Deep Neural Networks for Automatic ECG Analysis

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Online presentation @ Systems Control Group, LCSB
University of Luxembourg
March 30, 2022

The electrocardiogram (ECG) exam

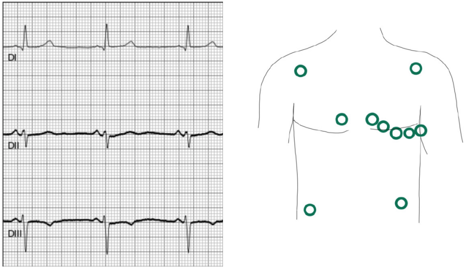
Cardiovascular diseases:

- leading cause of death globally.
- ≈18 million deaths in 2019 (32% of all deaths).
- 3/4 of them in low- and middle-income countries.

The ECG is the major diagnostic tool.

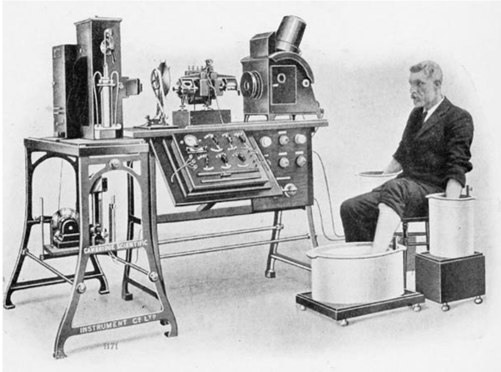
- Cheap, safe and non-invasive
- Can detect: Arrhthmias, Coronary heart diseas, heart attacks, cardiomyopathy...

In this presentation, we focus on the analysis of **resting ECG** (10 seconds / 12 leads)



Left: ECG signal **Right:** Electrode placement.

Computational electrocardiography



Left: An early ECG device built by Willem Einthoven in 1911. **Right:** First automated ECG interpretation system - Glasgow Royal Infirmary 1971.

Presentation outline

Paper I **Automatic diagnosis of the 12-lead ECG using a deep neural network**
Ribeiro, A. H., *Ribeiro, M. H., Paixão, G. M. M., Oliveira, D. M., Gomes, P. R., Canazart, J. A., Ferreira, M. P. S., Andersson, C. R., Macfarlane, P. W., Meira Jr., W., Schön, T. B., Ribeiro, A. L. P.*
Nature Communication, 2020.

Paper II **Deep neural network estimated electrocardiographic-age as a mortality predictor**
*Lima, E. M.**,**Ribeiro, A. H.***, *Paixão, G. M. M.*, Ribeiro, M. H., Filho, M. M. P., Gomes, P. R., Oliveira, D. M., Sabino, E. C., Duncan, B. B., Giatti, L., Barreto, S. M., Meira, W., Schön, T. B., Ribeiro, A. L. P.*
Nature Communications, 2021. **Equal Contribution*

Paper III **Artificial Intelligence-Based ECG Diagnosis of Myocardial Infarction in Emergency Department Patients**
*Gustafsson, S *, Gedon, D.*, Lampa. E.*, **Ribeiro, A.H.**, *Holzmann, M. , Schön T., Sundström J.*
NeurIPS Workshop, 2021
Under review, 2022.

Paper IV **Atrial fibrillation risk prediction from the 12-lead ECG using digital biomarkers and deep representation learning**
Biton, S., Gendelman, S., **Ribeiro, A. H.**, *Miana, G., Moreira, C., Ribeiro, A. L. P., Behar, J. A.*
European Heart Journal - Digital Health., 2021

Paper V **Overparametrized Linear Regression under Adversarial Attacks**
Ribeiro, A.H., *Schön, T.*
Workshop on the Theory of Overparameterized Machine Learning (TOPML), 2021
Under review, 2022.

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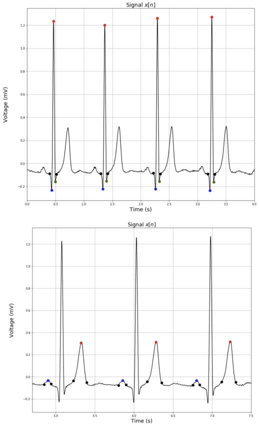
Work in progress

Classical ECG automated analysis



ECG segmented using signal processing.
Top: QRS complex. **Bottom:** T and P waves.

