Modeling and Simulation of the Gliding and Aggregation of Myxobacteria

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Abstract

This paper is an extended abstract of the authors PhD-thesis, which will be published elsewhere.
Up to now the phenomena of gliding and aggregation of Myxobacteria is not fully understood. To get further inside into the problem a stochastic cellular automaton model is constructed, where the gliding of the bacteria is simulated. The results of these simulations suggest that the bacteria prefer to glide on slime paths, secreted by themselves, to build preaggregation patterns. A second mechanism is necessary to produce the final aggregation. In the model described here, chemotaxis of the bacteria towards a diffusing chemical substance is implemented. This leads to the final aggregation. To be able to use the simulations not only like an experiment, a simplification of the stochastic cellular automaton is connected to an interacting stochastic many particle system. From this many particle system then a system of partial differential equations is derived, a so called chemotaxis-system, giving informations about the particle densities. This system now is a model where one can get qualitative and quantitative results.

The Biological Phenomenon

This work is dealing with the mathematical modeling of the aggregation of bacteria. From a biological point of view these phenomena are not only interesting in each individual case, but also serve as model problems for questions in morphogenesis, e.g.:
How do cells manage to come together and build higher organized structures?

Up to now no definitive answer to such problems can be given. So a mathematical approach may help to test different biological hypotheses, which try to give an answer, and to ask new questions. On the other hand, interesting biological phenomena often result in interesting mathematical problems.

Starting point of this work are the phenomena of social gliding and aggregation of the ubiquitous myxobacteria which are mainly living in soil. In laboratory ex-

periments it was observed that the bacteria are gliding very slowly on the agar. They build long cell tracks and glide in loops and spirals. Under starvation conditions the bacteria aggregate and finally build so called fruiting bodies. This behavior is presented in great detail in the films of REICHENBACH et al. (1968) and KÜHLWEIN et al. (1968), (1971). But it is still not completely known which mechanisms cause the social gliding and final aggregation of the myxobacteria.

The Stochastic Cellular Automaton

Various biological hyptheses are discussed, which try to explain these phenomena. The questions resulting from these ideas motivated the construction of a stochastic cellular automaton model where some of the biological hypotheses are tested. The model incorporates those parameters which are known from laboratory experiments, like for instance the length and width of the bacteria and their gliding velocity.

The simulations suggest that the bacteria, which glide on slime trails produced by themselves, use these trails to build preaggregation patterns like loops and cell tracks. But the trail following does not account for the final aggregation. It seems that another mechanism is necessary for the stabilization of the preaggregation patterns and for the final aggregation.

To achieve this effect, in the simulations a diffusing chemo-attractant is secreted by the bacteria. When a certain threshold density of cells is reached by the mechanism of slime trail following, one bacterium starts to produce the chemo-attractant. All bacteria sensing a density high enough start to produce it too and stop, if this concentration is decreasing below the threshold. The diffusion coefficient of the chemo-attractant is very small. This finally leads to stable aggregation centers.

A short overview of these results is already given in STEVENS (1990, 1991, to appear). A detailed description is given in STEVENS (1992).

The Interacting Stochastic Many Particle System

Up to now not much theory is done about such complex cellular automata. There exist for instance results about reinforced random walks in one dimension (DAVIS, 1990). But the methods used there, are far from being applicable to two dimensional problems. One possibility to get qualitative and quantitative results from stochastic cellular automaton simulations is, to use them like an experiment. One defines suitable quantities, whose average is taken after sufficiently many simulations. From a mathematical point of view this is not satisfying. The idea is to set the cellular automaton model into context with a mathematical concept which allows defined calculations.

The cellular automaton is a stochastic model discrete in time, space and population size. The discretization especially in space is theoretically not easy to overcome. In the easiest case a heuristic derivation of a continous model for the probability of one bacterium to be located at a certain place can be done. This

leads to a stochastic differential equation for the location of the bacterium. Now one needs a model for many bacteria or population densities. So the idea is to start with a similar stochastic model for each bacterium of a big population, but with interaction: an interacting stochastic many particle system, which is continous in time and space but discrete in population size. From this many particle system then a system of partial differential equations can be derived, describing the behavior of the population densities. This is done like follows:

For any $N \in \mathbb{N}$ a population of $\approx N$ particles is considered. It is divided into two subpopulations, the bacteria and the particles of a chemical substance, produced by the bacteria. For simplicity only the effect of the chemo-attractant is modeled. The particles move around in $\mathbb{R}^d$, $d \in \mathbb{N}$, each one changing its position due to a stochastic differential equation. The bacteria are reacting to the particles of the chemical substance and to the other bacteria close to them. The particles of the chemical substance are changing position due to Brownian motion and they may die. As population size tends to infinity, the interaction between the particles is rescaled in a moderate way. This means that the essential domain of interaction of one particle with the other ones is macroscopically small and microscopically large. So for $N \to \infty$ the volume of the essential interaction domain tends to 0 and the number of particles inside this domain tends to infinity.

Let $S_u(N,t)$ denote the set of all bacteria and $S_v(N,t)$ denote the set of all particles of the chemical substance. Let the particles be numbered consecutively and let $P_N^k(t)$ denote the position of the k^{th} particle. Then one defines the following empirical processes:

$$S_{Nu}(t) = \frac{1}{N} \sum_{k \in S_u(N,t)} \delta_{P_N^k(t)} \quad , \quad S_{Nv}(t) = \frac{1}{N} \sum_{k \in S_v(N,t)} \delta_{P_N^k(t)} \ ,$$

where δ_x denotes the Dirac measure at a point $x \in \mathbb{R}^d$.

The main result of the thesis is, that for large N the empirical processes of the two subpopulations converge to the solution of a system of partial differential equations, a so called chemotaxis–system:

$$\partial_t u = \nabla \cdot \left(\mu \nabla u - \chi(u,v) u \nabla v \right)$$

$$\partial_t v = \eta \Delta v + \beta(u,v) u - \gamma(u,v) v$$

$$u(0,x) = u_0(x) \quad \text{and} \quad v(0,x) = v_0(x) \ .$$

This is well known as a system describing cell aggregation (KELLER and SEGEL, 1970, 1971 and KELLER, 1980). The considerations are based on results of OELSCHLÄGER (1989), who solved the problem of convergence for $\chi < 0$. In the case described here one has $\chi > 0$. This causes the main difficulties for the mathematical proof.

The main point in the future is to compare the interaction behavior of the 'real Myxobacteria' with the possible interaction ranges of the particles in a limiting procedure for equations describing aggregation.

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