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Voice atypicalities in Schizophrenia; replicability of machine learning approaches

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Abstract

Can machine learning (ML) applied to voice data be used as a tool to help diagnose people with schizophrenia? Numerous studies have shown high accuracies when classifying schizophrenia, but results are widely heterogenous, as concluded in the latest meta study within the field (Parola et al., 2019). Little work has investigated the validity and robustness of the previous findings, and few replications shed light on the generalizability of the studies. Currently there is no consensus on which machine learning pipeline should be applied for optimal classification of schizophrenic patients.

This study provides a proposal for a general machine learning pipeline suitable for future research into this topic, along with the information necessary for implementing both rigorous and conservative machine learning models. As the pipeline is meant to be broad and general, an example of its more specific implementation is also provided for clarifying purposes. It is exemplified through a replication of the promising study by Chakraborty et al (Chakraborty et al., 2018), and thus also has the benefit of contributing to science within this area that is largely deprived of replications. A macro average F1-score of 0.70 was found – notably lower than the original study’s 0.77. As the replication employed a dissimilar dataset and slightly diverging methods, these differences were discussed in relation to the results. Subsequently, the proposed overall pipeline was scrutinized and given its limitations, further development on the pipeline was suggested. Finally, this paper advocates for a more open and cumulative scientific community.

Keywords: schizophrenia, speech signal, acoustic features, biomarker, machine learning

# 1. Introduction

## 1.1 Schizophrenia and voice as a biomarker

Schizophrenia is a diagnosis which has long been defined by disturbances in both thought, perception and communication (Bleuler, 1950). Although schizophrenia has been known to be a group of great heterogeneity, patients oftentimes suffer from similar symptoms (Picardi et al., 2012; Tsuang et al., 1990). They are generally thought to be divided up into two types of symptoms; negative and positive. Positive symptoms are those that are present during a psychotic episode in schizophrenia and include delusions and hallucinations (Andreasen et al., 1995). Negative symptoms are those that either diminishes or halts thought processes or normal emotional functioning and include, but are not limited to asociality, alogia – poverty of speech, latency of speech and blocking, and blunted affect – a decrease in emotional expression and a lack of vocal intonation (Andreasen et al., 1995; Cohen et al., 2012).

Schizophrenia is furthermore associated with several other speech impairments in addition or in relation to the qualitatively described symptoms of alogia and blunted affect. These range from higher-order semantic language impairments and semantic processing (Covington et al., 2005; Kuperberg, 2010), to differences in low-level acoustic signals such as shimmer and jitter (Kliper et al., 2016). A recent meta-analytic study from 2019 by Alberto et al., has systematically reviewed the accumulated evidence for distinctive acoustic patterns in schizophrenia (Parola et al., 2019). They found modest effects for proportion of spoken time, speech rate, pauses, and pitch variability, while pause duration proved to be a relatively strong predictor.

The language and speech disturbances are used in the clinical assessment process and have also been known to be helpful for both identifying those individuals that are at a high risk for developing psychosis – even before onset (Bearden et al., 2011; DeVylder et al., 2014; Sichlinger et al., 2019). They have furthermore allowed for tracking psychotic symptoms and predicting progression in symptoms (Bearden et al., 2011; Corcoran et al., 2020; Morice & Ingram, 1983; Solomon et al., 2011). Voice has in short been used as an important biomarker for psychosis. There is, however, a big drawback to the current use of speech in schizophrenia. Speech is being manually annotated or rated by expert raters, which is not only very time extensive but also requires training of the raters. The gathering of data is expensive and makes using it on a large scale impractical. Moreover, there is a chance that only the most extreme cases are picked up on, when using these manual assessments (Hitczenko et al., 2020).  
As the prospects of using speech in clinical psychiatry/psychology are ample but merely impractical on a larger scale, recent endeavors have been made to automate this method using supervised machine learning (ML) approaches.

## 1.2 Machine learning of acoustic patterns for detection of schizophrenia

### 1.2.1 Prospects of machine learning in classifying schizophrenia

Supervised ML classification works by learning patterns in some data set and can then subsequently be used to predict, using the learned patterns. The ‘learning’ part practically means building a model of the distribution of class labels (e.g. schizophrenic/non-schizophrenic) from predictor variables (e.g. acoustic features from speech). The ‘machine’ entails that the process is automated, which allows for finding complex, multivariate and sometimes non-linear relationships between multiple features in conjunction and class labels (Kotsiantis et al., 2007). This model is then used to assign class labels to the testing instances where the class labels are unknown, but where the predictor values are known.

ML has the potential of improving the ability of using information from speech in clinical contexts as it both gives objective judgements that scalable to large use given its automated nature (Hitczenko et al., 2020). Using a wide array of methods and both high and low-level speech features, different classification algorithms have categorized samples of schizophrenics and controls with accuracies between 70% and 95% (Martínez-Sánchez et al., 2015; Rapcan et al., 2010; Stassen et al., 1995; Tahir et al., 2019). If computational methods can achieve these rates of correct predictions, then the practical applications are countless. It would allow for preemptively identifying those with at risk of developing psychosis on a large scale as well as giving clinicians an effortless way of tracking and predicting symptom progression.

### 1.2.2 Current limitations in the literature

Although the results look entirely immensely promising at first glance, some substantial hurdles are still standing in the way before computational methods can be instantiated clinically.

One hurdle comes from the large discrepancies in results across studies – they undermine the confidence in the generalizability of the models (Hitczenko et al., 2020). A recent study from 2009 suggested that these purely data-driven approaches might be prone to overfitting, i.e. that the models have learned and relied on spurious correlations between features and diagnosis that might appear randomly in a particular dataset (Voleti et al., 2019). If this is the case for some of the models, the models then would predict poorly to data outside each of these studies (Dietterich, 1995). Given that predictive algorithm performance generally have been found to be greatly modulated by the data the algorithm is tested on, it is probable that it occurs to some extent within this field as well (Bone et al., 2013; Foody, 2017; James et al., 2013).

