

Design, implementation and evaluation of data integration methods for biomedical cancer data

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Preface

I would like to thank everybody who kept me busy the last year, especially my promotor and my assistants. I would also like to thank the jury for reading the text. My sincere gratitude also goes to my wife and the rest of my family.

Michiel Ruelens

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Abstract

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Samenvatting

In dit **abstract** environment wordt een al dan niet uitgebreide Nederlandse samenvatting van het werk gegeven. Wanneer de tekst voor een Nederlandstalige master in het Engels wordt geschreven, wordt hier normaal een uitgebreide samenvatting verwacht, bijvoorbeeld een tiental bladzijden.

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List of Abbreviations and Symbols

Abbreviations

LoG	Laplacian-of-Gaussian
MSE	Mean Square error
PSNR	Peak Signal-to-Noise ratio

Symbols

42	“The Answer to the Ultimate Question of Life, the Universe, and Everything” according to [?]
c	Speed of light
E	Energy
m	Mass
π	The number pi

Chapter 1

Introduction

The first contains a general introduction to the work. The goals are defined and the modus operandi is explained.

1.1 The need for data integration methods

1.2 Goals

1.3 Modus operandi

Chapter 2

Generalized Linear Models

In this chapter I will explain the current standard in machine learning when it comes to generalized linear models. This term indicates a generalization of simple linear regression that allows for a wide range of output variables.

First I will go over the basics of linear models, gradually building up to the definition of generalized linear models. Next, I will describe what actual data looks like and how this data is transformed into a useful model.

After that I will tackle the more recent innovation of regularization that will greatly improve our previous models by exploiting the bias-variance trade-off to reduce overfitting. Lastly I will outline the validation method that will be used to test the performance of the models.

2.1 Classical linear models

When we think of classical linear models, we can imagine a set of numeric explanatory (or input) variables and a numerical dependent (or output) variable. By making a linear combination of the explanatory variables we attempt to estimate a value for the dependent variable. Depending on the type of dependent variable the linear method gets a different name. In the following sections I will outline several of them.

2.1.1 Linear Regression

The simplest version of a linear model is called linear regression. In this case the input variables are combined using a linear combination, and the result of this calculation is immediately used as the final estimate.

//TODO MATH

For the other linear methods we will define a function each time that is applied to the result of the linear combination. We could do the same for linear regression and say that the applied function is the identity function. We could schematize this computation as follows:

//TODO SCHEMA

2.1.2 Linear Classification

The next method is called linear classification. The difference with linear regression is that we have a different type of output variable. In a classification task we want to predict a class from a list of potential classes. For instance, we could try to predict whether tomorrow will be a sunny day or not. Notice that there are only 2 possible outcomes: 'sunny' or 'not sunny' and we could represent these outcomes as 0 and 1 in our model. This form would be called binary classification because we have 2 possible classes. It is very easy to extend this method to multi-class classification. The computation in this method starts out exactly the same, combining the input variables using a linear combination. Next, we have to define a threshold to indicate which examples belong to one class or another. In the case of binary classification we would define 1 threshold, and if the result of the linear combination is higher than the threshold we would predict one class. If it is lower, we would predict the other class. The function used here would be called a sign function, which maps real values onto one of 2 possible outcomes. We could represent this computation with the following formula and schema:

//TODO MATH AND SCHEMA

2.1.3 Logistic Regression

The third method I want to present is called logistic regression. In this case, the output variable we want to predict comes from a binomial distribution. This means that they are the result of a probabilistic event. An example would be tossing a coin and checking whether the result is heads or tails. While the outcome is binary (heads or tails) we know that there is an underlying probability for the coin to be heads or tails, and we would like to know this probability.

The idea is still the same. We will make a linear combination of the input variables. However this time we will use a logistic function to produce our estimate. The logistic function is a function that maps real numbers onto the range $[0, 1]$. This result can then be interpreted as an estimate for the probability. We can schematize logistic regression as follows:

//TODO MATH AND SCHEMA

The logistic regression method is the one that will be most widely used throughout this thesis.

2.2 Training a model

In order to understand the integration strategies that will be explained later on, it is useful to know how exactly the models come to be. This section will explain what the input data for our linear models actually looks like, and how we get from this data to a model that we can use for future predictions.

2.2.1 The data

The data we use consists of two parts: the input data, which can be seen as a matrix where the columns are the explanatory variables and each row is an example (or patient). And secondly the output data, which can be seen as a vector where each value indicates the value of the dependent variable for a single example.

It is easy to see that the length of the output vector has to be equal to the amount of rows in the input matrix, indeed there should be one output value for each example. This amount is often called the size of the dataset and we would like it to be as big as possible. Especially when we are dealing with a large number of explanatory variables, it is essential to have a reasonably amount of examples aswell. This will be discussed in more detail later on //TODO REFERENCE.

2.2.2 Gradient descent

In this section I will explain how we get from the input data to the model. The idea here is that we have some for of error measure. The error measure is a sort of rating for our current model as it indicates how big the mistakes are that our current model is making. There are many different error measures we could use. The one that is used in logistic regression is explained in more detail in the following section.

Once we have a way of computing the error that our current model makes, we can try to minimize this error to obtain our 'best' possible model.

Error measure

In logistic regression the error measure we use is called the cross-entropy error. The formula for this error is the following:

$$E_{in}(w) = \frac{1}{N} \sum_{n=1}^N \ln(1 + e^{-y_n w^T x_n})$$

where

- x_n is the vector of values for the explanatory variables for example n .
- y_n is the value of the dependent variable for example n .
- w^T is the transpose of the weights vector. These are the parameters of our model that we can adjust.
- N is the size of our dataset.
- $E_{in}(w)$ is the in-sample error. This is the cross-entropy error that we make on the examples in our dataset. It is a function of the weights w .

The origin of this function is explained in appendix //TODO ADD APPENDIX AND REFERENCE. We can however easily notice that this is a reasonable error measure. It is an averaged sum over all examples, where for each example we compute an

individual error made on that example.

