The metabolic niche and its applications

Antoine Régimbeau

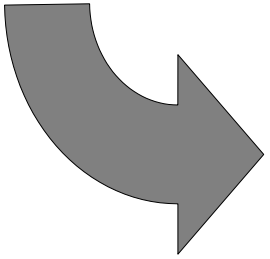
Functional omics

Genomics

DNA

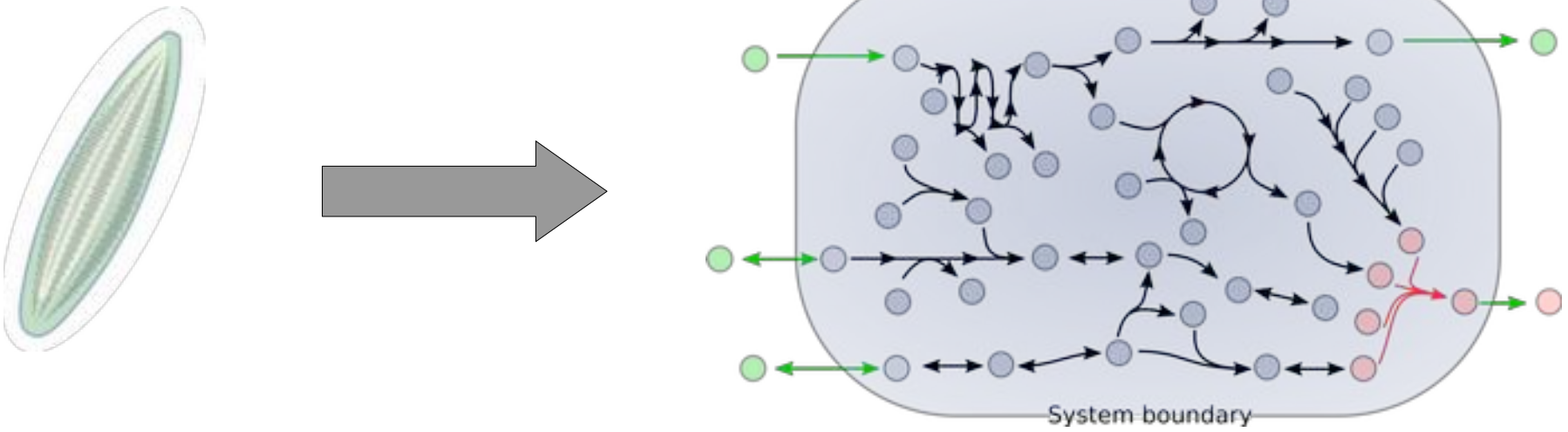
Transcriptomics

RNA



Responsible for most of the biological functions of an organism

Metabolic network

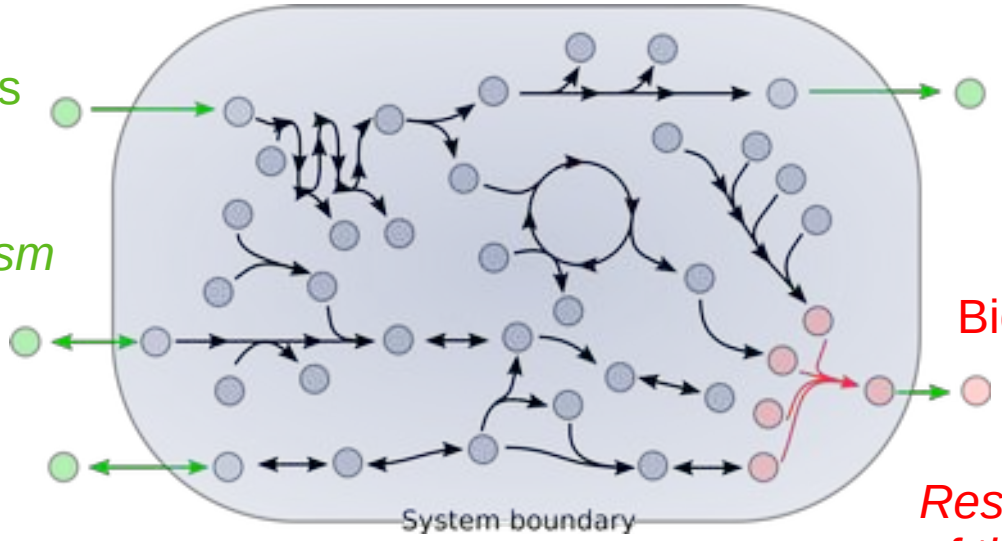


Abstracting a system through its metabolic abilities

Metabolic network: Modeling reactions

Exchange reactions

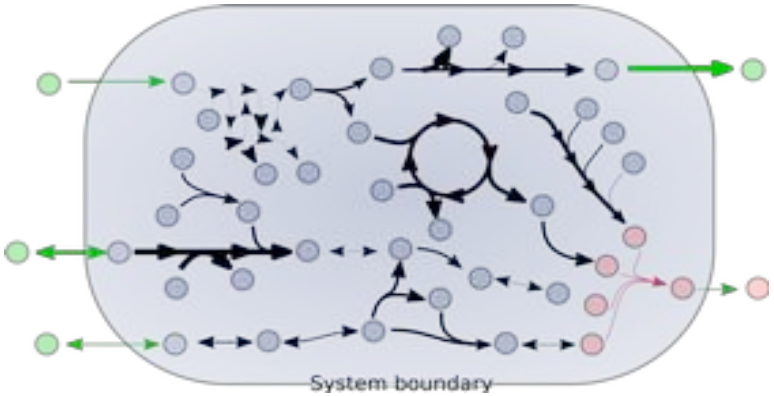
Responsible for the interactions of the organism with its environment.



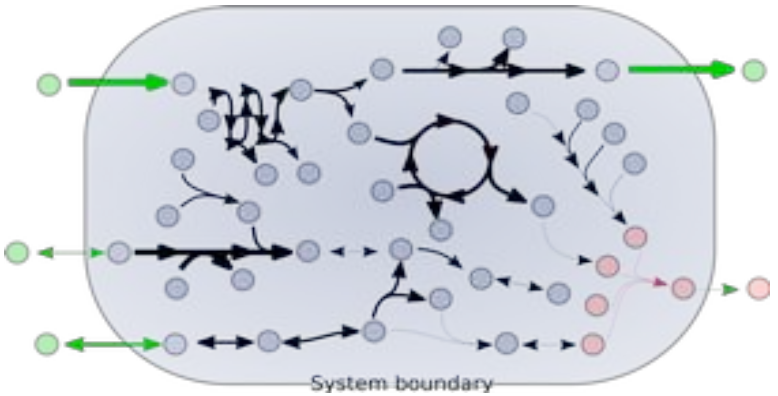
Biomass reaction

Responsible for the growth of the organism.
Mainly developed in a bio-engineering context.

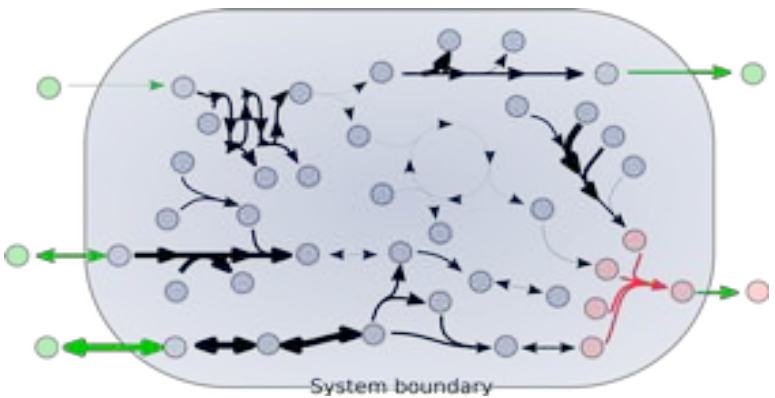
Metabolic network: Fluxes



State 1



State 3



State 2

Genome Scale Model: Mathematical formulation

GSM of a system:

$$\begin{cases} \mathbf{S}\mathbf{v} = \mathbf{0} \\ \mathbf{l_b} \leq \mathbf{v} \leq \mathbf{u_b} \end{cases}$$

Solution space of the GSM:

$$\mathcal{F} := \{\mathbf{v} \in \mathbb{R}^n, \mathbf{S}\mathbf{v} = 0, \quad \mathbf{lb} \leq \mathbf{v} \leq \mathbf{ub}\}$$

