Moment closure methods for cell motion in fiber structures

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Content

- Kinetic models
- Balance equations and moment closures
- Application: Tumor cell migration in tissue
- Application: Chemotaxis on networks

Kinetic equation

Consider $x \in \mathbb{R}^n$, and $v \in V = \mathbb{S}^2$, $\epsilon > 0$.
The kinetic equation for the cell density function f is

$$\partial_t f + \frac{1}{\epsilon} v \cdot \nabla_x f = (\frac{1}{\epsilon^2}\mathcal{L}_1 + \frac{1}{\epsilon}\mathcal{L}_2)f,$$

The turning operators $\mathcal{L}_1$ and $\mathcal{L}_2$ are

$$\mathcal{L}_i f = \int_V \left(k_i(x, v, v')f(v') - k_i(x, v', v)f(v)\right) dv', \quad i \in \{1, 2\}.$$

with

$$\int_V \mathcal{L}_i(f)(v)dv = 0.$$

Chalub, F., Markowich, P., Perthame, B., Schmeiser, C.: Kinetic models for chemotaxis and their drift-diffusion limits. (2004)

Hillen, T., Othmer, H.G.: The diffusion limit of transport equations derived from velocity jump processes. (2000)

Assume an equilibrium probability distribution $F = F(x, v) > 0$, $\langle F \rangle = \int_V f(v)dv = 1$ that is first-order symmetric,

$$\langle vF \rangle = 0$$

and fulfills for each $x \in \mathbb{R}^n$ the detailed balance condition

$$k_1(x, v', v)F(x, v) = k_1(x, v, v')F(x, v').$$

Density and mean flux

$$\rho = \int_V f dv = \langle f \rangle, \quad q = \langle vf \rangle.$$

As $\epsilon \to 0$ one obtains convergence to a drift-diffusion equation for ρ. We consider two examples for turning kernels.

Haptotaxis-kernels

Choose the kernels k_1 and k_2 as

$$k_1(x, v, v') = \eta F,$$
$$k_2(x, v, v') = -\lambda_H \nabla_x Q \cdot v' F.$$

- $\eta =$ constant: part of the turning rate independent of the cell-state.
- $F = F(x, v)$: normalized directional distribution of tissue fiber, in general not isotropic, $\langle vF \rangle = 0$.
- $Q = Q(x)$: macroscopic volume fraction of tissue fibers.
- $\lambda_H = \lambda_H(Q(x))$: cell-state dependent part of the turning rate.
- $\epsilon = \frac{x_0}{t_0 c}$, c the cell-velocity.

Then

$$\partial_t f + \frac{1}{\epsilon} \nabla_x \cdot (vf) = -\frac{\eta}{\epsilon^2} (f - F\rho) + \frac{1}{\epsilon} \lambda_H \nabla_x Q \cdot (fv - Fq).$$

As ϵ tends to 0 the macroscopic approximation is

$$\partial_t \rho - \nabla_x \cdot (\nabla_x \cdot (\rho D) - \rho \lambda_H \nabla_x Q D) = 0$$

with

$$\eta D = \int_V v \otimes v F dv = D_F$$

which is a generally anisotropic drift-diffusion equation.

Engwer, C., Hillen, T., Knappitsch, M., Surulescu, C.: Glioma follow white matter tracts: a multiscale DTI-based model. (2015)

Chemotaxis-kernels

Consider

$$k_1(x, v, v') = \lambda F(x, v) = \frac{\lambda}{|\mathbb{S}^2|},$$
$$k_2(x, v, v') = \alpha \overline{\nabla m} \cdot v F,$$

with constants λ and α and a limiter chosen for example as

$$\overline{x} = \frac{x}{\sqrt{1 + |x|^2}}.$$

The kinetic equation is given by

$$\partial_t f + \frac{1}{\epsilon} \nabla_x \cdot (vf) = -\frac{\lambda}{\epsilon^2} (f - F\rho) + \frac{1}{\epsilon} \alpha \rho \overline{\nabla m} \cdot v F.$$

Rem.: The chemoattractant concentration $m(t, x)$ is governed by a reaction-diffusion equation.

Rem.: As ϵ tends to 0 the macroscopic approximation is a flux-limited Keller-Segel model.

