On synthetic data with predetermined subject partitioning and cluster profiling, and pre-specified categorical variable marginal dependence structure

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ABSTRACT.

A standard approach for assessing the performance of partition or mixture models is to create synthetic data sets with a pre-specified clustering structure, and assess how well the model reveals this structure. A common format is that subjects are assigned to different clusters, with variable observations simulated so that subjects within the same cluster have similar profiles, allowing for some variability. In this manuscript, we consider observations from nominal, ordinal and interval categorical variables. Theoretical and empirical results are utilized to explore the dependence structure between the variables, in relation to the clustering structure for the subjects. A novel approach is proposed that allows to control the marginal association or correlation structure of the variables, and to specify exact correlation values. Practical examples are shown and additional theoretical results are derived for interval data, commonly observed in cohort studies, including observations that emulate Single Nucleotide Polymorphisms. We compare a synthetic dataset to a real one, to demonstrate similarities and differences.

Key words: Nominal variables; Ordinal variables; Interval variables; Cohort studies; Dirichlet process; Bayesian clustering; Simulated data; Single Nucleotide Polymorphisms
1 Introduction

Partitioning and mixture models are often used to reveal the clustering structure within a sample. For example, to discover if combinations of risk factors are associated with the risk of disease (Müller et al. 2011), or to reveal dependencies in a population, whilst reducing the dimensionality of the problem; Yau and Holmes (2011). The combination of clustering with other methods can potentially lead to significant improvements in the exploration of the joint effect of covariates. See Bhattacharya and Dunson (2012) and Yang and Dunson (2013), where tensor factorizations are employed to characterize the joint density of variables that form high-dimensional data. In Zhou et al. (2015) and Papathomas and Richardson (2016), marginally independent variables are detected with the use of modelling that is directly related to Bayesian partitioning algorithms. An overview of clustering approaches is given in Hennig et al. (2016).

Assessing the performance of partitioning models involves the creation of synthetic data with a pre-specified clustering structure. The model is then fitted to the simulated data to assess its performance in terms of revealing this structure. Usually, profiles are created for a number of subjects, by simulating observations from a set of variables. The subjects are assigned to different clusters, and variable observations are simulated so that subjects within the same cluster have similar profiles, allowing for some variability. The investigator controls the strength of the signal in the clustering structure (i.e. how distinct the different clusters are), and the variability of the observations within each cluster. Sometimes partitioning the variables is of interest, rather than the subjects (Marbac et al. 2014). In this manuscript we focus on the former set-up, as the two frameworks are interchangeable for simulated observations.

Partitioning models for continuous observations (Jasra et al. 2005) often assume a specific correlation structure for the variables, given the cluster allocation. This typically involves a multivariate normal distribution. Such modelling does not have any adverse effect on the predetermined clustering structure. See, for example, Melnykov et al. (2012) or Waller and Jones (2016). In contrast to continuous observations, clustering approaches for categorical observations typically prescribe that variables are independent given the clustering of the subjects (Dunson and Xing, 2009; Liverani et al. 2015). The resulting dimensional-
ity reduction is the main advantage of this local independence modelling, as determining a fully specified joint distribution between $P$ categorical variables with $M$ levels requires the specification of $M^P$ probabilities, a task that quickly becomes cumbersome and unwieldy. Celeux and Govaert (2016) comment on this notable difference in the modelling of continuous and categorical observations, mentioning that, in many applications, the assumption of independence given the clustering has proven successful in achieving the main objective of a clustering algorithm, which is to bring together similar observations. In Oberski (2016), local dependence is discussed, given well defined substantive interest. In this manuscript we concentrate on categorical variables, and thus adopt the widely espoused local independence assumption.

Importantly, when creating a synthetic dataset of categorical observations, departing from the within-cluster independence assumption can interfere with the predetermined clustering structure, generating additional clusters. For example, assume the aim is to create 2 clusters of subjects, using 5 variables with three levels each (0, 1, 2). For the first cluster, define probabilities (0.1, 0.1, 0.8) for observing (0, 1, 2) respectively. For the second cluster, define a high probability for observing 0, through probabilities (0.8, 0.1, 0.1). Assume now a high positive correlation imposed on the variables, given the cluster. (See Supplemental material, Section S1, for generating correlated categorical variable observations.) This specification will generate one prominent group of subjects with observations (2, 2, 2, 2), and another with observations (0, 0, 0, 0, 0). Crucially, a smaller but notable group of subjects will also be created, with profile (1, 1, 1, 1, 1), and this will form a third cluster, despite the simulation specifications. This was demonstrated in Tackney (2014, Summer student project). This is an artifact of the strong within-cluster correlation, and not of non-identifiability. In subsequent analyses, we ensure that all generated clustering structures are identifiable by following the guidelines of Allman et al. (2009) in terms of the required number of variables, so that the model parameters are identifiable up to label swapping. Denoting by $C$ the number of clusters, all synthetic datasets satisfy the identifiability condition, $P \geq 2[\log_M(C)] + 1$.

Our focus is on Bayesian clustering with the Dirichlet process (Bigelow and Dunson, 2009; Molitor et al. 2010). Our work concerns nominal, ordinal, and interval variables, where the numerical distance between categories is meaningful and known. Interval variables are
of particular interest to us, as data from epidemiological and association cohort studies, such as number of children, are often in the form of interval observations. Furthermore, continuous observations are often categorized when data from cohort studies are analyzed. This is done to alleviate the adverse effect of outlier observations (for example in dietary observations; see Bingham and Riboli, 2004), or to allow for the flexible modelling of interactions (for example in air pollution variables; see Papathomas et al. 2011). Importantly, interval categorical variables allow for the use of covariances and correlations through expectations. This enables the derivation of the mathematical results in Sections 2.4 and 4.2, further increasing the investigator’s control over the marginal dependence structure of the variables.

The variables are independent given the clustering of the subjects, but marginally dependent. In synthetic data sets, this dependence can be at odds with the dependence structure observed in real data sets. The creation of synthetic data with predetermined clustering structure is straightforward, as long as the marginal dependence structure between the variables, generated as a by-product of the clustering structure, is ignored. To the best of our knowledge, no algorithm has yet been proposed where the clustering structure is predetermined, whilst there is also control over the dependence structure between the variables. In this manuscript, an algorithm is proposed that allows to control the categorical variables’ marginal correlation structure. In turn, this enables the creation of simulated data sets that share more characteristics with real ones, compared to synthetic data created with standard methods. Wang and Sabo (2015) discuss the simulation of correlated binary observations, incorporating cluster specific random effects, but the aim of the proposed algorithm is not to generate clusters with distinct variable profiles. The proposed methods are generally applicable, as shown in the first six examples in this manuscript. One of the application of our methodology is to the generation of partitioned data that emulate Single Nucleotide Polymorphism (SNP) observations. We do not touch on issues relevant to recombination and imputation (Ioannidis et al. 2009), as this is beyond the scope of this manuscript.

In Section 2, we describe the generic approach for generating data with a predetermined clustering structure, introduce association measures for nominal and ordinal variables, and explore the marginal dependence structure between interval variables, deriving theoretical
results. In Section 3, we introduce a specific algorithm for constructing clusters with distinct variable profiles, and examine its properties. In Section 4, this algorithm is modified to allow for a more flexible dependence structure. The effected control on the marginal dependence of the variables is extended, and exact correlation values can be specified. Practical examples are shown and additional theoretical results are derived. In Section 5, a real data set containing SNP observations is compared to a synthetic one, demonstrating similarities and differences. We conclude with a discussion in Section 6.

