

Modèles mathématiques pour des écosystèmes complexes

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Outline

1. Optimisation of phototrophic biofilm productivity,
 - ▶ Colon & gut microbiota in a nutshell,
 - ▶ Mathematical model,
 - ▶ Simulations,
 - ▶ Conclusion & Perspectives,
2. Gut ecology,
 - ▶ Colon & gut microbiota in a nutshell,
 - ▶ Fluids mechanics of the gut,
 - ▶ Generalisation toward a more detail model,
 - ▶ Simulations,
 - ▶ Conclusion & Perspectives,

Phototrophic biofilm

Phototrophic?

Biofilm using light and inorganic carbon source to growth.



(a) Rotating microalgae biofilm device
Hans C. Bernstein et al. 2014

Motivation:

Credible alternative for biofuels

Why?

- ▶ High production yield for lipids,
 - ▶ Easy to harvest (just scalp),
 - ▶ A wide variety of species,
 - ▶ Can develop in sea and oceans,
 - ▶ Combined with wastewater treatment?

Objective:

Quantify the influence of growing conditions and harvest on productivity.



Fig. 2 The vertical phototrophic biofilm reactor (**a**), a close-up of the biofilm before harvesting (**b**), harvesting part of the biofilm with the adhesive comb (**c**), and the biofilm setup after harvesting (**d**)

Figure: Boelee et al. 2014

- ▶ **Observation:** Harvesting pattern impact biofilm productivity
- ▶ **Question:** What is the optimal harvesting strategy?
- ▶ **Context:**
 - Collaboration with biologist and experimentalist:
 - O. Bernard (Lov & Inria),
 - F. Lopes (CentraleSupélec),
 - A. Fanesi (CentraleSupélec),
 - M. Ribot (Institut Denis Poisson)

Theoretical framework for mixture theory

Mixture of $K \geq 1$ constituents: \mathbf{C}_k , each constituent is described by:

- ▶ Its volume fraction: $\phi_k(t, x) := \lim_{\mathbb{V} \rightarrow 0} \frac{\text{volume of } \mathbf{C}_k \text{ in } \mathbb{V}}{\text{volume of } \mathbb{V}}$
- ▶ Its speed $V_k(t, x)$
- ▶ Its mass density ρ_k (assumed constant)

Fundamental properties:

- ▶ Total volume conservation: $\sum_{k=1}^K \phi_k = 1$
- ▶ Mass balance equation:

$$\underbrace{\partial_t(\phi_k \rho_k) + \nabla_x \cdot (\phi_k \rho_k V_k)}_{\text{transport}} = \underbrace{\nabla_x \cdot (D_k \nabla_x(\phi_k \rho_k))}_{\text{diffusion}} + \underbrace{\Gamma_k}_{\text{exchanges}}$$

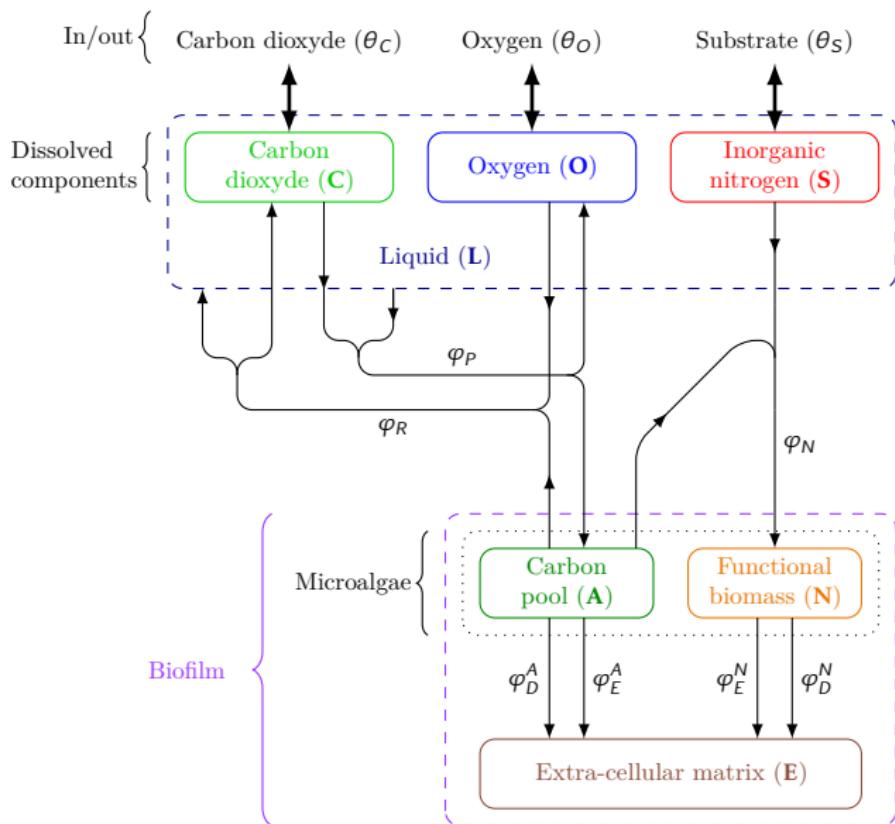
- ▶ Momentum conservation (Force balance equation):

$$\underbrace{\partial_t(\phi_k \rho_k V_k) + \nabla_x \cdot (\phi_k \rho_k V_k \otimes V_k)}_{\text{inertial terms}} = \underbrace{-\phi_k \nabla_x P}_{\text{pressure}} + \underbrace{F_{\text{fric}} + F_{\text{visc}} + \dots}_{\text{other forces}}$$

Advantages:

- Mesoscale
- Physical constraints included
- Different properties for each \mathbf{C}_k
- Interfaces without free boundary

Schematic representation of the system



Mixture framework – Mass balance

- Total volume conservation: $A + N + E + L = 1$
- Mass conservation: Transport

$$\text{Microalgae} \quad \left\{ \begin{array}{ll} \text{Carbon pool:} & \partial_t A + \nabla_x \cdot (A \mathbf{V}_M) = \Gamma_A / \rho \\ \text{Functional biomass:} & \partial_t N + \nabla_x \cdot (N \mathbf{V}_M) = \Gamma_N / \rho \\ \text{Extracellular matrix:} & \partial_t E + \nabla_x \cdot (E \mathbf{V}_E) = \Gamma_E / \rho \\ \text{Liquid:} & \partial_t L + \nabla_x \cdot (L \mathbf{V}_L) = \Gamma_L / \rho \end{array} \right.$$

- Pseudo incompressibility: Mass transfers \Rightarrow Pressure

$$\nabla_x \cdot ((A + N) \mathbf{V}_M + E \mathbf{V}_E + L \mathbf{V}_L) = \frac{1}{\rho} (\Gamma_A + \Gamma_N + \Gamma_E + \Gamma_L)$$

- Dissolved components: Transport by the liquid & Diffusion

$$\theta = \begin{cases} S & \text{Substrate} \\ C & \text{Carbon dioxide} \\ O & \text{Oxygen} \end{cases} \quad \partial_t(\theta L) + \nabla_x \cdot (\theta L \mathbf{V}_L) = \underbrace{\nabla_x \cdot \left(D_\theta \mathbf{L} \nabla_x \theta \right)}_{\text{diffusion}} + \frac{\Gamma_\theta}{\rho_L}$$

Mixture framework – Force balance

- Biological phases: $\phi = A + N, E$

$$\partial_t(\phi \rho_\phi v_\phi) + \nabla_x \cdot (\phi \rho_\phi v_\phi \otimes v_\phi) =$$
$$- \underbrace{\phi \nabla_x P}_{\text{Pressure}} + \underbrace{\nabla_x(\gamma_\phi \phi)}_{\text{Elastic}} + \underbrace{\sum_{\ell \neq \phi} m_{\ell, \phi} (v_\phi - v_\ell)}_{\text{Friction}} + \underbrace{\Gamma_\phi v_\phi}_{\text{Exch.}}$$

