Metagenome sequencing and *in silico* design for biogeoengineering by synthetic microbiology

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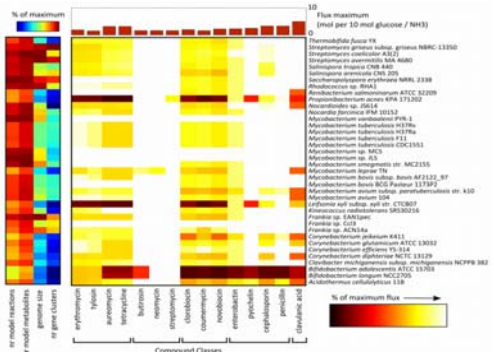
Introduction:

We will exploit the new emerging technology of Synthetic Biology and the abundant genome sequences available, to address very important ecological/environmental questions such as how to eliminate toxic (e.g.radioactive) elements using engineered microbes. We will do this by designing microbes to, e.g., accumulate these elements or alter their mobilization and deposition.



Predicted maximum fluxes of secondary metabolite production using genome-scale metabolic models[1)]

Project Summary

In this project, we will use large-scale genomic sequence data, which are available from both public databases, and genome-scale computational modelling of metabolism to identify the molecular machinery and possible genetic engineering strategies for the development of designer microbial strains. These designer strains will be developed to engineer global nutrient and element cycles and the fixation / mobilisation of (potentially toxic or valuable) minerals.

Year 1: Gather genome sequences and complete genome-scale computational modelling. Database searching will be augmented by targeted genome sequencing of key model organisms identified from previous work in Manchester on bacteria able to grow and metabolise toxic elements in extreme environments.

Year 2: From metabolite modelling completed in Year 1, identify target metabolism for modification by using synthetic biology (entire pathways or individual enzymes and regulators). The synthetic biology approaches to use are, e.g., genome editing by CRISPR/Cas or the Multiplex Automated Genome Engineering (MAGE) systems; rewriting the DNA of biosynthesis pathways by DNA synthesis and assembling of enzymes into newly designed pathways, incorporating synthetic promoters, ribosomal binding sites and terminators. The target organism(s) will be decided based on accessibility, genetic amenability and geo(bio)chemical importance, as well as the modelling results of Year 1 (e.g., strains that can survive in highly radioactive or toxic environments may be considered).

Year 3: The engineered strains will be tested, e.g., for their robustness in growth, element fixation, mobilisation and accumulation of toxic compounds by changing the growth conditions and potential alternative designs will be explored experimentally and by modelling.

The student will acquire interdisciplinary skills from a unique combination of computational systems biology; synthetic and environmental microbiology; and geochemistry / geomicrobiology.

References

1) Zakrzewski P, Medema MH, Gevorgyan A, Kierzek AM, **Breitling R**, **Takano E**. MultiMetEval: comparative and multi-objective analysis of genome-scale metabolic models. ***PLoS ONE***. (2012) 7: e51511

2) Medema MH, **Breitling R**, Bovenberg RAL, and **Takano E**. Exploiting Plug-and-Play Synthetic Biology for Drug Discovery and Production in Microbes. ***Nature Rev Microbiol*** (2011) 9:131–137.

3) Newsome, L., Morris, K. and **Lloyd**, **J.R**. The biogeochemistry and bioremediation of uranium and other priority radionuclides ***Chemical Geology*** (2014) 363:164–184