)$. Then Z satisfies

$$\frac{\varepsilon}{\gamma}Z_{tt} + Z_t - \frac{d}{\gamma^2}Z_{xx} = \varepsilon^2\left(\frac{1}{\gamma}m_{0tt}^{(1)} - \frac{1}{2\gamma}(m_{2txx} + m_{3xxx})\right), \tag{4.54}$$

with initial conditions $Z(0,x) = 0, Z_t(0,x) = 0$. We now use Theorem 3.2 in Hillen and Müller[32], which states that

$$\|Z(t,.)\|_\infty \leq C(T)\left(\varepsilon^2\int_0^t \left\|\frac{1}{\gamma}m_{0tt}^{(1)} - \frac{1}{2\gamma}(m_{2txx} + m_{3xxx})\right\|_\infty d\tau\right).$$

The term $m_{2txx} + m_{3xxx}$ has been bounded above, it remains to estimate $m_{0tt}^{(1)}$. From (4.47) it follows that $m_0^{(1)}$ solves the parabolic problem

$$m_{0t}^{(1)} = \frac{d}{\gamma^2}m_{0xx}^{(1)} - \frac{1}{\gamma}m_{0tt}^{(0)}, \qquad m_0^{(1)}(0,x) = 0.$$

The perturbation term $m_{0tt}^{(0)}$ comes from $m_0^{(0)}$ which in turn solves the initial value problem (4.46)

$$m_{0t}^{(0)} = \frac{d}{\gamma^2}m_{0xx}^{(0)}, \qquad m_0^{(0)}(0,x) = m_0(0,x).$$

Assuming that initial data are smooth, we find that $m_0^{(0)} \in C^2([0,T], C^\infty(\mathbb{R}))$, which implies $m_{0tt}^{(0)} \in C^0([0,T], C^\infty(\mathbb{R}))$. Then $m_0^{(1)} \in C^2([0,T], C^\infty(\mathbb{R}))$ which gives $m_{0tt}^{(1)} \in C^0([0,T], C^\infty(\mathbb{R}))$. Hence, there is a constant $C_3 > 0$ such that

$$\|m_{0tt}^{(1)}(t,.)\|_\infty \leq C_3.$$

This ends the proof. □

4.4. *Moment Approximation for the Kramers reaction equation*

For the linear Kramers equation we have seen that the moment approximations first lead to a telegraph equation and then to a diffusion equation. Here we study the question whether a similar result holds true for the nonlinear equation (2.15). For this equation the first three moments satisfy the equations

$$m_{0t} + m_{1x} = f(m_0) \tag{4.55}$$

$$m_{1t} + m_{2x} = -\gamma m_1 - g(m_0)m_1 \tag{4.56}$$

$$m_{2t} + m_{3x} = -2\gamma m_2 + 2dm_0 + \sigma^2 m(m_0)m_0 - g(m_0)m_2. \tag{4.57}$$

In (4.55) we have used $f(u) = m(u)u - g(u)u$, in (4.56) we have used the symmetry of H, and in (4.57) we denote the variance of H by

$$\sigma^2 = \int v^2 H(v)dv.$$

Repeating the procedure for the linear case, we find the analogue of (4.33) as

$$\begin{aligned} m_{0tt} + (\gamma - f'(m_0))m_{0t} = \; & m_{2xx} + \gamma f(m_0) \\ & + g'(m_0)m_{0x}m_1 + g(m_0)m_{1x}. \end{aligned}$$

Differentiating (4.57) twice with respect to x yields the analogue of (4.34) as

$$m_{2txx} + m_{3xxx} + 2\gamma m_{2xx} = dm_{0xx} + [\sigma^2 m(m_0)m_0 - g(m_0)m_2]_{xx}. \tag{4.58}$$