Notice that $w^T x_n$ is the linear combination of the input variables that our current model suggests. This is the prediction that our current model would make for example n and is a real valued number. On the other hand y_n is the actual correct prediction for example n and has a value of 0 or 1.

If the signs of $w^T x_n$ and y_n agree then our current model actually makes a correct prediction for this example. We can see that in this case the exponential becomes close to 0, making our error for example n very small, as we would expect.

If however their signs are opposite, the exponential becomes larger as our incorrect prediction becomes larger. This in turn will increase the error, again as we would expect.

Thus we can see that if we were to minimize this error, we are moving towards a model that tries to make correct predictions.

The gradient descent method

When trying to minimize a function, a general approach would be to try and compute the derivative of the function, and find the spot where this derivative equals zero. In the case of linear regression it is actually possible to compute this minimum in one step. More details about this can be found in appendix //TODO ADD AND REFERENCE APPENDIX.

In the case of logistic regression however it is not possible to find an analytic solution to this problem. The best we can do is put ourselves somewhere on the error curve and try to move towards the minimum in small steps. This is called an iterative approach.

Remember that our error function looks like this:

$$E_{in}(w) = \frac{1}{N} \sum_{n=1}^N \ln(1 + e^{-y_n w^T x_n})$$

We can now compute its derivative with respect to w :

$$\nabla E_{in}(w) = -\frac{1}{N} \sum_{n=1}^N \frac{y_n x_n}{1 + e^{y_n w^T x_n}}$$

The problem is to find the set of weights w for which the derivative becomes 0 (or that minimizes the error). We can start out with an initial set of weights $w(0)$ and then iteratively update these weights so we move towards the minimum. Let's call the direction in which we update our weights v . The update we make to w then becomes:

$$w(t+1) = w(t) + \eta v$$

where

- $w(t+1)$ are the updated weights for this iteration.
- $w(t)$ are the current weights before we make a move.

- v is a unit vector pointing in the direction we want to move.
- η is a number that indicates how big the move is that we make, also called the step size.

Remember that the gradient of a function at a certain point always points towards the steepest slope upwards. In our case we would like to find the minimum, so it is a good idea to move our weights in the direction of steepest descent. The direction v that we are moving towards then becomes the normalized opposite direction of the gradient:

$$v = -\frac{\nabla E_{in}(w(t))}{\|\nabla E_{in}(w(t))\|}$$

We can now summarize the gradient descent method as follows:

```
Data: x, y
initialize weights  $w(0)$ 
while Stopcondition is not met do
    Compute gradient  $\nabla E_{in}(w(t))$ 
    Compute update direction  $v$ 
    Update weights  $w(t+1) = w(t) + \eta v$ 
end
```

Algorithm 1: Gradient Descent algorithm

There are two more non-trivial issues in this computation: the initialization of the weights and the stopcondition.

Weight initialization is sometimes a very tricky thing to do, in the case of logistic regression however it is acceptable to set $w(0)$ equal to the zero-vector as this corresponds to no correlation between any of the input variables and the output variable, and the result of the sigmoid function would be 0.5 or 50% meaning the model has no preference for either outcome.

The stopcondition however is a bigger issue and usually the way to go here is to make a combination of several stop criteria. One criteria would be to simply limit the amount of iterations to a fixed number. This could avoid endlessly overfitting. Another criteria is to set up a target error we want to achieve (a small number), and stop when we have reached this target. This however raises the question of picking the target error, and this is mostly an application dependent choice.

In the version of logistic regression explained here, it can however be shown that the error surface we are dealing with is a very nice convex surface. This makes it very easy to find its minimum and we don't need very complex initialization and stopping criteria to get good results. In other machine learning methods however these surfaces aren't always as nice, and the issue of local minima versus global minima becomes a big deal. There has been much research on this topic however and many sophisticated methods have been developed to deal with this issue.

2.3 Overfitting

Now that we have established a method of computing our models, it is time to deal with an issue known as overfitting. Overfitting points to the fact that there are several mechanisms at work when we are building a model that prevent us from reaching the perfect model (a model that predicts correctly at all times). These mechanisms essentially originate from noise and uncertainty in many aspects of the learning process (the input data, choice of model, choice of algorithm, ...). We can however try to decompose this noise into several components and then attempt to influence them by making changes to our model computation. I will present two ways in which overfitting can be tackled: regularization and validation.

2.3.1 The problem of overfitting

Let's introduce some notation. From now on I will refer to the notion of 'in-sample error' or in symbolic notation E_{in} as the error that a model makes on the examples in our training set. The training set consists of the examples that were used to train (compute) the model in the first place.

Similarly I will define 'out-of-sample error' or E_{out} as the error we make on examples that were not used for training the model. Notice that E_{in} is something we could compute because we have access to the training data, but E_{out} is a quantity we cannot exactly compute but we could try to estimate it if we have some examples left that we did not use for training. Notice also that it is E_{in} that we minimize during our model computation, but it is E_{out} that we actually want to minimize! Indeed, E_{out} corresponds to the error that we get when we are going to deploy our model in practice and use it on examples we have never seen before. We can do this because we believe that E_{in} tracks E_{out} to a certain degree. And thus if we manage to minimize E_{in} we also minimize E_{out} to some extent.

We can only speak of overfitting when we are comparing two models. We say that one model, call it model A, is overfitting with respect to another model, model B, when model A managed to get a lower E_{in} than model B, but model B has a lower E_{out} .

Another way of looking at it is during the learning process. Let's have model A be the model that we computed when we started from model B and performed one more iteration of the training algorithm. Thus model A is 'more trained' than model B. Now let's suppose model A is overfitting:

$$E_{in}^{modelA} < E_{in}^{modelB} \quad (2.1)$$

$$E_{out}^{modelA} > E_{out}^{modelB} \quad (2.2)$$

The additional iteration has decreased the in-sample error, and thus we are able to fit our training data better, but the out-of-sample error has increased, meaning that our model doesn't generalize as well to other examples outside the training set. This means that we are actually fitting our training data too well, while we are not really getting a better grasp of the underlying pattern that we wish to learn. We are

overfitting the training data.

