

Using machine learning to identify thyroid diseases

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Data introduction

The data was originally gathered from Garvan Institute. Consisting of 9172 records from 1984 to early 1987. There are 30 columns and a lot of instances. Although there are significantly more healthy than sick instances.

The data is all about people and their thyroid values. All of the thyroid related hormones have been measured, but also external factors are accounted for. Such as medication, a swollen thyroid or a tumour. These factors affect the hormone cycle of the thyroid, changing a persons mental health. The data has a lot of instances, all of these columns contain a true or false. The patient uses medication or not for example. There are only a few numeric columns, these are for the hormone expression values. If the specific hormones (T3 and T4) are measured, the expression value is noted under the `__measured` column.

Table 1: Codebook of all the columns from the data

Name	Data Type	Unit	Description
age	integer	years	The age in years of the person.
sex	char	NA	The sex of the person.
on thyroxine	bool	NA	If the person uses thyroxine medication at this point.
query on thyroxine	bool	NA	If the person is on a waiting list for thyroxine medication or in the medical process of getting thyroid medication.
on antithyroid medication	bool	NA	If the person uses antithyroid medication, lowering the effect of the thyroid in general.
sick	bool	NA	If the person is sick, having a thyroid issue which is medically proven.
pregnant	bool	NA	If the person is carrying a child, since this can effect your mental health. Because the body is working extra hard.
thyroid surgery	bool	NA	If the person has had surgery related to the thyroid, in the past or future.
I131 treatment	bool	NA	A ratiation treatment where the radioactive isotope iodine (I-131) is used to effect the thyroid.
query hypothyroid	bool	NA	If the person has hypothyroid where the thyroid will producte too little hormones, causting an overreaction
query hyperthyroid	bool	NA	If the person has hyperthyroid where the thyroid produces too much hormones and causing an overreaction.

Name	Data Type	Unit	Description
lithium	bool	NA	Lithium is an element that circulates in the body and helps different processes. Patients can take extra to stimulate the thyroid and becoming more active. Which will result in true in the data.
goitre	bool	NA	A goitre is a major increase in size of the thyroid or local swelling. Which can be diagnosed, if this is the case then the value is true in the data.
tumor	bool	NA	If the person has a tumor or not, since that will drastically effect your body and mental health. Leading to the same symptons with a different cause.
hypopituitary	bool	NA	Hypopituitary is a rare case of the pituitary gland does not produce enough hormones.
psych	bool	NA	If the person is seeing a psychologist, since thyroid issues will have an effect on mental health.
TSH measured	bool	NA	Thyroid stimulating hormone measured: will measure the amount of thyroid stimulating hormones in the blood.
TSH	float	continuous	Thyroid stimulating hormone: this hormone helps the thyroid release the T3 and T4 hormones. Without TSH, the thyroid would not be able to function at all. If there is too much TSH, the thyroid isn't releasing enough T3 and T4. TSH is released from the hypothalamus and targets the thyroid.
T3 measured	bool	NA	Triiodothyronine measured: will measure the amount of T3 in the blood. Since all transport of the thyroid hormones is done via blood cells, this will give an accurate amount of hormones.
T3	float	continuous	Triiodothyronine: is one of the two thyroid hormones, the hormones will influence each other and affect a lot of different processes in the body. Such as metabolism of glucose, the breakdown of cholesterol or increasing the heart rate.
TT4 measured	bool	NA	Thyroxine measured: will measure the total amount of free T4 and bound to blood T4. Since there are two types of T4, the way that it's used can differ. It can be bound to the blood or roam in the fluid. There for it is also provable by the test.
TT4	float	continuous	Thyroxine: this is the other hormone that will cooperate with the T3 hormone. They have the same function and are involved in the same general processes of the body: Metabolism, growth and increased catecholamine.
T4U measured	bool	NA	Thyroxine unbound measured: will measure the amount of T4 Uptake, which tests the usage of available T4.
T4U	float	continuous	Thyroxine unbound: T4 wich is free T4 hormone in the cell. This is transported via the blood so it can be measurable.
FTI measured	bool	NA	Free T4 Index measured: will measure the amount of Free T4, Total Free (T4) Index. This can range between 0.7-1.9 nanogram per decilitre of blood.
FTI	float	continuous	Free T4 Index: amount of free T4 which roams free in the body, being unbound and roaming free. Helping other processes in the body.
TBG measured	bool	NA	Thyroxine binding globulin measured: will measure the amount of TBG enzymes. Which means this is an indirect test to measure T4.
TBG	float	continuous	Thyroxine binding globulin: this is the amount of helper enzymes which is cleaved to make T4 hormones.
referral source	String	NA	External factors which are sets of strings in the data, indicating diagnosed conditions. A diagnosis "-" indicates no condition requiring comment.
diagnosis letter	char	NA	Additional diagnose with the letter with the patient's condition.

