Multilevel Stochastic Optimization for Imputation in Massive Medical Data Records

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Abstract—It has long been a recognized problem that many datasets contain significant levels of missing numerical data. A potentially critical predicate for application of machine learning methods to datasets involves addressing this problem. However, this is a challenging task. In this paper, we apply a recently developed multi-level stochastic optimization approach to the problem of imputation in massive medical records. The approach is based on computational applied mathematics techniques and is highly accurate. In particular, for the Best Linear Unbiased Predictor (BLUP) this multi-level formulation is *exact*, and is significantly faster and more numerically stable. This permits practical application of Kriging methods to data imputation problems for massive datasets. We test this approach on data from the National Inpatient Sample (NIS) data records, Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality. Numerical results show that the multi-level method significantly outperforms current approaches and is numerically robust. It has superior accuracy as compared with methods recommended in the recent report from HCUP. Benchmark tests show up to 75% reductions in error. Furthermore, the results are also superior to recent state of the art methods such as discriminative deep learning.

Index Terms—Massive Datasets, Machine Learning, Best Linear Unbiased Predictor, Computational Applied Mathematics, Numerical Stability

1 INTRODUCTION

TITH the growing emphasis on massive datasets in many modern applications, the need for sophisticated and precise approaches to high dimensional and heterogeneous data analysis is increasing. As an example, in healthcare research and personalized medicine, many Electronic Medical Records (EMR) include data on millions of patients, harboring large numbers of variables (e.g., demographics, diagnostic/procedure codes, lab/imaging results). These massive biomedical datasets, among others, provide opportunities to advance clinical and biomedical research, including clinical phenotyping (i.e., learning clinical trait-related features), but such analyses require shifting from human-guided solutions toward machine-learning (ML)-driven approaches. ML can increase clinical prediction accuracy and contribute to clinical phenotyping. However, many of these datasets are incomplete and include significant components of missing data.

ML algorithms cannot function without complete data matrices. Removing or imputing missing data can reduce sample sizes or bias outcomes. A critical foundational element for studying large datasets includes properly addressing the problem of missing and incorrect data ([1]).

There is extensive work on statistical and ML methods for data imputation. These are seen in two categories. The first category involves constructing statistical and/or deterministic models for specific types of datasets, including single-cell RNA-sequencing data [2], [3], [4], image data [5], time series data [6], [7], and traffic data [8], [9]. The second category includes general methods that apply to a large class of datasets. Popular methods include k-nearest neighbors [10], discriminative deep learning methods [11], and generative deep learning methods [12], [13], [14], [15], [16]. See, for example, [17], [18], [19], [20] for surveys of this area.

Many ad hoc techniques have been developed to deal with this problem, including sample deletion, mean value or nearest neighbor imputation, etc.; in general these suffer from information loss that leads to inaccurate predictions.

Missing data form an important problem in medical record datasets. In particular, the HCUP Report #2015-01 by [21], *stresses* the need to address missing data in the National Inpatient Sample (NIS) and State Inpatient Databases (SID). As an example, suppose that there are missing data for discharges (total charge) in rural hospitals. Such missing data can lead to erroneous estimates of total charges, potentially biasing or otherwise misdirecting state/federal funding policies. It is important to obtain accurate and unbiased estimates of missing data.

In the HCUP Report #2015-01 the missing data is spread out to the whole dataframe. For example, about 20% of the data is missing for the important total charge variable for the Michigan SID dataset. In this paper we impute the missing values from a column of the dataframe by using the rest of the information including other columns. For example, for the total charge variable we use the data available for total charge, length of stay, number of procedures, number of diagnoses and age.

Current imputation algorithms recommended by the HCUP report #2015-01 include Predicted Mean Matching (PMM), Predicted Posterior Distribution (PPD) and linear regression ([22], [23]). These algorithms often are sub-optimal, in particular for noisy signals. Furthermore, Bayesian methods such as Data Augmentation (DA) see [24]) and Bootstrapping Expectation Maximization (BEM) algorithms (see [25]) suffer from poor accuracy. We note

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that a recent approach by [26] improves on the accuracy of traditional methods such as PMM, PPD, BEM, etc, by using a so-called optimization layer. More modern state of the art methods such as Discrimitative Deep Learning (DDL) [11] produces excellent results. This has been quantified in the recent benchmark paper [17].

In this paper we apply stochastic optimization approaches, such as Kriging/Best Linear Unbiased Predictor (BLUP) [27]. We note that we refer to Kriging as both the estimation of the coefficients of the covariance function and BLUP, although we mostly use Kriging/BLUP for clarification purposes. The technique is based on a principled optimal probabilistic representation of the data. These methods can lead to optimized imputation by taking advantage of essentially all available data. Kriging is a popular method for imputation for Geostatistics [28] and has been extended to other applications such as traffic flow [29] due to its high accuracy it is popular in many fields. However, Kriging methods in their general application are often costly and unstable numerically on massive datasets. A common technique is to apply a nugget to the covariance matrix. However, this changes the covariance function model and does not solve the original problem. This has been a limiting factor for application of Kriging to imputation for massive datasets outside of the spatio-temporal domain.

One of the goals of this paper is to motivate the application of Computational Applied Mathematical (CAM) techniques to solve large scale stochastic optimization problems. In particular, to address the above challenges, we propose to apply the recently developed multi-level Kriging approach that is designed to tackle computing cost effectiveness and numerical instability ([30], [31], [32]). These techniques originate from the fields of numerical analysis and uncertainty quantification ([32], [33], [34], [35], [36], [37], [38]) and have been effective in solving (stochastic) partial differential equations. Indeed, the present Kriging optimization problem has many connections to the solution of Partial Differential Equations (PDEs). We introduce the above techniques in the context of statistical methods including Kriging, and demonstrate their power to solve hard stochastic optimization large scale problems.

By remapping an original stochastic optimization problem onto a multi-level space, we can significantly mitigate numerical instabilities and reduce computational burdens. In particular, the BLUP is remapped onto an equivalent formulation with multi-level spaces. Mathematically the multi-level prediction is *exact*, i.e., it precisely solves the original BLUP problem. In practice, numerical efficiency augmentations involving factors of the order of tens of thousands can be gained for 20 dimensional problems, as compared with traditional Conjugate Gradient (CG) approaches for estimates with the same accuracy, as is shown in Section (4).

