

Supplementary Information

1 The brief description of the HOSVD algorithm

For demonstration, consider the tensor $x_{ijk} \in \mathbb{R}^{N \times M \times K}$. HOSVD is an algorithm that applies SVD to the unfolded tensor, either $x_{i(jk)} \in \mathbb{R}^{N \times MK}$, $x_{j(ik)} \in \mathbb{R}^{M \times NK}$, or $x_{k(ij)} \in \mathbb{R}^{K \times NM}$,

$$x_{i(jk)} = \sum_{\ell_1=1}^{\min(N, MK)} \lambda_{\ell_1} u_{\ell_1 i} v_{\ell_1 jk} \quad (1)$$

$$x_{j(ik)} = \sum_{\ell_2=1}^{\min(M, NK)} \lambda_{\ell_2} u_{\ell_2 j} v_{\ell_2 ik} \quad (2)$$

$$x_{k(ij)} = \sum_{\ell_3=1}^{\min(K, NM)} \lambda_{\ell_3} u_{\ell_3 k} v_{\ell_3 ij} \quad (3)$$

$$(4)$$

where $u_{\ell_1 i} \in \mathbb{R}^{\min(N, MK) \times N}$, $v_{\ell_1 jk} \in \mathbb{R}^{\min(N, MK) \times MK}$, $u_{\ell_2 j} \in \mathbb{R}^{\min(M, NK) \times M}$, $v_{\ell_2 ik} \in \mathbb{R}^{\min(M, NK) \times NK}$, $u_{\ell_3 k} \in \mathbb{R}^{\min(K, NM) \times K}$, $v_{\ell_3 ij} \in \mathbb{R}^{\min(K, NM) \times NM}$. A core tensor $G(\ell_1 \ell_2 \ell_3)$ can be calculated as

$$G(\ell_1 \ell_2 \ell_3) = \sum_{i=1}^N \sum_{j=1}^M \sum_{k=1}^K x_{ijk} u_{\ell_1 i} u_{\ell_2 j} u_{\ell_3 k}. \quad (5)$$

Subsequently, we obtain the following

$$x_{ijk} = \sum_{\ell_1=1}^N \sum_{\ell_2=1}^M \sum_{\ell_3=1}^K G(\ell_1 \ell_2 \ell_3) u_{\ell_1 i} u_{\ell_2 j} u_{\ell_3 k} \quad (6)$$

where $u_{\ell_1 i} \in \mathbb{R}^{N \times N}$, $u_{\ell_2 j} \in \mathbb{R}^{M \times M}$, and $u_{\ell_3 k} \in \mathbb{R}^{K \times K}$. When $u_{\ell_1 i}$, $u_{\ell_2 j}$, and $u_{\ell_3 k}$, are smaller than those computed in eqs. (1), (2), and (3), missing values are filled with zero. Then, $u_{\ell_1 i}$, $u_{\ell_2 j}$, and $u_{\ell_3 k}$ are the resultant orthogonal matrices obtained.

2 TD-based unsupervised FE with SD optimization

HOSVD was applied to x_{ijkmst} , and we obtained the following:

$$x_{ijkmst} = \sum_{\ell_1=1}^5 \sum_{\ell_2=1}^5 \sum_{\ell_3=1}^2 \sum_{\ell_4=1}^2 \sum_{\ell_5=1}^3 \sum_{\ell_6=1}^{31099} G(\ell_1 \ell_2 \ell_3 \ell_4 \ell_5 \ell_6) u_{\ell_1 j} u_{\ell_2 k} u_{\ell_3 m} u_{\ell_4 s} u_{\ell_5 t} u_{\ell_6 i} \quad (7)$$

where $G(\ell_1 \ell_2 \ell_3 \ell_4 \ell_5 \ell_6) \in \mathbb{R}^{5 \times 5 \times 2 \times 2 \times 3 \times 31099}$ is a core tensor and $u_{\ell_1 j} \in \mathbb{R}^{5 \times 5}$, $u_{\ell_2 k} \in \mathbb{R}^{5 \times 5}$, $u_{\ell_3 m} \in \mathbb{R}^{2 \times 2}$, $u_{\ell_4 s} \in \mathbb{R}^{2 \times 2}$, $u_{\ell_5 t} \in \mathbb{R}^{3 \times 3}$, and $u_{\ell_6 i} \in \mathbb{R}^{31099 \times 31099}$ are singular value matrices and orthogonal matrices.