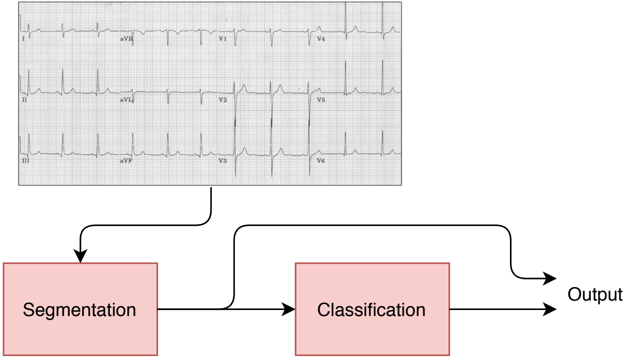
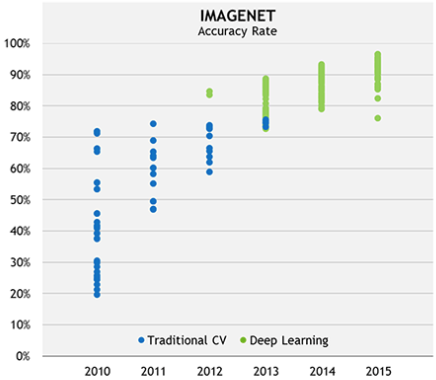


Figure: Two step analysis procedure

P. W. Macfarlane, B. Devine, and E. Clark, "The university of glasgow (Uni-G) ECG analysis program," in Computers in Cardiology, 2005, pp. 451–454. doi: 10.1109/CIC.2005.1588134.

Image classification with deep neural networks

Imagenet



Left: dataset samples. **Right:** Models accuracy on benchmark.

J. Deng, W. Dong, R. Socher, L.-J. Li, K. Li, and L. Fei-Fei, "Imagenet: A large-scale hierarchical image database," in 2009 IEEE conference on computer vision and pattern recognition, 2009, pp. 248–255.

Automatic ECG classification

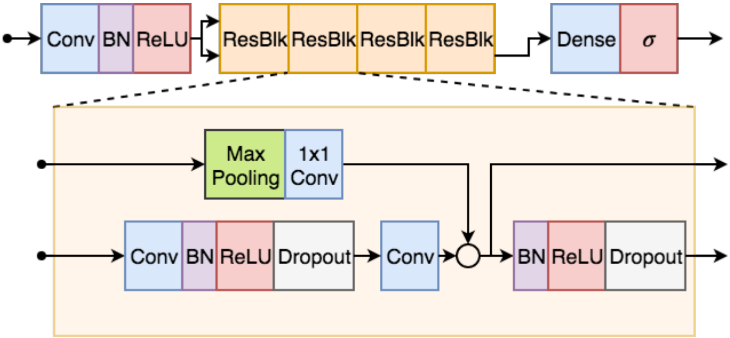


Figure: Uni-dimensional residual neural network architecture used for ECG classification.

[Paper I] A. H. Ribeiro, M. H. Ribeiro, G. M. M. Paixão et al., "Automatic diagnosis of the 12-lead ECG using a deep neural network," Nature Communications, vol. 11, no. 1, p. 1760, 2020, doi: 10.1038/s41467-020-15432-4.

Telehealth Network of Minas Gerais and CODE group

Year	# Municipalities
2006	82
2007	102
2008	97
2009	328
2011	54
2013	106
2015	42
Total	811

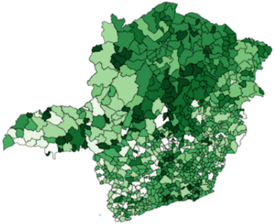


Figure: The CODE (*Clinical outcomes in eletrocardiography*) group was created to conduct clinical studies using storical data from the telehealth network.

M. B. Alkmim et al., "Improving patient access to specialized health care: the Telehealth Network of Minas Gerais, Brazil," Bulletin of the World Health Organization, vol. 90, no. 5, pp. 373–378, May 2012, doi: 10/f3x7px.

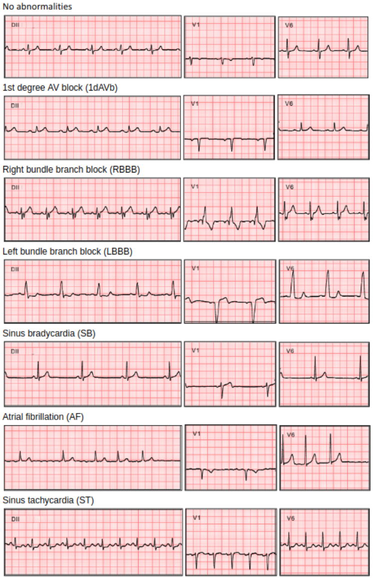
The CODE dataset

Training dataset:

- 2.3 million exams, 1.6 million patients;
- Annotated by telehealth center cardiologist;
- Refined by comparing with University of Glasgow software results. 30 000 exams manually reviewed.

