On a System of Hyperbolic Balance Laws Arising from Chemotaxis (14rit198)

Dong Li (University of British Columbia)
Kun Zhao (Tulane University)
03/30/2014 - 04/06/2014

1. Background and Motivation.

In contrast to random diffusion without orientation, chemotaxis is the biased movement of cells/particles toward the region that contains higher concentration of beneficial or lower concentration of unfavorable chemicals. The former often refers to the attractive chemotaxis and latter to the repulsive chemotaxis. Well-known examples of biological species experiencing chemotaxis include the slime mold amoebae *Dictyostelium discoideum*, the flagellated bacteria *Escherichia coli* and *Salmonella typhimurium*, and the human endothelial cells (cf. [16]). Chemotaxis has been advocated as a leading mechanism to account for the morphogenesis and self-organization of a variety of biological coherent structures such as aggregates, fruiting bodies, clusters, spirals, spots, rings, labyrinthine patterns and stripes, which have been observed in experiments (cf. [4, 5, 7, 8, 16]). In the last 30-35 years, among several works investigating taxes, chemotaxis research shows a significantly high ratio (>95%). Between the year 1975 and 2006, more than 22,000 papers in the scientific and medical literature were devoted to this phenomenon (PubMed), with the frequency of publication continuing to increase, which points to the underlined importance of chemotaxis research both in biology and medicine.

In a 1966 article published in *Science* (cf. [1]), Adler reported an important experimental result regarding the traveling bands of motile *Escherichia coli*. In the experiment, bands of *Escherichia coli* were observed to travel at constant speed when the bacteria were placed in one end of a capillary tube containing oxygen and an energy source. Four years later, in a series of seminal works (cf. [11, 12, 13]), Keller and Segel developed an effective mathematical model which nowadays is known as the Keller-Segel Chemotaxis Model (KSCM), and successfully reproduced the experimental result of Adler from a rigorous mathematical aspect. In its general form, the KSCM reads

$$\begin{cases} \partial_t u = D\Delta u - \nabla\cdot(\chi u\nabla\phi(v)), \\ \partial_t v = \varepsilon\Delta v + g(u,v), \end{cases} \tag{0.1}$$

where u and v denote the cell density and chemical concentration, respectively; $D>0$ and $\varepsilon\geq 0$ are cell and chemical diffusion coefficients, respectively; and χ is the chemotactic sensitivity coefficient. The chemotaxis is called to be attractive if $\chi>0$ and repulsive if $\chi<0$, where $|\chi|$ measures the strength of the chemical signal. Here $\phi(v)$ is referred to as the chemotactic sensitivity (CS) function describing the signal detection mechanism and $g(u,v)$ is a function characterizing the chemical growth and degradation. In [11, 12, 13], based on a phenomenological observation, the authors chose the CS function to be the *logarithmic* function: $\phi(v)=\log(v)$, which reflects the fact that bacteria are sensitive to very small change in oxygen if the concentration of oxygen is also very small. The logarithmic sensitivity also indicates that cell chemotactic response to the chemical signal follows the Weber-Fechner law which has prominent applications in biological modelings (cf. [2, 3, 6, 13]). Also in [11, 12, 13], the chemical production function was chosen as $g(u,v)=uv^m(0\leq m<1)$ to entail that the chemical signal grows algebraically. By using these functions, the authors provided sufficient conditions under which traveling wave

solutions to the KSCM exist and are stable. The results were consistent with the experimental observations reported in [1]. Since then, the KSCM has provided a cornerstone for many of works in chemotaxis research, its success being a consequence of its intuitive simplicity, analytical tractability and capability to model the basic dynamics of chemotactic populations. An extensive body of literature is devoted to the mathematical analysis of such model, see e.g. the survey papers [9, 10] and the references therein.

