Max-Planck-Institut für Mathematik in den Naturwissenschaften Leipzig

A Hydrodynamic Limit for Chemotaxis in a Given Heterogeneous Environment

by

Stefan Grosskinsky, Daniel Marahrens, and Angela Stevens

Preprint no.: 46 2015

A HYDRODYNAMIC LIMIT FOR CHEMOTAXIS IN A GIVEN HETEROGENEOUS ENVIRONMENT

IN HONOR OF WILLI JÄGER, ON THE OCCASION OF HIS 75TH BIRTHDAY.

STEFAN GROSSKINSKY, DANIEL MARAHRENS, AND ANGELA STEVENS

Abstract. In this paper the first equation within a class of well known chemotaxis systems is derived as a hydrodynamic limit from a stochastic interacting many particle system on the lattice. The cells are assumed to interact with attractive chemical molecules on a finite number of lattice sites, but they only directly interact among themselves on the same lattice site. The chemical environment is assumed to be stationary with a slowly varying mean, which results in a non-trivial macroscopic chemotaxis equation for the cells. Methodologically the limiting procedure and its proofs are based on results by Koukkus [18] and Kipnis/Landim [17]. Numerical simulations extend and illustrate the theoretical findings.

Contents

1. Introduction and result 1
2. The general result 5
3. Proof of Theorem 2.1 8
3.1. One block estimate 9
3.2. Two blocks estimate 14
4. Outlook and Examples: numerical simulations 14
5. Concluding remarks 19
References 19

1. Introduction and result

In this paper we derive chemotaxis-like equations as a hydrodynamic limit of a stochastic lattice gas. Chemotaxis describes the directed motion of mainly biological species towards higher or lower concentrations of chemical signals. Here we consider positive chemotaxis of *cells*, i.e. motion towards higher concentrations of a chemical signal, therefore the chemical signal is denoted as *chemo-attractant*.

Keller and Segel proposed in [16] a phenomenological chemotaxis model on the macroscopic level for the aggregation and self-organization of the cellular slime mold amoeba *Dictyostelium discoideum* (Dd). This can be written as

$$\begin{aligned} \partial_t \rho &= \nabla \cdot \big(k(\rho,\vartheta)\nabla\rho - \chi(\rho,\vartheta)\nabla\vartheta \big) \\ &= \nabla \cdot \big(k(\rho,\vartheta)\nabla\rho - \tilde{\chi}(\rho,\vartheta)\rho\nabla\vartheta \big), \end{aligned} \tag{1.1}$$

$$\partial_t \vartheta = \Delta\vartheta + r(\rho,\vartheta), \tag{1.2}$$

Date: August 14, 2015.

Key words and phrases. chemotaxis, interacting stochastic many particle system, hydrodynamic limit, stochastic lattice gas, block estimates.

where ρ is the (volume) density of amoebae, ϑ is the density of the attractive chemical molecules, k and $\tilde{\chi} = \chi/\rho$ are functional parameters describing the strength of random motion of the cells and their chemotactic sensitivity, respectively, and r comprises the reaction mechanisms. In [16], this cross-diffusion system was motivated by the macroscopic phenomenon being experimentally observed, namely movement of the amoebae in direction of higher concentrations of a chemical signal, i.e. their movement up chemical gradients. Such general types of chemotaxis systems are relevant also in the context of other biological species. One expects this system to be an accurate description for chemotaxis phenomena occuring in systems of many cells and signal molecules. There is a large literature on the formal derivation of macroscopic equations from microscopic particle systems in such settings. Rigorously this has been achieved in much fewer cases, e.g. by hydrodynamic or so-called moderate limits. The lack of an ellipticity condition for the limiting PDE-system, respectively the strong clustering of the cells is a major technical problem in this case.
The first rigorous derivation of a general class of chemotaxis systems from a stochastic interacting many particle system was given in [37], where the cells and the chemical molecules interact moderately with each other in the sense described in [28]. The motion of the cells and the molecules are governed by interacting stochastic differential equations, and production and decay of the chemical molecules are modeled via Poisson point processes. In [37] explicit error estimates could be given, which show that the total number of particles does not have to be too large for the limiting PDE-system to be a good approximation for the particle model. The moderate rescaling requires that in the limiting procedure, when the total particle number (cells and chemical molecules) tends to infinity, the main range of interaction of the particles tends to zero. The number of particles sensed in this main range of interaction tends to infinity too, while this number is still only a vanishing fraction of the total particle number. This is sufficient for correlations to become small enough in the limit. The main technical complication in the proof is the cross-diffusion structure of the chemotaxis system. The ellipticiy condition, heavily used in [28], is no longer valid in this case. To overcome this problem, two shadow systems were introdcued, in order to freeze the critical non-linearity and a priori estimates were derived. This technique applies also to more general systems of PDEs.

In principle it would be desirable to also derive chemotaxis like systems as hydrodynamic limits in the sense of [17]. In this paper, we rigorously derive equation (1.1) from a microscopic stochastic many particle system on a lattice, so only one equation, not the full system. The cells are assumed to interact via a finite number of lattice sites with the chemical molecules. This corresponds to the assumption that the cells detect chemical molecules in a fixed small region around themselves. They do not change the chemical environment in this case. The interaction of the cells among themselves takes place only at the same lattice site and not among cells located on neighboring sites. This interaction is described by a function g which among others fulfills conditions comparable to an ellipticity condition for the related limiting PDE. These will be specified later. So we consider the case, where a too strong clustering/aggregation of cells - a typical and important effect of chemotaxis and self-organization in Dd - is avoided.
Such an interaction with a finite number of lattice sites introduces specific mathematical difficulties. One has to deduce a weak equation for the limit density from empirical measures (see Section 2) which converge weakly, cf. the discussion in [27, Introduction]. To be more precise, we are modeling the cells/particles by an interacting particle system as introduced in [34] and derive limit equations via a

hydrodynamic limit, analogous to the procedure in [17]. Interacting particle systems in this sense are continuous-time Markov jump processes which also involve discrete particles moving on a lattice.

So far we were not able to derive the full system (1.1), (1.2) as hydrodynamic limit. It seems to be a major challenge to identify suitable particle models with invariant product measures. This would be one option in order to prove a hydrodynamic limit for systems of equations such as (1.1) and (1.2). Hydrodynamic limits without product measures for single-species monotone particle systems where established in [4, 5]. Stochastically monotone systems preserve a partial order on state space over time, which allows the use of coupling techniques following first results in [32]. Monotonicity usually leads to homogeneous mass distributions, and indeed it has been shown recently that particle systems with invariant product measures that exhibit a particular form of clustering are necessarily non-monotone [31].
A generic example which exhibits invariant product measures is given by the *zero-range process* (ZRP), where the jump rate of particles at any given site depends only on the occupation number at this site. It is known, see [13], that multi-species ZRPs have invariant product measures if the jump rates of particles satisfy certain symmetry relations, i.e. the *Onsager relations*. However, in our case this would not allow for purely diffusive motion of the chemo-attractant in (1.2). Instead, the attractive chemical molecules would need to undergo a kind of chemotactic motion too, in order for the Onsager relations to hold. From the modeling point of view this is definitely not the case here.
Another method to derive a system of a PDE coupled to an ODE via a hydrodynamic limit without the use of invariant product measures was introduced in [10] for a specific two-species cellular system on the lattice. The authors new method employs energy estimates for the mesoscopic empirical averages of the particles occupation number by which they obtain H_1^2 a-priori bounds and thus are able to derive a substitute for the two block estimates. For the most crucial terms in their setting homogenization techniques are used, which play the role of the one block estimates. For a discussion of the respective particle model itself see also [23]. It would be interesting to see whether in our case one can find scaling regimes where the existence of gradients (and not only densities as in [10]) can rigorously be proved for the full limiting PDE system.
One typical approximation of system (1.1), (1.2) is to assume a quasisteady chemo-attractant density, i.e. to set the left hand side of (1.2) equal to zero. Formally, this is justified by assuming that the diffusivity of the chemo-attractant is much larger than the random motion of the cells, see e.g. [14]. There are also recent results on random walks in dynamic random environments driven by exclusion processes [3], which are based on separation of time-scales argument. Otherwise there are only very few rigorous results on hydrodynamic limits for two-species systems, see e.g. [11, 7], since such processes are in general also non-monotone.
It is obvious from a modeling point of view, how a full chemotaxis model for the behavior of particles on a lattice could look like, compare e.g. [29]. One ansatz relates to attractive reinforced random walks for many particles with diffusion and decay of the attractive weight. Deriving a hydrodynamic limit for such, or similar models would be the final goal. We expect the Keller-Segel model to also hold in this context, but a proof is still missing.

As a first step towards understanding chemotaxis as a hydrodynamic limit, we therefore consider chemotaxis of cells in a stationary, but random, environment. In order to obtain a non-trivial macroscopic chemotactic motion, we impose a slowly

varying mean on the random chemical environment. There have been several studies of hydrodynamic limits of particles in random media: The hydrodynamic limit for a ZRP a with stationary, ergodic environment on the sites has been obtained in [18], and corresponding large deviations have been considered in [19]. The case of a stationary, ergodic environment on the edges was treated in [12]. The hydrodynamic limit for the ZRP with slowly varying but not random environment is given in [9]. For a result unifying all these situations of "locally convergent" media in the special case of the simple exclusion processes compare [15]. Our main result in the present paper concerns the modeling of chemotaxis via a ZRP in a random environment with slowly varying mean and it is summarized in Theorem 2.1, Section 2. A special case of this result is given in Corollary 1.1 below.