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- Hypothesis: Conservation of total momentum supply

Mixture framework – Force balance

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- Hypothesis: Conservation of total momentum supply
- Liquid phase:

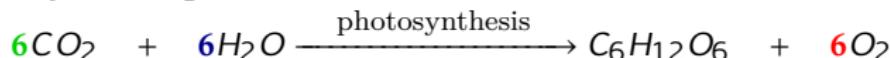
$$\partial_t(L \rho_L V_L) + \nabla_x \cdot (L \rho_L V_L \otimes V_L) =$$

$$- \underbrace{L \nabla_x P}_{\text{Pressure}} - \underbrace{\sum_{\phi \neq L} m_{\phi, L} (V_L - V_\phi)}_{\text{Friction}} - \underbrace{\sum_{\phi \neq L} \Gamma_\phi V_\phi}_{\text{Exch.}}$$

Source terms modelling

► Construction of source terms:

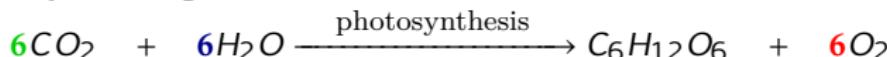
1. Identify a biological mechanism



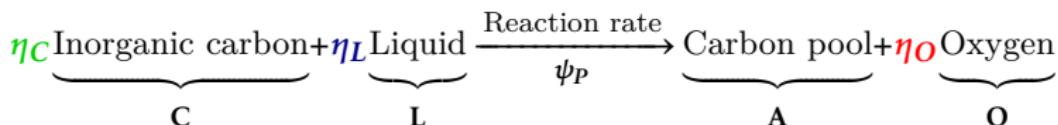
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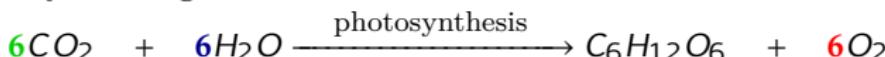
2. Translate in term of considered components



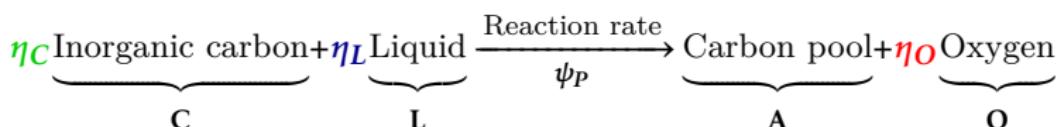
Source terms modelling

► Construction of source terms:

1. Identify a biological mechanism



2. Translate in term of considered components



3. Express the information in the source terms:

$$\Gamma_C = -\eta_C \psi_P + \dots$$

$$\Gamma_A = \psi_P + \dots$$

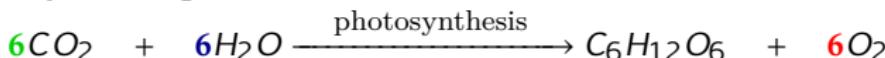
$$\Gamma_L = -\eta_L \psi_P + \dots$$

$$\Gamma_O = \eta_O \psi_P + \dots$$

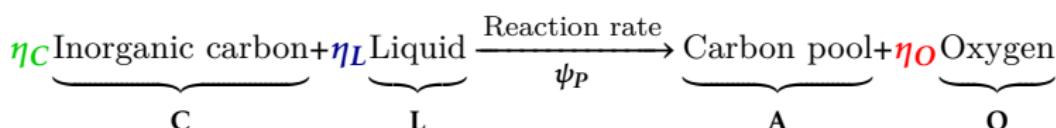
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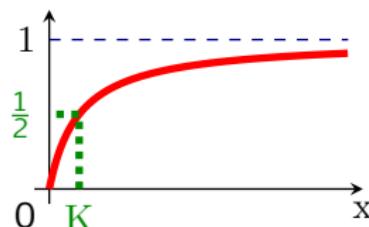
$$\Gamma_O = \eta_O \psi_P + \dots$$

► Considered mechanisms:

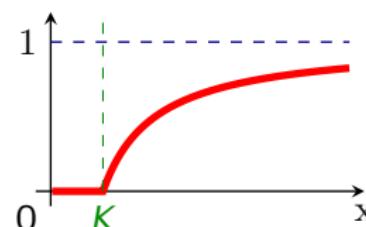
1. Photosynthesis
2. Respiration
3. Functional biomass synthesis
4. Extra-cellular matrix excretion
5. Mortality

Reaction rates modelling: ψ

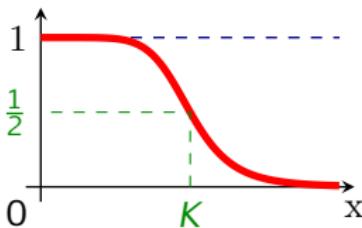
$$\psi := \prod_{i \geq 0} f_i(\phi) \quad \begin{cases} f_i & \text{elementary functions} \\ \phi & \text{volume or mass fraction} \end{cases}$$



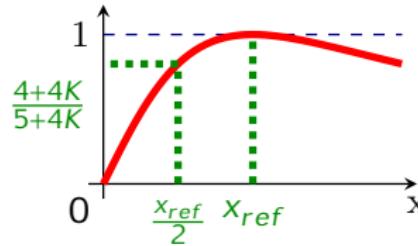
(a) Monod's law $f(x) = \frac{x}{K+x}$



(b) Droop's law $f(x) = \max\left\{0, 1 - \frac{K}{x}\right\}$



(c) Sigmoidal law $f(x) = \frac{1}{1+(x/K)^\alpha}$



(d) Haldane's law $f(x) = \frac{2(1+K)\tilde{x}}{\tilde{x}^2 + 2K\tilde{x} + 1}, \tilde{x} = x/x_{ref}$

Reaction rates modelling

- Highly nonlinear reaction rates:
Example:

$$\psi_P = \mu_P \rho_M N \frac{C}{\mathcal{K}_C + C} \frac{(1 + \mathcal{K}_L)L}{\mathcal{K}_L + L} \frac{2(1 + \mathcal{K}_I)\hat{I}}{\hat{I}^2 + 2\mathcal{K}_I\hat{I} + 1} \frac{\max\left\{0, 1 - \frac{Q_{min}}{\min\{Q, Q_{max}\}}\right\}}{Q_{max} - Q_{min}} \frac{1}{1 + \left(\frac{Q}{\mathcal{K}_O}\right)^\alpha},$$

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- Received light intensity:

$$\hat{I}(z) = \frac{I_0}{I_{opt}} \exp\left(- \int_z^H \tau_L L + \tau_M (A + N + E) d\xi\right)$$

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- Coupled mass balances:

$$\partial_t A + \nabla_x \cdot (AV_M) = \frac{1}{\rho_M} (\psi_P - \psi_R - \eta_N^A \psi_N - \psi_E^A - \psi_D^A)$$

$$\partial_t (CL) + \nabla_x \cdot (CLV_L) - \nabla_x \cdot (\mathcal{D}_C L \nabla_x C) = \frac{1}{\rho_L} (\eta_R^C \psi_R - \eta_P^C \psi_P),$$

Numerical scheme overview

- Semi-implicit approach for the mass balance equations:

$$\frac{(\theta L)^{n+1} - (\theta L)^n}{dt} + \nabla_x \cdot (\theta L V_L)^n = \nabla_x \cdot \left(D_\theta L^n \nabla_x \frac{(\theta L)^{n+1}}{L^n} \right) + f(U^n) - g(U^n)(\theta L)^{n+1}$$

- $f(U)$ production terms,
- $g(U)\theta L$ consumption terms.

