Two edge-count tests and relevance analysis in k high-dimensional samples

Xiaoping Shi∗

Abstract

For the task of relevance analysis, the conventional Tukey’s test may be applied to the set of all pairwise comparisons. However, there were few studies that discuss both nonparametric k-sample comparisons and relevance analysis in high dimensions. Our aim is to capture the degree of relevance between combined samples and provide additional insights and advantages in high-dimensional k-sample comparisons. Our solution is to extend a graph-based two-sample comparison and investigate its availability for large and unequal sample sizes. We propose two distribution-free test statistics based on between-sample edge counts and measure the degree of relevance by standardized counts. The asymptotic permutation null distributions of the proposed statistics are derived, and the power gain is proved when the sample sizes are smaller than the square root of the dimension. We also discuss different edge costs in the graph to compare the parameters of the distributions. Simulation comparisons and real data analysis of tumors and images further convince the value of our proposed method. Software implementing the relevance analysis is available in the R package Relevance.

Keywords: Graph-based nonparametrics; distribution-free tests; permutation null distribution; power; edge costs.

∗Irving K. Barber School of Arts and Sciences, University of British Columbia, Kelowna, BC V1V 1V7, Canada. E-mail: xiaoping.shi@ubc.ca
1 Introduction

We are now in an era of data explosion. Due to transparency and the right to data, improved technology for accessing data, and increased data storage capacity, vast amounts of high-dimensional data, including thousands of variables (features or attributes) and hundreds of instances are being entered into commercial, humanities, medical, scientific, and government databases around the world. Here are some examples of high-dimensional data.

**Microarray data:** The gene expression microarray technology, which can measure tens of thousands of gene expression levels in a single experiment (Shalon et al., 1996), have proven to be a very mature technology. With the illumina HiSeq platform, 20,531 gene expression levels were extracted from 801 patients to compare five different types of tumors for effective therapies (Weinstein et al., 2013). These data are available from https://archive.ics.uci.edu/ml/datasets/gene+expression+cancer+RNA-Seq.

**Proteomic data:** Aptamers, single-stranded oligonucleotides, are advanced tools for measuring plasma proteins (Zhou and Rossi, 2017). Through venipuncture, Lehallier et al. (2019) measured 2,925 plasma proteins to capture aspects of aging in different cell types and tissues. They compared dozens of instances with thousands of protein levels by applying the so-called sliding window analysis. Some of the high-dimensional data can be obtained from the R package DEswan at https://lehallib.github.io/DEswan/.

**Functional magnetic resonance imaging (fMRI) data:** The physiological monitoring system (Model 1030, Small Animal Instruments, Stony Brook, USA) allows continuous measurement of eletrocardiogram (ECG) and motion-sensitive respiration signals. By inserting 30G needle electrodes, Jung et al. (2019) collected blood oxygen level-dependent (BOLD) fMRIs from seven adult males under 9.4 T and 15.2 T magnetic resonance (MR)
conditions. Their aim was to compare the functional detection of BOLD responses to certain stimuli by these two MR conditions under different experimental periods: pre-stimulus (40s), stimulus (20s) and post-stimulus groups (60s). The size of the collected fMRI images is $228 \times 160 \times 132 \times 120$.

1.1 Problems

In traditional data collection, limited by technology, we usually have many observations and several variables. In order to compare whether the linear combination of the created mean vectors differs from one sample to another, we can perform a classical multivariate analysis of variance (MANOVA) with two important assumptions: multivariate normality and homogeneity of variance.

Nowadays, we collect data on genes, proteins or images. The dimensionality of each observation is in the thousands, while there are only tens or hundreds of instances available for study. MANOVA simply cannot cope with this high dimensionality, nor can it compare sample covariances. As an example of a proteomic comparison, we have four samples: males after age $t$ (MA), females after age $t$ (FA), males before age $t$ (MB), and females before age $t$ (FB). We assume that the mean vectors of the protein samples are $\mu_{MA}$, $\mu_{FA}$, $\mu_{MB}$ and $\mu_{FB}$, respectively. The linear combination of mean vectors, $(\mu_{MA} - \mu_{MB}) + (\mu_{FA} - \mu_{FB})$, represents the difference between two different age samples before and after $t$. However, in practical applications, there may be a negative correlation between males and females. Therefore, the weighted sum of norms, $w_1||\mu_{MA} - \mu_{MB}|| + w_2||\mu_{FA} - \mu_{FB}||$, should be more reasonable. But it is not trivial to determine the weights $w_1$ and $w_2$, which could be related to sample sizes and covariances. Developing nonparametric methods may be a good way to compare sample distributions and perform relevance analysis simultaneously in high dimensions.
1.2 Literature review

In a two-sample comparison, the classical Hotelling’s $T^2$ statistic is $(\bar{X}_1 - \bar{X}_2) S^{-1} (\bar{X}_1 - \bar{X}_2)^\top$, where $\bar{X}_1$ and $\bar{X}_2$ are the two sample mean vectors and $S$ is the pooled sample covariance. If the dimensionality is larger than the sample size, the inverse of $S$ may not exist, so Hotelling’s $T^2$ statistic does not work. An important progress was initially made by Bai and Saranadasa (1996) by introducing $(\bar{X}_1 - \bar{X}_2) (\bar{X}_1 - \bar{X}_2)^\top$. They derived its asymptotic distribution under normality and homogeneous covariance. Chen and Qin (2010) extended this by considering an U-statistic. Cai et al. (2014) proposed an extreme statistic by comparing each component. Xu et al. (2016) considered a $\gamma$-norm ($1 \leq \gamma < \infty$) of $\bar{X}_1 - \bar{X}_2$. The $\gamma$-norm of $d$-dimensional vector $X$ is defined by $||X||_\gamma = (\sum_{q=1}^d |X_q|^{\gamma})^{1/\gamma}$, where $X_q$ is the $q$th component of this vector. Thereafter, $||\bar{X}_1 - \bar{X}_2||_2^2 = (\bar{X}_1 - \bar{X}_2)^\top (\bar{X}_1 - \bar{X}_2)$. The introduction of the $\gamma$-norm paved the way for the graph method; see the cost (8). He et al. (2021) further proposed a family of U-statistics as an unbiased estimate of the $\gamma$-norm.

Along the development of U statistics, Srivastava and Kubokawa (2013) compared the means of several samples with a common covariance matrix, while Hu et al. (2017) relaxed it to unequal covariance matrices. These research advances indicate the feasibility of extending the two-sample comparison to the k-sample comparison in terms of the combination of the U-statistic and the $\gamma$-norm. It should not be overlooked that there is also a graph method based on graphical optimization that treats data of arbitrary dimension as points and minimizes the total costs under some constraints such as tree and path.

