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European Research Council

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iMinds

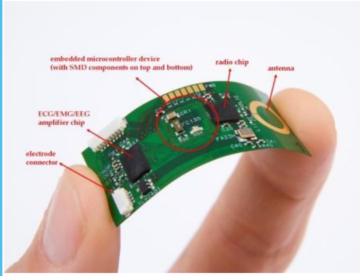
Medical Information Technologies Department

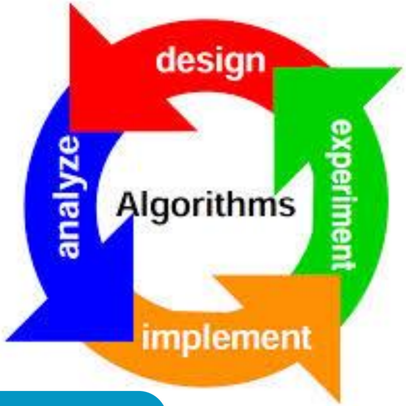
Smart Diagnostics: Applications and Future Challenges

Wetenschapsdag Faculteit Geneeskunde
Universiteit Gent, BE
March 16, 2016

Prof. Sabine Van Huffel

- Personalized: "customized" diagnosis and treatment
- Preventive: prevention is always better than curation, tailored to the individual patient
- Predictive: precise predictions with modern technology, determine risk profiles, predict progression and outcome
- Participatory: correct and complete information for the patient to participate in the decision process





Brain monitoring for neurological dise

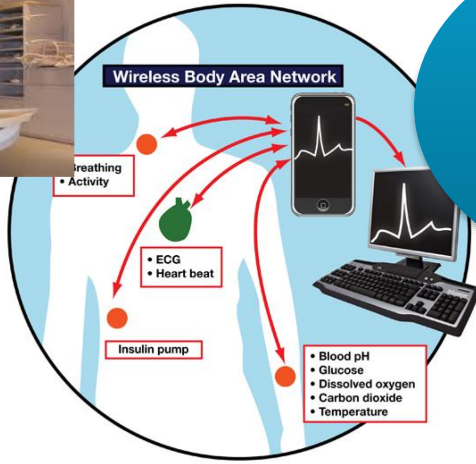
Algorithms (Technology)

Vital signs monitoring: sleep, stress, cardio risk stratification

Sensors (Carriers)

Pathologies (Applications)

Oncology: cancer diagnosis and prognosis



Smart Diagnostics

Chronic disease management & telemonitoring application

Hospital of the FUTURE

Knack,21.10.2015

Move healthcare away from hospitals to HOME environment

- UNOBTRUSIVE
- MULTIMODAL
- LONG-TERM

Challenges:
- ARTEFACTS
- BIG DATA
- AUTOMATED

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Current research

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Metabolite quantification & brain tumor tissue typing using Magnetic Resonance Spectroscopic Imaging;

Smart patient monitoring (sleep, epilepsy, sudden cardiac death, stress);

Neonatal brain monitoring using EEG and Near-Infrared Spectroscopy;

Cardiorespiratory dynamics and heart-rate variability analysis,

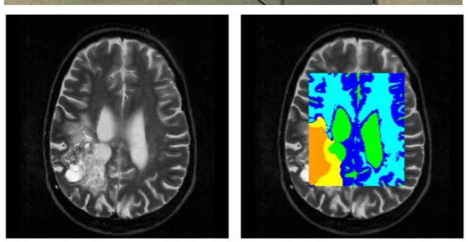
Cognitive brain functioning and seizure zone localization using EEG and functional MR Imaging

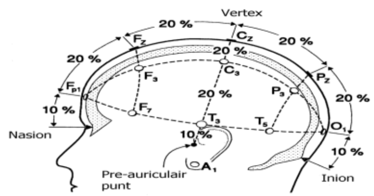
Decision support systems for medical diagnosis based on clinical data,

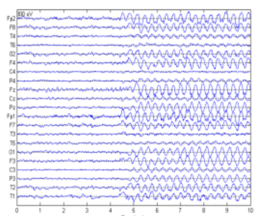
EEG-based auditory attention detection for hearing prostheses (Bertrand)

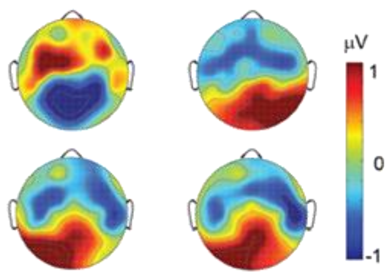
Distributed signal processing algorithms for body area networks and EEG sensor networks (Bertrand)

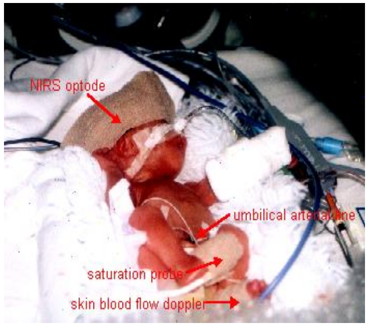
Distributed spike sorting algorithms for next-generation high-density neuroprobes (Bertrand)

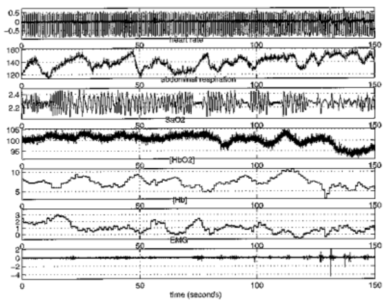


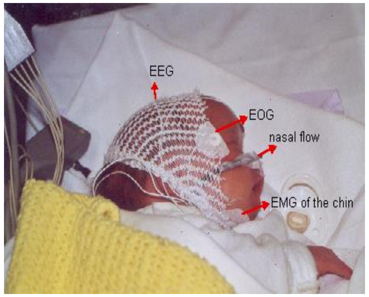












STADIUS
Center for Dynamical Systems, Signal Processing and Data Analytics

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KEYTOOL : Blind source separation

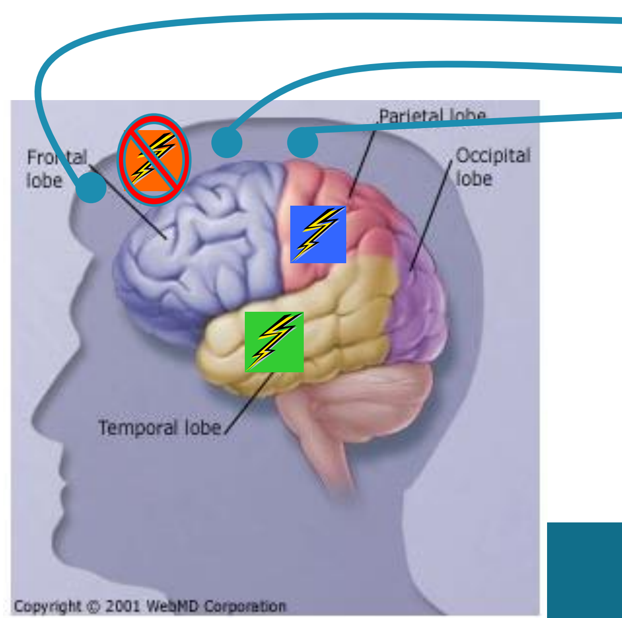
Signal analysis difficult because of artefacts → REMOVE

Matrix based Blind Source Separation (BSS)

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

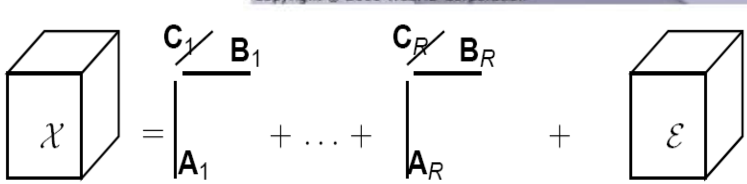
TENSOR based BSS: unique under mild conditions

ADD extra problem-specific constraints (nonnegative, sparse)



$$\mathrm{EEG}_1 = a_{11}\mathbf{s_1} + a_{12}\mathbf{s_2} + a_{13}\mathbf{s_3}$$
$$\mathrm{EEG}_2 = a_{21}\mathbf{s_1} + a_{22}\mathbf{s_2} + a_{23}\mathbf{s_3}$$
$$\mathrm{EEG}_3 = a_{31}\mathbf{s_1} + a_{32}\mathbf{s_2} + a_{33}\mathbf{s_3}$$

EEG = A ? S^T ?



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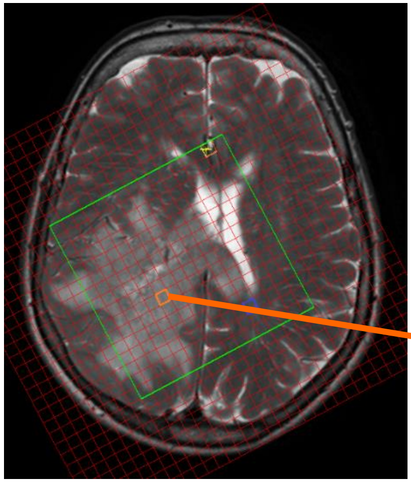
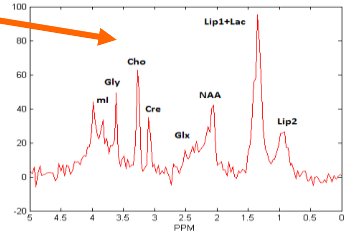
Unsupervised tissue type differentiation: Blind Source Separation for MRSI data



MRSI

$\boldsymbol{X}$ = matrix of spectra, $\boldsymbol{X} \approx \boldsymbol{W}\,\boldsymbol{H}$

