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Multi-scale PDE Inverse Problem in Bacterial Movement

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Abstract By their nature, biological systems evolve to complex structures, posing challenges for mathematical modelling that involve partial differential equations (PDEs). Experimental data is used to bridge the gap between simplified models and real world applications. The models as well as the associated inverse problems exhibit a multi-scale structure. In this article, we summarize recent studies on the multi-scale behaviour of PDE inverse problems for models of bacterial movement.

Keywords Inverse problems · Multi-scale modelling · Kinetic chemotaxis model · Parameter reconstruction · Keller-Segel model · Diffusion scaling limit

1 Introduction

Biological systems are complex and fundamental principles of operation are frequently not fully understood or extremely detailed as they incorporate influences of a vast number of external and internal stimuli. In both cases, deriving general ab initio models for biological phenomena is often not realizable. One such example is the motion of organisms: even similar species such as different bacteria can develop at least 6 different types of motility [14], each one operating according to its own mechanism. Under these circumstances, one not only has to rely on the physical intuition, but also on measurements collected in the laboratories to fit free parameters in mathematical models, see discussions in [7, 9, 19] for some examples in various settings. In all these examples, some mathematical models are formulated according to some general principles, and experimental data is collected to fit the unknown

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parameters in the models. This procedure falls into the category of inverse problems and is becoming increasingly important in the whole study of mathematical biology. Thanks to the fast advancement in mathematical inverse theory and the increasing power of computation, these problems are also becoming more and more accessible. The detailed inversion procedure heavily depends on the structure of the forward model. In this article we will present this approach on the so-called run-and-tumble model that is used to characterize bacterial motion.

Bacteria such as Escherichia coli (E. coli) possess organs (e.g. flagella) that they use to rotate in different directions so to perform a run-and-tumble movement. In particular, counter-clockwise rotation of the flagella results in a 'running' movement along a straight line in a certain direction while clockwise rotation initiates a 'tumble' movement so to search for a new direction to run in afterwards [17]. This motion of tumbling is frequently induced by an external force such as a chemical gradient, a light source, a food source etc. We consider the example of an attracting chemical substance, in which case the phenomenon is referred to as chemotaxis. The bacterium then steers towards the so called chemoattractant by changing the frequency of its tumbling [3].

Albeit having this general principle, the precise response of the bacteria to the chemoattractant is unknown. In particular, the value of the tumbling parameter typically cannot be directly derived or measured. Different species [3], different chemoattractant concentrations [4], and different environments [24] can also alter the precise value of the parameters. Because the tumbling parameter cannot directly be observed, biologists collect data on the density distribution of bacteria in the lab. One then formulates the inverse problem to infer the tumbling parameter from these data.

We will consider this problem for models in different space-time scales. For this type of systems, the naturally emerging model scales are:

- The *microscopic description* focuses on the individual motion and models the trajectories of single bacteria by stochastic differential equations [26, 29].
- On the *mesoscopic level*, the phenomenon is described from a statistical point of view: models are formulated to evolve the distribution densities of bacteria on the phase space and the bacteria's motion in different directions are incorporated [1, 10].
- The *macroscopic description* is of fluid type. The models describe the evolution of the bacteria density as a function of space and time [15, 22].

In a fixed experimental setup, the scale of the problem is roughly set fixed, and in this fixed regime, some models might be more suitable and would be selected as the fundamental model. However, these models are not completely independent of each other. In particular, there are studies that reveal the relation between these models, and it can be shown that models, in certain asymptotic regimes, are equivalent to each other [4, 21].

Associated to these models, one may have various options of the inverse problems. In this paper we review recent results on parameter inference for mesoscopic and macroscopic chemotaxis systems, where we are particularly interested in the scaling behaviour of the inverse problem.

The article is structures as follows. At first, the mesoscopic chemotaxis model is introduced and the inverse problem is explained. We then present results that guarantee a unique reconstructability of the tumbling parameter in this case. Afterwards, the macroscopic model (named Keller-Segel equation) and the associated inverse problem are explained. The connection between the two inverse problems in mesoscopic and the macroscopic scale is studied in the Bayesian framework. The article concludes with an outlook on open problems.