2.3.2 The bias and variance trade-off

There are several ways of looking at overfitting and pointing out its origins. I will introduce the notions of bias and variance and how they can describe the noise in our system.

Average hypothesis

First, let me explain the playing field. We are in a situation of learning, where we are given a set of examples that are produced by some target function f . It is this target function f that we wish to learn (or in other words model). In order to do this we have to decide on the type of functions that we will use to model. In machine learning this is called the hypothesis set. It is the set of all functions that we consider possible candidates to fit our target f . And we will use the examples x in our dataset D to decide which hypothesis we will pick.

Next, let's introduce the notion of average hypothesis \bar{h} . Imagine we have a very large number of datasets. For each of these datasets we apply the learning process and we will pick a certain hypothesis h from our hypothesis set. The average hypothesis is then equal to the average of all the hypothesis' just learned. Or in a formula:

$$\bar{h} = \mathbf{E}_D[h^{(D)}]$$

where

- \bar{h} is the average hypothesis.
- \mathbf{E}_D is the expected value over an infinite number of datasets
- $h^{(D)}$ is the hypothesis that was learned for a specific dataset D

We can also look at this average hypothesis as sort of the best we can do with the given hypothesis set. Indeed, when we imagine having an infinite number of datasets we would end up cancelling out much of the variation in the learned hypothesis' and end up with a very good one.

Bias

We can now define the bias as the distance between the average hypothesis \bar{h} and our target function f .

$$bias = (\bar{h} - f)^2$$

We can see the bias as an error we make due to our own choices. Namely our choice of hypothesis set. If we choose a very simple hypothesis set, we cannot expect to

be able to find a fit for a very complex function. The target function simply isn't contained in our hypothesis set. There exists no function in our hypothesis set that exactly fits our target.

Therefore we introduced the notion of average hypothesis. We can view this as the best we can do given our current hypothesis set, and the distance to the target is what we call the bias.

Variance

This however is not the full story. In a real learning situation we generally never find this average hypothesis, because remember it required a large amount (or even infinite amount) of datasets. We never have this luxury! In reality we always have only one dataset and that is all we can use to navigate through the hypothesis set. This is where the notion of variance comes in. We can define variance as the error we get from not having the best hypothesis possible in our hypothesis set. Or in other words as the distance between the hypothesis set that we actually found by learning from our dataset and the average hypothesis.

$$variance = (h^{(D)} - \bar{h})^2$$

Error due to variance mainly comes from two sources: the first is our finite dataset, the second is the complexity of the hypothesis set.

In reality we are given a dataset of N examples and that's all you've got. Most of the time this dataset is not sufficient to find the best hypothesis and thus there will be a variance error made.

Secondly, as we increase the complexity of the hypothesis set, it becomes increasingly difficult to navigate through this set. There are simply many more hypothesis to choose from. Again this makes it harder for our learning process to find the optimal hypothesis and as such will introduce a variance error.

The tradeoff

Having both bias and variance defined we can see that they are not disconnected, there is a tradeoff. If we look purely at bias we could think that simply choosing a super complex hypothesis set is always optimal. Indeed our bias will be zero since the target function will always be inside our hypothesis set.

However, an increasingly complex hypothesis set makes it harder to actually find the optimal hypothesis. We know that the optimal hypothesis is there, but we just cannot find it. The take-away message here is that we have to choose a hypothesis set complexity based on the resources that we have. In this case the resource is our dataset. The larger the dataset that we can learn from, the more complex hypothesis sets we can afford, and the better our results will be. But there is no gain in choosing overly complex hypothesis sets when you don't have the resources to afford them. This will simply cause you to find hypothesis' that fit your training data very well (imagine fitting 3 datapoints with a 7th order polynomial, you would get an exact fit) but this model will not generalize to anything in the real world, it is a complete overfit.

2.3.3 Regularization

Now that we have the concepts of bias and variance, let's use this information to try and improve our models. The first method is called regularization. In very simple terms this method will add a very small amount of bias in order to greatly decrease the amount of variance, reducing the overall error we make.

Adding bias

Remember that bias is defined as the distance between the average (or best) hypothesis \bar{h} and our target function f . Adding bias effectively means we are going to make another choice, which will impact the average hypothesis. The choice we are about to introduce is based on the following observation: when confronted with a set of similarly performing models, the simplest model is usually the best. Or in other words we should try to prefer simple models over very complex ones.

This observation does not have a mathematical proof, it is rather an observation from experience and reason. One good argument is the fact that noise is usually of high frequency. Meaning that distortions of our dataset (for instance measurement errors) will often be very scattered and random, while the underlying pattern that really makes up the data will be rather smooth. A similar argument can be made for the error due to bias, when we choose a hypothesis set that does not contain the target function, the error due to bias will be mostly random and of high frequency. Therefore if we want to reduce the impact of this noise in our final model, we should prefer models that are not able to fit these high frequencies exactly. Lastly we can remark that if we look at our current understanding of nature (let's say at a larger scale), systems almost always have smooth transitions. The most important laws of nature that we find are all written down in small, simple formulas. Nature doesn't work with instantaneous changes (high frequency), but rather it has smooth functions that govern the basic principle, and then it adds random noise and fluctuations on top of it. This principle is what we try to extrapolate here to machine learning. Thus, the choice we will make is that we will prefer simple models over complex ones by adding a constraint to the weights.

Regularization types

There are many kinds of constraints that we could add to the weights and, depending on the constraint we choose, the regularization gets a different name and it will have a different effect. One of the most famous regularizers is called ridge or weight-decay. The constraint for this regularizer is the following:

$$\sum_{i=1}^N w_i^2 \leq C$$

where

- w_i is the weight (model parameter) for the i 'th explanatory variable.