Steady state approximation

Thermodynamic constraints

A bit of ecology in Genome-Scale Models

$$\mathcal{F} := \{\mathbf{v} \in \mathbb{R}^n, \mathbf{S}\mathbf{v} = 0, \quad \mathbf{lb} \leq \mathbf{v} \leq \mathbf{ub}\}$$

The survival of the organism is assured if its growth rate is higher than its death rate:

$$\delta \leq v_{bio}$$

$$\mathcal{NF} := \{\mathbf{v} \in \mathbb{R}^n, \mathbf{S}\mathbf{v} = 0, \quad \mathbf{lb} \leq \mathbf{v} \leq \mathbf{ub}, \quad \delta \leq v_{bio}\}$$

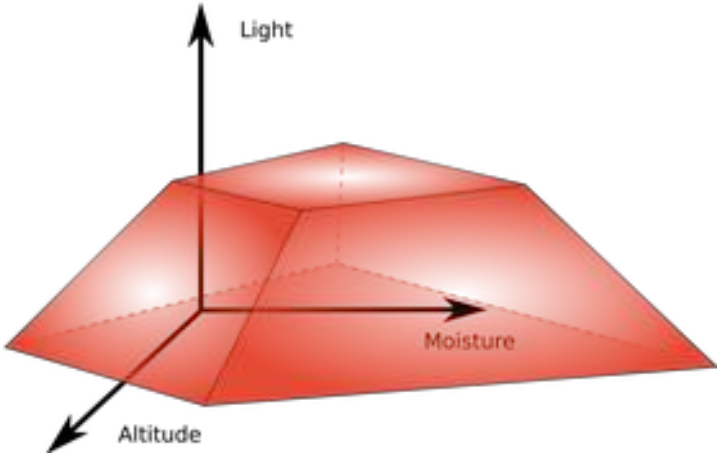
Survival condition

The ecological niche concept

Introduced by Joseph Grinnell in 1917

Formalized by Hutchinson in 1957 through the niche hypervolume:

Set of environmental conditions that assure the species survival



Concluding Remarks

G. Evelyn Hutchinson

Cold Spring Harb Symp Quant Biol 1957 22: 415-427
Access the most recent version at doi:10.1101/SQB.1957.022.01.039

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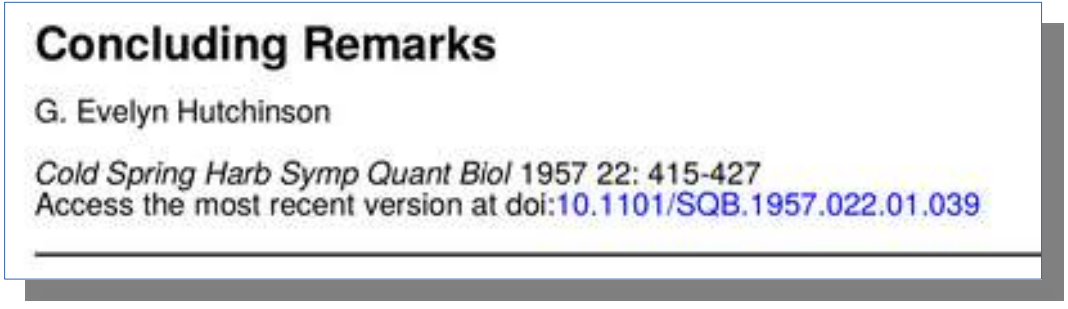

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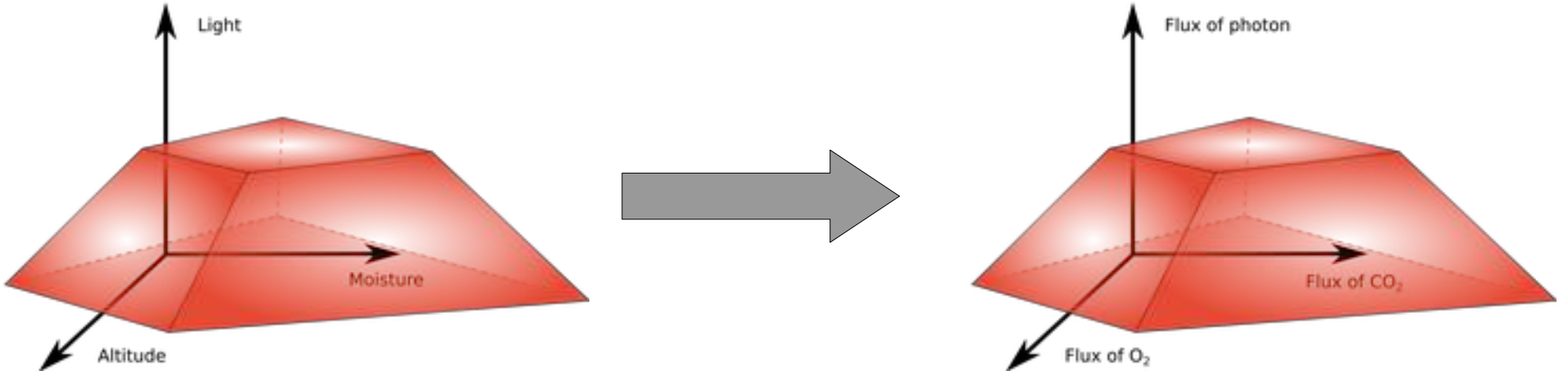
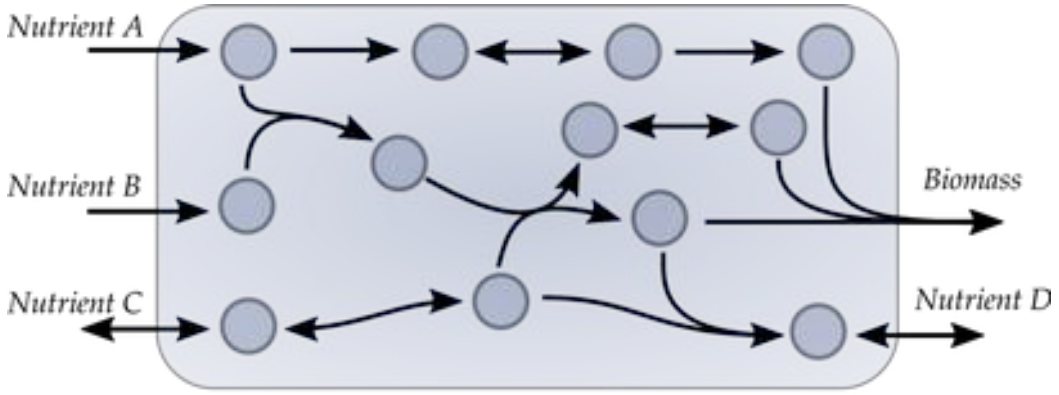
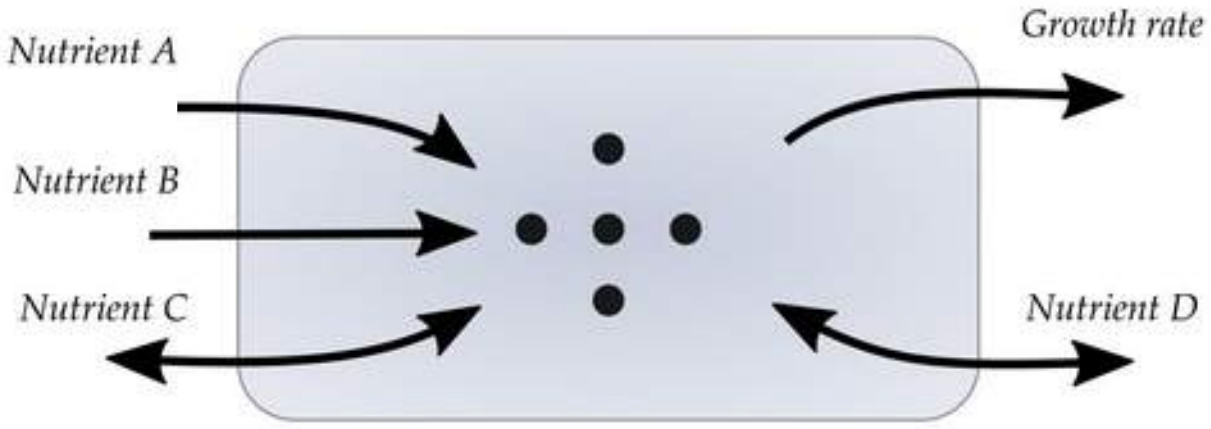
Translation in metabolic modeling

Set of environmental conditions: set of fluxes through the exchange reactions



Translation in metabolic modeling





$$\begin{cases} \mathbf{Sv} = \mathbf{0} \\ \mathbf{l_b} \leq \mathbf{v} \leq \mathbf{u_b} \end{cases}$$

?