Material and Methods

For the exploratory data analysis, R and Markdown have been used. The version of R is 4.0.4, R has been used as tool for Markdown. R is a programming language used for statistics and data analysis. Graphs can be programmed and is a great tool for research. The graphs were made via the GGplot2 library. dplyr and tidyr were also used as additional tools for data transformation. Finally the pander library was used for displaying tables in a better way than base R.

All code for the data analysis and workflow can be found in the logbook. The logbook can be found via GitHub on: <https://github.com/Reindert1/Project-praktijk>

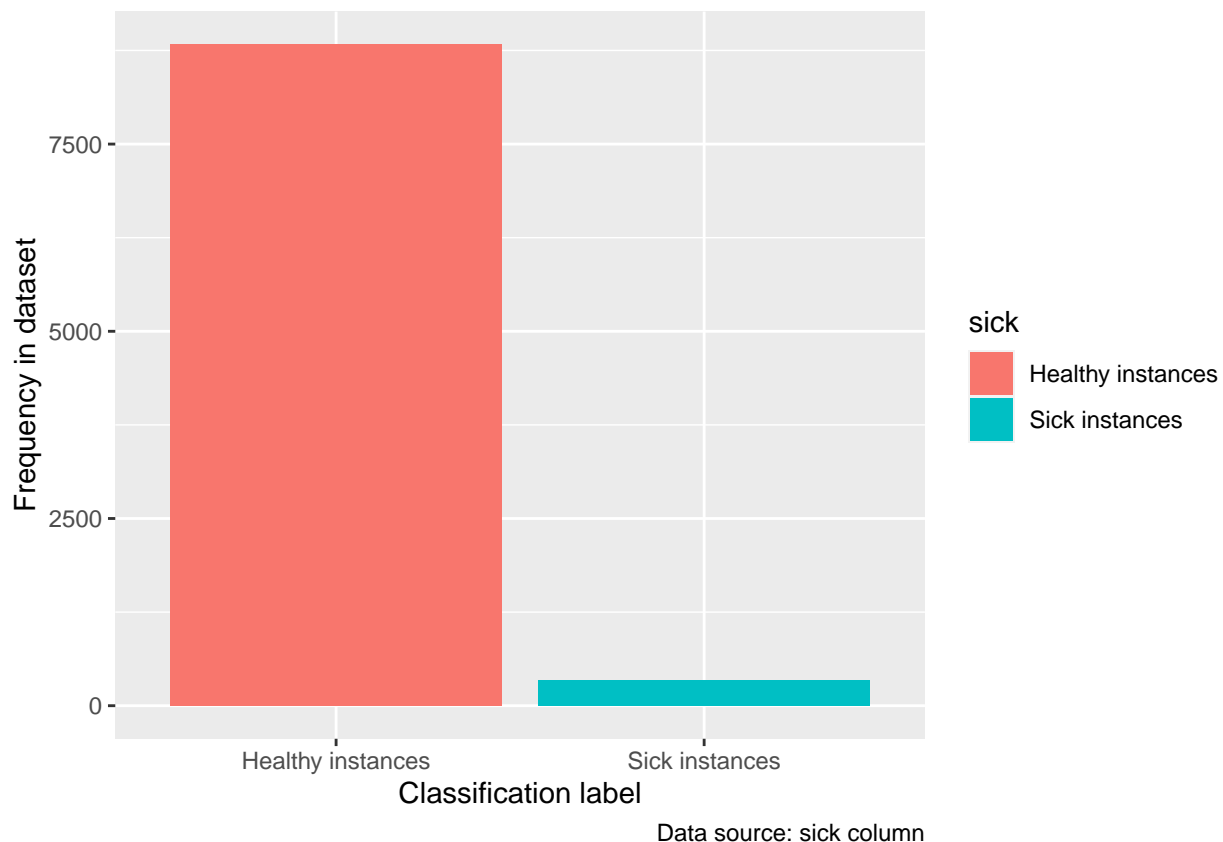
For the wrapper, the programming language Java has been used. The Java wrapper is made and tested on Java version 16. Via the command line, hormone values can be given and the wrapper will follow the model made in Weka version 3.9.5.

The Java wrapper also uses multiple dependencies, the common CLI version 1.4 for command line arguments. And the Weka stable version 3.8.5 was used for making the instance object, preparing this object and using the model to classify. Classifying the user's instance and showing this in the terminal output.