- C is the constraint value

Using this regularizer will result in a preference for models with smaller weights. This keeps certain weights from getting out of control. This form of regularization is also often called the L_2 penalty.

Another popular regularizer is called the lasso penalty (or L_1 penalty). The constraint in this case is:

$$\sum_{i=1}^N |w_i| \leq C$$

In addition to keeping the weights small, this form of regularization also performs parameter selection. This means that instead of just keeping the weights small it will also prefer to make weights actually zero. This will cause the resulting model to have fewer parameters, but the parameters that do survive the penalty are sure to be very important. This regularizer is often used when there is a huge number of explanatory variables, and we wish to find only those that are really descriptive. Later in the thesis I will use datasets that contain gene expression information about cancer patients, these datasets often have thousands of explanatory variables and will provide a good example for using the lasso regularization.

The last form of regularizer I wish to demonstrate is called the elastic net penalty. This regularizer is simply a linear combination of the ridge and lasso penalties and provides a way of balancing the two. It has the following constraint:

$$\alpha \sum_{i=1}^N w_i^2 + (1 - \alpha) \sum_{i=1}^N |w_i| \leq C$$

Lambda

Using a regularizer introduces a constraint, this means that we now have to deal with a constrained optimization problem which is much harder to solve than an unconstrained problem. Fortunately, through some clever mathematics it is possible to convert the constrained minimization problem to an unconstrained one by incorporating the regularization constraint in the formula for the error itself. //TODO ADD APPENDIX WITH FULL DERIVATION OR NOT ... The formula for the error with regularization then becomes:

$$E_{in}(w) = \frac{1}{N} \sum_{n=1}^N e(x_n, y_n, w) + \lambda R(w)$$

where

- $E_{in}(w)$ is the in-sample error.
- $e(x_n, y_n, w)$ is the individual error made on example n . In the case of logistic regression this would be a cross-entropy error term $\ln(1 + e^{-y_n w^T x_n})$.
- λ is the regularization parameter that will be explained below.

- $R(w)$ is the regularization term dependent on the type of regularization used. For instance: $\sum_{i=1}^N |w_i|$ for lasso, $\sum_{i=1}^N w_i^2$ for ridge, ...
- x_n is the n'th sample in the dataset.
- y_n is the outcome for the n'th sample in the dataset.
- w is the vector of weights, our model parameters that we are trying to find.

Notice that we now again have an error measure that we want to minimize, and it is an unconstrained optimization problem. The important new part is λ . This is the amount of regularization we want to use. It is a new form for the constraint constant C that was earlier introduced in the types of regularization. The higher λ the tighter the constraint (lower C) and vice versa. The value of λ will prove to be critical in getting good models. And the way in which we calculate it is through validation.

2.3.4 Validation

The sample size dilemma

Cross-validation

2.4 Conclusion

Chapter 3

The Next Chapter

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3.1 The First Topic of this Chapter

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3.1.1 An item

A master thesis is never an isolated work. This means that your text must contain references. On-line documents[?] as well as books[?] can be referenced.

3.2 Figures

Figures are used to add illustrations to the text. The Figure 3.1 shows the KU Leuven logo as an illustration.



FIGURE 3.1: The KU Leuven logo.

gnats	gram	\$13.65
	each	.01
gnu	stuffed	92.50
emu		33.33
armadillo	frozen	8.99

TABLE 3.1: A table with the wrong layout.

Item		
Animal	Description	Price (\$)
Gnat	per gram	13.65
	each	0.01
Gnu	stuffed	92.50
Emu	stuffed	33.33
Armadillo	frozen	8.99

TABLE 3.2: A table with the correct layout.

3.3 Tables

Tables are used to present data neatly arranged. A table is normally not a spreadsheet! Compare Table 3.1 en Table 3.2: which table do you prefer?

3.4 Lorem Ipsum

This section is added to check headers and footers. So this chapter must at least contain three pages. To make sure that we get the required amount, the `lipsum` package isn't used but the text is put directly in the text.

3.4.1 Lorem ipsum dolor sit amet, consectetur adipiscing elit

Sed nec tortor id felis tristique sodales. Nulla nec massa eu dui fermentum tincidunt. Integer ullamcorper ante eget eros posuere faucibus. Nam id ligula ut augue pulvinar vulputate id at purus. Aenean condimentum tortor eu mi placerat eget eleifend massa mollis. Nam est mi, sagittis quis euismod eget, sagittis in nibh. Proin elit turpis, aliquam et imperdiet sed, volutpat eu turpis.

Pellentesque vel enim tellus, vitae egestas turpis. Praesent malesuada elit non nisi sollicitudin non blandit lacus tincidunt. Morbi blandit urna at lectus ornare laoreet. Suspendisse turpis diam, lobortis dictum luctus quis, commodo at lorem. Integer lacinia convallis ultricies. Sed quis augue neque, eu malesuada arcu. Nullam vehicula, purus vitae sagittis pulvinar, erat eros semper massa, eu egestas nibh erat quis magna. Cras pellentesque, nisl eu dapibus volutpat, urna augue ornare quam, quis egestas lectus nulla a lectus.

Vivamus dictum libero in massa cursus sed vulputate eros imperdiet. Donec lacinia, libero ac lobortis egestas, nibh dui ornare arcu, luctus porttitor velit massa sit amet quam. Maecenas scelerisque laoreet diam, vitae congue quam adipiscing vitae. Aliquam cursus nisl a leo convallis eleifend fermentum massa porta. Nunc libero quam, dapibus dapibus molestie sit amet, faucibus vel nunc.

3.4.2 Praesent auctor venenatis posuere

Sed tellus augue, molestie in pulvinar lacinia, dapibus non ipsum. Fusce vitae mi vitae enim ullamcorper hendrerit eu malesuada est. Proin iaculis ante sed nibh tincidunt vel interdum libero posuere. Vivamus accumsan metus quis felis congue suscipit dapibus enim mattis. Fusce mattis tortor eget ipsum interdum sagittis auctor id metus.

