Models from mixture theory for biofilm growth

Magali Ribot

Laboratoire IDP, Université d'Orléans, Université de Tours, CNRS

Joint work with :

F. Clarelli, C. Di Russo, R. Natalini

O. Bernard, B. Polizzi, F. Lopes, A. Fanesi

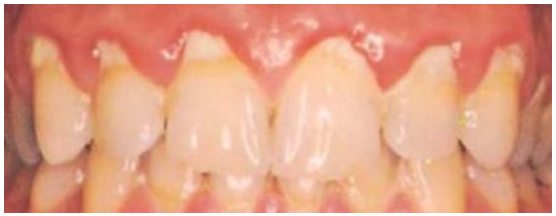
T.Goudon, S.Labarthe, B.Laroche, T. Phan, B. Polizzi

CIRM, 29 March 2022

Outline

Outline

Biofilm - examples

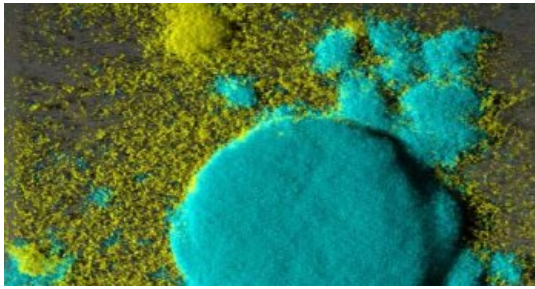


← Dental plaque

← Industry

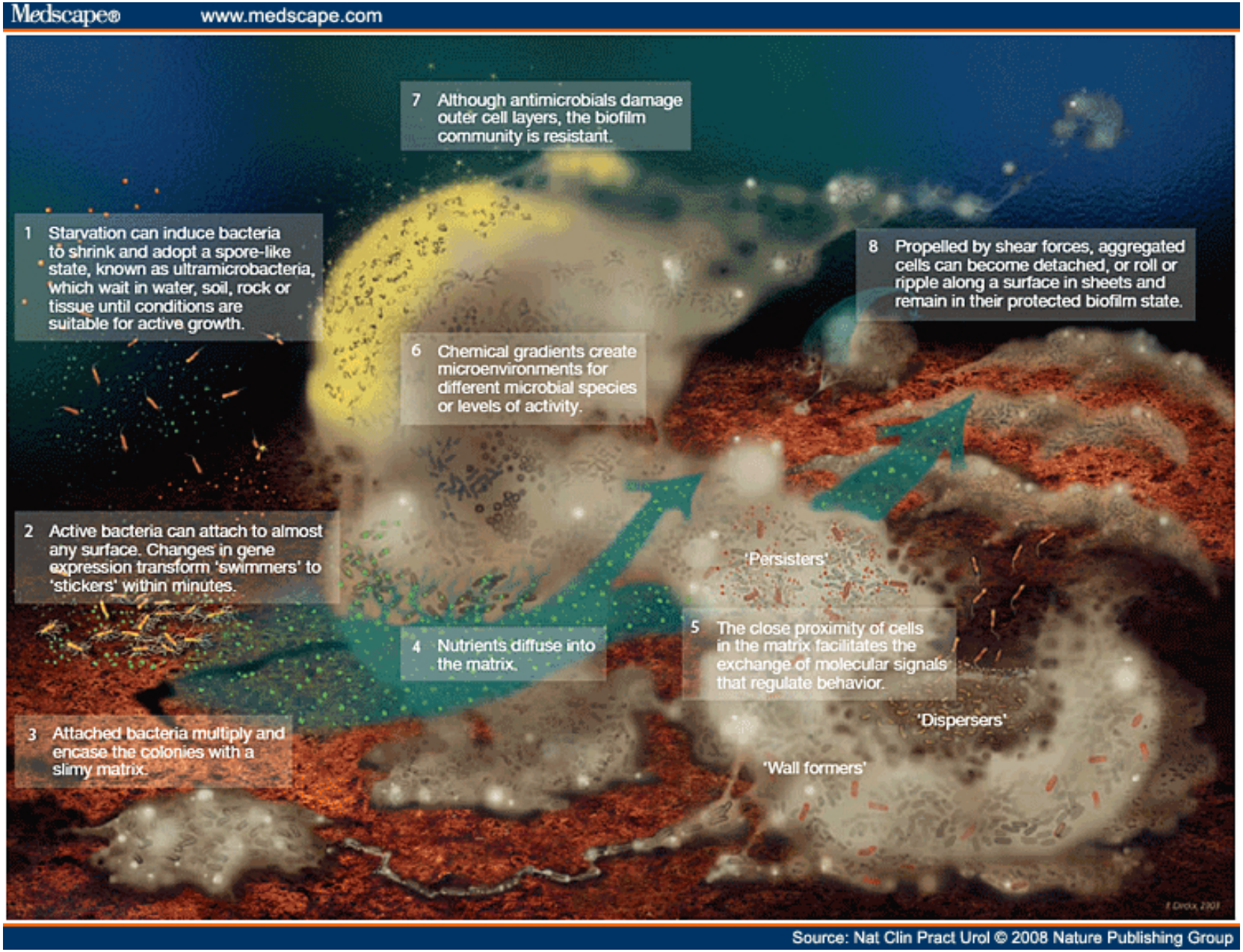
Monuments →

Pseudomonas aer. →

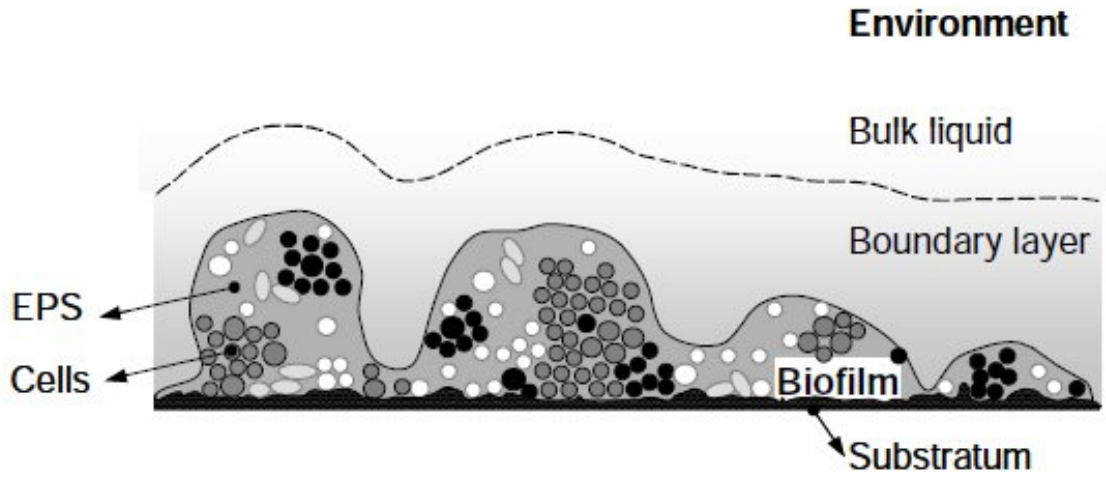


Biofilms are now considered as the preferred form of microbial life [Costerton, 78].

