ERA CoBioTech

ERA CoBioTech Status Webinar Series 2020

Kick Off Meeting SyCoLim

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Project name: Synthetic microbial communities for the production of limonene derived products

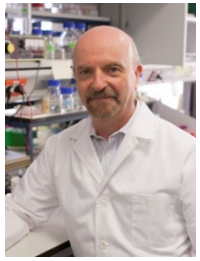
Project acronym: SyCoLim

Rodrigo Ledesma-Amaro, Victor de Lorenzo, Markus Ralser, Martin Kavscek and Guy-Bart Stan

SyCoLim

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant 722361

Project partners



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Molecular Environmental Microbiology lab
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Martin Kavscek
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Slovenia

Charite-Universitatsmedizin Berlin
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Biochemistry and Systems Biology of Metabolism
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Rodrigo Ledesma-Amaro
Synthetic Biology and Metabolic Engineering lab
UK

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Guy-Bart Stan
Control Engineering Synthetic Biology lab
UK

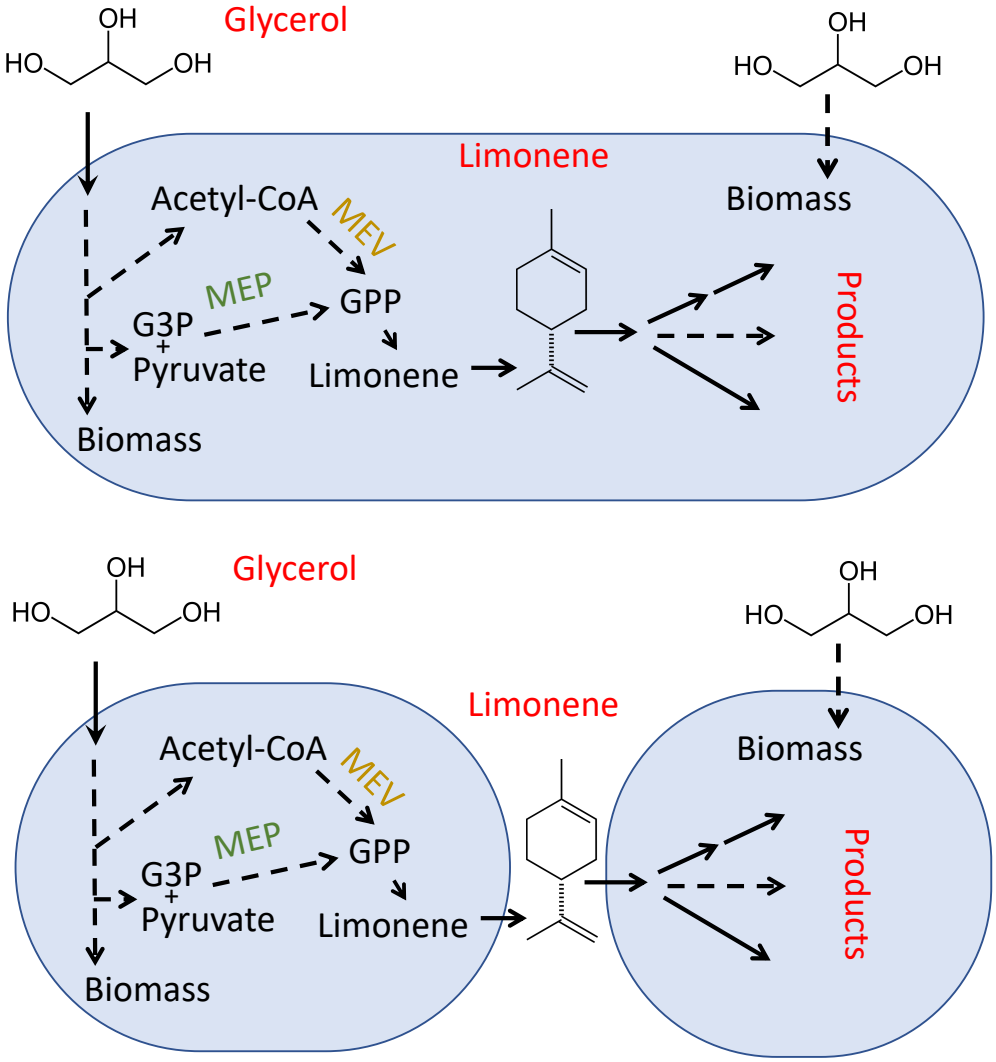
- Project objectives

Produce high value compounds, limonene-derived molecules from glycerol, a low-cost carbon source and industrial by-product.

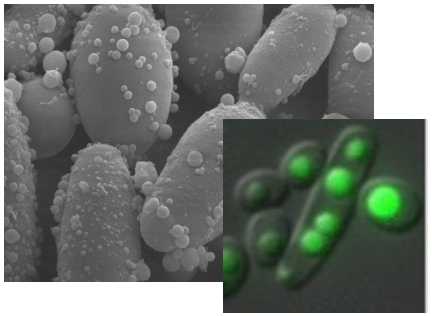
	T p.a.	$ /kg
Glycerol	2M	0.34

	Application	T p.a.	$ /kg
Limonene	Solvent, fragnance…	45000	5-10
Carvone	Additive, fragnance…	2000	50

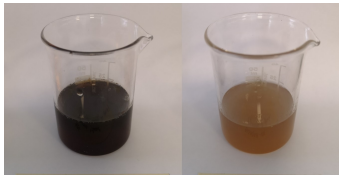
Overall strategy



Yarrowia lipolytica



Pseudomonas putida



Waste glycerol as feedstock

Biodiesel production side-product

Pseudomonas putida + *Y. lipolytica*

Co-culture

Production oprimization: Inoculation, pH, C/N ratio...