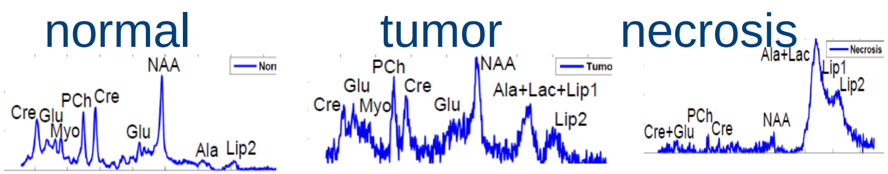


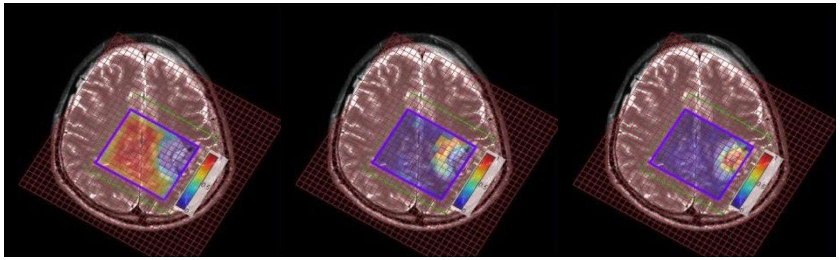
min || $\boldsymbol{X} - \boldsymbol{W}\boldsymbol{H}$ ||
such that $\boldsymbol{W} \geq 0, \boldsymbol{H} \geq 0$

non-negative matrix/tensor factorization

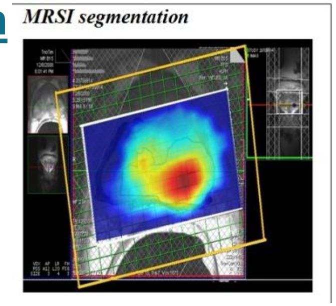
Applications

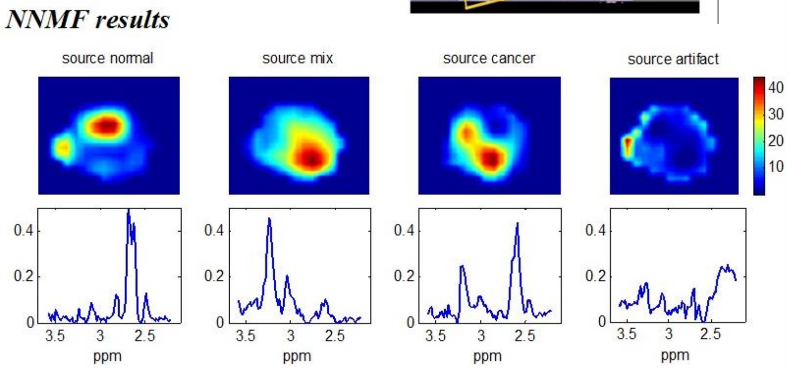
Brain tumor tissue typing





Prostate segmentation





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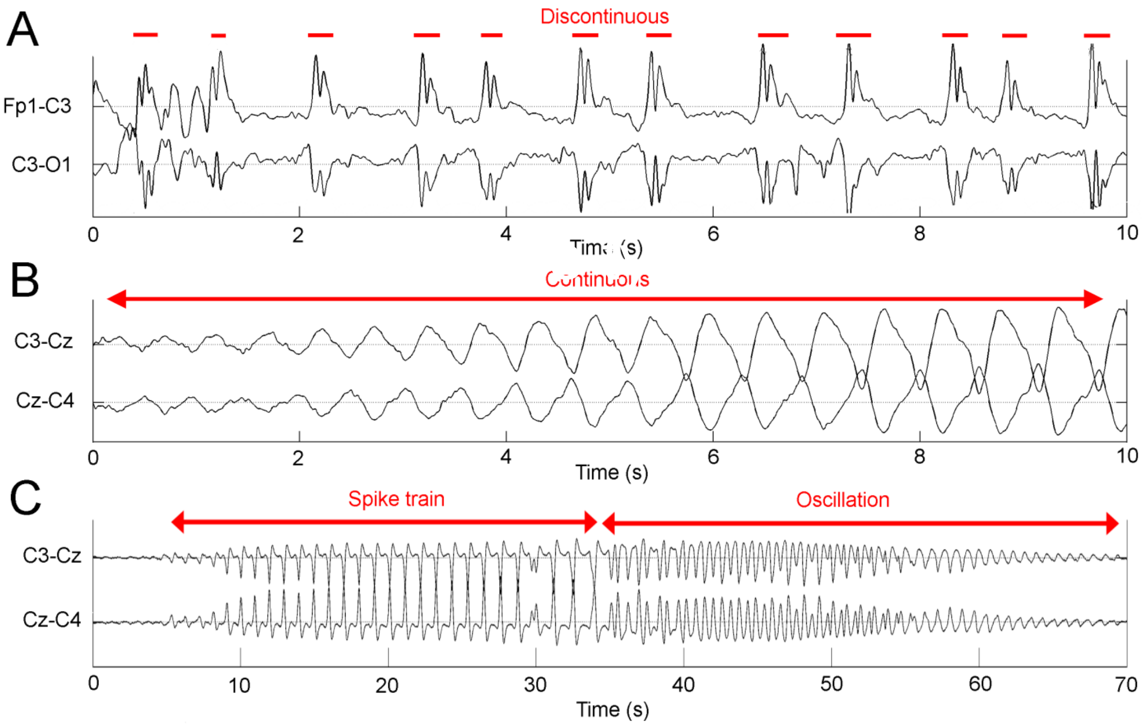
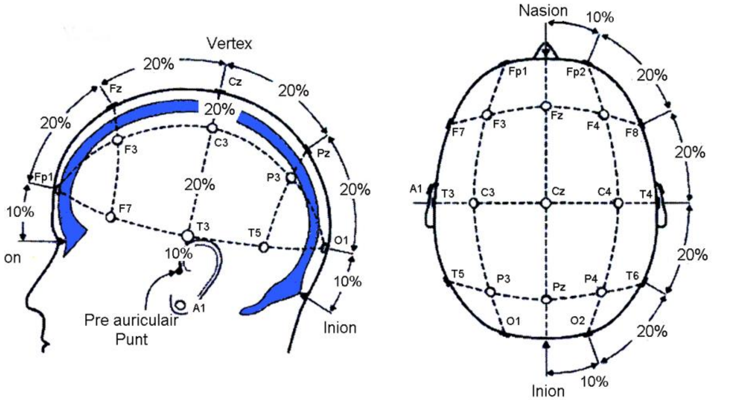
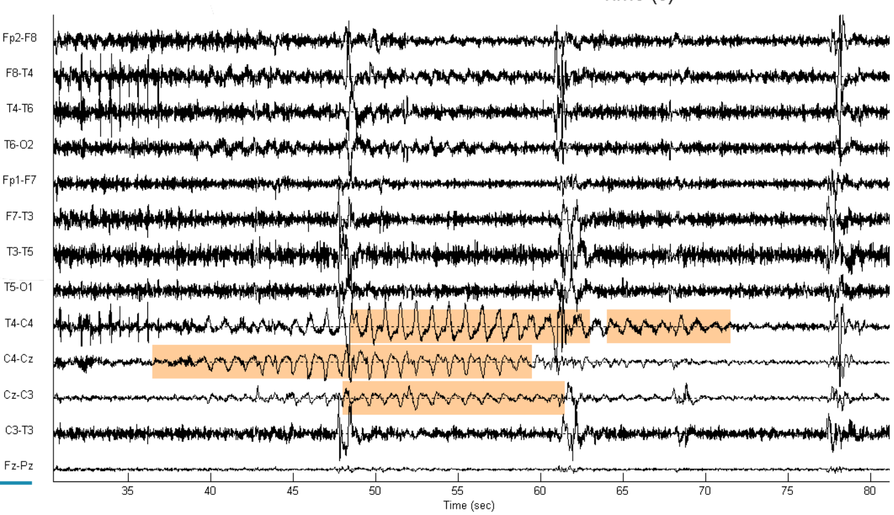
Neonatal Brain Monitoring:

Seizure detection







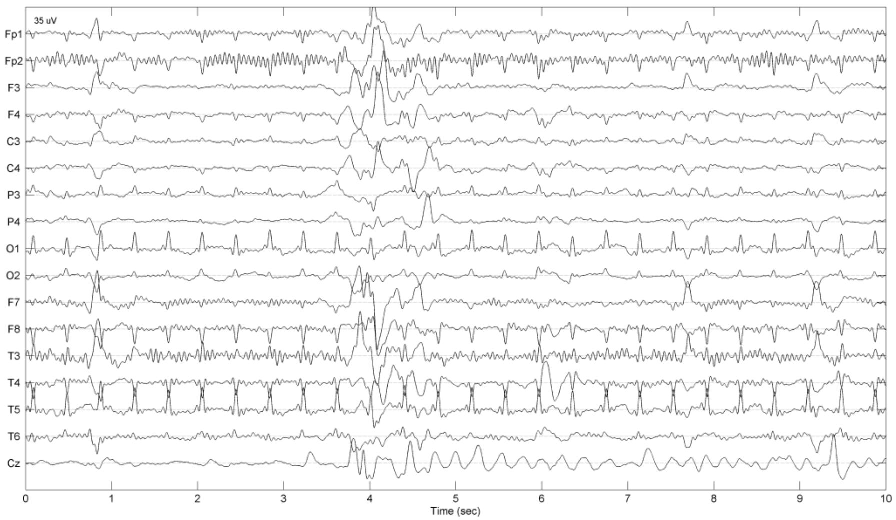
Deburchgraeve, PhD thesis, 2011; P.J. Cherian 2011; W. Deburchgraeve et al, Clin. Neurophys. 2008 & 2009
Alternatives using classification: See pubs of Temko, G. Boylan, etc.