As before, we add both equations, divide by γ and introduce the scaling (2.13). Then we get

$$\begin{aligned} & \frac{\varepsilon}{\gamma}m_{0tt} + (1 - \frac{\varepsilon}{\gamma}f'(m_0))m_{0t} + \frac{\varepsilon^2}{2\gamma^2}(m_{2txx} + m_{3xxx}) \\ = \; & \frac{d}{\gamma^2}m_{0xx} + f(m_0) + \frac{\varepsilon}{\gamma}g'(m_0)m_{0x}m_1 \\ & + \frac{\varepsilon}{\gamma}g(m_0)m_{1x} + \frac{\varepsilon^2}{2\gamma^2}[\sigma^2 m(m_0)m_0 - g(m_0)m_2]_{xx}. \end{aligned} \tag{4.59}$$

Next, we drop all terms containing ε^2 and arrive at

$$\begin{aligned} \frac{\varepsilon}{\gamma}m_{0tt} + (1 - \frac{\varepsilon}{\gamma}f'(m_0))m_{0t} = \; & \frac{d}{\gamma^2}m_{0xx} + f(m_0) \\ & + \frac{\varepsilon}{\gamma}g'(m_0)m_{0x}m_1 + \frac{\varepsilon}{\gamma}g(m_0)m_{1x}. \end{aligned}$$

Here we experience the failure that is known from carrying Cattaneo systems into wave equations ([15]). Unless the mortality function g is a constant we cannot get a wave equation. We can proceed in two ways.

Case 1: g is a constant. Then we replace m_{1x} by $f(m_0) - m_{0t}$ and get an approximation to the reaction Kramers equation in the form of a wave equation

$$\frac{\varepsilon}{\gamma}\bar{u}_{tt} + \left(1 - \frac{\varepsilon}{\gamma}(f'(\bar{u}) - g)\right)\bar{u}_t = D\Delta\bar{u} + \left(1 + \frac{\varepsilon}{\gamma}g\right)f(\bar{u}), \tag{4.60}$$

where $D = d/\gamma^2$. Hadeler[14] derived a similar wave equation from a correlated random walk with birth-death term (2.16), however, the term g seems to enter the corresponding wave equations in different ways. If we let $\varepsilon \to 0$ in (4.60) then we get the reaction diffusion equation

$$\bar{u}_t = D\Delta\bar{u} + f(\bar{u}). \tag{4.61}$$

Case 2: g is not constant. Then there is no way to eliminate m_1 and to obtain a wave equation. But omitting also the first order terms in ε leads directly to the reaction diffusion equation (4.61).

5. Application: Chemotaxis

The moment approximation for the Kramers equation can be applied to derive the classical Patlak-Keller-Segel model for *chemotaxis* ([38,22]). Chemotaxis, or more generally, chemosensitive movement, describes the active orientation of organisms along chemical gradients. In many examples, e.g. the slime mold *Dictyostelium discoideum* ([46]) individuals choose a direction upward a gradient of a chemical signal $S(t,x)$. For *Dictyostelium* this behavior leads to the formation of *aggregates* and *fruiting bodies*. A similar mechanism can be observed in bacteria such as *Escherichia coli*, or *Salmonella typhimurium* ([6]). The aggregation mechanism of the slime molds can be seen as a prototype of many other organization mechanisms of cell populations, like the development of organs in an embryo, the triggered defense of an infection or the blood supply of a growing tumor and many more applications. Because of these wide spread applications it is worthwhile to study the basic chemotaxis model (the Keller-Segel equations) from many different points of view. Here we choose the Langevin approach.

For a stochastic process for chemosensitive movement, corresponding to the Langevin equation, we follow the ideas of Stevens and Schweitzer[48] assuming that individual cells choose their direction of movement in the direction of the gradient of the signal distribution. We assume that this adaptation requires some relaxation time τ and we assume that there is some uncertainty in this adaptation,

$$\begin{aligned} dx &= v\,dt \\ \tau dv &= \chi \nabla S dt - v\,dt + \sqrt{D}\xi(t)dt, \end{aligned} \tag{5.62}$$

where χ is a proportionality constant and $\xi(t)dt$ again denotes white noise. For the scaling procedure later we use the parameters τ and D, rather than γ and d as in previous sections. They are related as $\gamma = \tau^{-1}$ and $d = D\tau^{-2}$.