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- Chorin-Temam's projection method for the conservation of momentum:

1. Projection step for V_ϕ , $\phi = M, E, L$:

$$\begin{aligned} & (\phi V_\phi)^{n+\frac{1}{2}} - (\phi V_\phi)^n + dt \nabla_x \cdot (\phi V_\phi \otimes V_\phi)^n \\ &= \frac{dt}{\rho_\phi} \left(-\nabla_x (\gamma_\phi \phi^n) + \sum_{\phi' \neq \phi} m_{\phi, \phi'} (V_\phi - V_{\phi'})^{n+\frac{1}{2}} + (\Gamma_\phi V_\phi)^n \right) \end{aligned}$$

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2. Elliptic equation for P : Variable coefficients & Nonhomogeneous

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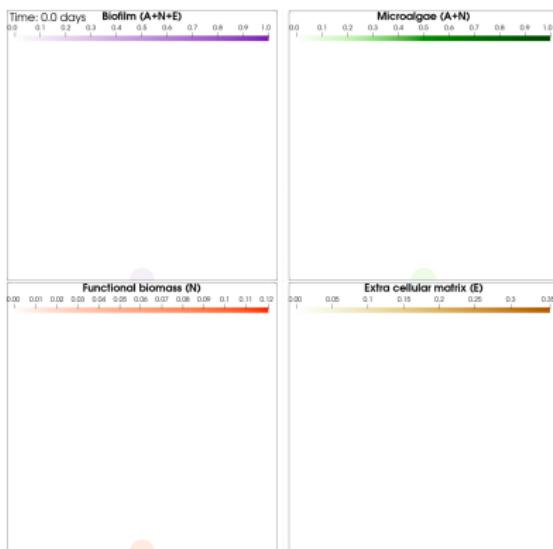
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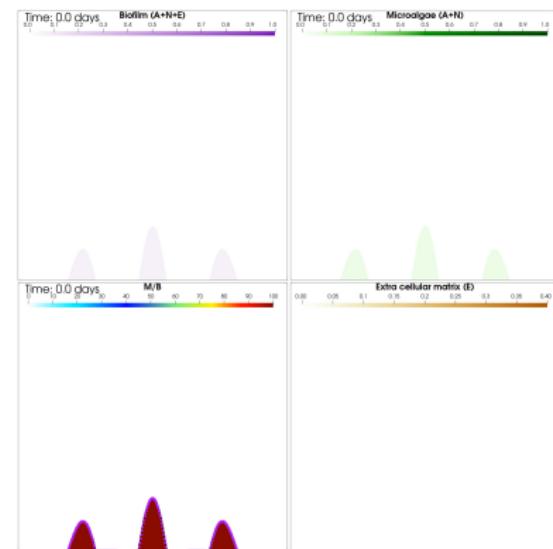
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2. Elliptic equation for P : Variable coefficients & Nonhomogeneous
3. Correction step: $V_\phi^{n+1} = V_\phi^{n+\frac{1}{2}} - \frac{dt}{\rho_E} (\nabla_X P)^{n+1}$

2D numerical simulations

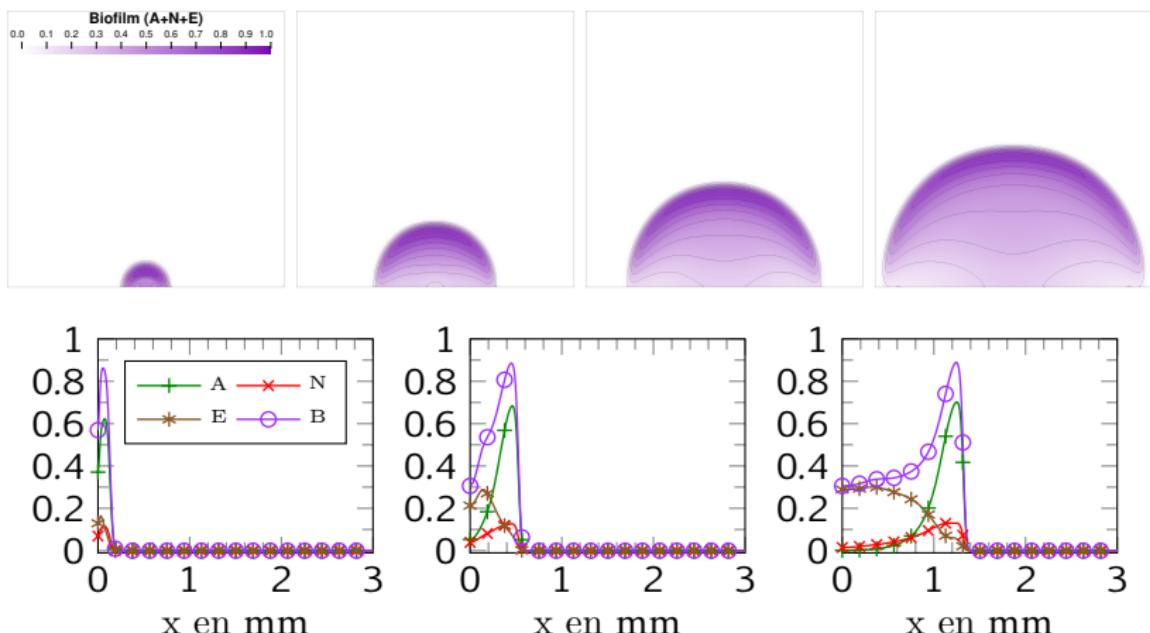


(a) Single spot colonie

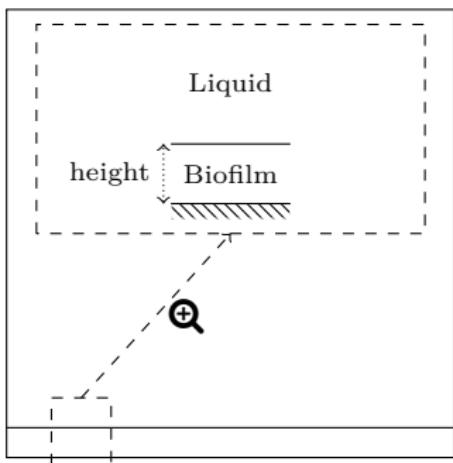


(b) Three spots colonie

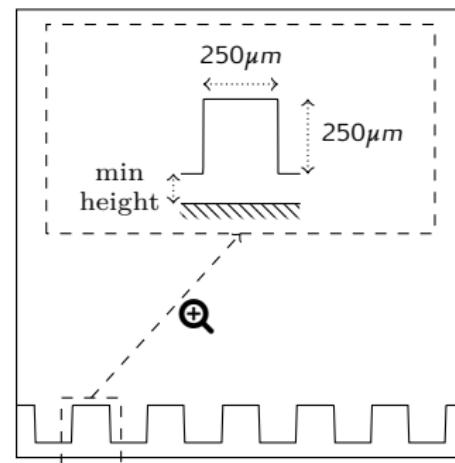
1D versus 2D numerical simulations



Harvest policy: Battlement versus uniform



(a) Uniform harvesting



(b) Battlement harvesting

Example: Battlement harvesting video.

Harvest policy: Impact of height and frequency?