A "simplified" description of biofilms



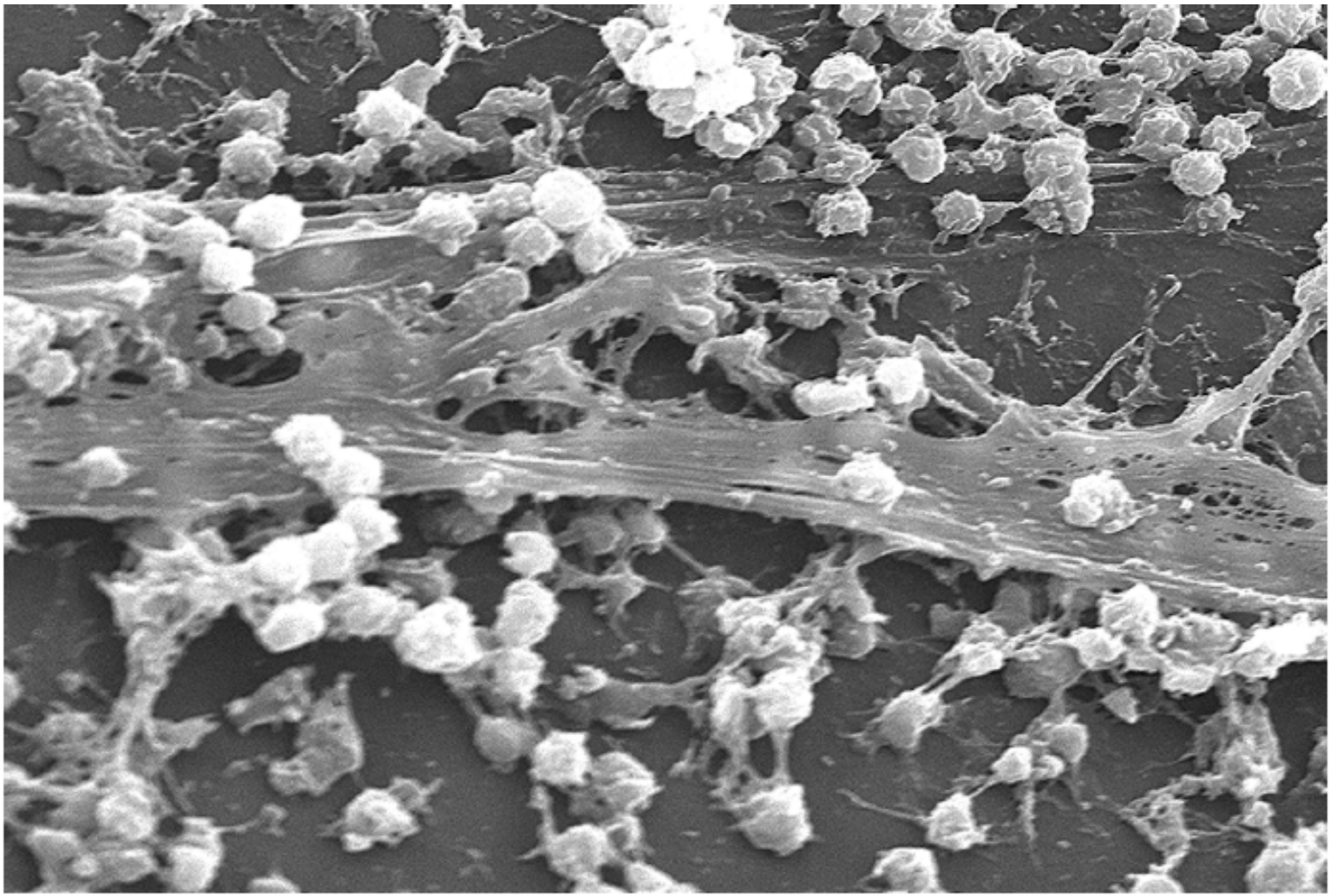
Main characteristics of a biofilm



A biofilm is a complex mixture of microorganisms in interaction

- anchored to a substratum surface,
- embedded in a Extracellular matrix of Polymeric Substances (EPS),
- in contact with water or moisture,
- influenced by nutrients.

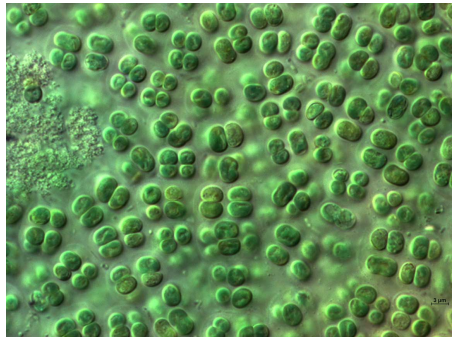
Main characteristics of a biofilm



Staphylococcus aureus on a catheter surface

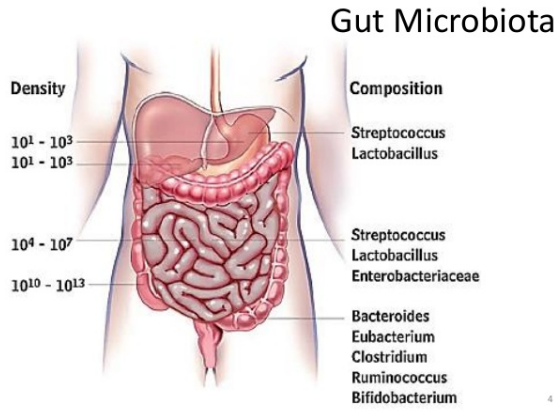
Biofilms studied in this talk

* *Gloeocapsa Chroococcales* cyanobacteria on fountain walls



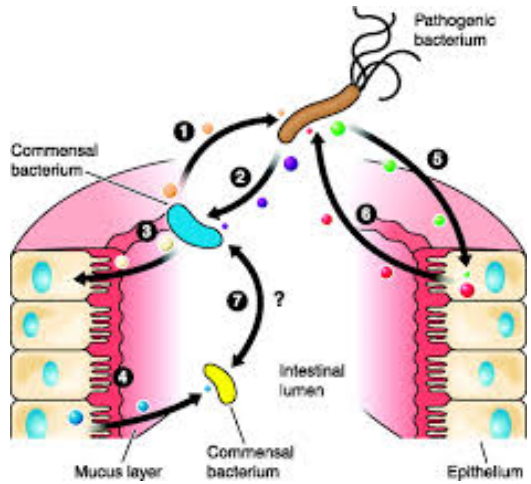
* Microalgae producing lipids

* Gut microbiota



Common features to the considered systems

* Dependency in time and space
* Huge number of organisms and interactions between them
* Coupling between the system and its environment



$\Rightarrow$ Description at the macroscopic level

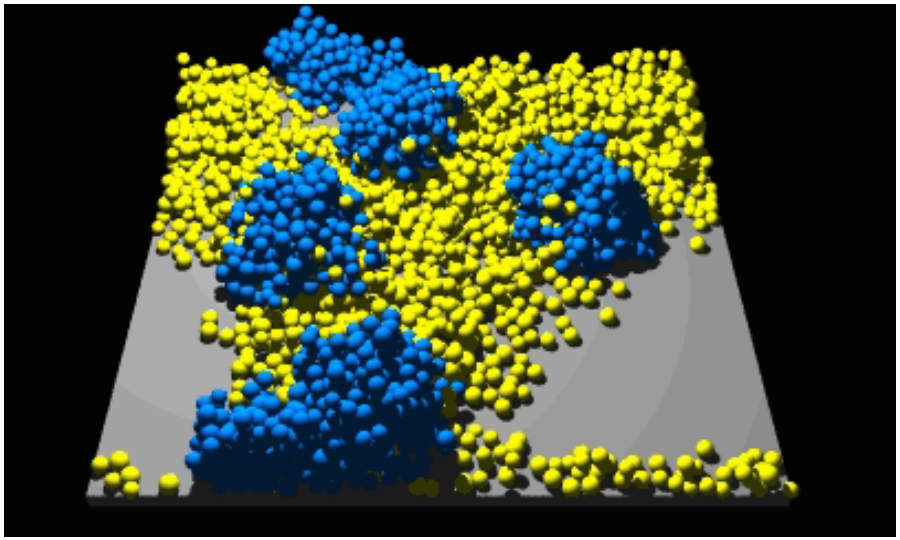
$\Rightarrow$ Partial Differential Equations

Outline

Agent-based models

[Delft team : Picioreanu, Noguera et al.,Water Science and Technology, 2006]

* Cell displacement by a random movement
* Rules for bacteria contact or division
* Growth according to the nutrient availability



Growth of a biofilm of motile (yellow) and non-motile (blue) Pseudomonas cells

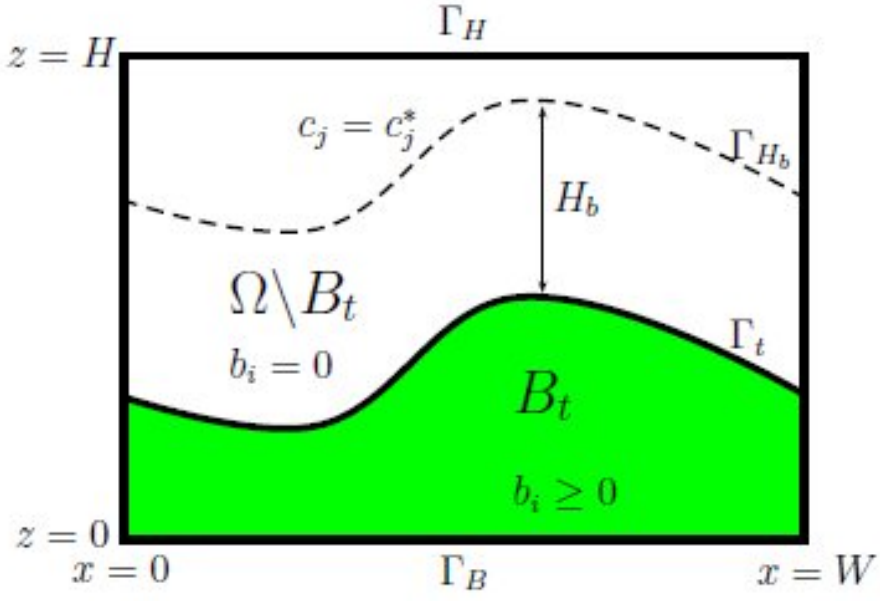
Problems :

