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Voice atypicalities in Schizophrenia; replication of machine learning approaches

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To do list:

1. Methods er bade I nutid og datid. Ret det til det rigtige??
2. Provide graphs and plots and flow charts for methods section
3. Read through and see if any ‘notes to section’ should be included in the sections, depending on space. This in OneNote!
4. Write about “software used” somewhere in the methods section
5. Explain why random forest/cvsm/others is good in the paper.
6. Remember to evaluate accuracy not to chance but to majority group

# Abstract

**Actual paper:**  
  
**Notes for section:**

**(Fabio exercise):**

Can machine learning (ML) applied to voice data be used as a tool to help diagnose people with schizophrenia? Numerous studies have shown high ML accuracy when classifying schizophrenia, but the ways in which they do so differ widely, as concluded in the latest metastudy within the field. Little work has been done to replicate these previous ML methods on new data, and there is currently no consensus on which methods should be used.  
This study replicated two promising ML studies on new data, using an improved validation technique and an inclusion of sensitivity and specificity rates. Accuracy rates found through replication were dissimilar to the original studies, with study X\* and study Y\* having overall accuracy rates for classification at 60% and 67%. In other words a drop of 6 and 3 percentage points for the two studies, respectively. Through discussion, this study has found that the difference in scores in the replication points toward low ecological validity and robustness. The rest of the litterature was also discussed, and I found that the widely heterogeneous results within the field indicate similar trends.  
As a consequence, this study has attempted to establish a ML pipeline less prone to the pitfalls of ML, with the intention of establishing a general procedure for future research. Finally this paper advocates for a more open and cumulative scientific community.

How to write abstract:  
<https://blackboard.au.dk/bbcswebdav/pid-2793891-dt-content-rid-9152972_1/courses/BB-Cou-Hold-36086/L1%20-%20Getting%20started.pdf>  
p. 14 - p. 18

**Keywords:** Schizophrenia, Machine Learning, Voice, SVM

# 1. Introduction

## 1.1 Research into voice atypicalities in schizophrenia

**Actual paper:**  
  
**Notes for section:**

Voice atypicalities in SZ’s have always been known (Bleuler, 1911; Kraepelin, 1919).  
Schizophrenia has certain distinctive features vocally. Qualitatively the atypicalities have been described using numerous different terms (Alogia, blunt affect, "poverty of speech", "latency of speech", increased pauses, distinctive tone, intensity of voice etc.).  
  
  
Effect sizes of acoustic features is partially determined by task (and task difficulty):  
\*\*sas  
  
  
The atypicalities have been studied using 3 methods;  
Qualitative perceptual ratings, quantitative acoustic analysis and ML investigations.  
Qualitative perceptual ratings have found relatively robust differences in voice between SZ and TD. Relying on raters to assess perceptual differences has some limitations. A feature such as “latency of speech” is interpretable and must be rated on the basis of human intuition – this requires comprehensive training for the rater. Moreover, the complex interplay between multiple acoustic features is hardly very accessible, even given proper and rigorous training.  
  
Quantitative acoustic analyses have identified acoustic features on the basis of automated processes, leaving the assessment of the acoustic features more reliable. Using automation, the features of a set of voice data will identical over multiple feature detections, given the same feature detection hard- and software.  
Here, fewer robust differences were found with varying effect sizes and direction, depending on the features investigated (Cohen et al., 2014; https://www.biorxiv.org/content/10.1101/583815v4.full.pdf).  
  
Multivariate ML investigations have found promising results. Focus on minimizing out-of-sample-error instead of within sample-error as when using more traditional analyses, makes the applicability of the method more practically generalizable. It also allows for analyzing multiple features in conjunction. High correlation between almost all features (3.3, correlation <https://www.biorxiv.org/content/10.1101/583815v4.full.pdf> ).  
It does, however, not allow for transparency as to wherein the acoustic differences between SZ and HC lie.