Another hurdle within the literature comes from the wide difference in how ML is being implemented between studies. As this field of research is relatively new, no universally accepted way of conducting this type of research exists. As a result, studies vary considerably in the acquisition of data, the use of methods and levels of method quality, transparency and documentation. Not only does this make it hard to compare studies, but it also makes it difficult to pinpoint which methods, feature sets, or datatypes produces the best results. When a study finds a classification rate of 87.5% (Martínez-Sánchez et al., 2015), while another finds a rate of 79.5% (Chakraborty et al., 2018) is the difference then the result of one using LDA classification as a method, while the other uses SVM? Or is it because one used a feature set related to emotion, while the other uses prosody, syllabic dynamics and pause duration as predictors? It is hard to pinpoint which factors cause what. The fact that studies potentially might be subject to overfitting even further convolutes the effects of using particular feature sets or algorithms.  
The thorough study by Hitczenko et al. that was very recently published, reviews the promises of the computational methods for clinical markers of schizophrenia after going into depth with publicized studies within this area (Hitczenko et al., 2020). Among other important insights, they establish this need for making direct comparisons to past work – using a similar critique of the current literature. A way of doing so would be to compare models on the same datasets, to perform replications - or studies that use similar courses of action.

## 1.3 Alleviating current limitations

### 1.3.1 Through replications and conservative ML implementation

Replications per definition make direct comparisons to past work and are useful in tackling the issues within this research area. By redoing a study and only differing on a few factors (such as nationality of participants) the results would give clear insights into the impact of these factors (e.g. showing that cross-cultural differences impact results).

However, these inferences are of course only possible if the studies are: 1) replicable – the studies have to be transparent and properly document the entire process of conducting the study. 2) proper and conservative methods – the results of replications and original studies alike are uninsightful if the models producing them either have problems of overfitting or if they elicit biases. Another way of alleviating the previously mentioned limitations of the research area would therefore be to ensure that these two criteria are met. But what constitutes a proper conservative ML implementation? To try and provide the foundation for further research, this paper will try and provide a rigorous conservative pipeline. If implemented, not only would it help by applying good ML practice – but if used more broadly, it would also allow for better comparison of results between studies.

### 1.3.2 A rigorous ML pipeline

A ML pipeline consists of several steps to train a model and operate workflow guidelines, from which predictive algorithms can be created. A well-organized pipeline will guide and support research and given wide implementation will also streamline research, making comparison to other work easier (Guzzetta et al., 2010; Olson & Moore, 2016; Samad & Witherow, 2018). In turn, this will enable insights of the impact of specific methods, features or populations on machine learning within a given research field.

The pipeline that this paper is presenting is broad, with aspirations of being widely inclusive and applicable regardless of data and specific algorithm while still managing to enclose the options to ensure that the strictly necessary requirements for good ml conduct are being met. To allow for comprehensive clarification, the pipeline will be divided up into 9 steps. As with all research, but perhaps especially within a field that suffers from little replicability, proper and thorough documentation of the specific implementation of the pipeline is crucial. Moreover, choices for the study ought to be scrutinized and evaluated both prior and subsequent to the analysis.

Data acquisition:

Preprocessing:

Data partitioning:

Feature scaling:

Feature selection:

Model training, tuning and testing:

Validation:

1. What is a pipeline?
2. This pipeline will be broad
3. Pipeline proposal:
   1. Data acquisition
   2. Preprocessing
   3. Data partitioning
   4. Feature scaling
   5. Feature selection
   6. Model tuning (training, tuning and testing cycle)
   7. Validation (and evaluation)
   8. (Reflection + proper documentation)

### 1.3.3 Purpose of paper

Short summary of introduction

1. Voice is an important biomarker with practical applications if automated
2. Machine learning proves promising but there are issues with:
   1. Overfitting
   2. Difference in implementation making it impossible to specify what works
   3. Lack of replications and testing across datasets
3. Pipeline alleviates problems of
   1. 1) overfitting
   2. 2) difference in implementation
   3. 3) lack of replications (by making it easier)

Thesis statement:

1. Provide pipeline
2. Show example of implementation
3. Evaluate implementation

# 2. Methods

## 2.1 Pipeline implementation and summary of methods section

The replication of this paper follows and provides an exemplification of the use of a rigorous pipeline - following the overall principles presented in the introduction (see section 1.3.2). The rest of the methods section will provide a detailed description of the course of action taken to specifically replicate the paper by Chakraborty et al. from 2018 (Chakraborty et al., 2018). Additionally, a short summary will be provided along with two figures in order to provide an overview of the process and showcase how it followed our proposed pipeline. One figure which attempts to visualize the pipeline (figure 1) and one which attempts to visualize the complex multi-leveled process of partitioning of the data (figure 2).

Diagram

Description automatically generated

Figure 1.

*An overview of the proposed pipeline. Purple boxes refer to the general pipeline whereas the green refer to the specifics implementation of the pipeline used in this replication.*

The pipeline for this replication is divided up into 8 steps which are as follows:

**1) Data acquisition.** Recorded voice data from 4 studies was acquired. **2)** **Data preprocessing.** Prior to this study, all data had gone through a cleaning process and all 988 features extracted in the original experiment were extracted from the data in this replication. **3) Partitioning.** The data was partitioned into a training and a holdout set of 80% and 20%, respectively. **4) Feature scaling.** Features were min-max normalized. **5) Feature selection.** The training data was split up into 5 folds. These folds were used in 5 different splits – with each split having a training set consisting of 4 out of the 5 folds and a testing set consisting of the remaining fold. All training sets had their features L2 regularized; meaning the feature estimates of the features that were less important were shrunk to zero, and thus essentially removed. This process resulted in a feature set with fewer than the original 988 features for each split. These feature sets only contained the most relevant features for the classification of schizophrenia patients.   
This process did in other words produce 5 splits of training and testing data. It also produced 5 feature sets. Each of these feature sets had been selected on the basis of 4/5th of the full training data, which meant that the remaining 1/5th of the training data (the testing set) could be used for testing. For an overview, see figure 2.