To demonstrate the accuracy of the multi-level Kriging imputation method, we benchmark it on the U.S. National Inpatient Sample (NIS) datasets (see [39], Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality). Significant improvements over methods including PPM, PPD, DA and EM are shown. More importantly, it is shown that the imputed values accurately reflect the overall statistics of the population. This contrasts with other approaches, including kNN-R, kNN, GLS, PPM, etc, which often also suffer from poor accuracy. Furthermore our results show improvements over the recent Discrimitative Deep Learning state of the art method.

2 PROBLEM SETUP

Suppose that for a Gaussian random field Y we have the model:

$$Y(\mathbf{x}) = \mathbf{k}(\mathbf{x})^{\mathrm{T}} \boldsymbol{\beta} + \varepsilon(\mathbf{x}), \qquad \mathbf{x} \in \mathbb{R}^{d}, \tag{1}$$

where *d* is the number of spatial dimensions, $\mathbf{k} : \mathbb{R}^d \to \mathbb{R}^p$ is a functional vector of the spatial location $\mathbf{x} \in \mathbb{R}^d$, $\boldsymbol{\beta} \in \mathbb{R}^p$ is an unknown vector of coefficients. The noise model ε is a stationary Gaussian random field with mean zero and parametric covariance function $\phi(\mathbf{x}, \mathbf{y}; \boldsymbol{\theta}) \equiv \operatorname{cov}(\varepsilon(\mathbf{x}), \varepsilon(\mathbf{y})) :$ $\mathbb{R}^d \times \mathbb{R}^d \to \mathbb{R}$, where $\boldsymbol{\theta} \in \mathbb{R}^d$ is an unknown vector of parameters. We assume $\phi(\mathbf{x}, \mathbf{y}; \boldsymbol{\theta})$ is positive definite.

Suppose that we collect $N \ge p$ observations of the Gaussian random field process Y at different locations in \mathbb{R}^d , i.e. the vector of observations $\mathbf{Y} = (Y(\mathbf{x}_1), \ldots, Y(\mathbf{x}_N))^{\mathrm{T}}$ is obtained from locations in the set $\mathbb{S} := \{\mathbf{x}_1, \ldots, \mathbf{x}_N\}$, where the elements in \mathbb{S} are assumed non-collinear. Denote $\mathbf{C}(\boldsymbol{\theta}) = \operatorname{cov}(\mathbf{Y}, \mathbf{Y}^{\mathrm{T}}) \in \mathbb{R}^{N \times N}$ bas the covariance matrix of \mathbf{Y} . Furthermore, assume that $\mathbf{C}(\boldsymbol{\theta})$ is positive definite for all $\boldsymbol{\theta} \in \mathbb{R}^w$. Let $\mathbf{X} = (\mathbf{k}(\mathbf{x}_1) \ldots \mathbf{k}(\mathbf{x}_N))^{\mathrm{T}} \in \mathbb{R}^{N \times p}$ and assume that it is full column rank. Since the model (1) is a Gaussian random field, the samples in \mathbb{S} can be written in vector form as

$$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon},\tag{2}$$

where $\boldsymbol{\varepsilon}$ is a Normal random vector, more precisely $\boldsymbol{\varepsilon} \sim N(0, \mathbf{C}(\boldsymbol{\theta}))$. The aim is to *estimate* the unknown vectors $\boldsymbol{\beta}$ and $\boldsymbol{\theta}$ and *predict* $Y(\mathbf{x}_0)$ for a new spatial location \mathbf{x}_0 with a stochastic optimization method. The unknown vectors $\boldsymbol{\beta}$ and $\boldsymbol{\theta}$ are estimated from the data using a log-likelihood function (see [31])

$$\ell(\boldsymbol{\beta}, \boldsymbol{\theta}) = -\frac{n}{2} \log(2\pi) - \frac{1}{2} \log \det\{\mathbf{C}(\boldsymbol{\theta})\} -\frac{1}{2} (\mathbf{Y} - \mathbf{X}\boldsymbol{\beta})^{\mathrm{T}} \mathbf{C}(\boldsymbol{\theta})^{-1} (\mathbf{Y} - \mathbf{X}\boldsymbol{\beta}),$$
(3)

which can be profiled by Generalized Least Squares (GLS) with

$$\hat{\boldsymbol{\beta}}(\boldsymbol{\theta}) = (\mathbf{X}^{\mathrm{T}} \mathbf{C}(\boldsymbol{\theta})^{-1} \mathbf{X})^{-1} \mathbf{X}^{\mathrm{T}} \mathbf{C}(\boldsymbol{\theta})^{-1} \mathbf{Y}.$$
 (4)

For the prediction problem, consider the Best Linear Unbiased Predictor (BLUP) $\hat{Y}(\mathbf{x}_0) = \boldsymbol{\lambda}^T \mathbf{Y}$, where $\boldsymbol{\lambda} = (\lambda_1, \dots, \lambda_N)^T$. The BLUP is formulated as the minimization of $\mathbb{E} \left[(Y(\mathbf{x}_0) - \boldsymbol{\lambda}^T \mathbf{Y})^2 \right]$ under the unbiased constraint $\mathbf{X}^T \boldsymbol{\lambda} = \mathbf{k}(\mathbf{x}_0)$. The solution to this problem ([27]) is given as

$$\hat{Y}(\mathbf{x}_0) = \mathbf{k}(\mathbf{x}_0)^{\mathrm{T}} \hat{\boldsymbol{\beta}} + \mathbf{c}(\boldsymbol{\theta})^{\mathrm{T}} \mathbf{C}(\boldsymbol{\theta})^{-1} (\mathbf{Y} - \mathbf{X} \hat{\boldsymbol{\beta}}), \qquad (5)$$

where $\mathbf{c}(\boldsymbol{\theta}) = \operatorname{cov}\{\mathbf{Y}, Y(\mathbf{x}_0)\} \in \mathbb{R}^N$ and $\hat{\boldsymbol{\beta}}$ is defined in equation (4).

Solving the Kriging estimation and prediction problem involves inverting the covariance matrix $C(\theta)$. Two main approaches exist. Direct methods, such as Gaussian elimination and Cholesky factorizations are popular for small datasets, but as the number of observations N increases the memory constraints grow as $O(N^2)$, which makes it infeasible for large datasets. Iterative methods, such as the Conjugate Gradient method (CG), avoid computing the covariance matrix, thus making them a good choice for large datasets.

