Modelling of cross linked fiber networks: from agent-based to continuum models

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Summary

1. Context of the research

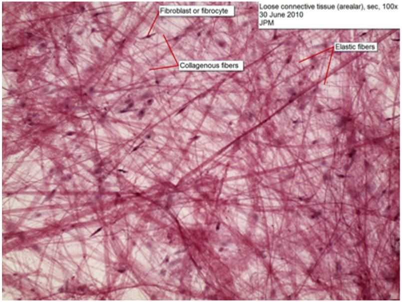
2. Microscopic model for interconnected fiber networks

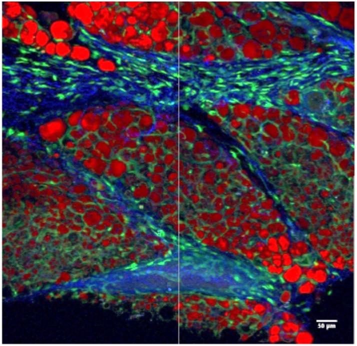
3. Derivation of a macroscopic model for interconnected fibers

4. Summary/perspectives

Biological Framework

Goal: Model the Extra-Cellular Matrix as a network of cross-linked fibers having the ability to reorganize





Derive a hierarchy of models to account for several scales

Use it as a component of a model of tissue self-organization

Modelling process

Goal: Mathematical modelling of cross-linked networks

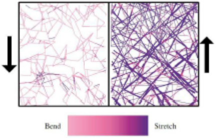
	Microscopic scale **Agent based models**	Macroscopic scale **Continuum models**
Variables	Agent position, speed $(X_i(t), v_i(t)),\ i \in [1, N] \dots$	Density, mean variables $\rho(x,t), \bar{\theta}(x,t) \dots$
Advantages	- Description of each interaction - Link with experimental data	- Computationally efficient - Mathematical framework
Drawbacks	- Computationally challenging - Lack of theoretical results	- Lost of information at the agent scale

Intermediate scale : Mesoscopic scale (Kinetic models)
Variables: probability density $f(x,t)$

Literature: Microscopic and Macroscopic models for cells in fibrous networks

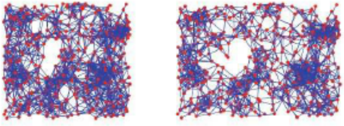
Microscopic models

Cross-linked fibers/ lattice spring models



[Astrom et al], [Broedersz et al], [Head et al], [Buxton and Clarke], ...

Fiber flocking model [Alonso et al]...



Macroscopic models

Phenomenological continuum models

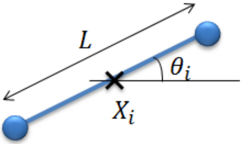
[Joanny, Jülicher, Kruse, Prost, New J. Phys. 07], [Oelz, Schmeiser, Small, Cell Adh Migr 08], ...

Micro to macro approaches: [Degond et al], [Barocas and Tranquillo], [Cacho et al], [Gasser], ...

Microscopic model for an interconnected fiber network

Biological features:

- Fiber cross-linking/unlinking
- Random motion and reorientation



Mechanical features:

- External potential
- Cross-linked fibers retraction force
- Cross-linked fiber alignment force

Global potential:

$$W_{\text{tot}} = W_{\text{ext}} + W_{\text{links}} + W_{\text{align}} + W_{\text{noise}}.$$

Motion (overdamped regime):

$$\frac{dX_i}{dt} = -\mu \nabla_{X_i} W_{\text{tot}}, \qquad \frac{d\theta_i}{dt} = -\lambda \partial_{\theta_i} W_{\text{tot}}, \qquad i \in \{1, \ldots, N\}$$

μ and λ are mobility coefficients.

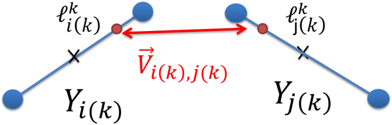
Detail of the potential elements

$$W_{\text{tot}} = W_{\text{ext}} + W_{\text{links}} + W_{\text{align}} + W_{\text{noise}}.$$

External potential U

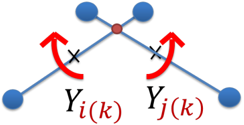
Fiber links:

- Retraction potential between linked fibers



$$W_{\text{links}} = \frac{\kappa}{2} \sum_{k=1}^{K} |V_{i,j}|^2.$$

- Alignment force between linked fibers:



$$W_{\text{align}} = \frac{\alpha}{2} \sum_{k=1}^{K} |\sin(\theta_i - \theta_j)|.$$

