Chapter 7

Chemotaxis

7.1 Introduction

Organisms often direct their movement by external cues, a process called taxis. Depending on the cue in question, we may term such directed movement thermotaxis (warmth), phototaxis (light), chemotaxis (chemical substances), and so on, and this may be both an attracting or repelling movement. Several kinds of common bacteria, such as *E. coli*, *Salmonella*, or the slime mould *Dictyostelium* (*Dicty* in short) have been shown to form intricate patterns when grown in semi-solid or liquid media in the laboratory. An example pattern showing spirals of the chemoattractant cyclic AMP (cAMP) in *Dictyostelium* is presented in Figure 7.1.

The reason for aggregation or repulsion may be many. Bacteria use scents to find food; immune cells chemotactically find enemies such as bacteria; insects use pheromones to find each other, either for reproduction as in moths, or to hunt collectively, as in army ants; reproduction is also the main drive behind Dicty aggregation.

Because of the simplicity of this organism, and the richness of its collective behaviour, *Dicty* has been used as a model organism for many years, especially to understand how signal transduction of cAMP induces aggregation and subsequent development (Othmer and Schaap, 1998).

Aggregation in *Dicty* is basically done through a feedback loop, in which the individual cells release cAMP into the environment while reacting to the cAMP levels they perceive. When general food levels become too low to sustain the slime mold cells individually, the cells start to produce cAMP in order to aggregate. They first form centra, which then concentrate to become 'slugs'. These slugs move about for a while until a suitable place is found. There, the multicellular slug undergoes cell differentiation to form a (pre)stalk on which a (pre)spore is formed. The stalk contains nonreproducing *Dicty* cells, i.e., there is cooperation among the cells so that few may reproduce. This is indeed an intricate evolutionary question, and to find the answer you should read the Selfish Gene and The Extended Phenotype by Richard Dawkins! The fruiting body on top finally contains spores which are dispersed by the wind. Some excellent videos of this remarkable progression may be found on the internet, including those made by the person who started much of this field, John Bonner, whilst still an undergraduate.

Mathematically, the description of the evolution of concentrations of organisms in some domain Ω begins with a general conservation law. This states that the total amount of organisms in Ω at time $t + \delta t$ must be equal to the total amount at time t plus the net concentration of particles which either flows out of Ω or is created inside Ω within the timespan δt. If we denote this net flow out of Ω by a

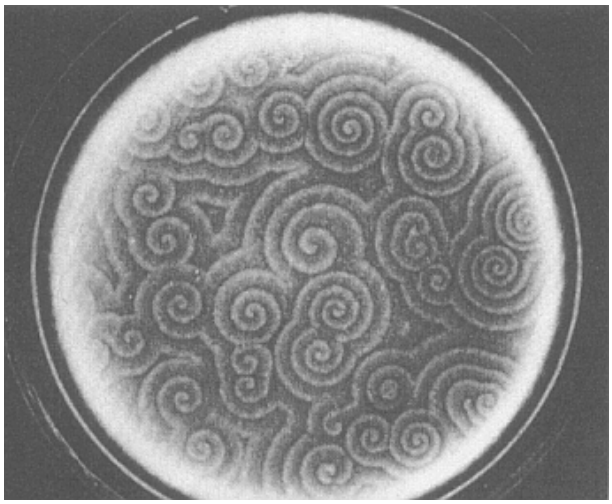

FIGURE 7.1. Spiraling waves of cyclic AMP, the chemoattractant used by colonies of *Dictyostelium* bacteria

flux $J(t,x)$ then we can write

$$\int_\Omega u(t+\delta t,x)dx = \int_\Omega u(t,x)dx - \delta t \int_{\partial\Omega} J(t,x)dS \tag{7.1.1}$$