Again, we understand (5.62) as generalized characteristic equations. The corresponding Kramers equation for the mean field population density $u(t,x,v)$ reads

$$u_t + v\cdot\nabla_x u - \frac{1}{\tau}\mathrm{div}_v(vu) + \frac{\chi}{\tau}\nabla_x S\cdot\nabla_v u = \frac{D}{\tau^2}\Delta_v u \tag{5.63}$$

which we call the *Kramers equation for chemosensitive movement*. The signal $S(t,x)$ is produced by the species itself and decays. Since the signal molecules are much smaller in magnitude than the individual organisms, we assume simple diffusion equation for S,

$$\kappa S_t = D_S\Delta S + g(S,\bar{u}), \tag{5.64}$$

where $\bar{u}$ is again given by (2.14). The function $g(S,\bar{u})$ describes the production and decay of the signal. A typical example is $g(S,\bar{u}) = -\beta S + \alpha\bar{u}$, where $\alpha,\beta > 0$ are constants. The constant κ allows for different time scales for u and S. Equations (5.63) and (5.64) form a *Kramers system for chemosensitive movement*.

There is a direct analogy to electrostatic and to gravitational movement of (physical) particles. We consider $g(S,\bar{u}) = \alpha\bar{u}$ and assume that the signal diffuses so fast

that it achieves its quasi steady state immediately. Then S satisfies a *potential equation*

$$D_S \Delta S = -\alpha \bar{u}. \tag{5.65}$$

In the physical context equations (5.63) and (5.65) are known as the *Vlasov-Poisson-Fokker-Planck system* ([4,25,39]). All the results known for the VPFP-system directly carry over to the biological interpretation of chemosensitive movement in a quasi-stationary chemical potential. It is a challenge for further research to study the full Kramers chemotaxis system (5.63) and (5.64) with the methods developed in the physical context.

We now apply the moment approximation developed in Section 4 to derive the Patlak-Keller-Segel model for $m_0 = \bar{u}$ from (5.63) and (5.64). For simplicity we restrict ourselves to the one dimensional case. Corresponding to (4.27–4.30) we now get

$$\begin{aligned}
m_{0t} + m_{1x} &= 0 \\
m_{1t} + m_{2x} &= -\frac{1}{\tau} m_1 - \frac{\chi}{\tau} S_x m_0 \\
m_{2t} + m_{3x} &= -\frac{2}{\tau} m_2 + \frac{2\chi}{\tau} S_x m_1 + \frac{2D}{\tau^2} m_0 \\
m_{3t} + m_{4x} &= -\frac{3}{\tau} m_3 + \frac{3\chi}{\tau} S_x m_2 + \frac{6D}{\tau^2} m_1.
\end{aligned}$$

Following the same procedure as above we find the equation corresponding to (4.35) as

$$\tau m_{0tt} + m_{0t} - D m_{0xx} = -\frac{\tau^2}{2}(m_{2txx} + m_{3xxx}) - (\chi S_x m_0)_x + \tau(\chi S_x m_1)_{xx} \tag{5.66}$$

Note that so far we are still using the original parameters τ, D as in (5.62). Now, for fast velocity relaxation, i.e. for $\tau << 1$, we get as a first order approximation:

$$m_{0t} = D m_{0xx} - (\chi S_x m_0)_x, \tag{5.67}$$

which, together with (5.64), forms the classical Patlak[38]-Keller-Segel[22] model for chemosensitive movement. Hence, if we assume that the signal diffuses fast, then we find the same parabolic limit as Poupaud[39]. There, the approximation property was proved rigorously using weak L^1 compactness of sequences of solutions.

