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MSc in Statistical Science

Final thesis

Missing data imputation for Haemorrhagic shock prediction

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Abstract

Lorem ipsum dolot sit amet nunc cui Brexit.

Acknowledgements

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Introduction

Main outline: Haemorrhagic shock is a condition that can be life-threatening but that has much higher survival rates if treated early. In addition, doctors tend to have a fairly bad record of detecting it. Because of this, we want to build a tool that predicts it based on measurement on trauma patients. For this we use Traumabase, a large patient-records database. Problem: lots of missing data in it. Solutions: use algorithms specifically made for missing data or impute missing data. Nice thing about imputation: once it is done, you can use any existing method -> here we only work on imputation (not so much the prediction part).

We present the data (Chapter 1), then present the state of the art in imputation (Chapter 2). Then, we derive some theory on imputation when it is performed with prediction as a goal (Chapters 3 and 4). We then come back to the data to apply what we learn, in order to choose the best imputation method for this problem (Chapter 5) and present our final results (Chapter 6).

Chapter 1

Goal and data

1.1 The problem of haemorrhagic shock

1.1.1 Importance as a medical condition

Descibe HS + hospital context

1.1.2 Need for an assistance tool

Prediction is very hard, as described in [1] + possible to treat if taken early

1.2 The Traumabase data

1.3 Exploratory data analysis

1.3.1 Variables

1.3.2 Missing data

1.4 Objective of this work

As explained in Section 1.1, we want to enable the conception of a tool that would detect haemorrhagic shock in trauma patients. In this work, we focus more specifically on handling the missing data

... explain the specificity: patient by patient predicition, analyst has no access to the training data

Chapter 2

Imputation methods

2.1 Main types of imputation

2.1.1 Joint parametric specification

2.1.2 Fully conditional specification: the MICE algorithm

2.1.3 Low-rank approximation for imputation

2.1.4 ML-based

2.2 Multiple imputation

2.2.1 Principle

2.2.2 Rubin's rule and prediction aggregation

2.3 Normality hypothesis: transforming the data

Chapter 3

Methodology: imputation and the validation split

The task we are trying to solve is quite peculiar: we are trying to impute the missing values in the data, not to perform a statistical analysis, but to select and train a prediction model. Our final benchmark of performance is not parameter estimation but predictive loss. As the next two chapters will show, although this seems like a small difference, this actually leads to some major changes.

It is interesting to note in that regard how the communities of statistics and machine learning seem to lack any point of convergence on the subject. Missing data have been an active field of research in statistics for a long time [2], and many complex methods have been developed and proven for statistical inference [3] (such as those described in Chapter 2).

On the other hand, there is almost no research on these methods when applied to prediction. Even recent manuals for machine learning [4] generally make only a quick mention of missing data, and in practice it is extremely rare for anything else than imputation by the mean to be used. *Scikit-learn* [5], by far the most-used machine learning package, only proposes imputation by the mean as of now.

A few research papers [6] [7] try to assess the performance of more recent imputation methods when used in a predictive context. However, they do not propose any framework or theory on this endeavour. They take it for granted that they can impute the whole dataset before performing the subsequent analysis. However, when performing prediction there is one significant difference with statistical inference, which we describe further in this chapter: the data is split into one dataset to learn the model, and another one to validate its performance. This raises many questions that we discuss here and in Chapter 4.

After laying out the general framework of Empirical Risk Minimization [8], which is the general paradigm used for prediction, we adapt it to fit the context of missing data. We notice that current implementations of modern imputation methods are incompatible with this framework, and try to devise solutions for this issue.

3.1 Empirical risk minimization (ERM): classical context

We first describe Empirical Risk Minimization (ERM) without missing data, as described in [8].

3.1.1 Context and notations

We are provided with a matrix X of size $n \times p$ and response vector y of size n. Our goal is to learn a model in the form $\hat{y} = f(x, \psi)$, where ψ is some parameter to choose, $\hat{y}$ is a predicted value for y and f is a fixed parametric predictive function (usually corresponding to a choice of function in a given class).

The quality of a prediction is evaluated with the loss $L(y, \hat{y})$. The end goal in this context is to find the parameter $\hat{\psi}$ which minimizes the risk: $R = \mathbb{E}(L(y, f(X)))$. However, we do not have access to the real expectation of the risk, so we must use a proxy for this value. We define the empirical risk:

$$R_{\mathrm{emp}}(y, f(X, \psi)) = \frac{1}{n} \sum_{i=1}^{n} L(y_i, f(X_i, \psi))$$

Empirical Risk Minimization corresponds to choosing ψ minimizing R_{emp} for our X and y. However, this is not enough. We do not just want the optimal ψ, we also want a measure of how well the final model would perform on new data. This is important because this is what we will take into account to make our choice of f. But the empirical risk gives us no measure of how well our model generalizes whatsoever, only of how closely it can fit known data.

To address the issue of model selection, the standard practice is to measure the error on some data that were not used to learn the model: it is the principle of cross-validation.

