MISSING VALUE KNOCKOFFS

Deniz Koyuncu  
Department of Electrical, Computer, and Systems Engineering  
Rensselaer Polytechnic Institute  
Troy, NY  
koyund@rpi.edu

Bülent Yener  
Department of Computer Science  
Rensselaer Polytechnic Institute  
Troy, NY  
byener@gmail.com

ABSTRACT

One limitation of the most statistical/machine learning-based variable selection approaches is their inability to control the false selections. A recently introduced framework, model-x knockoffs, provides that to a wide range of models but lacks support for datasets with missing values. In this work, we discuss ways of preserving the theoretical guarantees of the model-x framework in the missing data setting. First, we prove that posterior sampled imputation allows reusing existing knockoff samplers in the presence of missing values. Second, we show that sampling knockoffs only for the observed variables and applying univariate imputation also preserves the false selection guarantees. Third, for the special case of latent variable models, we demonstrate how jointly imputing and sampling knockoffs can reduce the computational complexity. We have verified the theoretical findings with two different exploratory variable distributions and investigated how the missing data pattern, amount of correlation, the number of observations, and missing values affected the statistical power.

Keywords  Model-x knockoffs · false discovery rate · FDR control · missing data · imputation · posterior sampling · knockoff sampling · generative models · latent variable models

1 Introduction

Coping with increasing number of variables, optimizing predictive performance, and selecting among candidate scientific hypothesis are all valid reasons for using a variable selection algorithm. Another reality of today’s datasets are missing values. Although there are existing methods for handling the missing values if applied directly, they can interfere with the assumptions of variable selection algorithms.

In this work, we will discuss how model-x knockoffs (Candes et al. 2017), a new approach in principled variable selection, can be applied to datasets that contain missing values. By principled variable selection we refer to algorithms that aims to identify the Markov Blanket (MB) of a response variable (Tsamardinos and Aliferis 2003) while providing a control of the false selections. Identifying the MB is by definition optimal as the MB refers to the smallest subset of variables that is sufficient to describe the conditional distribution of the response variable. Controlling the false selections refers to limiting the variables that are selected due to random chance and is especially important in applications where a selected variable corresponds to a scientific discovery.

Model-x knockoffs provides a framework for repurposing existing statistical/machine learning feature scorers for MB discovery. When the assumptions of the model-x framework holds, the expected fraction of selections that are conditionally pairwise independent with the response variable is controlled. Formally given exploratory variables \(X_1, \ldots, X_p\) and a response variable \(Y\), let \(X_{\neg j} = \{X_l : l \neq j\}\) denotes the variables except \(X_j\), then the conditionally pairwise independent variables set is given by \(\mathcal{H}_0 : \{ j : Y \perp \!\!\!\!\perp X_j \mid X_{\neg j}\}\) (Candes et al. 2017). Given the resulting subset \(S \subseteq \{1, \ldots, p\}\) from the procedure, the False Discovery Rate (FDR) (Benjamini and Yekutieli 2001) is controlled at a selected level \(q\) i.e.:

\[
E \left[ \frac{|S \cap \mathcal{H}_0|}{\max(1, |S|)} \right] \leq q
\]
Moreover, under widely used assumptions in the probabilistic graphical models literature, that is equivalent to controlling the expected fraction of selections that are outside of the MB of the response (Candes et al. 2017). As an alternative assumption, we also show that strict positiveness of the joint distribution is sufficient in the Appendix Theorem 6.

One assumption of the model-x knockoffs is the accurate knowledge of the distribution of the exploratory variables and the imputation of the missing values can alter the distribution. To describe the problems imputation can cause, we briefly review how the exploratory variable distribution is used in the knockoffs framework. In knockoffs methodology, given an input data matrix $X \in \mathbb{R}^{N \times p}$ an additional matrix (called knockoffs) $\tilde{X} \in \mathbb{R}^{N \times p}$ is sampled such the two matrices are pairwise exchangeable i.e.

$$(X, \tilde{X})_{\text{swap}(S)} \overset{d}{=} X, \tilde{X}$$

holds for all $S \in \{1, \ldots, p\}$ (Candes et al. 2017). The symbol $\overset{d}{=} \text{denotes the equality in distribution}$ and swap$(S)$ operator given two matrices swaps the columns indexed by $S$ in the first matrix with the ones in the second and vice versa. For that condition to hold, assuming rows of $X$ are i.i.d each row of $\tilde{X}$ is sampled using a knockoff sampler i.e. $\tilde{X}^{(i)} \sim P_{X|X(\cdot; X^{(i)})}$ s.t. $\tilde{X}^{(i)}$ and $X^{(i)}$ are pairwise exchangeable.

The effect of an imputation algorithm is on the joint distribution of the imputed variables and the observed variables. Given the observed variables $X_{o}^{(i)} = \{X_i : i \in o\}$ where $o \subseteq \{1, \ldots, p\}$ the missing variables are imputed using a function $g(\cdot): \mathbb{R}^{|o|} \rightarrow \mathbb{R}^{p-|o|}$ i.e. $\hat{X}_{m}^{(i)} = g(X_{o}^{(i)})$. In general the joint distribution of the observed and imputed random vectors is not equal to the joint distribution of the fully observed random vector i.e. $(X_{o}^{(i)}, \hat{X}_{m}^{(i)}) \overset{d}{=} (X_{o}^{(i)}, X_{m}^{(i)})$ where $m = \{1, \ldots, p\} \setminus o$. Therefore, if one samples the knockoff for the imputed vector using the original distribution $P_X$ in general the pairwise exchangeability would not hold. To sample valid knockoffs the joint distribution of $\hat{X}^{(i)} = (X_{o}^{(i)}, \hat{X}_{m}^{(i)})$ needs to be known accurately and that leads to two problems. First, deriving $P_{\hat{X}^{(i)}}$ using $P_X$ might not be practical for all functions $g(\cdot)$ and second even if the derivation is possible sampling valid knockoffs for the new distribution might not be tractable.

A simple solution to this problem is would be keeping $P_{\hat{X}^{(i)}} \overset{d}{=} P_X$. Once that is done any knockoff sampler that works for $P_X$ will also work for the imputed vector $\tilde{X}^{(i)}$. That is very practical as the existing code written for sampling knockoffs can be used directly with the imputed data. In this work we introduce an imputation algorithm that preserves the input distribution.

Our contributions in this paper are:

• Extending the knockoffs framework to missing data setting
• Introducing computationally efficient missing data knockoffs
• Quantifying the joint effect of correlation and missing data on power
• Describing the trade-off between the number of missing data and observations

2 Background

One of the challenges of the model-x framework is sampling knockoffs. If it was possible to sample knockoffs for an arbitrary probability distribution, knockoffs method can be used with any imputation algorithm whose resulting distribution can be derived. However, the lower bounds for the computational complexity of sampling knockoffs indicate the operation is not tractable in general (Bates et al. 2021). That suggests while imputing one has to consider the structure of the resulting probability distribution.

Instead of using a separate imputation model, one can treat missing values as hidden variables. Although there are existing algorithms for sampling knockoffs for the hidden variable models they only guarantee the pairwise exchangeability of the observed variables (Sesia et al. 2019; Gimenez et al. 2019). Therefore, even those algorithms essentially impute the hidden variables they do not guarantee the pairwise exchangeability of the imputations.

We have also reviewed how missing values are handled previously in the applications of model-x framework. For example, in (Candes et al. 2017; Masud et al. 2021) missing values are first imputed and the Multivariate Normal (MVN) distribution is fit to the resulting imputed matrix. Even if the initial distribution is indeed MVN that doesn’t guarantee it will remain after the imputation. Another problem can be the dependence among the rows of the resulting imputed
are pairwise exchangeable. Sampling the missing values independently helps with satisfying the pairwise exchangeability.

Following from Lemma 1, Proof of Theorem 1.

Theorem 1. Let \( \hat{X} = (\hat{X}_1, \ldots, \hat{X}_p)^T \) denote the imputed vector where \( \hat{X}_m \sim P_{X_m|X_o}(\cdot; X_o) \) and \( \hat{X}_o = X_o \). If the distribution \( P_{X,R} \) satisfies MCAR or MAR then \( P_X = P_{\hat{X}} \).

The proof is in Appendix B.2

3 Knockoffs and Missing Values

In this work, we will introduce different ways for dealing with missing data under the knockoffs framework. Throughout this work, we denote \( X = (X_1, \ldots, X_p)^T \) as the exploratory R.Vs and \( R = (R_1, \ldots, R_p)^T \) denote the missing value indicator R.Vs. \( R_i \) takes values in \{0, 1\} and \( R_i = 1 \) denotes \( X_i \) is missing. Let \( m = \{ i : R_i = 1 \} \) and \( o = \{1, \ldots, p\} \setminus m \) denote the sets of missing and observed values. Given a set \( S \subseteq \{1, \ldots, p\} \), \( X_S = \{ X_i : i \in S \} \) denotes the R.Vs indexed by set \( S \).