Since the initiation of the KSCM, researchers gradually recognized that many biological systems can be more accurately modeled by random walkers that deposit non-diffusible chemical signals that modify the local environment for succeeding passages. This phenomenon corresponds to one of the limiting cases of the KSCM, that is, when the diffusion of chemical substance is so small that it is negligible, i.e., $\varepsilon \to 0$. The resulting system of equations is of *hybrid* (PDE-ODE) type:

$$\begin{cases} \partial_t u = D\Delta u - \nabla \cdot (\chi u \nabla \phi(v)), \\ \partial_t v = g(u, v). \end{cases} \tag{0.2}$$

Twenty-seven years later since the pioneering work of Keller and Segel, Othmer and Stevens [17] proposed a version of (0.2) by taking $\phi(v) = \log(v),\ g(u, v) = uv - \mu v$. The resulting equations then take the form:

$$\begin{cases} \partial_t u = D\Delta u - \nabla \cdot (\chi u \nabla \log(v)), \\ \partial_t v = uv - \mu v, \end{cases} \tag{0.3}$$

where $\mu \geq 0$ is a constant describing the natural degradation rate of the chemical signal. Direct applications of (0.3) include modeling of haptotaxis and initiation of angiogenesis.

Although the hybrid model looks similar to the KSCM, the two models differ significantly from each other. From the biological point of view, the chemical signal in the hybrid model is non-diffusive and grows exponentially instead of algebraically, which suggests that finite-time blowup may occur (cf. [17]). From the mathematical perspective, because the chemical diffusion coefficient of the hybrid model is zero and its chemical production function corresponds to a limiting case of the KSCM ($g(u, v) = uv^m$, $0 \leq m < 1$ for KSCM, $m = 1$ for hybrid model), many existing methods for handling the KSCM do not work for the hybrid model. In spite of the widely appreciated magnitude of research conducted on the classic KSCM, there has been little work in the literature investigating the analytical and biological aspects of the hybrid model. A comprehensive analysis of such a nonlinear/degenerate system under general conditions is important for understanding fundamental phenomena in chemotaxis. Immediately after the hybrid model was developed, Levine and Sleeman [14] provided a comprehensive qualitative and numerical analysis for the model. In particular, explicit solutions describing aggregation and blow up of attractive chemotaxis and collapse of repulsive chemotaxis were constructed in one-dimensional space by choosing special initial data. The result was subsequently generalized in [18, 19]. Such evidence has led researchers in the field to appreciate that the hybrid model is capable of describing fundamental phenomena in chemotaxis.

However, the aforementioned research ceased when facing the challenge of validating the results obtained in [14] under *general conditions* on initial data, due to the lack of effective technical devices for handling the degeneracy of the system. This leaves the questions of global existence, finite-time blowup and long-time behavior of smooth solutions of the hybrid model widely open.

2. Recent Development and Open Problems.

From the biological point of view, when the spatial domain is large or the size of objectives considered (like bacteria) is small, the Cauchy problem of (0.3) becomes particularly relevant. Recently in [15], by developing a novel technique, we obtained the following results for the Cauchy problem of (0.3) in multi-dimensional spaces:

- local well-posedness and a blowup criteria of large smooth solutions in $\mathbb{R}^n,\ \forall\ n \in \mathbb{N}$,
- global well-posedness of small smooth solutions in $\mathbb{R}^n,\ n = 1, 2, 3$,
- a novel explicit (*frequency-by-frequency stretched-exponential*) decay rate of small smooth solutions in $\mathbb{R}^n,\ n \geq 4$.

The results have been widely appreciated by researchers and inspired many related work in the field. However, none of those results gives a definite answer to the question of *global well-posedness and long-time behavior of large smooth solutions* of (0.3), even in $\mathbb{R}^1$. The question is directly related to validating the results obtained in [14] under general conditions on initial data. Furthermore, the frequency-by-frequency time decay rate of small smooth solutions is restricted to the case in which the spatial dimension is greater than three which is unrealistic from the biological point of view.

3. Scientific Progress Made.

We have made significant progress during the one-week workshop at BIRS. Here is a list of results obtained during the meeting.

- We developed a novel energy method and proved the global well-posedness and long-time behavior of *large* smooth solutions of the Cauchy problem of (0.3) in $\mathbb{R}^1$. The results showed that constant ground states of the Cauchy problem is *globally stable*. It thus rigorously demonstrated the phenomenon of collapse in chemotactic repulsive problems with non-diffusible signal and logarithmic sensitivity under general conditions. The result is consistent with the explicit and numerical solutions constructed in [14].
- We identified the algebraic time decay rate of of one-dimensional smooth solutions towards constant ground states under very mild conditions on initial data, based on the global well-posedness result and by using weighted energy method.
- We re-developed our Fourier method (cf. [15]) and established a frequency-by-frequency stretched-exponential decay rate of small smooth solutions in $\mathbb{R}^1$ which makes the result biologically meaningful.
- We proved the global well-posedness of *almost large* smooth solutions in $\mathbb{R}^n,\ n = 2, 3$ under very mild conditions on initial data, which improved our previous result obtained in [15].
- The analytic techniques we developed during the workshop are of independent interest and can be applied to a family of chemotaxis models and models in other scientific research areas. Furthermore, they are expected to generate positive outcome in the investigation of the global stability of one-dimensional traveling wave solutions of (0.3) which is an important biological problem and a significant mathematical challenge.