3.1.2 Cross-validation

To perform Cross-validation, we divide the data in two datasets: first we choose $n_A < n$ entries in the dataset to be used to loearn ψ: this is the training dataset X_A and response y_A. We denote $I_A = (i_1, \dots, i_{n_A})$ the set of indices chosen for the training data. The rest of the observations are noted X_V and y_V and called the validation dataset.

Once this is done, ERM is performed as before, using only the training data. The obtained parameter $\hat{\psi}$ can then be evaluated with the validation error:

$$R_V = \frac{1}{n_V} \sum_{i=1, i \notin I_A}^{n} L(y_i, f(X_i, \hat{\psi}))$$

It is this value that we can compare to choose our our model class f.

3.2 ERM with missing data: the problem of current methodologies

We now place ourselves in the same context as before, except some values are missing from X, both in the training and the validation data. The context is almost the same as before: choosing a parametric model that takes as input the observed data and outputs a prediction for y.

3.2.1 Imputation seen as an ERM

Remember that the purpose of this work is to impute the data independently of the predictive model used afterwards. This does not change the framework of ERM but it does mean that we cannot use any function we like to go from X to $\hat{y}$. The prediction is the composition of two steps.

Imputation step First we choose an imputation model $X^{\text{complete}} = g(X, \phi)$ where X^{complete} is the completed dataset and ϕ some parameter. This is similar to predicting y as we did previously with one caveat: we do not know the true data, even on the training dataset. Thus we choose $\hat{\phi}$ to minimize some unsupervised loss

$$L'(g(X, \phi), \phi)$$

measuring the fit of the model to the data. Generally, this means that we choose a parameter that maximizes the likelihood of the observed data according to some generative model (though it is not always the case). Once this is done, we obtain a completed dataset $\hat{X}$.

Prediction step Once the imputation is done, we can perform as before to choose a parameter $\hat{\psi}$ that minimizes the empirical risk when using the completed data:

$$R_{\text{emp}}(y, f(\hat{X}_i, \psi)) = \frac{1}{n} \sum_{i=1}^{n} L(y_i, f(\hat{X}_i, \psi))$$

Putting it all together, we can define

$$h(X, (\psi, \phi)) = f(X^{imp}, \psi) = f(g(X, \phi), \psi)$$

the combined model that takes the observed data as input and outputs a predicted y. This is optimized as

$$\begin{aligned} \hat{\phi} &= \arg\min_{\phi} L'(g(X, \phi, \phi) \\ \hat{\psi} &= \arg\min_{\psi} R_{\text{emp}}(y, h(X, (\psi, \hat{\phi}))) \end{aligned}$$

We choose to use this notation to illustrate our point that imputation is an integral part of the ERM, not a separate, preliminary process. In particular, it means that in theory its parameters *must* be subjected to cross-validation just like those of the prediction. That is X_A the training data are used to estimate $(\hat{\psi}, \hat{\phi})$ as shown just above. Then, we can compute a prediction $\hat{y}_V = h(X_V, (\hat{\psi}, \hat{\phi}))$ which can be compared to y_V to evaluate the choice of model.

The bottom line is that just like for the prediction, the imputation parameter ϕ should be estimated only on the training data and then used on the validation data. As we will see, this raises an issue with the way current imputation methods are implemented.

3.2.2 Unsuitability of current methods

Over the years, many imputation methods have been proposed, and we describe some in Chapter 2. They have various assumptions and principles but they have one thing in common: they are all implemented (usually in R) via a single function. That function takes a dataset with missing values as an input and returns the dataset completed by the method of choice, *without giving the user any access to the model itself.*

This is a problem because of how cross-validation is supposed to be performed. Normally, one would estimate $(\hat{\psi}_A, \hat{\phi}_A)$ through ERM, and then make a prediction on the validation set as $h(X_V, (\hat{\psi}_{X_A}, \hat{\phi}_{X_A}))$. But here, all we have access to is a function $g' : X \mapsto g(X, \hat{\phi}_X)$ where $\hat{\phi}_X$ is the optimised parameter for the argument X. It is straightforward to see that using such a function, one can no longer separate the estimation of the parameters and the imputation in itself.

Incidentally, this issue was mentioned recently [9], as part of a larger effort to port the MICE [10] imputation method to Scikit-learn [5]. This package is developed for data scientists, who are used to having separate functions for training and prediction. Likewise, several other mentions of this problem arose in the last two years [11][12][13] with no mention of it earlier. It seems that as more elaborate imputation methods become popular with the machine learning community, the need arises for a change in the way those methods are implemented. However, it is clear that such changes take time, and for now we can do one of two things: make do with what is available, or build our own implementation to adapt one of these methods to our goals.

3.3 Possible solutions

3.3.1 Using current implementations

Methods

There are many ways we can use to approximate the correct procedure, though none of them is theoretically satisfactory. We describe the most natural ones and their caveats.