Since this argument holds for any domain Ω, and $\int_{\partial\Omega} J(t,x)dS = \int_\Omega \nabla \cdot J dx$, we have the general evolution equation

$$u_t + \nabla \cdot J = 0. \tag{7.1.2}$$

This flux J may be due to different kinds of motion, such as diffusion or taxis. We could also easily take creation of particles in Ω into account. If we let $f(t,x)$ denote the creation of organisms at time t and position x, then the above equation becomes simply

$$u_t + \nabla \cdot J - f = 0$$

Phenomenologically, we may pose the following equation for organisms whose movements are described as stochastic random walks with a bias towards chemoattractant concentrations:

$$u_t + \nabla \cdot (d\nabla u - u\chi(s)\nabla s) \tag{7.1.3}$$

known as a Keller-Segel equation (Keller and Segel, 1971). Here the chemotactic flux J_c due to attraction by the chemical s is

$$J_c = u\chi(s)\nabla s$$

where $\chi(s)$ is termed the *chemotactic sensitivity*. The Keller-Segel equation (7.1.3) is often coupled to an equation for the chemoattractant s, which usually diffuses and is produced either by the cells itself or by an external source, e.g.

$$s_t = \Delta s + u - s.$$

Note that we have conveniently scaled the diffusion constant for s to 1 by rescaling space, the production rate by u to 1 by rescaling u and the degredation rate of s to 1 by rescaling time. We supply no-flux BCs to the equations for u and S to complete the Keller-Segel model.

The plan for the rest of the chapter is as follows. First we will study the initiation of pattern formation for a Keller-Segel model in one spatial dimension, and briefly discuss whether solutions exist for all time or may blow up in finite

time. Lastly, we will try to derive macroscopic Keller-Segel-like equations from microscopic behaviour of the individual cells, such as run-and-tumble movement in bacteria, signal transduction, and so on.

7.2 Initiation of pattern formation

Let us focus on the following set of equations on a domain $[0, L]$, with no-flux BCs,

$$\frac{\partial u}{\partial t} = d\frac{\partial^2 u}{\partial x^2} - \chi\frac{\partial u}{\partial x}\frac{\partial s}{\partial x} - \chi u\frac{\partial^2 s}{\partial x^2}, \tag{7.2.1}$$

$$\frac{\partial s}{\partial t} = \frac{\partial^2 s}{\partial x^2} + u - s. \tag{7.2.2}$$

The last term in the u equation is due to cross diffusion. Note that there is conservation of mass for u, since $\frac{d}{dt}\int u\,dx = 0$.

There exists a uniform steady state $u = \bar{u}$, $s = \bar{s}$, as long as $\bar{u} = \bar{s}$, and we can thus treat $\bar{u}$ as a parameter. Introducing $u = \bar{u} + U$ and $s = \bar{s} + S$. Linearizing around $(\bar{u}, \bar{s})$ gives

$$\frac{\partial U}{\partial t} = d\frac{\partial^2 U}{\partial x^2} - \chi\bar{u}\frac{\partial^2 S}{\partial x^2}, \tag{7.2.3}$$

$$\frac{\partial S}{\partial t} = \frac{\partial^2 S}{\partial x^2} + U - S. \tag{7.2.4}$$

Making the usual separation of variables Ansatz

$$\begin{pmatrix} U \\ S \end{pmatrix}(t, x) = e^{\lambda t}\cos\mu x \begin{pmatrix} U_0 \\ S_0 \end{pmatrix}$$

gives

$$\lambda U_0 = \mu^2 d U_0 + \chi\bar{u}\mu^2 S_0,$$
$$\lambda S_0 = -\mu^2 S_0 + U_0 - S_0,$$

which in matrix form reads

$$\begin{pmatrix} \lambda + \mu^2 d & -\chi\bar{u}\mu^2 \\ -1 & \lambda + \mu^2 + 1 \end{pmatrix}\begin{pmatrix} U_0 \\ S_0 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}.$$

The condition for a nontrivial solution is thus given by requiring that this matrix has determinant zero, i.e.,

$$(\lambda + \mu^2 d)(\lambda + \mu^2 + 1) - \chi\bar{u}\mu^2 = 0,$$

which is written more transparently as

$$\lambda^2 + (\mu^2(d+1) + 1)\lambda + \mu^2(d(\mu^2+1) - \chi\bar{u}) = 0.$$

Denoting the first and zeroth order coefficients of this polynomial in λ by B and C, we know that

$$\lambda_\pm = \frac{-B \pm \sqrt{B^2 - 4C}}{2}.$$

Observe that if $\Im\lambda \neq 0$ then $\Re\lambda < 0$, and that if $\Im\lambda = 0$ then $\lambda_- < 0$ and $\lambda_+ > 0$ if and only if $C < 0$.