Artefact removal: ECG, respiration, pulsation

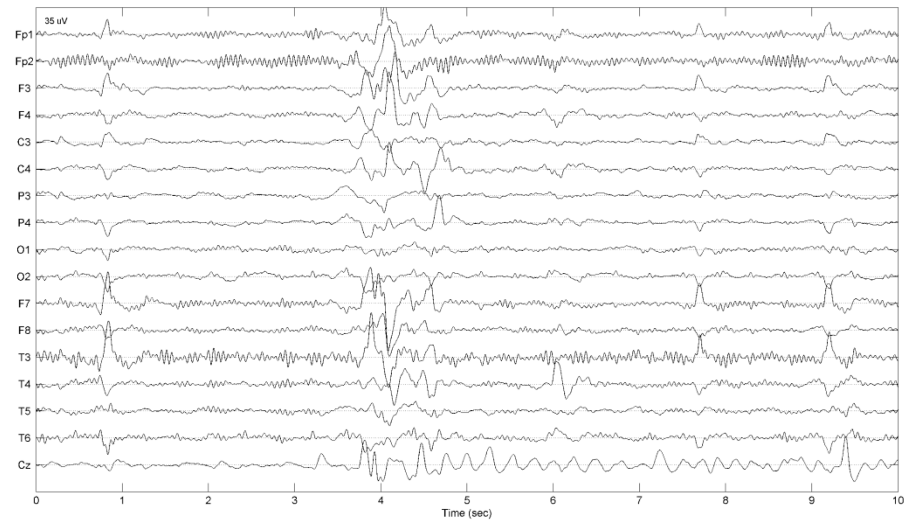
BSS based algorithm removes these 3 artifacts **before** seizure detection starts

ECG artefact removal: *with RobustICA* (spiky)
Respiration & Pulsation removal: *with SOBI* (oscillatory, autocorrelated)
Number of sources: *estimated with PCA and variance threshold*
IC source recognition: *correlation with reference after transformation*

ECG spike artefact



Cleaned EEG



VALIDATION study artefact-removal: *M. De Vos et al., Clinical Neurophys., Dec. 2011*

•13 patients: asphyxia (9 with artefacts, 4 artefact-free), 8h EEG per patient

	Fp/h	Seizure detection Rate (%)
No-AR:	0.38 (0-5)	87.1 (20-100)
With-AR:	0.00 (0-0.875)	100 (20-100)

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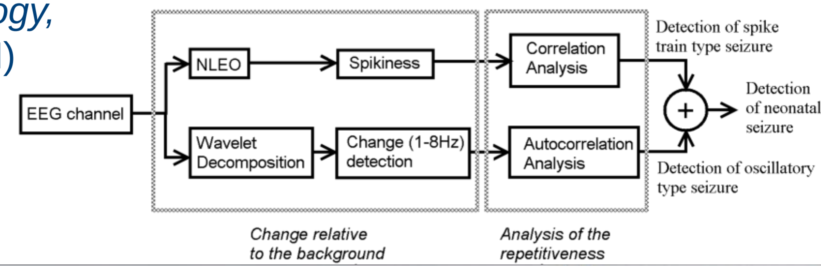
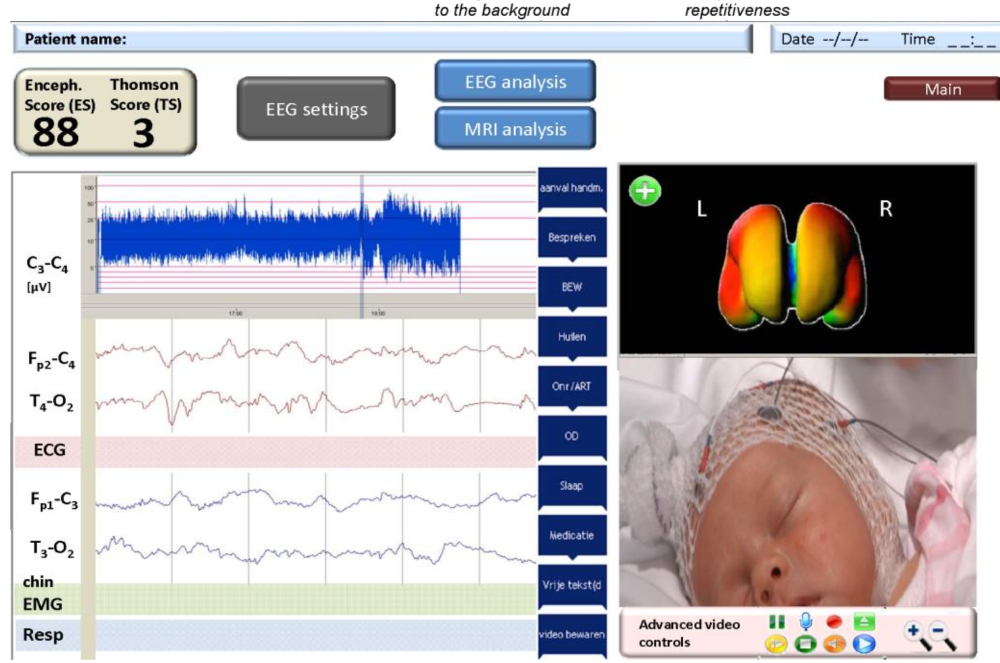
NeoGuard : decision support

Partners

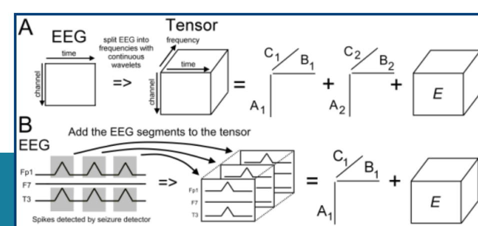
KU Leuven-ESAT (Stadius & MICAS), *UZ Leuven neonatology, EMC Rotterdam, ZNA Middelheim*, Ghent University (TELIN)

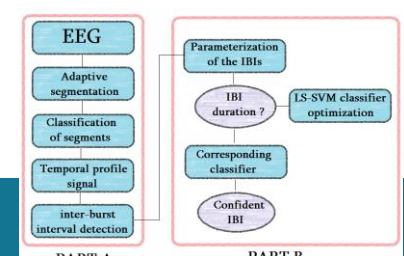


- Brain injury estimate
  - Detection of neonatal epileptic seizures
  - Seizures localization
  - Inter-burst intervals

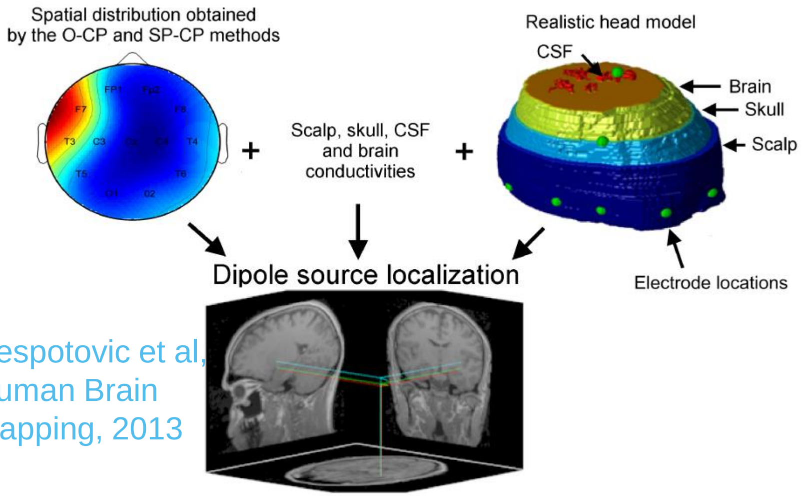


- Incorporated expertise
  - Knowledge of neurophysiologists are incorporated into algorithms
- Monitoring
  - Recovery after brain damage
  - Brain Maturation in prematures
- Outcome prediction
  - Good
  - Poor

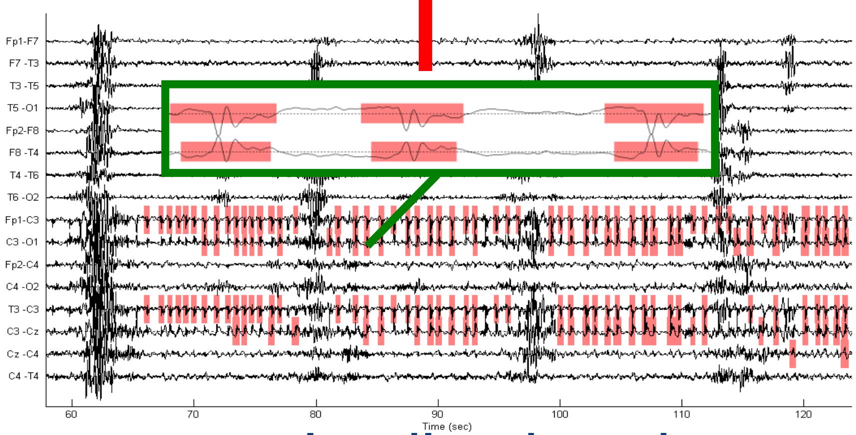




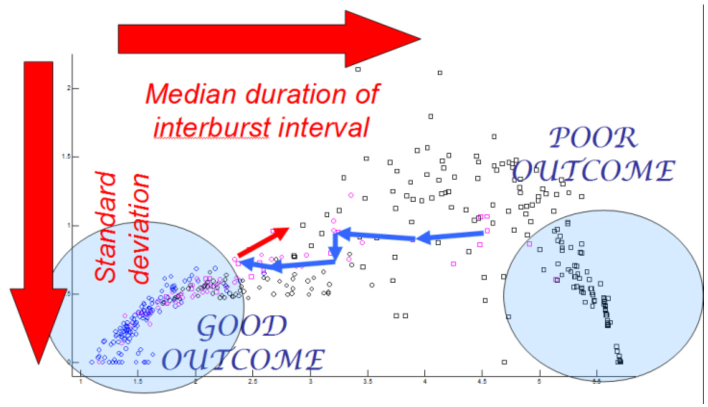
NeoGuard : Clinical Research



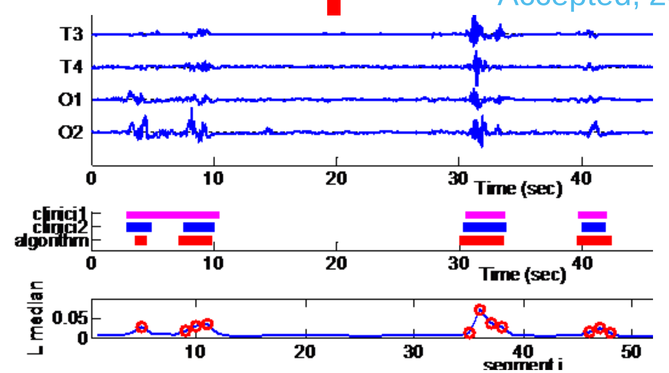
Despotovic et al, Human Brain mapping, 2013