Tissue movements: Random noise of intensity d

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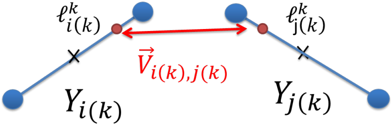

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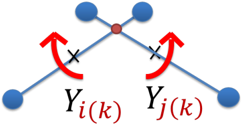

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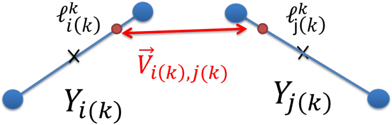

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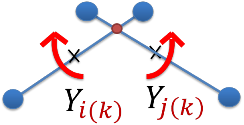

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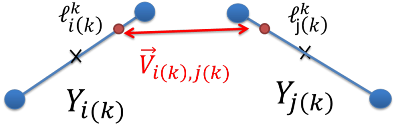

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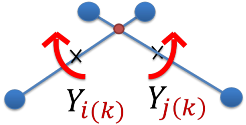

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Tissue movements: Random noise of intensity d

Kinetic model

Density distributions: One and two particle distribution functions

- $f^N(x, \theta, t)$: density distribution of the N individual fibers
- $g^K(x_1, \theta_1, \ell_1, x_2, \theta_2, \ell_2, t)$: density distribution of the K fiber links.

For all observable function $\Phi(x, \theta)$, $\Psi(x_1, \theta_1, \ell_1, x_2, \theta_2, \ell_2)$:

$$\langle f^N, \Phi \rangle = \frac{1}{N} \sum_{i=1}^{N} \Phi(X_i(t), \theta_i(t))$$

$$\langle g^K, \Psi \rangle = \frac{1}{K} \sum_{i=1}^{K} \Psi(X_{i(k)}(t), \theta_{i(k)}(t), \ell^k_{i(k)}, X_{j(k)}, \theta_{j(k)}, \ell_{j(k)}).$$

Limit of large number of individuals

Théorème P. Degond, F. Delebecque, D.P.

In the formal limit $K, N \to \infty$, $\frac{K}{N} \to \xi$, where $\xi > 0$ is a fixed parameter, the kinetic equation for the density distribution of individual fibers reads:

$$\frac{df}{dt} - \mu\Big(\nabla_x \cdot ((\nabla_x U_{ext})f) + \xi \nabla_x \cdot F_1 + d\Delta_x f\Big) - \lambda\Big(\partial_\theta((\partial_\theta U_{ext})f) + \xi \partial_\theta F_2 + d\partial_\theta^2 f\Big) = 0,$$

where

$$F_1(x_1, \theta_1) = \int g \nabla_{x_1} V \, d\ell_1 d\ell_2 \frac{d\theta_2}{\pi} dx_2,$$

$$F_2(x_1, \theta_1) = \int g(\partial_{\theta_1} V + \partial_{\theta_1} b) d\ell_1 d\ell_2 \frac{d\theta_2}{\pi} dx_2$$

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External potential U_{ext}.

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Restoring force between linked fibers V : force terms F_1 and F_2.

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Alignment force between linked fibers b: force term F_2.

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Random motion and reorientation: diffusion terms.

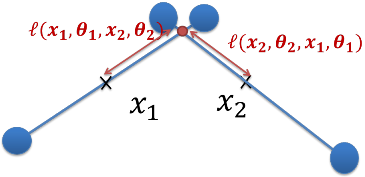
Equation for g

System for g has a similar structure

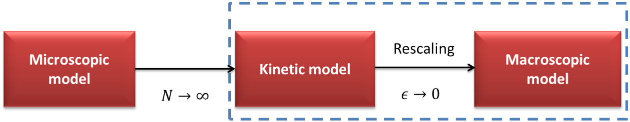
$$\partial_t g - \mu \nabla_{x_1} . \Big[g\big(\nabla_x (U + d \log f) + \xi(F_1/f)\big)|_{(x_1,\theta_1)} \Big]$$
$$- \lambda \partial_{\theta_1} \Big[g\big(\partial_\theta (U + d \log f) + \xi(F_2/f)\big)|_{(x_1,\theta_1)} \Big]$$
$$- \mu \nabla_{x_2} .[\dots] - \lambda \partial_{\theta_2} [\dots] = S(g)$$

Source term $S(g)$ describes link creation/removal:

$$S(g) = \nu_f f(x_1, \theta_1) f(x_2, \theta_2) \delta_{\ell(x_1,\theta_1,x_2,\theta_2)}(\ell_1) \delta_{\ell(x_2,\theta_2,x_1,\theta_1)}(\ell_2) - \nu_d g$$