Grouped imputation Impute all of the data at once before performing the cross-validation split. That is, estimate $\hat{\phi}_X$ on the whole data then

$$\hat{\psi}_{X_A} = \arg\min_{\psi} R_{emp}(y, h(X, (\psi, \hat{\phi}_X)))$$

and $\hat{y}_V = h(X_V, (\psi_{X_A}, \phi_X))$.

In that case, the parameter ϕ is imputed using the validation data. In particular, imputed values in X_A *depend on those in* X_V, which is contrary to the basic principles of cross-validation where validation data must be held out during parameter estimation. In theory this could falsify the validation error by making it too optimistic (if some hard-to-predict observations are present in the test set, that would otherwise have high validation error but will not in this case because of our 'cheating').

Separate imputation Divide the data first, then impute each dataset separately:

$$\begin{aligned}
\hat{\phi}_{X_A} &= \arg\min_{\phi} R'_{emp}(X_A, \phi) \\
\hat{\phi}_{X_V} &= \arg\min_{\phi} R'_{emp}(X_V, \phi) \\
\hat{\psi}_{X_A} &= \arg\min_{\psi} R_{emp}(y, h(X, (\psi, \hat{\phi}_{X_A}))) \\
\hat{y}_V &= h(X_V, (\psi_{X_A}, \phi_{X_V}))
\end{aligned}$$

Contrarily to grouped imputation, this does not violate cross-validation at all. However, we are using parameter ϕ_{X_V} to impute the validation data and then apply a predictive model that uses ψ_{X_A}, optimized for data imputed with ϕ_{X_A}. If sample size is not large enough, it is possible that ϕ_{X_A} and ϕ_{X_V} will be noticeably different. In that case, there is no guarantee that ψ_{X_A} will still be valid for prediction on the validation dataset that was imputed differently.

Line by line imputation The last option we mention here is to first impute the training data on its own. Then for every line of the validation data we impute it by stacking it with the imputed training data and imputing the whole dataset. Since it is just one line, we can safely assume that the imputation parameters will be those of the training data. The main issue with this method is that is the validation data is rather large, this will be computationally infeasible.

Need for a correct implementation

We want to understand if the alternatives proposed here are good enough to be used if a correct implementation is impossible. To do that, we need to be able to compare these with the correct method. That means that for at least one imputation method we need to build an implementation that allows us to separate the estimation and the imputation. That way we will be able to compare its performance with the other alternatives we propose

Moreover, in addition to this theoretical pursuit, we need this because of what we are trying to achieve with Traumabase: the end goal is to make a recommendation system that can produce a prediction for *a single new patient* arriving to the hospital, ideally without needing to have access to the whole Traumabase data (which is hard to share because it contains sensitive patient information). Without access to the initial training data, this means that only a fully parametric approach can be taken in this particular case (separate imputation is impossible on just one line of data, and the other ones require access to the full data).

Below, we design a very simple imputation method for those purposes.

3.3.2 A new variant: Multivariate Normal Mode with reserved data

The principle of this imputation is inspired from R package *Amelia* [14], and a large part of the code is from the *norm* package [15]. The idea is to assume that both X_A and X_V follow a normal distribution $\mathcal{N}(\mu, \Sigma)$ with unknown parameters.

Parameter estimation It is possible to approximate maximum-likelihood estimators for μ and σ iteratively, using the EM algorithm [16] [17]. First, the missing values of X are imputed randomly to give $X^{(1)}$. Then we repeat the following steps:

For $t = 1...$

1. $(\mu^{(t)}, \Sigma^{(t)})$ are computed as the maximum likelihood estimators on the completed data $X^{(t)}$ for the normal distribution (empirical mean and covariance)
2. $X^{(t+1)}$ is computed by replacing the missing values by their expected value under the new parameters:
$$X^{(t+1)} = \mathbb{E}(X|X^{\text{obs}}; \mu^{(t)}, \Sigma^{(t)})$$
The conditional expectation is easily derived using the Schur complement [18].

Once this converges we have an estimated parameter $\hat{\phi} = (\hat{\mu}, \hat{\Sigma})$.

Imputation Once we have the parameters, it is very straightforward to get an imputation of the missing data. There are two different ways of doing this:

- Replace missing values by their expectation conditional on the observed data:
$$\hat{X} = \mathbb{E}(X|X^{\text{obs}}; \hat{\mu}, \hat{\Sigma})$$
That is, pick the mode of the conditional distribution.

- Draw the missing values from the conditional distribution

In the second case, the *norm* package provides all that is needed. This is what would be used for multiple imputation. However, as we see in Chapter 4, the mode is the optimal choice if we want a single best imputation to use for a prediction model. We implemented this method. We use it below in order to compare the methods mentioned before.

3.3.3 Comparison on simulated data

In order to compare the methods used for imputation

Chapter 4

Error sources and best imputation: the case of linear regression with missing data

In order to make good decisions for imputation, it is important to understand how it impacts prediction. In order to get an idea on this issue, we solve a very simple case of cross-validated regression with missing data. We found no theoretical results whatsoever about the relationship between imputation and prediction.