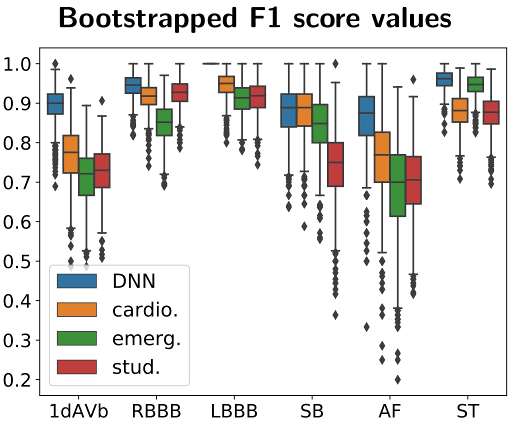
Test dataset:

- 827 tracings from distinct patients;
- Annotated by 3 different cardiologists.



Results

	F1 Score			
	DNN	cardio.	emerg.	stud.
1dAVb	**0.897**	0.776	0.719	0.732
RBBB	**0.944**	0.917	0.852	0.928
LBBB	**1.000**	0.947	0.912	0.915
SB	**0.882**	**0.882**	0.848	0.750
AF	**0.870**	0.769	0.696	0.706
ST	**0.960**	0.882	0.946	0.873



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Work in progress

Predicted age from the ECG

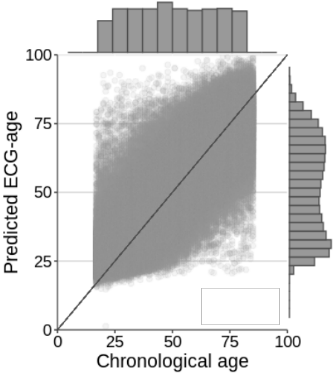
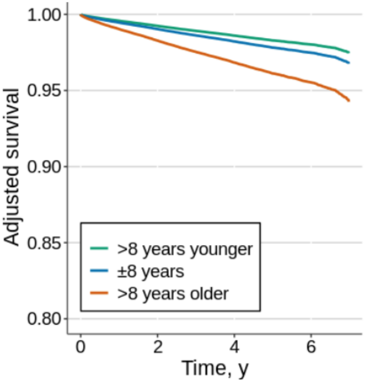


Figure: Predicted vs estimated age in 15% hold-out test set (n = 218,169 patients). Mean absolute error of 8.38 years.

Δ age = ECG-age - age

Predicted age from the ECG as a mortality predictor

	All ECGs	Only Normal ECGs
Adjusted by age and sex		
Δ age $<$ - 8 y	0.78	0.66
Δ age $>$ 8 y	1.79	1.53
Adjusted by age, sex and comorbities		
Δ age $<$ - 8 y	0.78	0.66
Δ age $>$ 8 y	1.78	1.52



Left: Hazard ratio from Cox model. **Right:** Survival curves (adjusted by sex and age)
Aditional external validation: Elsa-Brazil (n=14263 patients) Sami-Trop (n=1631).

[Paper II] E. M. Lima, A. H. Ribeiro, G. M. M. Paixão et al., "Deep neural network estimated electrocardiographic-age as a mortality predictor," Nature Communications, vol. 12, 2021, doi: 10.1038/s41467-021-25351-7.

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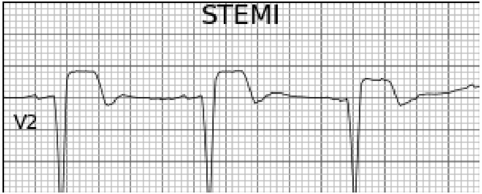
Myocardial Infarction

Myocardial Infarctions:

- 9M deaths/year, 200M disability-adjusted life years/year
- False negatives: 10-50,000 missed cases/year at EDs in the US
- False positives: Less than half of those hospitalized for a suspected MI are diagnosed.

Diagnosis:

- ST-elevation MI (STEMI) $\rightarrow$ ECG.
- non-STEMI $\rightarrow$ blood testing



Diagnosing myocardial infarction in emergency department patients

Dataset: (Stockholm region between 2007 and 2016)

- 492,226 ECGs from the emergency department
- 5,416 NSTEMI (1.1%)
- 1,818 STEMI (0.4%)
- MI annotated using blood testing.

