

# ANALYSIS OF EEG-BASED DEPRESSION BIOMARKERS

USING MACHINE LEARNING & NONLINEAR ANALYSIS

MIROSLAV KOVÁŘ

SEBASTIÁN BASTERRECH

FNSPE, CTU

MAY 17, 2019

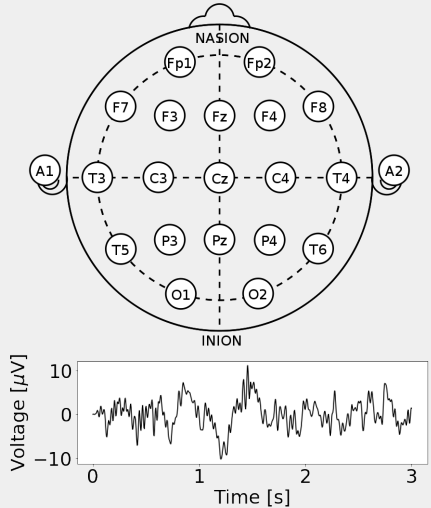


# **PROBLEM STATEMENT AND APPROACH**

# DEPRESSION TREATMENT IS EXPENSIVE

■ MDD

■ EEG

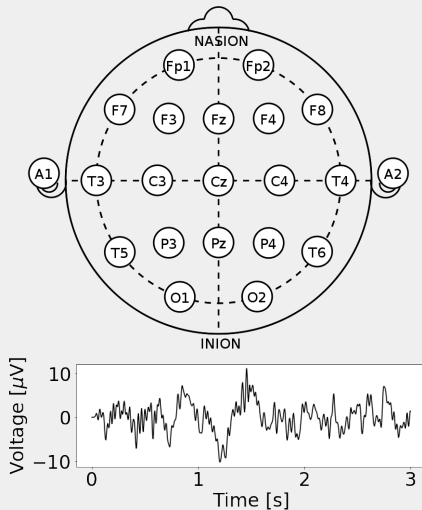


# DEPRESSION TREATMENT IS EXPENSIVE

## ■ MDD

- ▶ 300 million suffering worldwide

## ■ EEG

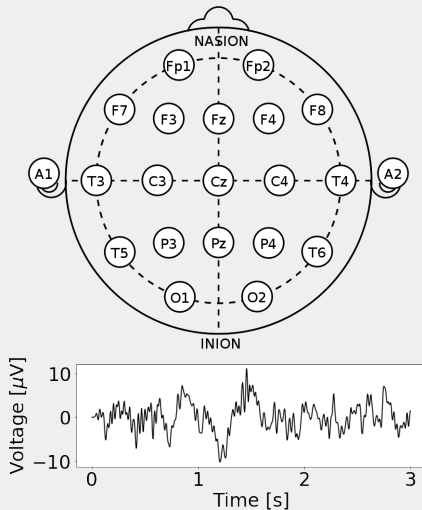


# DEPRESSION TREATMENT IS EXPENSIVE

## ■ MDD

- ▶ 300 million suffering worldwide
- ▶ diagnosis requires time of trained professionals

## ■ EEG



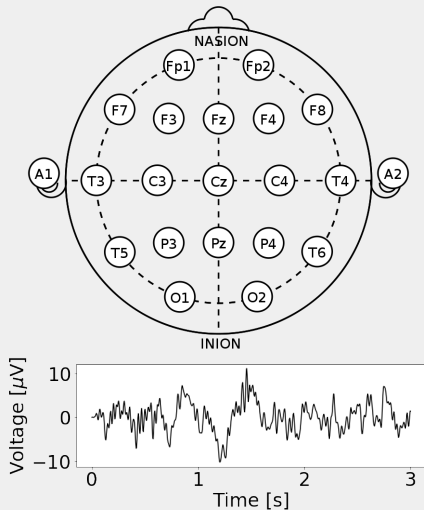
# DEPRESSION TREATMENT IS EXPENSIVE

## ■ MDD

- ▶ 300 million suffering worldwide
- ▶ diagnosis requires time of trained professionals