At each site $x \in \mathbb{T}_N^d$ on the periodic lattice $\mathbb{T}_N^d = \{1, \dots, N\}^d$ one distributes $\zeta(x) \in \mathbb{N}$ molecules of the chemo-attractor such that $\zeta(x)$ is a Poisson random variable with parameter $\vartheta(\frac{x}{N})$ and these are kept fixed for all time. Let $f : \mathbb{N} \to [a, b]$ for some $a, b > 0$ and set

$$\widetilde{f}\big(\vartheta(\tfrac{x}{N})\big) := \mathbb{E}\bigg[\frac{1}{f(\zeta(x))}\bigg]^{-1}.$$

Now we specify the type of chemotactic motion we consider here for the cells. We start with an initial distribution of $\eta(x)$ cells at $x \in \mathbb{T}_N^d$. All cells perform independent random walks with a site-dependent jump-rate which is $N^2 f(\zeta(x))$. Thus each cell remains at its current site $x \in \mathbb{T}_N^d$ for an exponentially distributed random waiting time with parameter $N^2 f(\zeta(x))$ and then jumps to a random neighboring site on the lattice. In this way, particles are more likely to stay at a site x if $f(\zeta(x))$ is large and therefore f is one way of formulating the microscopic behavior which results in a chemotactic drift towards higher concentrations of the chemical signal. To take the limit as $N \to \infty$, we embed the discrete torus $\mathbb{T}_N^d$ into the continuous torus $\mathbb{T}^d = \mathbb{R}^d/\mathbb{Z}^d$ via $x \mapsto \frac{x}{N}$. Thus the number of cells in an interval $I \subseteq \mathbb{T}^d$ is given by

$$\#\{\text{cells in } I\} = \sum_{x \in NI \cap \mathbb{T}_N^d} \eta(x),$$

where NI is I rescaled by N. The cell density in I is then obtained as $\sum_{x \in NI} \eta(x)/(|I|N^d)$.

Corollary 1.1. *Let $\eta_0(x)$ be distributed with a profile $\rho_0(u)$, i.e. for each interval $I \subseteq \mathbb{T}^d$, the density converges in probability:*

$$\lim_{N\to\infty} \frac{\#\{\textit{cells in } I\}}{|I|N^d} = \int_I \rho_0(u)\, du.$$

Then for all later times $t > 0$ and all intervals I, almost surely with respect to the distribution of chemical molecules ζ, it holds that

$$\lim_{N\to\infty} \frac{\#\{\textit{cells in } I\}}{|I|N^d} = \int_I \rho_t(u)\, du$$

in probability, where ρ_t solves

$$\partial_t \rho_t(u) = \Delta\big[\widetilde{f}(\vartheta(u))\rho_t(u)\big] = \nabla \cdot \Big[\widetilde{f}(\vartheta(u))\nabla\rho_t(u) + \widetilde{f}'(\vartheta(u))\rho_t(u)\nabla\vartheta(u)\Big], \tag{1.3}$$

which is of the form (1.1).

For the derivation of this result from Theorem 2.1 we refer to the discussion in Section 4. Let us first make several remarks concerning this result.

Remark 1.2. (1) The assumption of independent random walks treated in Corollary 1.1 yields a linear limit equation and is much weaker than necessary, see Theorem 2.1. It is presented here in order to give the reader an intuition for the connection between the macroscopic bias $\widetilde{f}(\vartheta(u))$ induced by the chemical signal and the related microscopic bias $f(\zeta(x))$.
(2) Note that instead of the Poisson distribution, we can let the environment be given by any distribution in $\mathbb{N}$ depending continuously (in distributional topology) on its parameter.
(3) In case of a stationary chemical environment, the solution is always global and no blow-up can occur, thus excluding a prominent feature of the full chemotaxis system, where the possibility of finite time blow-up in two space dimensions for a suitable parameter range is of important biological relevance for self-organization phenomena in the cellular slime mold amoebae Dd, [8], [14].
(4) Finally, let us mention that some microscopic descriptions for chemotactic cell motion are based on the feature that the cells can detect concentration gradients along their cell surface. Our result supports the idea that chemotactic effects can also occur if the cells only sense the absolute values of the concentration of the chemo-attractant without needing to sense its (local) gradients. An alternative approach would be to let each particle perform asymmetric random walks (and its nonlinear versions involving a zero range interaction $g(\cdot)$, see below) with jump rates across edges of the lattice proportional to $p(x, y)$. Here x, y are neighboring sites, and $p(x, y)$ is a random variable, which in our case is determined by the attractive chemical environment $\zeta(x)$., see also [29] and the microscopic approaches in [2]. A typical example for an asymmetric random walk would be $p(x, y) = f\big(\zeta(y)-\zeta(x)\big)$, representing a microscopic gradient for an appropriate function f. This approach would lead us to consider problems of the type investigated in [12].
(5) For positive chemotaxis effects, i.e. clustering/aggregation of the cells the sign of the second term on the right hand side of (1.1), (1.3) is crucial. Further, already in [33] it was pointed out that the diffusivity $\tilde{f}$, k and the chemotactic sensitivity $-\tilde{f}'$, $\tilde{\chi}$ of the cells are not completely independent functionals. A suggestion in [33] is that the diffusivity $\tilde{f}$ in (1.3) relates to the chemotactic sensitivity $-\tilde{f}'$, which is supposed to have a positive sign in case of positive chemotaxis, as follows:
$\tilde{f}' = -\chi_0 \tilde{f}\tilde{\Phi}'(\vartheta)$ for a suitable function $\tilde{\Phi}$, e.g. $\tilde{\Phi}(\vartheta) = \vartheta$ and $\chi_0 > 0$.
This results in $\tilde{f} = C\exp(-\chi_0\tilde{\Phi}(\vartheta))$, e.g. $\tilde{f} = C\exp(-\chi_0\vartheta)$.
So for large chemical concentrations $\tilde{f}$ becomes small.

The outline of the paper is as follows. In Section 2, we present a general result on hydrodynamic limits in a random environment with slowly varying mean. Its proof is given in Section 3 where we highlight the differences to the proofs found in [18, 17]. Then in Section 4, we show how to deduce Corollary 1.1 from the general result and present numerical simulations of the particle system.

2. The general result

In this paper, we apply the *entropy method* as given in [25] to obtain a generalization of equation (1.3), namely for the chemotactically moving cells, in a stationary, yet random, environment, which represents the density of a heterogeneously distributed attractive chemical signal. To avoid technicalities concerning boundary conditions, we shall work in a periodic domain. Thus we consider a Markov (Feller) process, describing the motion of the cells, with state space $\mathbb{N}^{\mathbb{T}_N^d}$, where $\mathbb{T}_N^d = \{1, \dots, N\}^d$ denotes the perodic lattice with $N + 1 \equiv 1$. Elements of the state space will be called *particle configurations* and denoted by the Greek letters η, ζ, ξ. Thus $\eta(x) \in \mathbb{N}$ denotes the number of particles of the configuration η at site x. The

elements of $\mathbb{T}_N^d$ will be denoted by the letters x, y, z and are called *microscopic* variables. Two microscopic sites $x, y \in \mathbb{T}_N^d$ are called *neighbors*, in short $x \sim y$, if $|x - y| = 1$. The discrete torus is embedded in the continuous torus $\mathbb{T}^d = \mathbb{R}^d/\mathbb{Z}^d$ via $x \mapsto x/N$. Elements of the continuous torus will be denoted by u and are called *macroscopic* variables. For simplicity, we consider only symmetric nearest-neighbor jumps; then the Markov process is given by the generator

$$\mathcal{L}_N f(\eta) = \sum_{x \sim y} g(\eta(x)) p_x^N \big(f(\eta^{x,y}) - f(\eta) \big) \tag{2.1}$$

for all $f \in C_b(\mathbb{N}^{\mathbb{T}_N^d})$, where the sum is taken over all (ordered) pairs of neighbors x and y. Here $\eta^{x,y}$ denotes the configuration obtained from η after one particle has jumped from site x to y and $p_x^N > 0$ describes the chemical environment. Throughout this article, we assume that

$$p_x^N = v(\tfrac{x}{N}) + q_x,$$

where $v \in C^1(\mathbb{T}^d, \mathbb{R})$ describes the slowly varying mean of the environment and $(q_x)_{x \in \mathbb{Z}^d} \subset \mathbb{R}^{\mathbb{Z}^d}$ is a uniformly bounded *stationary* and *ergodic* sequence of random variables with zero mean. In order to avoid degeneracies, we assume strictly positive jump rates, i.e. without loss of generality we assume $p_x^N, q_x \in [a, b]$ with $0 < a < b$. We denote the law of q by m, so that m is a probability measure on $\mathbb{R}^{\mathbb{Z}^d}$.
It is also possible to think of p_x^N as a random variable. Note, however, that for technical reasons in what follows we fix the ergodic part q of the environment independently of N. The dependence of the jump rates on the number of cells is given by the function $g : \mathbb{N} \to [0, \infty)$. In addition to the standard condition

$$g(n) = 0 \quad \Leftrightarrow n = 0$$

to avoid degeneracies, we make the following regularity assumptions on g throughout the paper.

