Computational development of metabolic reaction networks for degradation pathways in bacterial communities

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seit 1558

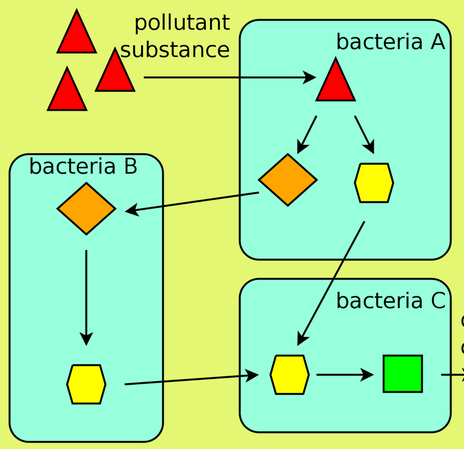
introduction

Systems biology aims to combine gathered biological data, approved mathematical methods and the power of modern computers to find solutions to biological problems.

In our project, we develop comprehensive computational metabolic models spanning various bacterial species.

We face the fact, that scientists have collected data for metabolic paths and also whole cell metabolisms over the last decades, but those data have been investigated only on single strains grown under laboratory conditions.

The ultimate goal is to create a set of prediction tools. This toolchain shall help to find an optimal remediation strategy for a given environmental setup.



Contrary to common models of the last decades, normally dozens of bacterial species interact in natural environments. It is now the time to illuminate those interaction processes and how they may be utilized for biodegradation purposes.

Incriminatory substances in the soil (triangles) may be degraded by communities of bacteria. Every functional member (blue shapes) may perform it's own degradation steps (arrows within the shapes) and may share intermediates (yellow and orange boxes) with other species.

Full degradation is only performed, if all community members interact.

our approach:

user provides environmental data:

Temperature
pH-values

present pollutant substances

present electron acceptors

present bacterial species

data is passed to the program

via database selection and sbml input

algorithm application:

models for given bacteria are collected from databases
↓
target substances are searched within the models
↓
inputs and outputs are calculated
↓
prediction of potential community members and nutrient additions

algorithm output

is written to tables and sbml models

prediction results:

list of present bacteria involved in degradation

list of bacteria that should be added to community

list of chemical substances that should be added

sbml models for simulation

list of non-degradable compunds (unsolvable requirement)

theoretical work

A great deal of data for theoretical predictions and experiment design is taken from online databases, such as

BSD,
KEGG,
EcoCyc,
MetaCyc,
BioModels,
Microbes Online

Theoretical work is divided in two main aspects:

network assembly from databases and

analysis of metabolic paths within the constructed networks

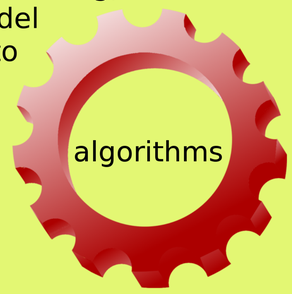
linear integer programming

Libraries providing LIP algorithms will help

- to determine inputs and outputs of assembled metabolic networks

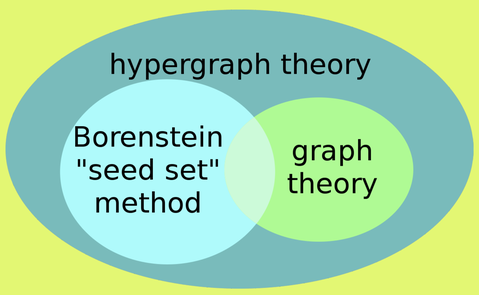
- to guess unknown parameters by specification of required network behaviour

For integrated data mining, evaluation and model prediction, we try to adopt algorithms from different sciences:



basic graph algorithms
linear integer programming
chemical organization theory
petri nets and hypergraph theory

Development of a method to calculate possible nutrient substances based on hypergraph theory



current work:

We develop algorithms, to identify sets of nutrients required to grow bacteria and additional substances that may allow contaminant degradation.

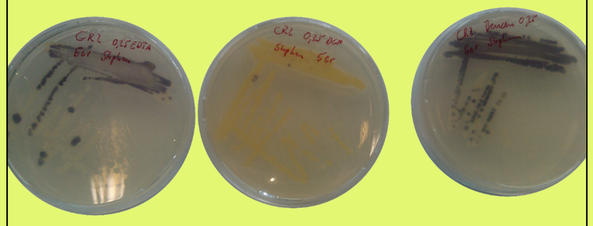
Those algorithms shall help to identify which bacteria may be combined to utilize terminal substances to fully decompose a compound of interest.

laboratory experiments

One important criterion on interaction investigation is, that observed strains can be distinguished from each other.

simplest possibility: using strains forming colonies of different color

Potential bacteria strains are selected by screening experiments:



Grown on minimal culture media, we select strains, which are able to utilize different pollutant substances

Sequencing of environmental probes
- helps to identify abundant species
- can give an overview, which genetic and therefore metabolic potential is present

A bacterial genomic sequence allows prediction of buildable enzymes and thus automated creation of metabolic models.

Concurrently to the deduction of theoretical information, laboratory experiments are carried out for:

checking deduced thesis: It may be tested, for example, whether a proposed consortium really shows a predicted compound degradation capability.

degradation tests:
- basic tests can be done in small flasks
- wetland experiments allow investigations under more realistic conditions

gathering fundamental data to develop hypothesis
- determination of model parameters
- genome analysis to investigate and assemble cross-species metabolic networks
- screening experiments:

We try to gain new insights to which bacteria from our reference collections come into consideration for degradation experiments.

The first of these experiments has recently been undertaken:
We tested bacteria of the following strains for their viability on minimal media loaded with contaminants:

bacteria family	minimal medium loaded with...
Agrobacterium	benzene
Micrococcus	tetrahydrofurane
Janthinobacterium	dichlorphenole
Williamsia	EDTA.
Rhodococcus	

References:
Elhanan Borenstein, Martin Kupiec, Marcus W. Feldman, and Eytan Ruppin (2008): Large-scale reconstruction and phylogenetic analysis of metabolic environments, PNAS vol. 105 no. 38 14482-14487
Peter Dittrich, Pietro Speroni di Fenizio (2007): Chemical Organization Theory, Bull. Math. Biol., 69(4):1199-1231