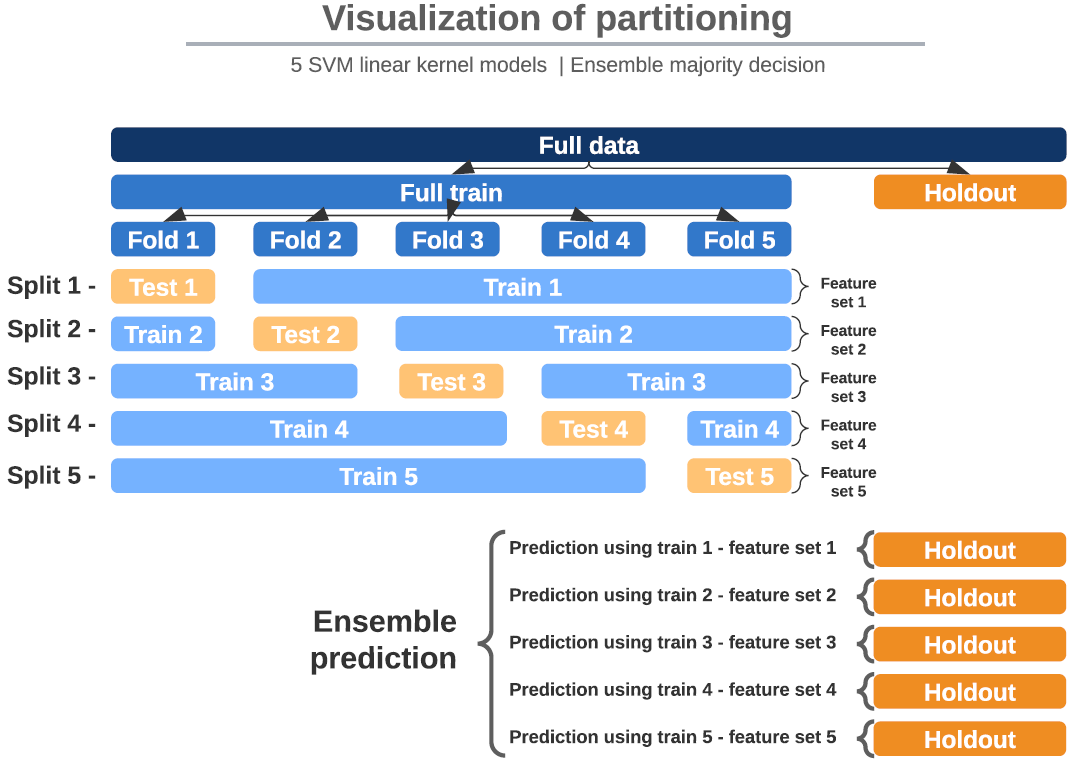


Figure 2.

*A visualization of the data structures used for this ML replication. Shows the process of partitioning and dividing the data up into multiple folds and outlines which sets were used for what.*

**6), 7), 8) Model training, parameter tuning, model testing.**

5 SVM linear kernel models were then constructed to classify patients from controls. Each of these models were fit on training sets (4/5th of the full training data) using the respective feature sets. The fit models were then tested on the matching test set (last 1/5th). The predictions were then evaluated based on their classification performance and C and Gamma parameters were tuned in the models. After tuning, the models were then tested again – repeating this process until need for a satisfactory performance level was met.

**9) Validation on holdout set.** Finally, the 5 models were tested on the holdout set. An ensemble model was also constructed. This model also predicted the holdout data, but by using the majority vote of the other 5 models as its prediction. Performance on the holdout set was then evaluated for the 6 models with the use of relevant metrics. Moreover, performance was also calculated separately for the two sexes. This allowed for insights into potential ML classification biases, given the different nature of voices between males and females.

## 2.2 Literature search for choice of replication

A literature search for papers, dissertations and unpublished manuscripts was conducted for finding a paper to replicate. The complete list of papers listed in the meta-analysis by Parola et al. in 2019 (Parola et al., 2019) was manually screened – first by title and since by content. As their search was last updated as of April 12 2018, the search was continued from that date and forward in time by the use of search using Google Scholar on the Sep 15 2020, using the same search terms (schizo\* AND machine learning AND prosody OR inflection OR intensity OR pitch OR fundamental frequency OR speech rate OR voice quality OR acoustic OR intonation OR vocal).

This search yielded an additional 709 papers that were manually screened for relevance by their title. Relevant papers – both from the meta-analysis and from the manual screening, were then explored by content, looking for papers that, 1) implemented ML to classify schizophrenia patients from healthy controls using acoustic features, 2) were transparent and well-documented, 3) were thorough in applying proper ML methods, 4) had larger amounts of data.

This narrowed the number of papers down to 8 papers (see appendix, 7.1). The study by Chakraborty et al. from 2018 was chosen for replication after carefully assessing relevant literature on these parameters (Chakraborty et al., 2018).

## 2.3 Data

### 2.3.1 Data sources

The data used in this paper consists of speech recordings gathered from 3 published studies (Beck et al., 2020; Bliksted et al., 2014, 2019) and an unpublished study by Vibeke Bliksted.   
Although the data was acquired in separate studies, the speech data has several qualities which makes it suitable for combining into a single study.