2 Simulating a predetermined clustering structure and the implied correlation matrix

2.1 The clustering model

Assume $P$ categorical variables $x_p, p = 1, \ldots, P$. Without any loss of generality, assume that each variable takes values $x_p = 1, \ldots, M_p$. Let $x = (x_1, \ldots, x_p)$. Following Papathomas and Richardson (2016), for subject $i, i = 1, \ldots, n$, a variable profile $x_i$ is a vector of categorical values $x_i = (x_{i1}, \ldots, x_{ip})$. Let $z = \{z_1, \ldots, z_n\}$, where $z_i$ is an allocation variable, so that $z_i = c$ denotes that subject, $i$, belongs to cluster $c$. Denote by $\phi^c_p(x)$ the probability that $x_p = x$, when the individual belongs to cluster $c$. Given the clustering allocation, the variables are assumed independent, following a multinomial distribution with cluster specific parameters $\phi^c_p = [\phi^c_p(1), \ldots, \phi^c_p(M_p)]$. Denote by $\psi = \{\psi_1, \psi_2, \ldots, \psi_C\}$ the probabilities that a subject belongs to cluster $c, c = 1, \ldots, C$.

2.2 A generic algorithm for a predetermined clustering structure for the subjects

A generic algorithm for creating observations from $P$ variables, for subjects that are partitioned in $C$ clusters, is given as:
• Specify the number of clusters $C$.

• Specify the number of subjects $n_c$, $c = 1, \ldots, C$, allocated to cluster $c$, in accordance with cluster allocation probabilities $\psi_c$. Allocate each subject to one of the $C$ clusters in accordance with $n_c$.

• Specify the variable profile of the subjects within each cluster, i.e. probabilities $P(x_p = x_{ip}|z_i = c) = \phi_p^c(x_{ip})$, for all $c = 1, \ldots, C$, $p = 1, \ldots, P$, and $x_{ip} = 1, \ldots, M_p$, to generate a distinct variable profile for the subjects in each cluster.

• To generate $x_{ip}$, sample $t$ from the standard normal distribution. For, $s = 0, \ldots, M_p - 1$, if $t \in [\Phi^{-1}(\sum_{x=0}^{s} \phi_p^c(x)), \Phi^{-1}(\sum_{x=0}^{s+1} \phi_p^c(x))]$, then $x_{ip} = s$. Here, by definition, $\phi_p^c(0) = 0$.

2.3 Association measures for nominal and ordinal variables

Pairwise association measures for nominal variables are typically based on the chi-square statistic. A standard choice is Cramer’s $V$, defined as,

$$V = \frac{\chi^2}{n \times \min\{M_p, M_q\}}.$$

Here,

$$\chi^2 = \sum_{i=1}^{M_p} \sum_{j=1}^{M_q} \frac{(n_{i,j} - \hat{\mu}_{i,j})^2}{\hat{\mu}_{i,j}},$$

where, $n_{i,j}$ denotes the number of subjects classified in the cross-tabulation cell $(x_p = i, x_q = j)$, $\hat{\mu}_{i,j} = n_{i+} n_{+j}/n$, $n_{i+} = \sum_{j=1}^{M_q} n_{i,j}$, and, $n_{+j} = \sum_{i=1}^{M_p} n_{i,j}$. Other measures describe the proportional reduction in variance from the marginal of $x_p$ to the conditional distribution of $x_p$ given $x_q$. Agresti (2002, p.69) suggests the concentration coefficient, $V_{cc}$, as a possible choice.

$$V_{cc} = \frac{\sum_{i=1}^{M_p} \sum_{j=1}^{M_q} \frac{\pi_{i,j}^2}{\pi_{i+} \pi_{+j}} - \sum_{j=1}^{M_q} \pi_{+j}^2}{1 - \sum_{j=1}^{M_q} \pi_{+j}^2},$$

where, $\pi_{i,j}$ denotes the probability a subject is classified in the cross-tabulation cell $(x_p = i, x_q = j)$, $\pi_{i+} = \sum_{j=1}^{M_q} \pi_{i,j}$, and, $\pi_{+j} = \sum_{i=1}^{M_p} \pi_{i,j}$. Those probabilities are estimated by $\hat{\pi}_{i,j} = n_{i,j}/n$. Measures $V$ and $V_{cc}$ vary within $[0, 1]$. One difficulty associated with these
measures is developing intuition on how large a value constitutes a strong association (Agresti, 2002, p.57).

The association between two ordinal variables is commonly measured by Spearman’s coefficient or Kendall’s tau. The two measures typically produce similar results (Collwell and Gillett, 1982). We opt to evaluate Kendall’s tau, as it has a more intuitive interpretation in terms of concordant and discordant observations. Kendall’s tau is defined as,

\[ \tau = \frac{n_c - n_d}{0.5n(n-1)}, \]

where \( n_c \) is the number of concordant pairs and \( n_d \) the number of discordant pairs. Two observed pairs \((x_p^{(1)}, x_q^{(1)})\) and \((x_p^{(2)}, x_q^{(2)})\) are concordant either if \(x_p^{(1)} < x_p^{(2)}\) and \(x_q^{(1)} < x_q^{(2)}\), or if \(x_p^{(1)} > x_p^{(2)}\) and \(x_q^{(1)} > x_q^{(2)}\). When \(x_p^{(1)} = x_p^{(2)}\), or \(x_q^{(1)} = x_q^{(2)}\), the two pairs are neither concordant nor discordant. When ties occur, the modified Stuart-Kendall \(\tau_c\) is often adopted (Berry et al. 2009), where,

\[ \tau_c = \frac{2(n_c - n_d)}{n^2(\min\{M_p, M_q\} - 1)/\min\{M_p, M_q\}}. \]

### 2.4 The marginal correlation structure of interval variables

Assume that \(x\) is a vector of interval categorical variables. The marginal variance-covariance matrix \(\text{Var}(x)\) is,

\[ \text{Var}(x) = E(xx^\top) - E(x)E(x)^\top = \text{E}_z\text{E}_{x|z}(xx^\top|z) - \left(\text{E}_z\text{E}_{x|z}(x|z)\right) \left(\text{E}_z\text{E}_{x|z}(x|z)^\top\right). \]

Element \((p,p), p = 1, \ldots, P\), in the diagonal of \(\text{Var}(x)\) is,

\[ \text{Var}(x_p) = E(x_p^2) - E(x_p)^2 = \sum_{x_p=1}^{M_p} x_p^2 P(x_p = x_p) - \left[\sum_{x_p=1}^{M_p} x_p P(x_p = x_p)\right]^2 \]

\[ = \sum_{c=1}^{C} P(z_i = c)\left[\sum_{x_p=1}^{M_p} x_p^2 P(x_p = x_p|z_i = c)\right] - \left[\sum_{c=1}^{C} P(z_i = c)\left[\sum_{x_p=1}^{M_p} x_p P(x_p = x_p|z_i = c)\right]\right]^2 \]

\[ = \sum_{c=1}^{C} \psi_c \left[\sum_{x_p=1}^{M_p} x_p^2 P(x_p = x_p|z_i = c)\right] - \left[\sum_{c=1}^{C} \psi_c \left[\sum_{x_p=1}^{M_p} x_p P(x_p = x_p|z_i = c)\right]\right]^2. \]  \(1\)