2 Chemotaxis Equation—Forward and Inverse

Mesoscopic, also called kinetic, descriptions of chemotaxis were first proposed in [1, 27]. They model the propagation of the population density $f(x, t, v)$ of bacteria as a function of space $x \in \mathbb{R}^3$, time $t \in [0, T]$ and velocity $v \in V$ that these bacteria run into. We use a standard simplification that tumbling happens instantaneously and bacteria run exactly at the same speed, without loss of generality $V = \mathbb{S}^2$. Furthermore, we assume that the chemoattractant concentration is a fixed function $c(x)$ independent of time and of the bacteria density (in particular bacteria do not consume or produce it). For a given initial condition $\phi \in C_c^\infty(\mathbb{R}^3 \times V)$, the kinetic model reads

$$\begin{aligned} &\partial_t f + v \cdot \nabla f = \int_V K(x, v, v') f(x, t, v') - K(x, v', v) f(x, t, v) \, \mathrm{d}v', \qquad (1) \\ &f(x, t = 0, v) = \phi(x, v) \end{aligned}$$

where $K(x, v, v')$, the so called tumbling kernel, encodes the probability of tumbling from velocity v' to v at location x. This kernel is implicitly affected by the chemoattractant concentration.

The inverse problem amounts to reconstructing K from measurements of f. In the lab experiment, we assume bacteria are placed in the environment in a controlled fashion. After some time, the bacteria density is measured locally in time and space. One problem arising in this context is that velocity dependent measurements $f(x, t, v)$ require specially designed equipment and are barely feasible. Instead, macroscopic measurements of the velocity averaged bacteria density

$$\rho(x, t) := \langle f\ (x, t) \langle f \rangle := \int_V f(x, t, v) \, \mathrm{d}v,$$

though more common, lose out on the velocity information. As such, one may naturally not suspect the possibility of reconstruction the collision kernel $K(x, v, v')$.

To be more precise, we assume knowledge of the following measurement generating map

$$\Lambda_K : \ C^\infty_{c,+}(\mathbb{R}^3 \times V) \times C^\infty_{c,+}(\mathbb{R}^3 \times [0,T]) \to \mathbb{R}, \qquad (2)$$
$$(\phi, \mu) \mapsto M_\mu(f^\phi) = M_\mu(\rho^\phi) := \int_0^T \int_{\mathbb{R}}^3 \rho^\phi(x,t)\mu(x,t)\,\mathrm{d}x\,\mathrm{d}t,$$

where ρ^ϕ is the macroscopic bacteria density corresponding to the solution f^ϕ of (1) with initial condition ϕ, and μ denotes a test function in space time. We abuse the notation and allow M_μ to either act on f^ϕ or ρ^ϕ directly. If clear from the context, we sometimes omit ϕ, μ in the notation. The map Λ_K is influenced by K, which determines the evolution of f^ϕ.

The precise question is then: Can one reconstruct K using the data coded in the map Λ_K? In [13], we give it a positive answer when we restrict ourselves to an a-prior defined admissible set

$$\mathcal{A}_K := \{K \in C_+(\mathbb{R}^3 \times W) \mid \|K\|_\infty \leq C_K\},$$

with $W := \{(v, v') \in V \times V \mid v \neq v'\}$ and slightly abuse notation, by excluding v from integration domain in (1).

Theorem 1 (Unique reconstruction of K; [13]) *Let $K \in \mathcal{A}_K$. The map Λ_K uniquely determines $K(x, v, v')$. In particular, for any $(x, v, v') \in \mathbb{R}^3 \times V$, by a proper choice of ϕ and μ, one can explicitly express $K(x, v, v')$ in terms of $M_\mu(\rho_\phi)$, with ρ_ϕ being the density associated with f_ϕ that solves* (1).

The proof relies on the singular decomposition technique [2, 6, 18]. We decompose

$$f = f_0 + f_1 + f_{\geq 2},$$

where the part $f_i(x, t, v)$ collects all bacteria in $f(x, t, v)$ that tumbled exactly i times up to time t for $i \in \{0, 1, \geq 2\}$. The different f_i attain different regularity and we use this fact by explicitly constructing initial data ϕ and measurement test function μ with compatible singularities so to trigger this regularity. This helps us to extract the part $M(f_1)$ from the full measurement

$$M(f) = M(f_0) + M(f_1) + M(f_{\geq 2}).$$

We then show that we can reconstruct K from $M(f_1)$.

Intuitively speaking, f_0 cannot contain any information about K, because the bacteria in there did not tumble. Those in $f_{\geq 2}$ tumbled at least twice, so we cannot distinguish the influence of the two tumblings. As a consequence, the only chance of recovering K relies on whether f_1 information can be singled out.