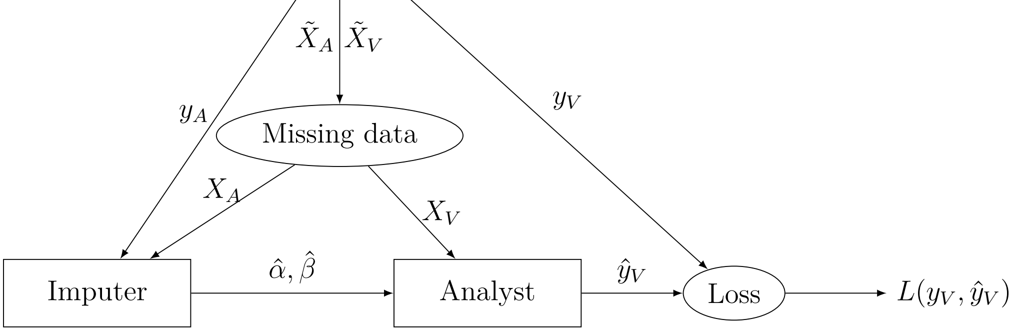

Ground truth
$\tilde{X}_A$ $\tilde{X}_V$
y_A
y_V
Missing data
X_A
X_V
Imputer
$\hat{\alpha}, \hat{\beta}$
Analyst
$\hat{y}_V$
Loss
$L(y_V, \hat{y}_V)$

Figure 4.1: Imputation framework

4.1 Problem set-up

We place ourselves in a simple linear regression context with two covariates, where one observation is missing in the training dataset, and one in the validation dataset.

4.1.1 Notations

True data

The true, unobserved data is a standard regression setup, with the exception that one line of the data is reserved as ’validation data’ [1] , with the rest called ’training data’ — as is standard in predictive contexts (cf Chapter 3). The response variable y is a noised linear combination of the covariates in X:

$$\tilde{X}_A = \begin{pmatrix} x_{11} & x_{12} \\ \vdots & \vdots \\ x_{n1} & x_{n2} \end{pmatrix} \quad \text{and} \quad y_A = X_A\beta + \epsilon_A \quad \text{with} \quad \epsilon_A \sim \mathcal{N}(0, \sigma^2)$$

$$\tilde{X_V} = \begin{pmatrix} x_1^V & x_2^V \end{pmatrix} \quad \text{and} \quad y_V = X_V\beta + \epsilon_V \quad \text{with} \quad \epsilon_V \sim \mathcal{N}(0, \sigma^2)$$

The end goal is to learn an estimator on the training set that minimizes the expected loss on the validation set:

$$L(y_V, \hat{y}_V) = (y_V - \hat{y_V})^2$$

This is a well known problem with a simple solution. The regression estimator can be expressed as:

$$\tilde{\beta} = (\tilde{X}_A^T\tilde{X}_A)^{-1}\tilde{X}_A^T y_A$$

with and estimated response

$$\tilde{y}_V = \tilde{X}_V\tilde{\beta}$$

But there is one caveat: the data is actually not fully observed.

---

[1] For this calculation we only need one line of validation data since we will be using expected values.

Observed data

What we actually have access to is slightly different: one observation is missing in the training set, as is one of the entries in the testing set. We observe the full y^A, but the covariate matrices we actually have access to are:

$$X^A = \begin{pmatrix} ? & x_{12} \\ \vdots & \vdots \\ x_{n1} & x_{n2} \end{pmatrix} \quad \text{and} \quad X^V = \begin{pmatrix} ? & x_2^V \end{pmatrix}$$

4.1.2 Imputed data and regression

Principle

To perform a linear regression similarly to what we did previously, we first have to fill in the blanks: we impute the missing data by replacing them with chosen values ϕ and ψ (which we choose using the value of what we observe).

$$\hat{X}^A = \begin{pmatrix} \phi & x_{12} \\ \vdots & \vdots \\ x_{n1} & x_{n2} \end{pmatrix} \quad \text{and} \quad \hat{X}^V = \begin{pmatrix} \psi & x_2^V \end{pmatrix}$$

This in turn allows us to perform the regression just like before:

$$\hat{\beta} = (\hat{X}_A^T \hat{X}_A)^{-1} \hat{X}_A^T y_A \quad \text{and} \quad \hat{y}_V(\phi, \psi) = \hat{X}_V \hat{\beta}$$

This means that what we really want to minimize is the following risk function:

$$R(\phi, \psi) = \mathbb{E}[(y_V - \hat{y}_V(\phi, \psi))^2 | X_A, X_V]$$

where the only thing we choose is our decision rule for ϕ and ψ.

Distribution hypotheses

Lastly, for this last expression to have any meaning, we need to make some assumption on the distribution of X.

We make a very simple hypotheses of a multivariate normal distribution for the covariates — the parameters are assumed to be known, in real life they would be estimates.

$$\tilde{X}_A \sim \mathcal{N}(\mu, \Sigma) \quad \tilde{X}_V \sim \mathcal{N}(\mu, \Sigma)$$

With these, we know the distribution of the missing observations x_{11} and X_1^V conditional of the observed ones and we can try to find the ϕ and ψ values that give us the best expected loss.

