Aplicació de la Intel·ligència Artificial per la millora del tractament i seguiment del Parkinson

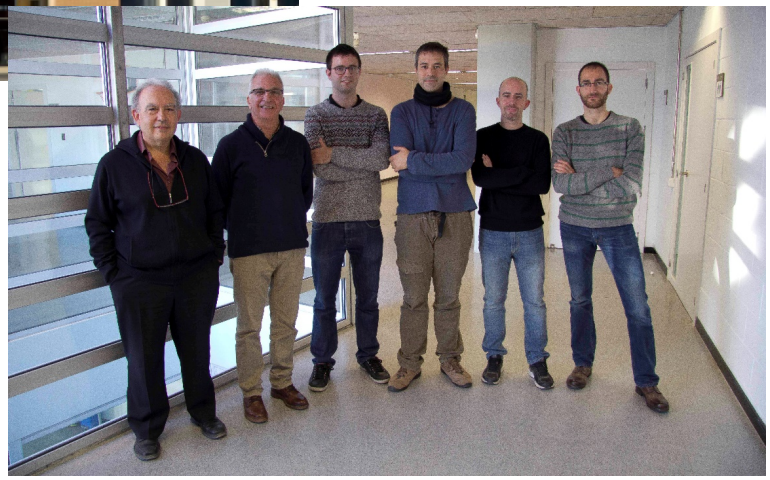
Joan Cabestany

- UPC professor
- Co-founder of Sense4Care SL

El guió de la meva presentació:

- Breu introducció.
  - Un marc de recerca aplicada. La transferencia de coneixament a la societat.
- El Parkinson
- Sobre el nostre producte. Caracteristiques i prestacions
- Com s'ha desenvolupat.
  - La Intel.ligència Artificial al rerafons.
  - Implementació
- Algunes conclusions.

Context de recerca aplicada: bàsicament suportada per finançament de projectes en lliure concurrència i activitat de tesis doctorals.



CETpD
Technical Research Centre for Dependency Care and Autonomous Living

UPC

La transferencia de coneixament a la societat com a repte…

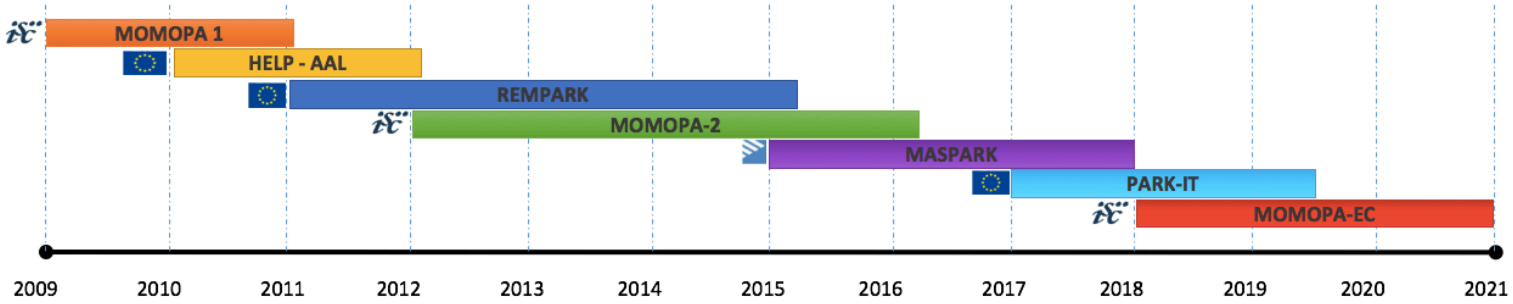
CETpD
Technical Research Centre for Dependency Care and Autonomous Living

Knowledge Transference

SENSE4CARE

MARKET

Background



RESEARCH & DEVELOPMENT

2009-2011	MOMOPA 1	15 patients, set the sensor on the waist, first algorithms and analysis of results.
2010-2013	HELP - AAL	1st approach with an apomorphine pump, tests with 6 patients.
2011-2015	REMPARK	>150 patients. Biggest database with inertial data known at patients' home. Focused on algorithms to detect motor symptoms.
2012-2016	MOMOPA-2	40 patients and project focused to determine the ON and OFF state with an inertial sensor.
2015-2018	MASPARK	Use of the sensor as a gold-standard. Cueing system and enhancement of algorithms to detect bradykinetic gait and freezing of gait

STAT-ON DEVELOPMENT

2017-2019	PARK-IT	SME Instruments Phase II project to re-design, industrialise, certify, and commercialise a wearable medical device to monitor PD motor symptoms

Sense4Care team:

Carlos Pérez, PhD

CEO

Electronics

Project management
Clinical trials design
+45 publications

Daniel Rodríguez, PhD

CTO

Industrial Engineering

Machine Learning
Quality control and HW
+45 Publications

Joan Calvet

COO

Business Management
Master in Marketing

Business development
+10 years experience in Start-ups

Martí Pié

Software

Electronics and Automation

Firmware, Hardware and Software design

Anna Santamaria

Assistant

Social and Economics Administration

ERP Management
Logistics
Customer service

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Alejandro Rodríguez, MD, PhD

CONSORCI SANITARI GARRAF

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Joan Cabestany, PhD

Xavier Castillo, PhD

TEMPOS 21 now Worldline

Andreu Català, PhD

El producte:

HOLTER FOR PARKINSON

STAT·ON

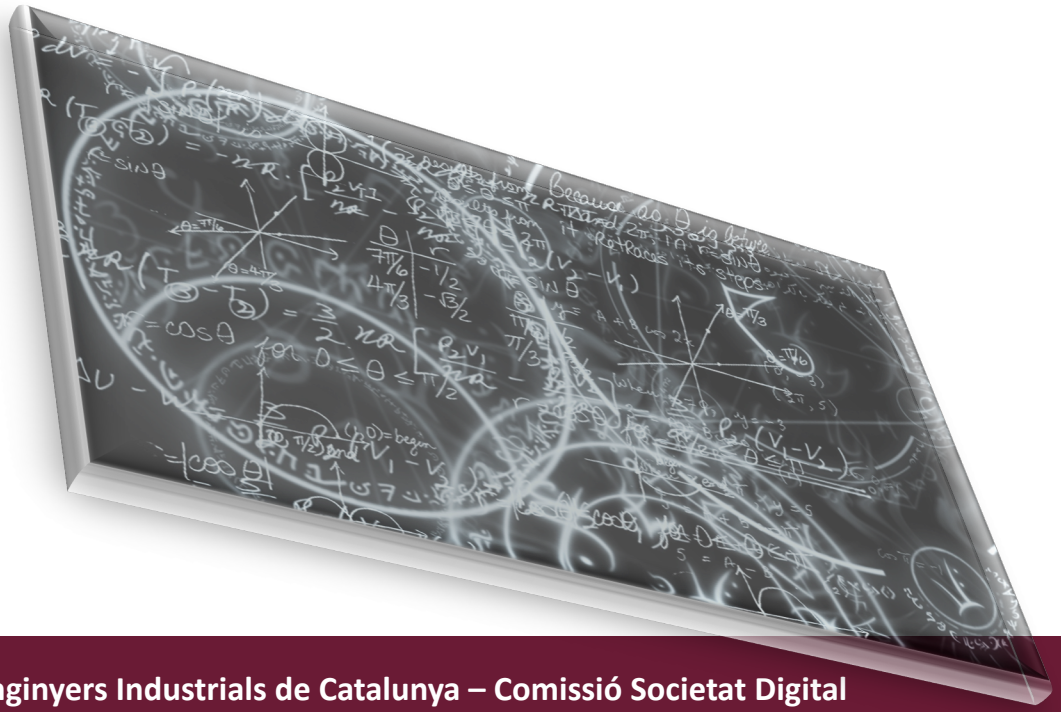
Designed at **PARK-IT 2.0,** SME Instrument Phase 2, H2020 – SMEINST – 2 – 2016 – 2017, Project number: 756861

PARK-IT2

CE
0051
EC CERTIFICATE
Certificate No 2042/MDD

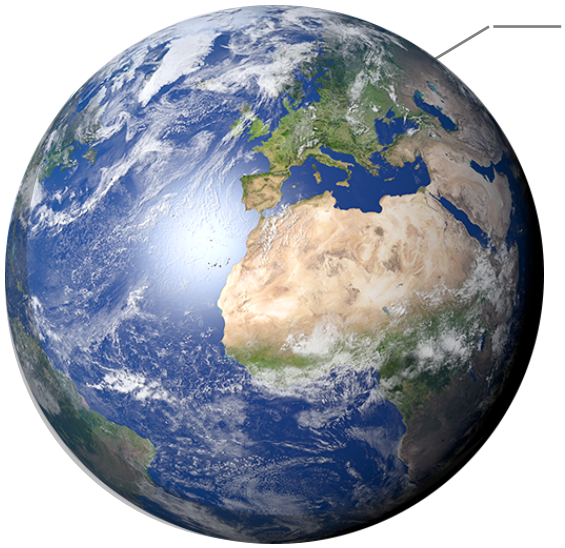
La enfermedad de Parkinson

- ***No se conoce con certeza su origen***
- Origina esencialmente la pérdida de neuronas dopaminérgicas y otras subcorticales en la ***Substantia Nigra***
- ***A dia de hoy, no tiene curación.***



Parkinson's disease

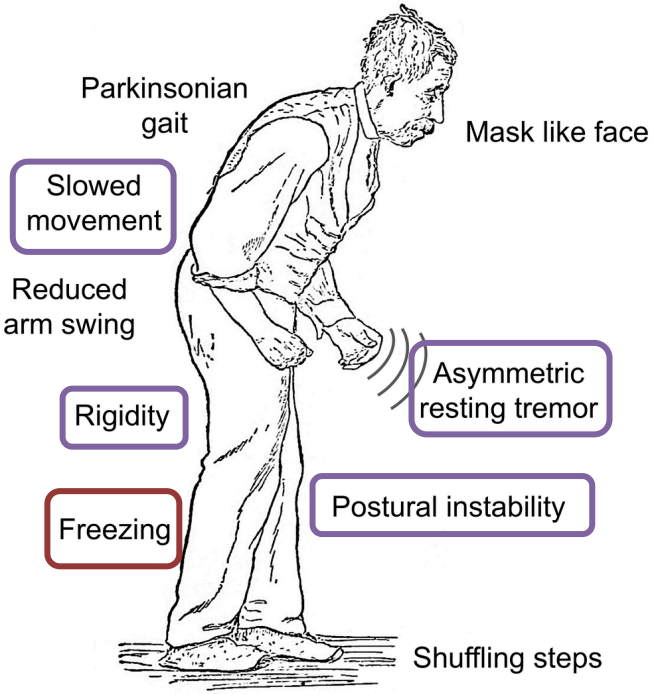
Is the 2nd most common neurodegenerative disease



1.200.000
Affected in EUROPE

People with PD in the world

Parkinson's disease

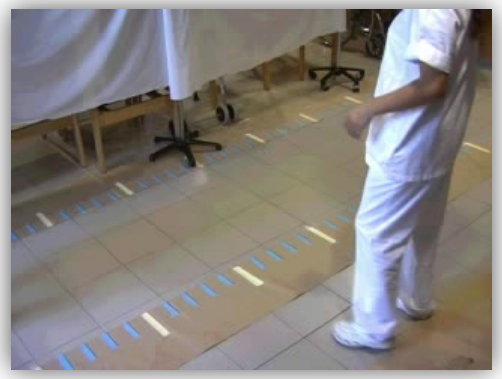


Síntomas del Parkinson

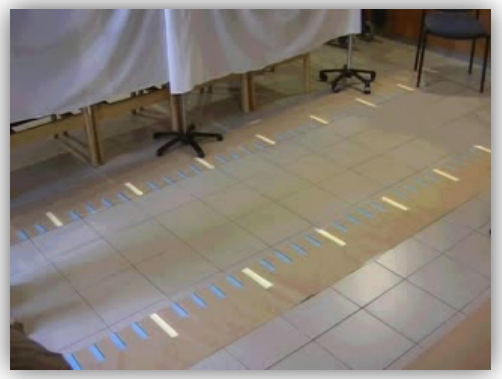
- Bradicinesia
  - *-Lentitud de movimiento*
- Bloqueo de la marcha (Freezing of Gait, FoG)
  - *-Parada repentina de la acción de caminar*
- Discinesias
  - *-Movimientos coreicos incontrolados*