The key problem with direct and iterative methods is that they are sensitive to the condition number of the covariance matrix. Large condition numbers leads to numerical instability with the consequence of inaccurate solutions. It can be shown that the accuracy for *any* inversion numerical algorithm is $\approx \kappa(\mathbf{C}(\theta))\epsilon_M$ (see [40]), where $\kappa(\mathbf{C}(\theta))$ is the condition number of $\mathbf{C}(\theta)$ and ϵ_M is the relative machine precision. For most computers, double precision $\epsilon_M \approx 10^{-16}$. Furthermore, iterative methods such as CG are slow for matrices with large condition numbers (see [41]). For many practical covariance functions, the condition numbers of $\mathbf{C}(\theta)$ are large.

Challenge: The number of observations is large and the covariance matrix $\mathbf{C}(\boldsymbol{\theta})$ can be highly ill-conditioned. This can lead to inaccurate estimates of the Kriging / BLUP predictor. In the paper written by [31], the authors propose a new transformation of the data vector \mathbf{Y} , leading to a decoupled multi-level description of the Kriging model without any loss of structure for \mathbb{R}^2 and \mathbb{R}^3 problems. As discussed in the introduction, missing data in the NIS and SID datasets form an important issue that is underscored in the HCUP report #2015-01 ([21]). The report shows as an example, the problem of missing data for discharges (total charge) in rural hospitals. This can potentially lead to erroneous statistics of the total charge, leading to sub-optimal or misinformed state and federal policy decisions. Missing data rates for total charge are at 2.08% for the NIS 2012 dataset. However, the Michigan SID dataset missing data rate for total charge is significantly higher at, 19.79%, underscoring the episodic problems of much higher impact for missing data in certain communities. The total number of samples is 7,296,968.

In this section we contrast the accuracy performance of the multilevel Kriging/BLUP method with the recommended imputation algorithms in HCUP report #2015-01, which include Predicted Mean Matching (PMM). We make further comparison with more traditional methods such as K-Nearest Neighbors (KNN) and KNN regression. In particular, we test the accuracy of the various methods on the above-mentioned total charge variable, containing the highest missing data rate. The different methods where tested on the 2013 NIS dataset, which was available to us for analysis. Our calculations show the overall missing data rate is 2% for total charge. The multi-level representation leads to significant computational benefits when computing β and the prediction $\hat{Y}(\mathbf{x}_0)$ in equation (5).

There is a wealth of publications that attempt to address computational costs of the above approaches. Most of these approaches are challenged by stringent a priori assumptions on the statistical properties of data ([42], [43], [44], [45], [46], [47], [48], [49]).

Recently, from the computational mathematics community, a promising hierarchical matrix approach has been developed by [50] to accurately compress covariance matrices, leading to significant speed-ups. However, the application is restricted to zero-mean data without a component trend. Another promising approach is based on the pivoted Cholesky decomposition developed in [51]. Nonetheless, if the condition number of the covariance matrix is large, as happens in practice often, these numerical methods will have difficulty solving the Kriging problem with any accuracy. A common ad hoc technique to improve the condition number involves the use of a so-called nugget; however, it is known that this leads to numerical inaccuracies.

Ill-conditioned matrices cannot be inverted with accuracy (see [40]). Furthermore, a covariance matrix can in general be large and unable to reside in computer memory. Thus the solution of the GLS would require inverting the covariance matrix p times using an iterative method, with p the number of columns of the design matrix.

The multi-level approach developed in [30], [31], [32], avoids forming the covariance matrix **C**, by transforming the problem into a multi-level form with significantly smaller condition numbers. In particular, for the BLUP problem the transformation is one-to-one and onto. *This implies that the solution for the multi-level form exactly solves the original BLUP problem* (5). Although this appears impossible due to the ill-conditioning and accuracy issue mentioned above, it can be shown that the prediction is a solution to a constrained optimization problem (e.g. unbiased constraint). Constructing a multi-level basis that spans a complementary constrained space leads to well-conditioned and accurate numerical algorithms. Furthermore, a single matrix inversion is all that is required.

3 METHODS: MULTILEVEL APPROACH

We describe the main ideas of the multilevel approach are used to tackle the above-mentioned numerical challenges. The details of this method developed by [32] can be involved for the reader not well versed in advanced numerical analysis; here We present a simplified exposition.

Let $\mathcal{P}^p(\mathbb{S})$ be the span of the columns of the design matrix **X**. Suppose that there exist orthogonal projections $\mathbf{L} : \mathbb{R}^N \to \mathcal{P}^p(\mathbb{S})$ and $\mathbf{W} : \mathbb{R}^N \to \mathcal{P}^p(\mathbb{S})^{\perp}$, where $\mathcal{P}^p(\mathbb{S})^{\perp}$ is the orthogonal complement of $\mathcal{P}^p(\mathbb{S})$. The operators **L** and **W** are constructed efficiently with an oct or binary kd-tree as shown in Theorem 3.1.

Remark. The operator \mathbf{L} and \mathbf{W} are constructed from a multilevel decomposition of the location of predictors. This process is somewhat elaborate and the reader is referred to [31] and [32] for all of the details. However, for the exposition in this section it sufficient to know what the properties of the operators \mathbf{L} and \mathbf{W} are.

Theorem 3.1. Suppose that we have a kd-tree representation, with t levels, of all the observation locations in S. Then:

- *i)* The linear operators \mathbf{L} and \mathbf{W} can be constructed in $\mathcal{O}(Nt)$ computational steps and memory.
- *ii)* The linear operators \mathbf{L} and \mathbf{W} have at most $\mathcal{O}(Nt)$ non-zero elements.
- iii) The operator $\begin{bmatrix} \mathbf{W} \mathbf{L} \end{bmatrix}$ is orthogonal.

Remark. For most practical datasets S, the number of levels of the kd-tree t is $\approx \log_2 N$.

