KU LEUVEN

imec

Slimme Gezondheidszorg

Algoritmen en Toepassingen

Prof. Sabine Van Huffel

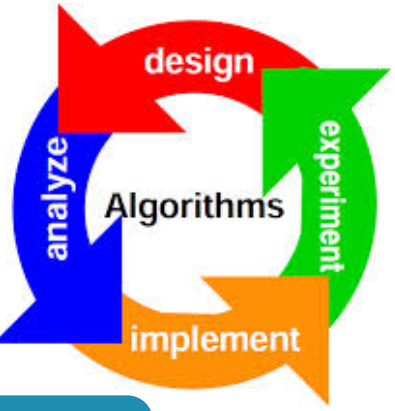
Koninklijke Vlaamse Academie van België voor Wetenschappen en Kunsten
10 januari 2018

erc
European Research Council
Established by the European Commission

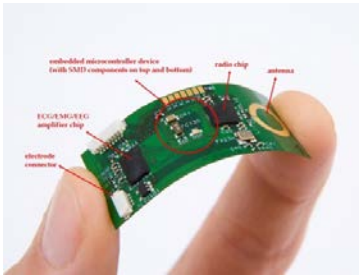
Contents Overview

- **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

KU LEUVEN



Brain monitoring for neurological diseases

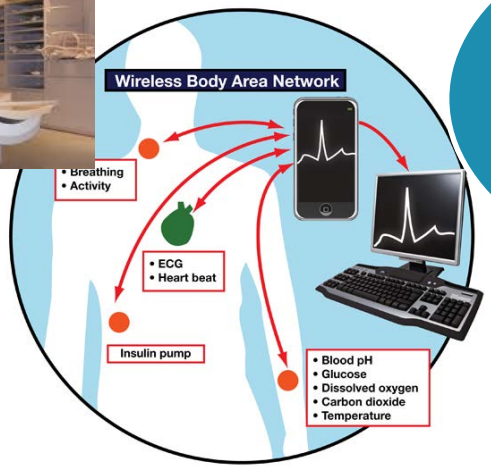


Algorithms (Technology)

Sensors (Carriers)

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

Knack,21.10.2015

Move healthcare
away from hospitals
to HOME environment

- UNOBTRUSIVE
- MULTIMODAL
- LONG-TERM

Challenges:
- ARTEFACTS
- BIG DATA
- AUTOMATED

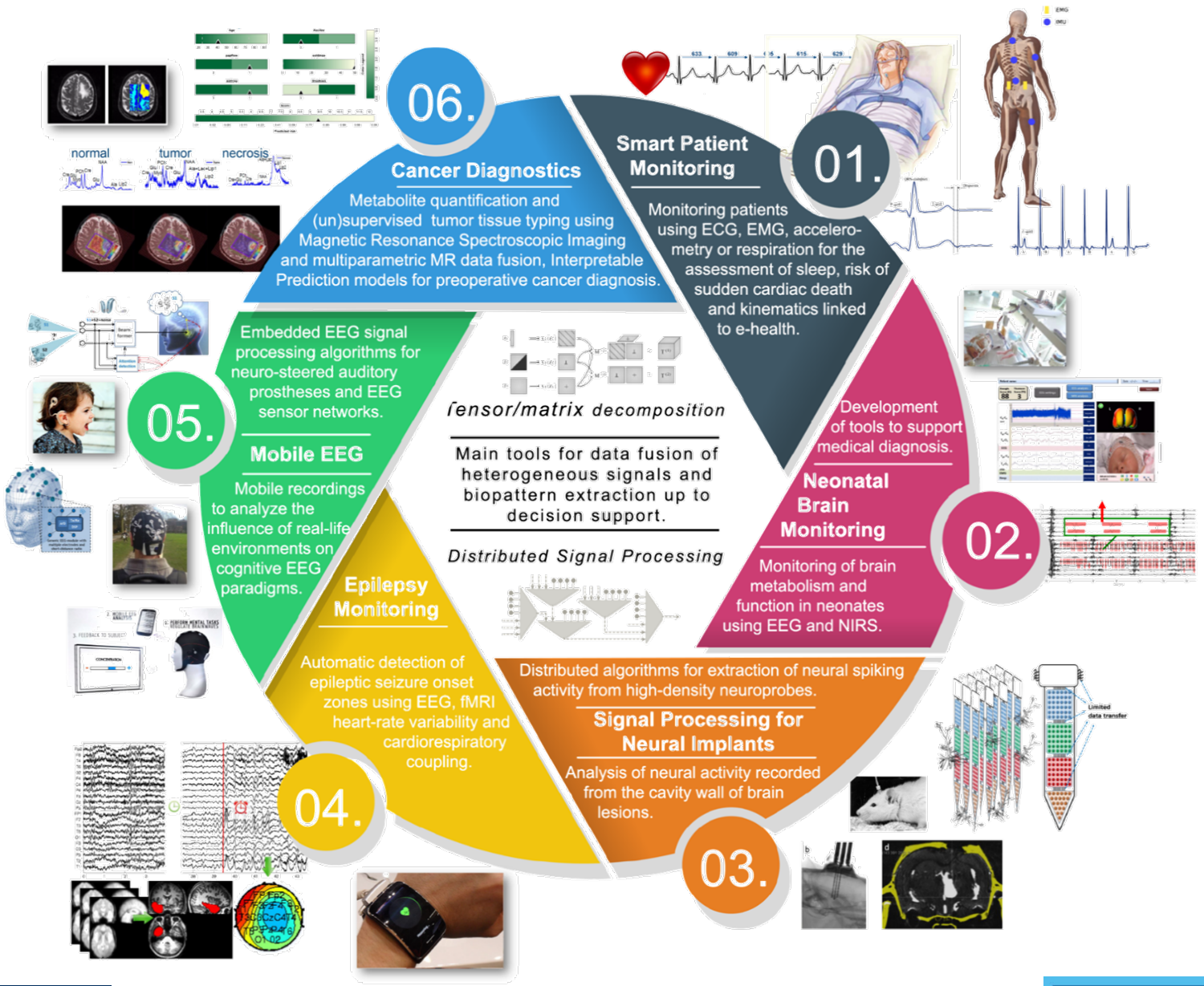
Facts and Figures

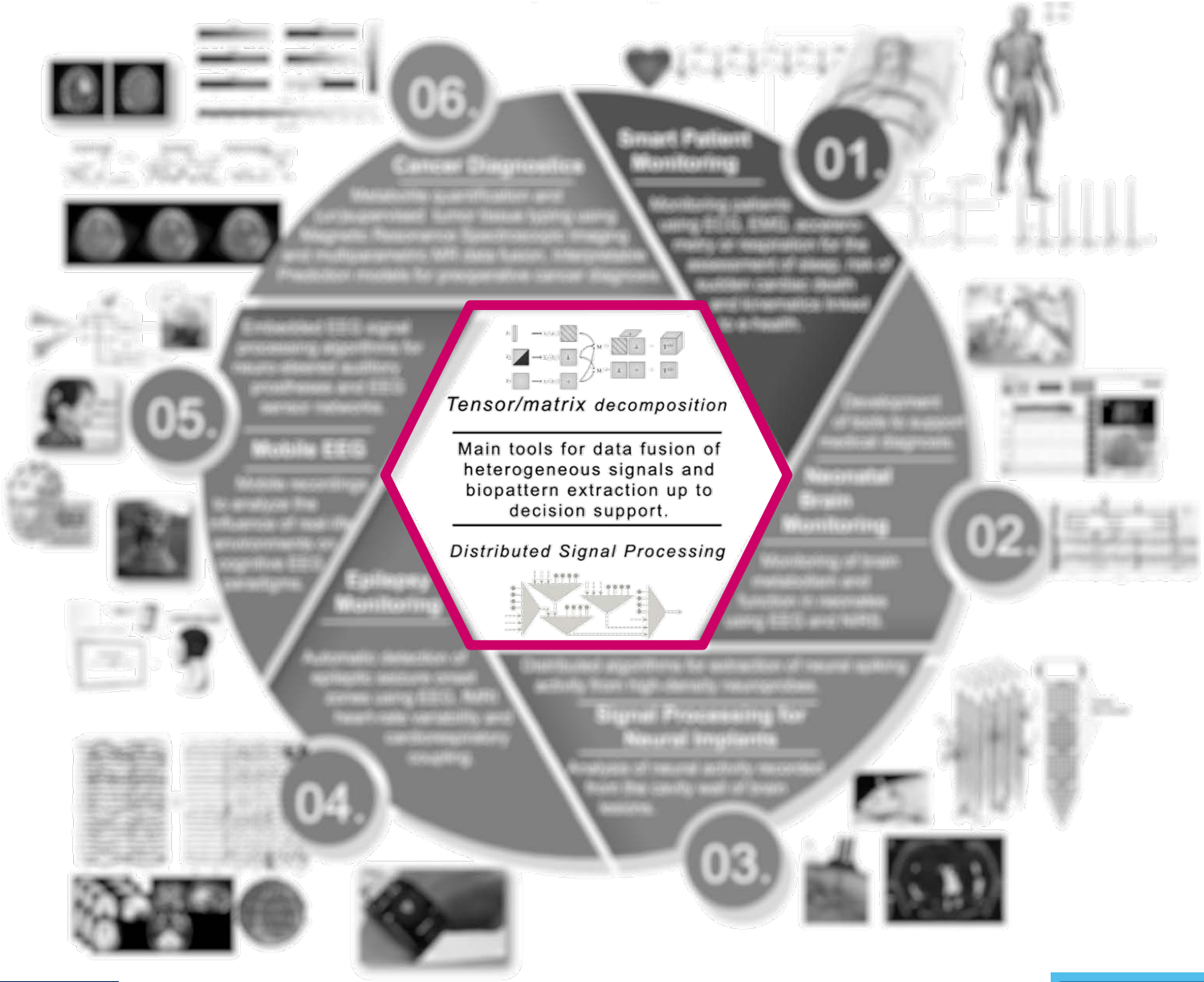
ESAT: Department of Electrical Engineering (±600 people)
STADIUS: Division (±80 pp.), Focus: Mathematical Engineering
BioMed: Biomedical Data Processing Research group in STADIUS

- Staff: S. Van Huffel (head), A. Bertrand (TT), S. Vandeput (IOF)
- 6 postdocs
- approx. 25 PhD students

Keywords: **Biomedical data Processing**, Biomonitoring, pattern recognition, multilinear algebra, numerical software, decision support, MR, EEG, ECG, cancer diagnosis, distributed signal processing,

Collaboration: with **UZ Leuven**, Psychology, Thomas More Kempen, R.U.Nijmegen, EMC Rotterdam, UMC Utrecht, **TU/e**, **IMEC/NERF,** etc.