Síntomas del Parkinson

- Estados motores



Con medicación: ON



Sin medicación: OFF

Síntomas del Parkinson

- Bradykinesia

- Slowness of movement
- Reduction of step length
- Less cadence
- Less stride speed
- Less fluidity
- Movement difficulties
- Speech affected

Síntomas del Parkinson

- Dyskinesia

- Blood dopamine excess
- Uncontrolled choreic movements
- Produces injuries, anxiety, depression, gait assimetry, and fall risk

Síntomas del Parkinson

- Freezing of Gait

- Sudden incapacity to keep an efficient gait
- According to patients: “as if feet were glued to ground”
- Direct relation with falls

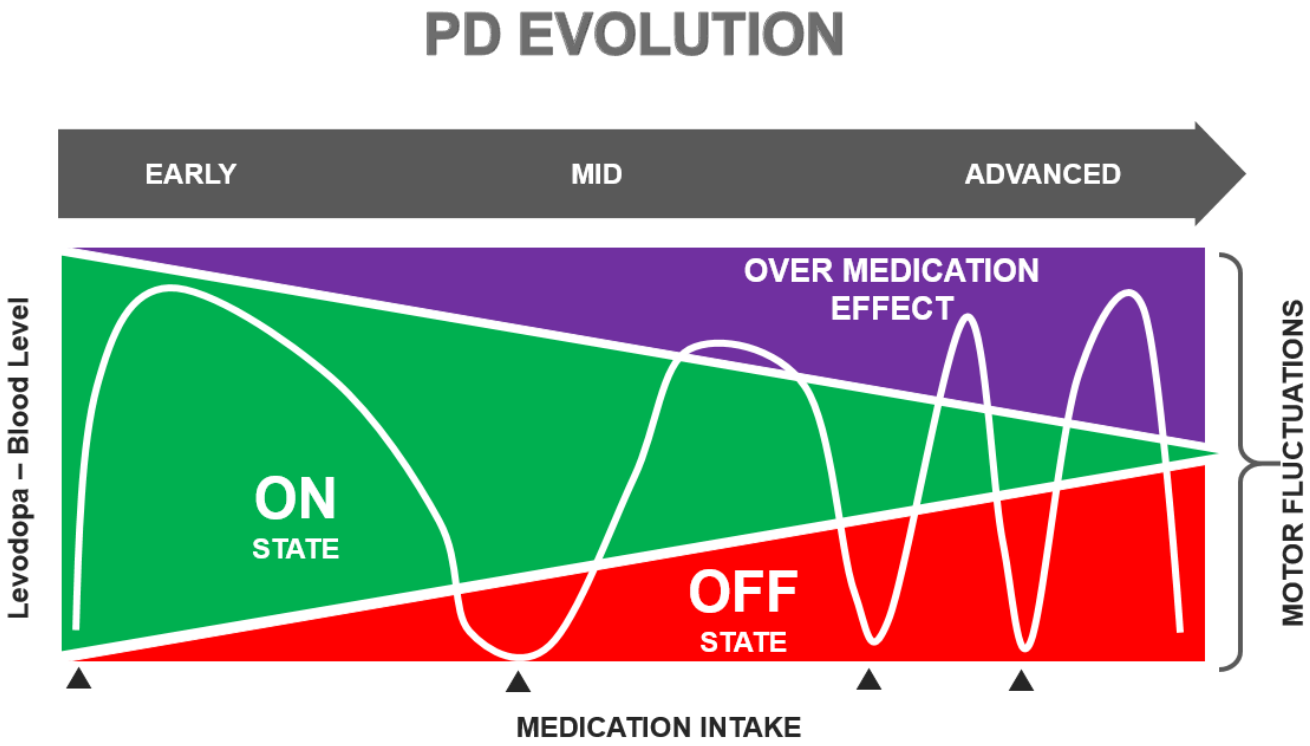
Context dependent

Síntomas del Parkinson

- Cueing at Freezing of Gait

- Unfreeze trick
- Works in some patients
- Useful at bradykinetic gait, too
- Visual, auditive, haptic

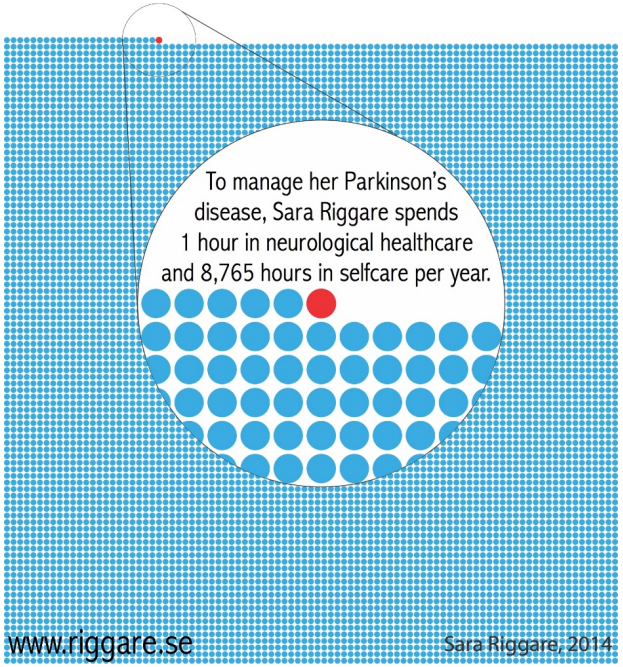
Parkinson symptoms



Síntomas y tratamiento del Parkinson

Sara Riggare, Parkinson's Disease patient (45)

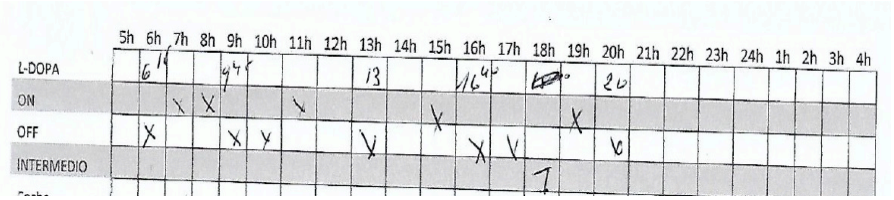
"Veo a mi neurólogo 2 veces al año. Media hora en cada visita. Es un total de 1 hora de cuidado de salud profesional sobre mi enfermedad. Durante el año me cuido durante 8765 horas, aplicando mi conocimiento y experiencia, junto con la información que me dice el neurólogo lo mejor que puedo."

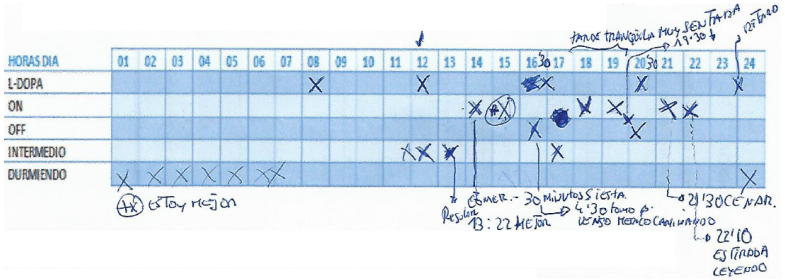


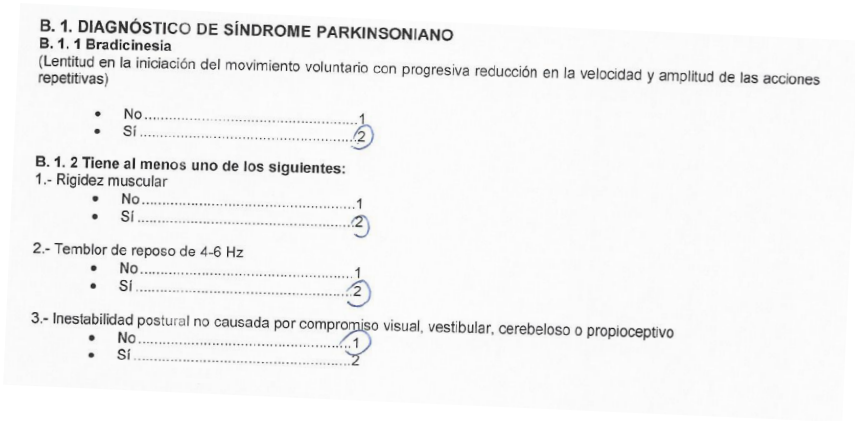
https://www.youtube.com/watch?v=-bqS-Y5RtoI

El problema: la necesidad de una evaluación más objetiva y en condiciones de vida normal.

- **Punctual and short evaluations**
- **Subjective questionnaires, chaotic diaries…**







B. 1. DIAGNÓSTICO DE SÍNDROME PARKINSONIANO

B. 1. 1 Bradicinesia

(Lentitud en la iniciación del movimiento voluntario con progresiva reducción en la velocidad y amplitud de las acciones repetitivas)

- No 1
- Sí 2

B. 1. 2 Tiene al menos uno de los siguientes:

1.- Rigidez muscular

- No 1
- Sí 2

2.- Temblor de reposo de 4-6 Hz

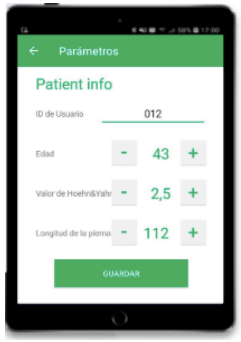
- No 1
- Sí 2

3.- Inestabilidad postural no causada por compromiso visual, vestibular, cerebeloso o propioceptivo

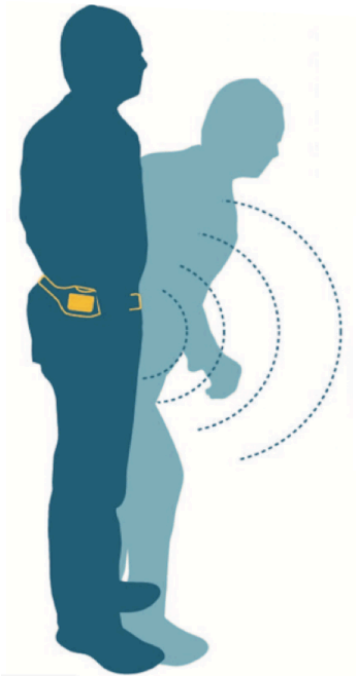
- No 1
- Sí 2

STAT-ON: How it Works?

Auto-calibration (the device adapts to each patient)
7 battery life working continuously



Only 3 parameters to set up the device



1

THE NEUROLOGIST CONFIGURES THE APP ACCORDING TO EACH PATIENT

2

THE PATIENT WEARS IT 7 DAYS IN DAILY LIVING CONDITIONS

3

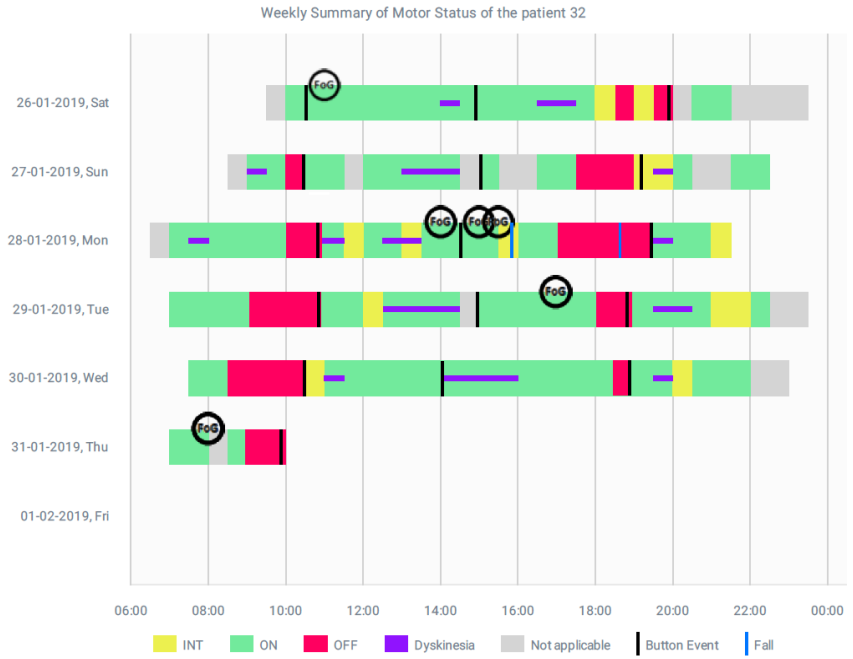
THE NEUROLOGIST DOWNLOADS IN FEW SECONDS THE REPORT OF THE PATIENT'S STATE VIA BLUETOOTH