* Costly computations if realistic (population size)
* High sensibility to initial data

MultiD & multi-species models [Alpkvist & Klapper, 2007]

A multidimensional multispecies continuum model for heterogeneous biofilm development

Erik Alpkvist [a,*], Isaac Klapper [b,c]



2 regions : biomass B_t and liquid $\Omega \backslash B_t$.
Biomass components θ_i :

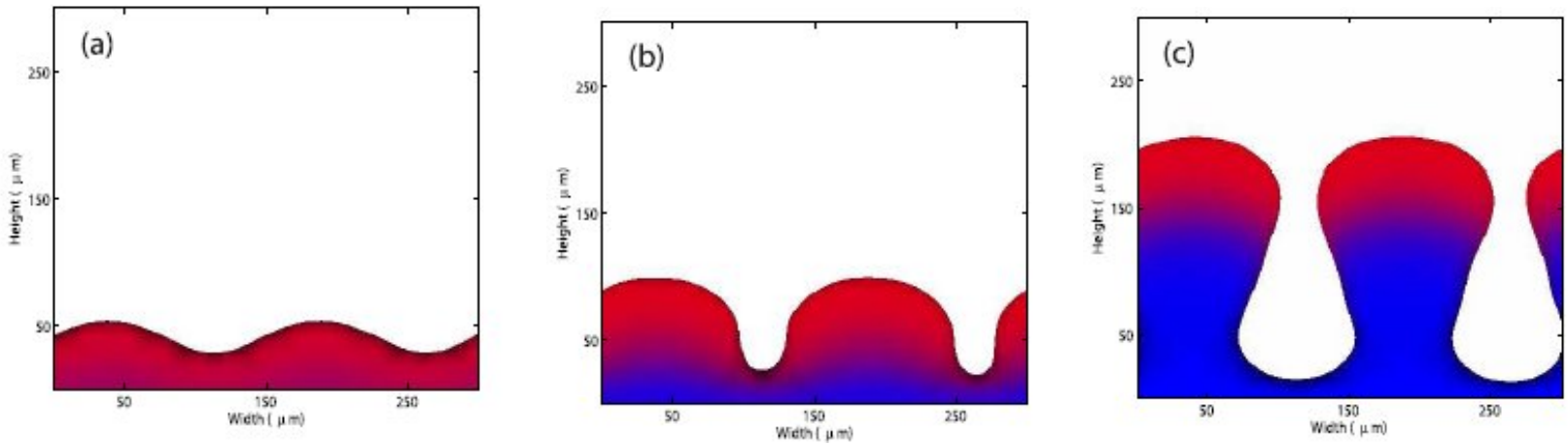
$$\partial_t \theta_i + \mathrm{div}(\theta_i \mathsf{v}) = g_i,$$

$$\mathsf{v} = -\lambda \nabla p$$

Level set formula for the boundary $\Gamma_t = \{\phi(x,t) = 0\}$, with :

$$\phi_t + \mathsf{v} \cdot \nabla \phi = 0$$

MultiD & multi-species models [Alpkvist & Klapper, 2007]



Time evolution of a biofilm (red : active biomass ; blue : inert biomass)

Quorum sensing modeling [Anguige, King & Ward, 2006]

A multi-phase mathematical model of quorum sensing in a maturing *Pseudomonas aeruginosa* biofilm

K. Anguige [a], J.R. King [b], J.P. Ward [c,*]

- 4 phases : living cells(B), dead cells(D), EPS(E) and liquid(L).
- 1 common velocity for B, D and E and 1 velocity for L.
- Influence of Quorum Sensing (QS) and treatments

Equations :

* Mass conservation for B, D, E and L.

$$\partial_t B + \mathrm{div}(B\mathbf{v}) = ...,$$

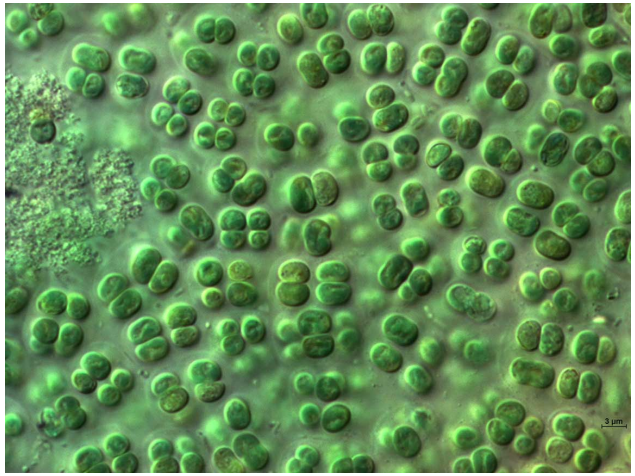
* Advection-diffusion equations for oxygen, antibiotics, antiQS...

Problems :

* Closure of the system thanks to the condition : $L = L_0 + \alpha E$.
* Multi-species 1D PDE model.

Cyanobacteria biofilms in fountains

[Clarelli, Di Russo, Natalini, R., J. Math. Biol. 2013 & Math. Med. Biol.,2016]



Model characteristics :

* Spatial dependency without interface
* Natural closure of equations in 2D, 3D
* Water = limiting factor (death during cold and dry seasons)
* Cyanobacteria embedded within EPS $\Rightarrow$ same velocity
* Influence of light

Mass conservation equations

adapted from [Anguige, King & Ward, 2006]

Unknowns :

* B,D,E, L = volume fractions of cyanoBacteria, Dead cyanobacteria , EPS and Liquid.
* v_S= cells and EPS velocities ; v_L = liquid velocity.

- **Mass conservation equations** are :

$$\begin{aligned}
\partial_t B + \operatorname{div}(B v_S) &= \Gamma_B, \\
\partial_t D + \operatorname{div}(D v_S) &= \Gamma_D, \\
\partial_t E + \operatorname{div}(E v_S) &= \Gamma_E, \\
\partial_t L + \operatorname{div}(L v_L) &= \Gamma_L.
\end{aligned}$$

$\Gamma_B, \Gamma_D, \Gamma_E, \Gamma_L$
= mass exchange rates

- **Volume constraint** :

$$B + D + E + L = 1.$$

Mass exchange rates

Modeling biology !

* **Mass conservation** : $\Gamma_B + \Gamma_D + \Gamma_E + \Gamma_L = 0.$
* Mass exchange rate for B (cyanobacteria) :

$$\Gamma_B = \underbrace{k_B(I)\, LB}_{\text{birth term for bacteria}} - \underbrace{k_D\, B}_{\text{death term for cyanobacteria}}$$

* Mass exchange rate for D (dead bacteria) :

$$\Gamma_D = \underbrace{\alpha k_D\, B}_{\text{bacteria death}} - \underbrace{k_N\, D}_{\text{natural decrease}}$$

* Mass exchange rate for E (EPS) :

$$\Gamma_E = \underbrace{k_E\, LB}_{\text{EPS production}} - \underbrace{\varepsilon E}_{\text{natural decrease}}$$

* I : Influence of light [Thebault, Rabouille, 2003]

Velocity equations

Modeling physics !

Recall :

$$\partial_t \rho + \operatorname{div} F = 0, \text{with } F = \rho \mathsf{v}$$

Velocity given by momentum conservation equation :

$$\partial_t(\rho \mathsf{v}) + \overbrace{\operatorname{div}(\rho \mathsf{v} \otimes \mathsf{v})}^{\text{inertial term}} = \text{ Ext. forces}$$

Velocity equations

Velocity given by momentum conservation equation :

$$\overbrace{\partial_t(\rho \mathsf{v}) + \mathrm{div}(\rho \mathsf{v} \otimes \mathsf{v})}^{\text{inertial term}} = \text{Ext. forces}$$

[Rajagopal-Tao, 1995 ; Byrne Preziosi, 2001 ; Ambrosi Preziosi, 2002 ; Astanin Preziosi, 2008]

- **Force balance for B, D and E :**

$$\partial_t((1-L)\mathsf{v}_S) + \mathrm{div}((1-L)\mathsf{v}_S \otimes \mathsf{v}_S) = F_{solid}$$

where

$$F_{solid} = \overbrace{\nabla\Sigma}^{\text{constraints}} - \overbrace{(1-L)\nabla P}^{\text{hydro. pressure}} + \underbrace{M(\mathsf{v}_L - \mathsf{v}_S)}_{\text{interaction forces}} \overbrace{-\Gamma_L \mathsf{v}_L}^{\text{momentum cons.}}$$