To do so, we design singular initial data that starts off the dynamics at a specific location with a specific velocity, and take measurement also at a very specially designed time and location. This designing is to make sure that there is only one trajectory for a bacterium to start off from the initial location and velocity and end at a particular location at a certain time. So we are ensuring the measured density

reflect all bacteria that tumble at an exact tumbling point, changing exactly from the initial velocity to the new direction.

In [13], we derived the explicit formula for the measurement $M(f_1)$ and see that we can reconstruct $K(x', v', v_i)$ from $M(f_1)$. We also proved that the contribution of f_0 and $f_{\geq 2}$ is negligible in this setting, so $M(f) = M(f_1)$. Altogether, we are able to reconstruct K from the measurements in this setting.

3 Keller-Segel Equation—Forward and Inverse

Another classical description of chemotaxis is given by the Keller-Segel equation on the macroscopic level [15, 22]. Denoting the macroscopic bacteria density by $\rho(x, t)$, for $x \in \mathbb{R}^3, t \in [0, T]$, we have

$$\begin{aligned} &\partial_t \rho - \nabla \cdot (D \cdot \nabla \rho) + \nabla \cdot (\rho \Gamma) = 0, \\ &\rho(x, t = 0) = \psi(x) \in C^\infty_{c,+}(\mathbb{R}^3). \end{aligned} \tag{3}$$

The symmetric diffusion matrix $D(x)$ and drift vector $\Gamma(x)$ are again influenced by the fixed independent chemoattractant concentration $c(x)$.

The macroscopic inverse problem amounts in finding D and Γ, given measurements of ρ. We now assume that we have access to pointwise measurements $\rho(x_m, t_m)$ for all for measurement locations x_m and small times $0 < t_m < t^\star$, i.e. we have knowledge on the measurement generating mapping

$$\Lambda_{D,\Gamma} : C^\infty_{c,+}(\mathbb{R}^3) \times \mathbb{R}^3 \times [0, t^\star] \ni (\psi, x_m, t_m) \mapsto \rho^\psi(x_m, t_m),$$

where ρ^ψ denotes the solution to (3) with initial condition $\rho(x, t = 0) = \psi$. Compared to the kinetic description, it would be a much simpler strategy to show the unique reconstruction of the quantities D and Γ from the above measurements. Since both the unknowns (D and Γ) and the data (ψ and ρ) are of macroscopic nature, presented on the spatial domain (instead of the phase domain), the reconstruction is expected to be feasible. To summarize we have the following theorem on the uniqueness of the reconstruction of D, Γ in the admissible set

$$\mathcal{A}_{D,\Gamma} = \{(D, \Gamma) \mid D \in C^2(\mathbb{R}^3, \mathbb{R}^{3\times 3}) \text{ symmetric\&positive definite}, \Gamma \in C^2(\mathbb{R}^3, \mathbb{R}^3)\}.$$

Theorem 2 (Unique reconstruction of D, Γ) *Let $(D, \Gamma) \in \mathcal{A}_{D,\Gamma}$. The map $\Lambda_{D,\Gamma}$ uniquely determines $D(x), \Gamma(x)$. The pointwise reconstruction $D(x)$, $\Gamma(x)$ can be explicitly expressed by the measurements $\rho^\psi(x_m, t_m)$, the solutions to (3), as functions of time, for specifically designed ψ.*

The proof of the theorem is significantly simpler than that for the previous theorem. We lay out the strategy below.

From knowledge of ρ by $\Lambda_{D,\Gamma}$, we can derive the time derivative of ρ at any location. The linearity of (3) allows a simple reconstruction of D, Γ by a suitable choice of initial data. Indeed, we construct the following algorithmic pipeline to gradually reveal comments of D and Γ at location $a \in \mathbb{R}^3$:

- Step 1—Reconstruct $\nabla \cdot \Gamma(a)$: We set the initial condition $\psi_1(x) \equiv 1$ in a neighbourhood of a. At $t = 0$ we observe

$$\partial_t \rho^{\psi_1}(a, t = 0) + \nabla \cdot \Gamma(a) = 0.$$

  Since we retrieve $\partial_t \rho^{\psi_1}(a, t = 0)$ from the measurements, we have a reconstruction of $\nabla \cdot \Gamma(a)$.
- Step 2—Determine the (k, l)-th entry $D_{kl}(a)$ of $D(a)$: Use the initial data $\psi_2(x) = (x_k - a_k)(x_l - a_l) + 1$ in a neighbourhood of a, where v_i denotes the i-th entry of a vector v. Then