The distribution of the missing values can also change the distribution of the observed variables. We focus our attention on two missing data configurations namely configurations Missing Completely At Random (MCAR) and Missing At Random (MAR). MCAR holds if \( X \perp \!\!\!\!\perp R \) holds and MAR holds if \( X_m \perp \!\!\!\!\perp R \mid X_o \) holds for any \( X_m, X_o \) (Little and Rubin 2002; Mohan 2017).

We start by introducing the posterior sampled missing value knockoffs method which allows reusing the existing knockoff samplers under MAR and MCAR.

Lemma 1. Let \( \hat{X} = (\hat{X}_1, \ldots, \hat{X}_p)^T \) denote the imputed vector where \( \hat{X}_m \sim P_{X_m|X_o}(\cdot; X_o) \) and \( \hat{X}_o = X_o \). If the distribution \( P_{X,R} \) satisfies MCAR or MAR then \( P_X = P_{\hat{X}} \).

The proof is in Appendix B.2

3.1 Knockoffs for Posterior Sampled Missing Values

The knockoffs framework assumes that the input distribution \( P_X \) is known or known to a certain accuracy. That information can be used for imputation in such a way that the FDR control is maintained. The idea is if we can sample \( \hat{X}_m \) from the posterior distribution \( P_{X_m|X_o} \) than the joint distribution of \( \hat{X} \) will remain unchanged. More importantly existing knockoff samplers can be used with the same FDR guarantees.

Definition 1. Following (Barber et al. 2019) a conditional distribution \( P_{\hat{X} | X} \) is pairwise exchangeable with respect to a probability distribution \( Q_X \) if given \( X \sim Q_X(\cdot) \) and \( \hat{X} \sim P_{\hat{X} | X}(\cdot; X) \), \( X \) and \( \hat{X} \) are pairwise exchangeable.

Theorem 1. Let \( \hat{X} = (\hat{X}_1, \ldots, \hat{X}_p)^T \) denote the imputed vector where \( \hat{X}_m \sim P_{X_m|X_o}(\cdot; X_o) \) and \( \hat{X}_o = X_o \). We assume the distribution \( P_{X,R} \) satisfies MCAR or MAR. If \( \hat{X} \sim P_{\hat{X} | X}(\cdot; \hat{X}) \) and \( P_{\hat{X} | X} \) is pairwise exchangeable with respect to \( P_X \), then \( \hat{X} \) and \( \hat{X} \) are pairwise exchangeable.

Proof of Theorem 1. Following from Lemma 1 \( P_X(x) = P_X(x) \) holds for all \( x \) under MAR or MCAR. Then \( P_{\hat{X} | X} \) is pairwise exchangeable with respect to \( P_X \) and by the definition of a pairwise exchangeable distribution \( \hat{X} \) and \( \hat{X} \) are pairwise exchangeable.

The advantage of Theorem 1 lies in reusing an existing sampler of \( P_{\hat{X} | X} \). Algorithm 1 illustrates how it can be applied to N i.i.d. observations \( \{x_o^{(n)}, x_{o'}^{(n)}\}_{n=1}^N \) with varying missing values indices \( \{m^n, o^n\}_{n=1}^N \). Because of the i.i.d. assumption the resulting imputed matrix and knockoffs matrix will be pairwise exchangeable as well. The only additional step of Algorithm 1 is sampling the missing values from the posterior.

3.2 Knockoffs for Univariate Sampled Missing Values

In scenarios where sampling from the posterior is challenging but knockoffs for the observed R.Vs \( X_o \) can be sampled, an alternative method can be using univariate imputation. First the knockoffs for the observed variables \( \hat{X}_o \) will be sampled then the missing values of the originals \( X_m \) and the knockoffs \( \hat{X}_m \) will be imputed independent from \( X_o, \hat{X}_o \). Sampling the missing values independently helps with satisfying the pairwise exchangeability.
Algorithm 1 Posterior sampled missing value knockoffs

Input: \( \{x_o^{(i)}\}_{i=1}^N, \{m^i, o^i\}_{i=1}^N, P_{\hat{X}|X}, P_X \)

for \( i = 1, \ldots, N \) do
  \( m \leftarrow m^i \)
  \( o \leftarrow o^i \)
  \( \hat{x}_m \sim P_{X_m|X_o}(\cdot; x_o^{(i)}) \)
  \( \hat{x}_o^{(i)} \leftarrow (x_o^{(i)}, \hat{x}_m) \)
  \( \hat{x}^{(i)} \sim P_{\hat{X}|X}(\cdot; \hat{x}_o^{(i)}) \) \{Knockoff Sampling\}
end for

Output: \( \{\hat{x}^{(i)}, \hat{x}_o^{(i)}\}_{i=1}^N \)

Theorem 2. Let \( \hat{X} = (\hat{X}_1, \ldots, \hat{X}_p)^T \) denote the imputed vector where \( \hat{X}_o = X_o \) and \( \hat{X}_{m_j} \sim P_{X_{m_j}} j = 1, \ldots, |m| \). We assume \( P_{X,R} \) satisfies MCAR. If \( \hat{X}_o \sim P_{\hat{X}_o|X_o}(\cdot; \hat{X}_o) \), \( P_{\hat{X}_o|X_o} \) is pairwise exchangeable with respect to \( P_{X_o} \), and \( \hat{X}_{m_j} \sim P_{X_{m_j}} j = 1, \ldots, |m| \) then \( \hat{X} \) and \( \hat{X} \) are pairwise exchangeable.

The proof is in Appendix B.1.

In Algorithm 2, we have described how this can be applied to \( N \) i.i.d. observations. Notice that for each different set of observed variables \( o^i \) a different knockoff sampler \( P_{\hat{X}_o|X_o} \) is required. That is computationally a disadvantage compared to Algorithm 1. But Algorithm 2 has a computationally easier imputation step as it samples from the univariate distribution instead of the posterior.

Algorithm 2 Univariate sampled missing value knockoffs

Input: \( \{x_o^{(i)}\}_{i=1}^N, \{m^i, o^i\}_{i=1}^N, \{P_{\hat{X}_o|X_o}^{(i)}\}_{i=1}^N, P_X \)

for \( i = 1, \ldots, N \) do
  \( m \leftarrow m^i \)
  \( o \leftarrow o^i \)
  \( \hat{x}_o \sim P_{\hat{X}_o|X_o}(\cdot; x_o^{(i)}) \)
  for \( j = 1, \ldots, |m| \) do
    \( \hat{x}_{m_j} \sim P_{X_{m_j}} \)
    \( \hat{x}_{m_j} \sim P_{X_{m_j}} \) \{Uni. Imputation of Knockoffs\}
  end for
  \( \hat{x}_o^{(i)} \leftarrow (x_o^{(i)}, \hat{x}_m) \)
  \( \hat{x}^{(i)} \leftarrow (\hat{x}_o, \hat{x}_m) \)
end for

Output: \( x_c, \hat{x} \)

3.3 Mean Squared Errors (MSEs) of Two Imputation Methods

We also analyzed how the posterior sampling and univariate sampling imputations compare in terms of Mean Squared Error (MSE).

Theorem 3. The MSE of the posterior imputation (Algorithm 1) cannot exceed the univariate imputation (Algorithm 2).

Proof is in B.3

These results suggest that assuming lower imputation error leads to a better performance, posterior imputation should be preferred over the univariate. However, our goal is not to have the optimal MSE estimator which is given by \( Y'' = E[Y \mid X] \) because in general \( Y'' \not\overset{d}{=} Y \) and one cannot directly use the existing knockoff samplers.
4 Missing Value Knockoffs For Latent Variable Models

In the preceding section, we have treated imputation and knockoff sampling as two different stages and shown how that enables reusing existing knockoff samplers. In this section, we will show how jointly imputing and knockoff sampling can have computational advantages in latent variable models. The intuition is in certain latent variable models posterior imputation and knockoff sampling requires two separate samples from the latent variable posterior distribution and we can actually reduce that to one sample by modifying the knockoff sampler. To illustrate the idea we will modify the two existing latent variables knockoff samplers: HMM knockoff sampler (Sesia et al. 2019) and GZ knockoff sampler (Gimenez et al. 2019) for the missing data setting.

Algorithm 3 Modified Sesia HMM Knockoffs

Input: $x_o, P_Z, P_{X|Z}, P_{Z|Z}, m, o$
\[ \hat{z} \sim P_{Z|x}(\cdot; x_o) \]  \{Posterior Sampling with $X_o$\}
\[ \hat{x}_m \sim P_{X_m|Z}(\cdot; \hat{z}) \]  \{Imputing Originals\}
\[ z' \sim P_{Z|Z}(\cdot; \hat{z}) \]
\[ \hat{x}_m \sim P_{X_m|Z}(\cdot; z') \]
\[ \hat{x}_o \sim P_{X_o|Z}(\cdot; z') \]

Output: $\hat{x}, \hat{x}$

We have provided the modified version of the HMM knockoff sampler (Sesia et al. 2019) in Algorithm 3. The only differences from the original sampler is the first two steps: sampling from the posterior and imputing the originals. We have demonstrated in Appendix Theorem 7 that HMM structure allows tractable sampling from the posterior $P_Z$ and provided the Algorithm 5. The second step is to impute the originals using $X_{X_m|Z}$ and it’s relatively easy as given the hidden states emission probabilities factors out.

