Autonomous Medical Monitoring and Diagnostics (AMIGO)

AO/1-8112/14/F/MOS

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FM - Final meeting

Mathieu Lemay, Project Manager
Alia Lemkaddem, Signal Processing and Data Mining Expert

Division Systems, CSEM SA

Köln, 26th of October 2016

Outline

- Introduction
- Amigo's status
- Mission scenarios
- Medical database selection
- Feature extraction
- Technical and medical validation
- Evaluation platform & matrix
- Data mining techniques
- Anomaly detection and classification
- Clinical investigation
- AMIGO in future missions
- Open discussion

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Introduction - Amigo's objectives

AMIGO proposes to **evaluate** if and how **data mining** can be of benefit for an **autonomous** medical **monitoring/diagnostic** system.

AMIGO targets:

- **astronauts** and **medical crewmember** as users;
- **long-term spaceflight** and **non-space** related applications; and
- **ISS** medical examination protocols.

AMIGO shall be evaluated on **substantial** and **representative** numerical database compliant with **regulation** rules.

AMIGO data mining and feature extraction algorithms shall be **iteratively designed/evaluated** on **relevant medical data**.

AMIGO shall provide **faster awareness** and **resolution** than with ground interactions.

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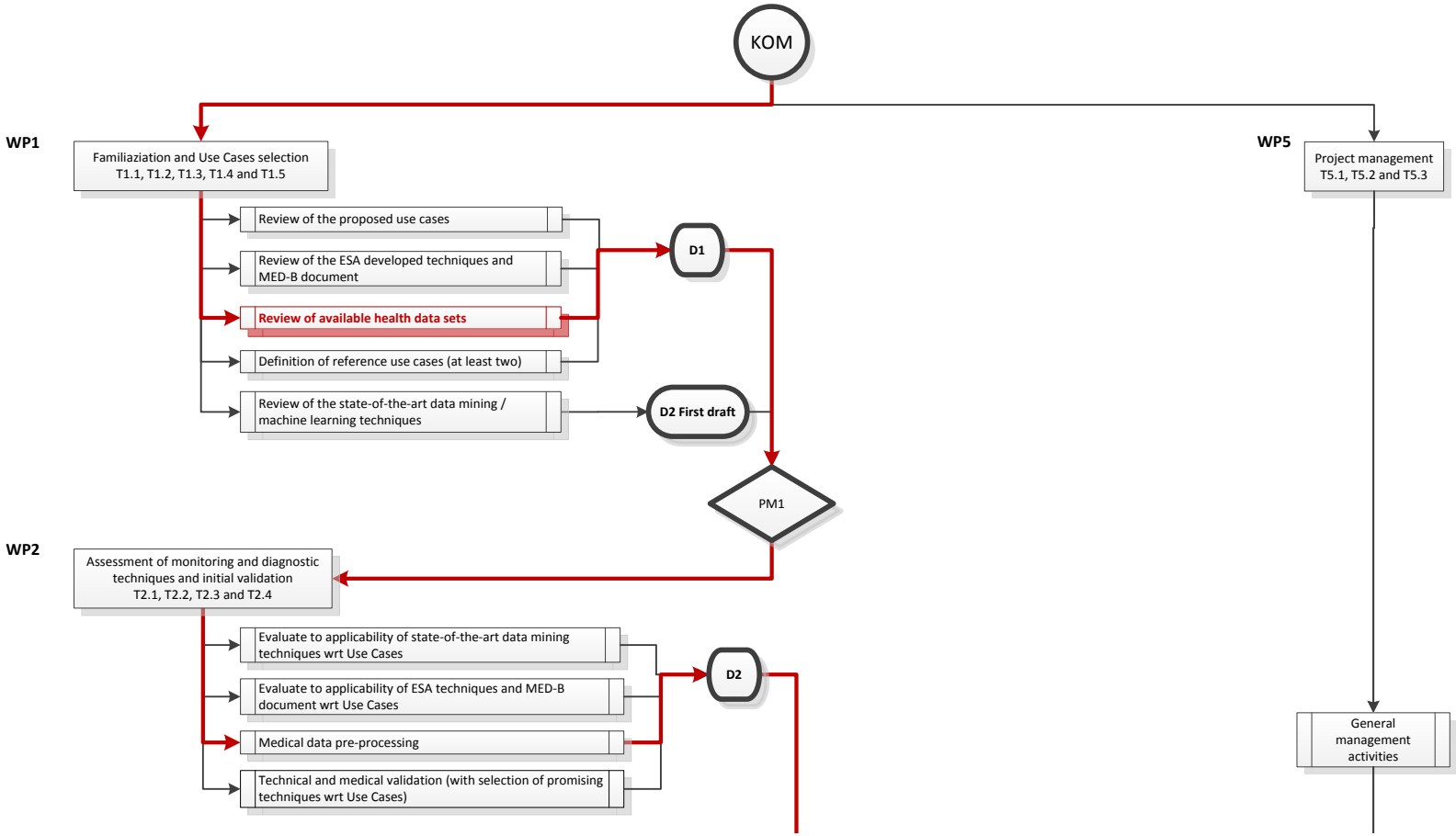
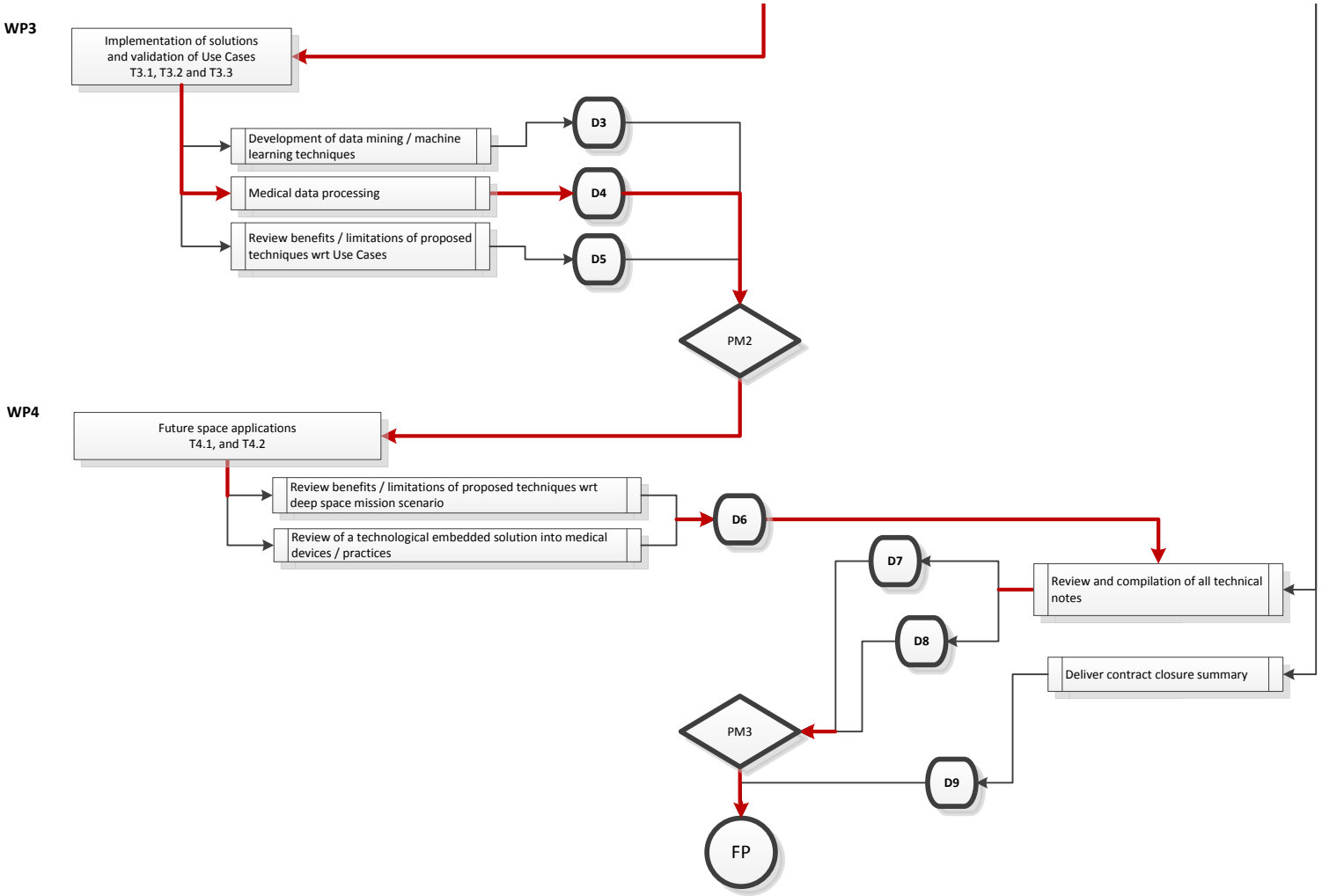
Amigo's status - WP definitions

- WP1 is untitled "*Familiarization and Use Case selection*" and is mainly dedicated to the **review** of proposal and corresponding documents and **definition** of **scenarios** and **Medical Use C**ase.
- WP2 is untitled "*Assessment of monitoring and diagnostic techniques and initial validation*" and is mainly dedicated to the **definition** and **evaluation** of the proposed **development**.
- WP3 is untitled "*Implementation of solutions and validation of Use Cases"* and is mainly dedicated to **development** of the evaluation platform, its **performance evaluation** and the review of its **benefits/limitations**
- WP4 is untitled "*Future space applications for medical monitoring and diagnostics"* and is mainly dedicated to **review** of **AMIGO benefits / limitations** and **review** of **technological embedded solutions** and their **applicability** into AMIGO framework.