Now that we have these notations and hypotheses, it is possible to solve the problem of the choice of imputation. Here we give a full expression of the loss and partial resolution.

4.2 Partial resolution

4.2.1 General loss

To be able to estimate the expected loss, we break it up into several components

$$\begin{aligned}
L(y_V, \hat{y_V}) &= (y_V - \hat{y_V})^2 \\
&= (\tilde{X}_V\beta + \epsilon_V - \hat{X}_V\hat{\beta})^2 \\
&= (\tilde{X}_V(\beta - \tilde{\beta}) + \tilde{X}_V(\tilde{\beta} - \hat{\beta}) + (\tilde{X}_V - \hat{X}_V)\hat{\beta} + \epsilon_V)^2 \\
&= (\tilde{X}_V(\beta - \tilde{\beta}))^2 && (1)\\
&\quad + (\tilde{X}_V(\tilde{\beta} - \hat{\beta}))^2 && (2)\\
&\quad + ((\tilde{X}_V - \hat{X}_V)\hat{\beta})^2 && (3)\\
&\quad + \tilde{X}_V(\beta - \tilde{\beta})\tilde{X}_V(\tilde{\beta} - \hat{\beta}) && (4)\\
&\quad + \tilde{X}_V(\beta - \tilde{\beta})(\tilde{X}_V - \hat{X}_V)\hat{\beta} && (5)\\
&\quad + \tilde{X}_V(\tilde{\beta} - \hat{\beta})(\tilde{X}_V - \hat{X}_V)\hat{\beta} && (6)\\
&+ \epsilon_V^2 \\
&+ \epsilon_V K
\end{aligned}$$

Where K is some term that will not matter (because when we take the expectation it will be zero). The risk we want to minimize is the expectation of this loss.

4.2.2 When the validation set is fully observed

Imputation

The first thing we can easily do is to study the situation where the only missing data is in the validation set. In that case, $\tilde{X}_A = \hat{X}_A$ and so $\tilde{\beta} = \hat{\beta}$, and all we have to choose is ψ. In the previously computed loss, it means that terms (2), (4) and (6) are zero.

Furthermore, Cochran's theorem ensures that $(\beta - \tilde{\beta})$ and $\tilde{\beta}$ are independent so term (5) can be factorized and will have zero expectation (since $(\beta - \tilde{\beta})$ has zero expectation).

Term (1) depends only on the true values of X_V, independent of psi, so the choice of ψ is not impacted by this term.

This leaves us with only term (3), with expectation:

$$\begin{aligned}\mathbb{E}[((\tilde{X}_V - \hat{X}_V)\tilde{\beta})^2 | x_2^V, X_A] &= \mathbb{E}[(x_1^V - \psi)^2 \tilde{\beta}_1^2 | x_2^V, X_A] \\ &= \mathbb{E}[\tilde{\beta}_1^2 | x_2^V, X_A](\mathbb{E}[(x_1^V)^2 | x_2^V, X_A] \\ &\quad - 2\psi \mathbb{E}[x_1^V | x_2^V, X_A] + \psi^2)\end{aligned}$$

Once we are there, we can differentiate this expression to easily derive the optimal expression for ψ: $\hat{\psi} = \mathbb{E}[x_1^V | x_2^V]$, the conditional expectation of the missing value.

Incidentally, this does not use any assumption on the distribution of X: this would be true for any joint distribution we choose for the covariates.

Expected loss

First note:

$$\begin{aligned}\eta = \beta - \tilde{\beta} = \beta - (\tilde{X}_A^T \tilde{X}_A)^{-1} \tilde{X}_A^T y_A \\ = (\tilde{X}_A^T \tilde{X}_A)^{-1} \tilde{X}_A^T (\tilde{X}_A \beta + \epsilon_A) \\ = (\tilde{X}_A^T \tilde{X}_A)^{-1} \tilde{X}_A^T \epsilon_A\end{aligned}$$

That is, the difference between the estimated and real parameter is distributed following some centred normal distribution. Let us denote its covariance matrix by $S = \sigma^2 (\tilde{X}_A^T \tilde{X}_A)^{-1}$.

Now, term (1) can be expressed as :

$$\begin{aligned}\mathbb{E}[(\tilde{X}_V \eta)^2 | x_2^V] &= \mathbb{E}[(x_1^V \eta_1 + x_2^V \eta_2)^2 | x_2^V] \\ &= S_{11} \mathbb{E}[(x_1^V)^2 | x_2^V] + 2 x_2^V S_{12} \mathbb{E}[x_1^V | x_2^V] + S_{22} (x_2^V)^2\end{aligned}$$

Term (3) can be expressed as:

$$\begin{aligned}\mathbb{E}[((\tilde{X}_V - \hat{X}_V)\hat{\beta})^2 | x_2^V] &= \mathbb{E}[((x_1^V - \hat{\psi})\tilde{\beta}_1)^2 | x_2^V] \\ &= \mathbb{E}[((x_1^V - \hat{\psi})(\beta_1 + \eta_1))^2 | x_2^V] \\ &= \beta_1^2 \mathrm{Var}[x_1^V | x_2^V] + S_{11}^2 \mathrm{Var}[x_1^V | x_2^V]\end{aligned}$$

The terms from (1) would be more or less the same if the test data were fully observed. They represent the impact on the prediction of the error made when estimating β.