Participants from all studies went through the same tasks; namely the Frith Happé animations task (Abell et al., 2000). All participants went through 8 such trials that were recorded, except for in the study from 2014 by Bliksted et al., where the they also recorded 2 practice trials – meaning this dataset included voice recordings from 10 trials (Bliksted et al., 2014). This totaled in 1900 recordings with a duration mean of 18.18 seconds and a standard deviation of 14.84.   
\* kan man skrive det op sådan?? \*

Moreover, recording equipment and recording setting was constant within study, but unique across studies. This results in data corpora of diverse speech recordings suitable for testing whether implementation of a certain ML algorithm proves to be versatile in its predictions across data sets. \* move to discussion? \*

### 2.3.2 Participants

222 Danish participants were included in this study. Out of the 222 participants 106 were clinically diagnosed with schizophrenia by trained psychiatrists in accordance with the standards of ICD-10 DCR (Zivetz, 1992). Patients were recruited through OPUS, Clinic for people with schizophrenia, Aarhus University Hospital Risskov.  
The patient group was originally matched one-to-one with healthy control subjects (N = 116), using the following criteria: age, sex, handedness, ethnicity, community of residence and parental social economic status (based on the highest parental education and expected parental income according to Statistics Denmark regarding wages) and educational level (based on the last commenced education) (*Statistics Denmark*, n.d.). Healthy control subjects were recruited via advertisements in four local newspapers. All participants in the healthy group (and their first-degree relatives) had no history of any psychological disorders. Although the control group was originally matched one-to-one with the patient group, 14 patients and 4 controls were excluded due to poor recording quality or other similar factors. This explains the uneven number of participants within each group. For further information on participants, see table 1.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Study | N() | Diagnosis | N(Females) | N(Males) | Mean(Age) | SD(Age) | Range(Age) |
| Beck et al., 2020 | 70 | SZ | 16 | 18 | 22.8 | 3.13 | 18-31 |
| HC | 17 | 19 | 22.7 | 3.19 | 18-30 |
| Bliksted et al., 2014 | 46 | SZ | 6 | 17 | 23.3 | 3.94 | 18-33 |
| HC | 7 | 16 | 23.7 | 3.61 | 18-34 |
| Bliksted et al., 2019 | 48 | SZ | 11 | 8 | 40.8 | 12.4 | 20-61 |
| HC | 13 | 16 | 37.5 | 13.1 | 21-62 |
| Bliksted et al., n.d. | 58 | SZ | 12 | 18 | 24.8 | 3.66 | 18-31 |
| HC | 13 | 15 | 24.4 | 4.65 | 18-34 |
| Total | 106 | SZ | 45 | 61 | 26.7 | 9.02 | 18-61 |
| 116 | HC | 50 | 66 | 26.7 | 9.22 | 18-62 |

Table 1:

*Demographic data on the sex and diagnosis within each of the different studies. N means number and SD standard deviation. HC refers to the healthy control group, while SZ refers to the schizophrenic group.*

### 2.3.2 Procedure/task

The participants from all studies went through the Frith Happé animations task (Abell et al., 2000). This task consisted of watching a 2D top-view video of animated triangles. There were two distinct triangles; one large red and one small blue, both of which moved around on the screen. The videos differed their movement; some animations had the triangles move randomly, while others had either goal-directed movement or interactive movement between the triangles.

After watching an animation from one of these conditions, the participants were interviewed and asked to describe what happened in the animation. Each description of a trial thus ended up as a single .wav file.

## 2.4 Preprocessing

### 2.4.1 Cleaning of audio files

The cleaning of the audio files was carried out by Ludvig Olsen in 2018 (Olsen, 2018)  
The audio files were converted to 16-bit .wav files, with a sample rate of 16k. They were subsequently denoised by stacking multiple instances of the Voice De-noise and De-hum tools in the iZotope RX 6 audio editor (iZotope Inc., 2018). A small equalizer tilt was applied at 1085Hz with the Fabfilter Pro-Q2 equalizer to bring more brightness to the signal (FabFilter Software Instruments, 2018). The signal was normalized to peak at -1dB both before and after the cleaning steps.

### 2.4.2 Feature extraction from audio files

The toolkit openSMILE 2.3.0 was used for extracting the features needed for the classification algorithm. From within the openSMILE software package, the base-set configuration file of emotion recognition features called ‘emobase’ was chosen for feature extraction.

The feature set specified by emobase contains 988 features used for emotion recognition:

Intensity, Loudness, 12 MFCC’s, F0 Pitch, Probability of voicing, F0 envelope, 8 LSFs (Line

Spectral Frequencies), Zero-Crossing Rate. Delta regression coefficients are then computed from all these previously mentioned low-level descriptors (LLD). Both the LLDs and their delta coefficients are smoothed by a moving average window that filters with a window size of 3 seconds. Furthermore, the following functionals are applied to the LLDs and the delta coefficients:

Max./Min. values and their respective relative position within input, range, arithmetic mean, 2 linear

regression coefficients and linear and quadratic error, standard deviation, skewness, kurtosis,

quartile 1-3, and 3 inter-quartile ranges.

This resulted in the feature set consisting of 988 features. In other words; 26 LLDs, a delta regression coefficient for each LLD and 19 functionals for each of the LLDs and for each of the delta regression coefficients (26 \* 2 \* 19 = 988). The process of feature extraction was executed on each of the speech recordings, yielding a single feature vector for each trial of each participant. These feature vectors functioned as data points for the model.

## 2.5 Partitioning

To be able to evaluate the performance of the model the dataset was partitioned into a training set and a holdout set consisting of 80% and 20% of the total data, respectively. The partitioning was done using the package groupdata2 and was carried out semi-randomly (Olsen, 2020). The partitioning kept each participant ID only within either the resulting training set or the resulting holdout set. This prevented leakage of information from the training set to the holdout set, which otherwise would have led to overfitting and as a result an unprecise evaluation of out-of-sample performance \* introduction??? Or discussion? \* . Moreover, to avoid a skewed distribution of sex or diagnosis in the holdout set (e.g. ending up with only males/controls in the holdout set as a result of a random partitioning), sex and controls/patients were evenly distributed in the holdout set. The constituents of the holdout set were the feature vectors for each trial from:  
11 female controls, 10 female patients, 12 male controls and 11 male patients.   
A properly balanced holdout set ensures that performance across sexes and diagnosis can be accessed without too much statistical uncertainty; calculating performance of females with predictions on a single female would either yield a 100% or 0% accuracy, neither of which would necessarily be telling for a models true performance. \*Discussion or introduction??\*

## 2.6 Normalization

All feature parameters were normalized using the min-max feature scaling formula in order to achieve a dataset with a common scale without losing information or distorting differences in the range of values.