- **Force balance for L :**

$$\partial_t(L\mathsf{v}_L) + \mathrm{div}(L\mathsf{v}_L \otimes \mathsf{v}_L) = -L\nabla P - M(\mathsf{v}_L - \mathsf{v}_S) + \Gamma_L \mathsf{v}_L$$

Final system

* **Equations for the volume fractions** :

$$\begin{aligned}
&\partial_t B + \operatorname{div}(B\mathsf{v}_\mathsf{S}) = B\left(Lk_B(I,\theta,N) - k_D(I,\theta,N)\right),\\
&\partial_t D + \operatorname{div}(D\mathsf{v}_\mathsf{S}) = \alpha B k_D(I,\theta,N) - D k_N(\theta),\\
&\partial_t E + \operatorname{div}(E\mathsf{v}_\mathsf{S}) = BLk_E(\theta) - \varepsilon E,\\
&L = 1 - (B + D + E)
\end{aligned}$$

* **Equations for the velocities** :

$$\begin{aligned}
\partial_t((1-L)\mathsf{v}_\mathsf{S}) + \operatorname{div}((1-L)\mathsf{v}_\mathsf{S}\otimes\mathsf{v}_\mathsf{S}) + (1-L)\nabla P = \nabla\Sigma\\
+ (M - \Gamma_L)\mathsf{v}_\mathsf{L} - M\mathsf{v}_\mathsf{S},\\
\partial_t(L\mathsf{v}_\mathsf{L}) + \operatorname{div}(L\mathsf{v}_\mathsf{L}\otimes\mathsf{v}_\mathsf{L}) + L\nabla P = -(M-\Gamma_L)\mathsf{v}_\mathsf{L} + M\mathsf{v}_\mathsf{S}
\end{aligned}$$

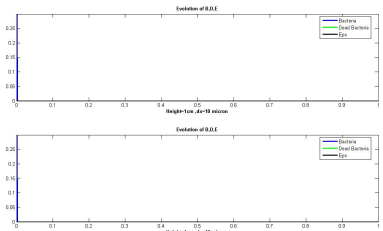
* **Incompressibility** :

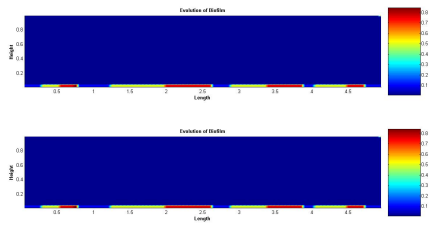
$$\operatorname{div}\left((1-L)\mathsf{v}_\mathsf{S} + L\mathsf{v}_\mathsf{L}\right) = 0.$$

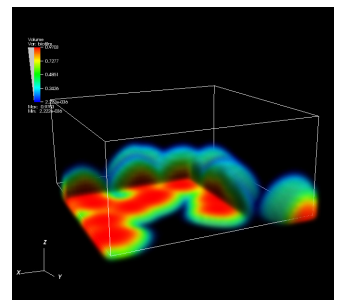
Cyanobacteria biofilms : contributions

[Clarelli, Di Russo, Natalini, R., J. Math. Biol. 2013 & Math. Med. Biol.,2016]

* Multi-phases hyperbolic model from mixture theory
  accounting for physics and biology
* Modeling the dependency on light
* Stationary solutions and their stability in 1D
* 1D, 2D analysis [Bianchini-Natalini 2016 - 2019]
* Numerical study
  - Numerical scheme : problems of vacuum and pressure
  - Parameter estimates
  - Sensibility analysis
* Simulations in 1D , 2D, 3D





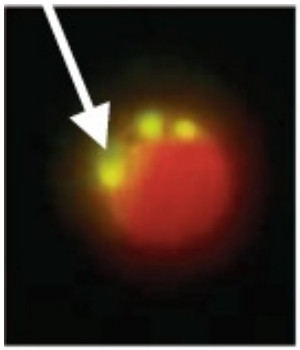
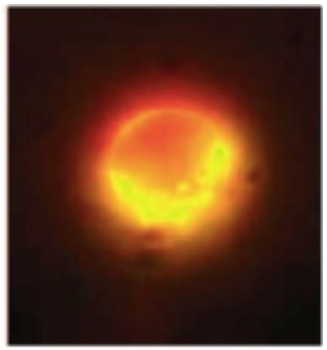


1D (60 days) , 2D (180 days), 3D (30 days)

Outline

Microalgae

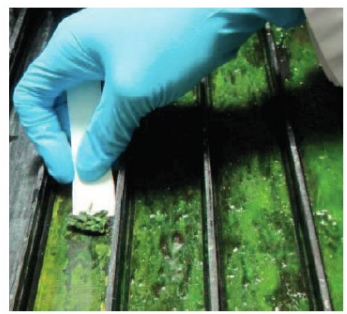
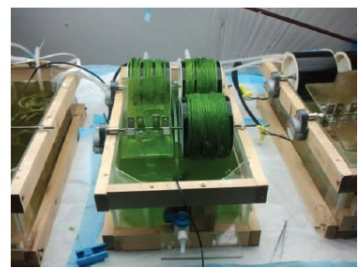
Use : biofuel, alimentary, cosmetic, water treatment,...

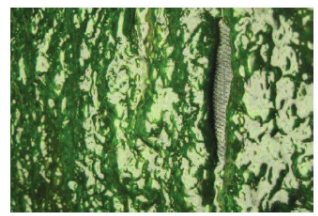



Production :

Raceways

Biofilms

Microalgae biofilms producing lipids

[Polizzi, Bernard, R., J. Math. Biol. 17 & Polizzi, Fanesi, Lopes, R., Bernard, PLOS Comp. Biol. 22]

Aims of the model :

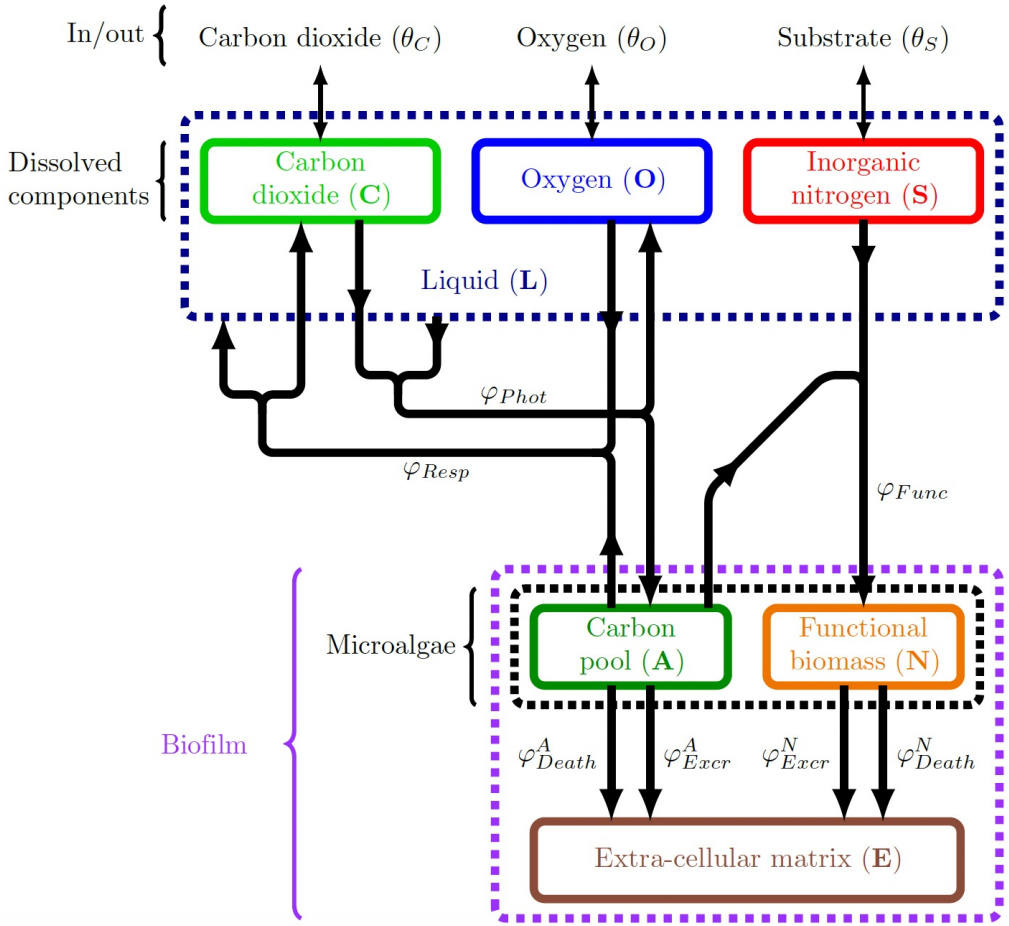
* Modeling in details photosynthesis & other chemical reactions
* Extra-cellular matrix excretion
* Influence of nutrient deficiency

