Modeling and inference of bacterial swimmers in biofilms

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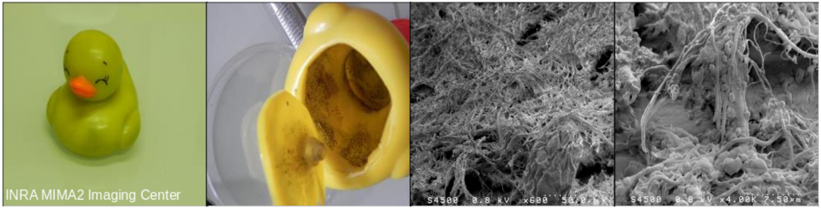
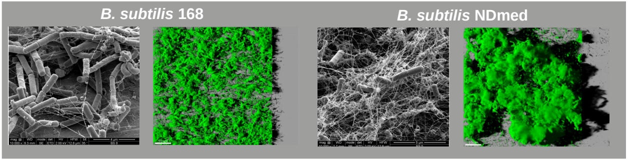
Introduction

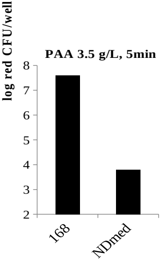
Context : biofilms

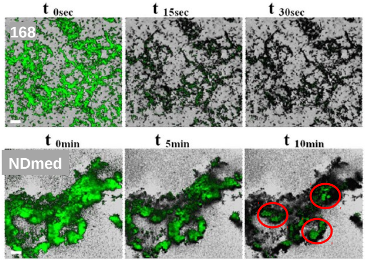


Structural resistance

Biofilms (vs plantonic phase) provide resistance to biocides

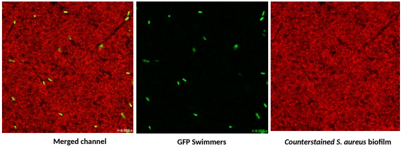




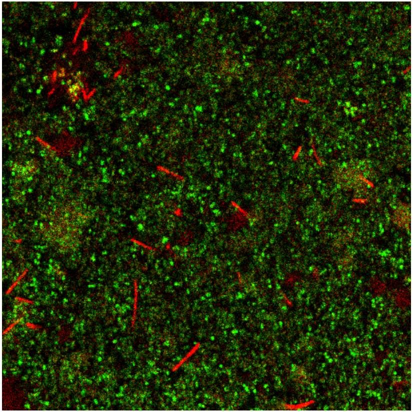


Bridier et al., Plos One 2011

Bacterial swimmers in biofilms



Images : courtesy of Romain Briandet



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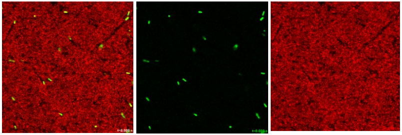
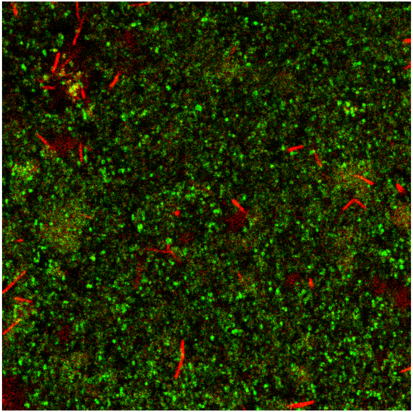


Merged channel GFP Swimmers *Counterstained S. aureus* biofilm

Images : courtesy of Romain Briandet



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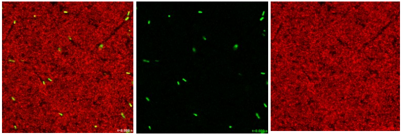

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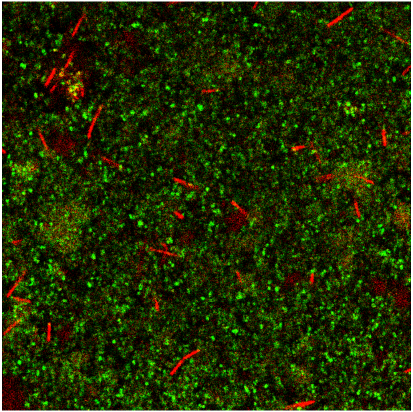
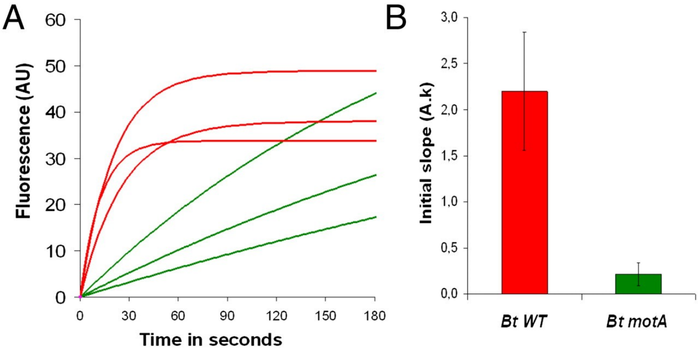


Swimmers facilitate diffusion

Penetration of macromolecules in biofilms is facilitated by swimmer bacteria.