Denote a set of points (nodes or vertices) by $\mathcal{V} = \{v_1, \ldots, v_N\}$. Let $\mathcal{G}$ be a connected and costed graph with a set of edges $\mathcal{E}(\mathcal{G})$. We assign $\gamma$-norm to the cost of each edge. An information graph can have some features sensitive to alternatives. Currently, two kinds of optimized graphs are studied: minimum spanning tree (MST) and shortest Hamiltonian
path (SHP). Both tests based on MST (Friedman and Rafsky, 1979) and SHP (Biswas et al., 2014) can be generalized from the Wald-Wolfowitz run test (Wald and Wolfowitz, 1940). However, the MST-based test that counted the between-sample edges can result in the power loss (Chen and Zhang, 2013; Chen et al., 2018). Some improvements in power gain have been made through counting the within-sample edges (Chen and Friedman, 2017; Zhang and Chen, 2021). For other developments in nonparametric tests, see the recent work of (Mukhopadhyay and Wang, 2020).

1.3 Contributions

Our main contributions include:

1. It is still unknown whether the two-sample edge counts can be used to solve the k-sample comparison problem. In addition, the power gain at large sample sizes is uncertain. We convince the applicability and power gain of this counting by requiring the sample sizes to be smaller than the square root of the dimension. This allows the sample sizes to grow with the dimension.

2. We propose two distribution-free tests based on the weighted sum of between-sample counts and minimum of standardized between-sample counts, and derive asymptotic permutation null distributions. The degree of relevance between combined samples can be measured by the standardized between-combined-sample counts.

3. We also discuss how to accurately assess the degree relevance by choosing appropriate edge costs. We call our technique relevance, short for related entire variety analysis of counts of edges; it is implemented in the R package Relevance. The simulation study demonstrates the advantage of our test for the k-sample comparison problem. Two real data analyses further convince the value of relevance analysis.
For convenience, we make these notations. Write the vectors $X_t = (X_{t,1}, \ldots, X_{t,d})^\top$, the difference vectors $\dot{X}_t = (X_{t,2} - X_{t,1}, \ldots, X_{t,d} - X_{t,d-1})^\top$, and the partial sums $X_{t,*} = \sum_{j=1}^d X_{t,j}$ for $1 \leq t \leq N$. Denote $k$ samples indexed by $g_t$, where for any $t$, there exists only one $G_\ell \subseteq \mathbb{N}$ with $1 \leq \ell \leq k$ such that $g_t \in G_\ell$. Denote each size as $n_\ell = |G_\ell|$ or $\#\{G_\ell\}$ and total size as $N = \sum_{\ell=1}^k n_\ell$. Write $\theta(F_{G_\ell})$ as the parameter vector of the common distribution $F$ of the sample $G_\ell$. The multivariate normal distribution is denoted as $N(0, \Sigma)$ with a mean vector $0 = (0, 0, \ldots, 0)^\top$ and a covariance matrix $\Sigma$. In particular, $I$ is an identity matrix. We denote the $N!$ distinct paths as $\mathcal{P}_{\text{all}} = \{\text{all distinct paths } v_{q_1}, \ldots, v_{q_N} | (q_1, \ldots, q_N) \text{ is every permutation of } (1, \ldots, N)\}$. $E_{\text{all}}(\cdot)$ and $\text{Var}_{\text{all}}(\cdot)$ refer to the expectation and variance under permutations of $N!$ paths.

The rest of this paper is organized as follows. Section 2 proposes two edge-count statistics and a relevance analysis. The power analysis is given in Section 3. Section 4 compares the proposed statistics and related statistics numerically. The applications are illustrated in Section 5. Finally, we conclude with a discussion in Section 6.

## 2 Edge-count statistics

Suppose we have random vectors $X_t$ that are indexed by the sample $G_1, \ldots, G_k$. We consider the problem of testing the hypothesis:

$$H_0 : \theta(F_{G_1}) = \cdots = \theta(F_{G_k}) \quad \text{vs} \quad H_1 : \exists \ell, m \neq \ell, \theta(F_{G_m}) \neq \theta(F_{G_\ell}).$$

We treat vectors $X_t$ as nodes or points $v_t$ for $t = 1, \ldots, N$. Consider a graph $\mathcal{G}$ that is a path $\mathcal{P}$ with edges $(v_i, v_{i+1})$ for $i = 1, \ldots, N - 1$. The path $\mathcal{P}$ can be considered as $(v_1, \ldots, v_N)$ or $(v_N, \ldots, v_1)$. The number of edges connecting any two sets of nodes between
$G_m$ and $G_\ell$ is defined as follows:

$$S_p(G_m, G_\ell) = \sum_{i=1}^{N-1} I \left[ \{(v_i \in G_m) \cap (v_{i+1} \in G_\ell)\} \cup \{(v_i \in G_\ell) \cap (v_{i+1} \in G_m)\} \right],$$

where $1 \leq m, \ell \leq k$ and $I(\cdot)$ is an indicator function that takes 1 if true and 0 otherwise.

Given a path $P$, for any two samples $G_m$ and $G_\ell$, $S_p(G_m, G_\ell)$ counts the edges between samples for $m \neq \ell$ or within samples for $m = \ell$. We first illustrate this edge counting with an example, and then give some properties of it.

**Example 1.** Suppose there are two samples $G_1 = \{1, 2, 3, 4\}$ and $G_2 = \{5, 6, 7, 8\}$. In light of the relevance analysis, we divide each sample into two subsamples $X_A = \{1, 2\}$, $X_B = \{3, 4\}$, $Y_A = \{5, 6\}$, and $Y_B = \{7, 8\}$. Suppose we have a path $P = (2, 3, 4, 1, 5, 7, 8, 6)$.

Fig. 1 provides two representations of these connected edges, namely the rainbow and matrix representations. Four subsamples $X_A, X_B, Y_A$ and $Y_B$ are blue, brown, purple and red, respectively. Only the edges connecting different subsamples are colored, otherwise are connected by dashed lines. It can be seen that $S_p(X_A, X_B) = \#\{(1, 4), (2, 3)\} = 2$, $S_p(X_A, Y_A) = \#\{(1, 5)\} = 1$, $S_p(X_A, Y_B) = 0$, $S_p(X_B, Y_A) = 0$, $S_p(X_B, Y_B) = 0$, $S_p(Y_A, Y_B) = \#\{(5, 7), (6, 8)\} = 2$, and $S_p(G_1, G_2) = \#\{(1, 5)\} = 1$.

To study the asymptotic distribution of $S_p(G_m, G_\ell)$ shown in (2) under all permutations, we provide the following properties of edge counts.

**Lemma 1.** For any non-empty and disjoint samples $\{G_i, 1 \leq i \leq k\}$ ($k \geq 2$), we have properties:

1. $S_p(G_1, G_2) = S_p(G_2, G_1)$ (symmetric);
2. $S_P(G_1 \cup G_2, G_3) = S_P(G_1, G_3) + S_P(G_2, G_3)$ if $k \geq 3$ (additive);

3. $E_{\text{all}}\{S_P(G_1, G_2)\} = \frac{2n_1n_2}{N}$;

4. $E_{\text{all}}\{S_P(G_1, G_1)\} = \frac{n_1(n_1-1)}{N}$;

5. $E_{\text{all}}\{S_P(G_1, G_2)^2\} = \frac{2n_1n_2}{N} + \frac{2n_1n_2(n_1+n_2-2)}{N(N-1)} + \frac{4n_1(n_1-1)n_2(n_2-1)}{N(N-1)}$;

6. $E_{\text{all}}\{S_P(G_1, G_1)^2\} = \frac{n_1(n_1-1)}{N} + \frac{2n_1(n_1-1)(n_1-2)}{N(N-1)} + \frac{n_1(n_1-1)(n_1-2)(n_1-3)}{N(N-1)}$;

7. $E_{\text{all}}\{S_P(G_1, G_2)S_P(G_3, G_4)\} = \frac{4n_1n_2n_3n_4}{N(N-1)}$ if $k \geq 4$;

8. $E_{\text{all}}\{S_P(G_1, G_2)S_P(G_2, G_3)\} = \frac{2n_1n_2n_3(2n_2-1)}{N(N-1)}$ if $k \geq 3$;

9. $E_{\text{all}}\{S_P(G_1, G_1)S_P(G_2, G_2)\} = \frac{n_1(n_1-1)n_2(n_2-1)}{N(N-1)}$. 