Balance equations and moment closure approaches

We start with the kinetic equation

$$\epsilon^2 \partial_t f + \epsilon v \cdot \nabla_x f = \mathcal{L}_1 f + \epsilon \mathcal{L}_2 f.$$

Multiplication with 1 and v and integrating with respect to v gives the continuity and momentum equations

$$\begin{aligned} \epsilon \partial_t \rho + \nabla_x \cdot q &= 0, \\ \epsilon^2 \partial_t q + \epsilon \nabla_x \cdot P &= \langle v \mathcal{L}_1 f \rangle + \epsilon \langle v \mathcal{L}_2 f \rangle . \end{aligned}$$

The pressure tensor $P := \langle v \otimes v f \rangle$ contains the second moments of f. These equations have to be closed by an approximation of P (and potentially $\langle v \mathcal{L}_i f \rangle$) using only ρ and q.

One uses an ansatz function $f^A(v;\rho,q)$ with $\left\langle f^A\right\rangle = \rho$ and $\left\langle vf^A\right\rangle = q$. Then

$$P = \langle v \otimes vf\rangle \approx \left\langle v \otimes vf^A\right\rangle = P^A.$$

Resulting system of equations is

$$\begin{aligned}\epsilon\partial_t\rho + \nabla_x \cdot q &= 0,\\ \epsilon^2\partial_t q + \epsilon\nabla_x \cdot P^A(\rho,q) &= \left\langle v\mathcal{L}_1 f^A(\rho,q)\right\rangle + \epsilon\left\langle v\mathcal{L}_2 f^A(\rho,q)\right\rangle.\end{aligned}$$

In the following we consider different ansatz functions and the resulting equations.

Hillen, T.: Hyperbolic models for chemosensitive movement. (2002)

Linear ($P_1^{(F)}$-)closure

One uses the simple linear perturbation ansatz

$$f^A = a(1 + \epsilon v \cdot b)F(v).$$

The multipliers a and b are chosen to fulfill the moment constraints $\langle f^A \rangle = \rho$ and $\langle v f^A \rangle = q$. With $\hat{q} = \frac{q}{\rho}$ one obtains

$$P^A = \rho \hat{P}^A(\hat{q}),$$

with

$$\hat{P}^A(\hat{q}) = \frac{\langle v \otimes v f^A \rangle}{\langle f^A \rangle} = D_F + \epsilon \langle v \otimes v v \cdot b F(v) \rangle ,$$

where $D_F = \langle v \otimes v F(v) \rangle$.

Rem: Closure function might become negative!

Nonlinear ($M_1^{(F)}$-)closure

Use the approximating function

$$f^A = a \exp(\epsilon v \cdot b) F(v) > 0.$$

Again, the multipliers a and b are determined from the moment constraints on f^A

$$(\rho, q) = \left\langle (1, v) f^A \right\rangle = \langle (1, v) a \exp(\epsilon v \cdot b) F(v) \rangle .$$

This gives

$$\hat{q}(b) = \frac{\langle v \exp(\epsilon v \cdot b) F(v) \rangle}{\langle \exp(\epsilon v \cdot b) F(v) \rangle} \quad \text{and} \quad \hat{P}^A(b) = \frac{\langle v \otimes v \exp(\epsilon v \cdot b) F(v) \rangle}{\langle \exp(\epsilon v \cdot b) F(v) \rangle}.$$

Inverting the relation for $\hat{q}(b)$ one obtains $\hat{P}^A(\hat{q})$.

Anile, A.M., Pennisi, S., Sammartino, M.: A thermodynamical approach to Eddington factors. (1991)

Levermore, C.D.: Moment closure hierarchies for kinetic theories. (1996)

Simplified nonlinear closure ($K_1^{(F)}$)

We determine the second moment P^A via an interpolation between the free-streaming value $P_{free} = \rho \frac{q \otimes q}{|q|^2}$ and the equilibrium solution $P_{eq} = \rho D_F$ and make the ansatz

$$P^A = \rho \hat{P}^A(\hat{q}) := \rho \left(\alpha D_F + (1-\alpha) \frac{\hat{q} \otimes \hat{q}}{|\hat{q}|^2} \right),$$

where $\alpha = \alpha(\hat{q})$ has to be chosen such that the realizability conditions, i.e. the fact that the moments can be generated by a non-negative distribution function, are satisfied.