Resultados en formato de informe:

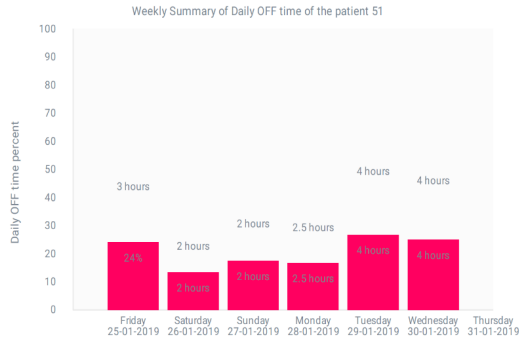
SENSE4CARE STAT·ON

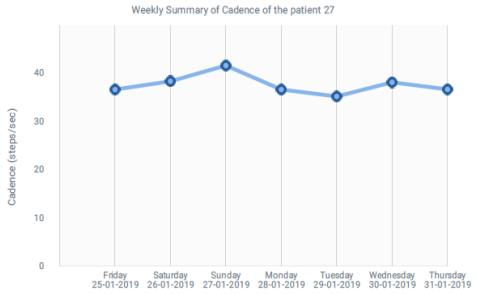
User ID:	171113-S01
Age:	68
Hoehn & Yahr:	OFF: 3, ON: 2
Study start date:	3/28/2018
Study ending date:	4/1/2018
Total days monitored	5

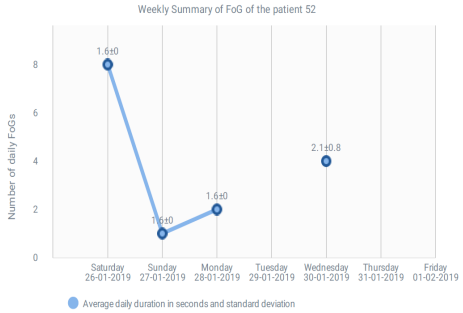
Total FoG Episodes	87
Average FoG Episodes per day	18±4
Average minutes walking per day	58±19
Average number of steps per day	3094±560
Number of falls	4
Time in OFF (% regarding total time monitored)	7.2 hours (34.5 %)
Time in Intermediate (% regarding total time monitored)	9.6 hours (43.6 %)
Time in ON (% regarding total time monitored)	8.4 hours (38.2%)
Time with dyskinesias (% regarding total time monitored)	1.6 hours (7.3 %)
Total time monitored	22 hours

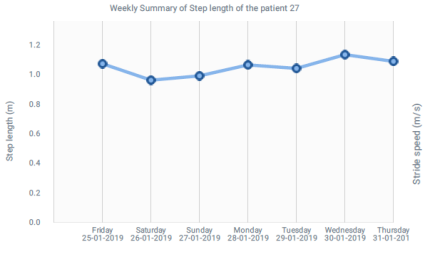


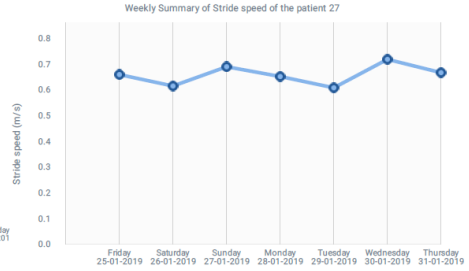
Resultados en formato de informe:

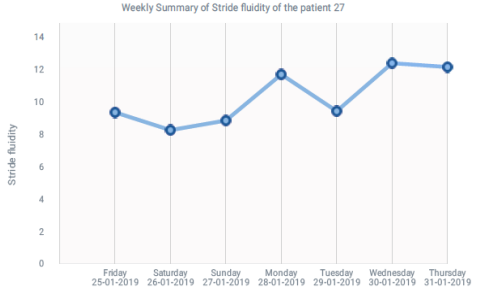


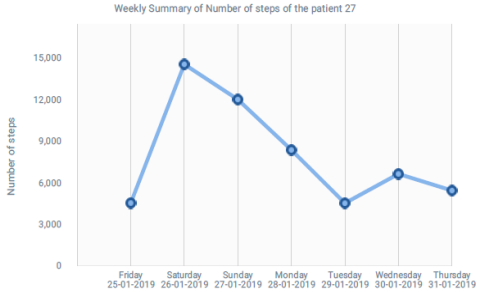






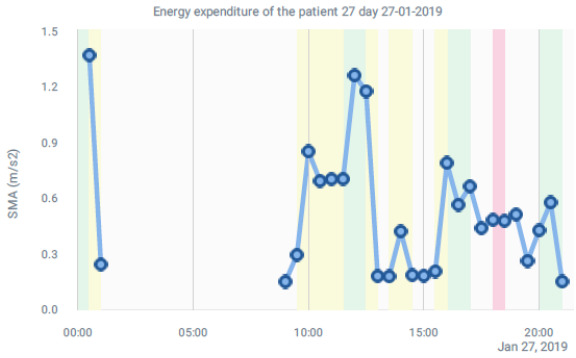


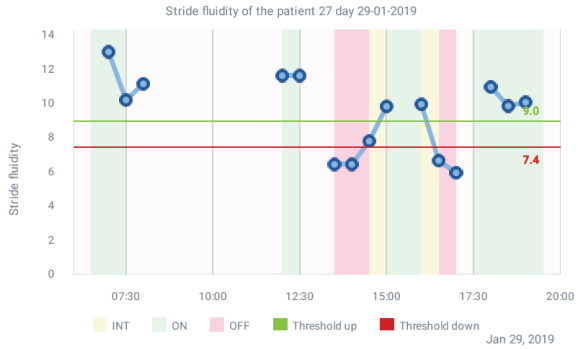


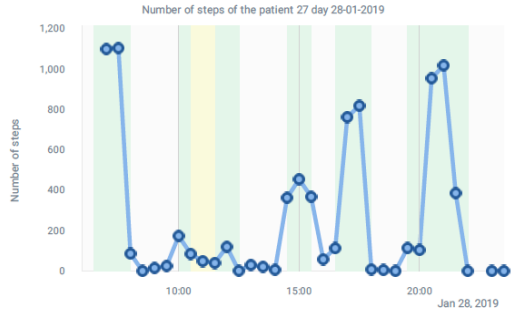


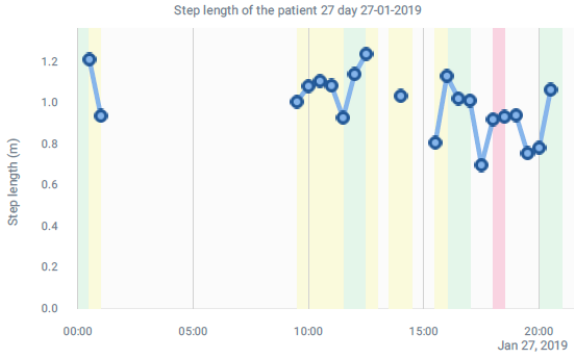
Hours in OFF	Cadence	Step length	Stride Speed	Stride Fluidity	Number of Steps	Minutes walking	Energy Expenditure

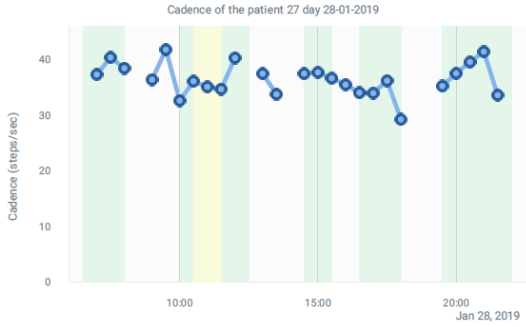
Resultados en formato de informe:

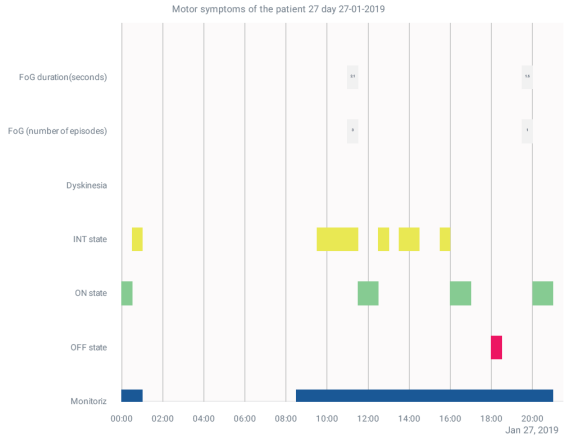






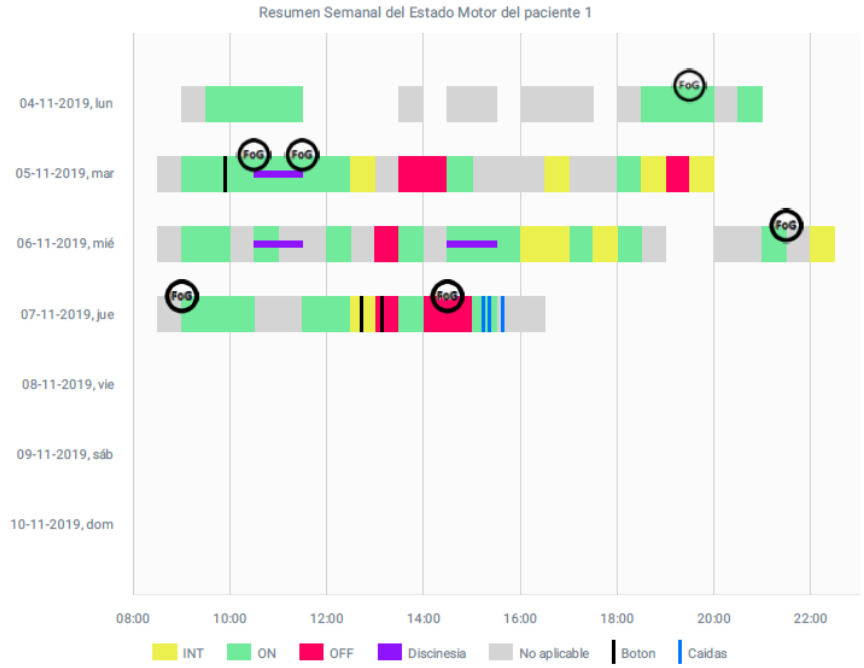


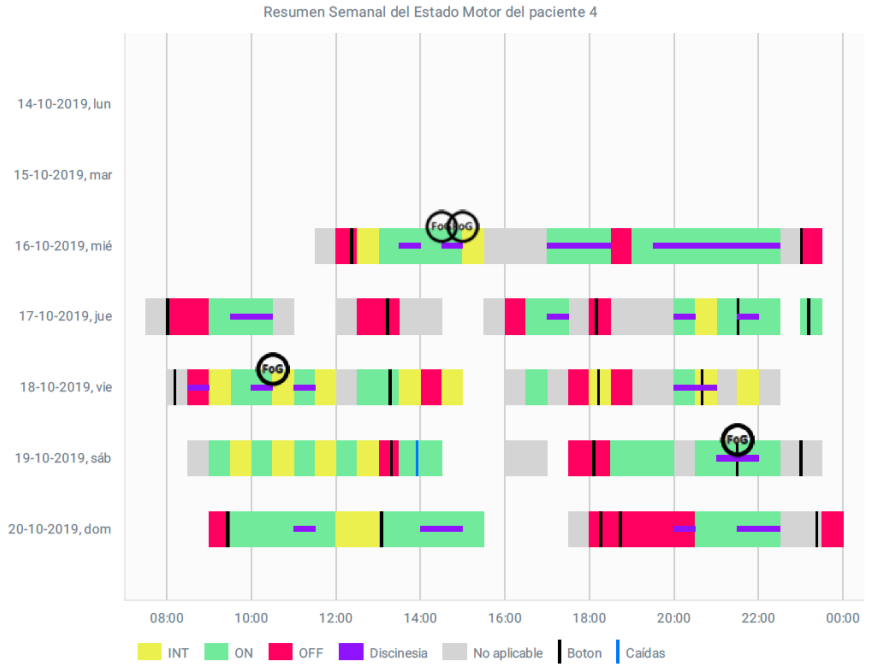




Daily information of each item

Results


Resumen Semanal del Estado Motor del paciente 1
04-11-2019, lun
05-11-2019, mar
06-11-2019, mié
07-11-2019, jue
08-11-2019, vie
09-11-2019, sáb
10-11-2019, dom
FoG
08:00
10:00
12:00
14:00
16:00
18:00
20:00
22:00
INT
ON
OFF
Discinesia
No aplicable
Boton
Caidas