After identifying $u_{\ell_1 j}$, $u_{\ell_2 k}$, $u_{\ell_3 m}$, $u_{\ell_4 s}$, and $u_{\ell_5 t}$ of interest, we attempted to identify $G(\ell_1 \ell_2 \ell_3 \ell_4 \ell_5 \ell_6)$ with the largest absolute value and fixed ℓ_1 to ℓ_5 . Then, we attributed P -values to i by assuming that $u_{\ell_6 i}$ obeys a Gaussian distribution as follows:

$$P_i = P_{\chi^2} \left[> \left(\frac{u_{\ell_6 i}}{\sigma_{\ell_6}} \right)^2 \right] \quad (8)$$

where $P_{\chi^2} [> x]$ is the cumulative χ^2 distribution under the assumption that it is larger than x and σ_{ℓ_6} is the SD. P_i is corrected with the BH criterion [?].

The SD is optimized so that $u_{\ell_6 i}$ obeys the Gaussian distribution (null hypothesis) as much as possible [?], and the optimization process is as follows. Initially, we compute the histogram h_p , which includes the number of i values that satisfy the following:

$$\frac{p}{N_p} \leq 1 - \text{adjusted}P_i \leq \frac{p+1}{N_p}, 0 \leq p \leq N_p - 1 \quad (9)$$

Then, the standard deviation of h_p for $\text{adjusted}P_i > p_0$ for the threshold value p_0 ,

$$\Delta h_p = \frac{1}{N'_p} \sum_{\text{adjusted} \frac{p}{N_p} > p_0} (h_p - \langle h_p \rangle)^2 \quad (10)$$

$$\langle h_p \rangle = \frac{1}{N'_p} \sum_{\text{adjusted} \frac{p}{N_p} > p_0} h_p \quad (11)$$

$$N'_p = \sum_{\text{adjusted} \frac{p}{N_p} > p_0} 1 \quad (12)$$

is minimized. Therefore, for $1 - \text{adjusted}P_i < 1 - p_0$, h_p takes a constant value (i.e., it obeys the null hypothesis) as much as possible, whereas for $1 - \text{adjusted}P_i > 1 - p_0$, h_p presents a peak value.

The P_i values are finally calculated using the optimized SD, and i values associated with adjusted P -values less than 0.01 are selected. Probes, is , are converted to gene symbols using the gene ID conversion tool in DAVID [?].

The genes selected are presumed to be coincident with the profiles associated with selected u_{ℓ_1j} , u_{ℓ_2k} , u_{ℓ_3m} , u_{ℓ_4s} , and u_{ℓ_5t} ; this corresponds to the identification of differentially expressed genes.

For details, check sample R source code in supplementary materials.

3 Gene sepections

The results indicated that u_{2j} represents the dependence on time, u_{2m} represents the distinction between the controls and treatment, u_{1k} represents the independence of the replicate, u_{1s} represents the independence of strains, and u_{1t} represents the independence of tissues (Fig. S1). Table S1 presents

Table S1: The core tensor defined in eq. (7) when HOSVD is applied to data sets, $G(2, 1, 2, 1, 1, \ell_6)$.