Integer diam lacus, pharetra sit amet tempor et, tristique non lorem. Aenean auctor, nisi eu interdum fermentum, lectus massa adipiscing elit, sed facilisis orci odio a lectus. Proin mi nibh, tempus quis porta a, viverra quis enim. In sollicitudin egestas libero, quis viverra velit molestie eget. Nulla rhoncus, dolor a mollis vestibulum, lacus elit semper nisi, nec sollicitudin sem urna eu magna. Nunc sed est urna, euismod congue mi.

3.4.3 Cras vulputate ultricies venenatis

Vivamus eros urna, sodales accumsan semper vel, lobortis sit amet mauris. Etiam condimentum eleifend lorem, ullamcorper ornare lectus aliquet vitae. Praesent massa enim, interdum sit amet semper et, venenatis ut elit. Quisque faucibus, quam ac lacinia imperdiet, nulla neque elementum purus, tempus rutrum justo massa porta sapien. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Sed ultrices interdum mi, et rhoncus sapien rutrum sed.

Duis elit orci, molestie quis sollicitudin sed, convallis non ante. Maecenas tincidunt condimentum justo, et ultricies leo tristique vitae. Vestibulum quis quam non lectus dapibus eleifend a vitae nibh. Nam nibh justo, pharetra quis iaculis consequat, elementum quis justo. Etiam mollis lacinia lacus, nec sollicitudin urna lobortis ac. Nulla facilisi.

Proin placerat risus eleifend erat ultricies placerat. Etiam rutrum magna nec turpis euismod consectetur. Phasellus tortor odio, lacinia imperdiet condimentum sed, faucibus commodo erat. Phasellus sed felis id ante placerat ultrices. Aenean tempor justo in tortor volutpat eu auctor dolor mollis. Aenean sit amet risus urna. Morbi viverra vehicula cursus.

3.4.4 Donec nibh ante, consectetur et posuere id, tempus nec arcu

Curabitur a tellus aliquet ipsum pellentesque scelerisque. Etiam congue, risus et volutpat rutrum, est purus dapibus leo, non cursus metus felis eget ligula. Vivamus facilisis tristique turpis, ut pretium lectus luctus eleifend. Fusce magna sapien, ullamcorper vitae fringilla id, euismod quis ante.

Phasellus volutpat, nunc et pharetra semper, sem justo adipiscing mauris, id blandit magna quam et orci. Vestibulum a erat purus, ut molestie ante. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Proin turpis diam, consequat ut ullamcorper ut, consequat eu orci. Sed metus risus, fringilla nec interdum vel, interdum eu nunc. Suspendisse vel sapien orci.

3.4.5 Morbi et mauris tempus purus ornare vehicula

Mauris sit amet diam quam, eget luctus purus. Sed faucibus, risus semper eleifend iaculis, mi turpis bibendum nisl, quis cursus nibh nisl sit amet ipsum. Vestibulum tempor urna vitae mi auctor malesuada eget non ligula. Nullam convallis, diam vel ultrices auctor, eros eros egestas elit, sed accumsan arcu tortor eget leo. Vestibulum orci purus, porttitor in pharetra eget, tincidunt eget nisl. Nullam sit amet nulla dui, facilisis vestibulum dui.

Donec faucibus facilisis mauris ac cursus. Duis rhoncus quam sed nisi laoreet eu scelerisque massa tincidunt. Vivamus sit amet libero nec arcu imperdiet tempor quis non libero. Sed consequat dignissim justo. Phasellus ullamcorper, velit quis posuere vulputate, felis erat tincidunt mauris, at vestibulum justo lectus et turpis. Maecenas lacinia convallis euismod. Quisque egestas fermentum sapien eu dictum. Sed nec lacus in purus dictum consequat quis vel nisl. Fusce non urna sem. Curabitur eu diam vitae elit accumsan blandit. Nullam fermentum nunc et leo dictum laoreet. Donec semper varius velit vel fringilla. Vivamus eu orci nunc.

3.5 Conclusion

The final section of the chapter gives an overview of the important results of this chapter. This implies that the introductory chapter and the concluding chapter don't need a conclusion.

Nunc sed pede. Praesent vitae lectus. Praesent neque justo, vehicula eget, interdum id, facilisis et, nibh. Phasellus at purus et libero lacinia dictum. Fusce aliquet. Nulla eu ante placerat leo semper dictum. Mauris metus. Curabitur lobortis. Curabitur sollicitudin hendrerit nunc. Donec ultrices lacus id ipsum.

Chapter 4

The Final Chapter

Morbi malesuada hendrerit dui. Nunc mauris leo, dapibus sit amet, vestibulum et, commodo id, est. Pellentesque purus. Pellentesque tristique, nunc ac pulvinar adipiscing, justo eros consequat lectus, sit amet posuere lectus neque vel augue. Cras consectetur libero ac eros. Ut eget massa. Fusce sit amet enim eleifend sem dictum auctor. In eget risus luctus wisi convallis pulvinar. Vivamus sapien risus, tempor in, viverra in, aliquet pellentesque, eros. Aliquam euismod libero a sem.

4.1 The First Topic of this Chapter

4.1.1 Item 1

Sub-item 1

Nunc velit augue, scelerisque dignissim, lobortis et, aliquam in, risus. In eu eros. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Curabitur vulputate elit viverra augue. Mauris fringilla, tortor sit amet malesuada mollis, sapien mi dapibus odio, ac imperdiet ligula enim eget nisl. Quisque vitae pede a pede aliquet suscipit. Phasellus tellus pede, viverra vestibulum, gravida id, laoreet in, justo. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Integer commodo luctus lectus. Mauris justo. Duis varius eros. Sed quam. Cras lacus eros, rutrum eget, varius quis, convallis iaculis, velit. Mauris imperdiet, metus at tristique venenatis, purus neque pellentesque mauris, a ultrices elit lacus nec tortor. Class aptent taciti sociosqu ad litora torquent per conubia nostra, per inceptos hymenaeos. Praesent malesuada. Nam lacus lectus, auctor sit amet, malesuada vel, elementum eget, metus. Duis neque pede, facilisis eget, egestas elementum, nonummy id, neque.