Neonatal epileptic seizures



Koolen et al, Clini.Neurophys. Accepted, 2014



Inter-burst intervals in premature EEG

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NeoGuard: Future Challenges in Development

Monitor development

- Multilevel: *Bedside version for daily clinical use (only show clinical relevant information) and Extensive research version*
- Validation: *improved interobserver agreement*
- *Telemedicine kit for mobile neonatal healthcare*

Algorithm development and optimization

- EEG background activity quantification : *more features, multichannel, connectivity, dynamics evolution*
- Source localization: *including dynamics of seizures*
- Patient customized settings
- Adding non-linear entropy analysis, autoregulation

Clinical studies

(combined with EEG and MRI findings)

- Improvement outcome by monitoring:
- Improved understanding clinical relevance seizure types : *spike versus oscillation, rhythmicity, frequency, etc*
- Improved understanding clinical relevance EEG background characteristics: *SW cycling, frequency content bursts, sharp waves, etc*

Multimodality monitoring

- NIRS
- EEG cap: dry electrodes, smart textile
- Polygraphy: ECG, HRV, Respiration, SaO_2, CO_2
- Movement (automated video recognition?)

integrated, BAN, wireless improved comfort

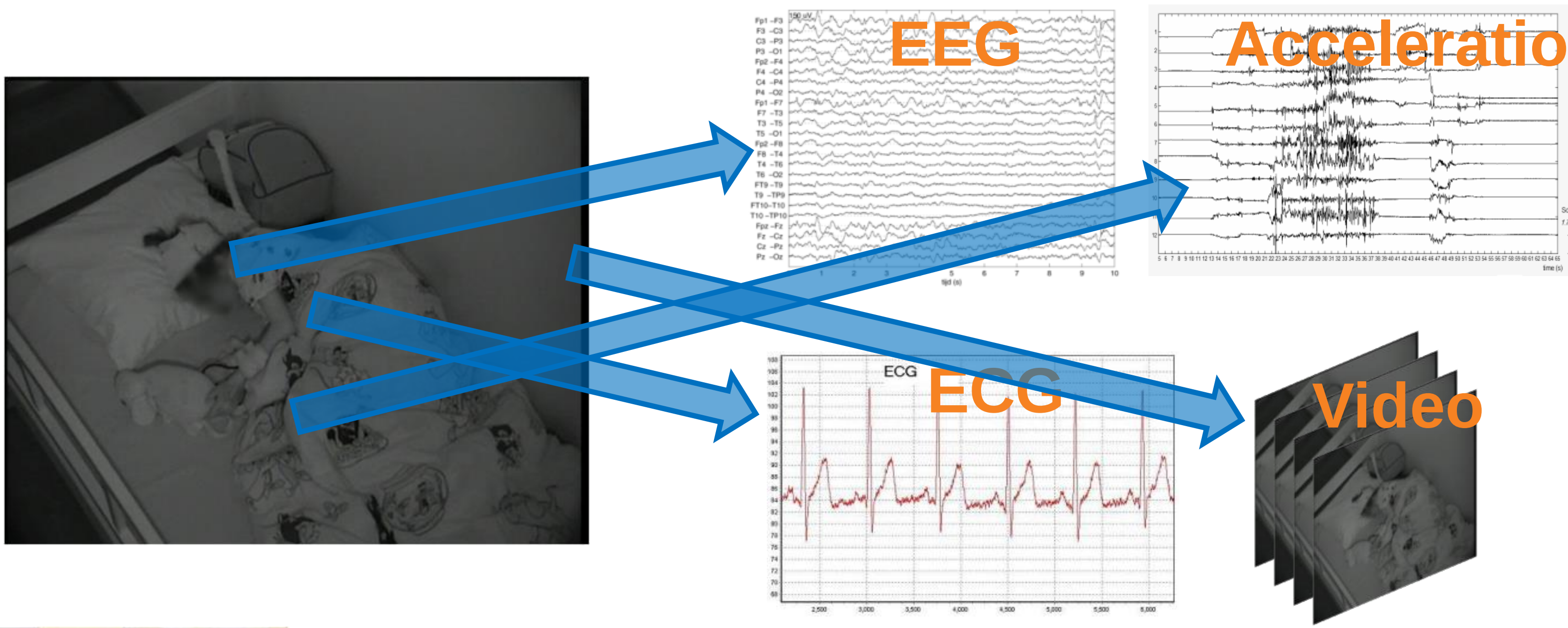
Epilepsy monitoring

- EEG (clinic) → golden standard for epilepsy monitoring
- Non-EEG → video, audio, radar, ECG, respiration, EMG,ACM

- Commercially available systems:
  → Efficiency lacks (long, intense & repetitive movements, excessive false alerts)
  → Few seizure logging (EpiWatcher, SmartWatch, EpiCare)
  → Single modality, no video storage



Future Challenges in Epilepsy monitoring: Home Monitoring & multimodal data acquisition

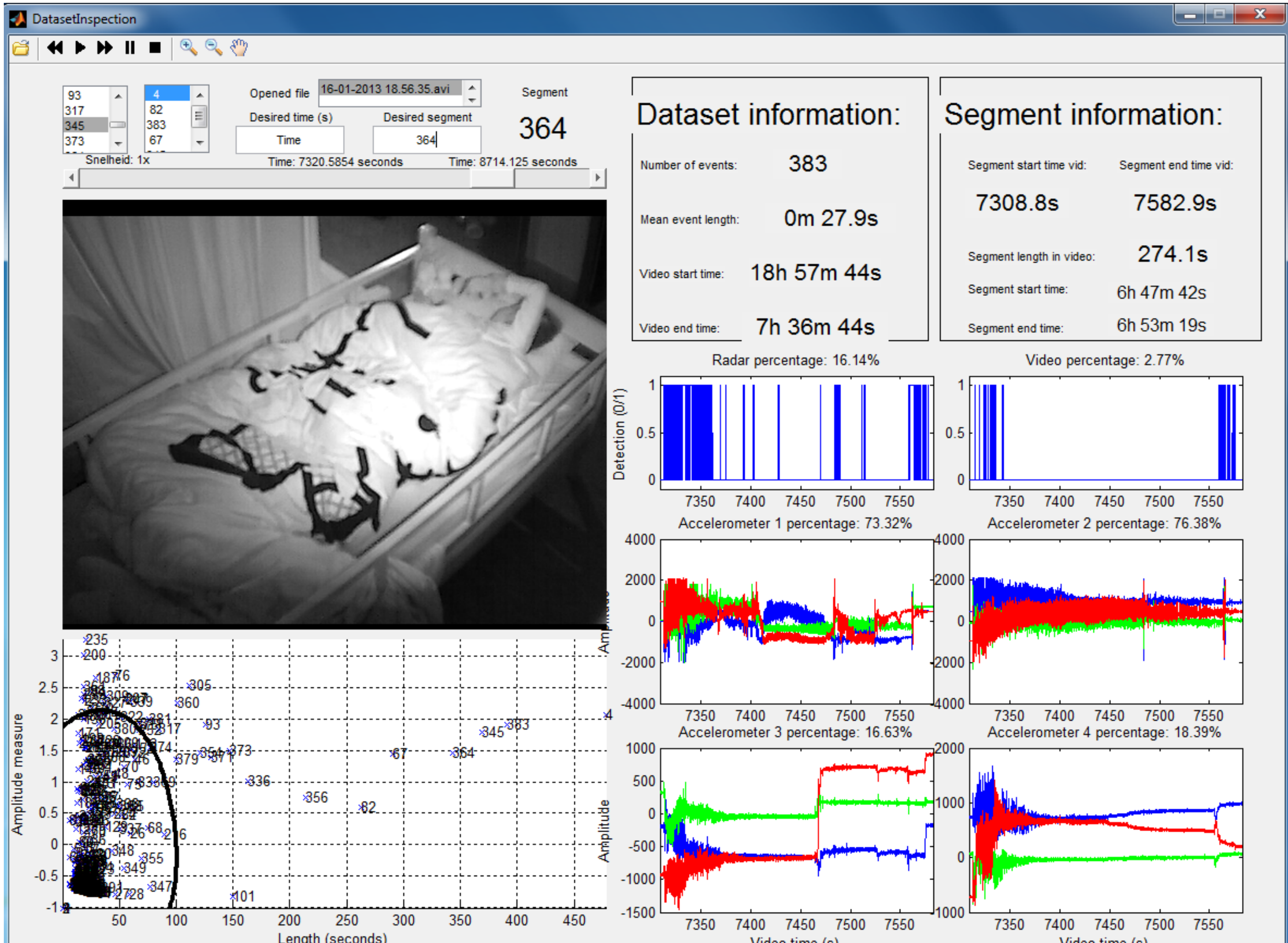


EEG
ECG
EMG
EOG
video
audio
acceleration

Myoclonic and tonic-clonic seizure

Long-term home Epilepsy monitoring: first results

- Equipment:
  - Video-triggered accelerometry plus radar
  - No EEG!