Objective

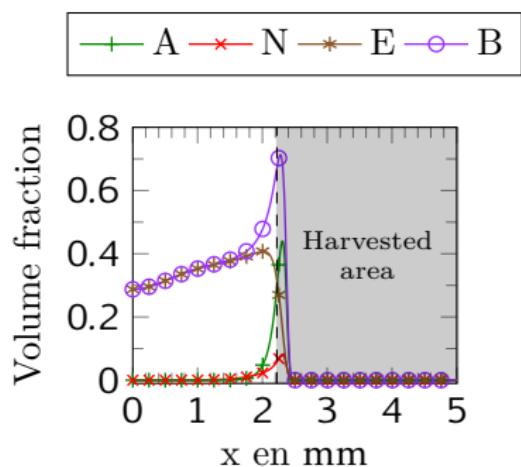
Quantify the impact of harvesting parameters on productivity.

Limitation

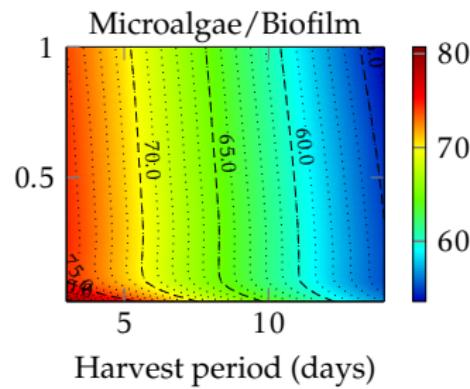
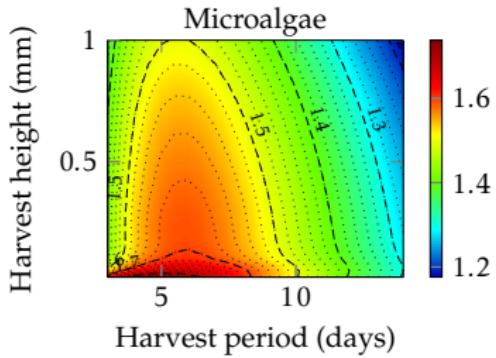
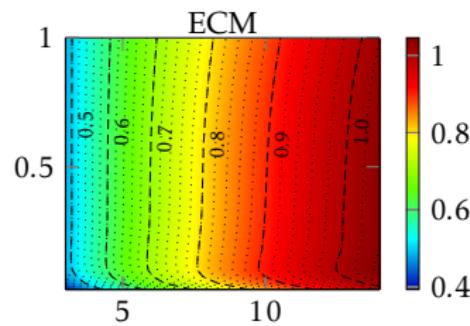
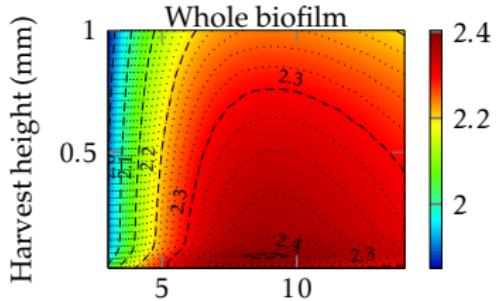
2D numerical simulation of ~ 50 days takes about two weeks on 2.40GHz Xeon.

Methodology

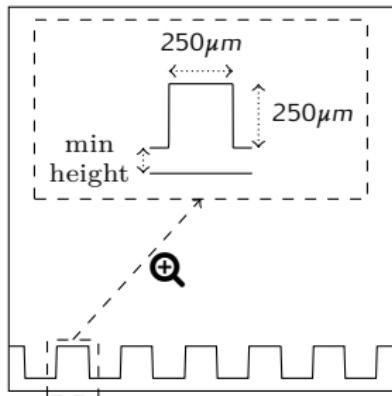
Investigate the impact of harvest height and frequency with 1D numerical simulation (about ~ 1 h for 90 days).



Harvest policy: Impact of height and frequency



Harvest policy: Impact of scraping pattern



Battlement harvest shape:

- ▶ significantly increases productivity,
- ▶ modifies components productivity.

Period	(days)	4	6.5	9
Min height	(μm)	100	100	75
A	(%)	10.33	9.98	1.90
M	(%)	8.87	8.97	1.77
E	(%)	-19.77	-2.44	10.58
B	(%)	-1.31	4.92	4.90

 Conclusion & Perspectives

Results:

- ▶ Structure formation,
- ▶ Role of dissolved components in the development of structures,
- ▶ Quantification of limiting factors: light, Oxygen, ...
- ▶ Optimal strategy quantification for uniform harvest,
- ▶ Battlement scrapping harvest induce productivity increase.

Perspectives:

- ▶ Include the water flow,
- ▶ Take into account the viscosity,
- ▶ Multi-species biofilm,
- ▶ Calibration and comparison with experimental data.

CEMRACS 2022 project

Advanced numerical schemes for mixture ecosystems

► Aims:

1. Design and implement a numerical scheme preserving at the discrete level the constraints,
2. Include additional physical forces: viscosity, gravity,
3. Explore modeling and numerical approaches for frictions and elastic tensors.

- **Idea:** Use the numerical flux for the pseudo incompressibility constraint.
- **Difficulty:** Incompressibility constraint becomes non-linear equation,

Participants:

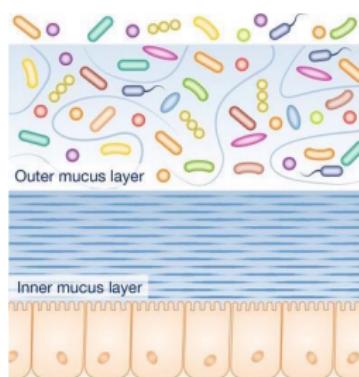
Students: Mickael Bestard, Leo Meyer, Florent Noisette,

Advisor: Olivier Bernard, Thierry Goudon, Sebastian Minjeaud, Bastien Polizzi.

Colon & gut microbiota in a nutshell



(a) Human gut



(b) Mucus layers &
Microbiota

Gut's role

- ▶ Last stage of digestion,
- ▶ Body hydration.

Gut's operating mechanisms

- ▶ Microbiota: all the bacteria contained in the gut
 - ▶ Fiber degradation,
 - ▶ Synthesize neuro-transmitters,
 - ▶ Pathogens domination,
 - ▶ Regulate immunity.
- ▶ Host:
 - ▶ Excretion of protective mucus layers,
 - ▶ By-products assimilation,
 - ▶ Water pumping: 90% of the gastric broth's water.

Colon & gut microbiota in a nutshell

Motivations: Understand the complex symbiotic relationship between the host and its microbiota.

Why: Dysbiosis¹ is associated with many diseases such that metabolic, inflammatory, mental, autoimmune, ...

Objectives: Quantify the influence of mechanical, ecological and chemical mechanisms in the functioning of the gut.

Context: Collaboration with scientists from Institut National de Recherche en Agronomie (INRA): B. Laroche & S. Labarthe.

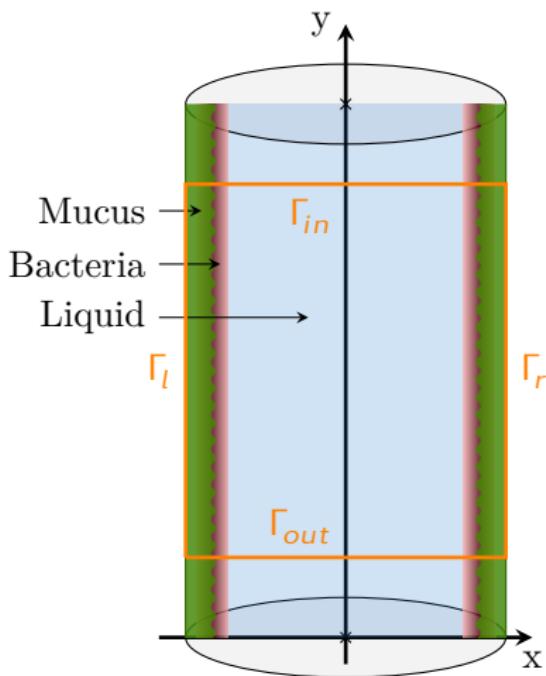
¹Qualitative and functional alteration of the microbiota.