Theorem 4. Let $X$ denote a p-dimensional random vector which is distributed according to an HMM i.e.
\[ Z_1 \sim P_{Z_1} \]
\[ Z_t \sim P_{Z_t|Z_{t-1}}(\cdot; Z_{t-1}), t = 2, \ldots, p \]
\[ X_t \sim P_{X_t|Z_t}(\cdot; Z_t), t = 1, \ldots, p \]

We assume the distribution $P_{X,R}$ satisfies MCAR or MAR. Given $\hat{X}$ and $\hat{X}$ resulting from Algorithm 3 if $P_{Z|Z}$ is pairwise exchangeable with respect to $P_Z$ then $\hat{X}$ and $\hat{X}$ are pairwise exchangeable.

Proof is in Appendix B.4

In Algorithm 4 we have extended the GZ knockoff sampler (Gimenez et al. 2019) to the missing data setting. GZ knockoff sampler supports a broader class of latent variable models than the HMM sampler as it doesn’t require $P_Z$ to form a Markov Chain. Compared to the original, the modified algorithm restricts the order of sampling to first $Z'$ and then $\hat{X}$. Moreover, just as in the HMM case it has two additional steps: sampling from the posterior and imputing the missing values. We denote $Z_{k:i} = \{Z_i : i \geq k & i \leq l\}$.

Algorithm 4 Modified GZ Knockoffs

Input: $x_o, P_Z, P_{X|Z}, m, o$
\[ \hat{z} \sim P_{Z|x}(\cdot; x_o) \]  \{Posterior Sampling with $X_o$\}
\[ \hat{x}_m \sim P_{X_m|Z}(\cdot; \hat{z}) \]  \{Imputing Originals\}
for $i = 1, \ldots, L$ do
\[ z'_i \sim P_{Z_i|X, Z_{i+1:L}, Z_{i-1}}(\cdot; \hat{x}, \hat{z}_{i+1:L}, z'_{i-1}) \]
end for
\[ \hat{x}_m \sim P_{X_m|Z}(\cdot; z') \]
\[ \hat{x}_o \sim P_{X_o|Z}(\cdot; z') \]

Output: $\hat{x}, \hat{x}$

Theorem 5. Let $X \sim P_X$ and $P_X$ can be denoted as a latent variable model i.e.
\[ Z \sim P_Z \]
\[ X_j | Z \sim P_{X_j|Z}(\cdot; Z) \quad j = 1, \ldots, p \]
where \( Z \) is a \( L \) dimensional random vector. We assume the distribution \( P_{X,R} \) satisfies MCAR or MAR. If \( \hat{X} \) and \( \tilde{X} \) are resulting from Algorithm 4 then \( \hat{X} \) and \( \tilde{X} \) are pairwise exchangeable.

The proof is in Appendix B.5

Figure 1: Constant power contours of the posterior imputation knockoffs (Algorithm 1). The missing value positions are restricted to true features on the left, to null features on the middle, and are not restricted on the right. Each cross is a searched pair. X axis is \( \rho \) and y axis is \( p_0 \). Interpolation is used to to draw the constant power lines.

5 Simulation Experiments

Because of the difficulty of obtaining ground truth variables in real world datasets simulation studies are commonly used in the model-x knockoffs literature (Candes et al. 2017; Barber and Candès 2015; Nguyen et al. 2020). We’re currently working on applications in genomics datasets with missing values which require domain specific treatments and interpretation. Therefore, we have found it not suited to the scope of this paper.

In our experiments, we have investigated the effect of missing values in the knockoffs framework by simulating a variable selection problem in different settings. The simulations are divided into two categories based on the probability distribution of the exploratory variables, namely multivariate normal (MVN) distributed and HMM distributed simulations.

Simulation Setup, Response Distribution: Throughout our experiments, we have followed the simulations of (Sesia et al. 2019) and used a Logistic Regression model as the response conditional distribution. In our simulations, we have also simulated missing data in the exploratory variables. Let \( X \) be a random vector with a specified \( P_X \), \( \beta^* \in \mathbb{R}^p \) and \( \sigma \) denotes the sigmoid function. The response variable is given by:

\[
Y \sim \text{Bernoulli}(p = \sigma(X^T \beta^*)), \quad \beta^*_i = \begin{cases} a, & \text{if } i \in S^* \\ 0, & \text{otherwise} \end{cases}
\]

where \( a \) denotes the amplitude of the coefficient and \( S^* \) denotes the indices of the subset of covariates with non-zero coefficient. The \( |S^*| \) is an experiment parameter and elements of \( S^* \) are randomly selected from \( \{1, \ldots, p\} \) with equal probability and kept the same for different trials.

Missing Values: After generating \( N \) i.i.d samples from \( \{X^{(i)}\}_{i=1}^N \) from \( P_X \), we simulate missing completely at random as follows:

\[
\epsilon_j^{(i)} \sim \text{Bernoulli}(p = 1 - p_0) \quad j = 1, \ldots, p
\]

\[
o^{(i)} = \{j : \epsilon_j^{(i)} = 1, \ j \in M\}
\]

where \( M \subseteq \{1, \ldots, p\} \) denotes the position of the missing values and \( p_0 \) denotes the probability of observing a missing value. The \( N \) i.i.d samples of observed variables and the response variables i.e. \( \{X^{(i)}_{o^{(i)}}, Y^{(i)}\}_{i=1}^N \) are then used as the input to the knockoffs procedure.

Knockoffs Setup: In the model-x knockoffs framework one has to specify the feature-scorer and the final weighted score of each variable. As the feature-scorer we have used the coefficients of an L1 regularized logistic regression of the concatenated matrix \( [X, \tilde{X}] \) which optimizes the following objective function:
\[ \hat{\beta}, \hat{\beta}_0 = \arg \min_{\beta, \beta_0} \sum_{i=1}^{N} \log(1 + e^{-y_i(\beta^T x^{(i)} + \beta_0)}) + \lambda \| \beta \|_1 \]

In each trial \( \lambda \) is selected using 5-fold cross-validation with area under the curve metric and search space \{1e-10, 1e-2, 1e-1, 1, 1e1\} is used. Let \( \lambda_{cv} \) denote the resulting parameter and \( \hat{\beta}(\lambda_{cv}) \in \mathbb{R}^2p \) denote the estimated coefficients, the feature scores and the final scores are given by: \( i = 1, \ldots, p \)

\[
T_i = |\hat{\beta}(\lambda_{cv})_i| \\
\hat{T}_i = |\hat{\beta}(\lambda_{cv})_{i+p}| \\
W_i = T_i - \hat{T}_i
\]

5.1 MVN Simulations: Correlation and Missing Values

In the MVN simulations, our goal was to observe how the amount the missing data and the correlation among the exploratory variables affected the performance of the developed missing value knockoffs methods. For that reason, following (Barber and Candes 2015; Nguyen et al. 2020) we have used a zero-mean MVN with a special correlation matrix \( \Sigma \) whose \( i \)’th row and \( j \)’th column of \( \Sigma \) is given by \( \Sigma_{ij} = \rho^{i-j} \). By that way we’re able to control the correlation amount with a single parameter \( \rho \in (0, 1) \). Another question we had was whether where the missing value occurs affected the performance. For that reason we used three different missing value configurations. In the first and the second experiments the missing values are restricted to occur at the true variables (\( M = S^t \)) and the null variables (\( M = \{1, \ldots, p\} \setminus S^t \)) respectively. While in the third experimental setting we didn’t restrict the location (\( M = \{1, \ldots, p\} \)). In each experiment setting, we have searched the grid of different missing value amounts (\( p_0 = \{0, 0.1, \ldots, 0.4\} \)), and correlation values (\( \rho = \{0, 0.1, \ldots, 0.8\} \)) to investigate the bivariate relationship.

Other experimental parameters we selected are as follows: we have used \( p = 700 \) different exploratory variables and set \( N = 1050 \) which is slightly higher than \( p \). Six \% of the variables are selected as true i.e. | \( S^t \) | = 42 and the effect size is set to \( a = 10/\sqrt{N} = 0.38 \). Each setting in the grid is repeated 31 times to obtain empirical averages. For the knockoff samplers required in Algorithms 1 and 2 we have used the Model-x MVN knockoffs introduced in (Candes et al. 2017) which requires solving a convex optimization problem. To sample from the posterior distribution \( P_{X_{true}|X_{null}} \) (as required in Algorithm 1), we have used the exact inference formulas for the the MVN distribution.