Element \((p,q), p \neq q, p,q = 1, \ldots, P\), in the off-diagonal of \(\text{Var}(x)\) is,

\[ \text{Cov}(x_p, x_q) = E(x_p x_q) - E(x_p) \times E(x_q) \]
\[
\sum_{x_p=1}^{M_p} \sum_{x_q=1}^{M_q} x_p \times x_q P(x_p = x_p, x_q = x_q) - \sum_{x_p=1}^{M_p} x_p P(x_p = x_p) \times \sum_{x_q=1}^{M_q} x_q P(x_q = x_q) = \sum_{c=1}^{C} P(z_i = c) \left[ \sum_{x_p=1}^{M_p} \sum_{x_q=1}^{M_q} x_p x_q P(x_p = x_p, x_q = x_q | z_i = c) \right] - \{ \sum_{c=1}^{C} P(z_i = c) \left[ \sum_{x_p=1}^{M_p} x_p P(x_p = x_p | z_i = c) \right] \} \times \{ \sum_{c=1}^{C} P(z_i = c) \left[ \sum_{x_q=1}^{M_q} x_q P(x_q = x_q | z_i = c) \right] \}
\]

As \( x_p \) and \( x_q \) are independent given \( z \),

\[
\text{Cov}(x_p, x_q) = \sum_{c=1}^{C} P(z_i = c) \left[ \sum_{x_p=1}^{M_p} x_p P(x_p = x_p | z_i = c) \right] \left[ \sum_{x_q=1}^{M_q} x_q P(x_q = x_q | z_i = c) \right] - \{ \sum_{c=1}^{C} P(z_i = c) \left[ \sum_{x_p=1}^{M_p} x_p P(x_p = x_p | z_i = c) \right] \} \times \{ \sum_{c=1}^{C} P(z_i = c) \left[ \sum_{x_q=1}^{M_q} x_q P(x_q = x_q | z_i = c) \right] \}
\]

Denote by \( f_{p,c} \) the expected value for \( x_p \) in cluster \( c \), i.e. \( f_{p,c} = \text{E}(x_p | z_i = c) = \sum_{x_p=1}^{M_p} x_p P(x_p = x_p | z_i = c) \). Then, for \( p \neq q \),

\[
\text{Cov}(x_p, x_q) = \sum_{c=1}^{C} \psi_c f_{p,c} f_{q,c} - \left( \sum_{c=1}^{C} \psi_c f_{p,c} \right) \left( \sum_{c=1}^{C} \psi_c f_{q,c} \right).
\] (2)

**Example 1:** Consider \( C = 2 \). Then, \( f_{p,1} = f_{q,1} \) and \( f_{p,2} = f_{q,2} \) implies positive correlations, as,

\[
\text{Cov}(x_p, x_q) = \psi_1 f_{p,1}^2 + \psi_2 f_{p,2}^2 - \psi_1 f_{p,1}^2 - \psi_2 f_{p,2}^2 - 2\psi_1 \psi_2 f_{p,1} f_{p,2} = \psi_1 \psi_2 (f_{i,1} - f_{i,2})^2 > 0.
\]

**Example 2:** Consider \( C = 4 \), and assume that \( f_{p,1} = f_{q,1} = f_{p,3} = f_{q,3} \) and \( f_{p,2} = f_{q,2} = f_{p,3} = f_{q,4} \). Then, for \( p \neq q \), it follows from (2) that,

\[
\text{Cov}(x_p, x_q) = (\psi_1 + \psi_3)(\psi_2 + \psi_4)(f_{p,1} - f_{p,2})^2 > 0.
\]

In the Supplemental material, Section S2, we present extended versions of the two examples above, including additional inferences after utilizing equation (2). However, the
larger the number of clusters, the less helpful (2) becomes for understanding the effect of the clustering on the marginal covariance structure of the variables. More helpful is the following Theorem.

**Theorem 1**: Assume that $x_p$ and $x_q$ are interval categorical variables. Under the condition that $\psi_1 = \psi_2 = \ldots = \psi_C = \psi$, for $p \neq q$, $p, q = 1, \ldots, P$,

$$\text{Cov}(x_p, x_q) = \sum_{\{c_1, c_2 = 1, \ldots, C, c_1 < c_2\}} \psi^2(f_{p,c_1} - f_{p,c_2})(f_{q,c_1} - f_{q,c_2}). \quad (3)$$

*Proof*: The proof is given in the Appendix.

Equation (3), although restricted to $\psi_1 = \psi_2 = \ldots = \psi_C = \psi$, is more helpful for examining the effect of the clustering on the covariance structure of the variables. For any number of clusters, if, for all $c_1 < c_2$, the sign of $(f_{p,c_1} - f_{p,c_2})$ is the same as the sign of $(f_{q,c_1} - f_{q,c_2})$, the correlation between $x_p$ and $x_q$ is positive. If, for all $c_1 < c_2$, the sign of $(f_{p,c_1} - f_{p,c_2})$ is different to the sign of $(f_{q,c_1} - f_{q,c_2})$, the correlation between $x_p$ and $x_q$ is negative. The correlation is zero if, for every term in $\text{Cov}(x_p, x_q)$, as given by (3), either $(f_{p,c_1} - f_{p,c_2})$ is zero or $(f_{q,c_1} - f_{q,c_2})$ is zero.

### 3 A specific algorithm for a predetermined clustering

The algorithm in this Section allows for the creation of synthetic data with a partitioning signal of adjustable strength. The signal’s strength depends on how distinct probability vectors $H_p$ and $L_p$, $p = 1, \ldots, P$, are. Markedly different vectors $H_p$ and $L_p$ create distinct variable profiles for the different clusters. The algorithm is given as:

- Define the number of clusters $C$.
- For $C$ even, define the number of variables $P$ so that, $P = l \times 2^{C/2-1}$, where $l$ is an integer, $l \geq 1$. For $C$ odd, define $P$ so that, $P = l \times 2^{(C+1)/2-1}$.
- Specify the number of subjects $n_c$ allocated to cluster $c$, in accordance with cluster allocation probabilities, $\psi_c = \psi = 1/C$, $c = 1, \ldots, C$. Allocate each subject to one
of the $C$ clusters in accordance with $n_c$.

- For each variable $x_p$, consider two sets of probabilities, $H_p = [\phi_p^H(1), \ldots, \phi_p^H(M_p)]$ and $L_p = [\phi_p^L(1), \ldots, \phi_p^L(M_p)]$, so that, $\sum^{M_p}_{m=1} \phi_p^H(m) = 1$, and, $\sum^{M_p}_{m=1} \phi_p^L(m) = 1$. The two sets could be distinct in the sense that the first elements of $H_p$ are considerably higher than subsequent elements, whilst the first elements of $L_p$ are considerably lower that subsequent elements. When the same probabilities apply to all variables, subscript $p$ is omitted, so that, $H_1 = \ldots = H_P = H$, and, $L_1 = \ldots = L_P = L$.