Production of limonene and perillyl alcohol

Optimal co-culture and production conditions

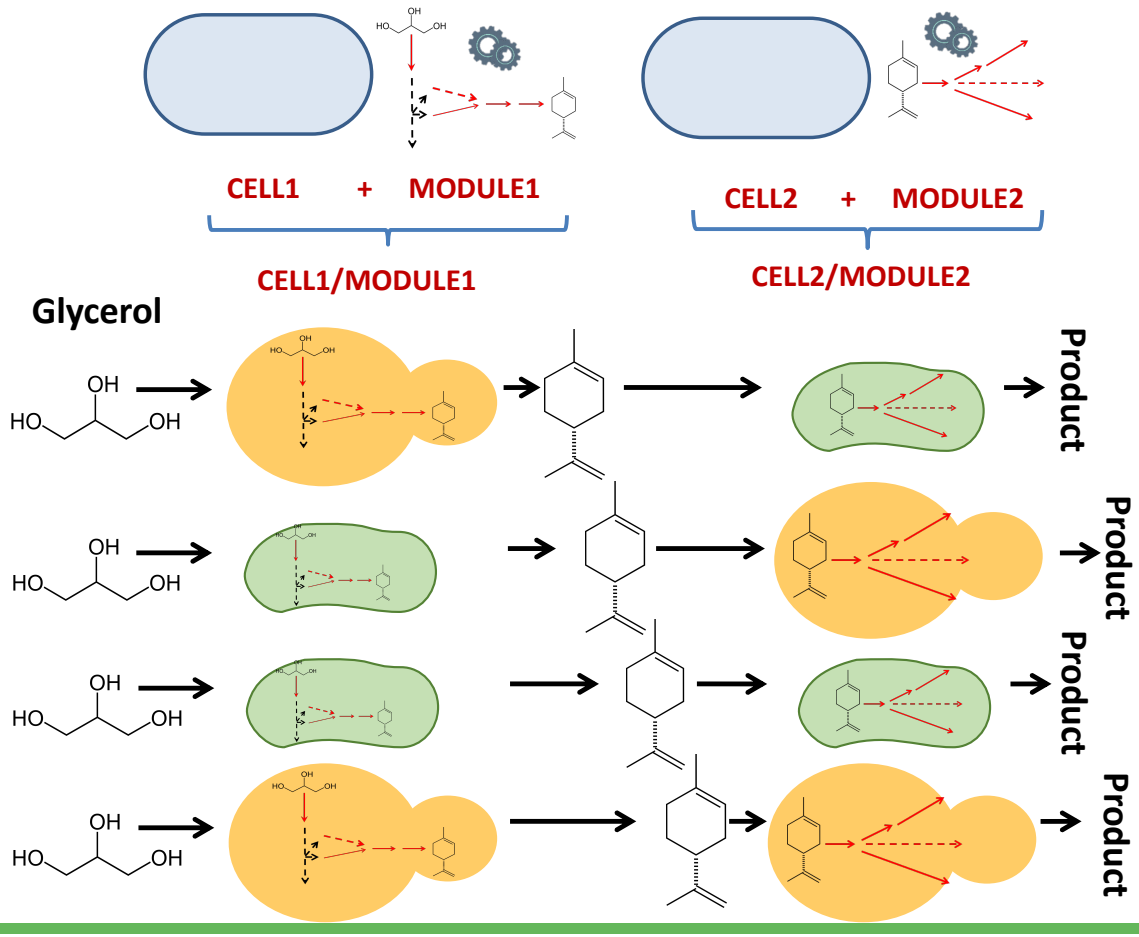
Scale-up

Business development