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.
normal
tumor
necrosis
01.
Smart Patient Monitoring
Monitoring patients using ECG, EMG, accelero-metry or respiration for the assessment of sleep, risk of sudden cardiac death and kinematics linked to e-health.
05.
Embedded EEG signal processing algorithms for neuro-steered auditory prostheses and EEG sensor networks.
Mobile EEG
Mobile recordings to analyze the influence of real-life environments on cognitive EEG paradigms.
Tensor/matrix decomposition
Main tools for data fusion of heterogeneous signals and biopattern extraction up to decision support.
Distributed Signal Processing
Development of tools to support medical diagnosis.
Neonatal Brain Monitoring
Monitoring of brain metabolism and function in neonates using EEG and NIRS.
02.
04.
Epilepsy Monitoring
Automatic detection of epileptic seizure onset zones using EEG, fMRI heart-rate variability and cardiorespiratory coupling.
Distributed algorithms for extraction of neural spiking activity from high-density neuroprobes.
Signal Processing for Neural Implants
Analysis of neural activity recorded from the cavity wall of brain lesions.
03.
Limited data transfer


06.
Cancer Diagnostics
01.
Smart Patient Monitoring
05.
Mobile EEG
02.
Neonatal Brain Monitoring
04.
Epilepsy Monitoring
03.
Signal Processing for Neural Implants
Tensor/matrix decomposition
Main tools for data fusion of heterogeneous signals and biopattern extraction up to decision support.
Distributed Signal Processing

KEYTOOL : Blind source separation

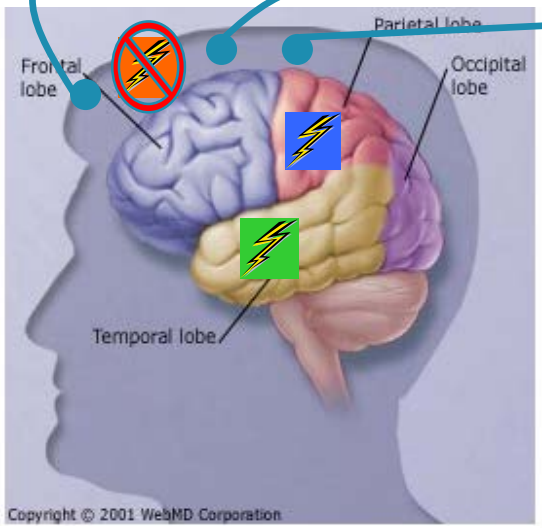
Signal analysis difficult because of artefacts → REMOVE

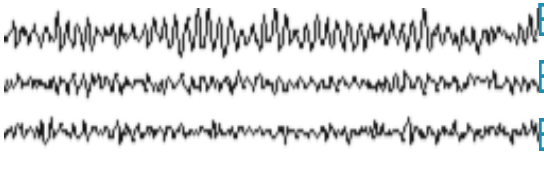
Matrix based Blind Source Separation (BSS)

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

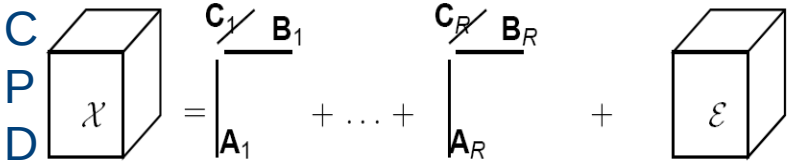
TENSOR based BSS: unique under mild conditions

ADD extra problem-specific constraints (nonnegative, sparse)





$$EEG_1 = a_{11}s_1 + a_{12}s_2 + a_{13}s_3$$
$$EEG_2 = a_{21}s_1 + a_{22}s_2 + a_{23}s_3$$
$$EEG_3 = a_{31}s_1 + a_{32}s_2 + a_{33}s_3$$

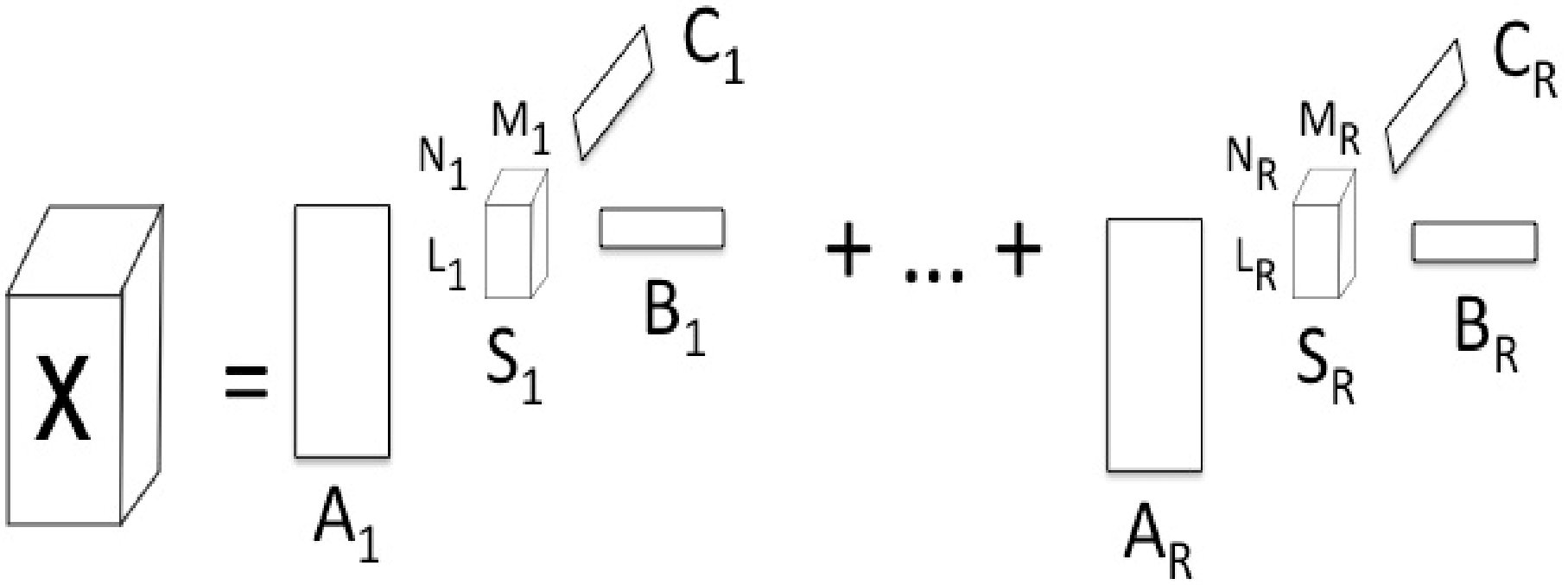


EEG = A ? S^T ?

KU LEUVEN

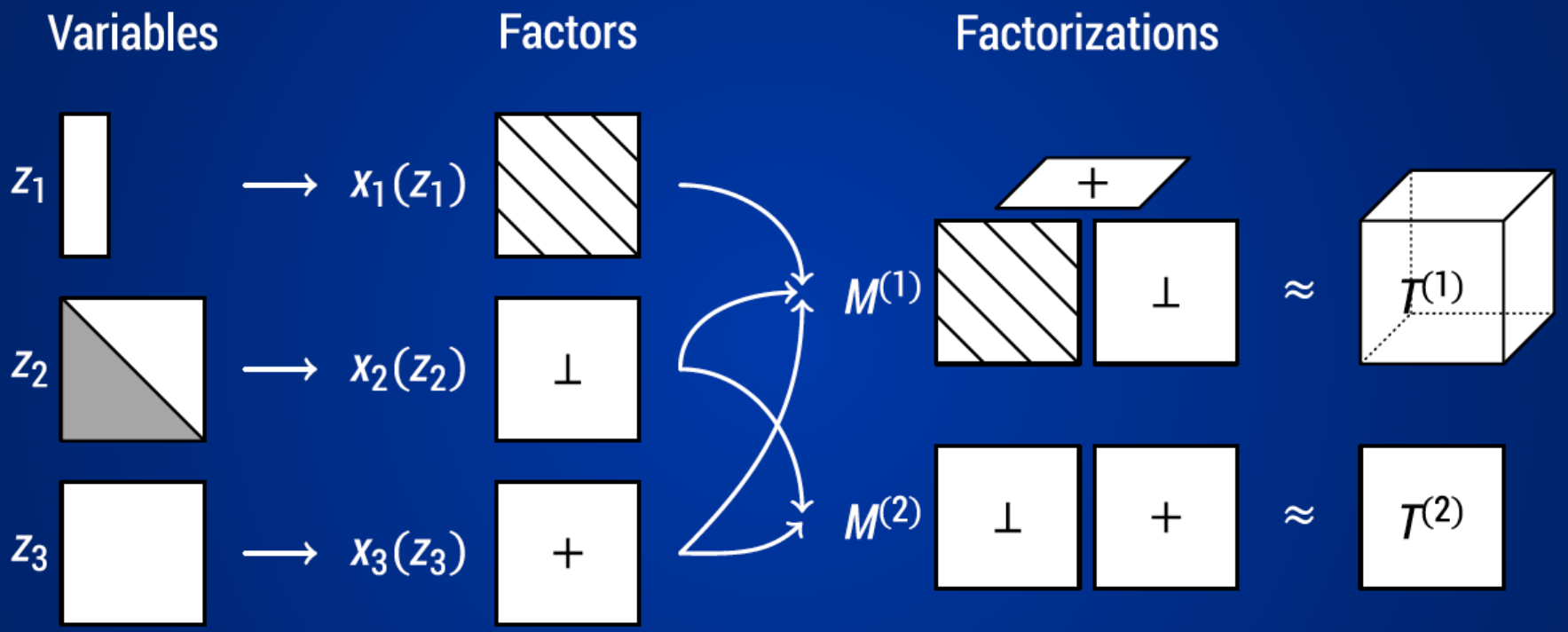
From CPD to Block Tensor Decomposition

see www.tensorlab.net



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

STRUCTURED DATA FUSION



$$\underset{z}{\text{minimize}} \quad \sum_d \omega_d \left\| M^{(d)}(X(z)) - T^{(d)} \right\|^2$$

