

CHALLENGES in SMART PATIENT MONITORING: from Raw Data to Decision Support



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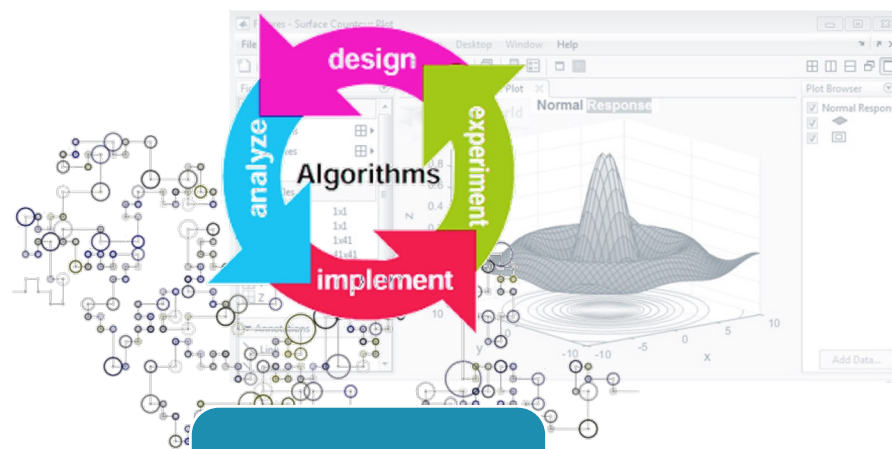
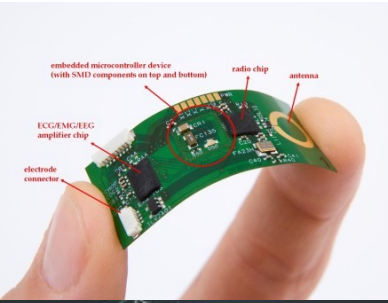
Contents Overview

1. Introduction

- Smart Patient Monitoring
- Research Overview
- Blind Source Separation
- Tensor Decompositions
- AI: From Machine Learning to Deep Learning

2. Examples

3. Future Challenges



Brain monitoring for neurological diseases

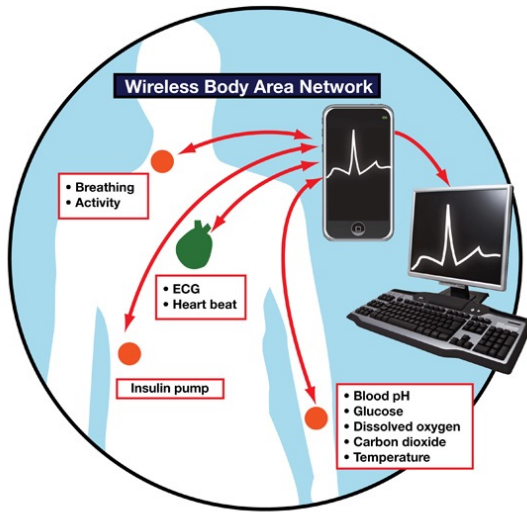


Sensors
(Carriers)

Algorithms
(Technology)

Pathologies
(Applications)

Smart
Patient
Monitoring



Vital signs monitoring:
sleep, stress, cardio risk
stratification



Oncology: cancer
diagnosis and prognosis



Chronic disease management
& telemonitoring application

Hospital of the FUTURE

Move healthcare away from hospitals to HOME environment

- UNOBTRUSIVE
- MULTIMODAL
- LONG-TERM

Challenges:

- ARTEFACTS
- BIG DATA
- AUTOMATED



Imagine a surgeon is perched in front of a telecommunications console in New York City while his patient lies on an operating table 3,870 miles away at a hospital in Strasbourg, France. From the console, the physician remotely guides the movement of a three-armed surgical robot named Zeus to remove the 68-year-old patient's diseased gallbladder. The operation takes less than an hour, and the patient recovers as expected, returning home two days later.

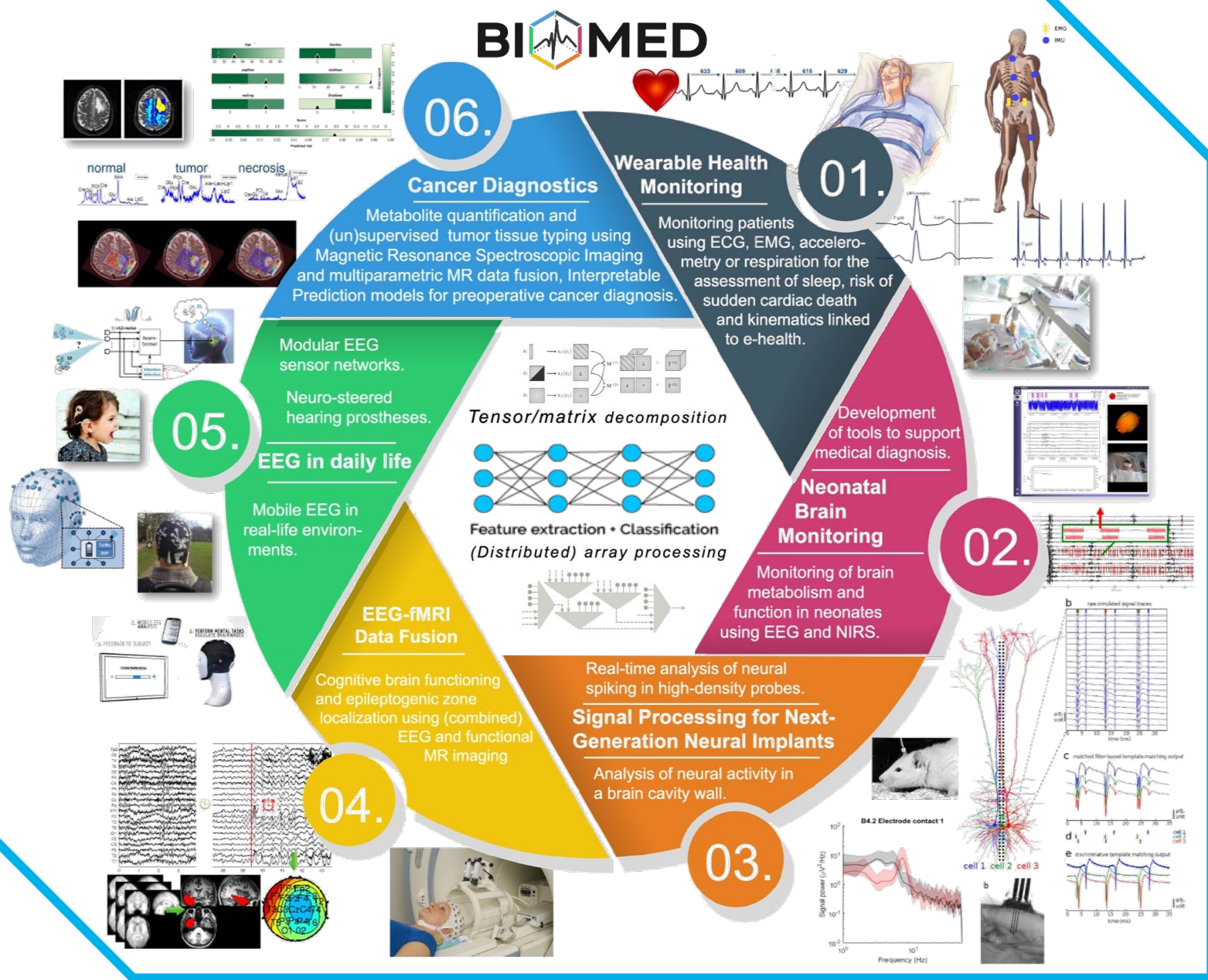
Sounds like something out of science fiction, doesn't it? It's not.

The transatlantic procedure actually happened in 2001. Known as Operation Lindberoh, named after American aviator Charles Lindberoh, the breakthrough event

The Guardian, 6.11.2016



Research in close collaboration with



06. Cancer Diagnostics
Metabolite quantification and (un)supervised tumor tissue typing using Magnetic Resonance Spectroscopic Imaging and multiparametric MR data fusion, Interpretable Prediction models for preoperative cancer diagnosis.

05. EEG in daily life
Modular EEG sensor networks.
Neuro-steered hearing prostheses.
Mobile EEG in real-life environments.

04. EEG-fMRI Data Fusion
Cognitive brain functioning and epileptogenic zone localization using (combined) EEG and functional MR imaging

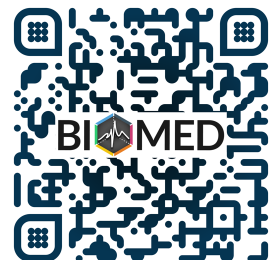
03. Signal Processing for Next-Generation Neural Implants
Real-time analysis of neural spiking in high-density probes.
Analysis of neural activity in a brain cavity wall.

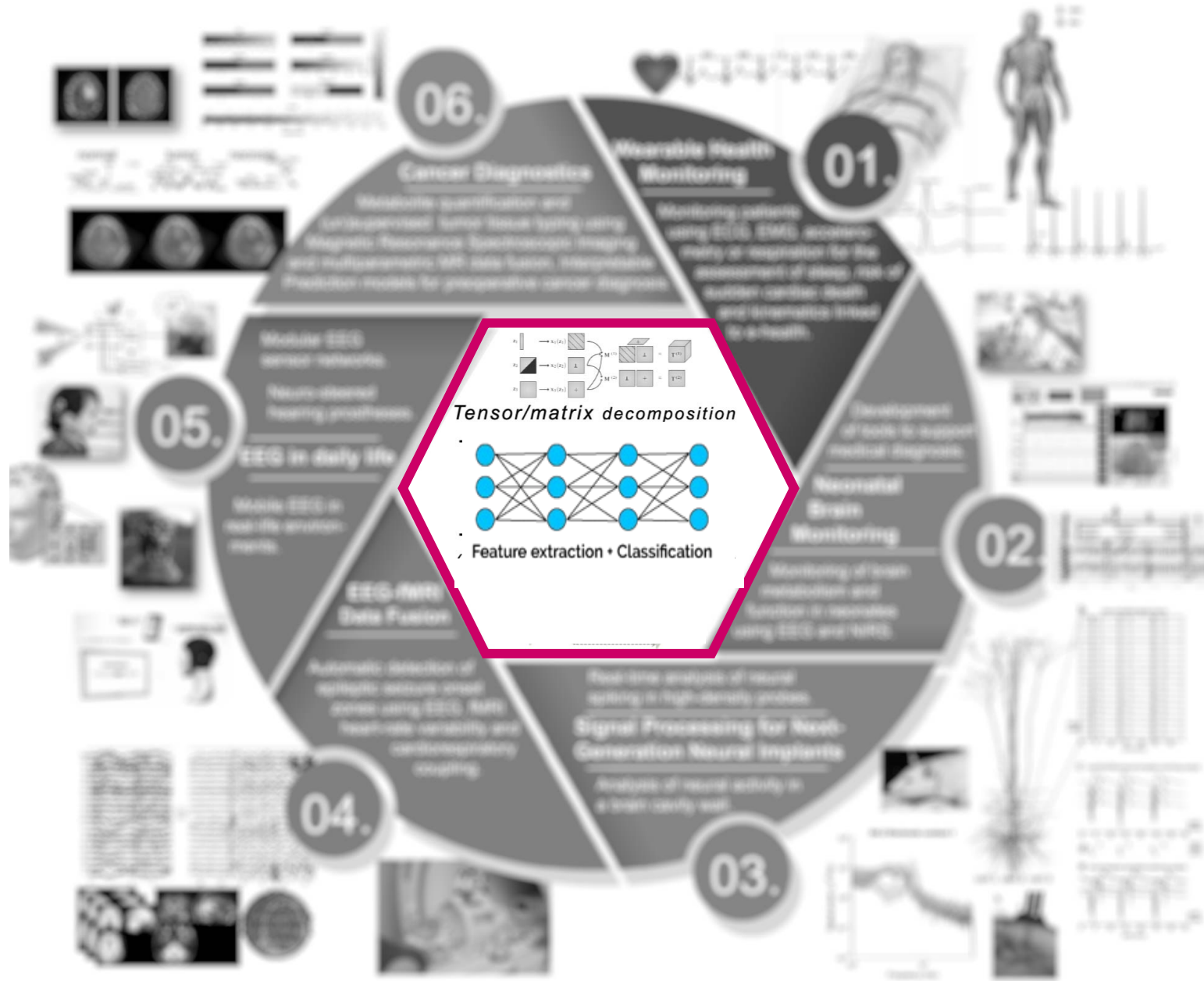
02. Neonatal Brain Monitoring
Monitoring of brain metabolism and function in neonates using EEG and NIRS.

01. Wearable Health Monitoring
Monitoring patients using ECG, EMG, accelerometry or respiration for the assessment of sleep, risk of sudden cardiac death and kinematics linked to e-health.

Tensor/matrix decomposition

Feature extraction • Classification (Distributed) array processing





KEYTOOL : Blind source separation

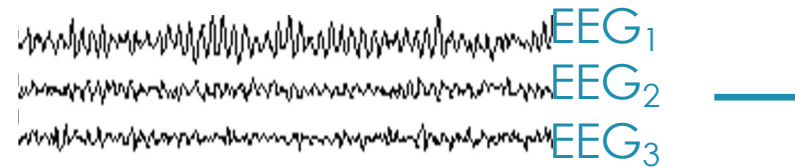
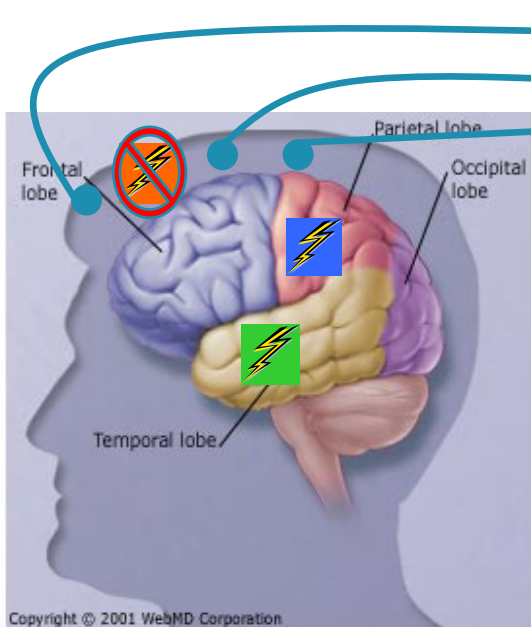
Signal analysis difficult because of artefacts → REMOVE

Matrix based Blind Source Separation (BSS)

- **Non-unique** → Constraints are needed (orthogonal, independency)

TENSOR based BSS: unique under mild conditions

ADD extra problem-specific constraints (nonnegative, sparse)



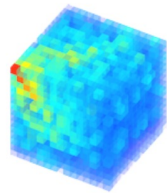
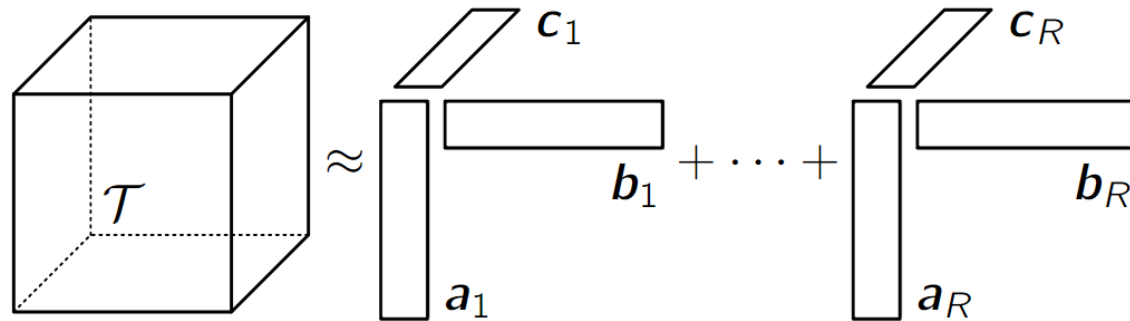
$$\begin{aligned} \text{EEG}_1 &= a_{11}\mathbf{s}_1 + a_{12}\mathbf{s}_2 + a_{13}\mathbf{s}_3 \\ \text{EEG}_2 &= a_{21}\mathbf{s}_1 + a_{22}\mathbf{s}_2 + a_{23}\mathbf{s}_3 \\ \text{EEG}_3 &= a_{31}\mathbf{s}_1 + a_{32}\mathbf{s}_2 + a_{33}\mathbf{s}_3 \end{aligned}$$

The coefficient a_{13} in the first equation is circled in red with a slash, indicating it is to be removed.

$$\begin{matrix} C \\ P \\ D \end{matrix} \begin{matrix} \text{ } \\ \text{ } \\ \text{ } \end{matrix} \begin{matrix} \text{ } \\ \text{ } \\ \text{ } \end{matrix} \begin{matrix} \mathcal{X} \\ \text{ } \\ \text{ } \end{matrix} = \begin{matrix} C_1 \\ \text{ } \\ \text{ } \end{matrix} \begin{matrix} \text{ } \\ \text{ } \\ \text{ } \end{matrix} \begin{matrix} B_1 \\ \text{ } \\ \text{ } \end{matrix} + \dots + \begin{matrix} C_R \\ \text{ } \\ \text{ } \end{matrix} \begin{matrix} \text{ } \\ \text{ } \\ \text{ } \end{matrix} \begin{matrix} B_R \\ \text{ } \\ \text{ } \end{matrix} + \begin{matrix} \text{ } \\ \text{ } \\ \text{ } \end{matrix} \begin{matrix} \text{ } \\ \text{ } \\ \text{ } \end{matrix} \begin{matrix} \text{ } \\ \text{ } \\ \text{ } \end{matrix} \begin{matrix} \mathcal{E} \\ \text{ } \\ \text{ } \end{matrix}$$

$$\text{EEG} = \begin{matrix} A \\ ? \end{matrix} \begin{matrix} S^T \\ ? \end{matrix}$$

Canonical Polyadic Decomposition - CPD

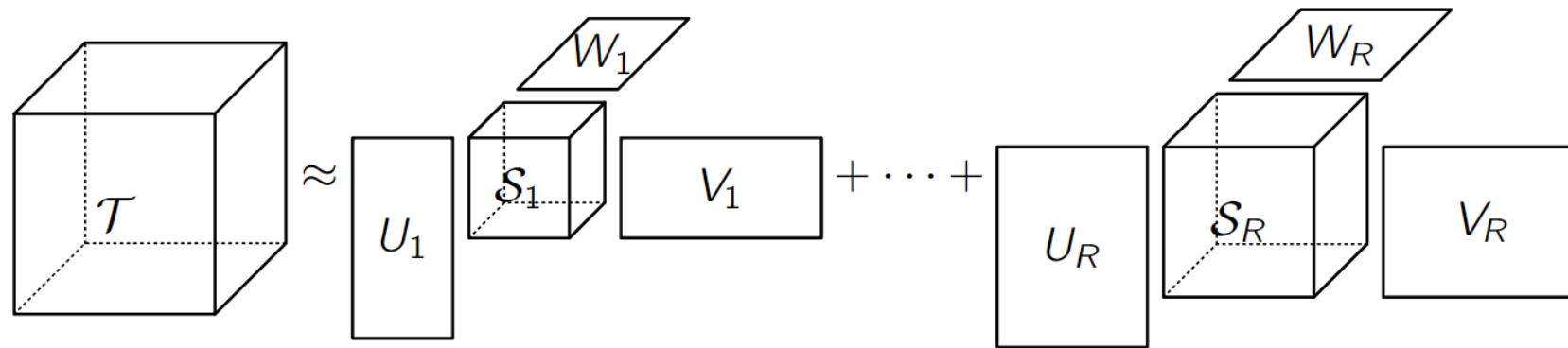


Tensorlab

A MATLAB package for
tensor computations.

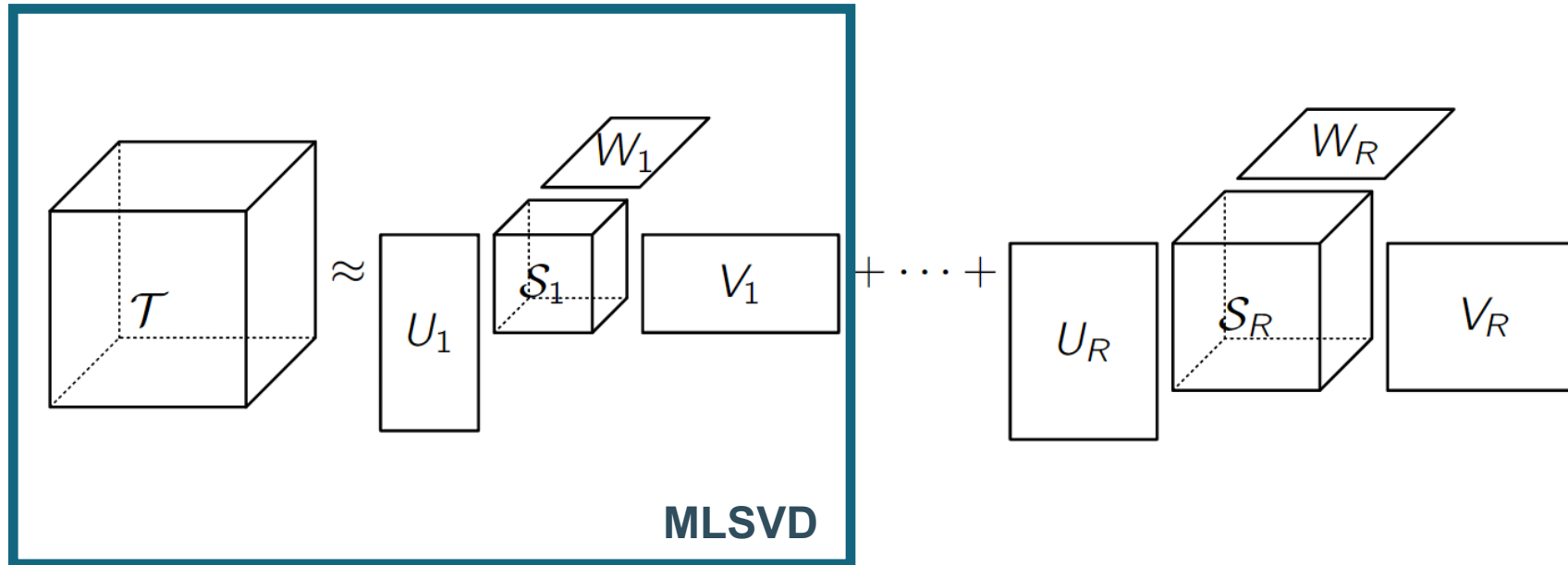
www.tensorlab.net

From CPD to Block Tensor Decomposition



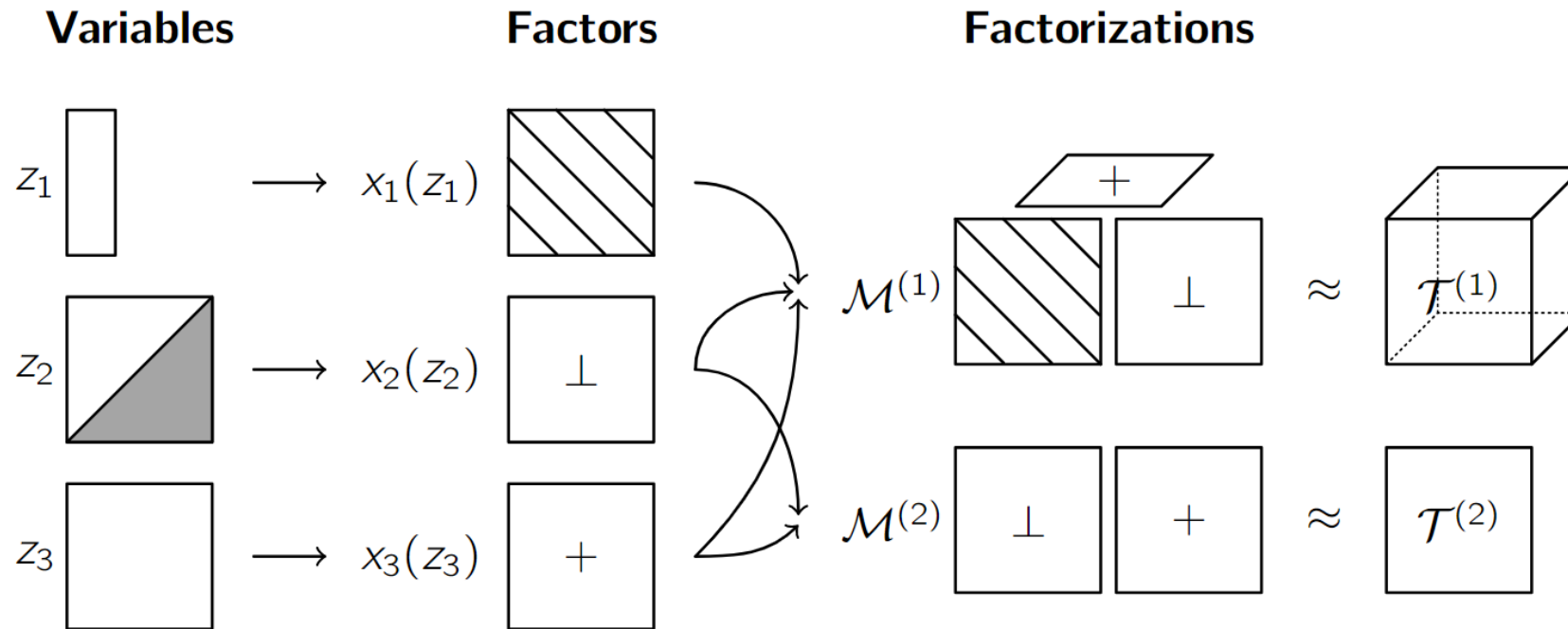
De Lathauwer et al., SIMAX, 2008; Sorber et al., SIOPT, 2013

From CPD to MLSVD and Block Tensor Decomposition



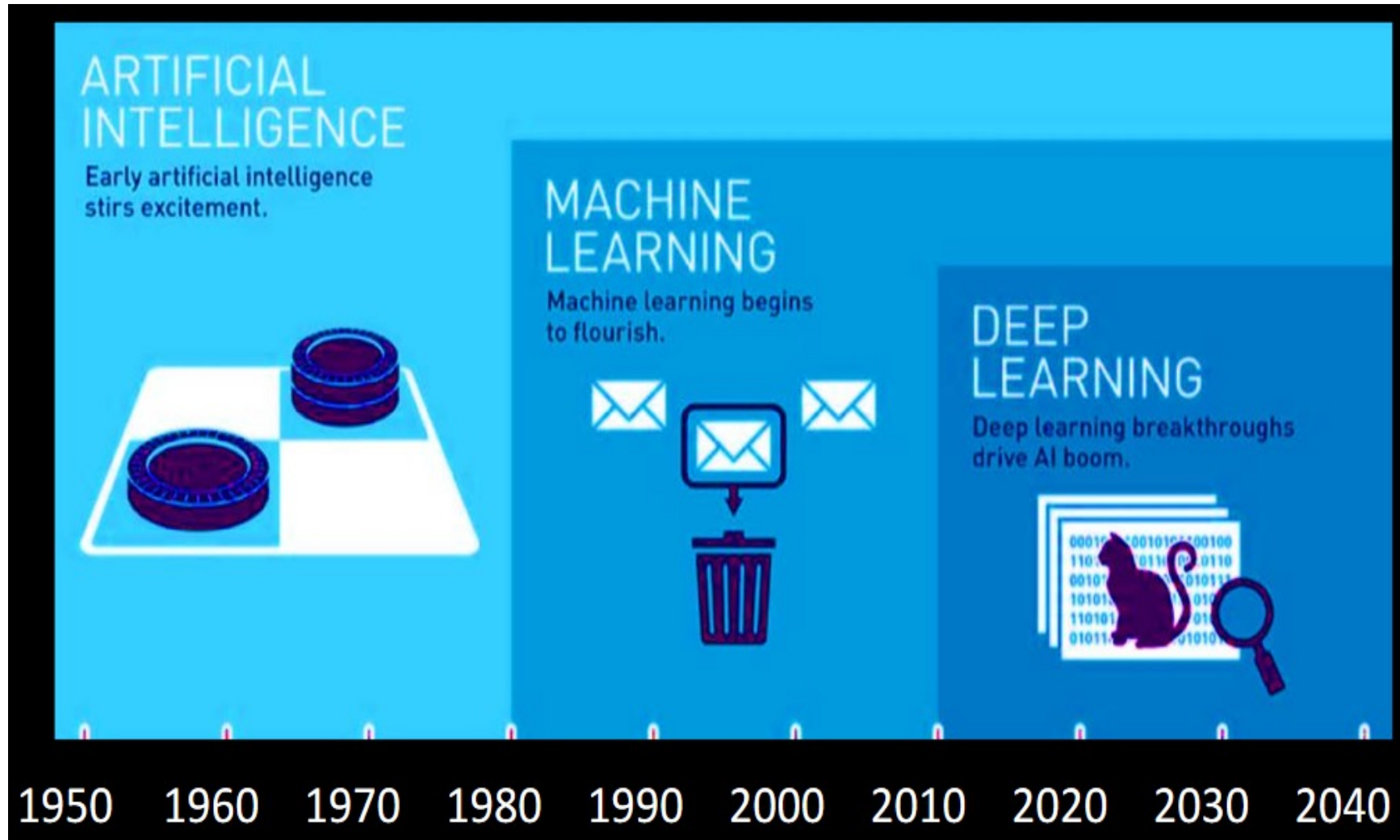
De Lathauwer et al., SIMAX, 2008; Sorber et al., SIOPT, 2013