- Data:
  - 2 patients
  - 24 nights

- Efficiency:
  - 25 % missed (due to defects, reporting mistakes, misclassified seizures)
  - Not yet sufficiently reliable for detection or alarm but
  - screening tool to detect the 50 % extra seizures

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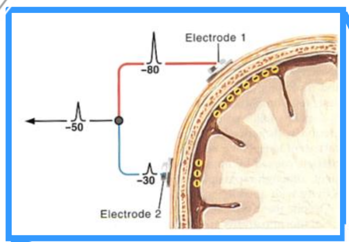
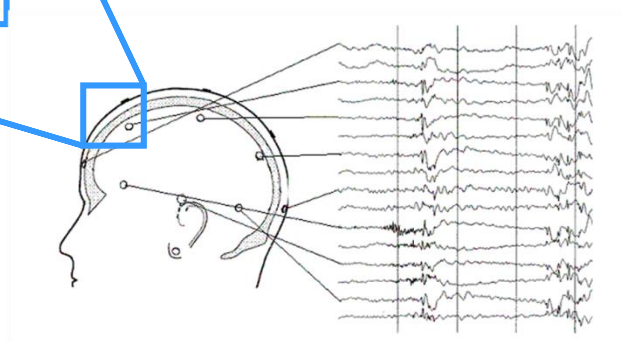
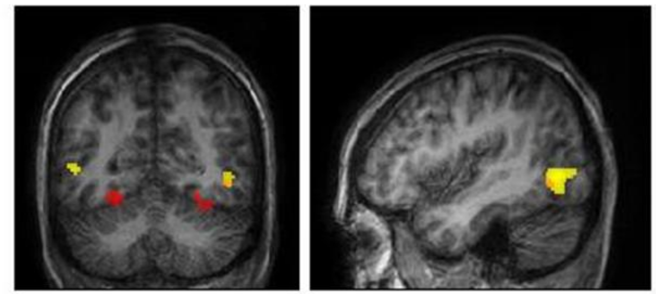
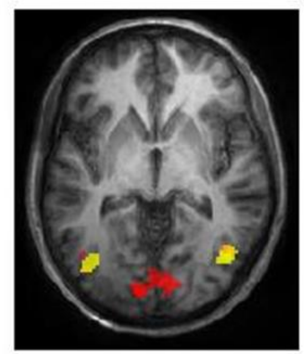
Combined EEG-fMRI analysis



EEG measures electrical potentials on the scalp







fMRI

localizes active brain regions

Combining EEG and fMRI:

- ***EEG*** *good* ***temporal resolution*** *(~ ms)*
- ***fMRI*** *good* ***spatial resolution*** *(~ mm)*

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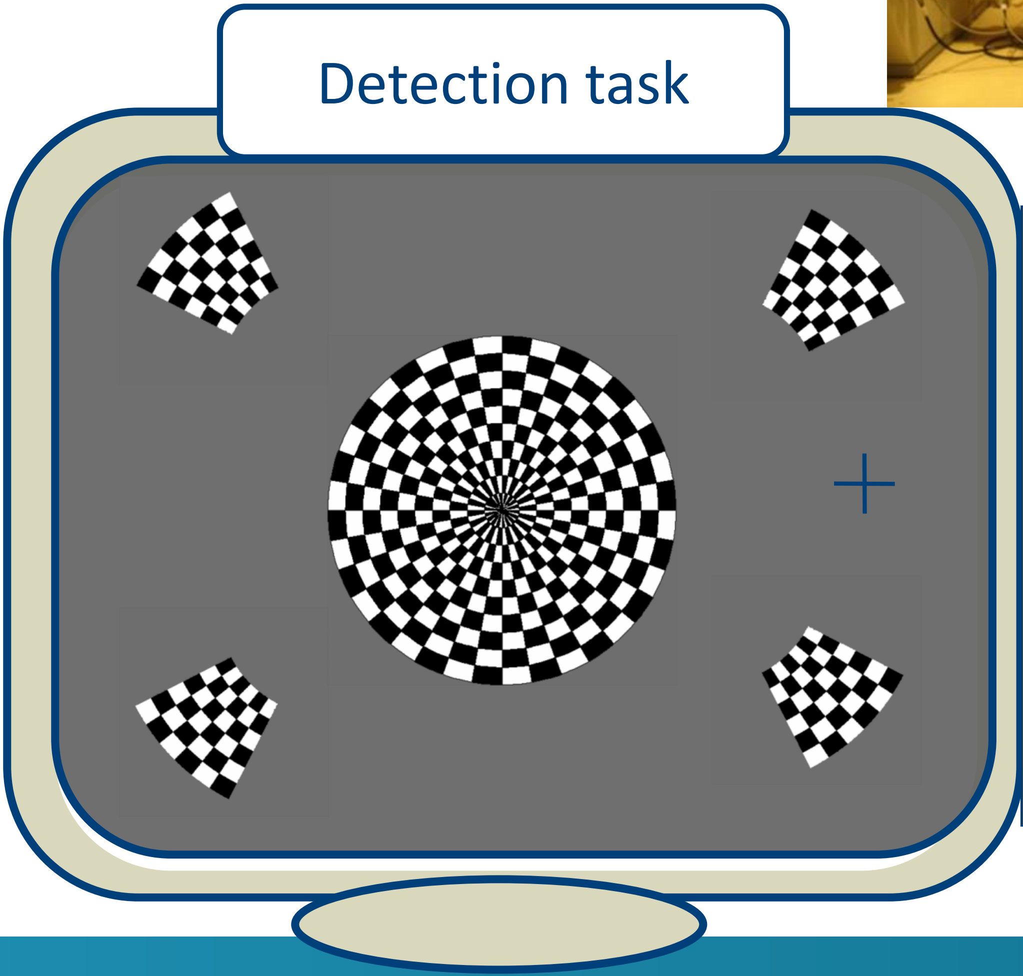
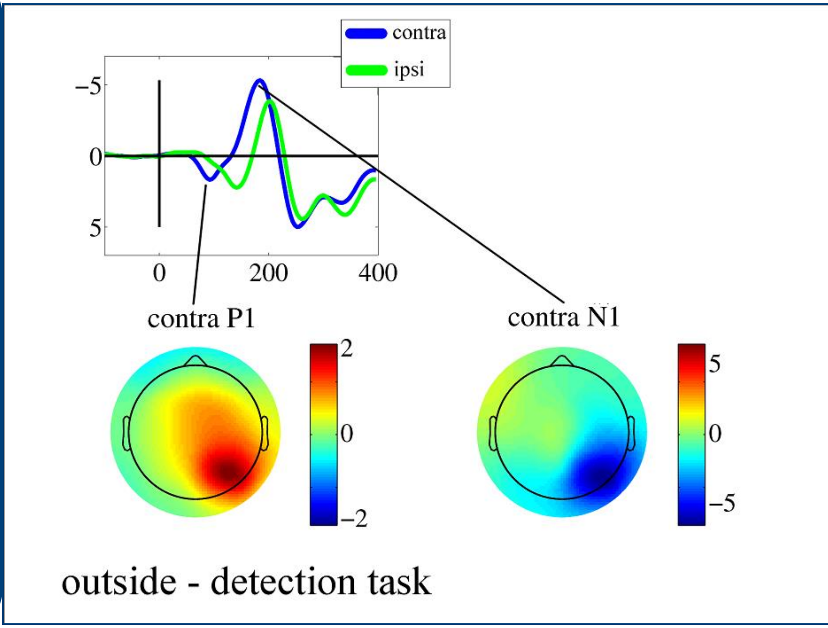
ERP analysis:

Brain responses evoked due to mental task





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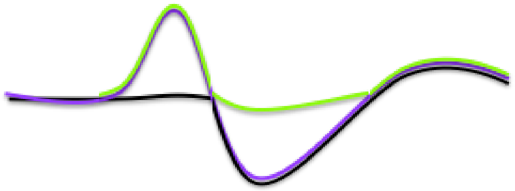
Symmetric EEG-fMRI approaches: Joint BSS

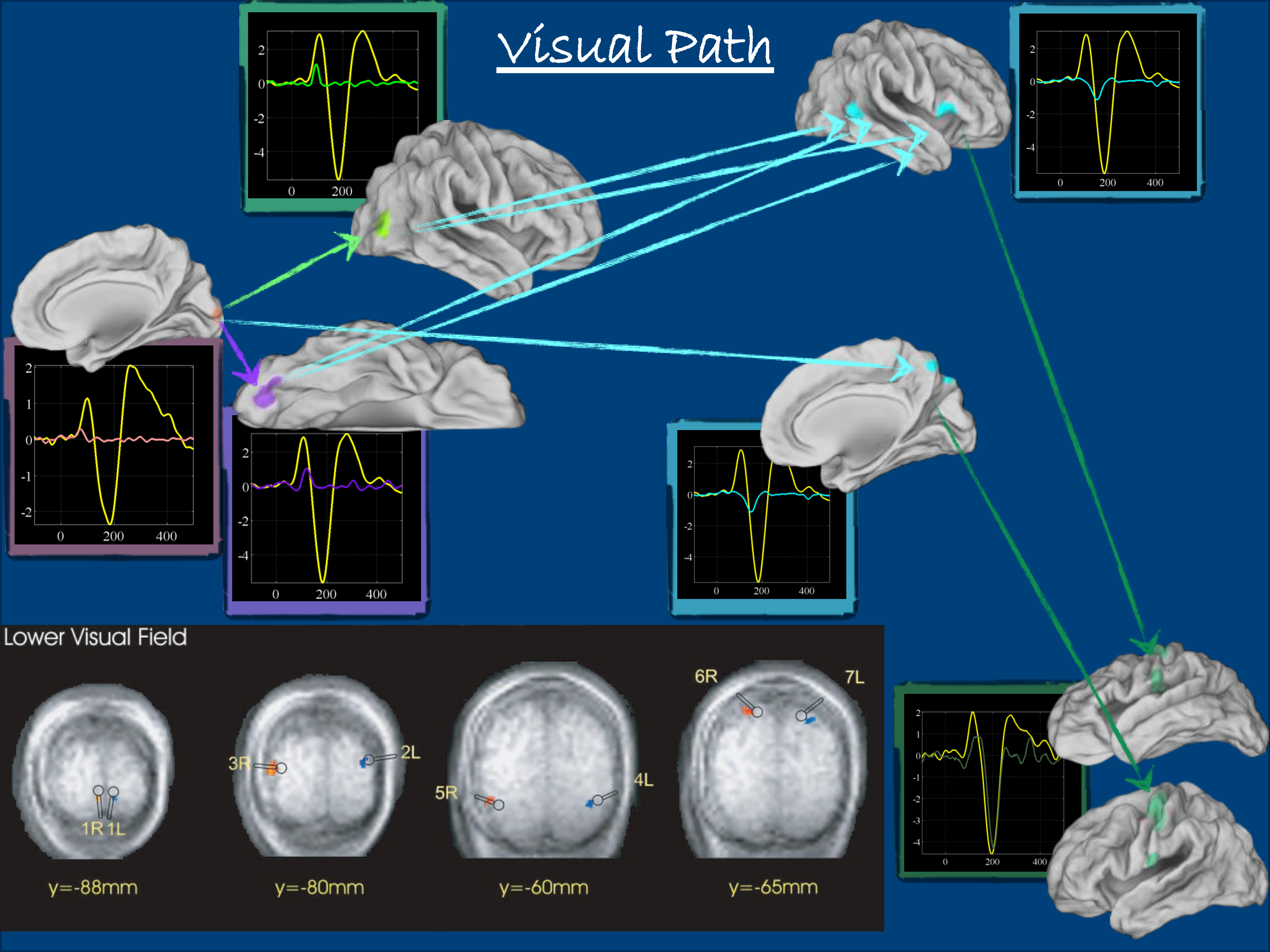
Calhoun et al., (2006), NeuroImage



Joint BSS Output

X^{fMRI} X^{EEG} = Mixing Matrix ○ **Estimated** Sources (fMRI) Estimated Sources (EEG)