Assumption 1. *(i) Suppose that g is uniformly Lipschitz-continuous, i.e. there exists a constant g^* such that*

$$\sup_{n \in \mathbb{N}} |g(n+1) - g(n)| \le g^*.$$

(ii) Further assume that g grows at least linearly, i.e. there exists $g_0 > 0$ such that

$$\inf_{n \in \mathbb{N}} \frac{g(n)}{n} \ge g_0.$$

These assumptions are not optimal but they are standard in the literature, see e.g. [17, Theorem 5.1.1], on which our proof is based. Under these assumptions, the process with generator (2.1) has invariant product measures $\nu^{N,p}$ that satisfy the *detailed balance condition*

$$\begin{aligned} p_x^N g(n) \nu^{N,p}[\eta(x) = n] \nu^{N,p}[\eta(y) = k] \\ = p_y^N g(k+1) \nu^{N,p}[\eta(x) = n-1] \nu^{N,p}[\eta(y) = k+1] \end{aligned}$$

for all neighbors $x, y \in \mathbb{T}_N^d$ and $k, n \in \mathbb{N}$.
Indeed for any $\varphi \ge 0$, there exists such a measure $\nu_\varphi^{N,p}$ given by

$$\nu_\varphi^{N,p}(\eta) = \prod_{x \in \mathbb{T}_N^d} \frac{\big[(p_x^N)^{-1}\varphi\big]^{\eta(x)}}{Z((p_x^N)^{-1}\varphi) g(\eta(x))!} \quad , \tag{2.2}$$

where $g(n)! = g(1)g(2)\dots g(n)$, $g(0)! = 1$ and

$$Z(\varphi) = \sum_{n=0}^{\infty} \frac{\varphi^n}{g(n)!} \tag{2.3}$$

is the partition function. The detailed balance condition ensures that the generator $\mathcal{L}_N$ in (2.1) is $L^2(\nu_\varphi^{N,p})$-selfadjoint and in particular the measure $\nu_\varphi^{N,p}$ is an invariant product measure. Let ν_φ^1 denote the one-site marginal without environment, i.e.

$$\nu_\varphi^1(n) = \frac{\varphi^n}{Z(\varphi)g(n)!} \quad .$$

The associated density then is

$$M(\varphi) = \mathbb{E}_{\nu_\varphi^1}[\eta(0)]. \tag{2.4}$$

Assumption 1 implies that Z is finite on $[0,\infty)$. Hence the product measure $\nu_\varphi^{N,p}$ exists for all $\varphi \in [0,\infty)$ and environments $(p_x^N)_{x\in\mathbb{T}_N^d}$. The parameter $\varphi \geq 0$ is called fugacity, and it controls the expected particle density which is given by

$$R(u,\varphi) := \mathbb{E}_m\Big[M\Big(\tfrac{\varphi}{v(u)+q_0}\Big)\Big] \tag{2.5}$$

for all $u \in \mathbb{T}^d$. The family of distributions (2.2) is also called the grand-canonical ensemble. One can show that for each $u \in \mathbb{T}^d$, the function $R(u,\cdot)$ is strictly increasing, cf. [17], and we then define $\Phi(u,\cdot)$ to be its inverse function. Note that

$$\mathbb{E}_m\Big[\mathbb{E}_{\nu^{N,p}_{\Phi(\frac{x}{N},\rho)}}\big[\eta(0)\big]\Big] = \rho \quad \text{and} \quad \mathbb{E}_m\Big[\mathbb{E}_{\nu_\varphi^{N,p}}\big[g(\eta(x))p_x^N\big]\Big] = \Phi(\tfrac{x}{N},\varphi).$$

We shall see that the limit equation is given by

$$\partial_t \rho_t(u) = \Delta\Phi(u,\rho_t(u)). \tag{2.6}$$

Finally we need a suitable notion of distance between probability measures, which in our case is given by the relative entropy. Consider measures $\nu,\mu \in P(\mathbb{N}^{\mathbb{T}_N^d})$ such that μ is absolutely continuous with respect to ν (i.e. $\mu \ll \nu$). Then the relative entropy is given by

$$H(\mu|\nu) = \int_{\mathbb{N}^{\mathbb{T}_N^d}} \log\frac{d\mu}{d\nu}(\eta)\, d\mu(\eta),$$

where $\frac{d\mu}{d\nu}$ denotes the Radon-Nikodym derivative of μ with respect to ν. The main result of this section is the following.

Theorem 2.1. *Let $\mu_0^N \in P(\mathbb{N}^{\mathbb{T}_N^d})$ be the initial datum of the particle process with an associated initial profile $\rho_0 \in L^\infty(\mathbb{T}^d)$, i.e. it holds*

$$\lim_{N\to\infty} \mu_0^N\Big(\Big|\frac{1}{N^d}\sum_{x\in\mathbb{T}_N^d} G(\tfrac{x}{N})\eta(x) - \int_{\mathbb{T}^d} G(u)\rho_0(u)\,du\Big| \geq \delta\Big) = 0 \qquad m\text{-almost surely}$$

for all $G \in C(\mathbb{T}^d)$ and $\delta > 0$. Furthermore we suppose the bounds

$$H(\mu_0^N|\nu_\varphi^{N,p}) \leq CN^d \quad \text{and} \quad \mathbb{E}_{\mu_0^N}\Big[\sum_{x\in\mathbb{T}_N^d}\eta(x)^2\Big] \leq CN^d$$

to hold for some (and hence all) $\varphi > 0$. Denote by $\mu_t^N \in P(\mathbb{N}^{\mathbb{T}_N^d})$ the measure obtained from the evolution of the ZRP with rate function g and by $\rho_t \in L^\infty(\mathbb{T}^d)$ the density obtained from equation (2.6). Then under Assumption 1, it holds that

$$\lim_{N\to\infty} \mu_t^N\Big(\Big|\frac{1}{N^d}\sum_{x\in\mathbb{T}_N^d} G(\tfrac{x}{N})\eta(x) - \int_{\mathbb{T}^d} G(u)\rho_t(u)\,du\Big| \geq \delta\Big) = 0 \qquad m\text{-almost surely}$$

for all $t > 0$, $G \in C(\mathbb{T}^d)$ and $\delta > 0$.

Remark 2.2. In order to fully connect Corollary 1.1 with Theorem 2.1, we note that weak convergence of the empirical measures implies convergence of the densities over intervals by the Portmanteau theorem [6, Theorem 2.1]. This follows from the absolute continuity (with respect to the Lebesgue measure) of the limit measure $\rho_t(u)\,du$.

To prove this result, we adapt the method in [18] to a random environment with slowly varying mean. The paper [18] is based on the entropy method given in [25] and proves a hydrodynamic limit for a zero range process in a stationary (ergodic) random environment. The case of a zero range process in a slowly varying deterministic environment was treated in [9]. Thus, from a purely technical point of view, our result is a combination of the previous two. Indeed, our method is close to the methods presented in [18]. Therefore we mainly highlight the differences here. The basic idea of the proof lies in the fact that the slowly varying mean is locally almost constant and hence in small boxes we are essentially in the situation of [18].

3. Proof of Theorem 2.1

The first step of the proof is to obtain a priori bounds and tightness of the particle process. Indeed we can understand the convergence result of Theorem 2.1 in terms of the empirical measure

$$\alpha_\eta^N(du) = \frac{1}{N^d} \sum_{x\in\mathbb{T}_N^d} \eta(x)\delta_{\frac{x}{N}}(du) \in \mathcal{M}_+,$$

where δ_u denotes a Dirac delta, $u \in \mathbb{T}^d$, and $\mathcal{M}_+$ is the space of all positive Radon measures on $\mathbb{T}^d$. For all $t \geq 0$, the configuration η_t is a random variable distributed according to μ_t^N. Note that it suffices to prove Theorem 2.1 for all $0 \leq t \leq T$ with a fixed, but arbitrary, $T > 0$. Since for any environment p the ZRP is a jump process on the state space, $(\eta_t)_{t\in[0,T]}$ is a random variable on the path space $D([0,T];\mathbb{N}^{\mathbb{T}^d})$. Here $D([0,T];\mathbb{N}^{\mathbb{T}^d})$ denotes the space of functions $[0,T] \to \mathbb{N}^{\mathbb{T}^d}$ that are right-continuous in time with left limits. We denote the distribution of $(\eta_t)_{t\in[0,T]}$ by μ^N. In the same vein, $(\alpha_{\eta_t}^N)_{t\in[0,T]}$ is a random variable on the path space $D([0,T];\mathcal{M}_+)$; let $Q^{N,p}$ denote its distribution. The entropy dissipation of μ_t^N can be defined in terms of the Dirichlet form

$$\mathcal{D}(\mu_t^N|\nu_\varphi^{N,p}) := \int_{\mathbb{N}^{\mathbb{T}_N^d}} \sqrt{\frac{d\mu_t^N}{d\nu_\varphi^{N,p}}}\mathcal{L}_N\sqrt{\frac{d\mu_t^N}{d\nu_\varphi^{N,p}}}\,d\nu_\varphi^{N,p}.$$

Throughout this paper we suppose that the assumptions of Theorem 2.1 are satisfied.

Lemma 3.1. *It holds that*

$$H(\mu_t^N|\nu_\varphi^{N,p}) \leq CN^d \text{ for all } t\in[0,T] \quad \text{and} \quad \frac{1}{T}\int_0^T \mathcal{D}(\mu_t^N|\nu_\varphi^{N,p})\,dt \leq CN^d.$$

Lemma 3.2. *For any environment p, the sequence of probability measures $(Q^{N,p})_{N\in\mathbb{N}}$ is tight.*

Lemma 3.3. *For any environment p, all limit points $Q^{*,p}$ of $(Q^{N,p})_{N\in\mathbb{N}}$ are supported on $\{\pi \in D([0,T];\mathcal{M}_+(\mathbb{T}^d)) : \pi_t(du) \ll du\}$, i.e. at each time t, the limit measures are absolutely-continuous with respect to the Lebesgue measure.*

Lemma 3.4. *For any environment p, if $\pi_t(du) = \rho_t(u)\,du$ is distributed according to $Q^{*,p}$, then $\rho_t(u)$ is the unique solution of (2.6) in $L^2((0,T)\times\mathbb{T}^d)$.*

The proofs of Lemma 3.1 – 3.4 are similar to the proofs of the corresponding results for the usual ZRP, see Lemma 2.1 – 2.4 in [18] and Lemma V.1.5 and V.1.6 in [17]. Once these results have been obtained, Theorem 2.1 is a straight-forward consequence. The main difficulty consists in the proof of the so-called replacement lemma, which is the key to Lemma 3.4. In order to state the replacement lemma, we need some additional notation to describe averages over mesoscopic blocks. Set

$$\eta^l(x) = \frac{1}{(2l+1)^d} \sum_{|x-y|\le l} \eta(y)$$

and

$$V^p_{x,l}(\eta) := \left| \frac{1}{(2l+1)^d} \sum_{|x-y|\le l} p^N_y\, g(\eta(y)) - \Phi(\tfrac{x}{N}, \eta^l(x)) \right|.$$

Lemma 3.5 (Replacement Lemma)**.** *For every $\delta > 0$, m-almost surely it holds that*

$$\limsup_{\epsilon\to 0} \limsup_{N\to\infty} \mu^N \left(\int_0^T \frac{1}{N^d} \sum_{x\in\mathbb{T}^d_N} V^p_{x,\epsilon N}(\eta_t)\, dt \ge \delta \right) = 0,$$

where τ_x denotes the translation by $x \in \mathbb{T}^d_N$.