Figure 1: Visualizations of edge counts
The first two properties are obvious. The proofs of the other properties are given in the Appendix. In particular, if \( k = 2 \) and \( n_1 + n_2 = N \), then properties 3 and 5 are consistent with the moments shown in \cite{Wald} [eq. 12 and eq. 13].

2.1 Weighted sum statistic

We propose a weighted sum statistic:

\[
\bar{Z}_P = \sum_{m=1}^{k-1} \sum_{\ell=m+1}^{k} w_{m,\ell} S_P(G_m, G_\ell),
\]

where \( w_{m,\ell} \geq 0 \). In particular, if \( k = 2 \), then it is the classical edge-count statistic \cite{Friedman}. For multiple samples with \( k > 2 \), it is reasonable to set \( w_{m,\ell} \) to be \( \left\{ \text{Var}_{\text{all}}(S_P(G_m, G_\ell)) \right\}^{-1/2} \) for unbalanced sample sizes, or zero for subsample analysis (see Example 2). Its asymptotic normal distribution is established in Theorem 1, a direct result of Lemma 1.

**Theorem 1.** Assume \( \min \ell n_\ell \to \infty \).

\[
\frac{\bar{Z}_P - E_{\text{all}}(\bar{Z}_P)}{\sqrt{\text{Var}_{\text{all}}(\bar{Z}_P)}} \to_d N(0,1),
\]

where \( \text{Var}_{\text{all}}(\bar{Z}_P) = \sum_{m=1}^{k-1} \sum_{\ell_1=m+1}^{k} \sum_{m_2=1}^{k-1} \sum_{\ell_2=m_2+1}^{k} w_{m,\ell_1} w_{m_2,\ell_2} C_{m_1,\ell_1,m_2,\ell_2}, C_{m_1,\ell_1,m_2,\ell_2} \) is the covariance \( E_{\text{all}}\{S_P(G_{m_1}, G_{\ell_1})S_P(G_{m_2}, G_{\ell_2})\} - E_{\text{all}}\{S_P(G_{m_1}, G_{\ell_1})\}E_{\text{all}}\{S_P(G_{m_2}, G_{\ell_2})\} \), and \( E(\bar{Z}_P) = \sum_{m=1}^{k-1} \sum_{\ell=m+1}^{k} w_{m,\ell} E_{\text{all}}\{S_P(G_m, G_\ell)\} \).

Theorem 1 follows by the functional limiting theory. The expectation \( E_{\text{all}}(\bar{Z}_P) \) and variance \( \text{Var}_{\text{all}}(\bar{Z}_P) \) can be calculated by properties 3-6 in Lemma 1.

As we know, the SHP is the path with the lowest total cost. Finding SHP is a non-deterministic polynomial (NP) problem. A heuristic algorithm (HA) is due to Biswas et
al. (2014). HA first arranges all the edges in order of increasing cost. First, the edge with the minimum cost must be selected. Then, subsequent edges are selected one by one from the remaining list of sorted edges according to the requirements of the path. If the current edge does not form a cycle with the previously selected edges and the degree of each vertex connected by the current edge or the previously selected edges is not greater than 2, then the current edge must be selected. HA terminates when $N - 1$ edges are selected. The approximate SHP is formed by the selected $N - 1$ edges and is represented as a set of vertices $P^* = (v_1^*, \ldots, v_N^*)$. The observed weighted sum statistic is $\bar{Z}_{P^*}$.

Given a significance level $\alpha$, we reject the null hypothesis as shown in (1) if

$$\bar{Z}_{P^*} < E_{\text{all}}(\bar{Z}_P) - z_\alpha \sqrt{\text{Var}_{\text{all}}(\bar{Z}_P)},$$

where $z_\alpha$ is the $\alpha$th quantile of standard normal distribution.

### 2.2 Minimum statistic

We define a minimum statistic:

$$Z_P = \min_{1 \leq m < \ell \leq k} w_{m,\ell} \{ S_P(G_m, G_{\ell}) - E_{\text{all}}(S_P(G_m, G_{\ell})) \}.$$  

(4)

Since we need to express its distribution, we define $L(i, j) = j - i + (2k - i)(i - 1)/2$ for $1 \leq i < j \leq k$. Then, $1 \leq L(i, j) \leq k(k - 1)/2$. Given any $1 \leq \ell \leq k(k - 1)/2$, only one pair $(i_\ell, j_\ell)$ exists such that $i_\ell < j_\ell$ and $L(i_\ell, j_\ell) = \ell$. According to the functional limiting theory, we have the following asymptotic distribution of the minimum statistic.
Theorem 2. For any \( x \),

\[
P(Z_P \leq x) - 1 + P(Z > x\sigma) \to 0, \tag{5}
\]

where the normal random vector \( Z \sim N(0, \Sigma) \), the entries of covariance matrix \( \Sigma \) are

\[
\Sigma_{\ell_1, \ell_2} = E_{\text{all}}\{S_P(G_{\ell_1}, G_{\ell_2})S_P(G_{\ell_2}, G_{\ell_1})\} - \{E_{\text{all}}S_P(G_{\ell_1}, G_{\ell_1})\}\{E_{\text{all}}S_P(G_{\ell_2}, G_{\ell_2})\}
\]

for \( 1 \leq \ell_1, \ell_2 \leq k(k - 1)/2 \), and the \( \ell \)th (\( 1 \leq \ell \leq k(k - 1)/2 \)) component of \( \sigma \) is equal to \( w_{i_t,j_t} \) if \( w_{i_t,j_t} \) is positive, otherwise the \( \ell \)th component is \( -\infty \).

The proof of Theorem 2 is intuitive because \( 1 - P(Z_P \leq x) \) can be expressed as the probability of a multivariate normal variable. Unlike the weighted sum statistic, the minimum statistic is based on the standardized value of \( S_P(G_m, G_\ell) \).

The numerical computation of \( P(Z > x\sigma) \) is implemented by the R function \textit{pmvnorm} \citep{Genz1992}. Assume that the critical values \( z_\alpha \) satisfies \( 1 - P(Z > z_\alpha\sigma) = \alpha \). Given a significant level \( \alpha \), we reject the null hypothesis when \( Z_{P^*} \leq z_\alpha \).

