A nonparametric Bayesian test of dependence

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Abstract

In this article, we propose a new method for the fundamental task of testing for dependence between two groups of variables. The response densities under the null hypothesis of independence and the alternative hypothesis of dependence are specified by nonparametric Bayesian models. Under the null hypothesis, the joint distribution is modeled by the product of two independent Dirichlet Process Mixture (DPM) priors; under the alternative, the full joint density is modeled by a multivariate DPM prior. The test is then based on the posterior probability of favoring the alternative hypothesis. The proposed test not only has good performance for testing linear dependence among other popular nonparametric tests, but is also preferred to other methods in testing many of the nonlinear dependencies we explored. In the analysis of gene expression data, we compare different methods for testing pairwise dependence between genes. The results show that the proposed test identifies some dependence structures that are not detected by other tests.

Key words: Test of independence, nonparametric Bayesian, Dirichlet process mixture, reversible jump MCMC.
1 Introduction

A fundamental task in statistics is to determine whether two groups of variables are dependent. For example, in genomic analysis, we might want to test whether two groups of genes are associated to identify dependence between genetic pathways. In the brain imaging research, we may want to discover whether sets of voxels from different parts of the brain are related to explore functional connectivity. In general, high-dimensional data analysis can be simplified by identifying sets of independent variables.

Testing of dependence is often reduced to testing for linear dependence. Pearson correlation coefficient is a classical and widely-used method for quantifying the strength of linear dependence between two univariate variables. Spearman’s rank correlation coefficient [Spearman 1904] is a ranked-based version of Pearson correlation coefficient which quantifies monotone correlation. Tests based on correlation are powerful for testing specific types of association, but lose power for other general types.

For testing more general associations, the $\chi^2$ test of independence and Hoeffding’s test of independence [Hoeffding 1948] are two classical nonparametric methods. These tests are based on partitioning data into a contingency table. The main drawback for $\chi^2$ test is that the result is sensitive to the way the data are partitioned. Several approximations of the test statistics of the Hoeffding’s test are studied: Blum et al. [1961] introduce an approximation by the concordances and discordances of a $2 \times 2$ contingency tables, and Wilding & Mudholkar [2008] propose an approximation by using two Weibull extensions. A relation between the Hoeffding’s test and the $\chi^2$ test statistics was noted by Thas & Ottoy [2004], and they also suggested extending the idea of Blum et al. [1961] to a $k \times k$ contingency tables, for $k > 2$. More recent methods related to the Hoeffding’s test have been proposed by Heller et al. [2013] and Kaufman et al. [2013]. Both of these tests are consistent under general types of associations. Other methods for testing for independence include the distance correlation test of Szekely et al. [2007] and the maximal information coefficient of Reshef et al. [2011]. Both the tests of Heller et al. [2013] and Szekely et al.
(2007) can be extended to higher dimensions for testing joint independence of two or more random vectors. Several Bayesian methods are available for testing of independence. The simplest test of linear dependence between two univariate random variables can be achieved by fitting a linear model and inspecting the posterior distribution of the correlation coefficient. Other methods were proposed for testing of independence based on a contingency table (Nandram & Choi 2006, 2007, Nandram et al. 2013).

In this article, we propose a nonparametric Bayesian test of independence between two groups of variables. We test the null hypothesis of independence and the alternative hypothesis of dependence. We specify nonparametric Bayesian models for the response density under both hypotheses. Under the null hypothesis, the joint distribution is taken to be the product of two independent densities, both with nonparametric priors; under the alternative, the full joint density has a nonparametric prior. The test is based on the posterior probability of the alternative hypothesis. By specifying nonparametric Bayesian models under each hypothesis, we obtain an extremely flexible test which can capture both linear and complex nonlinear relationships between groups of variables.

The remainder of the article proceeds as follows. In Section 2 we introduce the statistical algorithm. The details of the reversible jump MCMC algorithm use to compute the posterior probability of the alternative hypothesis are provided in Section 3. In Section 4 we present a simulation study to compare the power of the proposed test with other tests of linear and nonlinear relationships. The method is illustrated using a genetic data analysis in Section 5. Section 6 concludes.

2 Statistical model

Let $X_1 \in \mathbb{R}^{D_1}$ and $X_2 \in \mathbb{R}^{D_2}$ be random vectors in $D_1$ and $D_2$ dimensions, respectively, and denote $X = (X_1, X_2)$. The objective is to test whether $X_1$ and $X_2$ are independent. The
hypotheses are

\[ H_0 : \ X_1 \text{ and } X_2 \text{ are independent and } f(X) = f_1(X_1)f_2(X_2) \]

\[ H_1 : \ X_1 \text{ and } X_2 \text{ are dependent and } f(X) \text{ cannot be factorized} \]

In other words, when they are independent, the joint density can be factorized as the product of two lower-dimensional densities.

Under both hypotheses, the densities are modeled using Dirichlet process mixture (DPM) prior. Under \( H_0 \), \( f_1(X_1) \) and \( f_2(X_2) \) follow independent DPM priors; under \( H_1 \) when \( X_1 \) and \( X_2 \) are not independent, the joint distribution is assumed to follow a DPM prior. The following subsections describe the independent and joint DPM priors.