Rescaling



Macroscopic scaling and scaling assumptions:

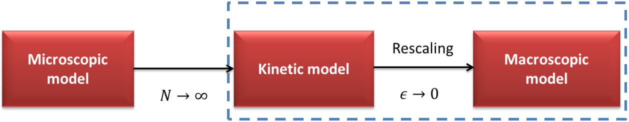
$$\tilde{x} = \sqrt{\varepsilon}x, \quad \tilde{t} = \varepsilon t, \quad f^\varepsilon = \frac{f}{\varepsilon} \quad g^\varepsilon = \frac{g}{\varepsilon^3},$$

- External potential: $U(x, \theta) = U^0(x) + \varepsilon U^1(\theta)$
- Alignment potential between linked fibers: $\alpha = O(\varepsilon^{-1})$,
- Restoring force between linked fibers: $\kappa = O(\varepsilon)$,
- Random motion and reorientation: $d, \xi = O(1)$.
- process of linking/unlinking is supposed to occur at a very fast time scale, i.e. $\tilde{\nu}_f = \varepsilon^2 \nu_f$ and $\tilde{\nu}_d = \varepsilon^2 \nu_d$.

$\Rightarrow$ simplification of g^ε

$$g^\varepsilon = \frac{\nu_f}{\nu_d} f(x_1, \theta_1) f(x_2, \theta_2) \delta_{\ell(x_1,\theta_1,x_2,\theta_2)}(\ell_1) \delta_{\ell(x_2,\theta_2,x_1,\theta_1)}(\ell_2)$$

Rescaled equation



$$\partial_t f^\varepsilon - \nabla_x \cdot (\nabla_x U^0 f^\varepsilon) - \partial_\theta \left(\left[\partial_\theta U^1 + \xi G[f^\varepsilon](x,\theta) \right] f^\varepsilon \right) - d\Delta_x f^\varepsilon = \frac{1}{\varepsilon} Q(f^\varepsilon), \tag{1}$$

where $Q(f^\varepsilon)$ is the collision operator:

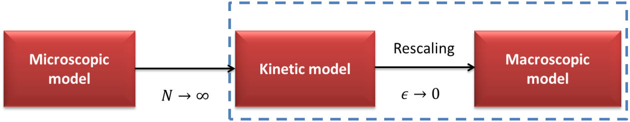
$$Q(f^\varepsilon) = \xi \partial_\theta \left(\partial_\theta \Phi[f^\varepsilon](x,\theta) f^\varepsilon \right) + d\partial_\theta^2 f^\varepsilon$$

External potential
Fibers links:

- ~~Restoring force between linked fibers~~.
- Alignment force between linked fibers.

Random motion and reorientation

Rescaled equation



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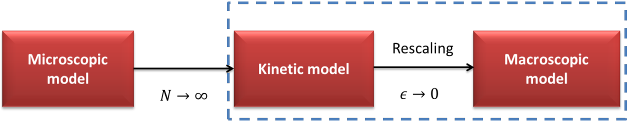

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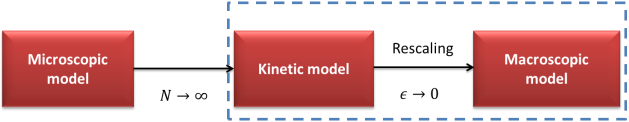

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Random motion and reorientation

Equilibria

Equilibria of the collision operator:

$$Q(f^0) = 0 \quad \Rightarrow \quad f^0 = \rho M_{\theta_0}(\theta) \qquad (\textit{equilibrium}),$$

with $M_{\theta_0}(\theta)$ a generalized Von Mises distribution of θ with θ_0 mean and variance r:

$$M_{\theta_0} = \frac{e^{r\cos 2(\theta-\theta_0)}}{\int_{-\frac{\pi}{2}}^{\frac{\pi}{2}} e^{r\cos 2(\theta-\theta_0)} \frac{d\theta}{\pi}},$$

$$r = \frac{\xi \alpha L^2 \rho c(r) \nu_f}{4 d \nu_d}, \quad c(r) = \frac{\int_{-\frac{\pi}{2}}^{\frac{\pi}{2}} \cos 2\theta e^{r\cos 2\theta} \frac{d\theta}{\pi}}{\int_{-\frac{\pi}{2}}^{\frac{\pi}{2}} e^{r\cos 2\theta} \frac{d\theta}{\pi}}.$$