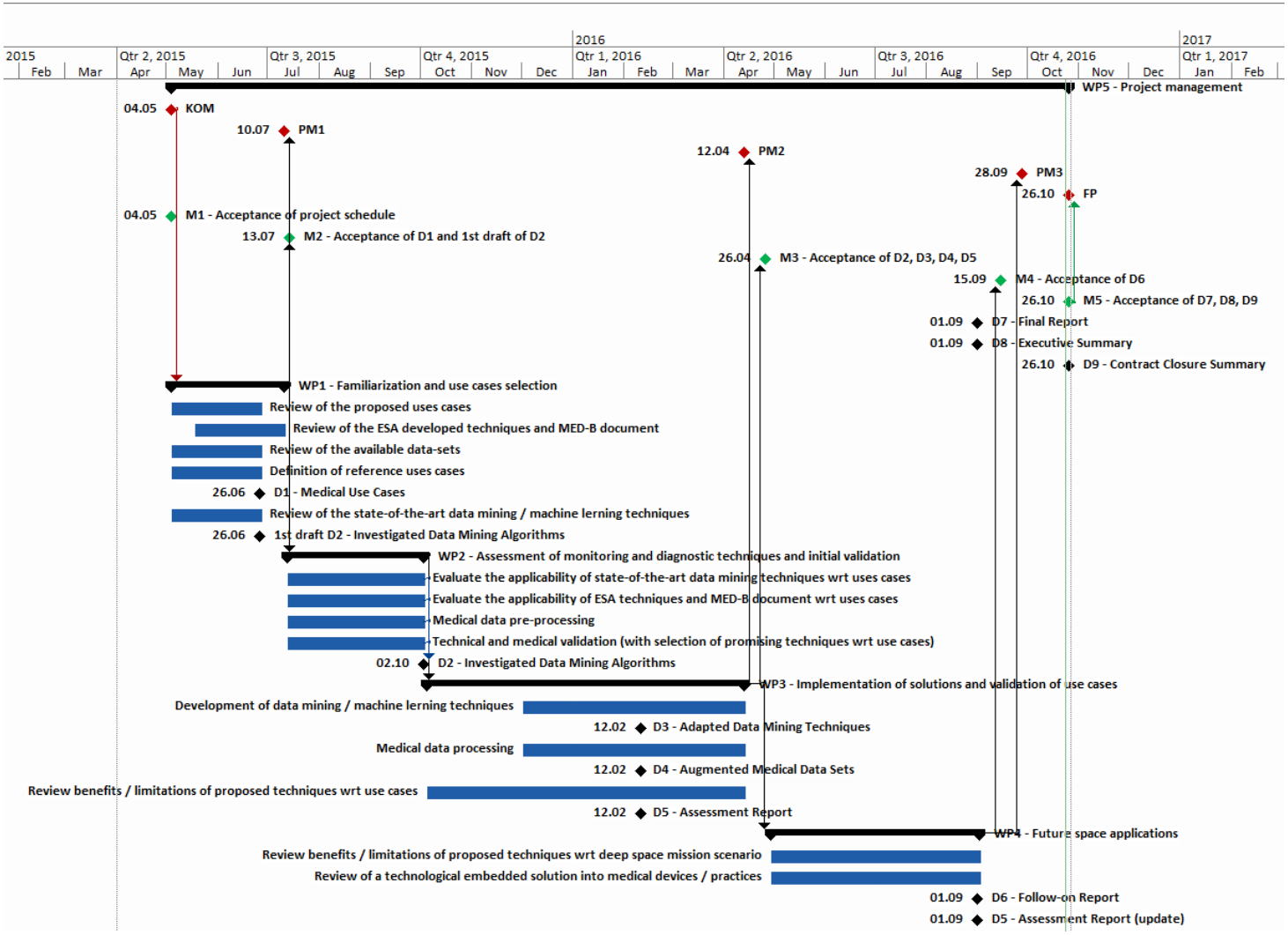
Amigo's status - Deliverables (part I)



Amigo's status - Deliverables (part II)



Amigo's status - planning



Amigo's status - budget

WP	Title	total budget (PSS A8:12+13)	Current costs (partners)	Current costs (CSEM)	Current costs (ALL)	Cost in %	w.i.p.
WP1	Use Cases	45'892	35'000	3'661	38'661	84.2	100
WP2	Assessment of monitoring and diagnostic techniques and initial validation	33'538	0	33'538	33'538	100.0	100
WP3	Implementation of solutions and validation of Use Cases	44'717	0	97'495	97'495	218.0	100
WP4	Future space applications	30'000	30'000	0	30'000	100.0	100
WP5	Project Management	16'769	0	17'023	17'023	101.5	100
	Travel and/or material	4'083	0	2'500	2'500	61.2	100
	Total	**174'999**	**65'000**	**165'178**	**230'178**	**125.3**	**100**

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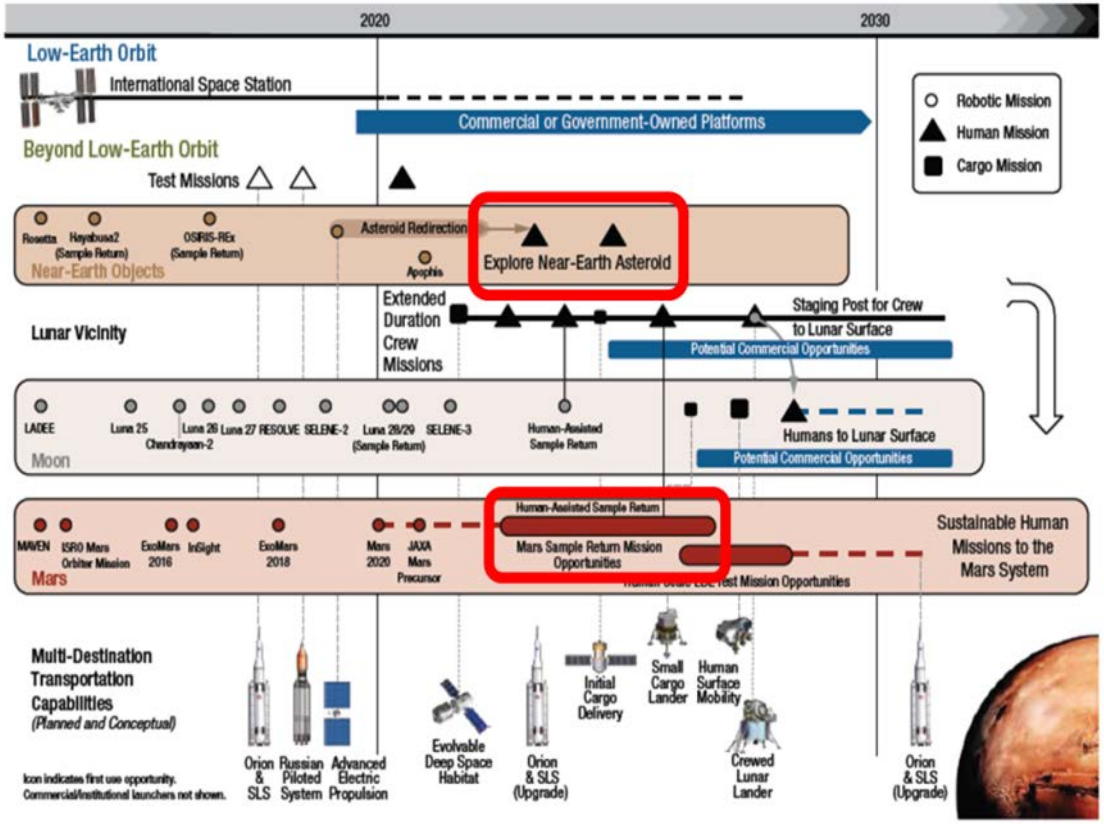
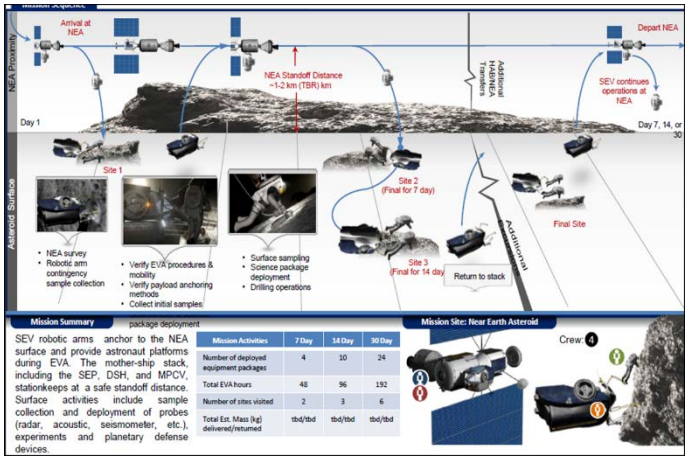
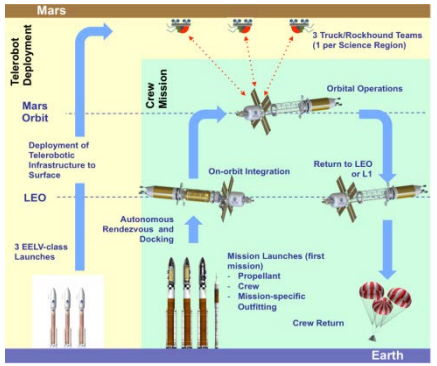
Mission scenarios

Based on International Space Exploration Coordination Group roadmap, **Explore Near-Earth Asteroid** and **Mars Sample Return Mission** scenario's were selected.







Mission scenarios

This scenarios are characterized by:

- **higher medical risk** due to expected human missions / tasks with EVA for the asteroid mission for sample extraction and planetary surface exploration for the Mars mission;
- requires Delta-V impulsion in a range of 10-35 km/sec;
- the crew size would be four or six;
- the mission duration would be **around 430 or 630 days** including 30 days on the asteroid to “visit” up to six sites or 180 days on Mars orbit for tele-robotic exploration of 3 science regions;
- the **crewmember workload** would be fully occupied (8 hours / day by shift); and
- this mission has been predesigned.

Mission scenarios

The related medical conditions are:

- De Novo cardiac arrhythmia, characterized by **high occurrence** (**3** and **0.15** person/year during transfer and planetary/asteroid surface activities respectively[1]) especially when the subject is under stress environment and under microgravity with a relative dehydration / hemoconcentration as observed on astronaut after some days under microgravity; and
- Sleep apnea, characterized **by high occurrence** (**10%** of astronaut during 1 to 3 days at gravity changes during transfer and planetary/asteroid surface activities respectively[1]).

[1] Source space specific, astronaut epidemics data

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Medical database selection

De Novo cardiac arrhythmia (MIT-BIH Arrhythmia, MIT-BIH Noise Stress, CU Ventricular Tachyarrhythmia, Long-Term AF Databases)

Monitoring duration: from 30 minutes up to 24 hours

Population: 94 (44 + 6 + 15 + 35) subjects

Monitoring parameters:

- multi-lead ECG recordings (from 2 to 12-lead ECG) with useful medical-condition dependent features and classification.

Medical database selection

Sleep apnea syndrome (MIT-BIH Polysomnographic Database)

Monitoring duration: from 97 minutes up to 6 ½ hours

Population: 16 subjects (18 recordings)

Monitoring parameters:

- ECG, invasive blood pressure signal, EEG, respiratory signals (EOG, EMG, stroke volume and oxygen saturation are optional) with useful medical-condition dependent features and classification.