Sorber L, Van Barel M, De Lathauwer L, *IEEE J. of Selected Topics in Signal Proc., 2015*

Contents Overview

1. Introduction

2. Examples

3. Future Challenges

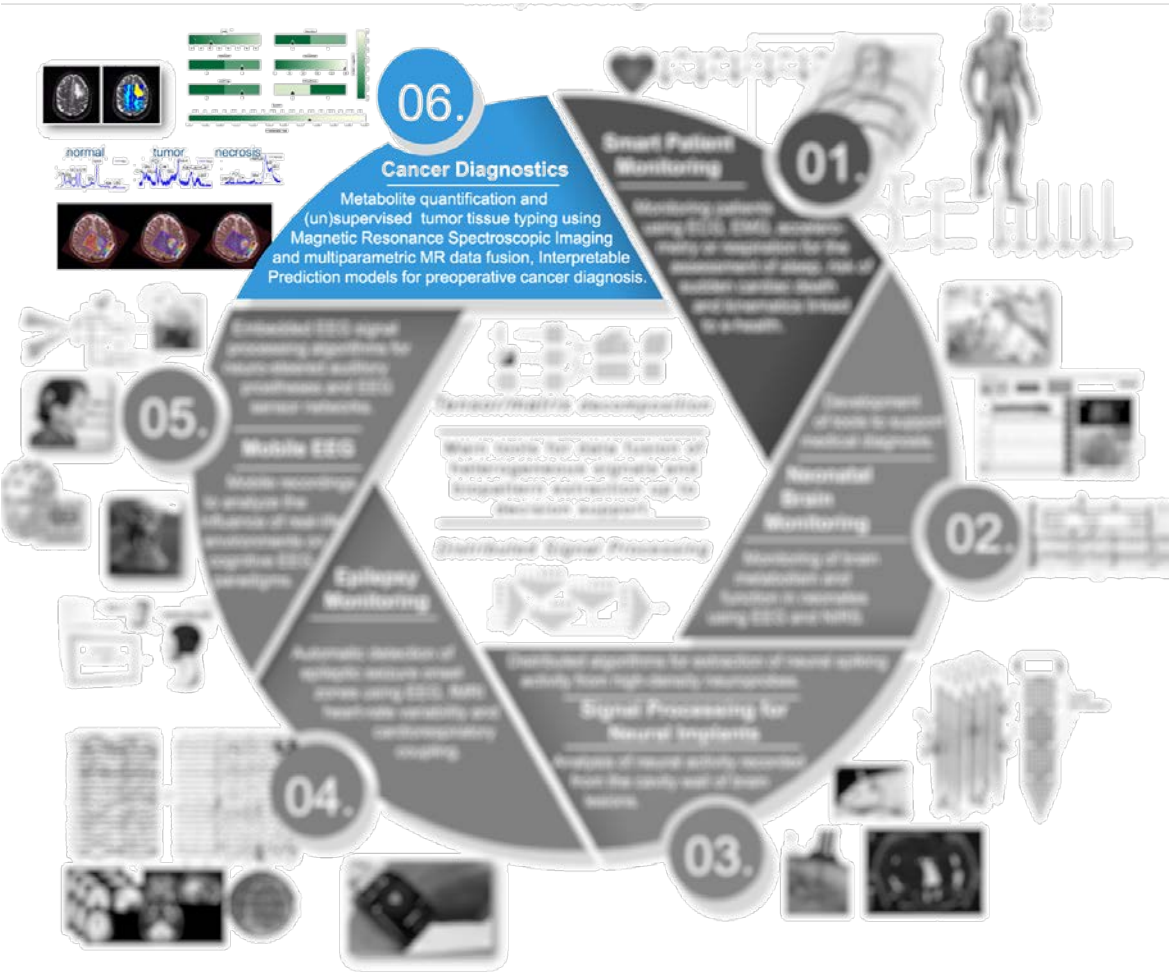
Classification for Magnetic Resonance Spectroscopy and multi-modal MRI

Diana M. Sima, Anca R. Croitor Sava, Nicolas Sauwen, Adrian Ion-Margineanu, Bharath HN, Michal Jablonski, Claudio Stamile

UZ Leuven partners:

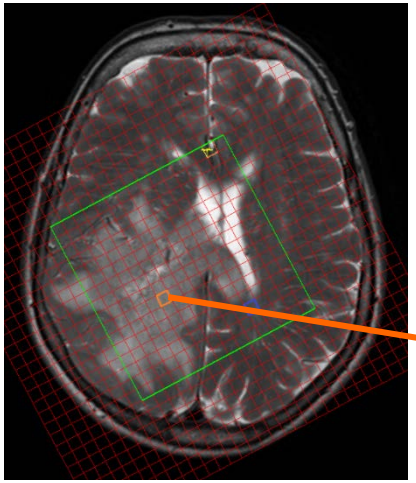
Uwe Himmelreich, Sofie Van Cauter, Stefan Sunaert

ESAT-PSI: Frederik Maes



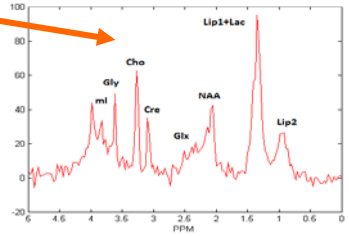
EXAMPLE

Unsupervised tissue type differentiation: Blind Source Separation for MRSI data



Applications

MRSI

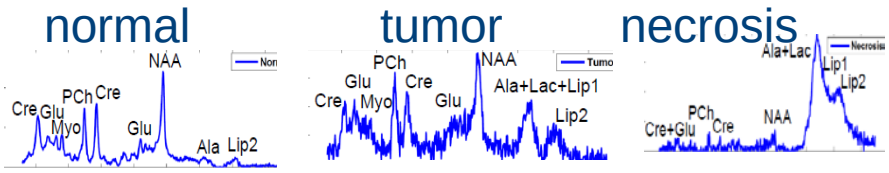


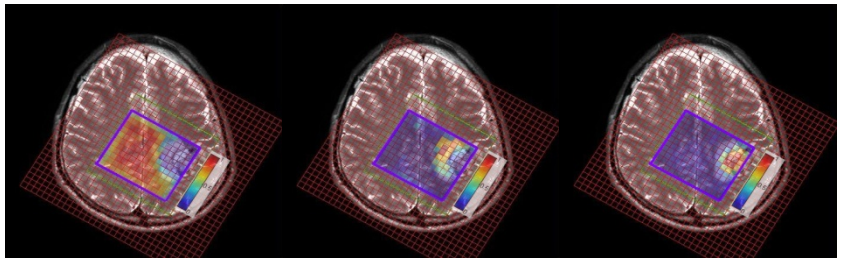
X = matrix of spectra, ***X*** ≈ ***W H***

min || *X* - *W H* ||
such that ***W*** ≥ **0**, ***H*** ≥ **0**

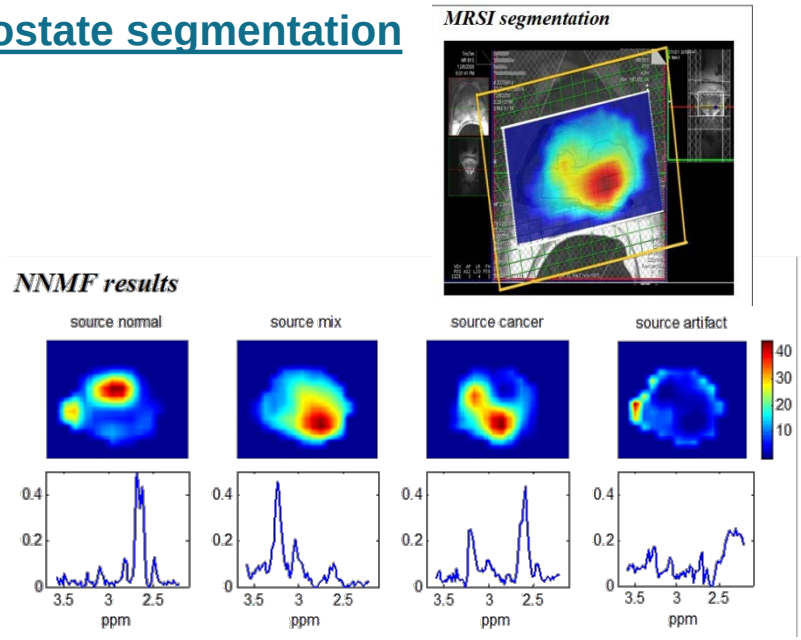
non-negative matrix/tensor factorization