Resumen Semanal del Estado Motor del paciente 4
14-10-2019, lun
15-10-2019, mar
16-10-2019, mié
17-10-2019, jue
18-10-2019, vie
19-10-2019, sáb
20-10-2019, dom
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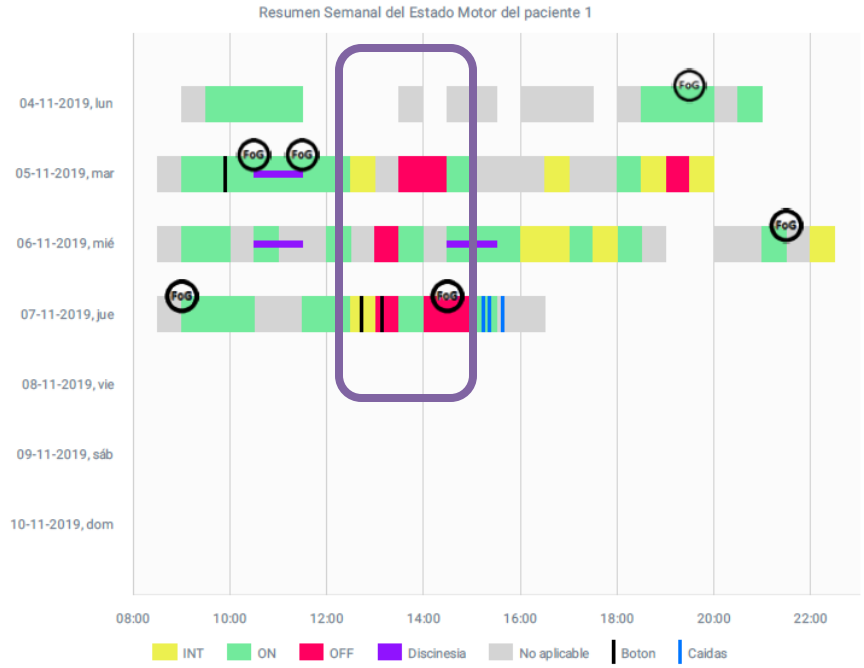
Caídas

Results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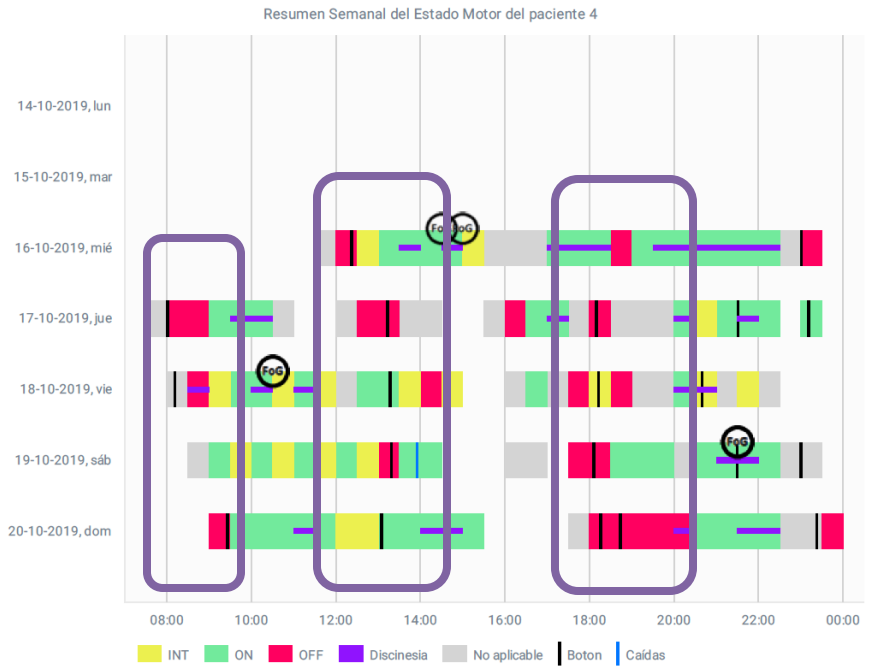
Resumen Semanal del Estado Motor del paciente 4
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16-10-2019, mié
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18-10-2019, vie
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Boton
Caídas

Artificial Intelligence concepts

According B.Mesko (2017) or J.Qi (2017): "*AI is the science and engineering of making **intelligent machines**, especially intelligent computer programs*", or more concrete: "*…is the capacity of a computer program to **perform tasks or reasoning processes** that we usually associate to intelligence in a human being*"

eHealth

+

IoT

Generation of data

Benefits?
Challenges?

Extract knowledge

How?

- **Reasoning**
- **Better management**
- **Personalization**

AI: a personal view

Data coming from:

- Wearables
- EHR (Electronic Health Record)

Learning Database

- Structured
- Non-structured

Rule based Engines (server or Fog level)

Treatment of Data

- Machine learning
- Expert knowledge

Extracted Knowledge

Possible outputs:

- Personalized diagnosis
- Personal treatments
- Recommendations
- Alarms, alerts and re-adjustments

AI: a personal view (2)

How to get a good Learning Database?

- Structures Database from specific experiments (pilots) with real participants, generating data according a given approved protocol.

  DATA + labelling by experts + annotations → GOLD STANDARD

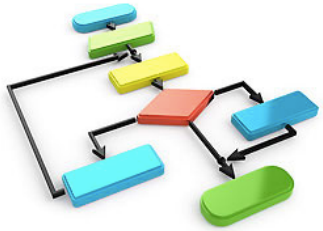
- Non-structured Database from people just giving access to their data, compiled from sensors or wearables

  DATA + methods of analysis + similitude methods → No GOLD STANDARD
  → Intrinsic patterns

Learning process: model parameters calculation

Model to be applied: depends on the problem and the computational requirements.

- **Calculated parameters**
- **Generalization capability**

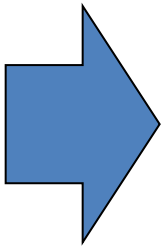


Obtained results on data not contained in the learning Database

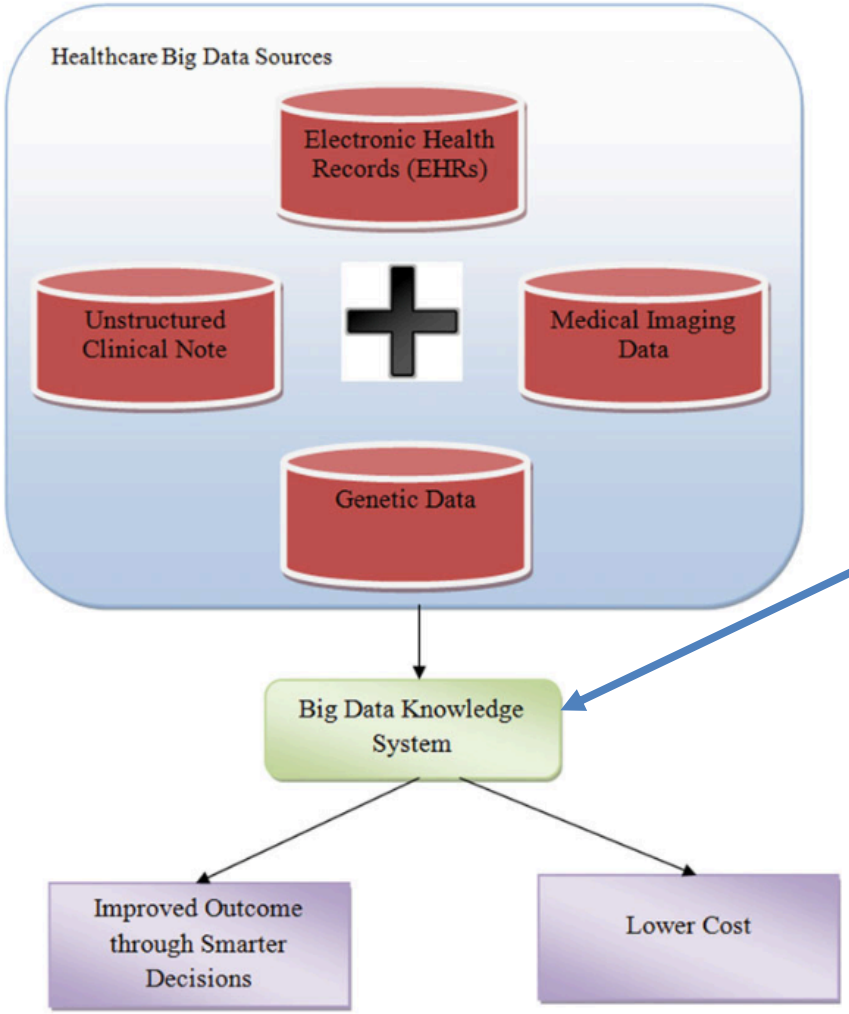
Usual question: how big must be the learning Database?

- ***Artificial intelligence***: Designates a set of techniques implemented for purposes of **allowing machines to simulate human intelligence** in order to resolve complex problems. It can be used in a variety of approaches, notably **automatic learning** (or machine learning) and **deep learning**. The latter imitates neuronal function in the human brain for purposes of teaching a machine how to independently identify and classify data.

Thanks to artificial intelligence, the ever-increasing volume of data and growing computing power, it is now possible to construct algorithms that generate automatic and more accurate solutions to medical problems.



- How to extract knowledge from specific or formal data?
- Implementation of learning approaches?
- Can be done in real time?



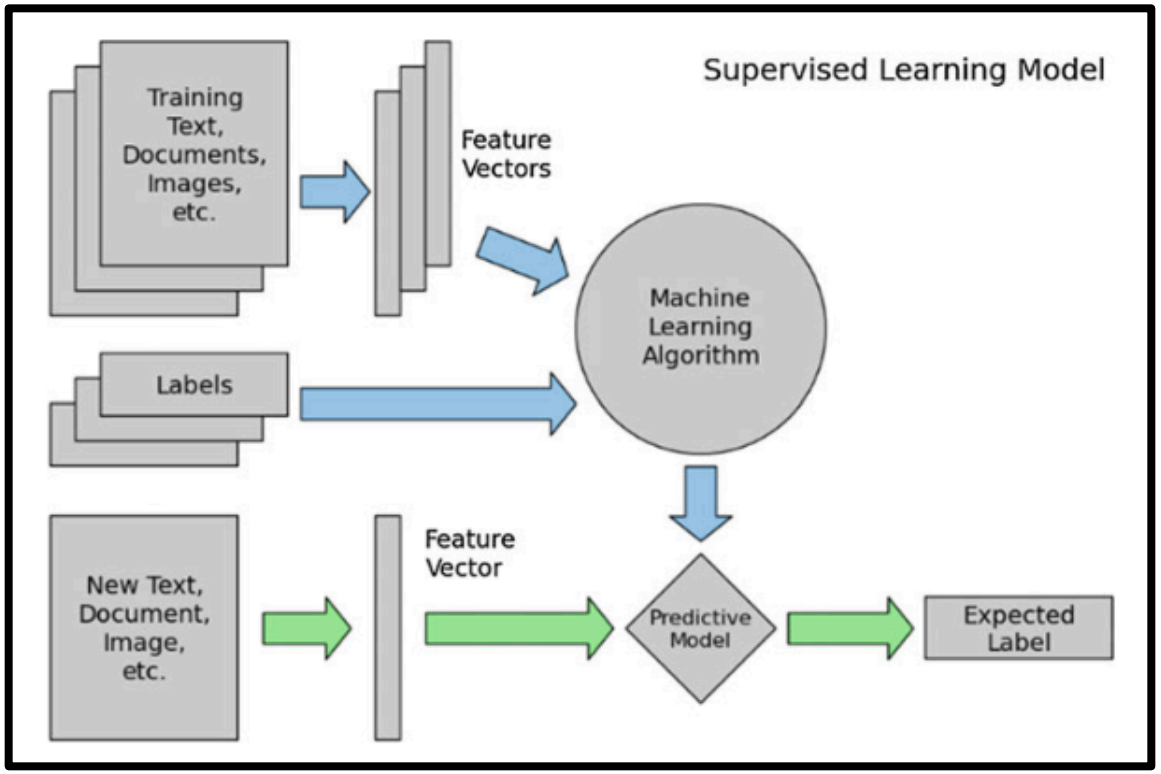
Provider Knowledge: Medical experts have both tacit and explicit knowledge. In general, every doctor is required to identify typical medical diagnosis or details from various available sources. Years of experience in medical diagnosis is used to take better decisions.