$\Rightarrow$ Particular care to mass exchange terms

Model components :

* Microalgae = functional part N & carbon storage (lipids...) A
* Extra-cellular matrix E
* Liquid phase L
* Nutrients : nitrates S, carbon (bicarbonate)C, oxygen O

Considered reactions

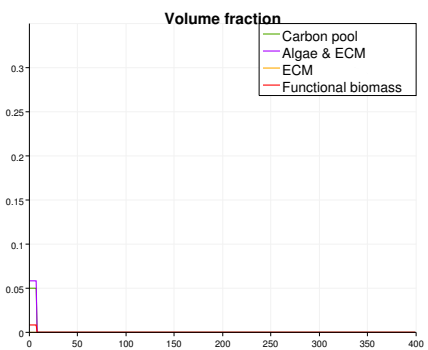


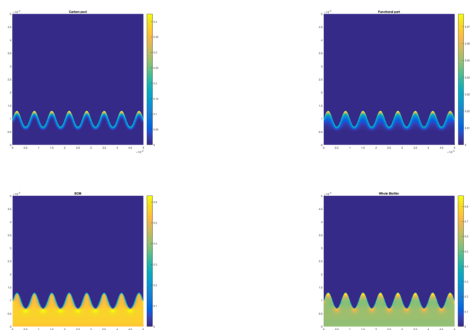
- Photosynthesis : assimilation of inorganic carbon (C) to (A)
- Respiration
- Biomass growth : from carbon (A) to functional part (N)
- Extra polymeric substrate excretion (organic carbon) (E)
- Death : from (A) and (N) to (E)

Contributions

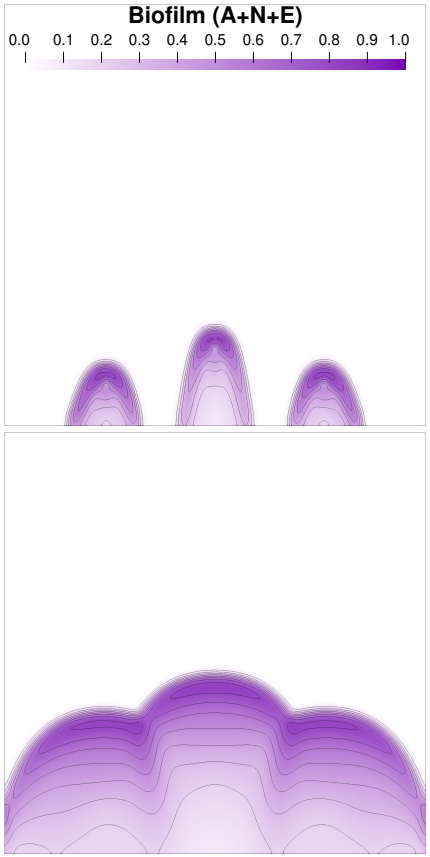
[Polizzi, Bernard, R., J. Math. Biol. 17 & Polizzi, Fanesi, Lopes, R., Bernard, PLOS Comp. Biol. 22]

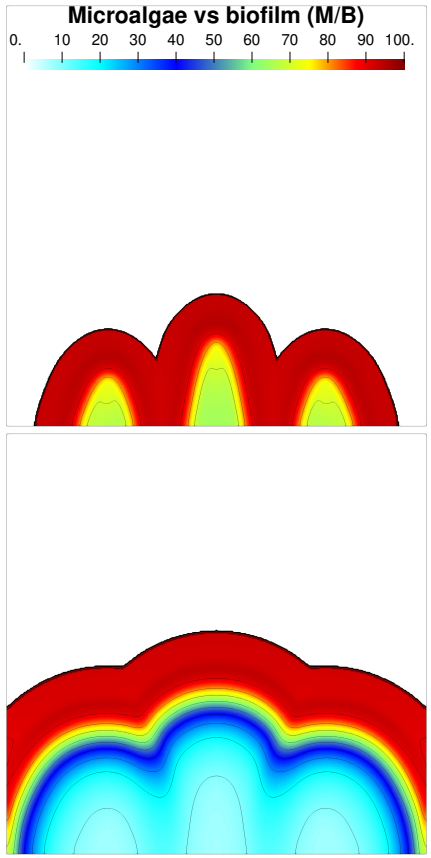
* Source terms from chemical reactions with saturation/ inhibition/threshold/optimal value effects
* Supplementary equations for nutrients
* Numerical study
  - Numerical scheme : problems of stiff source terms + more complex incompressibility equation
  - Estimate and influence of various parameters
* Simulations in 1D, 2D
* Optimization of the harvesting technique