Need for two equations BUT **momentum not preserved $\Rightarrow$ Generalized Collision Invariants**: function Ψ_{θ_0} such that for functions f with local orientation θ_0

$$\int Q(f) \Psi_{\theta_0} d\theta = 0$$

To find Eqs. for ρ and θ_0:

- Integrate Eq (1)
- Multiply (1) by GCI associated with θ_{f^ε} and integrate

Continuum model

General case:

$$\partial_t \rho - \nabla_x \cdot (\nabla_x U^0 \rho) - d\Delta_x \rho = 0,$$

$$\begin{aligned}
&\rho \partial_t \theta_0 - \rho \nabla_x U^0 \cdot \nabla_x \theta_0 - 2\alpha_2 \nabla_x \rho \cdot \nabla_x \theta_0 - \alpha_2 \rho \Delta_x \theta_0 \\
&\quad + \alpha_3 (\rho \nabla_x^2 \theta_0 + \nabla_x \theta_0 \otimes \nabla_x \rho + \nabla_x \rho \otimes \nabla_x \theta_0) : [\omega_0 \otimes \omega_0 - \omega_0^\perp \otimes \omega_0^\perp] \\
&\qquad + \left(2\rho\alpha_3 \nabla_x \theta_0 \otimes \nabla_x \theta_0 - \alpha_4 \nabla_x^2 \rho\right) : [\omega_0 \otimes \omega_0^\perp + \omega_0^\perp \otimes \omega_0] + \alpha_5 \rho \langle \partial_\theta U^1 \rangle = 0,
\end{aligned}$$

where $\alpha_2, \ldots, \alpha_5$ are fully determined by the model parameters.

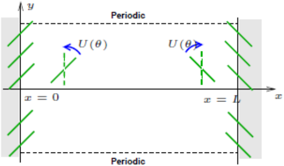
Special case: $\rho = Constant$, $U^0 = 0$

$$\begin{aligned}
\partial_t \theta_0 - \alpha_2 \rho \Delta_x \theta_0 &+ \alpha_3 \nabla_x^2 \theta_0 : [\omega_0 \otimes \omega_0 - \omega_0^\perp \otimes \omega_0^\perp] \\
&+ 2\alpha_3 \nabla_x \theta_0 \otimes \nabla_x \theta_0 : [\omega_0 \otimes \omega_0^\perp]^s + \alpha_5 \langle \partial_\theta U^1 \rangle = 0
\end{aligned}$$

- Problem is parabolic
- Existence of solutions to the stationary problem

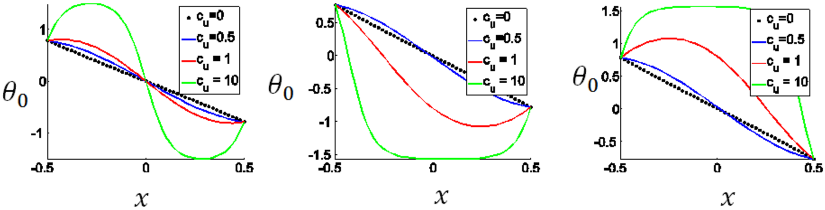
Buckling

Experimental setting:



Numerical method:
Finite differences, Newton algorithm, Continuation method

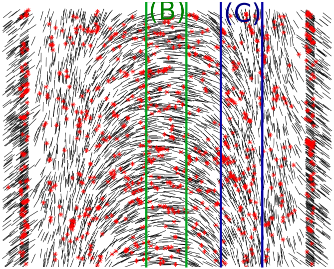
Simulation results:



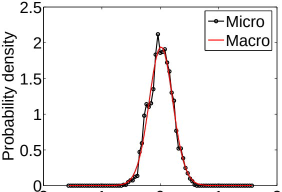
Typical behavior of non linear elastic media

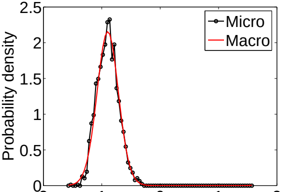
Numerical Micro-Macro comparison: Von Mises distribution

Goal: Compare Individual-based VS Continuum model in the case of homogeneous fiber density