### 2.3 Relevance analysis

We define the \( z \)-score as

\[
z_{(m), (\ell)} = \frac{S_P(G_m, G_\ell) - E_{\text{all}}(S_P(G_m, G_\ell))}{\sqrt{\text{Var}_{\text{all}}(S_P(G_m, G_\ell))}}, \tag{6}
\]

for \( 1 \leq m \neq \ell \leq k \). The defined \( z \)-score is a nonparametric measure of the degree of relevance based on pairs of two samples. In particular, if \( k = 2 \) for two samples, then both the weighted sum statistic and the minimum statistic are related to the \( z \)-score between
the two samples. For combined samples, we can define

$$|z_{A_1,A_2}| = \frac{|SP(\cup_{m \in A_1} G_m, \cup_{\ell \in A_2} G_\ell) - E_{all}(\cup_{m \in A_1} G_m, \cup_{\ell \in A_2} G_\ell)|}{\sqrt{\text{Var}_{all}(\cup_{m \in A_1} G_m, \cup_{\ell \in A_2} G_\ell)}},$$

(7)

where $A_1$ and $A_2$ are disjoint subsets of $\{1, \ldots, k\}$.

To illustrate the relevance analysis, we give the following example.

**Example 2.** The motivation for this example is Simpson’s paradox, where a trend appears in several different samples of data, but disappears or reverses when these samples are combined together. Here, we consider four samples, as shown in Table 1.

| Samples | $G_1$ | $G_2$ | $G_3$ | $G_4$ |
|---------|-------|-------|-------|-------|
| Sizes   | 20    | 24    | 26    | 28    |
| Distributions with $d = 1000$ | $N_d(0, I)$ | $N_d(0.01 + 0, 1.1I)$ | $N_d(0.01 + 0, 1.1I)$ | $N_d(0, I)$ |

Table 1: Individuals are distributed along each sample.

We draw data along each sample according to Table 1. The approximate SHP, $P^*$, is plotted in Figure 2 where four blue edges connect samples $G_1$ and $G_2$, eight purple edges connect samples $G_1$ and $G_3$, twenty green edges connect samples $G_1$ and $G_4$, eleven brown edges connect samples $G_2$ and $G_3$, six yellow edges connect samples $G_2$ and $G_4$, and ten red edges connect samples $G_3$ and $G_4$. The $z$-scores of these edge counts are listed in Table 2.

|       | $G_2$ | $G_3$ | $G_4$ |
|-------|-------|-------|-------|
| $G_1$ | -2.3  | -1.0  | 3.2   |
| $G_2$ | -0.6  | -2.6  |       |
| $G_3$ |       | -1.6  |       |

Table 2: The $z$-scores of edge counts for measuring the degree of relevance.
From Table 2 the four smallest $z$-scores are: $z_{\{2\} \cup \{4\}} = -2.6$, $z_{\{1\} \cup \{2\}} = -2.3$, $z_{\{3\} \cup \{4\}} = -1.6$, $z_{\{1\} \cup \{3\}} = -1.0$. They correspond to different samples. Suppose we want to compare the difference between combined samples: $G_1 \cup G_2$ and $G_3 \cup G_4$, ignoring the within-sample differences, i.e., test

$$H_0 : \theta(F_{G_1 \cup G_2}) = \theta(F_{G_3 \cup G_4}) \text{ vs } H_1 : \theta(F_{G_1 \cup G_2}) \neq \theta(F_{G_3 \cup G_4}).$$

The combined $z$-score $z_{\{1,2\} \cup \{3,4\}}$ is -0.7. In addition, both the weighted sum test (3) and the minimum test (4) give the same $p$-values of 0.237. To make meaningful comparisons,
we test for the difference between $G_1$ and $G_3$ or between $G_2$ and $G_4$, i.e.,

$$H_0 : \theta(F_{G_1}) = \cdots = \theta(F_{G_4}) \quad \text{vs} \quad H_1 : \theta(F_{G_1}) \neq \theta(F_{G_3}) \quad \text{or} \quad \theta(F_{G_2}) \neq \theta(F_{G_4}).$$

We set the weights $w_{1,2}$, $w_{1,4}$, $w_{2,3}$ and $w_{3,4}$ to be zeros and focus only on the purple and yellow edges in Figure[2]. The weighted sum test gives a $p$-value of 0.009, while the minimum test give a $p$-value of 0.007. This comparison is more meaningful. Thus, differences between samples are apparent but disappear when these samples are combined.

3 Power

In this section, we discuss the effect of edge costs on power. Denote the cost between $X_{t_1}$ and $X_{t_2}$ as $C(t_1, t_2)$ and its limit as $C^*(t_1, t_2)$. We make the following regular assumptions.

A1. $C(t_1, t_2) > 0, t_1 \neq t_2$, almost surely.

A2. $C(t_1, t_2) = C(t_2, t_1)$ (symmetry).

A3. $C(t_1, t_2) \leq C(t_1, t_3) + C(t_2, t_3)$ (triangular inequality).

A4. $C(t_1, t_2) - C^*(g_{t_1}, g_{t_2}) = O_p(d^{-1/2})$ and $Nd^{-1/2} \rightarrow 0$ (rates).

A5. If $\theta(F_{g_{t_1}}) \neq \theta(F_{g_{t_2}})$, then $C^*(g_{t_1}, g_{t_2}) > \min\{C^*(g_{t_1}, g_{t_1}), C^*(g_{t_2}, g_{t_2})\}$ (increased cost).

Here, we consider continuous random vectors and therefore require A1. Because we actually apply the permutation test, we need the symmetric condition A2. Due to the ordering of costs, we need A3. Since we consider that $d$ converges to $\infty$, by the law of large numbers it is natural to assume that the limit of cost exists: $C(t_1, t_2) \rightarrow_p C^*(g_{t_1}, g_{t_2})$. Since
there are $N(N - 1)/2$ random costs, we further assume some rates in A4. These reflect the relationship between the sample size $N$ and dimension $d$ and lead to

$$P \left\{ \bigcup_{1 \leq t_1 < t_2 \leq N} |C(t_1, t_2) - C^*(g_{t_1}, g_{t_2})| > \varepsilon \right\} = O(N^2 d^{-1}) \to 0,$$

for any $\varepsilon > 0$. To obtain power, we require the between-sample cost must be greater than one of within-sample costs in A5.