## ■ EEG

- ▶ accessible diagnosis-aid tool



# DEPRESSION TREATMENT IS EXPENSIVE

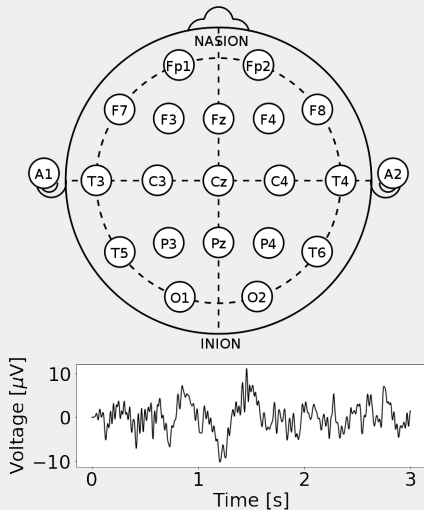
## ■ MDD

- ▶ 300 million suffering worldwide
- ▶ diagnosis requires time of trained professionals

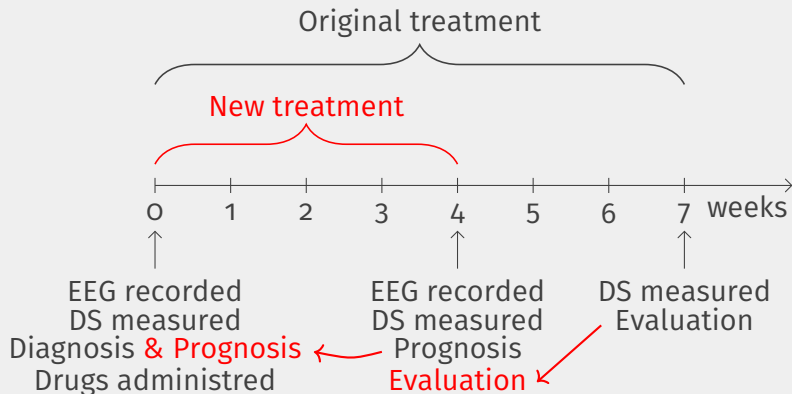
## ■ EEG

- ▶ accessible diagnosis-aid tool
- ▶ still not reliable enough!

Research into effective analysis techniques is ongoing...