Medical database selection

The existing anomalies within the databases with a sufficient number of occurrences:

Anomaly	Training dataset		Testing dataset		Included in AMIGO
	NTot	NSubj	NTot	NSubj	
Atrial fibrillation	6'716	4	14'131	4	A
Supraventricular ectopic	0	0	4	1	R
Ventricular ectopic	6'780	17	7'456	20	A
Ventricular tachycardia	0	0	0	0	R
Ventricular flutter	0	0	0	0	R
Ventricular fibrillation	0	0	0	0	R
Supraventricular tachycardia	6	2	0	0	R
Ventricular bigeminy	1'244	5	1'596	6	A
Ventricular trigeminy	772	5	784	5	A
Idioventricular rhythm	0	0	0	0	R
Atrial bigeminy	74	1	0	0	R
Sinus bradycardia	0	0	0	0	R
Sleep apnea syndrome	10'236	8	11'784	8	A

De Novo cardiac arrhythmias

- Atrial fibrillation
- Ventricular ectopic
- Ventricular bigeminy
- Ventricular trigeminy

Sleep apnea syndromes:

- Hypopnea
- Hypopnea with arousal
- Obstructive apnea
- Obstructive apnea with arousal
- Central apnea
- Central apnea with arousal

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Feature extraction

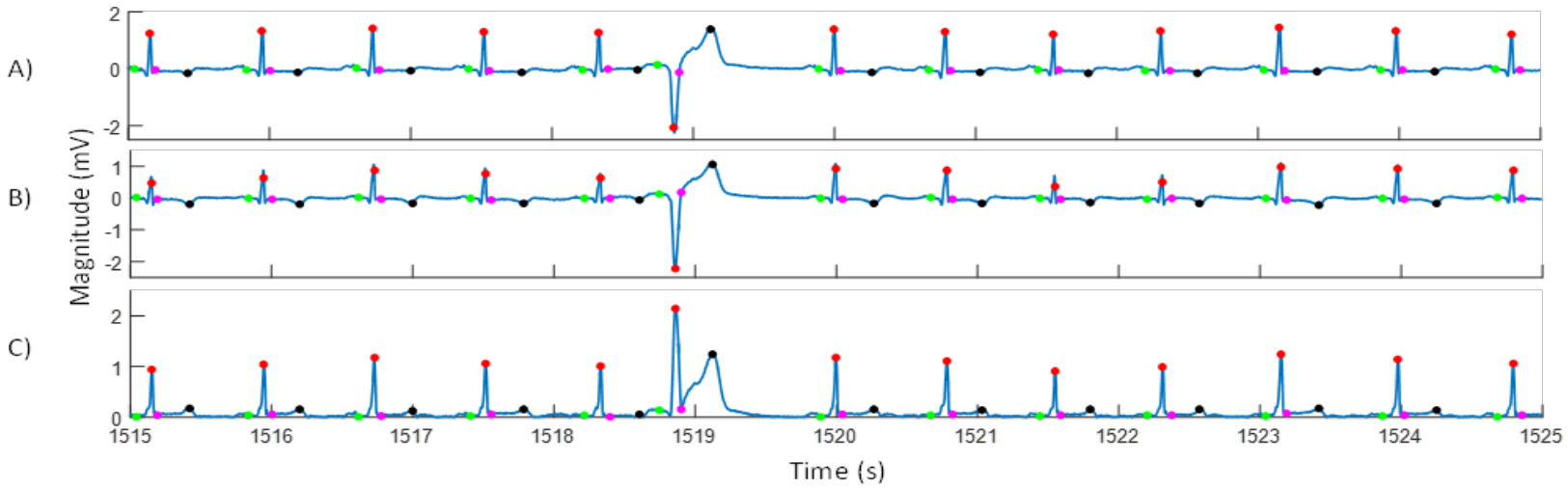
Non-specific signals:

- 10 statistic-based features on moving time windows (mean, standard deviation, skewness, kurtosis, magnitude extrema, quartiles, power, average first derivative).
- 3 frequency-based features on moving time windows (dominant frequency, kurtosis of spectrum, skewness on spectrum).

Feature extraction

ECG-specific signals:

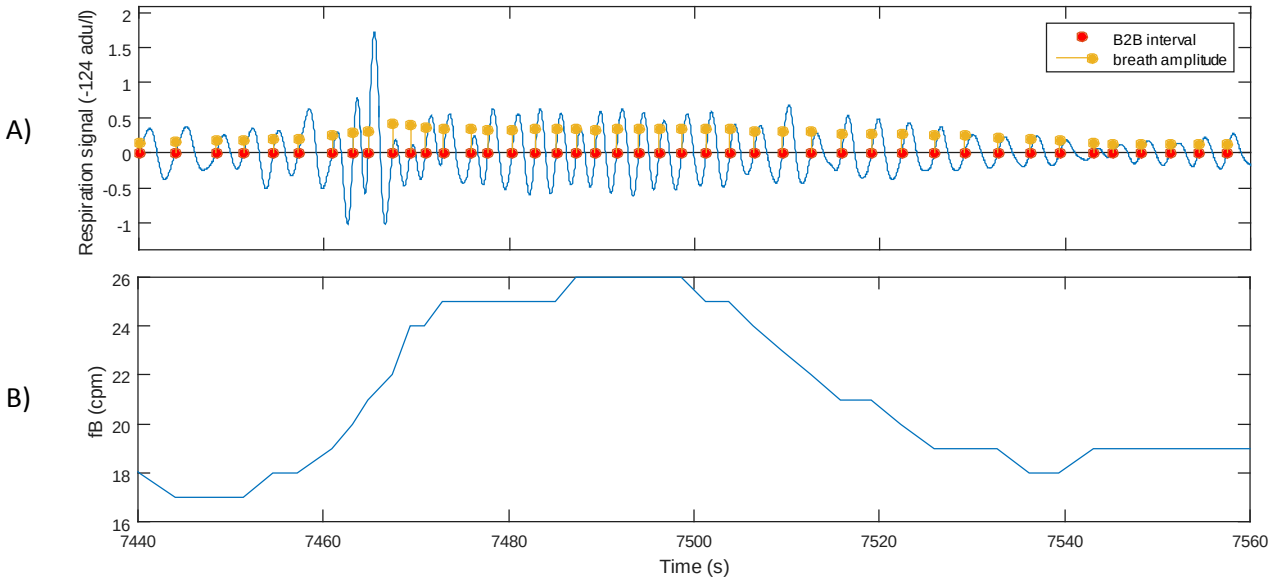
- 7 fiducial point detections
- 55 fiducial point non-specific derived features
- 20 statistical features from separate atrial and ventricular activities
- 4 spatial dynamic features from separate atrial and ventricular activities



Feature extraction

Respiration-specific signals:

- 14 respiration non-specific derived features
- 3 respiration event detections
- 14 non-specific features from time series of breath-2-breath (B2B) intervals

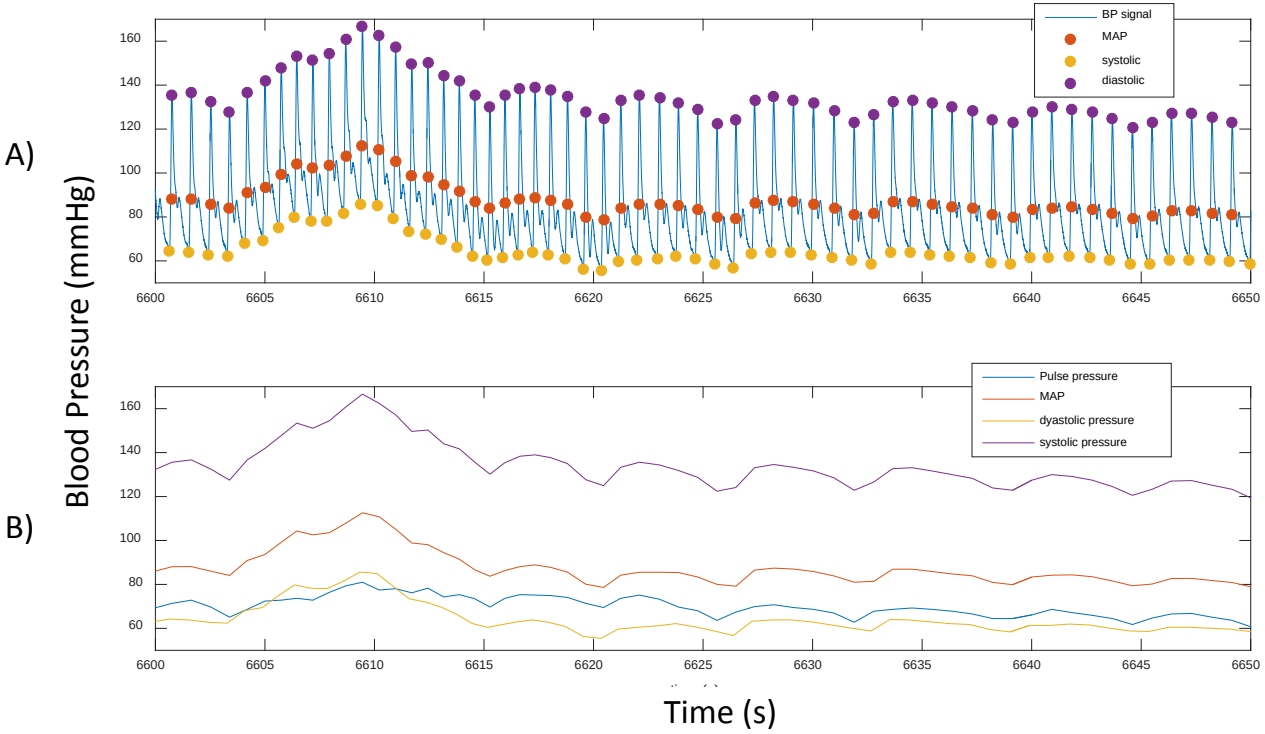


A) Pre-processed respiratory signal, B) The evolution of the breathing frequency

Feature extraction

Blood pressure-specific signals:

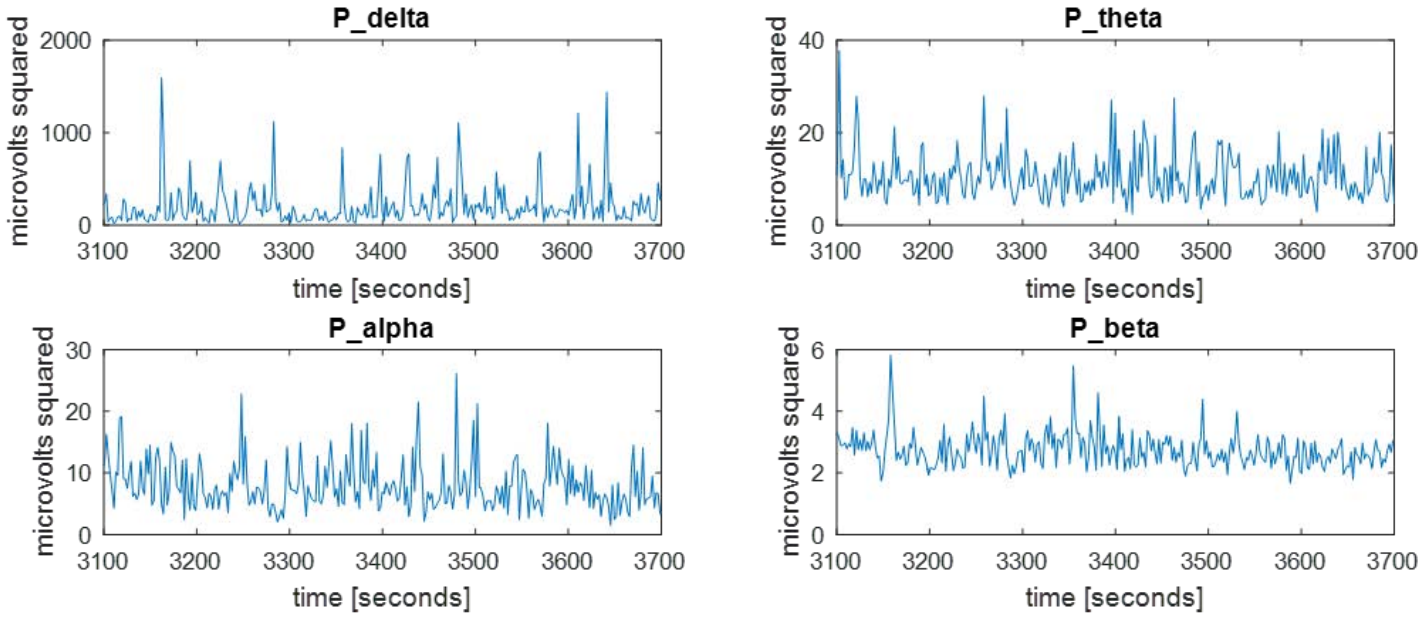
- 4 BP-specific features (systolic, diastolic, pulse pressure and MAP)



Feature extraction

EEG-specific signals:

- 7 EEG-specific features (Delta, Theta, Alpha, Power ratio, MF and SE)



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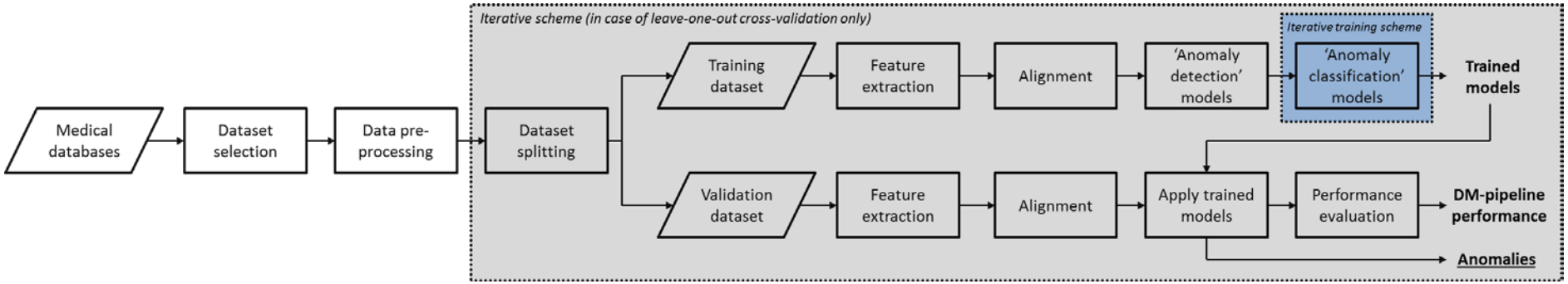
Technical and medical validation

Technical validation (implementation)

- Each block have been validated by **visual inspection** of the block outputs using recordings of the **training** set.
- Each **feature extraction** and **alignment** implementation has been thoroughly inspected using result **visualization,** and **result distributions and performance** (when ground truth is available).
- The complete data flow (from raw data to performance results) validates in itself the API implementation.



Technical and medical validation

Medical validation

- Most of the implemented features and other methods are justified with scientific publications (58).

Anomaly (medical condition) vs extracted features	PR interval	QRS interval	ST segment	RR interval	PP intervals	AA signals (non-specific features)	VA signals (non-specific features)	Eigenvalues of C	Blood pressure-based features	Respiration-based features	EEG-based features
Atrial fibrillation	x			x	x	x		x	x		
Supraventricular ectopic	x				x	x					
Ventricular ectopic				x	x	x	x	x			
Paced beats											
Ventricular tachycardia				x			x	x	x		
Ventricular flutter	x			x			x	x			
Ventricular fibrillation				x				x	x		
Supraventricular tachycardia					x	x					
Ventricular bigeminy		x	x	x							
Ventricular trigeminy		x	x	x							
Idioventricular rhythm		x		x		x	x	x			
Atrial bigeminy	x			x	x						
Sinus bradycardia					x	x					
Sleep apnea syndrome			x	x					x	x	x

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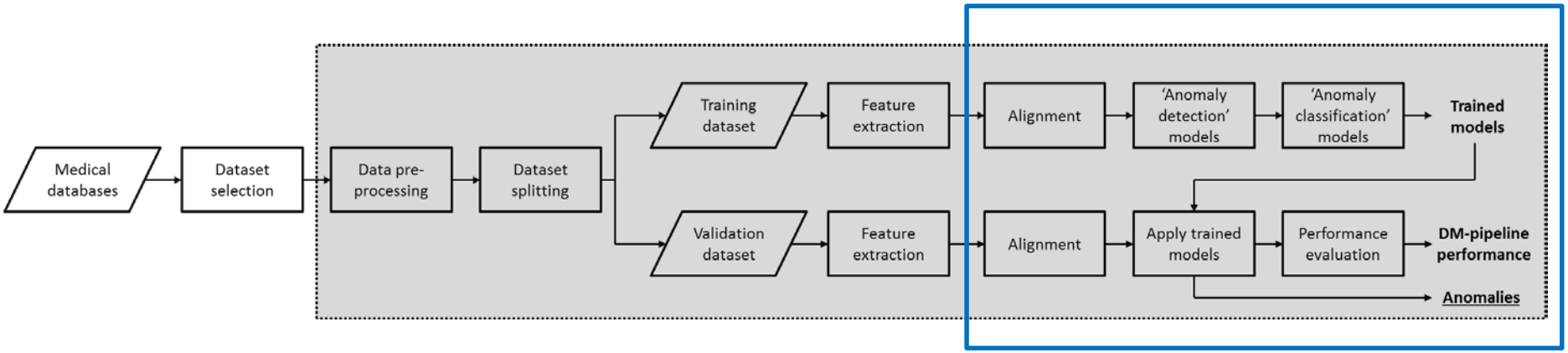
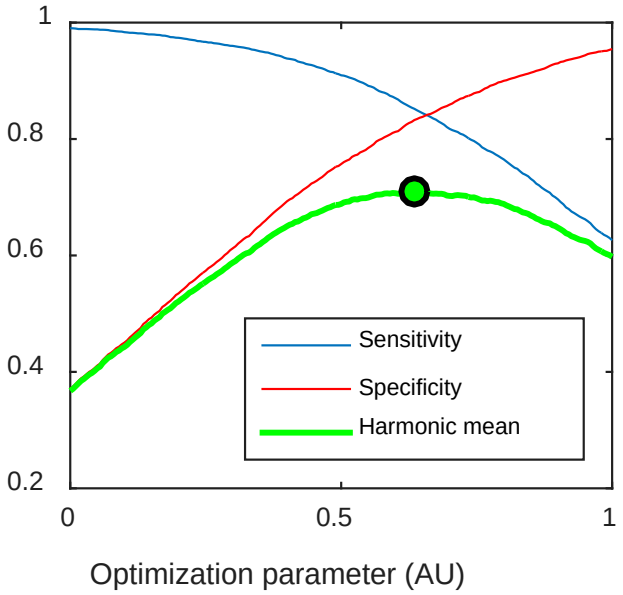
Evaluation platform



Evaluation matrix

The used algorithm will be evaluated in term of:

- Sensitivity (SE) = TP / (TP+FN)
- Specificity (SP) = TN / (TN+FP)
- Harmonic mean (HM) = 2*SE*SP / (SE + SP)



where

TP = abnormal instances correctly identified as abnormal.

FP = normal instances incorrectly identified as abnormal.

TN = normal instances correctly identified as normal.

FN = abnormal instances incorrectly identified as normal.

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Data mining techniques

Evaluation criteria:

- **Transparency:** degree to which the algorithm is understandable by a human (white-/gray-/black-box model)
- **Amount of training data:** quantity of training data required to avoid over-fitting (model is specific to training data but obtain poor performances on unseen data)
- **Explanation:** the output of the model gives an "explanation" of the decision
- **Computational complexity:** computation power and memory required by the algorithm
- **Adaptability**: potentialities to adapt the system to changing conditions
- **Algorithm availability**: availability of the algorithm in Matlab
- **Distribution *a priori***: the approach applies a feature distribution model

Data mining techniques

Type of model	Transparency	Data requirements	Explanation	Computational load	Adaptability	Distribution *a priori*
Linear classifiers	**High**	**Low**	**High**	**Very low**	**High**	High
Quadratic classifiers	**High**	Medium	Medium	Low	**High**	High
GMM	Medium	High	Medium	High	Medium	**Low**
HMM	Low	Very high	Low	Very high	Low	**Low**
ANN	Very low	Very High	Very low	Very High	Very low	**Low**
***k*-NN**	**High**	**Low**	**High**	Medium	Medium	Medium
Decision tree	**High**	**Low**	**High**	Medium	**High**	Medium
Bayes network	Medium	Medium	Medium	High	Medium	High
Random forest	Medium	High	Medium	Medium	Medium	High

Data mining techniques

Novelty detection

Advantages: (1) user friendly interface, (2) accessible and ready-to-use (4) provide flexible solution in terms of input parameters (extremely generic)