Brain tumor tissue typing



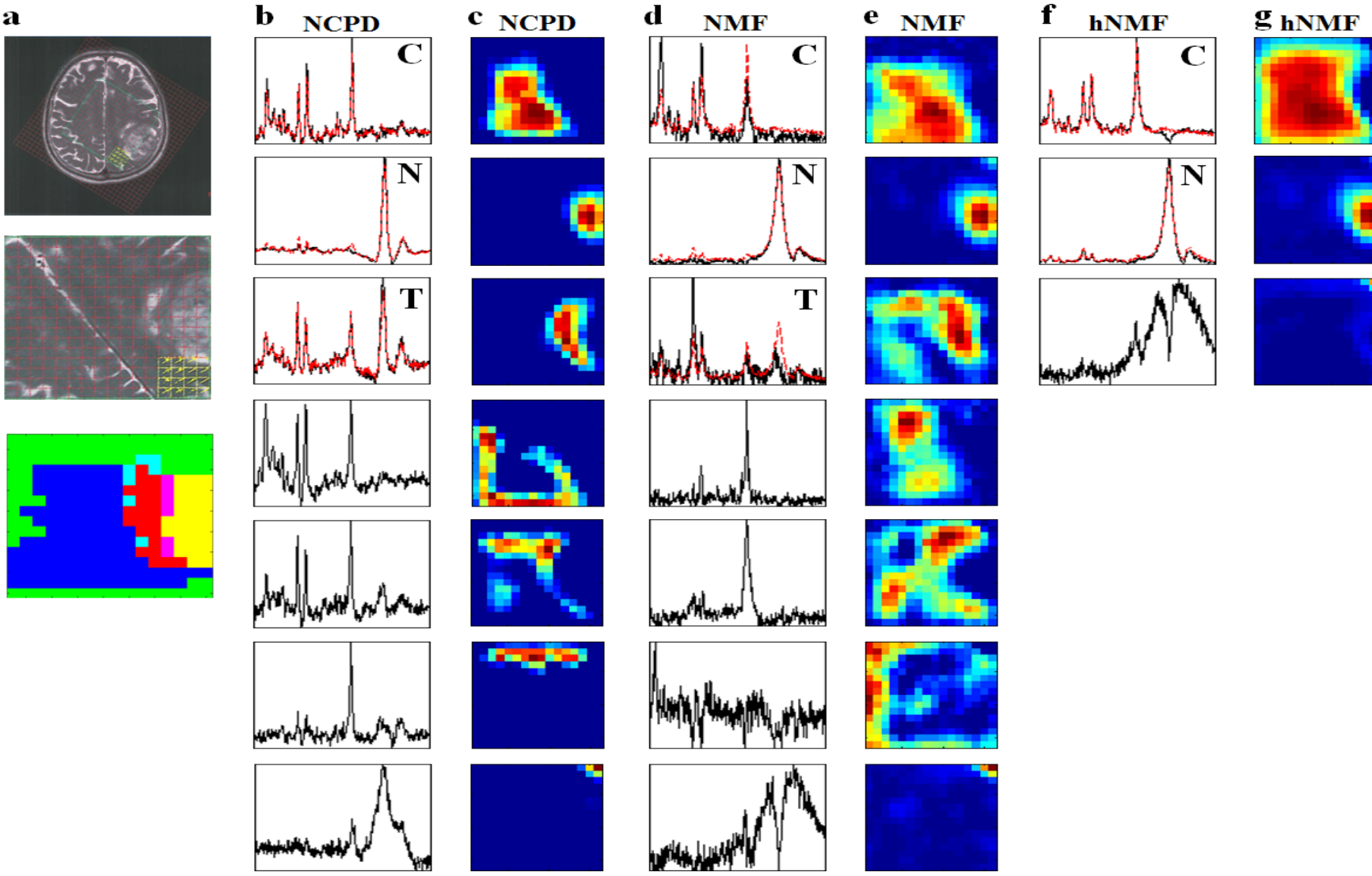


Prostate segmentation



KU LEUVEN

Brain tumor recognition using Non-negative CPD



EEG-fMRI data fusion for the study of brain function

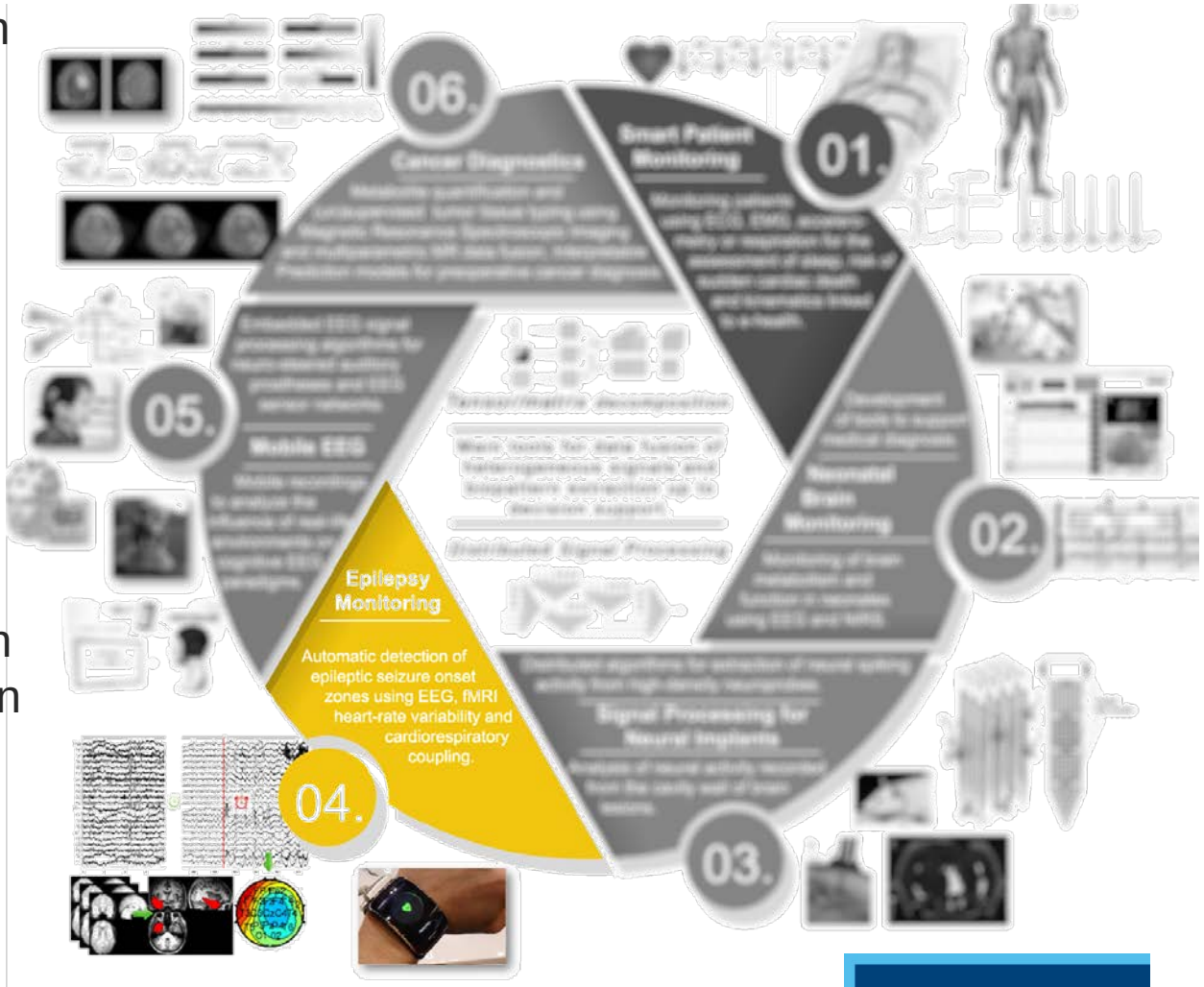
Borbála Hunyadi, Simon Van Eyndhoven, and Bogdan Mijović