On the other hand, those from (3) are both positive and unique to the incomplete case. They do not depend on the test data at all. The first term reflects how an error in the imputation of X_V is amplified by the regression coefficient when predicting y. The second one shows how errors in the estimation of β and of X_V combine when predicting y.

Most importantly, the least squares estimator is a strongly consistent one[19], which implies that the only error terms that matter with large n are those that remain when η is set to zero:

$$\beta_1^2 \mathrm{Var}[x_1^V | x_2^V] + \sigma^2$$

The missing data in the validation set adds a term that does not vanish for large n.

When there are more than two covariates An important point is that in a context with more than two covariates, the conditional variance of an observation increases when the number of unobserved variables increases: this means that when the dimension increases, not only do new error terms appear, but the existing ones also increase.

For X_V with $p > 2$ covariates, we denote X_V^{miss} and X_V^{obs} the missing and observed values in X_V. We can now write (3) again:

$$\begin{aligned}\mathbb{E}[((\tilde{X}_V - \hat{X}_V)\beta)^2 | X_V^{\mathrm{obs}}] &= \mathbb{E}[(\sum_{\substack{i=1 \\ i \in X_V^{\mathrm{miss}}}}^{p} (x_i^V - \hat{x}_i^V)\beta_i)^2 | X_V^{\mathrm{obs}}] \\ &= \mathbb{E}[\sum_{\substack{i=1 \\ i \in X_V^{\mathrm{miss}}}}^{p} \sum_{\substack{j=1 \\ j \in X_V^{\mathrm{miss}}}}^{p} (x_i^V - \hat{x}_i^V)(x_j^V - \hat{x}_j^V)\beta_i\beta_j | X_V^{\mathrm{obs}}]\end{aligned}$$

If, as previously, we choose $\hat{x}_i^V = \mathbb{E}[x_i^V | X_V^{\mathrm{obs}}]$, we end up with:

$$\mathbb{E}[((\tilde{X}_V - \hat{X}_V)\beta)^2 | X_V^{\mathrm{obs}}] = \sum_{\substack{i,j=1 \\ i,j \in X_V^{\mathrm{miss}}}}^{p} \beta_i\beta_j Cov(x_i^V, x_j^V | X_V^{\mathrm{obs}})$$

4.2.3 When the data is large and the training data is fully observed

We can suppose that n is large and that we know $\tilde{X}_V$. In that case, we can take the approximation that $\beta = \tilde{\beta}$, that is, the only error in the estimation of β comes from the missing data in the training set. Then, the only error term that is nonzero is (2):

$$(\tilde{X}_V(\hat{\beta} - \tilde{\beta}))^2$$

To complete

4.3 Analysis

4.3.1 Implications

Theoretical consequences If the results above are any indication as to how things go in more complex settings, there are some interesting implications.

First, this confirms our intuition that using the conditional mode is the right thing to do to impute the validation data. This is important, especially as most imputation packages were made for multiple imputation and draw from the conditional distribution instead.

Second, there is a major asymmetry between the training and validation dataset: in the training set, every line works together with the others to help estimate some parameter. In particular, this means that even if all of the imputations are imperfect, with enough observations we can obtain a satisfactory estimate of the parameters (this is similar to the case of statistical inference with missing data, where under some assumptions the estimators are asymptotically consistent [20]). More data adds information, and even if it is incomplete it helps with the estimation.

The validation data is in a completely different situation. Missing data in the validation dataset adds error terms to the data that can be very large and do not vanish asymptotically. Intuitively, even if we have exactly the right β for regression, any error in the estimation of the data will be directly reflected as a prediction error proportional to the regression coefficient, while in the training set this effect is much more indirect. Such errors are inevitable, even if we know the exact distribution of the data, because it is random. The expected loss will be the same for every line on the validation set (with the same missingness pattern), so adding more validation lines will do nothing to reduce the mean error if they also have missing data. This is important not only from the standpoint of model selection, but also because the validation error gives us an idea of how our model will perform on real-world data: missing data in the data we use for prediction can be a much more severe issue than missing data in our training database.

Implications for our data This could actually be a positive find. Take the example of Traumabase and haemorrhagic shock prediction: part of what our results mean is that the Traumabase can indeed be used to build a prediction tool, even if it has a significant amount of missing data. If the missing data is mostly due to errors of recording, this may mean that it is available in the real world when a doctor uses the tool: if the data used to make important predictions (that is, not a posteriori from the base but in a hospital when a patient needs care) can be kept full, then our estimates will have a chance of being very good, as long as we built our model with a large enough database.

The flip size, of course, is that when data is indeed missing from the validation dataset, there is little we can do to offset the resulting penalty. The missing value has a natural variability, even when controlling for every other observed variable, so even our best guess could have a high error.