In the remainder of this section we will mainly prove Lemma 3.5, where we sketch the modifications necessary to adapt the proof in [18] in order to take into account the slowly varying average of the environment $v(\frac{x}{N})$. First we prove the replacement over small boxes of size $l \in \mathbb{N}$.

3.1. **One block estimate.**

Lemma 3.6 (One Block Estimate)**.** *It holds that*

$$\limsup_{l\to\infty} \limsup_{N\to\infty} \mathbb{E}_{\mu^N} \left[\int_0^T \frac{1}{N^d} \sum_{x\in\mathbb{T}^d_N} V^p_{x,l}(\eta_t)\, dt \right] = 0$$

m-almost surely.

Setting

$$f^N_t(\eta) = \frac{d\mu^N_t}{d\nu^{N,p}_\varphi}(\eta), \qquad F^N(\eta) = \int_0^T f^N_t(\eta)\, dt,$$

we see that

$$\mathbb{E}_{\mu^N} \left[\int_0^T \frac{1}{N^d} \sum_{x\in\mathbb{T}^d_N} V^p_{x,l}(\eta_t)\, dt \right] = \frac{1}{N^d} \sum_{x\in\mathbb{T}^d_N} \int_{\mathbb{N}^{\mathbb{T}^d_N}} V^p_{x,l}(\eta) F^N(\eta)\, d\nu^{N,p}_\varphi(\eta)\ .$$

Lemma 3.1, together with convexity of the entropy and Dirichlet form, yields the bounds

$$\begin{aligned} H^{N,p}(F^N) &:= H(F^N\, d\nu^{N,p}_\varphi |\, d\nu^{N,p}_\varphi) \le CN^d, \\ \mathcal{D}^{N,p}(F^N) &:= \mathcal{D}(F^N\, d\nu^{N,p}_\varphi |\, d\nu^{N,p}_\varphi) \le CN^{d-2}. \end{aligned} \tag{3.1}$$

For future reference, we also note the following expression of the Dirichlet form via the density F^N. It holds that

$$\mathcal{D}^{N,p}(F^N) = \sum_{x\sim y} \int_{\mathbb{N}^{\mathbb{T}^d_N}} \frac{1}{2} p^N_x\, g(\eta(x)) \big[\sqrt{F^N(\eta^{x,y})} - \sqrt{F^N(\eta)} \big]^2\, d\nu^{N,p}_\varphi\ . \tag{3.2}$$

The next lemma allows us to restrict ourselves to bounded particle configurations. Its proof is analogous to the proof of [17, Lemma V.4.2] with the entropy inequality as additional ingredient.

Lemma 3.7. *Under the conditions of Theorem 2.1, we have*

$$\limsup_{A\to\infty}\limsup_{l\to\infty}\limsup_{N\to\infty}\sup_{p,f}\int_{\mathbb{N}^{\mathbb{T}_N^d}}\frac{1}{N^d}\sum_{x\in\mathbb{T}_N^d}V_{x,l}^p(\eta)\chi_{\{\eta^l(x)>A\}}(\eta)f(\eta)\,d\nu_\varphi^{N,p}(\eta)=0.$$

where the supremum is taken over all densities f such that $H^{N,p}(F^N)\le CN^d$, $\mathcal{D}^{N,p}(F^N)\le CN^{d-2}$ and all environments $p=p^N\subset[a,b]^{\mathbb{T}_N^d}$. For every set $\mathcal{A}$, we denote by $\chi_{\mathcal{A}}$ the characteristic function of $\mathcal{A}$.

Therefore we just need to prove

$$\limsup_{l\to\infty}\limsup_{N\to\infty}\frac{1}{N^d}\sum_{x\in\mathbb{N}^{\mathbb{T}_N^d}}\int_{\mathbb{N}^{\mathbb{T}_N^d}}V_{x,l,A}^p(\eta)F^N(\eta)\,d\nu_\varphi^{N,p}(\eta)=0$$

m-almost surely, where we set $V_{x,l,A}^p(\eta):=V_{x,l}^p(\eta)\chi_{\{\eta^l(x)\le A\}}(\eta)$. In fact, due to the bounds (3.1) on the Dirichlet form of F^N, it suffices to find an upper bound for

$$\frac{1}{N^d}\sum_{x\in\mathbb{T}_N^d}\int_{\mathbb{N}^{\mathbb{T}_N^d}}V_{x,l,A}^p(\eta)F^N(\eta)\,d\nu_\varphi^{N,p}(\eta)-\gamma CN^{2-d}\mathcal{D}^{N,p}(F^N)\tag{3.3}$$

for all $\gamma>0$. Next we restrict the problem to translations of the small box $\Lambda_l:=\{-2l,\dots,2l\}$. Denote by $\nu_\varphi^{x,l,p}$ the $\Lambda_{x,l}$-marginal of $\nu_\varphi^{N,p}$ and by $F_{x,l}(\eta)$ the density of the $\Lambda_{x,l}$-marginal of the measure $F^N(\eta)d\nu_\varphi^{N,p}(\eta)$ with respect to $\nu_\varphi^{x,l,p}$. We will sometimes drop the index for $x=0$ for such quantities when taken at the origin. Furthermore we define a Dirichlet form on $\Lambda_{x,l}$ by

$$\mathcal{D}_{x,l}^p(f)=\sum_{\substack{y\sim z\\ y,z\in\Lambda_{x,l}}}I_{y,z}^p(f),\qquad\text{where we have set}$$

$$I_{y,z}^p(f)=\frac{1}{2}\int_{\mathbb{N}^{\mathbb{T}_N^d}}p_y^Ng(\eta(y))\Big(\sqrt{f(\eta^{y,z})}-\sqrt{f(\eta)}\Big)^2d\nu_\varphi^{N,p}.$$

By convexity of the "bond"-Dirichlet forms $I_{x,y}^p$, we have $I_{y,z}^p(F_{x,l})\le I_{y,z}^p(F^N)$ for all neighbors $x,y\in\Lambda_{x,l}$ and thus

$$\frac{1}{N^d}\sum_{x\in\mathbb{T}_N^d}\mathcal{D}_{x,l}^p(F_{x,l})\le\frac{C(l)}{N^d}\mathcal{D}^{N,p}(F^N).$$

Hence instead of expression (3.3), we just need to find an upper bound for

$$\frac{1}{N^d}\sum_{x\in\mathbb{T}_N^d}\Big\{\int_{\mathbb{N}^{\mathbb{T}_N^d}}V_{x,l,A}^p(\eta)F_{x,l}(\eta)\,d\nu_\varphi^{x,l,p}(\eta)-\gamma C(l)N^2\mathcal{D}_{x,l}^p(F_{x,l})\Big\}.\tag{3.4}$$

Next we need to take care of the random part of the environment. The method to keep track of the environment is due to [18] and constitutes the main deviation from the proof of the hydrodynamic limit for the usual ZRP as exhibited in [17]. Thus we fix $\alpha,\delta>0$ and let $n\in\mathbb{N}$ be sufficiently large such that $\frac{1}{n}<\delta$. Divide the interval $[a,b]$ into sub-intervals of length not greater than $\delta(b-a)$ via $I_j^\delta=[\beta_j,\beta_{j+1})$ for $0\le j\le n-2$ where

$$\beta_j=a+(b-a)\frac{j}{n}\qquad(j=0,\dots,n-1)$$

and $I_{n-1}^\delta=[\beta_{n-1},b]$. Fix $k<l$ and let $L=[(2l+1)/(2k+1)]^d$, where $[x]$ denotes the Gaussian bracket, i.e. the largest integer smaller than or equal to $x\in\mathbb{R}$. Now we divide Λ_l into disjoint cubes of the form $x+\Lambda_k$, where we take B_i, $i=1,\dots,L-1$, such that

$$B_i\subseteq\Lambda_l,\quad B_i\cap B_j=\emptyset\text{ for }i\ne j,\quad\text{ and }B_i=x_i+\Lambda_l\text{ for some }x_i\in\mathbb{Z}^d.$$

Then set $B_L = \Lambda_l \setminus \bigcup_{i=1}^{L-1} B_i$ and without restriction take $x_1 = 0$, i.e. $B_1 = \Lambda_k$. Also set $B_i(x) = x + B_i$ for $x \in \mathbb{Z}^d$. For $x \in \mathbb{T}_N^d$, $\alpha \in (0,1)$ and $q \in [a,b]^{\Lambda_l}$, set

$$
\begin{aligned}
N_{x,j,i}^{l,k,\delta}(q) &:= \frac{1}{(2k+1)^d} \sum_{z \in B_i(x)} \chi_{I_j^\delta}(q_z), \\
A_{x,i,\alpha}^{l,k,\delta} &:= \left\{ (q_z)_{z\in\Lambda_l} : \left| N_{x,j,i}^{l,k,\delta}(q) - \mathbb{E}_m[\chi_{I_j^\delta}(q_z)] \right| \le \alpha, j = 0, \dots, n-1 \right\}, \qquad (3.5) \\
A_{x,\alpha}^{l,k,\delta} &:= \left\{ (q_z)_{z\in\Lambda_l} : \frac{1}{L} \sum_{i=1}^{L} \chi_{A_{x,i,\alpha}^{l,k,\delta}}(q) \ge 1 - \alpha \right\}.
\end{aligned}
$$