Sub-item 2

Proin non sem. Donec nec erat. Proin libero. Aliquam viverra arcu. Donec vitae purus. Donec felis mi, semper id, scelerisque porta, sollicitudin sed, turpis. Nulla in urna. Integer varius wisi non elit. Etiam nec sem. Mauris consequat, risus nec

congue condimentum, ligula ligula suscipit urna, vitae porta odio erat quis sapien. Proin luctus leo id erat. Etiam massa metus, accumsan pellentesque, sagittis sit amet, venenatis nec, mauris. Praesent urna eros, ornare nec, vulputate eget, cursus sed, justo. Phasellus nec lorem. Nullam ligula ligula, mollis sit amet, faucibus vel, eleifend ac, dui. Aliquam erat volutpat.

4.1.2 Item 2

Fusce vehicula, tortor et gravida porttitor, metus nibh congue lorem, ut tempus purus mauris a pede. Integer tincidunt orci sit amet turpis. Aenean a metus. Aliquam vestibulum lobortis felis. Donec gravida. Sed sed urna. Mauris et orci. Integer ultrices feugiat ligula. Sed dignissim nibh a massa. Donec orci dui, tempor sed, tincidunt nonummy, viverra sit amet, turpis. Quisque lobortis. Proin venenatis tortor nec wisi. Vestibulum placerat. In hac habitasse platea dictumst. Aliquam porta mi quis risus. Donec sagittis luctus diam. Nam ipsum elit, imperdiet vitae, faucibus nec, fringilla eget, leo. Etiam quis dolor in sapien porttitor imperdiet.

4.2 The Second Topic

Cras pretium. Nulla malesuada ipsum ut libero. Suspendisse gravida hendrerit tellus. Maecenas quis lacus. Morbi fringilla. Vestibulum odio turpis, tempor vitae, scelerisque a, dictum non, massa. Praesent erat felis, porta sit amet, condimentum sit amet, placerat et, turpis. Praesent placerat lacus a enim. Vestibulum non eros. Ut congue. Donec tristique varius tortor. Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas. Nam dictum dictum urna.

Phasellus vestibulum orci vel mauris. Fusce quam leo, adipiscing ac, pulvinar eget, molestie sit amet, erat. Sed diam. Suspendisse eros leo, tempus eget, dapibus sit amet, tempus eu, arcu. Vestibulum wisi metus, dapibus vel, luctus sit amet, condimentum quis, leo. Suspendisse molestie. Duis in ante. Ut sodales sem sit amet mauris. Suspendisse ornare pretium orci. Fusce tristique enim eget mi. Vestibulum eros elit, gravida ac, pharetra sed, lobortis in, massa. Proin at dolor. Duis accumsan accumsan pede. Nullam blandit elit in magna lacinia hendrerit. Ut nonummy luctus eros. Fusce eget tortor.

Ut sit amet magna. Cras a ligula eu urna dignissim viverra. Nullam tempor leo porta ipsum. Praesent purus. Nullam consequat. Mauris dictum sagittis dui. Vestibulum sollicitudin consectetur wisi. In sit amet diam. Nullam malesuada pharetra risus. Proin lacus arcu, eleifend sed, vehicula at, congue sit amet, sem. Sed sagittis pede a nisl. Sed tincidunt odio a pede. Sed dui. Nam eu enim. Aliquam sagittis lacus eget libero. Pellentesque diam sem, sagittis molestie, tristique et, fermentum ornare, nibh. Nulla et tellus non felis imperdiet mattis. Aliquam erat volutpat.

4.3 Conclusion

Vestibulum sodales ipsum id augue. Integer ipsum pede, convallis sit amet, tristique vitae, tempor ut, nunc. Nam non ligula non lorem convallis hendrerit. Maecenas hendrerit. Sed magna odio, aliquam imperdiet, porta ac, aliquet eget, mi. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Vestibulum nisl sem, dignissim vel, euismod quis, egestas ut, orci. Nunc vitae risus vel metus euismod laoreet. Cras sit amet neque a turpis lobortis auctor. Sed aliquam sem ac elit. Cras velit lectus, facilisis id, dictum sed, porta rutrum, nisl. Nam hendrerit ipsum sed augue. Nullam scelerisque hendrerit wisi. Vivamus egestas arcu sed purus. Ut ornare lectus sed eros. Suspendisse potenti. Mauris sollicitudin pede vel velit. In hac habitasse platea dictumst.

Suspendisse erat mauris, nonummy eget, pretium eget, consequat vel, justo. Pellentesque consectetur erat sed lacus. Nullam egestas nulla ac dui. Donec cursus rhoncus ipsum. Nunc et sem eu magna egestas malesuada. Vivamus dictum massa at dolor. Morbi est nulla, faucibus ac, posuere in, interdum ut, sapien. Proin consectetur pretium urna. Donec sit amet nibh nec purus dignissim mattis. Phasellus vehicula elit at lacus. Nulla facilisi. Cras ut arcu. Sed consectetur. Integer tristique elit quis felis consectetur eleifend. Cras et lectus.

Ut congue malesuada justo. Curabitur congue, felis at hendrerit faucibus, mauris lacus porttitor pede, nec aliquam turpis diam feugiat arcu. Nullam rhoncus ipsum at risus. Vestibulum a dolor sed dolor fermentum vulputate. Sed nec ipsum dapibus urna bibendum lobortis. Vestibulum elit. Nam ligula arcu, volutpat eget, lacinia eu, lobortis ac, urna. Nam mollis ultrices nulla. Cras vulputate. Suspendisse at risus at metus pulvinar malesuada. Nullam lacus. Aliquam tempus magna. Aliquam ut purus. Proin tellus.