Kershaw, D.S.: Flux Limiting Nature's Own Way: A New Method for Numerical Solution of the Transport Equation. (1976)

Realizability

For every $\rho \geq 0$ and $|\hat{q}| \leq 1$ we need (Cauchy-Schwarz and $v \in \mathbb{S}^2$)

$$\hat{P} - \hat{q} \otimes \hat{q} \geq 0 \text{ and } \operatorname{tr}(\hat{P}) = 1.$$

The trace equality immediately follows for all $\alpha \in \mathbb{R}$ since $\operatorname{tr}(D_F) = \operatorname{tr}(\frac{\hat{q}\otimes\hat{q}}{|\hat{q}|^2}) = 1$. Plugging in the definition of P^A gives that

$$\hat{P}^A - \hat{q} \otimes \hat{q} = \alpha D_F + (1 - \alpha - |\hat{q}|^2)\frac{\hat{q} \otimes \hat{q}}{|\hat{q}|^2}$$

is positive semidefinite if $\alpha \geq 0$ and $1 - \alpha \geq |\hat{q}|^2$. We use

$$\alpha = 1 - |\hat{q}|^2.$$

Rem.: In the special case $D_F = \frac{I}{3}$ the original Kershaw model is recovered.

Higher-order moment models and other angular bases

Let $\boldsymbol{a}(v) = (a_0(v), \ldots a_{K-1}(v))$ be the basis of a K- dimensional subspace of $L^2(V)$. The corresponding moments are defined as $\boldsymbol{u} := \langle f\boldsymbol{a}\rangle$. As before we get a system of equations for the moments

$$\partial_t \boldsymbol{u} + \frac{1}{\epsilon}\nabla_x \cdot \langle v\boldsymbol{a}f\rangle = \left\langle (\frac{1}{\epsilon^2}\mathcal{L}_1(f) + \frac{1}{\epsilon}\mathcal{L}_2(f))\boldsymbol{a} \right\rangle .$$

f is approximated by an ansatz function

$$f^A[\boldsymbol{u}](v) \approx f(v)$$

which depends on the moments, such that we get a closed form

$$\partial_t \boldsymbol{u} + \nabla_x \cdot \left\langle v\boldsymbol{a}f^A \right\rangle = \frac{1}{\epsilon^2}\left\langle \mathcal{L}_1(f^A)\boldsymbol{a} \right\rangle + \frac{1}{\epsilon}\left\langle \mathcal{L}_2(f^A))\boldsymbol{a} \right\rangle .$$

The classical P_N and M_N methods use the ansatz functions

$$f^A = \boldsymbol{\alpha}_N \cdot \boldsymbol{a} \qquad \text{and} \qquad f^A = \exp(\boldsymbol{\alpha}_N \cdot \boldsymbol{a}),$$

respectively. Analogously to the first-order methods we define the modified $P_N^{(F)}$ and $M_N^{(F)}$ as

$$f^A = (\boldsymbol{\alpha}_N \cdot \boldsymbol{a})F(v) \qquad \text{and} \qquad f^A = \exp(\boldsymbol{\alpha}_N \cdot \boldsymbol{a})F(v),$$

respectively, in order to incorporate the equilibrium of the reorientation kernel $F(v)$.

Half moments - Partial moments in one dimension

Given a density function $f(t,x,v)$ with $t \in \mathbb{R}^+$, $x \in \mathbb{R}$ and $v \in V = [-1,1]$, we define half-moments as

$$(\rho_\pm, q_\pm, P_\pm, \cdots) := \int_{V_\pm} (1, v, v^2, \cdots) f dv,$$

with $V_- := [-1,0]$, $V_+ := [0,1]$.
Then one proceeds similarly to the full moment case closing the equations with different closure functions.

Partial moments in higher dimension

- Similarly to the one-dimensional setting one may define higher order partial moment equations in higher dimensions, for example, quarter-moments in 2D. This gives QP_N and QM_N models.
- For the minimum-entropy closures one uses suitable lookup tables .
- A more refined division of angular space and the use of higher order moments yields a hierarchy of discretizations ($\sim$ hp-FE).

Application: Tumor cell migration

- The system of moment equations is discretized using second-order realizability-preserving Finite-Volume schemes with realizability limiters.
- The source code for the numerical simulations builds upon DUNE and DUNE PDELab [4], a C++ numerics framework for PDE'S.
- Goal: Decision support for cancer treatment

Corbin, G., Hunt, A., Schneider, F., Klar, A., Surulescu, C.: Higher-order models for glioma invasion. (2018)