2.1 The independent DPM prior

When \( X_1 \) and \( X_2 \) are independent, \( f_j(X_j), \ j = 1, 2, \) are assumed to follow the DPM prior independently. The DPM prior can be written as the infinite mixture

\[
 f_j(X_j) = \sum_{l=1}^{\infty} w_{lj} \phi_j(X_j \mid \mu_{lj}, \Sigma_j),
\]

where \( w_{lj} \) is the mixture weight, \( \phi_j \) is assigned to be the \( D_j \)-dimensional multivariate normal distribution (MVN) in this analysis, \( \mu_{lj} \) is the mean vector of the \( l^{th} \) mixture component, and \( \Sigma_j \) is the covariance matrix.

The mixture weights \( w_{lj} \) are modeled by the stick-breaking construction with concentration parameter \( d_j \). The weights \( w_{lj} \) are modeled in terms of latent \( v_{lj} \sim \text{Beta}(1, d_j) \). The first weight is \( w_{1j} = v_{1j} \). The remaining elements are modeled as \( w_{lj} = v_{lj} \prod_{i=1}^{l-1} (1 - v_{ij}) \), where \( \prod_{i=1}^{l-1} (1 - v_{ij}) = 1 - \sum_{i=1}^{l-1} w_{ij} \) is the remaining probability after accounting first \( l - 1 \) mixture weights. The number of mixture components is truncated by a sufficiently large number \( K \) (i.e. \( l = 1, \ldots, K \)), where the last term \( v_K \) is fixed to be 1 to ensure that \( \sum_{l=1}^{K} w_{lj} = 1 \).
The mean vectors $\mu_{lj}$ have priors $\mu_{lj} \sim \text{MVN}(0, \Omega_j)$. The covariance matrices $\Sigma_j$ and $\Omega_j$ are parameterized as $\Sigma_j = rS_j$, and $\Omega_j = (1 - r)S_j$. Under this model, $S_j$ is the covariance matrix for $X_j$ marginally over the mixture means $\mu_{lj}$, and $r$ is the proportion of the total variance attributed to the variance within each mixture component. The marginal covariance $S_j$ is assigned to have inverse Wishart prior distribution, and to facilitate computing, the prior of $r$ is a discrete uniform distribution with support $r \in \{0, 0.01, ..., 1\}$. The concentration parameter $d_j$ has prior distribution Gamma($a, b$).

### 2.2 The joint DPM prior

When $X_1$ and $X_2$ are not independent, $f(X)$ is assumed to follow the joint DPM prior

$$f(X) = \sum_{l=1}^{\infty} w_l \phi(X | \mu_l, \Sigma), \quad (2)$$

where $w_l$ is the mixture weight, $\phi$ is the $(D_1 + D_2)$-dimensional MVN distribution, $\mu_l$ is the mean vector of the $l^{th}$ mixture component, and $\Sigma$ is the covariance matrix. The number of mixtures is truncated by the same number $K$ as in the independent model. The mixture weights $w_l$ are again modeled by the stick-breaking algorithm with concentration parameter $d$. The mean vectors $\mu_l$ have priors $\mu_l \sim \phi(0, \Omega)$. The covariance matrices $\Sigma$ and $\Omega$ are modeled as $\Sigma = r \text{diag}(S)$ and $\Omega = (1 - r)S$, where $S$ is the covariance matrix for $X$, and $\text{diag}(S)$ is the diagonal form of $S$. In other words, under the joint DPM prior, we assign non-diagonal structure for the $\Omega$, and diagonal structure for the $\Sigma$. We found that diagonalizing $\Sigma$ greatly improved computational stability.

The priors for $S$, $r$, and $d$ are the same as in the independent DPM prior.

### 2.3 Bayesian test of independence

The Bayesian hypothesis test of independence is based on the Bayes factor (BF)

$$BF = \frac{P(H_1 | X) / P(H_0 | X)}{P(H_1) / P(H_0)} = \frac{P(X | H_1)}{P(X | H_0)}. \quad (3)$$
The null is rejected if BF > $T$, where $T$ is a threshold parameter. The threshold parameter $T$ can be chosen based on rules of thumb about the weight of evidence favoring $H_1$. For example, Kass & Raftery (1995) suggest that BF = 10 is a strong evidence for $H_1$. Alternatively, in the simulation study in Section 4 we select $T$ to control the Type I error rate. In the analysis of genetic data in Section 5, multiple tests are performing simultaneously, therefore we select $T$ to control the Bayesian false discovery rate.

3 Computing details

Computing the Bayes factor requires computing the posterior probability of each hypothesis. This is accomplished using a reversible jump MCMC (RJMCMC) algorithm as described below.

3.1 Reparameterization and hyperparameters

The updating algorithm of the DPM prior is facilitated by introducing the equivalent clustering model. The mixture form in (1) can be written as

$$f_j(X_j \mid g_j = l) = \phi_j(X_j \mid \mu_{lj}, \Sigma_j),$$

which draws an auxiliary cluster label $g_j \in \{1, \ldots, K\}$ with $P(g_j = l) = w_{lj}$. Similarly, the model in (2) is equivalent to

$$f(X \mid g = l) = \phi(X \mid \mu_l, \Sigma),$$

with cluster label $g$ and $P(g = l) = w_l$. Under the clustering model, the full conditionals of all the parameters are conjugate.