To avoid overfitting as a result of carrying data from the test set to the training set, the normalization was carried out separately for the training and the testing set. The scaling of both sets used the minimum and the maximum value for each feature, only from the training set. This had the advantage of having both the training and the test features on the same scale, while not letting information from the test set flow to the training set (Myrianthous, 2020). This procedure is common practice when applying most ML algorithms. \* move to discussion or introduction? \*

## 2.7 Feature selection using LASSO

### 2.7.1 Motivation for using LASSO

As the 988 acoustic features from the ‘emobase’ package were originally designed to distinguish emotions from speech, some features were less important for the purpose of distinguishing between patients and controls. As a measure to counterfeit this, a rigorous feature selection method was applied to rid the model of potentially superfluous features. This was done in order to simplify the model and thereby reduces both complexity, computational power needed to run the model and in order to improve both predictive power and interpretability of the classifier. \* move to introduction or discussion? \*

Feature selection was done using L2 regularization, also called the Least Absolute Shrinkage and Selection Operator (LASSO) analysis regression. To carry out this process, the ‘glmnet’ R Package was utilized for the purpose of this paper. (Friedman et al., 2010)

Although the parameters could have been regularized using Ridge or ElasticNet, LASSO regularization has the advantage of being able to shrink irrelevant parameters all the way to zero – as opposed to Ridge regularization. ElasticNet is a combination of Ridge and Lasso and would therefore be a compromise between the two (Hastie et al., 2009). The shrinking of parameter estimates to zero gives a smaller number of features. This has the benefit of reducing the probability of a spurious feature-target correlation that would result in an overfit ML model (Hawkins, 2004).

### 2.7.2 What is L2 regularization?

This method optimizes beta estimates for all parameters not only through misclassification error but also adding a L2 regularization term. The latter adds a penalty to each beta estimate on the basis of a lambda value multiplied with the beta estimate.

In other words; performing L2 regularization means fitting a LASSO regression model and thus finding the optimal beta values for all parameters using the loss function seen below.

The loss function used for finding parameter estimates using LASSO:  
\* Brug eget lavet \*

Since this method requires a lambda value (λ), the optimal lambda value for all 5 feature sets also had to be found. The lambda value producing the minimum value in the loss function (lambda.min) was first computed. This was done by testing a range of lambda values using 5-fold cross-validation. Subsequently the lambda value resulting in the fewest number of parameters within 1 SE from the lambda.min was chosen (lambda.1se). Although lambda.min has the lowest level of misclassification, lambda.1se has the advantage of acknowledging the fact that the fits are estimated with some error (Friedman et al., 2010).

This process thus generates a list of parameter estimates for each time it is performed. Those that have not been shrunken to zero are selected as relevant features for predicting patients from controls. For a visualization of lambda misclassification plot, see figure 3.



Figure 3:

*A range of lambda values (x-axis) and the resulting 1) misclassification error, and 2) number of features (seen at the top). From left to right, the dotted lines represent lambda.min and lambda.1se, respectively. \* which data was this from? \**

### 2.7.4 Feature selection

The training data was partitioned into 5 folds, and thus also 5 splits (see fig. 2). The previously mentioned L2 regularization was carried out on all 5 training splits, resulting in a feature set for each of them (see appendix x\* for list of these feature sets). An illustration of the feature selection for a single split (split 1), can be seen below in figure 4.

Graphical user interface, diagram

Description automatically generated

Figure 4:

*Figure showing the process of feature selection on train 1:*

*The training data is divided up into 5 folds. One fold is then excluded (yellow). Using cross-validation, the LASSO regression fit for a specific lambda value is then computed with each of the folds being omitted once. The misclassification error for each of these fits is then accumulated and stored. The process is then reiterated using a new lambda value from the lambda grid, until all accumulated errors from all relevant lambda values have been obtained.*

*This entire procedure is then repeated for each of the remaining 4 training splits.*

## 2.8 Model training, testing and parameter tuning

Using the 5 training sets and the appertaining feature sets for each split, 5 SVM linear kernel classifier models were constructed. The models were fit on the trainings sets, using only the appertaining feature sets. SVM classifiers were then tested on the appropriate test sets - the model fit on training set 1 was tested on test set 1, etc. Performance was then evaluated based on relevant metrics (see section 2.7). After testing, the models were tested again using a self-specified range of C-parameters around default (1) to see if they allowed for better predictions. The default C-parameter of 1 was found optimal for classification.

The 5 models were then implemented into an ensemble model. This model merely predicted using the majority vote of the 5 previously mentioned constituent models. If for example 3 out of 5 models predicted ‘schizophrenia’ for a recording, then this was also the vote of the ensemble model.

## 2.9 Evaluation metrics

For evaluating the performance of the models, several metrics conveying information about the classification was provided. Precision (positive predictive value) is the ratio between true positives and all positive predictions. Recall on the other hand is the ratio of positives that were correctly classified. Although both precision and recall are typically only provided for the model as a whole, additional information can be acquired be calculating them for each class (i.e. getting precision and recall for both the patient and the control group). Since a model might have a high precision and a low recall rate (or vice versa), a F1-score used often used. A such score gives the harmonic mean of the two ratios and gives an overall understanding of the classification performance for each class. By calculating the arithmetic mean of the two F1-scores (one F1-score for the classification of patients, and one for controls), the single score of macro-F1 provides clear and quick overall insight into classification performance.   
Accuracy – the percentage of correct classifications - is said to give an intuitive impression of the performance and is regarded common practice. However, it can often be misleading (e.g. when evaluating performance on an unbalanced test set). By providing information about the baseline accuracy it is possible to compare accuracy, since baseline accuracy depicts the accuracy rate of a model that merely predicted the majority group.   
Moreover, confusion matrices are provided as they convey the whole picture of evaluation and provide all the information needed for all other evaluation metrics to be calculated.