Structured Data Fusion



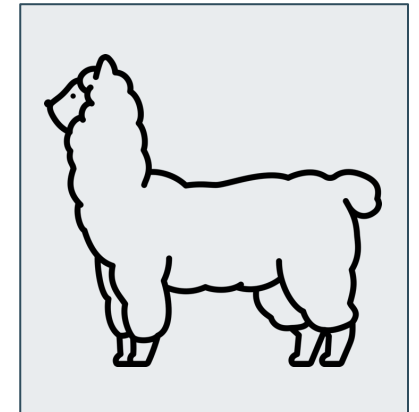
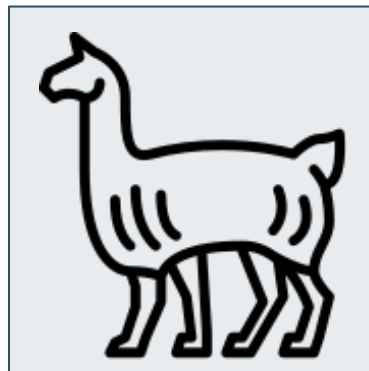
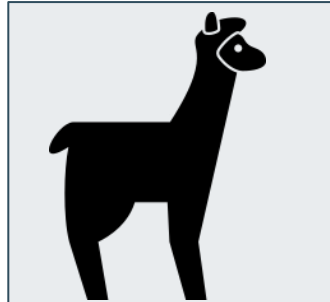
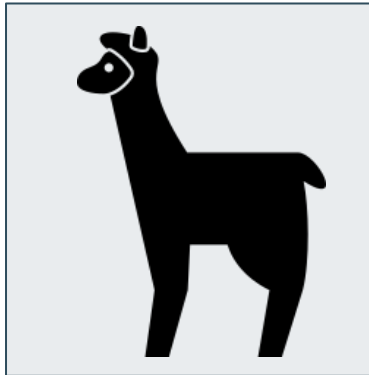
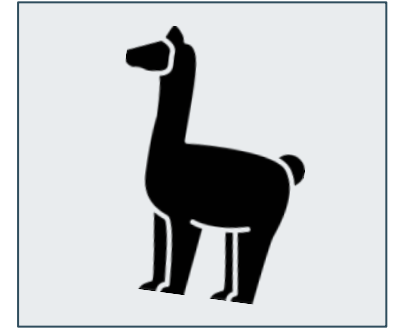
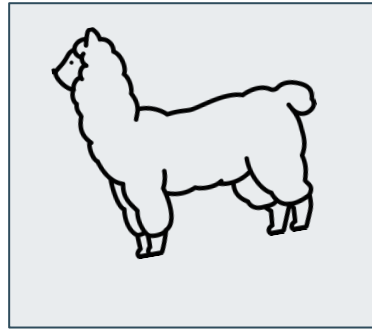
$$\underset{z}{\text{minimize}} \quad \sum_{d=1}^D \frac{\omega_d}{2} \left\| \mathcal{M}^{(d)}(\mathcal{X}(z)) - \mathcal{T}^{(d)} \right\|_{\mathcal{W}^{(d)}}^2,$$

Evolution of AI: from machine learning to deep learning

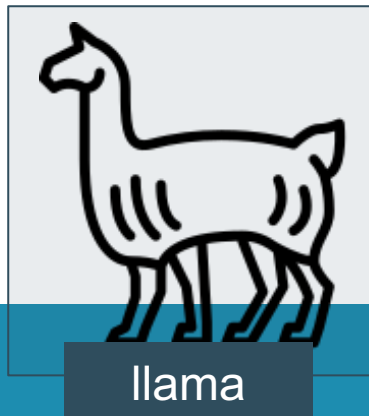
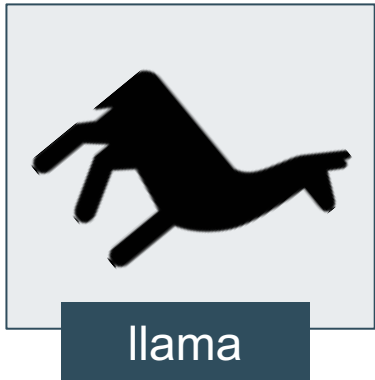
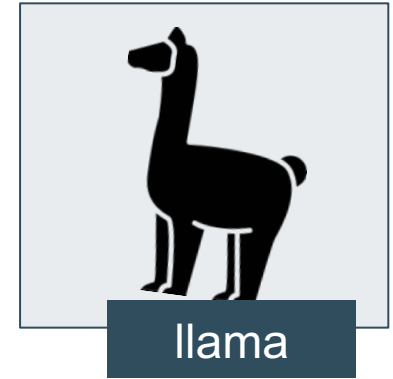
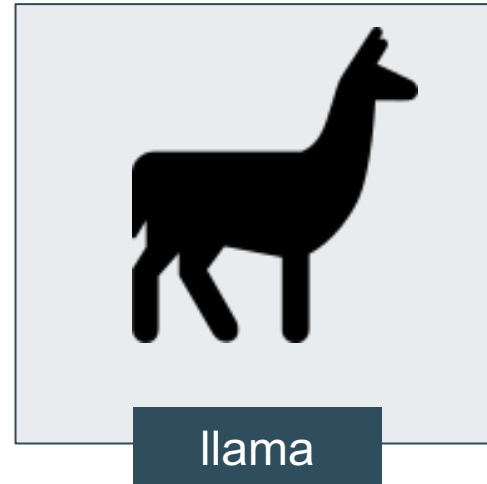
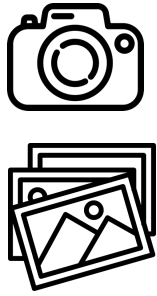


<https://blogs.nvidia.com/blog/2016/07/29/whats-difference-artificial-intelligence-machine-learning-deep-learning-ai/>

Introduction to Machine Learning



Machine Learning



- 1.
- 2.
- 3.

alpaca



llama



Feature	Angle Ears [degrees]	Relative Shoulder Height [%]	Relative Tail Length [%]
Average Value			
Average Value			

alpaca



llama



Feature	Angle Ears [degrees]	Relative Shoulder Height [%]	Relative Tail Length [%]
Average Value	90		
Average Value	45		

alpaca



llama



Feature	Angle Ears [degrees]	Relative Shoulder Height [%]	Relative Tail Length [%]
Average Value	90	80	10
Average Value	45	73	35

alpaca

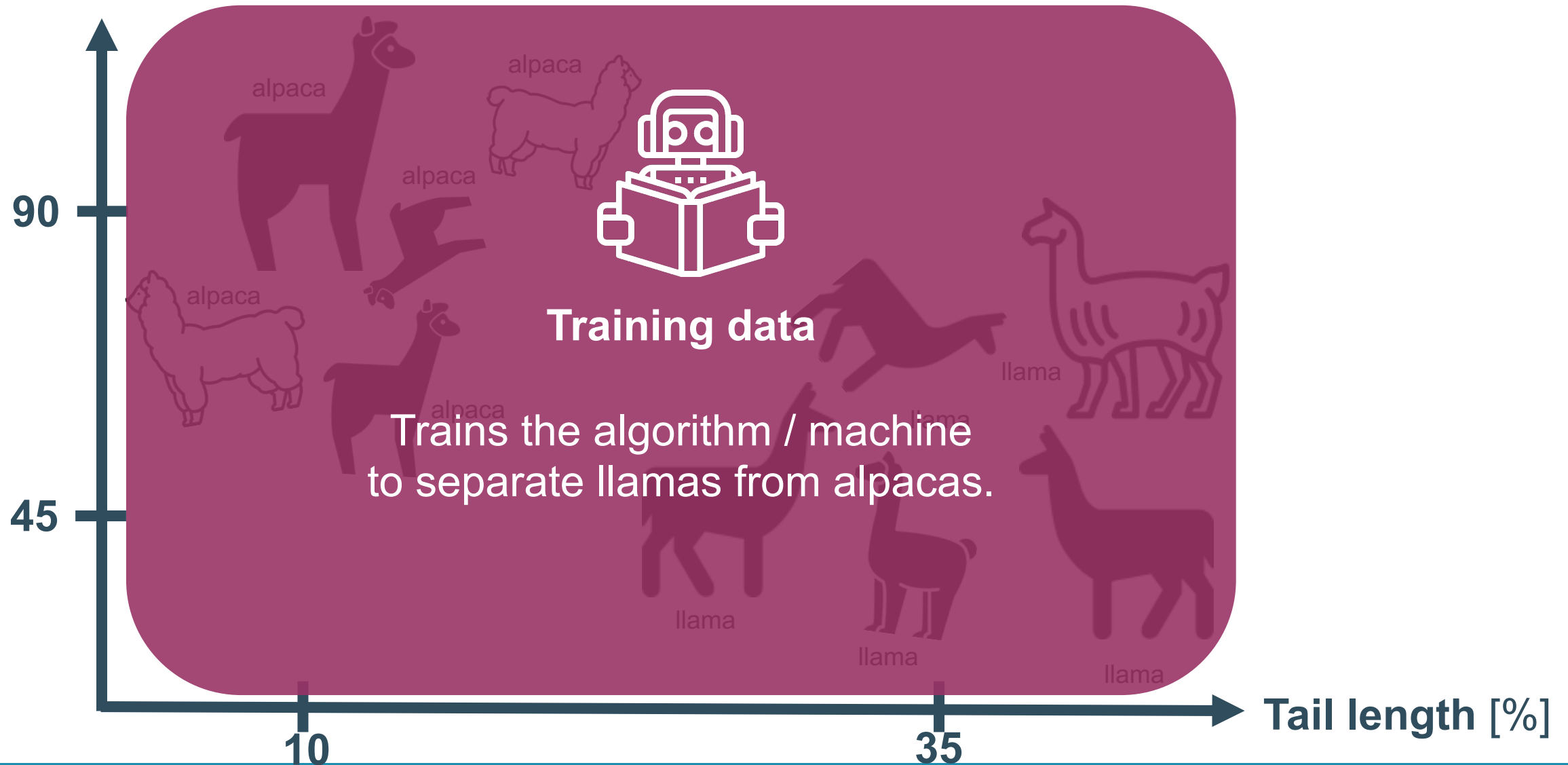


llama

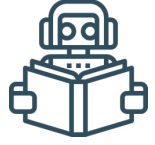


Feature	Angle Ears [degrees]	Relative Shoulder Height [%]	Relative Tail Length [%]
Average Value	90	80	10
Average Value	45	73	35

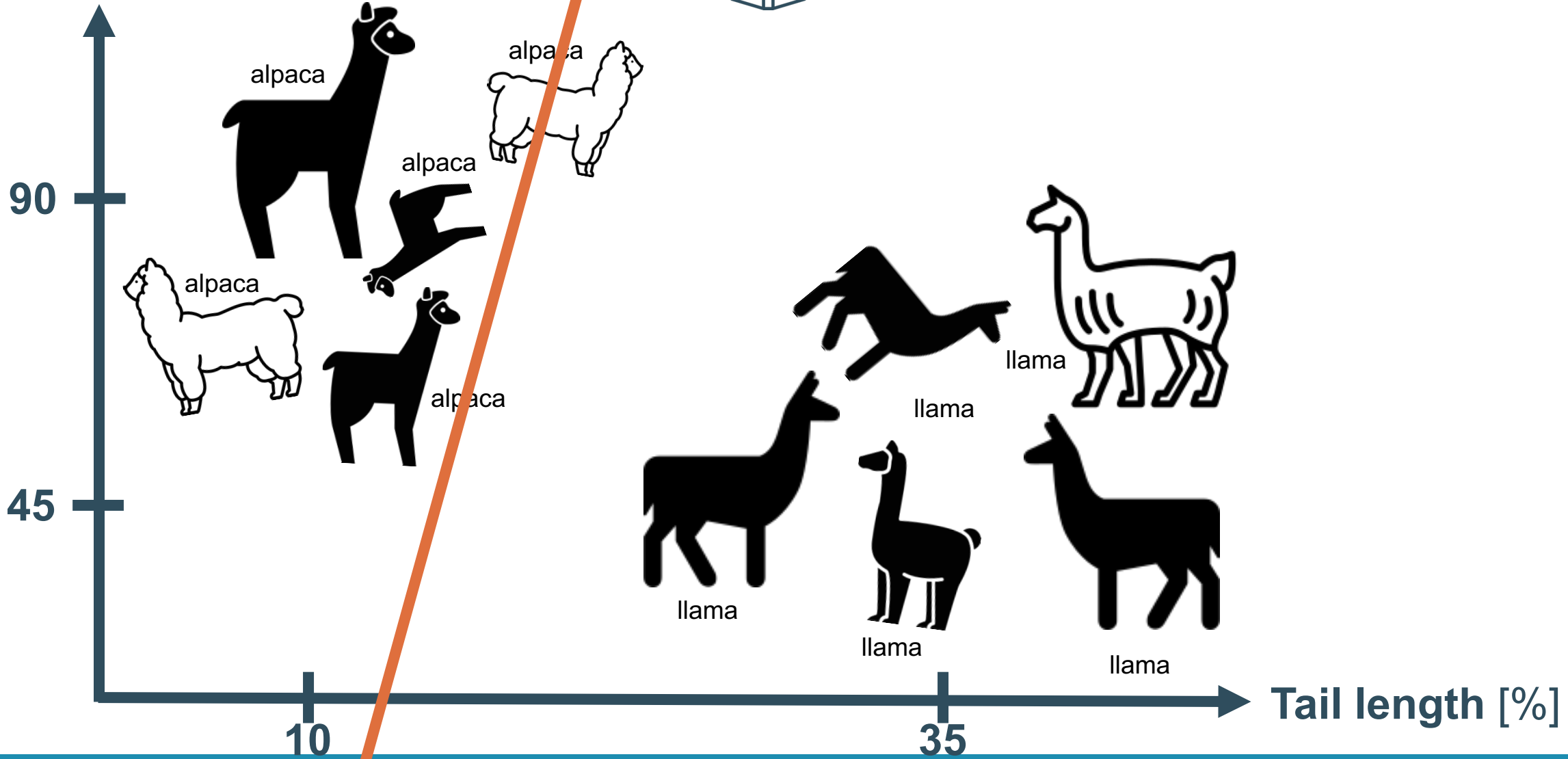
Angle Ears [°]



Learning process

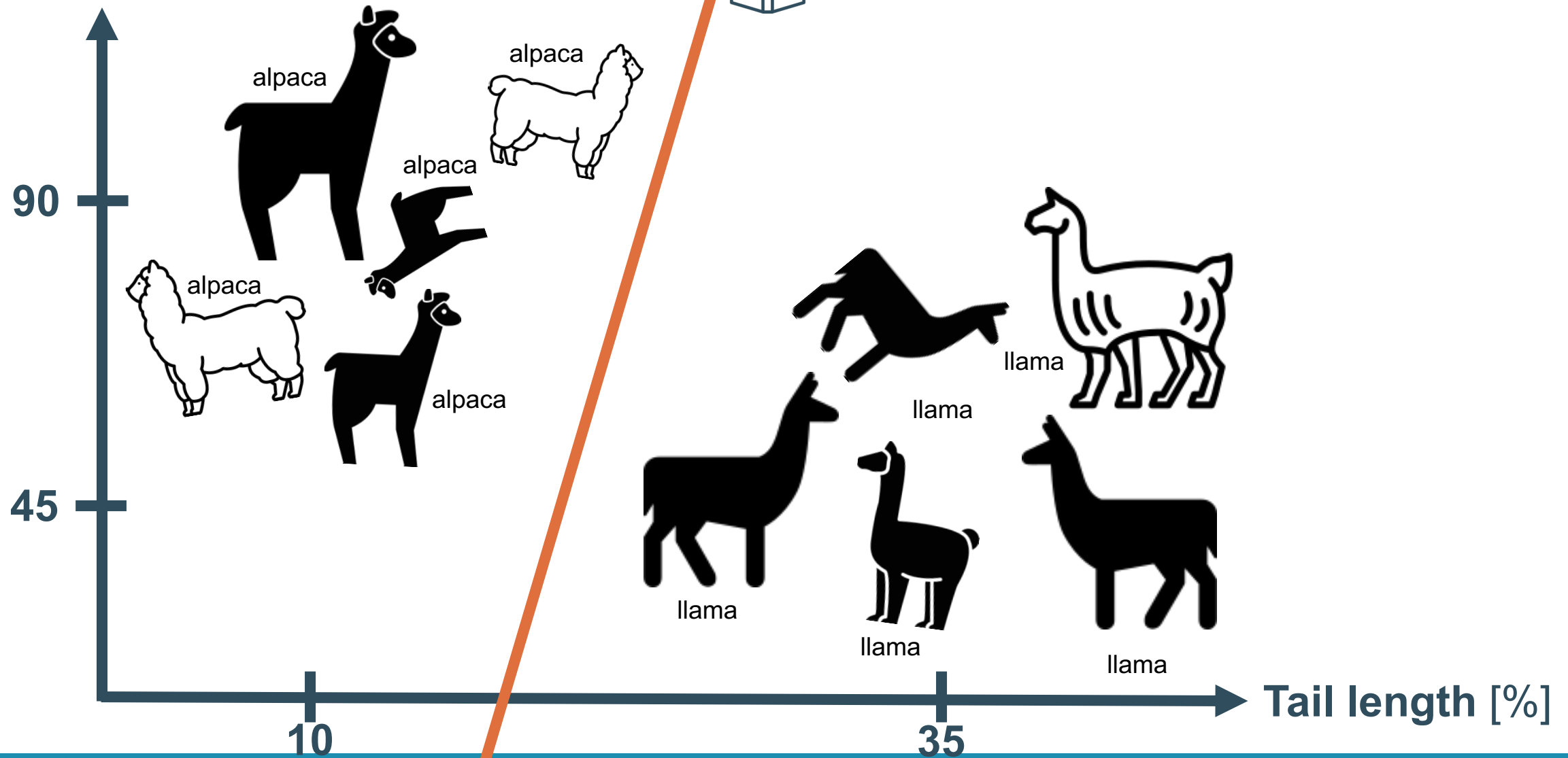


Angle Ears [°]



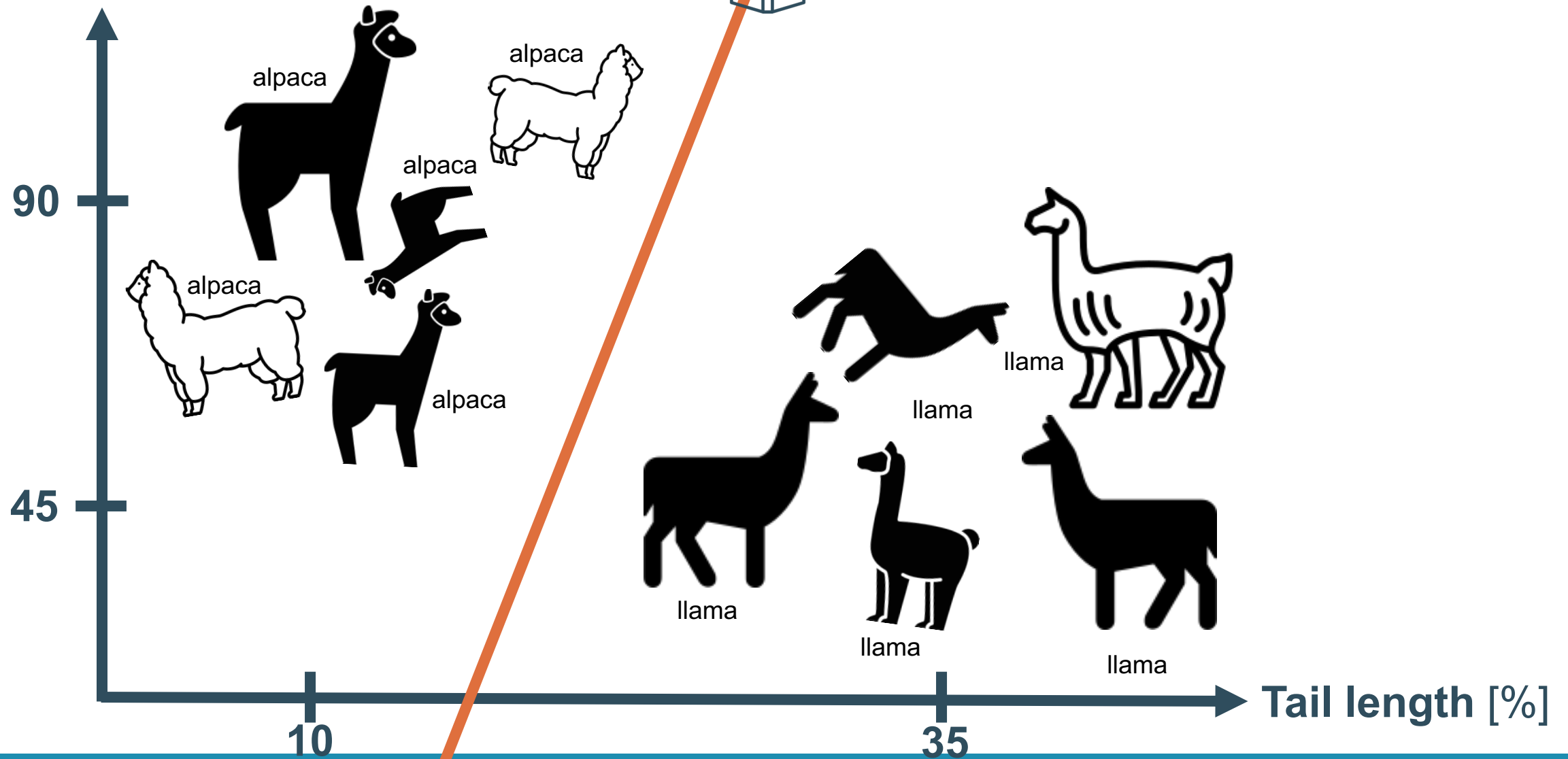
Learning process

Angle Ears [°]



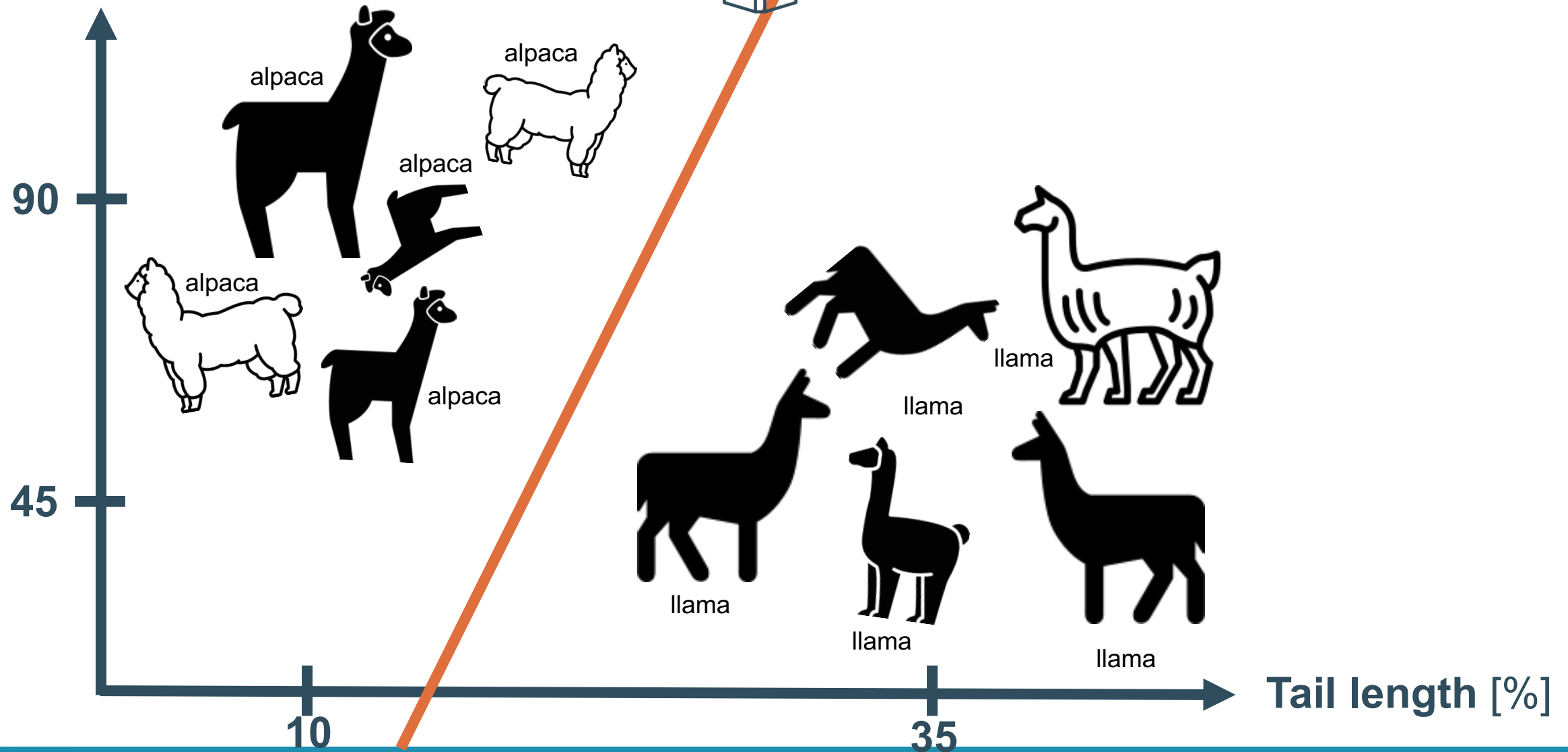
Learning process

Angle Ears [°]



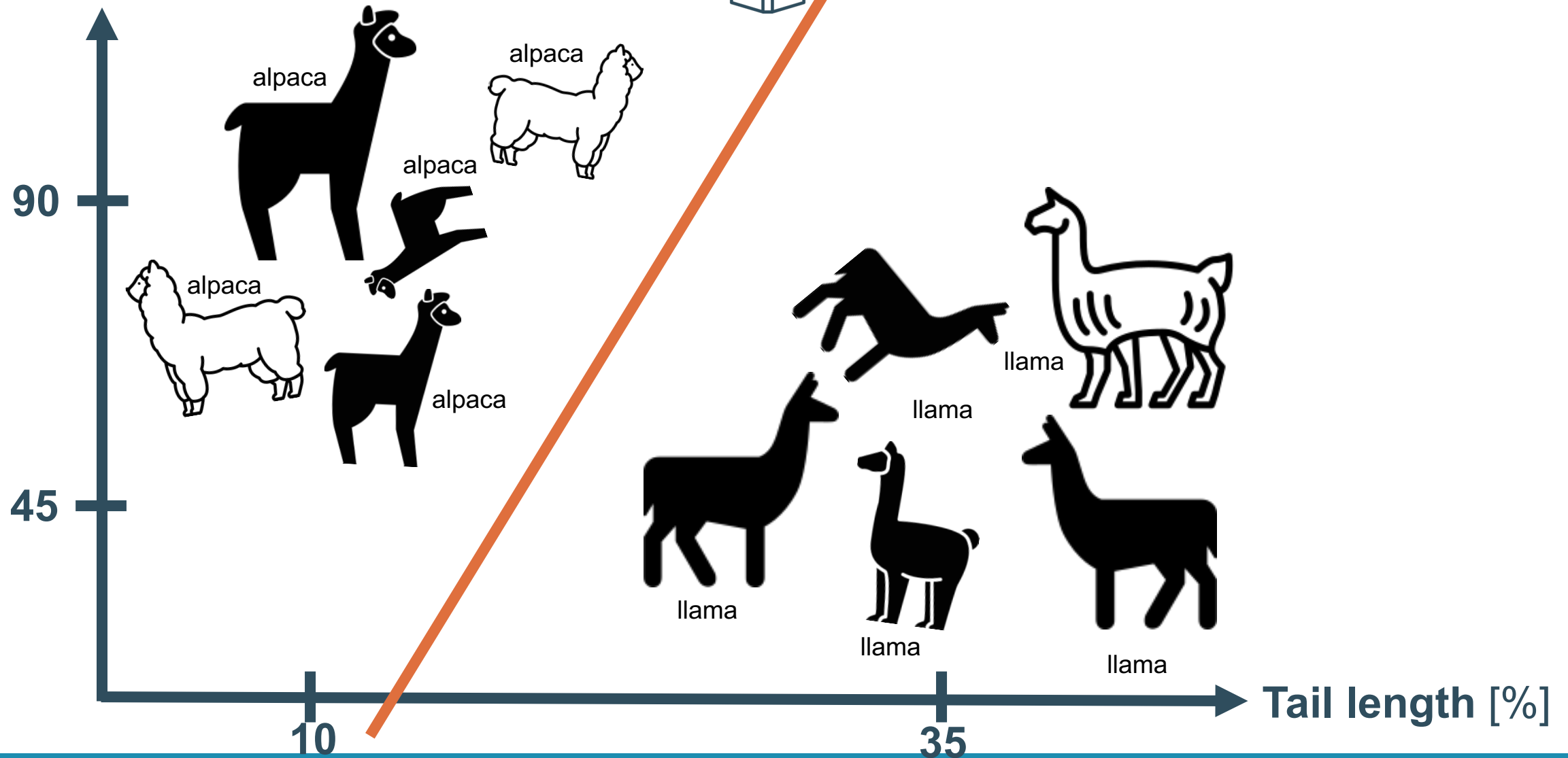
Learning process

Angle Ears [°]