It should be noted that from (5.66) one cannot derive a telegraph equation for m_0 since the next order approximation contains the term $\chi S_{xxx} m_1$ and the equation for m_0 does not decouple.

We can generalize the equations by allowing the *chemotactic sensitivity* χ to depend on the signal S. Moreover, density control effects, as studied by Hillen and Painter[19], can be included. Then the Langevin equation becomes

$$\begin{aligned}
dx &= v\, dt, \\
\tau dv &= \chi(S)\beta(m_0)\nabla S\, dt - v\, dt + \sqrt{D}\xi(t)\, dt,
\end{aligned} \tag{5.68}$$

where $\beta(m_0)$ is a decreasing function which describes reduced chemotaxis at high population densities. The corresponding Kramers equation reads

$$u_t + v \cdot \nabla_x u - \frac{1}{\tau}\nabla_v \cdot (vu) + \frac{\chi(S)}{\tau}\beta(m_0)\nabla_x S \cdot \nabla_v u = \frac{D}{\tau^2}\Delta_v u. \tag{5.69}$$

In the parabolic limit $\tau \to 0$ in one dimension we finally get

$$m_{0t} = Dm_{0xx} - (\chi(S)\beta(m_0)S_x m_0)_x. \tag{5.70}$$

This equation together with (5.64) has been analyzed in detail by Hillen and Painter[19] and emerging patterns have been studied.

Appendix A. The Green's function

For convenience of the reader, we cite the Greens function for the linear Kramers equation from Bouchut[4].

$$G(t,x,v,y,\nu) = \left[\frac{1}{4\pi d\sqrt{\phi(t)}}\right]^N \times \tag{A.1}$$

$$\exp\left\{-\frac{1}{4d\phi(t)}\int_0^t \left|\frac{1-e^{-\gamma s}}{\gamma}v + \frac{e^{-\gamma s}-e^{-\gamma t}}{\gamma}\nu - e^{-\gamma s}(x-y)\right|^2\right\}, \tag{A.2}$$

where

$$\phi(t) = \frac{1}{\gamma^2}\left[\frac{1-e^{-2\gamma t}}{\gamma}t - \left(\frac{1-e^{-\gamma t}}{\gamma}\right)^2\right], \tag{A.3}$$

Note that, even though equation (2.10) contains only the first derivative in the space variable x, solutions become smooth in space. The first exponential term of the Green's function (A.1) looks similar to the Green's function of the heat equation in $2n$ dimensions. The time dependent factor in (A.1) however, shows that the smoothing effect is much slower than in the heat equation. The function ϕ approaches 0 faster than any polynomial as $t \to 0$ and hence $1/\phi$ is larger than $t^{-\gamma}$ for all $\gamma > 0$.

Appendix B. The counterexample

We show that a smooth, bounded integrable function on $\mathbb{R}^2$ does not necessarily yield a bounded function when integrated over one of the two variables, i.e., in terms above

$$u \in \mathcal{C}_b^\infty(\mathbb{R}^2) \cap L^1(\mathbb{R}^2) \qquad \not\Rightarrow \qquad \bar{u} \in \mathcal{C}_b(\mathbb{R}). \tag{B.1}$$

In the x,v-plane, let $v(x)$ be an integrable function with a pole at zero, for example

$$v(x) = \frac{1}{\sqrt{x}}, \qquad x \in [-1,1].$$

Let $\chi(x,v)$ be the characteristic function of the set under the graph of v. Then χ is bounded and integrable over $\mathbb{R}^2$, since v is integrable over $\mathbb{R}$. However, the integral with respect to v, i.e., $\bar{\chi}$ is unbounded as a function of x, in fact $\bar{\chi} \to \infty$ as $x \to 0$. Now, choose $u(x,v)$ as a C^∞-function such that $u = \chi$ on the support of χ and $u = 0$ above the graph of $2v(x)$. Then the same considerations apply to u.

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