Letting $\mathbf{Y}_{\mathbf{W}} := \mathbf{W}\mathbf{Y}$, from equation (2) it follows that $\mathbf{Y}_{\mathbf{W}} = \mathbf{W}(\mathbf{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon}) = \mathbf{W}\boldsymbol{\varepsilon}$. Note that trend $\mathbf{X}\boldsymbol{\beta}$ is filtered

 \square

$$\ell_{\mathbf{W}}(\boldsymbol{\theta}) = -\frac{n}{2}\log(2\pi) - \frac{1}{2}\log\det\{\mathbf{C}_{\mathbf{W}}(\boldsymbol{\theta})\} - \frac{1}{2}\mathbf{Y}_{\mathbf{W}}^{\mathrm{T}}\mathbf{C}_{\mathbf{W}}(\boldsymbol{\theta})^{-1}\mathbf{Y}_{\mathbf{W}},$$
(6)

where $\mathbf{C}_{\mathbf{W}}(\boldsymbol{\theta}) = \mathbf{W}\mathbf{C}(\boldsymbol{\theta})\mathbf{W}^{\mathrm{T}}$ and $\mathbf{Y}_{\mathbf{W}} \sim \mathcal{N}_{N-p}(\mathbf{0}, \mathbf{W}\mathbf{C}(\boldsymbol{\theta})\mathbf{W}^{\mathrm{T}})$. One immediate consequence is that the likelihood function is decoupled. Furthermore, the following theorem shows that $\mathbf{C}_{\mathbf{W}}(\boldsymbol{\theta})$ is more stable numerically than $\mathbf{C}(\boldsymbol{\theta})$.

Theorem 3.2. If $\kappa(A) \to \mathbb{R}$ is the condition number of the matrix $A \in \mathbb{R}^{N \times N}$, then

$$\kappa(\mathbf{C}_{\mathbf{W}}(\boldsymbol{\theta})) \leq \kappa(\mathbf{C}(\boldsymbol{\theta})).$$

Proof. See [31], [32].

Remark. Evaluating the likelihood function $\ell_{\mathbf{W}}(\boldsymbol{\theta})$ requires the computation of $\log \det \{ \mathbf{C}_{\mathbf{W}}(\boldsymbol{\theta}) \}$ and solving $\mathbf{C}_{\mathbf{W}}(\boldsymbol{\theta})^{-1}$ $\mathbf{Y}_{\mathbf{W}}$. This can be done by constructing a Cholesky factor (see [41]) of C_W . From Theorem 3.2 this is more stable numerically than evaluating $\ell(\boldsymbol{\theta})$. Nonetheless, the computational efficiency can be significantly increased by constructing a sparse matrix version of C_W , which we refer to as C_W , that is close to the full dense matrix. The sparse matrix C_W is built using a distance criterion approach ([31], [32]). A sparse Cholesky factorization can now be computed. An alternative method for evaluating $C_{W}(\theta)^{-1} Y_{W}$ is an iterative method such as CG iteration ([41]). This is discussed more in detail below. Note that in practice to estimate θ accurately, it is unnecessary to compute the Cholesky factor of the entire sparse matrix C_W , but just sparse sub-blocks. The computational burden will be significantly reduced (See [31], [32] for details).

We now show how to construct a multilevel predictor that gives rise to well conditioned multilevel covariance matrices. As pointed out in our problem setup, this is equivalent to a best linear unbiased predictor but much easier to solve numerically, making it suitable for missing data problems in large datasets. Consider the system of equations

$$\begin{pmatrix} \mathbf{C}(\boldsymbol{\theta}) & \mathbf{X} \\ \mathbf{X}^{\mathrm{T}} & \mathbf{0} \end{pmatrix} \begin{pmatrix} \hat{\boldsymbol{\gamma}} \\ \hat{\boldsymbol{\beta}} \end{pmatrix} = \begin{pmatrix} \mathbf{Y} \\ \mathbf{0} \end{pmatrix}$$

In [27] the authros show that the solution of (3) is given by the GLS estimate of β (equation (4)) and $\hat{\gamma}(\theta) = \mathbf{C}^{-1}(\theta)(\mathbf{Y} - \mathbf{X}\hat{\beta}(\theta))$. The BLUP at the targe point \mathbf{x}_0 is given by

$$\hat{Y}(\mathbf{x}_0) = \mathbf{k}(\mathbf{x}_0)^{\mathrm{T}} \hat{\boldsymbol{\beta}}(\boldsymbol{\theta}) + \mathbf{c}(\boldsymbol{\theta})^{\mathrm{T}} \hat{\boldsymbol{\gamma}}(\boldsymbol{\theta}).$$
(7)

Furthermore, the Mean Squared Error (MSE) at the target point \mathbf{x}_0 is given by

$$1 + \tilde{\mathbf{u}}^{\mathrm{T}} (\mathbf{X}^{\mathrm{T}} \mathbf{C}(\boldsymbol{\theta})^{-1} \mathbf{X})^{-1} \tilde{\mathbf{u}} - \mathbf{c}(\boldsymbol{\theta})^{\mathrm{T}} \mathbf{C}^{-1}(\boldsymbol{\theta}) \mathbf{c}(\boldsymbol{\theta}),$$

where $\tilde{\mathbf{u}}^{\mathrm{T}} := (\mathbf{X}\mathbf{C}^{-1}(\boldsymbol{\theta})\mathbf{c}(\boldsymbol{\theta}) - \mathbf{k}(\mathbf{x}_0)).$

From (3) the key observation is that $\mathbf{X}^{\mathrm{T}} \hat{\boldsymbol{\gamma}}(\boldsymbol{\theta}) = \mathbf{0}$, which implies that $\hat{\boldsymbol{\gamma}} \in \mathbb{R}^N \setminus \mathcal{P}^p(\mathbb{S})$. Thus it can be rewritten as $\hat{\boldsymbol{\gamma}} = \mathbf{W}^{\mathrm{T}} \boldsymbol{\gamma}_{\mathbf{W}}$ for some $\boldsymbol{\gamma}_{\mathbf{W}} \in \mathbb{R}^{N-p}$. From equation (3) rewrite $\mathbf{C}(\boldsymbol{\theta}) \hat{\boldsymbol{\gamma}} + \mathbf{X} \hat{\boldsymbol{\beta}} = \mathbf{Y}$ as

$$\mathbf{C}(\boldsymbol{\theta})\mathbf{W}^{\mathrm{T}}\boldsymbol{\gamma}_{\mathbf{W}} + \mathbf{X}\hat{\boldsymbol{\beta}} = \mathbf{Y}.$$
 (8)