In addition, we introduce model indicator parameter $M$, where

$$M \in \begin{cases} 
I & \text{if } X_1 \text{ and } X_2 \text{ are independent (H}_0 \text{ is true)} \\
J & \text{if } X_1 \text{ and } X_2 \text{ are not independent (H}_1 \text{ is true)}.
\end{cases}$$
Under each MCMC step, we propose a new indicator $M'$ in the Markov chain, and decide whether to accept the new status $M'$. The probability $P(H_1 \mid X)$ is then approximated by $\sum_{i=1}^{N} I(M^{(i)} = J)/N$, where $N$ is the number of MCMC samples and $M^{(i)}$ is the model status for the $i^{th}$ MCMC sample.

Throughout this article, we let the number of mixture components truncated at $K = 20$ and the hyperparameters in the stick-breaking procedure $(a, b)$ are fixed under different sample sizes $n$ as presented in Table 1.

| $n$ | $a$ | $b$ |
|-----|-----|-----|
| 100 | 1.5 | 2.5 |
| 200 | 1.0 | 4.0 |
| 300 | 1.0 | 4.5 |
| 500 | 0.8 | 4.6 |

### 3.2 Pseudo code for the DPM test of independence algorithm

Let $\Theta_M$ denote the DPM parameters ($\Theta_M = \{\mu_{11}, ..., \mu_{K2}, r, S_1, S_2, w_{11}, ..., w_{K2}, d_1, d_2\}$ if $M = I$, and $\Theta_M = \{\mu_1, ..., \mu_K, r, S, w_1, ..., w_K, d\}$ if $M = J$). The algorithm of the DPM test of independence is described as follows:

**Step 0:** Select initial values for $M$ and $\Theta_M$.

**Step 1:** Update $\Theta_M$ given $M$ using the Gibbs sampling.

**Step 2:** Update $M$ given the parameters $\Theta_M$.

**Step 2.1:** Generate proposed model status $M'$ with $P(M' = I) = P(M' = J) = 0.5$.

**Step 2.2:** If $M = M'$, then so back to **Step 1**.

**Step 2.3:** If $M = I$ and $M' = J$, then propose $\Theta_{M'}$ required for the joint DPM prior ($H_1$).

**Step 2.4:** If $M = J$ and $M' = I$, then propose $\Theta_{M'}$ required for the independent DPM prior ($H_0$).
Step 2.5: Accept \( M' \) with probability \( \min\{1, \alpha(M, M')\} \).

Step 3: Back to Step 1.

The full conditionals requires for Step 1 are all standard and are given in Appendix A.1 for \( M = I \), and Appendix A.2 for \( M = J \). Details on the RJMCMC steps are provided below in Section 3.3.

3.3 Steps of the RJMCMC algorithm

The parameter spaces under the independent and the joint DPM priors are different, so moving between these two parameter spaces becomes a trans-dimensional problem. Reversible jump MCMC (RJMCMC) was first introduced by Green (1995), which can be thought of as a generalized Metropolis-Hastings algorithm for the trans-dimensional updates.

Under the current model status \( M \), the propose model status \( M' \) is randomly assigned to be either \( I \) or \( J \) with acceptance probability \( \min\{1, \alpha(M, M')\} \), where

\[
\alpha(M, M') = \frac{l_{M'} \cdot \pi_{M'} \cdot q_{M}} {l_{M} \cdot \pi_{M} \cdot q_{M'}},
\]

where \( l_{M} \) and \( \pi_{M} \) are the likelihood function and the prior distribution under model \( M \), \( q_{M'} \) is the candidate distribution of the parameters when proposing for model \( M' \) under model \( M \), \( p_{M \rightarrow M'} \) is the probability of proposing \( M' \) conditional on the current status \( M \), and \( |3| \) is the Jacobian. As \( M' \) is randomly picked from \{I, J\}, \( p_{M \rightarrow M'} \) and \( p_{M' \rightarrow M} \) are equal in the algorithm. Note that when \( M = M' \), it becomes the usual fixed-dimensional MCMC algorithm as \( \alpha(M, M') = 1 \); when \( M \neq M' \), the candidate distribution of the parameters \( q \) is then for balancing the parameter spaces between the independent and joint models.

Recall that \( \Theta_{M} \) and \( \Theta_{M'} \) denote the DPM parameters under models \( M \) and \( M' \), respectively, and the truncated number \( K \) under both models are assigned to be identical. We first examine the case when \( X_1 \) and \( X_2 \) are univariate random variables \((D_1 = D_2 = 1)\) with the current model status \( M = I \), and the proposed model is \( M' = J \). Denote the covariance matrix under the joint model as \( \mathbf{S} = \begin{pmatrix} s_{11} & s_{12}\rho_j \\ s_{12}\rho_j & s_{22} \end{pmatrix} \). We assign the \( 2 \times K \) mean vector \( \mu \) to be the same in both the
independent and joint DPM models. Also, we assign the variances $S_{11}^2$ and $S_{22}^2$, and $r$ to be the same across different model statuses. Therefore, this move only requires proposing the parameters under the joint DPM prior in (2): the cluster label $g'_J$, $\rho'_J$, the concentration parameter $d'_J$, and the mixture weights $w'_J$. The concentration parameter $d'_J$ is proposed by $d'_J \sim \text{Gamma}(\bar{d}_I, 1)$, where $\bar{d}_I$ is the mean of $d_I$, and then the mixture probabilities $w'_J$ is proposed from the stick-breaking procedure with concentration parameter $d'_J$. The cluster label $g'_J$ is proposed from the full conditional distribution given in Appendix A. The details of the mapping for each parameter is described in the end of this section.