The wrapper can be found on: <https://github.com/Reindert1/wekawrapper/tree/master/src/main/java> Readme and support can be directly found on: <https://github.com/Reindert1/wekawrapper/blob/master/README.txt>

Results

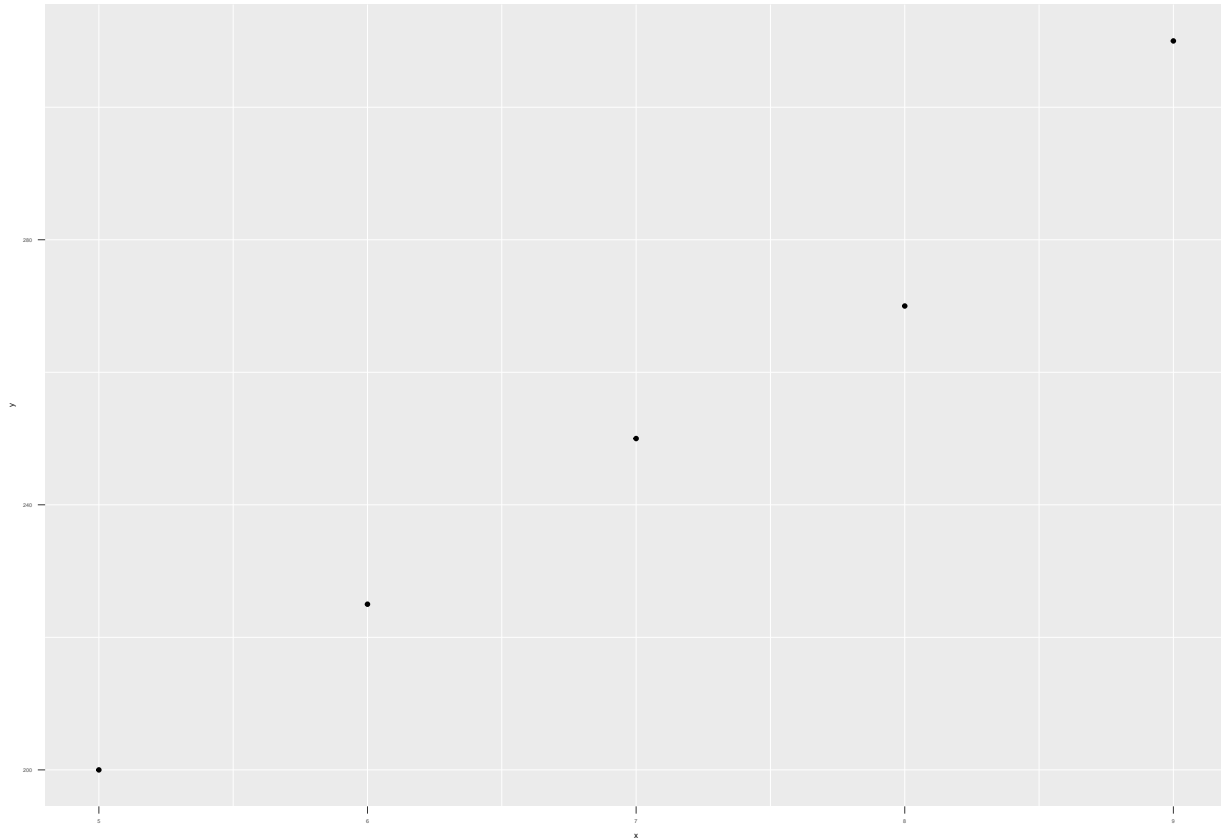
Of all the 9000 instances, only around the 200 are sick. Since sick is the most valuable column, this will become the class column. The data tells if the patient is either sick or not, so the machine learning algorithm will predict if the patient is sick or not.



There are a lot more healthy instances than the sick instances. So in order to successfully go to the machine learning process, some trimming needs to be done. 60% of the sick instances have been deleted, this will be done at random to maintain integrity.

```
df_1 = data.frame(x=c(5, 6, 7, 8, 9), y = c(200, 225, 250, 270, 310))
```

```
options(repr.plot.width = 1, repr.plot.height = 0.75)
ggplot(df_1, aes(x = x, y = y)) + geom_point(size = 0.3) +
  theme(text = element_text(size = 3), element_line(size = 0.1))
```



Overall the data is of pretty high quality, there are a lot columns that tell you enough information. The data is relatively complete, not extreme amounts of missing values (NAs).