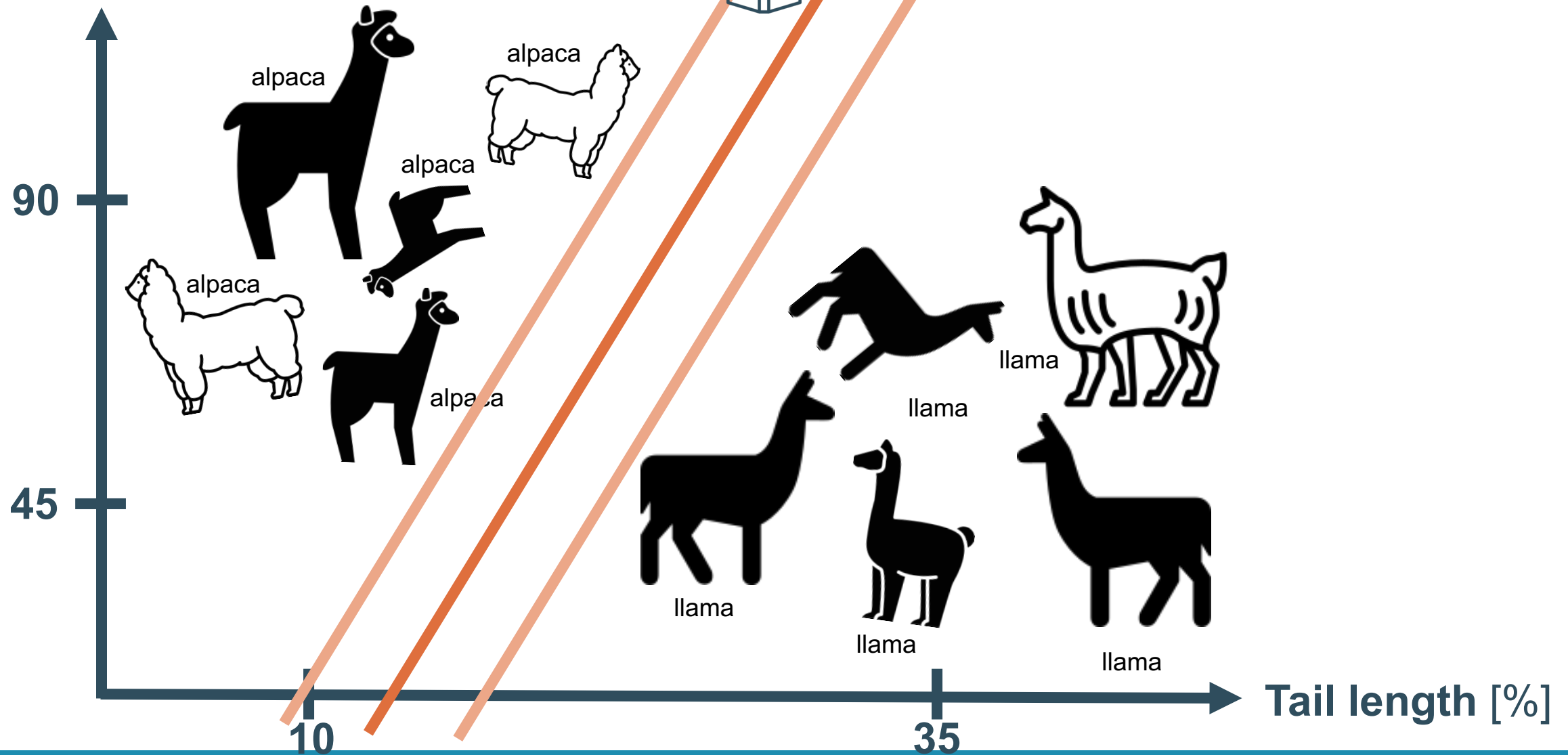
Learning process

Angle Ears [°]



Learning process

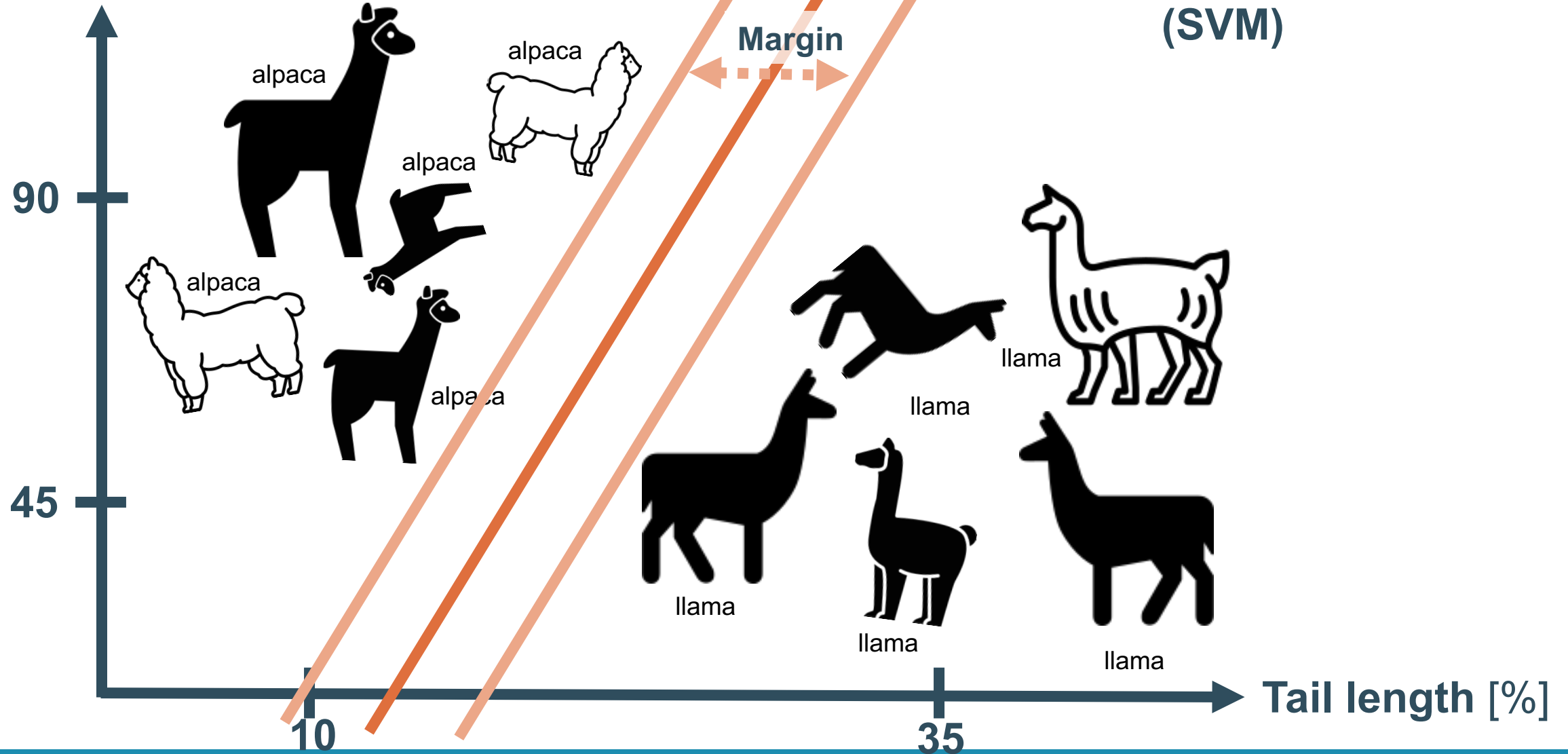
Angle Ears [°]



Angle Ears [°]

Decision boundary

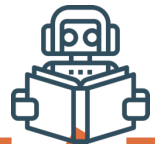
→ Support Vector Machines (SVM)



Angle Ears [°]

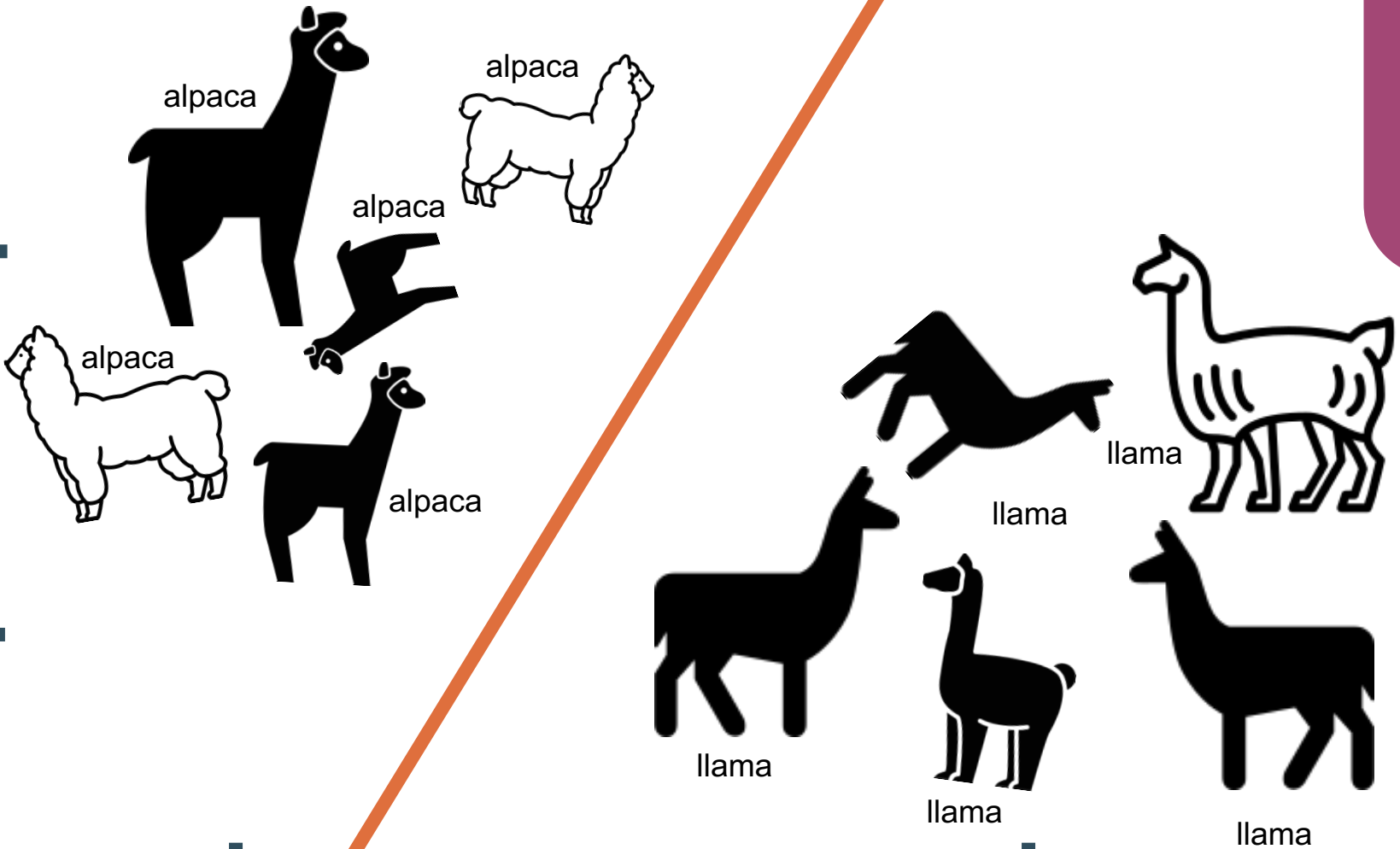
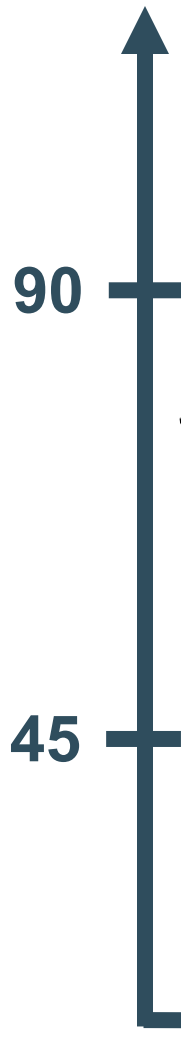
alpaca

llama



Test data
Data the machine has never seen before.

alpaca or llama ?



10

35

Tail length [%]

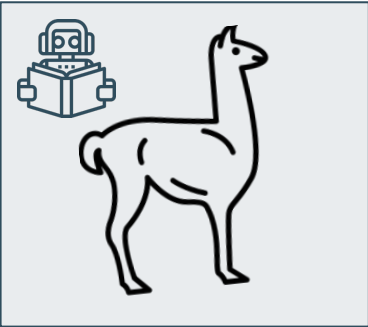
Angle Ears [°]

90

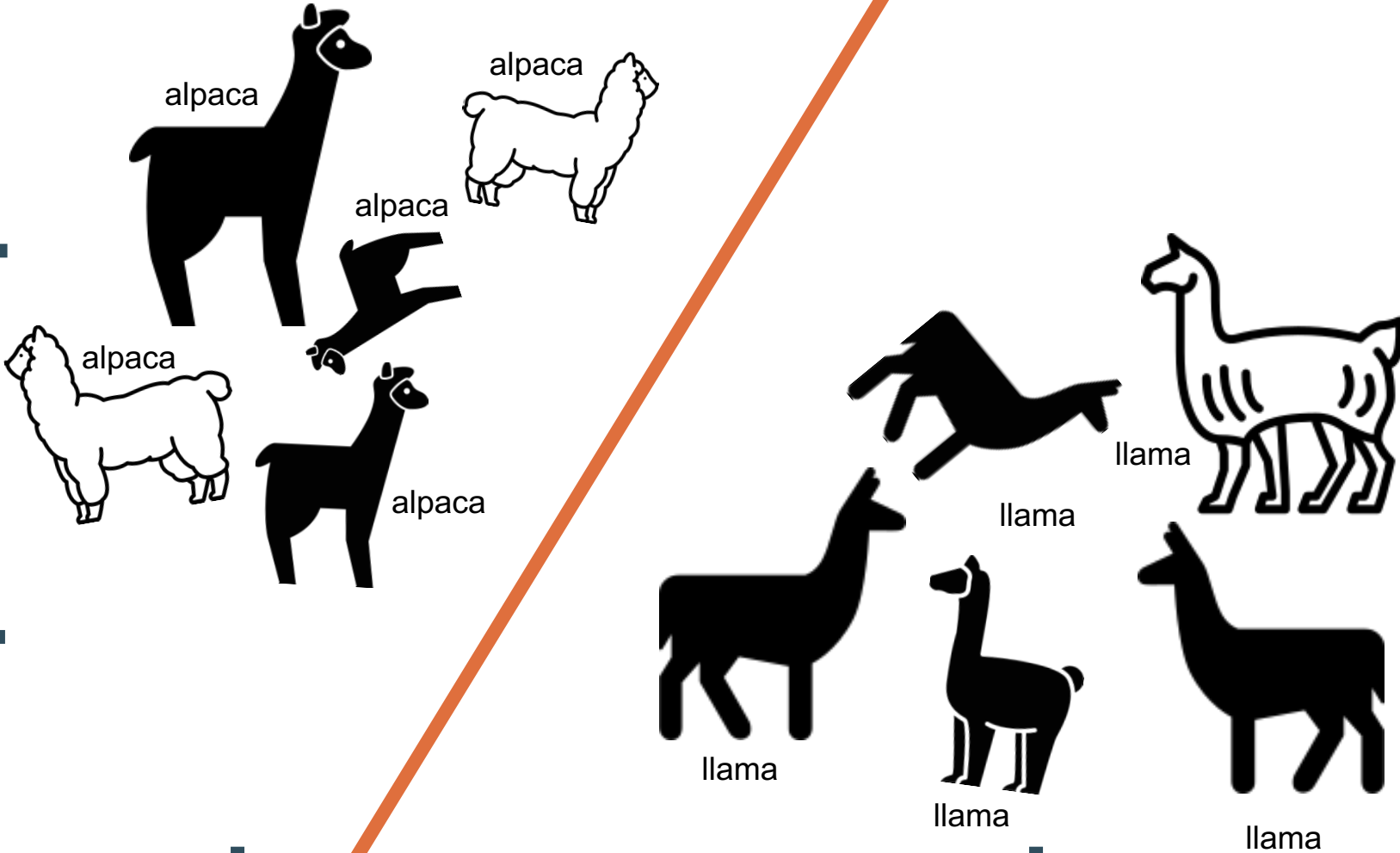
45

alpaca

llama



alpaca or
llama ?



10

35

Tail length [%]

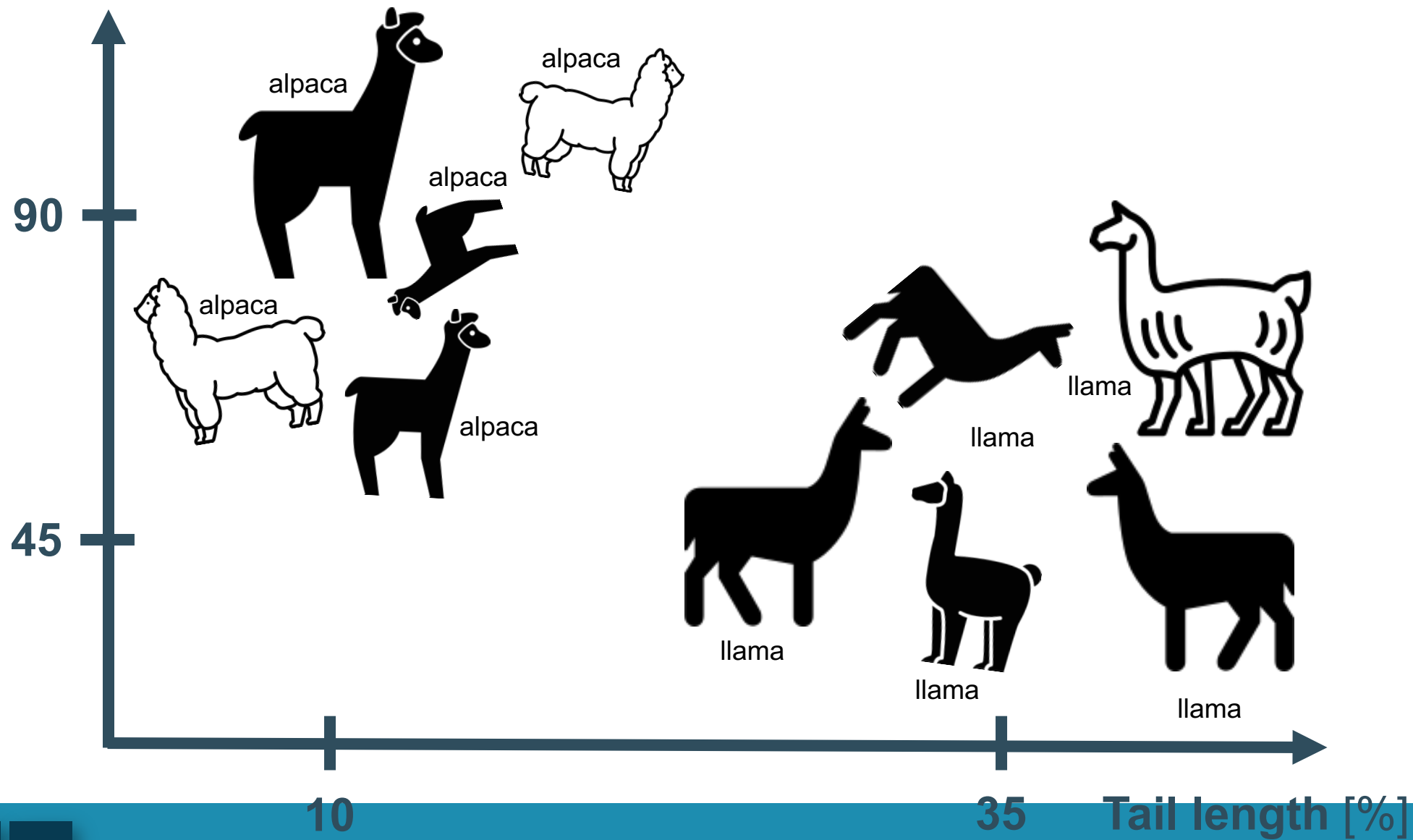
1.

2.

3.

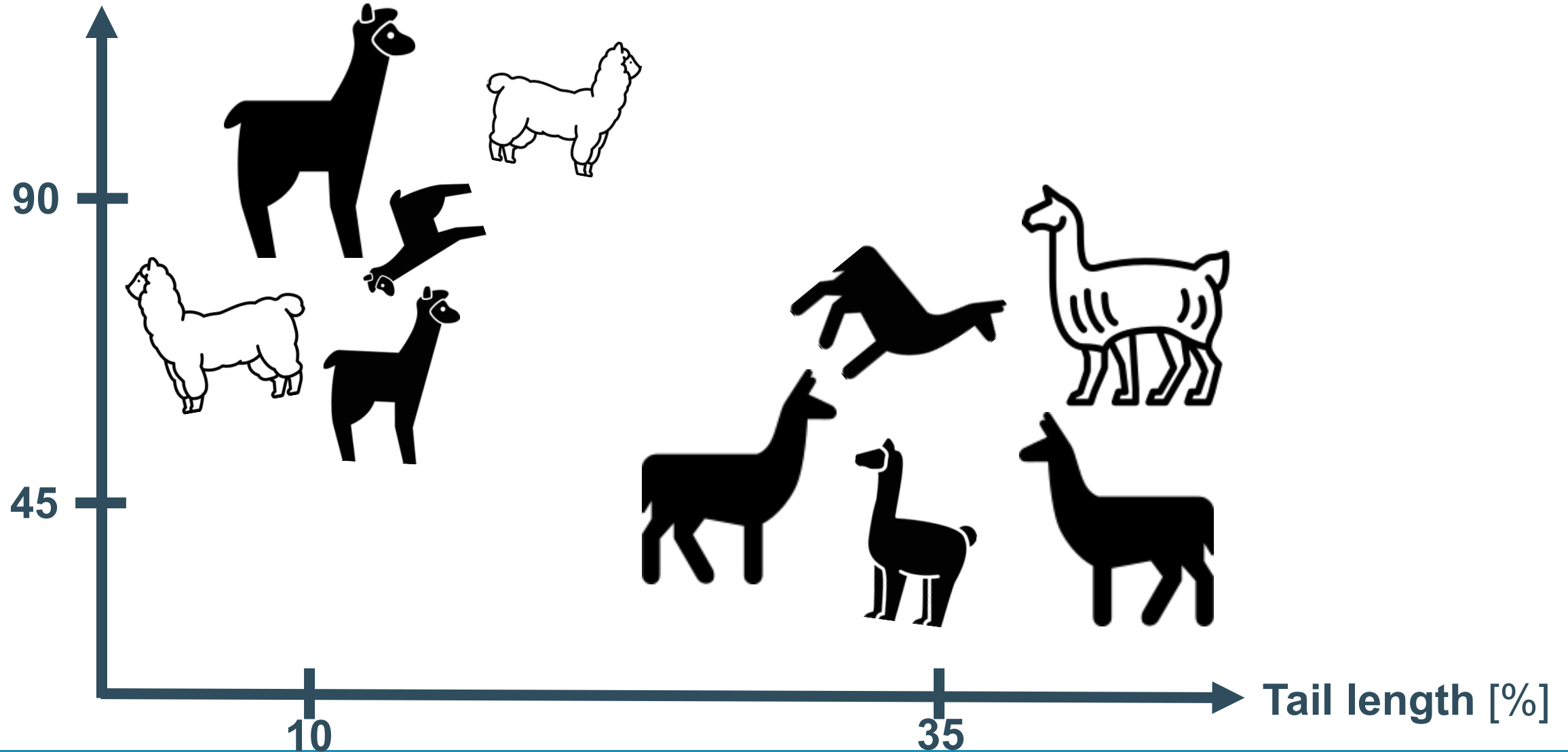
Angle Ears [°]

Supervised learning



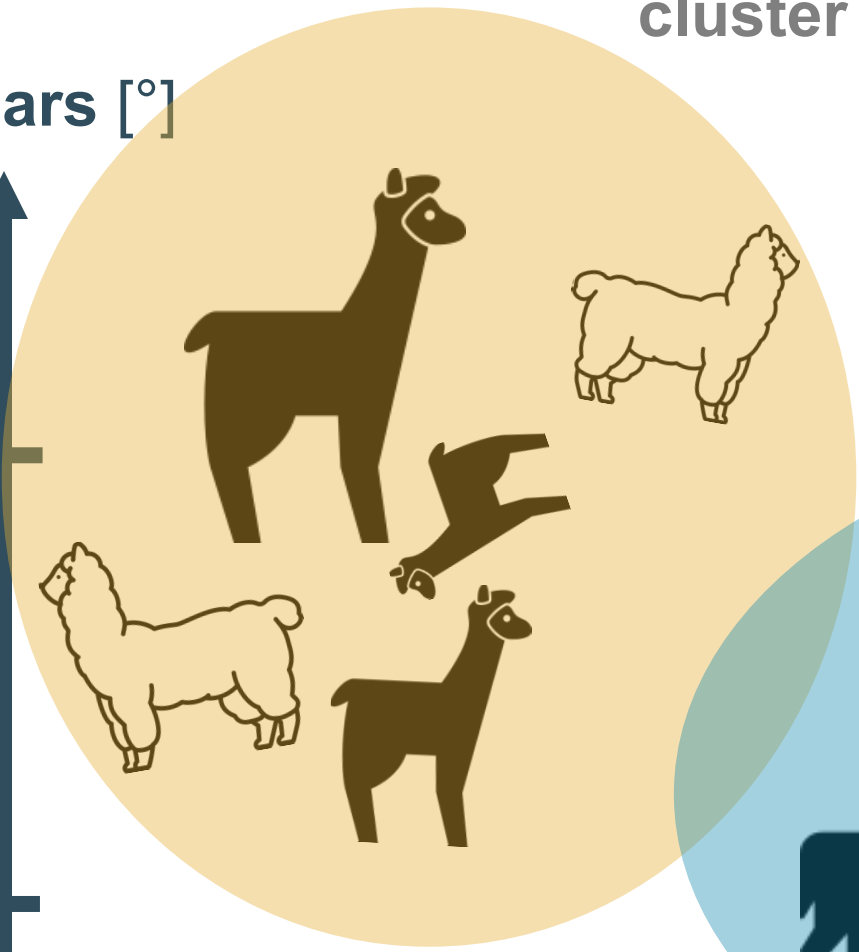
Angle Ears [°]