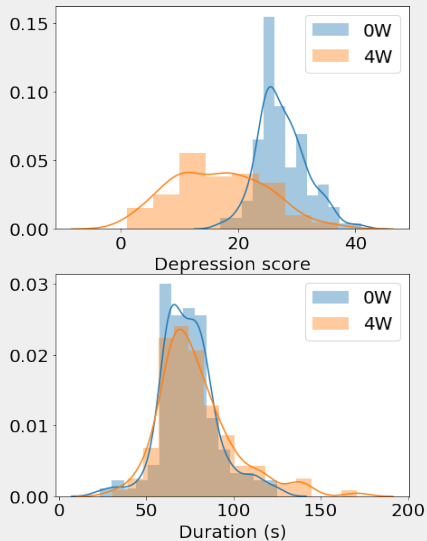
# OUR GOALS





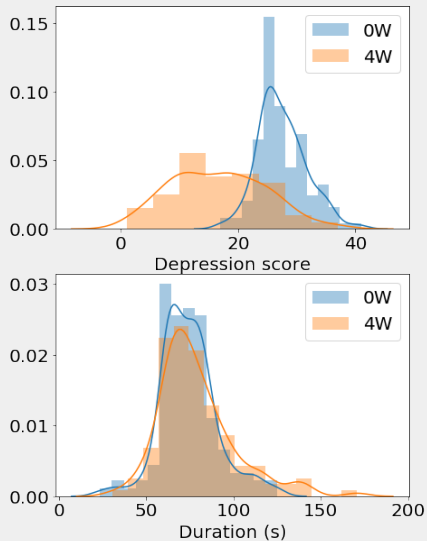
# OUR DATASET

■ Czech National Institute of Mental Health



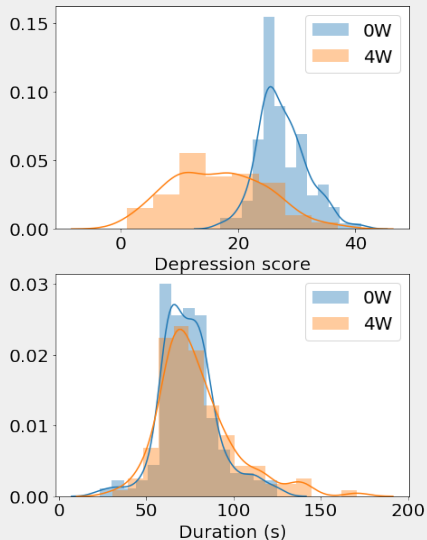
# OUR DATASET

- Czech National Institute of Mental Health
- 133 patients



# OUR DATASET

- Czech National Institute of Mental Health
- 133 patients
- EEG recordings
  - ▶ 250 Hz or 1000 Hz
  - ▶ Various duration
  - ▶ 19 channels



# OUR DATASET

- Czech National Institute of Mental Health

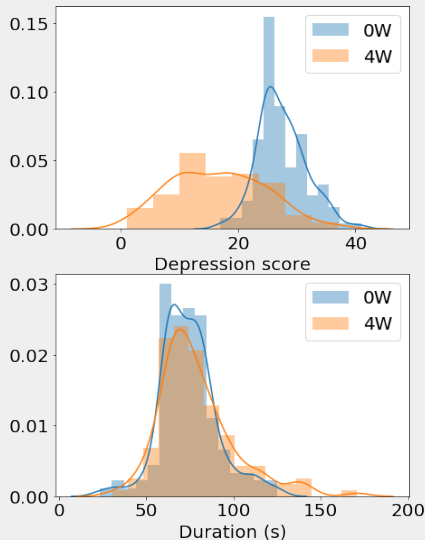
- 133 patients

- EEG recordings

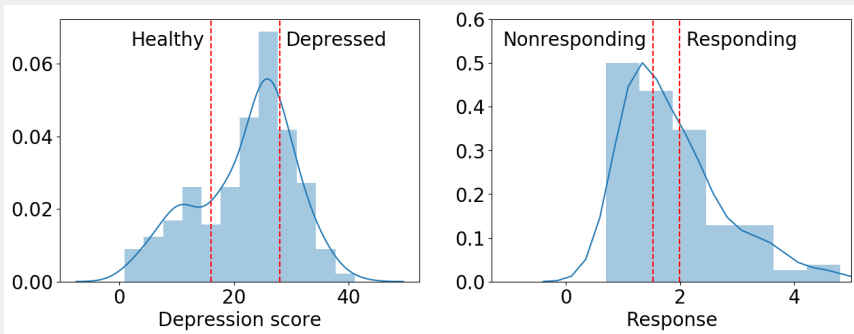
- ▶ 250 Hz or 1000 Hz
- ▶ Various duration
- ▶ 19 channels

- Metadata

- ▶ Depression scores
  - Week 0
  - Week 4
- ▶ Age, gender, drugs

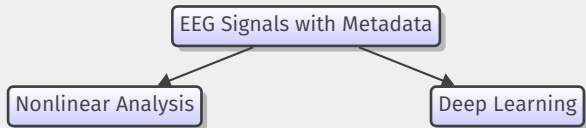


# LABELS

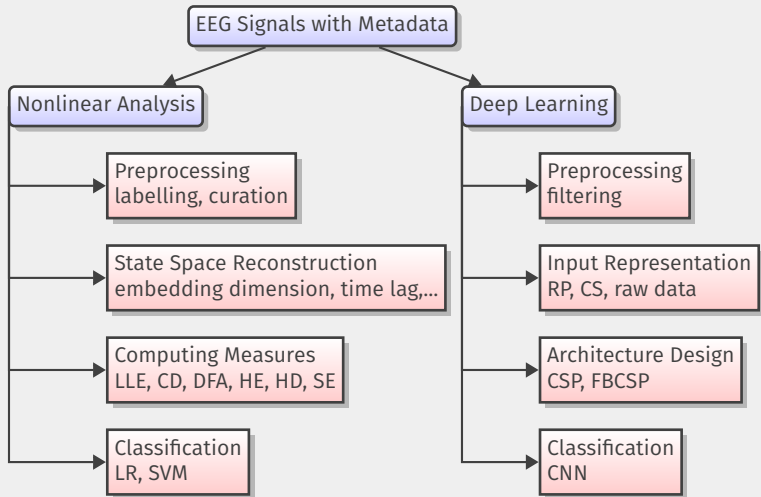


$$\text{Response} = \frac{\text{Depression score}_{\text{Week 4}}}{\text{Depression score}_{\text{Week 0}}}$$