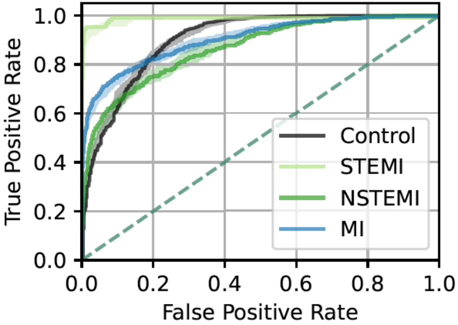


Figure: Our method for screaning MI from the ECG using DNN.

[Paper III] S. Gustafsson, D. Gedon et al., "Artificial Intelligence-Based ECG Diagnosis of Myocardial Infarction in Emergency Department Patients," Under review, 2022.

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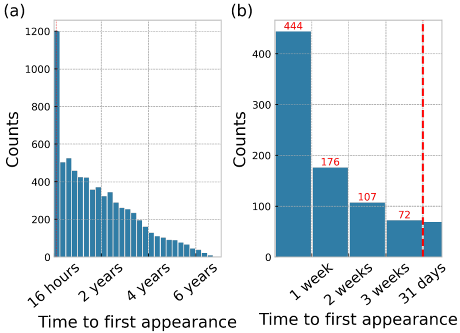
Atrial Fibrilation (AF) in CODE dataset

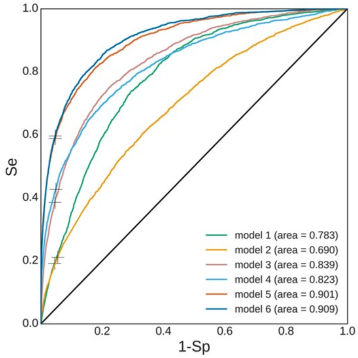
- CODE dataset: $\sim$ 400 thousand patients underwent multiple exams;
- $\sim$ 7 thousand have an exam baseline exam without AF followed by an exam with AF.



Left: Time to the follow up exam (all patients). **RIght:** Patients who were diagnosed for AF within 31 days of the baseline examination.

[Paper IV] S. Biton et al., "Atrial fibrillation risk prediction from the 12-lead ECG using digital biomarkers and deep representation learning," European Heart Journal - Digital Health, 2021, doi: 10.1093/ehjdh/ztab071.

Atrial Fibrilation risk prediction



model 1 Patient Information,

model 2 Heart rate variability;

model 3 ECG Morphology;

model 4 Deep Neural Networks features; and,

model 5/6 Combinations of these.

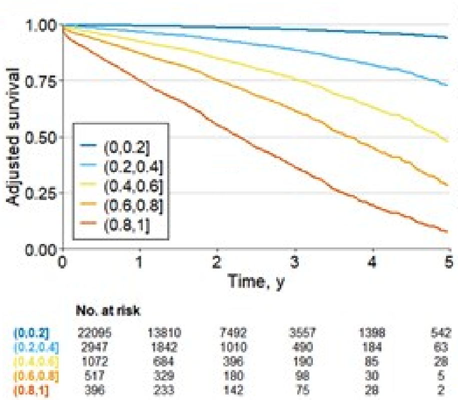


Figure: Adjusted (by age and sex) survival curves. Grouped acording to the output probability.

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Neural networks in critical applications

- Neural networks can be vulnerable:

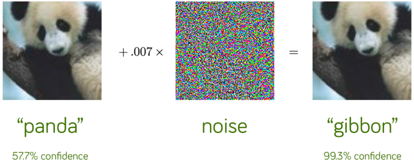


Figure: Effect of adversarial training on image classification.

Source: I. J. Goodfellow, J. Shlens, C. Szegedy , *"Explaining and Harnessing Adversarial Examples"*, ICLR 2015

- Neural networks in ECG applications display the same behavior:

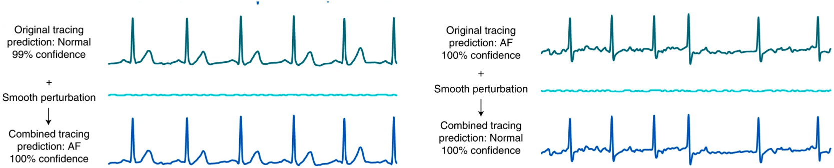


Figure: Effect of adversarial training on ECG Classification.