Conversely, if the current model status is $M = J$ and the proposed model status is $M' = I$, the parameters of the independent model described in (1) are proposed as follow: The concentration parameter $d'_I \sim \text{Gamma}(d_J, 1)$, and the mixture weights $w'_I$ are again proposed by the stick-breaking procedure with concentration parameter $d'_I$. The cluster label $g'_I$ is again proposed by the full conditional distribution given in Appendix A.

For dimension matching under the RJMCMC algorithm, the bijection map is described below for the case where $M = I$ and $M' = J$. The reverse move uses the same map. Let

\[
\begin{align*}
\theta_M &= \{\mu, S_{11}, S_{22}, r, w_I, d_I, g_I\} \\
u &= \{\rho'_J, w'_J, d'_J, g'_J\} \\
\theta_{M'} &= \{\mu, S_{11}, S_{22}, r, w_J, d_J, g_J, \rho_J\} \\
u' &= \{w'_J, d'_J, g'_J\}.
\end{align*}
\]

Then we assign $\Theta_M = \{\theta_M, u\}, \Theta_{M'} = \{\theta_{M'}, u'\}$. The bijection function $h$ has the form

\[
h(\Theta_M) = h(\theta_M, u) = \Theta_{M'} = \{\theta_{M'}, u'\},
\]

which is a one-to-one bijection map with: $w_I \rightarrow w'_I, d_I \rightarrow d'_I, g_I \rightarrow g'_I, \rho'_J \rightarrow \rho_J, w'_J \rightarrow w_J, d'_J \rightarrow d_J$, and $g'_J \rightarrow g_J$. Hence, the Jacobian $|J| = \left| \frac{\partial(\theta_{M'}, u')}{\partial(\theta_M, u)} \right| = 1$.
When $\sum_i D_i > 2$, the transition of the covariance matrices between the independent and joint models becomes more complicated as the off-diagonal elements are harder to propose than in the bivariate case. One way to alleviate this concern is to assume the covariance matrix $S$ under the joint model is a block-diagonal matrix $S = \begin{pmatrix} S_1 & 0 \\ 0 & S_2 \end{pmatrix}$, where $S_i$ is a $D_i \times D_i$ covariance matrix of $X_i$ for $i = 1, 2$. However, in the simulation study and the real data analysis of this article, we will focus on the case where $X_1$ and $X_2$ are univariate random variables.

4 Simulation Study

The simulation study focuses on testing for dependence between two univariate variables. The objective is to compare the power of each method under linear and nonlinear dependence. In the following subsections, we introduce the data generation procedure, the competing methods, and the simulation results.

4.1 Data generation

The seven different types of data sets are simulated. Scenarios 5 and 6 are designed from [Kaufman et al. (2013)].

1. Independent normal (Null): $X_j \sim N(0, 1)$, for $j=1,2$.

2. Bivariate normal (BVN): $(X_1, X_2) \sim \text{BVN} \left[0, \begin{pmatrix} 1 & \rho \\ \rho & 1 \end{pmatrix} \right]$, where $\rho = 0.2$.

3. Horseshoe (HS): $X_1 \sim N(0, 1)$, $X_2 | X_1 \sim N(\rho X_1^2, 1)$, where $\rho = 0.2$.

4. Cone: $X_1 \sim U(0, 1)$, $X_2 | X_1 \sim N \left[0, (\rho X_1^2 + 0.1)^2 \right]$, where $\rho = 0.1$.

5. W: $X_1 \sim \frac{1}{n} \sum_{i=1}^{n} U(a_i, a_i + \frac{1}{3})$, $X_2 | X_1 \sim U \left[3(X_1^2 - \frac{1}{2})^2, 3(1 + X_1^2 - \frac{1}{2}) \right]$, where $a_1 = -1$, $n$ is the number of samples, and $a_i = a_{i-1} \frac{2}{n}$, for $i > 1$.

6. Circle: $(X_1, X_2) \sim \frac{1}{n} \sum_{i=1}^{n} \text{BVN} \left[\theta_i, \begin{pmatrix} \frac{1}{n} & 0 \\ 0 & \frac{1}{n} \end{pmatrix} \right]$, where $\theta_i = [\sin(a_i \pi), \cos(a_i \pi)]$, and $a_i$ is defined as in W.
Each scenario is generated with the algorithms introduced above with sample size \( n = 100, 200, \) and 500. Then for each dimension, we standardize the data to have mean zero and variance one. We plot the data when \( n = 200 \) in Figure 1 along with the true density. The responses are dependent for designs 2-6. Design 3-6 are all examples of the challenging dependent but uncorrelated random variables and thus the usual test of correlation will miss this dependence.

**Figure 1:** True log density (background color) and one simulated data set (points) for each simulation design.
4.2 Methods for testing of independence

We compare six methods in the simulation study (described in detail in the Appendix). Each method is controlled to have type I error rate approximately equal to 0.05.

1. Linear regression (LR): The model \( X_2 = \beta_0 + \beta_1 X_1 + \epsilon, \epsilon \sim N(0,1) \) is fitted by least squares and the linear association is determined by the test of \( \beta_1 = 0 \).