Visual Path


Lower Visual Field
1R 1L
3R
2L
5R
4L
6R
7L
y=-88mm
y=-80mm
y=-60mm
y=-65mm

Cardiorespiratory Monitoring

Ambulatory ECG system

- Few sensors
- Low cost
- Accurate information

Improve

- Diagnosis
- Monitoring
- Follow-up

Sleep

Stress

Sports

Epilepsy

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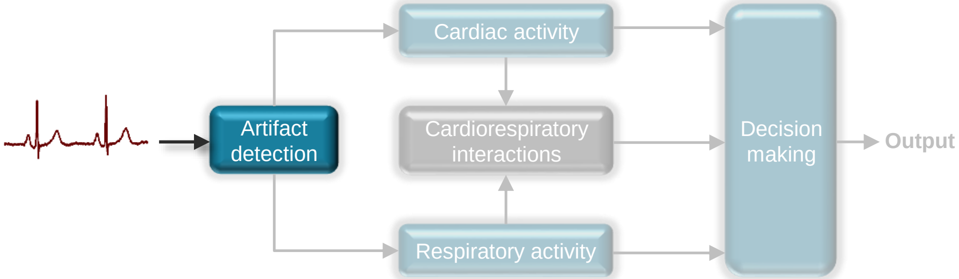
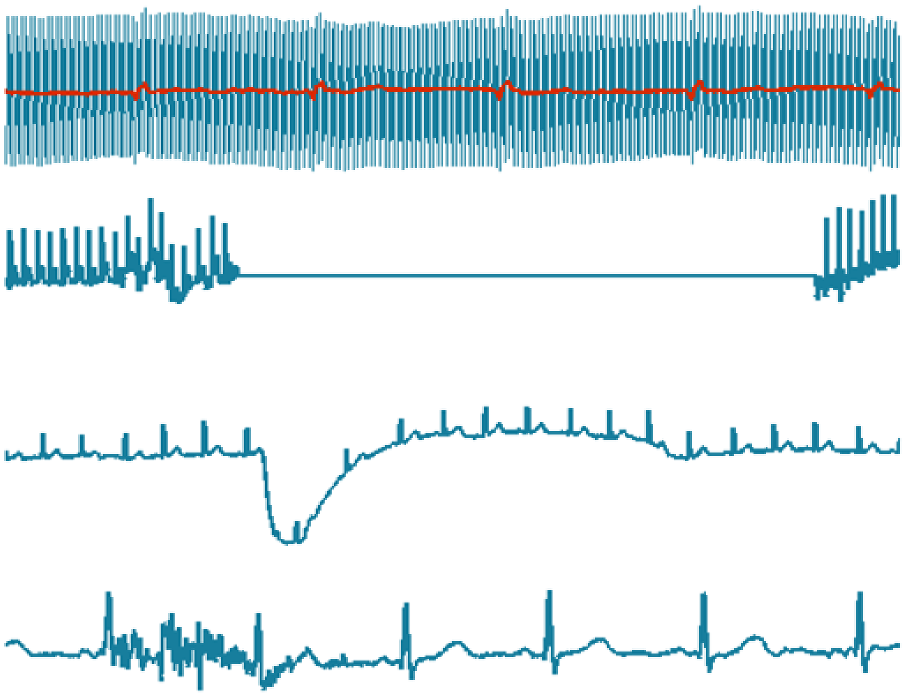
Artifact Detection

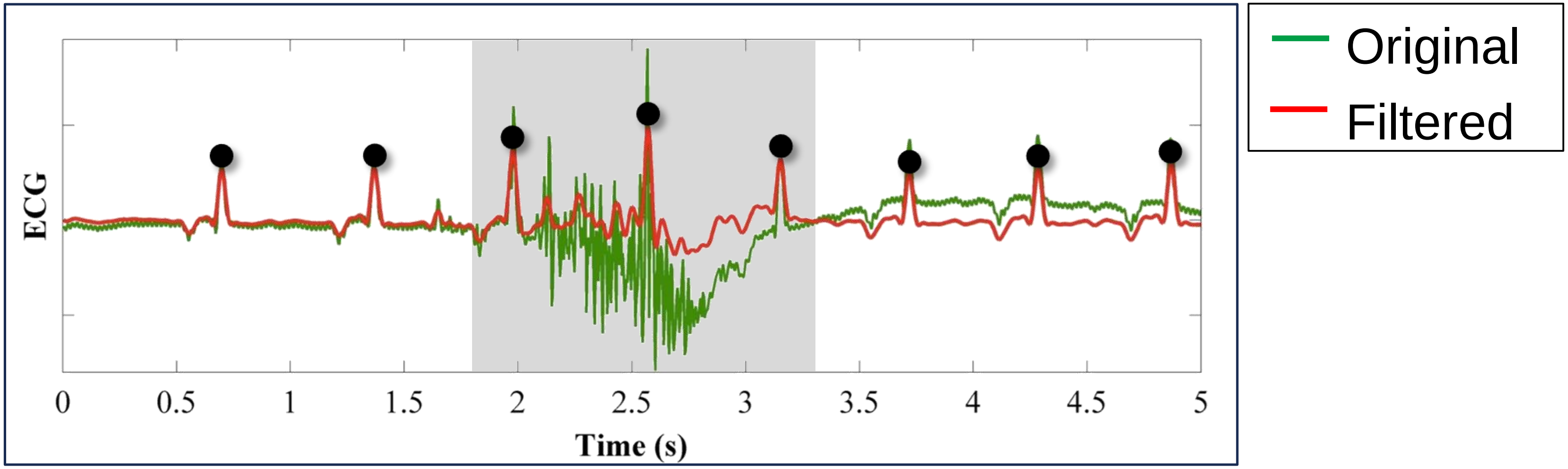




Sources:

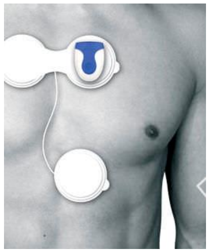
- Electrode motion
- Contact noise
- Muscle activity
- Interferences (50Hz-60Hz)
- Baseline drift
- …

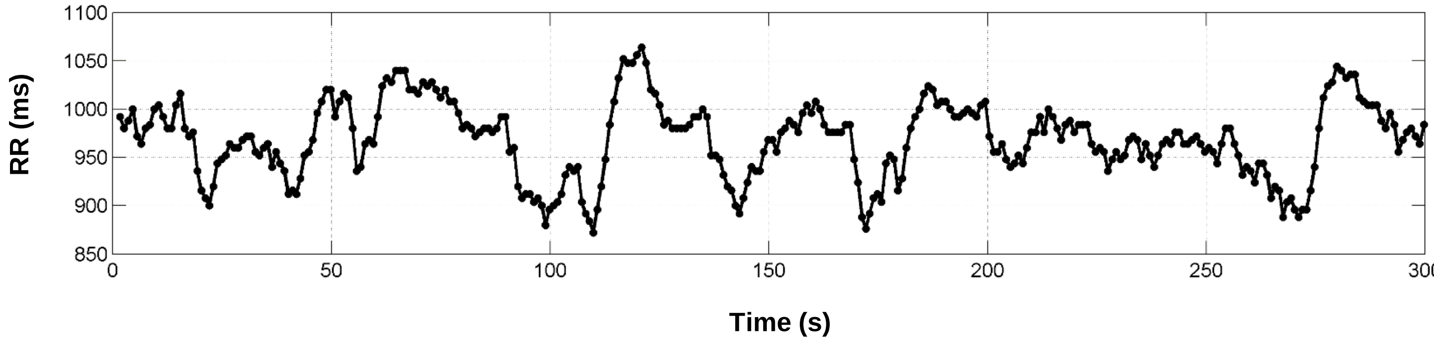
Artifact Detection



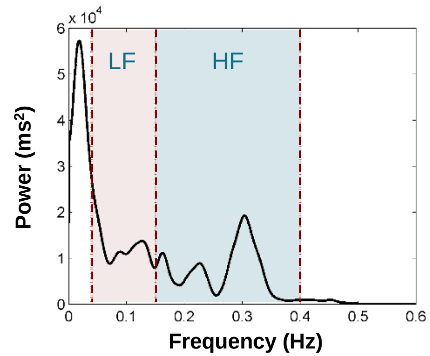
- Location of contaminated segments → Visual inspection
- Easy to compute

Cardiac Activity





Feature extraction:

Time domain	Frequency domain	Non-linear
mean SDNN SDANN RMSSD NN50 pNN50 : Geometric measures		DFA 1/f slope Corr. dimension Lyapunov exponent Fractal dimension Sample entropy