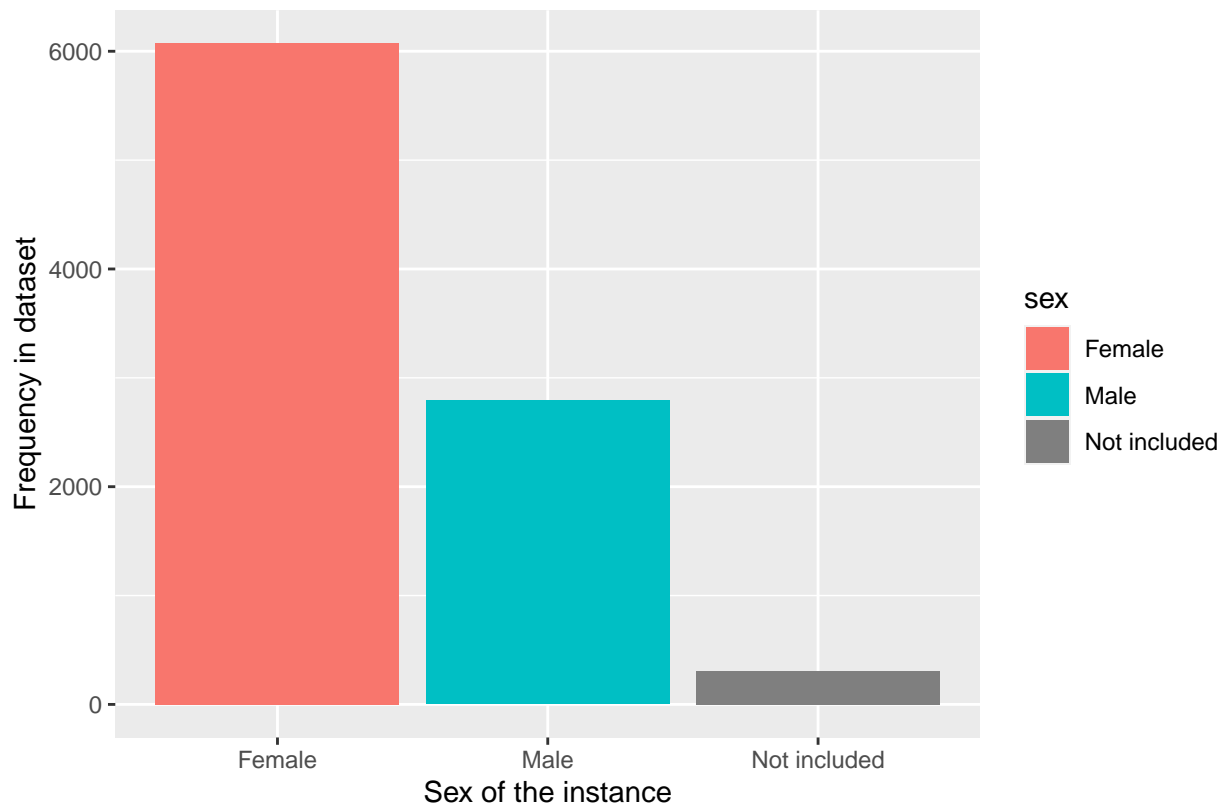
Table 2: Amounts of NA found in the data.

	x
age	0
sex	307
on_thyroxine	0
query_on_thyroxine	0
on_antithyroid_medication	0
sick	0
pregnant	0
thyroid_surgery	0
I131_treatment	0
query_hypothyroid	0
query_hyperthyroid	0
lithium	0

	x
goitre	0
tumor	0
hypopituitary	0
psych	0
TSH_measured	0
TSH	842
T3_measured	0
T3	2604
TT4_measured	0
TT4	442
T4U_measured	0
T4U	809
FTI_measured	0
FTI	802
TBG_measured	0
TBG	8823
referral_source	0
Diagnose_letter	0

Only the sex column has a lot of NAs, this could be because people wouldn't like to include their gender. There are also a lot of NAs in the hormone columns.

All of thyroid hormones are included in the data, and extra hormones like Thyroid stimulating hormone (TSH) are included. So it creates a complete picture of hormones. Most of the patients are healthy, only a small portion of the instances are sick, this might become a problem for the algorithm. Since the algorithm will most likely say "Not sick" and have 80% correct, while the patients with actual thyroid issues might get wrongfully diagnosed.

