Introduction to Flux Balance Analysis

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What is Flux Balance Analysis?

- Metabolic networks operate at steady-state
- Network structure is reflected in stoichiometry matrix
- Flux Balance Analysis (FBA) considers constraints on reaction fluxes
  - Irreversibility of some reactions: sign constraints
  - More generally, bounds are imposed on all fluxes
- FBA aims at identifying 'optimal' metabolic flux patterns

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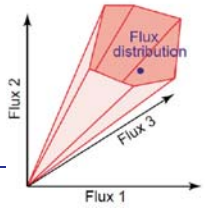
$$\mathbf{N} \cdot \mathbf{J} = \mathbf{0}$$

- Flux Balance Analysis (FBA) considers constraints on reaction fluxes
- This defines a convex set of possible fluxes, a flux cone
- Fluxes can be written as linear combinations of rays of the flux cone: extreme pathways



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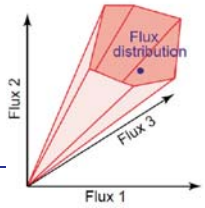
- FBA aims at identifying flux patterns optimizing specific linear combinations of fluxes
  - Biomass production
  - ATP synthesis, etc.



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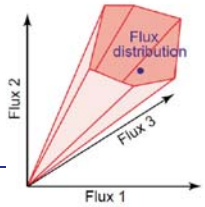
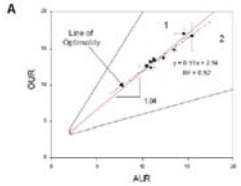
- This is achieved by linear programming

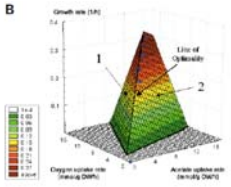


Applications of FBA

- Optimal flux combinations on whole-cell metabolic models
- For instance, which flux patterns achieve the highest growth yield at given input fluxes?
- Example of *E. coli* growing on acetate with oxygen

  Optimal line fits well with growth experiments (Edwards *et al.*, 2001), suggesting *E. coli* growth yield is indeed optimized on acetate





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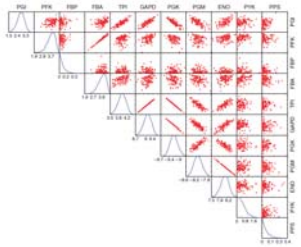
- Optimal flux combinations on whole-cell metabolic models
- For instance, which flux patterns achieve the highest growth yield at given input fluxes?
- Model allows to predict growth consequences of missing reactions in mutant strains, changes of input fluxes, etc.

Sampling flux space

- Instead of looking for optimal solutions, it is also possible to sample the cone of possible fluxes
- This provides a view of flux correlations and variability
  - Here under the constraint of growth yield above 90% of its optimum
- Note that even optimal solutions are usually not unique
  - Flux Variability Analysis



Conclusion

- FBA models provide genome-scale pictures of metabolism
- They yield experimentally testable predictions of flux ratios and yields, assuming a known objective function
- However the choice of an objective function will depend on the system under study
- FBA cannot inform on quantities such as nutrient or metabolite concentrations, or even reaction rates
  - It is informative on flux ratios
- It is uneasy to incorporate regulation into FBA
  - It amounts to modulating flux bounds