Fluids mechanics of the gut

Objective: Design a simple fluid mechanic model for the gut's rheology.

Mechanisms considered:

- ▶ Flow of the gastric broth's
- ▶ Water pumping
- ▶ Mucus production
- ▶ Viscosity gradient



Components considered:

- ▶ Liquid: \mathcal{L}
- ▶ Mucus: \mathcal{M}
- ▶ Microbiota (in a second step): \mathcal{B}

Tools: Mixture theory & Stokes equation

Mixture theory framework

► Total volume conservation: $\mathcal{L} + \mathcal{M} = 1$

► Mass conservation:

- Transport at velocity V $\partial_t \mathcal{M} + \nabla_x \cdot (\mathcal{M}V - D_M \nabla_x \mathcal{M}) = 0$
- Radial diffusion D_ϕ , $\phi = \mathcal{L}, \mathcal{M}$ $\partial_t \mathcal{L} + \nabla_x \cdot (\mathcal{L}V - D_L \nabla_x \mathcal{L}) = 0$

► Pseudo incompressibility constraint:

$$\nabla_x \cdot V = \nabla_x \cdot ((D_M - D_L) \nabla_x \mathcal{M})$$

► Stokes equation: with viscosity $\mu(\mathcal{M})$ and pressure P

$$\nabla_x \cdot \left(\mu(\mathcal{M}) (\nabla_x V + \nabla_x V^T) \right) - \nabla_x P = 0.$$

Boundary conditions

Boundary condition on \mathcal{M} and \mathcal{L}

- Robin condition on Γ_L and Γ_R :

$$(\mathcal{M}\mathbf{V} - \mathbf{D}_{\mathcal{M}}\nabla\mathcal{M}) \cdot \vec{n} = -f(\mathcal{M}), \quad f(\mathcal{M}) = \theta_{\mathcal{M}}[\mathcal{M} - \mathcal{M}^{\star}]$$

$$(\mathcal{L}\mathbf{V} - \mathbf{D}_{\mathcal{L}}\nabla\mathcal{L}) \cdot \vec{n} = -g(\mathcal{L}), \quad g(\mathcal{L}) = -\theta_{\mathcal{L}} [\mathcal{L} - \mathcal{L}^{\star}]^{+}$$

- Neumann boundary conditions on Γ_{in} and Γ_{out}

Boundary condition for $V(u, v)$

- Dirichlet boundary condition on Γ_{in} :

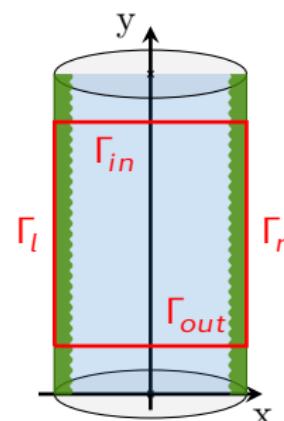
$$(u, v) = (0, v_{i_n})$$

- Dirichlet boundary conditions on Γ_L and Γ_R :

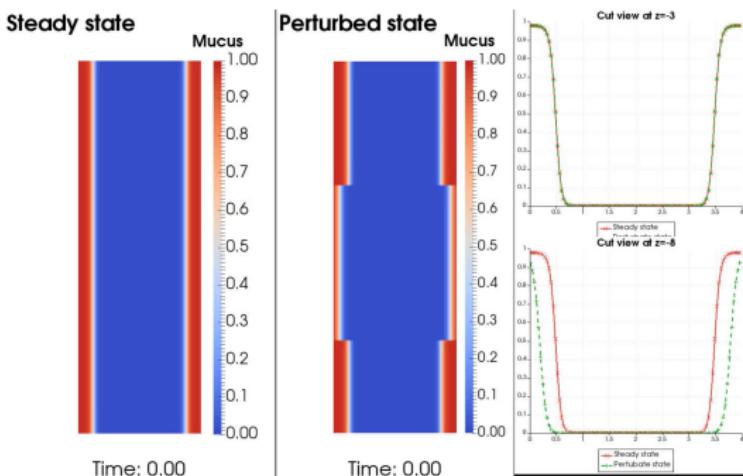
$$V = (u, v) = \left(\pm \frac{f(\mathcal{M}) + \frac{D_M}{D_L} g(\mathcal{L})}{\mathcal{M} + \frac{D_M}{D_L} \mathcal{L}}, 0 \right).$$

- Neumann boundary conditions on Γ_{out} :

$$\left(\mu(\mathcal{M}) (\nabla_x V + \nabla_x V^T) - \nabla_x P \right) \cdot \vec{n} = 0$$



Numerical results



Conclusions

- ▶ Numerical scheme: VF4 on a staggered grid
- ▶ The model preserves the mucus layer,
- ▶ The model can reconstruct the mucus layer,
- ▶ Steady state independent of \mathcal{M}_0 (numerical).
- ▶ Viscosity gradient is the key ingredient

Extension including the micorbiota

- Total volume conservation:

$$\mathcal{L} + \mathcal{M} + \mathcal{B} = 1$$

- Mass conservation:

- Transport at velocity V

$$\partial_t \mathcal{M} + \nabla_x \cdot (\mathcal{M} V - D_{\mathcal{M}} \nabla_x \mathcal{M}) = 0$$

- Radial diffusion D_{ϕ} , $\phi = \mathcal{L}, \mathcal{M}$

$$\partial_t \mathcal{L} + \nabla_x \cdot (\mathcal{L} V - D_{\mathcal{L}} \nabla_x \mathcal{L}) = 0$$

$$\partial_t \mathcal{B} + \nabla_x \cdot (\mathcal{B} V + \mathcal{B} \nabla_x \phi - D_{\mathcal{B}} \nabla_x \mathcal{B}) = 0$$

- Chemotaxis for bacteria:

$$-\Delta_x \phi = \mathcal{F}(\mathcal{M}) - \frac{1}{|\Omega|} \int_{\Omega} \mathcal{F}(\mathcal{M}) \cdot dx$$

$$\mathcal{F}(\mathcal{M}) = 1 - \frac{1}{\eta(\mathcal{M} - \mathcal{M}_{ref})^2 + 1}, \quad \eta > 0$$

- Pseudo incompressibility constraint:

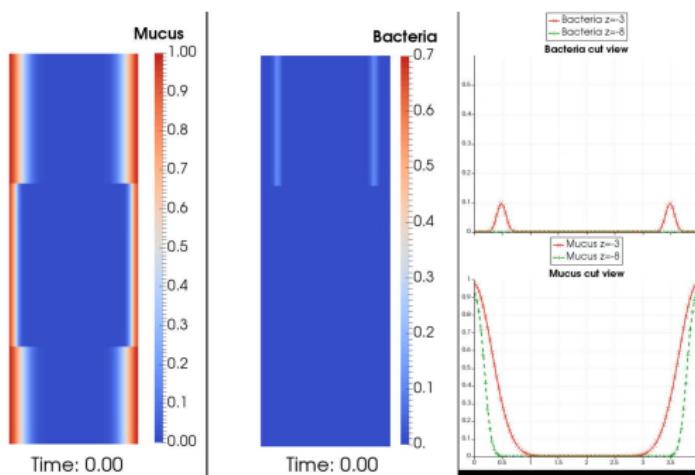
$$\nabla_x \cdot V = \nabla_x \cdot ((D_{\mathcal{M}} - D_{\mathcal{L}}) \nabla_x \mathcal{M} + (D_{\mathcal{B}} - D_{\mathcal{L}}) \nabla_x \mathcal{B} - \mathcal{B} \nabla_x \phi)$$

- Stokes equation:

$$\nabla_x \cdot \left(\mu(\mathcal{M}) (\nabla_x V + \nabla_x V^T) \right) - \nabla_x P = 0.$$

Extension including the microbiota

Numerical results



Conclusions

- The model preserves the mucus & microbiota layers,
- The model can reconstruct the mucus & microbiota layers,
- Steady state independent of \mathcal{M}_0 .