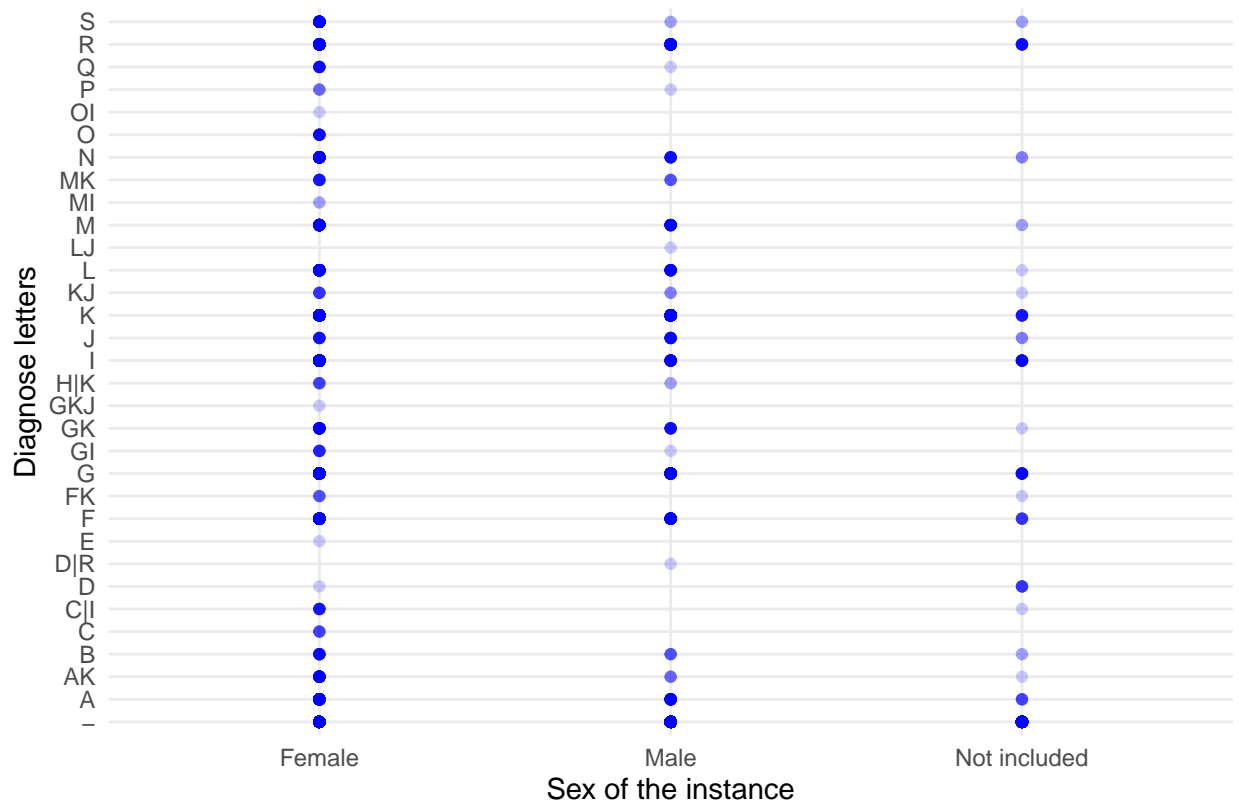


Data source: patients' sex in the dataset

Since sex is a sensitive topic, the NAs have not been filtered out or filled in. This is because the column does not give a lot of information, because the ratio is not near 50/50. Editing the data will result in major integrity loss, so these instances will stay the way they are. Although it does not give an complete picture and an actual representation of the population.

Since there are differences between sexes, not only body but also in hormones. The thyroid might act different, this might affect the effects people feel and how they respond to this.

```
## `geom_smooth()` using formula 'y ~ x'
```