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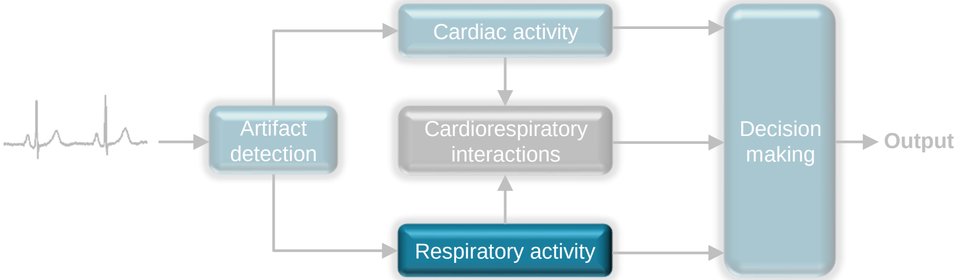
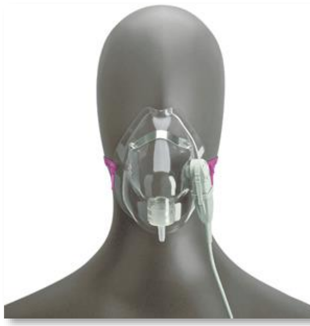
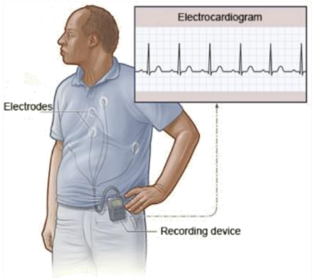
Respiratory activity

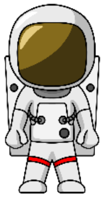


Respiratory sensors:

- Interfere with natural breathing
- Increase costs
- Uncomfortable







ECG-derived Respiration

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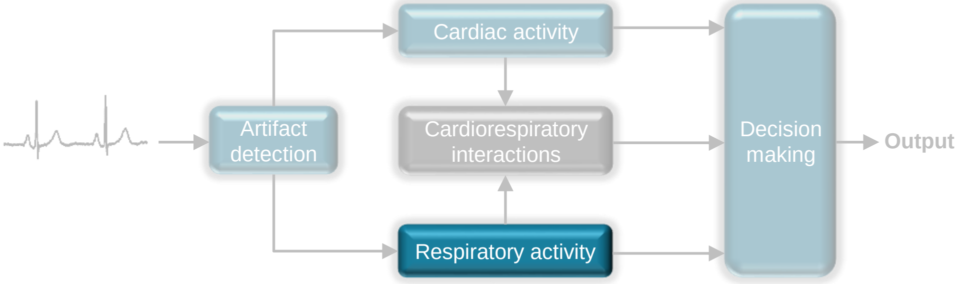
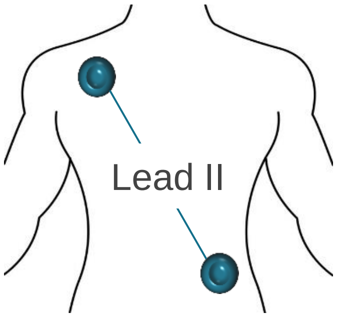
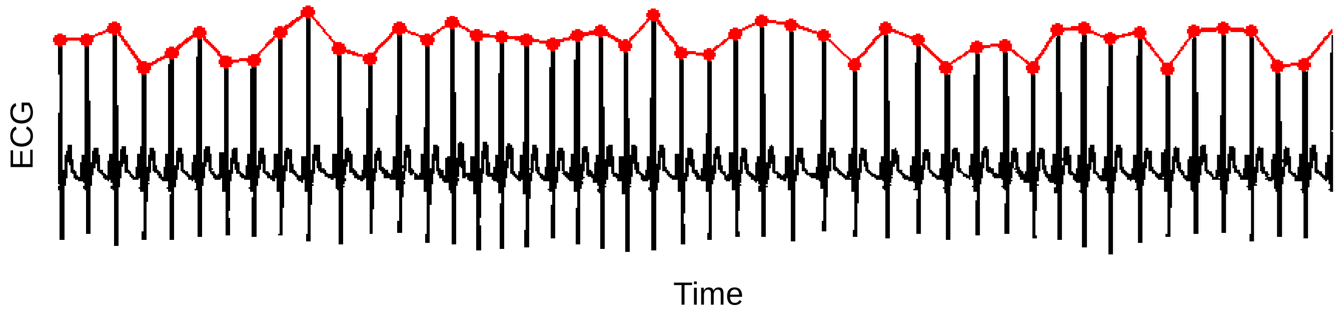
Respiratory activity





- ➢ Change in relative position of cardiac vector
- ➢ Change in impedance due to filling of the lungs



ECG-derived respiration (EDR)

- R-peak amplitude (Moody et al. 1985)
- PCA (Langley et al. 2010)
- kPCA (Widjaja et al. 2012, Varon C. et al., IEEE TNNLS, 2015)

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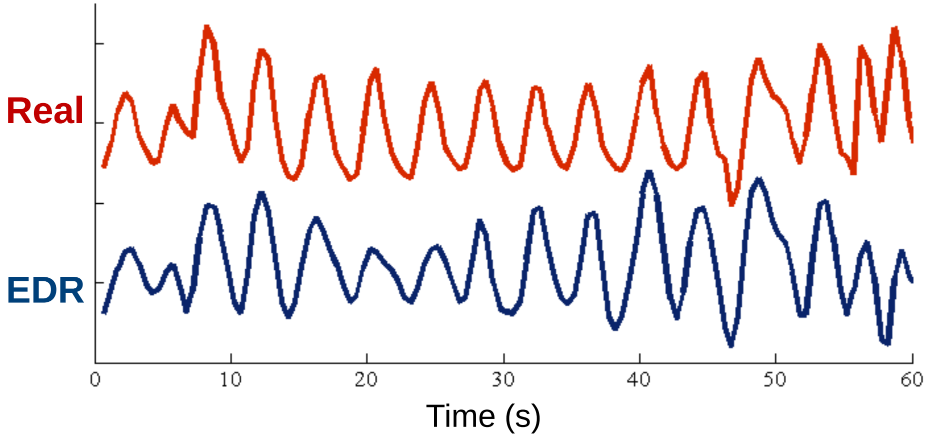
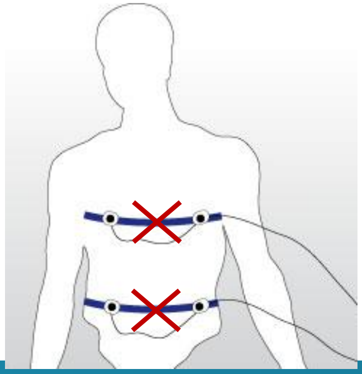
ECG-derived respiration

- Four different algorithms for EDR computation
- Three public datasets
- Correlation
- Coherence



- ✓ R-peak amplitude is more robust in the presence of artifacts
- ✓ Simpler and sufficient - Low computational costs