Usually we assign the $\gamma$-norm as the cost: for $0 < \gamma \leq 2$,

$$C(t_1, t_2) = d^{-1/\gamma}||X_{t_1} - X_{t_2}||_\gamma. \quad (8)$$

When $\gamma = 2$, the 2-norm is the scaled Euclidean distance, $C(t_1, t_2) = d^{-1/2}||X_{t_1} - X_{t_2}||_2$. It is obvious that A1-A3 are satisfied. A4 can be confirmed by using the Markov inequality under some weak conditions. In particular, if the components of the random vectors $X_t$ are independent and identically distributed (IID), and $\theta(F_{g_t})$ is a parametric vector including mean and variance, denoted as $(\mu_{g_t}, \sigma_{g_t}^2)^\top$, then

$$C^*(g_{t_1}, g_{t_1}) = \sqrt{2\sigma_{g_{t_1}}^2}, \quad C^*(g_{t_2}, g_{t_2}) = \sqrt{2\sigma_{g_{t_2}}^2},$$

and $C^*(g_{t_1}, g_{t_2}) = \sqrt{(\mu_{g_{t_1}} - \mu_{g_{t_2}})^2 + \sigma_{g_{t_1}}^2 + \sigma_{g_{t_2}}^2}$. As $\sqrt{\sigma_{g_{t_1}}^2 + \sigma_{g_{t_2}}^2} \geq \min\{\sqrt{2\sigma_{g_{t_1}}^2}, \sqrt{2\sigma_{g_{t_2}}^2}\}$, $C^*(g_{t_1}, g_{t_2}) > \min\{C^*(g_{t_1}, g_{t_1}), C^*(g_{t_2}, g_{t_2})\}$ when $\mu_{g_{t_1}} \neq \mu_{g_{t_2}}$ or $\sigma_{g_{t_1}}^2 \neq \sigma_{g_{t_2}}^2$. This implies that A5 holds.

Next, we consider other values of $\gamma$: $C(t_1, t_2) = d^{-1/\gamma}||X_{t_1} - X_{t_2}||_\gamma$ for $0 < \gamma < 2$. In particular, if $\gamma = 1$, that is the scaled Mahalanobis distance that is widely used in cluster analysis and classification. We proceed to the case of IID. Similarly, we can verify the conditions A1-A4. Since $C^*$ has no closed form, we apply the results of [Szekely and Rizzo (2005)] to prove A5, which is shown in Lemma 2.

**Lemma 2.** Suppose the components of the random vectors $X_t$ are IID. If $F_{g_{t_1}} \neq F_{g_{t_2}}$, then

$$2\{C^*(g_{t_1}, g_{t_2})\}^\gamma > \{C^*(g_{t_1}, g_{t_1})\}^\gamma + \{C^*(g_{t_2}, g_{t_2})\}^\gamma.$$
By Lemma 2, \( \{C^*(g_{t_1}, g_{t_2})\}^\gamma > \min\{\{C^*(g_{t_1}, g_{t_1})\}^\gamma, \{C^*(g_{t_2}, g_{t_2})\}^\gamma\} \) that leads to A5.

If we only need to detect changes in the common mean, we can consider the average cost

\[
\overline{C}(t_1, t_2) = d^{-1} ||X_{t_1\bullet} - X_{t_2\bullet}||_1,
\]

(9)

which was applied in Shi, Wu and Rao (2018). It is clear that \( \overline{C}(t_1, t_2) \) satisfies A1-A5.

When the covariances may not be equal, we can consider another cost to capture the change in mean or covariance:

\[
\dot{C}(t_1, t_2) = d^{-1/2} \sqrt{||X_{t_1} - X_{t_2}||^2_2 + ||\dot{X}_{t_1}||^2_2 + ||\dot{X}_{t_2}||^2_2}.
\]

(10)

This new cost obviously satisfies A1-A4. To verify the condition A5, we consider two autoregressive (AR) processes \( X_{t_\ell,j} = \mu_\ell + \phi_\ell g_{t_\ell} X_{t_\ell,j-1} + \varepsilon_j \), where \( |\phi_\ell g_{t_\ell}| < 1 \), \( \varepsilon_j \) is white noise with variance \( \sigma^2_{g_{t_\ell}} \), and \( \ell = 1, 2 \). We have that \( ||X_{t_1} - X_{t_2}||^2_2 \) converges to

\[
(\mu_{g_{t_1}} - \mu_{g_{t_2}})^2 + \frac{\sigma^2_{g_{t_1}}}{1 - \phi^2_{g_{t_1}}} + \frac{\sigma^2_{g_{t_2}}}{1 - \phi^2_{g_{t_2}}}.
\]

Moreover, it can be seen that \( X_{t_\ell,j} - X_{t_\ell,j-1} \) are autoregressive moving average (ARMA) processes with mean AR coefficient \( \phi_{\ell} \) and MA coefficient \( -1 \). Thus, \( ||\dot{X}_{t_\ell}||^2_2 \) converges to

\[
\frac{(2 - 2\phi_{g_{t_\ell}})\sigma^2_{g_{t_\ell}}}{1 - \phi^2_{g_{t_\ell}}}.
\]

Now, we write \( \dot{C}^*(g_{t_1}, g_{t_2}) = \sqrt{\frac{(\mu_{g_{t_1}} - \mu_{g_{t_2}})^2}{1 - \phi^2_{g_{t_1}}} + \frac{3 - 2\phi_{g_{t_2}}\sigma^2_{g_{t_1}}}{1 - \phi^2_{g_{t_1}}} + \frac{(3 - 2\phi_{g_{t_2}})\sigma^2_{g_{t_2}}}{1 - \phi^2_{g_{t_2}}}}. \) Furthermore, we write \( \dot{C}^*(g_{t_1}, g_{t_1}) = \sqrt{\frac{(6 - 4\phi_{g_{t_1}})\sigma^2_{g_{t_1}}}{1 - \phi^2_{g_{t_1}}} \) and \( \dot{C}^*(g_{t_2}, g_{t_2}) = \sqrt{\frac{(6 - 4\phi_{g_{t_2}})\sigma^2_{g_{t_2}}}{1 - \phi^2_{g_{t_2}}}}. \) When \( \mu_{g_{t_1}} \neq \mu_{g_{t_2}} \) or
\[
\frac{(3-2\phi_{g_1})\sigma_{g_1}^2}{1-\phi_{g_1}} \neq \frac{(3-2\phi_{g_2})\sigma_{g_2}^2}{1-\phi_{g_2}}, \quad \hat{C}^*(g_1, g_2) > \min\{\hat{C}^*(g_{t_1}, g_{t_1}), \hat{C}^*(g_{t_2}, g_{t_2})\}.
\]

To show how power is obtained, we first provide an upper bound of the count \(S_P(g_{t_1}, g_{t_2})\).

**Theorem 3.** Assume that conditions A1-A5 are satisfied. If \(\theta(F_{g_{t_1}}) \neq \theta(F_{g_{t_2}})\), then
\[S_P^*(g_{t_1}, g_{t_2}) \leq 2\] in probability as \(d \to \infty\).

The proof is placed in the Appendix. The upper bound is determined by the degree constraint of the vertices. We remark that one can equivalently consider a degree-constrained minimum spanning tree (DCMST) where the maximum vertex degree is limited to a certain constant 2.

**Theorem 4.** Assume that conditions A1-A5 are satisfied. If \(\lim_{N \to \infty} n_i/N > 0\) and there exists at least one pair \((i, j)\) such that \(w_{i,j} > 0\) and \(\theta(F_{G_i}) \neq \theta(F_{G_j})\). The power of the \(k\)-sample test based on \(\bar{Z}_P\) in (3) or \(Z_P\) in (4) tends to 1 as \(d \to \infty\).

The proof is placed in the Appendix. Theorem 4 justifies why the proposed \(k\)-sample tests can obtain power.

