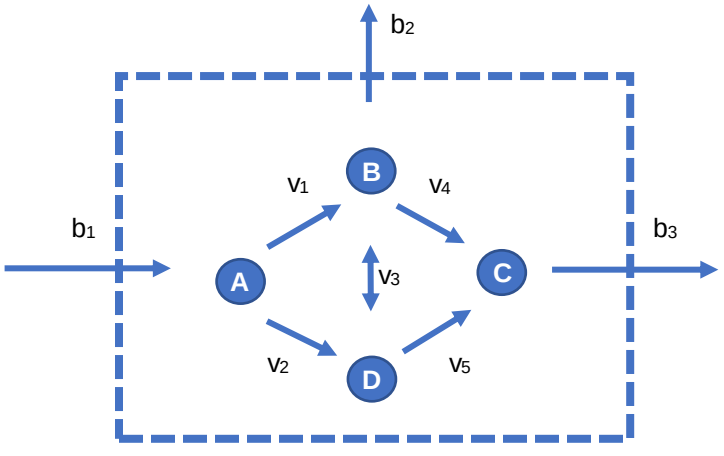
Exercise for Constraint-based Modeling of Cellular Networks

26 January 2023

Homework should be sent to Anika (ankueken@uni-potsdam.de)

Hand in your commented code / answers for all exercise tasks as homework.

Each Elementary Flux Mode (EFM) of a metabolic network represents a minimal set of reactions that can work together in a steady state. Use this definition to convert the problem of finding EFMs to a mixed-integer linear programming (MILP) problem. Then use your approach to find EFMs in a small sample network illustrated in figure below. The lower bounds and upper bounds are -1000 and 1000 for reversible reactions, respectively and they are 0 and 1000 for irreversible reactions.



1. Split all reversible reactions in the model by two irreversible reactions.
2. Finding minimal reactions that can work together in a steady state is equivalent to finding maximal reactions with zero fluxes that the remaining reactions with non-zero fluxes can work together in a steady state. A binary variable can be defined for each reaction to represent its presence in the network ($y_i = 0 \leftrightarrow v_i = 0$). Make sure that not all the reactions in the network get zero flux.
3. To identify all EFMs in the network (alternative solutions), iteratively solve the same MILP problem augmented with additional constraints (known as **integer cuts**), which come from previously found solutions.