4.3.2 Partial multiple imputation

This suggests an idea that could help mitigate this drawback while keeping the computational cost rather low. Using X_A the training data, we can estimate parameters ϕ, ψ, β as usual. Then, keeping these parameters constant, we can make draws from the conditional distribution of X_V and make predictions on the datasets generated this way. Using the quantiles of these predictions, we can build intervals that approximate the possible location of the true value of y and account for uncertainty. The idea behind this is that it is not necessary to multiply impute X_A because with lare n the estimated parameters will not really vary. It is also computationally intensive because it means we have to fit a new model for every imputed dataset. With our method, just one fit is needed and we only perform multiple predictions, which are usually cheaper.

To illustrate these results, we perform an analysis on some very simple simulated data, and check if the properties we derived are visible.

4.3.3 Verification on real and simulated data

We ran an analysis on two sets of data:

1. A simulated dataset designed to respect the assumptions of our model: the X data is generated as a multivariate normal for some random covariance matrix (with $p = 10$ variables), and the response are obtained linearly by scalar product with some parameter β (plus some noise)

2. A very simple real world dataset: the Abalone dataset. It is a regression dataset where the goal is to predict the age of a shell based on 7 measurements. It has no missing data and the covariates have high correlation.There are more that 4000 observations.

On both dataset, we ran the following procedure:

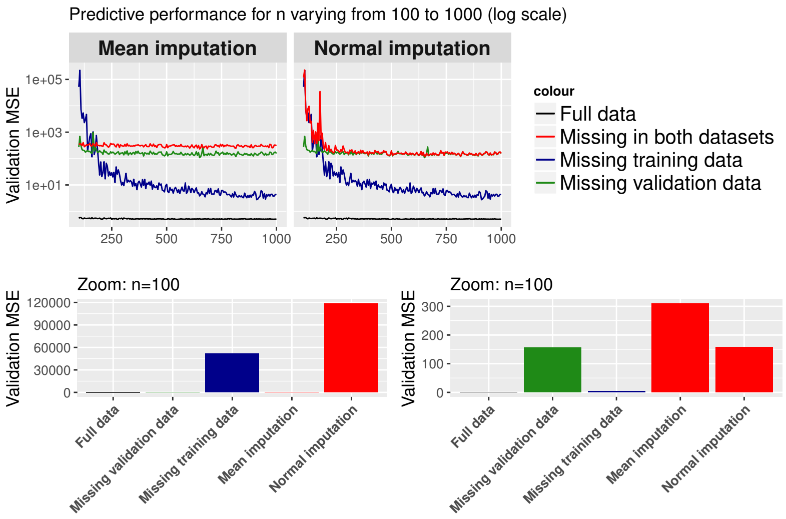
- Split the data in a training and a validation datasets.
- Perform one linear regression on the complete dataset.
- Add some (30%) missing data completely at random.
- Impute the data by the mean, perform a regression.
- Using the complete training data and the validation data with missing values, impute the data as a multivariate normal and perform a regression.
- Using the training data data with missing values and the complete validation, impute the data as a multivariate normal and perform a regression.
- Using both datasets with missing values, impute the data as a multivariate normal and perform a regression.
- Compute the mean squared prediction error for each of the five regressions on the validation data.

This is repeated multiple times to smooth out the variability of the results. We do this for a broad range of n values (for Abalone we select n rows at random for the analysis, for the simulated data we generate n rows each time).

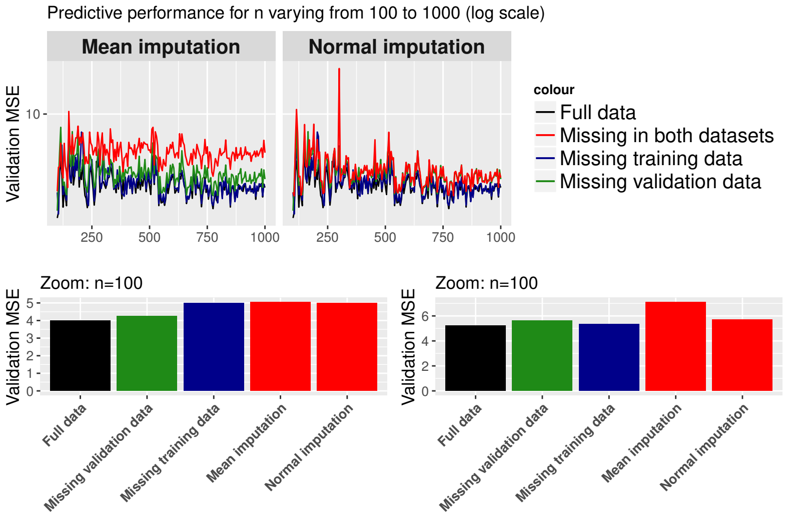
The results are shown in Figure 4.2.

The trends are less visible in the Abalone data, most likely because the base error from model misspecification is higher so the relative variations are smaller. However, we can see some general trends emerge.