Oxford University:
Maarten de Vos

ESAT-Stadius:
Lieven De Lathauwer

UZ Leuven partners: Stefan Sunaert, Wim Van Paesschen

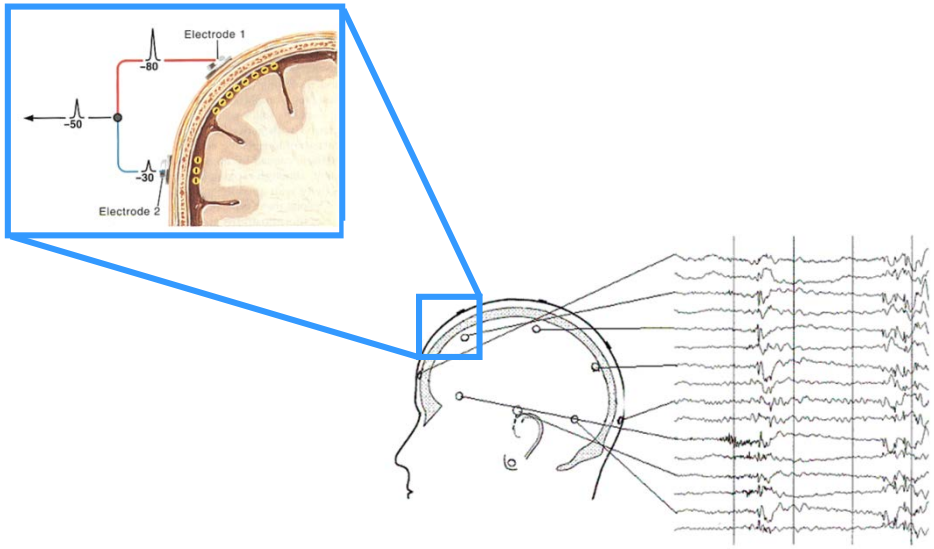
Dept. of Psychology:
Johan Wagemans

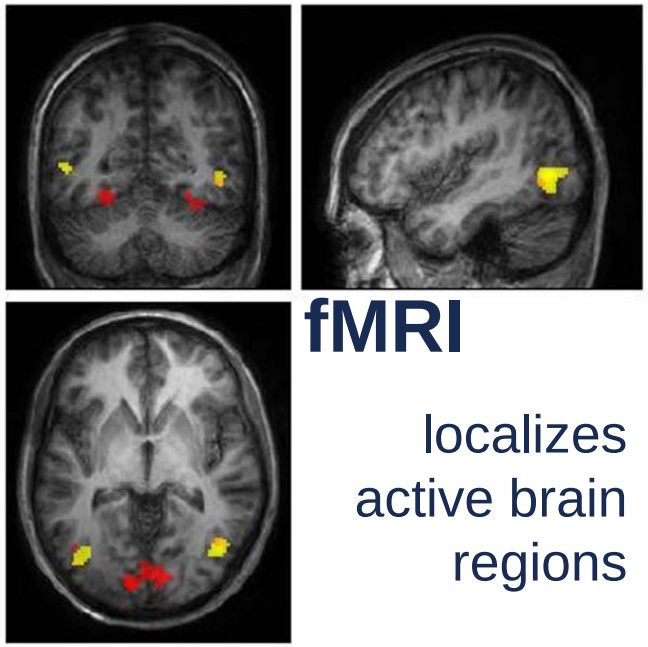


EXAMPLE II

Combined EEG-fMRI analysis

EEG measures electrical potentials on the scalp





fMRI

localizes active brain regions

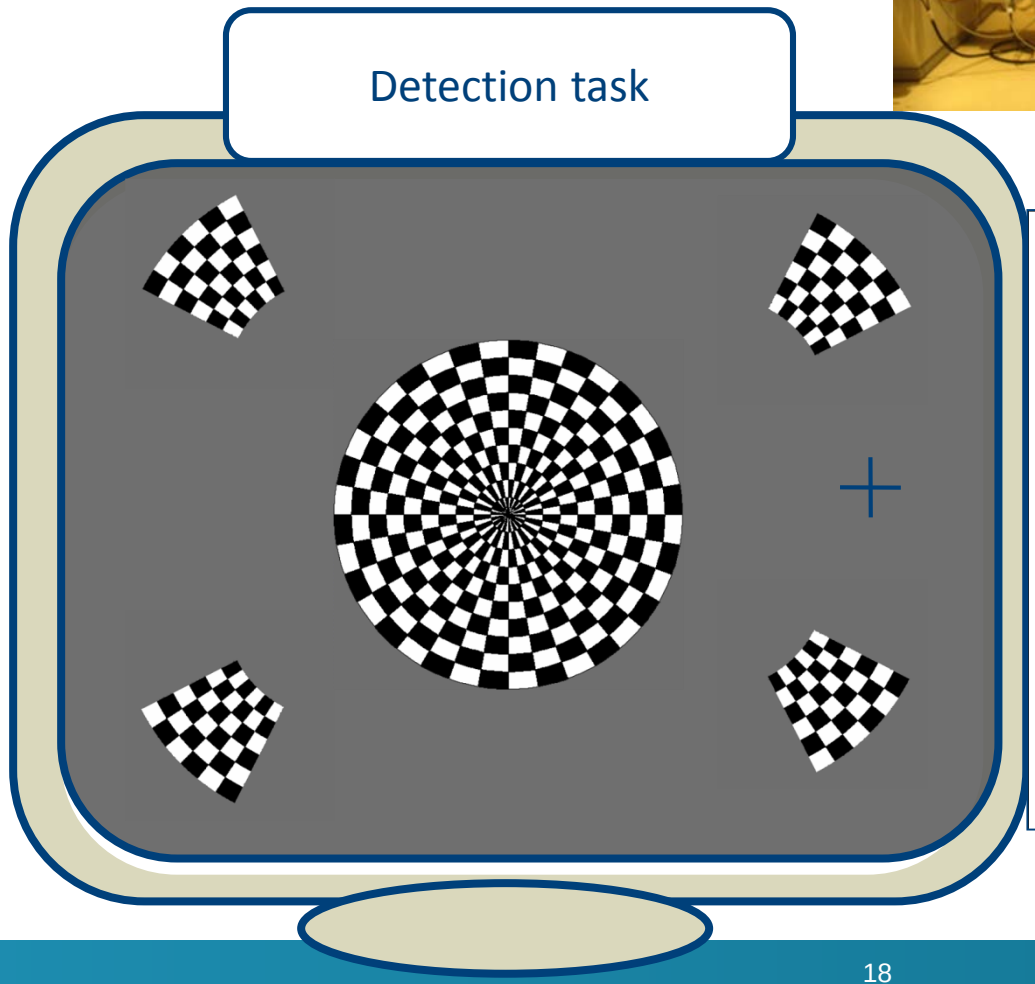
Combining EEG and fMRI:

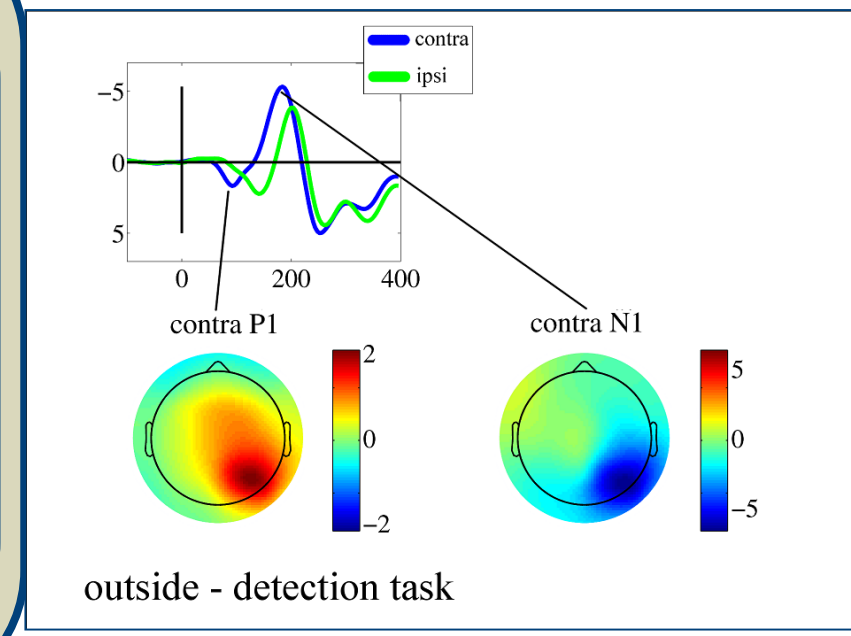
- ***EEG** good **temporal resolution** (~ ms)*
- ***fMRI** good **spatial resolution** (~ mm)*

KU LEUVEN

ERP analysis:

Brain responses evoked due to mental task



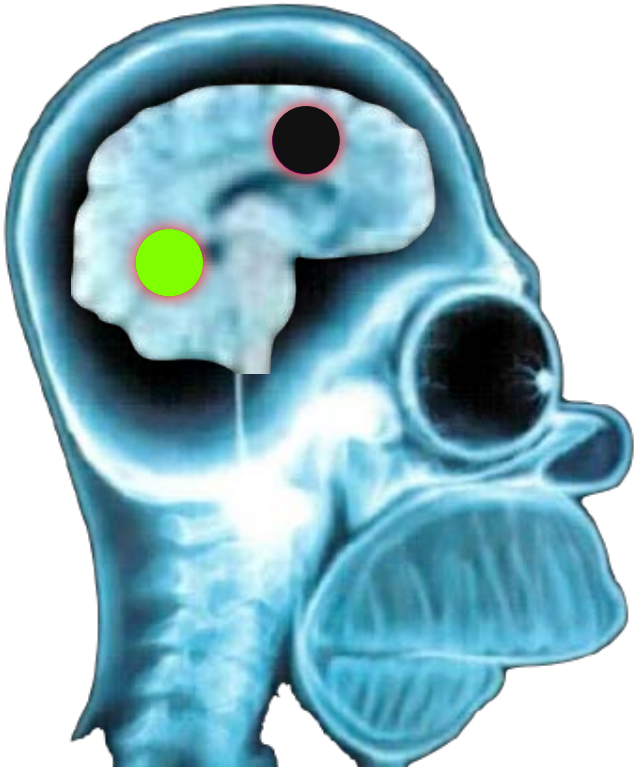


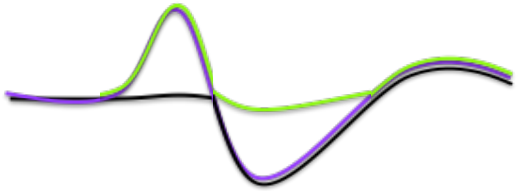
outside - detection task

KU LEUVEN

Symmetric EEG-fMRI approaches: Joint BSS

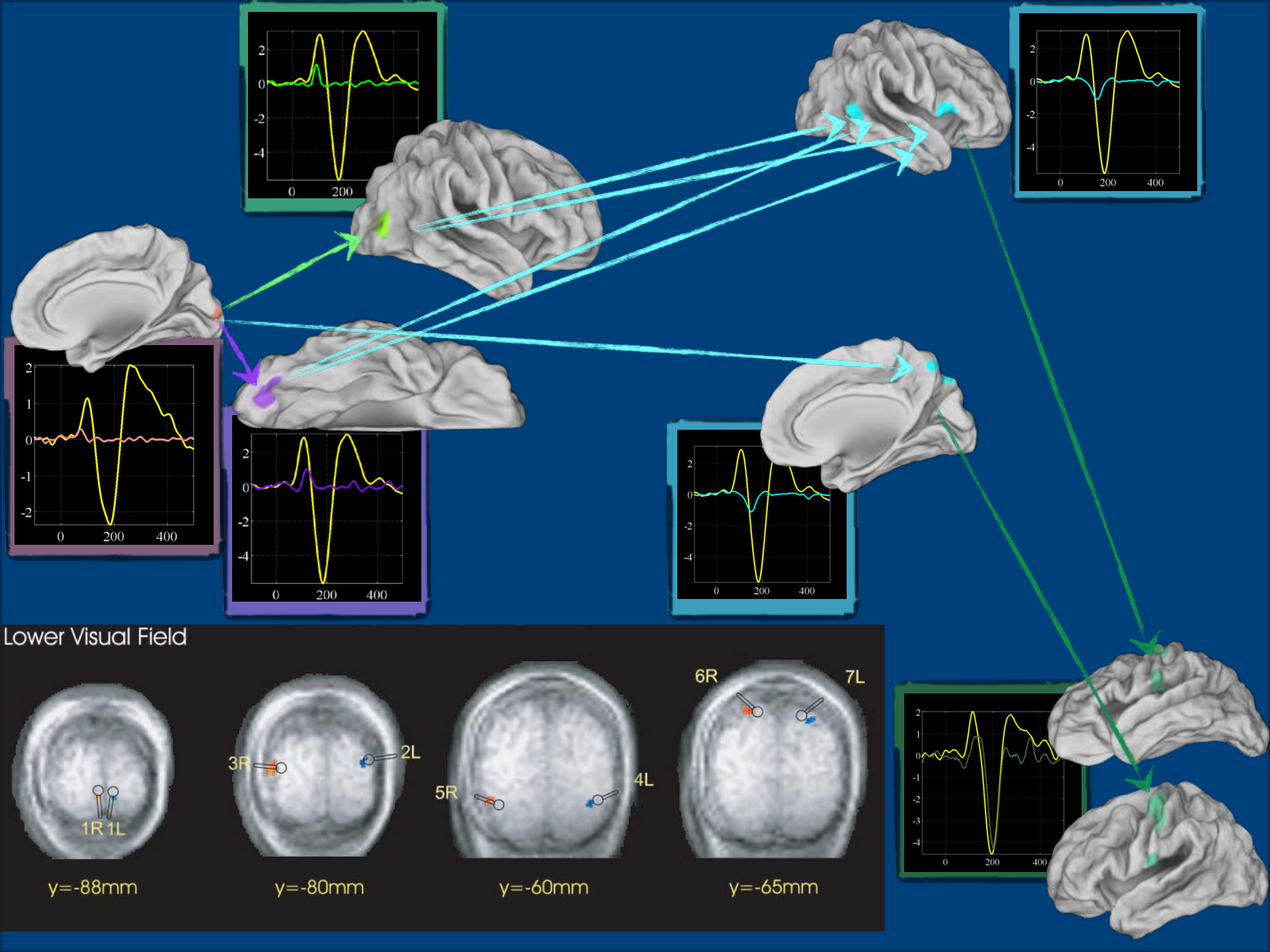
Calhoun et al., (2006), NeuroImage





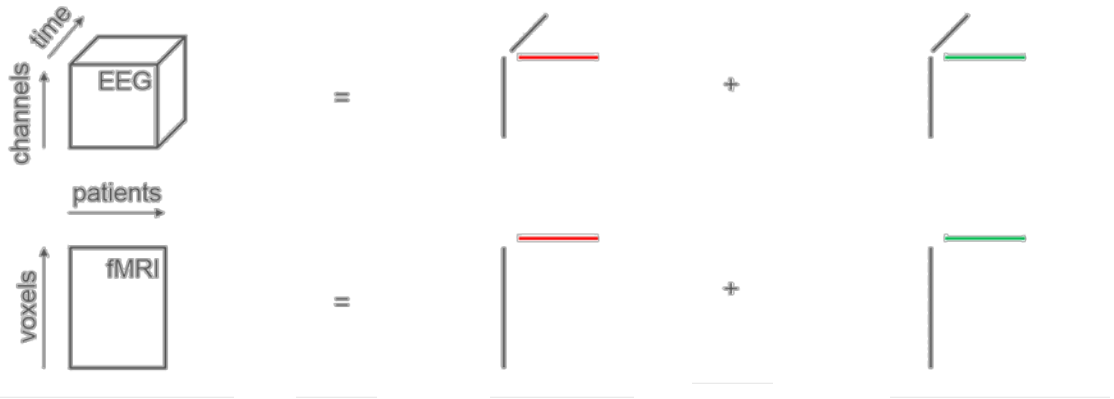
Joint BSS Output

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


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

Exploring the epileptic network

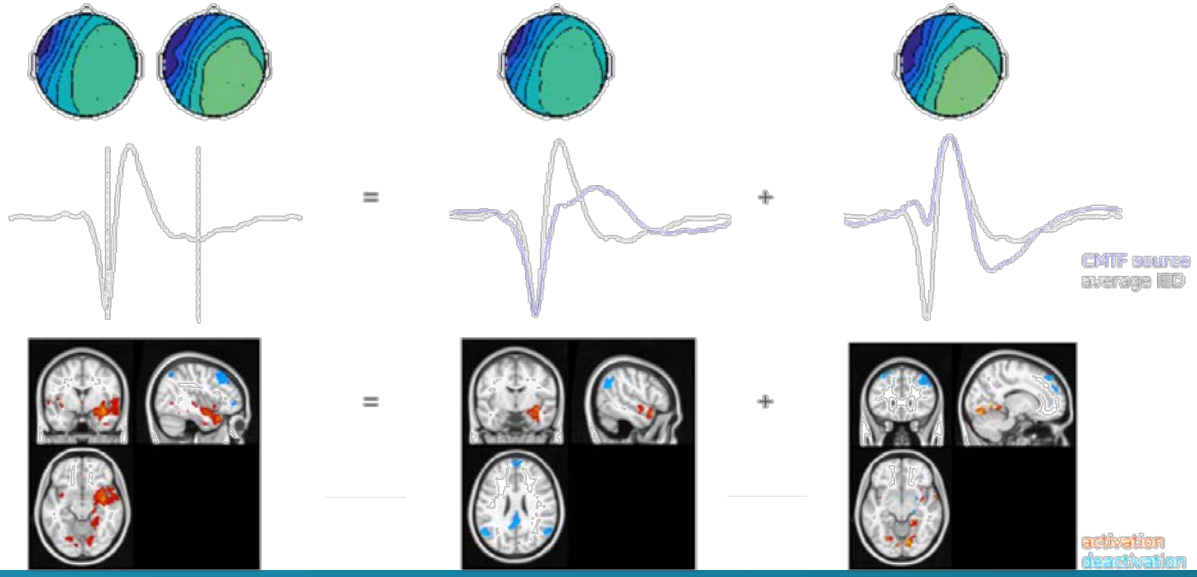
Coupled tensor-matrix factorization:



Average epileptic discharge and BOLD activation:

spike (onset)

slow wave (propagation)



KU LEUVEN

Neonatal Brain Monitoring

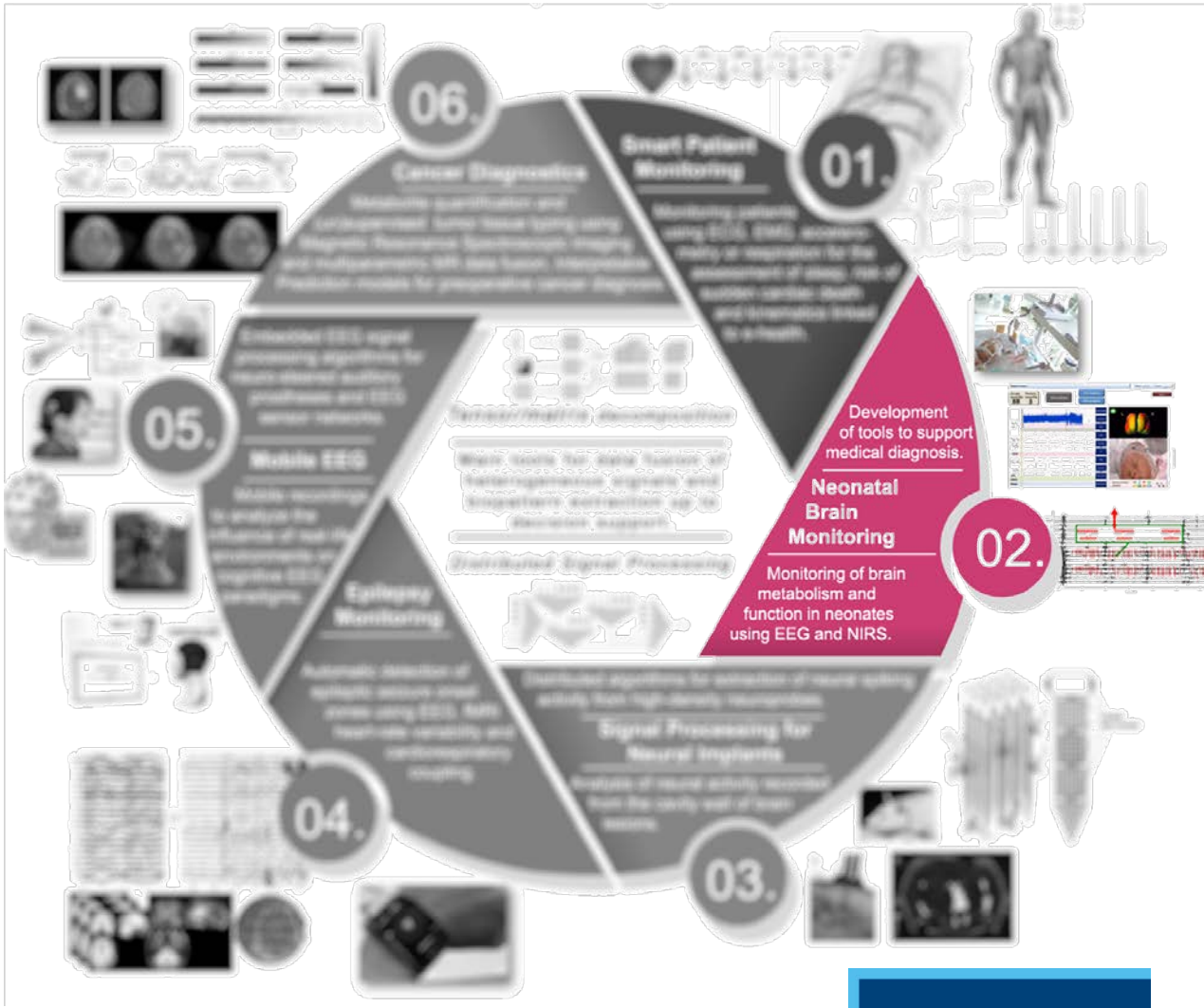
Amir H. Ansari, Alexander Caicedo Dorado, Ofelie De Wel, Ninah Koolen, Mario Lavanga, Vladimir Matic

UZ Leuven partners:

G. Naulaers, J. Vervisch, K. Jansen, A. Dereymaeker

Oxford University:

Maarten De Vos



EXAMPLE III

Neonatal Brain Monitoring

Neonatal Brain Monitoring

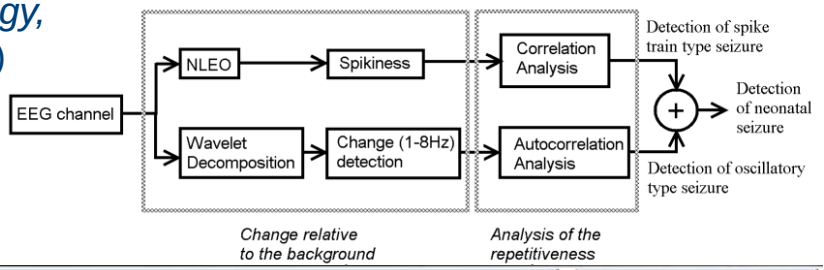
- **Newborn baby is admitted at the Neonatal Intensive Care Unit**
  - Prematurity
- EEG monitoring Starts promptly !
- What are the brain functions?
  - No neurological experts present 24/7
  - No scans for small babies
  - No MRIs
- Limited time window for interventions
  - therapeutic hypothermia has to start within the 6 hours after birth

