

Max Mass Objective

The MaxMass algorithm contains the following objective function:

$$\max \sum_{k \in K} y_k \sum_{i=1}^k m_i - \sum_{k \in K} x_k \sum_{i=1}^k m_i$$

where the variables are

$$x_k = \begin{cases} 1, & \text{if gene or promoter } k \text{ is the first gene or promoter within the deleted segment} \\ 0, & \text{otherwise} \end{cases}$$

and

$$y_k = \begin{cases} 1, & \text{if gene or promoter } k \text{ is immediately after the end of the deleted segment} \\ 0, & \text{otherwise} \end{cases}$$

where

$$\sum_{k \in K} x_k = 1$$

and

$$\sum_{k \in K} y_k = 1$$

and the parameters are

- d_k : Position of the first nucleotide of the deleted sequence starting from the origin of replication when gene or promoter k is selected to be deleted in the beginning of the stretch. Note that d_k is not always the start site of a gene or promoter. It is the first nucleotide of the nonoverlapped region between the gene/promoter k and gene/promoter $k - 1$
- d'_k : Position of the first nucleotide of the gene or promoter k immediately after the deleted sequence
- m_i is the measured protein mass of gene i and $\sum_{i=1}^k m_i$ is the cumulative protein mass of all genes from the origin of replication to the k th gene. By subtracting the cumulative protein mass of the start gene (x_k) from the cumulative protein mass of the end gene (y_k), we obtain the cumulative protein mass of the interval for the optimal solution

We maximize the mass that is knocked out based on absolute quantitative proteomics [Schmidt et al 2015](http://www.nature.com/articles/nbt.3418) (<http://www.nature.com/articles/nbt.3418>) in (fg/cell)

MaxMass constraints

$\sum_{j \in J} S_{i,j} v_j = 0$	$i = 1, \dots, N$	Steady state conservation of metabolite i requirement
$\sum_{k \in K} y_k = 1$	$\sum_{k \in K} x_k = 1$	Ensure only one gene knockout per iteration
$\sum_{j=1}^k x_j - \sum_{j=1}^k y_j = z_k$	$k = 1, \dots, K$	Ensures all genes between start and end area also knocked out
$v_{\text{biomass}} \geq f \cdot v_{\text{biomass, max}}$		Requires that the KO must be capable of growing at the specif
$z_g = \prod_{p \in p^s} z_p$	$p = 1, \dots, P$	Ensures that a gene is not functional if all of its promoters are

Gene Protein Reaction constraints

Single gene catalyzes reaction: $z_k \rightarrow v_j$

$$(1 - z_k) \cdot LB \leq v_j \leq (1 - z_k) \cdot UB$$

Enzyme dimer complex catalyzes reaction: $(k_1 \text{ AND } k_2) \rightarrow v_j$

$$(1 - z_{k_1}) \cdot LB \leq v_j \leq (1 - z_{k_1}) \cdot UB$$

$$(1 - z_{k_2}) \cdot LB \leq v_j \leq (1 - z_{k_2}) \cdot UB$$

Two Isozymes catalyze reaction: $(k_1 \text{ OR } k_2) \rightarrow v_j$

$$(2 - z_{k_1} - z_{k_2}) \cdot LB \leq v_j \leq (2 - z_{k_1} - z_{k_2}) \cdot UB$$

$$LB \leq v_j \leq UB$$

Complex Gene Protein Reaction: $(k_1 \text{ AND } k_2) \text{ OR } (k_1 \text{ AND } k_3) \rightarrow v_j$

$$(2 - z_{k_2} - z_{k_3}) \cdot LB \leq v_j \leq (2 - z_{k_2} - z_{k_3}) \cdot UB$$

$$(1 - z_{k_1}) \cdot LB \leq v_j \leq (1 - z_{k_1}) \cdot UB$$