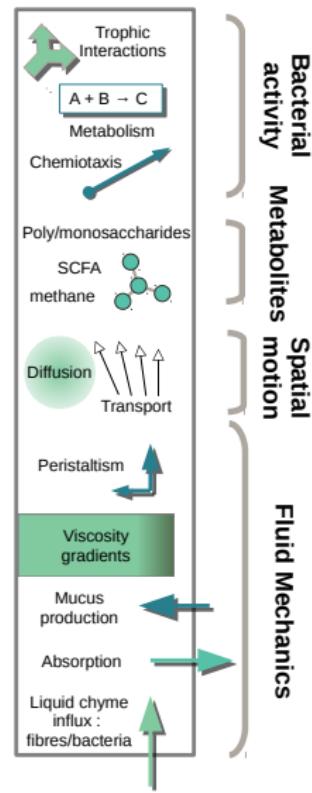
Toward a more detail model

Aim of the model

- ▶ Describe the microbiota in its physical environment,
- ▶ Understand how bacteria remain in the colon and resist the overcoming flow,
- ▶ Study the ecology of bacteria in competition in the gut.

Features of the model

- ▶ Hydrodynamical description: luminal flow, water pumping, viscosity gradient, mucus structure, ...
- ▶ Spatial behaviour: chemotaxis, peristaltism, ...
- ▶ Metabolic description of the digestion process:
 - ▶ Dissolved metabolites,
 - ▶ Different bacteria communities.



Geometry and unknowns



Mixture model with

- 8 fluid components:
 1. mucus,
 2. indigestible residuals,
 3. liquid chyme,
 4. polysaccharides
 5. bacteria \mathcal{B}_{mon} ,
 6. bacteria \mathcal{B}_{la} ,
 7. bacteria \mathcal{B}_{H_2a} ,
 8. bacteria \mathcal{B}_{H_2m} .
- 8 dissolved compounds:
 1. monosaccharides,
 2. lactate,
 3. hydrogen,
 4. acetate
 5. butyrate,
 6. propionate,
 7. methane,
 8. carbon dioxyde.
- A common velocity field, with a correction for bacteria,
- The hydrostatic pressure

Mixture theory framework

- Fluid components: $\phi_i = \text{Volume fractions}, i \in [1, 8]$

Mass balance

$$\partial_t \phi_i + \nabla_x \cdot (\phi_i V_i) - \nabla_x \cdot (\sigma \nabla_x \phi_i) = \mathcal{F}_i$$

Total volume conservation

$$\sum_{i \in [1, 8]} \phi_i = 1$$

Velocity, $v_i = \text{chemotactic speed}$ $V_i = V + v_i$

Phase transfert constraint

$$\sum_{i=1}^8 \mathcal{F}_i = 0$$

Incompressibility

$$\nabla_x \cdot (V + \sum_{i=1}^8 \phi_i v_i) = 0$$

- Solutes: $\mathcal{S}_i = \text{concentration}, i \in [1, 8]$

Mass balance

$$\partial_t \mathcal{S}_i + \nabla_x \cdot (\mathcal{S}_i \tilde{V}) - \nabla_x \cdot (\sigma_i \nabla_x \mathcal{S}_i) = \mathcal{G}_i$$

Mixture average velocity

$$\tilde{V} = \sum_{i=1}^8 \phi_i V_i$$

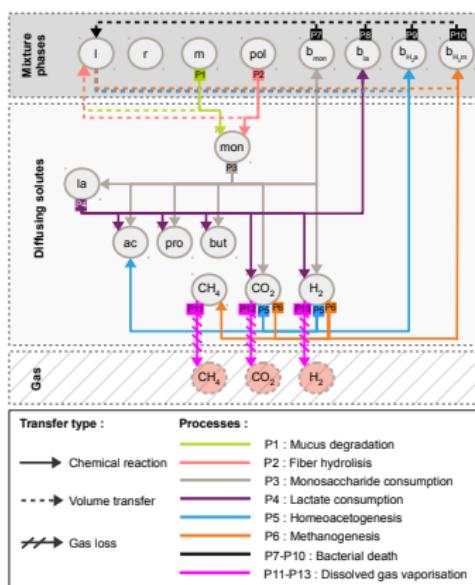
- Stokes equation:

Viscosity $\mu(\mathcal{M}, \mathcal{L})$ depending on mucus and liquid P pressure

$$\nabla_x \cdot \left(\mu(\mathcal{M}, \mathcal{L}) (\nabla_x V + \nabla_x V^T) \right) - \nabla_x P = 0.$$

Metabolic model: modelling source terms

Knowledge-based microbiota
metabolic model: Muñoz Tamayo
et al. JTB 2010



- Petersen matrix,
- Complex reaction rates including:
inhibition, limitation mechanisms,
...
- General form:

$$\mathcal{F}_i(\phi, \mathcal{S}) = \sum \mu_{max} \frac{\mathcal{S}_j \phi_i}{K_j + \mathcal{S}_j}$$

Chemotactic speed

Observations:

- ▶ Chemotactic speed ~ 1 cm/day
- ▶ Gut half average surface inflow ~ 40 cm/day

Consequence: Chemotactic speed \ll Gut average inflow

Hypothesis: Consider only the radial chemotactic speed

Keller-Segel model:

$$v_i = \sum_j \lambda_{i,j} \nabla_r \psi_j \quad \text{and} \quad -\Delta \psi_j = \mathcal{S}_j - \frac{1}{R} \int_0^R \mathcal{S}_j(r, z) \cdot dr$$

whith $\lambda_{i,j}$ chemosensitivity coefficient of \mathcal{B}_i to \mathcal{S}_j ,
 ψ_j chemotactic potential of \mathcal{S}_j ,
 R gut radius,
 $\nabla \psi_j \cdot \vec{n} = 0$ boundary condition.

Boundary conditions: In/out & Peristaltism

- Mucosal exchanges: robin boundary conditions

$$(\phi_i V_i - \sigma \nabla_x \phi_i) \cdot \vec{n} = \gamma_{\phi_i}$$

$$(S_i \tilde{V} - \sigma_i \nabla_x S_i) \cdot \vec{\eta} = \gamma_{S_i}$$

where γ is the exchange rate which depends on the local composition.

- Peristaltism:

$$V \cdot \vec{n} = \sum_{i \in [1,8]} \gamma_{\phi_i} + V_{per} \cdot \vec{n} \quad \text{and} \quad V \cdot \vec{\tau} = V_{per} \cdot \vec{\tau}$$

with V_{per} is the velocity peristaltism induced.

Notation: \vec{n} normal unit vector,
 $\vec{\tau}$ tangential unit vector.