Disadvantages: (1) not suited for anomaly classification

***k*-NN**

- Advantages: (1) no need to train parameters/settings and (2) simple and powerful algorithm
- Disadvantages: (1) high computational cost and (2) high in data storage

Data mining techniques

SVM

- Advantages: (1) robust against low amount of data and (2) flexibility of the techniques

GMM

- Advantages: (1) flexible, (2) no *a priori* on feature distribution and (3) exploit prior information (confidence indexes) via EM algorithm
- Disadvantages: (1) require enough data

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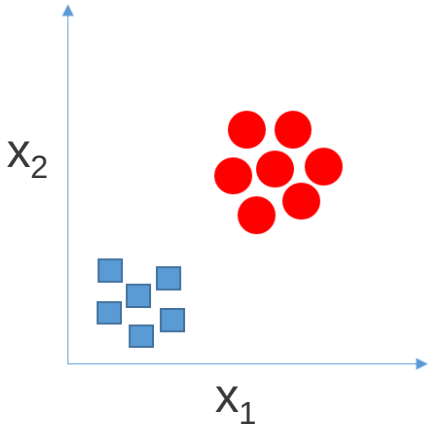
Anomaly detection and classification

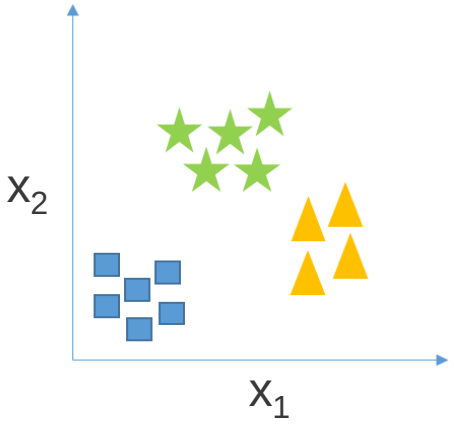
Anomaly detection

- Binary classifier is enough
- Two classes => Normal and Abnormal



Anomaly classification

- Binary classifier is *not* enough.
- Multiple Classes = Normal, Atrial fibrillation, Ventricular ectopic, etc.



Anomaly detection

Results: Novelty Detection

De Novo cardiac arrhythmias	Sleep apnea syndrome
SE = 0.0957	SE = 0.0097
SP = 0.8440	SP = 0.9825
HM = 0.1720	**HM = 0.0193**

SE = sensitivity, SP = specificity, HM = Harmonic mean

+ Completely generic.
+ Distribution of data does not need to be known a priori.

- Binary classifier
- Rely on simple statistical features

Anomaly detection

Results: *k*-Nearest Neighbours algorithm (*k*-NN) on MITDB

De Novo cardiac arrhythmias	Sleep apnea syndrome
SE = 0.8711 (1.0000)	SE = 0.4905 (1.0000)
SP = 0.7575 (0.9971)	SP = 0.4641 (0.9027)
HM = 0.8103 (0.9985)	**HM = 0.4769 (0.9489)**

SE = sensitivity, SP = specificity, HM = Harmonic mean

+ Distribution of data does not need to be known *a priori*.
+ Easy to implement

- Computationally expensive

Anomaly detection

Results: *Support Vector Machine* (*SVM*)

Linear (MITDB)

De Novo cardiac arrhythmias	Sleep apnea syndrome
SE = 0.8890 (0.9860)	SE = 0.4536 (0.7670)
SP = 0.9535 (0.9893)	SP = 0.6664 (0.8715)
HM = 0.9201 (0.9876)	**HM = 0.5398 (0.8159)**

Non-Linear (MITDB)

De Novo cardiac arrhythmias	Sleep apnea syndrome
SE = 0.8957 (0.9994)	SE = 0.2521 (0.9184)
SP = 0.9022 (0.9984)	SP = 0.9425 (0.9565)
HM = 0.8990 (0.9989)	**HM = 0.3978 (0.9371)**

SE = sensitivity, SP = specificity, HM = Harmonic mean

\+ Big choice of parameters to tweak for optimal performance.

\- Distribution of data needs to be known in advance.

\- Proper parameters needs to be selected.

\- Binary classifier.

\- Computationally expensive

Anomaly detection

Results: Gaussian Mixture Model (GMM)

MITDB

De Novo cardiac arrhythmias
SE = 0.8923 (0.9986)
SP = 0.7483 (0.9798)
HM = 0.8140 (0.9891)

ALL

De Novo cardiac arrhythmias
SE = 0.4795 (0.5385)
SP = 0.4724 (0.6519)
HM = 0.4759 (0.5898)

+ Distribution of data does not need to be known a priori.

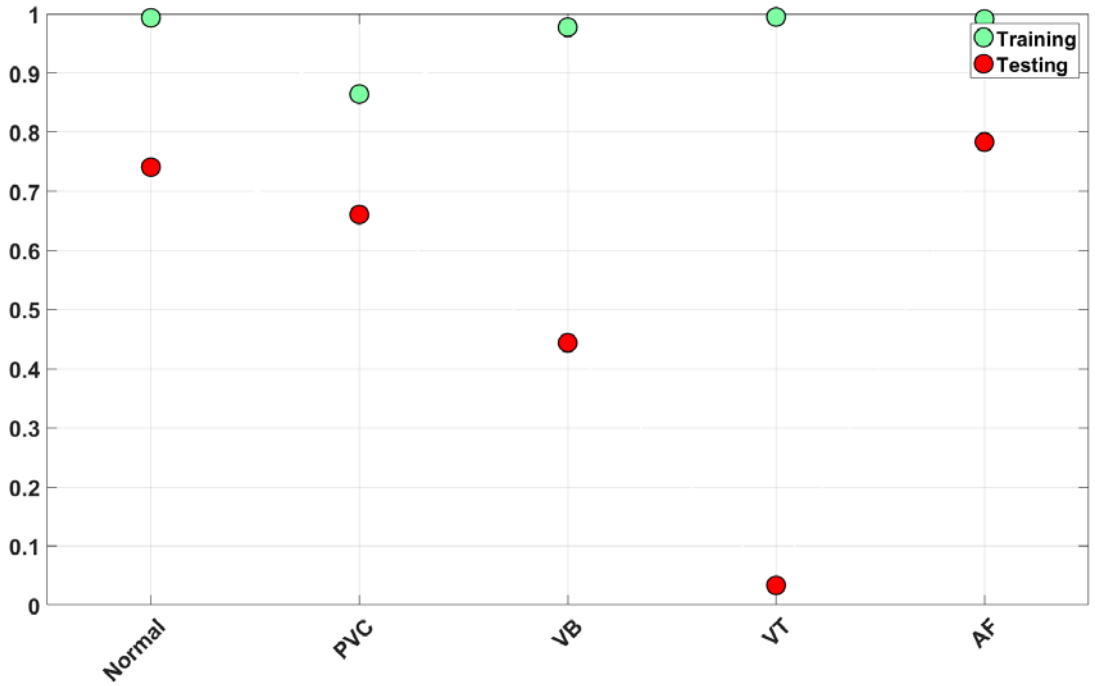
- Requires a big set of data .
- Sensitive to the initialization.
- Can not handle highly correlated features.

Anomaly classification

k-Nearest Neighbours algorithm (*k*-NN) on MITDB

Results of *De Novo cardiac arrhythmias*

- The class with the highest Harmonic mean score is the **AF**, **78%**.
- The class "**Normal**" had a score of **74%**.
- The *k*-NN did not mange to classify the "**VT**" class.



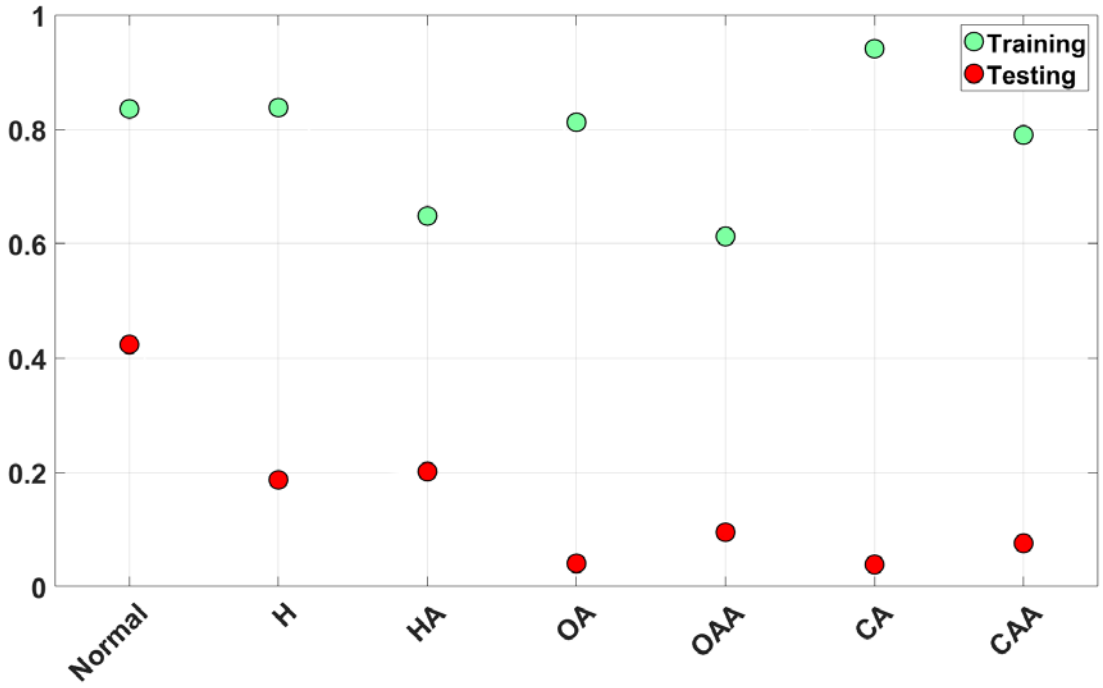
PVC = Premature ventricular contraction, VB = Ventricular bigeminy, VT = Ventricular trigemini, AF = Atrial fibrillation.

Anomaly classification

k-Nearest Neighbours algorithm (*k*-NN)

Results of *Sleep apnoea syndromes*

- The class with the highest Harmonic mean score is the Normal class, **42%**.
- Very low classification scores.



H = Hypopnea, HA = Hypopnea with arousal, OA = Obstructive apnoea , OAA = Obstructive apnoea with arousal ,CA = Central apnoea , CAA = Central apnea with arousal .