- For a subject in cluster $c$, $c$ odd, define its profile so that the first $P/(2^{c/2} - 0.5)$ variables are simulated in accordance with $L_p$, the next $P/(2^{c/2} - 0.5)$ variables in accordance with $H_p$, and so on and so forth. This is done in accordance with the fourth step of the algorithm in Section 2.2.

- For a subject in cluster $c$, $c$ even, define its profile so that the first $P/(2^{c/2} - 1)$ variables are simulated in accordance with $H_p$, the next $P/(2^{c/2} - 1)$ variables in accordance with $L_p$, and so on and so forth.

- If required, to generate observations from variables $x_q$, $q > P$, that do not contribute to the clustering, consider $A_q = [\phi_q^A(1), \ldots, \phi_q^A(M_q)]$, distinct from $H_p$ and $L_p$. For all subjects, generate observations from $A_q$ irrespectively of cluster allocation.

For even $C$, this specification generates $k = 2^{C/2-1}$ groups of associated variables, where the dependence between variables within a group is stronger compared to the dependence between variables in different groups. Henceforth, we refer to those groups as homogenous. $l$ is the number of variables within each homogenous group. This dependence structure is shown empirically for nominal and ordinal variables in Examples 3 and 4, where we also present derived correlations assuming interval variables. Proposition 1, determines theoretically the dependence structure described above for interval variables.

**Proposition 1:** For the algorithm proposed in Section 3, for even $C$, and for $H_1 = \ldots = H_P = H$, and, $L_1 = \ldots = L_P = L$, the covariance within each homogenous group is the same for all groups, and the highest observed in the interval variables’ covariance matrix.
Proof: Without any loss of generality, assume that all variables contribute to the clustering. Each of the $2^{C/2-1}$ homogenous groups contains $l = P/(2^{C/2-1})$ adjoined variables with the same cluster profile characterized by H or L. For the variables within a homogenous group, the differences $(f_{p,c_1} - f_{p,c_2})$ and $(f_{q,c_1} - f_{q,c_2})$ always carry the same sign, for any $c_1$ and $c_2$. This is not true for variables in different groups. This translates to within-group covariances $\text{Cov}(x_p,x_q)$ that are always positive and larger than between-group covariances, as the algorithm determines balanced sized clusters and Theorem 1 holds.

Example 3: For 8 clusters ($C = 8$) and 16 variables ($P = 16$), the variable profile for each cluster is shown in Table 1. In the Supplemental material, Section S3, Figure S1, we show the clustering of simulated data for 800 subjects, using $H = (0.9025, 0.0950, 0.025)$ and $L = (0.0625, 0.3750, 0.5625)$. The clustering of the simulated data is in accordance with the predetermined clustering. This is observed in subsequent Examples too. (Throughout the manuscript, simulated subject profiles are clustered using the R package PReMiuM (Liverani et al. 2015), which implements Bayesian clustering with the Dirichlet process.) The number of variables in each homogenous group is $l = 2$, and the number of homogenous groups is $k = 8$. In Figure 1(a) we show a heatmap for the derived pairwise concentration coefficient $V_{cc}$, which corresponds to simulated observations from nominal variables. Cramer’s $V$ gave the same dependence structure, with slightly smaller correlations. In Figure 1(b) we present the derived Stuart-Kendall $\tau_c$ measure, assuming ordinal observations. Results using Spearman’s coefficient were very similar. In Figure 1(c), we present a heatmap of the theoretical correlations between the variables, and in Figure 1(d) the sample correlations assuming interval observations. Note that blocks of negative and zero correlations are also observed in the correlation matrix, due to the symmetry in the clustering structure. We observe that the dependence structure measured by $\tau_c$ in Figure 1(b) is very similar to the sample correlations in Figure 1(d). In Figures S2 and S3 in the Supplemental material, we present the derived correlation matrices for $C = 6$ and $C = 4$ respectively.

Example 4: For odd $C$, the number of homogenous groups of variables, is $2^{(C+1)/2-1}$. The homogenous groups are not defined as clearly as for even $C$ (see Example 3). For 5 clusters
Table 1: Cluster profiles for 16 variables \((P = 16)\) and 8 clusters \((C = 8)\) for Example 3. Observations are simulated using probability vectors \(L\) and \(H\).

| \(x_1\) | \(x_2\) | \(x_3\) | \(x_4\) | \(x_5\) | \(x_6\) | \(x_7\) | \(x_8\) | \(x_9\) | \(x_{10}\) | \(x_{11}\) | \(x_{12}\) | \(x_{13}\) | \(x_{14}\) | \(x_{15}\) | \(x_{16}\) |
|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| Cluster 1 | L | L | L | L | L | L | L | L | L | L | L | L | L | L | L |
| Cluster 2 | H | H | H | H | H | H | H | H | H | H | H | H | H | H | H |
| Cluster 3 | L | L | L | L | L | L | L | L | L | L | L | L | L | L | L |
| Cluster 4 | H | H | H | H | H | H | H | H | L | L | L | L | L | L | L |
| Cluster 5 | L | L | L | L | H | H | H | H | L | L | L | L | L | L | L |
| Cluster 6 | H | H | H | H | L | L | L | L | H | H | H | H | L | L | L |
| Cluster 7 | L | L | H | H | L | L | H | H | L | L | H | L | L | L | H |
| Cluster 8 | H | H | L | L | H | H | L | H | L | L | H | L | H | H | L |

Table 2: Cluster profiles for 14 variables \((P = 12)\) and 5 clusters \((C = 5)\) for Example 4. Observations are simulated using probability vectors \(L\), \(H\) and \(A\).

| \(x_1\) | \(x_2\) | \(x_3\) | \(x_4\) | \(x_5\) | \(x_6\) | \(x_7\) | \(x_8\) | \(x_9\) | \(x_{10}\) | \(x_{11}\) | \(x_{12}\) | \(x_{13}\) | \(x_{14}\) |
|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| Cluster 1 | L | L | L | L | L | L | L | L | L | L | L | A | A |
| Cluster 2 | H | H | H | H | H | H | H | H | H | H | H | L | A |
| Cluster 3 | L | L | L | L | L | L | H | H | H | H | H | A | A |
| Cluster 4 | H | H | H | H | H | H | L | L | L | L | L | L | A |
| Cluster 5 | L | L | L | H | H | L | L | L | H | H | H | A | A |

\((C = 5)\) and 14 variables \((P = 12, \text{as two additional variables do not contribute to the clustering})\), the variable profile for each cluster is shown in Table 2. In the Supplemental material, Section S4, Figure S4, we show the clustering structure for simulated data for 500 subjects, using \(H = (0.9025, 0.0950, 0.025)\), \(L = (0.0625, 0.3750, 0.5625)\), and \(A = (0.5625, 0.3750, 0.0625)\). The number of variables in each homogenous group is \(l = 3\), and the number of homogenous groups is \(k = 4\). In figure 2(a) we show the derived pairwise association measure \(V_{cc}\). Again, Cramer’s \(V\) gave a very similar structure, with slightly smaller correlations. In Figure 1(b) we present the derived Stuart-Kendall \(\tau_c\) measure. Results using Spearman’s coefficient were very similar. In Figure 2(c), we present a heatmap of the theoretical correlation matrix for the 12 variables that contribute to the clustering. Figure 2(d), shows the sample correlation matrix for all 14 variables, given the simulated observations. When we assume that the simulated observations are ordinal [Figure 2(b)], the derived association measure is very similar to the correlations in Figure 2(d).
4 A modified algorithm

The algorithm introduced in Section 3 is modified in Section 4.1, to allow for homogenous groups of different size. Observations are generated from variables split into \( k \) homogenous groups, not necessarily in a balanced manner. In Section 4.2, we derive a theoretical result for interval variables that allows to first specify the within homogenous group covariances or correlations. In turn, this specification determines \( H_p \) and \( L_p \). The number of homogenous groups \( k \) is a power of 2. We assume the number of clusters \( C \) is even, as this generates a clearly defined dependence structure. The categorical variables are positively associated (nominal/ordinal data) or correlated (interval data) within each homogenous group.