Now apply the matrix **W** to equation (8) and obtain $\mathbf{W}{\mathbf{C}(\boldsymbol{\theta})\mathbf{W}^{\mathrm{T}}\boldsymbol{\gamma}_{\mathbf{W}} + \mathbf{X}\hat{\boldsymbol{\beta}}} = \mathbf{W}\mathbf{Y}$. Since the columns for **X** are in $\mathcal{P}^{p}(\mathbb{S})$, it follows $\mathbf{W}\mathbf{X} = \mathbf{0}$ and

$$\mathbf{C}_{\mathbf{W}}(\boldsymbol{\theta})\boldsymbol{\gamma}_{\mathbf{W}} = \mathbf{Y}_{\mathbf{W}}.$$
(9)

The advantage of this form is that $\mathbf{C}_{\mathbf{W}}(\boldsymbol{\theta})$ is better conditioned due to Theorem 3.2 and γ_W can be solved by applying a numerical inversion algorithm. Next, $\hat{\gamma}$ can be computed by applying the transformation $\hat{\gamma} = \mathbf{W}^{\mathrm{T}} \gamma_{\mathbf{W}}$. Finally, the GLS estimate $\hat{\boldsymbol{\beta}}$ can solved from (8) by applying the least squares

$$\hat{\boldsymbol{\beta}} = (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{X}^T (\mathbf{Y} - \mathbf{C}(\boldsymbol{\theta}) \hat{\boldsymbol{\gamma}}).$$
(10)

In Figure 1 a workflow of the imputation method is shown. *Remark.* It is remarkable that $\hat{\gamma}$ can be solved for independently of the GLS estimate $\hat{\beta}$ and in turn, $\hat{\beta}$ can be solved as a least squares problem without the need to invert the covariance matrix $\mathbf{C}(\theta)$. Furthermore the multilevel solution of the BLUP using equation (5), (9) and (10) leads to the same exact answer as the original BLUP in equation (5). However, from Theorem 3.2 the multilevel BLUP is numerically more stable. See Table 1 for the differences in condition numbers for \mathbf{C} and $\mathbf{C}_{\mathbf{W}}$. This is of particular importance since it is known that if matrices are ill-conditioned they cannot be inverted (directly or indirectly) with accuracy [40]. This is the reason that a nugget is usually added to the covariance matrix. However, this changes the model to make it easier to solve, but does not solve the original BLUP.

The linear system of equations (9) can be solved using a direct or iterative approach. If *N* is relatively small, a direct method such as a Cholesky factorization ([41]) will work well. However, for large *N*, due to well-conditioning of the matrix $\mathbf{C}_W(\theta)$, a CG ([41]) method is a better approach. Let $\gamma_{\mathbf{W}}^n$ be the n^{th} conjugate gradient estimate of $\gamma_{\mathbf{W}}$, where $\gamma_{\mathbf{W}}^0$ is the initial guess. The main cost of the CG method is in computing the matrix vector products $\mathbf{C}_{\mathbf{W}}(\theta)\gamma_{\mathbf{W}}^n$. This can be done in 3 steps as:

$$\gamma_{\mathbf{W}}^{n} \xrightarrow[(1)]{\mathbf{W}^{\mathrm{T}} \gamma_{\mathbf{W}}^{n}} \mathbf{a}_{n} \xrightarrow[(2)]{\mathbf{C}(\boldsymbol{\theta}) \mathbf{a}_{n}} \mathbf{b}_{n} \xrightarrow[(3)]{\mathbf{W} \mathbf{b}_{n}} \mathbf{C}_{\mathbf{W}}(\boldsymbol{\theta}) \gamma_{\mathbf{W}}^{n}.$$

- (1) The first step transforms $\gamma_{\mathbf{W}}^n$ into a single level (original) representation in \mathbb{R}^N .
- (2) The matrix vector product C(θ)a_n is computed with a summation method. For problems in R² and R³ this we can achieve this efficiently (O(N) computational cost) using a Kernel Independent Fast Multipole Method (KIFMM) ([31], [52]) or a Hierarchical Matrix ([50]). For d > 3 dimensions the direct approach is used with a cost of O(N²).
- (3) For the last step, \mathbf{b}_n is transformed to a multilevel representation and the matrix vector product $\mathbf{C}_{\mathbf{W}}(\boldsymbol{\theta})\gamma_{\mathbf{W}}^n$ is obtained.

Remark. A preconditioner $\mathbf{P}_{\mathbf{W}}$ can be used to speed up the convergence rate of the CG method, and the system of equations

$$\mathbf{P}_{\mathbf{W}}^{-1}\mathbf{C}_{\mathbf{W}}(\boldsymbol{\theta})\boldsymbol{\gamma}_{\mathbf{W}} = \mathbf{P}_{\mathbf{W}}^{-1}\mathbf{Y}_{\mathbf{W}}$$
(11)

is solved instead of (9). For the multilevel method, $\mathbf{P}_{\mathbf{W}}$ can be constructed using the diagonal entries of $\mathbf{C}_{\mathbf{W}}$. Note that it is possible that $\mathbf{C}_{\mathbf{W}}(\boldsymbol{\theta})$ will have small condition numbers. If this is the case no preconditioner is used.

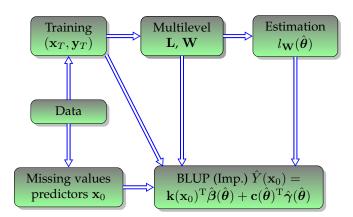


Fig. 1: Multilevel Kriging/BLUP flowchart. **Training:** The data is split into the predictors \mathbf{x}_T and the observation data \mathbf{y}_T corresponding to the variable that will be imputed. **Multilevel:** The multilevel operators are constructed (\mathbf{L}, \mathbf{W}). **Estimation:** The coefficients $\hat{\boldsymbol{\theta}}$ of the covariance coefficients are estimated. **BLUP (Imputation):** Given the multilevel operators for the missing values \mathbf{x}_0 imputing the missing variable.

Remark. Given k CG iterations, the total computational cost for computing $\hat{\mathbf{Y}}(\mathbf{x}_0)$ from (7) using the multilevel approach is $\mathcal{O}(p^3 + (k + 1)N^{\alpha} + 2Nt)$. For 2 and 3 dimensional problems, the parameter α is 1 with the use of the KIFMM method. For higher dimensions, a direct approach is used, and thus $\alpha = 2$. The residual error for the CG method decays exponentially with respect to k and at a rate that is a function of the condition number. Small condition numbers lead to fast convergence, see [41] for details.

