Sensitivity of a Flux Balance Analysis solution

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Consider a biochemical network with m molecular species interconverted by n biochemical reactions, represented by a stoichiometric matrix $S \in R^{m\times n}$. Given lower and upper bounds on reaction rates, $l, u \in R^n$, a vector of changes in molecular species concentrations $b \in R^m$ and a coefficient vector $c \in R^n$, flux balance analysis is the optimisation problem

$$\begin{array}{ll} \max & c^T v \\ \text{s.t.} & Sv = b \\ & l \leq v \leq u \end{array} \tag{1}$$

where $v \in R^n$ is a vector of net reaction rates. Problem (1) is a minimisation of a scalar valued objective $\psi(v) \coloneqq c^T v$, subject to m mass balance constraints, n lower bound constraints and n upper bound constraints. We seek to analyse the sensitivity of the optimal objective $\psi(v^\star) \coloneqq c^T v^\star$ to (1) with respect to perturbations to the input data $\{b, l, u\}$.

Problem (1) written as

$$\begin{array}{ll} \max & c^T v \\ \text{s.t.} & Sv = b \\ & v - s_l = l \\ & v + s_u = u \\ & s_u \geq 0 \\ & s_l \geq 0 \end{array} \tag{2}$$

where the pair of inequality constraints bounding v in (1) are reformulated as a pair of equality constraints by introducing a pair of non-negative slack variables $s_u, s_l \in R^n_{\geq 0}$. Any optimal flux vector $v^\star$that is a solution to (2) must satisfy a set of equations termed *optimality conditions.* These conditions may be derived by representing (2) as an unconstrained scalar minimisation problem. To do this, we introduce we introduce dual variables $y \in R^m$, $w_l \in R^n_{\geq 0}$ and $w_u \in R^n_{\geq 0}$ to weight equality, lower bound and upper bound constraints, respectively. Problem (1) with dual variables included is written as

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$$
\begin{array}{ll}
\max & c^T v \\
\text{s.t.} & Sv = b : y \\
& v - l - s_l = 0 : w_l \\
& u - v - s_u = 0 : w_u \\
& s_u \geq 0 \\
& s_l \geq 0
\end{array} \tag{3}
$$

The objective function augmented with a weighted sum of the constraint functions [1] is

$$
\mathcal{L}(v, y, w_u, w_l) \coloneqq c^T v + y^T (Sv - b) + w_l^T (v - l + s_l) + w_u^T (u - v - s_u) \tag{4}
$$

which is termed the *Lagrangian* function for Problem (1). Consider the unconstrained scalar optimisation problem

$$
\max \mathcal{L}(v, y, w_u, w_l, s_u, s_l) \tag{5}
$$

An optimum of $\mathcal{L}(v, y, w_u, w_l)$ is attained when each partial derivative of$\mathcal{L}(v, y, w_u, w_l, s_u, s_l)$ is equal to zero, that is

$$
\begin{aligned}
\frac{\partial \mathcal{L}}{\partial v} &= c + S^T y^\star + w_l^\star - w_u^\star = 0, \\
\frac{\partial \mathcal{L}}{\partial y} &= Sv^\star - b = 0, \\
\frac{\partial \mathcal{L}}{\partial w_l} &= v^\star - l + s_l^\star = 0, \\
\frac{\partial \mathcal{L}}{\partial w_u} &= u - v^\star - s_l^\star = 0.
\end{aligned} \tag{6}
$$

Using Equations (6), the optimal value of the objective in Problem (5) is

$$
\begin{aligned}
\mathcal{L}^\star \coloneqq \mathcal{L}(v^\star, y^\star, w_u^\star, w_l^\star, s_u^\star, s_l^\star) &= c^T v^\star + y^{\star T} (Sv^\star - b) + w_l^{\star T} (v^\star - l + s_l^\star) + w_u^{\star T} (u - v^\star - s_l^\star) \\
&= c^T v^\star
\end{aligned}
$$

Therefore, to compute the sensitivity of the optimal value of the objective of Problem (3), with respect to the input data data $\{b, l, u\}$, we take the partial derivatives of the Lagrangian at the optimum, that is

$$
\begin{aligned}
\frac{\partial \mathcal{L}^\star}{\partial b} &= y^\star, \\
\frac{\partial \mathcal{L}^\star}{\partial l} &= -w_l^\star, \\
\frac{\partial \mathcal{L}^\star}{\partial u} &= w_u^\star.
\end{aligned} \tag{7}
$$

This means that a change of ∂b_i will change optimal value of the objective by $y_i^\star$. Likewise, a change of ∂l_j to l_j will change optimal value of the objective by $w_{lj}^\star$ and a change of ∂u_j to u_j will change the optimal value of the objective by $-w_{uj}^\star$. One can combine the dual variables to the inequality constraints into a single dual vector by defining

$$
w \coloneqq w_l - w_u
$$

so $w_j = 0 \Rightarrow w_l = 0, w_u = 0$, $w_j > 0 \Rightarrow w_l > 0, w_u = 0$ and $w_j < 0 \Rightarrow w_l = 0, w_u > 0$. Note that, if Problem (1) and its subsequent reformulations are minimisation problems, rather than maximisation problems, then the signs of each of the dual variables is the opposite of those in (7).

References

[1] S. P. Boyd, L. Vandenberghe. *Convex Optimization*. Cambridge University Press. (document)