4. Outcome of the Meeting.

Our results obtained for the one-dimensional Cauchy problem have been submitted to a peer-reviewed journal for publication. We are currently in the process of writing up the multi-dimensional results. One of the participants (K. Zhao) presented the one-dimensional results at the SIAM Conference on the Life Sciences which was held in Charlotte, North Carolina, USA, on August 4 - 7, 2014. K. Zhao is also an invited speaker at the 2015 International Congress on Industrial and Applied Mathematics which will be held in Beijing, China. The results obtained during the workshop will be reported at the conference.

References

[1] J. Adler. Chemotaxis in Bacteria. *Science* **153** (1966): 708–716.

[2] W. Alt and D. Lauffenburger. Transient behavior of a chemotaxis system modeling certain types of tissue inflammation. *J. Math. Biol.* **24** (1987): 691–722.

[3] D. Balding and D.L. McElwain. A mathematical model of tumour-induced capillary growth. *J. Theor. Biol.* **114** (1985): 53–73.

[4] E. Budrene and H. Berg. Complex patterns formed by motile cells of Escherichia coli. *Nature* **349** (1991): 630–633.

[5] E. Budrene and H. Berg. Dynamics of formation of symmetrical patterns by chemotactic bacteria. *Nature* **376** (1995): 49–53.

[6] F. W. Dahlquist, P. Lovely, and D. E. Jr Koshland. Qualitative analysis of bacterial migration in chemotaxis. *Nature, New Biol.* **236** (1972): 120–123.

[7] R.M. Ford and D.A. Lauffenburger. Measurement of bacterial random motility and chemotaxis coefficients: II. application of single cell based mathematical model. *Biotechnol. Bioeng.* **37** (1991): 661–672.

[8] R.M. Ford, B.R. Phillips, J.A. Quinn and D.A. Lauffenburger. Measurement of bacterial random motility and chemotaxis coefficients: I. stopped-flow diffusion chamber assay. *Biotechnol. Bioeng.* **37** (1991): 647–660.

[9] T. Hillen and K. Painter. A user's guide to PDE models for chemotaxis. *J. Math. Biol.* **58** (2009): 183–217.

[10] D. Horstmann. From 1970 until present: the Keller-Segel model in chemotaxis and its consequences: I. *Jahresber. Deutsch. Math.-Verein* **105** (2003): 103–165.

[11] E.F. Keller and L.A. Segel. Initiation of slime mold aggregation viewed as an instability. *J. Theor. Biol.* **26** (1970): 399–415.

[12] E.F. Keller and L.A. Segel. Model for chemotaxis. *J. Theor. Biol.* **30** (1971): 225–234.

[13] E.F. Keller and L.A. Segel. Traveling bands of chemotactic bacteria: a theoretical analysis. *J. Theor. Biol.* **26** (1971): 235–248.

[14] H. Levine and B. Sleeman. A system of reaction diffusion equations arising in the theory of reinforced random walks. *SIAM J. Appl. Math.* **57** (1997): 683–730.

[15] D. Li, T. Li and K. Zhao. On a hyperbolic-parabolic system modeling repulsive chemotaxis. *Math. Models Methods Appl. Sci.* **21** (2011): 1631–1650.

[16] J.D. Murray. *Mathematical Biology I: An Introduction*. Springer, Berlin, 3rd edition, 2002.

[17] H. Othmer and A. Stevens. Aggregation, blowup and collapse: The ABC's of taxis in reinforced random walks. *SIAM J. Appl. Math.* **57** (1997): 1044–1081.

[18] Y. Yang, H. Chen, and W. Liu. On existence of global solutions and blow-up to a system of the reaction-diffusion equations modeling chemotaxis. *SIAM J. Math. Anal.* **33** (2001): 763–785.

[19] Y. Yang, H. Chen, W. Liu and B. Sleeman. The solvability of some chemotaxis systems. *J. Differential Equations* **212** (2005): 432–451.