The metabolic niche in equations

$$\mathcal{F} := \{\mathbf{v} \in \mathbb{R}^n, \mathbf{S}\mathbf{v} = 0, \quad \mathbf{lb} \leq \mathbf{v} \leq \mathbf{ub}\}$$

Projection

$$\mathcal{N} := \{\mathbf{x} \in \mathbb{R}^p | \exists \mathbf{y} \in \mathbb{R}^{n-p}, \mathbf{S}\begin{pmatrix}\mathbf{x}\\ \mathbf{y}\end{pmatrix} = \mathbf{0}, \mathbf{lb} \leq \begin{pmatrix}\mathbf{x}\\ \mathbf{y}\end{pmatrix} \leq \mathbf{ub}\}$$

Vector linear programming

$$\begin{cases} min \begin{pmatrix} I_p \\ -\mathbf{1}_p^T \end{pmatrix} \mathbf{x} \\ \text{subject to} \quad \begin{pmatrix}\mathbf{x}\\ \mathbf{y}\end{pmatrix} \in \mathcal{F} \end{cases}$$

The metabolic niche in ~~equations~~ papers

Equivalence between polyhedral projection, multiple objective linear programming and vector linear programming

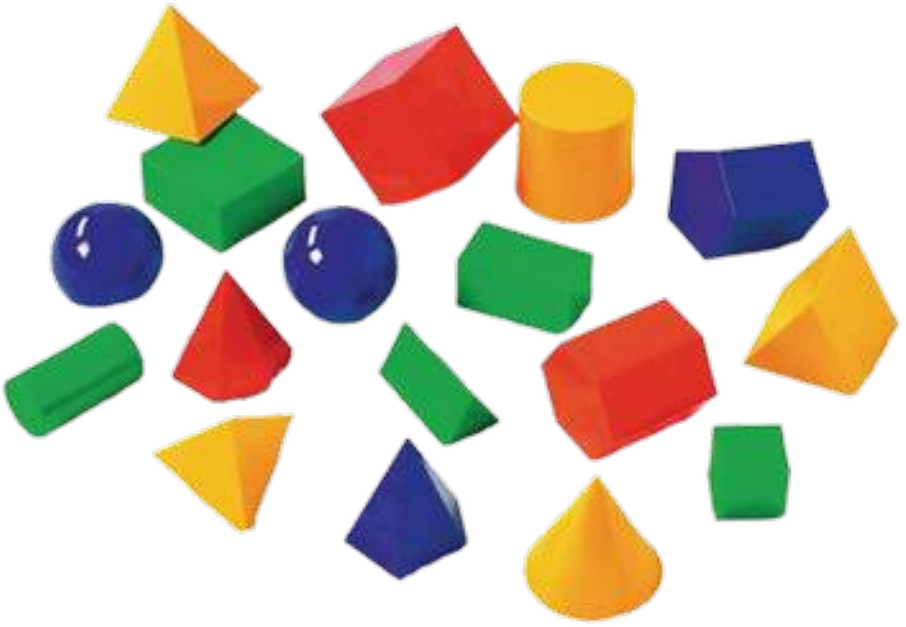
Andreas Löhne * Benjamin Weißing †

July 25, 2016

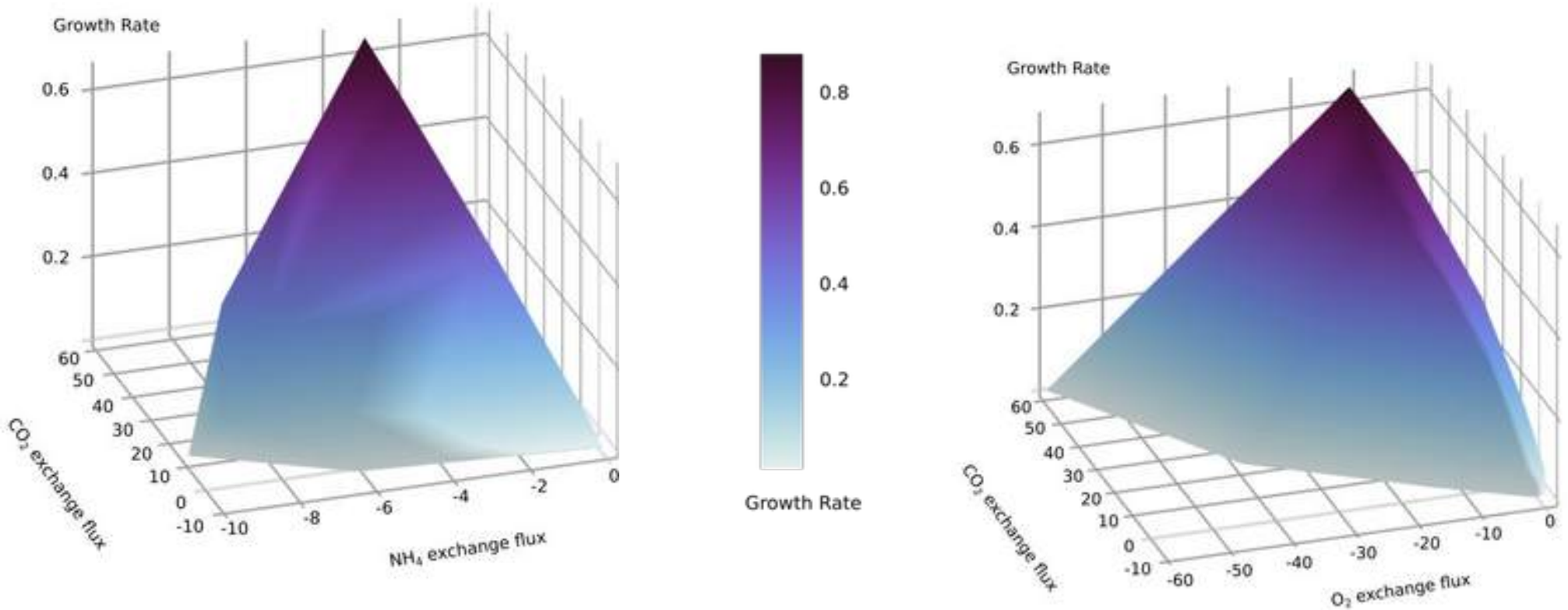
Contribution of genome-scale metabolic modelling to niche theory

Antoine Régimbeau[1] | Marko Budinich[1] | Abdelhalim Larhlimi[1] |
Juan José Pierella Karlusich[2] | Olivier Aumont[3] | Laurent Memery[4] |
Chris Bowler[2,5] | Damien Eveillard[1,5]