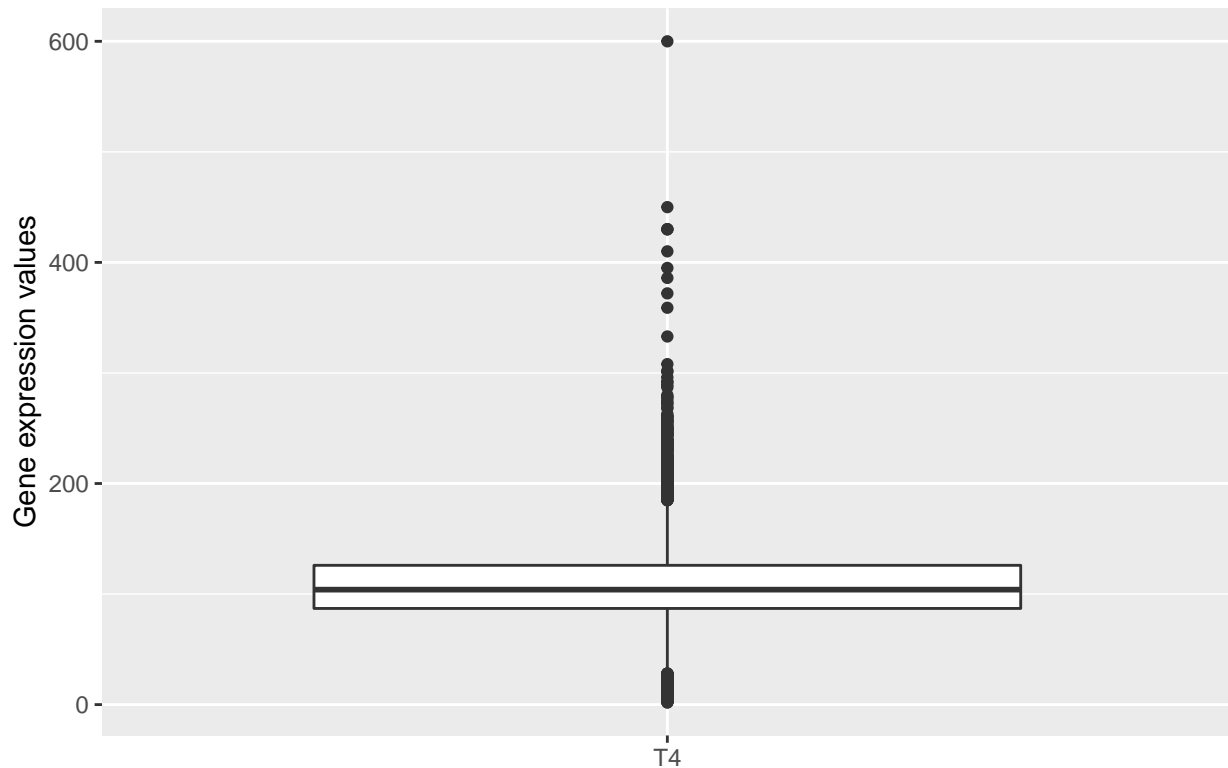


Data source: sex and diagnose columns

Not all males have the same problems as females, some more frequent than others. NA is added this time to give a general overview of the data.

One of the few numeric columns in the data set, are the hormone expression columns.

Warning: Removed 442 rows containing non-finite values (stat_boxplot).



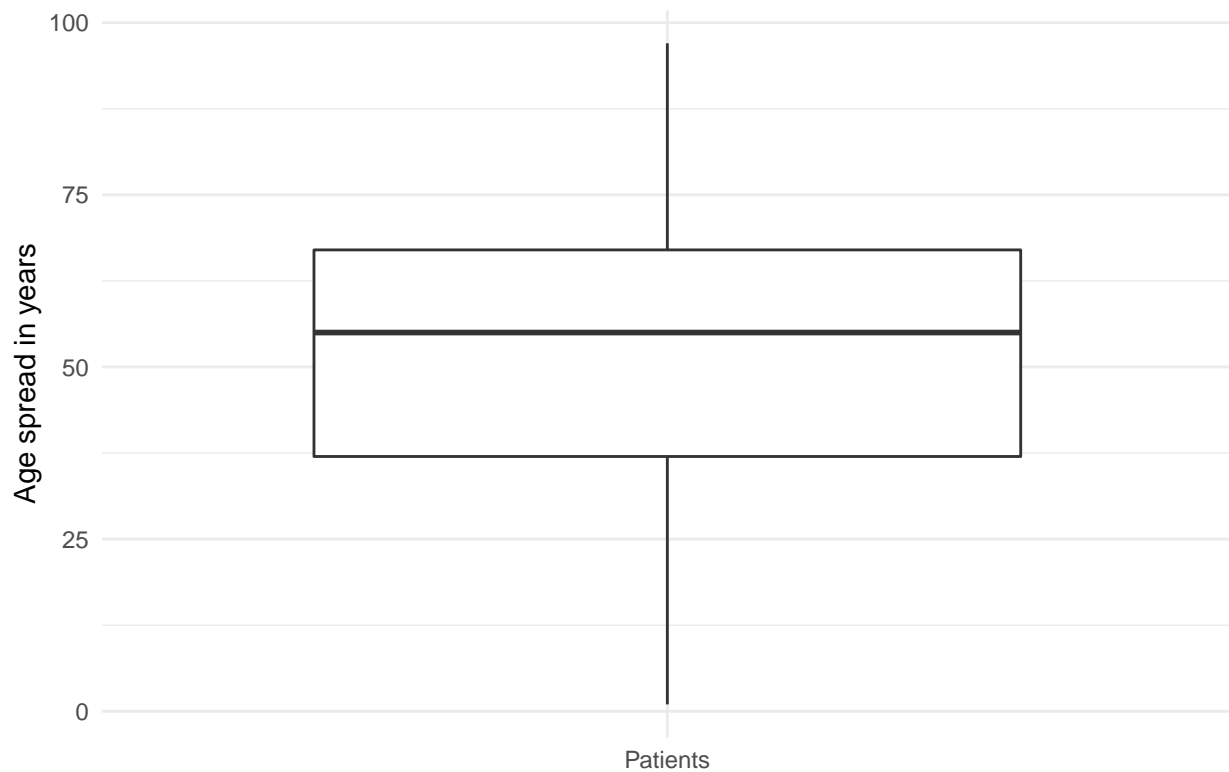
Data source: patients' expression values from the data

The hormones are of more value since these columns are numeric. Which is why the machine learning algorithm will most likely chose these columns to start with.