We conclude that the uniform steady state is *unstable* iff

$$C < 0 \quad \Longleftrightarrow \quad d(\mu^2 + 1) < \chi\bar{u}. \tag{7.2.5}$$

We may offer directly the following biological interpretation of this inequality. Instability, and thus the initiation of pattern formation, is promoted by a high initial concentration of cells, a high chemotactic sensitivity χ, or a low random

motility d. Additionally, we do well to remember that several quantities were hidden inside the nondimensional equations by the rescaling of variables we had assumed. Making these explicit again revels that a high rate of cAMP production and low degredation rate of cAMP also promote pattern formation. Finally, we focus on the spatial mode $\mu = k\pi/L$ of the perturbation we have analyzed. Inequality (7.2.5) is more easily satisfied for small μ, i.e. for long waves, or equivalently, on large intervals $[0, L]$.

Overall, we may conclude that the feedback loop of involving signal production and moving towards stronger signals may lead to growing peaks provided the "equalizing" influence of diffusion is not too strong.

Finally we make some remarks on the *asymptotic behaviour* for large t. If the spatial dimension is 1, then solutions stay bounded. (Note that $\int u\,dx$ remains constant, so there is never blow up in the L^1-norm. Also $\int S \to \int u$ as $t \to \infty$.) If the spatial dimension is two, then if $\int u$ is large enough, a Dirac may form in finite time. If the spatial dimension is 3, then Dirac's may form in infinite time. Keller-Segel chemotaxis in the plane may thus account for aggregation in one spot. (There are are some ways to extend the model in order to capture the subsequent movement of Dirac's.)

The literature on Keller-Segel-like models has grown enormously since the early 1970s. The interested reader may consult (Horstmann, 2003) or (Perthame, 2007).

7.3 Derivation of chemotaxis models

One of the main obstacles to use (7.1.3) directly is that one has to specify $\chi(S)$. There is no general theory which allows us to translate the bacteria's perception of the chemoattractant and their subsequent change of behaviour (moving towards higher chemoattractant concentrations) to a macroscopic chemotactic sensitivity function.

In this section we will show how one can obtain Keller-Segel equations, or other evolution equations for chemotactic bacteria, using the dynamics at a *mesoscopic* scale as starting point. The main point is that it is often easier to describe dynamics on a level at which pattern is *not* observed, and then lift these equations to the level at which it *is* observed. In the current context, it is easy to specify how individual particles change their direction due to external cues or random motion. This gives us evolution equations for a density $u(t, x, v)$, say, which thus depends on velocities v. The mathematical goal is then to derive an evolution equation for a function n, say, which does not depend on v anymore, but only on time and space (which is the quantity one observes when one describes the bacterial patterns such as in Figure 7.1).

The simplest example in which we can derive a parabolic equation from a mesoscopic one is in one space dimension. Let particles move according to a so-called velocity-jump process. In this process, the particles move at a certain speed (here assumed to be a constant s), and reorient at random instants in time according to a Poisson process with intensity λ. In one space dimension, the particles can only move in two directions. Let $u^{\pm}(t, x)$ be the density of particles at (t, x) and moving to the right (+) or left (-) respectively. Then $u^{\pm}$ satisfy the hyperbolic equations

$$\frac{\partial u^+}{\partial t} + s\frac{\partial u^+}{\partial x} = -\lambda u^+ + \lambda u^- \tag{7.3.1}$$

$$\frac{\partial u^-}{\partial t} - s\frac{\partial u^-}{\partial x} = -\lambda u^- + \lambda u^+ \tag{7.3.2}$$