After conducting the experiments, we have observed that the average FDR is generally controlled at the target \( q = 0.1 \) regardless of the missing value pattern, number of missing values, and the correlation amount (Fig 3). We also noticed that as \( \rho \) increased the average power consistently decreased in all three missing value configurations (Fig 1). On the contrary, the the affect of missing value amount (\( p_0 \)) depended on the missingness pattern. Specifically when the missing values are not restricted or are restricted to the true variables, increasing the number of missing values (\( p_0 \)) decreased the power (Fig 1 left and right). But when the missing values are restricted to the nulls, the power didn’t change with \( p_0 \) in almost all configurations and only decreased when \( \rho = 0.7 \) and \( \rho = 0.8 \) (Fig 1 centre). Interestingly although the third setting (Fig 1 right) has missing values on the null variables in addition to the missing values on the true variables it’s performance is similar to the setting where missing values are restricted to the true variables (Fig 1 left).

We have compared the statistical power of posterior and univariate imputation knockoffs in three experiments with different missing value patterns (Fig 2). In the setting where the missing values occur only in the null features, we have observed an interesting phenomena. Despite having theoretically higher MSE than posterior imputation, univariate imputation had higher statistical power (Fig 2 centre). The gap became even more visible when we increased the amount of correlation and missing values. The results suggests that the imputation quality of the null features may be insignificant and univariate imputation by removing the correlation between the nulls and the true variables can increase the power.

In the first and the most realistic third experimental settings where the missing values are allowed to occur on the true variables, the posterior imputation has an advantage (Fig 2 left and right). That advantage is less visible for lower \( \rho \) values and one reason is the MSE of the posterior imputations depends on \( \rho \). As \( \rho \) increases, the conditional variance of the missing values decreases. That doesn’t change the MSE of the univariate imputation but translates into a to lower MSE for the posterior imputation. As \( \rho \) increases further the power difference starts to shrink again, possibly because of resulting intrinsically difficulty problem. The results in the third experimental setting (Fig 2 right) suggest that, having lower MSE on the imputed true variables is more beneficial than removing the correlation of the null variables.
Another comparison we made was between the three readily available imputation methods and the methods we introduced. Those three methods are K-nearest neighbour (KNN) imputation (Troyanskaya et al. 2001), SoftImpute (Mazumder et al. 2010), and sample mean imputation. We have used scikit-learn for KNN imputation which fills the missing values of a row by the average of the closest (in Euclidean geometry) K rows (Pedregosa et al. 2011) and sample mean imputation which imputes the missing values with the column’s sample mean. SoftImpute, implemented in (Rubinsteiny 2021) fancyimpute package, is an SVD decomposition-based iterative matrix completion algorithm. We have used the third experimental setting i.e. no restriction on the position of missing values.

We have observed that the off-the-shelf methods had generally higher power than the posterior and univariate methods (Figure 4 left). Despite the three off-the-shelf methods violate the independence assumption of the rows and the equality between the distributions $P_{\hat{X}}$ and $P_X$, we observed that they control the FDR (Figure 4 right). That can possibly be due to $P_{\hat{X}}$ being “close” to $P_X$ in our experiments, and the robustness of the knockoffs framework (Barber et al. 2019). More experimentation with different predictor and target distributions can help to understand the conditions of FDR control with off-the-shelf imputation methods.

5.2 HMM simulations: Compensating Missing Values

As the knockoffs method supports an arbitrary $P_X$ so does the missing value knockoffs. To show that, in this simulation we used an HMM distribution which also has applications in modeling the distribution of genetic markers in the human genome (Sesia et al. 2019). Our second goal was to quantify the affect of changing the missing value amount $p_0$ and the observation amount $N$ simultaneously. To observe that in detail we have done a fine grid search with parameter spaces $p_0 = \{0, 0.05, \ldots, 0.5\}$ and $N = \{500, 625, 750, \ldots, 2000\}$. We also increased number of simulation repetitions to 128 for a clearer picture of the performance.

The HMM distribution is specified following the simulations in (Sesia et al. 2019). The emission and trasmission matrices are given in Appendix D.1.

Before using the exploratory variables for simulating the response variable to shift their values around to zero we subtract 4 as in (Sesia et al. 2019). We have restricted the missing values to true indices and the remaining experiment parameters are given as: $p = 1000$, $\alpha = 0.32$, $|S| = 60$.

We have only tested posterior imputation (Algorithm 1) in this setting and used the Sesia HMM Knockoffs (Sesia et al. 2019) for sampling the knockoffs. We refer to this combination as posterior sampling + Sesia HMM. HMM structure allows sampling from $P_{X_m|X_s}$ by first sampling from $P_{Z|X_s}$ then sampling from $P_{X_m|Z}$. We also compared Algorithm 1 with our modified Sesia HMM Knockoffs (Algorithm 3).

The experiment results showed that the posterior imputation knockoffs almost always controlled the FDR at the target level ($q = 0.1$) irrespective of the amount of missing values and observations (Fig. 5 right). We also observed that...
increasing the amount of observations ($N$) increased the statistical power while increasing the amount of missing values ($p_0$) decreased it (Fig. 5 left). As a matter fact as $p_0$ got closer to 0.45 the power reduced to 0 irrespective of $N$.

As the amount of missing data and the number of observations both have contradicting affects on the statistical power, a natural question arises as whether the power can be kept constant. As an example, 2000 samples with 15% missing values have power comparable to 1125 samples. For that purpose we have drawn the constant power contours (Fig. 6). We have observed that the constant power contours are not linear and tolerating a increase in missing value amount gets more challenging. For example, when $N = 1000$ to tolerate an increase in $p_0$ by one unit, additional two units of
samples are required. However, when \( N = 1625 \) to compensate a one unit increase in \( p_0 \), three units of samples are required.

We observed that Algorithm 3 also controlled the FDR control (Appendix Fig. 7 right). In terms of power it’s difficult to distinguish the Algorithm 3 and Algorithm 1 (Fig. 6). That suggests the computational advantages of Algorithm 3 do not have a shortcoming in performance.

![Figure 4: Comparison of different imputation methods. Left column is power vs \( \rho \) and right column is FDR vs \( \rho \). Rows corresponds to different amounts of missing data. From top to bottom \( p_0 \) takes the values \( \{0.2, 0.4\} \). The corresponding color and line style of the imputation methods are denoted in the legend. The full figure is given in Appendix Figure 8.](image)

![Figure 5: Heatmap of power on the left, FDR on right. The posterior imputation + Sesia HMM Knockoffs is used (Algorithm 1). On the left darker red (blue) indicates higher (lower) power. On the right values above \( q = 0.1 \) are red and below are blue.](image)

6 Discussion

In this work, we have shown how to impute the missing values while preserving the guarantees of the model-x knockoffs method. We have proved that posterior imputation allows using the existing knockoffs setups without changing them in the missing data setting. The second method we introduced, univariate sampling is an alternative that allows...
using model-x knockoffs with missing values when the posterior sampling is not available. Moreover, we also shown how the computational requirements can be reduced when the imputation and the knockoff sampling are done jointly. To do that we have have modified two latent variable knockoff samplers to work with missing values while preserving the FDR.

Our experiments also demonstrate that FDR control is possible under the knockoffs methodology even when missing values are imputed. In the simulations, we first investigated the bivariate affect of correlation and missing data mount on the statistical power and FDR. Next, through the constant power contours we have quantified the amount of additional data required for mitigating the affects of missing values.

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We denote $X$ as a $p$-dimensional random vector, $Y$ a R.V., $X_j$ $j$'th R.V. of $X$, and $X_{-j} = \{X_l : l \neq j\}$. Given set $M$, $X_M = \{X_l : l \in M\}$ denotes the corresp. R.V.s and the complement of $M$ is denoted by $M' = \{1, \ldots, p\} \setminus M$.

**Definition 2.** Let $M \subseteq \{1, \ldots, p\}$. $X_M$ is the Markov Blanket (MB) of $Y$ if it’s the smallest subset such that

$$Y \perp X_M' \mid X_M$$
Theorem 6. Let $X, Y$ denote two random vector and $X_M$ denote the MB of $Y$. Given $P_{X,Y}(x,y) > 0 \forall x, y$, $Y \not\perp X_i | X_{-i}$ holds iff $i \in M$.