The metabolic niche in ~~equations~~ ~~papers~~ practice



Metabolic niche of E. Coli



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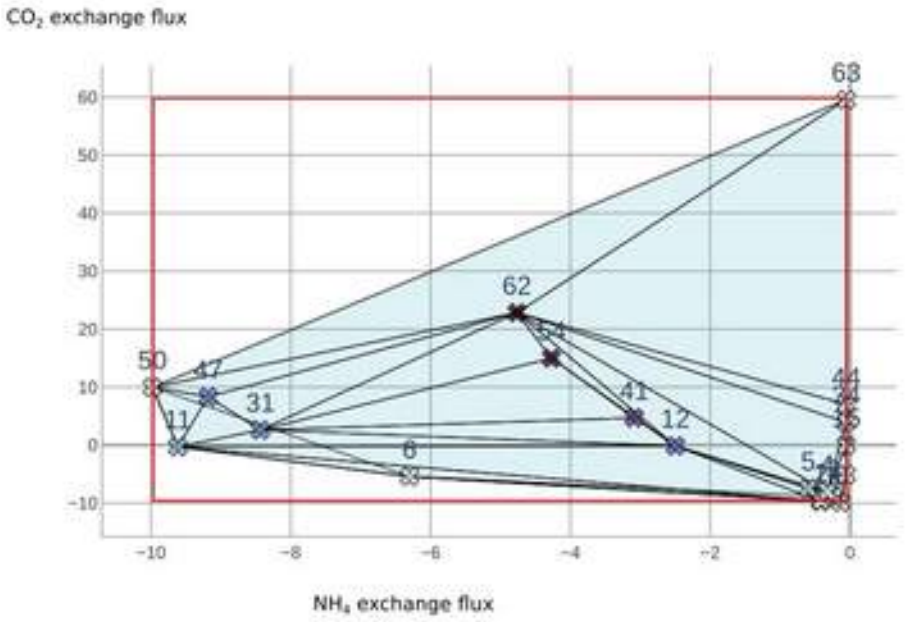
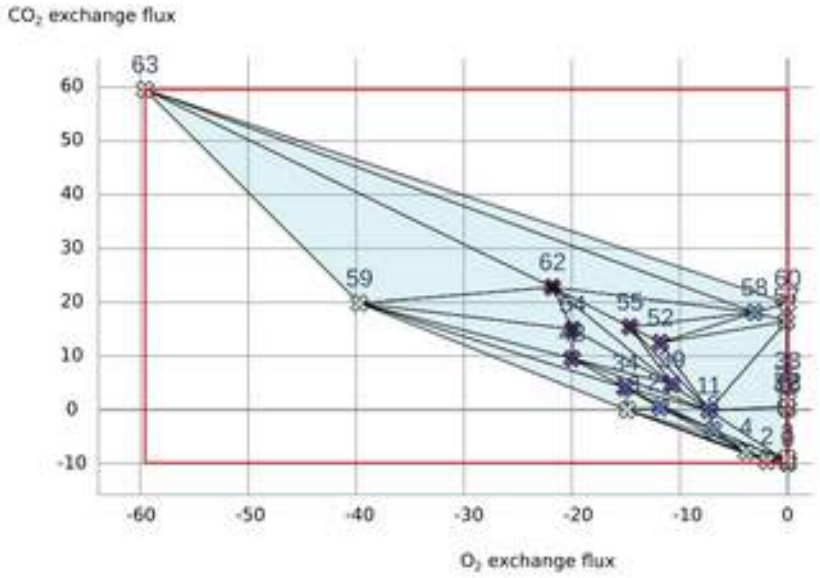




What can we do with metabolic niches?

Comparison of organisms through their niche

Considered nutrients (niche axes) :

- NH4
- SO4
- H2S
- Glucose
- NO3

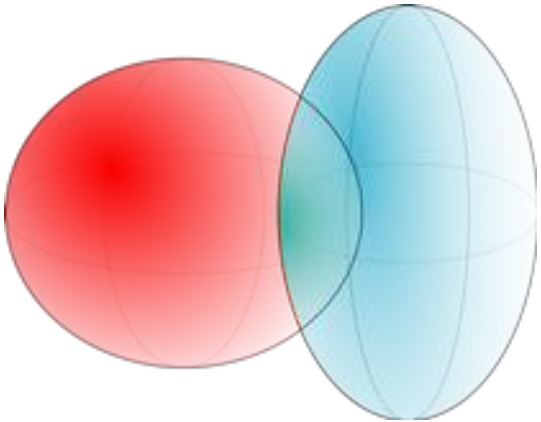
Metabolic Networks : bacteria reconstructed with CarveMe

How to compare metabolic niches?

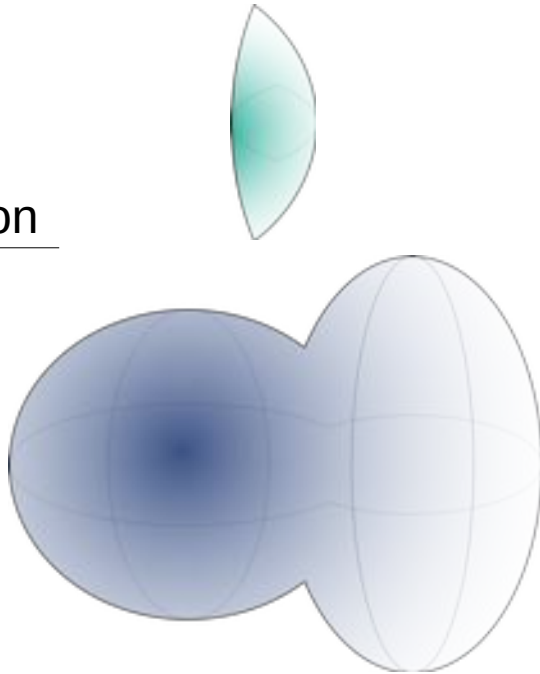
A measure of similarity between two volumes:

Blue volume

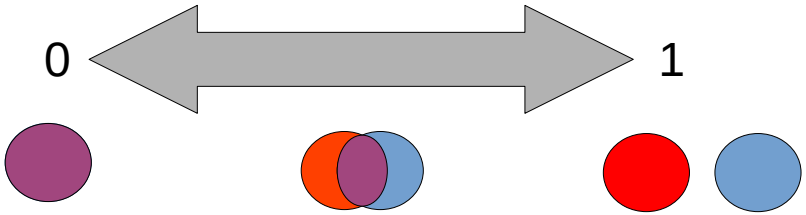
Red volume



Jaccard index : $\frac{\text{Intersection}}{\text{Union}}$

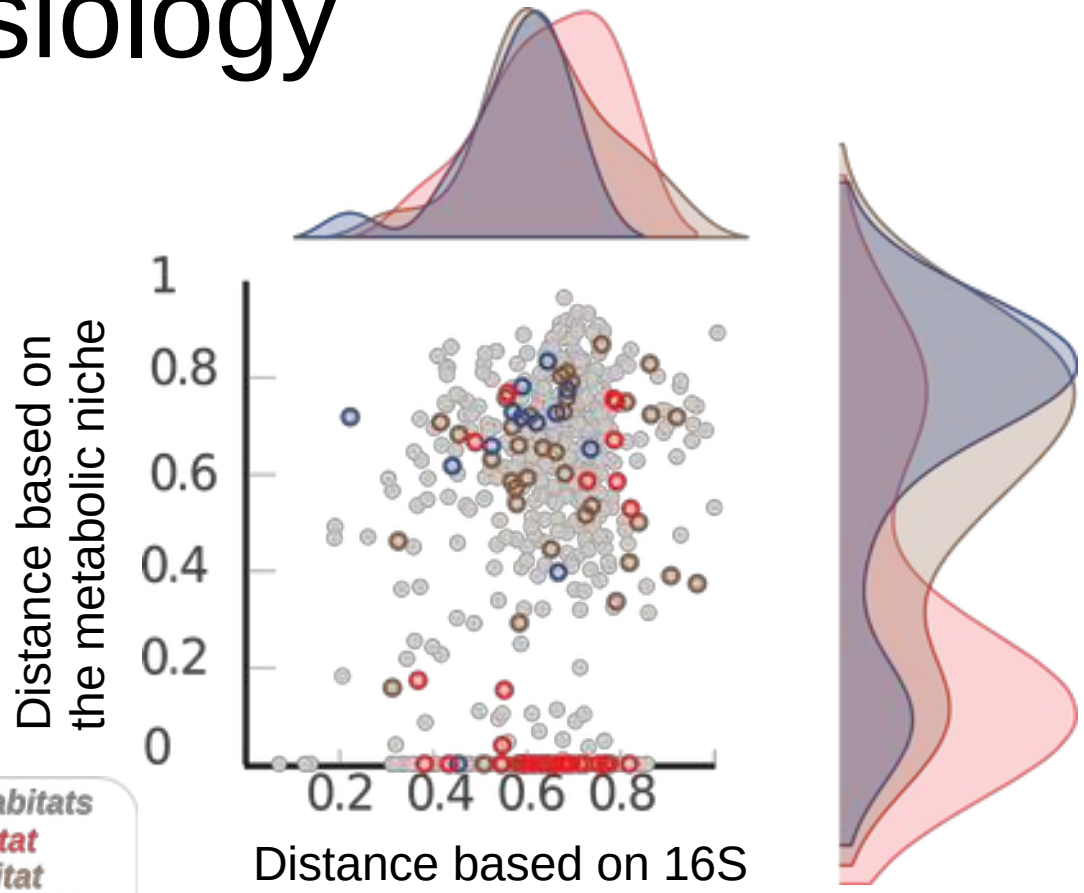


Jaccard distance : 1 - index



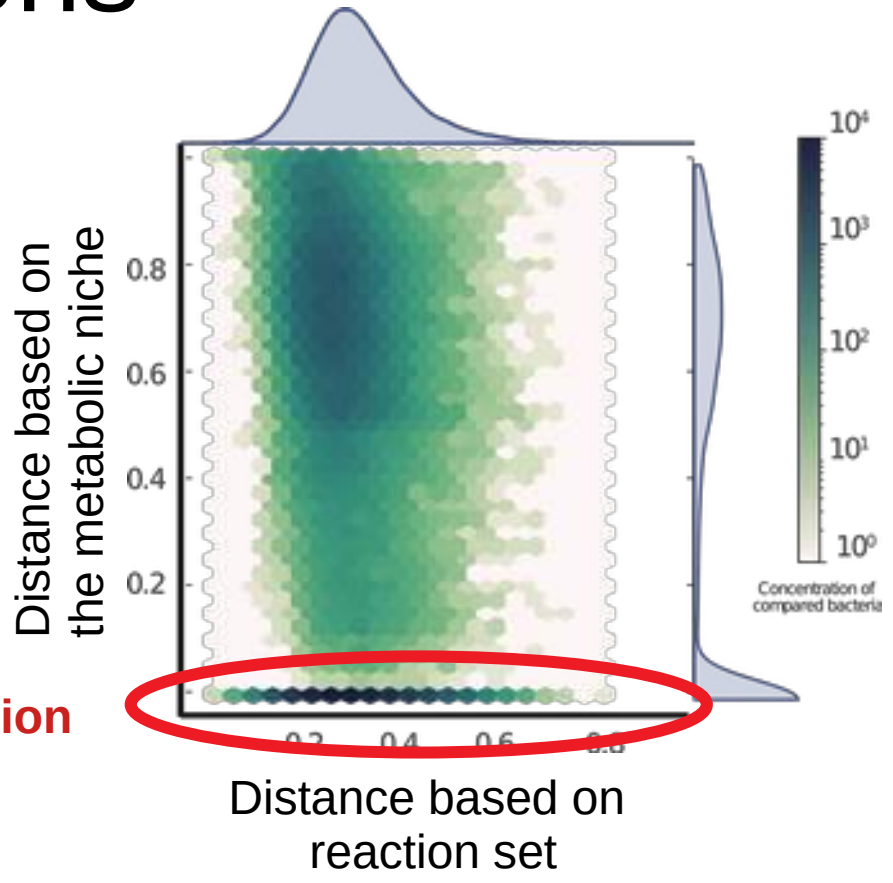
Phylogeny is not the same as physiology

Comparison of 39 bacteria from diverse environments



Functionalities are keys, not reactions

Comparison of 500 Tara Ocean bacteria



Metabolic niche inclusion

Ordering the living through its niche size

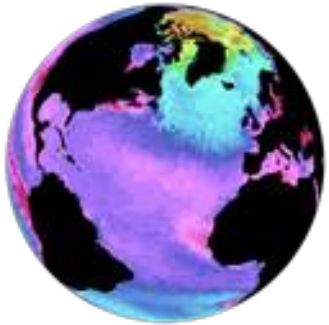
The niche size is the witness of the plasticity of the organism.

What can we do with metabolic niches?