Von Mises distribution for the fiber mean local orientation

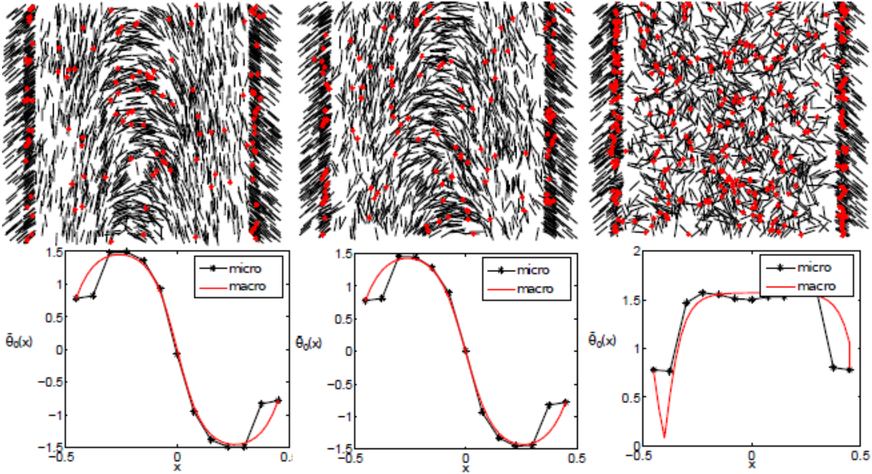




Numerical Micro-Macro comparison: case of small link concentration

Methodology:

- Fit the order parameter from the microscopic simulation
- Use the value for the macroscopic model

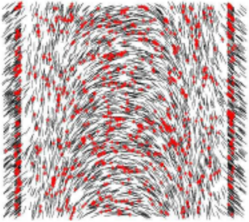


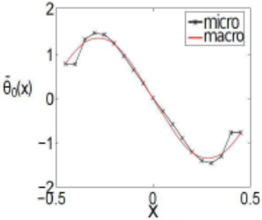
Micro-Macro comparison: case of large link concentration

Methodology:

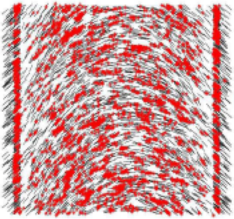
- Fit the order parameter from the microscopic simulation does not work
- Fit the order parameter such that macro simulation match

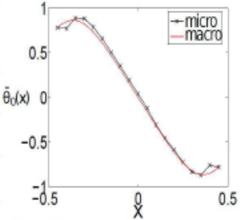
Medium link concentration (10 × higher)





Large link concentration (100 × higher)





Conclusions/perspectives of the works

Summary:

- Derivation of a physically relevant macroscopic model for interconnected fibers
- Macroscopic model in good agreement with the microscopic dynamics

Future works:

- Rigorous derivation of the macroscopic model
- Numerical and theoretical analysis for a non homogeneous fiber density
- Case of non instantaneous linking/unlinking

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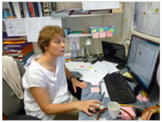

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Thank you for your attention

Equations for ρ and θ_0

Main tools:

- Integrate in θ ($\int Q(f^\varepsilon)d\theta = 0$):

$$\int_\theta \left(\partial_t f^\varepsilon - \nabla_x \cdot (\nabla_x U^0 f^\varepsilon) - \partial_\theta \left(\left[\partial_\theta U^1 + \xi G[f^\varepsilon](x,\theta) \right] f^\varepsilon \right) - d\Delta_x f^\varepsilon \right) d\theta = 0,$$

Equations for ρ and θ_0

Main tools:

- Integrate in θ ($\int Q(f^\varepsilon)d\theta = 0$):

$$\int_\theta \left(\partial_t f^\varepsilon - \nabla_x \cdot (\nabla_x U^0 f^\varepsilon) - \partial_\theta \left(\left[\partial_\theta U^1 + \xi G[f^\varepsilon](x,\theta) \right] f^\varepsilon \right) - d\Delta_x f^\varepsilon \right) d\theta = 0,$$

- Integrate against Collision Invariants Ψ:

$$\int_\theta \left(\partial_t f^\varepsilon - \nabla_x \cdot (\nabla_x U^0 f^\varepsilon) - \partial_\theta \left(\left[\partial_\theta U^1 + \xi G[f^\varepsilon](x,\theta) \right] f^\varepsilon \right) - d\Delta_x f^\varepsilon \right.$$
$$\left. = \frac{1}{\varepsilon} Q(f^\varepsilon)\Psi \right) d\theta,$$

Problem: Momentum **not** preserved $\Rightarrow$ integrate against **Generalized** collision invariant Ψ_{θ_0}, i.e function Ψ_{θ_0} such that for functions f with local orientation θ_0

$$\int Q(f)\Psi_{\theta_0} d\theta = 0$$