# OUR APPROACH



# OUR APPROACH



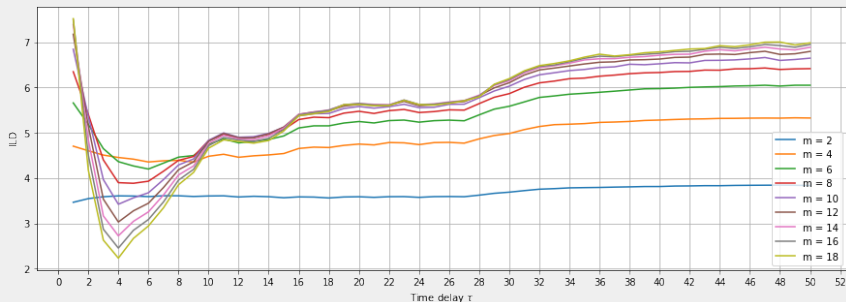
# **NONLINEAR ANALYSIS APPROACH**



# NONLINEAR MEASURES

<b>LLE</b>	Largest Lyapunov exponent	}	“stability”
<b>SE</b>	Sample entropy		
<b>CD</b>	Correlation dimension	}	“complexity”
<b>HD</b>	Higuchi fractal dimension		
<b>DFA</b>	Detrended fluctuation analysis	}	LRTC
<b>HE</b>	Hurst exponent		

# ESTIMATION OF EMBEDDING PARAMETERS



## Parameters

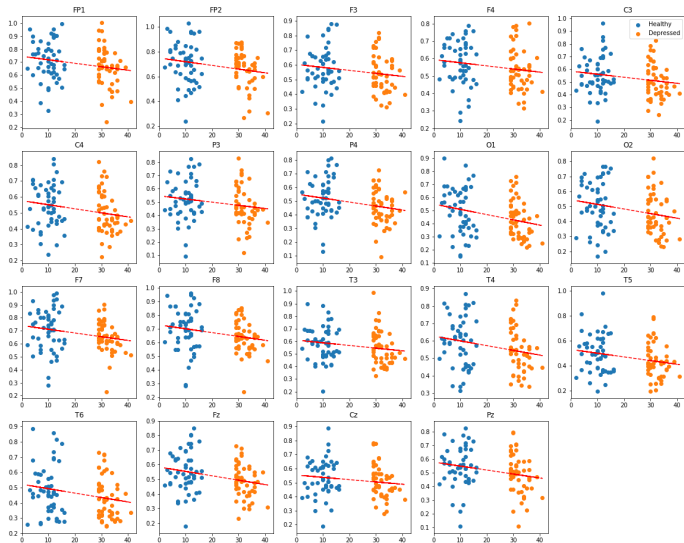
- Embedding dimension
- Time delay
- Scaling regions
- ...

## Methods

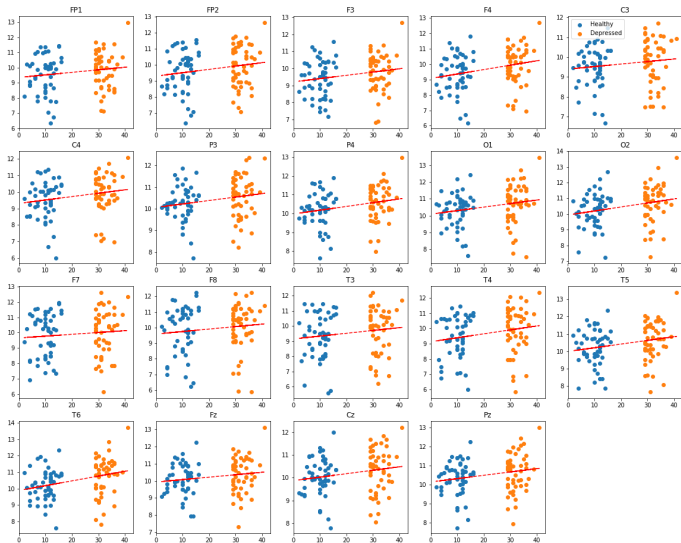
- Literature review
- Estimation algorithms (FNN, AFN, ADFD, ILD, ...)
- Result analysis