2. E-statistics (ES) (Szekely et al. 2007): The testing procedure is by calculating the distance covariance between \( X_1 \) and \( X_2 \).

3. Heller-Heller-Gorfine method (HHG) (Heller et al. 2013): The test statistic is based on the sum of all likelihood ratio tests of 2 × 2 contingency tables formed by the pairwise distances within each of \( X_1 \) and \( X_2 \).

4. Data Derived Partitions method (DDP) (Kaufman et al. 2013) with 3 × 3 contingency tables: The DDP method is similar to the HHG method, but only designed for univariate random variables. The test statistic is based on the sum of all likelihood ratio tests of 3 × 3 contingency tables formed by the observed values.

5. Maximal Information Coefficient method (MIC) (Reshef et al. 2011): It is a rank-order test statistic which is calculated from the largest achievable mutual information under different grid sizes.

6. The DPM test of independence (DPM): The proposed test is described in Section 2. \( X \) is first marginally transformed to be standard normal distribution. The normal score transformation makes the proposed method a distribution-free testing procedure. Therefore, the threshold for the BF in Section 2 that controls Type I error can be determined by the permutations of the transformed data. The threshold \( T \) for the Bayes factor is computed from 300 permutations of the sample.
4.3 Simulation results

The results are presented in Table 2 with sample sizes $n = 100, 200$ and $500$. The first three rows of the table are the type I error rate for each method under different sample sizes, which is controlled for all methods (Type I error rate is between 0.03 to 0.09). The following rows give the power of each method under different scenarios and sample sizes. It is clear that as the sample size $n$ increases, the powers increase for all the methods except the LR method under the HS, Cone, and Circle scenarios because of the nonlinear associations of these scenarios.

When the data are generated from bivariate normal distribution, the LR method has the highest power. This is expected because the LR method is theoretically the most powerful test under this scenario. The ES and DPM tests are the second best among other comparing tests.

The DPM test outperforms all other methods when data are generated from the HS and the W shapes. Under the Cone shape data, the HHG and the DPM tests both perform well. For the Circle design, the HHG, DDP, and DPM tests all have power greater than 0.9 starting from small sample sizes, and the ES and MIC have lower power.

In summary, the LR method is able to capture linear association but loses power in the nonlinear cases. The ES method is able to capture linear and nonlinear associations, but loses power in some of the nonlinear cases. The HHG and DDP methods both have high power in testing of nonlinear associations, but lose power in the linear association, especially the HHG method. The MIC method is a relatively conservative test compared to all other methods, and this problem is discussed by [Heller et al. (2012)](Heller2012). The proposed method not only shows the ability to capture the linear association, but is also powerful for detecting nonlinear associations in the simulation study.
Table 2: Power of each test (columns) for each simulation settings and sample size $n$ (rows). A * indicates that the power is significantly different than the power of DPM test.

| Type  | $n$ | LR  | ES  | HHG | DDP | MIC | DPM |
|-------|-----|-----|-----|-----|-----|-----|-----|
| Null  | 100 | 0.06| 0.04| 0.03| 0.02| 0.03| 0.03|
|       | 200 | 0.06| 0.05| 0.03| 0.02| 0.07| 0.05|
|       | 500 | 0.09| 0.08| 0.05| 0.09| 0.02| 0.09|
| BVN   | 100 | 0.57*| 0.49| 0.24*| 0.38*| 0.13*| 0.43|
|       | 200 | 0.84*| 0.78| 0.37*| 0.61*| 0.25*| 0.76|
|       | 500 | 0.99| 0.99| 0.83*| 0.99| 0.40*| 0.99|
| HS    | 100 | 0.11*| 0.22*| 0.42| 0.39| 0.12*| 0.44|
|       | 200 | 0.05*| 0.48*| 0.53*| 0.60*| 0.25*| 0.68|
|       | 500 | 0.10*| 0.96| 0.99| 1.00| 0.42*| 1.00|
| Cone  | 100 | 0.03*| 0.25*| 0.54*| 0.33| 0.17*| 0.36|
|       | 200 | 0.08*| 0.56*| 0.87| 0.73*| 0.37*| 0.84|
|       | 500 | 0.09*| 1.00| 1.00| 1.00| 0.80*| 1.00|
| W     | 100 | 0.54*| 0.42*| 0.55*| 0.75*| 0.34*| 0.92|
|       | 200 | 0.84*| 0.83*| 0.92*| 1.00| 0.70*| 1.00|
|       | 500 | 1.00| 1.00| 1.00| 1.00| 0.98| 1.00|
| Circle| 100 | 0.00*| 0.00*| 0.96| 0.99| 0.20*| 0.99|
|       | 200 | 0.00*| 0.22*| 1.00| 1.00| 0.37*| 1.00|
|       | 500 | 0.00*| 1.00| 1.00| 1.00| 0.95*| 1.00|