*Where,   
tp, fp, tn, fn, refers to true positives, false positives, true negatives, false negatives - while i and N refers to class and number of classes respectively.*

## 2.10 Differences between replication and original study

This replication employed principles from the proposed general pipeline, which means that it diverges from the original study on several aspects. These discrepancies can all be seen in table x \* below

|  |  |  |
| --- | --- | --- |
|  | **Original** | **Replication** |
| **N (participants)** | 78 | 222 |
| **Origin** | Malay, Chinese, Indian | Danish |
| **SZ rate** | 66.67% | 48.2% |
| **Task  language** | English | Danish |
| **N (recordings)** | 78  (1 per participant) | 1900  (8-10 per participant) |
| **Mean (length of recordings)** | 26 min | 18.8 sec |
| **Feature  selection** | PCA | LASSO regularization |
| **Feature scaling** | Min-max  normalization | No  information provided |
| **ML  algorithm** | Single SVM | Majority  vote ensemble – SVM |
| **Final  testing set** | Cross- validation (full dataset) | Holdout (separate set for final test) |

Table x \* :

*An overview of the differences between the original paper by Chakraborty et al. and this replication.*

# 3. Results

This section presents the performance of the ML models when predicting various parts of the full data. A crude overview of the performance of the 5 models on the various test sets is given in table 2. An in-depth look at the ensemble models performance; both for controls and for the patient group is provided in table 3. The latter also provides insight into performance differences between the sexes. Finally, confusion matrices (table 4, 5 and 6) provide the necessary details that would underlie calculations for any and all additional performance metrics. The latter uses the abbreviations HC and SZ which mean ‘healthy controls’ and ‘schizophrenia”, respectively.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Testing set** | **Training and feature set** | **Macro avg. F1-score** | **Accuracy** | **Baseline accuracy** |
| Train 1 | Train 1 | 0.896 | 89.64% | 53.05 |
| Train 2 | Train 2 | 0.930 | 93.03% | 51.52 |
| Train 3 | Train 3 | 0.897 | 89.73% | 52.21 |
| Train 4 | Train 4 | 0.899 | 89.91% | 51.89 |
| Train 5 | Train 5 | 0.898 | 89.85% | 51.80 |
|  | | | | |
| Test 1 | Train 1 | 0.687 | 68.68% | 51.85 |
| Test 2 | Train 2 | 0.630 | 63.05% | 54.34 |
| Test 3 | Train 3 | 0.678 | 67.84% | 51.62 |
| Test 4 | Train 4 | 0.613 | 61.31% | 52.94 |
| Test 5 | Train 5 | 0.658 | 65.80% | 53.29 |
|  | | | | |
| Holdout | Train 1 | 0.644 | 64.44% | 51.87% |
| Train 2 | 0.652 | 65.19% | 51.87% |
| Train 3 | 0.735 | 73.51% | 51.87% |
| Train 4 | 0.740 | 74.05% | 51.87% |
| Train 5 | 0.716 | 71.64% | 51.87% |
| **Ensemble (majority vote of set 1:5)** | **0.703** | **70.32%** | **51.87%** |

Table 2:

*Prediction performance for all 5 SVM linear kernel models, on various testing data.*

*Within-sample prediction performance can be seen in the first 5 rows, while row 5-10 depicts performance tested on the 5 test sets. Finally, the performance for the models’ predictions on the holdout set along with the majority decision vote can be seen in the bottommost 6 rows.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Test set | Model | Sex | Acc. | Baseline acc. | Class | Precision | Recall | F1-score |
| Holdout | Ensemble | Male | 70.62% | 52.58% | SZ | 0.664 | 0.772 | 0.714 |
| HC | 0.759 | 0.647 | 0.698 |
| Female | 70.00% | 51.11% | SZ | 0.689 | 0.705 | 0.697 |
| HC | 0.711 | 0.696 | 0.703 |
| Both | 70.32% | 51.87% | SZ | 0.675 | 0.739 | 0.706 |
| HC | 0.734 | 0.670 | 0.700 |

Table 3:

*Performance of the ensemble model - within both the sexes and diagnosis.*

|  |  |  |  |
| --- | --- | --- | --- |
| N = 374  *(m = 194,*  *f = 180)* | Predicted group | | |
| True group |  | HC | SZ |
| HC | 130  *(m = 66*  *f = 64)* | 64  *(m = 36*  *f = 28)* |
| SZ | 47  *(m = 21*  *f = 26)* | 133  *(m = 71*  *f = 62)* |

Table 4:  
*Confusion matrix for the ensemble model predictions. Information on the proportion of males (m) and females (f) is also provided*

# 4. Discussion (update this!!)

This discussion section will first compare the results of this replication with the results of the original paper. Focus will be on the metrics: precision, recall and F1-score for classification of each of the two groups. A potential model bias coming from the physiological difference between the sexes, will furthermore be investigated.

Secondly, the implementation of the general pipeline in this replication will be discussed – going into depth with the choices for each step. The question “*How did an implementation of the proposed pipeline in this replication work out?*“ will be addressed. This will be done on two levels:  
1) with regards to this specific replication (evaluating the choices for the 9 steps) and

2) with regards to the original paper (what differed in the replication, and what impact did it have?)

Finally, the use of the proposed general pipeline will be assessed, using the insights of this replication. Future research using the pipeline will also be discussed, looking into both the benefits and limitations that it holds, as well as potential future development. On this basis, the prospects for conducting further research are then assessed.

## 4.1 Performance results and comparison of performance to original study

This section will compare the original papers performance with the performance of the ensemble model on the holdout set from this study.

The reason for looking at the performance when predicting the holdout set is because it gives information about the out-of-sample capabilities of the model. This contrasts with predicting the training data, as this would give no idea of the generalizability of the model.   
The reason for looking at the performance of the ensemble model instead of for example the best performing model, is because it is likely to be the most robust model. The fact that some of the training sets and their appertaining feature sets produced better predictions on this specific holdout set (e.g. train 4), is likely only due to random chance. The holdout dataset will undoubtedly have more in common with some of the training splits than others. The ensemble model will be more robust and generalizable since it simply is based on more data. Larger samples will more closely approximate the true population \* cite \*.

