# Contrasting Flux-Balance Analysis and Metabolic Flux Analysis

In the course you have learned about two different approaches for the analysis of metabolic fluxes in biological systems. These approaches were flux balance analysis (FBA) and metabolic flux analysis (MFA). The following questions are intended to contrast these two methods so that their differences become clear.

**Please feel free to discuss these questions with the other course participants on the course forum**. (The forum can be found under the "information" tab on the course's Moodle page)

## Question 1: What's not to like about flux balance analysis?

Flux balance analysis (FBA) is computationally fast, requires as input only readily available reaction stoichiometries, predicts metabolic fluxes for all reactions in a metabolic system and has had considerable success in a number of biotechnological applications (e.g. genetic engineering of microorganisms to optimize the biotechnological production of industrially important chemicals).

By contrast metabolic flux analysis (MFA) utilizes experimental data that needs to be collected by growing cells on isotope-labeled substrates and analyzing these cells with sophisticated analysis techniques. These data are then analyzed by comparing experimental observations with model predictions via complex data fitting procedures.

Based on these descriptions it may seem that flux balance analysis is a far superior approach. Is this really the case?

Please use your knowledge from the course to explain why and when the extra effort required for MFA may be a good investment.

## Question 2: Choice of objective function in FBA?

The choice of the objective function employed in flux-based analysis has a very large impact on the final metabolic model. Here is a table of some commonly used objective functions.

|  |  |
| --- | --- |
| Objective Function | Rationale |
| Maximization of biomass yield | Greater biomass yield equates to faster cell proliferation. Evolution selects organisms that can outgrow competitors. |
| Maximization of ATP yield | Evolution drives maximal energy efficiency |
| Minimization of overall intracellular flux | Most efficient use of cell's protein resources (enzymes) translates to faster and more efficient cellular growth. |
| Maximization of biomass yield per flux unit | Cells operate to maximize biomass yield while minimizing enzyme (protein) usage |
| Minimization of ATP producing fluxes | Cells grow while using the minimal amount of energy, thus conserving energy. |
| Maximization of ATP producing fluxes | Cells produce as much ATP as possible |

Which of these objective functions seem reasonable to you and in what biological contexts (exponential growth, starvation etc.) would they be applicable.

Can you think of unusual growth conditions and the objective functions that might be appropriate for them?

## Question 3: The role of the objective function in FBA?

Please clarify the role of the objective function in FBA. To do so please:

a) Explain what will happen if you choose the wrong objective function for FBA. Will the analysis tell you that your choice of objective function was wrong?

b) Please discuss the following statement: "In FBA the objective function takes over the role experimental data plays in MFA"