Make biology for stubborn physician oceanographer

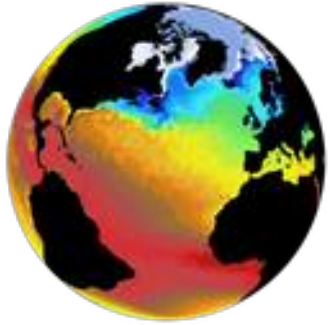
Ocean **Bio**geochemical Models

pH

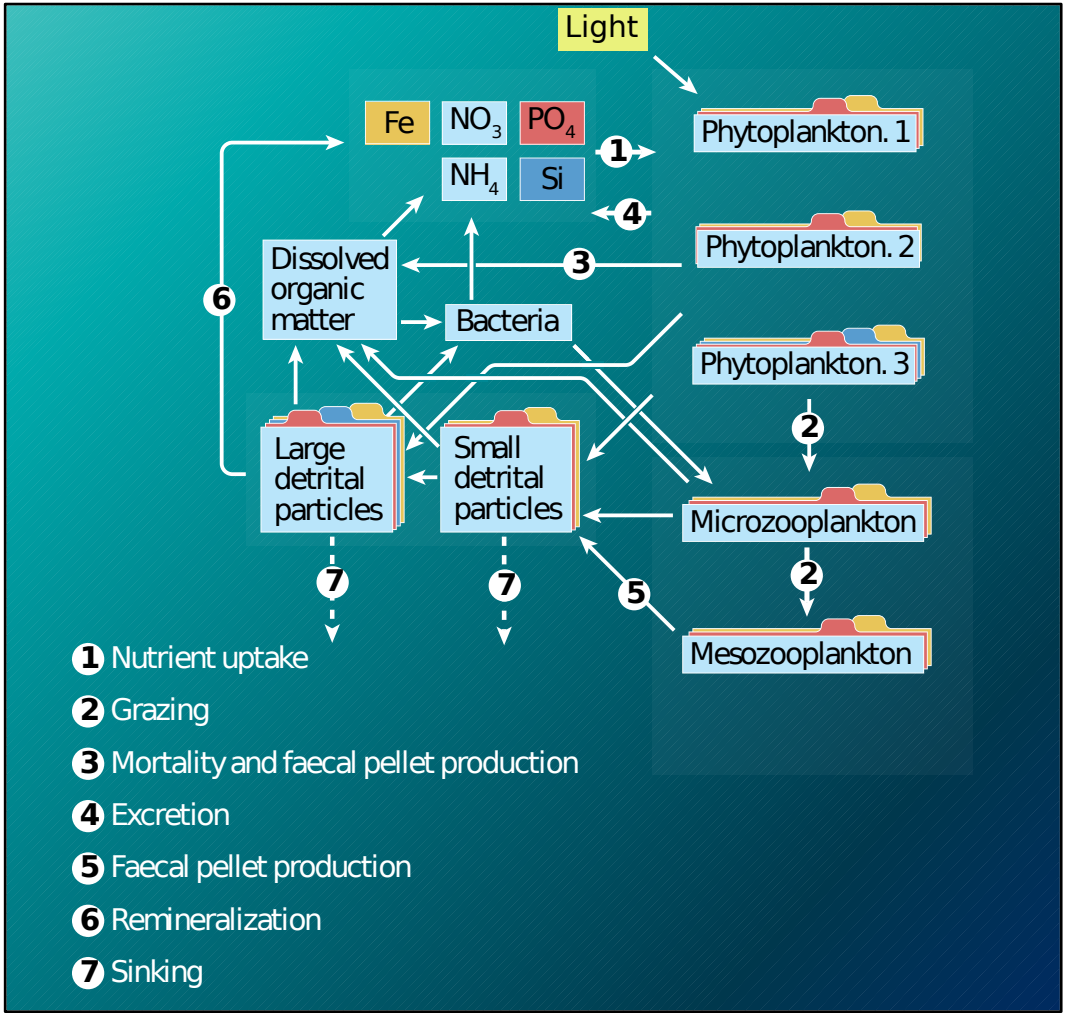


Chlorophyll

Temperature



Velocity field



Source: Fennel et *al.* 2022 Ocean biogeochemical modelling

Plug & Play

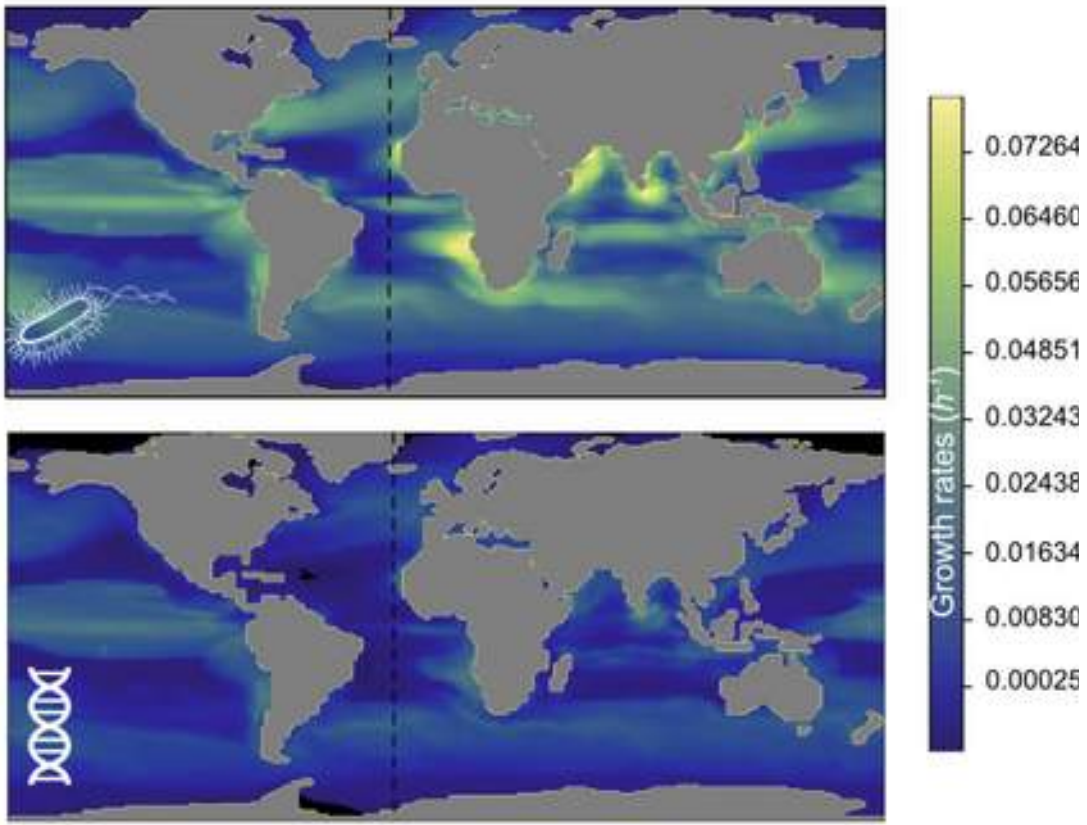
$$\mathcal{N} := \{\mathbf{x} \in \mathbb{R}^p | \exists \mathbf{y} \in \mathbb{R}^{n-p}, \mathbf{S}\begin{pmatrix}\mathbf{x}\\ \mathbf{y}\end{pmatrix} = \mathbf{0}, \mathbf{lb} \leq \begin{pmatrix}\mathbf{x}\\ \mathbf{y}\end{pmatrix} \leq \mathbf{ub}\}$$ (*$\mathcal{N}$ is convex*)

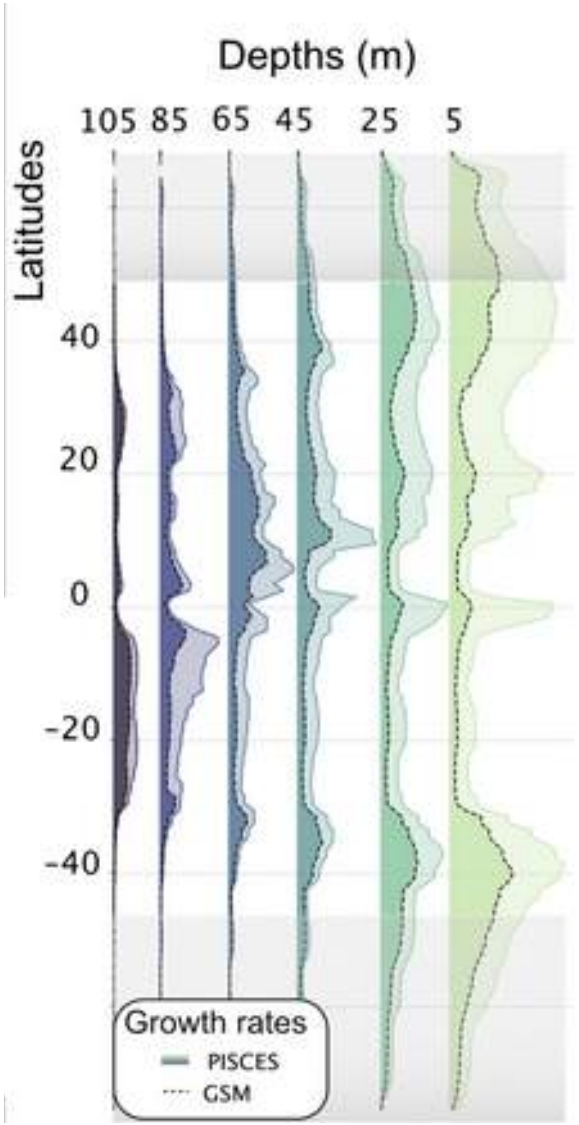
Let us split **x** into the biomass flux, and the environmental fluxes: $\mathbf{x} = \begin{pmatrix}\mathbf{x}_{env}\\ x_{bio}\end{pmatrix}$

For any given environmental conditions, we are able to compute the maximal growth rate of the modeled organism:

$$\begin{cases} max \quad x_{bio} \\ \mathbf{x} = \begin{pmatrix}\mathbf{x}_{env}\\ x_{bio}\end{pmatrix} \in \mathcal{N}, \end{cases}$$

Results on *Prochloroccocus*





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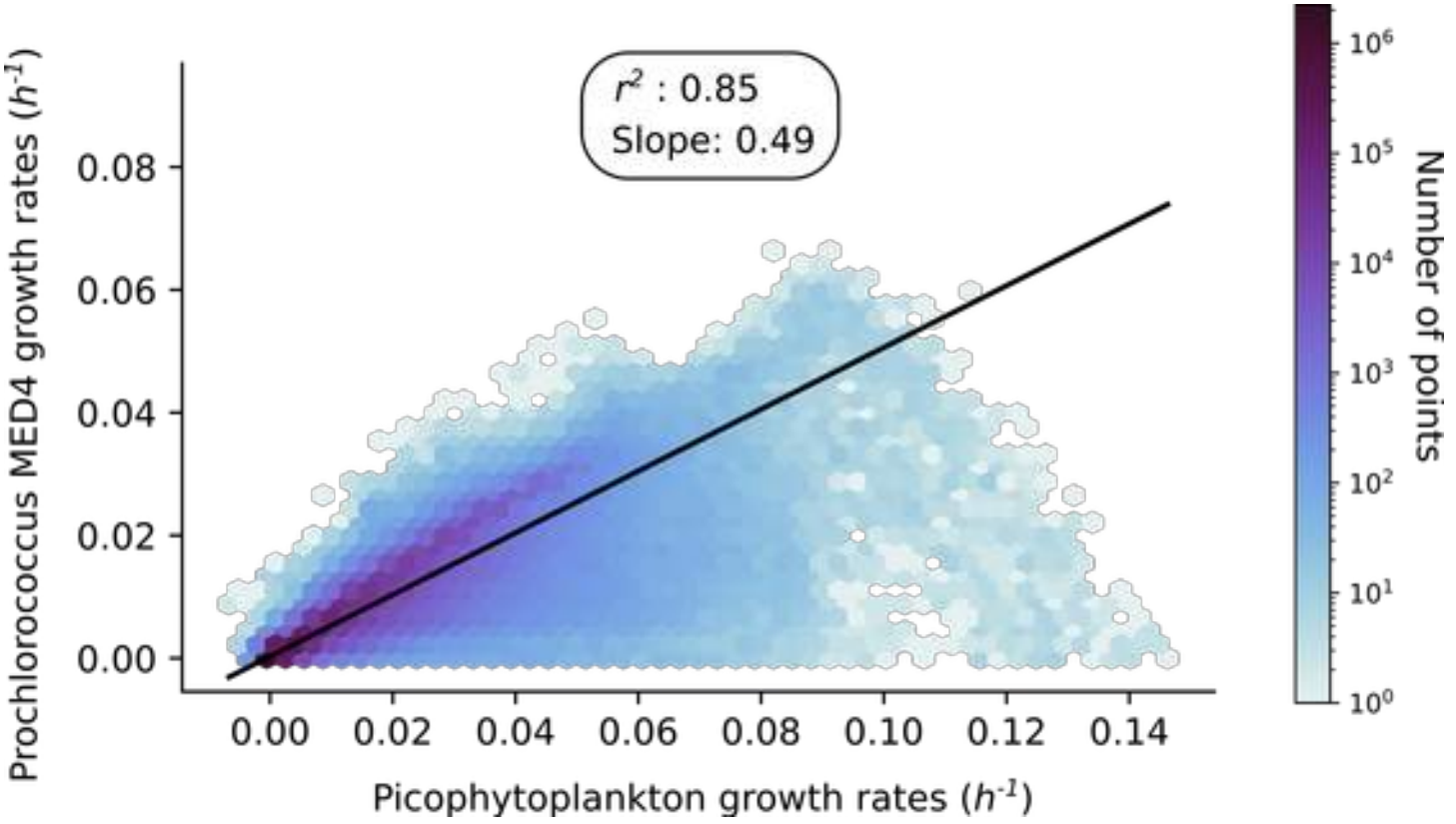
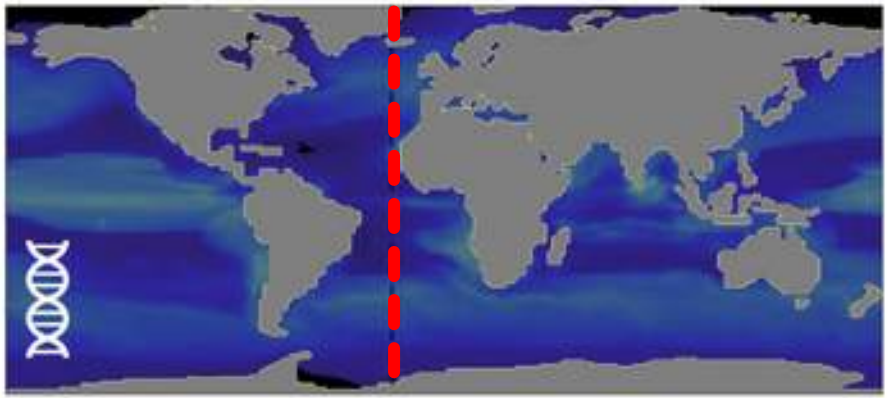