## 1.2. Practical appliance of ML

**Actual paper:**  
  
**Notes for section:**

ML can perhaps help with showing:  
a) Severity of schizophrenic symptoms  
b) Diagnosis, schizophrenia  
  
Practical applications:   
1. Assisting tool for assessing diagnosis (Parola, Fusaroli et. al 2019)

2. Clinical application -> given schizophrenia, and given samtaleterapi or drugs, see how they're doing along the way by them talking every week on their phone.  
"*In addition, voice analysis may potentially allow to assess the response to psychosocial or pharmacological treatment over longer periods using objective and quantitative indices, and enhance the capability of clinicians to capture the complex relationship between emotion regulation, expressive behavior, social perception and cognitive and clinical features of the disorder (e.g. Ben-Zeev et al., 2017; Dahlgren et al., 2018; Tahir et al., 2019)*" (Parola, Fusaroli et. al 2019)Va [(Bush et al., 1998)](https://www.zotero.org/google-docs/?KFKj12).  
  
but no validation between datasets exist. Moreover, language differences?

## 1.3 What this paper aims to do

**Actual paper:**  
  
**Notes for section:**

Need for replication. Need for clear pipeline within the field

On prediction of severity of clinical features from acoustic measures:  
(Püschel et al., 1998)

## 1.4 Notes for all sections below, here

**Actual paper:**  
  
**Notes for section:**

A nificantly higher brain activation ex

**History of the project:**

1. Schizophrenia has certain distinctive features vocally. (Alogia, blunt affect, "poverty of speech", "latency of speech" etc.). This has been known since forever (Bleuler, 1911; Kraepelin, 1919).

Voice atypicalities have been studied using 3 methods. Qualitative perceptual ratings, quantitative acoustic analysis and ML investigations.

Qualitative perceptual ratings have found robust differences between SZ and TD.

Quantitative acoustic analyses have found fewer robust differences, with varying effect sizes and sometimes direction.

ML investigations have found promising results, but no validation between datasets and/or languages exist.

Overall:

We don't know which features proves to have differences between SZ and TD

The litt. is a mess - results in different directions.

Different ways of conducting studies

Systematic review, for both ASD and Schizo. Finds all acoustic measures (not perceptual). They have found everything that is in the litterature.

Might have been additional new papers.

Replicate in a new corpus with 2 languages - even though metanalysis tells us it is robust. (These are the ones in Google Docs).

Other studies have used ML - but support vector machine, different data, some overfit.

1. There's already a metastudy on Schizophrenia; which found atypicalities on different voice/speaking parameters - with varying effect sizes.

Large heterogeneity between studies.

More demanding tasks meant larger effect sizes.

**Applicability of Bachelors project:**

Meta-science, open science.

Assisting tool for assessing diagnosis (Parola, Fusaroli et. al 2019)

Clinical application -> given schizophrenia, and given samtaleterapi or drugs, see how they're doing along the way by them talking every week on their phone.

"*In addition, voice analysis may potentially allow to assess the response to psychosocial or pharmacological treatment over longer periods using objective and quantitative indices, and enhance the capability of clinicians to capture the complex relationship between emotion regulation, expressive behavior, social perception and cognitive and clinical features of the disorder (e.g. Ben-Zeev et al., 2017; Dahlgren et al., 2018; Tahir et al., 2019)*" (Parola, Fusaroli et. al 2019)

Companies interested in this (Lasse Hansen), Switzerland Internship on this in depression

**Thesis statement idea 1 (Maries):**

This thesis aims to investigate the capabilities of existing machine-learning classifying individuals with ASD from acoustic features. We will review previous literature, extract strong voice-features and machine-learning models, and validate models on new data. We predict that support vector machine will achieve higher accuracy but will have less x and that naive bayes will x. Additionally, we predict that validation methods x,y,z will make results stronger in specific case/weaker generalization. By this, we will attempt to establish a procedure for machine-learning studies that achieve the most robust and ecologically valid measures.