Source: Han, X., Hu, Y., Foschini, L. et al. Deep learning models for electrocardiograms are susceptible to adversarial attack. Nature Medicine 26, 360–363 (2020). https://doi.org/10.1038/s41591-020-0791-x

The role of high-dimensionality

- High-dimensionality as a source of vulnerability:
  - I. J. Goodfellow, J. Shlens, C. Szegedy , *"Explaining and Harnessing Adversarial Examples"*, ICLR 2015
  - J. Gilmer et al., *"Adversarial Spheres,"* arXiv:1801.02774, Sep. 2018.
  - D. Tsipras, S. Santurkar, L. Engstrom, A. Turner, and A. Ma, "Robustness May Be At Odds with Accuracy," ICLR, p. 23, 2019.
- High-dimensionality as a source of robustness:
  - S. Bubeck and M. Sellke, "A Universal Law of Robustness via Isoperimetry," Advances in Neural Information Processing Systems, 2021

Double-descent

- The idea was proposed by (Belkin et al., 2019)

  M. Belkin, D. Hsu, S. Ma, and S. Mandal (2019), "Reconciling modern machine-learning practice and the classical bias–variance trade-off," Proc Natl Acad Sci USA, vol. 116, no. 32, pp. 15849–15854, doi: 10.1073/pnas.1903070116.

- Reproducible in a large number of scenarios:

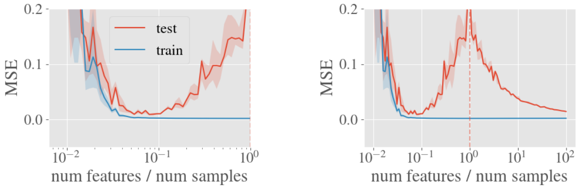


Figure: Nonlinear ARX performance in Couple Eletric Drives benchmark. **Left:** Underparametrized models. **Right:** Overparametrized models using minimum-norm solution.

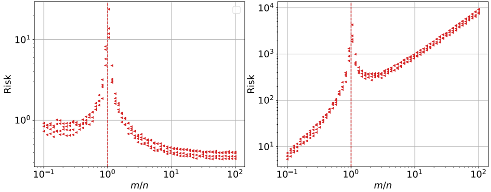
Antônio H. Ribeiro, Johannes N. Hendriks, Adrian G. Wills, Thomas B. Schön. "Beyond Occam's Razor in System Identification: Double-Descent when Modeling Dynamics". Proceedings of the 19th IFAC Symposium on System Identification (SYSID), 2021. *Honorable mention: Young author award*

- Can be observed in purely linear models:

  T. Hastie, A. Montanari, S. Rosset, and R. J. Tibshirani, "Surprises in High-Dimensional Ridgeless Least Squares Interpolation," arXiv:1903.08560, Nov. 2019.

Overparametrized linear models under adversarial attacks

Understand and conciliate the two types of behavior in linear models.



(a) Adversarial ℓ_2 risk (b) Adversarial ℓ_∞ risk

[Paper V] A. H. Ribeiro and T. B. Schön, "Overparametrized Linear Regression under Adversarial Attacks," Under reviews. 2022.

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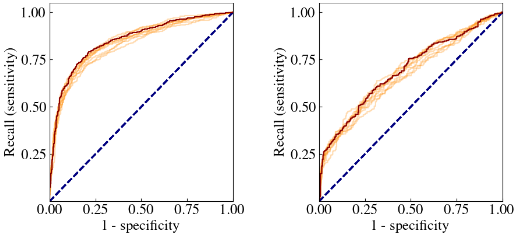
Work in progress

- CODEv2 dataset.
  - $n = 1\,184\,656$ patients
  - Annotated for 60 classes
  - June 2018 - December of 2020
  - Potential to improve tele-health service in short/medium term;
- Screaning for Chagas Diasease;
  - SamiTrop, CODE, REDS
  - Self-reported noisy labels in CODE
- Predicting Electrolyte values;
  - Use Gaussian/Laplace approximations
  - Uncertainty prediction



Left: Performance on SamiTrop. **Right:** on REDs.

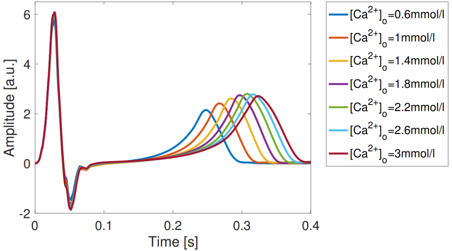


Figure: Predicted influence of Calcium on the ECG.

Figure from N. Pilia et al. "ECG as a tool to estimate potassium and calcium concentrations in the extracellular space," CinC, 2017