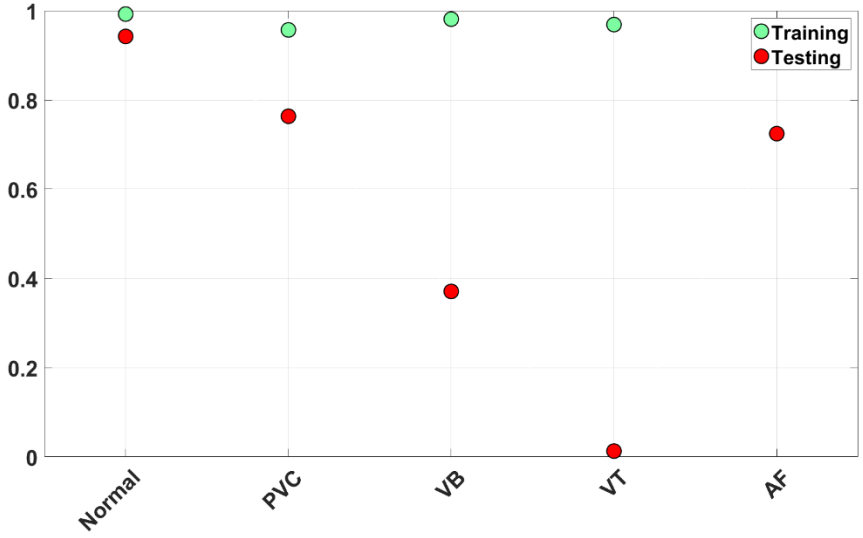
Anomaly classification

Support Vector Machine (SVM)

Results of *De Novo cardiac arrhythmias*

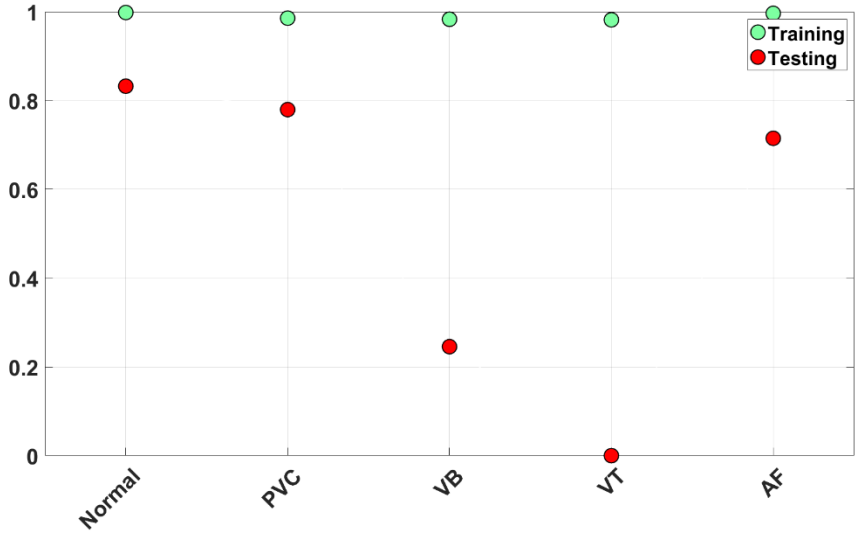
Linear (MITDB)

The "**normal**" class resulted in the highest HM scores (**94%**).



Non-Linear (MITDB)

The "**normal**" class resulted in the highest HM scores (**83%**).



PVC = Premature ventricular contraction, VB = Ventricular bigeminy, VT = Ventricular trigemini, AF = Atrial fibrillation.

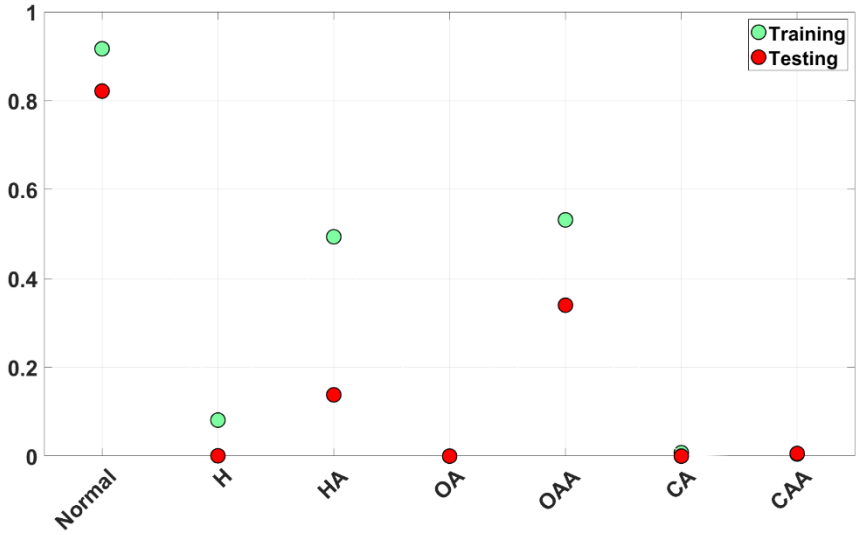
Anomaly classification

Support Vector Machine (SVM)

Results of *Sleep apnea syndromes*

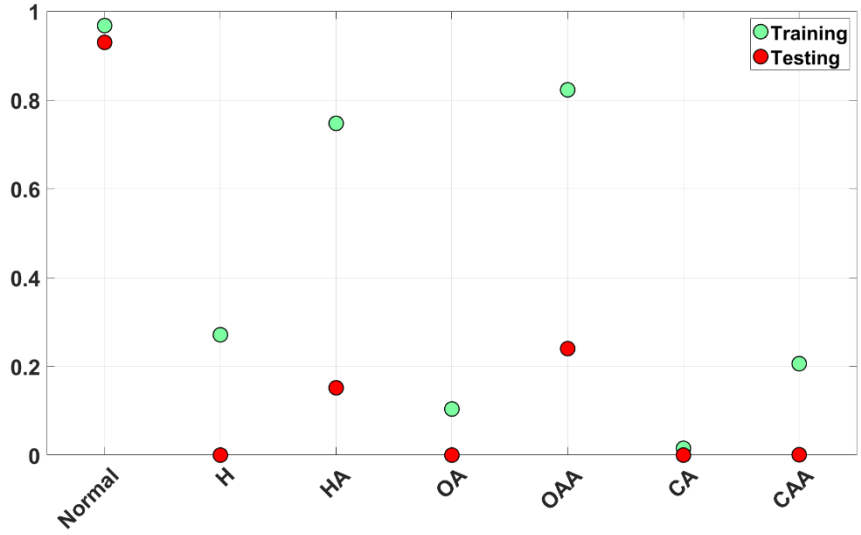
Linear

The "**normal**" class resulted in the highest HM scores (**82%**).



Non-Linear

The "**normal**" class resulted in the highest HM scores (**93%**).



H = Hypopnea, HA = Hypopnea with arousal, OA = Obstructive apnea , OAA = Obstructive apnea with arousal ,CA = Central apnea , CAA = Central apnea with arousal.

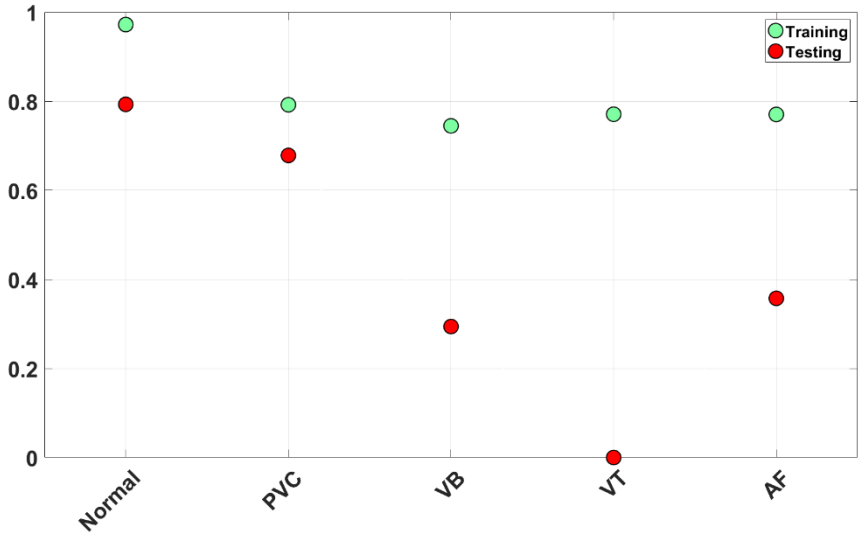
Anomaly classification

Gaussian Mixture Model (GMM)

Results of *De Novo cardiac arrhythmias*

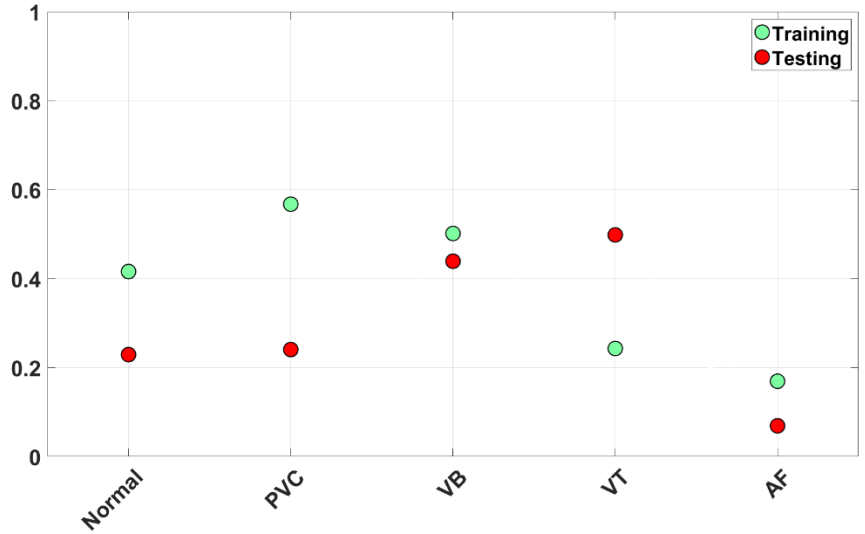
MITDB

The "**normal**" class resulted in the highest HM scores (**79%**).



ALL

The "**VT**" class resulted in the highest HM scores (**50%**).



PVC = Premature ventricular contraction, VB = Ventricular bigeminy, VT = Ventricular trigemini, AF = Atrial fibrillation.