**Thesis statement idea 2:**

This thesis aims to replicate two promising findings of machine learning classification of schizophrenia, using voice data. Since the litterature on the area has very hetereogeneous findings, I expect worse performance given the new data that I will test on. Given the inrobustness and low ecological validity of ML attempts, I will attempt to establish a ML pipeline less prone to the pitfalls of ML, with the intention of establishing a general procedure for future research.

# 2. Materials and Methods

Læs Tour de Bachelors:

<https://docs.google.com/document/d/1qc3tDtAg6sc2-zfnxaxqKl_WydK3AAgaDLb1V7QjTTU/edit?fbclid=IwAR1JB53UmJcDEI8GnXEEvA4PcuWXvVeX_ZN43VEamHHxMWsHYdAR_Wo3vKY#>

## 2.0 Pipeline

**Actual paper:**

**Notes for section:**

General on pipeline

Flowchart of general pipeline (along with this study)  
Look at Ludvigs

## 2.1 Literature search

**Actual paper:**A literature search for papers, dissertations and unpublished manuscripts was conduced for finding the paper to replicate. The complete list of papers listed in the meta-analysis by Alberto et al. in 2019 (Alberto 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).

The manual search explored the papers by the author, looking for papers that 1) were transparent and well-documented, 2) were thorough in applying proper machine learning methods, 3) had larger amounts of data. The study by Chakraborty et al. from 2018 was chosen for replication on basis of these factors (Chakraborty et al., 2018).

\* Expand on this? \*

## 2.1 Data

### 2.1.1 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 (FHA) (Abell et al., 2000). All participant went through 8 such trials, except for in the study from 2015 by Bliksted et al., where the participants were presented with 10 trials (Bliksted et al., 2014).

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 machine learning algorithm proves to be versatile in its predictions across data sets.

### 2.1.2 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 this 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 x \*.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **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 |
| TD | 17 | 19 | 22.7 | 3.19 | 18-30 |
| Bliksted et al., 2014 | 46 | SZ | 6 | 17 | 23.3 | 3.94 | 18-33 |
| TD | 7 | 16 | 23.7 | 3.61 | 18-34 |
| Bliksted et al., 2019 | 48 | SZ | 11 | 8 | 40.8 | 12.4 | 20-61 |
| TD | 13 | 16 | 37.5 | 13.1 | 21-62 |
| Bliksted et al., n.d. | 58 | SZ | 12 | 18 | 24.8 | 3.66 | 18-31 |
| TD | 13 | 15 | 24.4 | 4.65 | 18-34 |
|  |  |  |  |  |  |  |  |
| **Total** | **106** | **SZ** | **45** | **61** | **26.7** | **9.02** | **18-61** |
| **116** | **TD** | **50** | **66** | **26.7** | **9.22** | **18-62** |

Table x \* :

*Demographic data on the sex and diagnosis within each of the different studies. N means number and SD standard deviation.*

### 2.2.2 Procedure/task

The participants went through the Frith Happé animations task. 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 and most videos furthermore contained an enclosure in the center of the video. There were three conditions with multiple videos for each condition:

**1. Random movement sequences.** There was no obvious interaction between the triangles and movement appears random. **2. Goal-directed (G-D) movement sequences.** An interaction between the triangles in which actions are directed toward each other in order to achieve specific goals.

**3. Mental interaction (ToM)**. An interaction between the triangles involving the manipulation of the emotions and thoughts of one triangle by the other.

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.

## 2.3 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 then 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 SVM 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 results 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.

### 2.4.3 Partitioning

To be able to evaluate the performance of the model the dataset was partitioned into a training set and a test set consisting of 80% and 20% of the total data, respectively. The partitioning was carried out using the package groupdata2 and was done semi-randomly (Olsen, 2020). The partitioning kept each participant ID only within one of the two resulting training and test sets. This prevented leakage of information from the training set to the test set, which otherwise would have led to overfitting and finally unprecise values for the evaluation.  
Moreover, to avoid a skewed distribution of sex or diagnosis between sets (e.g. ending up with only males/controls in the test set as a result of a random partitioning), sex and controls/patients were evenly distributed in the partitioning.