5 Real data analysis

We compare the six methods in the simulation study on the gene expression data set from Hughes et al. (2000). Studies of associations between genes can be found in de la Fuente et al. (2004) and Bhardwaj & Lu (2005). The number of observations is $n = 300$ for each gene, and we select 94 genes on chromosome 1 after removing samples with missing values. The objective is to test the pairwise associations within these 94 genes. A total of $\binom{94}{2} = 4371$ hypotheses tests of independence are performed. Because of the large number of tests, we control false discovery rate (FDR) at the 0.05 level rather than Type I error. The Bayesian FDR (BFDR) control procedure is applied (Efron & Tibshirani 2002, Newton et al. 2004, Storey et al. 2004, Muller et al. 2006) for the DPM test, and the Benjamini–Hochberg procedure (Benjamini & Hochberg 1995) is applied for the other methods.
The Cohen’s κ statistic (Cohen 1960) is used to measure agreement between tests. The κ statistic is

\[ \kappa = \frac{P_a - P_e}{1 - P_e}, \]

where \( P_a \) is the proportion of agreements between the two methods among the \( N = 4371 \) tests, and \( P_e \) is the theoretical proportion of agreements under independence. Larger values of \( \kappa \) represents more agreement between the tests. The number of rejections among \( N = 4371 \) tests and the κ statistics of pairwise methods are presented in Table 3.

### Table 3: Numbers of rejections (of the \( N = 4371 \) tests), and Cohen’s κ statistics for each pair of methods.

| Methods | Number of rejections | LR   | ES   | HHG  | DDP  | MIC  | DPM  |
|---------|----------------------|------|------|------|------|------|------|
| LR      | 2404                 | 1.000| 0.472| 0.301| 0.404| 0.082| 0.452|
| ES      | 3352                 | –    | 1.000| 0.686| 0.830| 0.036| 0.779|
| HHG     | 3442                 | –    | –    | 1.000| 0.751| 0.032| 0.720|
| DDP     | 3350                 | –    | –    | –    | 1.000| 0.036| 0.814|
| MIC     | 249                  | –    | –    | –    | –    | 1.000| 0.042|
| DPM     | 3231                 | –    | –    | –    | –    | –    | 1.000|

The κ statistics show that the ES, HHG, DDP, and the DPM tests have similar testing powers in this gene expression data sets, and the number of rejections among these tests are similar (3231 to 3442). The LR test only captures the linear associations between genes, and the MIC has the lowest power as in the simulation study.

In Figure 2, we plot six pairs of genes where there are disagreements among the tests. In the upper two plots (gene 94 versus gene 8, and gene 88 versus gene 15), the associations between these pairs of genes are detected by the DPM test, but not the other tests. The figure shows that between gene 94 and gene 8, there is a horseshoe pattern of dependence, and a nonlinear relationship between gene 88 and gene 15. In the middle two plots (gene 17 versus gene 1, and gene 89 versus gene 24), the ES, HHG, DDP, and DPM tests all flag associations between genes, but not the LR and the MIC tests. The figure shows that gene 17 and gene 1 have a cone-shape
association, and genes 89 and 24 have a clustering relationship. The bottom two plots (gene 92
versus gene 2 and gene 30 versus gene 6) are the cases where only the LR, ES and DPM tests flag
associations between genes. These three tests are powerful in testing the linear associations, and
the figure shows linear relationships between genes in these two pairs.

Figure 2: Six pairs of genes where there are disagreements among the tests. The red lines are the linear
regression fitted lines.

6 Conclusion

We propose a nonparametric Bayesian test of dependence by calculating the Bayes factor using
the Dirichlet process mixture model and the reversible jump MCMC algorithm. We compare
our method with the linear model, distance correlation method, HHG, DDP, and MIC in the
simulation study and also in the gene expression data sets. The simulation results show that the
proposed test is competitive in testing both linear and nonlinear relationships.

In the gene expression data analysis, we performed 4371 multiple testing on the gene expression data in comparing pairwise genes. The proposed test shows similar performance with the distance correlation, DDP, and HHG methods, and detects some cases that other methods do not detect. It also shows that the proposed method is powerful on both linear and nonlinear relationships in the pairwise gene comparisons.
A Full conditional distributions

A.1 Full conditionals for the independent DPM prior

Let $X_j = \{X_{ij} : i = 1, ..., N\}$, where $X_{ij}$ is the $i$th observation of $X_j$ and $N$ is the number of observations. The prior of $S_j$ is $S_j \sim IW_{D_j}(\rho_j, W_j)$. The full conditional distribution for each parameters under the independent DPM prior of $X_j$ are

\[
\begin{align*}
\mu_{ij} | \text{rest} &\sim MVN_{D_j}[(n_{lj} \Sigma_j^{-1} + \Omega_j^{-1})^{-1} \Sigma_j^{-1} (\sum_{i:g_{ij}=l} X_{ij}), (n_{lj} \Sigma_j^{-1} + \Omega_j^{-1})^{-1}] \\
S_j | \text{rest} &\sim IW[N + K + \rho_j, A] \\
P(r = r_m | \text{rest}) &= \frac{\prod_{i=1}^{N} \phi_j(X_{ij} | \mu_{g_{ij},j}, r_m S_j) \prod_{l=1}^{K} \phi_j(\mu_{lj} | 0, (1 - r_m) S_j)^{\frac{1}{n_r}}}{\sum_{q=1}^{n_r} \prod_{i=1}^{N} \phi_j(X_{ij} | \mu_{g_{ij},j}, r_q S_j) \prod_{l=1}^{K} \phi_j(\mu_{lj} | 0, (1 - r_q) S_j)^{\frac{1}{n_r}}} \\
P(g_{ij} = l | \text{rest}) &= \frac{\phi_j(X_{ij} | \mu_{lj}, S_j) w_{lj}}{\sum_{s=1}^{K} \phi_j(X_{ij} | \mu_{sj}, S_j) w_{sj}} \\
v_{lj} | \text{rest} &\sim Beta \left( \sum_{i=1}^{N} I(g_{ij} = l) + 1, \sum_{i=1}^{N} I(g_{ij} > l) + d_j \right) \\
d_j | \text{rest} &\sim Gamma \left( K + a - 1, b - \sum_{l=1}^{K-1} \log(1 - v_{lj}) \right),
\end{align*}
\]