$$\partial_t \rho^{\psi_2}(a, t = 0) - D_{kl}(a) - D_{lk}(a) + \nabla \cdot \Gamma(a) = \partial_t \rho^{\psi_2}(a, t = 0) - 2D_{kl}(a) + \nabla \cdot \Gamma(a) = 0,$$

  where $\partial_t \rho^{\psi_2}(a, t = 0)$ is known from the experiment and $\nabla \cdot \Gamma(a)$ can be reconstructed as above.
- Step 3—Find the entries $\Gamma_k(a)$ of $\Gamma(a)$: For a fixed k, choose the initial data $\psi_3(x) = (x_k - a_k) + 1$ in a neighbourhood of a, so

$$\partial_t \rho^{\psi_3}(a, t = 0) = \sum_i \partial_{x_i} D_{ik}(a) - \Gamma_k(a) - \nabla \cdot \Gamma(a).$$

  We can measure $\partial_t \rho^{\psi_3}(a, t = 0)$ and reconstruct $\partial_{x_i} D_{ik}(a)$ from the reconstructions on D_{ik} in a neighbourhood of a. Because $\nabla \cdot \Gamma(a)$ is known from Step 1, this gives $\Gamma_k(a)$.

We should note that generally speaking D and Γ are linearly reflected in the solution. Like all other linear algebra problems $A \cdot x = b$, there are many ways to design the testing matrix A to infer x, as long as A has the full column rank. What was listed above is simply one version in which we can explicitly represent the unknown variables. A more interesting question is how to design the "testing matrix" A so it is well-conditioned and inversion is robust to error. We leave out that part of the discussion from here.

4 Fluid Limit for the Inverse Problem

In this section, we specifically focus on the limit-passing from chemotaxis equation to the Keller-Segel equation, two fundamental models in math biology that simulate bacteria motion. We discuss the connection between these two inverse problem.

In the forward setting, one can prove that under certain assumptions, these models are asymptotically equivalent [1, 4, 21], i.e. the Keller-Segel equation (3) emerges as the diffusion limit $\varepsilon \to 0$ of the chemotaxis Eq. (1) in a parabolic scaling

$$\begin{aligned} \varepsilon^2 \partial_t f_\varepsilon + \varepsilon v \cdot \nabla f_\varepsilon &= \int_V K_\varepsilon(x, v, v') f_\varepsilon(x, t, v') - K_\varepsilon(x, v', v) f_\varepsilon(x, t, v) \, \mathrm{d}v', \quad (4) \\ f_\varepsilon(x, t = 0, v) &= \phi(x, v). \end{aligned}$$

To be specific, under mild continuity assumptions on K, one can prove that $f_\epsilon \to \rho F$ in $L^\infty([0, T]; L^1_+ \cup L^\infty(\mathbb{R}^3 \times V))$ norm, where F is an equilibrium distribution in velocity and ρ solves (3) with the initial condition $\psi = \langle \phi \rangle$. The diffusion matrix D and drift vector Γ in (3) can be expressed in terms of the zeroth and first order terms K_0, K_1 of the asymptotic expansion $K_\varepsilon = K_0 + \varepsilon K_1 + O(\varepsilon^2)$ of the tumbling kernel. We should stress that ε stands for the spatial and temporal scaling. Small ε means we are looking at a system for which the observation time/space scaling is significantly larger than that of the chemotaxis scattering, i.e. we are in the frequent scattering domain.

In [12], we investigate whether this relation holds true for the inverse problems as well, i.e. if the reconstruction of the tumbling parameters, using the scaled chemotaxis (ε, chem) Eq. (4) as an underlying model, converges to the reconstruction with underlying macroscopic Keller-Segel (KS) model (3). A similar question was studied in [20] for the stationary radiative transfer equation and the diffusion equation.

To exercise the comparison, it would be fair to set up the problem in two different regimes using the same parameter configuration. For example, it would be meaningless to compare the reconstruction of K in the kinetic regime to the reconstruction of (D, Γ) in the parabolic regime. To unify the notations, we assume we are looking to reconstruct the parameters K_0 and K_1, the first two terms in the asymptotic expansion of K in the following admissible set:

$$\begin{aligned} \mathcal{A}'_K = \{ \quad & K_\varepsilon = K_0 + \varepsilon K_1 \quad \forall \varepsilon > 0 \mid K_i \in C^1(\mathbb{R}^3 \times [0, \infty) \times V \times V), \|K_i\|_{C^1} \le C, \quad (5) \\ & i = 0, 1, \text{ and } 0 < \alpha \le K_0 \text{ symmetric and } K_1 \text{ antisymmetric in } (v, v')\}. \end{aligned}$$

Together with further (mild) requirements it is guaranteed that the two forward models converge uniformly over this admissible set. Generalizations to other admissible sets are possible, see also [12].