Proof. We start with the direction $Y \not\perp X_i | X_{-i} \Rightarrow i \in M$. Proof by contradiction, assume $i \in M$ and $Y \perp X_i | X_{-i}$. Then, $\forall x, y$

$$P_{Y|X_{-i}}(y;x-i) = P_{Y|X}(y;x) \quad (1a)$$
$$P_{Y|X_{-i}}(y;x-i) = P_{Y|X,M}(y;x_M) \quad (1b)$$
$$P_{Y,X_{-i}}(y,x-i) = P_{Y|X,M}(y;x_M)P_{X_{-i}}(x-i) \quad (1c)$$
$$\sum_{x_M'} P_{Y,X_{-i}}(y,x-i) = \sum_{x_M'} P_{Y|X,M}(y;x_M)P_{X_{-i}}(x-i) \quad (1d)$$
$$\sum_{x_M'} P_{Y,X_M',X_M\setminus\{i\}}(y,x_M',x_M\setminus\{i\}) = P_{Y|X,M}(y;x_M)\sum_{x_M'} P_{X_M',X_M\setminus\{i\}}(x_M',x_M\setminus\{i\}) \quad (1e)$$
$$P_{Y,X_M\setminus\{i\}}(y,x_M\setminus\{i\}) = P_{Y|X,M}(y;x_M)P_{X_M\setminus\{i\}}(x_M\setminus\{i\}) \quad (1f)$$
$$P_{Y|X_M\setminus\{i\}}(y|x_M\setminus\{i\}) = P_{Y|X,M}(y;x_M) \quad (1g)$$
$$= P_{Y|X}(y;x) \quad (1i)$$

The explanation of the properties used in each line of Eq. 1:

(a) $Y \perp X_i | X_{-i}$
(b) Definition of Markov Blanket
(c) Definition of conditional probability
(d) Strict positivity
(e) Both sides summed
(f) Constant outside the summation, splitting the variables using $i \in M$
(g) Total law of probability
(h) Definition of conditional probability
(i) Definition of Markov Blanket

Eq. 1 implies $Y \perp X_{(M\setminus\{i\})'} | X_{M\setminus\{i\}}$ which contradicts the assumption that $M$ is the MB of $Y$ since cardinality of $M \setminus \{i\}$ is one less than of $M$. Note if we use integration instead of the summation the proof can be used for the continuous R.Vs. An alternative proof for the discrete R.Vs can be done using the Intersection condition in [Pearl 1988].

We next proceed to proving the second direction $i \in M \Rightarrow Y \not\perp X_i | X_{-i}$. We use proof by contradiction and assume $i \notin M$.

$$Y \perp X_M | X_M$$
$$\Rightarrow Y \perp X_{M\setminus\{i\}} | X_{-i} \quad (2)$$

The first implication follows from marginalizing $X_i$. The next one follows from the strict positiveness and $x_{M\cup M'\setminus\{i\}} = x_{-i}$. 

$\blacksquare$
B Proofs

B.1 Theorem 2

Proof of Theorem 2

\[ P_{\hat{X},\hat{X}}((\hat{x}, \hat{\tilde{x}})_{\text{swap}(S)}) = P_{X_o,\hat{X}}((x_o, \hat{x})_{\text{swap}(S)}; o) \prod_{j \in S} P_{\hat{X}_{m_j}}(\hat{x}_{m_j})P_{\tilde{X}_{m_j}}(\tilde{x}_{m_j}) \prod_{j \notin S} P_{\hat{X}_{m_j}}(\hat{x}_{m_j})P_{\tilde{X}_{m_j}}(\tilde{x}_{m_j}) \]

From MCAR assumption we have \( P_{\hat{X}_o} = P_\theta \). \( \hat{x} \) follows from the definition of the swap operator and the univariate sampling of the imputed missing values. \( 3b \) follows from \( P_{\hat{X}_o|X_o} \) being a pairwise exchangeable distribution with respect to \( P_{X_o} \) and \( P_{\tilde{X}_{m_j}} = P_{\hat{X}_{m_j}} \).

B.2 Proof of Lemma 1

Proof of Lemma 1

We first prove it for MCAR setting. Let \( \mathcal{R} := \{r \in \{0, 1\}^p : P_{\hat{X},R}(\hat{x}, r) > 0\}, \forall \hat{x} \)

\[ P_{\hat{X}}(\hat{x}) = \sum_{r \in \mathcal{R}} P_{\hat{X}|R}(\hat{x}; r)P_R(r) \]

\[ = \sum_{r \in \mathcal{R}} P_{\hat{X}_m|X_o,R}(\hat{x}_m; \hat{x}_o, r)P_{X_o|R}(\hat{x}_o; r)P_R(r) \] \( \tag{4a} \)

\[ = \sum_{r \in \mathcal{R}} P_{\hat{X}_m|X_o,R}(\hat{x}_m; \hat{x}_o, r)P_{X_o|R}(\hat{x}_o; r)P_R(r) \] \( \tag{4b} \)

\[ = \sum_{r \in \mathcal{R}} P_{X_m|R}(\hat{x}_m; \hat{x}_o)P_{X_o}(\hat{x}_o)P_R(r) \] \( \tag{4c} \)

\[ = \sum_{r \in \mathcal{R}} P_{X_m|R}(\hat{x}_m; \hat{x}_o)P_{X_o}(\hat{x}_o)P_R(r) \] \( \tag{4d} \)

\[ = \sum_{r \in \mathcal{R}} P_{X_m|R}(\hat{x}_m; \hat{x}_o)P_{X_o}(\hat{x}_o)P_R(r) \] \( \tag{4e} \)

\[ = P_{X_m|R}(\hat{x}_m; \hat{x}_o)P_{X_o}(\hat{x}_o) \]

\[ = P_X(\hat{x}) \] \( \tag{4f} \)

\( \hat{x} \) follows from law of total probability and chain rule. \( \hat{x} \) follows from \( m = \{i : R_i = 1\} \) and \( o = \{i : R_i = 0\} \). \( \hat{x} \) uses \( \hat{X}_o = X_o \). \( \hat{x} \) follows from posterior sampling and MCAR i.e. \( X \perp\!\!\!\!\perp R \). We next proceed with the more general MAR setting. \( \forall \hat{x} \)

\[ P_{\hat{X}}(\hat{x}) = \sum_{r \in \mathcal{R}} P_{X_m|R}(\hat{x}_m; \hat{x}_o)P_{X_o|R}(\hat{x}_o; r)P_R(r) \] \( \tag{5a} \)

\[ = \sum_{r \in \mathcal{R}} P_{X_m|R}(\hat{x}_m; \hat{x}_o)P_{X_o|R}(\hat{x}_o; r)P_R(r) \] \( \tag{5b} \)

\[ = \sum_{r \in \mathcal{R}} P_{X,R}(\hat{x}, r) \] \( \tag{5c} \)

\[ = P_X(\hat{x}) \] \( \tag{5d} \)

\( \hat{x} \) follows from the posterior sampling. \( \hat{x} \) follows from MAR assumption i.e. \( X_m \perp\!\!\!\!\perp R \mid X_o \) and \( P_{X_o,R}(x_o, r) > 0 \). \( \forall \hat{x} \) implies \( P_{X_o,R}(\hat{x}_o, r) > 0 \) which implies \( P_{X_o,R}(x_o, r) > 0 \). The \( P_{X_m|X_o} = P_{X_m|X_o,R} \) property was inspired by the Example 2 of Section 3.1.1. (Mohan 2017).
B.3 Theorem 3

We begin with proving two lemmas.

Lemma 2. Let $Y$ denote a R.V and $X$ denote a random vector. Let $\hat{Y}$ denote the estimate resulting from posterior sampling (as in Algorithm 1) i.e. $\hat{Y} \sim P_{Y \mid X}(\cdot ; X)$. It’s MSE is given by:

$$E[(Y - \hat{Y})^2] = 2(\text{Var}(Y) - \text{Var}(E[Y \mid X]))$$

Proof.

$$E[(Y - \hat{Y})^2 \mid X] = E[Y^2 \mid X] + E[\hat{Y}^2 \mid X] - 2E[Y \mid X]E[\hat{Y} \mid X]$$
$$= 2E[Y^2 \mid X] - 2E[Y]^2$$
$$= 2\text{Var}(Y \mid X)$$

(6a)
(6b)
(6c)

The first line uses $Y \perp \perp \hat{Y} \mid X$ and expectation is a linear operator. The second line uses $Y \overset{d}{=} \hat{Y}$.

$$E[(Y - \hat{Y})^2] = E[E[(Y - \hat{Y})^2 \mid X]]$$
$$= 2E[\text{Var}(Y \mid X)]$$
$$= 2(\text{Var}(Y) - \text{Var}(E[Y \mid X]))$$

(7a)
(7b)
(7c)

The first line uses law of iterated expectations and the last line uses the law of total variance.

Lemma 3. Let $Y$ denote a R.V and $Y'$ denote the estimate resulting from univariate sampling (as in Algorithm 2) i.e. $Y' \sim P_Y(\cdot)$. It’s MSE is given by:

$$E[(Y - Y')^2] = 2\text{Var}(Y)$$

Proof.

$$E[(Y - Y')^2] = E[Y^2] + E[Y'^2] - 2E[Y]E[Y']$$
$$= 2E[Y^2] - 2E[Y]^2$$
$$= 2\text{Var}(Y)$$

(8a)
(8b)
(8c)

The first line uses $Y \perp \perp \hat{Y}$ and expectation is a linear operator. The second line follows from $Y \overset{d}{=} Y'$.

Proof of Theorem 3 From Lemma 2 and 3 $E[(Y - \hat{Y})^2] \leq E[(Y - Y')^2]$}

B.4 Theorem 4

We first prove a useful Lemma.