where $l = 1, ..., K$, $m = 1, ..., n_r$, $i = 1, ..., N$, $A = r^{-1} \sum_{i=1}^{N} (X_{ij} - \mu_{g_{ij}})(X_{ij} - \mu_{g_{ij}})^T + (1 - r)^{-1} \sum_{l=1}^{K} \mu_{lj} \mu_{lj}^T + \rho_j W_j$, $n_{lj} = \sum_{i=1}^{N} I(g_{ij} = l)$, $g_{ij}$ is the cluster label of the $i$th observation, $n_r$ is the number of discrete $r$ values, $\phi_j$ is the $D_j$-dimensional multivariate normal density function, and $(a, b)$ is the tuning parameter of the stick-breaking algorithm.

A.2 Full conditionals for the joint DPM prior

Let $X = \{X_i : i = 1, ..., N\}$, where $X_i$ is the $i$th observation of $X$ and $N$ is the number of observations. The prior of $S$ is $S \sim IW_{D_1 + D_2}(\rho, W)$. The full conditional distribution for each
parameters under the joint DPM prior of $X$ are

$$
\mu_l \mid \text{rest} \sim \text{MVN}_{D_1+D_2}((n_l \Sigma^{-1} + \Omega^{-1})^{-1} \Sigma^{-1} (\sum_{i:g_i=l} X_i), (n_l \Sigma^{-1} + \Omega^{-1})^{-1})
$$

$$
S \mid \text{rest} \sim \text{IW}[N + K + \rho, B]
$$

$$
P(r = r_m \mid \text{rest}) = \frac{\prod_{i=1}^{N} \phi(X_i \mid \mu_{g_i}, r_m S) \prod_{l=1}^{K} \phi(\mu_l \mid 0, (1 - r_m) S)^{\frac{1}{m_r}}}{\sum_{q=1}^{n_r} \left[ \prod_{i=1}^{N} \phi(X_i \mid \mu_{g_i}, r_q S) \prod_{l=1}^{K} \phi(\mu_l \mid 0, (1 - r_q) S)^{\frac{1}{n_r}} \right]}
$$

$$
P(g_{ij} = l \mid \text{rest}) = \frac{\phi_j(X_{ij} \mid \mu_{s_j}, \Sigma_j)w_{ij}}{\sum_{s=1}^{K} \left[ \phi_j(X_{ij} \mid \mu_{s_j}, \Sigma_j)w_{sj} \right]}
$$

$$
v_l \mid \text{rest} \sim \text{Beta} \left[ \sum_{i=1}^{N} I(g_i = l) + 1, \sum_{i=1}^{N} I(g_i > l) + d \right]
$$

$$
d \mid \text{rest} \sim \text{Gamma} \left[ K + a - 1, b - \sum_{i=1}^{K-1} \log(1 - v_l) \right],
$$

where $l = 1, \ldots, K$, $m = 1, \ldots, n_r$, $i = 1, \ldots, N$, $B = r^{-1} \sum_{i=1}^{N} (X_i - \mu_{g_i})(X_i - \mu_{g_i})^T + (1 - r)^{-1} \sum_{l=1}^{K} \mu_l \mu_l^T + \rho W$, $n_l = \sum_{i=1}^{N} I(g_i = l)$, $g_i$ is the cluster label of the $i^{th}$ observation, $n_r$ is the number of discrete $r$ values, $\phi$ is the $D$-dimensional multivariate normal density function, and $(a, b)$ is the tuning parameter of the stick-breaking algorithm.

### B Test of independence by E-statistics

The test of independence by E-statistics, which calculates the distance covariance measures (dCov), was first introduced by [Szekely et al. (2007)](https://link.to.szekely.et.al.2007). The dCov between two random variables (or vectors) $X_1 \in \mathbb{R}^p$ and $X_2 \in \mathbb{R}^q$ with finite first moments is the nonnegative number defined as