To characterize the limit-passing procedure of the two associated inverse problems, we take on the Bayesian perspective [8, 28]. It is a numerical strategy to assign the probability measure of all possible configurations of the unknown parameter that may produce data that matches the measurement. Due to the flexibility of this Bayesian framework, one also can relax the requirement of needing the entire measurement map but rather utilize finite data set. This relaxation permits a much more practical use of the framework.

We once again restrict ourselves to macroscopic data, where this time, we assume fixed time measurement. The data is thus given by

$$\mathcal{G}_{ij}^{\varepsilon,\mathrm{chem}}(K_\varepsilon) := \mathcal{M}_{\chi_i}\left(\langle f_\varepsilon^{\phi}\rangle\right) = \int_{\mathbb{R}^3}\int_V f_\varepsilon^{\phi_j}(x,t_i,v)\ \mathrm{d}v\ \chi_i(x)\,\mathrm{d}x\,,$$

$$\mathcal{G}_{ij}^{\mathrm{KS}}(K_\varepsilon) := \mathcal{M}_{\chi_i}\left(\rho^{\langle\phi\rangle}\right) = \int_{\mathbb{R}^3}\rho^{\langle\phi_j\rangle}(x,t_i)\,\chi_i(x)\,\mathrm{d}x, \qquad 1\le i\le I, 1\le j\le J,$$

where $f_\varepsilon^{\phi_j}$ solves (4) with initial condition $\phi_j \in C^1_{c,+}(\mathbb{R}^3, V)$ and $\rho^{\langle\phi\rangle}$ solves (3) with initial condition $\langle\phi_j\rangle$. We stipulate a $L^1\cap L^\infty$ bound on the initial conditions ϕ_j uniformly in j. The measurement times t_i are in $[0,T]$ and the measurement test functions $\chi_i \in C_c(\mathbb{R}^3)$ are uniformly in i bounded in $L^1\cap L^2\cap L^\infty$ with uniformly bounded support volume. All measurements are collected in a matrix $\mathcal{G} = (\mathcal{G}_{ij})_{i,j} \in \mathbb{R}^{I\times J}$.

The available data is supposed to be the polluted version $y = \mathcal{G} + \eta$ of the measurements, where $\eta \in \mathbb{R}^{I\times J}$ has independent and identically $N(0,\gamma^2)$ distributed entries of known variance $\gamma^2 > 0$.

Bayes' theorem states that if an a-priori guess on the distribution is known, termed μ_0 and supported on $\mathcal{A}'_K$, then given the measurements $y\in\mathbb{R}^{I\times J}$, the posterior distribution given this knowledge is:

$$\mu_\star^y(K_\varepsilon) = \frac{1}{Z^\star} e^{-\frac{1}{2\gamma^2}\|\mathcal{G}^\star(K_\varepsilon)-y\|^2}\,\mu_0(K_\varepsilon)\,, \qquad \star\in\{(\mathrm{chem},\varepsilon),\mathrm{KS}\} \tag{6}$$

where $Z^\star$ is a normalization constant to ensure that $\mu_\star^y$ is a probability distribution again. The posterior distribution $\mu_\star^y$ is the solution to the Bayesian inverse problem with underlying model $\star$. The norm $\|\mathcal{G}^\star(K_\varepsilon)-y\|$ should be understood in the Frobenius manner.

The goal now becomes to precisely characterize the similarity and differences between the posterior distributions produced by the two distinct forward models (4) and (3). It would be natural to expect that as the two forward models asymptotically approximate each other, the associated Bayesian inverse distribution would also get close.

To measure the distance of two probability distributions μ_1,μ_2, we use the Kullback-Leibler (KL) divergence d_{KL} and the Hellinger metric d_{Hell}, assuming μ_1,μ_2 are absolutely continuous w.r.t. each other or w.r.t. a third probability measure μ_0

$$d_{\mathrm{KL}}(\mu_1,\mu_2) := \int_{\mathcal{A}'_K}\left(\log\frac{d\mu_1}{d\mu_2}(u)\right)d\mu_1(u),$$

$$d_{\mathrm{Hell}}(\mu_1,\mu_2)^2 := \frac{1}{2}\int_{\mathcal{A}'_K}\left(\sqrt{\frac{d\mu_1}{d\mu_0}(u)}-\sqrt{\frac{d\mu_2}{d\mu_0}(u)}\right)^2 d\mu_0(u).$$

Finally, we could show the following theorem.