Chapter 5

Conclusion

The final chapter contains the overall conclusion. It also contains suggestions for future work and industrial applications.

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Ut purus elit, vestibulum ut, placerat ac, adipiscing vitae, felis. Curabitur dictum gravida mauris. Nam arcu libero, nonummy eget, consectetur id, vulputate a, magna. Donec vehicula augue eu neque. Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas. Mauris ut leo. Cras viverra metus rhoncus sem. Nulla et lectus vestibulum urna fringilla ultrices. Phasellus eu tellus sit amet tortor gravida placerat. Integer sapien est, iaculis in, pretium quis, viverra ac, nunc. Praesent eget sem vel leo ultrices bibendum. Aenean faucibus. Morbi dolor nulla, malesuada eu, pulvinar at, mollis ac, nulla. Curabitur auctor semper nulla. Donec varius orci eget risus. Duis nibh mi, congue eu, accumsan eleifend, sagittis quis, diam. Duis eget orci sit amet orci dignissim rutrum.

Nam dui ligula, fringilla a, euismod sodales, sollicitudin vel, wisi. Morbi auctor lorem non justo. Nam lacus libero, pretium at, lobortis vitae, ultricies et, tellus. Donec aliquet, tortor sed accumsan bibendum, erat ligula aliquet magna, vitae ornare odio metus a mi. Morbi ac orci et nisl hendrerit mollis. Suspendisse ut massa. Cras nec ante. Pellentesque a nulla. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Aliquam tincidunt urna. Nulla ullamcorper vestibulum turpis. Pellentesque cursus luctus mauris.

Nulla malesuada porttitor diam. Donec felis erat, congue non, volutpat at, tincidunt tristique, libero. Vivamus viverra fermentum felis. Donec nonummy pellentesque ante. Phasellus adipiscing semper elit. Proin fermentum massa ac quam. Sed diam turpis, molestie vitae, placerat a, molestie nec, leo. Maecenas lacinia. Nam ipsum ligula, eleifend at, accumsan nec, suscipit a, ipsum. Morbi blandit ligula feugiat magna. Nunc eleifend consequat lorem. Sed lacinia nulla vitae enim. Pellentesque tincidunt purus vel magna. Integer non enim. Praesent euismod nunc eu purus. Donec bibendum quam in tellus. Nullam cursus pulvinar lectus. Donec et mi. Nam vulputate metus eu enim. Vestibulum pellentesque felis eu massa.

Quisque ullamcorper placerat ipsum. Cras nibh. Morbi vel justo vitae lacus tincidunt ultrices. Lorem ipsum dolor sit amet, consectetur adipiscing elit. In

hac habitasse platea dictumst. Integer tempus convallis augue. Etiam facilisis. Nunc elementum fermentum wisi. Aenean placerat. Ut imperdiet, enim sed gravida sollicitudin, felis odio placerat quam, ac pulvinar elit purus eget enim. Nunc vitae tortor. Proin tempus nibh sit amet nisl. Vivamus quis tortor vitae risus porta vehicula.

Fusce mauris. Vestibulum luctus nibh at lectus. Sed bibendum, nulla a faucibus semper, leo velit ultricies tellus, ac venenatis arcu wisi vel nisl. Vestibulum diam. Aliquam pellentesque, augue quis sagittis posuere, turpis lacus congue quam, in hendrerit risus eros eget felis. Maecenas eget erat in sapien mattis porttitor. Vestibulum porttitor. Nulla facilisi. Sed a turpis eu lacus commodo facilisis. Morbi fringilla, wisi in dignissim interdum, justo lectus sagittis dui, et vehicula libero dui cursus dui. Mauris tempor ligula sed lacus. Duis cursus enim ut augue. Cras ac magna. Cras nulla. Nulla egestas. Curabitur a leo. Quisque egestas wisi eget nunc. Nam feugiat lacus vel est. Curabitur consectetur.

Suspendisse vel felis. Ut lorem lorem, interdum eu, tincidunt sit amet, laoreet vitae, arcu. Aenean faucibus pede eu ante. Praesent enim elit, rutrum at, molestie non, nonummy vel, nisl. Ut lectus eros, malesuada sit amet, fermentum eu, sodales cursus, magna. Donec eu purus. Quisque vehicula, urna sed ultricies auctor, pede lorem egestas dui, et convallis elit erat sed nulla. Donec luctus. Curabitur et nunc. Aliquam dolor odio, commodo pretium, ultricies non, pharetra in, velit. Integer arcu est, nonummy in, fermentum faucibus, egestas vel, odio.

Sed commodo posuere pede. Mauris ut est. Ut quis purus. Sed ac odio. Sed vehicula hendrerit sem. Duis non odio. Morbi ut dui. Sed accumsan risus eget odio. In hac habitasse platea dictumst. Pellentesque non elit. Fusce sed justo eu urna porta tincidunt. Mauris felis odio, sollicitudin sed, volutpat a, ornare ac, erat. Morbi quis dolor. Donec pellentesque, erat ac sagittis semper, nunc dui lobortis purus, quis congue purus metus ultricies tellus. Proin et quam. Class aptent taciti sociosqu ad litora torquent per conubia nostra, per inceptos hymenaeos. Praesent sapien turpis, fermentum vel, eleifend faucibus, vehicula eu, lacus.

Appendices

Appendix A

The First Appendix

Appendices hold useful data which is not essential to understand the work done in the master thesis. An example is a (program) source. An appendix can also have sections as well as figures and references[?].

A.1 More Lorem

Quisque facilisis auctor sapien. Pellentesque gravida hendrerit lectus. Mauris rutrum sodales sapien. Fusce hendrerit sem vel lorem. Integer pellentesque massa vel augue. Integer elit tortor, feugiat quis, sagittis et, ornare non, lacus. Vestibulum posuere pellentesque eros. Quisque venenatis ipsum dictum nulla. Aliquam quis quam non metus eleifend interdum. Nam eget sapien ac mauris malesuada adipiscing. Etiam eleifend neque sed quam. Nulla facilisi. Proin a ligula. Sed id dui eu nibh egestas tincidunt. Suspendisse arcu.