The density of particles at (t,x), $u(t,x)$, is the sum of $u^+(t,x)$ and $u^-(t,x)$, and the particle flux j equals $s(u^+ - u^-)$. These satisfy

$$\frac{\partial u}{\partial t} + \frac{\partial j}{\partial x} = 0 \tag{7.3.3}$$

$$\frac{\partial j}{\partial t} + 2\lambda j = -s^2 \frac{\partial u}{\partial x} \tag{7.3.4}$$

Differentiating the first of these equations with respect to t and the second to x and combining both equations leads to the telegraph equation

$$\frac{\partial^2 u}{\partial t^2} + 2\lambda \frac{\partial u}{\partial t} = s^2 \frac{\partial^2 u}{\partial x^2}$$

The diffusion equation follows formally in the limit $\lambda \to \infty$, $s \to \infty$, while keeping

$$\frac{s^2}{\lambda} =: d \tag{7.3.5}$$

constant.

To understand pattern formation in bacteria or other chemotactic organisms such as ants, we need to derive continuum models in higher dimensions. Now particles can travel in an infinity of directions, and we denote by $p(t,x,v)$ the density of particles at time t and position $x \in \mathbb{R}^n$ moving in the direction $v \in V := sS^{n-1}$ (still with constant speed s). This density now satisfies the transport equation

$$\frac{\partial u}{\partial t} + \nabla \cdot (vu) = -\lambda u + \lambda \int_V T(v,v')u(t,x,v')dv'$$

which resembles the Boltzmann equation, but it is linear in u rather than quadratic. It is nothing but a conservation equation like (7.1.2), but now over the domain $\mathbb{R}^n \times V$ rather than a domain $\Omega \subset \mathbb{R}^n$. Within the current context, $T(v,v')$ is a turning kernel, and signifies the probability of changing direction from v' to v if a switch is made, which happens with probability λ. It has a number of obvious properties. Most importantly, $T \geq 0$ and

$$\int_V T(v,v')dv' = 1$$

The main goal here is to find an evolution equation for $n(t,x) := \int u(t,x,v)dv$ such as a diffusion equation or a Keller-Segel equation. The method makes crucial use of a small parameter which has to be identified in the mesoscopic model. Within the current context, this parameter, ε, is usually the ratio sL/T, where L is a typical length scale of the pattern and T a measure of the typical time scale. The method now consists of three steps

(1) introduce a scaling which reflects the type of model you want to find using a small parameter
(2) write u as an asymptotic expansion in this small parameter
(3) find out what equations the different parts of this expansion have to satisfy in order for the problem to be solvable. In many cases, these solvability conditions give rise to the evolution equations you are after

In our case, we will study a parabolic scaling, i.e., $\xi = \varepsilon x$ and $\tau = \varepsilon^2 t$. Hyperbolic scalings are also often useful, and give rise to chemotaxis models with quite different properties. The rescaled transport equation now becomes

$$\varepsilon^2 \frac{\partial u}{\partial \tau} + \varepsilon \nabla_\xi \cdot (vu) = -\lambda u + \lambda \int_V T(v,v')u(\tau,\xi,v')dv' \tag{7.3.6}$$

The second step is two write u as an asymptotic expansion

$$u(\tau,\xi,v) = \sum_{i=0}^{k} \varepsilon^i u_i(\tau,\xi,v) + \mathcal{O}(\varepsilon^{k+1}) \tag{7.3.7}$$

Let us denote

$$\mathcal{L}\phi(v) = -\lambda\phi(v) + \lambda \int_V T(v,v')\phi(\tau,\xi,v')dv'$$

for functions $\phi \in L^2(V)$. Note that the natural choice of function space here would be $L^1(V)$, but choosing L^2 makes the exposition more straightforward, since the dual of L^2 is again L^2.

