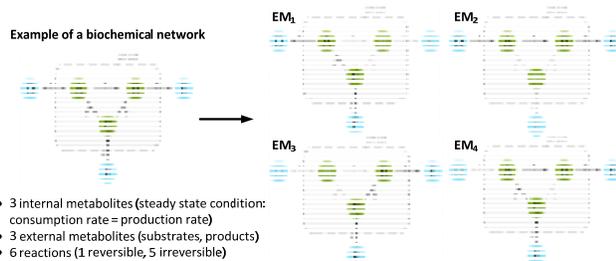


## Towards a platform organism for terpenoid production

*In silico* comparison of metabolic networks of *E. coli* and *S. cerevisiae* as potential hosts  
Evamaria Gruchattka, Oliver Kayser, Verena Schütz

Terpenoids are one of the largest classes of natural products and possess important medicinal and industrial applications. The heterologous production of plant terpenoids in microorganisms is a concept to overcome supply problems and high purification costs as several compounds are rare and produced only in low amounts in plants. Our focus is on the development of a platform organism for the efficient supply of isopentenylpyrophosphate (IPP), the biosynthetic precursor of all terpenoids. *E. coli* and the yeast *S. cerevisiae* are potential hosts that use two different pathways to produce IPP. (Fig 1.)

*E. coli* and *S. cerevisiae* are compared by means of elementary flux mode analysis (EMA) regarding their metabolic potential to supply IPP. EMA allows the calculation of a solution space containing all steady state flux distributions of a metabolic network considering stoichiometry, topology and thermodynamics (Fig. 2).



**Figure 2:** Concept of elementary flux mode analysis

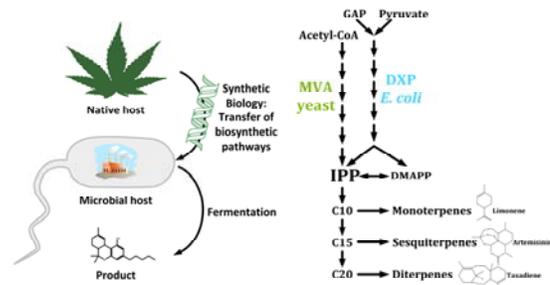
Models of the central carbon metabolism of both organisms were constructed considering current knowledge from genome scale models and literature. The theoretical maximum IPP yield was calculated. Exchange and combination of the DXP and MVA pathway were analyzed. (Fig. 3)

The data obtained from EMA will now be used for the rational identification of targets for metabolic engineering. A proof of concept will be performed using patchouli synthase producing the plant sesquiterpene patchouliol.

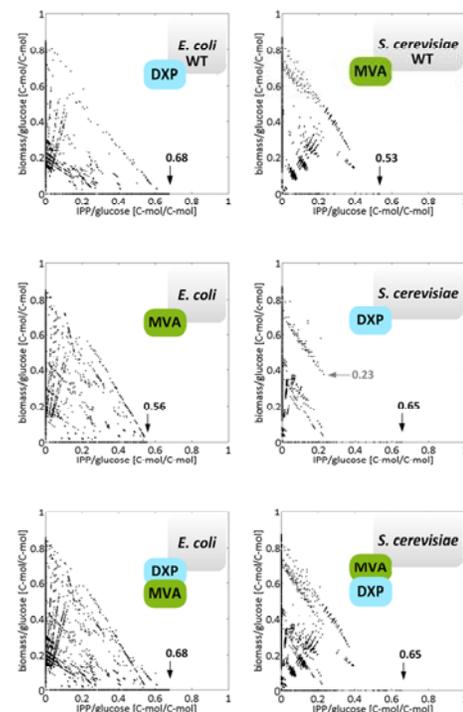
[verena.schuetz@bci.tu-dortmund.de](mailto:verena.schuetz@bci.tu-dortmund.de)

[evamaria.gruchattka@bci.tu-dortmund.de](mailto:evamaria.gruchattka@bci.tu-dortmund.de)

[oliver.kayser@bci.tu-dortmund.de](mailto:oliver.kayser@bci.tu-dortmund.de)



**Figure 1:** Synthetic biology for the production of plant terpenoids. Yeast and *E. coli* use different IPP pathways to supply the common terpenoid precursor IPP.



**Figure 3:** IPP and biomass yields for the obtained elementary modes with glucose as carbon source. *E. coli* wild type shows a higher potential to supply IPP than *S. cerevisiae* wild type, with and without biomass formation. The exchange of DXP and MVA pathway lowers the maximum theoretical carbon yield for *E. coli*. The exchange enhances the  $Y_{IPPmax}$  for *S. cerevisiae*, however, the maximum theoretical IPP yield with biomass formation is lowered. The exchange of the terpenoid pathways is stoichiometrically not efficient.

### Publikationen:

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*E. coli* versus *S. cerevisiae* – On the Competition for Terpenoid Production, Conference: New Biotrends to smarter drugs, Dortmund, Germany, 08. – 09. December 2011, book of abstracts: page 25