$$
\mathcal{V}^2(X_1, X_2) = \| f(X) - f_1(X_1) f_2(X_2) \|_w^2,
$$

where $\| \cdot \|_w^2$ is the $L_2$-norm with weight function $w$. The $w$ is described more details in [Szekely et al. (2007)](https://link.to.szekely.et.al.2007), and in this article, we use the identical $w$ as suggested. The empirical distance covariance of $n$ observed samples $\mathcal{V}_n^2(X_1, X_2)$ is also defined in [Szekely et al. (2007)](https://link.to.szekely.et.al.2007). A test
statistic $T(\mathbf{X}_1, \mathbf{X}_2, p, n)$ that rejects the null hypothesis that two random variables (or vectors) if
\[
\frac{n \chi^2_n(\mathbf{X}_1, \mathbf{X}_2)}{S_2} > (\Phi^{-1}(1 - \alpha/2))^2
\]
has an asymptotic significance level at most $\alpha$, and
\[
S_2 = \frac{1}{n^2} \sum_{k,l=1}^{n} |\mathbf{X}_{1k} - \mathbf{X}_{1l}|^p \frac{1}{n^2} \sum_{k,l=1}^{n} |\mathbf{X}_{2k} - \mathbf{X}_{2l}|^q,
\]
where $|\cdot|_r$ is the $L_r$-norm, and $\Phi$ is the standard normal distribution. However, the test decision based on $\Phi$ is quite conservative for many distributions, so the testing decision in this article is determined by 300 permutation samples under the null hypothesis with Type I error rate $p = 0.05$ level under each data set. The R package “energy” with function “indep.test” is used in the analysis.

A distribution-free version of distance covariance was also introduced in [Szekely & Rizzo 2009], which uses the ranks of the observations instead of the values. In this article, the distribution-free version of dCov performs similar to the original version, so we only present the original version of the dCov.

C Heller-Heller-Gorfine test of association based on Euclidean distance metric

This test was first introduced by [Heller et al. 2013]. The test is based on the pairwise distances within $\mathbf{X}_1$ and $\mathbf{X}_2$ respectively. Let the pairwise distances within $\mathbf{X}_j$, $j = 1, 2$, denoted as $\{d(\mathbf{X}_{ij}, \mathbf{X}_{i'j}) : i, i' \in \{1, \ldots, n\}\}$, where $\mathbf{X}_{ij}$ is the $i$th observation in $\mathbf{X}_j$, and $d(\cdot, \cdot)$ is assigned to be the Euclidean distance metric in this article. The idea is to first randomly select two samples $i$ and $i'$ in each of $\mathbf{X}_1$ and $\mathbf{X}_2$, and then use the distances $d(\mathbf{X}_{i1}, \mathbf{X}_{i'1})$ and $d(\mathbf{X}_{i2}, \mathbf{X}_{i'2})$ as the references to construct a $2 \times 2$ contingency table among the remaining $n - 2$ samples. Then
the likelihood ratio test of independence for summarizing this table denoted as \( S(i, i') \) gives test statistic
\[
T = \sum_{i=1}^{n} \sum_{i' = 1, i' \neq i}^{n} S(i, i').
\]
The 0.05 Type I error rate is controlled by 300 permutation samples under the null hypothesis of each data set. The R package “\( HHG \)” with function ”\( hhg.test \)” is used in the analysis.

A distribution-free version of HHG test was suggested in [Heller et al., 2013] for comparison. We found that in this article the results are similar to the original version of HHG test. Therefore, we only present the original version of the HHG results.

D Distribution-free tests of association based on data derived partitions

This test was first introduced in [Kaufman et al., 2013], which is designed for testing two univariate random variables (i.e. \( D_1 = D_2 = 1 \)). The idea follows the HHG test but with different ways of forming the contingency tables. The data values are now used directly instead of using the distances. In forming a \( 2 \times 2 \) contingency table, one sample point is randomly selected as the reference, and then a \( 2 \times 2 \) contingency table can be constructed and a test statistic of this table is calculated. The same procedure can be applied to form \( m \times m \) contingency tables (\( m > 2 \)) with randomly selected \( m - 1 \) data values as references. More specifically, the \( m \times m \) contingency table is defined by the range \((-\infty, X^*_1(1)), (X^*_1(2), X^*_1(3)), \ldots, (X^*_1(m-1), \infty) \) in \( X_1 \), and \((-\infty, X^*_2(1)), (X^*_2(2), X^*_2(3)), \ldots, \) (\( X^*_2(m-1), \infty \)) in \( X_2 \), where \( X^*_j(r) \) is the \( r \)th ordered selected observation in \( X_j \), \( j = 1, 2 \). In this article, the summation of the likelihood ratio test statistics with each \( 3 \times 3 \) \((m = 3)\) contingency table is used as the test statistics. This setting was shown to perform the best in most of the scenarios in [Kaufman et al., 2013]. The testing decision is again based on 300 permutation samples under the null hypothesis for each data set controlled under 0.05 Type I error rate in this study. The R package ”\( HHG \)” with function ”\( xdp.test \)” is used in this article.
E Maximal information coefficient for measuring dependence of two variables

The Maximal Information Coefficient (MIC) method is first introduced by [Reshef et al. 2011]. The intuition is that if a relationship exists between two univariate random variables, then a grid (a square) can be drawn on the scatter-plot of these two variables which can partition the data to capture the relationship. The method explores all size of grids up to a maximal grid resolution. For grid size $x$-by-$y$, the largest achievable normalized mutual information (MI) is denoted as $m_{xy}$

$$m_{xy} = \max \{I_{xy}\}/\log(\min\{x, y\}),$$

where computation of $I_{xy}$ can be found in [Jiang et al. 2010], and the MIC is the maximum of $m_{xy}$ over all pair $(x, y)$ such that $xy < B$, where $B$ depends on the sample size $n$. In this article, we use $B = n^{0.6}$ as suggested in [Reshef et al. 2011], and the p-value is calculated from the p-value table given in [www.exploredata.net/Downloads/P-Value-Tables]. The R package "minerva" with function "mine" is used in this article.
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