Ali Houry et al. PNAS 2012;109:32:13088-13093

ANR GreenSwimmers

GreenSwimmers (A.Briandet/INRAE)

- swimmers bank ($\simeq$ 120 swimmer strains) + images
- image analysis (A.Trubuil, MaIAGE/INRAE).
- Swim descriptor and statistics $\Rightarrow$typology

Linking swimmer types with underlying biofilm

"foragers" (explore a lot) vs "bulldozers" (dig big pores) vs "ants" (explore again pores made by others) vs ...

$\Rightarrow$Do bacteria adapt their swimming to the underlying biofilm ? Are there species-specific patterns ?

Question

Goal

- Understand the link between underlyning biofilm and bacterial swimming.
- Characterize and discriminate bacterial species according to their swimming strategy.

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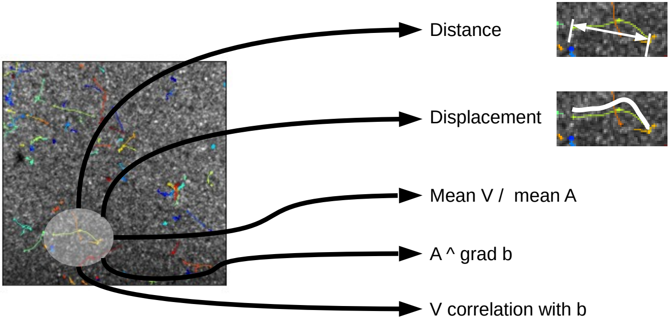
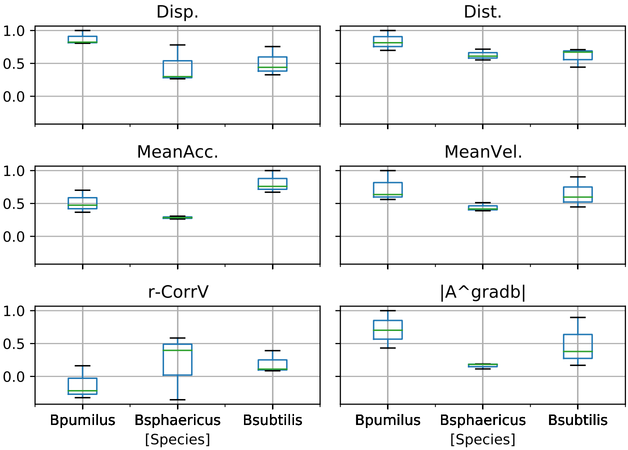
2 › Characterizing bacterial swimming

Swimming characteristics



Swimming characteristics



3 Swimmer model

IBM definition

Random walk model (Langevin equation)

Let X^i the position of the swimmer i, $dX^i = dV^i dt$

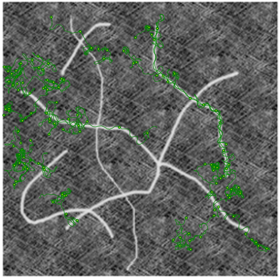
$$dV^i = (\gamma(\alpha(b) - ||V^i||)V^i + \beta \frac{\nabla b}{||\nabla b||})dt + \varepsilon\sqrt{dt}$$

where $\alpha(b) := v_{bio} + b(v_{mat} - v_{bio})$ defines the (b dependant) swimming speed, γ is a relaxation time, β a directional force, and ε a brownian noise.

Qualitative assessment

Random walk model (Langevin equation)

$$dV^i = (\gamma(\alpha(b) - ||V^i||)V^i + \beta \frac{\nabla b}{||\nabla b||})dt + \varepsilon\sqrt{dt}$$



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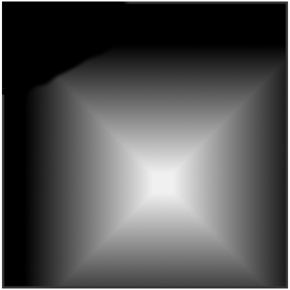
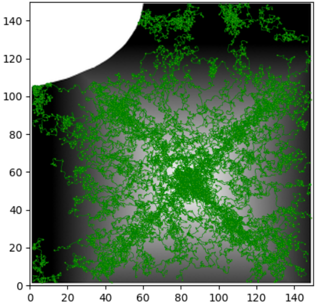