Anomaly detection and classification

Resume:

- Important tasks has been done concerning data processing development.
- Important validation and double-checking of the extracted features in terms of robustness is needed
- All classification methods **performed globally well** (**HM of 92%**) besides *Novelty Detection*.
- Classification methods that do not assume any distribution of the data are more suitable.
- Some anomalies more challenging to classify compared to others.
- *De Novo Cardiac arrhythmias* resulted in better performance compared to *Sleep Apnea Syndromes* => **The importance of good features**.
- Reference to CinC Challenge performance of **82%** only on AF.
- Even though **GMM** has a slightly lower score in performance, it has a **major potential** in the scope of AMIGO project.

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- **Clinical investigation**
- AMIGO in future missions
- Open discussion

Clinical investigation

During the last meeting (PM2), the following open actions were defined (from MOM 221-ES-1577-MOM-20160412):

- **AI-15** Comparison with SOTA medical systems
- **AI-18** Define the methodology for the two extra investigations to improve D5
  1st investigation: the optimization (subset) of feature selection and
  2nd investigation: the evaluation of a new performance approach based on disease episode classification and not on cardiac beat classification
- **AI-19** Applied the methodology (feature subset and AMIGO's performance relevant for clinicians)

Clinical investigation

With the help of the **Arrhythmia Unit** of the **Lausanne University Hospital**, a short **clinical investigation** was conducted on AMIGO performance against AF classification.

Methodology:

- A subset of 20 patients were selected with sequences of sinus rhythm and AF.
- AMIGO solution was applied with a subset of features (**11 features based on interbeat intervals**)
- **Statistical difference analysis** was applied to each feature **wrt AF/SR distributions**
- AMIGO classifier based on a **SVM approach** (linear kernel) was used to **separate both classes**
- Based on resulting cardiac beat classification, a **sub-layer mimicking clinician analyze** was added (convert isolated positive events (AF) into negative ones (SR)

Clinical investigation

List of features with corresponding Fischer linear discriminant value

Feature	Variable	Fisher linear discriminant
'Moving Average with RR series'	F_ecg(8)	**0.6825**
'Moving STD with RR series'	F_ecg(9)	**2.3739**
'Moving Skewness with RR series'	F_ecg(10)	0.4965
'Moving Kurtosis with RR series'	F_ecg(11)	0.0167
'Moving Minima with RR series'	F_ecg(12)	**2.2469**
'Moving Maxima with RR series'	F_ecg(13)	0.3526
'Moving 25th percentile - WL:5 and Overlap: with RR series'	F_ecg(14)	**2.2251**
'Moving 50th percentile - WL:5 and Overlap: with RR series'	F_ecg(15)	0.2890
'Moving 75th percentile - WL:5 and Overlap: with RR series'	F_ecg(16)	**2.2050**
'Moving Power - WL:5 and Overlap: with RR series'	F_ecg(17)	0.2451
'Moving Derivative Average - WL:5 and Overlap: with RR series'	F_ecg(18)	0.2658

Clinical investigation

Classification scores of the AF and SR with clinician's analysis mimic

Measures	Scores
True positives	1927
False positives	6
False negatives	11
True negatives	294
Sensitivity	**99.43%**
Specificity	**98.00%**
Harmonic mean	98.71%
Accuracy	**99.24%**

Clinical investigation

- These results **derived from the subset** of the total database confirms the **reliability** of the outcome using AMIGO.

- **AMIGO results challenge** the actual **gold standard AF monitoring solutions (**implantable cardiac monitoring performance of 66%[1]**)**

[1] Podd *et al.* "Are implantable cardiac monitors the 'gold standard' for atrial fibrillation detection? A prospective randomized trial comparing atrial fibrillation monitoring using implantable cardiac monitors and DDDRP permanent pacemakers in post atrial fibrillation..," *Europace,* vol. 18, pp. 1000-1005, 2016.

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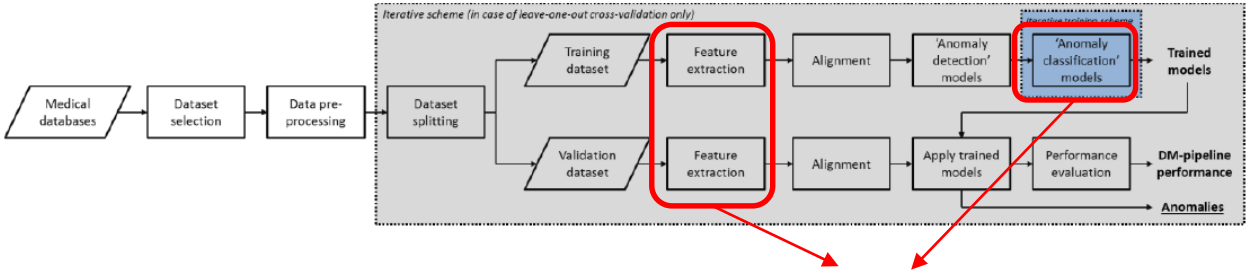
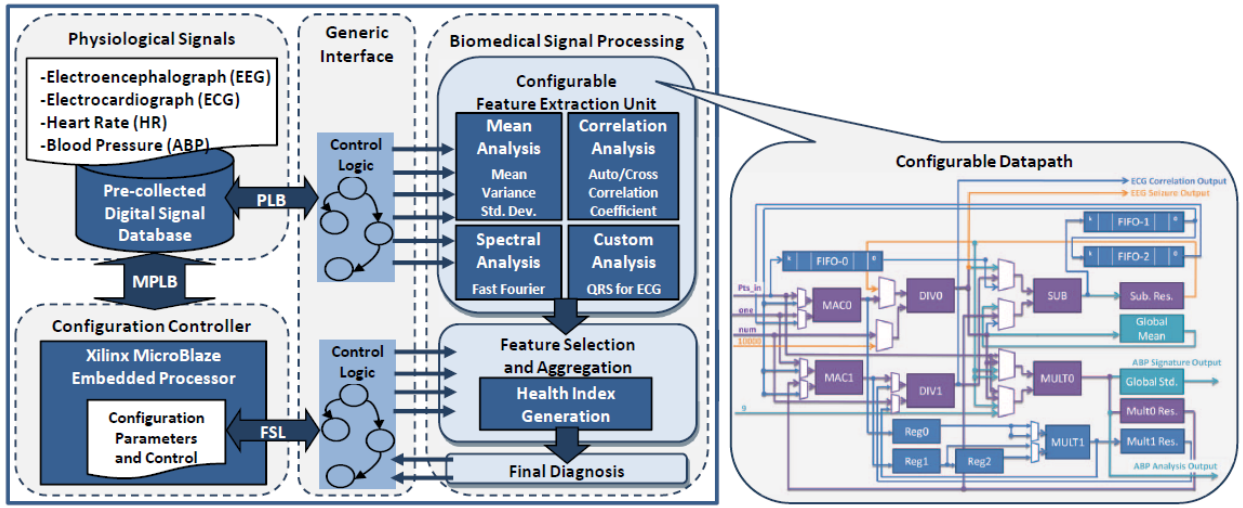
AMIGO in future missions

AMIGO in future missions - Data processing



Computationally expensive

(experience on NPAL, SPARTAN, ExoMars Rover and others)



RMED Architecture Framework with Configurable Data path prototyped on an FPGA platform

AMIGO in future missions - Data processing

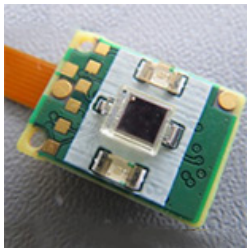
- ARM® processors widely used on wearable health and sport monitoring
- Only basic data sampling and processing performed
- Interesting insight into trade-offs of miniaturization, processing power and power consumption

Tom Tom Spark
(powered by ARM® Cortex® M7)

FitBit Surge
(powered by ARM® Cortex® M3)

AMIGO in future missions - New sensors

LifeQ LENS integrated in a wearable device (miniaturized multi-wavelength optical sensor module)



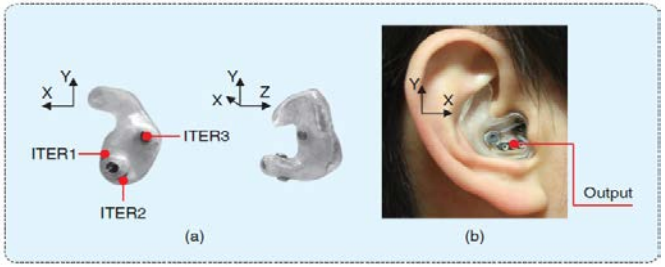
Miniaturized optical ECG sensor by Philips

Miniaturized accelerometers by ST Microelectronics

CSEM Long Term Medical Survey System (LTMS-S) system

Emotiv EPOC+ EEG

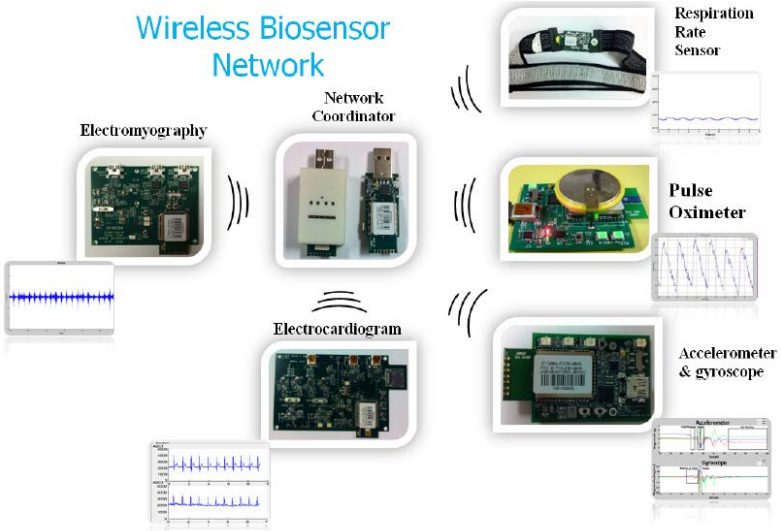
Emotiv Insight EEG



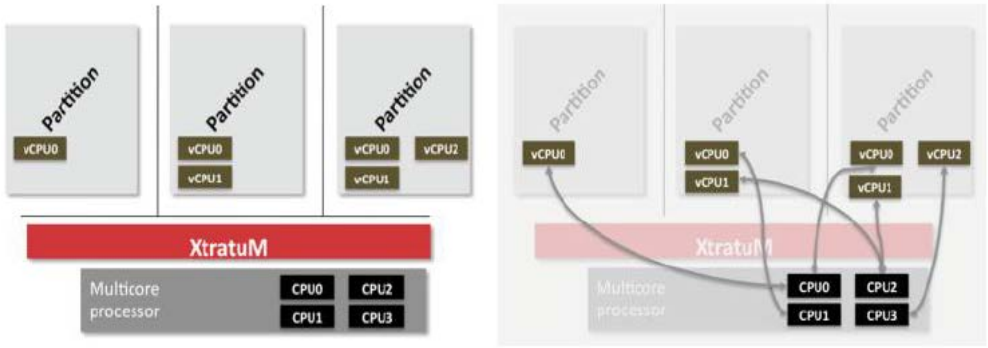
Ear-EEG earpieces (Imperial College London)