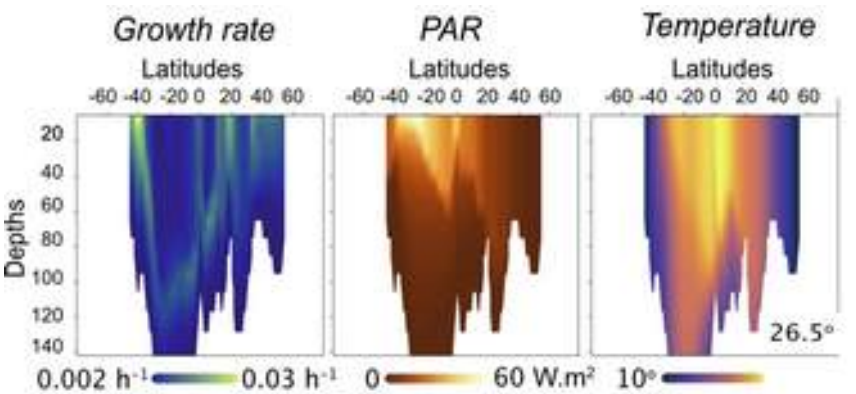
(Prochlorococcus, *Synechococcus, Florenciella, Bolidomonas, Pelagomonas, Imantonia, Micromonas, Ostreococcus, Pycnococcus, Nannochloris*...)