## 4 Simulations

### 4.1 Two-sample comparison

We generate data \(\{X_t, 1 \leq t \leq 60\}\) from \(N_d(\mu_t, \Sigma_t)\). We consider two samples \(G_1\) and \(G_2\) whose sizes are \(n_1 = 20\) and \(n_2 = 40\), respectively. We set the parameters:

\[
\mu_t = \begin{cases} 
\mu^{(1)}, & 1 \leq t \leq n_1, \\
\mu^{(2)}, & n_1 < t \leq n_1 + n_2,
\end{cases} \quad \Sigma_t = \begin{cases}
\Sigma^{(1)}, & 1 \leq t \leq n_1, \\
\Sigma^{(2)}, & n_1 < t \leq n_1 + n_2.
\end{cases}
\]

To examine the effect of parameters on power, we consider the following three cases.

**Case 1.** \(\mu^{(1)} = \mu^{(2)} - 0.1 = 0\) and \(\Sigma^{(1)}_{i,j} = \Sigma^{(2)}_{i,j} = 0.2|^{i-j}|\).

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Case 2. $\mu^{(1)} = \mu^{(2)} = 0$, $\Sigma_{i,j}^{(1)} = 0.2|i-j|$, and $\Sigma_{i,j}^{(2)} = 0.4|i-j|$.

Case 3. $\mu^{(1)} = \mu^{(2)} - 0.1 = 0$, $\Sigma_{i,j}^{(1)} = 0.2|i-j|$, and $\Sigma_{i,j}^{(2)} = 0.4|i-j|$.

The original test was proposed by Bai and Saranadasa (1996) and denoted as T-1. Some variants were proposed by Chen and Qin (2010) and Cai et al. (2014) denoted as T-2 and T-3, respectively. These variants can treat equal covariances for case 1 and unequal covariances for cases 2 and 3, respectively. Four MST-based tests have been proposed by Friedman and Rafsky (1979), Chen and Friedman (2017), Chen et al. (2018), Zhang and Chen (2021), which are denoted by T-4, T-5, T-6, and T-7, respectively. The latest test to be compared was proposed by Mukhopadhyay and Wang (2020), which is denoted as K-1.

Since we are considering here a comparison of two samples, both weighted sum statistic (3) and minimum statistic (4) are equivalent. We only consider the weighted sum statistic (3). We consider the cost (8) for $\gamma = 2$, denoted by K-2. For a fair comparison, we apply the cost (9) in case 1 and the cost (10) in cases 2 and 3, which we denote both as K3.

Fig. 3 shows the estimated power, a percentage in the 200 trials (%) when the null hypothesis is rejected at the 0.05 level for each of the two-sample tests. We can see that K-3 has highest power; T-1 and T-3 are comparable and can gain power when the mean value changes; the others have little powerful; and overall, K-2 does not perform poorly.

### 4.2 Three-sample comparison

Similar to the two-sample setup, we allow $t$ to vary from 1 to 90. We consider three samples $G_1$, $G_2$ and $G_3$ with sizes $n_1 = 20$, $n_2 = 30$ and $n_3 = 40$, respectively. We set the parameters:
We consider another three cases.

Case 4. \( \mu^{(1)} = \mu^{(2)} = \mu^{(3)} - 0.1 = 0 \)
\( \Sigma^{(1)} = \Sigma^{(2)} = 0.2|i-j| \),
\( \Sigma^{(3)} = 0.4|i-j| \).

Case 5. \( \mu^{(1)} = \mu^{(2)} = \mu^{(3)} - 0.1 = 0 \)
\( \Sigma^{(1)} = 0.2|i-j| \),
\( \Sigma^{(2)} = 0.4|i-j| \),
\( \Sigma^{(3)} = 0.6|i-j| \).

Case 6. \( \mu^{(1)} = \mu^{(2)} + 0.1 = \mu^{(3)} - 0.1 = 0 \)
\( \Sigma^{(1)} = 0.2|i-j| \),
\( \Sigma^{(2)} = 0.4|i-j| \),
\( \Sigma^{(3)} = 0.6|i-j| \).

Since K-1 can be applied for multiple-sample comparison, we include it here for further comparison. Here, the weighted sum statistic (3) and the minimum statistic (4) are not the same. For the weighted sum statistic (3), we consider the cost (8) with \( \gamma = 2 \) denoted by K-2 and the cost (10) denoted as K3, while for minimum statistic (4), we consider the cost (8) with \( \gamma = 2 \) denoted by K-4 and the cost (10) denoted as K5.
Similarly, Fig. 4 presents the estimated power. It can be seen that all of our tests are comparative in case 4; K-3 and K-5 obtain more power in cases 5 and 6; and K-1 has a worse performance.

![Figure 4: Power comparison of three-sample tests.](image)

5 Real data analysis

5.1 Microarray data analysis

We analyze the tumor data \( \{X_t \in \mathbb{R}^d, 1 \leq t \leq 801, d = 20, 531\} \) indexed to five samples of BRCA, COAD, KIRC, LUAD and PRAD. The sizes of all samples are 300, 78, 146, 141, and 136. Using the proposed relevance analysis, we compared gene expression levels across 5 tumor types. The following table lists the \( z \)-scores between each two samples, as in (6).

From Table 3, we can see that the two types of tumors BRCA and KIRC are mostly irrelevant, and the other two types of tumors COAD and LUAD are mostly relevant. Both the weighted sum statistic (3) and minimum statistic (4) return extremely small \( p \)-values.
Table 3: The $z$-scores between each two samples, as in (6).

|       | COAD | KIRC | LUAD | PRAD |
|-------|------|------|------|------|
| BRCA  | -9.86| -13.62| -12.72| -12.84|
| COAD  | -6.13| -5.13 | -5.88 |
| KIRC  |       | -8.54 | -8.36 |
| LUAD  |       |       | -8.19 |

To compare the relevance for significant components, we perform a one-way ANOVA test on each component. The $p$-value of each test is adjusted by the Benjamini-Hochberg correction \cite{Benjamini1995}. We select 19,565 significant components whose tests have $p$-values less than 0.05. Table 4 presents the relevance analysis based on the significant components.

Table 4: The $z$-scores between each two samples on significant components, as in (6).

|       | COAD | KIRC | LUAD | PRAD |
|-------|------|------|------|------|
| BRCA  | -9.69| -13.74| -12.97| -13.10|
| COAD  | -6.13| -5.35 | -5.88 |
| KIRC  |       | -8.37 | -8.19 |
| LUAD  |       |       | -8.19 |

From Table 4 we can see the small differences compared to the Table 3.

5.2 Functional magnetic resonance imaging data analysis

BOLD was measured from each subject in 7 mice, under the conditions of 9.4 T and 15.2 T MR systems. The output of this measurement was a 3D volume of each subject, where each voxel contained pixel values with dimensions of $228 \times 160 \times 132$. All of these
were concatenated into a 4D image, where the fourth dimension was the time point, \( t \), varying from 1 to 120. The time period includes 40-s pre-stimulus, 20-s stimulus, and 60-s post-stimulus.