Plugging this expansion (7.3.7) into (7.3.6) and grouping the terms in the resulting equation by orders of ε, we find

$$\mathcal{O}(\varepsilon^0): \qquad \mathcal{L}u_0 = 0 \tag{7.3.8}$$

$$\mathcal{O}(\varepsilon^1): \qquad \mathcal{L}u_1 = v \cdot \nabla u_0 \tag{7.3.9}$$

$$\mathcal{O}(\varepsilon^2): \qquad \mathcal{L}u_2 = \frac{\partial u_0}{\partial t} + v \cdot \nabla u_1 \tag{7.3.10}$$

$$\vdots$$

$$\mathcal{O}(\varepsilon^i): \qquad \mathcal{L}u_i = \frac{\partial u_{i-2}}{\partial t} + v \cdot \nabla(u_{i-1}) \quad 3 \le i \le k \tag{7.3.11}$$

The properties of T imply that 0 is a simple eigenvalue of $\mathcal{L}u = -\lambda u + \lambda \int_V T(.,v')u(v')dv'$ with eigenfunction $u \equiv 1$. We can hence conclude that, since $\mathcal{L}u_0 = 0$, u_0 does not depend on v! This means that u_0 only depends on τ and ξ and is the dependent variable for which we are trying to derive an evolution equation.

Were $\mathcal{L}$ invertible, we could simply proceed by first setting

$$u_1 = \mathcal{L}^{-1}(v \cdot \nabla u_0)$$

and then

$$u_2 = \mathcal{L}^{-1}\frac{\partial u_0}{\partial t} + v \cdot \nabla(\mathcal{L}^{-1}(v \cdot \nabla u_0))$$

and so on. But $\mathcal{L}$ is singular, and is only invertible on the orthogonal complement in $L^2(V)$ of the eigenspace at eigenvalue 0, $\langle 1 \rangle^\perp$. This is nothing but those functions $\phi \in L^2$ such that

$$\int_V \phi(v)dv = 0$$

Hence, to be able to express u_1 in u_0, we have to make sure that the right hand side of (7.3.9) satisfies this orthogonality condition, which reads

$$\int_V (v \cdot \nabla u_0)dv = 0. \tag{7.3.12}$$

Then $u_1 = \mathcal{F}(v \cdot \nabla u_0)$, where $\mathcal{F}$ is the pseudoinverse of $\mathcal{L}$ (i.e., the inverse of $\mathcal{L}$ where it is well-defined).

To solve (7.3.10) we similarly have to require that

$$\int_V \frac{\partial u_0}{\partial t} + v \cdot \nabla u_1 dv = 0$$

Using $u_1 = \mathcal{F}(v \cdot \nabla u_0)$ this becomes

$$\int_V \frac{\partial u_0}{\partial t} + v \cdot \nabla(\mathcal{F}(v \cdot \nabla u_0))dv = 0$$

Since u_0 is independent of v, the integrand vanishes, and we find the desired evolution equation for u_0,

$$\frac{\partial u_0}{\partial t} + v \cdot \nabla(\mathcal{F}(v \cdot \nabla u_0)) = 0 \tag{7.3.13}$$

which can be written in the more familiar form

$$\frac{\partial u_0}{\partial t} - \nabla \cdot (d \nabla u_0) = 0 \tag{7.3.14}$$

where

$$d = -\frac{1}{|S^{n-1}|} \int_V v \mathcal{F} v dv$$

Fortunately, in many cases this pseudoinverse $\mathcal{F}$ can be computed explicitly. In the simplest case, when $T(v, v') = 1/|S^{n-1}|$ and $V = sS^{n-1}$, we find

$$d = \frac{s^2}{\lambda n}$$

This is a straighforward generalisation of the diffusion constant (7.3.5) we found in the one-dimensional telegraph equation.

This technique of scaling, substituting an asymptotic expansion and finding an evolution equation as a solvability condition, is a very general one and occurs in many applied mathematics problems. Let us here extend this idea to incorporate sensing of a chemoattractant, with a Keller-Segel model as the final result.

The main ingredient we need to add to include chemotaxis is to change the turning kernel T. We suppose that this is now a function of an external signal $S(t, x)$. Intuitively, if a bacterium senses the signal it should swim in the direction of highest concentration. The probability of choosing a new direction should thus depend on the concentration around the position x, in other words on ∇S. We will make this assumption at the very end.