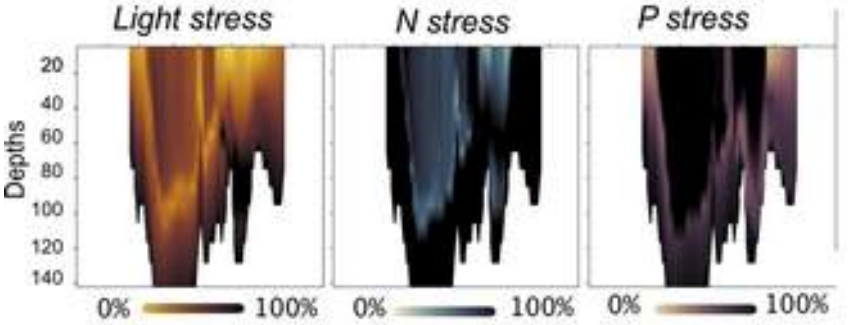
Physiology of *Prochloroccocus*

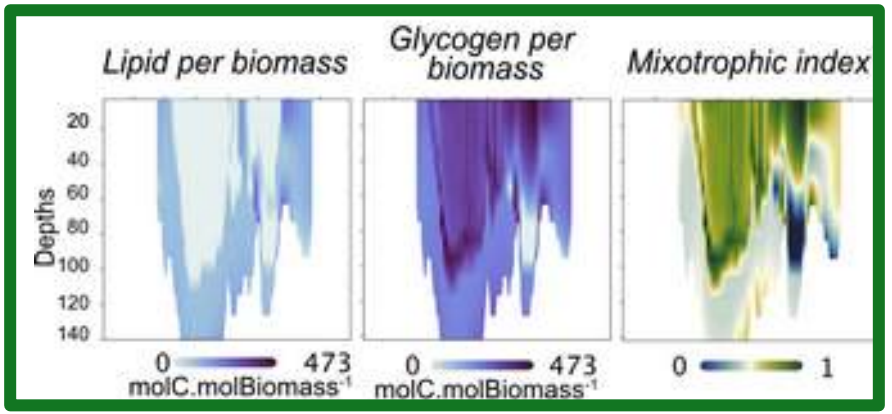
-24°



Consequence of stresses

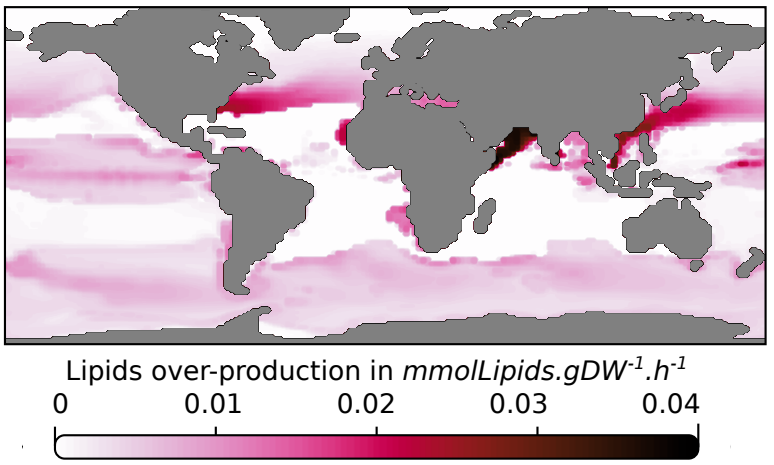




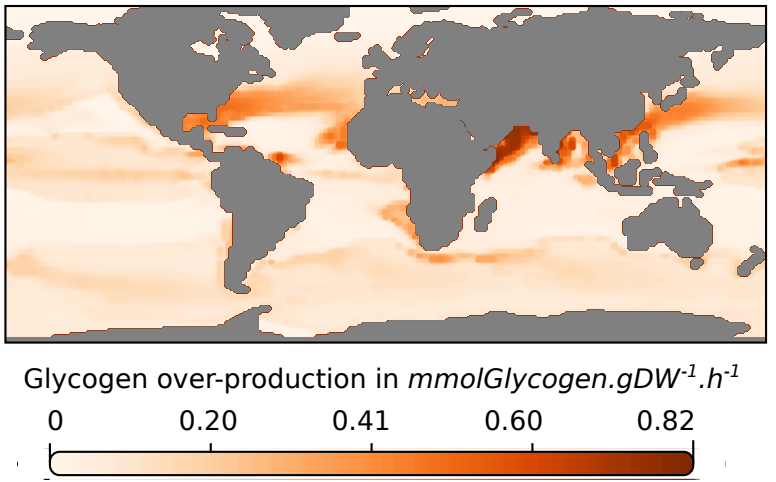


Physiology of *Prochloroccocus*

Two types of energy storage



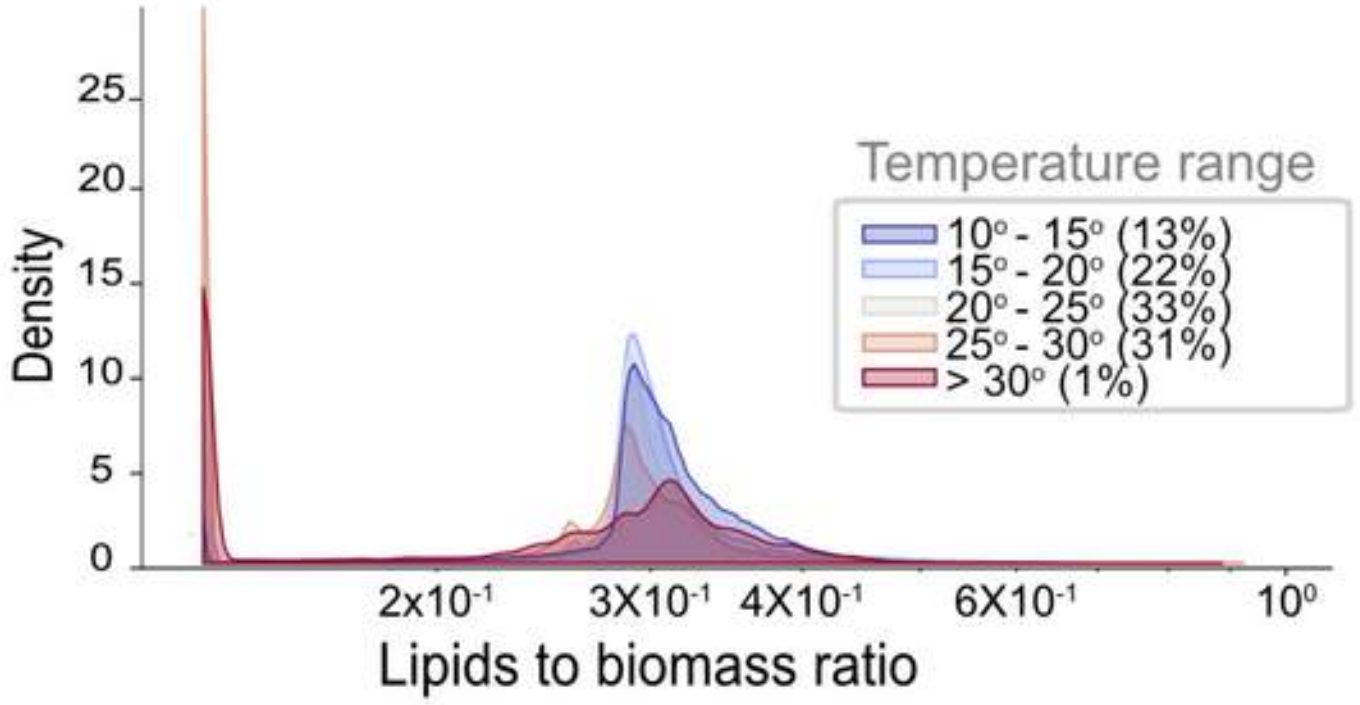
Long term storage



Short term storage

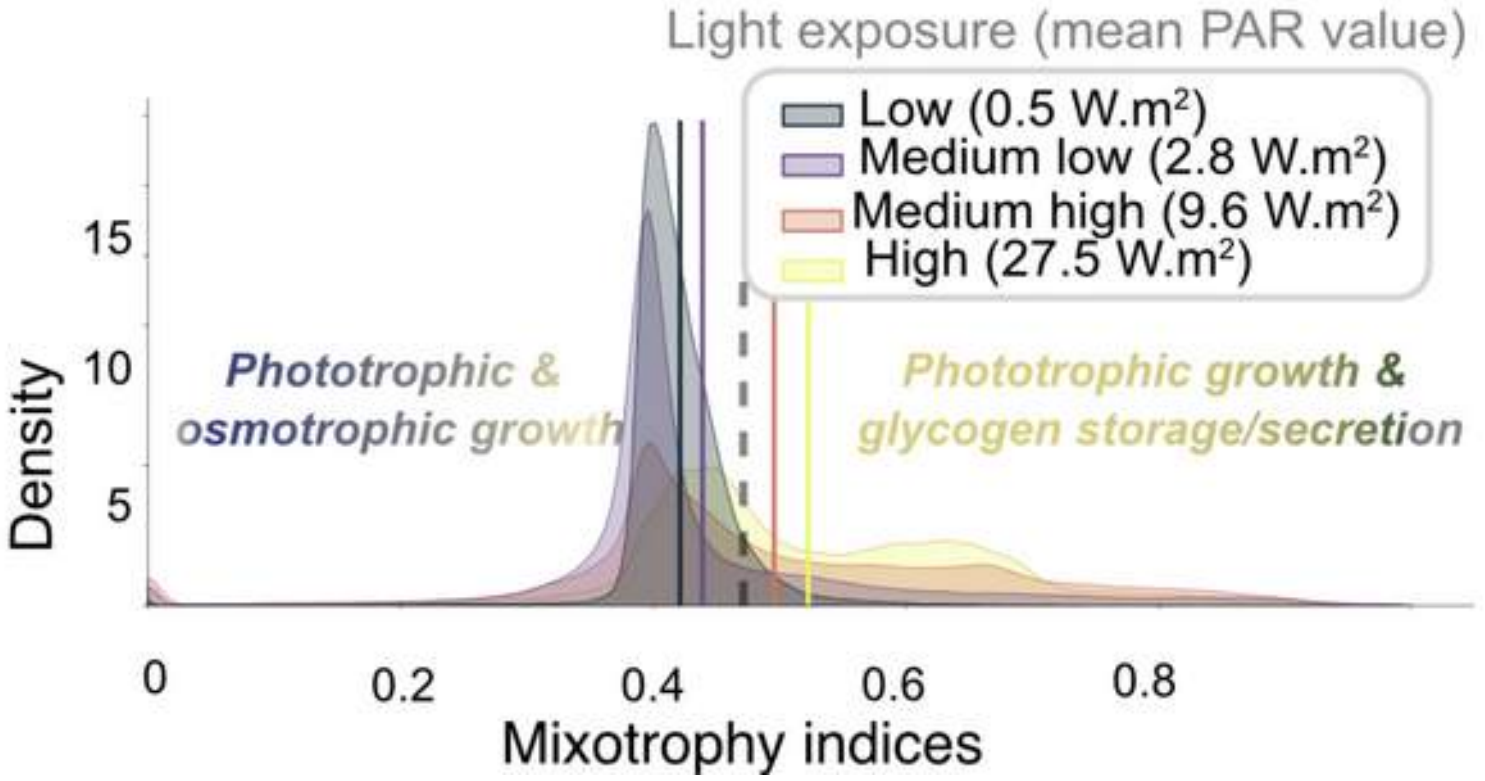
Physiology of *Prochloroccocus*

Le gras c'est la vie



Result consistent with:
Guyet, U. *et al*. Synergic effects of temperature and irradiance on the physiology of the marine synechococcus strain WH7803.

Physiology of *Prochloroccocus*



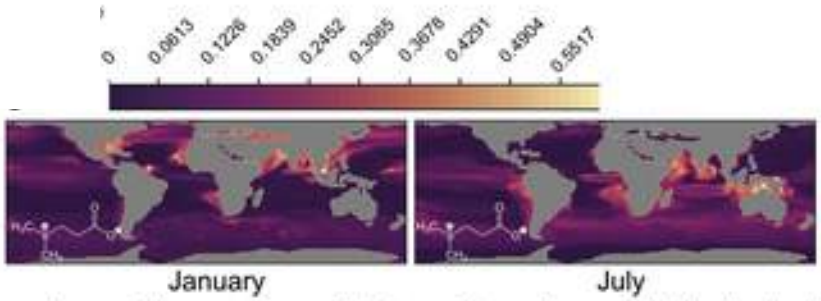
Take home messages

Genome-Scale Models are well suited to model microorganisms

The metabolic niche is a theoretical concept

The metabolic niche is a numerical tool

If physicians can handle it we are ready to introduce new metabolites and more biodiversity in ocean models



DMSP production

Thank you for your attention!

And a special thanks to :

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Olivier Aumont
Chris Bowler
Lionel Guidi
George Jackson
Eric Karsenti
Laurent Memery
Damien Eveillard
Daniele Ludicone
Alejandro ++

Any questions?