LCA

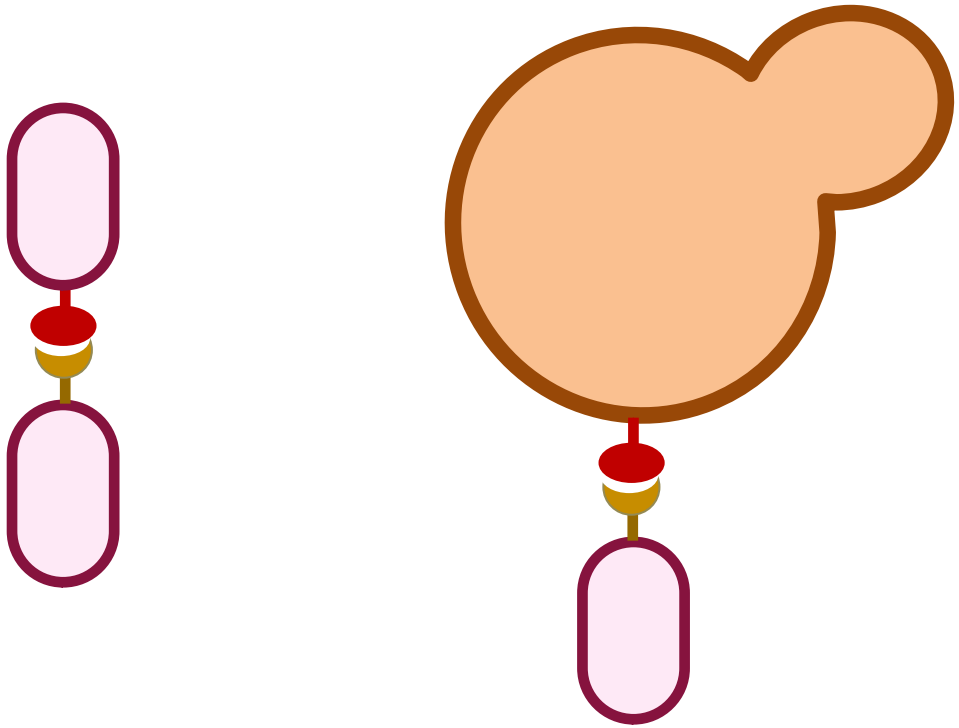
Sustainability profile

Engineering Division of labour for the production of limonene-derived compounds.