Patient Knowledge: Tacit knowledge is developed from the patients and it is considered "health status". Generally speaking, practitioners and doctors may not know about the current and past medical conditions of the patients.

Organizational Knowledge is also a vital role in patient treatments and diagnoses for preventative maintenance and illnesses. Most medical organizations have other familiar resources that are available for doctors and patients to contact.

Machine learning algorithms: supervised learning

Supervised learning is a type of learning which is appropriate when correct results are assigned to the training instances that can predict the progress of learning. This is a very common method in classification problems where the goal is mostly to get the computer to learn a classification system that is already created.



Steps in Supervised Learning:

- Data Preparation
- Choosing appropriate Algorithm
- Fit appropriate Model
- Selection of appropriate validation methodology.
- Test and Update
- Using final model for prediction

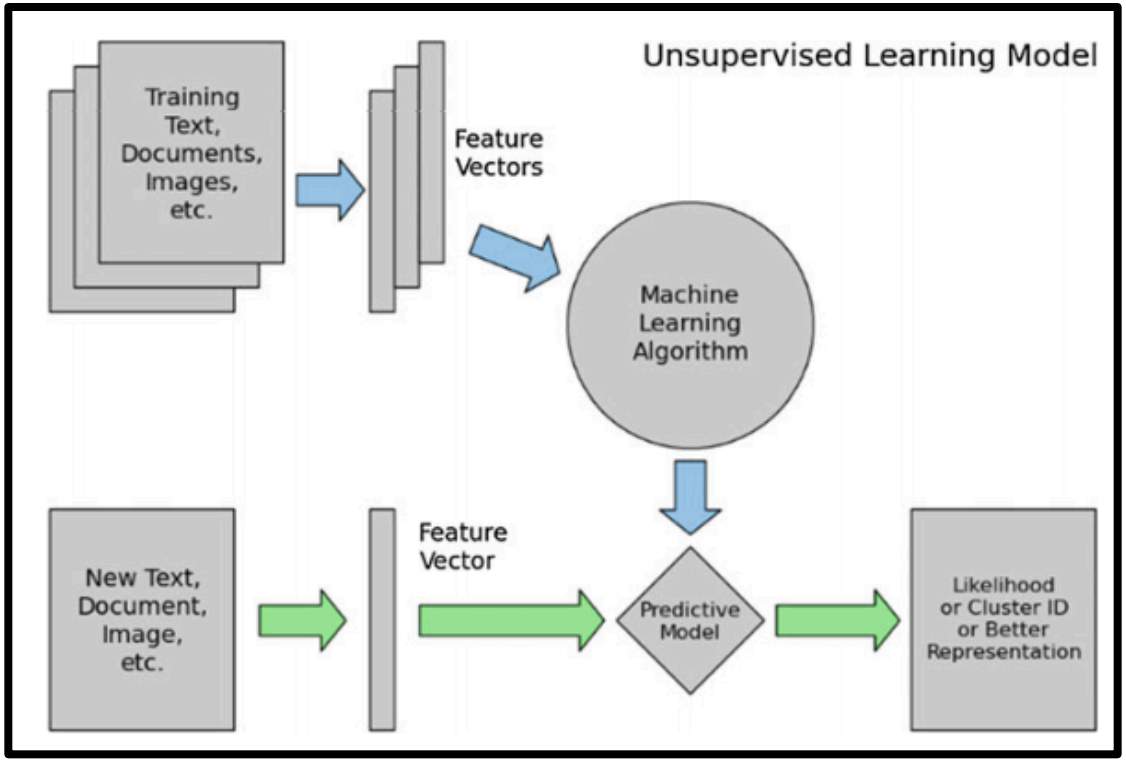
Importance of Supervised Learning Algorithms in Big data Analytics: Machine learning is a very ideal solution for exploiting new opportunities from a huge volume of data as it requires **minimum human interaction**. Also this methodology is **data driven** and runs at machine scale. It is also capable of handling **huge variety of variables** coming from **heterogeneous sources**.

Very common used algorithms in supervised learning:

- SVM – Support Vector Machines (useful both for classification and regression)
- Naïve Bayes algorithm (useful for classification purposes)
- Decision Trees Classifiers

Machine learning algorithms: unsupervised learning

Unsupervised learning is more complicated approach than supervised learning. Here the **objective is to learn something by the computer by its own**. There are primarily two approaches available in this type of learning.



- The first approach is teaching the agent with the help of **reward system** which is an **indicator of success**. This approach is most suitable into the **decision problem** framework where the goal is making decisions for maximizing rewards instead of producing a classification.
- The second type of approach is **clustering** where the goal is finding **similar patterns** in the training dataset instead of **maximizing a utility function**.

Common Algorithms in Unsupervised learning:

- **Clustering Algorithms**: Clustering is a popular concept which groups organization of unlabeled data based on similarity.
  - Bayesian Algorithms: The major goal of this kind of algorithm is to generate a posteriori distribution over the collection of all partitions of the data.
  - Hierarchical Algorithms: These type of algorithms find successive clusters using the clusters used previously.
  - Partition Algorithms: These type of algorithms find all clusters at the same time but can also be used as divisive algorithms in the hierarchical clustering. **K-means clustering** algorithm resides in this group.

- **Dimensionality Reduction Techniques**: In the world of big data, the volume of dataset increased tremendously and it leads to lots of redundancy. So it needs a treatment of dimensionality reduction to remove unwanted dimension.
  - Missing values
  - Random Forest
  - Principal Component Analysis - PCA

Please, take a look on main results and applicability of the REMPARK project…

River Publishers Series in Biomedical Engineering

Parkinson's Disease Management through ICT: The REMPARK Approach

Editors:
Joan Cabestany, Universitat Politècnica de Catalunya UPC, Barcelona, Spain
Àngels Bayés, Uparkinson Teknon, Grupo Hospitalario Quirón, Barcelona, Spain
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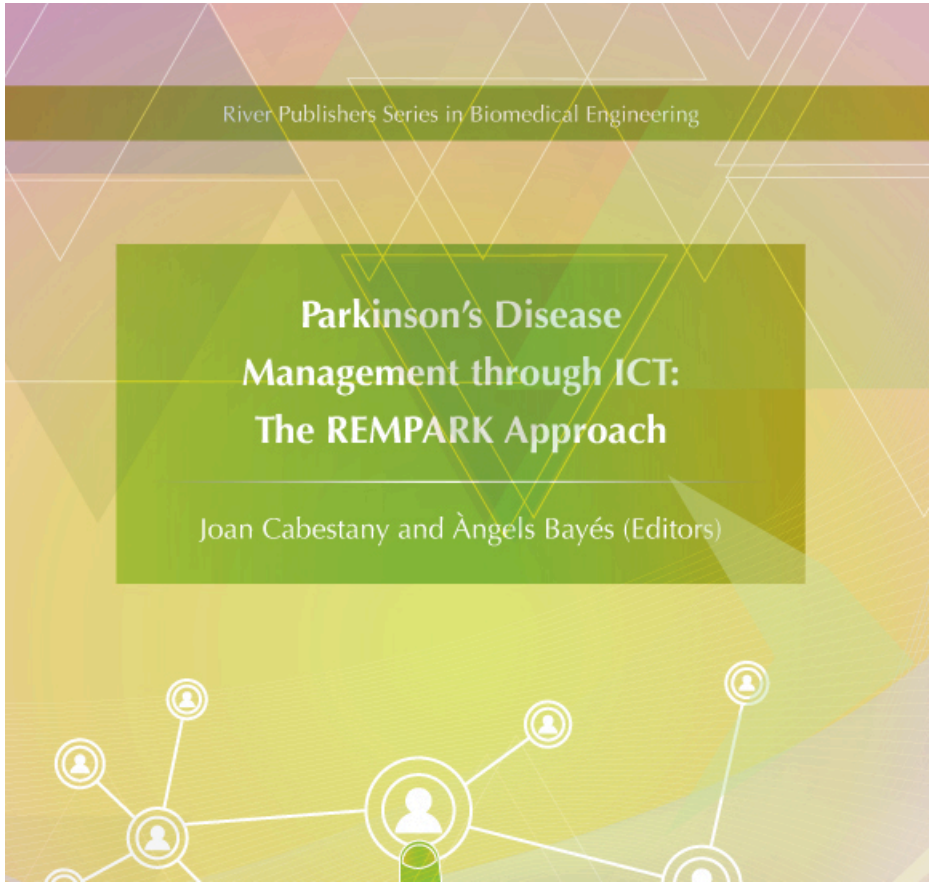
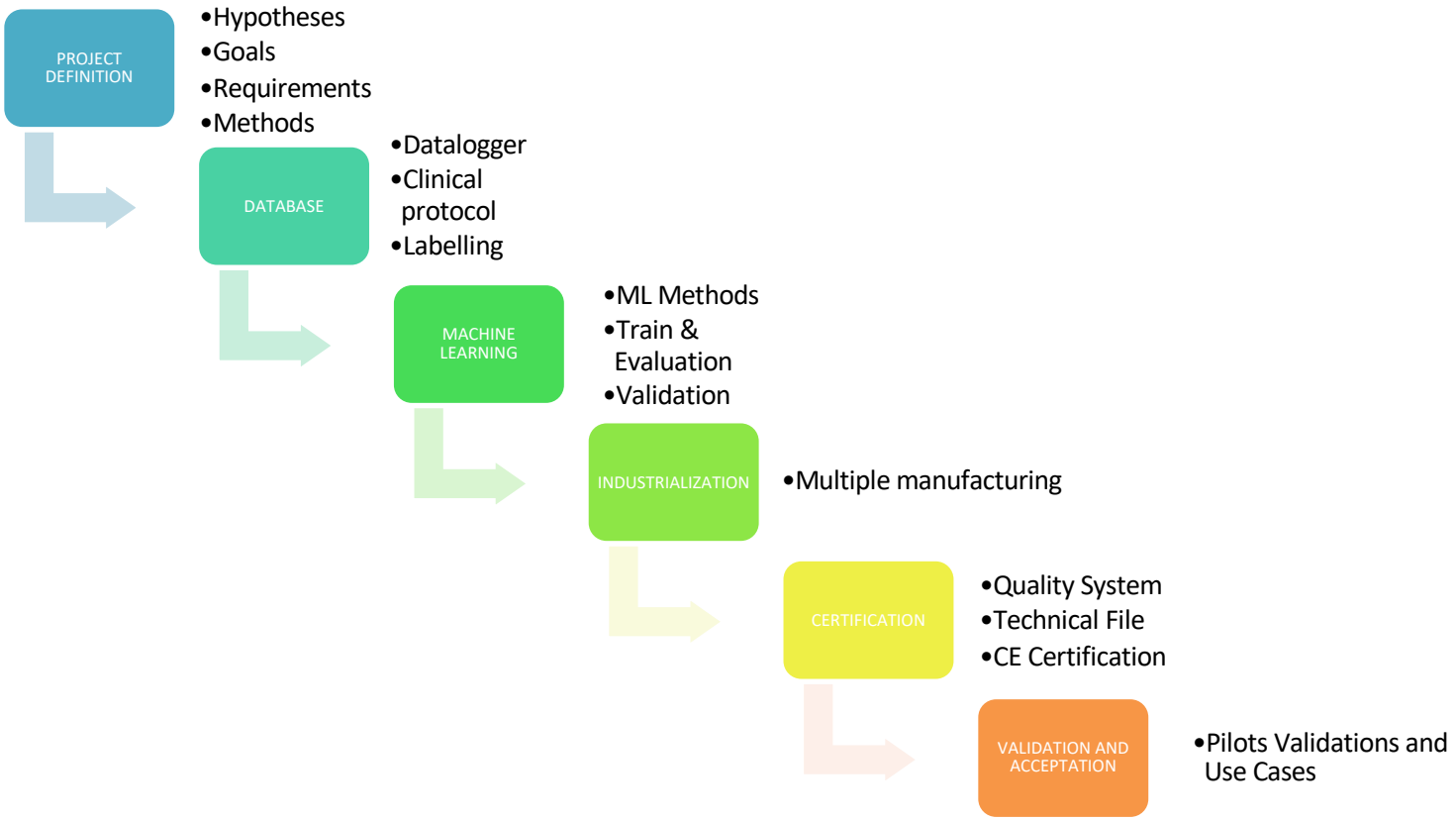
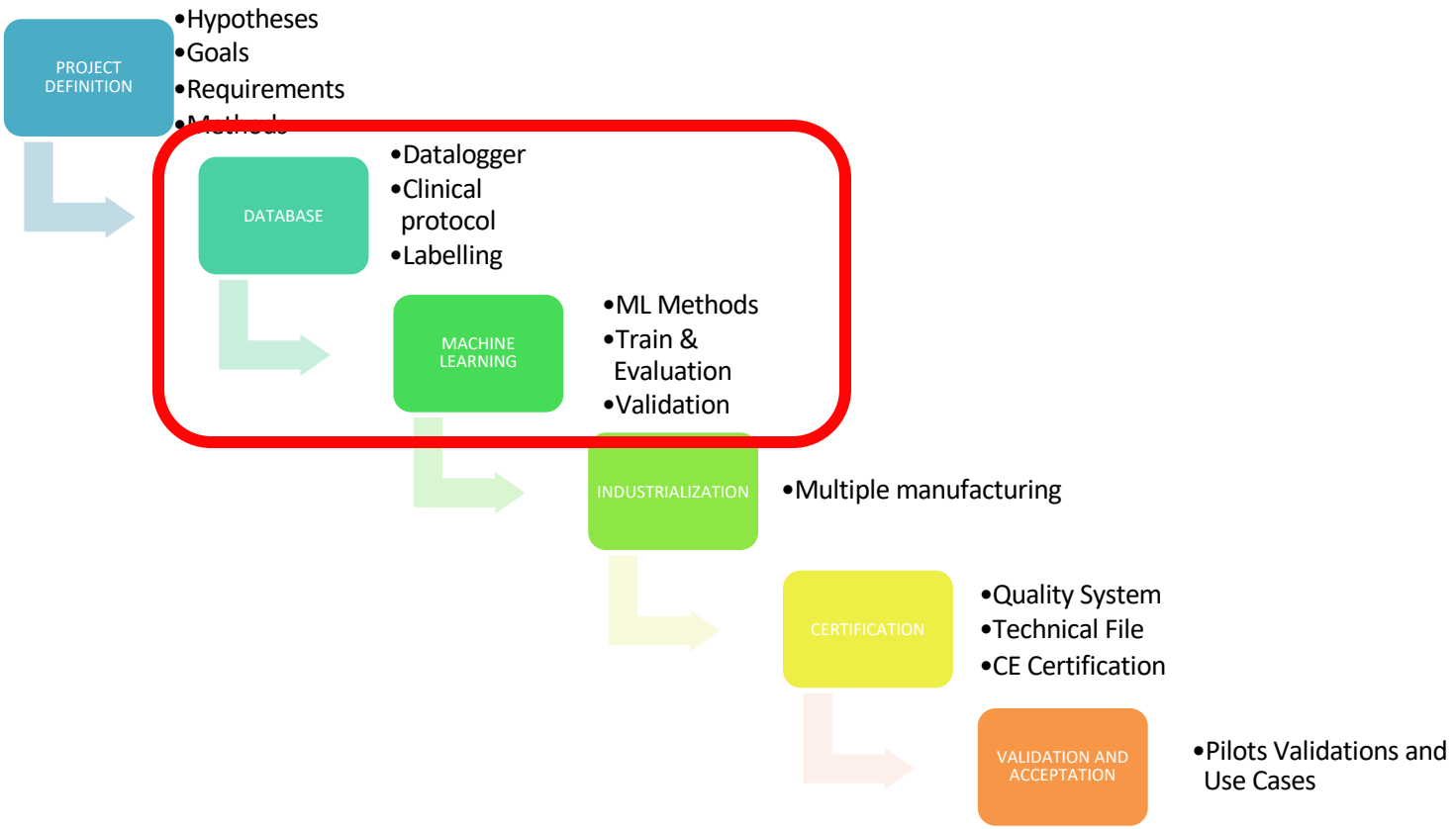