4.1 The proposed algorithm

The proposed algorithm is shown below. Explanatory comments are added in brackets.

- Define the number of homogenous groups \( k \), where \( k \) is a power of 2.
- Define the number of variables \( l_v \) in each homogenous group \( v, v = 1, \ldots, k \).
- \{Solving \( k = 2^{C/2-1} \) gives the even number of clusters, \( C = 2 \times [\ln(k)/\ln(2) + 1] \). \}
- Define the number of subjects, \( n_1 = \ldots = n_C \), within each cluster.
- For each variable \( x_p \), consider two sets of probabilities, \( H_p = [\phi_H^p(1), \ldots, \phi_H^p(M_p)] \), and, \( L_p = [\phi_L^p(1), \ldots, \phi_L^p(M_p)] \), so that, \( \sum_{m=1}^{M_p} \phi_H^p(m) = 1 \), and, \( \sum_{m=1}^{M_p} \phi_L^p(m) = 1 \).
  The two sets could be distinct so that the first elements of \( H_p \) are considerably higher than subsequent elements, whilst the first elements of \( L_p \) are considerably lower.
- For odd \( c \), define the profile of cluster \( c \) so that:
  - the first \( l_1 + \ldots + l_{k/(2^{c/2-0.5})} \) variables are simulated in accordance with \( \{L_1, \ldots, L_P\} \)
  - the next \( l_{k/(2^{c/2-0.5})+1} + \ldots + l_{k/(2^{c/2-0.5})+k/(2^{c/2-0.5})} \) variables in accordance with \( \{H_1, \ldots, H_P\} \)
the next $l_k/(2^{c/2-0.5})+k/(2^{c/2-0.5})+1 + \ldots + l_k/(2^{c/2-0.5})+k/(2^{c/2-0.5})$ variables in accordance with \{L_1, \ldots, L_P\}

- and so on and so forth.

- For even $c$, define the profile of cluster $c$ so that:

  - the first $l_1+\ldots+l_k/(2^{c/2-1})$ variables are simulated in accordance with \{H_1, \ldots, H_P\}
  
  - the next $l_k/(2^{c/2-1})+1 + \ldots + l_k/(2^{c/2-1})+k/(2^{c/2-1})$ variables in accordance with \{L_1, \ldots, L_P\}
  
  - the next $l_k/(2^{c/2-1})+k/(2^{c/2-1})+1 + \ldots + l_k/(2^{c/2-1})+k/(2^{c/2-1})+k/(2^{c/2-1})$ variables in accordance with \{H_1, \ldots, H_P\}
  
  - and so on and so forth.

- \{ When $l_1 = \ldots = l_k$, the two steps above simplify as follows: for odd $c$, define the profile of cluster $c$ so that the first $P/(2^{c/2-0.5})$ variables are simulated in accordance with \{L_1, \ldots, L_P\}, the next $P/(2^{c/2-0.5})$ variables considering \{H_1, \ldots, H_P\}, and so on and so forth. For even $c$, the first $P/(2^{c/2-1})$ variables are simulated considering \{L_1, \ldots, L_P\}, the next $P/(2^{c/2-1})$ variables in accordance with \{H_1, \ldots, H_P\}, and so on and so forth. \}

- If required, to generate observations from variables $x_{q}$, $q > P$, that do not contribute to the clustering, consider $A_q = [\phi^A_q(1), \ldots, \phi^A_q(M_q)]$, distinct from $H_p$ and $L_p$. For all subjects, generate observations from $A_q$ irrespectively of cluster allocation.

**Example 5:** Assume 6 clusters ($C = 6$), 12 variables ($P = 12$), and, $l_1 = 2$, $l_2 = 2$, $l_3 = 5$, and $l_4 = 3$. Consider 600 subjects. Observations were simulated using $H = (0.9025, 0.0950, 0.025)$ and $L = (0.0625, 0.3750, 0.5625)$. Figure 3(a) shows the derived pairwise association measure $V_{cc}$. In Figure 3(b) we present the derived Stuart-Kendall $\tau_c$ measure. In Figure 3(c), we present a heatmap of the theoretical correlation matrix for this specification. In Figure 3(d), we present the sample correlation matrix for the simulated observations. Inferences are very similar to those in Examples 3 and 4.
4.2 Allowing for a predetermined covariance or correlation within each homogenous group for interval variables

**Theorem 2:** Assume that interval variables $x_p$ and $x_q$ belong to the same homogenous group. For the algorithm in Section 4.1, and for $\psi_1 = \psi_2 = \ldots = \psi_C = \psi = 1/C$, so that Theorem 1 holds,

$$\text{Cov}(x_p, x_q) = 0.25 \times (f_{(p,H)} - f_{(p,L)}) \times (f_{(q,H)} - f_{(q,L)}),$$

where, $f_{(p,H)} = \sum_{x_p=1}^{M_p} x_p P(x_p = x_p | H_p)$, and, $f_{(p,L)} = \sum_{x_p=1}^{M_p} x_p P(x_p = x_p | L_p)$.

*Proof:* See Appendix.

For $x_p$ and $x_q$ in the same homogenous group, given $\text{Cov}(x_p, x_q)$, cluster specific probabilities for $x_p$ and $x_q$ should be set so that,

$$(f_{(p,H)} - f_{(p,L)}) \times (f_{(q,H)} - f_{(q,L)}) = 4\text{Cov}(x_p, x_q). \tag{4}$$

In practice, one may consider the simplified scenario where variables in the same homogenous group share the same set of possible values, and $(f_{(p,H)} - f_{(p,L)}) = (f_{(q,H)} - f_{(q,L)})$. Then, given $\text{Cov}(x_p, x_q)$, set cluster specific probabilities so that, for all $x_p$ in the same homogenous group,

$$|f_{(p,H)} - f_{(p,L)}| = \sqrt{4\text{Cov}(x_p, x_q)}, \tag{5}$$

where $|.|$ denotes absolute value. Example illustrations are given below, starting with a rudimentary example involving binary variables.