(re)-programming bacterial adhesion for synthetic consortia

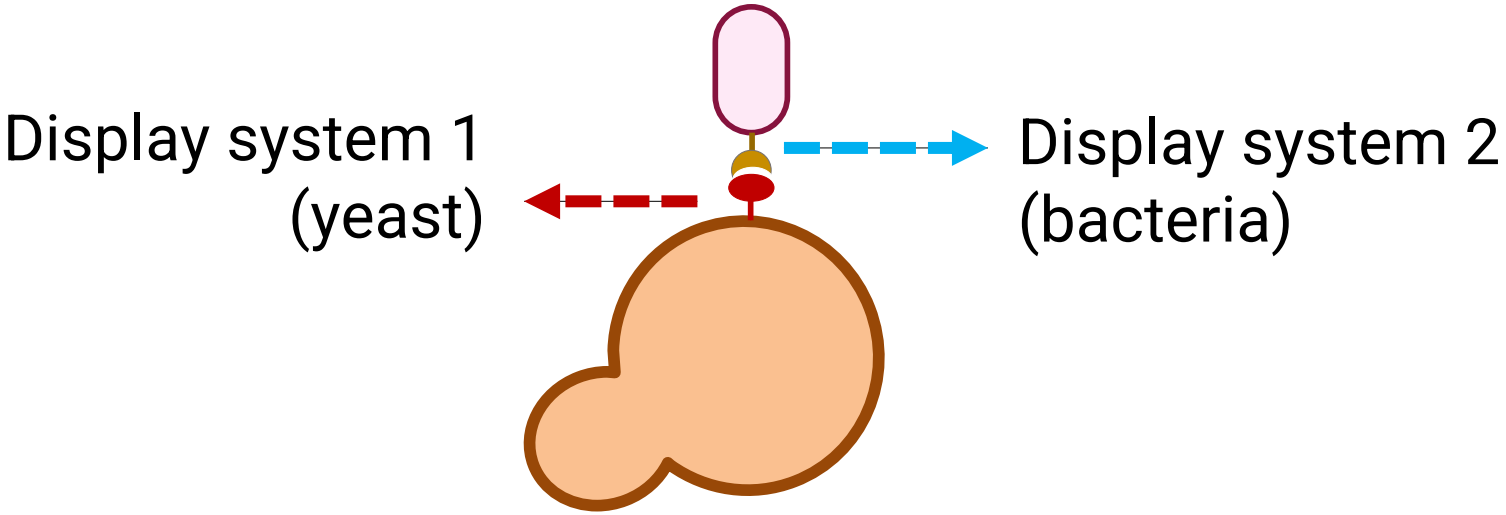
What do we need to engineer a consortia?