-> automated procedure

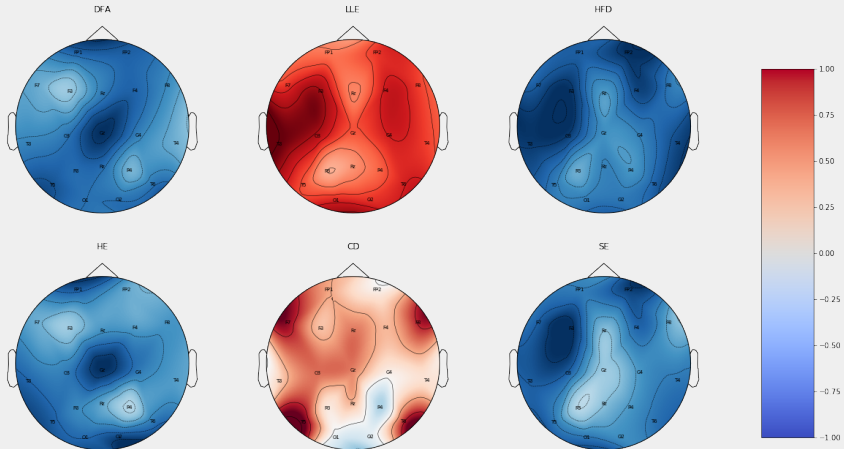
# CORRELATION OF DFA WITH DS



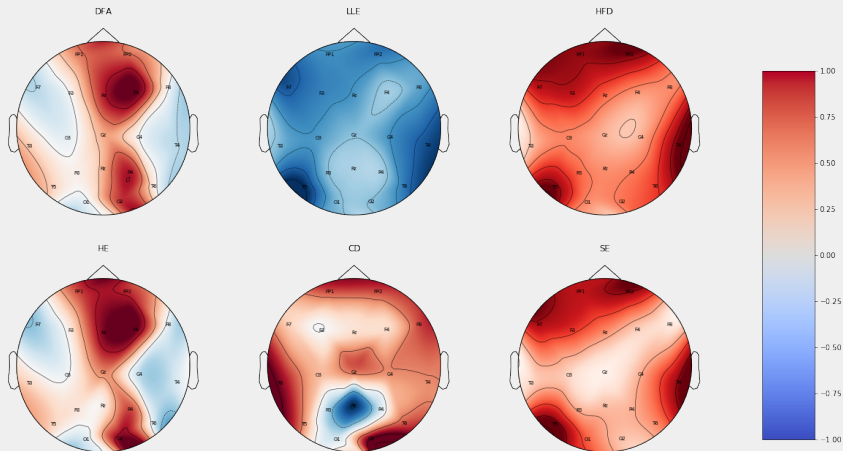
# CORRELATION OF LLE WITH DS



# CORRELATIONS WITH DS



# CORRELATIONS WITH RESPONSE



# RESULTS

Measure	Classifier	Accuracy	
		Mean	Std
<b>LLE, CD</b>	SVM (lin.)	<b>0.74</b>	0.04
<b>LLE, SE</b>	SVM (lin.)	<b>0.75</b>	0.10
LLE, HE	SVM (lin.)	0.73	0.06
LLE, SE, DFA	SVM (lin.)	0.73	0.09
CD, HD	LR	0.73	0.10
<b>LLE</b>	SVM (lin.)	<b>0.72</b>	0.04
<b>CD</b>	SVM (lin.)	<b>0.71</b>	0.05
SE	LR	0.68	0.12
HD	SVM (rbf)	0.67	0.11
DFA	LR	0.67	0.16
HE	LR	0.67	0.17