To obtain the differences in conditions among all subjects, we first average the 3D voxels along the third dimension. Fig. 5 presents the projected 2D voxels for two conditions (9.4 T and 15.2 T) and three time points (\( t = 1, 60, 120 \)). We then take the differences in the projected 2D voxels for each subject across conditions, and finally consider the cumulative differences for all 7 subjects. We convert each cumulative difference matrix into a vector of length \( 228 \times 160 \), which consists of all columns of the original matrix. Let \( X_t \) represent the vector of time point \( t \).

Table 5 provides the \( z \)-score values in the pre-stimulus, stimulus, and post-stimulus samples. Pre-stimulus and stimulus are mostly irrelevant, while stimulus and post-stimulus are mostly relevant. This can be explained by the fact that the response increases rapidly in the stimulus period and decreases slowly in post-stimulus period.

Table 5: The \( z \)-scores between each two time periods, as in (6).

|          | Stimulus | Post-stimulus |
|----------|----------|---------------|
| Pre-stimulus | 3.63    | 2.92          |
| Stimulus    | 0.64    |               |

The minimum statistic-based test (4) captures the change between pre-stimulus and stimulus and returns a \( p \)-value of 0.0004, while the weighted sum statistic-based test (3) has a \( p \)-value of 0.1472. One can set the weight between pre-stimulus and post-stimulus to be zero, ignoring the comparison between them. Then, the \( p \)-values based on the weighted sum statistic (3) and the minimum statistic (4) are 0.00001 and 0.0003, respectively. Overall, these tests confirm the change in the difference between conditions from pre-stimulus to
Figure 5: Multi-slice averaged fMRI maps of one animal projected along one of the dimensions.

post-stimulus.

6 Discussion

Based on the graph method, we provide a technology to compare $k$ high-dimensional samples. The proposed $z$-scores can be used to measure the degree of relevance between the combined samples. We propose two nonparametric tests and show that powers can be obtained under weak conditions. Two datasets are analyzed for illustration.
We note that there is a connection between the k-sample problem and the multiple change point problem. Sliding window analysis can bridge them (Lehallier et al., 2019). We will further investigate this connection in our future work.

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References

Shalon, D., Smith, S. J. & Brown, P. O. (1996). A DNA microarray system for analyzing complex DNA samples using two-color fluorescent probehybridization. Genome Research 6, 639–645.

Weinstein, J. N., Collisson, E. A., Mills, G. B., Shaw, K. R., Ozenberger, B. A., Ellrott, K., Shmulevich, I., Sander, C. & Stuart, J. M. (2013). The Cancer Genome Atlas Pan-Cancer analysis project. Nature Genetics 45, 1113–1120.

Zhou, J. & Rossi, J. (2017). Aptamers as targeted therapeutics: current potential and challenges. Nature Reviews Drug Discovery 16, 181–202.

Lehallier, B., Gate, D., Schaum, N., Nanasi, T., Lee, S. E., Yousef, H., Losada, P. M., Berdnik, D., Keller, A., Verghese, J., Sathyan, S., Franceschi, C., Milman, S., Barzilai, N. & Wyss-Coray, T. (2019). Undulating changes in human plasma proteome profiles across the lifespan. Nature Medicine 25, 1843–1850.
JUNG, W. B., SHIM, H. J. & KIM, S. G. (2019). Mouse BOLD fMRI at ultrahigh field detects somatosensory networks including thalamic nuclei. NeuroImage 195, 203–214.

BAI, Z. & SARANADASA, H. (1996). Effect of high dimension: by an example of a two sample problem. Statistica Sinica 6, 311–329.

CHEN, S. & QIN, Y. (2010). A two-sample test for high-dimensional data with applications to gene-set testing. Annals of Statistics 38, 808–835.

CAI, T., LIU, W. & XIA, Y. (2014). Two-sample test of high dimensional means under dependence. Journal of the Royal Statistical Society: Series B 76, 349–372.

XU, G., LIN, L., WEI, P. & PAN, W. (2016). An adaptive two-sample test for high-dimensional means. Biometrika 103, 609–624.

HE, Y., XU, G., WU, C. & PAN, W. (2021). Asymptotically independent U-statistics in high-dimensional testing. Annals of Statistics 49, 154-181.

SRIVASTAVA, M. S. & KUBOKAWA, T. (2013). Tests for multivariate analysis of variance in high dimension under non-normality. Journal of Multivariate Analysis 115, 204–216.

HU, J., BAI, Z., WANG, C. & PAN, W. (2017). On testing the equality of high dimensional mean vectors with unequal covariance matrices. Annals of the Institute of Statistical Mathematics 69, 365–387.

FRIEDMAN, J. H. & RAFSKY, L. C. (1979). Multivariate generalizations of the Wald-Wolfowitz and Smirnov two-sample tests. Annals of Statistics 7, 697–717.

BISWAS, M., MUKHOPADHYAY, M. & GHOSH, A. K. (2014). A distribution-free two-sample run test applicable to high-dimensional data. Biometrika 101, 913–926.
Wald, A. & Wolfowitz, J. (1940). On a test whether two samples are from the same distribution. *Annals of Mathematical Statistics* **11**, 147–162.

Chen, H. & Zhang, N. R. (2013). Graph-based tests for two-sample comparisons of categorical data. *Statistica Sinica* **23**, 1479-1503.

Chen, H., Chen, X. & Su, Y. (2018). A weighted edge-count two sample test for multivariate and object data. *Journal of the American Statistical Association: Theory and Methods* **113**, 1146-1155.

Chen, H. & Friedman, J. H. (2017). A new graph-based two-sample test for multivariate and object data. *Journal of the American Statistical Association: Theory and Methods* **112**, 397-409.

Zhang, J. & Chen, H. (2021). Graph-based two-sample tests for data with repeated observations. *Statistica Sinica*, to appear.

WMukhopadhyay, S. & Wang, K. (2020). A nonparametric approach to high-dimensional k-sample comparison problems. *Biometrika* **107**, 555–572.

Genz, A. (1992). Numerical computation of multivariate normal probabilities. *Journal of Computational and Graphical Statistics* **1**, 141-150.

Székely, G. J. & Rizzo, M. L. (2020). Hierarchical clustering via joint between-within distances: extending Ward’s minimum variance method. *Journal of Classification* **22**, 151–183.

Benjamini, Y. & Hochberg, Y. (2014). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society: Series B* **57**, 289–300.
8 Appendix

8.1 Proof of Lemma 1

For the first moment, we calculate

\[
E_{all}\{S_P(G_1, G_2)\} = \sum_{i=1}^{n-1} P \left[ \{(v_i \in G_1) \cap (v_{i+1} \in G_2)\} \cup \{(v_i \in G_2) \cap (v_{i+1} \in G_1)\} \right],
\]

\[
= \sum_{i=1}^{n-1} \frac{2n_1n_2}{N(N-1)} = \frac{2n_1n_2}{N},
\]

(11)

where the calculation of the probability is illustrated in Fig. 6 (i).

When \(G_2 = G_1\), Property 4 follows by the fact that \(n_2 = n_1 - 1\).

For the second moment, we calculate

\[
E_{all}\{S_P(G_1, G_2)\}^2 = \sum_{i=1}^{n-1} \sum_{j=1}^{n-1} p_{i,j},
\]

(12)

where \(p_{i,j}\) is the expectation of two indicator functions as in (2) for indexes \(i\) and \(j\), respectively.