Remark. The multilevel method is implemented in MATLAB [53] and C/C++. More details can be found in the paper by [32]. However, for this paper we have further optimized the code which now runs at least twice as fast.

4 EXPERIMENTS AND RESULTS

As discussed in the introduction, missing data in the NIS and SID datasets form an important problem underscored in the HCUP report #2015-01 ([21]). The report highlights, the problem of missing data for discharge information (total charge) in rural hospitals with potential consequences involving erroneous statistics and consequently possibly sub-optimal and even misinformed state and federal policy decisions. The missing data rates for total charge are at 2.08% for the NIS 2012 data. The Michigan SID data has a total charge missing data rate significantly higher at 19.79%. We test the multilevel approach on the NIS 2013 dataset. The NIS 2013 missing data rate for total charge was 2.00 %.

In this section we contrast the accuracy performance of the multilevel Kriging/BLUP method against recommended imputation algorithms in HCUP report #2015-01, including Predicted Mean Matching and Predicted Posterior Distribution methods. We make further comparison with more traditional methods such as K-Nearest Neighbors (KNN) and KNN regression. In particular, we test the accuracy of the various methods on the total charge variable, with its highest missing data rate. The computational and accuracy performance of the multi-level Kriging method is analyzed with the following choice of Matérn covariance function

$$\phi(r,\rho,\nu) := \frac{1}{\Gamma(\nu)2^{\nu-1}} \left(\sqrt{2\nu}\frac{r}{\rho}\right)^{\nu} K_{\nu}\left(\sqrt{2\nu}\frac{r}{\rho}\right),$$

with Γ the gamma function, $\nu > 0$, $\infty > \rho > 0$, and where K_{ν} is the modified Bessel function of the second kind. The parameter ν controls the shape of the Matérn kernel and ρ is the length correlation. Thus for this case $\theta = (\nu, \rho)$, and the stochastic optimization approach seeks the estimate of θ that best explains the data.

To demonstrate the numerical efficiency of the multi-level method, we generate a series of random observation nodes on a n-sphere $S_{d-1} := {\mathbf{x} \in \mathbb{R}^d \mid ||\mathbf{x}||_2 = 1}$ with dimension d. We create a series of nested sets of nodes $\mathbf{S}_1^d \subset \cdots \subset \mathbf{S}_7^d$ that vary with N = 2000, 4000 to N = 128, 000 in size. The final set \mathbf{S}_7^d contains 128,000 randomly selected points on the n-sphere S_{d-1} . For the covariates we choose the first d-1 dimensions. In other words, forming a matrix of node coordinates (N) by the number of dimensions d, we pick the first d-1 columns as our covariate nodes. The last dimension (column) is chosen to be the observations. The polynomial basis chosen for the design matrix \mathbf{X} is Total Degree (**TD**) with maximum degree w.

The imputation performance of the multi-level Kriging method is tested on the National Inpatient Sample (NIS) datasets ([39]), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality with the 2013 data set. Among all 190 variables in this dataset, totchg (total charge), as, the most problematic, is a good candidate to test the performance of the multi-level method. The variables npr (number of procedures), ndx (number of diagnoses), los (length of stay) and age are used as predictors. Note that as an experimental comparison we also test los as a candidate response variable, though this would not be necessary in practice since its missing data rate is 0.004 % in the NIS 2013 dataset. We extract from the NIS 2013 data matrix these five variables and remove any incomplete rows. To test the imputation performance of the multi-level Kriging method, N rows are selected at random for $N = \{2, 000;$ $5,000; 10,000; 50,000; 100,000 \}.$

The error performance is measured using the relative root-mean-square error (rMSE), mean absolute percentage error (MAPE), and the mean of the log of the accuracy Ratio (lnQ). The relative RMSE represents the sample standard deviation of the differences between predicted and observed values normalized by the mean of the square of the observed values. The MAPE corresponds to the averaging the ratio of differences between predicted values and observed values to observed values; here there is a bias towards small predictions. lnQ overcomes this issue by using an accuracy measure based on the ratio of the predicted to actual value.

The Kriging predictor is compared with other methods such as the Generalized Least Squares (GLS), k-nearest neighbors (KNN) and KNN regression. Comparisons are also made with the following four well known imputation methods: PMM (predicted mean matching), PPD (posterior prediction distribution), BEM (bootstrapping EM), and DA (data augmentation). Furthermore, we obtain results for the Discrimitative Deep Learning (DDL) from the AutoML li-

	(a) $\boldsymbol{\theta} = (\nu, \rho)$	(5/4,	(10), d = 20	w = 3 (p)	= 1771)	
N	$\kappa(\mathbf{C})$	$\kappa(\mathbf{C}_{\mathbf{W}})$	itr(C)	$itr(\mathbf{C}_{\mathbf{W}})$	MB(s)	Itr(s)	Total(s)	$\mathrm{Eff}_{\boldsymbol{\gamma},\boldsymbol{\beta}}$
16,000	5×10^7	6	178	10	52	56	109	31,520
32,000	1×10^8	10	237	13	125	276	403	32,290
64,000	3×10^8	17	303	16	288	1405	1,695	33,540
	((b) $\boldsymbol{\theta} = (\nu, \mu)$	o) = (5/4)	(10), d = 2	5, w = 2 (p = 351)		
N	$\kappa(\mathbf{C})$	$\kappa(\mathbf{C}_{\mathbf{W}})$	itr(C)	$itr(C_W)$	MB(s)	Itr(s)	Total(s)	$\mathrm{Eff}_{\boldsymbol{\gamma},\boldsymbol{\beta}}$
16,000	3×10^7	17	139	17	7	89	98	3,510
32,000	8×10^7	33	183	22	16	462	480	2,920
64.000	2×10^8	64	231	29	35	2.400	2.437	2,800

TABLE 1: Multilevel BLUP Kriging results for the n-sphere data set with d = 20 and d = 25 dimensions, **TD** design matrix of degree w, and Matérn covariance function with parameters (ν, ρ) . (a) Computational wall-clock times for solving the Kriging prediction for d = 20 and $\theta = (5/4, 10)$. Due to the direct method to compute the matrix vector product, the computational burden increases somewhat faster than quadratic. However, compared to the single level iterative approach it is $\approx 33, 540$ faster for N = 64, 000 observations. (b) Kriging prediction for d = 25 and $\theta = (5/4, 10)$. For N = 64, 000 observations the efficiency of the multilevel BLUP is about 2,796 times faster for the same accuracy.