**(a)** Current DS

Measure	Classifier	Accuracy	
		Mean	Std
<b>LLE, CD</b>	SVM (lin.)	<b>0.75</b>	0.11
<b>LLE, SE</b>	SVM (lin.)	<b>0.75</b>	0.10
<b>LLE</b>	LR	<b>0.71</b>	0.08
<b>CD</b>	LR	<b>0.67</b>	0.09
HD	LR	0.66	0.05
SE	LR	0.66	0.09
DFA	SVM (lin.)	0.64	0.15
HE	SVM (rbf)	0.63	0.09

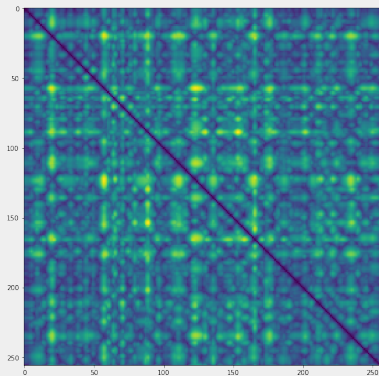
**(b)** Response prediction

- 60 s samples
- 5f-CV on 100 recordings

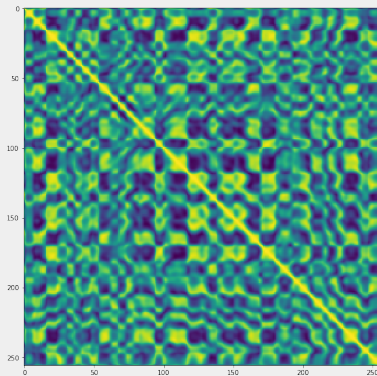
# DEEP LEARNING APPROACH



# INPUT REPRESENTATION



**(a)** Recurrence plot (RP)

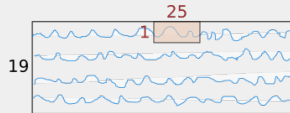


**(b)** Cosine similarity (CS)  
Multivariate GAFs?

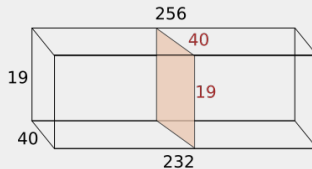
**(c)** Raw data

# ARCHITECTURE DESIGN - SHALLOW

**Temporal covolution**  
(1,25,40)

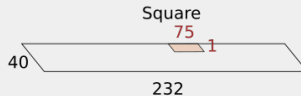


**Spatial filtering**  
(19,1,40)



Batch norm.

**Average pooling**  
(1,75,40)  
stride (1,15)



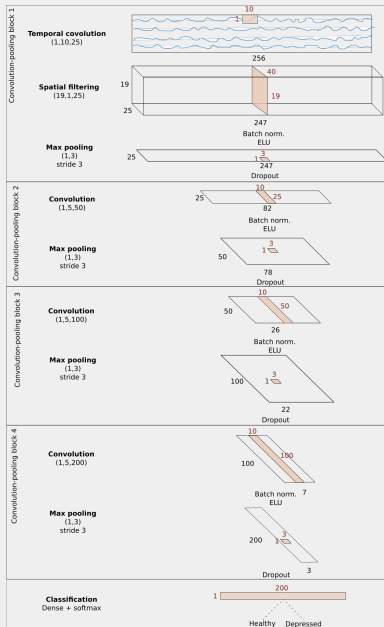
Log

Dropout

**Classification**  
Dense + softmax



# ARCHITECTURE DESIGN - DEEP



# RESULTS

Lab.	Freq.	Arch.	Accuracy	
			Mean	Std
DEP	$0 - f_{\text{fin}}$	SHAL	0.85	0.13
	$4 - f_{\text{fin}}$	SHAL	0.84	0.11
	$0 - f_{\text{fin}}$	DEEP	<b>0.86</b>	0.01
	$4 - f_{\text{fin}}$	DEEP	0.85	0.02
RES	$0 - f_{\text{fin}}$	SHAL	<b>0.94</b>	0.02
	$4 - f_{\text{fin}}$	SHAL	0.94	0.03
	$0 - f_{\text{fin}}$	DEEP	0.88	0.01
	$4 - f_{\text{fin}}$	DEEP	0.86	0.02