We continue the above technique at the rescaled transport equation, which now reads

$$\varepsilon^2 \frac{\partial u}{\partial \tau} + \varepsilon \nabla_\xi \cdot (vu) = -\lambda u + \lambda \int_V T(v, v', S) u(\tau, \xi, v') dv'$$

Next to the asymptotic expansion (7.3.7) of u, we also introduce an expansion for T. Let us assume that the influence of S only occurs in the order ε term:

$$T(v, v', S) = T_0(v, v') + \varepsilon T_1(v, v', S) \tag{7.3.15}$$

Substituting this gives

$$\varepsilon^2 \frac{\partial u}{\partial \tau} + \varepsilon \nabla_\xi \cdot (vu) = \mathcal{L}_0 u + \varepsilon \lambda \int_V T_1(v, v', S) u(\tau, \xi, v') dv'$$

where

$$\mathcal{L}_0 u = -\lambda u + \lambda \int_V T_0(., v') u(v') dv'$$

We continue by substituting the expansion for u. The u_i again satisfy a coupled set of equations analogous to (7.3.8)–(7.3.11), which can only be solved under certain solvability conditions. The lowest order contribution u_0 is still independent of v, and the solvability condition for u_0 at order ε^2 is now

$$\int_V \left(\frac{\partial u_0}{\partial t} + (v \cdot \nabla) \mathcal{F}_0 (v \cdot \nabla u_0) - \lambda (v \cdot \nabla) \mathcal{F}_0 \left(\int_V T_1(v, v') dv' u_0 \right) \right) dv$$
$$- \lambda_0 \int_V \int_V T_1(v, v', S) u_1(v') dv' dv = 0 \tag{7.3.16}$$

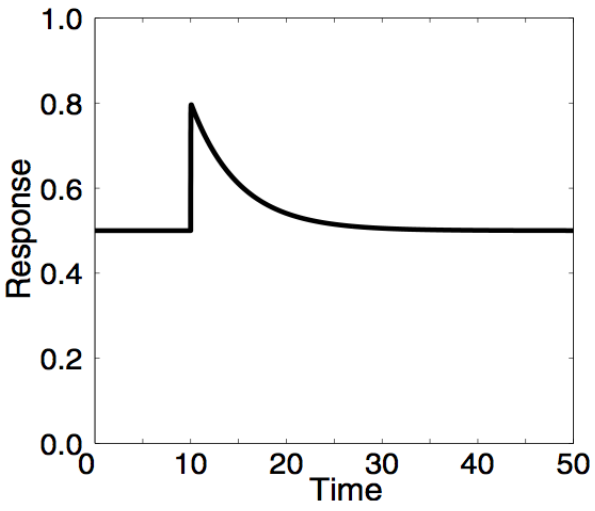

FIGURE 7.2. Typical dynamics of the internal excitation variable y_1 as the bacterium passes a sudden increase of chemoattractant. Note that the bacterium is first more excitable, but that this excitability slowly decreases back to a rest state. Adapted from Erban and Othmer (2004).

Here $\mathcal{F}_0$ is the pseudoinverse of $\mathcal{L}_0$. If we define

$$v_c = -\frac{\lambda}{|S^{n-1}|}\int_V\int_V v\mathcal{F}_0 T_1(v,v',S)dv'dv$$

as the chemotactic velocity, then u_0 satisfies an equation which starts to resemble a Keller-Segel equation

$$\frac{\partial p_0}{\partial \tau} = \nabla\cdot(d\nabla u_0 - v_c u_0)$$

If we moreover make the same simplifying assumptions as before, $T_0 = 1/|S^{n-1}|$, then

$$d = \frac{s^2}{\lambda n}, \quad v_c = \frac{1}{|S^{n-1}|}\int_V\int_V vT_1(v,v',S)dvdv'$$

Finally, to obtain the classical Keller-Segel model, we make the additional assumption that T_1 depends linearly on ∇S to which we hinted at the beginning of this derivation. Then v_c is of the form $\chi(S)\nabla S$, with

$$\chi(S) = \frac{\lambda k(S)}{|S^{n-1}|}d$$

Note, however, that we are effectively not very much further. Rather than having to choose an arbitrary function $\chi(S)$, we now have to choose an equally arbitrary $k(S)$.