It is an Open Access book, available at http://www.riverpublishers.com/research_details.php?book_id=430

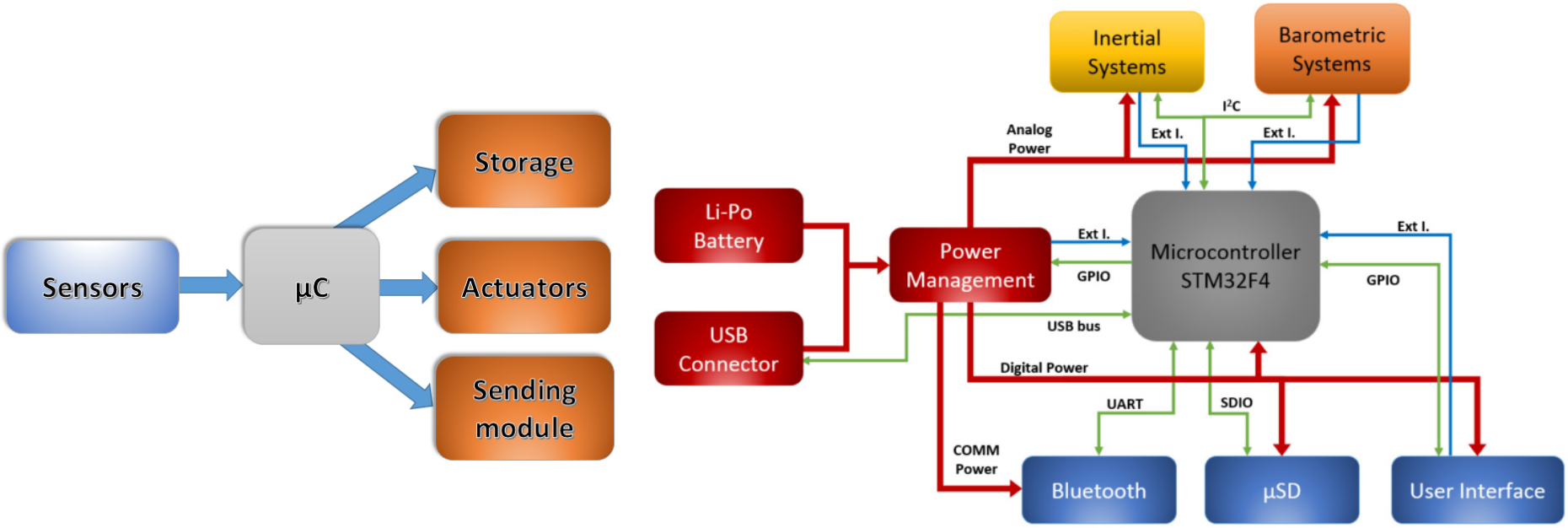
Project roadmap



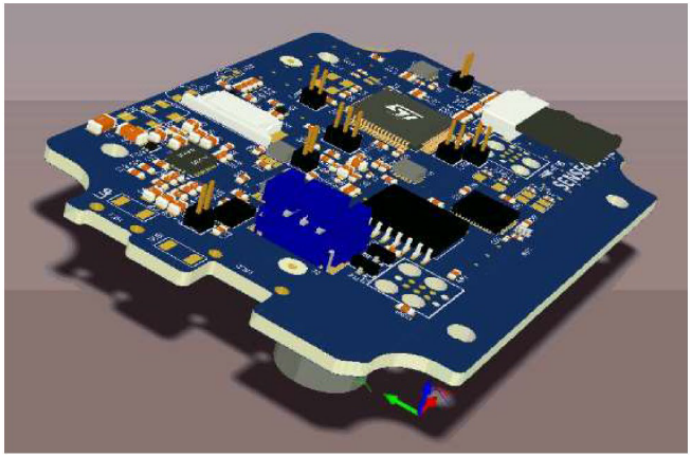
Project roadmap

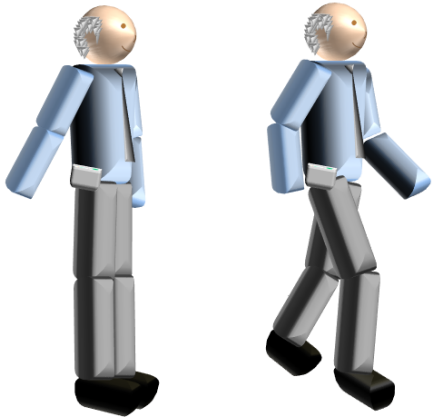


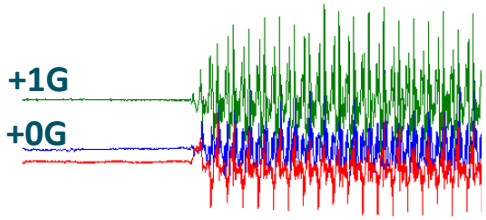
Inertial systems

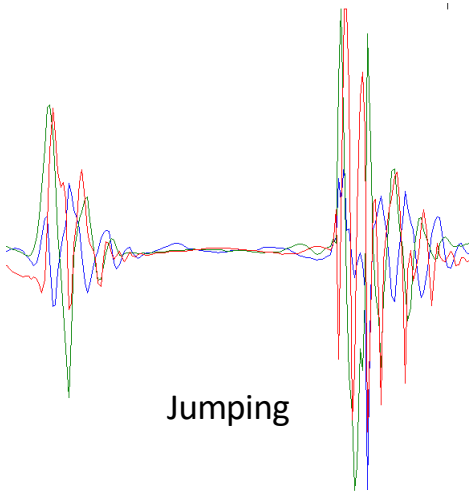


Inertial systems

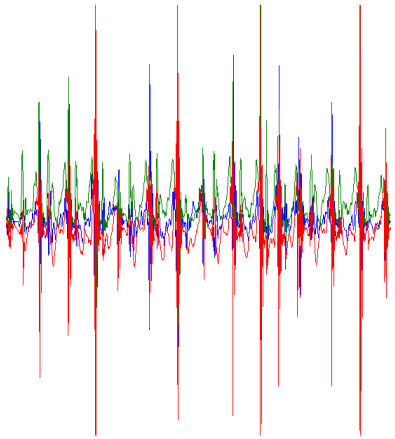




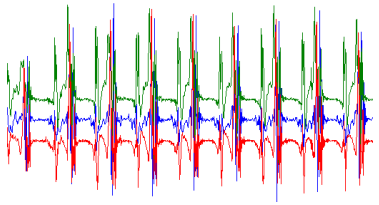




Jumping



Running

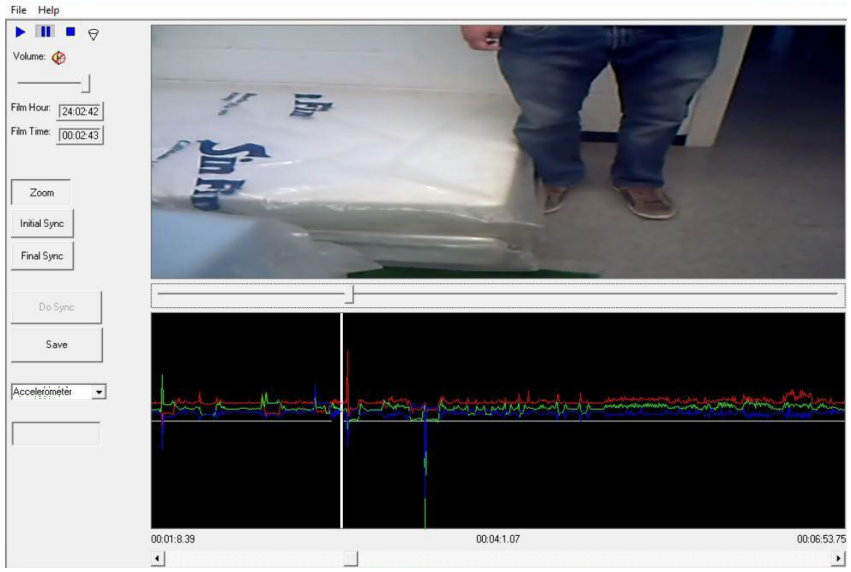


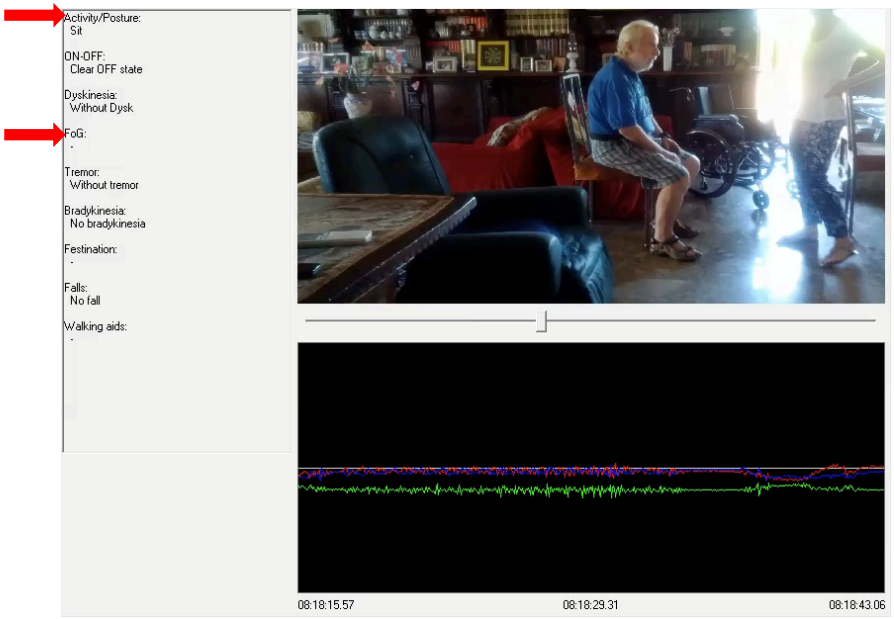
Walking

Clinical protocol

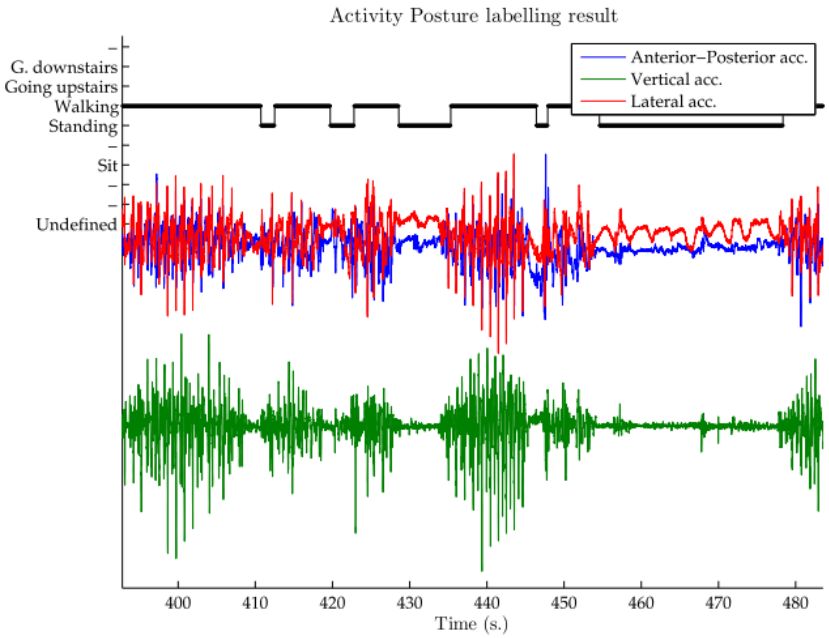
- **Cubrir todos los movimientos posibles**
- Criterios de inclusión y de exclusión
- Grupo control
- Ambientes lo más cercano a la realidad
- Cobertura tecnológica
  - Sensores
  - Cámaras
  - Expertos clínicos
- Comités éticos, aceptación de la AEMPS??

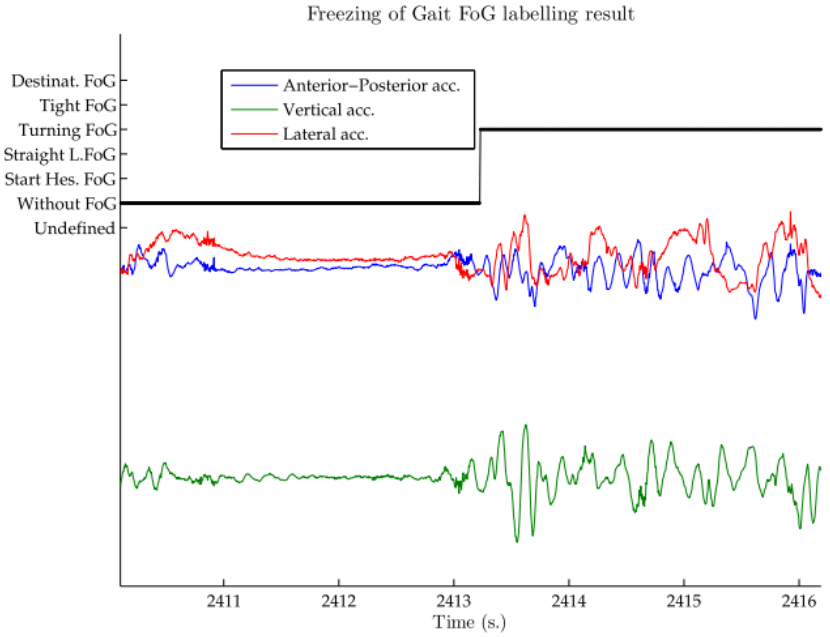
Clinical protocol: Data base construction