The ensemble model achieved an overall accuracy of 70.32% which is lower than the original paper’s 70.49%. This can be misleading however, as it does not account for differences in baseline accuracy. The original study had a baseline accuracy of 66.67% (2/3rd of the participants were patients), while this replication had a baseline accuracy of 51.87%.

The macro average F1-score gives a better measure of performance. The original paper had an F1-score of 0.77 – higher than the F1-score of 0.703 in this replication. When looking at the isolated F1-scores for classifying patients and controls both the ensemble model and the model of the original study classified controls equally well. The model from the original study did, however, achieve a higher F1-score when classifying patients compared to the model from this replication. This performance difference is what caused the macro average F1-score to be higher for the study by Chakraborty et al. Moreover, both models also had an evenly balanced rate between recall and precision – the metrics that constitute the basis for the F1-score calculation.

As voice is modulated by the physiological differences between the sexes, it is relevant to see if this fact resulted in a model that predicted one sex better than the other. The ensemble model classified equally well between males and females with macro average F1-scores of 0.706 for males and 0.7 for females. No information was provided by Chakraborty et al. on this issue, although performance metrics would have been informative in shedding light upon a potential sex bias.

All performance measures considered, a moderate difference in performance was found with this replication seemingly having slightly worse classification capabilities. Should this fact be interpreted as an indicator of the original study not being conservative enough for the implementation of ML methods? Perhaps this rigorous ML pipeline implementation resulted in a more robust and generalizable model and its performance more accurately reflects what can be achieved. Although this could be hypothesized to partially explain the drop in performance, it is very likely that the differences across studies in data, feature scaling and feature selection also had an impact. To shed light on this topic it is sensible to evaluate the specifics of the individual pipeline steps in this replication, as well as discussing the differences between the study by Chakraborty et al. and this replication.

## 4.2 Evaluating specific pipeline implementation (and discussing differences from original study)

The proposed overall pipeline provides an outline of the necessary steps in ML. However, it does not specify exactly how each step should be carried out (e.g. the feature extraction step could justifiably have extracted a different set of features). This means that the particular choices for courses of action within each step of the pipeline should be not only well documented but also scrutinized and evaluated. Each step will therefore be evaluated and if the step deviates from the original study, it will also be discussed in relation to the study by Chakraborty et al. (differences between the studies can be seen in table x \* )

**1) Data acquisition.** This study used data corpora of diverse speech recordings from multiple studies. Not only did this provide more data, but it also provided more diverse data since the recording setting differed across study. The ML model will therefore be more versatile, in that it is less bound to only learning patterns within a certain setting. \* måske slettes? \*

All participants in this study were Danish, which entails that the results are not necessarily entirely generalizable across nationalities or languages. As of yet, research suggests that symptoms such as alogia and the flat effect partially produce the differences in acoustic patterns in patients with schizophrenia. It is a probable that the extent to which they elicit these symptoms could be modulated by culture and language. Moreover, the nature of the schizophrenic participants might also vary slightly – people diagnosed with schizophrenia elicit different symptoms depending on culture, with for example westerners typically eliciting more depressive behavior (*Lundbeck Institute Campus*, 2016; Sartorius et al., 1986).

The number of recordings (N = 1900) was quite large in this replication given the large number of participants and the fact that each participant went through 8-10 trials with separate recordings. This meant that the feature extraction process produced a large number of feature vectors (1 per recording). As each feature vector represents a data point, the classification algorithm simply had many datapoints to learn from.

The data acquisition was widely different in the original study. Their recordings were substantially longer which meant that the feature vectors for each data point more accurately captured the true feature values as they were less prone to random variation \* cite \*. However, they did only have 78 data points, which is substantially fewer than the 1900 employed in this replication. Their participants were Malay, Indian or Chinese, but were instructed to speak English during the recording sessions. As mentioned, both language and culture might impact both symptoms and acoustic measures in patients. This means that the results between studies can have been impacted by the difference in data acquisition.

**2) Preprocessing.** The data was cleaned, ensuring that for example reverb qualities or noises specific to certain rooms was not allowed to confound the classification algorithm. This sometimes proves to be a confounding factor in classification using speech, leading to high but inaccurate accuracies (Bone et al., 2013). The sound level of the data was normalized before and after the cleaning steps, to avoid having the ML model learn from the volume level. Reflecting upon this retrospectively, it does technically allow for the training data to learn from the holdout set, since this process happened before the splitting into a training and a holdout set. Given that loudness of speech is only one feature out many, the author suspects that this have had a miniscule impact – if any.  
As for feature extraction, the ‘emobase’ feature set includes features originally found to be relevant for classifying emotions. Since emotional impairment is known to be one of the hallmark symptoms of schizophrenia, they also prove useful for classifying schizophrenia. However, many other acoustic features not included in ‘emobase’ have been found promising in this feat \*cite\*. It could also have been interesting to look at multiple different feature sets and compare them, or to use multiple in conjunction. The recent software development of ‘DigiVoice’ for example, supports feature extraction of not only acoustics features, but also features about linguistic complexity, natural language and semantic coherence features. (Zhang et al., 2019).

**3) Partitioning.** The data was partitioned into a training set and a holdout set of 80% and 20%, respectively. A larger training allows for the model to better learn the patterns in the data, while a larger holdout set allows for a more accurate measure of performance - having three voice recordings to predict could only result in an accuracy of either 0%, 33.33%, 66.67% or 100% accuracy even given a true accuracy 70% \* cite \*. Although there is some basis for choosing the split, the optimal split size is considered to be rather arbitrary – there is no scientific consensus on what exactly is optimal \* cite \*.  
It is however relevant to try and have both sets balanced. This study had a roughly even balancing of not only controls and patients, but also an almost even balancing between the sexes \* what balance – specifically? \*. The holdout set included enough male (N = 194) and female recordings (N = 180) to allow for insights into whether the slight imbalance in sex confounded the results. As discussed in 4.1.1 this was found not to be the case. An unbalanced training set of 4 male patients and 2 female controls, might simply lead to the model predicting ‘schizophrenic’ to all cases where the acoustic features are specific to males. Instead of learning the acoustic patterns of schizophrenia it would learn the acoustic patterns of males.  
An unbalanced holdout set consisting of too few members of a group – whether it be sex, nationality of diagnosis - has the problem previously mentioned problem of not allowing for an accurate measure of performance within that group. This performance measure within one group is the only way of seeing whether the model learned based on some confounding factor (such as sex – if for example all controls were female).