(a) Raw data

Lab.	Freq.	Arch.	Accuracy	
			Mean	Std
DEP	$0 - f_{\text{fin}}$	RP	<b>0.63</b>	0.02
	$4 - f_{\text{fin}}$	RP	0.61	0.01
	$0 - f_{\text{fin}}$	CS	0.59	0.02
	$4 - f_{\text{fin}}$	CS	0.58	0.01
RES	$0 - f_{\text{fin}}$	RP	0.61	0.03
	$4 - f_{\text{fin}}$	RP	<b>0.65</b>	0.02
	$0 - f_{\text{fin}}$	CS	0.55	0.02
	$4 - f_{\text{fin}}$	CS	0.63	0.01

(b) Image-encoded data

Dataset	DEP		RES	
	Neg.	Pos.	Neg.	Pos.
Training	3278	3230	2684	2705
Validation	826	802	686	662
Test	<b>1038</b>	<b>997</b>	<b>830</b>	<b>855</b>

1 s samples

# CONCLUSION

1. Largest Lyapunov exponent seem to be predictive of treatment response.

1. Largest Lyapunov exponent seem to be predictive of treatment response.
2. Analysis of correlations between nonlinear measures and
  - 2.1 depression score.
  - 2.2 treatment response.

1. Largest Lyapunov exponent seem to be predictive of treatment response.
2. Analysis of correlations between nonlinear measures and
  - 2.1 depression score.
  - 2.2 treatment response.
3. Analysis of spatial distribution across brain regions in depression.



1. Largest Lyapunov exponent seem to be predictive of treatment response.
2. Analysis of correlations between nonlinear measures and
  - 2.1 depression score.
  - 2.2 treatment response.
3. Analysis of spatial distribution across brain regions in depression.
4. Analysis of nonlinear measure and input parameter estimation algorithms and procedures for EEG analysis.

1. Largest Lyapunov exponent seem to be predictive of treatment response.
2. Analysis of correlations between nonlinear measures and
  - 2.1 depression score.
  - 2.2 treatment response.
3. Analysis of spatial distribution across brain regions in depression.
4. Analysis of nonlinear measure and input parameter estimation algorithms and procedures for EEG analysis.
5. Evaluation of FBCSP-inspired neural network architectures for depression diagnosis and prognosis.

# LIMITATIONS AND FUTURE WORK

## Limitations

- Binary output
- Most patients initially depressed and in remission

### NL approach

- Nonstationarity (windowing?)
- Spatially local
- Temporally global
- Inconclusive surrogate tests
- “Theoretically too ambitious”

### DL approach

- Short samples

## Future Work

- Implement application to aid treatment
- Generalization to other datasets (sample bias)
- Output depression severity measure
- Ensemble of models combining (neuroimaging) modalities
- Incorporate information about treatment details (drugs,...)





### NL approach

- Compare with spatial embedding
- New (spatiotemporal) measures

### DL approach

- Model interpretation
- Compare with FBCSP
- Dimensionality reduction techniques

# REFERENCES I

-  GALKA ANDREAS.  
***TOPICS IN NONLINEAR TIME SERIES ANALYSIS, WITH IMPLICATIONS FOR EEG ANALYSIS, VOLUME 14.***  
World Scientific, 2000.
-  HOLGER KANTZ AND THOMAS SCHREIBER.  
***NONLINEAR TIME SERIES ANALYSIS, VOLUME 7.***  
Cambridge university press, 2004.
-  ROBIN TIBOR SCHIRRMESTER AND JOST TOBIAS SPRINGENBERG.  
***DEEP LEARNING WITH CONVOLUTIONAL NEURAL NETWORKS FOR EEG DECODING AND VISUALIZATION.***  
*Human brain mapping*, 38(11):5391–5420, 2017.
-  KEES STAM.  
***NONLINEAR DYNAMICAL ANALYSIS OF EEG AND MEG: REVIEW OF AN EMERGING FIELD.***  
*Clinical Neurophysiology*, 116(10):2266–2301, 2005.

**THANK YOU FOR ATTENTION**