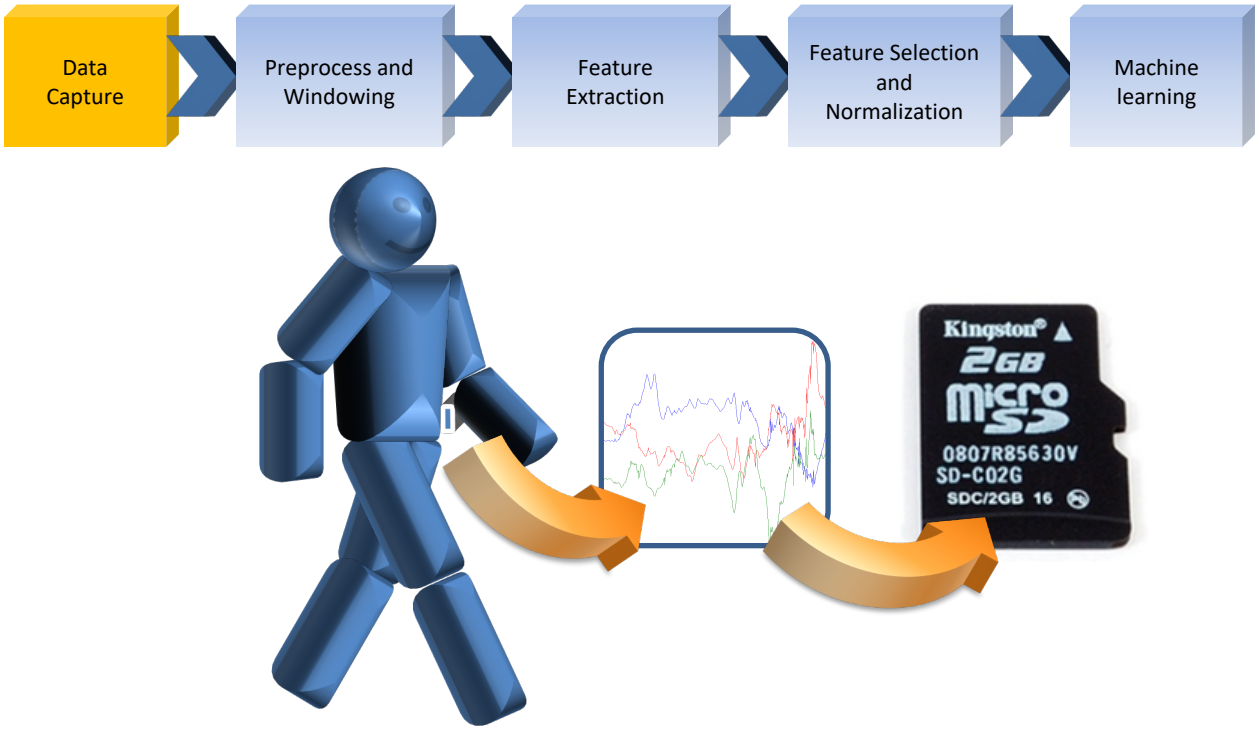


Machine learning





Machine learning



Machine learning

$$(x'_k, y'_k, z'_k) = (x_k, y_k, z_k) \cdot C_k$$

Calibration matrix

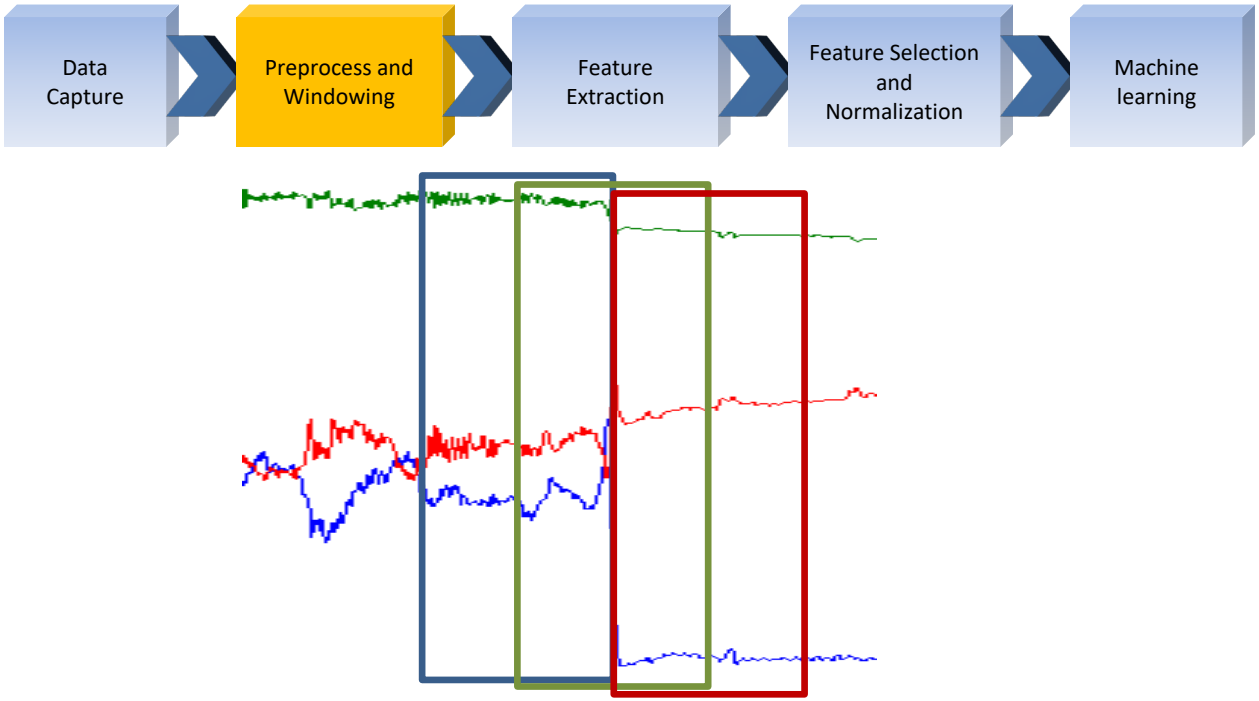
Acquired data

Calibrated data

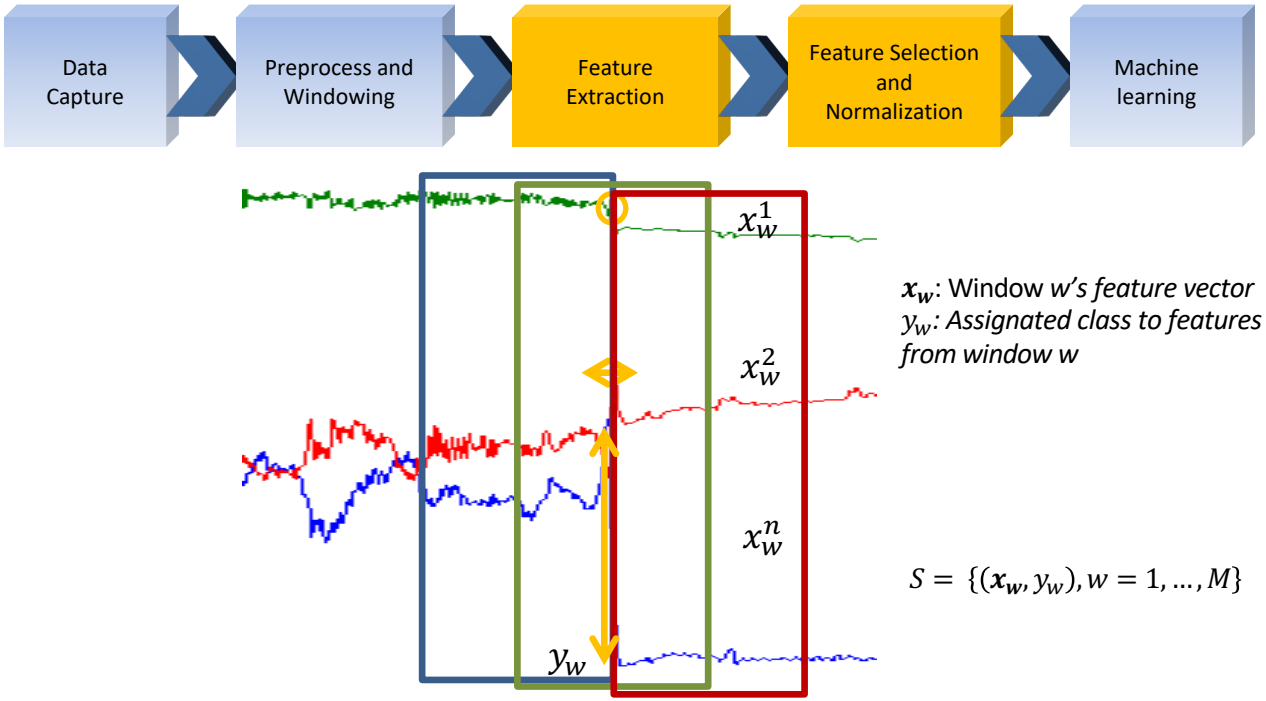
k is *a* (accelerometer), *g* (gyroscope), o *m* (magnetometer)

$$C_k = (L_k)(S_k)^T[(S_k)(S_k)^T]^{-1}$$

Machine learning

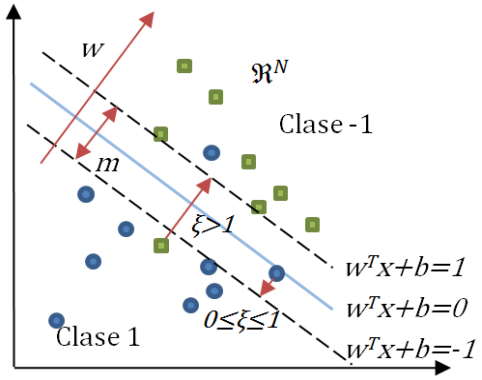


Machine learning



Machine learning

- Support Vector Machines
- Random Forest
- Tree Classifier
- Neural Networks
- ...



$$minimizar \left\{ \frac{1}{2}\|w\|^2 + C^* \sum_{i=1}^{l} \xi_i \right\}$$

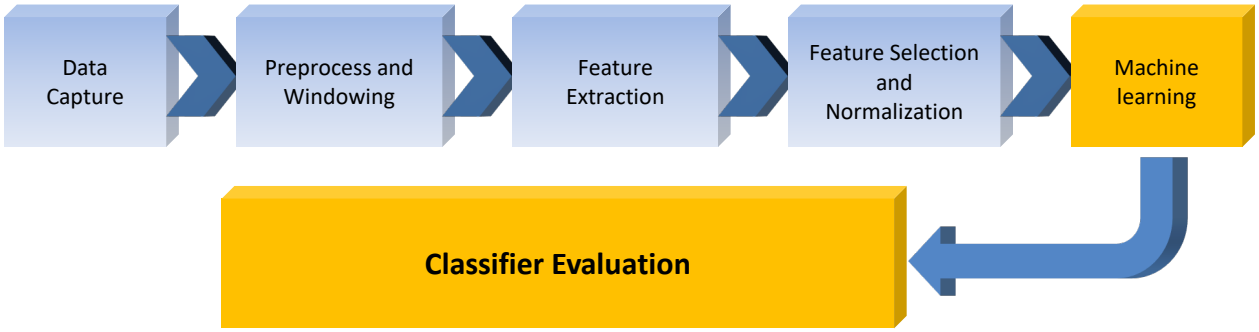
$$Sujeto\ a:\ y_i(w \cdot \varphi(x_i) + b) \geq 1 - \xi_i, \forall i$$

$$\xi_i \geq 0, \forall i$$

$$C^* = C_1 = C \cdot \rho_{-1}\ si\ y_i = 1$$

$$C^* = C_{-1} = C \cdot \rho_1\ si\ y_i = -1$$

Machine learning



$$Sensitivity = \frac{TP}{TP+FN}$$

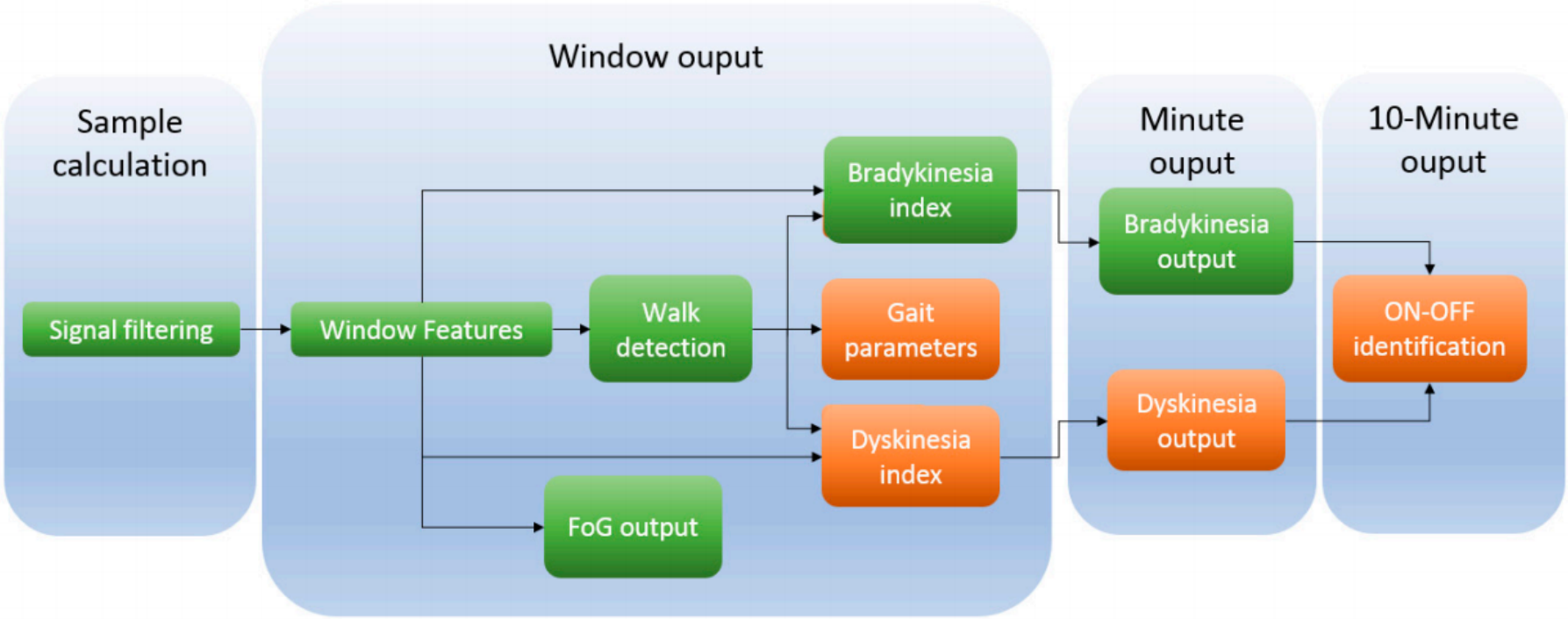
$$Specificity = \frac{TN}{TN+FP}$$

	Goal Class	No-Goal Class
Positive Test	TP	FP
Negative Test	FN	TN

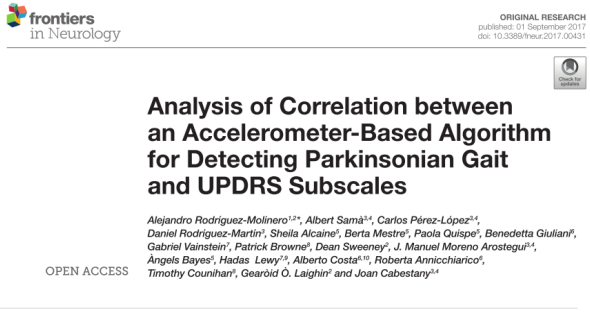
Sensitivity (also called the **true positive rate**) measures the proportion of actual positives that are correctly identified as such.

Specificity (also called the **true negative rate**) measures the proportion of actual negatives that are correctly identified as such

PD: motor symptoms evaluation



Algorithms validation



frontiers in Neurology

ORIGINAL RESEARCH
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Analysis of Correlation between an Accelerometer-Based Algorithm for Detecting Parkinsonian Gait and UPDRS Subscales

Alejandro Rodríguez-Molinero[1,2*], Albert Samà[3,4], Carlos Pérez-López[3,4], Daniel Rodríguez-Martín[3], Sheila Alcaine[5], Berta Mestre[5], Paola Quispe[5], Benedetta Giuliani[6], Gabriel Vainstein[7], Patrick Browne[8], Dean Sweeney[9], J. Manuel Moreno Arostegui[3,4], Àngels Bayes[5], Hadas Lewy[7,8], Alberto Costa[6,10], Roberta Annicchiarico[6], Timothy Counihan[9], Gearòid Ò. Laighin[2] and Joan Cabestany[3,4]