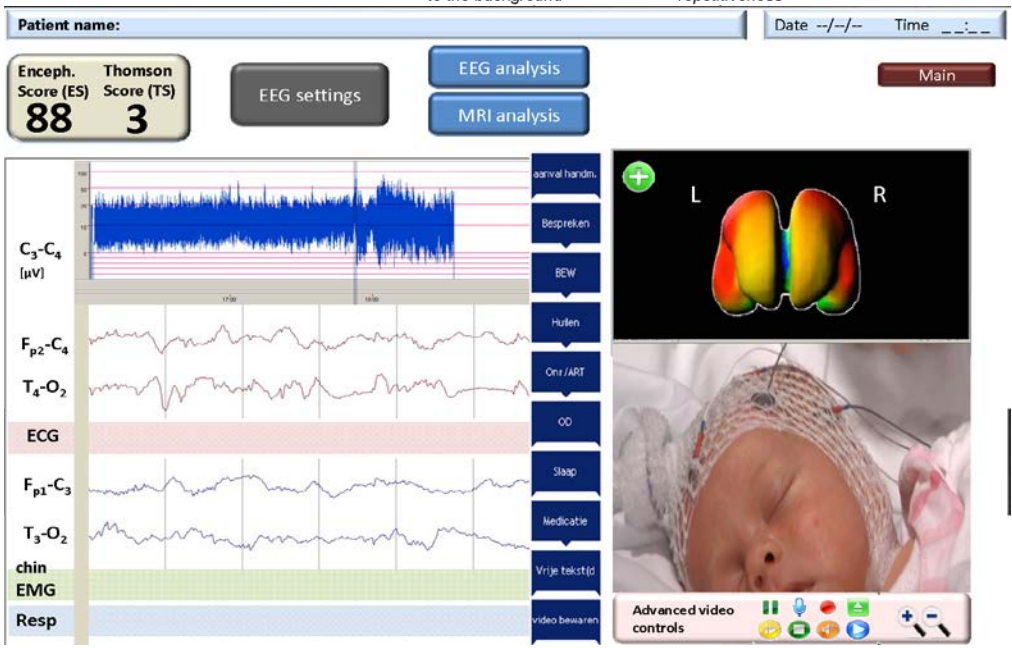
NeoGuard : decision support

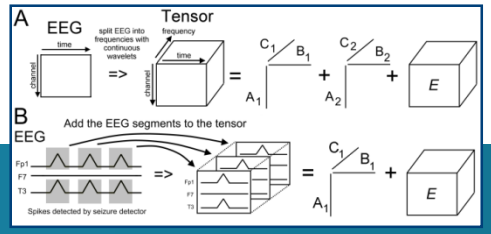
Partners

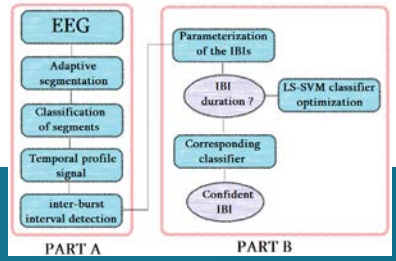
KU Leuven-ESAT (Stadius & MICAS), *UZ Leuven neonatology, EMC Rotterdam, ZNA Middelheim*, Ghent University (TELIN)

- 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

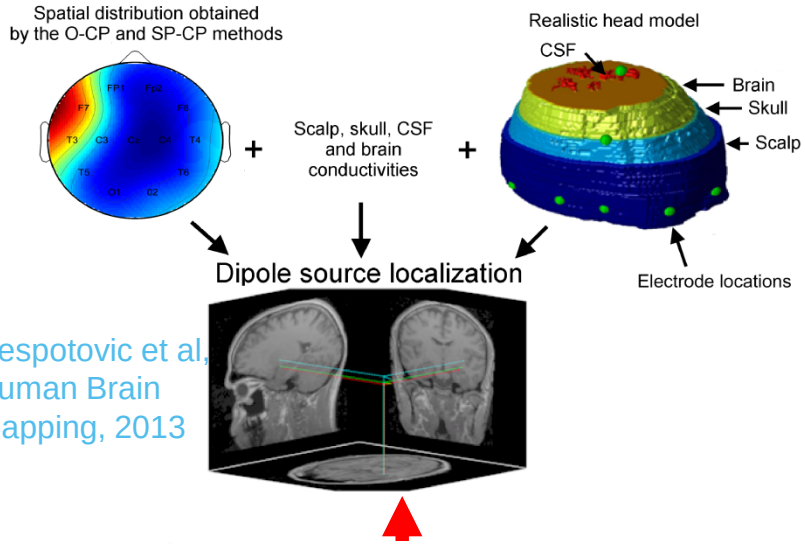




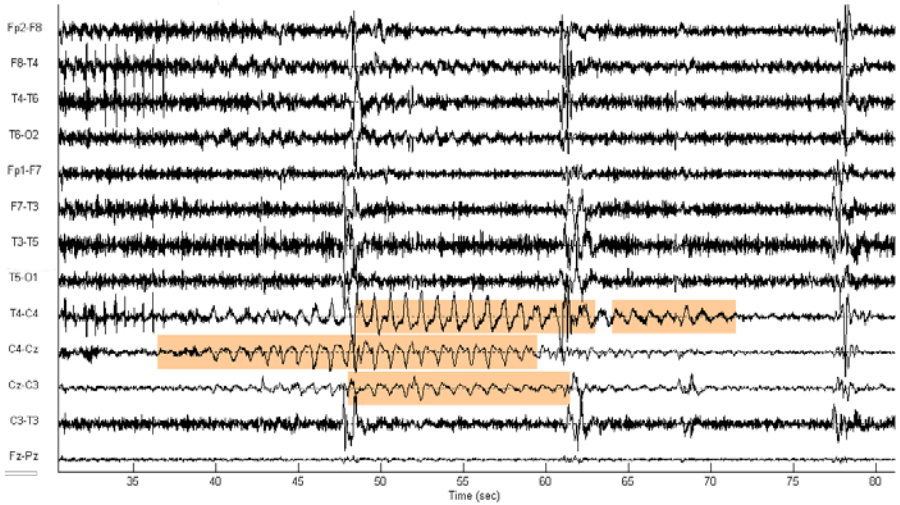




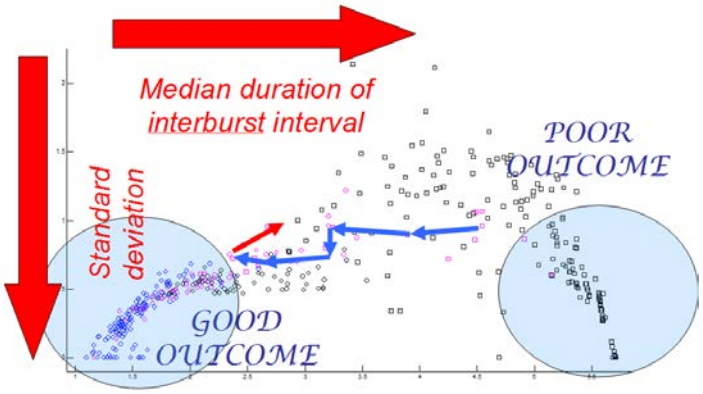
NeoGuard : Clinical Research



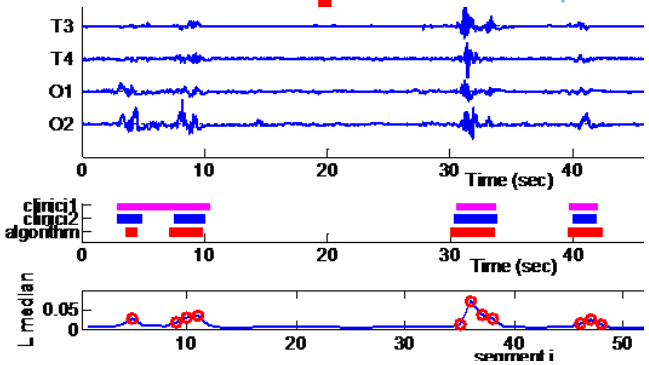
Despotovic et al, Human Brain mapping, 2013



Neonatal epileptic seizures



Koolen et al, Clini.Neurophys. Accepted, 2014



Inter-burst intervals in premature EEG

Effect of Perinatal Stress on the development of preterm infants

Assessment of development of preterm infants affected by perinatal stress through:

- Psychological measures
- Multimodal signal processing
  - EEG
  - HRV
- Epigenomic markers

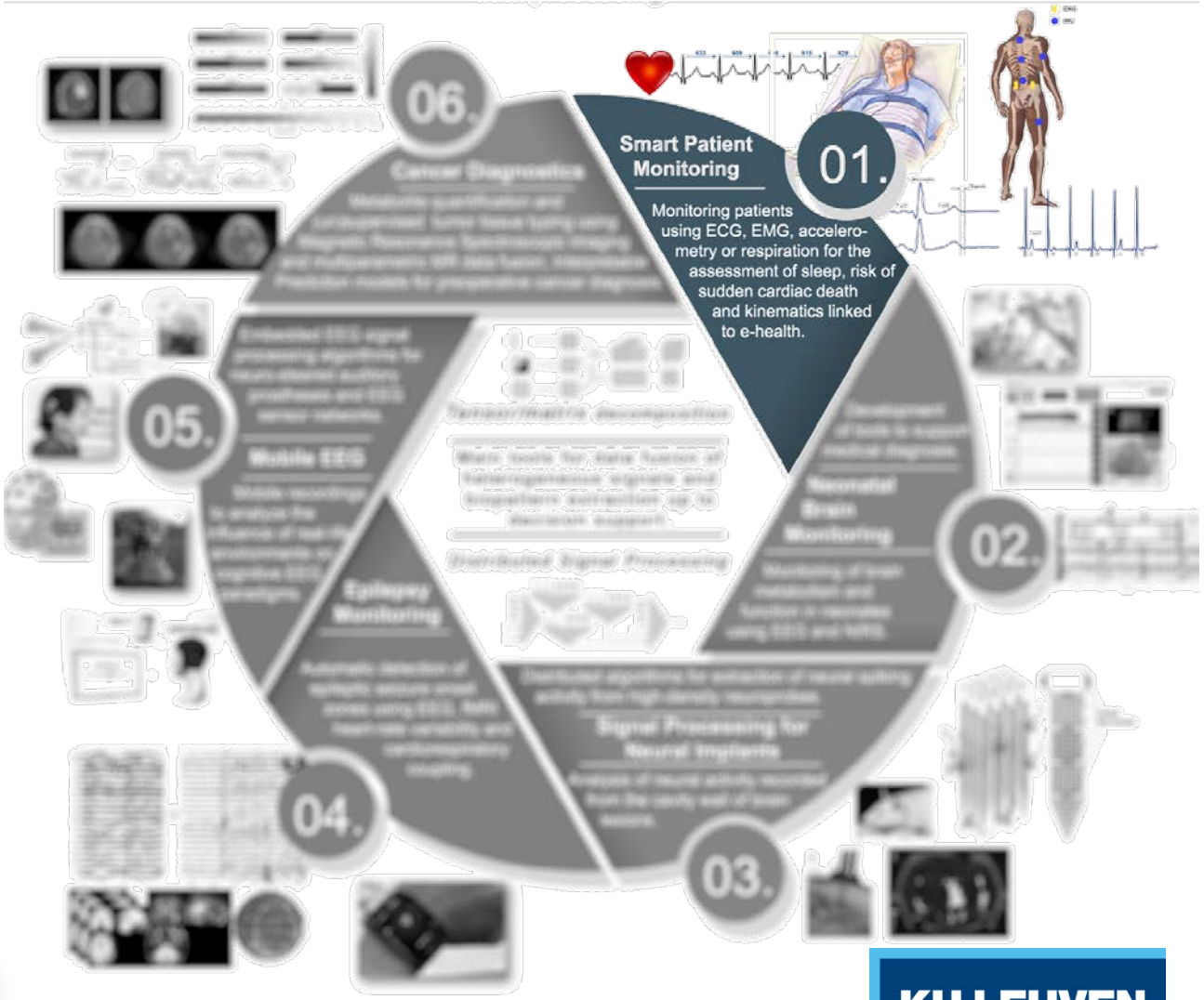
Development of a **mathematical** model, using machine learning techniques, to predict short-term clinical outcomes or neurological delay.