Haptotaxis and glioma invasion

We consider a water diffusion tensors D_W from a DTI scan of the human brain. This is used to obtain the equilibrium fiber distribution as

$$F(v) = \frac{3}{4\pi tr D_W} \left(v^\top D_W v \right).$$

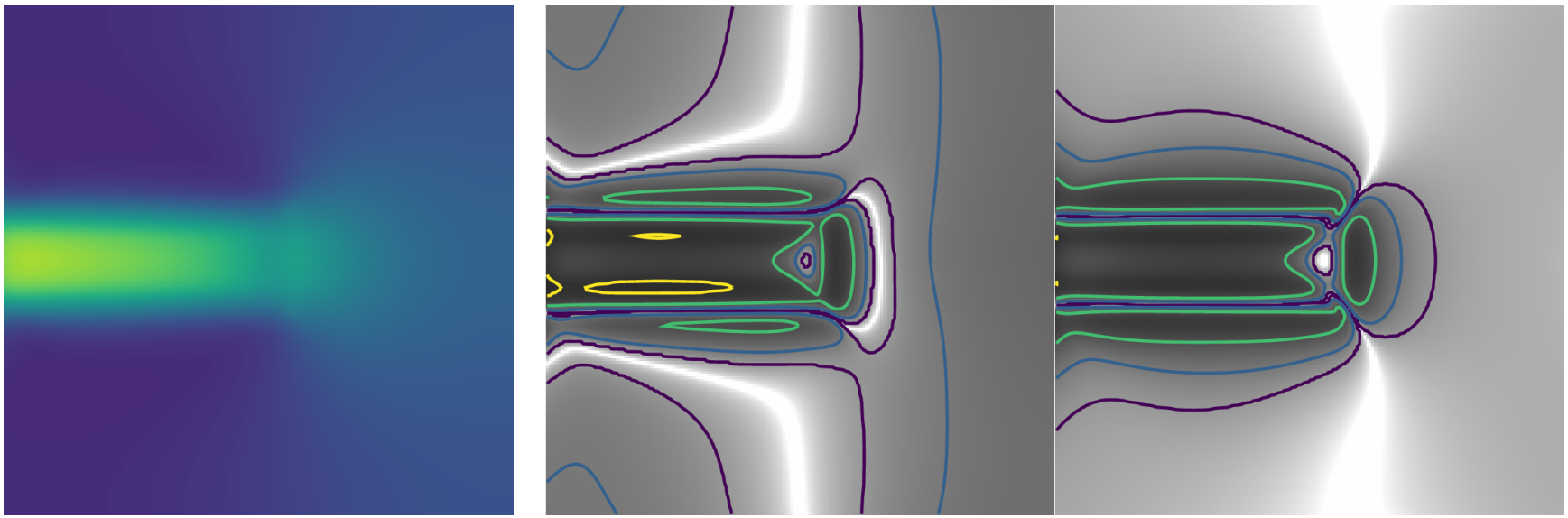
We use the following expression to obtain the volume fractions:

$$Q(x) = 1 - \left(\frac{tr D_W}{4\lambda_1} \right)^{\frac{3}{2}},$$

where λ_1 is the maximum eigenvalue of D_W.

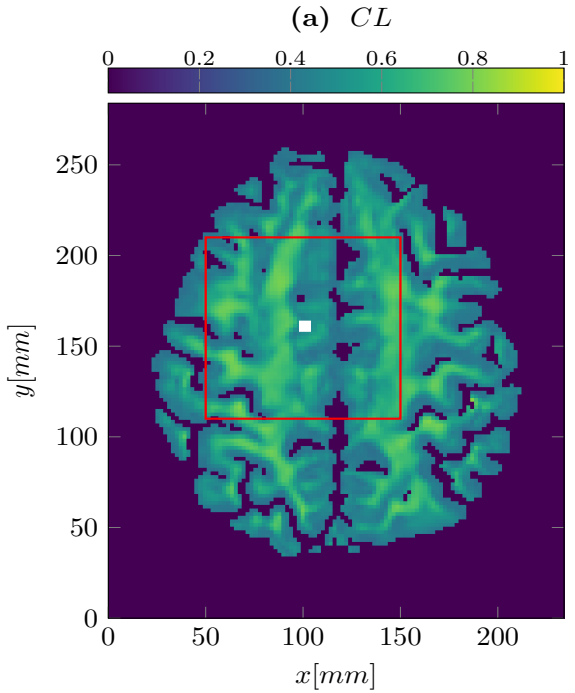
Engwer, C., Hillen, T., Knappitsch, M., Surulescu, C.: Glioma follow white matter tracts: a multiscale DTI-based model. (2015)

P_5^F, Diffusion, K_1^F, $\epsilon = 0.1$.