**4) Feature scaling.** As using SVM as an algorithm requires scaled parameters/features, this study employed a min-max normalization. The scaling of both the training and holdout set used the minimum and maximum values from the training set to ensure no information could flow from the training to the holdout set (Myrianthous, 2020). An alternative could have been to standardize the features instead. Standardization has the benefit of not being as affected as outliers as min-max normalization does, given that standardized data is generated from standard deviation and mean.  
As no information was provided in the original paper, it is unclear whether their acoustic features were scaled within each step of the cross-validation, ensuring to scale the test set using only information from the training set, or if they scaled prior to the cross-validation process. The latter could result in a small amount of overfitting. Performance would appear to be slightly better, but it would more poorly reflect out-of-sample performance. The reason for this would be that the classification algorithm could have learned from the testing data before seeing it for the validation (Géron, 2019).

**5) Feature selection.** LASSO regularization was utilized for feature selection in this study. Choosing one specific feature selection technique over another should in theory not have a large impact on performance in classification. Much theory supports the choice being somewhat arbitrary, but in practice it sometimes is not (Oreski et al., 2017). LASSO has in some studies found to be one of the best feature selection techniques, with great improvements of classification algorithms (Sun et al., 2019) \* cite more \*. However, a myriad of other feature selection techniques exists and could have been utilized instead – the best individually performing feature selection techniques depend on both the dataset and the classifier used. There simply is no silver bullet method (Jović et al., 2015). It would have been interesting to perform multiple feature selection techniques and compare performance, instead of choosing only one technique.

Principal Component Analysis (PCA) has, similarly to LASSO, often been found to be the feature selection technique which resulted in the best ML performance when comparing models. This was also the case in the original paper where multiple feature selection techniques were used. (Abdi & Williams, 2010; Chakraborty et al., 2018; Sun et al., 2019). PCA reduces the dimensionality (number of features) of each data point (each recording), by generating a smaller number of new ‘principal components’ (dimensions) while preserving as much as the variation in the data as possible (Abdi & Williams, 2010). The latter feature selection technique diminishes the interpretability of the model as opposed to the former, given that the original acoustic features are convoluted in the new principal components. LASSO allows for investigations into which features where most important for classification.  
Given that both PCA and LASSO have been known to perform similarly well, it is therefore unlikely that all the variation in performance between the two studies can be attributed solely to feature selection technique. If the method for using the acoustic features from ‘emobase’ for classification truly is robust and reliable, then either should in theory work.

**6, 7, 8) Model training, model testing and parameter tuning.** As this study had both a testing and a holdout set, it was possible to tune the parameters for optimal classification. The model was trained on the training data, and subsequently tested on the test data using a grid of different hyperparameters relevant to linear kernel SVM. The hyperparameter values resulting in the best classification on the test set were used for the models. This enabled an optimal tuning of the models for the best predictions on the holdout set, without overfitting to the holdout set. This is also the background for proposing a split that entails both having a training, testing and a holdout set in the general pipeline. Using cross-validation on the whole dataset would have allowed for using all of the data for training, but it does not allow for hyperparameter tuning.

**9) Validation.** When validating the model on the final testing set, it is important to evaluate performance. F1-scores gives an accurate, unbiased and easy overview for a model’s performance. Confusion matrices, however, remain the most important tool in documenting performance as they provide the raw scores that all performance measures are calculated from. If anything is missing, it should be ROC-curves – these could have showed the tradeoff between sensitivity and specificity at different classification thresholds could also have been provided.

As mentioned in the introduction, the implementation of the pipeline steps in solitude was not proposed to alleviate the issues in the current literature. The pipeline had to be accompanied by a proper and rigorous documentation. It also had to be supplemented by both reflection and scrutiny of the specific choices for each step in the pipeline – just as all good research has to. The description of the methods for this replication have been attempted to be both meticulous and exhaustive, enabling both replication and further scrutiny. The specific choices for each step have moreover been discussed, both in terms of their consequences but also in terms of their potential alternatives.

In summary; the pipeline implementation of this replication is unlikely to have been confounded by problems related to either small or unbalanced data. This model is also unlikely to be overfit, given that the feature scaling process was carried out appropriately and given that the data was cleaned so that any acoustic qualities the model picked up on were not due to specific room settings. Moreover, the validation on the final holdout set was both balanced and potential bias coming from differences between the sexes were ruled out by looking at the results for each sex individually. The differences in performance between the original and this replication is likely to be due to a) a difference in data, b) a difference in methods, or c) the very conservative nature of this replication. Since the data differs widely between studies, it is reasonable to assume that data has had an impact – it is however unfeasible to deciphering exactly why, how and to which magnitude.

## 4.3 Prospects and limitations of the proposed overall pipeline

Overall pipeline (not individual steps, but the thing from introduction)

1. Good things mentioned in the introduction, shortly summarized… end with “But limitations!”

2. Limitations (some of which were found from doing a replication)

3. Something about the future? Future development? Future research? Looking forwards

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# 6. Appendix

## 6.1 Relevant studies

(Chakraborty et al., 2018; Gosztolya et al., 2018; Kliper et al., 2016; Martínez-Sánchez et al., 2015; Püschel et al., 1998; Rapcan et al., 2010; Stassen et al., 1995; Tahir et al., 2019)

## 6.2 Feature lists after L2 Regularization

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