Signal processing for home monitoring of epileptic children

Thomas De Cooman, Carolina Varon, Kris Cuppens and Milica Milosevic

UZ Leuven partners: Lieven Lagae, Katrien Jansen

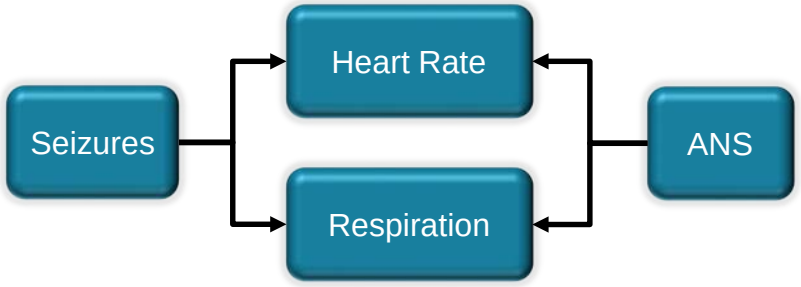
Pulderbos partners: Berten Ceulemans, Anouk Van de Vel

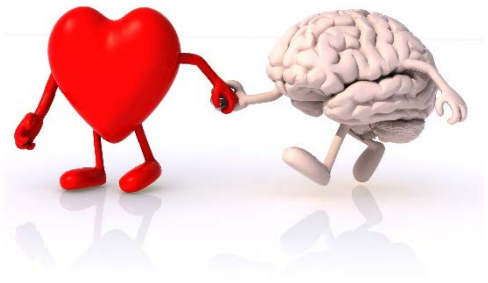


EXAMPLE IV

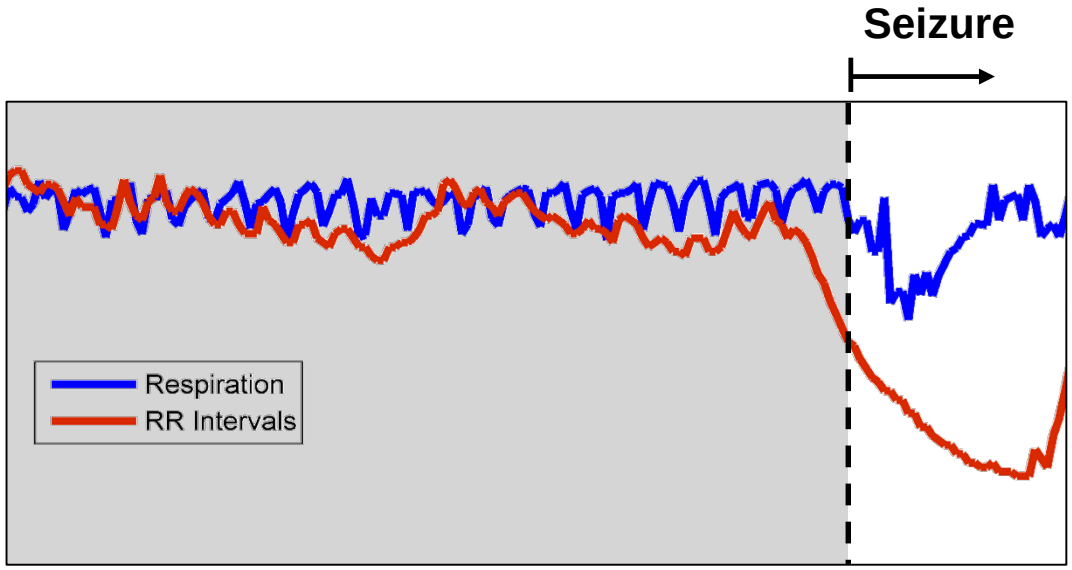
Epileptic seizure detectors based on ECG

Seizures and the autonomic nervous system (ANS)





Goal: Detect cardiac and respiratory changes caused by seizures



Seizures

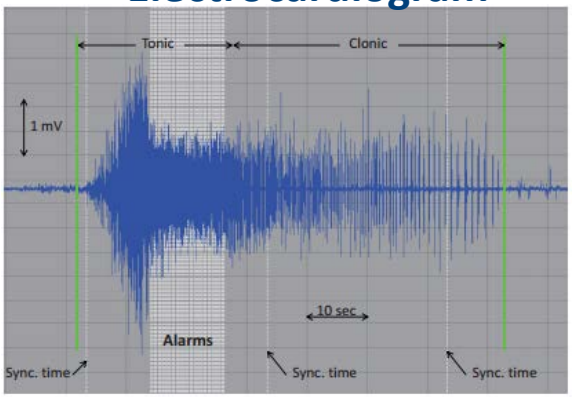
- ✓ Pre-ictal changes
- ✓ Autonomic symptoms
- ✓ Motor activity
- ✓ Stress response
- ✓ Apnea episodes
- ✓ Reduced HRV
- ✓ Tachycardia or bradycardia

KU LEUVEN

Epilepsy monitoring at home

wireless accelerometers

Electrocardiogram



Electromyogram

Combine modalities in optimal way

Single decision output

-Learn online which sensors are useful for the patient

-Other sensors can be removed after a while

-Minimal number of necessary sensors used for patient convenience

-Done by using online l0-norm optimization in SVM classifier

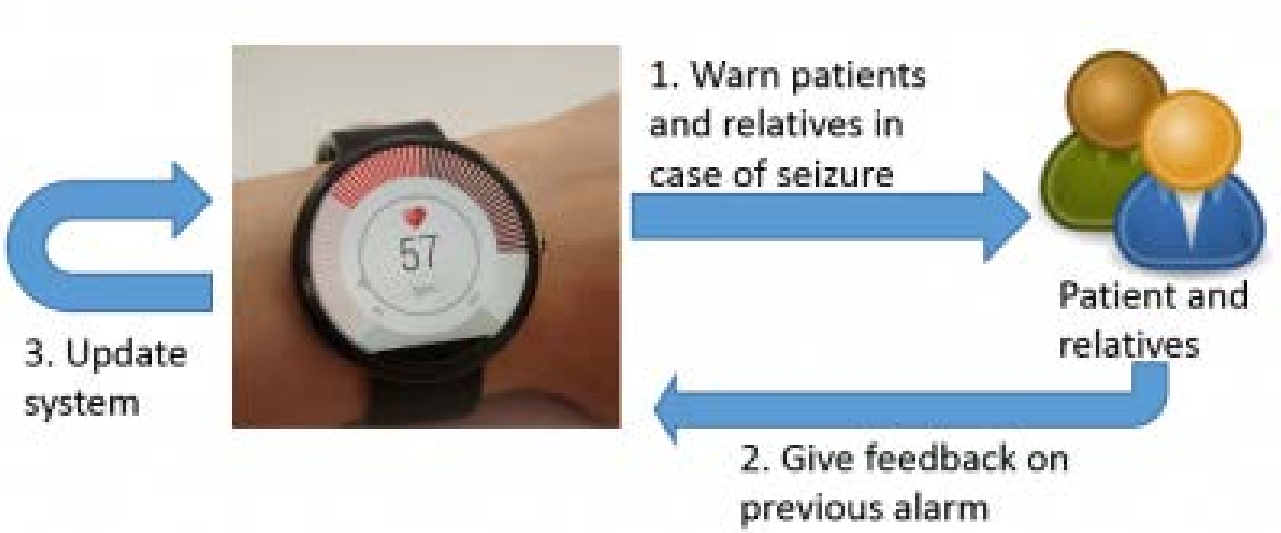
KU LEUVEN

Adaptive learning for improved usability

Problem: Seizure data very patient-specific

Collecting patient-specific data however too time consuming for short-term monitoring

Initially patient-independent system



Benefits compared to patient-specific algorithm:

-Directly usable

-No patient-specific seizure data required

-Quick adaption to patient-specific requirements

KU LEUVEN

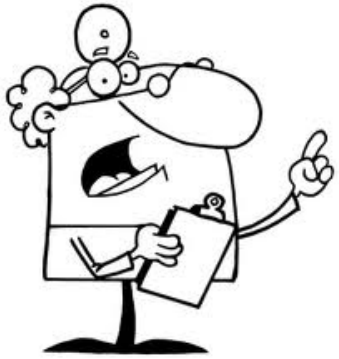
Epilepsy monitoring at home: applications

Comfort patient

Early seizure detection

	Data	Time	Description
1	22/01/2012	22:37:16	CLONIC-TONIC seizure
2	22/01/2012	23:13:36	TONIC seizure
3	…		

Logging of detected seizures



Inform neurologist

Alter treatment/ medication

KU LEUVEN

Contents Overview

1. Introduction

2. Examples

3. Future Challenges

Smart Patient Monitoring: Future Challenges

- **Hardware**: equipment, sensors, …
  → *wearable, unobtrusive, contactless, invisible*

- **Software**: long-term monitoring, (multiple) modalities
  → *low-quality data, 24/7 days reliability, big data*
- **Validation studi**es: long-term followup, GDPR regulations
  → *patient data labeling uncertain & labor-intensive*
- **Training**: learning platform, (online) courses, interdisciplinar
  → *new Ba/Ma programmes in Medicine and BME*

- **Tech transfer to market in medical technology tough job !**
  → *Non-trivial business models, many stakeholders*
  ethical and legal issues, hyper-regulated →CE/FDA approval
  niche market: societal value > economical value

Thank you!

Acknowledgments

University Hospitals Leuven Gasthuisberg
ZNA Middelheim, Queen Paola Children's hospital
EMC Rotterdam
KU Leuven, Dept. Electrical Engineering-ESAT, division STADIUS & MICAS
Ghent University, Dept. Telecommunication and Information Processing, TELIN-IPI
Eindhoven University of Technology

ERC advanced grant 339804 BIOTENSORS
in collaboration with L. De Lathauwer and group