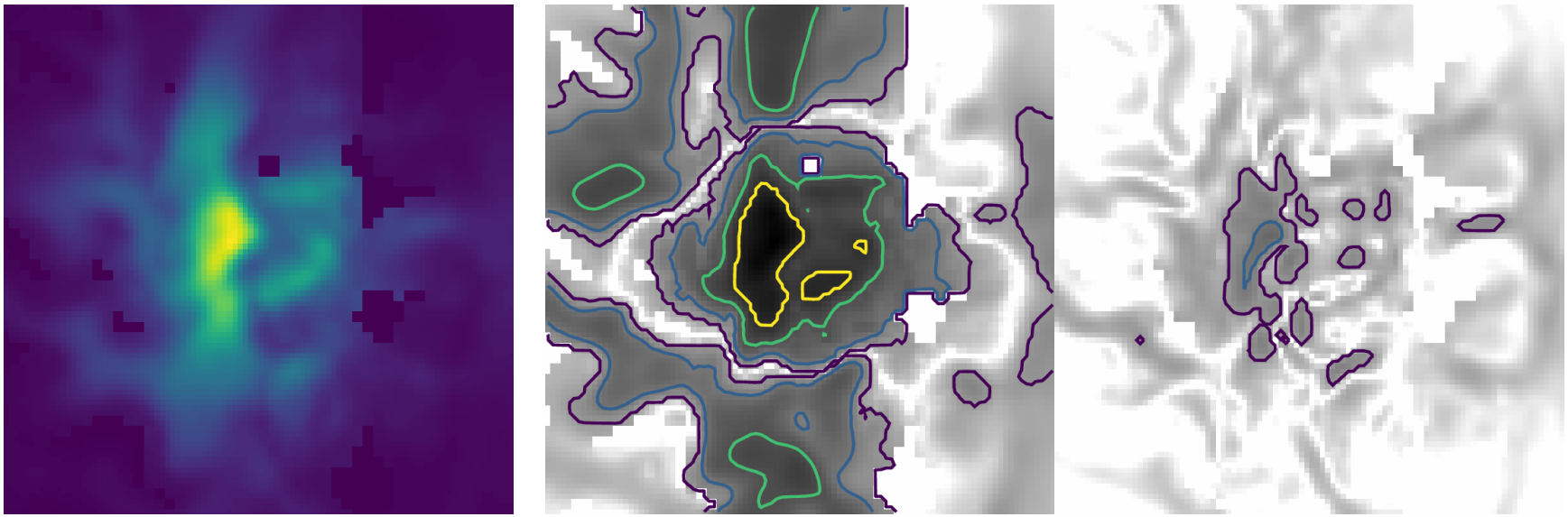


Yellow: 10 % error, green: 5 % , purple: 1 %

Volume fraction and domain of computation.



P_3^F, Diffusion, K_1^F.



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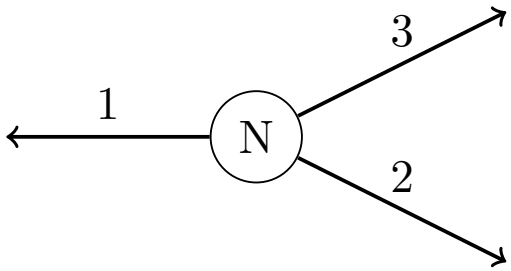
Application: Cell motion on networks

Consider hierarchy of 1D cell-motion equations on a graph



Crucial point: determine coupling conditions at the nodes
Procedure:

- define coupling conditions for kinetic equations
- derive coupling conditions for moment models.

Coupling condition for kinetic equations

Consider node with 3 outgoing edges.
The coupling conditions should assign on each edge a value to all $f(v)$ with $v > 0$. We require:

1. The coupling conditions should be linear and independent of v.
2. The total mass in the system should be conserved.
3. The values of f should remain positive all times.
4. In the limit $\epsilon \to 0$ the conditions should converge to reasonable coupling conditions for the limit equations.