Since $V_{l,A}^p \le C(A)$ is bounded, the expression (3.4) is bounded form above by

$$
\begin{aligned}
&\frac{1}{N^d} \sum_{x \in \mathbb{T}_N^d} \left\{ \chi_{A_{x,\alpha}^{l,k,\delta}}(p) \left(\int_{\mathbb{N}^{\mathbb{T}_N^d}} V_{x,l,A}^p(\eta) F_{x,l}(\eta)\, d\nu_\varphi^{x,l,p}(\eta) - \gamma C(l) N^2 \mathcal{D}_{x,l}^p(F_{x,l}) \right) \right. \\
&\qquad \left. + C(A)(1 - \chi_{A_{x,\alpha}^{l,k,\delta}}(q)) \right\}. \qquad (3.6)
\end{aligned}
$$

Now we take care of the non-random part of the enviroment. To this end, set

$$
\widetilde{A}_{x,u,\alpha}^{l,k,\delta} = \left\{ (p_z)_{z\in\Lambda_l} : p_z = q_z + v_z, q \in A_{x,\alpha}^{l,k,\delta}, \sup_{z\in\Lambda_l} |v_{x+z} - v(u)| \le \alpha \right\}
$$

Since v is smooth, in particular (uniformly) continuous, for every α we can choose N large enough such that $v_{x+z} := v((x+z)/N)$ does not differ from $v(x/N)$ by more than α. Thus (3.6) is bounded from above by

$$
\begin{aligned}
&\frac{1}{N^d} \sum_{x \in \mathbb{T}_N^d} \left\{ \chi_{\widetilde{A}_{x,\frac{x}{N},\alpha}^{l,k,\delta}}(p) \left(\int_{\mathbb{N}^{\mathbb{T}_N^d}} V_{x,l,A}^p(\eta) F_{x,l}(\eta)\, d\nu_\varphi^{x,l,p}(\eta) - \gamma C(l) N^2 \mathcal{D}_{x,l}^p(F_{x,l}) \right) \right. \\
&\qquad \left. + C(A)(1 - \chi_{A_{x,\alpha}^{l,k,\delta}}(q)) \right\}. \qquad (3.7)
\end{aligned}
$$

Since the random part q of the environment is stationary and ergodic by assumption, it holds

$$
\frac{1}{N^d} \sum_{x \in \mathbb{T}_N^d} \left(1 - \chi_{A_{x,\alpha}^{l,k,\delta}}(q) \right) \xrightarrow{N\to\infty} \mathbb{P}_m(q \notin A_{0,\alpha}^{l,k,\delta}),
$$

which in turn vanishes by ergodicity in the limit as $l \to \infty$ and $k \to \infty$. The remaining term in (3.7) is bounded from above by

$$
\begin{aligned}
&\sup_{u\in\mathbb{T}^d} \chi_{\widetilde{A}_{[uN],u,\alpha}^{l,k,\delta}}(p) \left(\int_{\mathbb{N}^{\mathbb{T}_N^d}} V_{[uN],l,A}^p(\eta) F_{[uN],l}(\eta)\, d\nu_\varphi^{[uN],l,p}(\eta) \right. \\
&\qquad \left. - \gamma C(l) N^2 \mathcal{D}_{[uN],l}^p(F_{[uN],l}) \right).
\end{aligned}
$$

Again $\tau_{-[uN]}p$ is in $\widetilde{A}_{0,u,\alpha}^{l,k,\delta}$ for large enough N and the term involving $\Phi(\frac{[uN]}{N}, \rho)$ which appears in $V_{[uN],l,A}^p$ converges uniformly in u and $\rho \le A$ to $\Phi(u,\rho)$. Thus we see that, up to an error that vanishes as $N \to \infty$, it suffices to estimate

$$
\sup_{u\in\mathbb{T}^d} \sup_{p \in \widetilde{A}_{0,u,\alpha}^{l,k,\delta}} \sup_f \left(\int_{\mathbb{N}^{\Lambda_l}} V_{l,A}^p(\eta) f(\eta)\, d\nu_\varphi^{l,p}(\eta) - \gamma C(l) N^2 \mathcal{D}_{0,l}^p(f) \right), \qquad (3.8)
$$

where the inner supremum is taken over all densities f on $\mathbb{N}^{\Lambda_l}$. For fixed $l \in \mathbb{N}$, the term $V^p_{0,l,A}$ is only non-zero on the compact space of configurations in $\mathbb{N}^{\Lambda_l}$ of at most $(2l+1)^d A$ particles, the Dirichlet form is lower-semicontinuous and this property is conserved by the supremum. Hence the limit superior of (3.8) is bounded from above by

$$\sup_{u\in\mathbb{T}^d} \sup_{p\in\widetilde{A}^{l,k,\delta}_{0,u,\alpha}} \sup_{f} \int_{\mathbb{N}^{\Lambda_l}} V^p_{l,A}(\eta) f(\eta)\, d\nu^{l,p}_{\varphi}(\eta), \tag{3.9}$$

where now the inner supremum is taken over all densities f on $\mathbb{N}^{\Lambda_l}$ with vanishing Dirichlet form $\mathcal{D}^p_l(f) = 0$. A density f has vanishing Dirichlet form if and only if it is constant along all hyperplanes of a given number of particles. With this in mind, we introduce the *canonical measures*

$$\nu^p_{l,K}(\,\cdot\,) := \nu^{0,l,p}_{\varphi}(\,\cdot\,|\textstyle\sum_{x\in\Lambda_l}\eta(x) = K)\ .$$

Since the probability density f is constant on $\{\sum_{x\in\Lambda_l}\eta(x) = K\}$, we can estimate (3.9) from above by

$$\sup_{u\in\mathbb{T}^d_N} \sup_{p\in\widetilde{A}^{l,k,\delta}_{0,u,\alpha}} \max_{0\le K\le(2l+1)^d A} \Bigg\{ \int_{\mathbb{N}^{\mathbb{T}^d_N}} \frac{1}{L}\sum_{i=1}^{L} \int \Big| \frac{1}{(2k+1)^d} \sum_{x\in B_i} p_x g(\eta(x)) - \Phi\big(u, \tfrac{K}{(2l+1)^d}\big)\Big|\, d\nu^p_{l,K}(\eta) \Bigg\}, \tag{3.10}$$

where we have inserted the explicit form of $V^p_{0,l,A}$ and applied the triangle inequality. For given u and $p \in \widetilde{A}^{l,k,\delta}_{0,u,\alpha}$, we define φ^p_K by

$$\mathbb{E}_{\nu^{l,p}_{\varphi^p_K}}[\eta^l(x)] = \frac{K}{(2l+1)^d}. \tag{3.11}$$

Note that $0 \le \varphi^p_K \le C(A)$ is uniformly bounded in $0 \le K \le (2l+1)^d A$ and $l \in \mathbb{N}$. The next lemma concerns the closeness of the grand-canonical and the canonical measures.

Lemma 3.8 (Equivalence of ensembles)**.** *For all $F : \mathbb{N}^{\Lambda_k} \to \mathbb{R}$ with finite second moments with respect to $\nu^{k,p}_{\varphi}$ for all $\varphi \le C(A)$, it holds that*

$$\lim_{l\to\infty} \sup_{p\in[a,b]^{\mathbb{Z}^d}} \max_{0\le K\le(2l+1)^d A} \Big| \mathbb{E}_{\nu^{l,p}_{\varphi^p_K}}\big[F(\eta)\big] - \mathbb{E}_{\nu^p_{l,K}}\big[F(\eta)\big]\Big| = 0.$$

Proof. Thanks to the uniform bounds $a \le p_x \le b$, the equivalence of ensembles can be proved as explained in [17, Appendix 2], see also [18, Lemma 3.3]. □

By applying Lemma 3.8 to

$$F(\eta) = \frac{1}{(2k+1)^d} \sum_{x\in B_i} p_x g(\eta(x)),$$

we just need to find an upper bound for

$$\sup_{u\in\mathbb{T}^d_N} \sup_{p\in\widetilde{A}^{l,k,\delta}_{0,u,\alpha}} \max_{0\le K\le(2l+1)^d A} \Bigg\{ \int_{\mathbb{N}^{\mathbb{T}^d_N}} \frac{1}{L}\sum_{i=1}^{L} \int \Big| \frac{1}{(2k+1)^d} \sum_{x\in B_i} p_x g(\eta(x)) - \Phi\big(u, \tfrac{K}{(2l+1)^d}\big)\Big|\, d\nu^{l,p}_{\varphi^p_K}(\eta) \Bigg\}. \tag{3.12}$$

The next two lemmas yield convergence of this expression in the limit as $l \to \infty$ and then $k \to \infty$. In a certain sense, the first lemma describes the "ergodic" error between spatial averages and the quenched grand-canonical average.

Lemma 3.9. *For all $\alpha, \delta > 0$, it holds that*

$$\limsup_{k\to\infty} \limsup_{l\to\infty} \sup_{u\in\mathbb{T}_N^d} \sup_{p\in\widetilde{A}_{0,u,\alpha}^{l,k,\delta}} \max_{0\le K\le(2l+1)^d A} \left\{ \int_{\mathbb{N}^{\mathbb{T}_N^d}} \frac{1}{L}\sum_{i=1}^{L} \int \Big| \frac{1}{(2k+1)^d} \sum_{x\in B_i} p_x g(\eta(x)) - \varphi_K^p \Big| \, d\nu_{\varphi_K^p}^{l,p}(\eta) \right\} = 0.$$

The second lemma describes the difference between the quenched and annealed grand-canonical averages.