Lemma 4. Given random vectors $X_m, X_o, Z$, let $\hat{Z} \sim P_{Z \mid X_o}(\cdot ; X_o)$ and $\hat{X}_m \sim P_{X_m \mid Z}(\cdot ; \hat{Z})$. If $X_m \perp \perp X_o \mid Z$, then $P_{X_m \mid X_o}(\hat{x}_m; x_o) = P_{X_m \mid X_o}(\hat{x}_m; x_o)$ holds for all $\hat{x}_m, x_o$.

Proof of Lemma 4 Let $Z := \{z : P_{\hat{X}_m, \hat{Z} \mid X_o}(\hat{x}_m, \hat{z} ; x_o) > 0\}$


\[ P_{X_m|X_o}(\hat{x}_m; x_o) = \sum_{\hat{z} \in \tilde{Z}} P_{X_m,\tilde{Z}|X_o}(\hat{x}_m, \hat{z}; x_o) \]  
(9a)

\[ = \sum_{\hat{z} \in \tilde{Z}} P_{X_m|\tilde{Z},X_o}(\hat{x}_m; \hat{z}, x_o) P_{\tilde{Z}|X_o}(\hat{z}; x_o) \]  
(9b)

\[ = \sum_{\hat{z} \in \tilde{Z}} P_{X_m|\tilde{Z},X_o}(\hat{x}_m; \hat{z}) P_{\tilde{Z}|X_o}(\hat{z}; x_o) \]  
(9c)

\[ = \sum_{\hat{z} \in \tilde{Z}} P_{X_m|\tilde{Z},X_o}(\hat{x}_m; \hat{z}) P_{\tilde{Z}|X_o}(\hat{z}; x_o) \]  
(9d)

\[ = \sum_{\hat{z} \in \tilde{Z}} P_{X_m|\tilde{Z},X_o}(\hat{x}_m; \hat{z}) P_{\tilde{Z}|X_o}(\hat{z}; x_o) \]  
(9e)

\[ = \sum_{\hat{z} \in \tilde{Z}} P_{X_m|\tilde{Z},X_o}(\hat{x}_m; \hat{z}, x_o) P_{\tilde{Z}|X_o}(\hat{z}; x_o) \]  
(9f)

\[ = \sum_{\hat{z} \in \tilde{Z}} P_{X_m|\tilde{Z},X_o}(\hat{x}_m; \hat{z}, x_o) \]  
(9g)

\[ = P_{X_m|X_o}(\hat{x}_m; x_o) \]  
(9h)

The equality \( P_{X_m|z} = P_{X_m|z,X_o} \) used in (9b) follows from \( X_m \perp X_o \mid z \) and \( z \in \tilde{Z} \). Because \( z \in \tilde{Z} \) implies \( P_{\tilde{Z},X_o}(\hat{z}, x_o) > 0 \) which then implies \( P_{\tilde{Z},X_o}(\hat{z}, x_o) > 0 \).

Proof of Theorem 5: Algorithm 3 uses \( \tilde{Z} \sim P_{\tilde{Z}|X_o}(\cdot ; X_o) \) and \( \hat{x}_m \sim P_{X_m|z}(\cdot ; \tilde{Z}) \). Therefore, from Lemma 4 we have \( P_{X_m|X_o}(\hat{x}_m; x_o) = P_{X_m|X_o}(\hat{x}_m; x_o) \) for all \( \hat{x}_m, x_o \). Then, combining that with Lemma 4 results in \( P_X = P_{\hat{X}} \) as MAR or MCAR holds.

\[ P_{X,\tilde{Z}|Z}(\hat{x}, \tilde{x}, \hat{z}, \tilde{z}) = P_{X_o|\tilde{Z}}(\tilde{x}_o; \tilde{z}') P_{X_m|Z}(\hat{x}_m; \tilde{z}) P_{\tilde{Z}|X}(x; \hat{z}) P_{\tilde{Z}|Z}(\hat{z}; \tilde{z}) \]  
(10a)

\[ = P_{X_o|\tilde{Z}}(\tilde{x}_o; \tilde{z}') P_{X_m|Z}(\hat{x}_m; \tilde{z}) P_{\tilde{Z}|X}(x; \hat{z}) P_{\tilde{Z}|Z}(\hat{z}; \tilde{z}) \]  
(10b)

\[ = P_{Z'}(z'; \tilde{z}) \prod_{i \in o} P_{X_i|Z_i}(x_i; \tilde{z}_i) \prod_{i \in m} P_{X_i|Z_i}(\tilde{x}_i; \tilde{z}_i) \prod_{i=1}^p P_{X_i|Z_i}(\tilde{x}_i; z_i) \]  
(10c)

\[ P_{\tilde{Z}, Z'}(z', \tilde{z})_{\text{swap}(S)}, (\tilde{z}', z')_{\text{swap}(S)}) = P_{Z'}(z'; \tilde{z})_{\text{swap}(S)} \prod_{i \in S} P_{X_i|Z_i}(x_i; \tilde{z}_i) \prod_{i \in o \setminus S} P_{X_i|Z_i}(\tilde{x}_i; \tilde{z}_i) \prod_{i \in m \setminus S} P_{X_i|Z_i}(\tilde{x}_i; \tilde{z}_i) \prod_{i \in \tilde{S}} P_{X_i|Z_i}(\tilde{x}_i; \tilde{z}_i) \prod_{i \in \tilde{S}} P_{X_i|Z_i}(x_i; \tilde{z}_i) \prod_{i \in \tilde{S}} P_{X_i|Z_i}(\tilde{x}_i; \tilde{z}_i) \prod_{i \in \tilde{S}} P_{X_i|Z_i}(x_i; \tilde{z}_i) \prod_{i \in \tilde{S}} P_{X_i|Z_i}(\tilde{x}_i; \tilde{z}_i) \]  

\[ P_{Z'}(z'; \tilde{z})_{\text{swap}(S)} = P_{Z'}(z'; \tilde{z}) \] follows from \( P_{\tilde{Z}|Z} \) is pairwise exchangeable with respect to \( P_Z \).

B.5 Theorem 5

To prove Theorem 5, we start by proving the following lemmas. For notational convenience if \( k > l \) or \( l < k \), \( Z_{k:l} \) is omitted from a function ex: \( P_{X,Z_{k:l}}(x, z_{k:l}) = P_X(x) \).
Lemma 5. Let us define:

\[ g_i(\hat{z}_{i+1:T}, z', x) := \sum_{\hat{z}_i} P_{Z|X,Z_{i+1:T},Z_{1:i-1}}(z'_i; x, \hat{z}_{i+1:T}, z'_{1:i-1}) g_{i-1}(\hat{z}_{i:T}, z', x), \forall i = 2, \ldots, T \]

\[ g_1(\hat{z}_{2:T}, z', x) := \sum_{\hat{z}_i} P_{Z|X,Z_{2:T}}(z'_1; x, \hat{z}_{2:T}) P_{X}(\hat{z}, x) \]

Then, \( \forall i = 1, \ldots, T \) and \( \hat{z}, z', x \)

\[ g_i(\hat{z}_{i+1:T}, z', x) = P_{Z_{1:i}, Z_{i+1:T}, X}(z'_{1:i}, \hat{z}_{i+1:T}, x) \]

Proof. Proof by induction

Base: \( \forall \hat{z}, z', x \)

\[ g_1(\hat{z}_{2:T}, z', x) = P_{Z_{1:1}, Z_{1:T}, X}(z'_1, \hat{z}_{1:T}, x) \]

(11)

(11b) follows from law of total probability. (11c) follows from definition of conditional probability.

Step k:

From step k-1, we have: \( \forall \hat{z}, z', x \)

\[ g_{k-1}(\hat{z}_{k:T}, z', x) = P_{Z_{1:k-1}, Z_{k:T}, X}(z'_{1:k-1}, \hat{z}_{k:T}, x) \]

Then, \( \forall \hat{z}, z', x \)

\[ g_k(\hat{z}_{k+1:T}, z', x) = P_{Z_{k}|X,Z_{k+1:T},Z_{1:k-1}}(z'_k; x, \hat{z}_{k+1:T}, z'_{1:k-1}) \sum_{\hat{z}_k} g_{k-1}(\hat{z}_{k:T}, z', x) \]

\[ = P_{Z_{k}|X,Z_{k+1:T},Z_{1:k-1}}(z'_k; x, \hat{z}_{k+1:T}, z'_{1:k-1}) P_{Z_{1:k-1}, Z_{k+1:T}, X}(z'_{1:k-1}, \hat{z}_{k+1:T}, x) \]

\[ = P_{Z_{1:k}, Z_{k+1:T}, X}(z'_{1:k}, \hat{z}_{k+1:T}, x) \]

(12a)

(12b)

(12c)

(12b) follows from step k-1 and total law of probability. (12c) follows from definition of conditional probability.