General form

$$f^+ = Af^-,$$

where $f_i^+ = f_i(v)$ and $f_i^- = f_i(-v)$ for $v > 0$. In order to conserve the total mass in the system the matrix $A \in \mathbb{R}^{3\times 3}$ has to fulfill

$$\sum_{i=1}^{3} a_{i,j} = 1 \qquad \forall j = 1, \ldots, 3 \ .$$

We require also

$$\sum_{j=1}^{3} a_{i,j} = 1 \qquad \forall j = 1, \ldots, 3 \ .$$

A typical choice where all edges are treated equally:

$$\begin{bmatrix} f_1^+ \\ f_2^+ \\ f_3^+ \end{bmatrix} = \begin{bmatrix} 0 & 1/2 & 1/2 \\ 1/2 & 0 & 1/2 \\ 1/2 & 1/2 & 0 \end{bmatrix} \begin{bmatrix} f_1^- \\ f_2^- \\ f_3^- \end{bmatrix} \ .$$

Coupling condition for the linear and non-linear half-moment model

We define the quantities $\rho_i^+, \rho_i^-, q_i^+, q_i^-$ for $i = 1, \dots, N$ on each edge. Coupling condition for the half moment model are obtained from the kinetic ones via integration

$$\begin{cases} \begin{bmatrix} \rho_1^+ \\ \rho_2^+ \\ \rho_3^+ \end{bmatrix} = \begin{bmatrix} 0 & 1/2 & 1/2 \\ 1/2 & 0 & 1/2 \\ 1/2 & 1/2 & 0 \end{bmatrix} \begin{bmatrix} \rho_1^- \\ \rho_2^- \\ \rho_3^- \end{bmatrix} \\ \begin{bmatrix} q_1^+ \\ q_2^+ \\ q_3^+ \end{bmatrix} = -\begin{bmatrix} 0 & 1/2 & 1/2 \\ 1/2 & 0 & 1/2 \\ 1/2 & 1/2 & 0 \end{bmatrix} \begin{bmatrix} q_1^- \\ q_2^- \\ q_3^- \end{bmatrix}. \end{cases}$$

These are six equations for six outgoing characteristics (2 per edge) of the half moment system.

Coupling condition for the linear full moment equations (Cattaneo)

Problem: Kinetic conditions are given for parts of the velocity domain. No simple integration over the full velocity domain.
Simple solution: Use the linear full moment closure function and insert it into the kinetic conditions. This gives

$$\begin{bmatrix} 2 & -1 & -1 \\ -1 & 2 & -1 \\ -1 & -1 & 2 \end{bmatrix} \begin{bmatrix} \rho_1 \\ \rho_2 \\ \rho_3 \end{bmatrix} + \epsilon \frac{3}{2} \begin{bmatrix} 2 & 1 & 1 \\ 1 & 2 & 1 \\ 1 & 1 & 2 \end{bmatrix} \begin{bmatrix} q_1 \\ q_2 \\ q_3 \end{bmatrix} = 0 \ .$$

Note that for the linear full moment equation we have one characteristic moving to the right ($\sim$ wave equation). This yields 3 conditions for a node with three edges.

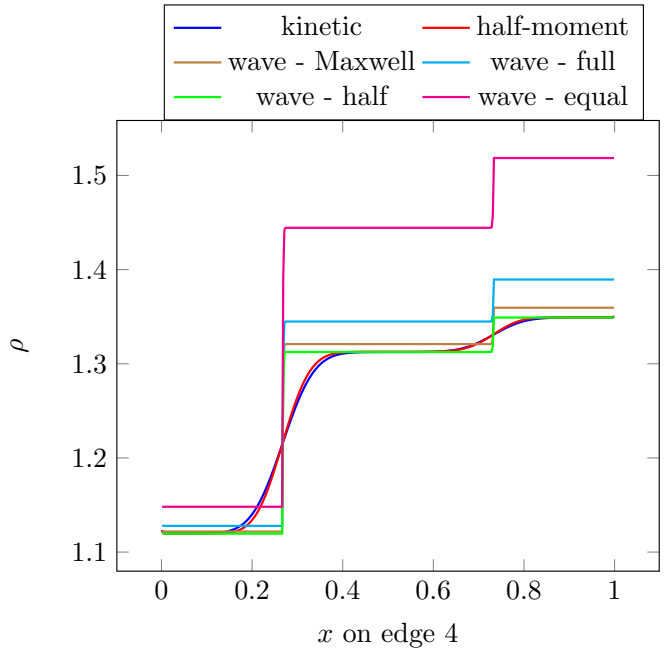
Remarks

- For the linear full moment case similar conditions are treated in

  Bretti, G., Natalini, R., Ribot, M.: A hyperbolic model of chemotaxis on a network: a numerical study. (2014)

- A more detailed analysis of the situation near the node based on kinetic layers leads to more accurate conditions. For a kinetic BGK model and the wave equation, see

  Borsche, R., Klar, A.: Kinetic layers and coupling conditions for macroscopic equations on networks. (2018)