ℓ_6	$G(2, 1, 2, 1, 1, \ell_6)$	ℓ_6	$G(2, 1, 2, 1, 1, \ell_6)$
1	3.505367	6	6.227675
2	8.092320	7	6.890919
3	-15.707937	8	-3.287872
4	9.134575	9	-1.529140
5	6.723113	10	-9.158979

$G(2, 1, 2, 1, 1, \ell_6)$, and it shows that $G(2, 1, 2, 1, 1, 3)$ has the highest absolute value. Then, u_{3i} (i.e., $\ell_6 = 3$) is used to select probes. The P_i values are determined using eq. (8), with $\ell_6 = 3$. SD optimization was performed, and $\sigma_3 = 0.001514603$. A histogram of $1-P_i$ after SD optimization is presented in Figure S2 and the histogram is more similar to that of the null hypothesis, i.e., the combination of a flat region and a sharp peak. Then, the P -values corresponding to the i th probe are determined with eq. (8), and the P_i values are corrected by BH criterion. Finally, 2,452 selected probes are associated with adjusted P -values less than 0.01, and they are further converted to 2,281 gene symbols.

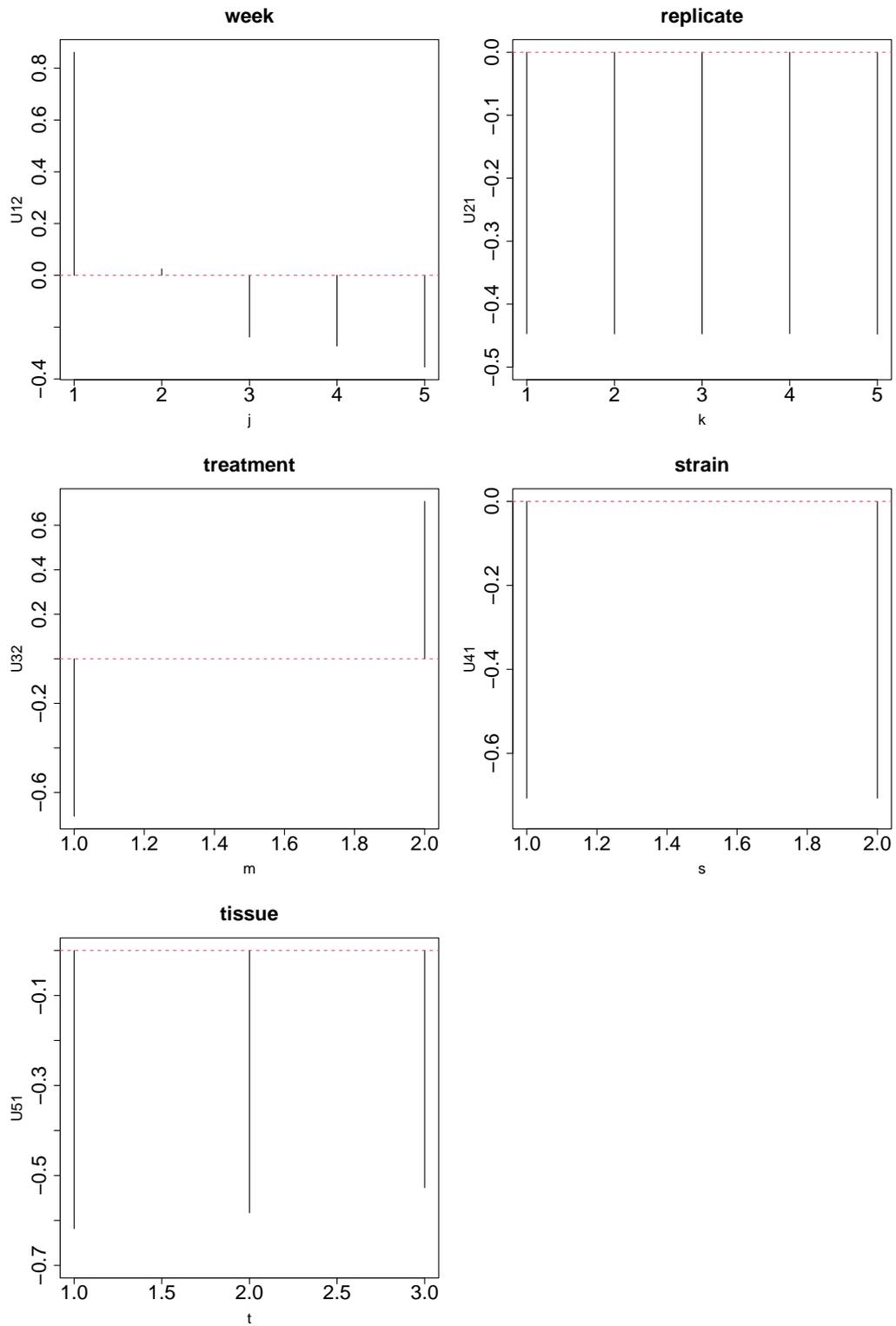


Figure S1: Singular value vectors defined in eq. (7) when HOSVD is applied to data sets. u_{2j} (week), u_{1k} (replicate), u_{2m} (treatment), u_{1s} (strain), and u_{1t} (tissue).

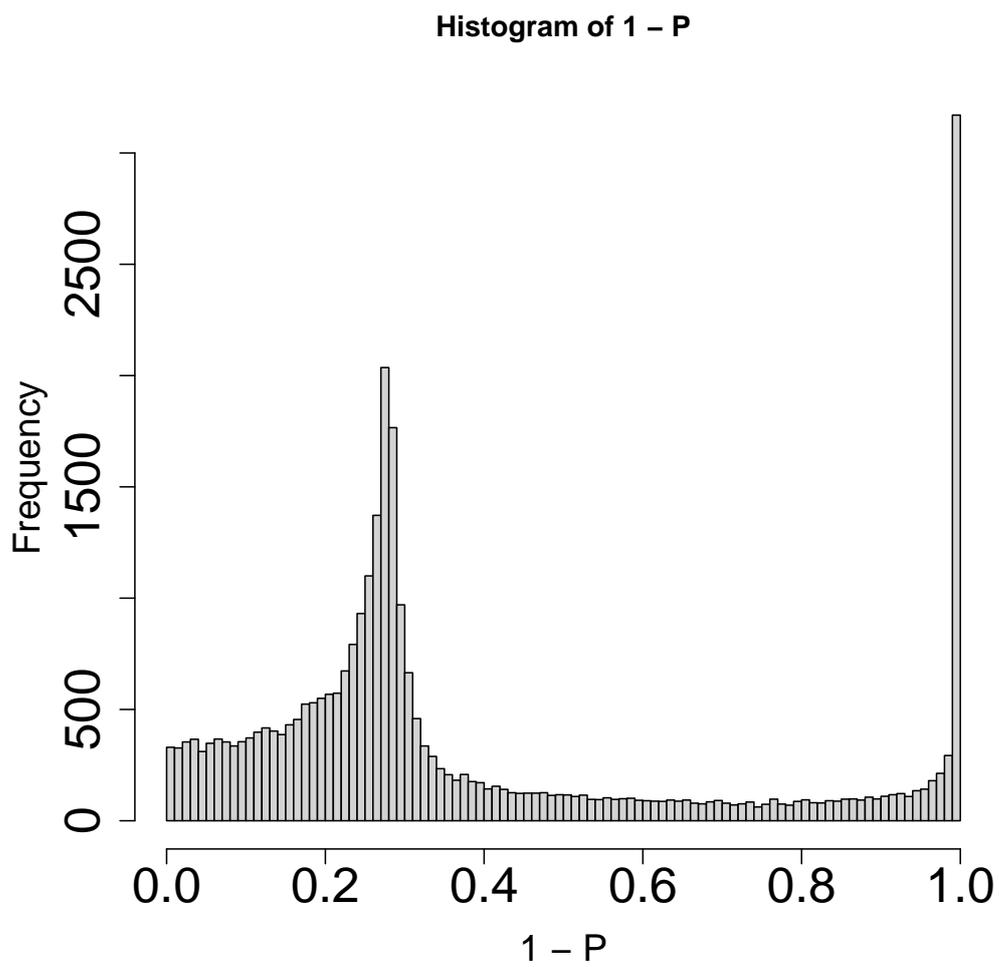


Figure S2: Histogram of $1 - P_i$.