There are many variations and extensions on this theme. We may also introduce dependence of the turning rate λ on the chemoattractant, and again find that the this dependence has to be of order ε to give us a Keller-Segel equation. Starting either with a turning kernel T or a turning rate λ in which this S-dependence is already present in the $\mathcal{O}(1)$ term (T_0 or λ_0) does not result in a Keller-Segel equation, but reduces the evolution equation to simple diffusion.

One of the most exciting extensions in this field has been the additional modelling of the signal transduction pathways by which bacteria sense the chemoattractant. Rather than modelling directly how the turning angle depends

on S (which resulted in our having to choose $k(S)$ in the chemotactic sensitivity $\chi(S)$), we let it depend on some internal state of the bacterium. This pathway is known to be very complex indeed, and mathematical models of its reaction dynamics often contain 30 or more dependent variables. Fortunately, it has been shown convincingly that this system may be approximated well using two phenomenologically chosen variables, a fast excitation variable y_1 changing at time scale τ_e, and a slow adaptation variable y_2 varying at time scale τ_a. See Figure 7.2 for the kind of dynamics this creates. These two ingredients of excitation and adaptation are very commonly found in many sensory systems following an external concentration. We now introduce an internal state $y = (y_1, y_2)$ for each individual particle, evolving according to

$$\frac{dy}{dt} = h(y, S) \tag{7.3.17}$$

or more specifically,

$$\tau_e \frac{dy_1}{dt} = g(S(x)) - (y_1 + y_2) \tag{7.3.18}$$

$$\tau_a \frac{dy_2}{dt} = g(S(x)) - y_2 \tag{7.3.19}$$

We may resort to the conservation equation (7.1.2) again, but now the flux is not in space or in velocity space, but in internal state space. The evolution of particle densities and their internal states can be given by

$$\frac{\partial u}{\partial t} + \nabla_y \cdot (hu) = 0$$

So rather than treating y as an dependent variable, we can treat it as an independent variable. This is entirely analogous to the situation in which $dx/dt = v$ and u solves $u_t + \nabla \cdot (vu) = 0$.

Putting this new ingredient into the transport equation is straighforward. Now $u(t, x, y, v)$ satisfies

$$\frac{\partial u}{\partial t} + \nabla_x \cdot (vu) + \nabla_y \cdot (hu) = -\lambda(y)u + \lambda(y) \int_V T(v, v', y)u(t, x, v', y)dv' \tag{7.3.20}$$

The three-step technique works also for this more elaborate example. Assuming that the turning rate depends linearly on the excitation variable (which detects the signal and thus influences when to change direction) we write $\lambda(y) = \lambda_0 - by_1$ for $\lambda_0 > 0$, $b > 0$. A macroscopic evolution equation for $U(x, t) = \int \int u(t, x, y, v)dydv$, can now be derived, and is indeed a classical Keller-Segel equation for large times

$$\frac{\partial U}{\partial t} = \nabla \cdot \Big(\frac{s^2}{\lambda_0} \nabla U - \Big[\frac{bs^2 \tau_a g'(S(x))}{\lambda_0 (1 + 2\lambda_0 \tau_a)(1 + 2\lambda_0 \tau_e)} \Big] U \nabla S \Big). \tag{7.3.21}$$

Not only have we understood under what circumstances mesoscopic dynamics give rise to Keller-Segel equations, we have also obtained insight how the parameters specifying the individual bacteria's behaviour influence the diffusion or aggregation parts of the final macroscopic equation (7.3.21).

This is but one way to derive Keller-Segel models from lower-level dynamics. One may also start from a stochastic description, see e.g. Stroock (1974); Stevens (1995). For more information and much detail on recent developments on velocity-jump processes and their relation to chemotaxis models, see Alt (1980); Othmer et al. (1988); Othmer and Hillen (2002); Erban and Othmer (2004, 2007); Xue and Othmer (2009). The analysis of the resulting chemotaxis models has become a large field. The interested reader may consult Horstmann Horstmann (2003) for a detailed review of many mathematical aspects of chemotaxis.