Remarks

- To derive coupling conditions for the nonlinear full-moment approximation from the kinetic ones is a challenging topic: nonlinear kinetic layers, change of the number of required coupling conditions. For a similar problem see

  Borsche, R., Klar, A.: Kinetic layers and coupling conditions for nonlinear scalar equations on networks. (2018)

- For theoretical work on the Keller-Segel model on a network see

  Camilli, F., Corrias, L.: Parabolic models for chemotaxis on weighted networks. (2017)

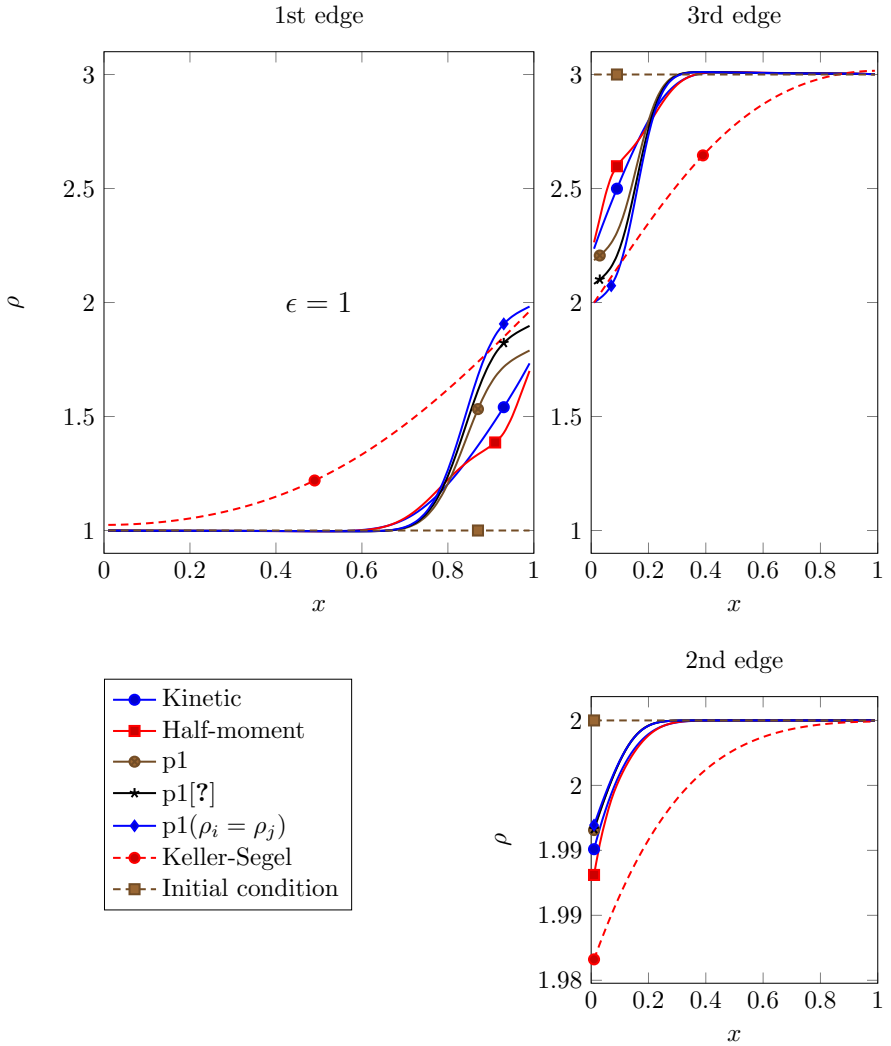
Numerical results on tripod networks

- Consider the chemotaxis model.
- We use for the nonlinear half-moment model the Kershaw approximation.
- The results of the nonlinear half-moment model with the corresponding coupling conditions are compared with the results of the kinetic, linear half and full moment and Keller-Segel model.