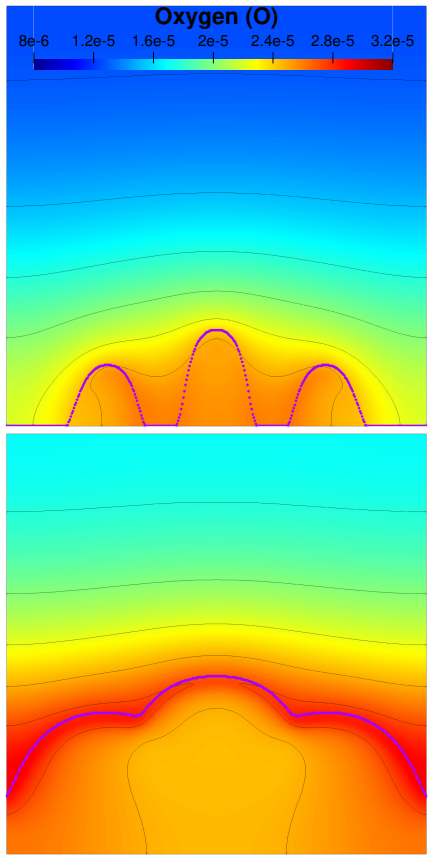


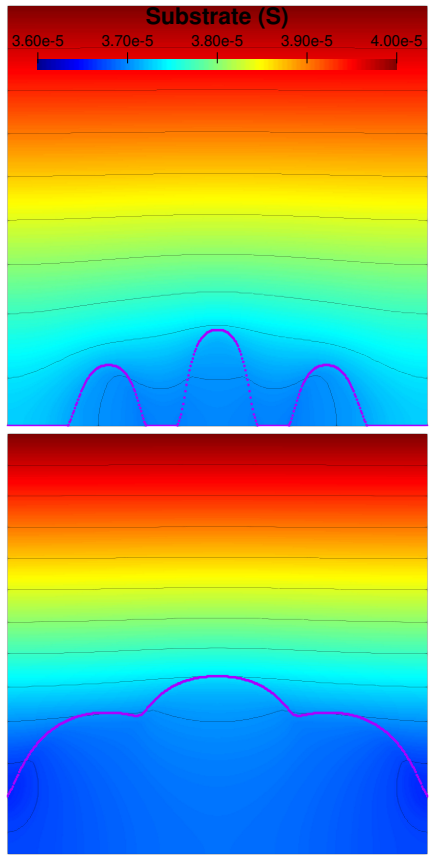


Numerical results (2D case)- T=5 and 20 days



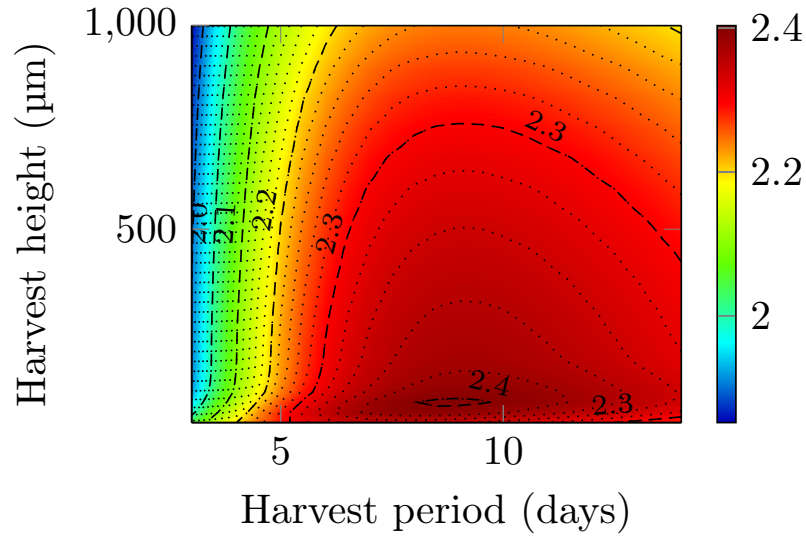




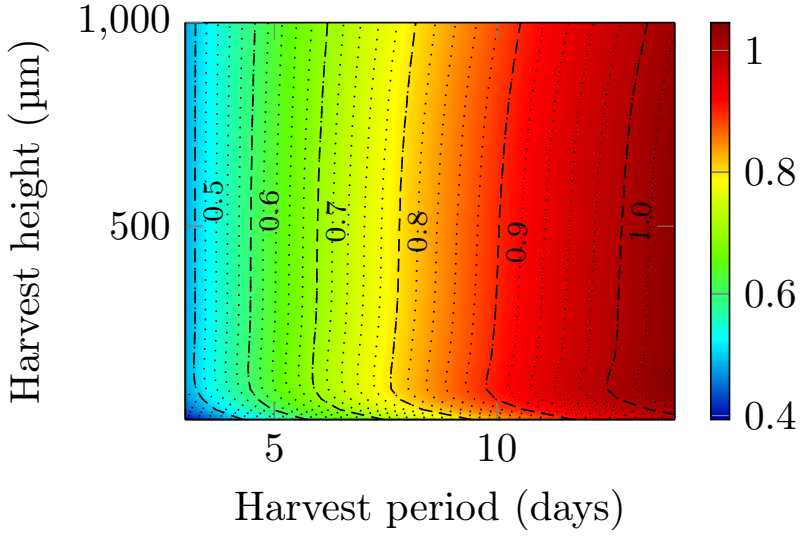


Optimization of the harvesting technique

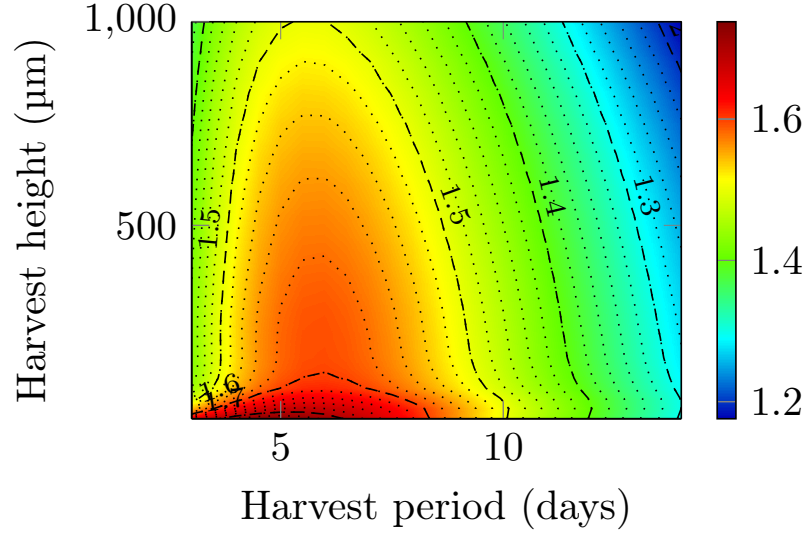
Daily production rates



Biofilm A + N + E



ECM E

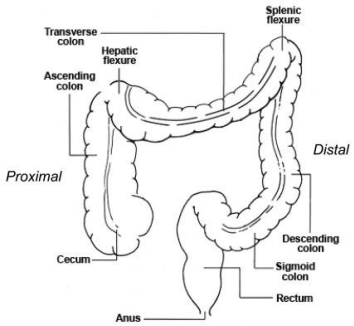


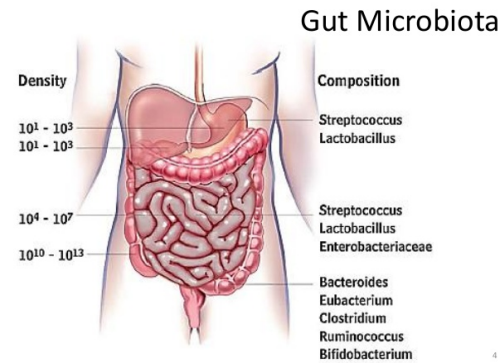
Microalgae A+N

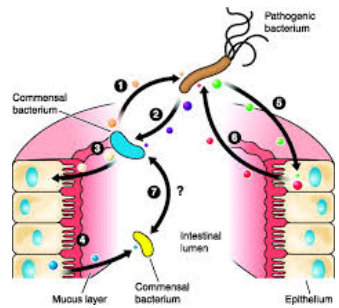
Outline

Colon & gut microbiota

- Largest number of bacteria and species in the body
- Disorders (dysbiosis) associated to metabolic, inflammatory, mental diseases
- Role : body hydration by pumping water
- Protective layer of mucus that separates bacteria from tissue
- Microbial community :
  - Digestion
  - Control pathogens
  - Regulate immune system







$\Rightarrow$ Important study in microbiology

Gut microbiota

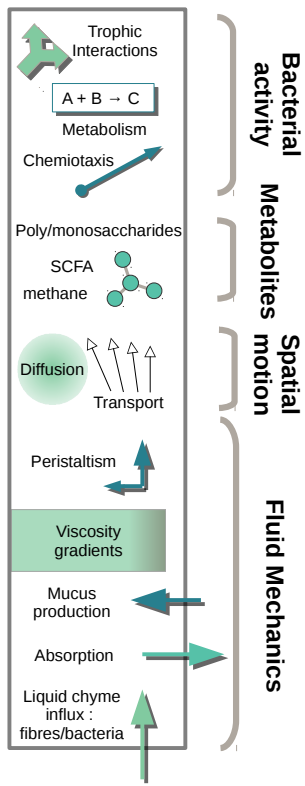
[El Bouti, Goudon, Labarthe, Laroche, Polizzi, Rachah, R., Tesson, ESAIM Proc 16], [Labarthe, Polizzi, Phan, Goudon, R., Laroche, J. Th. Biol. 2019]

Aims of the model :

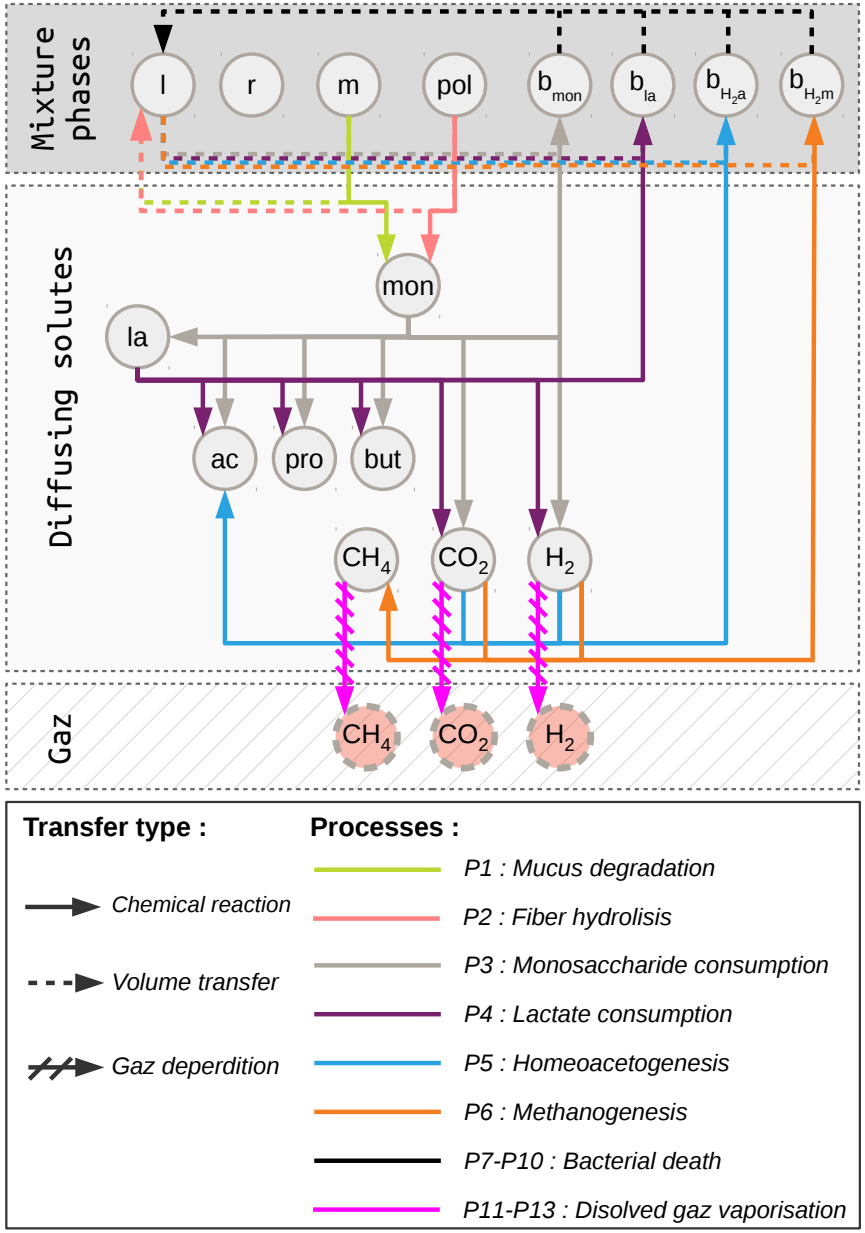
* Describe microbiota in its physical environment
* Understand how bacteria remain in colon, overcoming flow

Features of the model :

* Metabolic description of the digestion process in the colon [Muñoz-Tamayo et al, JTB 10 ; Moorthy et al., PLOS One 15]
* Hydrodynamical description (luminal flow, mucus structure,...)[Cremer, Hwa et al. PNAS 16 & 17]
* Bacteria patial behaviour (chemotaxis, peristalsis, ...)