**Example 6 (Application to binary variables):**

Given predetermined covariances: For a binary variable $x_p$, with levels 0 and 1, $f_{p,H} = P(x_p = 1 | H_p) = \Phi^H_p(1)$, and, $f_{p,L} = P(x_p = 1 | L_p) = \Phi^L_p(1)$. For $x_p$ and $x_q$ in the same homogenous group, given $\text{Cov}(x_p, x_q)$, set cluster specific probabilities for $x_p$ and $x_q$ so that, $|\Phi^H_p(1) - \Phi^L_p(1)| = \sqrt{4\text{Cov}(x_p, x_q)}$. In practice, set $\Phi^H_p(1) = \Phi^H(1)$ constant for all variables, and suitably high, say, close to 1. Then, allow $\Phi^L_q(1)$ to vary, in accordance with, $\Phi^H(1) - \Phi^L_q(1) = \sqrt{4\text{Cov}(x_p, x_q)}$. 

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Given predetermined correlations: From equation (1), and for \( \psi_1 = \ldots = \psi_C = \psi \),

\[
\text{Var}(x_p) = \psi \sum_{c=1}^{C} P(x_p = x_p | z_i = c) - \psi^2 \left\{ \sum_{c=1}^{C} [P(x_p = x_p | z_i = c)] \right\}^2.
\]

For even \( C \), for half of the clusters, \( P(x_p = x_p | z_i = c) = \Phi_p^L(1) \). For the remaining clusters, \( P(x_p = x_p | z_i = c) = \Phi_p^H(1) \). Thus, as \( \psi = 1/C \),

\[
\text{Var}(x_p) = \frac{1}{2} [\Phi_p^H(1) + \Phi_p^L(1)] - \frac{1}{4} (\Phi_p^H(1) + \Phi_p^L(1))^2.
\]

Therefore, denoting with \( \text{Cor}(x_p, x_q) \) the correlation between \( x_p \) and \( x_q \),

\[
\text{Cov}(x_p, x_q) = \text{Cor}(x_p, x_q) \left[ \sqrt{\text{Var}(x_p)} \sqrt{\text{Var}(x_q)} \right]
\]

\[
= \text{Cor}(x_p, x_q) \left[ \frac{1}{2} [\Phi_p^H(1) + \Phi_p^L(1)] - \frac{1}{4} (\Phi_p^H(1) + \Phi_p^L(1))^2 \right].
\]

To allow for different predetermined correlations within each homogenous group of variables, set \( \Phi_p^H(1) = \Phi(H) \) constant for all \( p = 1, \ldots, P \), and let \( \Phi_p^L(1) \) vary so that,

\[
\Phi(H) - \Phi_p^L(1) = \sqrt{4 \text{Cor}(x_p, x_q) \left[ \frac{1}{2} [\Phi_p^H(1) + \Phi_p^L(1)] - \frac{1}{4} (\Phi_p^H(1) + \Phi_p^L(1))^2 \right]}.
\]

**Example 7 (Application to SNP variables, given predetermined covariances):**

Single Nucleotide Polymorphisms (SNP) are categorical observations with 3 levels, usually denoted by 0, 1 and 2 for ‘Wild type’, ‘Heterozygous variant’ and ‘Homozygous variant’ respectively. For a SNP \( x_p \), due to the Hardy-Weinberg principle, (Ziegler and König, 2010), \( P(x_p = 0) = p^2_{S_p} \), \( P(x_p = 1) = 2p_{S_p}(1-p_{S_p}) \) and \( P(x_p = 2) = (1-p_{S_p})^2 \), where \( 0 < p_{S_p} < 1 \). Thus, \( \text{E}(x_p | z_i = c) = 2 - 2p_{S_p} \), \( \text{E}(x_p^2 | z_i = c) = (1 - p_{S_p})(4 - 2p_{S_p}) \), \( \text{Var}(x_p | z_i = c) = 2p_{S_p}(1-p_{S_p}) \), and, \( f(p,H) - f(p,L) = \text{E}(x_p | p^H_{S_p}) - \text{E}(x_p | p^L_{S_p}) = 2(p^H_{S_p} - p^L_{S_p}) \). Assume that for \( x_p \) and \( x_q \) in the same homogenous group, \( p^H_{S_p} = p^H_{S_q} \), and, \( p^L_{S_p} = p^L_{S_q} \), and therefore, \( f(p,H) = f(q,H) \) and \( f(p,L) = f(q,L) \). From (5), given a required covariance \( \text{Cov}(x_p, x_q) \), set cluster specific probabilities for \( x_p \) and \( x_q \) so that, \( 2|p^H_{S_p} - p^L_{S_p}| = \sqrt{4 \text{Cov}(x_p, x_q)} \). In practice, set \( p^H_{S_p} = p^H_{S} \) suitably high (say close to 1) and constant for all variables, and allow \( p^L_{S_p} \) to vary in accordance with, \( p^H_{S} - p^L_{S_p} = \sqrt{\text{Cov}(x_p, x_q)} \).

**Example 8:** Assume 6 clusters \( (C = 6) \), 12 variables \( (P = 12) \) that emulate SNPs, and \( l_1 = 2, l_2 = 2, l_3 = 5, l_4 = 3 \). Consider 600 subjects, and \( p^H_{S} = 0.95 \). Assume a covariance of 0.45 for the variables within homogenous groups. In Figure 4(a), we present a heatmap.
of the theoretical correlation matrix for the specifications in this example, whilst in Figure 4(b) the sample correlations for the simulated observations.

Example 9 (Application to SNP variables, given predetermined correlations):

From Section 2.3, equation (1), and for \( \psi_1 = \ldots = \psi_C = \psi \),

\[
\text{Var}(x_p) = \psi \sum_{c=1}^{C} [E(x_p^2|z_i = c)] - \psi^2 \sum_{c=1}^{C} [E(x_p|z_i = c)]^2.
\]

For even \( C \), for half of the clusters, \( E(x_p^2|z_i = c) = (1 - p_{S_p}^H)(4 - 2p_{S_p}^H) \) and \( E(x_p|z_i = c) = 2 - 2p_{S_p}^H \). For the remaining clusters, \( E(x_p^2|z_i = c) = (1 - p_{S_p}^L)(4 - 2p_{S_p}^L) \), and \( E(x_p|z_i = c) = 2 - 2p_{S_p}^L \). Therefore,

\[
\text{Var}(x_p) = \psi \frac{C}{2} (1 - p_{S_p}^H)(4 - 2p_{S_p}^H) + \frac{C}{2} (1 - p_{S_p}^L)(4 - 2p_{S_p}^L) - \psi^2 \frac{C}{2} (2 - 2p_{S_p}^H) + \frac{C}{2} (2 - 2p_{S_p}^L))^2
\]

\[
= \psi C (1 - p_{S_p}^H)(2 - p_{S_p}^H) + \psi C (1 - p_{S_p}^L)(2 - p_{S_p}^L) - \psi^2 C^2 (2 - p_{S_p}^H - p_{S_p}^L)^2.
\]

Then, denoting with \( \text{Cor}(x_p, x_q) \) the correlation between \( x_p \) and \( x_q \), and as \( \psi = 1/C \),

\[
\text{Cov}(x_p, x_q) = \text{Cor}(x_p, x_q)[(1 - p_{S_p}^H)(2 - p_{S_p}^H) + (1 - p_{S_p}^H)(2 - p_{S_p}^H) - (2 - p_{S_p}^H - p_{S_p}^L)^2].
\]