Model simplification

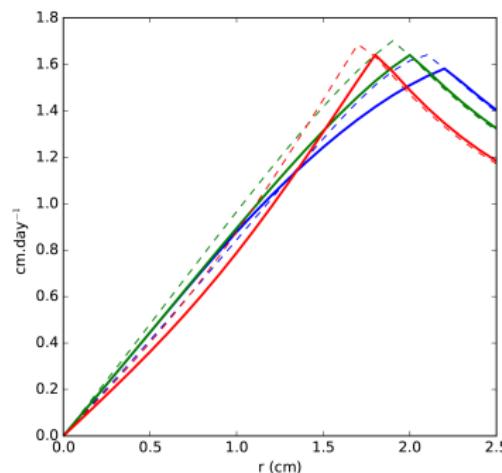
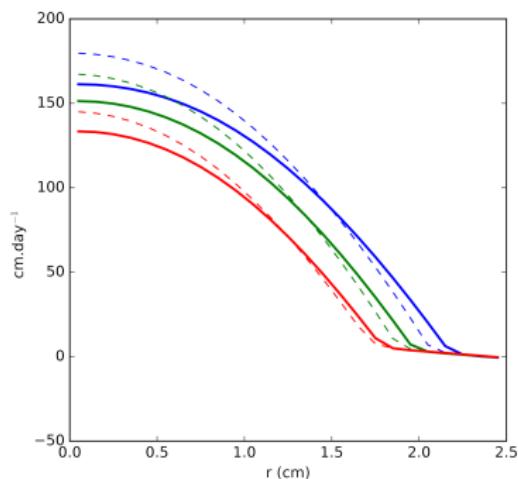
- ▶ Realistic hypothesis: Aspect ratio $\varepsilon = \frac{R}{L} \ll 1$.
- ▶ Model simplification method:
 - ▶ Use series expansion in ε , ie. $f = f_0 + \varepsilon f_1 + \dots$
 - ▶ Keep only the first orders.
- ▶ Simplified mass balance

$$\partial_t \phi_i + \nabla_x \cdot (\phi_i \mathbf{U}) + \frac{1}{r} \partial_r (r \phi_i u_{i,r}) - \frac{1}{r} \partial_r (r \sigma \partial_r \phi_i) = \mathcal{F}_i$$
$$\partial_t \mathcal{S}_i + \widetilde{\mathbf{U}} \cdot \nabla_x \mathcal{S}_i - \frac{1}{r} \partial_r (r \sigma_i \partial_r \mathcal{S}_i) = \mathcal{G}_i$$

- ▶ Simplified Stokes and Keller-Segel equations
 - ▶ Can be solved exactly
 - ⇒ Explicit formulas for the velocities \mathbf{U} and $u_{i,r}$ depending on: rehology, peristaltism, inflow and pumping.
- ▶ Speed up factor ~ 70 .

Comparison between full and simplified model

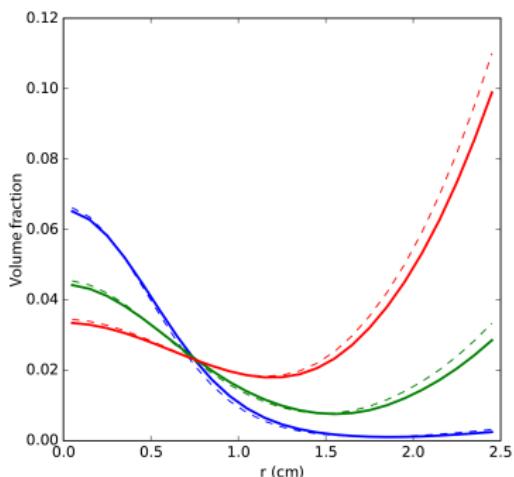
Discrepancies between velocities



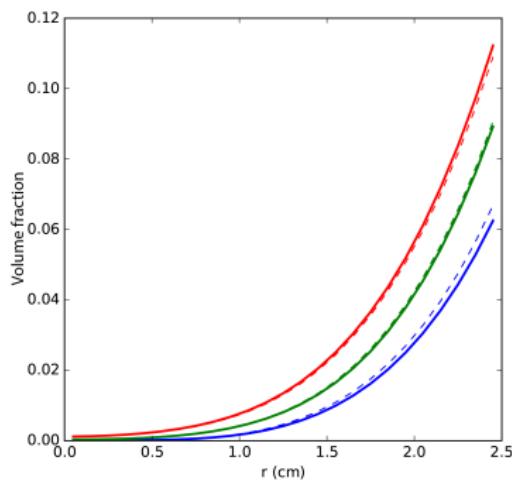
z in cm	-25	-50	-75
Reduce model	- - -	- - -	- - -
Full model	—	—	—

Comparison between full and simplified model

Discrepancies in composition



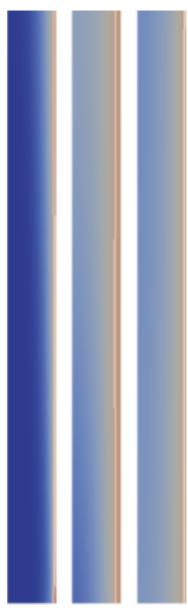
(a) Radial distribution of bacteria



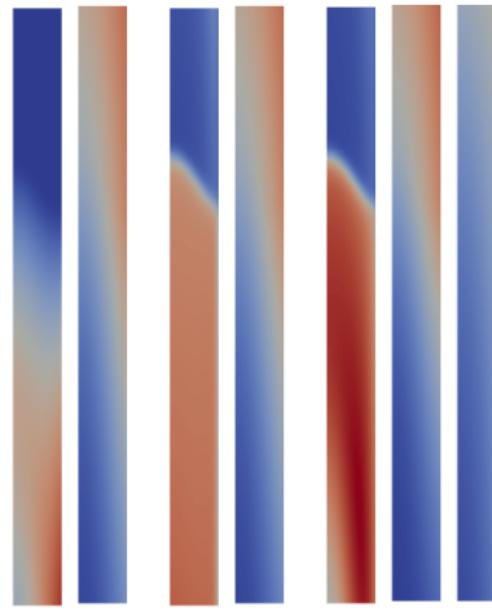
(b) Radial distribution of mucus

z in cm	-25	-50	-75
Reduce model	— - -	— - -	— - -
Full model	—	—	—

Persistence of the mucus layer & spatial structure



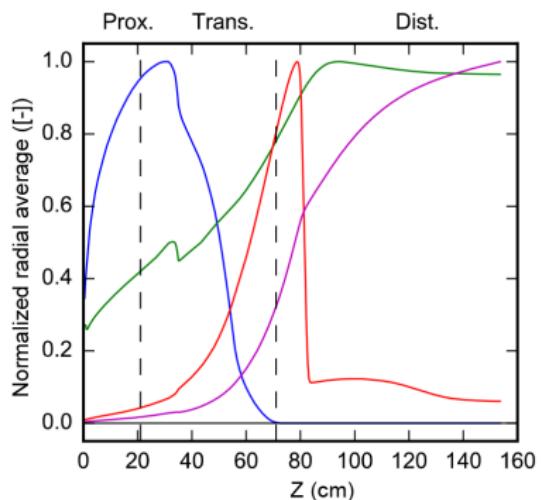
(a) Mucus distribution



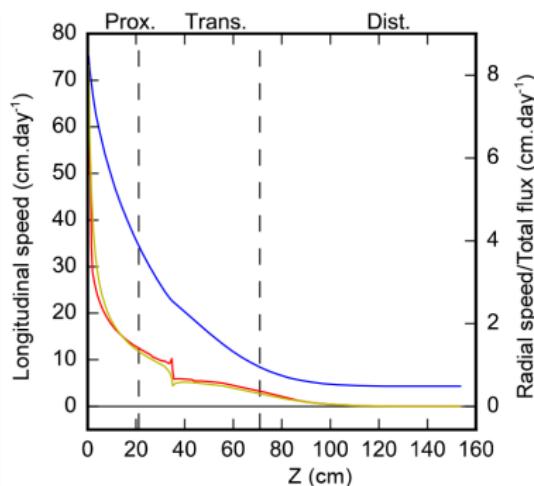
(b) Distribution of microbial densities and their corresponding substrate in the transverse colon