38

78

12,644

12,724

brary *autokeras* software package [54]. The model is optimized by setting the number of trials to 50 and the number of *epochs* to 50 also [17].

128,000

Kriging/BLUP provides 38% reduction in error for rMSE, 75% for MAPE and 72% for mean lnQ compared to PPD (see Table 2). Similar performance is also achieved compared to PPM, DA and BEM for rMSE, but significantly better for MAPE and lnQ. We will analyze this in more detail in this section. Our error rates are significantly lower than the state of the art methods recommended by HCUP report#2015-01, with up to a 75% reduction. Indeed, this can have a strong impact on funding as an example of policy decision-making. As an example, if for half of a group of rural hospitals the total charge is missing, mean estimates could be significantly off under recommended methods, with poor funding and related policies as a consequence. In particular, our numerical results show that MAPE errors for PPD, BEM, DA and can be more than 390% greater than the multilevel method, with a figure of 140% for PMM.

The numerical performance of the multilevel approach is tested on the datasets \mathbf{S}_k^d for $k = 4, \ldots, 7, d = 20$ and d = 25 dimensional problems. Since d > 3, a fast summation (convolution) method such as the KIFMM is unavailable. Each matrix-vector product of the conjugate gradient iterations is computed with the direct approach using a combination of the Graphics Processing Unit (GPU, Nvidia GTX 970) and a single i7-3770 CPU @ 3.40GHz processor.

We test the performance of BLUP only since the multilevel estimation computational burden is almost negligible in comparison (See [32] for more detail). In Table 1 (a) and (b) numerical results for computing the BLUP parameters $\hat{\gamma}$ and $\hat{\beta}$ for d = 20 and $\theta = (5/4, 10)$ are shown. The CG relative residual tolerance accuracy is set to $tol = 10^{-3}$, itr(**A**) is the number of CG iterations needed to achieve tol residual for any matrix **A**. MB(s) is the wall-clock time in seconds needed to compute the multilevel basis. Itr(s) is similarly time needed to solve for $\hat{\gamma}$ using the CG method. Total(s) is total time needed to solve for $\hat{\beta}$ and $\hat{\gamma}$. An efficiency comparison between the cost of computing $\hat{\beta}$ and $\hat{\gamma}$ with the original covariance matrix **C** and the multilevel approach is given by Eff_{γ,β}. We first notice that the condition number for **C** is large $(\kappa(\mathbf{C}) \approx 10^8)$ even for relatively small problems. This has several numerical stability implications including a sever downgrade for maximal accuracy using any numerical inversion algorithm. A single precision computation would lead to erroneous results. Using a double precision computation can ameliorate the accuracy problem, but still exhibit slow convergence. In comparison $\kappa(\mathbf{C}_{\mathbf{W}}) \approx 20$ is significantly smaller leading to a stable and fast matrix inversion algorithm.

Compared to the traditional iterative approach using the covariance matrix C (single level representation), *the multilevel method is thousands to tens of thousands times faster for the same accuracy*. This can be observed in Table 1 (a) and (b). The source of this efficiency is due to: i) The number of iterations for convergence to the same tolerance accuracy is significantly smaller. ii) The multilevel approach only needs one iterative matrix inversion, in comparison to p iterative matrix inversions needed for the traditional single level representation approach. This is relevant for large problems where the matrix cannot reside in memory.

We can now test the accuracy of the Kriging method. In particular we test the performance of the multi-level Kriging method with respect to the following regression problems: i) $los \sim totchg + npr + ndx$, ii) $totchg \sim los + npr + ndx$ + age and iii) $log(totchg) \sim log(los) + log(npr) + ndx + age (normalized).$

i) totchg ~ los + npr + ndx + age. For predicting total charge, we employ los, npr, ndx and age as predictors for datasets of size N = 2,000 to N = 100,000 with a 90% training and 10% validation split. This is a 4 dimensional problem, so we cannot use a fast summation method. In Figure 2 Kriging/BLUP is compared to kNN-R, kNN and GLS for the prediction on the validation set. Observe that as the number of observations increases, Kriging outperforms all the other methods. Furthermore from Figure 3 (a) the general shape of the population, including mean and variance, of the validation dataset is well captured by Kriging, but significantly degrades for kNN-R, KNN and GLS. The same phenomenon was also observed for PMM, PPD, BEM and DA. In addition, from the table in Figure 3 (b) we observe that Kriging outperforms GLS, kNN and DDL consistently in all

(a) totchg imputation

Methods	rMSE	MAPE	lnQ	Method
PMM	0.864	1.235	1.00	PMM
PPD	0.869	3.378	1.779	PPD
BEM	0.869	3.317	1.745	BEM
DA	0.867	3.449	1.787	DA
Kriging	0.535	0.861	0.492	Kriging

TABLE 2: Imputation performance comparison of Kriging/BLUP, PMM, PPD, BEM and DA for the totchg variable with N = 100,000 data points. (a) Imputation performance without transformation. The Kriging approach clearly outperforms the state of the art methods. (b) Imputation performance with log transformation. The Kriging also outperforms the state of the art methods. Furthermore, other methods such as DA degrade with the transformation.

(b) totchg Imputation (with log trans.)

MAPE

1.102

1.117

1.171

1.192

0.653

lnQ

0.888

0.924

0.943

0.935

0.418

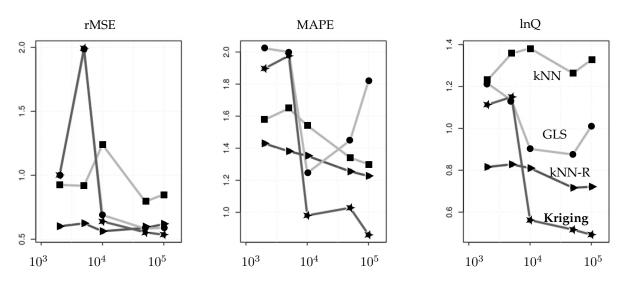


Fig. 2: Prediction error comparison (totchg) for the 2013 NIS Dataset with respect to the number of data points N, where 90% are used for training and 10% for validation.