Unsupervised learning

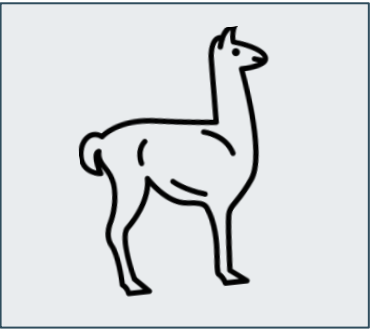
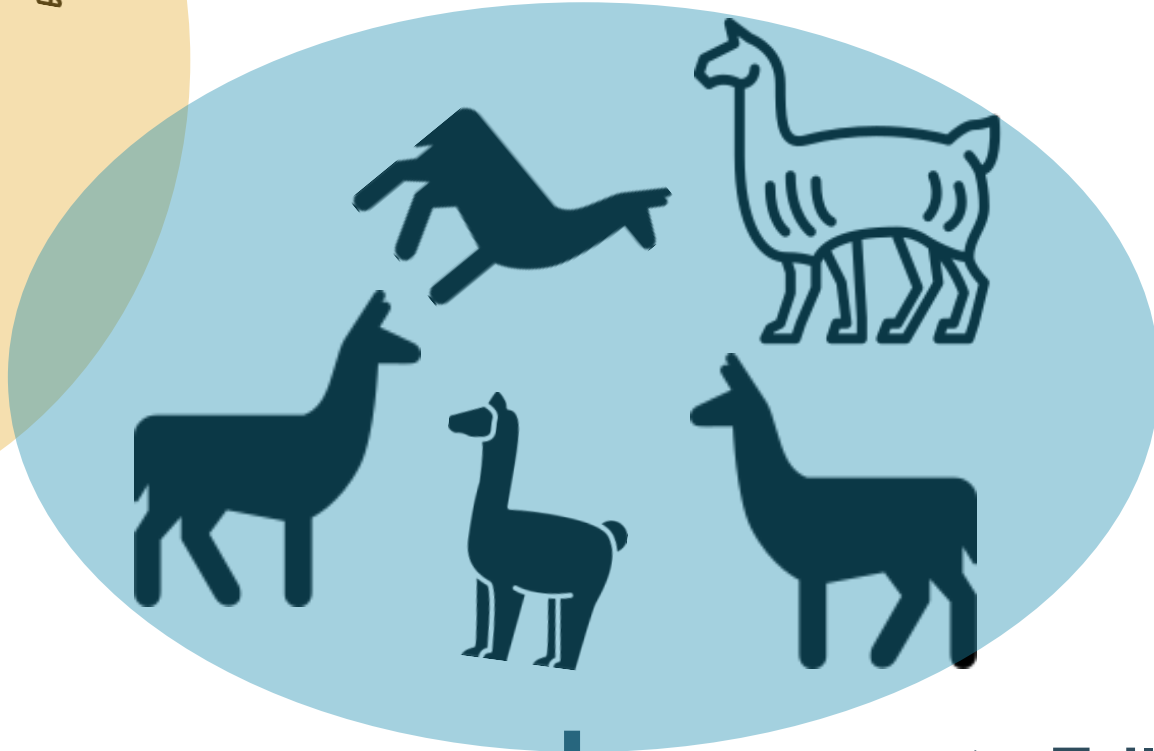


cluster 1

Angle Ears [°]



cluster 2



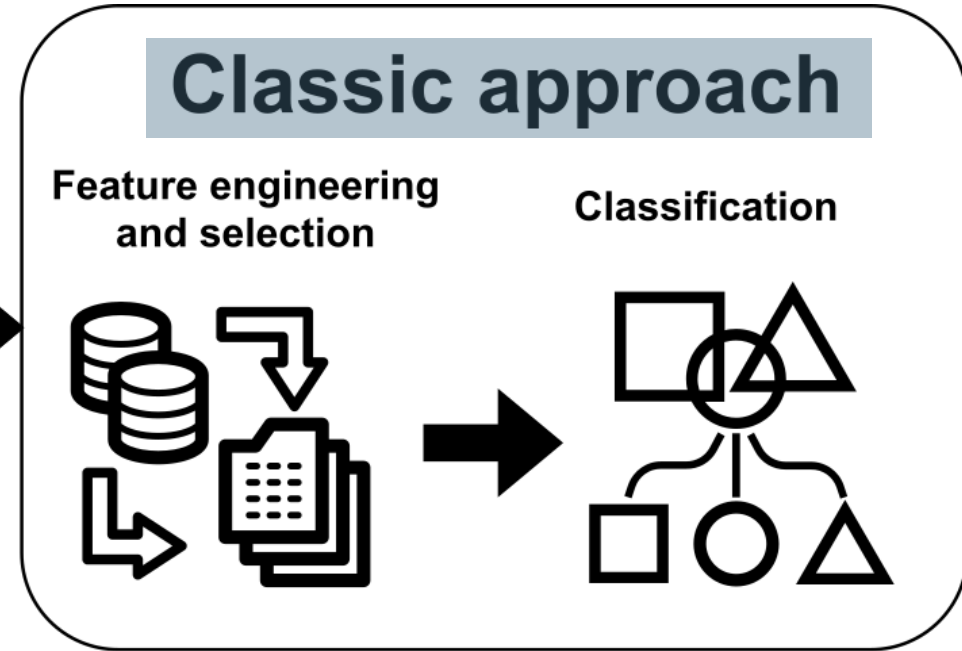
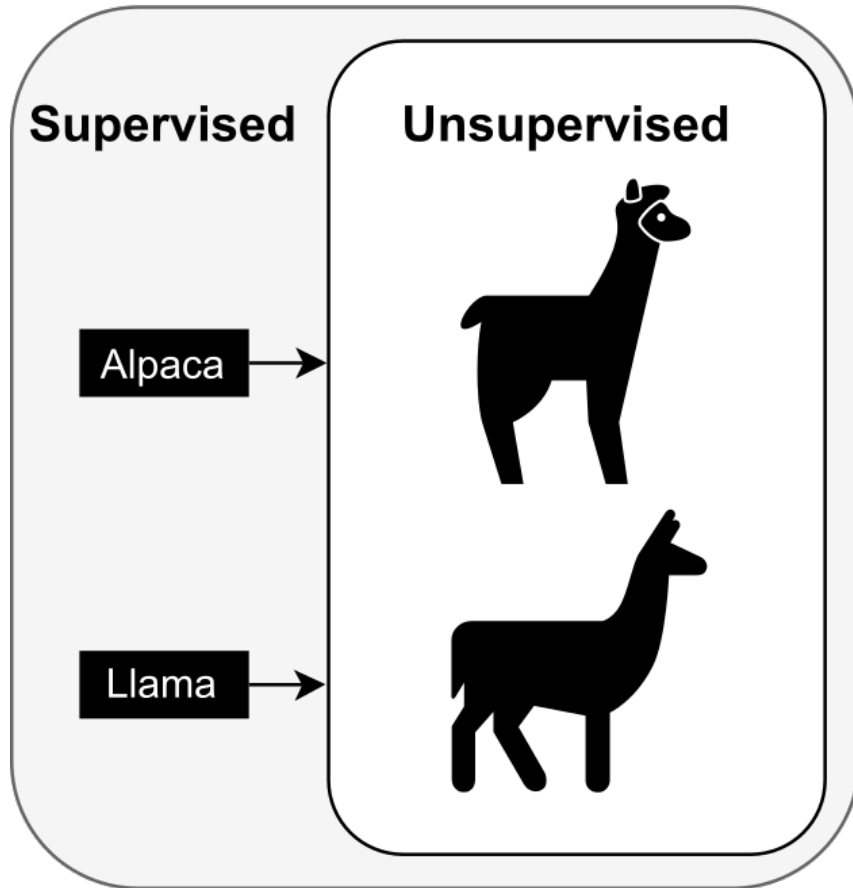
cluster 1 or cluster 2 ?

10

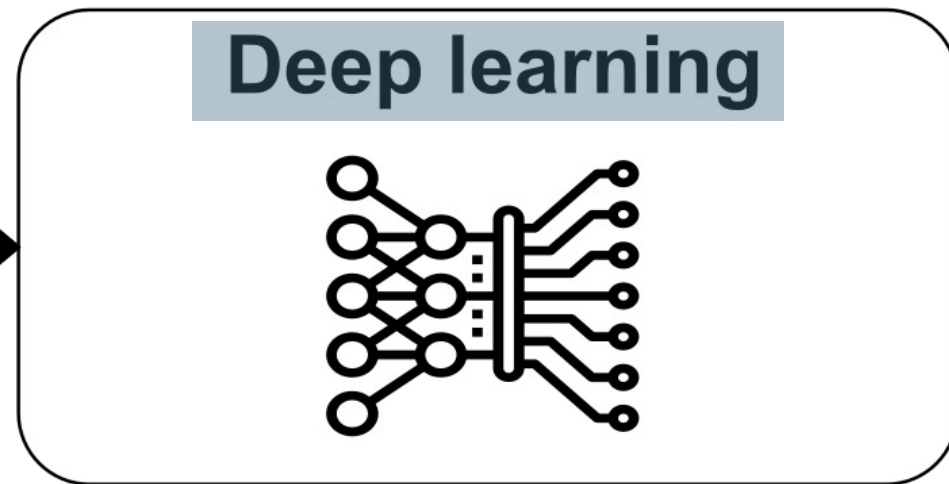
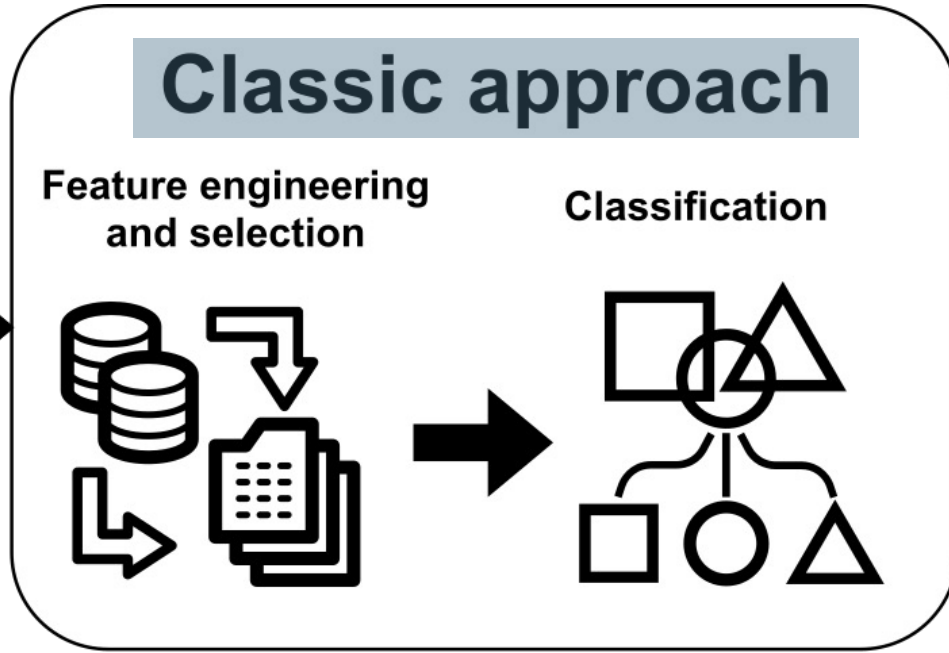
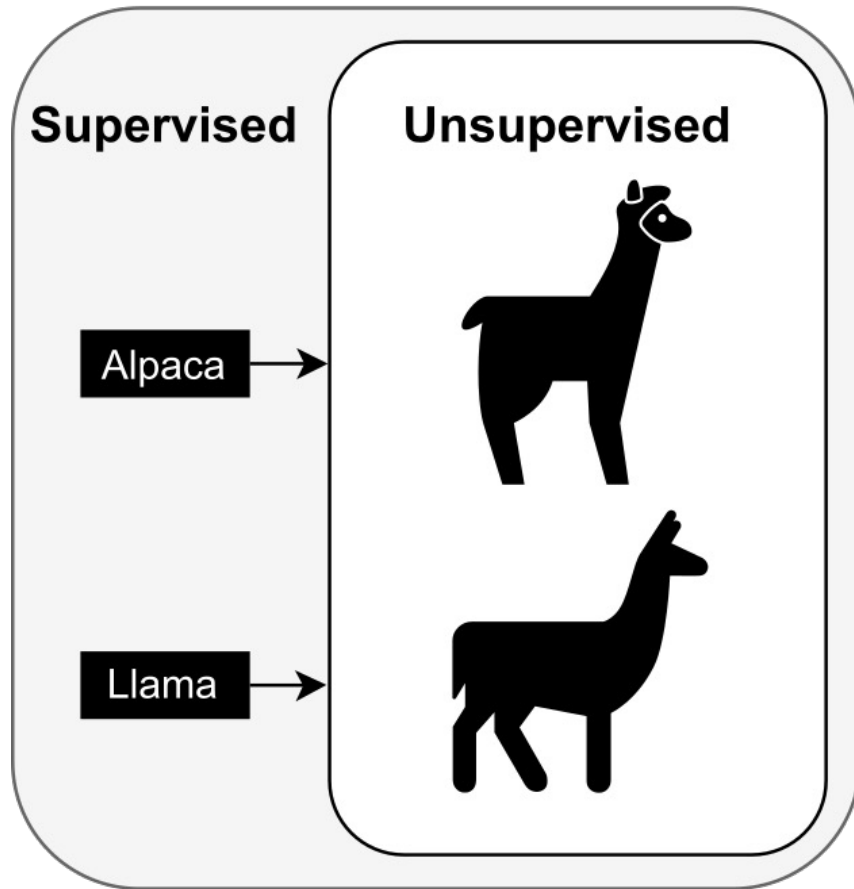
35

Tail length [%]

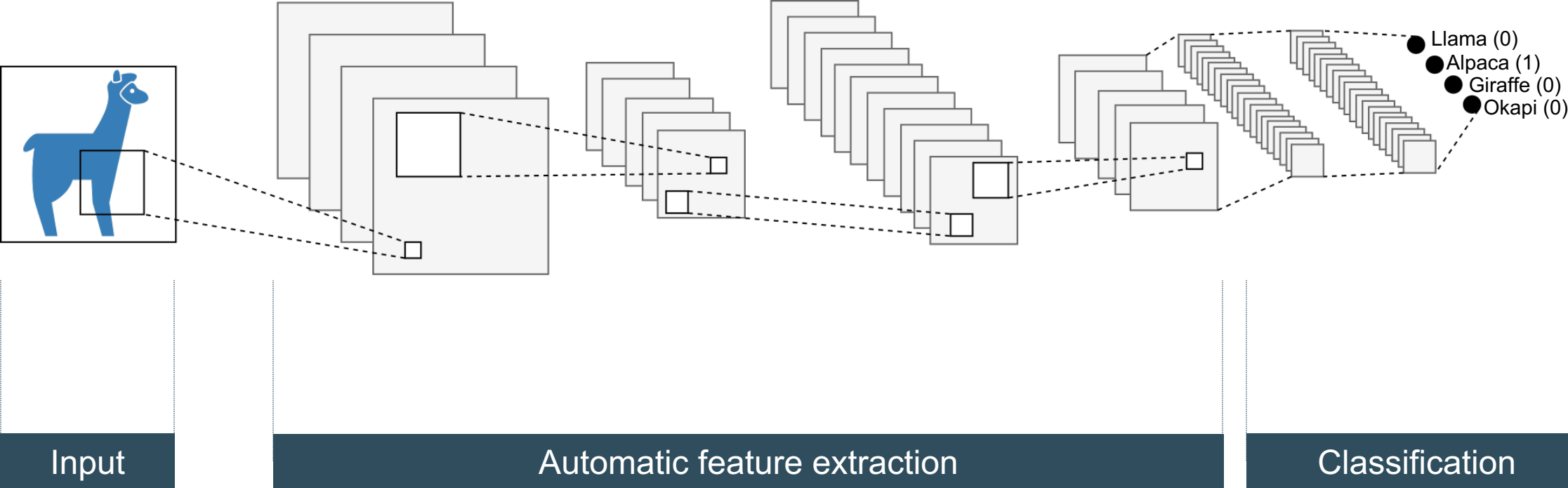
Machine learning



Machine learning



Deep Learning using convolutional neural networks (CNN)



Contents Overview



1. Introduction



2. Examples

- Cancer diagnostics
- Neonatal brain monitoring (epilepsy)
- EEG-fMRI data fusion (epilepsy)
- Wearable health monitoring (epilepsy, sleep)



3. Future Challenges

| Cancer Diagnostics

UZ Leuven departments

Imaging & Pathology

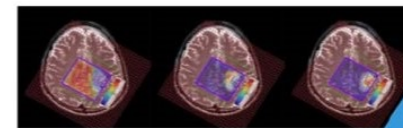
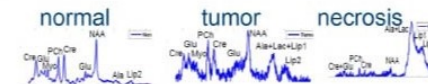
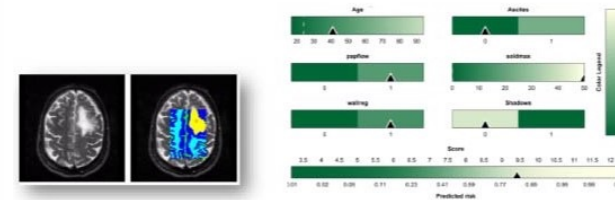
Radiology

Neurosurgery

Development and Regeneration

UZ Gent department

Radiology



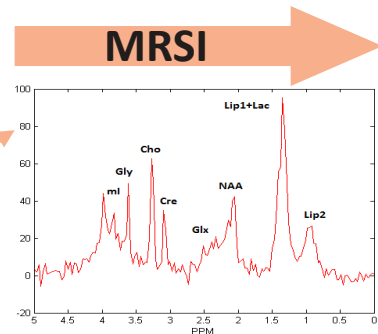
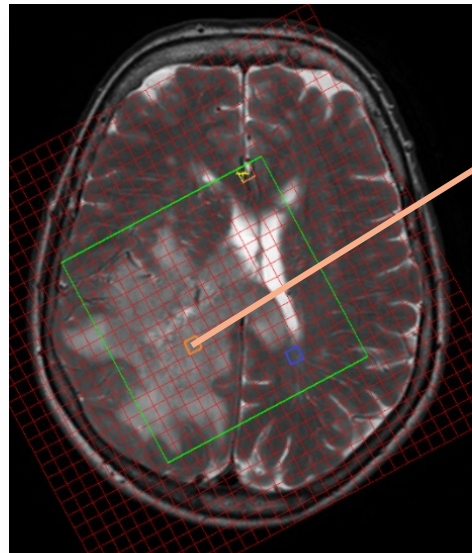
06.

Cancer Diagnostics

Metabolite quantification and (un)supervised tumor tissue typing using Magnetic Resonance Spectroscopic Imaging and multiparametric MR data fusion, Interpretable Prediction models for preoperative cancer diagnosis.

EXAMPLE

Unsupervised tissue type differentiation: Blind Source Separation for MRSI data



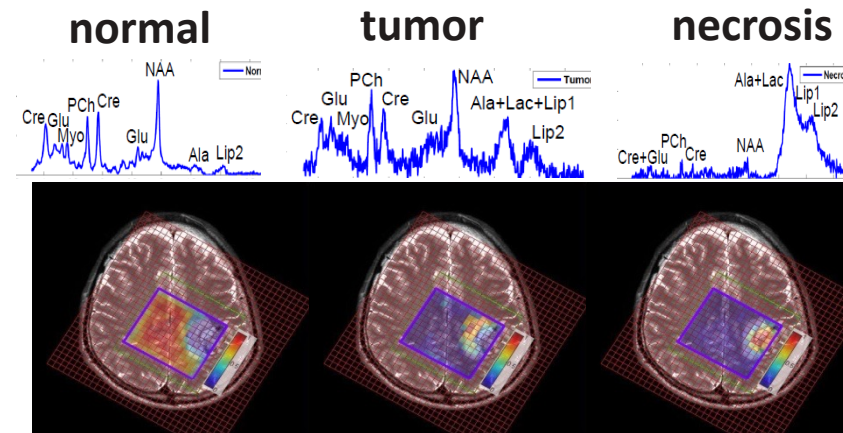
$X = \text{matrix of spectra, } X \approx WH$

$$\min ||X - WH||$$

such that $W \geq 0, H \geq 0$

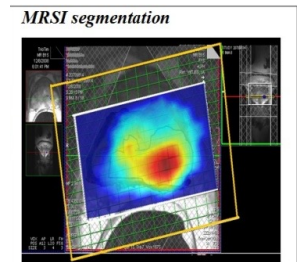
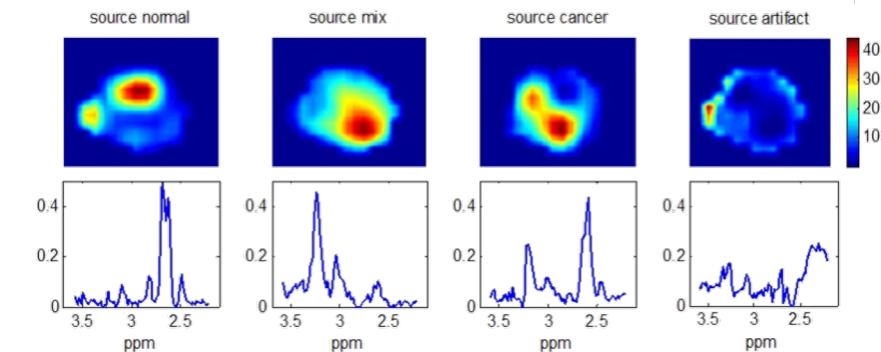
non-negative matrix/tensor factorization

Brain tumor tissue typing

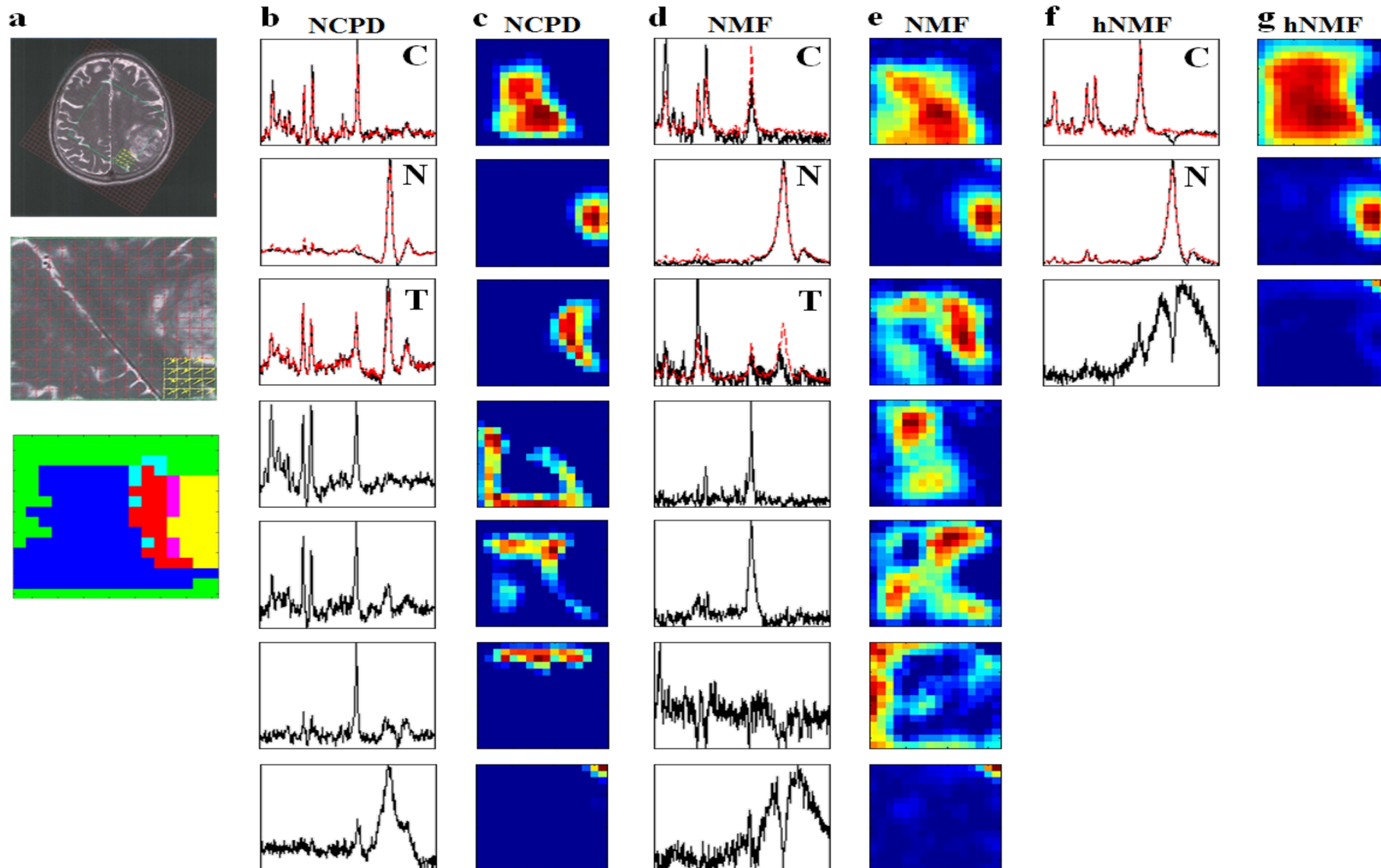


Prostate segmentation

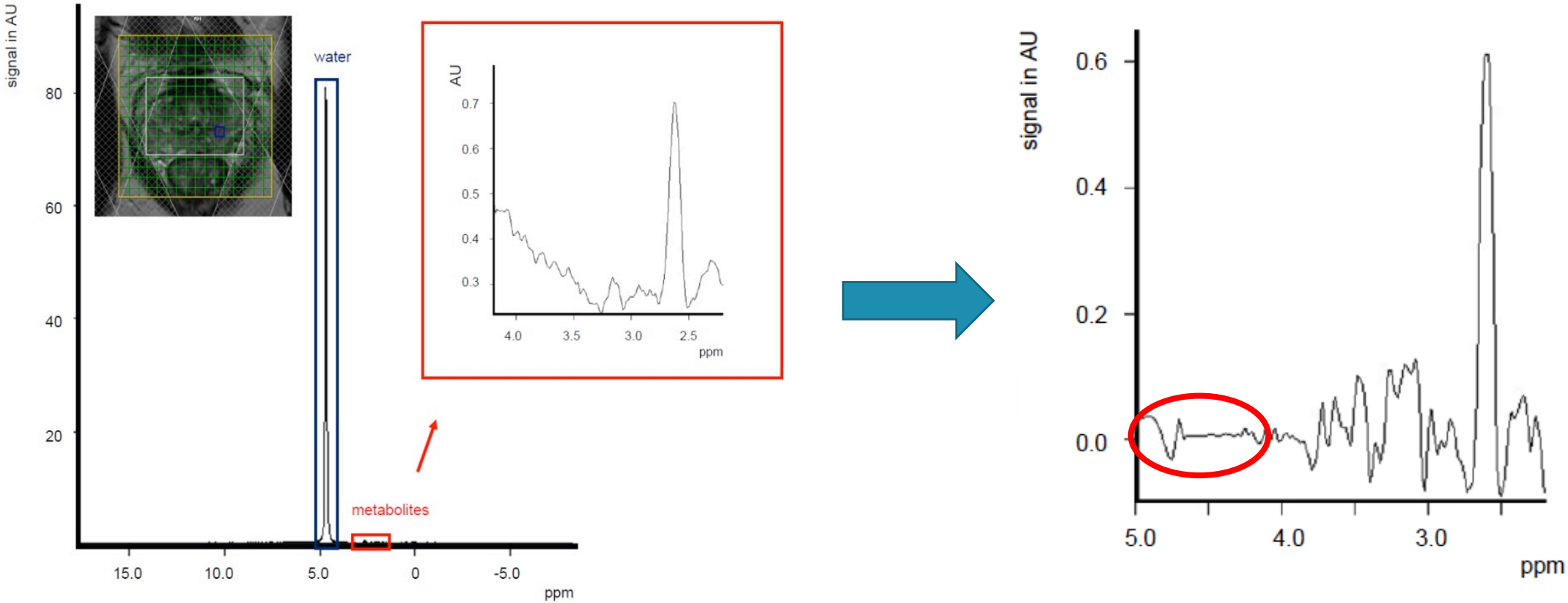
NNMF results



Brain tumor recognition using Non-negative CPD



Tensor based water suppression in MRSI



Frequency domain Model

$$S(f) = \sum_{r=1}^R \frac{a_r e^{j\phi_r} / 2\pi}{d_r + j2\pi(f - f_r)} + \eta(f)$$

Löwner Tensor → **ALL voxels** (2D or 3D)

Time domain Model

$$S(t) = \sum_{r=1}^R a_r e^{j\phi_r} e^{(-d_r + j2\pi f_r)t} + \eta(t)$$

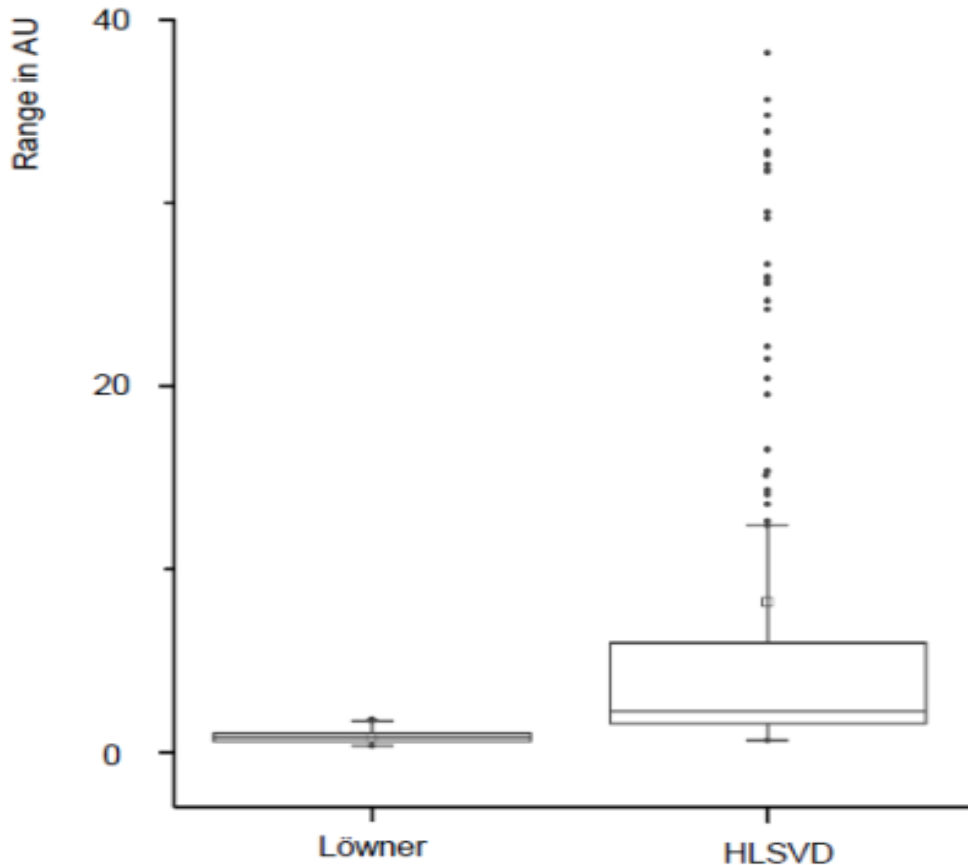
HSVD matrix based suppression → **voxel per voxel**

$$S = WH^T$$

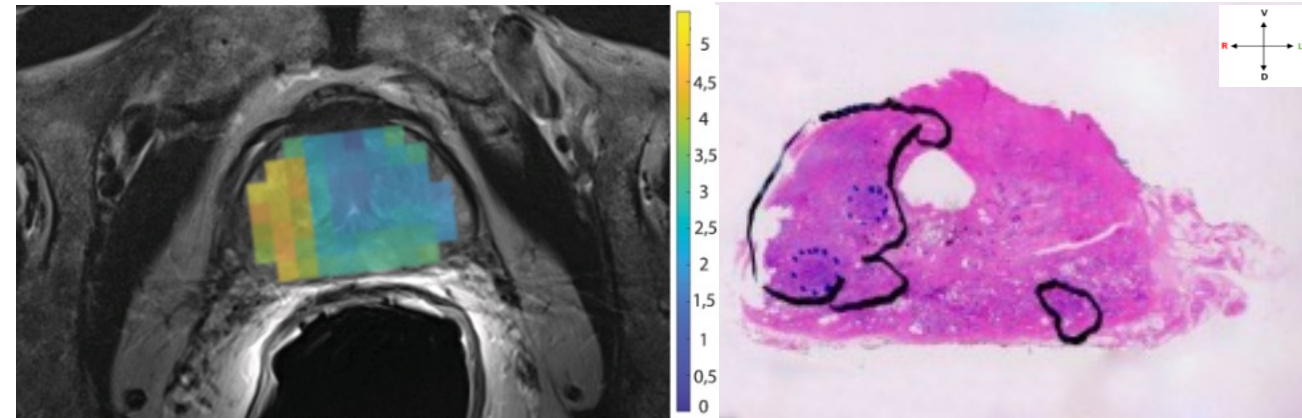
Tensor based water suppression in MRSI

Box-plot displays differences in variance in suppressed region of 306 in-vivo MRSI signals:

Tensor based BSS uses info from ALL voxels
while HLSVD does it voxelwise

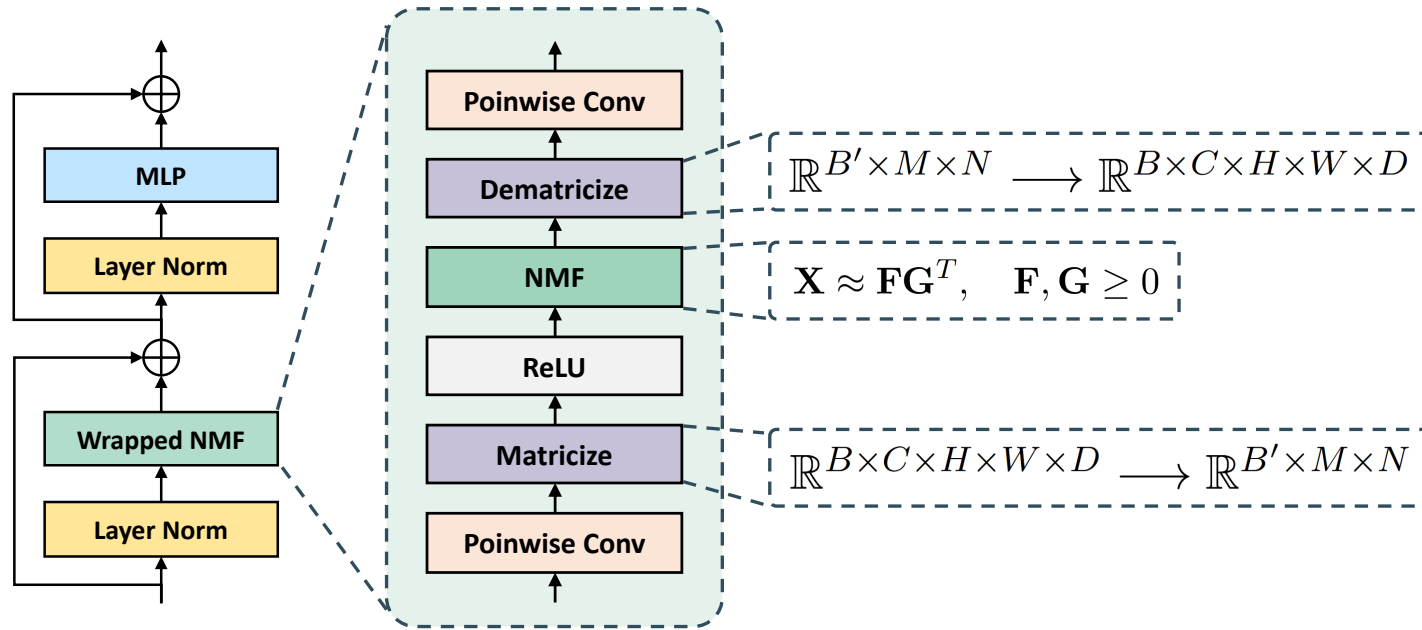


Metabolite maps of a patient with prostate cancer:
The two tumors in peripheral prostate zone have relatively high Cho levels



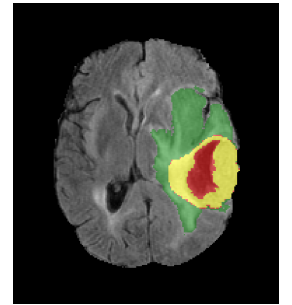
Factorizer: Interpretable Approach to Brain Tumor Segmentation

Factorizer Block



Interpretability

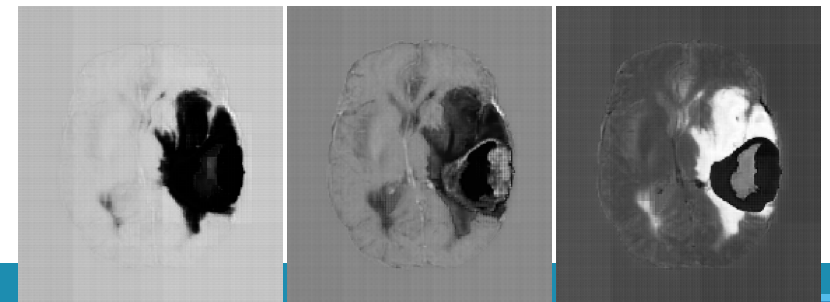
■ Necrosis
■ Enhancing
■ Tumor
■ Edema



Ground Truth

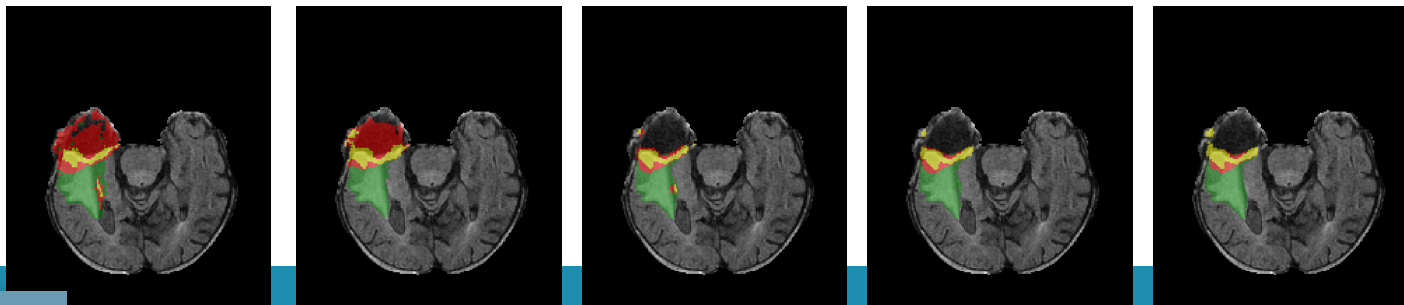


Shallowest NMF Layer Components



Deepest NMF Layer Components

Qualitative Results



1.

2.

Ground Truth

Factorizer

Transformer

Res-U-Net

U-Net

Neonatal Brain Monitoring

UZ Leuven departments:

Neonatology

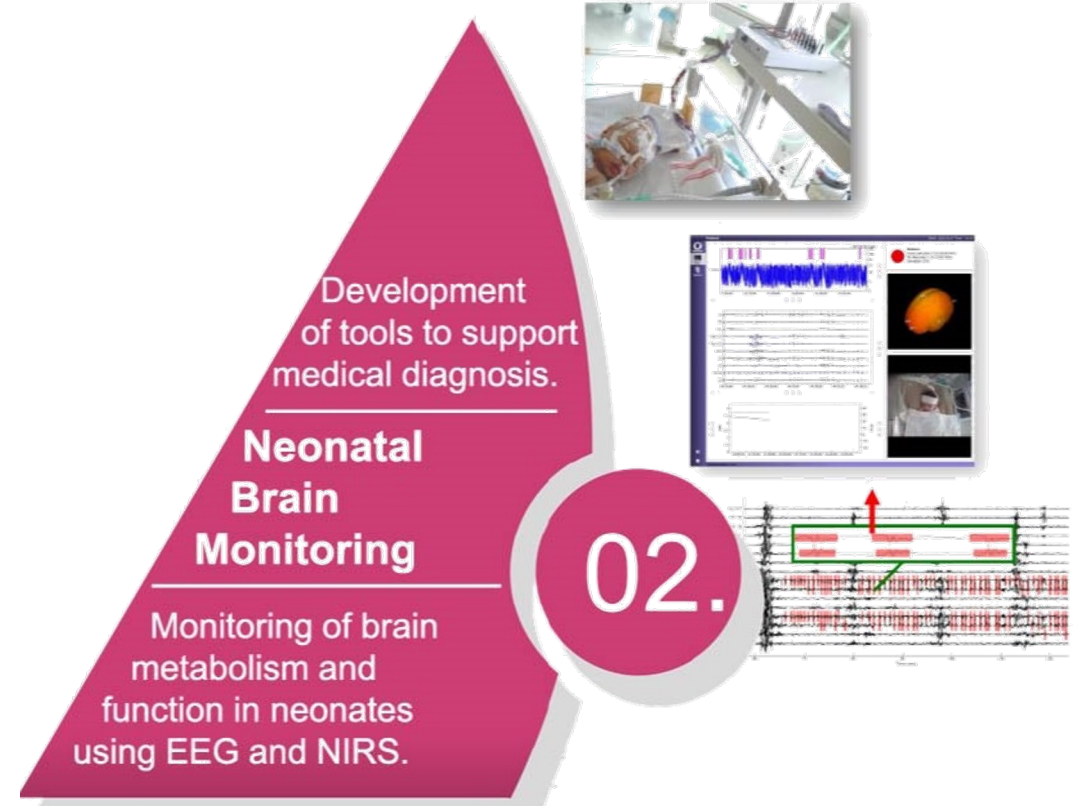
Pediatric neurology

Eindhoven University of Technology

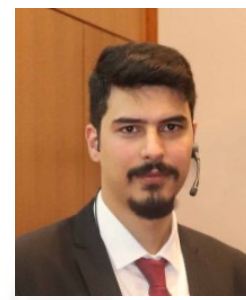
Maxima Medical Centre

Oxford University:

Dept. of Engineering Science



Monitoring in the NICU



Development of a Neonatal EEG Monitor for Automated Brain Analysis



de jong gortemaker algra

Neonatal brain monitoring: why?

Newborn baby is admitted at the
Neonatal Intensive Care Unit

- Prematurity (24-32w): 1/8 births in USA
- Hypoxic insult: 1-6/1000 births in USA

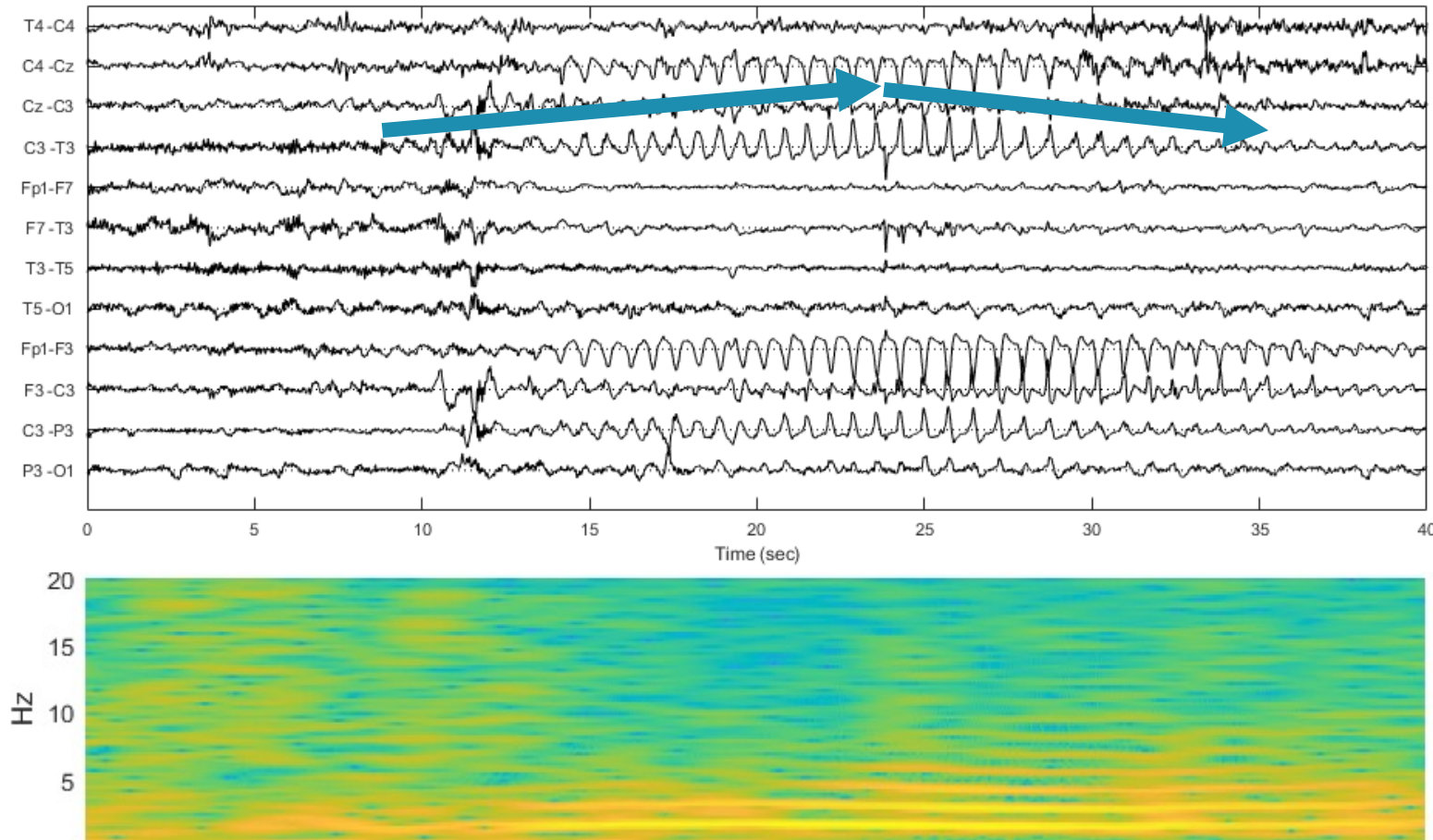


Shortage of oxygen supply to brain (or risk):

- Brain monitoring Starts promptly !
 - **Electro-EncephaloGraphy (EEG)**
 - Cerebral Functional Monitoring (CFM)
 - Near-InfraRed Spectroscopy (NIRS)
- Why brain monitoring?
 - No neurological experts present 24/7
 - No MRI scans for small babies
- Limited time window for interventions
 - Therapeutic hypothermia has to start within 6 hours after birth

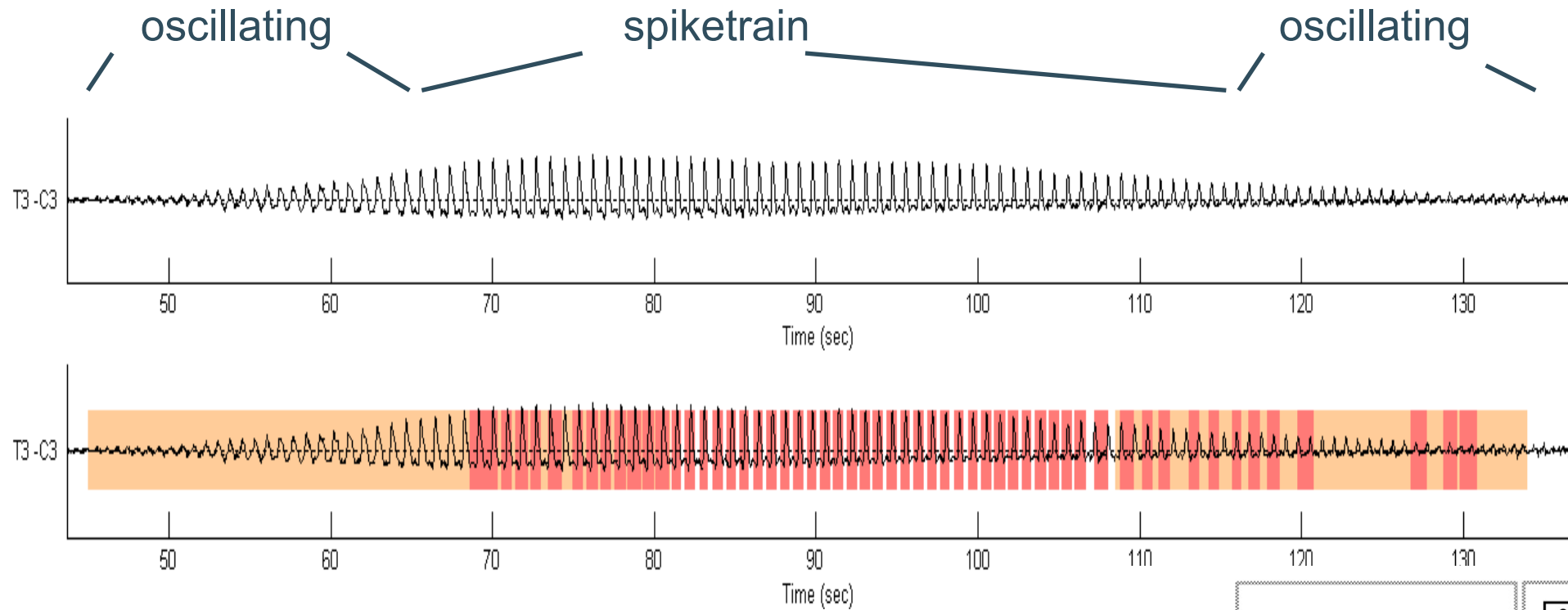
Neonatal Seizures

Abnormal, excessive, and synchronous neuronal activity in the brain

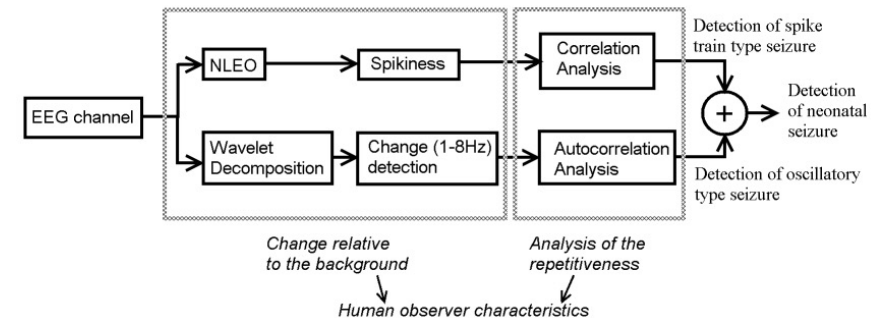


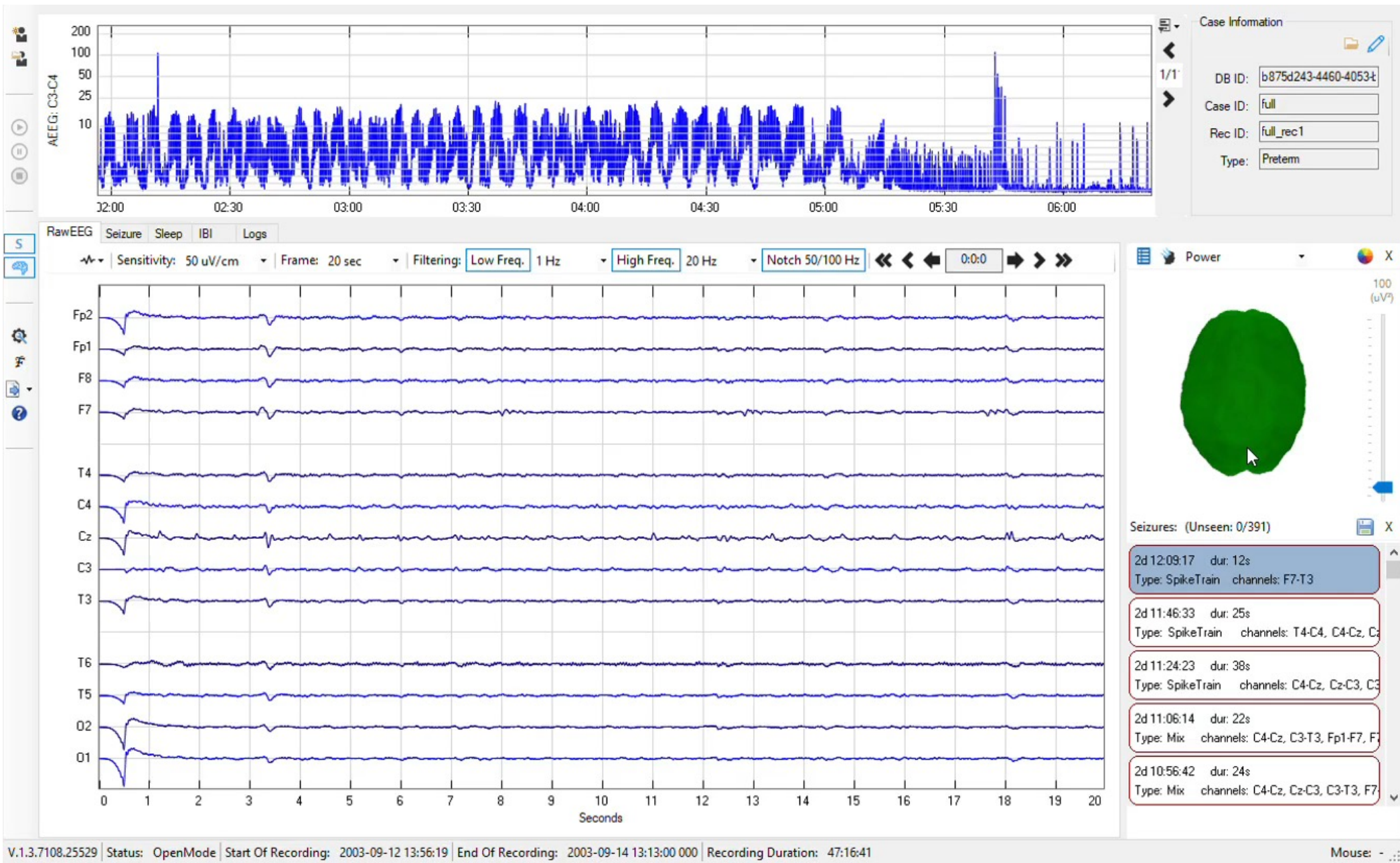
CHALLENGES:
How to automate seizure detection?
→ Scoring
→ Low interrater agreement

Seizure Detection: *heuristic approach*



Mimicking the neurologist: **heuristic**, feature based →



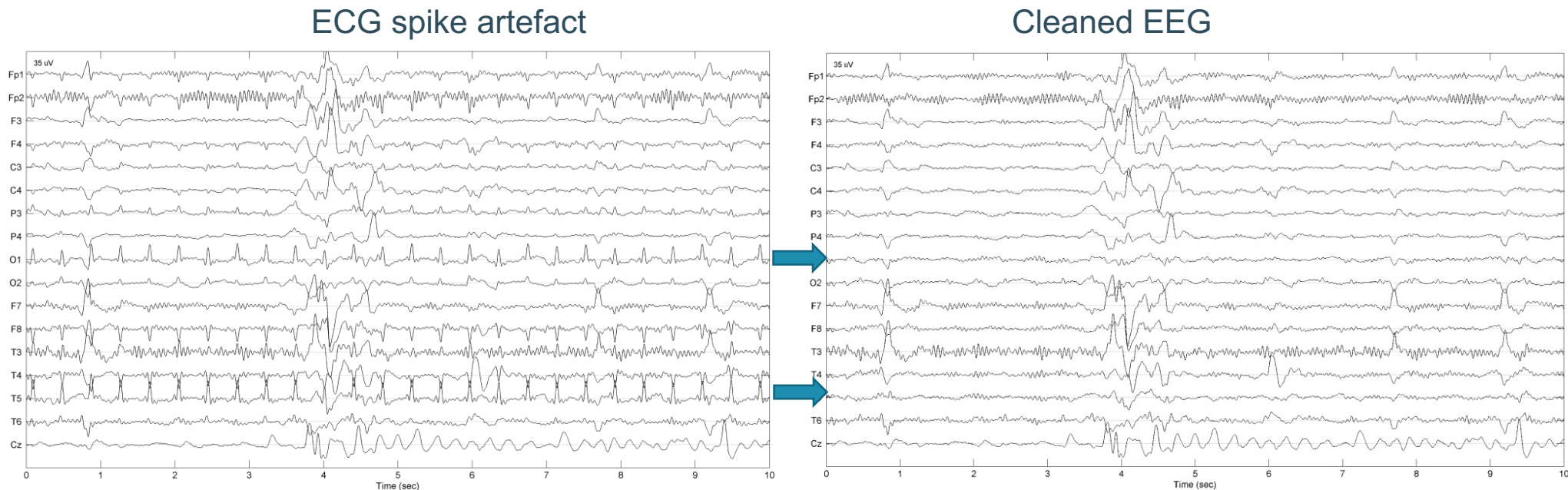


Improve Seizure Detection: *via Artefact removal*

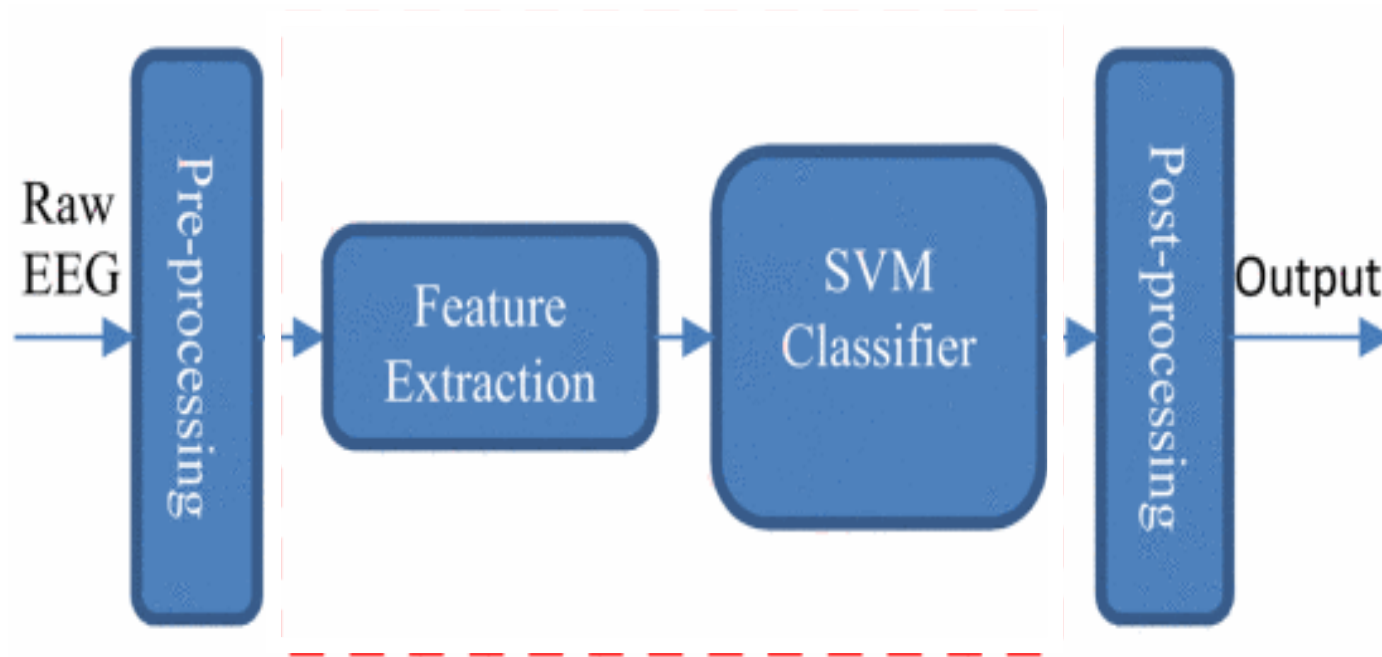
Artefacts: ECG, respiration, blood vessel pulsation most important ones
→ lead to false positive seizure detections