From Example 7, for a given \( \text{Cov}(x_p, x_q) \), \( (p_{S_p}^H - p_{S_p}^L) = \sqrt{\text{Cov}(x_p, x_q)} \). Thus, to allow for different predetermined correlations within each homogenous group of variables, one should set \( p_{S_p}^H \) suitably high (say, close to 1), and let \( p_{S_p}^L \) vary so that,

\[
p_{S_p}^H - p_{S_p}^L = \sqrt{\text{Cor}(x_p, x_q)[(1 - p_{S_p}^H)(2 - p_{S_p}^H) + (1 - p_{S_p}^H)(2 - p_{S_p}^H) - (2 - p_{S_p}^H - p_{S_p}^L)^2]}.
\]

Example 10: Assume 8 clusters \( (C = 8) \), 16 variables \( (P = 16) \) that emulate SNPs, and \( l_v = 2 \), \( v = 1, \ldots, 8 \). Consider 800 subjects, with observations simulated using \( p_{S_p}^H = 0.95 \), for predetermined correlations within the 8 homogenous groups given by \( (0.4, 0.5, 0.6, 0.7, 0.8, 0.6, 0.7, 0.4) \). In Figure 5(a), we present a heatmap of the theoretical correlation matrix, for the specifications in this example. In Figure 5(b) we present the sample correlation matrix for the simulated observations.
5 Application to subjects clustered according to genetic profiles defined by correlated SNPs

Data from a GWA study of lung cancer presented in Hung et al. (2008) are utilized. Genotyping was performed with the Illumina Sentrix HumanHap300 BeadChip, including 317,139 SNPs of subjects from the International Agency for Research on Cancer (IARC) lung cancer study. The top 200 SNPs, ranked by their p-value for association with lung cancer (adjusted for age, sex, and country) were selected. The correlation (Linkage Disequilibrium) structure is seen in Figure 6(a). We observe 27 groups of SNPs, where SNPs are correlated within each group and uncorrelated between groups. Correlations are overwhelmingly positive, with a small number of negative correlations observed. Table 3, shows the average sample correlation within each of the 27 groups, for the 89 SNPs that are correlated with at least one other polymorphism.

The algorithm in Section 4 is used to generate a predetermined clustering structure for 6000 subjects, using simulated observations from 200 SNPs, whilst the specified homogenous groups resemble those in the real data set. For 12 predetermined clusters, we consider 32 homogenous groups of SNPs. For the first 27 groups, we specify within-group correlations that match the within-group correlations in the real data set. For the last five groups, created to satisfy the requirements of the proposed algorithm, we determine a very small within-group correlation of 0.01. This is because each one of the 10 SNPs in the last 5 groups corresponds to a SNP in the real data that is not correlated with any other SNP. The clustering structure in the simulated data is exactly as pre-determined, with 12 clusters containing 500 subjects each (Supplemental material, Section S5, Figure S5). Within-group sample correlations for the simulated data are shown in Table 3. The simulated dataset replicates almost exactly the real within-group correlations. Such control is a considerable improvement compared to the standard algorithm implemented in Papathomas et al. (2012) and described in Section 2.

The Linkage Disequilibrium structure within the simulated data set can be seen in Figure 6(b). Due to the symmetry in the clustering algorithm, we observe a notable simulated correlation structure between homogenous groups, not observed in the real dataset. Figure
Table 3: Average within-group sample correlations for the 89 correlated SNPs from Hung et al. (2008), and for the simulated data. In parentheses the number of SNPs in each group.

| Group | 1 (2) | 2 (2) | 3 (3) | 4 (2) | 5 (2) | 6 (3) | 7 (2) | 8 (2) | 9 (3) | 10 (2) |
|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------|
| Corr (LD) - Real | 0.68  | 0.96  | 0.62  | 0.91  | 0.96  | 0.93  | 0.90  | 0.98  | 0.91  | 0.98   |
| Corr (LD) - Sim | 0.69  | 0.96  | 0.63  | 0.90  | 0.96  | 0.93  | 0.90  | 0.98  | 0.91  | 0.98   |

| Group | 11 (2) | 12 (2) | 13 (21) | 14 (5) | 15 (2) | 16 (2) | 17 (3) | 18 (2) | 19 (3) | 20 (4) |
|-------|--------|--------|---------|--------|--------|--------|--------|--------|--------|--------|
| Corr (LD) - Real | 0.96  | 0.98  | 0.59    | 0.94   | 0.32   | 0.92   | 0.41   | 0.96   | 0.63   | 0.66   |
| Corr (LD) - Sim | 0.96  | 0.98  | 0.59    | 0.94   | 0.31   | 0.92   | 0.41   | 0.96   | 0.64   | 0.66   |

* Actual correlation is 0.99. 0.98 used to avoid numerical instability
+ Actual average correlation is 0.15. 0.6 used, after excluding negative within-group correlations

S6, in the Supplemental material, Section S5, shows this more clearly, as the focus is on the first 99 SNPs, ignoring the last 101 uncorrelated Polymorphisms. In the next Section, we discuss in more detail the issue of controlling the between-group correlations independently of within-group correlations.

6 Discussion

Our work concerns nominal, ordinal and interval categorical variables. The proposed algorithm generates a similar dependence structure for observations that are treated as ordinal and interval. The dependence structure considering nominal data differs, as negative associations are not present. Nevertheless, we observed in all examples that the overall structure of positive associations was quite similar between ordinal/interval and nominal variables, albeit weaker for the latter. All empirical evidence from our analyses suggests that the manner in which we effect control over within-group correlations is also relevant to nominal and ordinal variables, in terms of the comparative magnitude of within-group associations. For example, the predetermined within-group correlations (0.4, 0.5, 0.6, 0.7, 0.8, 0.6, 0.7, 0.4) in Example 10, correspond to sam-
ple within-group associations $V_{cc} = (0.14, 0.18, 0.23, 0.32, 0.46, 0.28, 0.30, 0.12)$ and $\tau_c = (0.32, 0.43, 0.51, 0.60, 0.69, 0.57, 0.59, 0.33)$.

The proposed algorithm in Section 4 effects control over within-group correlations. Between-group correlations are present as a direct consequence of the symmetry in the clustering structure. Determination of between-group correlations independently of the within-group structure, in tandem with the predetermined clustering, is not straightforward. Equation (3) offers a direct link between the covariances $\text{Cov}(x_p, x_q)$, and the variable profiles in each cluster, through $f_{p,c}$, $p = 1, \ldots, P$, $c = 1, \ldots, C$. $P$ variables imply $P(P - 1)/2$ covariances, under the constraint that they form a positive definite matrix. The number of different $(f_{p,c_1} - f_{p,c_2})$ quantities is $\binom{C}{2}P$. It is straightforward to deduce that the number of unconstrained $(f_{p,c_1} - f_{p,c_2})$ quantities is $P(C - 1)$. For predetermined covariances, (3) generates a non-linear system of $P(P - 1)/2$ equations, with $P(C - 1)$ unknowns. Solving such a system could, in principle, allow to set between-group correlations independently of within-group associations. However, numerical solutions for simple examples (using the R package nleqslv) were not available, with no solution or an infinite number of solutions reported. This was true also for systems with equal number of equations and unknowns, for example for $P = 5$ and $C = 3$. This suggests that a generally applicable algorithm, such as the one proposed in Section 4, is a suitably pragmatic approach for achieving control over the marginal dependence of the variables, noting also that the resulting between-group dependence is less pronounced when the simulated data are viewed as observations from nominal variables.