Theorem 3 (Bayesian Multiscale Convergence; [12]) *In the above setting, the Bayesian posterior distribution for the tumbling kernel derived from the scaled kinetic*

chemotaxis Eq. (4) *and the macroscopic Keller Segel equation* (3) *as underlying models are well posed and asymptotically equivalent in the Kullback Leibler divergence and the Hellinger metric*

$$d_{KL}(\mu^y_{\varepsilon,chem}, \mu^y_{KS}) \xrightarrow{\varepsilon\to 0} 0, \qquad d_{Hell}(\mu^y_{\varepsilon,chem}, \mu^y_{KS}) \xrightarrow{\varepsilon\to 0} 0.$$

The proof can be summarized as follows:

- By boundedness of the initial data and the measurement test function, the conservation of total mass establishes the boundedness of the measurements $\mathcal{G}^\star_{ij}$.
- The measurability of the likelihoods $e^{-\frac{1}{2\gamma^2}\|\mathcal{G}^\star(K_\varepsilon)-y\|^2}$ is a consequence of the Lipschitz continuity of the measurements w.r.t. K_ε. The well-definedness and continuity of the posterior distributions w.r.t. each other and w.r.t. the prior distribution are mere consequences.
- Stability w.r.t. the data y originates from the relaxation introduced by the Bayesian posterior (6). In total, this gives well-posedness.
- For the convergence result, we additionally need uniform convergence $f_\varepsilon \to \rho F$ over the admissible set. Together with the boundedness of initial data and measurement test function, this gives uniform over $\mathcal{A}'_K$ convergence of the measurements $\mathcal{G}^{\text{chem},\varepsilon} \to \mathcal{G}^{\text{KS}}$.
- Together with the uniform boundedness of $\mathcal{G}$ on $\mathcal{A}'_K$ and in ε, we could follow the steps in [20] and show that the integrand of the Kullback-Leibler divergence asymptotically vanishes, uniformly on $\mathcal{A}'_K$.
- Convergence in KL divergence implies convergence in the Hellinger metric by the bound $d^2_{\text{Hell}} \le d_{\text{KL}}$.

In summary, this shows that the Bayesian inverse problems are asymptotically close in the KL divergence and the Hellinger metric.

5 Open Problems (Stabilize the Inverse System)

So far, the stability of the inverse problems in Sects. 2 and 3 has not been considered yet. Because of potential measurement errors, this is an important point in inverse problems and a lack of stability can, as for the Calderon problem, lead to severe problems. Tracing the stability in the scaling limit might lead to additional insights. An example is presented in [5, 16], where the authors show the stability degradation in the diffusion limit for the stationary radiative transport equation, explaining the seemingly contrast of a well-posed inverse problem for stationary radiative transport converging to an ill-posed one for the diffusion equation.

This poses another interesting question: Considering an instable macroscopic inverse problem as a scaling limit of a corresponding stable kinetic inverse problem, can we somehow hybridize the systems so to combine the computational efficiency of macroscopic low dimensional model with the stability of the kinetic system? How

can we merge the information from both systems and which mechanisms can be used to induce better stability? How could a corresponding experimental strategy look like?

These theoretical questions could help to develop efficient numerical strategies to solve the considered inverse problems and adapt the models to reality. Numerical inversion typically relies on PDE-constrained optimization or relaxation approaches, which might be adapted to exploit the multiscale nature of the models so to improve stability. These computationally more expensive methods are now more feasible than ever given the increasing computational power at hand. Apart from that, the downside of high dimensionality of a fully kinetic reconstruction may up to some extent be leveraged by incorporating the macroscopic knowledge. A very easy example could be using a macroscopic reconstruction as a starting point for an iterative kinetic reconstruction.

Sticking to the example of chemotaxis, new models have been developed improving the modelling on different scalings, compare for instance [11, 23, 25] just to mention some. Frequently, internal states of bacteria are incorporated in the model as an additional free variable. These model can not only describe the diffusive motion as in the Keller-Segel equation (3), but also super-diffusive motion, which can under certain circumstances be experimentally observed. Adapting these models to real experiments generates new inverse problems for which the same well-posedness and multiscale convergence questions apply.

In summary, the fields of multiscale inverse problems and inverse problems for biological systems pose many interesting opportunities to develop application driven mathematical tools.

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