Lemma 3.10. *It holds that*

$$\limsup_{\delta\to 0} \limsup_{\alpha\to 0} \limsup_{k\to\infty} \limsup_{l\to\infty} \sup_{u\in\mathbb{T}_N^d} \sup_{p\in\widetilde{A}_{0,u,\alpha}^{l,k,\delta}} \max_{0\le K\le(2l+1)^d A} \Big| \varphi_K^p - \Phi\big(u, \tfrac{K}{(2l+1)^d}\big) \Big| = 0.$$

Proof of Lemma 3.9. Under the law $\nu_{\varphi_K^p}^{l,p}$, the random variables $(p_x g(\eta(x)) - \varphi_K^p)_{x\in B_i}$ are independent with zero mean. Furthermore their variance is uniformly bounded by continuity in p and K. Thus the expression to be bounded vanishes by a law of large numbers. □

Proof of Lemma 3.10. The absolute value in the given equation is obviously continuous in p and K. Using the fact that $\widetilde{A}_{0,u,\alpha}^{l,k,\delta}$ is closed and $v(\cdot)$ is continuous, it is straight-forward to prove that the supremum over p and K is continuous with respect to u. Hence for every $l \in \mathbb{N}$, the supremum in the hypothesis is achieved for some $u \in \mathbb{T}^d$, $p \in \widetilde{A}_{0,u,\alpha}^{l,k,\delta}$ and $0 \le K \le (2l+1)^d A$. For these maximizers, let φ be a limit point as $l \to \infty$ and φ_K^p the corresponding subsequence. Then the absolute value in the given formula in Lemma 3.10 is bounded from above by

$$\begin{aligned} (3.13)\quad & \Big|\varphi_K^p - \varphi\Big| + \Big|\varphi - \Phi\Big(u, \tfrac{1}{(2l+1)^d}\textstyle\sum_{z\in\Lambda_l} M\big(\frac{\varphi}{p_z}\big)\Big)\Big| \\ & \quad + \Big|\Phi\Big(u, \tfrac{1}{(2l+1)^d}\textstyle\sum_{z\in\Lambda_l} M\big(\frac{\varphi}{p_z}\big)\Big) - \Phi\Big(u, \tfrac{1}{(2l+1)^d}\textstyle\sum_{z\in\Lambda_l} M\big(\frac{\varphi_K^p}{p_z}\big)\Big)\Big|, \end{aligned}$$

where we have used (2.4), (2.2) and (3.11). By continuity and since φ_K^p converges to φ as $l \to \infty$, the first and last terms vanish in the limit. Now by definition of Φ and (2.5), we write

$$\varphi = \Phi(u, R(u,\varphi)) = \Phi\Big(u, \mathbb{E}_m\Big[M\big(\tfrac{\varphi}{v(u)+q_0}\big)\Big]\Big).$$

Since $\Phi(u,\cdot)$ is Lipschitz continuous uniformly in $u \in \mathbb{T}^d$, the second term in (3.13) is bounded from above by a multiple of

$$\Big|\mathbb{E}_m\Big[M\big(\tfrac{\varphi}{v(u)+q_0}\big)\Big] - \frac{1}{(2l+1)^d}\sum_{z\in\Lambda_l} M\big(\tfrac{\varphi}{p_z}\big)\Big|.$$

By the triangle inequality and since $p \in \widetilde{A}_{0,u,\alpha}^{l,k,\delta}$ is of the form $p_z = q_z + v_z$ with $|v_z - v(u)| \le \alpha$, this term is bounded from above by

$$\frac{1}{L}\sum_{i=1}^{L} \chi_{A_{0,i,\alpha}^{l,k,\delta}}(q) \Big|\mathbb{E}_m\Big[M\big(\tfrac{\varphi}{v(u)+q_0}\big)\Big] - \frac{1}{(2k+1)^d}\sum_{z\in B_i} M\big(\tfrac{\varphi}{v(u)+q_z}\big)\Big| + C\alpha$$

for all small enough $\alpha > 0$. Hence it is enough to consider

$$\sup_{q \in A_{0,1,\alpha}^{l,k,\delta}} \left| \mathbb{E}_m \Big[M\big(\tfrac{\varphi}{v(u)+q_0}\big) \Big] - \frac{1}{(2k+1)^d} \sum_{z \in \Lambda_k} M\big(\tfrac{\varphi}{v(u)+q_z}\big) \right|.$$

For each q, the absolute value in this formula is bounded from above by

$$\begin{aligned} &\left| \mathbb{E}_m \Big[M\big(\tfrac{\varphi}{v(u)+q_0}\big) \Big] - \sum_{j=1}^{n-1} M\big(\tfrac{\varphi}{v(u)+\beta_j}\big) m(I_j^\delta) \right| \\ &\qquad + \left| \sum_{j=1}^{n-1} M\big(\tfrac{\varphi}{v(u)+\beta_j}\big) \big(m(I_j^\delta) - N_{j,1}^{l,k,\delta}(q) \big) \right| \\ &\qquad + \left| \frac{1}{(2k+1)^d} \sum_{z \in \Lambda_k} \sum_{j=0}^{n-1} \Big(M\big(\tfrac{\varphi}{v(u)+\beta_j}\big) - M\big(\tfrac{\varphi}{v(u)+q_z}\big) \Big) \chi_{I_j^\delta}(q_z) \right|. \end{aligned}$$

By the Lipschitz-continuity of M and since $n \leq C\delta^{-1}$, this expression is bounded from above by $C(\delta + \alpha\delta^{-1})$ for all $q \in A_{0,1,\alpha}^{l,k,\delta}$. Taking the limit, first for $\alpha \to 0$ and then for $\delta \to 0$, finishes the proof of the one block estimate. □

Remark 3.11. The above estimates correspond to the approximation of the integral with respect to the measure m by an integral of simple functions.

3.2. **Two blocks estimate.** Similarly, we can prove the two blocks estimate, which shows that the difference between averages over boxes of size l and ϵN is negligible in the limit.

Lemma 3.12 (Two Blocks Estimate)**.** *It holds that*

$$\limsup_{l \to \infty} \limsup_{\epsilon \to 0} \limsup_{N \to \infty} \sup_{|y| \leq \epsilon N} \mathbb{E}_{\mu^N} \left[\int_0^T \frac{1}{N^d} \sum_{x \in \mathbb{T}_N^d} \left| \eta_t^l(x+y) - \eta_t^{\epsilon N}(x) \right| \, dt \right] = 0$$

m-almost surely.

We will skip the proof here and just note that it follows in a similar manner like the one block estimate — the main difference lying in restricting the process to two boxes of size l (that are at most ϵN apart) instead of just one. For details, the reader may refer to [17, 18].

4. Outlook and Examples: numerical simulations

In this section, we present examples for chemotactic motion of particles in a slowly varying chemical attractive environment in a slightly more general setting than our theory has so far addressed. This is done in order to get further insight into the behavior of such particle systems. Consider the (smooth) function $\vartheta : \mathbb{T}^d \to (0, \infty)$. Assume that the attractive chemical environment $\zeta(x)$ on the lattice $\mathbb{T}_N^d$ is given by independent Poisson random variables with parameter $\vartheta(\frac{x}{N})$ at site $x \in \mathbb{T}_N^d$. As before, let m denote the law of this random environment. One might think of this distribution as resulting from independent diffusion of attractive chemical molecules on a time-scale much faster than the typical time-scale of the diffusive motion of cells so that it is effectively time independent with respect to the random motion of the cells. This assumption on the time-scales is biologically reasonable and helpful also for theoretical reasons as outlined in the introduction. We suppose that the cells motion is described by a Markov process with generator given by (2.1), where the environment p^N depends on the number of attractive chemical molecules ζ via

$$p_x^N = f(\zeta(x)) \qquad \text{for all } x \in \mathbb{T}_N^d \ .$$

Thus $f : \mathbb{N} \to (0, \infty)$ provides a microscopic description of the chemical bias. For simplicity, let us suppose for the rate $g(\eta) = \eta$, i.e. that the cells diffuse independently in the random environment p^N. Note that the "random part" $p_x^N - \mathbb{E}_m[f(\zeta(x))]$ consists of independent but not stationary random variables, so our theory given before does not apply directly in this case. However, on local boxes the density $\vartheta(\frac{x}{N})$ is approximately constant, say $\vartheta(u)$, and the environment consists of almost identically and independently distributed particles, so that we expect that with techniques as given above a hydrodynamic limit can be derived in this case, too. To identify this limit, consider M given as in (2.4). Since g is the identity, ν_φ^1 is a product of identical Poisson distributions with parameter φ and it follows $M(\varphi) = \varphi$. Therefore we see that R as defined in (2.5) is given by

$$R(u, \varphi) = \mathbb{E}_{\mathrm{Pois}(\vartheta(u))}\left[\frac{\varphi}{f(\zeta(x))}\right],$$

where the average on the right hand side is taken over a Poisson distribution with parameter $\vartheta(u)$. Solving for φ yields

$$\Phi(u, \rho) = \mathbb{E}_{\mathrm{Pois}(\vartheta(u))}\left[\frac{1}{f(\zeta(x))}\right]^{-1} \rho.$$