### 2.4.4 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 used the min. and the max. value for each feature, only from the training set, both for the training and for the testing 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 and is common practice when applying most machine learning algorithms.

## 2.4 Feature selection using LASSO

### 2.4.1 Motivation for feature selection using LASSO

As the 988 acoustic features from the ‘emobase’ package were originally designed to distinguish emotions from speech, some of the features were bound to be redundant 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 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.

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 unimportant parameters all the way to zero – as opposed to Ridge regularization. Elastic net is a combination of Ridge and Lasso and would therefore be a compromise between the two. The shrinking of parameter estimates to zero is beneficial given the many features that are unrelated to the distinction between schizophrenia and healthy individuals.

### 2.4.2 LASSO – L2 regularization

This method optimizes beta estimates for all parameters not only based on misclassification error but also adds 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.

The loss function used for finding parameter estimates using LASSO:  


Since this method requires a lambda value, the optimal lambda value also had to be found.

The lambda value producing the minimum value in the loss function (lambda.min) was first discovered. This was done by testing a range of lambda values using Leave-One-Out CV (LOO-CV). Subsequently the lambda value resulting in the fewest number of parameters within 1 SE from the lambda.min was chosen (lambda.se). For a visualization of the process of choosing lambda value, see figure x \*.  
  
Figure x \*:

*Different lambda values and the resulting number of features*  
  
The application of LASSO thus generates a list of parameter estimates and all those that have not been shrunken to zero are selected as features for predicting Schizophrenia from typically developing.

### 2.4.3 Cross-validation on the training data

Instead of just using LASSO method on the whole of the training set, cross-validation was applied in order to ensure the optimal number of features. To specify, the training data from the main partitioning was partitioned into 5 folds, with each of them appearing once as a test set in the subsequent cross-validation. The previously mentioned LASSO regularization process was thus carried out 5 times for each step in the cross-validation, resulting in 5 different feature sets (see appendix x \* .

To evaluate which features were optimal, the feature sets were evaluated. As each feature set was based upon 4/5th, and the last 1/5th had not been presented to the model, the last 1/5th was used as a test set using an SVM classifier with a linear kernel. The software Visual Studio Code was used, using the package SciKitLearn.

\* \* \* \* \*

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\* \* \* \* \*

Figure x \* :

*A flow chart showing the LASSO partitioning and cross-validation process*

\* \* \* \* \*

\* \* \* \* \*

\* \* \* \* \*

\* \* \* \* \*

\* \* \* \* \*

Table x \* :

*The test results from the different feature sets:*

## 2.5 Model and model tuning

**Actual paper:**?  
  
**Notes for section:**

Ensemble   
Each .wav file is being predicted

C-score fiddling for model tuning?

SVM, linear kernel

## 2.6 Evaluation metrics

**Actual paper:**The fitted models’ predictions of the sound files were evaluated not only on the per file level, but also by diagnosis and by sex. The evaluation was based the set of metrics, seen below:  
  
Math for the different metrics:

\* \* \* \* \*

\* \* \* \* \*

\* \* \* \* \*

\* \* \* \* \*

\* \* \* \* \*

Where, tp, fp, ….. means true positives (correctly classified schizophrenics), etc. etc… respectively

**Notes for section:**

Cohens kappa

Accuracy  
Precision

Recall

F1

For everything  
For each diagnosis  
For each diagnosis, for each gender

# 4. Results

## 4.1 Model predictions

**Actual paper:**  
  
**Notes for section:**

s

# 5. Discussion

## 5.1 ML results

**Actual paper:**  
  
**Notes for section:**

s

## 5.2 Differences in original vs. this

### 5.2.0 Performance differences

**Actual paper:**sssd

### 5.2.1 Feature selection methods

**Actual paper:**  
  
**Notes for section:**

LASSO, not PCA  
  
Hard to replicate, given the sparse information on how PCA was used to feature select.