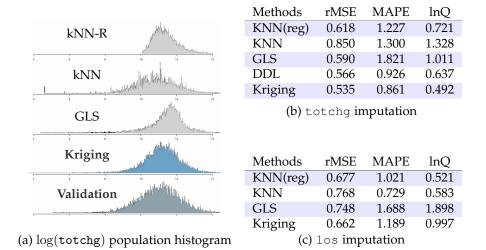


Fig. 3: (a) Population histogram statistical comparison of kNN-R, kNN, GLS and Kriging with respect to the validation data set for 90,000 training and 10,000 validation datasets (N = 100,000). Notice that Kriging more faithfully reproduces the population statistics of the validation total charge data set. This is the advantage of the unbiased constrained in the stochastic optimization. Note that PMM, PPD, BEM and DA methods also give similar results to kNN-R. (b) Total charge (totchg) imputation statistical errors comparisons. Kriging provides the best imputation performance for all error measures. (c) Length of stay (los) imputation statistical errors comparisons. For los, in general Kriging performs well.

8

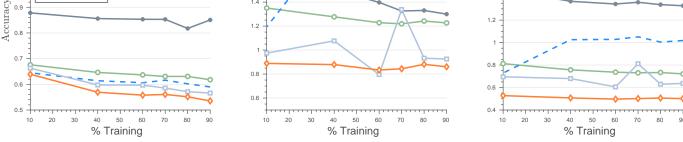


Fig. 4: Performance comparison for imputation of the total charge variable among Kriging/BLUP, KNN-Reg, KNN, GLS and DDL for different training/validation proportions of the data. On the horizontal axis we have the percentage proportion for the training dataset. The vertical axis corresponds to the rMSE, MAPE and mean lnQ metrics. As observed for all the metrics rMSE, MAPE and mean lnQ the Kriging/BLUP method produces in almost all cases the best results.

three measures of accuracy. In Table 2 (a) we observe that Kriging outperforms the imputation packages such as PMM, PPD, BEM and DA for N = 100,000 data points with the 90%-10% training/validation split.

rMSE

--KNN_Reg KNN

GLS

DDL Kriging

1 1

0.9

In Figure 4, we can observe a comparison of performance among different methods for the totchg (total charge) variable: Kriging/BLUP, KNN-Reg, KNN, GLS, and DDL. This comparison is conducted across varying training/validation proportions of the dataset (from (10%/90%) to (90%/10%) of the data. The horizontal axis depicts the percentage of the dataset used for training, while the vertical axis represents metrics such as rMSE, MAPE, and mean lnQ. Notably, the Kriging/BLUP method consistently outperforms the other methods across all metrics (rMSE, MAPE, and mean lnQ), with its superiority evident in nearly all scenarios.

- ii) los \sim totchg + npr + ndx. For the experiments of predicting length of stay, totchg, npr and ndx are used as predictors due to the high correlation with los and run the simulations for datasets (training set plus testing set) of size N = 100,000. Note that since this is a three dimensional problem, the Kriging multi-level code is significantly faster due to the application of the KIFMM. From Figure 3 (c) the result of the experiment shows that the Kriging was not always the best predictor consistently. However, it still appears to outperform most of the other methods. Intuitively, in this case, this could be due to the violation of the Gaussian assumption of the linear model.
- iii) $\log(\text{totchg}) \sim \log(\log) + \log(\operatorname{npr}) + \operatorname{ndx} + \operatorname{age}$. (normalized)

For this experiment the same dataset as in i) is used. However, a log transformation is and normalization step is applied. From Table performance:table1 (b) it is observed that the accuracy of traditional imputations methods improves. Although the accuracy of the Kriging method improves somewhat, it still outperforms all others. This indicates that the proposed Kriging method has the capacity of handling raw and rough models

when traditional methods tend to fail.

5 CONCLUSION

In this paper we introduce novel techniques from Computational Applied Mathematics to solve large scale statistical problems. In particular, the problem of imputation is solved with the new multi-level Kriging method. Due to the numerical and stability problems associated with the stochastic optimization Kriging method, until recently this had limited applicability to imputation for large datasets. Due to the introduction of multi-level methods from the CAM community, many of these limitations have been resolved. Our results show that the multi-level Kriging method is computationally feasible, stable numerically, accurate and mathematically principled. In particular, it is shown that the multilevel BLUP is exact and significantly outperforms current state-of-the-art methods. Furthermore, it is robust and applies to a large class of missing data problems such as massive medical records.

Multiple imputation is an important strategy for quantifying the uncertainty of predictions. There are many methods such as bootstrapping used to created multiple realizations of data. These realizations are used to quantify the variances of predictions. Such methods can also be used to create multiple realizations for the multilevel Kriging/BLUP approach. However, the extension is not trivial. To more faithfully reproduce realizations of the data, the bootstrapping approach needs to take into account the Cholesky decomposition (see [41]) of the covariance matrix **C**, which is very difficult since the matrix is large and ill-conditioned. However, alternatively we can use a Karhunen Loéve (KL) expansion (see [55]) to create multiple realizations with the Matérn covariance function from the Gaussian process representation of the data. This would involve computing the eigenstructure of the covariance function, which is significantly more stable to compute even if the matrix is ill-conditioned. Moreover, by using a Kernel Independent Fast Multipole (KIFMM) approach [52] the computation of the eigenstructure in principle can be relatively fast for problems in \mathbb{R}^3 . An advantage of the KL expansion is that it does not involve

inversion of the covariance matrix. However, for higher dimensional problems, such as predicting the total charge missing data involving 4 dimensions, there are no known fast summation methods such as the KIFMM. It is still possible to compute the eigenstructure for a relatively large dataset on a powerful Graphics Processing Unit (GPU).

Alternatively, there exists a set of linear equations for the BLUP that solve for the Mean Square Error (MSE) of the prediction. This involves inverting the covariance matrix **C**; thus for large datasets it can be numerically unstable and intractable. [31] show that there exists a formulation for the multilevel approach that is significantly faster and numerically stable. However, it can still be intractable for estimating large numbers of missing data. We shall investigate these approaches in more detail in a future publication.

Finally, we have not addressed the problem of imputation for categorical data, which is part of the HCUP dataset. Our approach can potentially deal with the categorical data by treating it as numerical and defining a cutoff. For example this is what is done with Support Vector Machines (SVMs). The question that arises is what choice of cutoff do we use ? We will deal with these types of variables in a future publication.

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