AMIGO in future missions - Miniaturisation

- Reduction of mass and volume can be achieved also by acting on the harness resulting from the connection of the modules (i.e. sensors and computing units).
- A number of studies have been investigating this problem in the domain of Wireless Body Area Network (WBAN)
- Separation of concerns is required in highly-integrated systems



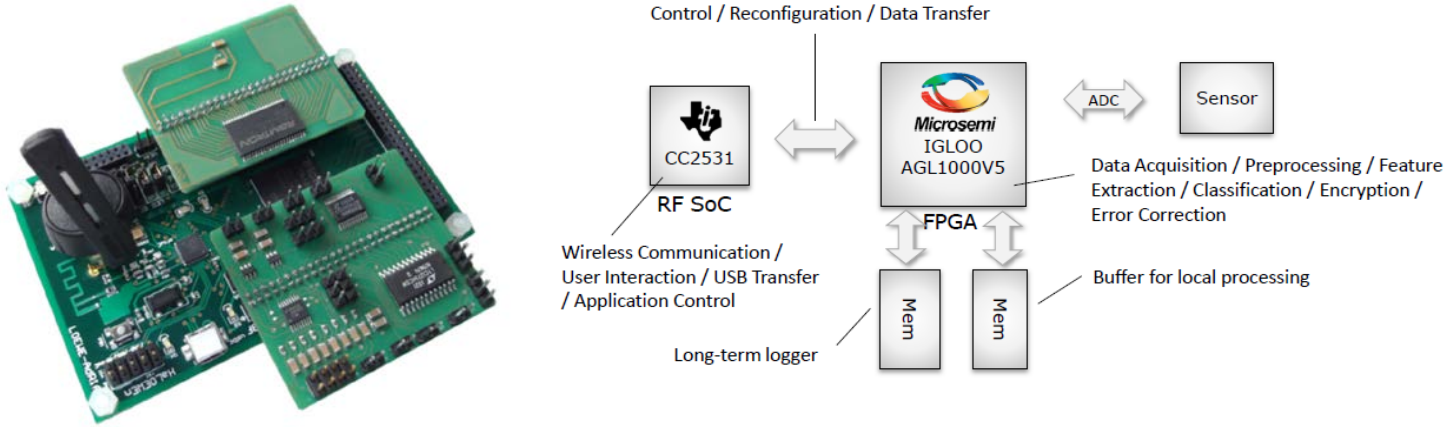
Target ZigBee-based wireless biosensor network



Time and Space Partitioning architecture with XtratuM

AMIGO in future missions - Reconfiguration

- AMIGO is supposed to be adaptable to different types of mission scenarios and integrate different types of sensors
- A computing architecture capable of being reconfigurable in case of change of mission profile or devices configuration is advisable
- Avionics reconfiguration is ESA projects: DRPM, MINAVIO

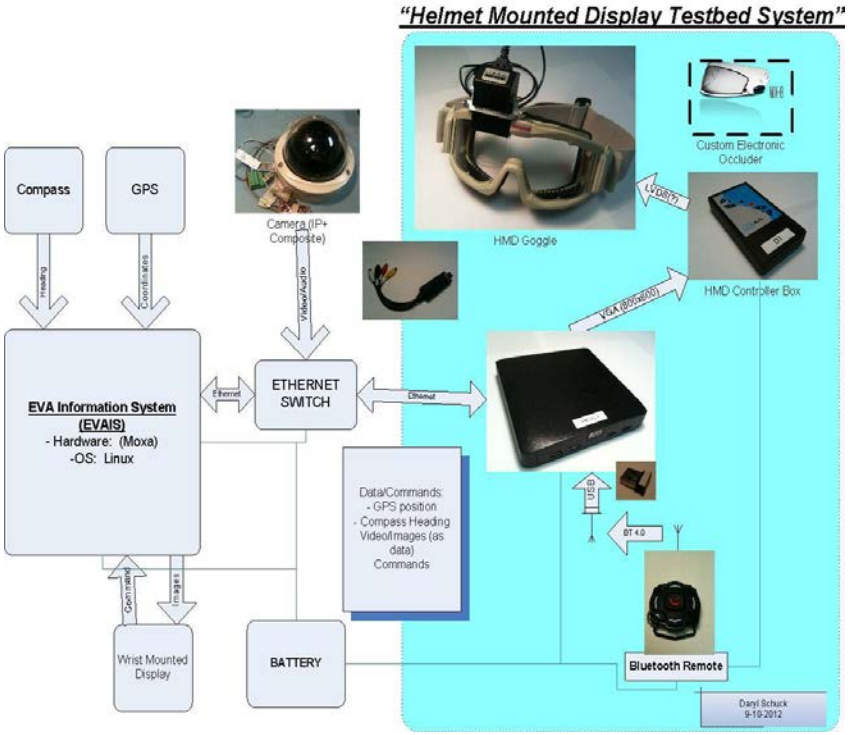


HaLOEWEn Platform with Sensor and Memory Extensions (left) and system architecture (right). The reconfigurable platform allows for connection and disconnection of new sensors in a plug-and-play fashion

Human-machine interaction

The capability of the system to interact in a timely manner with astronauts are paramount for the effectiveness of the overall health-monitoring and diagnostics service

Extravehicular Activities HMI information system (Moonwalk project)



Head-Mounted Display System Architecture

AMIGO in future missions - Eye Tracking Device

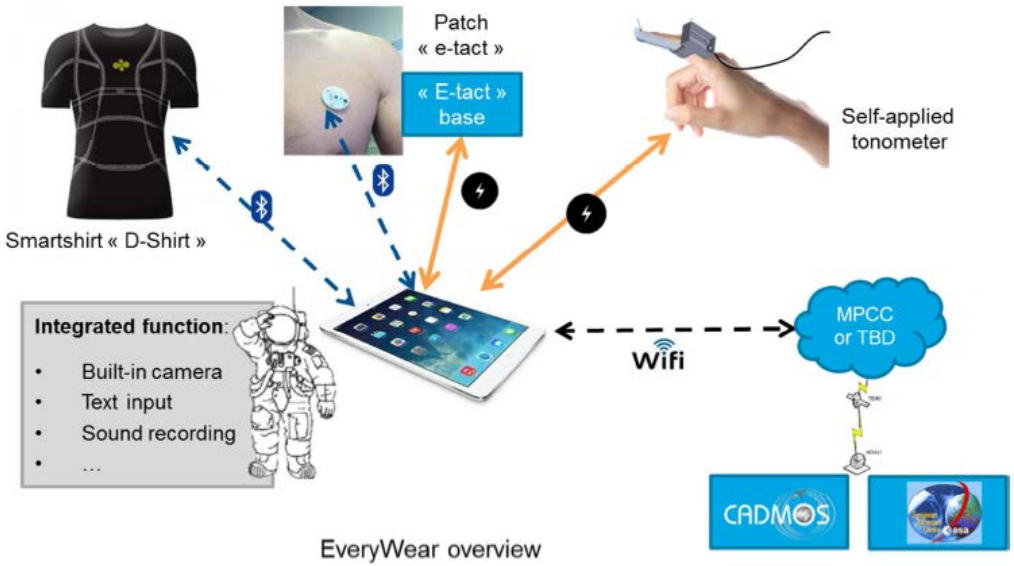
- Eye Tracking Device (ETD)
  - ESA investigation (2003-2007) on how the vestibular system adapts to microgravity
  - Relation to space adaptation syndrome
  - Insight into vestibular disorders like Meniere's disease

AMIGO in future missions - Airway monitoring

- Airway Monitoring
  - ISS investigation (6 months duration) into pulmonary nitric oxide turn-over in microgravity
  - Measurement of airway inflammation in Microgravity and reduced pressure

AMIGO in future missions - Everywear

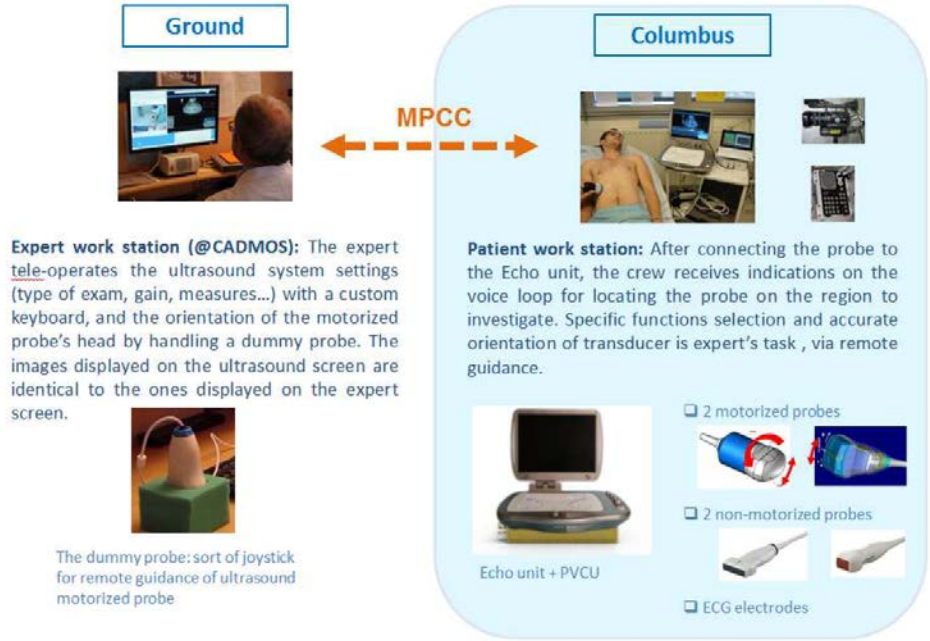
- Everywear (Thomas Pesquet monitoring Nov 2016 to May 2017)
  - Wearable monitoring sensors: ECG, Tonometry, temperature…
  - Data collection via iPad
  - Future: data visible on smartwatch



EveryWear overview

AMIGO in future missions - Echo

- Echo: tele-operated ultrasound (ISS project)
  - Tele-operated Ultrasound
  - Diagnostics require direct ground communications, therefore no option for deep sp



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OPEN DISCUSSION