“*the features of the training set were ranked using one of the following techniques: F-score (ANOVA), χ 2 , Mutual Information, Pearson correlation, Principal Components, linear SVM, Decision Trees, and Random Forests. Subsequently, the optimal number of features were selected according to the previous ranking methods*”  
PCA used to rank? Most common method is that PCA is used for defining new features, namely PC1 + PC2 + ... +PCn, until some desired threshold of accumulated variance is met.

There’s also the possibility that it truly was used to rank, e.g. by looking at the features with least shared variance in the different principal components to avoid covarying features, but also here it is not possible to replicate 1-1. The method is still not specified

Regardless, of method used by Chakraborty et al, the method used here is good. And if the method using speech for classification truly is robust, then either would work. If these results truly are reliable and reliable, they shouldn’t be dependent on PCA/LASSO / whatever

Link of idea of PCA for feature selection. (starts at 3:50). It shows that there are different methods (example with gain, here)

[https://www.youtube.com/watch?v=YEDOSOd44bU&list=PLBv09BD7ez\_5\_yapAg86Od6JeeypkS4YM&index=2&frags=wn&ab\_channel=VictorLavrenko](https://www.google.com/url?q=https://www.youtube.com/watch?v%3DYEDOSOd44bU%26list%3DPLBv09BD7ez_5_yapAg86Od6JeeypkS4YM%26index%3D2%26frags%3Dwn%26ab_channel%3DVictorLavrenko&sa=D&ust=1601362784622000&usg=AFQjCNERIVXMRd-YOHtyHEZ-n_Q_viBn-Q)

Link for example of PCA for feature selection (creating new features):

[https://www.quora.com/How-do-you-use-PCA-for-feature-selection](https://www.google.com/url?q=https://www.quora.com/How-do-you-use-PCA-for-feature-selection&sa=D&ust=1601362784622000&usg=AFQjCNEJOcJmuf_2J_jkzAGToPaZN4tLrg)

### 5.3 Feature extraction method

**Actual paper:**  
  
**Notes for section:**

**Feature extraction method:**  
Original paper:   
"*Both the LLDs and their delta coefficients are smoothed by a moving average filter with window size 3*" - it only specifies the frameSize, not the frameStep!  
  
Replication paper:   
Not necessarily done exactly the same way. The above was interpreted as a frameStep of 3 as well.

Machine generated alternative text:
B. Multiple summaries over fixed size (sliding) windows (5 seconds long, shifted forward at 
intervals of 2 seconds): 
frameMode = fixed 
frameSize = S 
frameStep = 2 
frameCenterSpecia1 
= left 

**OBS: EDIT YES IT WAS! It was just the default setting!**

### 5.3 Task

**Actual paper:**  
  
**Notes for section:**

Task the data is from:  
Storytelling of triangle moving meaningfully or sometimes not. Storytelling monologues, no social component in this data. (Mid-level)  
  
Replicated paper is highly difficult - interview. This likely has huge effects.

### 5.4 Sex bias

**Actual paper:**  
  
**Notes for section:**

No information on bias in terms of sex, but balanced datasets in the original.  
Here, perhaps a bit worse training, but balanced test-set

## 5.4 In general

### 5.4.1: Hard to replicate, given the sparse information given

**Actual paper:**  
  
**Notes for section:**

### 5.4.2 What new knowledge has been acquired?

**Actual paper:**  
  
**Notes for section:**

ML methods not robust to language differences and task differences.  
Also not as balanced  
Which of them and how much, is hard to tell.

### 5.6 Where should the research go from here?

**Actual paper:**  
  
**Notes for section:**

More replications, to better understand

# 6. Conclusion

**Actual paper:**  
  
**Notes for section:**

sd

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8. Appendix

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