# Mathematical formula for the metric Relative expression across cell type clusters

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## Abstract

This document provides the suggestion of Asli and Katelyn for the Relative expression across cell type clusters metric. The process for the similarity metric: Relative expression levels/probe efficiency is the same by converting the pairwise differences per gene for each cell to pairwise differences per cell for each gene.

### 0.1. Relative expression across cell type clusters

Let $n_c$ be the different numbers of clusters. Let $U = U_1, ..., U_{n_c}, V = V_1, ..., V_{n_c}$ be the set of sets of cells in each cluster for single-cell data and the spatial data. We have $|U| = |V| = n_c$.
Denote the shared genes as $I = I_1, ..., I_{n_c}$ as $I = U \cap V$ and subset $U$ to $V$ with $U = U \cap I$.

Define the mean expression levels for each modality as $M_{sc}$ and $M_{sp}$ :
$M_{sc} = \frac{(\sum_{i=0}^{n_c} U_i)}{n_c}$ and $M_{sp} = \frac{(\sum_{i=0}^{n_c} V_i)}{n_c}$

Calculate the pairwise difference between cell types for each column using the following idea:

For each unique pair of columns $(col_i, col_j)$ from both $M_{sc}$ and $M_{sp}$ such that $i < j$. We calculate the difference in between and store the values in $P_{sc}$ which represents the pairwise differences per gene for single cell data and analog for the spatial data: $P_{sp}$:

$P_{sc} = (p_{kj})$ with $(p_{kj})_{1 \leq k \leq \frac{c!}{(c-2)!*2!}, 1 \leq j \leq g}$

where $c$= Number of cells and $g$= Number of genes in $M_{sc}$. For $M_{sc} = (m_{il})_{1 \leq i \leq c, 1 \leq l \leq g}$ we have

$p_{kj} = \sum_{k=1}^{\frac{c*(c-1)}{2}-1} \sum_{j=i+1}^{g} [m_{j,col_i} - m_{k,col_l}]$

and analog for $P_{sp}$.

To define the mean normalized relative expression matrix for each gene, we define:

$$\mathfrak{M}_{i,j}^{sc} = \left( \frac{p_{i,j}}{\sum_{s=1}^{\frac{c*(c-1)}{2}} p_{s,j}} \right)_{1 \leq i \leq \frac{c*(c-1)}{2}, 1 \leq j \leq g}$$

Analog for $\mathfrak{M}_{i,j}^{sp}$.

As last step we define $S_i = \frac{|\mathfrak{M}^{sc} - \mathfrak{M}^{sp}|}{|\mathfrak{M}^{sc} - \mathfrak{M}^{sp}|}$

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