4 Setting the inference problem

Normalized model

Non-dimensioned model

$$\mathrm{d}\mathbf{v} = \gamma'(v_0' + b(v_1' - v_0') - \|\mathbf{v}\|)\frac{\mathbf{v}}{\|\mathbf{v}\|}\mathrm{dt} + \beta'\frac{\nabla b}{\|\nabla b\|}\mathrm{dt} + \eta'_{\mathbf{mod}}\mathrm{dt}$$

where :

$$\begin{cases} \gamma' = \dfrac{\gamma V^*}{A^*} \\ v_0' = \dfrac{v_0}{V^*} \\ v_1' = \dfrac{v_1}{V^*} \\ \beta' = \dfrac{\beta}{A^*} \\ \eta'_{mod} \sim \mathcal{N}(0, \epsilon') \\ \epsilon' = \dfrac{\epsilon}{A^*} \end{cases}$$

Normalized model

Non-dimensioned model

$$\mathrm{d}\mathbf{v} = \gamma'(v_0' + b(v_1' - v_0') - \|\mathbf{v}\|)\frac{\mathbf{v}}{\|\mathbf{v}\|}\mathrm{dt} + \beta'\frac{\nabla b}{\|\nabla b\|}\mathrm{dt} + \eta'_{\mathbf{mod}}\mathrm{dt}$$

Acceleration equation

$$\frac{\mathrm{d}\mathbf{v}}{dt} := Y_A = f_A(\theta, z, \mathbf{v}, b, \nabla b) + \eta'_{\mathbf{mod}}$$

where :

$$\begin{cases} \theta = (\gamma, v_0, v_1, \beta) \text{ the parameter vector} \\ f_A(z, \theta, b, \nabla b) = \gamma'(v_0' + b(v_1' - v_0') - \|\mathbf{v}\|)\frac{\mathbf{v}}{\|\mathbf{v}\|} + \beta'\frac{\nabla b}{\|\nabla b\|} \end{cases}$$

Inference problem

$$\frac{\mathrm{d}\mathbf{v}}{dt} := Y_A = f_A(\theta, z, \mathbf{v}, b, \nabla b) + \eta'_{\mathbf{mod}}$$

Data and preprocessing

Compute

$$X := (z, \mathbf{v}, b, \nabla b)$$

where

$$\begin{cases} z : \text{observed positions (assumption : no observation error).} \\ \mathbf{v} : \text{computation by finite difference from } z \\ b \text{ and } \nabla b : \text{computed by observations and finite difference on biofilm} \end{cases}$$

and

$$Y_A \text{ by finite difference}$$

.

Inference problem

$$\frac{\mathrm{d}\mathbf{v}}{dt} := Y_A = f_A(\theta, z, \mathbf{v}, b, \nabla b) + \eta'_{\mathbf{mod}}$$

Bayesian framework : regression problem

- Define priors on θ and ϵ'.
- Define the likelihood function

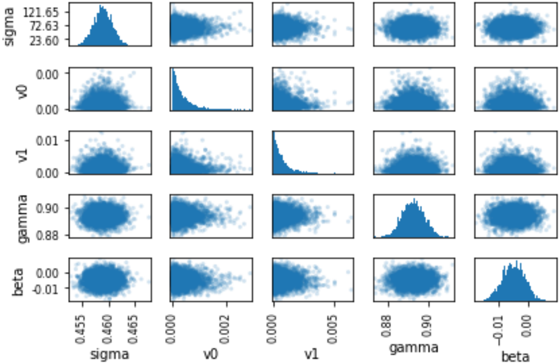
$$Y_A \sim \mathcal{N}(f_A(\theta|X), \epsilon')$$

Implementation : Stan (via pystan)