Metabolic description



Simplified mixture model - Case of 2 phases

[El Bouti, Goudon, Labarthe, Laroche, Polizzi, Rachah, R., Tesson, ESAIM Proc 16]

M =mucus volume fraction, L= liquid volume fraction,
V=velocity, P=pressure

* Mass conservation :

$$\partial_t M + \mathrm{div}(MV) - \mathrm{div}(\sigma_M \nabla M) = F(M,L)$$
$$\partial_t L + \mathrm{div}(LV) - \mathrm{div}(\sigma_L \nabla L) = -F(M,L)$$
$$M + L = 1$$

$\Rightarrow$ Incompressibility constraint :

$$\mathrm{div}\, V = \mathrm{div}((\sigma_M - \sigma_L)\nabla M)$$

* Stokes equation :

$$-\mathrm{div}\left(\mu(M)\left(\nabla V + \nabla^T V\right)\right) + \nabla P = 0$$

Generalization to 8 components + 8 solutes

- Mass balance eq. for 8 components (f_i=volume fraction) :

  (mucus, polysaccharides, indigestible residuals, liquid, 4 bacteria)

$$\partial_t f_i + \mathrm{div}(f_i u_i) - \mathrm{div}(\sigma \nabla f_i) = F_i$$

  * Volume constraint : $\sum_i f_i = 1$
  * Velocity : $u_i = u + \theta_{i,chem}$ ($\theta_{i,chem}$=chemotaxis velocity)

- Mass balance eq. for 8 solutes (c_j=concentration) :

  (monosaccharides, lactate, H2, acetate, propionate, butyrate, CH4 and CO2)

$$\partial_t c_j + \mathrm{div}(c_j \tilde{u}) - \mathrm{div}(\sigma_j \nabla c_j) = G_j$$

  * No volume
  * Velocity : $\tilde{u} = \sum_i f_i u_i$

- Stokes equation (u=velocity ; p=pressure)

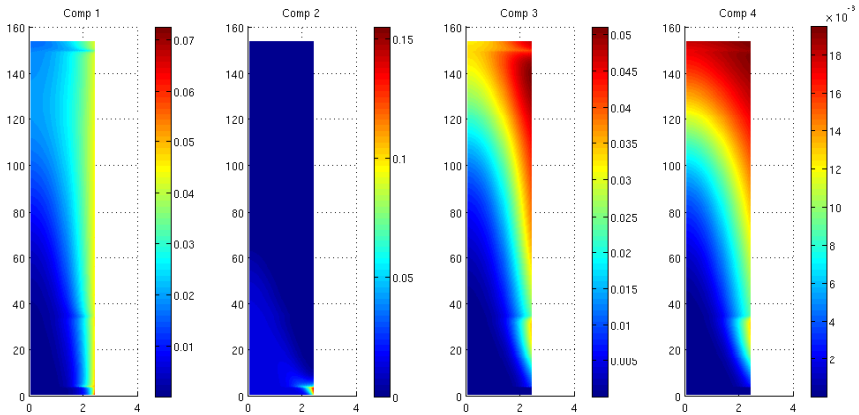
$$-\mathrm{div}(\mu(f_m, f_l)(\nabla u + \nabla u^T)) + \nabla p = 0$$

- On boundaries : peristalsis, water pumping, mucus production, SCFA absorption, ...

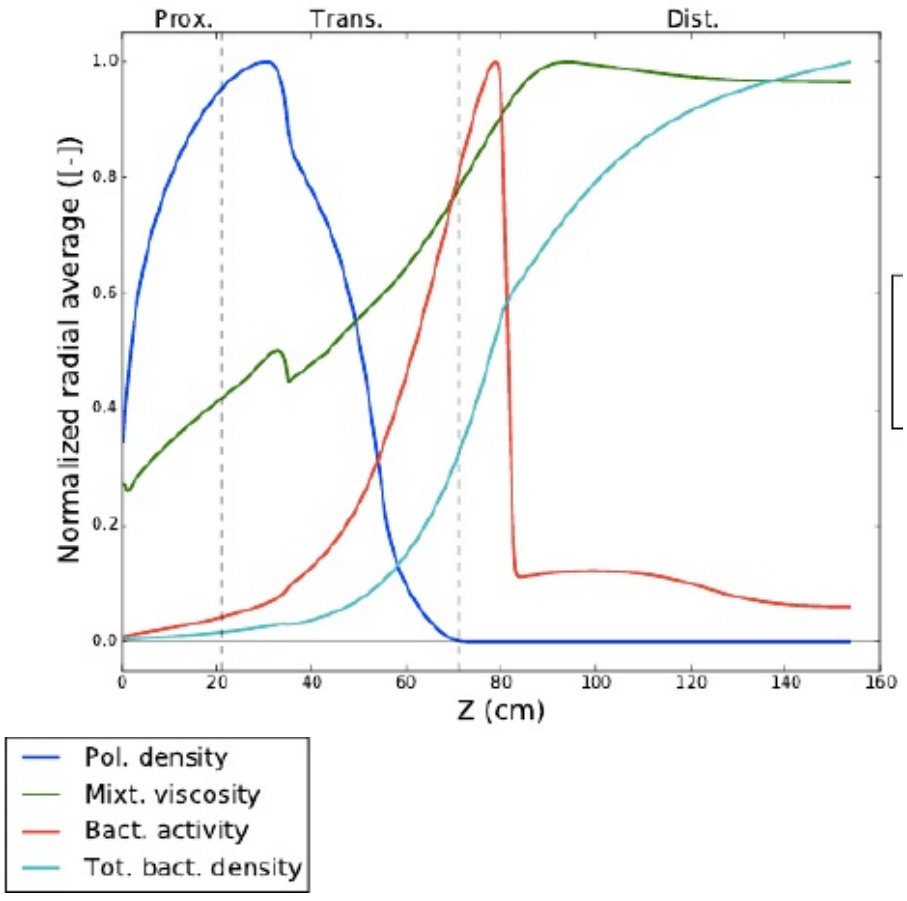
Contributions

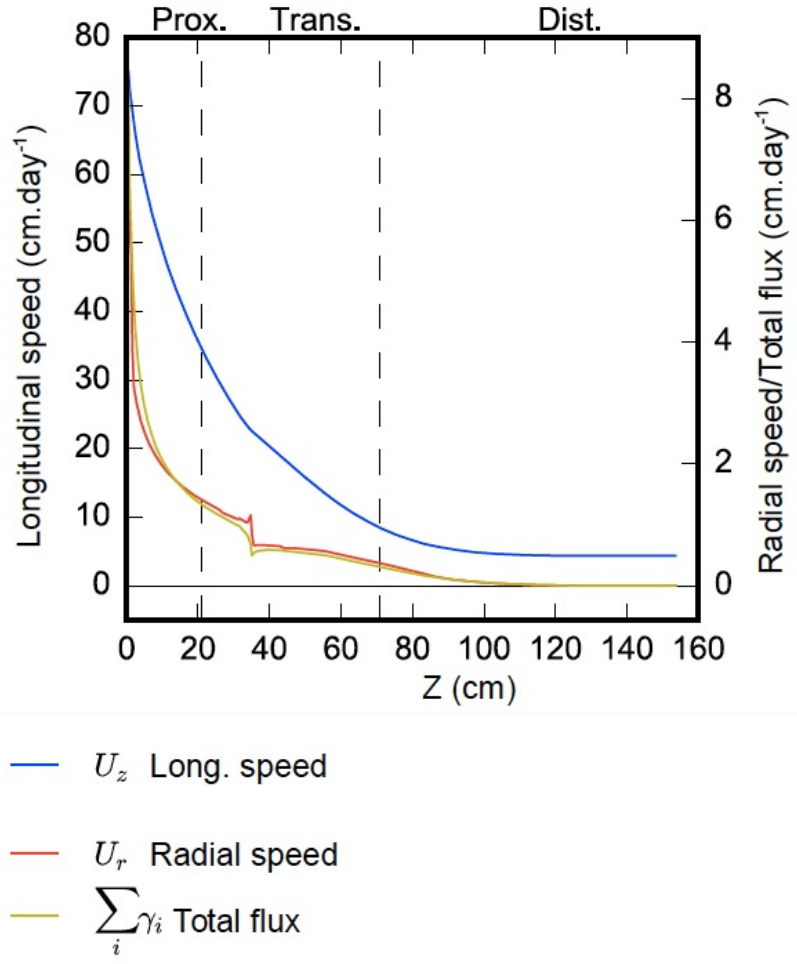
[El Bouti, Goudon, Labarthe, Laroche, Polizzi, Rachah, R., Tesson, ESAIM Proc 16], [Labarthe, Polizzi, Phan, Goudon, R., Laroche, J. Th. Biol. 2019]

