Supplementary note

Calculation of reaction score (pseudocode)

INPUT referenceGEM
INPUT mspGene (binary $n \times m$ matrix, n: number of genes; m: number of MSPs)
INPUT taxonomy ($m \times r$ table, m:number of MSPs; r: number of taxonomy level i.e. from genus to phylum, [m,r]: taxonomy name)
reactionState= zeros (length(referenceGEM.rules), m)
FOR h = 1 to m
    vect= gene names (mspGene(:,h)==1)
    FOR i=1 to length(vect)
        $index$=find (vect$_i$ in referenceGEM.rules)
        IF NOT empty (**$index$**) **THEN** reactionState($index$,i)=1 **ENDIF**
    ENDFOR
ENDFOR
% convert reaction state to reaction score
FOR i = 1 to m
    FOR j= 1 to r
        IF taxonomy (i,j) != "unclassified" **THEN**
            $index$=find (taxonomy (i,j) in taxonomy (:,j))
            state= reactionState (:,$index$)
            FOR k= 1 to length(referenceGEM.rules)
                ScoreMatrix(k,j) = sum(state(k,:)) /r;
            ENDFOR
        ELSE
            ScoreMatrix(:,j)=0
        ENDIF
    ENDFOR
    FOR k= 1 to length(referenceGEM.rules)
        ScoreMatrix(k,(r+1)) = sum(ScoreMatrix (k,:)) /r;
    ENDFOR
    reactionScore(:,i)= ScoreMatrix(k,(r+1))
ENDFOR
FOR i = 1 to length(referenceGEM.rules)
    IF empty **(**referenceGEM.rules(i)**) THEN**
        reactionState(i,:)=-1; reactionScore(i,:)=-1
    ENDIF
ENDFOR
% Define threshold
FOR j= 1 to r
threshold (1,j)= **MIN** ScoreMatrix(1,j)>0
ENDFOR

RETURN threshold
RETURN reactionScore
RETURN reactionState