(re)-programming bacterial adhesion for synthetic consortia

Adhesins: antibodies → Nanobodies

1. Synthetic (artificial) nanobodies
2. Natural nanobodies

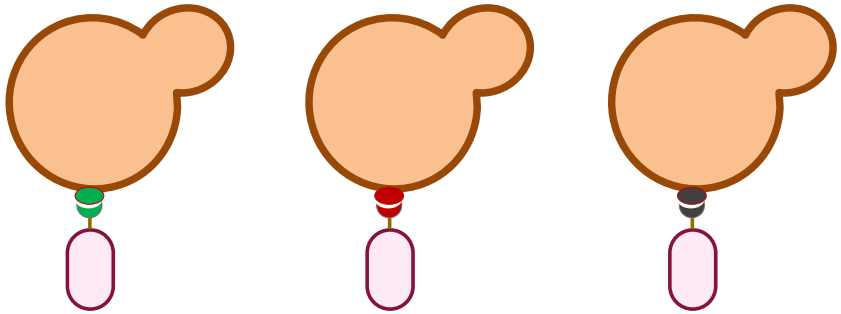


(re)-programming bacterial adhesion for synthetic consortia

Adhesins: antibodies → Nanobodies

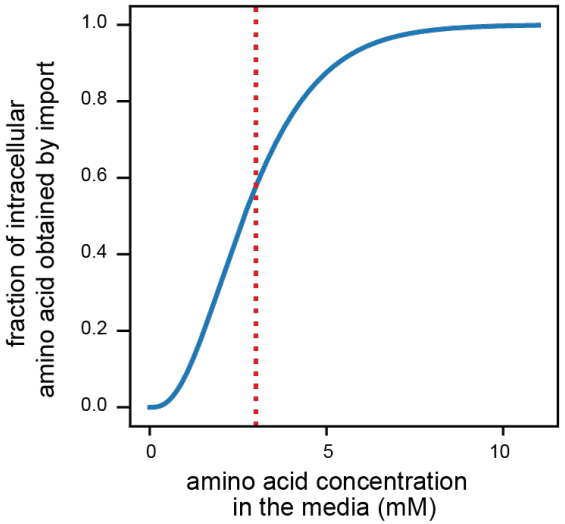
1. Synthetic (artificial) nanobodies
2. Natural nanobodies

Nanobody library against *Yarrowia lipolytica*

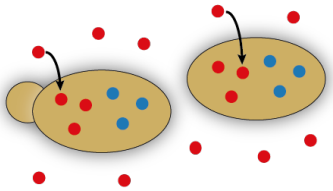


Does amino acid supplementation trigger heterogeneity?

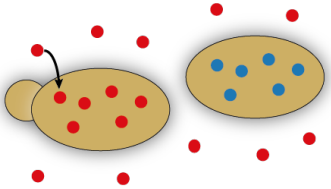
Phenotype observed at population level



Competing underlying models

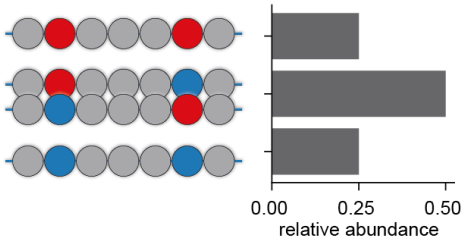


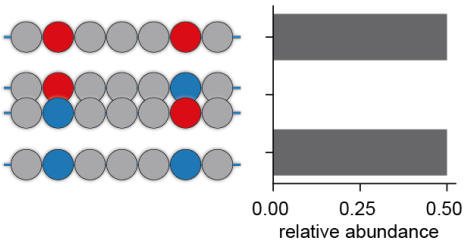
Homogeneous, mix of synthesis and uptake