In other words, the effective influence of the environment is given by its *harmonic mean*. This is reminiscent of analogous formulas in (one-dimensional) stochastic homogenization, cf. [30]. Let us denote

$$\widetilde{f}(\vartheta(u)) := \mathbb{E}_{\mathrm{Pois}(\vartheta(u))}\left[\frac{1}{f(\zeta(x))}\right]^{-1},$$

which yields the relationship between the microscopic chemical bias f and its macroscopic counterpart $\widetilde{f}$. Analogous to (2.6) the equation describing the limit of the empirical measures is then explicitly given by

$$\partial_t \rho(t, u) = \Delta\big[\widetilde{f}(\vartheta)\rho\big](t, u), \quad (t, u) \in [0, T] \times \mathbb{T}^d, \tag{4.1}$$

which we rewrite as

$$\partial_t \rho = \nabla \cdot \Big([\widetilde{f}(\vartheta)\nabla\rho + \widetilde{f}'(\vartheta)\rho\nabla\vartheta\Big],$$

which is of the form (1.1) with $k(\rho, \vartheta) = \widetilde{f}(\vartheta)$ and $\chi(\rho, \vartheta) = -\rho\widetilde{f}'(\vartheta)$, respectively $\tilde{\chi}(\rho, \vartheta) = -\widetilde{f}'(\vartheta)$. From (4.1) it follows that the stationary states are given by multiples of

$$\rho_\infty(u) = \frac{1}{\widetilde{f}(\vartheta(u))} = \mathbb{E}_{\mathrm{Pois}(\vartheta(u))}\left[\frac{1}{f(\zeta(x))}\right]. \tag{4.2}$$

The respective coefficient is determined by the initial mass, which is conserved. In order to perform numerical simulations, let us suppose that the dependence of $f(\zeta)$ on the attractive chemical molecules is explicitly given by

$$f(\zeta) = \nu + \frac{\chi_0}{1 + \zeta(x)}$$

with parameters $\nu, \chi_0 > 0$ describing the relative strengths of the free diffusion and the chemotactic motion. Specifically, we set $\chi_0 = 2$ and $\nu = 0.5$. Furthermore, let

$$\vartheta(u) = 30 \exp\big(-60((u_1 - 0.5)^2 + (u_2 - 0.5)^2)\big). \tag{4.3}$$

The simulations of the stochastic particle system are carried out with an algorithm based on random sequential updates. Here the particle densities are measured over balls in $\mathbb{T}^2$ of radius 0.05. The results are then compared with the numerical solution of the corresponding limiting PDE, which is obtained by using a standard finite difference method. Since we only deal with the first equation of a chemotaxis system and because we are not in the situation where blowup in finite time is

expected, we do not go into further details concerning more refined algorithms for the PDE in this illustrating section.
The simulations for a lattice size of $N \times N$ with $N = 250$ and uniform initial configuration $\eta(x) = 4$ for all $x \in \mathbb{T}^2_N$ are shown in Figs. 1–10.

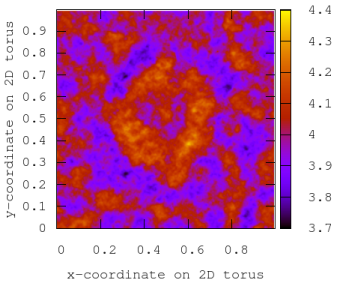

FIGURE 1. Cell density for particle system, $t = 0.0008$

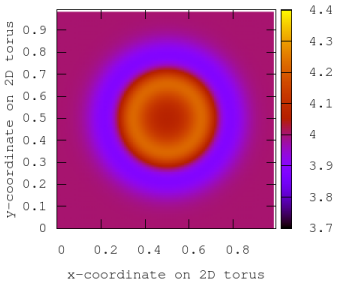

FIGURE 2. PDE solution, $t = 0.0008$

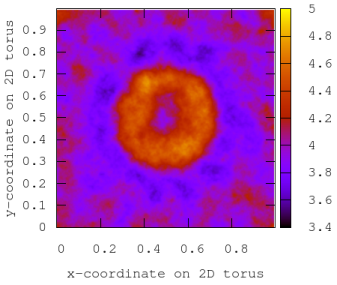

FIGURE 3. Cell density for particle system, $t = 0.004$

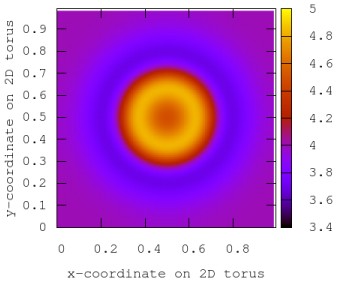

FIGURE 4. PDE solution, $t = 0.004$

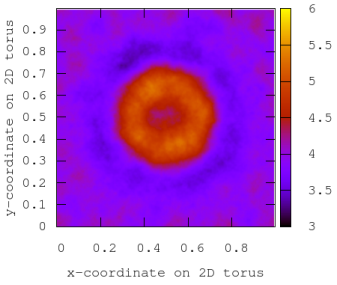

FIGURE 5. Cell density for particle system, $t = 0.01$

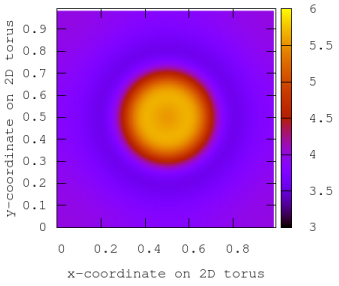

FIGURE 6. PDE solution, $t = 0.01$

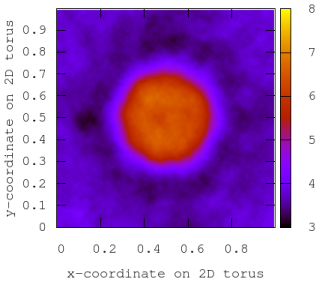

FIGURE 7. Cell density for particle system, $t = 0.04$

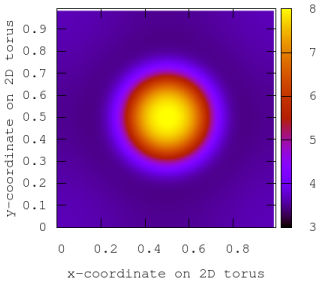

FIGURE 8. PDE solution, $t = 0.04$

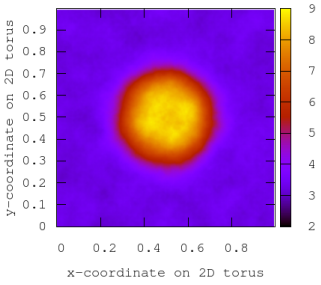

FIGURE 9. Cell density for particle system, $t = 0.2$

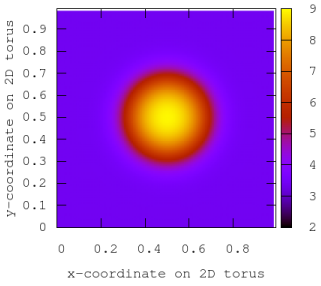

FIGURE 10. PDE solution, $t = 0.2$

The simulations for the cell density exhibit an interesting phenomenon near the boundary of the support of the positive density of the chemo-attractant, which itself is not visualized in the figures. Initially a ring of lower cell density forms around the area where the cells finally will concentrate due to positive chemotaxis, best visible as the blue ring in Figures 2 and 4. This can be explained by particles jumping out of the region of this ring into the domain of positive chemical attraction where they get stuck due to their lower motility there. If they jump out of this domain again, then they may not move very far away from it by random motion. This leads to a density profile which is a non-monotone function of the distance from the centre. For longer times this effect vanishes, however, and the density approaches the steady state, which (in the hydrodynamic limit as $N \to \infty$) is numerically indistinguishable from the solution of the PDE at time $t = 0.2$ shown in Figure 10. Initially, the fluctuations of the initial condition dominate in the simulation of the particle system, which explains the rather large difference to the deterministic solution of the PDE. Averaging over several realizations of the particle system would lead to closer resemblance between the two.

Finally, let us remark that it is possible to also consider models with a strong localization of particles. Again we assume that the chemical environment results from a random process. For the case considered below we do not have a proof for a hydrodynamic limit so far, but expect a similar outcome as before. Also, we do

not have stationarity in this case but convergence towards a stationary random variable. Now we simulate only the respective particle model, since the solution for the limiting PDE would require more refined numerical schemes than given above, because now blow-up phenomena may occur.
Our example here is the following, let us consider a zero range process within the range of so-called condensation. Specifically, we consider a ZRP with a constant jump rate $g(n) = g_0$ for all $n > 0$. As soon as $\varphi > g_0$, the partition function Z defined in (2.3) does not converge and the corresponding grand-canonical measure (2.2) does not exist. As shown in [20, 21], for large enough densities the particles tend to concentrate on only a few sites with the lowest exit rate. However, in this case, this behavior is not due to the reinforced interaction of the cells and the attractive chemical molecules, but instead it is solely due to the stochastic properties of the ZRP. Such strong localization effects may relate to finite time blow-up of solutions of related limiting objects.

Figs. 11–15 show the results of simulations for this model with $N = 100$, $g(n) = 3$, and all other parameters given as before, i.e. uniform initial configuration $\eta(x) = 4$, $\chi_0 = 2$, $\nu = 0.5$ and ϑ given in (4.3) with final averaging over the empirical measure with radius 0.05. In fact, this radius can be seen explicitly at points where many particles have clustered in the figures below. Figure 16 shows the random density of the chemo-attractant in order to compare with the location of the cell aggregate.

