• If \( u \not\geq 0 \), choose \( i \in I \) such that \( u_i < 0 \) and define the direction \( d \overset{\text{def}}{=} -A_i^{-1} e_i \), where \( e_i \) is the \( i \)-th unit basis vector in \( \mathbb{R}^I \).

• Next increase the objective function value by going from \( v \) in direction \( d \), while maintaining feasibility.

**Simplex Algorithm: Algebraic version**

1. If \( Ad \not\leq 0 \), the largest \( \lambda \geq 0 \) for which \( v + \lambda d \) is still feasible is

   \[
   \lambda^* = \min \{ \frac{b_p - A_p v}{A_p d} \mid p \in \{1, \ldots, m\}, A_p d > 0 \}.
   \]

   Let this minimum be attained at index \( k \). Then \( k \not\in I \) because \( A_i d = -e_i \leq 0 \).

   Define \( I' = (I \setminus \{i\}) \cup \{k\} \), which corresponds to the vertex \( v + \lambda^* d \).

   Replace \( I \) by \( I' \) and repeat the iteration.

2. If \( Ad \leq 0 \), then \( v + \lambda d \) is feasible, for all \( \lambda \geq 0 \). Moreover,

   \[
   c^T d = -c^T A_i^{-1} e_i = -u^T e_i = -u_i > 0.
   \]

   Thus the objective function can be increased along \( d \) to infinity and the problem is unbounded.

**Termination and complexity**

• The method terminates if the indices \( i \) and \( k \) are chosen in the right way (such choices are called pivoting rules).

• Following the rule of Bland, one can choose the smallest \( i \) such that \( u_i < 0 \) and the smallest \( k \) attaining the minimum in (PIV).

• For most known pivoting rules, sequences of examples have been constructed such that the number of iterations is exponential in \( m + n \) (e.g. Klee-Minty cubes).

• Although no pivoting rule is known to yield a polynomial time algorithm, the Simplex method turns out to work very well in practice.

**Simplex : Phase I**

• In order to find an initial feasible basis, consider the auxiliary linear program

   \[
   \max \{ y \mid Ax - by \leq 0, \ -y \leq 0, \ y \leq 1 \}, \quad \text{(Aux)}
   \]

   where \( y \) is a new variable.

• Given an arbitrary basis \( K \) of \( A \), obtain a feasible basis \( I \) for (Aux) by choosing \( I = K \cup \{m+1\} \). The corresponding basic feasible solution is 0.

• Apply the Simplex method to (Aux). If the optimum value is 0, then (LP) is infeasible. Otherwise, the optimum value has to be 1.

• If \( I' \) is the final feasible basis of (Aux), then \( K' = I' \setminus \{m+2\} \) can be used as an initial feasible basis for (LP).
Application: Metabolic networks

Stoichiometric matrix

- Metabolites (internal) \( \rightarrow \) rows
- Biochemical reactions \( \rightarrow \) columns

\[
\begin{array}{c}
\text{Reaction} \quad kA + lC \xrightarrow{i} mE + nH \\
\text{gives} \\
\begin{bmatrix}
A & \ldots & -k & \ldots \\
B & 0 \\
C & \ldots & -l \\
D & 0 \\
E & m \\
F & 0 \\
G & 0 \\
H & \ldots & n & \ldots 
\end{bmatrix}
\end{array}
\]

Flux cone

- Flux balance: \( Sv = 0 \)
- Irreversibility of some reactions: \( v_i \geq 0, i \in \text{Irr} \).
- Steady-state flux cone \( C = \{ v \in \mathbb{R}^n \mid Sv = 0, v_i \geq 0, \text{ for } i \in \text{Irr} \} \)

Flux balance analysis

- Use linear programming to study flux distribution in a cell
  \[
  \max \{ c^T v \mid Sv = 0, \; v_{\text{min}} \leq v \leq v_{\text{max}} \}
  \]
- Objective function
  - Maximize biomass production
  - Maximize metabolite production (e.g. biofuel)
- Metabolic engineering