Thresholding options

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| Approach | Threshold input | Visual representation | Example |
| **Global T1** | **One global threshold:**   * 1. exact value input   2. percentile input (25th, 75th,90th …) |  | Lower Threshold: 130  YDL227C 871  YDL226C 126  YDL225W 319  YDL224C 56  YDL223C 13  YDL222C 3  YDL221W 135 |
| **Local T1** | **One global threshold:**   * 1. exact value input   2. percentile input (25th, 75th,90th …)   **Multiple local thresholds:** calculated automatically across multiple transcriptomics data samples of the same conditions |  | Lower Threshold: 130  Local for YDL227C: 600  Local for YDL225W: 350   |  |  | | --- | --- | | YDL227C | 871 | | YDL226C | 126 | | YDL225W | 319 | | YDL224C | 56 | | YDL223C | 13 | | YDL222C | 3 | | YDL221W | 135 | |
| **Local T2** | **Two global thresholds:**   * 1. exact value input   2. percentile input (25th, 75th,90th …)   **Multiple local thresholds:** calculated automatically across multiple transcriptomics data samples of the same conditions |  | Lower Threshold: 50  Upper Threshold: 130  Local for YDL224C: 60  Local for YDL226C: 70   |  |  | | --- | --- | | YDL227C | 871 | | YDL226C | 126 | | YDL225W | 319 | | YDL224C | 56 | | YDL223C | 13 | | YDL222C | 3 | | YDL221W | 135 | |

**Gene Mapping and Constraining options**

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| **Requirement** | **Options** |
| Constraining options | 1. Only irreversible reactions 2. All reactions 3. Growth not affecting gene deletion only 4. Meet minimum growth requirements |
| Gene mapping approach | 1. AND/MIN and OR/MAX 2. AND/MIN and OR/SUM 3. AND/GM and OR/MAX 4. AND/GM and OR/SUM |

GM – geometric mean

The **constraining options** are used to implement transcriptome absolute values on reaction bounds in the GSM:

* **Only irreversible reactions** function. Enzymatic reactions have 3 different directions in GSM: irreversible, reversible and backward irreversible. This approach constraints only irreversible and backward irreversible reactions in oriented direction.
* **All reactions** function constraints all reactions. Irreversible and backward irreversible reactions in oriented direction, but reversible reactions are constrained in both directions.
* **Growth not affecting gene deletion only** option allows to delete only those genes with expression values below the given threshold and does not affect growth. Cobra Toolbox 3.0 *singleGeneDeletion* analysis with FBA method is performed before executing gene deletion for those genes. Only if the returned output *grRatio* returned by *singleGeneDeletion* function is equal to 1 (meaning that the wild type growth equals to the deletion strain growth) the gene gets deleted.
* **Meet minimum growth requirements** option allows to constrain only those reactions where the gene mapping end value (which is set as a reaction upper bound) is not below the minimum growth requirements for that reaction. Minimum growth requirements are obtained by creating another context-specific model where only the gene deletion and medium exchange reaction constraining is applied in order to calculate the Cobra Toolbox 3.0 FBA (*optimizeCbModel*) minimization of growth.