Lemma 6. Let \( Z' \) sampled as in Algorithm \( 4 \) then \( \forall i = 1, \ldots, T \) and \( \forall \hat{z}, z', x \)

\[ \sum_{\hat{z}_i} P_{Z'|X,\hat{z}}(z'; x, \hat{z}) P_{X}(\hat{z}, x) = g_i(\hat{z}_{i+1:T}, z', x) \prod_{i=0}^{T-1} P_{Z_{T-i}|X,Z_{T-i+1:T},Z_{1:T-i-1}}(z'_{T-i}; x, \hat{z}_{T-i+1:T}, z'_{1:T-i-1}) \]

Proof. Proof by induction:

Base: \( \forall \hat{z}, z', x \)
\[
\sum_{\hat{z}_{i}} P_{Z|X,\hat{Z}}(z'; x, \hat{z}) P_{X,\hat{Z}}(x, \hat{z}) \\
= \sum_{\hat{z}_{i}} P_{X,Z}(x, \hat{z}) \prod_{i=0}^{T-1} P_{Z_{T-i}|X,\hat{Z},z'_{i},z'_{i-1}}(z'_{T-i}; x, \hat{z}, z'_{1:T-i-1}) \\
= \sum_{\hat{z}_{i}} P_{X,Z}(x, \hat{z}) \prod_{i=0}^{T-1} P_{Z_{T-i}|X,Z_{T-i+1:T},z_{1:T-i-1}}(z'_{T-i}; x, \hat{z}_{T-i+1:T}, z'_{1:T-i-1}) \\
= \prod_{i=0}^{T-2} P_{Z_{T-i}|X,Z_{T-i+1:T},z_{1:T-i-1}}(z'_{T-i}; x, \hat{z}_{T-i+1:T}, z'_{1:T-i-1}) \sum_{\hat{z}_{1}} P_{X,Z}(x, \hat{z}) P_{Z_{1}|X,Z_{2:T}}(z'_{1}; x_{1}, \hat{z}_{2:T}) \\
= g_1(\hat{z}_{2:T}, z', x) \prod_{i=0}^{T-2} P_{Z_{T-i}|X,Z_{T-i+1:T},z_{1:T-i-1}}(z'_{T-i}; x, \hat{z}_{T-i+1:T}, z'_{1:T-i-1})
\]

\[13\text{b} \text{ from chain law.} \textbf{13c} \text{ follows from definition of sampling. In} \textbf{13d} \text{ the only term that depends on} \hat{z}_{1} \text{ is} P_{X,Z}. \textbf{In 13e} \text{ the definition of} g_1 \text{ is used (as defined in Lemma 5).}
\]

**Step k:** \(\forall \hat{z}, z', x \)

\[
\sum_{\hat{z}_{k}} \sum_{\hat{z}_{k-1}} P_{Z|X,\hat{Z}}(z'; x, \hat{z}) P_{X,Z}(x, \hat{z}) \\
= \sum_{\hat{z}_{k}} g_{k-1}(\hat{z}_{k:T}, z', x) \prod_{i=0}^{T-k-1} P_{Z_{T-i}|X,Z_{T-i+1:T},z_{1:T-i-1}}(z'_{T-i}; x, \hat{z}_{T-i+1:T}, z'_{1:T-i-1}) \\
= \prod_{i=0}^{T-k-1} P_{Z_{T-i}|X,Z_{T-i+1:T},z_{1:T-i-1}}(z'_{T-i}; x, \hat{z}_{T-i+1:T}, z'_{1:T-i-1}) \sum_{\hat{z}_{k}} g_{k-1}(\hat{z}_{k:T}, z', x) P_{Z_{k}|X,Z_{k+1:T},z_{k-1}}(z'_{k}; x, \hat{z}_{k+1:T}, z'_{1:T-1}) \\
= g_{k}(\hat{z}_{k+1:T}, z', x) \prod_{i=0}^{T-k-1} P_{Z_{T-i}|X,Z_{T-i+1:T},z_{1:T-i-1}}(z'_{T-i}; x, \hat{z}_{T-i+1:T}, z'_{1:T-i-1})
\]

\[14\text{b} \text{ follows from reordering of notation.} \textbf{14c} \text{ holds as step k-1 is assumed to hold. In step 14d and 14e only term depends on} \hat{z}_{k} \text{ is} g_{k-1}. \textbf{In step 14f}, \text{ the definition of} g_{k} \text{ is used (as defined in Lemma 5).}
\]

**Proof of Theorem 5:** In Algorithm 4, \(\hat{Z} \sim P_{Z|X,\cdot} (\cdot; X_{o})\) and \(\hat{X}_{m} \sim P_{X_{m}|Z} (\cdot; \hat{Z})\) is used. Combining Lemma 4 and Lemma 1 we have \(P_{X} = P_{X} \) under the MAR or MCAR assumption.

We prove another required equality. \(\forall \hat{x}, \hat{z}, z' \)

\[
P_{Z,X}(\hat{z}, \hat{x}) = P_{X_{m}|Z}(\hat{x}_{m}; \hat{z}) P_{Z|X_{o}}(\hat{z}; x_{o}) P_{X_{o}}(x_{o}) \\
= P_{X_{m}|Z}(\hat{x}_{m}; \hat{z}) P_{Z|X_{o}}(\hat{z}; x_{o}) P_{X_{o}}(x_{o}) \\
= P_{X_{m}|Z}(\hat{x}_{m}; \hat{z}) P_{X_{o}|Z}(x_{o}; \hat{z}) P_{Z}(\hat{z}) \\
= P_{Z,X}(\hat{z}, \hat{x})
\]

\[15\text{b} \text{ follows from chain rule and} \textbf{15c} \text{ follows from sampling definitions.} \textbf{15d} \text{ follows from definition of conditional independence.} \]
\begin{equation}
P_{\hat{X}, \check{X}, Z}(\hat{x}, \check{x}, z') = P_{\hat{X}|Z}(\hat{x}; z') \sum_{\hat{z}} P_{Z'|\hat{Z}, \check{X}}(z'; \hat{z}, \check{x}) P_{\hat{Z}, \check{X}}(\hat{z}, \check{x}) \tag{16a}
\end{equation}

\begin{equation}
P_{\hat{X}|Z}(\hat{x}; z') \sum_{\hat{z}} P_{Z'|\hat{Z}, \check{X}}(z'; \hat{z}, \check{x}) P_{\hat{Z}, \check{X}}(\hat{z}, \check{x}) \tag{16b}
\end{equation}

\begin{equation}
P_{\hat{X}|Z}(\hat{x}; z') \sum_{\hat{z}} P_{Z'|\hat{Z}, \check{X}}(z'; \hat{z}, \check{x}) P_{\hat{Z}, \check{X}}(\hat{z}, \check{x}) \tag{16c}
\end{equation}

\begin{equation}
P_{Z}(z') \prod_{i \in o} P_{X_i|Z}(\hat{x}_i; z') \prod_{i \in m} P_{X_i|Z}(\hat{x}_i; z') \prod_{i=1}^p P_{X_i|Z}(\hat{x}_i; z') \tag{16d}
\end{equation}

\begin{equation}
P_{Z}(z') \prod_{i \in o} P_{X_i|Z}(\check{x}_i; z') \prod_{i \in m} P_{X_i|Z}(\check{x}_i; z') \prod_{i=1}^p P_{X_i|Z}(\check{x}_i; z') \tag{16e}
\end{equation}

In (16b), \(P_{X_i|Z} = P_{\hat{X}|Z}\) follows from the sampling definitions and Eq. (15) is used for the joint distribution equality. In (16c), Lemma 6 is used. In (16d), Lemma 5 and (16e) follows from the conditional independence assumption assumed in Theorem 5.

\begin{equation}
P_{\hat{X}, \check{X}, Z}(\hat{x}, \check{x}, z') = P_{Z}(z') \prod_{i \in o} P_{X_i|Z}(\hat{x}_i; z') \prod_{i \in m} P_{X_i|Z}(\check{x}_i; z') \prod_{i \in o} P_{X_i|Z}(\hat{x}_i; z') \prod_{i \in m} P_{X_i|Z}(\check{x}_i; z') \prod_{i=1}^p P_{X_i|Z}(\hat{x}_i; z') \prod_{i \in m} P_{X_i|Z}(\check{x}_i; z') \prod_{i=1}^p P_{X_i|Z}(\check{x}_i; z') \tag{16f}
\end{equation}

The first equality uses Eq. (16) with the swap definition applied to each factor in Eq. (16e). The second equality follows grouping the variables. Pairwise exchangeability of \(\hat{X}, \check{X}\) follows as above statement holds for all \(z'\). For continuous variables summations can be replaced with integrations.