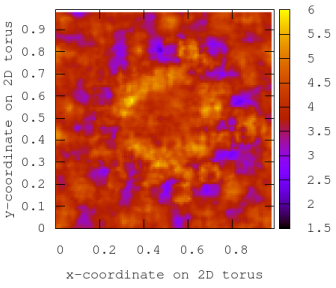

FIGURE 11. Cell density, $t = 0.008$

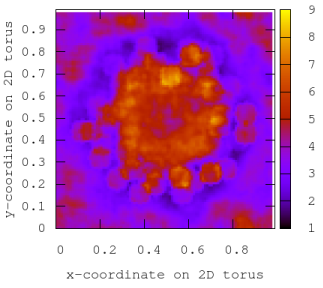

FIGURE 12. Cell density, $t = 0.04$

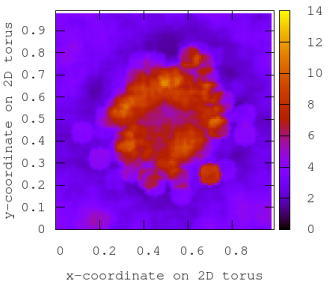

FIGURE 13. Cell density, $t = 0.1$

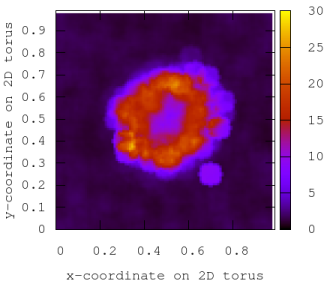

FIGURE 14. Cell density, $t = 0.4$

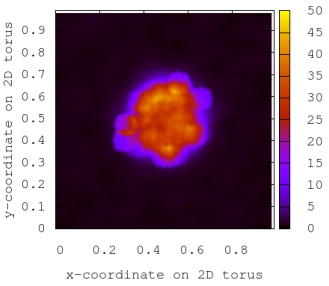

FIGURE 15. Cell density, $t = 2$

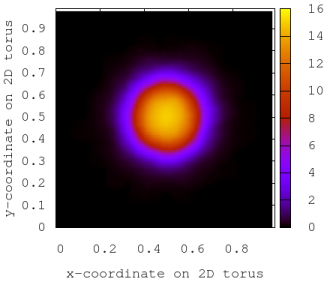

FIGURE 16. Density of the chemo-attractant ϑ (random)

If the total density in the system is high enough, we expect that eventually a finite fraction of all particles will concentrate on the site with the highest number of chemical molecules.

5. Concluding remarks

In this paper we derived the first equation of a general class of chemotaxis systems via a hydrodynamic limit of a stochastic lattice gas. The attractive chemical environment is prescribed in our case and assumed to be random and stationary, with a slowly varying mean. The situation of very strong clustering of the particles on single lattice sites is excluded in our theory, although this phenomenon can happen during selforganization of chemotactic particles in certain situations, and then it is of important biological relevance, like for the slime mold amoebae *Dictyostelium discoideum*. It would be interesting to be able to derive the full chemotaxis system from a hydrodynamic limit. Technically this is more challenging and methods of scale separation might play a role here.

Acknowledgements

Major parts of this work were done while D.M. and A.S. were working at the University of Heidelberg. This work was finished while A.S. took part in the CGP-program, 2015 at the Isaac Newton Institute, Cambridge.

References

[1] R. A. Adams and J. J. F. Fournier, *Sobolev Spaces*. Elsevier (2003)

[2] W. Alt *Biased random walk models for chemotaxis and related diffusion approximations*, J. Math. Biol. **9** (1980), no. 2, 147–177.

[3] L. Avena, T. Franco, M. Jara, F. Völlering, *Symmetric exclusion as a random environment: Hydrodynamic limits*, Ann. Inst. H. Poincaré Probab. Statist. **51** (2015), no. 3, 901–916.

[4] C. Bahadoran, H. Guiol, K. Ravishankar and E. Saada, *Euler hydrodynamics of one-dimensional attractive particle systems*, Ann. Probab. **34** (2006), no. 4, 1339–1369.

[5] C. Bahadoran, H. Guiol, K. Ravishankar and E. Saada, *Euler hydrodynamics for attractive particle systems in random environment*, Ann. Inst. H. Poincaré Probab. Statist. **50** (2014) no. 2, 403–424.

[6] P. Billingsley, *Convergence of probability measures*, 2nd ed. (1999), Wiley Series in Probability and Statistics, John Wiley & Sons Inc., New York.

[7] N. Braxmeier-Even and S. Olla, *Hydrodynamic Limit for an Hamiltonian System with Boundary Conditions and Conservative Noise*, Arch. Ration. Mech. Anal. **213** (2014), no. 2, 561–585.

[8] S. Childress and J. K. Percus, *Nonlinear aspects of chemotaxis*, Math. Biosci. **56** (1981), no. 3-4, 217–237.
[9] P. Covert P. and F. Rezakhanlou, *Hydrodynamic limit for particle systems with non-constant speed parameter*, J. Statist. Phys. **88** (1997), no. 1-2, 383–426.
[10] A. De Masi, S. Luckhaus, and E. Presutti, *Two scales hydrodynamic limit for a model of malignant tumor cells*, Ann Inst. H. Poincare Probab. Statist. **43** (2007), no. 3, 257–297.
[11] J. Fritz and B. Tóth, *Derivation of the Leroux system as the hydrodynamic limit of a two-component lattice gas*, Comm. Math. Phys. **249** (2004), no. 1, 1–27.
[12] P. Gonçalves and M. Jara, *Scaling limits for gradient systems in random environment*, J. Stat. Phys. **131** (2008), no. 4, 691–716.
[13] S. Großkinsky and H. Spohn, *Stationary measures and hydrodynamics of zero range processes with several species of particles*, Bull. Braz. Math. Soc. (N.S.) **34** (2003), no. 3, 489–507.
[14] W. Jäger and S. Luckhaus, *On explosion of solutions to a system of partial differential equations modelling chemotaxis*, Trans. Amer. Math. Soc. **329** (1992), no. 2, 819–824.
[15] M. Jara, *Hydrodynamic limit of the exclusion process in inhomogeneous media*, Dynamics, games and science (II) 449–465. Springer Proc. Math. **2**, Springer, Heidelberg (2011).
[16] E. F. Keller and L. A. Segel, *Initiation of slime mold aggregation viewed as an instability*, J. Theoret. Biol. **26** (1970), 399–415.
[17] C. Kipnis and C. Landim, *Scaling limits of interacting particle systems*. Springer (1999).
[18] A. Koukkous, *Hydrodynamic behavior of symmetric zero-range processes with random rates*, Stochastic Process. Appl. **84** (1999), no. 2, 297–312.
[19] A. Koukkous and H. Guiol, *Large deviations for a zero mean asymmetric zero range process in random media*, arXiv:math/0009110.
[20] J. Krug and P. A. Ferrari, *Phase Transitions in Driven Diffusive Systems With Random Rates*, J. Phys. A-Math. Gen. **29** (1996), L465–L471.
[21] C. Landim, *Hydrodynamical limit for space inhomogeneous one-dimensional totally asymmetric zero-range processes*, Ann. Probab. **24** (1996), no. 2, 599-638.
[22] T. M. Liggett *Stochastic interacting systems: contact, voter and exclusion processes*, Grundleheren der Mathematischen Wissenschaften **324**, Springer (1999).
[23] S. Luckhaus and L. Triolo, *The continuum reaction-diffusion limit of a stochastic cellular growth model*, Atti Accad. Naz. Lincei CI. Sci. Fis. Mat. Natur. Rend. Lincei (9) Mat. Appl. **15** (2004), no. 3-4, 215–223.
[24] D. Marahrens, *A hydrodynamic limit for a zero range process in a random medium with slowly varying average*, Diplomathesis, University of Heidelberg (2008).
[25] M. Z. Guo, G. C. Papanicolaou and S. R. S. Varadhan, *Nonlinear diffusion limit for a system with nearest neighbor interactions*, Commun. Math. Phys. **118** (1988), 31-59.
[26] L. C. Evans, *Partial Differential Equations, 2nd Edition*, Graduate Studies in Mathematics **19**, American Mathematical Society (2000).
[27] K. Oelschläger, *A law of large numbers for moderately interacting diffusion processes*, Z. Wahrsch. Verw. Gebiete **69** (1985), no. 2, 279–322.
[28] K. Oelschläger, *On the derivation of reaction-diffusion equations as limit dynamics of systems of moderately interacting stochastic processes*, Probab. Theory Rel. Fields **82** (1989), no. 4, 565–586.
[29] H. G. Othmer and A. Stevens, *Aggregation, blowup, and collapse: the ABCs of taxis in reinforced random walks*, SIAM J. Appl. Math. **57** (1997), no. 4, 1044–1081.
[30] G. C. Papanicolaou and S. R. S. Varadhan, *Boundary value problems with rapidly oscillating random coefficients*, Random fields, Vol. I, II (Esztergom, 1979) Colloq. Math. Soc. János Bolyai **27** (1981), 835–873.
[31] T. Rafferty, P. Chleboun, S. Grosskinsky, *Monotonicity and Condensation in Homogeneous Stochastic Particle Systems*, arXiv:1505.02049.
[32] F. Rezakhanlou, *Hydrodynamic limit for attractive particle systems on* $\mathbf{Z}^d$, Comm. Math. Phys. **140** (1991), no. 3, 417–448.
[33] R. Schaaf, *Stationary solutions of chemotaxis systems*, Trans. Amer. Math. Soc. **292** (1985), no. 2, 531–556.
[34] F. Spitzer, *Interaction of Markov processes*, Advances in Math. **5** (1970), 246–290.
[35] A. Stevens, *Trail following and aggregation of myxobacteria*, J. of Biol. Syst. **3** (1995), no. 4, 1059–1068.
[36] A. Stevens, *A stochastic cellular automaton modeling gliding and aggregation of myxobacteria*, SIAM J. Appl. Math. **61** (2000), no. 1, 172–182.

[37] A. Stevens, *The derivation of chemotaxis equations as limit dynamics of moderately interacting stochastic many-particle systems*, SIAM J. Appl. Math. **61** (2000), no. 1, 183–212.
[38] H.-T. Yau, *Relative Entropy and Hydrodynamics of Ginzburg–Landau Models*. Lett. Math. Phys. **22** (1991), no. 1, 63–80.

University of Warwick, Mathematics Institute, Zeeman Buildg., Coventry CV4 7AL, UK
E-mail address: S.W.Grosskinsky@warwick.ac.uk

Max-Planck-Institute for Mathematics in the Sciences (MPI MIS), Inselstr. 22, D-04109 Leipzig, Germany

Westfälische Wilhelms-Universität Münster, Applied Mathematics, Einsteinstr. 62, D-48149 Münster, Germany
E-mail address: angela.stevens@wwu.de