Heterogeneous, producer/consumer populations

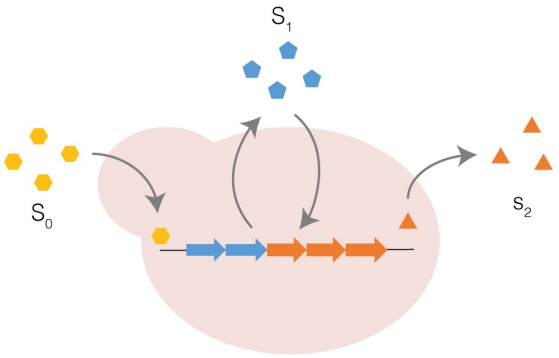
Expected peptide labelling patterns





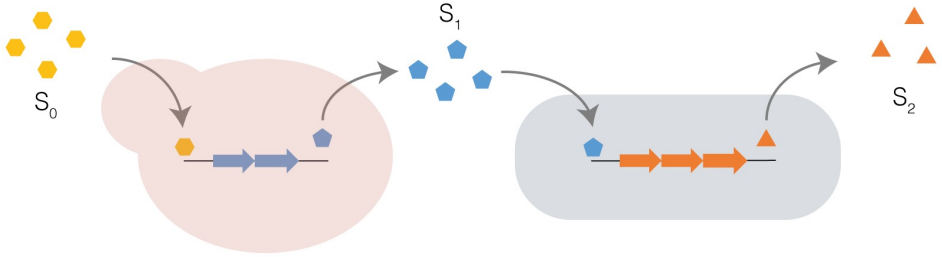
Kamrad, S., in preparation

A mathematical model for studying division of labour



Monoculture

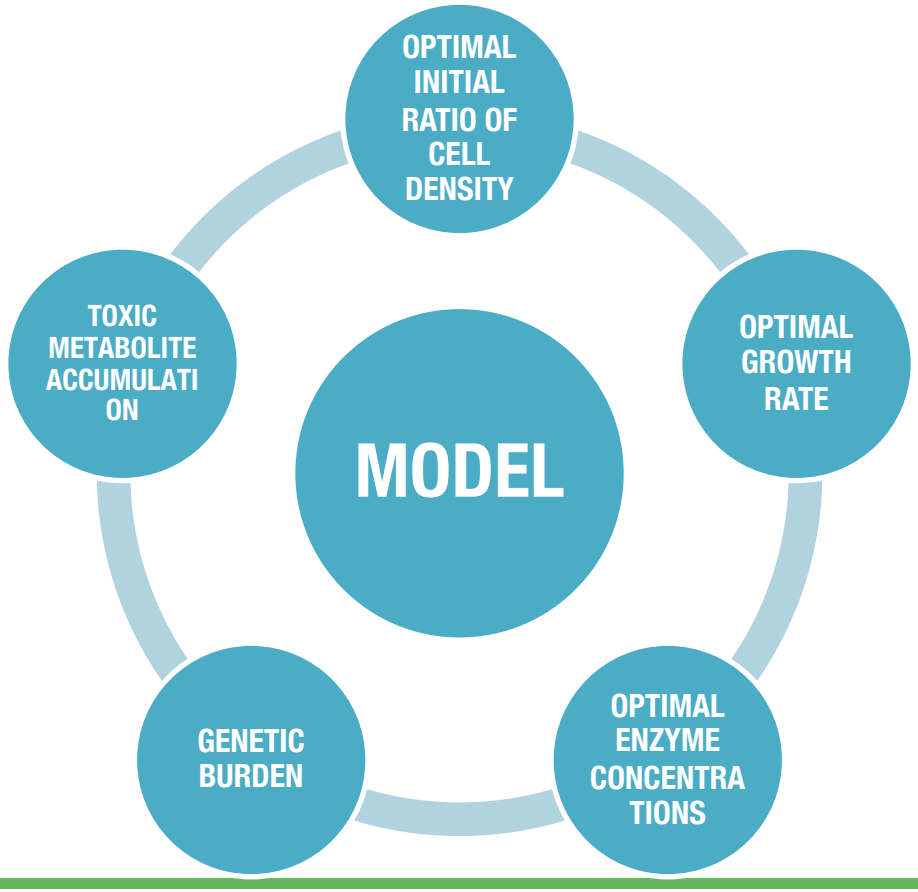
Keywords: Accurate, simple, dynamical, and general



Synthetic microbial community (DoL)

- **Our solution:** A coarse-grained dynamical model based on a set of ordinary differential equations
  - A compartment describing the **cell growth**:
    1. A single ODE to describe biomass dynamics (i.e., cell density concentration) for each strain
  - A compartment describing the **metabolic pathway**:
    1. Three ODEs to describe a two-step metabolic pathway

Our mathematical model: What can we do?



Strength: Adaptability

A matter of numerical parameters to simulate a different organism or metabolic pathway

Achievements

- Media optimized for co-culture
- Carbon source selected
- Limonene production
- Nanobodies libraries
- Synthetic antibodies
- Identified heterogeneity
- Model developed for Pseudomonas

In progress

- LCA
- Market analysis
- Co-cultures vs monocultures
- Omic analysis
- Model for Yarrowia
- Looking for next project: partners, calls, etc

Outcomes:

- Presentation in 5 international conferences
- 2 R packages released in Bioconductor
- 19 scientific publications

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