The algorithms described in this manuscript are available in the R package PReMiuM (Liverani et al. 2015), which performs flexible Bayesian clustering and profile regression (Molitor et al. 2010). \{ Note: Functions to become available in PReMiuM after publication. Currently available upon request, and for refereeing purposes. \}

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APPENDIX: Proof of Theorem 1: From (2),

\[
\text{Cov}(x_p, x_q | z_i = c) = \sum_{c=1}^{C} \psi_c f_{p,c} f_{q,c} - \left( \sum_{c=1}^{C} \psi_c f_{p,c} \right) \left( \sum_{c=1}^{C} \psi_c f_{q,c} \right)
\]

\[
= \sum_{c=1}^{C} \psi_c f_{p,c} f_{q,c} - \sum_{c=1}^{C} \psi_c^2 f_{p,c} f_{q,c} - \sum_{c_1 < c_2, c_2 = 2, \ldots, C} \psi_{c_1} \psi_{c_2} f_{p,c_1} f_{q,c_2} - \sum_{c_1 < c_2, c_2 = 2, \ldots, C} \psi_{c_1} \psi_{c_2} f_{p,c_2} f_{q,c_1}
\]

\[
= \sum_{c=1}^{C} (\psi_c - \psi_c^2) f_{p,c} f_{q,c} - \sum_{c_1 < c_2, c_2 = 2, \ldots, C} \psi_{c_1} \psi_{c_2} f_{p,c_1} f_{q,c_2} - \sum_{c_1 < c_2, c_2 = 2, \ldots, C} \psi_{c_1} \psi_{c_2} f_{p,c_2} f_{q,c_1}.
\]

(6)

Now,

\[
\sum_{c_1 < c_2, c_2 = 2, \ldots, C} (\psi_{c_1} f_{p,c_1} - \psi_{c_2} f_{p,c_2}) (\psi_{c_1} f_{q,c_1} - \psi_{c_2} f_{q,c_2})
\]

\[
= \sum_{c_1 < c_2, c_2 = 2, \ldots, C} [\psi_{c_1}^2 f_{p,c_1} f_{q,c_1} + \psi_{c_2}^2 f_{p,c_2} f_{q,c_2} - \psi_{c_1} \psi_{c_2} f_{p,c_1} f_{q,c_2} - \psi_{c_1} \psi_{c_2} f_{p,c_2} f_{q,c_1}]
\]

\[
= \sum_{c=1}^{C} (C - 1) \psi_c^2 f_{p,c} f_{q,c} - \sum_{c_1 < c_2, c_2 = 2, \ldots, C} \psi_{c_1} \psi_{c_2} f_{p,c_1} f_{q,c_2} - \sum_{c_1 < c_2, c_2 = 2, \ldots, C} \psi_{c_1} \psi_{c_2} f_{p,c_2} f_{q,c_1}.
\]

(7)

To complete the proof we show that, for \(\psi_1 = \ldots = \psi_C = \psi\), (6)=(7), i.e. that,

\[
\sum_{c=1}^{C} (\psi_c - \psi_c^2) f_{p,c} f_{q,c} = \sum_{c=1}^{C} (C - 1) \psi_c^2 f_{p,c} f_{q,c} \Leftrightarrow \sum_{c=1}^{C} (\psi_c - C \psi_c^2) f_{p,c} f_{q,c} = 0.
\]

To show this, notice that,

\[
\psi_c - \psi_c^2 = \psi_c (1 - \psi_c) = \psi_c (\psi_1 + \ldots + \psi_{c-1} + \psi_{c+1} + \ldots + \psi_C) = (C - 1) \psi^2
\]

\[
\Rightarrow \psi_c - C \psi_c^2 = \psi - C \psi^2 = \psi - \psi + \psi^2 - \psi^2 = 0,
\]

and the proof of Theorem 1 is complete.

APPENDIX: Proof of Theorem 2: From Theorem 1,

\[
\text{Cov}(x_p, x_q) = \sum_{\{c_1, c_2: c_1, c_2 = 1, \ldots, C, c_1 < c_2\}} \psi^2 (f_{p,c_1} - f_{p,c_2}) (f_{q,c_1} - f_{q,c_2}).
\]

The number of terms in the above sum is \(\binom{C}{2}\). For the algorithm in Section 4.1, and for all \(p = 1, \ldots, P\), all non-zero terms \((f_{p,c_1} - f_{p,c_2})\) are equal in absolute value, and we denote this absolute value by \(|f_{(p,H)} - f_{(p,L)}|\), where, \(f_{(p,H)} = \sum_{x_p=1}^{M_p} x_p P(x_p = x_p|H_p)\), and, \(f_{(p,L)} = \sum_{x_p=1}^{M_p} x_p P(x_p = x_p|L_p)\). The number of non-zero terms in either \(f_{(p,H)}\) or \(f_{(p,L)}\) is,

\[
\sum_{i=1}^{C/2} i + \sum_{i=1}^{(C-2)/2} i = \frac{(C + 1)C}{2} + \frac{(C-2)C-2}{2}
\]

22
\[
\frac{(C + 2)C}{2 \times 4} \times \frac{(C - 2 + 2)C - 2}{2 \times 4} = \frac{(C + 2)C + C(C - 2)}{2 \times 4} = \frac{C(2C)}{8} = \frac{C^2}{4}.
\]

For variables \(x_p\) and \(x_q\) in the same homogenous group, \((f_{p,c1} - f_{p,c2})\) and \((f_{q,c1} - f_{q,c2})\) always carry the same sign. Therefore,

\[
(f_{p,c1} - f_{p,c2}) \times (f_{q,c1} - f_{q,c2}) = |f_{(p,H)} - f_{(p,L)}| \times |f_{(q,H)} - f_{(q,L)}|.
\]

Thus, we can write,

\[
\text{Cov}(x_p, x_q) = \psi^2 \frac{C^2}{4} (f_{(p,H)} - f_{(p,L)})(f_{(q,H)} - f_{(q,L)}) = 0.25(f_{(p,H)} - f_{(p,L)}) \times (f_{(q,H)} - f_{(q,L)}).
\]

This completes the proof of Theorem 2.

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Figure 1(a): Example 3. Concentration coefficient $V_{cc}$.

Figure 1(b): Example 3. Stuart-Kendall $\tau_c$.

Figure 1(c): Example 3. Theoretical correlations.

Figure 1(d): Example 3. Sample correlations.
Figure 2(a): Example 4. Concentration coefficient $V_{cc}$.

Figure 2(b): Example 4. Stuart-Kendall $\tau_c$.

Figure 2(c): Example 4. Theoretical correlations.

Figure 2(d): Example 4. Sample correlations.
Figure 3(a): Example 5. Concentration coefficient $V_{cc}$.

Figure 3(b): Example 5. Stuart-Kendall $\tau_c$.

Figure 3(c): Example 5. Theoretical correlations.

Figure 3(d): Example 5. Sample correlations.
Figure 4(a): Example 8. Theoretical correlations.  Figure 4(b): Example 8. Sample correlations.

Figure 5(a): Example 10. Theoretical correlations.  Figure 5(b): Example 10. Sample correlations.
Figure 6(a): Real data Linkage Disequilibrium. Figure 6(b): Simulated data Linkage Disequilibrium.