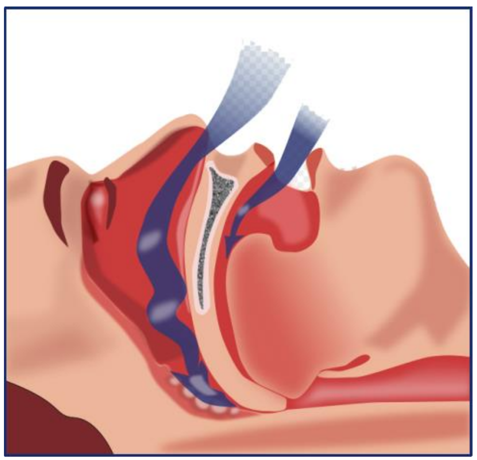


Ambulatory systems

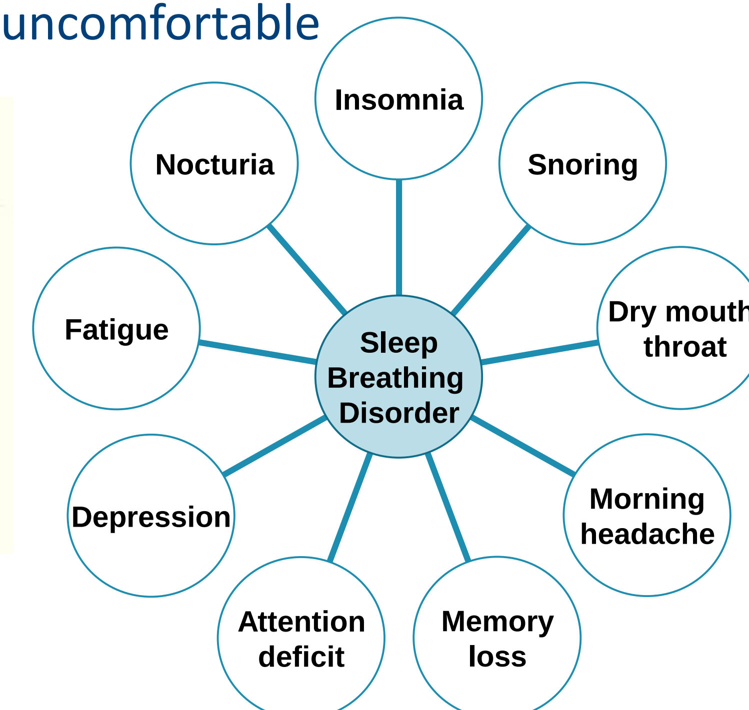
KU LEUVEN

NXT_SLEEP: next generation sleep monitoring platform

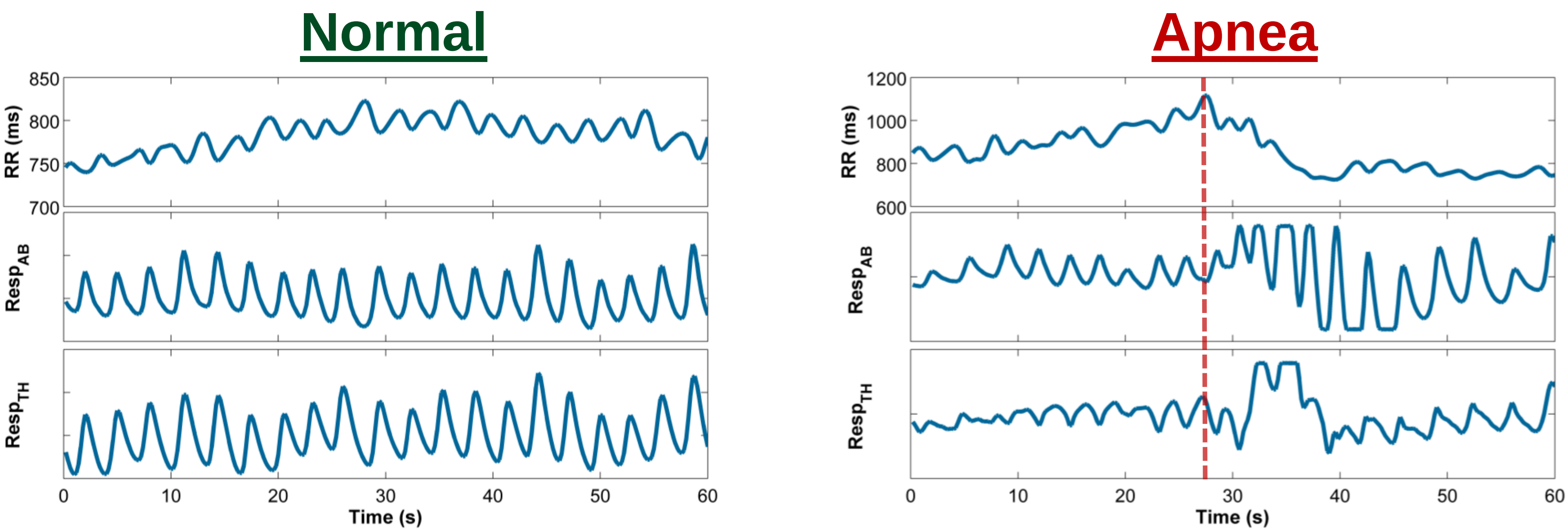
- Sleep-related breathing disorders
  - Major impact on cardiovascular health
  - Prevalence: around 4% in men and 2% in women.
- Severely under diagnosed
  - Limited availability of clinical screening
  - Polysomnography: time-consuming, costly, uncomfortable



Obstructive
Sleep Apnea

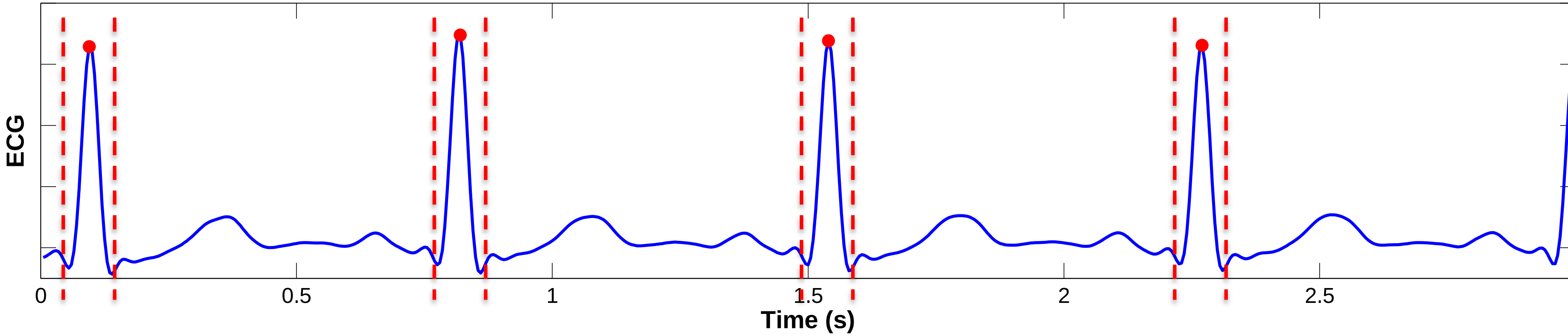


Sleep Apnea Detection

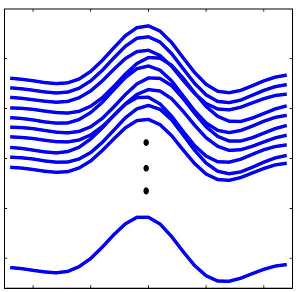


- Physionet: **34 313 ECG Minutes**
- Sleep Laboratory UZ Leuven: **3 847 ECG Minutes**

Sleep Apnea Detection

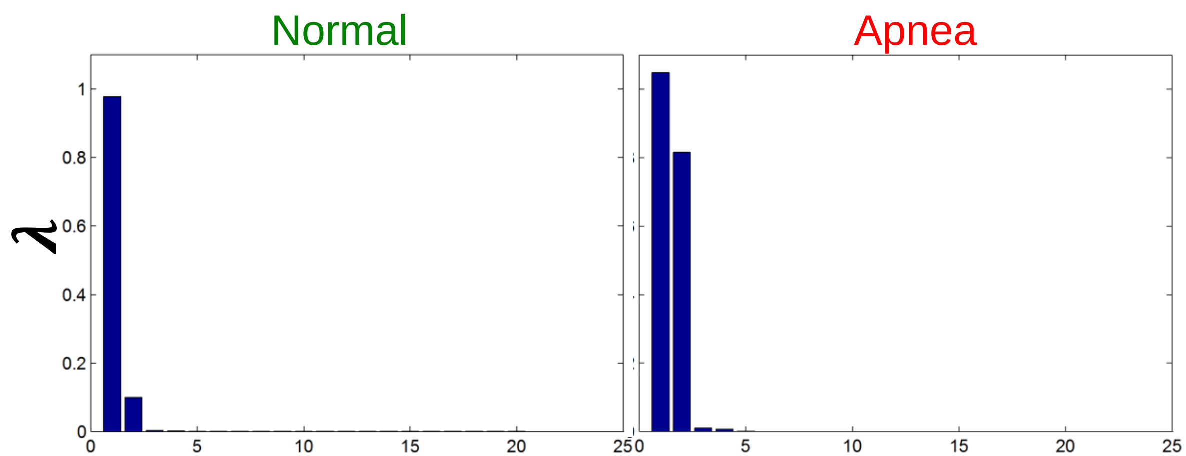


X =



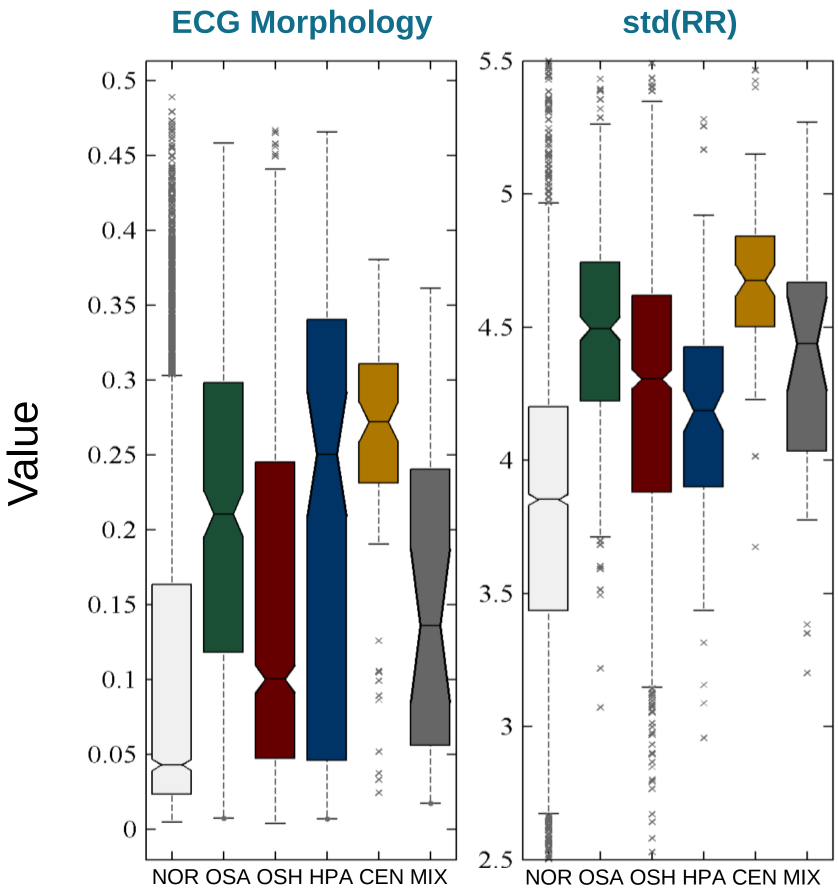
$$S = XX^T$$

$$S\alpha^{(i)} = \lambda_i \alpha^{(i)} \rightarrow \frac{\lambda_2}{\sum_i \lambda_i} \times 100$$



Varon C. et al. IEEE EMBC, 2013

Sleep Apnea Detection



- Using the RR series and the EDR separately
- Classification accuracy ≈ 79%

Added value of cardiorespiratory interactions?

Sleep Apnea Detection

- Time domain features of heart rate and respiration (Acc $\approx$ 79%)
- Cardiorespiratory features (only using the ECG)
- LS-SVM (RBF) classifier

Dataset	Sens.	Spec.	Acc	AUC
Physionet	84.71%	84.69%	84.74%	88.07%
Leuven	78.81%	84.56%	83.95%	89.97%

Comparable to the best results reported for fully automated algorithms and ECG and respiration based algorithms

Varon C. et al. IEEE TBME, 2015

VIDEO NXT_SLEEP: sleep monitoring of the future

iMinds ICON project NXT_SLEEP

Medical Information Technologies Department

Future Challenges in Tech Transfer

Technology transfer to market in medical technology is a though job !!

- many different stakeholders
- non-trivial business models
- hyper-regulated environment with separated policy levels
- totally different systems in other countries
- many ethical and legal issues
- niche market of medical diagnostics
  - societal valorization is often more important than a pure economic point of view
  - non-straightforward CE labeling or FDA approval

CE

economic

societal

iMinds

KU LEUVEN

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Eindhoven University of Technology

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Thank you!

KU LEUVEN