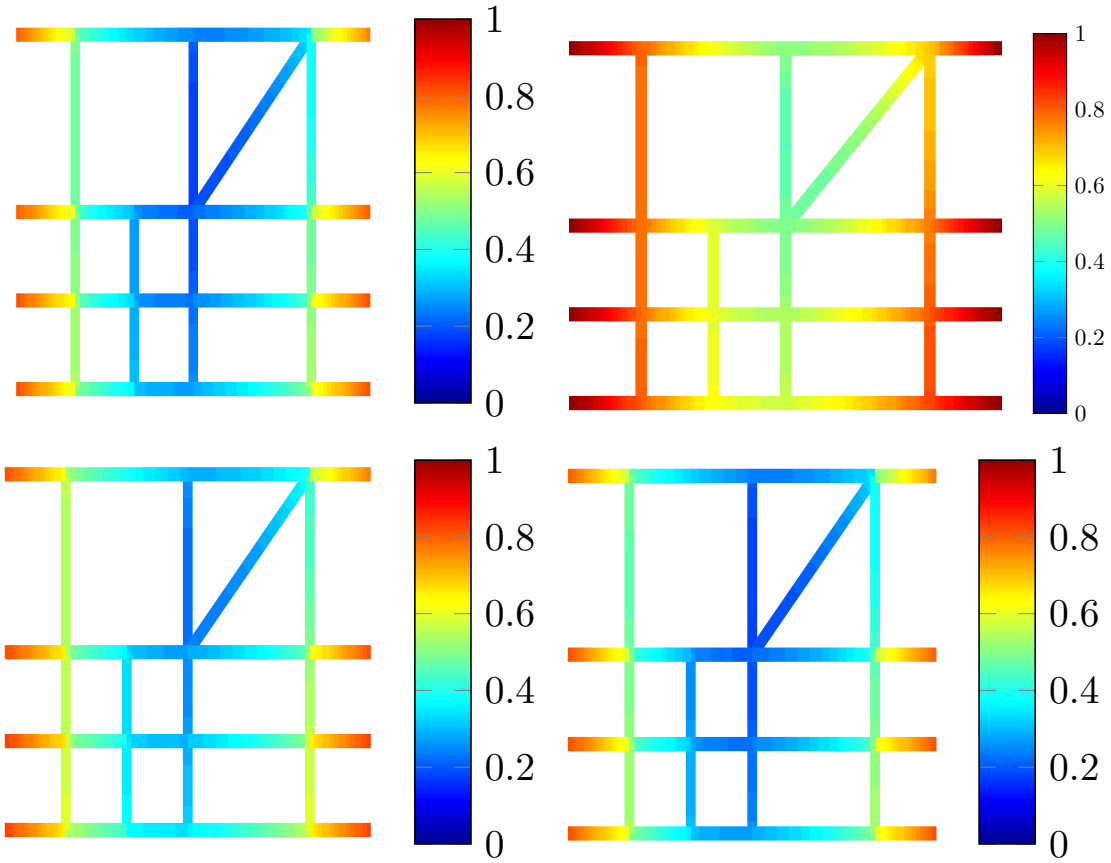
Borsche, R., Kall, J., Klar, A., Pham, T.: Kinetic and related macroscopic models for chemotaxis on networks. (2016)

Borsche, R., Klar, A., Pham, T.H.: Nonlinear flux-limited models for chemotaxis on networks. (2017)

Numerical solutions on a tripod network at time $t = 0.2$, $\Delta x = 0.02$, $\epsilon = 1$

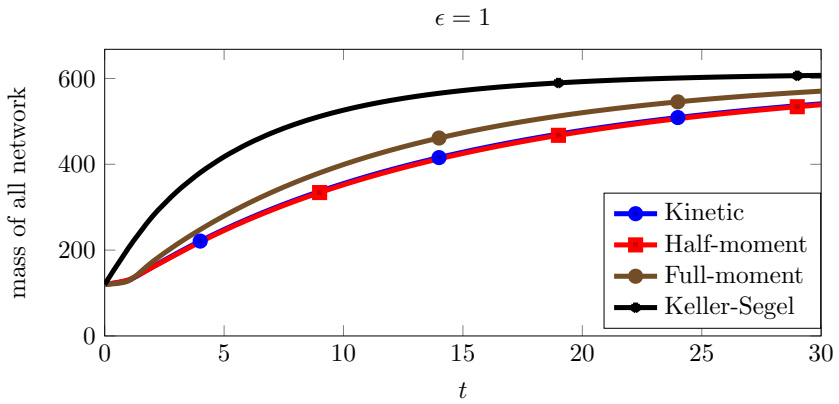


Numerical solutions on a larger network



Kinetic, Diffusion, Full-moment , Half-moment at $t = 5$.

Total mass over time in large network.



Outlook

- numerical method for kinetic equations based on automatic choice of moment expansion and subspace for integration, combination with asymptotic preserving methods for small values of ϵ.
- Calibration and validation of tumor migration models with clinical data: time resolution before and after surgery??
- network models: derivation of coupling conditions for more complicated nonlinear full moment models, e.g. Euler equations, from underlying kinetic models