For large n, the results match our expectations. The error is much lower when the validation data is known, while there is almost no difference with and without knowing the real training data: with enough information we make up for the missing data when estimating the parameters. Even on the Abalone data (which is not really normally distributed), the normal imputation performs much better than imputation by the mean.



(a) Simulated data



(b) Abalone data

Figure 4.2: Linear regression with missing data

For small n, everything is very different. The first striking result is that the main error term comes from the missing data in the training set, this time. This makes sense, as for such a small n it is very difficult to accurately estimate the covariance of the data, so missing values in the training data can seriously impact parameter estimation for the imputation. For the same reason, it is understandable that imputation by the mean works better than normal imputation in this context: with less parameters to estimate, we can at least have a fairly good estimation of the mean rather than a very bad estimation of both the mean and covariance.

Throughout the spectrum of n, we also see that the imputation with missing data everywhere tends to match whichever is worse between the full training data and the full validation data. These values act as lower bounds for the quality of prediction.

Chapter 5

Analysis: imputing the Traumabase data for prediction

5.1 Criteria for evaluation

5.2 Choosing the imputation method

Mention the fact that most methods have the same performance (even mean)

Imputation done before model selection (cf congeniality)

5.3 Multiple imputation

Chapter 6

Results

Conclusion

Bibliography

[1] Matthew J Pommerening, Goodman, et al. Clinical gestalt and the prediction of massive transfusion after trauma. *Injury*, 46(5):807–813, 2015.

[2] Donald B Rubin. Inference and missing data. *Biometrika*, 63(3):581–592, 1976.

[3] Roderick JA Little and Donald B Rubin. *Statistical analysis with missing data*, volume 333. John Wiley & Sons, 2014.

[4] Ian H Witten, Eibe Frank, Mark A Hall, and Christopher J Pal. *Data Mining: Practical machine learning tools and techniques.* Morgan Kaufmann, 2016.

[5] F. Pedregosa, G. Varoquaux, A. Gramfort, V. Michel, B. Thirion, O. Grisel, M. Blondel, P. Prettenhofer, R. Weiss, V. Dubourg, J. Vanderplas, A. Passos, D. Cournapeau, M. Brucher, M. Perrot, and E. Duchesnay. Scikit-learn: Machine learning in Python. *Journal of Machine Learning Research*, 12:2825–2830, 2011.

[6] Yvonne Vergouwe, Patrick Royston, Karel GM Moons, and Douglas G Altman. Development and validation of a prediction model with missing predictor data: a practical approach. *Journal of clinical epidemiology*, 63(2):205–214, 2010.

[7] José M Jerez, Ignacio Molina, Pedro J García-Laencina, Emilio Alba, Nuria Ribelles, Miguel Martín, and Leonardo Franco. Missing data imputation using statistical and machine learning methods in a real breast cancer problem. *Artificial intelligence in medicine*, 50(2):105–115, 2010.

[8] Vladimir Naumovich Vapnik. An overview of statistical learning theory. *IEEE transactions on neural networks*, 10(5):988–999, 1999.

[9] Basic version of MICE Imputation github pull request. `https://github.com/scikit-learn/scikit-learn/pull/8478`. Scikit-learn repository.

[10] Joseph L Schafer. *Analysis of incomplete multivariate data*. Chapman and Hall/CRC, 1997.

[11] Get at the final model used in the MICE iterations? `https://github.com/stefvanbuuren/mice/issues/32`, . Github MICE repository.

[12] R MICE impute new observations. `https://stackoverflow.com/questions/40115226/r-mice-impute-new-observations`, . Stackoverflow discussion.

[13] Imputation using MICE: Use the train data to impute the missing test data. `https://stats.stackexchange.com/questions/332342/imputation-using-mice-use-the-train-data-to-impute-the-missing-test-data` . Stackexchange discussion.

[14] James Honaker, Gary King, Matthew Blackwell, et al. Amelia ii: A program for missing data. *Journal of statistical software*, 45(7):1–47, 2011.

[15] Ported to R by Alvaro A. Novo. Original by Joseph L. Schafer <jls@stat.psu.edu>. *norm: Analysis of multivariate normal datasets with missing values*, 2013. URL `https://CRAN.R-project.org/package=norm`. R package version 1.0-9.5.

[16] Arthur P Dempster, Nan M Laird, and Donald B Rubin. Maximum likelihood from incomplete data via the em algorithm. *Journal of the royal statistical society. Series B (methodological)*, pages 1–38, 1977.

[17] Joseph L Schafer. *Analysis of incomplete multivariate data*. Chapman and Hall/CRC, 1997.

[18] Fuzhen Zhang. *The Schur complement and its applications*, volume 4. Springer Science & Business Media, 2006.

[19] TW Anderson, John B Taylor, et al. Strong consistency of least squares estimates in normal linear regression. *The Annals of Statistics*, 4(4): 788–790, 1976.

[20] Roderick JA Little and Donald B Rubin. *Statistical analysis with missing data*, volume 333. John Wiley & Sons, 2014.