- Coupling between metabolic processes and fluid mechanism (viscosity)
- Modeling of chemotaxis, of peristalsis, ...
- Asymptotic model in the limit $\varepsilon = R/L << 1$
- Numerical study
- Sensitivity analysis
- Simulations in 1D, 2D

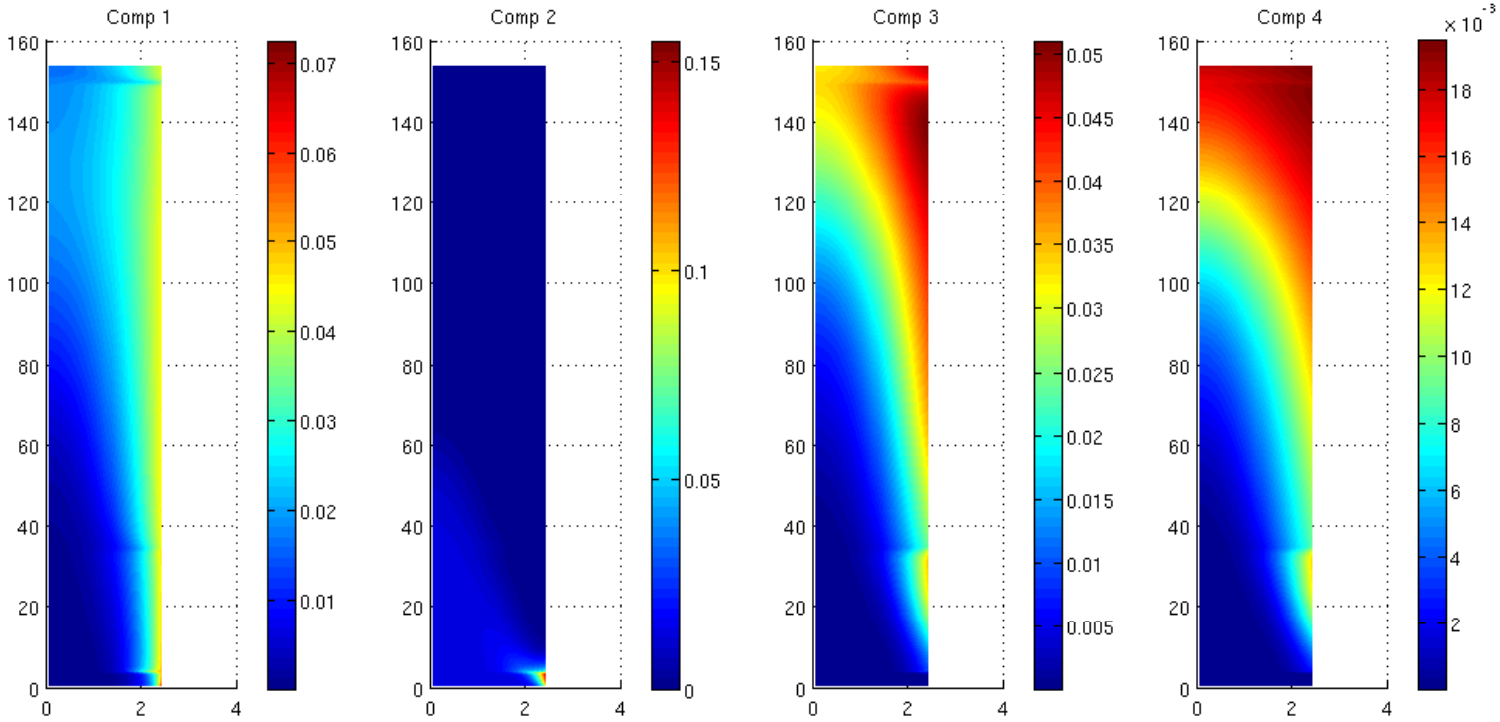


Reference state



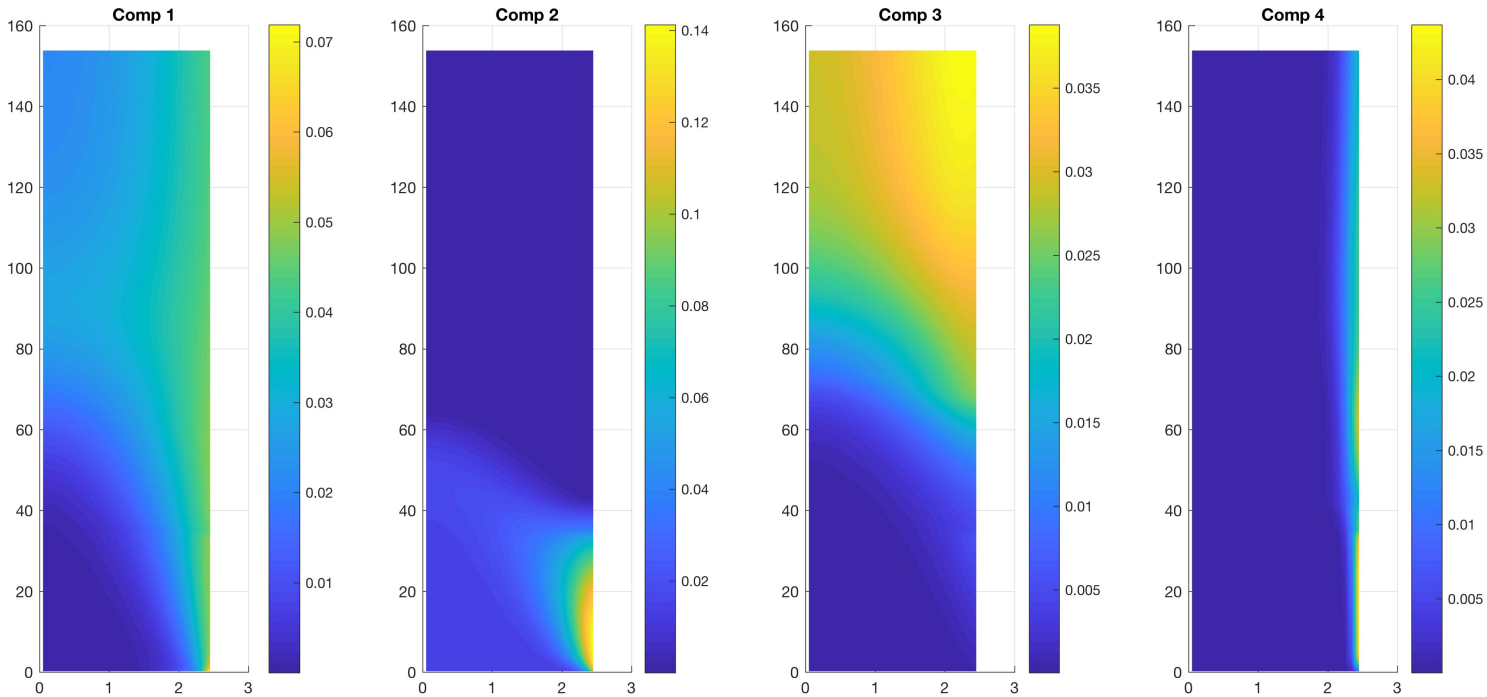


Persistence of mucus layer & bacteria - Spatial structure



from left to right :mucus, polysaccharides, bacteria (monosaccharides), bacteria (lactate)

Competition between bacteria in the gut



from left to right : mucus, polysaccharides, bacteria 1 & bacteria 2 (case when bacteria 1 $\geq$ bacteria 2 for metabolism ; bacteria 2 $\geq$ bacteria 1 for chemotaxis)