→ detect & remove using **various Blind Source Separation (BSS)** methods

Note: other artefacts (eye, tremor, nonbiological, ...) to be removed

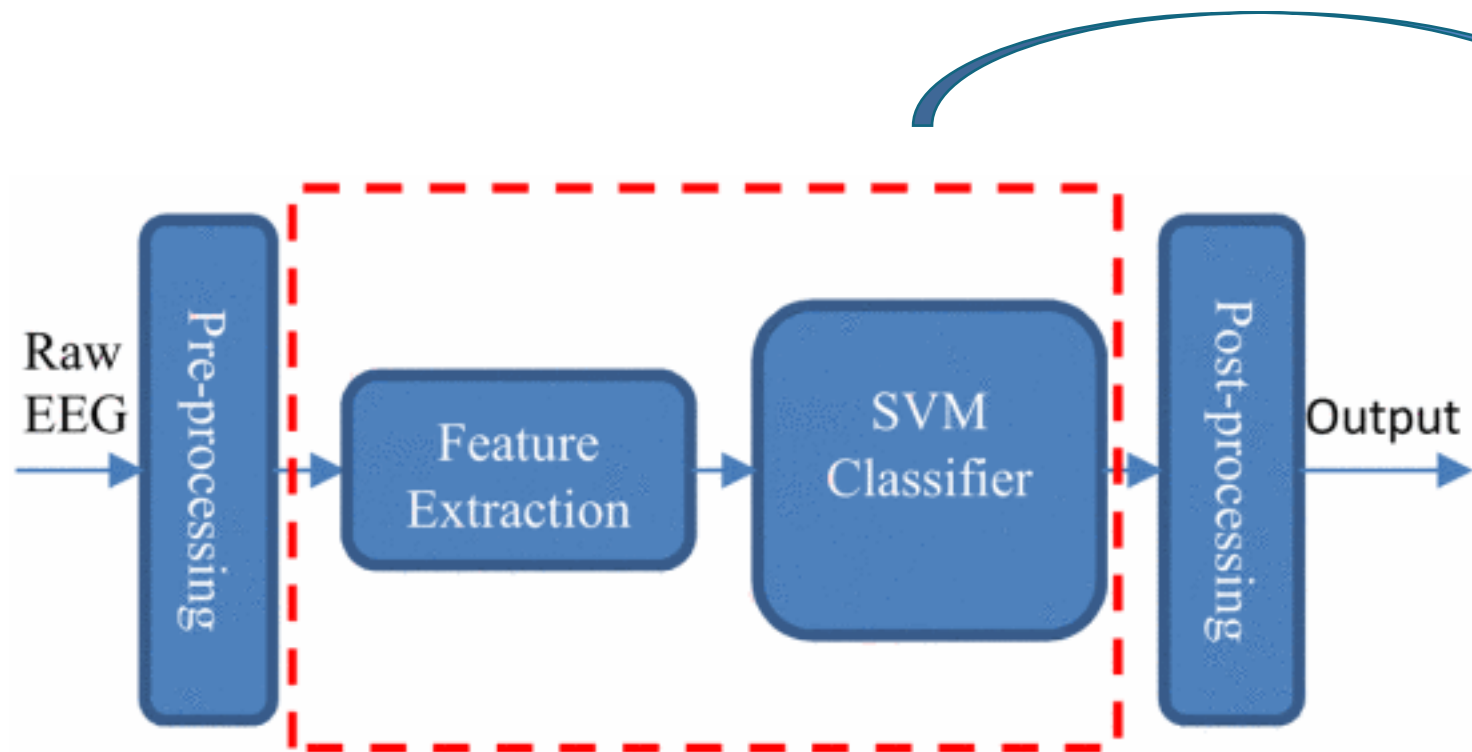


Seizure Detection: *Features-SVM*



Extracted Features	
Frequency Domain	Total power (0-12Hz) Peak frequency of Spectrum Spectral edge frequency (80%, 90%, 95%) Power in 2HZ wide sub-bands Normalized power in sub-bands Wavelet energy
Time Domain	Curve length Number of maxima and minima Root mean squared amplitude Hjorth parameters Zero crossings (raw epoch, Δ , $\Delta\Delta$) Autoregressive modelling error (order 1-9) Skewness Kurtosis Nonlinear energy Variance (Δ , $\Delta\Delta$)
Information Theory	Shannon entropy Singular value decomposition entropy Fisher information Spectral entropy

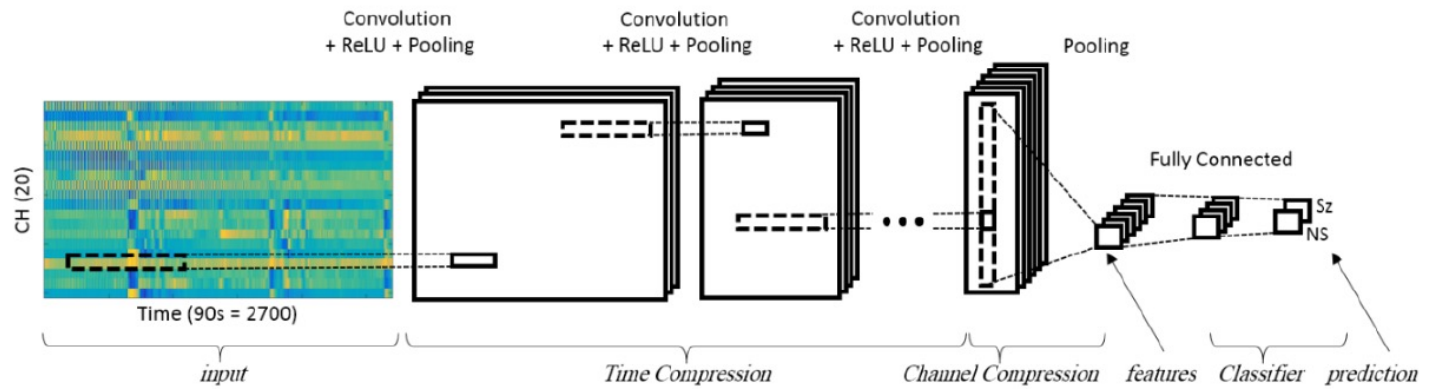
Seizure Detection: *Deep learning*



Layer Type	Shape	Output Shape	Parameters
Input	256	256x1	0
1D Convolution	32 filters 4x1 kernel Stride 1	32x253x1	160
1DConvolution	32 filters 4x1 kernel Stride 1	32x250x1	4128
1DConvolution	32 filters 4x1 kernel Stride 1	32x247x1	4128
Batch Norm.		32x247x1	64
Average Pooling	Pool 8 Stride 2	32x120x1	0
1DConvolution	32 filters 4x1 kernel Stride 1	32x117x1	4128
1DConvolution	32 filters 4x1 kernel Stride 1	32x114x1	4128
Average Pooling	Pool 4 Stride 2	32x56x1	0
1DConvolution	2 filters 4x1 kernel Stride 1	2x53x1	258
GAP		2x1	0
Softmax		2	0

Improve Convolutional Neural Networks architecture

		Layer Info	Output Size		
		Input:	(20,	2700,	1)
Feature Extraction	1	Conv (1, 5) × 5	(20,	2696,	5)
	2	MPool (1, 3), s: 2	(20,	1347,	5)
	3	ReLU	(20,	1347,	5)
	4	Conv (1, 5) × 8	(20,	1343,	8)
	5	MPool (1, 3), s: 2	(20,	671,	8)
	6	ReLU	(20,	671,	8)
	7	Conv (1, 5) × 10	(20,	667,	10)
	8	MPool (1, 3), s: 2	(20,	333,	10)
	9	ReLU	(20,	333,	10)
	10	Conv (1, 5) × 15	(20,	329,	15)
	11	MPool (1, 3), s: 2	(20,	164,	15)
	12	ReLU	(20,	164,	15)
	13	Conv (1, 20) × 20	(20,	145,	20)
	14	MPool (1, 10), s: 5	(20,	28,	20)
	15	ReLU	(20,	28,	20)
	16	MPool (1, 5), s: 3	(20,	8,	20)
	17	APool (1, 8), s: 1	(20,	1,	20)
	18	MPool (20, 1), s: 1	(1,	1,	20)
Classifier	19	Conv (1, 1) × 5	(1,	1,	5)
	20	Sigmoid	(1,	1,	5)
	21	Conv (1, 1) × 2	(1,	1,	2)
	22	Sigmoid	(1,	1,	2)
	23	Loss	(1,	1,	1)
		Total Number of Parameters:	7600		



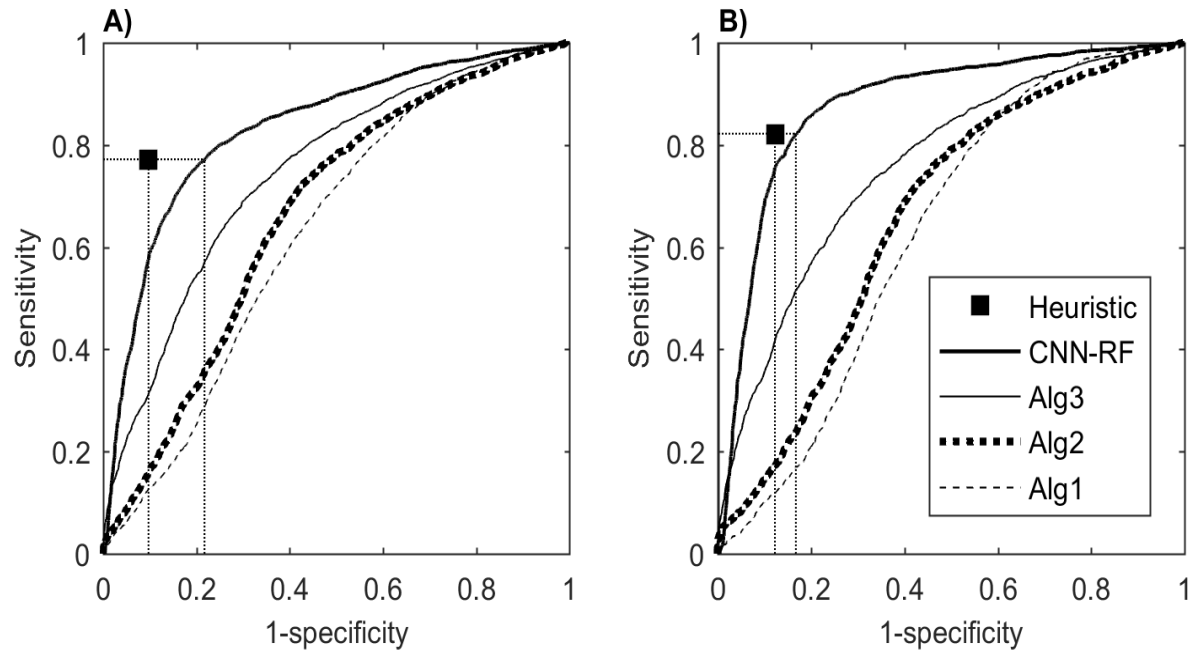
Using 39000 recordings of 48 Neonates (EMC Rotterdam)

X

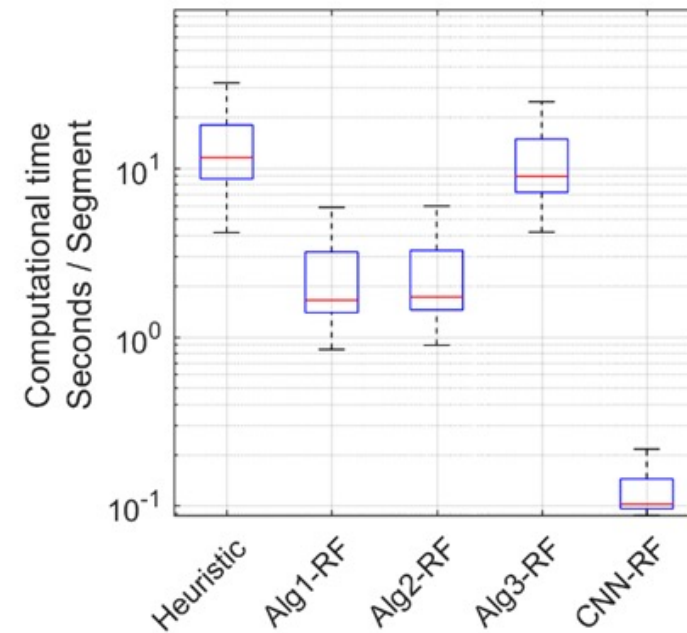
Seizure Detection: *Performance*



Results of the tested seizure detector: Heuristic, CNN, feature-based Alg 1-3.
A) all recordings, B) after excluding some recordings with unique pattern



Recall Speed of the tested seizure detectors:
Heuristic, CNN, feature-based Alg 1-3.



| EEG-fMRI data fusion

UZ Leuven Departments:

Radiology

Neurology

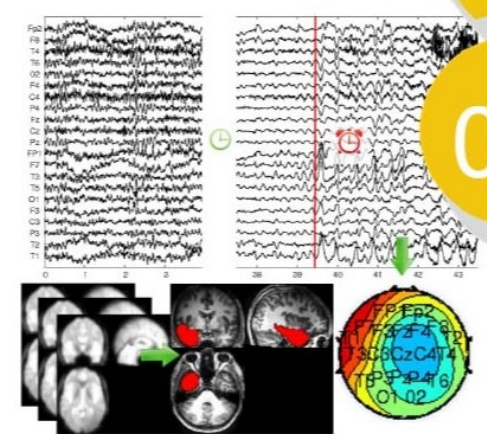
KU Leuven:

Dept. of Psychology

Dept. of Kinesiology and Rehabilitation Sciences

Oxford University:

Dept. of Engineering Science



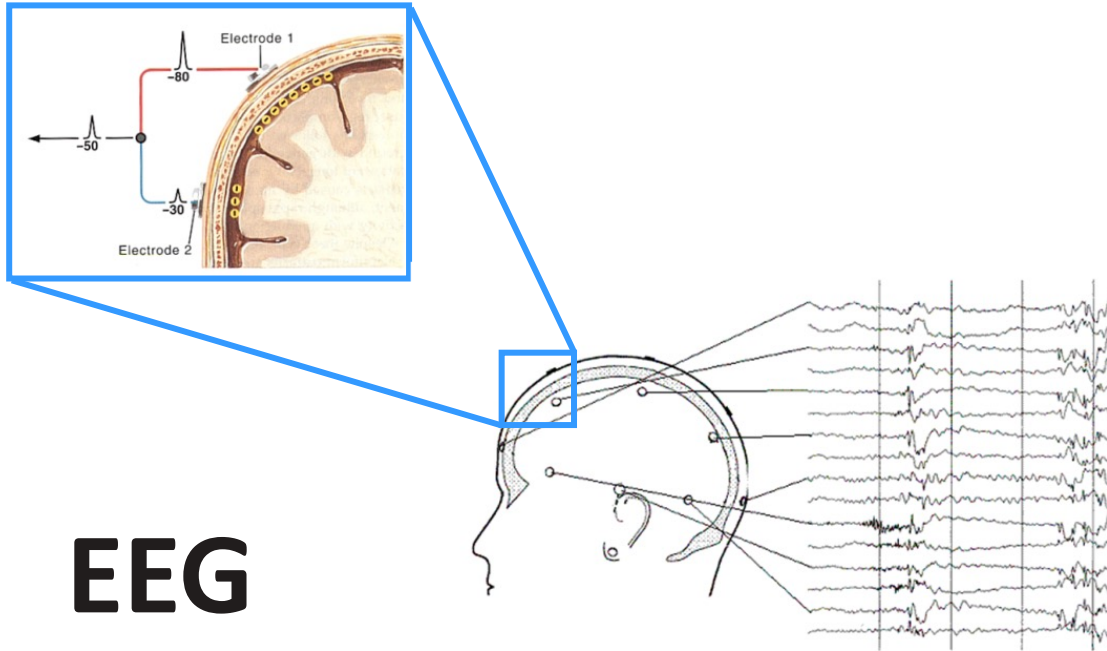
04.



EXAMPLE

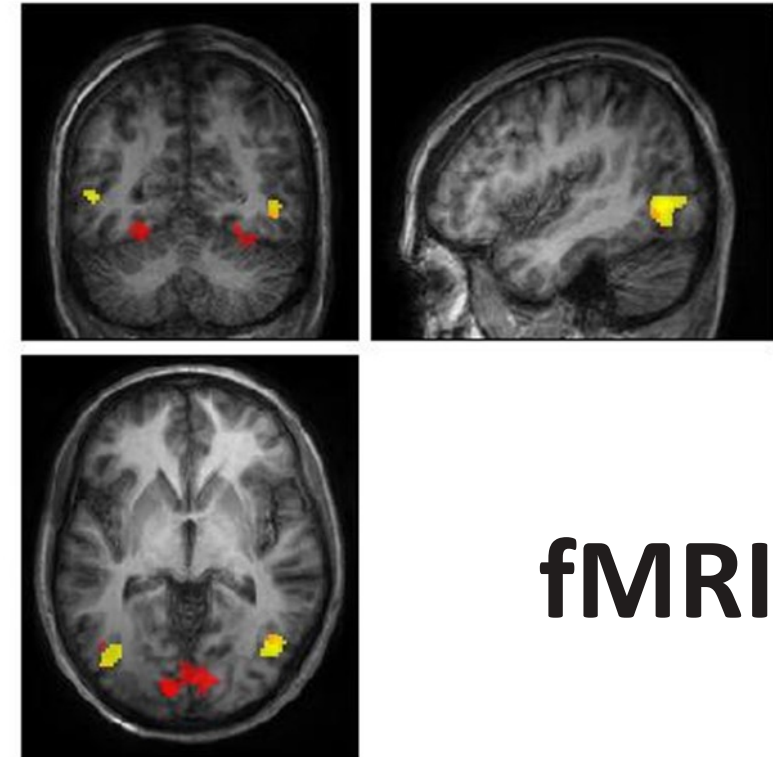
Combined EEG-fMRI analysis

EEG measures electrical potentials on the scalp



EEG

fMRI localizes active brain regions



fMRI

Combining EEG and fMRI:

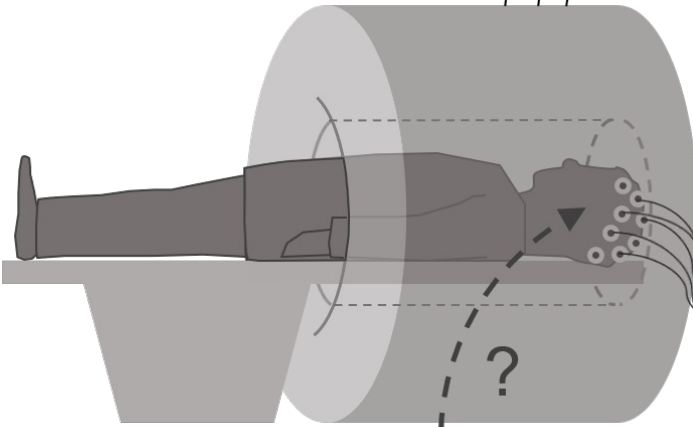
EEG good temporal resolution (~ ms)

fMRI good spatial resolution (~ mm)

Coupled MTF revealing neurovascular coupling localizes seizure onset

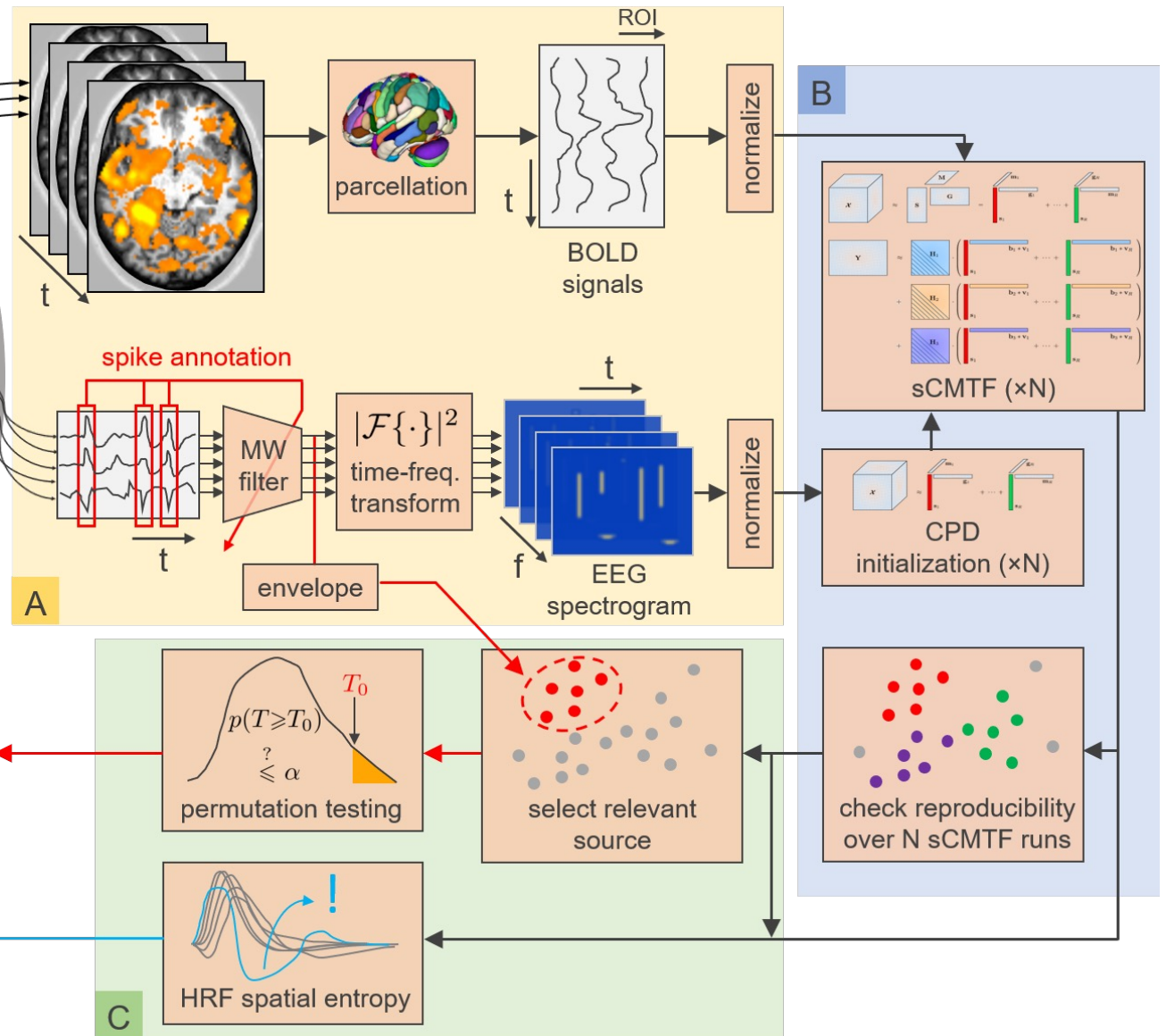
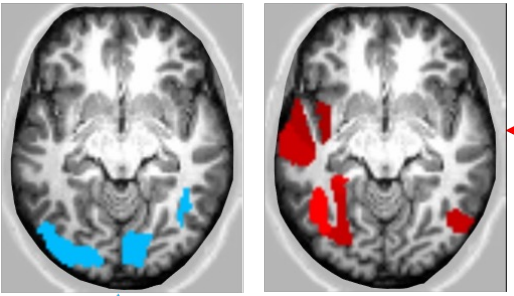
coupled matrix-tensor factorization:

mapping **interictal spikes**
+
neurovascular coupling



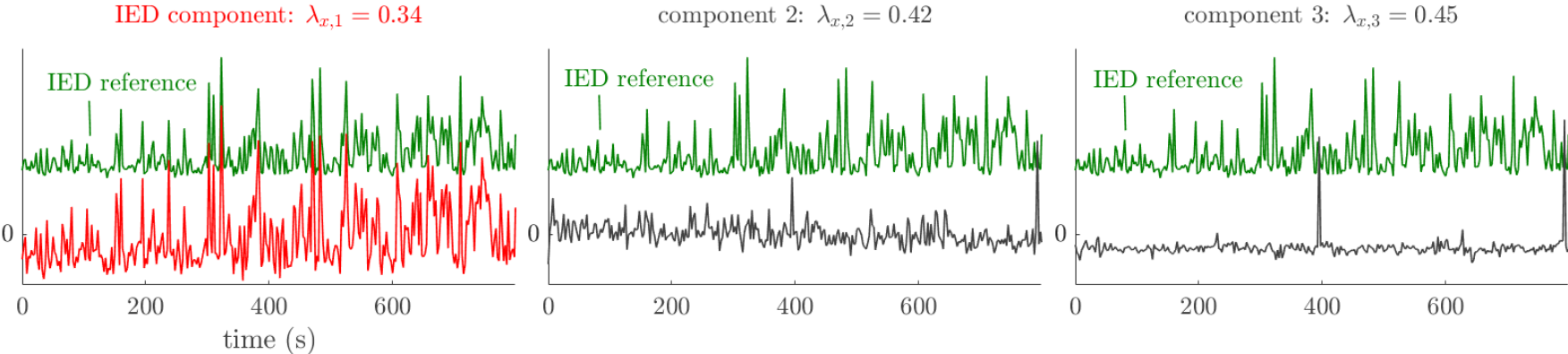
HRF entropy map

spike SnPM

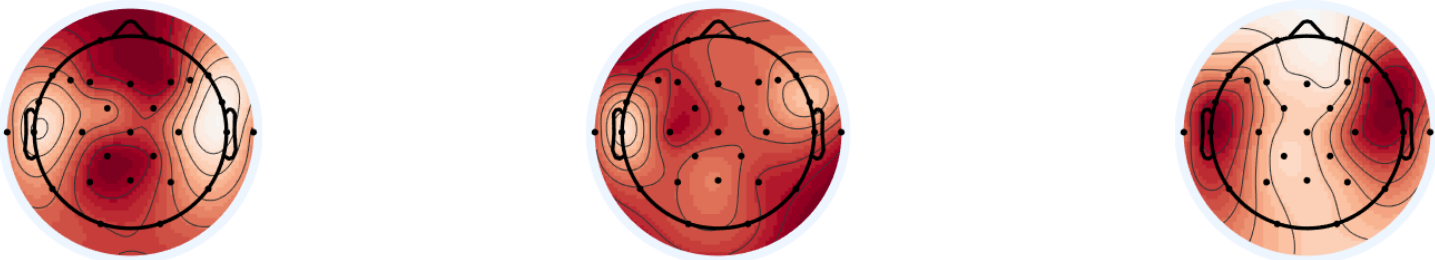


Low-rank models disentangle the EEG

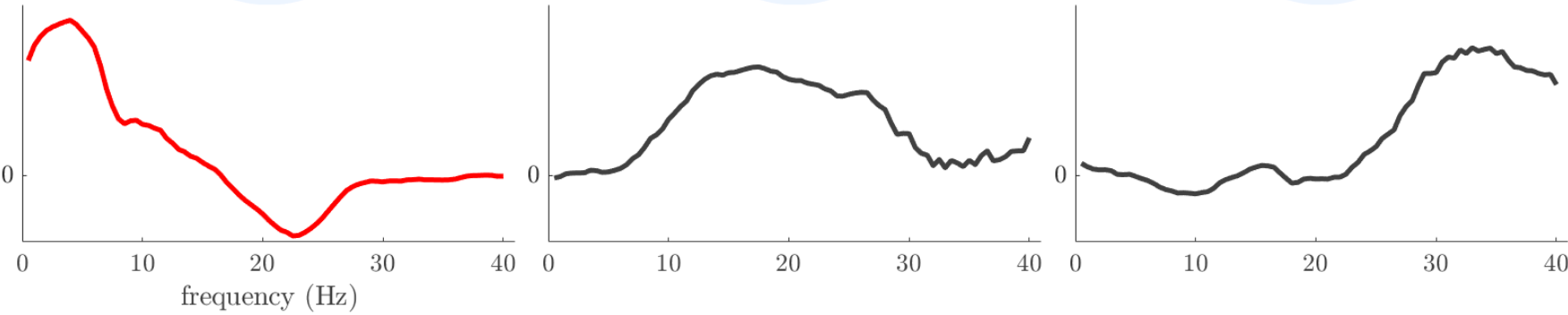
temporal



spatial



spectral



Wearable Health Monitoring

UZ Leuven departments:

Cardiology

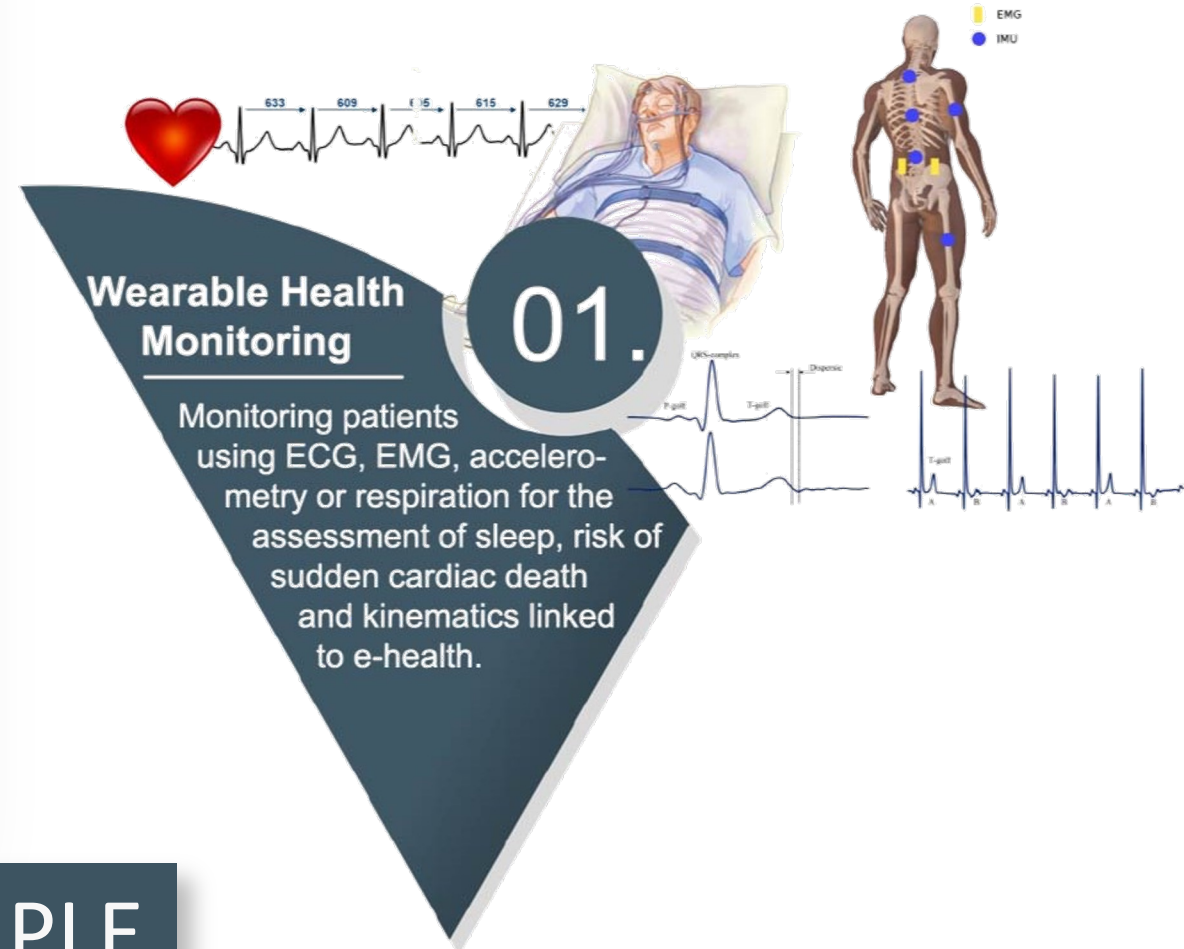
Neurology

Pneumology

Rheumatology

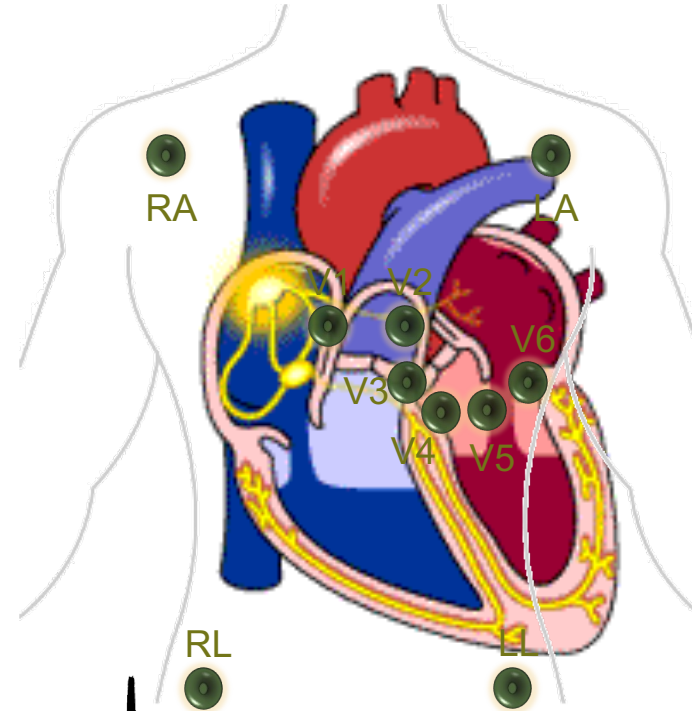
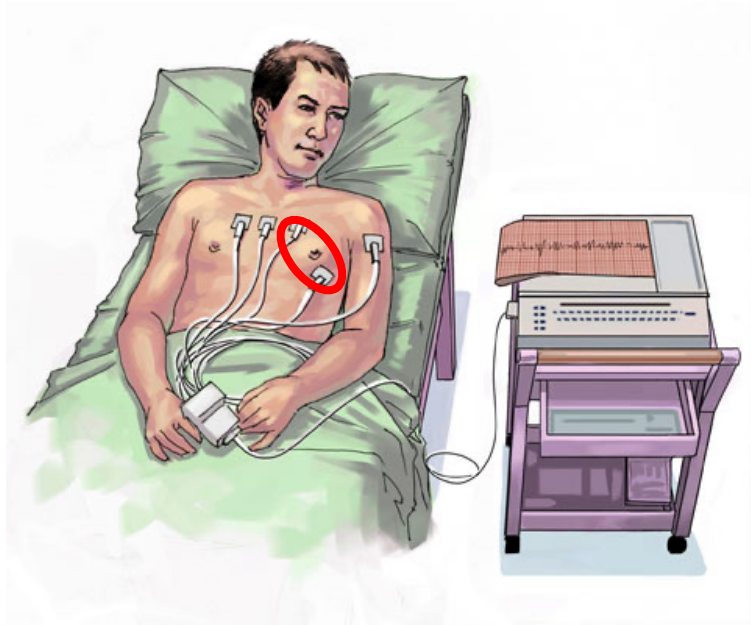
Pulderbos Revalidation Center

EXAMPLE

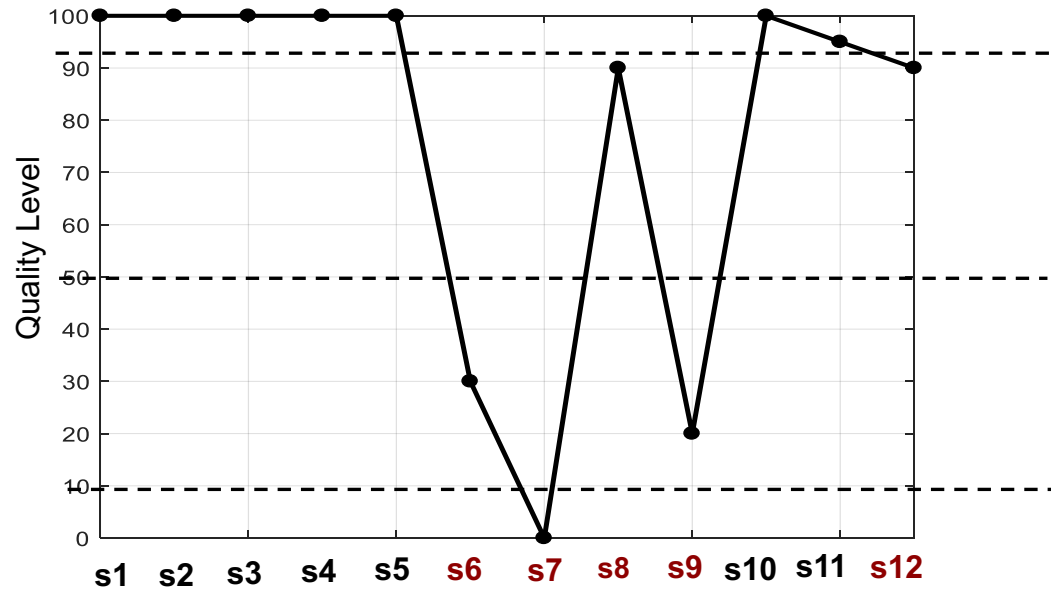
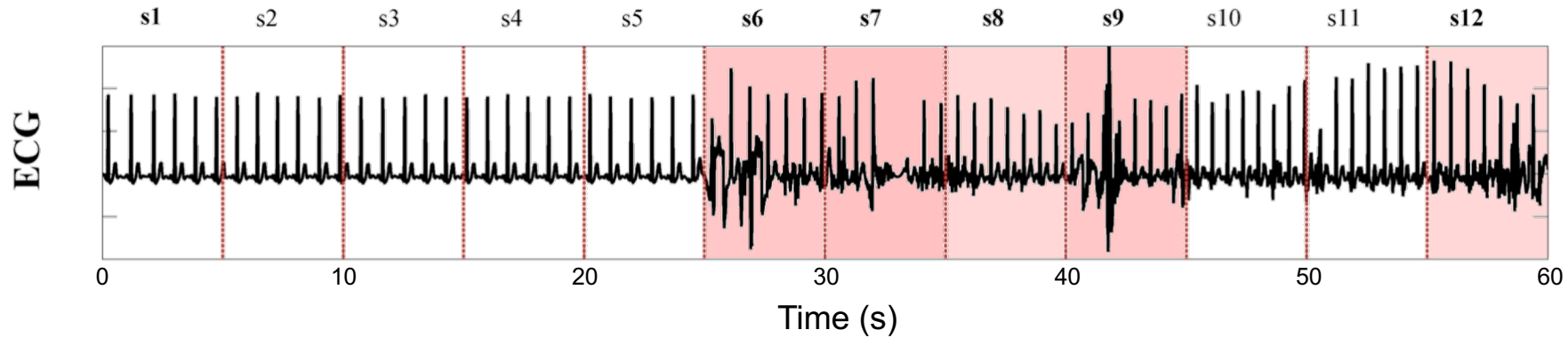


Introduction:THE ECG

Electrocardiogram (ECG)



ECG quality indication using supervised ML



Creation of an annotated ECG dataset

3 different recording systems

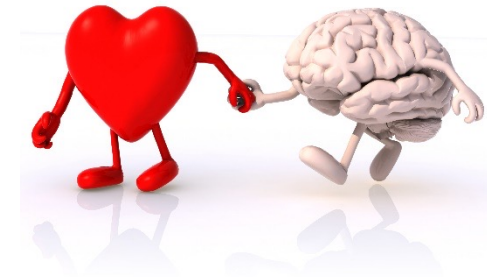
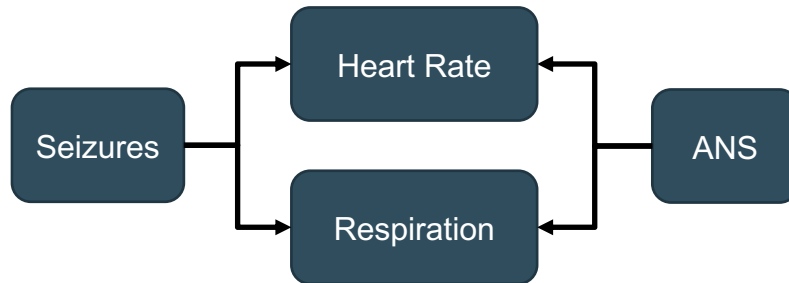
Continuous ECG Quality Index

Accuracy of about 99% in the detection of noisy segments

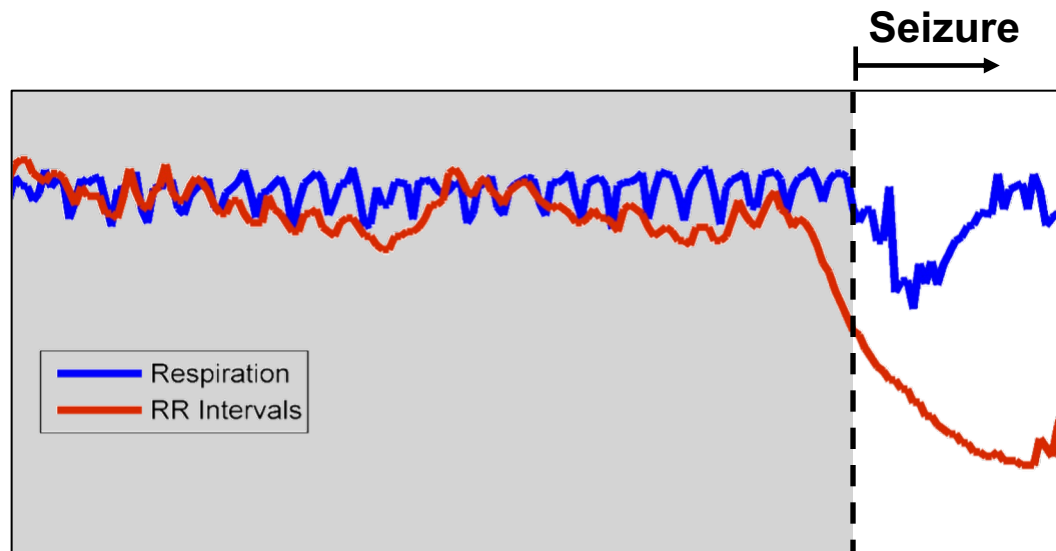
Easy to implement
LOW
Computational load

Epileptic seizure detectors based on ECG

Seizures and the autonomic nervous system (ANS)



Goal: Detect cardiac and respiratory changes caused by seizures



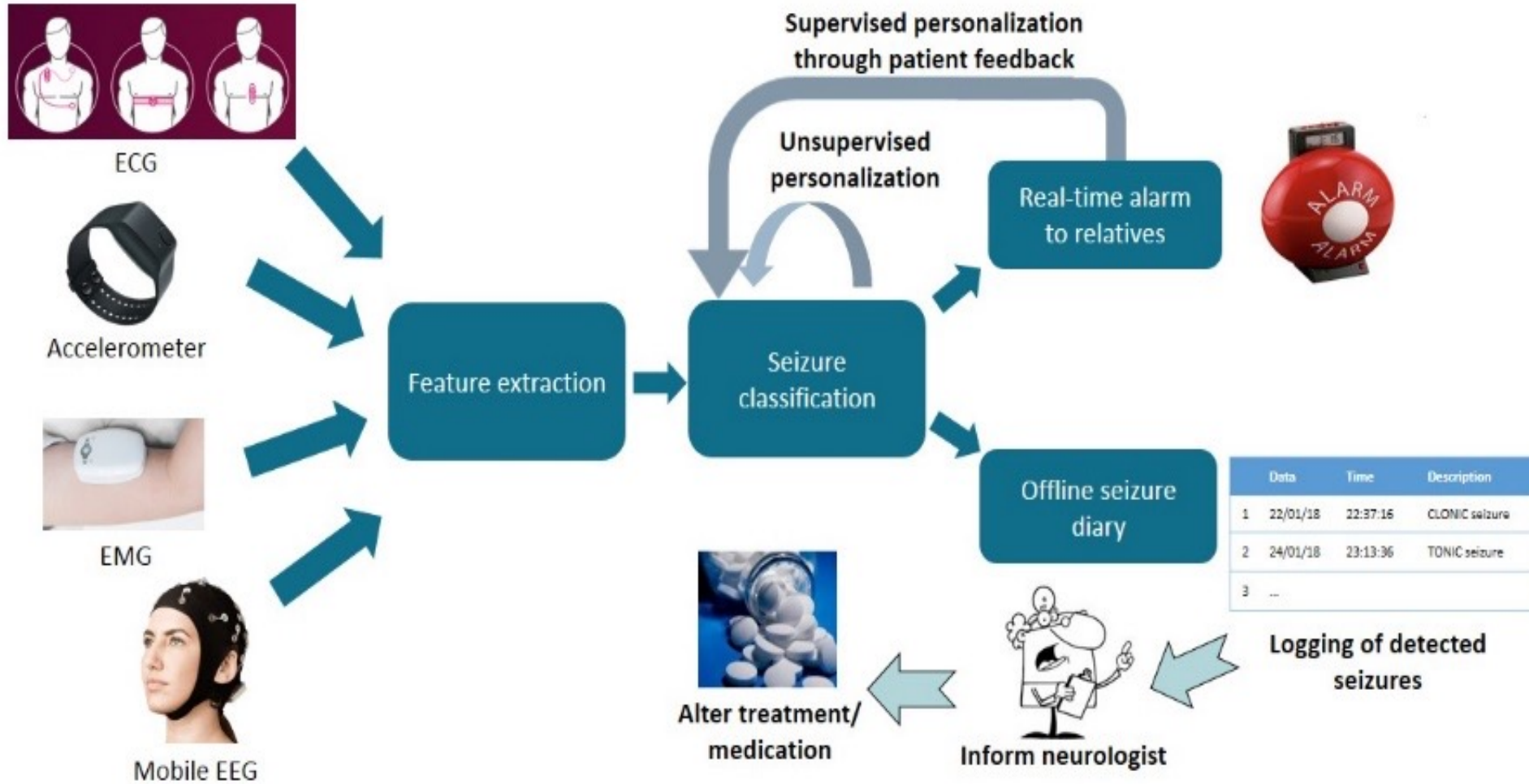
Seizures

- ✓ Pre-ictal changes
- ✓ Autonomic symptoms
- ✓ Motor activity
- ✓ Stress response
- ✓ Apnea episodes
- ✓ Reduced HRV
- ✓ Tachycardia or bradycardia

Varon C., Caicedo A., Testelmans D., Buyse B., Van Huffel S., A novel algorithm for the automatic detection of sleep apnea from single-lead ECG, *IEEE Transactions on Biomedical Engineering*, vol. 62, no. 9, Sep. 2015, pp. 2269-2278.

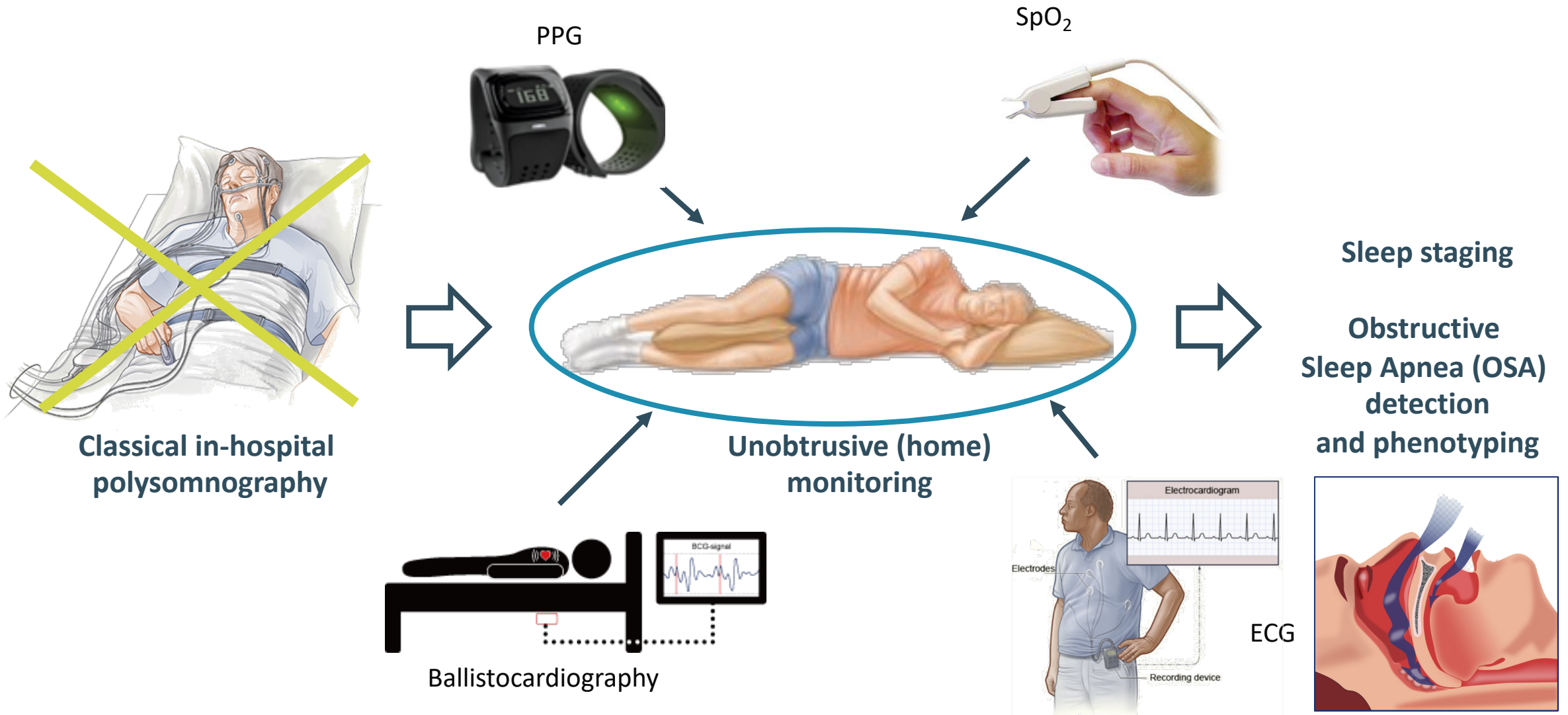
De Cooman T., Varon C., Hunyadi B., Van Paesschen W., Lagae L., Van Huffel S., Online Automated Seizure Detection In Temporal Lobe Epilepsy Patients Using Single-Lead ECG, *International Journal Of Neural Systems*, vol. 27, No. 7, Mar. 2017, pp. 1750022

Automated real-time seizure detection @ home



SeizelT prototype

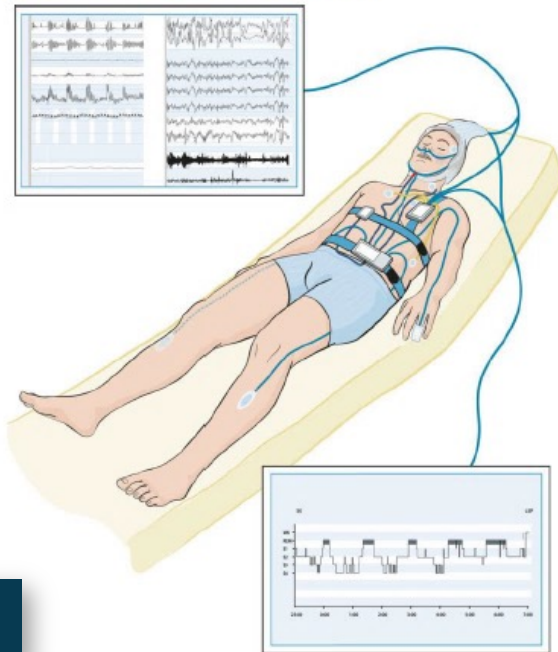
Sleep Monitoring @ home



Current situation

- Prevalence 6-33 % and increasing
- Clinical diagnosis
 - ☺ Highly accurate
 - ☹ Expertise required
 - ☹ Extensive equipment
 - ☹ Uncomfortable
 - ☹ Single night

→ Patients remain undiagnosed

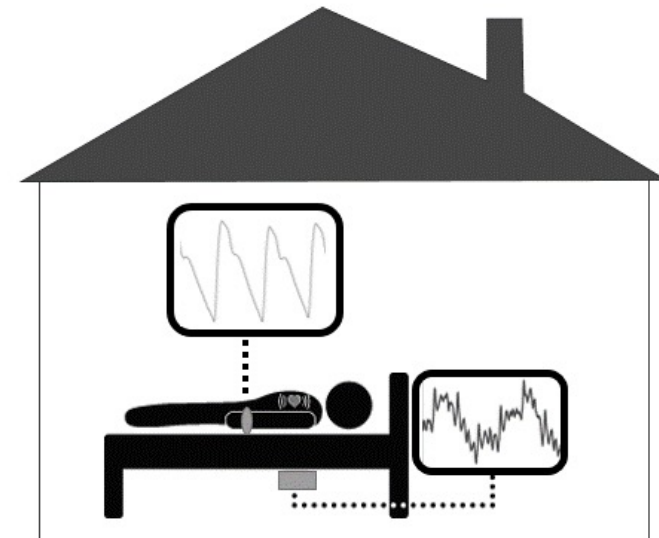


Goal

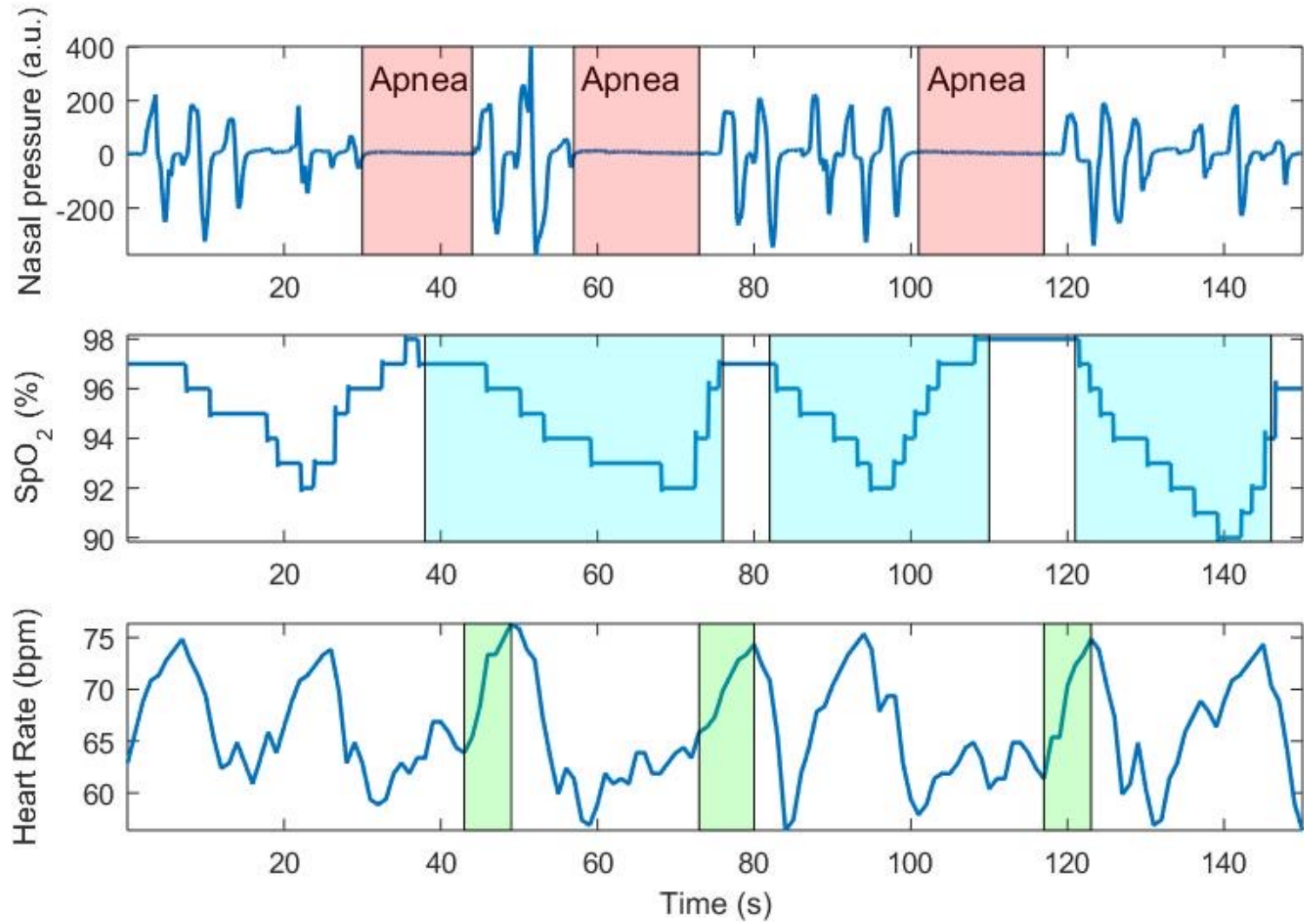
- Comfortable “unobtrusive” sensors
- Multiple nights
 - ☺ Captures normal sleeping pattern
 - ☺ Allows large scale monitoring

Unobtrusive sensors

- ☹ Lower quality
- ☹ Timing issues with other sensors



Sleep Apnea Detection



Cessation of breathing



Oxygen desaturation

Autonomic arousal

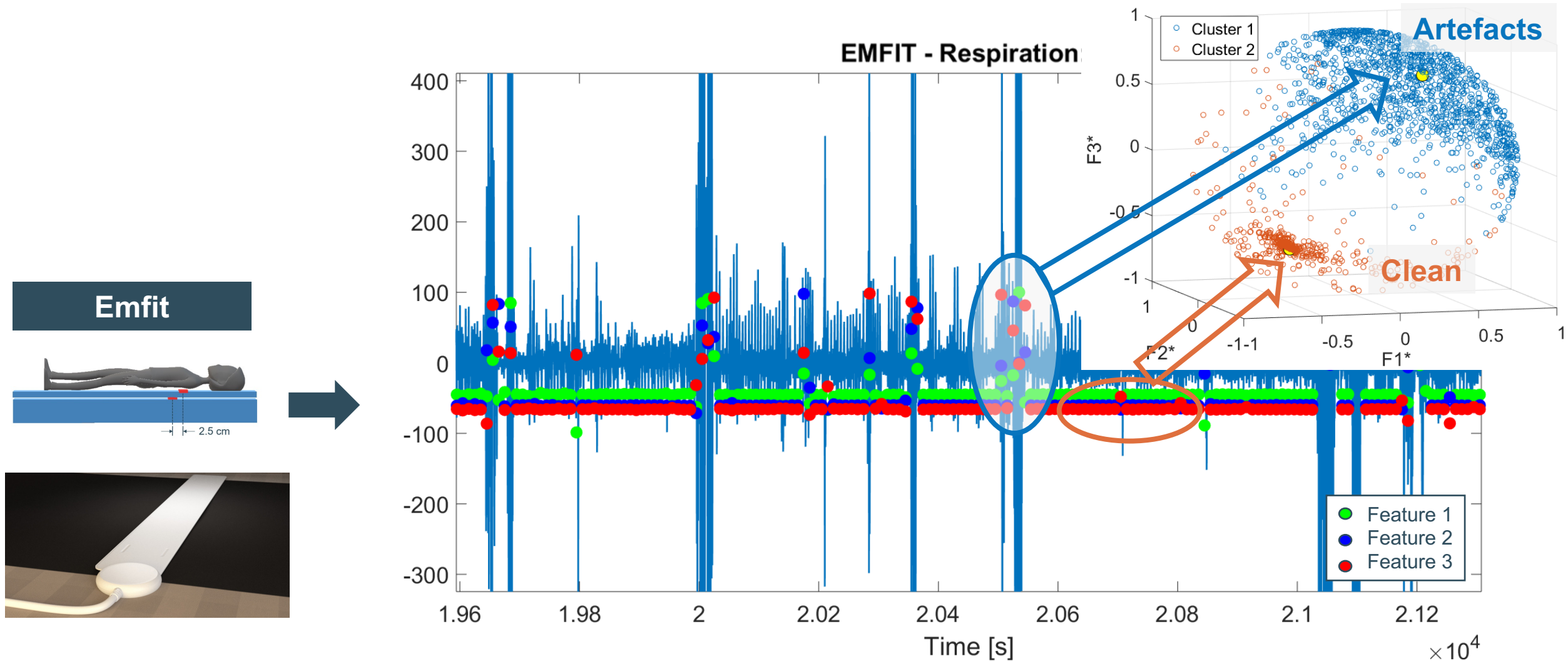
Apnea Hypopnea Index (AHI)

Apnea breathing stop
Hypopnea breathing reduction

Severity of sleep apnea ~ **AHI** =
$$\frac{\# \text{ (Hypo)Apneas}}{\text{Hours of sleep}}$$

No apnea	AHI < 5		No sleep apnea
Mild apnea	5 ≤ AHI < 15 + symptoms		
Moderate apnea	15 ≤ AHI < 30		Sleep apnea
Severe apnea	AHI ≥ 30		

Automated artefact detection in the novel Emfit sensor

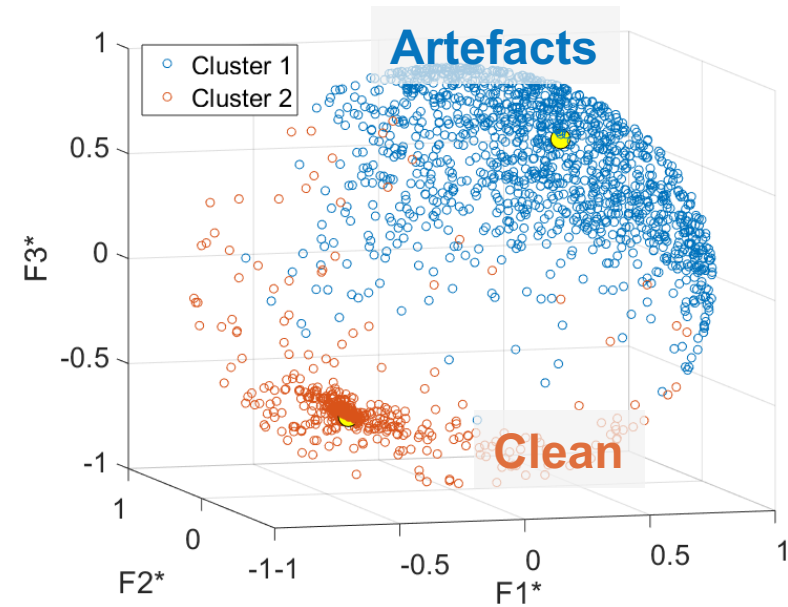


Contribution

- ✓ Artefacts detected automatically in a novel sensor w/o labeling

1. 2. 3.