Cleaning data

When it comes to the dataset, which consists of either True or False, cleaning will become an issue. There are no outliers or impossible values, so the data (when originally downloaded) is mostly clean. There are some measured columns, there are numerical values here, but there are no outliers. So this does not need a lot of work to be done.

The age column has a lot of outliers, there are a lot of people with inhumane ages. For example three people would be in the nine thousand, one would be eight thousand and one would be four hundred years old. This is not possible of course, these values have been modified to only use the first two digits. If someone would say "I'm forty and a half years" and write it down as 40.50. Due to the use of floats it might got mixed up and combined. To not delete the entire instance, the first two digits will be used to fix this problem. Although this is not the most accurate instance. But on a scale of eight thousand instances, this will not be weighted heavily and won't affect the data. The age of the instances makes a jump from 97 to 400 to 8000, the instances above 97 have been trimmed to their first two digits.

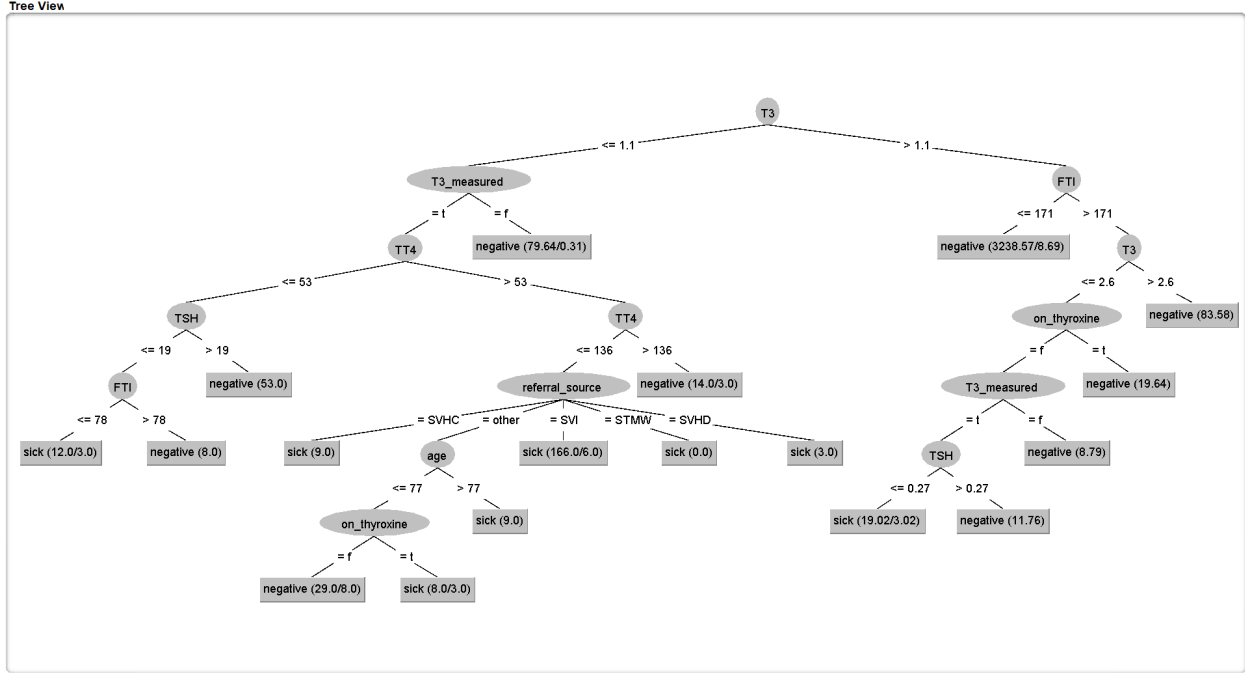


Data source: patients' ages from the data

Now that the data has been filtered of the outlying ages, the data looks a lot more believable. Since it is not possible for a person to be 8 thousand years, there must have gone something wrong with the data. This will increase the data's credibility and makes the conclusions of the algorithm more valid. Because there is no need to take these ages into account and split them in the design later on.

Machine learning

Multiple algorithms have been run, but certain algorithms performed better than others. Because of the way the algorithms work.



After multiple runs, with cross validations and no randomness factors or “lucky seeds”; the J48 tree algorithm performed the best out of them all.

Multiple test results have been run, the most important factors are displayed under the columns.

Table 3: Results of various machine learning algorithms

algorithm_name	speed	accuracy	error_rate	true_positives	false_positives	false_negatives	true_negatives
Zero R	0.01	0.94	0.062	3541	231	0	0
One R	0.01	0.96	0.040	3466	53	75	178
Naïve Bayes	0.02	0.93	0.070	3314	52	227	179
J48-Tree	0.14	0.99	0.010	3524	28	17	203
Ibk	0.00	0.96	0.040	3484	87	57	144
SMO	0.24	0.94	0.060	3540	231	1	0
Random Forest	0.42	0.98	0.020	3533	49	8	182

The J48-Tree proves to be best, since it has the lowest amount of false negatives and false positives. On top of that, it also runs the best with true negatives.

