SynBio 4Flav

Providing a path for the standardized production of flavonoids

Introduction

SynBio4Flav develops a standardized pipeline for the surrogate production of plant flavonoids using Synthetic Microbial Consortia (SMC) for systems-guided assembly of such complex natural products.

By facilitating component troubleshooting and reusability, instead of optimizing a single whole-cell biocatalyst, SynBio4Flav recreates the non-homogeneous scenario of natural flavonoid production processes. Specifically, it breaks down complex, highly regulated metabolic pathways into stand-alone modules and then assigns each module to a microorganism that is genetically engineered to deliver the optimal output for subsequent biosynthetic steps within the SMC.
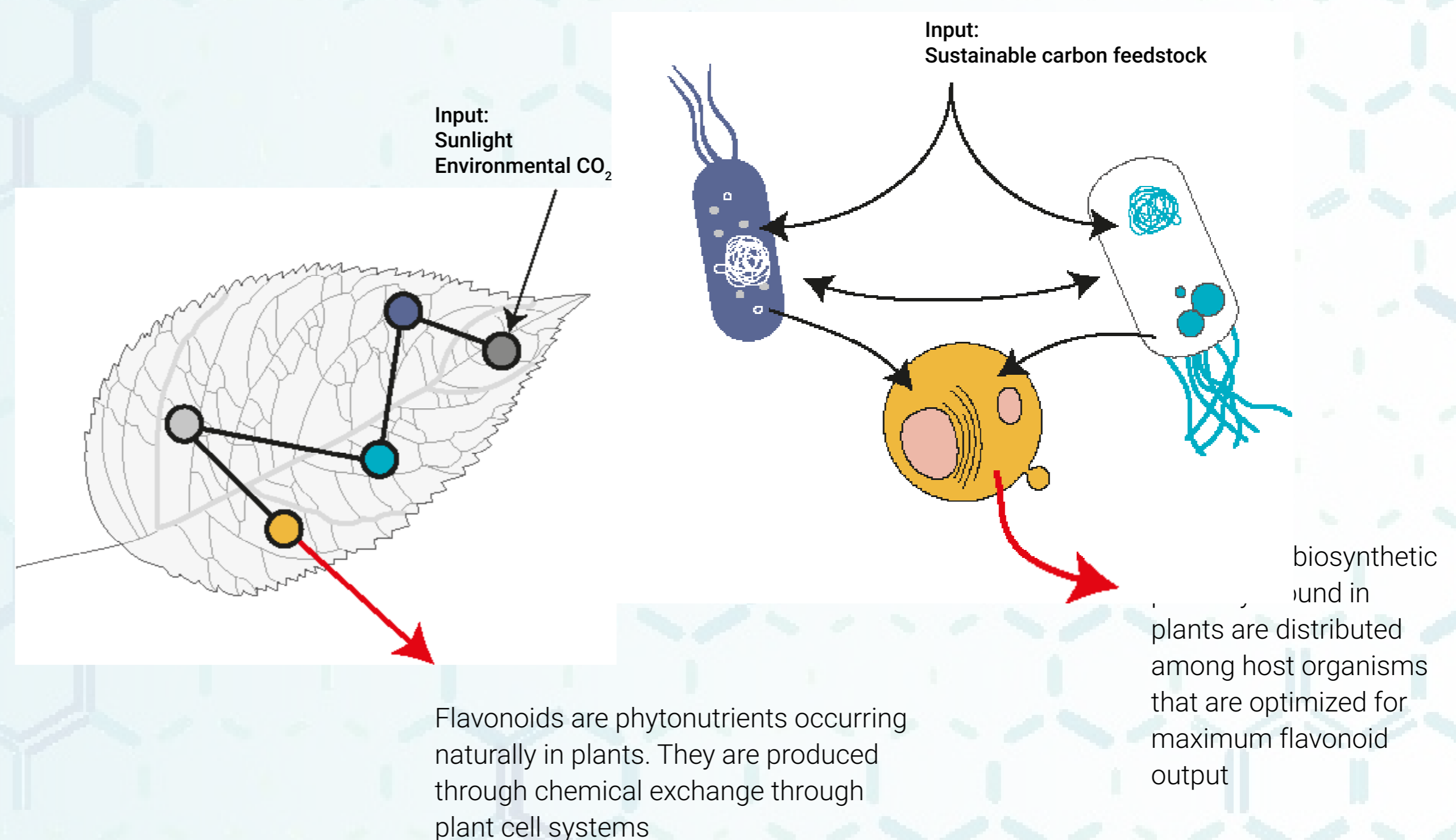
Expected results