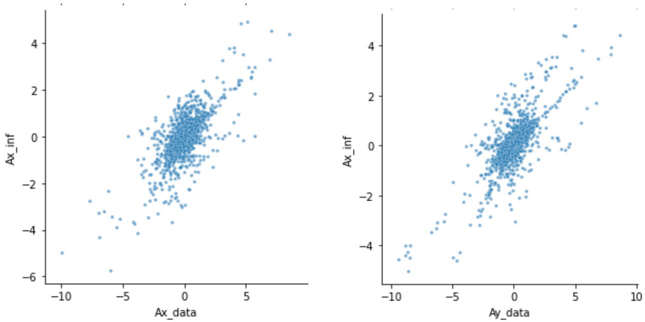
5 > Inference validation

Checking posteriors

Parameter chains pair-plot

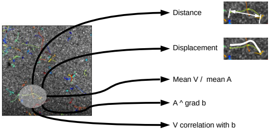


Y_A vs $f_A(X|\theta)$



$\frac{\sigma_i}{\sigma(y_i^A)}$	r^2
0.674	0.45

Simulated indicators

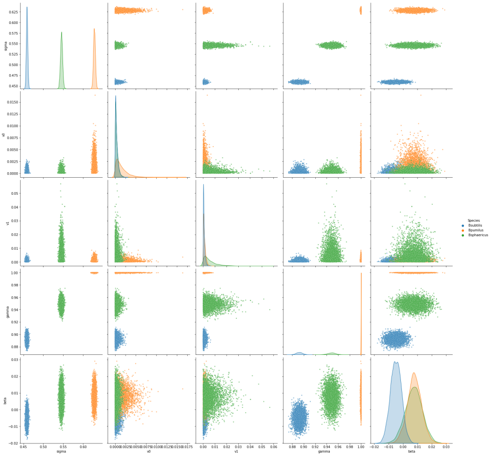


	Dist.	Disp.	Mean Vel.	Mean Acc.
REF	40.911	5.139	1.0	1.0
Mean (1000 simus)	54.276	7.740	0.998	0.959

[Bpumilus]

Interpretation

Parameter chains pair-plot



6 > Conclusion

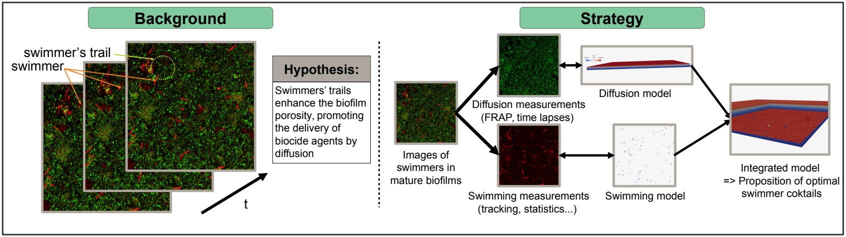
Conclusions

Characterizing bacterial swimming

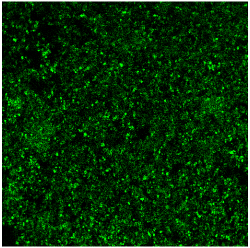
- mechanistic model of bacterial swimming with interaction with underlying biofilm
- bayesian inference
- Deterministic part of the random walk model accounts for 40 % of the variance.
- Allow to reproduce macroscopic indicators
- Allow to discriminate bacteria

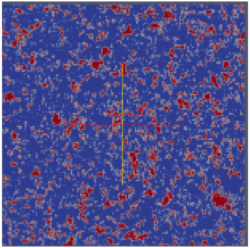
Perspective

Modeling bacterial swimmers coupled with diffusion



Diffusion model





We note c and b respectively the biocide and the biofilm bacteria concentrations.

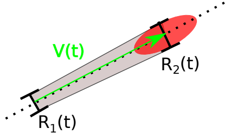
$$\partial_t c = \text{div}(\sigma(b)\nabla c) - d\frac{cb}{K+b} \text{ on } \Omega$$

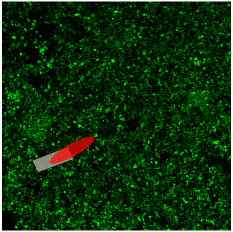
$$\nabla c \cdot \eta = 0 \text{ on } \partial\Omega \setminus \Gamma, \quad c = c_{in} \text{ on } \Gamma$$

where the isotropic diffusion tensor $\sigma(b) := \sigma_{min} + b(\sigma_{max} - \sigma_{min})$ depends on b, and the Michaelis-Menten parameters d and K are uniform.

Coupling swimmers and diffusion

Pore model





- Swimmers leave tails
- Due to biofilm mechanics, pores are plugged.
- Modeled phenomenologically with cones with time-dependent radius $R_i(t)$.

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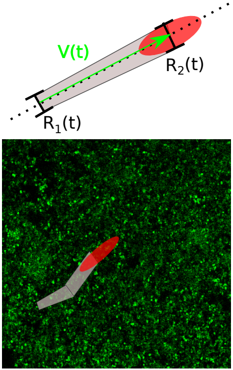

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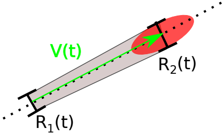

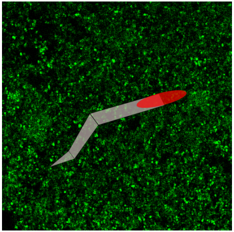

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