\end{document}
C  HMM Latent Variable Posterior Sampling

Given \( x_o \), we define \( o(t) := o \cap \{1, \ldots, t\} \)

Algorithm 5 HMM Latent Posterior Sampling with Missing Values

| Input: \( x_o, P_{Z_1}, P_{X|Z}, P_{Z|Z}, o \) |
| for \( t = 1, \ldots, T \) do |
| if \( t = 1 \) then |
| \( \alpha_t(z_t) \leftarrow P_{Z_1}(z_1) \) |
| else |
| \( \alpha_t(z_t) \leftarrow \sum_{z_{t-1}} P_{Z_t|Z_{t-1}}(z_t | z_{t-1}) \alpha_{t-1}(z_{t-1}) \) |
| end if |
| if \( t \in o \) then |
| \( \alpha_t(z_t) \leftarrow \alpha_t(z_t) P_{X|Z_t}(x_t; z_t) \) |
| end if |
| end for |
| for \( t = T, \ldots, 1 \) do |
| if \( t = T \) then |
| \( \hat{\alpha}_T(z_T; x_o) \leftarrow \frac{\alpha_t(z_t)}{\sum_{z'_T} \alpha_t(z'_T)} \) |
| \( \hat{z}_T \sim P_{Z_T|X_o}(z_T; x_o) \) |
| else |
| \( \hat{z}_t \sim P_{Z_t|Z_{t+1}, X_o(t)}(z_t; z_{t+1}, x_{o(t)}) \) |
| \( \hat{z}_t \sim P_{Z_t|Z_{t+1}, X_o(t)}(z_t; z_{t+1}, x_{o(t)}) \) |
| end if |
| end for |

Output: \( \{\hat{z}_t\}_{t=1}^{T} \)

Lemma 7. If \( \alpha_t(z_t) \) is calculated as in Algorithm 5 then, \( \alpha_t(z_t) = P_{Z_t|X_o(t)}(z_t, x_{o(t)}) \).

Proof. First, assume \( t \neq 1 \) and \( t \in o \), then

\[
P_{Z_t, X_o(t)}(z_t, x_{o(t)}) = P_{Z_t, X_{o(t-1)}}(z_t, x_t, x_{o(t-1)})
\]

\[
= P_{X_t|Z_t}(x_t; z_t) \sum_{z_{t-1}} P_{Z_{t-1}, X_{o(t-1)}}(z_t, z_{t-1}, x_{o(t-1)})
\]

\[
= P_{X_t|Z_t}(x_t, z_t) \sum_{z_{t-1}} P_{Z_{t-1}}(z_t | z_{t-1}) \alpha_{t-1}(z_{t-1})
\]

(17a)

(17b)

(17c)

The second equality uses the chain rule, the conditional independence properties of the HMM, and the total law of probability. The last line again uses the chain rule in combination with the conditional independence properties.

Now assume \( t \neq 1 \) and \( t \notin o \), then

\[
P_{Z_t, X_o(t)}(z_t, x_{o(t)}) = P_{Z_t, X_{o(t-1)}}(z_t, x_{o(t-1)})
\]

\[
= \sum_{z_{t-1}} P_{Z_{t-1}, Z_{o(t-1)}}(z_t, z_{t-1}, x_{o(t-1)})
\]

\[
= \sum_{z_{t-1}} P_{Z_t}(z_t | z_{t-1}) \alpha_{t-1}(z_{t-1})
\]

(18)

Now let's assume \( t = 1 \), then

\[
P_{Z_t, X_o(t)}(z_t, x_{o(t)}) = \begin{cases} P_{Z_t, X_1}(z_1, x_1), & \text{if } t \in o \\ P_{Z_t}(z_1), & \text{o.w.} \end{cases}
\]

(19a)

\[
= \begin{cases} P_{X_1}(z_1 | z_1) P_{Z_1}(z_1), & \text{if } t \in o \\ P_{Z_1}(z_1), & \text{o.w.} \end{cases}
\]

(19b)
In Algorithm 5, the Eq. 17 and first case of Eq. 19 are directly used in the first if else statement. Notice that if \( t \in o \) then there is an additional multiplication with \( P_{X_t|Z_t}(x_t; z_t) \) term. That is implemented in Algorithm 5 in an additional if statement.

Lemma 8. Let \( \hat{P}_t|X_o \) and \( \hat{P}_{Z_t|Z_{t+1},X_o(t)} \) denote the probabilities computed in Algorithm 5 then \( \hat{P}_{Z_t|Z_{t+1},X_o(t)} = P_{Z_t|Z_{t+1},X_o(t)} \) and \( \hat{P}_t|X_o = P_t|X_o \)

Proof.

\[
P_{Z_t|Z_{t+1},X_o(t)}(z_t; z_{t+1}, x_{o(t)}) = \frac{P_{Z_t,Z_{t+1},X_o(t)}(z_t, z_{t+1}, x_{o(t)})}{P_{Z_{t+1},X_o(t)}(z_{t+1}, x_{o(t)})} \tag{20a}
\]

\[
= \frac{P_{Z_{t+1}|Z_t}(z_{t+1}; z_t) \alpha_t(z_t)}{\sum_{z_t'} P_{Z_{t+1}|Z_t}(z_{t+1}; z_t') \alpha_t(z_t')} \tag{20b}
\]

\[
= P_{Z_t|Z_{t+1},X_o(t)}(z_t; z_{t+1}, x_{o(t)}) \tag{20c}
\]

The first line follows from the definition of conditional probability. The second line uses chain rule, conditional independence of the HMM and \( \alpha_t(z_t) = P_{Z_t,X_o(t)}(z_t, x_{o(t)}) \) from Lemma 7. Similarly,

\[
P_{Z_t|X_o}(z_t; x_o) = \frac{P_{Z_t,X_o}(z_T, x_o)}{P_{X_o}(x_o)} = \frac{\alpha_T(z_T)}{\sum_{z_T'} \alpha_T(z_T')} \tag{21b}
\]

Theorem 7. Let \( \hat{Z} \) denote the output of Algorithm 5 with the input \( X_o \), then \( \hat{P}_t|X_o = P_t|X_o \).

Proof. First, we factor \( P_{Z|X_o} \) using the conditional independence of the HMM.

\[
P_{Z|X_o}(z; x_o) = P_{Z_t|X_o}(z_T; x_o) \prod_{t=1}^{T-1} P_{Z_t|Z_{t+1:T},X_o}(z_t; z_{t+1:T}, x_o) \tag{22a}
\]

\[
= P_{Z_t|X_o}(z_T; x_o) \prod_{t=1}^{T-1} P_{Z_t|Z_{t+1},X_o(t)}(z_t; z_{t+1}, x_{o(t)}) \tag{22b}
\]

The first line follow from the chain rule and the second one from the d-separation applied to the HMM graph. The resulting \( P_{Z|X_o} \) can be factored using the sampling structure as follows:

\[
P_{Z|X_o}(z; x_o) = P_{Z|X_o}(z_T; x_o) \prod_{t=1}^{T-1} P_{Z_t|Z_{t+1:T},X_o}(z_t; z_{t+1:T}, x_o) \tag{23a}
\]

\[
= P_{Z|X_o}(z_T; x_o) \prod_{t=1}^{T-1} P_{Z_t|Z_{t+1},X_o}(z_t; z_{t+1}, x_o) \tag{23b}
\]

\[
= P_{Z|X_o}(z_T; x_o) \prod_{t=1}^{T-1} P_{Z_t|Z_{t+1},X_o}(z_t; z_{t+1}, x_o) \tag{23c}
\]

\[
= P_{Z|X_o}(z; x_o) \tag{23d}
\]

We first use the chain rule, then the conditional independence following from the sampling order. The third line follows from Lemma 8. The final equality follows from Eq. 22.
D HMM Experiments

D.1 HMM Simulation Parameters

Let \( Z_t \) denote the \( t \)'th hidden states and \( X_t \) the \( t \)'th exploratory variable both are categorical R.Vs with range \( \{0, \ldots, 8\} \). The transmission and emission probabilities given as follows:

\[
P_{Z_t}(x) = \begin{cases} 
1, & \text{if } x = 1 \\
0, & \text{otherwise}
\end{cases}
\]

\[
P_{Z_t|Z_{t-1}}(x; y) = \begin{cases} 
0.9, & \text{if } x = y, \\
0.1, & \text{if } x = y + 1 \\
0.1, & \text{if } x = 0, y = 8 \\
0, & \text{otherwise}
\end{cases}
\]

\[
P_{X_t|Z_t}(x; z) = \begin{cases} 
0.35/2, & \text{if } x = z \\
0.35/2, & \text{if } x = z + 1 \\
0.35/2, & \text{if } x = 0, z = 8 \\
0.65/7, & \text{otherwise}
\end{cases}
\]

D.2 Results

![Figure 7: Heatmap of power on the left, FDR on right. Modified Sesia HMM Knockoffs (Algorithm 3) is used. On the left darker red (blue) indicates higher (lower) power. On the right values above \( q = 0.1 \) are red and below are blue.](image-url)
E MVN Experiments

E.1 Results

Figure 8: Comparison of different imputation methods. Left column is power vs $\rho$ and right column is FDR vs $\rho$. Rows corresponds to different amounts of missing data. From top to bottom $p_0$ takes the values \{0, 0.1, 0.2, 0.3, 0.4\}. The corresponding color and line style of the imputation methods are denoted in the legend.