SynBio4Flav conceives a standardized platform containing hundreds of optimal optimally engineered cell systems for exploring the full combinatorial space of flavonoid biosynthesis. SynBio4Flav is expected to reach a Technology Readiness Level (TRL) 5 in the production of natural and new-to-nature glycosylated flavonoids.

Envisaged project outputs include:
- Standardized platform for à la carte flavonoid synthesis.
- New protocols for synthetic microbial assembly (including 3D assembly).
- Multi-chamber bioreactors for SMC-based bioprocesses.
- A new, standardized Synthetic Biology & System Biology toolkit.

Purpose

There are over 10,000 flavonoids that have been identified thus far, each with its unique set of bioactivities that may be important for health benefits. Depending on the chemical structure of a given flavonoid, they can exhibit anti-oxidative, anti-inflammatory, anti-mutagenic, and anti-carcinogenic properties. They could also support our immune and cardiovascular systems and help to modulate key functions of enzymes in our cells. Flavonoids are used in numerous applications including functional food & beverages, dietary supplements, cosmetics, and pharmaceuticals. Despite the growing market demand for flavonoids, current production is constrained by conventional manufacturing processes using plant-based sources. Furthermore, their production remains elusive to chemical synthesis and biotech-based approaches.
The SynBio4Flav project aims to provide a cost-effective alternative to current flavonoid production.

Input:
Sunlight
Environmental CO$_2$

Input:
Sustainable carbon feedstock

Flavonoids are phytonutrients occurring naturally in plants. They are produced through chemical exchange through plant cell systems

biosynthetic ... ound in plants are distributed among host organisms that are optimized for maximum flavonoid output

Research & Development areas

- Design, assembly, and optimization of synthetic pathways for flavonoid production; multi-step process analyzing, i) precursor molecules, ii) synthesis of the flavonoid and, iii) functionalization/ glycosylation of the flavonoid
- Microbial chassis systems – Optimization and consolidation; metabolism refactoring
- Synthetic microbial consortia design, construction and optimization; chemicals trafficking optimization

- Validation and demonstration of microbial synthetic platform; bottlenecks removal, fermentation optimization
- Standardization on synthetic biology; providing standardization along the hierarchy abstraction using SynBioTools for constructing efficient synthetic pathways and SMC
- System-level assessment of the SMC-based biocatalyst; functional states, simulation and evaluation of the metabolic networks, and characteristics and behaviours of all organisms

Platforms

The following platforms are used in project development. The developers of the specific platforms are partners in the SynBio4Flav project.

MODELLING & ENGINEERING

The Standard European Vector Architecture (SEVA) platform is a web-based resource and a material clone repository to assist the choice of optimal plasmid vectors for de-constructing and re-constructing complex prokaryotic phenotypes.

doulix

DOULIX is the first toolkit for synthetic biologists that provides an end-to-end solution to move from design to synthesis within one single cloud-based application using the SEVA Standard European Vector Architecture.

INSTRUMENTATION

LARA

LARA (Laboratory Automation Robotic Assistant) is a research platform allowing fully automated high-throughput protein screening and statistical evaluation of experimental data.

SOFTWARE

FLYCOP

FLYCOP (FLexible sYnthetic Consortium OPtimization) is a framework that improves the understanding of the metabolic behaviour of microbial consortia by automating the modelling of those communities.

Gecko

GECKO (Genome-scale model with Enzymatic Constraints using Kinetic and Omic data) is a toolbox that allows for reconstruction of enzyme-constrained models (ec-models) of metabolism.