As shown in Fig. 6, there are three possible values of \(p_{i,j}\), corresponding to three cases.

Figure 6: Illustrations of calculation of probabilities.
(i), (ii), and (iii). The first case (i) is \( \{ i = j, 1 \leq i, j \leq N - 1 \} \), which has size \( N - 1 \). The second case (ii) is \( \{|i - j| = 1, 1 \leq i, j \leq N - 1 \} \), which has size \( 2(N - 2) \). The third case (iii) is for \( \{|i - j| > 1, 1 \leq i, j \leq N - 1 \} \), whose size is \( (N - 2)(N - 3) \). Therefore,

\[
E_{\text{all}}\{S_P(G_1, G_2)\}^2 = (N - 1) \frac{2n_1n_2}{N(N - 1)} + 2(N - 2) \frac{n_1n_2(n_1 + n_2 - 2)}{N(N - 1)(N - 2)} + (N - 2)(N - 3) \frac{4n_1n_2(n_1 - 1)(n_2 - 1)}{N(N - 1)(N - 2)(N - 3)}.
\]

This is the same as the simplified Property 5.

Property 6 follows for the same samples \( G_1 = G_2 \), where

\[
E_{\text{all}}\{S_P(G_1, G_1)\}^2 = (N - 1) \frac{n_1(n_1 - 1)}{N(N - 1)} + 2(N - 2) \frac{n_1(n_1 - 1)(n_1 - 2)}{N(N - 1)(N - 2)} + (N - 2)(N - 3) \frac{n_1(n_1 - 1)(n_1 - 2)(n_1 - 3)}{N(N - 1)(N - 2)(N - 3)}.
\]

To prove Property 7, we note that \( G_1, G_2, G_3 \) and \( G_4 \) are disjoint groups. Therefore, the values of \( p_{i,j} \) for cases (i) and (ii) are zeroes. We only need to consider case (iii). This can be done by

\[
E_{\text{all}}\{S_P(G_1, G_2)S_P(G_3, G_4)\} = (N - 1) \times 0 + 2(N - 2) \times 0 + (N - 2)(N - 3) \frac{4n_1n_2n_3n_4}{N(N - 1)(N - 2)(N - 3)}.
\]

To prove Property 8, we note that

\[
S_P(G_1, G_2) + S_P(G_2, G_3) = S_P(G_1 \cup G_3, G_2).
\]

On both sides of this equation, we take their squares and calculate their expected values.
\[ 2E_{\text{all}}\{S_P(G_1, G_2)S_P(G_2, G_3)\} = E\{S_P(G_1 \cup G_3, G_2)\}^2 - E\{S_P(G_1, G_2)\}^2 - E\{S_P(G_2, G_3)\}^2. \]

By using Property 5, we obtain that

\[
2E_{\text{all}}\{S_P(G_1, G_2)S_P(G_2, G_3)\} = \frac{2(n_1 + n_3)n_2}{N} + \frac{2(n_1 + n_3)n_2(n_1 + n_3 + n_2 - 2)}{N(N - 1)} + \frac{4(n_1 + n_3)(n_1 + n_3 - 1)n_2(n_2 - 1)}{N(N - 1)} - \frac{2n_1n_2}{N} - \frac{2n_1n_2(n_1 + n_2 - 2)}{N(N - 1)} - \frac{4n_1(n_1 - 1)n_2(n_2 - 1)}{N(N - 1)} - \frac{2n_3n_2}{N} - \frac{2n_3n_2(n_3 + n_2 - 2)}{N(N - 1)} - \frac{4n_3(n_3 - 1)n_2(n_2 - 1)}{N(N - 1)} + \frac{4n_1n_3n_2(2n_2 - 1)}{N(N - 1)}.
\]

To prove Property 9, we again make use of the fact that the values of \(p_{i,j}\) for cases (i) and (ii) are zeroes. We only need to consider the case (iii). This can be done by

\[
E_{\text{all}}\{S_P(G_1, G_1)S_P(G_2, G_2)\} = (N - 1) \times 0 + 2(N - 2) \times 0 + (N - 2)(N - 3) \frac{n_1(n_1 - 1)n_2(n_2 - 1)}{N(N - 1)(N - 2)(N - 3)},
\]
8.2 Proof of Theorem 3

We first consider a two-sample case for \( k = 2 \) and \( \theta(F_{G_1}) \neq \theta(F_{G_2}) \). By condition A4, the total weight can be expressed as

\[
C^*(G_1, G_1) \sum_{i=1}^{N-1} I(v_i \in G_1, v_{i+1} \in G_1) + C^*(G_2, G_2) \sum_{i=1}^{N-1} I(v_i \in G_2, v_{i+1} \in G_2) \\
+ C^*(G_1, G_2) \sum_{i=1}^{N-1} I\{(v_i \in G_1, v_{i+1} \in G_2) \text{ or } (v_i \in G_2, v_{i+1} \in G_1)\} + o_p(1). \tag{13}
\]

Without loss of generality, we assume that \( C^*(G_1, G_1) < \min\{C^*(G_1, G_2), C^*(G_2, G_2)\} \) under condition A5. Since we need to minimize the total costs, \( \sum_{i=1}^{N-1} I(v_i \in G_1, v_{i+1} \in G_1) \) must be maximized. Therefore, the number of vertices belonging to \( G_1 \) and of degree 1 must be less than or equal to 2 in probability. Since the maximum vertex degree is limited to 2 and there are no cycles, \( S_{P^*}(G_1, G_2) \leq 2 \) in probability.

Since the analysis of the total costs applies to the case of \( k \) samples with \( k > 2 \), \( S_{P^*}(g_{t_1}, g_{t_2}) \leq 2 \) in probability if \( \theta(F_{g_{t_1}}) \neq \theta(F_{g_{t_2}}) \). Theorem 3 follows from this.

8.3 Proof of Theorem 4

Under the null hypothesis,

\[
\text{E}_{\text{all}}\{S_p(G_m, G_{\ell})\} = O(N) \quad \text{and} \quad \text{Var}_{\text{all}}\{S_p(G_m, G_{\ell})\} = O(N).
\]

Therefore, \( w_{i,j} = O(N^{-1/2}) \), and \( N^{-1/2} \bar{Z}_p = c_1 + o_p(1) \) for \( c_1 > 0 \).

By Theorem 3, under the alternative hypothesis, \( N^{-1/2} \bar{Z}_p = c_2 + o_p(1) \) with \( 0 < c_2 < c_1 \). Hence, the power based on \( \bar{Z}_p \) converges to 1.
For the minimum statistic, under the alternative hypothesis, we have

\[ P(Z_{p^*} \leq x) \geq P \left[ w_{i,j} \left\{ S_{p^*}(G_m, G_\ell) - E_{\text{all}} S_p(G_m, G_\ell) \right\} \leq x \right]. \]

As \( S_{p^*}(G_m, G_\ell) \leq 2 \) in probability and \( w_{i,j} E_{\text{all}} S_p(G_m, G_\ell) \to \infty \), the right probability converges to 1. Therefore, \( P(Z_{p^*} \leq x) \) converges to 1. The proof is finished.