Reference state

Without chemotaxis & peristaltism

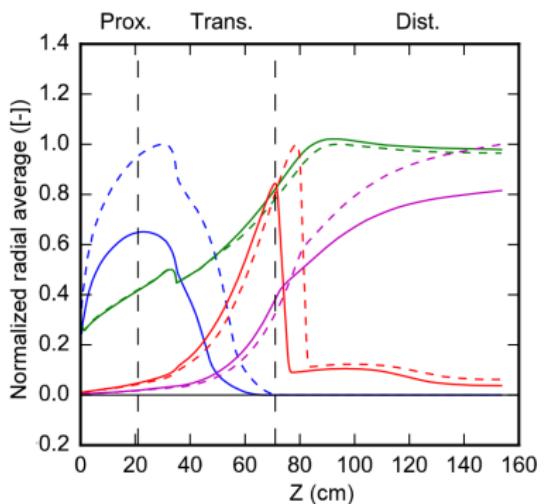


- Polysaccharid density
- Mixture viscosity
- Bacterial activity
- Total bacteria density

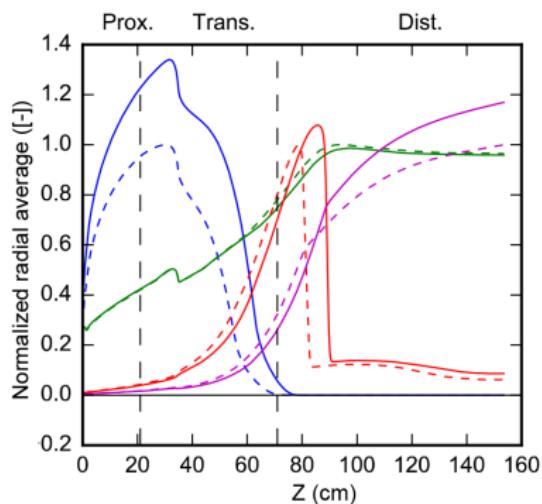


- Longitudinal speeds
- Radial speed
- Total flux: $\sum_{i \in [1,8]} \gamma_{\phi_i}$

Impact of the diet



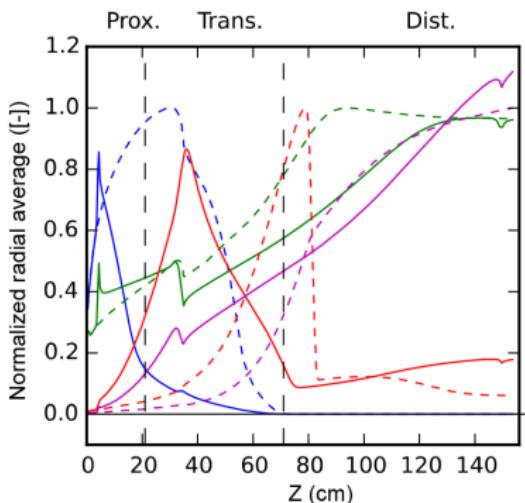
(a) Low fibre diet



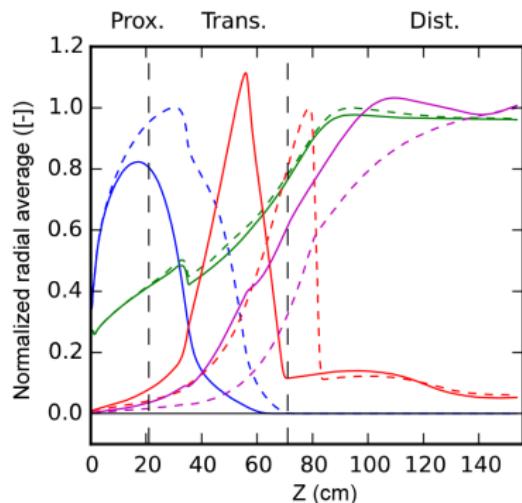
(b) High fibre diet

Curve	Poly. density	Mixt. viscosity	Bact. activity	Total bact. density
Reference	- - -	- - -	- - -	- - -
Low/High	—	—	—	—

Impact of peristaltims & chemotactism



(a) Impact of peristaltims

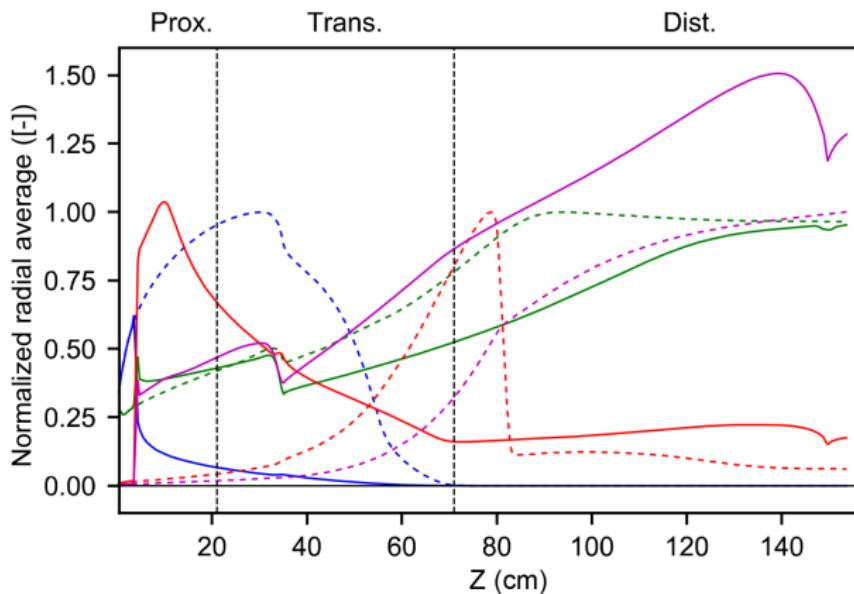


(b) Impact of chemotactism

Curve	Poly. density	Mixt. viscosity	Bact. activity	Total bact. density
Reference	- - -	- - -	- - -	- - -
Per./Chemo.	—	—	—	—

All mechanisms combined

Peristaltims & chemotactism



Curve	Poly. density	Mixt. viscosity	Bact. activity	Total bact. density
Reference	- - -	- - -	- - -	- - -
Per./Chemo.	—	—	—	—

Conclusion & Further work

Main results

- ▶ Coupled fluid mechanics-Population dynamics model.
- ▶ Simplified fluid mechanics.
- ▶ Assessment of the spatial structure of the gut microbiota.
- ▶ Chemotaxis has an impact on the gut's spatial structure and ecology.
- ▶ Quantification of the impact of peristaltism.

Mathematical perspectives

- ▶ Rigorous proof of the formal computations for the asymptotic limit

Modelling perspectives

- ▶ Include pathogens invasion
- ▶ Include drug delivery & immune response
- ▶ Different timescales for the source terms (slow-fast dynamics)

Thank you for your attention!

Questions?

References:

- ▶ Understanding photosynthetic biofilm productivity and structure through 2D simulation, B. Polizzi, A. Fanesi, F. Lopes, M. Ribot, O. Bernard, Plos Computational Biology (accepted).
- ▶ A time-space model for the growth of microalgae biofilms for biofuel production, B. Polizzi, O. Bernard, M. Ribot, Journal of Theoretical Biology, Volume 432, 7 November 2017, Pages 55-79.
- ▶ A mixture model for the dynamic of the gut mucus layer, T. El Bouti, T. Goudon, S. Labarthe, B. Laroche, B. Polizzi, A. Rachah, M. Ribot, R. Tesson, Esaim: proceedings and surveys, December 2016, Vol. 50, p. 111-130.
- ▶ A mathematical model to investigate the key drivers of the biogeography of the colon microbiota, Simon Labarthe, Bastien Polizzi, Thuy Phan, Thierry Goudon, Magali Ribot, Béatrice LAROCHE, Journal of Theoretical Biology - In revision.