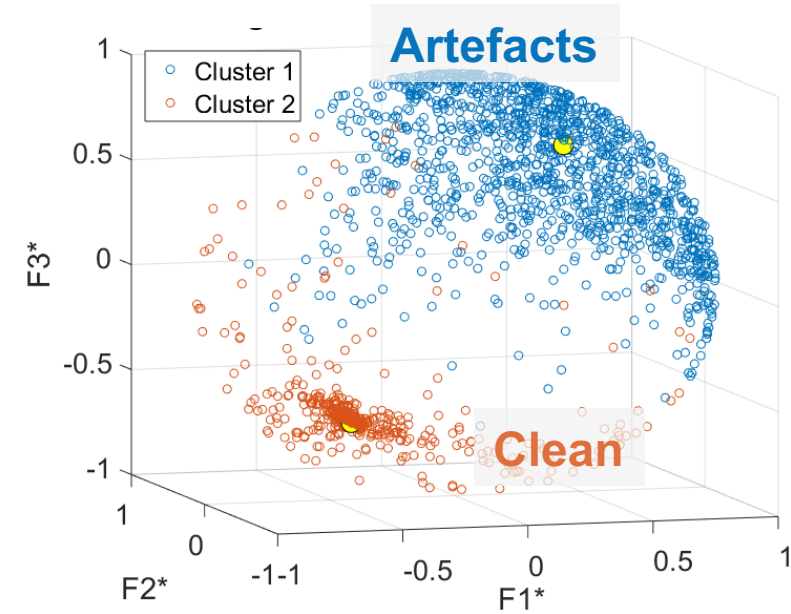
Identification of patients with OSA based on Emfit



Hypothesis

Emfit data of OSA patients contains more artefacts

Identification of patients with OSA based on Emfit

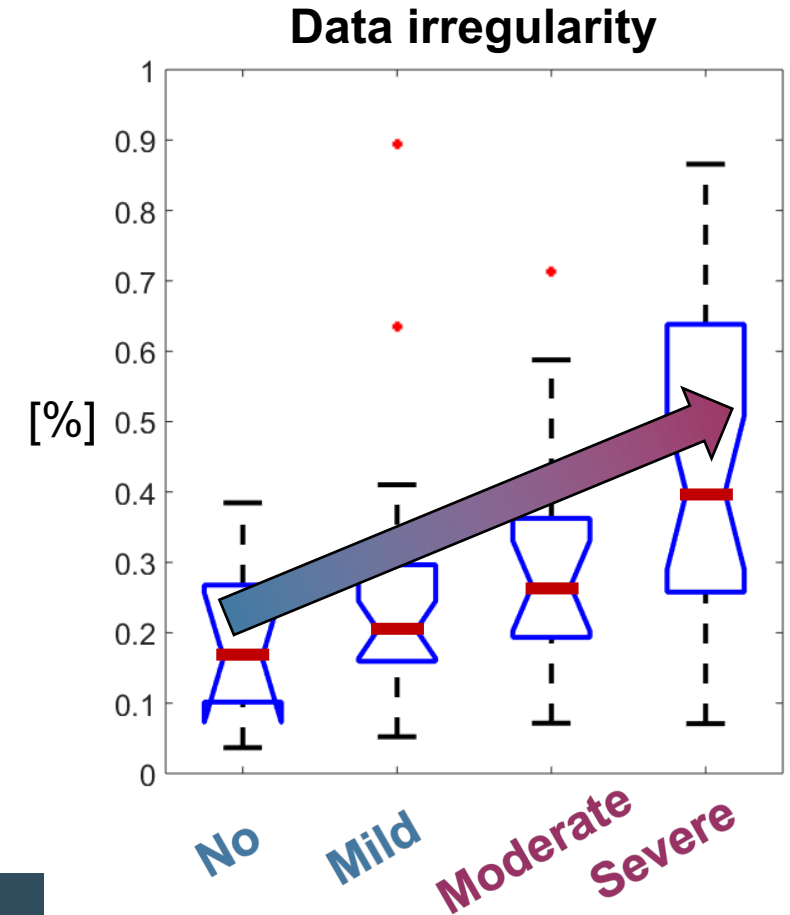


Hypothesis

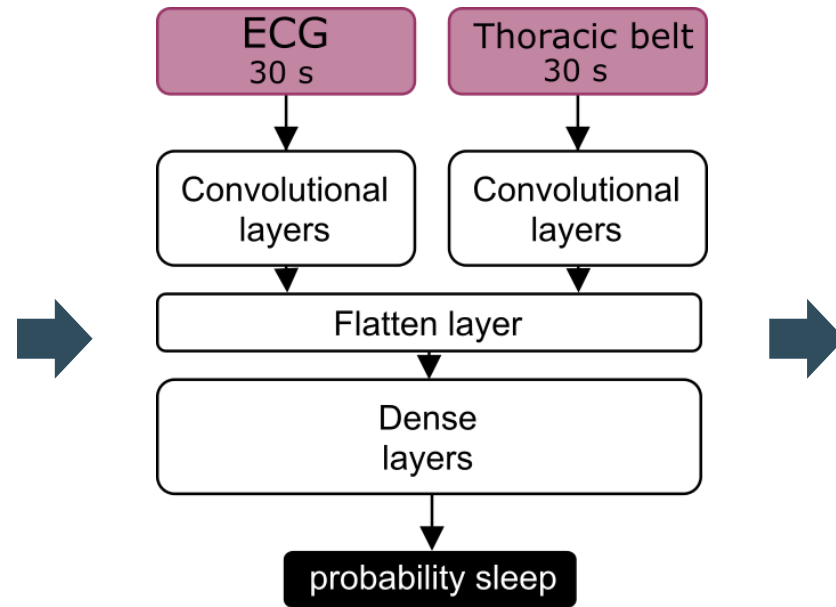
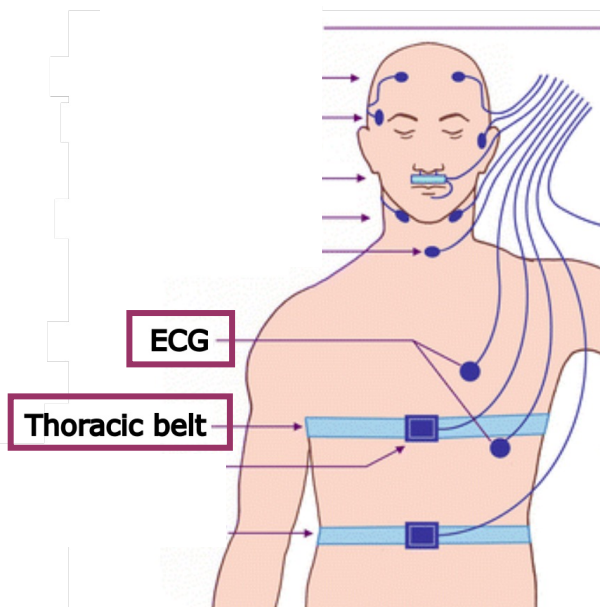
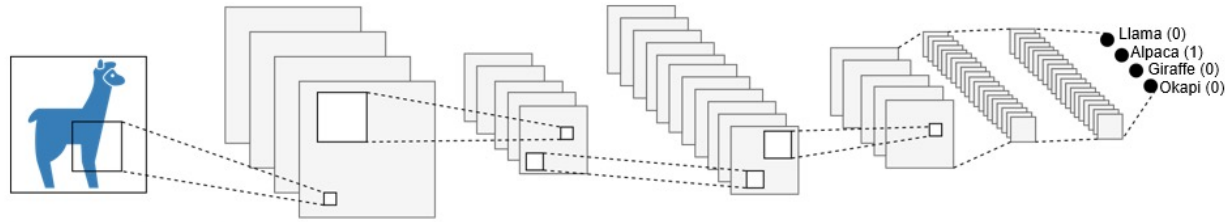
Emfit data of OSA patients contains more artefacts

Contribution

- ✓ Data irregularity as a marker for OSA
- ✓ Detection of OSA patients



Detection of sleep in OSA patients based on ECG and thoracic belt



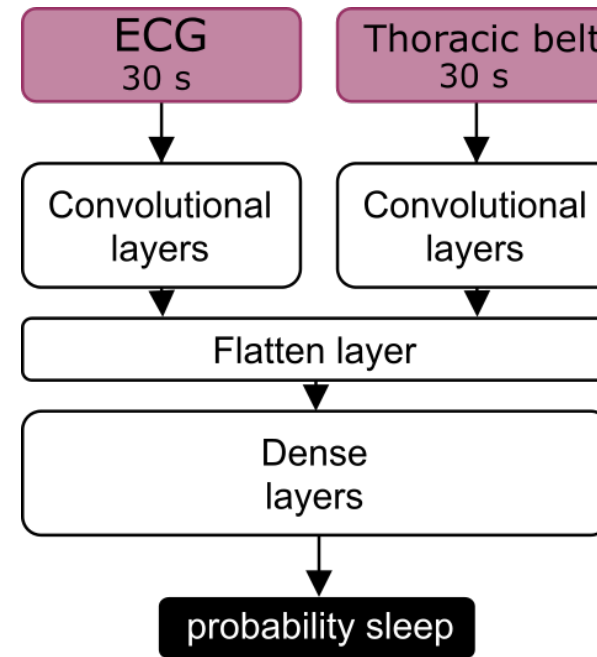
Contribution

- ✓ Sleep time estimation comparable to literature
- ✓ Short independent windows account for data loss and artefacts
↔ literature: long range features

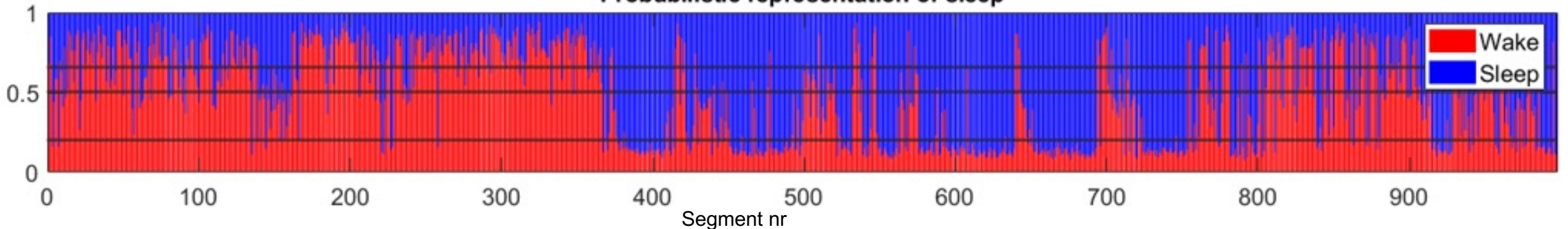
Identification of OSA patients based on ECG and thoracic belt

Hypothesis

- More uncertainty predictions in OSA patients
- More awakenings predicted in OSA patients



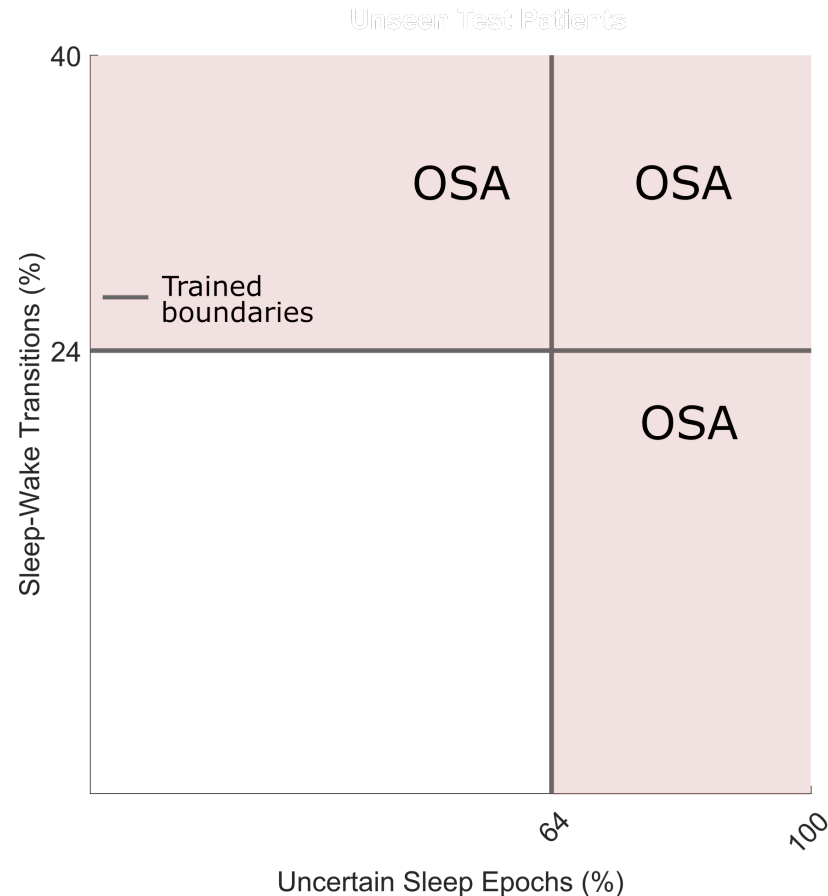
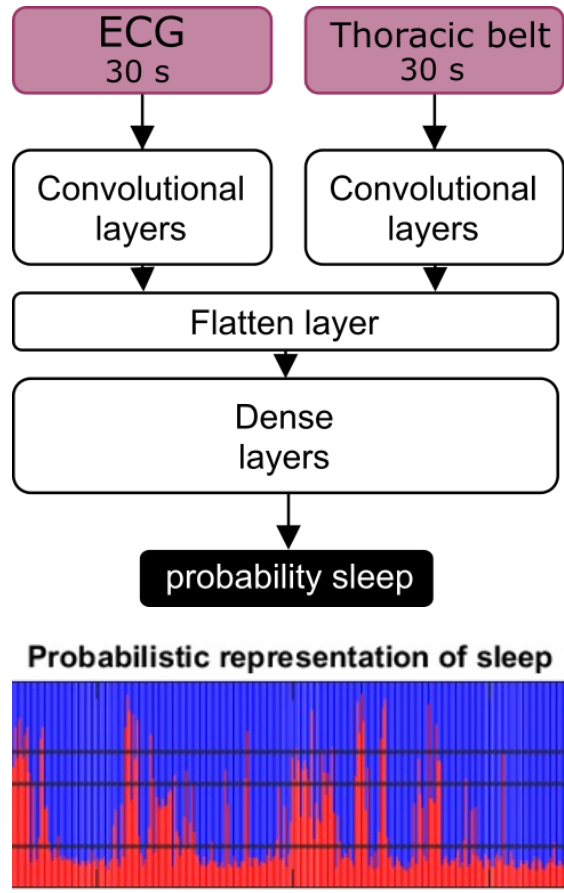
Probabilistic representation of sleep



Identification of OSA patients based on ECG and thoracic belt

Hypothesis

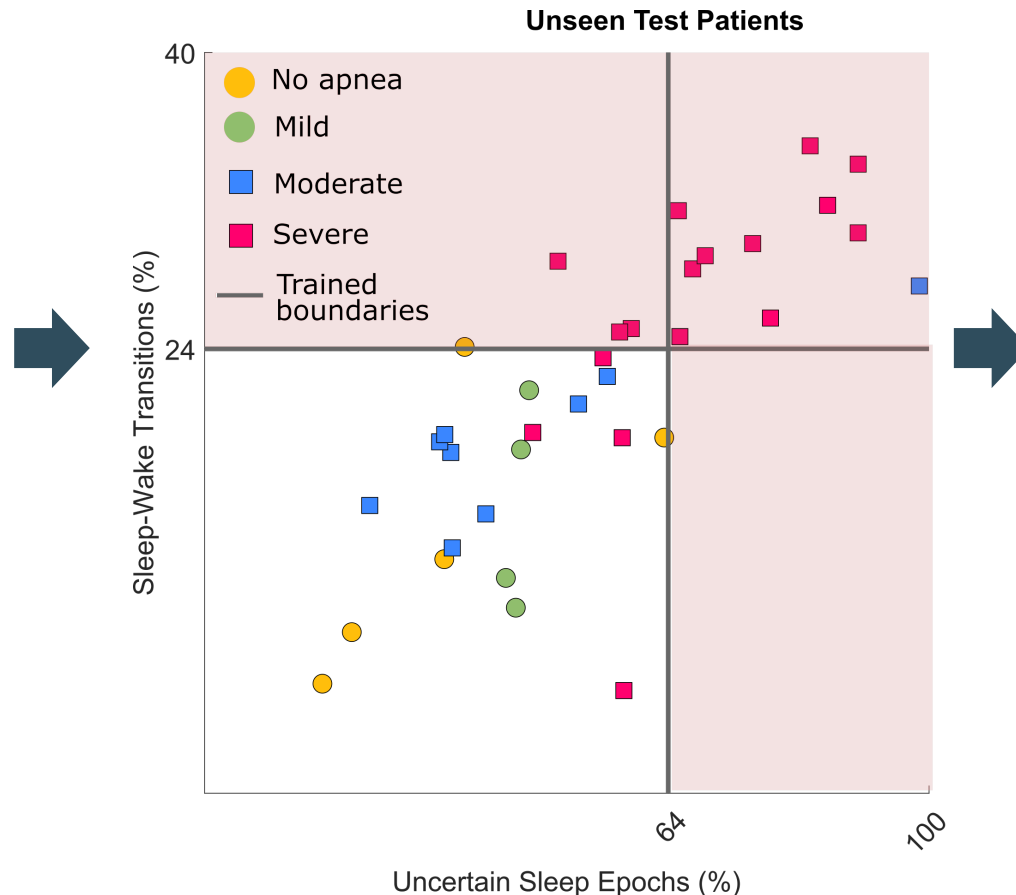
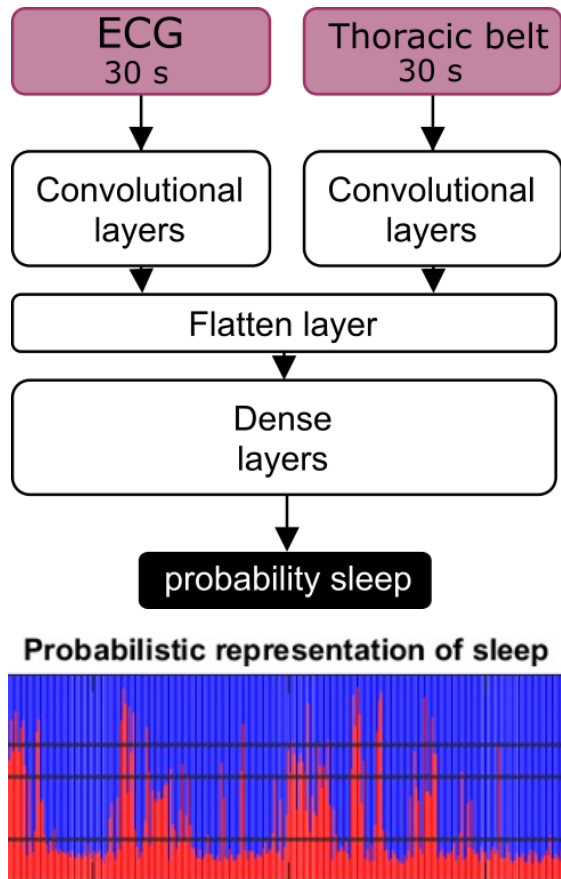
- More uncertainty predictions in OSA patients
- More awakenings predicted in OSA patients



Identification of OSA patients based on ECG and thoracic belt

Hypothesis

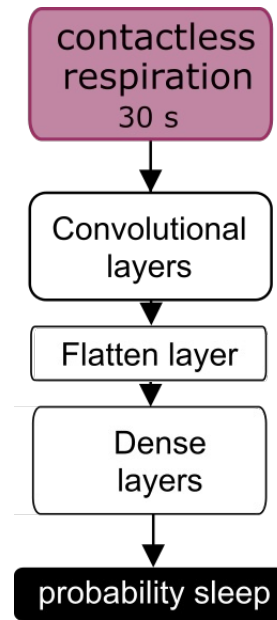
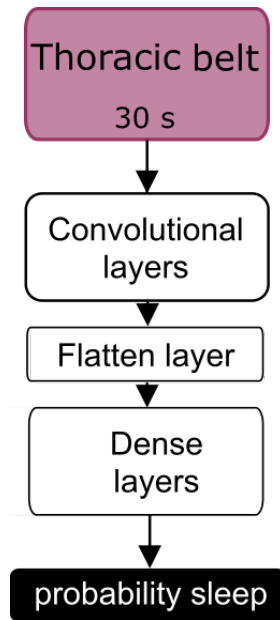
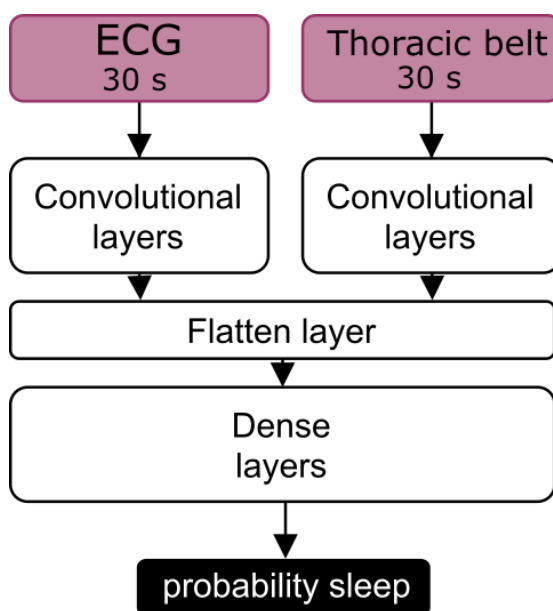
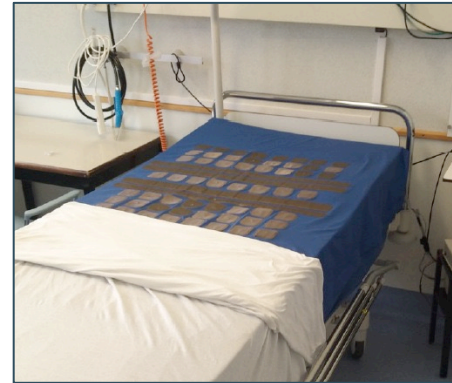
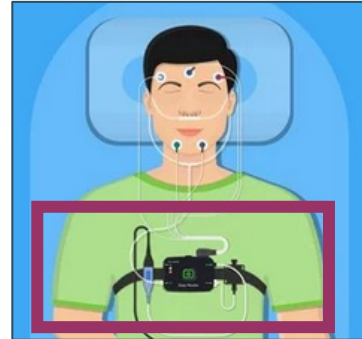
- More uncertainty predictions in OSA patients
- More awakenings predicted in OSA patients



Contribution

- ✓ Transformation of uncertainty into useful information
- ✓ Interpretable graph
- ✓ Detection of severe OSA patients
→ Refined methods for mild patients

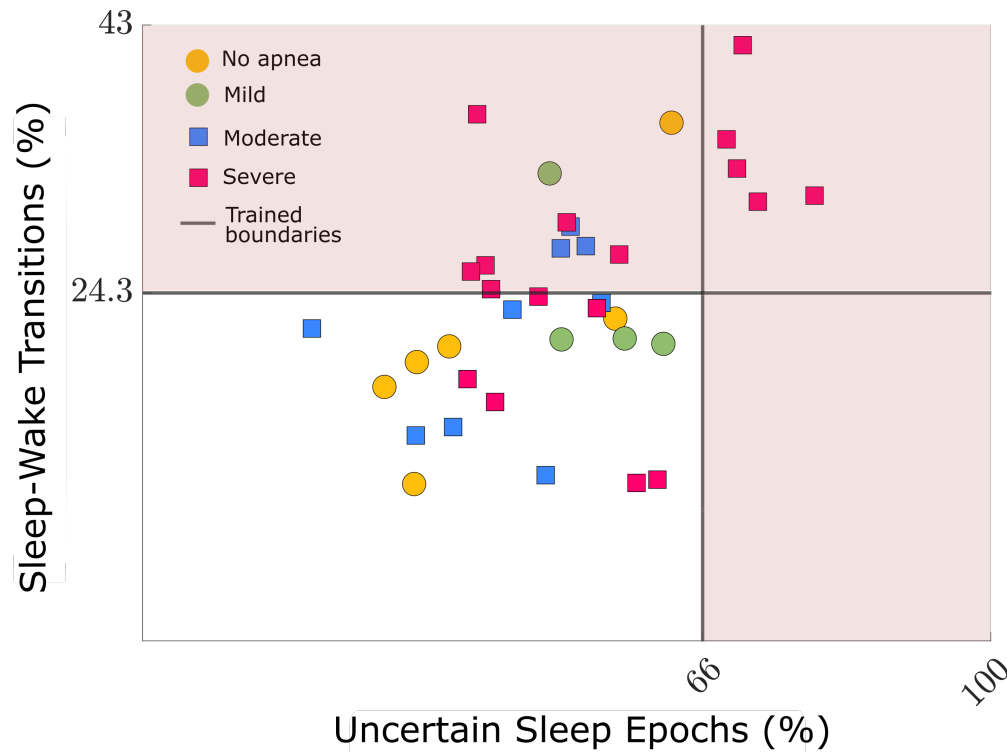
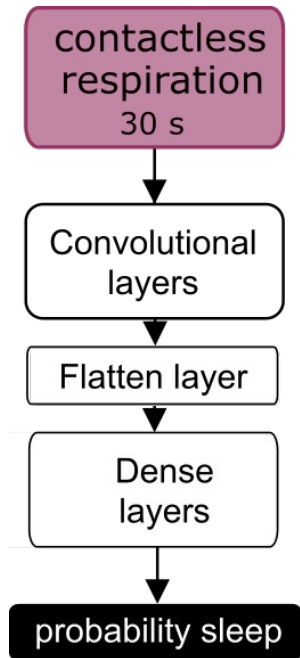
Detection of sleep in OSA patients based on contactless ECG & respiration



Contribution

- ✓ Sleep time based on contactless respiration

Identification of patients with OSA based on contactless ECG and contactless respiration



Contribution

- ✓ Detection of severe OSA patients using only contactless respiration
- ➔ Prioritization for treatment

Contents Overview



1. Introduction

- Smart Patient Monitoring
- Research Group Overview
- Blind Source Separation
- Tensor Decompositions



2. Examples



3. Future Challenges

Smart Patient Monitoring: *Future Challenges*

How to bridge the gap to clinical practice?

- **Hardware:** equipment, sensors, ...
→ *wearable, unobtrusive, contactless, invisible*
- **Software:** long-term monitoring, (multiple) modalities
→ *low-quality data, 24/7 days reliability, big data*
- **Validation studies:** long-term followup, GDPR regulations
→ *patient data labeling uncertain & labor-intensive*
- **Training:** learning platform, (online) courses, interdisciplinary
→ *new Ba/Ma programmes in Medicine and BME*
- **Tech transfer to market in medical technology tough job !**
→ *models, many stakeholders*
ethical and legal Non-trivial business issues, hyper-regulated → CE/FDA approval
small niche market: societal value > economical value



Acknowledgments



- | University Hospitals Leuven Gasthuisberg
- | ZNA Middelheim, Queen Paola Children's hospital
- | UMC Utrecht & EMC Rotterdam
- | Eindhoven University of Technology



European Research Council
Established by the European Commission



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