
Pseudocode of the reliability-based integrating (RBI) algorithm

Input :

${}_m\mathbf{X}_a$ // The stoichiometric matrix.
 $\mathbf{D}$ // The gene expression data.
 $\mathbf{g}$ // Vector of the metabolic genes (MG).
 $\mathbf{h}$ // Vector of the regulatory genes (RG).
 $\mathbf{a}$ // Vector of the boolean equation in GRNs.
 $\mathbf{b}$ // Vector of the boolean equation in GPR.
Parameters α, β, γ .

Output : v_{biomass} and $v_{\text{metabolite}}$

Process :

1	Determine k regulatory gene knocked out.	$O(1)$
2	Binarizing $\mathbf{D}$ based on α .	$O(n_1)$
3	for $i : 1$ to $n(h)$	$O(n_2)$
4	if RG_i is knocked out	
5	$p_{\text{RG}_i} \Leftarrow 0$	
5	else	
6	$p_{\text{RG}_i} \Leftarrow f(\text{RG}_i)$	
7	end	
8	end	
9	Compute r_{MG_j}	$O(n_1)$
10	Calculate r_{MR_k}	$O(n_3)$
11	Determine $[\text{lb}_k^*, \text{ub}_k^*]$ using FVA	$O(n_4.n_3)$
12	Generate $\tilde{\mathbf{v}}$ // It is a vector containing the metabolic reaction (MR) categorized as the transport reaction or the 'ATPM' reaction	$O(n_3)$
13	for $k : 1$ to a	$O(a)$
14	if $(r_{\text{MR}_k} < \beta)$ or $(\text{MR}_k \notin \tilde{\mathbf{v}})$	
15	$\text{ub}_k \Leftarrow r_{\text{MR}_k} \times \text{ub}_k^* + \gamma$	
16	$\text{lb}_k \Leftarrow r_{\text{MR}_k} \times \text{lb}_k^* - \gamma$	
17	end	
18	end	
19	Calculate v_{biomass} using FBA	$O(n_4)$
20	$\text{lb}_{\text{biomass}} \Leftarrow 0.1 \times v_{\text{biomass}}$	$O(1)$
21	Calculate $v_{\text{metabolite}}$ using FBA	$O(n_4)$