A.1.1 Lorem 15–17

Nulla in ipsum. Praesent eros nulla, congue vitae, euismod ut, commodo a, wisi. Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas. Aenean nonummy magna non leo. Sed felis erat, ullamcorper in, dictum non, ultricies ut, lectus. Proin vel arcu a odio lobortis euismod. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Proin ut est. Aliquam odio. Pellentesque massa turpis, cursus eu, euismod nec, tempor congue, nulla. Duis viverra gravida mauris. Cras tincidunt. Curabitur eros ligula, varius ut, pulvinar in, cursus faucibus, augue.

Nulla mattis luctus nulla. Duis commodo velit at leo. Aliquam vulputate magna et leo. Nam vestibulum ullamcorper leo. Vestibulum condimentum rutrum mauris. Donec id mauris. Morbi molestie justo et pede. Vivamus eget turpis sed nisl cursus tempor. Curabitur mollis sapien condimentum nunc. In wisi nisl, malesuada at, dignissim sit amet, lobortis in, odio. Aenean consequat arcu a ante. Pellentesque porta elit sit amet orci. Etiam at turpis nec elit ultricies imperdiet. Nulla facilisi.

In hac habitasse platea dictumst. Suspendisse viverra aliquam risus. Nullam pede justo, molestie nonummy, scelerisque eu, facilisis vel, arcu.

Curabitur tellus magna, porttitor a, commodo a, commodo in, tortor. Donec interdum. Praesent scelerisque. Maecenas posuere sodales odio. Vivamus metus lacus, varius quis, imperdiet quis, rhoncus a, turpis. Etiam ligula arcu, elementum a, venenatis quis, sollicitudin sed, metus. Donec nunc pede, tincidunt in, venenatis vitae, faucibus vel, nibh. Pellentesque wisi. Nullam malesuada. Morbi ut tellus ut pede tincidunt porta. Lorem ipsum dolor sit amet, consectetur adipiscing elit. Etiam congue neque id dolor.

A.1.2 Lorem 18–19

Donec et nisl at wisi luctus bibendum. Nam interdum tellus ac libero. Sed sem justo, laoreet vitae, fringilla at, adipiscing ut, nibh. Maecenas non sem quis tortor eleifend fermentum. Etiam id tortor ac mauris porta vulputate. Integer porta neque vitae massa. Maecenas tempus libero a libero posuere dictum. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Aenean quis mauris sed elit commodo placerat. Class aptent taciti sociosqu ad litora torquent per conubia nostra, per inceptos hymenaeos. Vivamus rhoncus tincidunt libero. Etiam elementum pretium justo. Vivamus est. Morbi a tellus eget pede tristique commodo. Nulla nisl. Vestibulum sed nisl eu sapien cursus rutrum.

Nulla non mauris vitae wisi posuere convallis. Sed eu nulla nec eros scelerisque pharetra. Nullam varius. Etiam dignissim elementum metus. Vestibulum faucibus, metus sit amet mattis rhoncus, sapien dui laoreet odio, nec ultricies nibh augue a enim. Fusce in ligula. Quisque at magna et nulla commodo consequat. Proin accumsan imperdiet sem. Nunc porta. Donec feugiat mi at justo. Phasellus facilisis ipsum quis ante. In ac elit eget ipsum pharetra faucibus. Maecenas viverra nulla in massa.

A.2 Lorem 51

Maecenas dui. Aliquam volutpat auctor lorem. Cras placerat est vitae lectus. Curabitur massa lectus, rutrum euismod, dignissim ut, dapibus a, odio. Ut eros erat, vulputate ut, interdum non, porta eu, erat. Cras fermentum, felis in porta congue, velit leo facilisis odio, vitae consectetur lorem quam vitae orci. Sed ultrices, pede eu placerat auctor, ante ligula rutrum tellus, vel posuere nibh lacus nec nibh. Maecenas laoreet dolor at enim. Donec molestie dolor nec metus. Vestibulum libero. Sed quis erat. Sed tristique. Duis pede leo, fermentum quis, consectetur eget, vulputate sit amet, erat.

Appendix B

The Last Appendix

Appendices are numbered with letters, but the sections and subsections use arabic numerals, as can be seen below.

B.1 Lorem 20-24

Nulla ac nisl. Nullam urna nulla, ullamcorper in, interdum sit amet, gravida ut, risus. Aenean ac enim. In luctus. Phasellus eu quam vitae turpis viverra pellentesque. Duis feugiat felis ut enim. Phasellus pharetra, sem id porttitor sodales, magna nunc aliquet nibh, nec blandit nisl mauris at pede. Suspendisse risus risus, lobortis eget, semper at, imperdiet sit amet, quam. Quisque scelerisque dapibus nibh. Nam enim. Lorem ipsum dolor sit amet, consectetur adipiscing elit. Nunc ut metus. Ut metus justo, auctor at, ultrices eu, sagittis ut, purus. Aliquam aliquam.

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B.2 Lorem 25-27

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Bibliography

Fiche masterproef

Student: Michiel Ruelens

Titel: Design, implementation and evaluation of data integration methods for biomedical cancer data

Nederlandse titel: Design, implementatie en evaluatie van data integratie methoden voor biomedische data

UDC: 621.3

Korte inhoud:

Hier komt een heel bondig abstract van hooguit 500 woorden. L^AT_EX commando's mogen hier gebruikt worden. Blanco lijnen (of het commando `\par`) zijn wel niet toegelaten!

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Thesis voorgedragen tot het behalen van de graad van Master of Science in de ingenieurswetenschappen: elektrotechniek, optie Elektronica en geïntegreerde schakelingen

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