Discussion

The data consists mainly of either True or False, so there is little room for outliers and illogical values such as typos or other human errors. This helps the end result in its integrity. Apart from the age column, which has been modified. Multiple instances have been modified, although this is on a scale on 3 of 9172. This is not significantly for the end result and won't affect the conclusions of the algorithm. Both of the instances are not thyroid patients, so this will fall under the mass of “Not sick”. Deleting the instance might result in loss of information, this was the right way to act with these instances. But since this is a human error, it is not certain if this would be the correct for the person. But there is no way to track these individuals down, so there is no other way to either delete or modify the data.

Learning pattern

The original data has class labels. Since the instances are patients and Sick is the class column, the data tells if the instance is sick or not. This helps the machine learning section, these labels create a supervised learning environment. This way the algorithm can learn what values the sick patients have and how it differs to the other instances. This has multiple benefits compared to unsupervised, since the criteria will be a lot better and the concept of the algorithm will be better. Supervised learning also prevents the classification errors that unsupervised machine learning has. Since the columns and classes are already readied and human errors have been resolved.

Data ratio

A minor issue with the data, is that the male/female ratio is not 50/50. Females stereotypically tend to go more to the doctor. Since the thyroid involves mental health, an adult man won't go to the doctor unless it's absolutely necessary. This is also represented in the data set. There are a lot more females than males in the data, so hormone expression might be different. But sickness is provable due to hormone expression and external factors, so the male/female ratio won't affect the results of the data set. Since the algorithm does not take the sex of the patient (or instance) into account, since this column gives the least amount of information. The information gain is very little since all instances will most likely be female. This won't score highly in bits per instance; so the information gain will be very low. So the results of the algorithm are valid, even though the sex leans more towards female than male. Ideally to isolate the hormone values, without other factors of sex, the ratio would be 50/50.

Penalty matrix

In the algorithm performance, some choices have been made. What is worse: a false negative or false positive? Since the instances are patients, the false negatives need to be the lowest. If a false positive (incorrectly declared sick) will under go further medical investigation, they'll be proven healthy in the process. This might affect the person a lot, but it will save more lives. Because of the false negatives are lower (incorrectly declared healthy) might have serious issues which have gone under the radar. To prevent bigger issues later on with these instances, the algorithm needed to weight the false negatives heavier than the false positives. The J48-algorithm handles this the best, but additionally the scoring matrix has been used to weight the incorrectly declared healthy instances heavier. This way the overall accuracy was lowered by 0.04 but there was a change of 16 instances, where 7 were sick and correctly classified. Resulting in a gain of 7 correctly classified sick on a scale of 200. And 9 newly wrong classified on a scale of three thousand in the subset data.

Conclusion

With the machine learning results and J48 scoring 98.5% accuracy, while classifying 211 correctly sick and the majority of healthy instances correctly. The overall result of the experiment is promising

To conclude the research project, the original data was relatively clean. Due to the nature of the data, there was little room for outliers and extreme values. The amount of NAs are also relatively low and all relevant columns for the thyroid have been included in the data. External factors are also included and these columns are a great addition to the credibility of the dataset. So the results of the algorithm are valid, biologically and human errors have been filtered out.

There was a subset used for the machine learning process, since there were too many healthy instances. Resulting in a skewed dataset. After a subset was made, the J48 tree performed exceedingly well. Using the hormone expressions and medication to classify. In order to lower the amount of incorrectly healthy declared instances, these were given a penalty of 4.0 in the matrix. Resulting in a slightly lower accuracy but overall better performance. J48 is also an algorithm which is easy to understand, since it uses a decision tree. With this model, a Java wrapper was made to classify new instances via the command line. Printing the classification label to the terminal output.

Future research

A possible follow-up machine learning project, for the high throughput/high performance biocomputing minor.

To take the hormone expression values of the sick instances, and calculate medication via machine learning. In order to bring the expression values within healthy range. With the effect that the sick instance will start to feel better again. Using machine learning for this, the dose can be exact for every patient and machine learning can determine what values would be most beneficial for the patient. The same dataset can be used again, only the algorithm becomes way more complex. But in order to upscale this, more data of thyroid patients need to be collected. Since the data originally had nine thousand healthy instances and only two hundred sick instances.

More maths is involved and the algorithm would be tested on more various levels, in more ways than just class label prediction. This algorithm needs to calculate the hormone up scaling per patient to bring them into more healthy ranges, taking into account all healthy instances. This would not only identify patients, but also help them.