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Full length article

A "HOLTER" for Parkinson's disease: Validation of the ability to detect on-off states using the REMPARK system

Àngels Bayés[a,*], Albert Samá[b], Anna Prats[e,k], Carlos Pérez-López[b], Maricruz Crespo-Maraver[a,c], Juan Manuel Moreno[b], Sheila Alcaine[a], Alejandro Rodriguez-Molinero[d,e,f], Berta Mestre[a], Paola Quispe[a], Ana Correia de Barros[g], Rui Castro[g], Alberto Costa[h], Roberta Annicchiarico[i], Patrick Browne[j], Tim Counihan[e,k], Hadas Lewy[l], Gabriel Vainstein[l], Leo R. Quinlan[e,m], Dean Sweeney[e,n], Gearóid ÓLaighin[e,m], Jord
Joan Cabestany[b]

JMIR MHEALTH AND UHEALTH — Rodríguez-Molinero et al

Original Paper

Validation of a Portable Device for Mapping Motor and Gait Disturbances in Parkinson's Disease

Alejandro Rodríguez-Molinero[1,2*], MD, PhD; Albert Samà[3*], PhD; David A Pérez-Martínez[4], MD, PhD; Carlos Pérez López[3], MSc; Jaume Romagosa[3], BSc; Àngels Bayés[5], PhD; Pilar Sanz[6], MD, PhD; Matilde Calopa[7], MD, PhD; César Gálvez-Barrón[8], MD; Eva de Mingo[8], BN; Daniel Rodríguez Martín[3], PhD; Natalia Gonzalo[8], NURSE AID; Francesc Formiga[9], MD, PhD; Joan Cabestany[3], PhD; Andreu Catalá[3], PhD

JMIR REHABILITATION AND ASSISTIVE TECHNOLOGIES — Rodríguez-Molinero et al

Original Paper

A Kinematic Sensor and Algorithm to Detect Motor Fluctuations in Parkinson Disease: Validation Study Under Real Conditions of Use

Alejandro Rodríguez-Molinero[1], MD, PhD; Carlos Pérez-López[2,3], PhD; Albert Samà[2,3], PhD; Eva de Mingo[4], RN; Daniel Rodríguez-Martín[2], PhD; Jorge Hernández-Vara[5], MD, PhD; Àngels Bayés[6], MD, PhD; Alfons Moral[7], MD, PhD; Ramiro Álvarez[8], MD, PhD; David A Pérez-Martínez[9], MD, PhD; Andreu Catalá[2,3], PhD

SCIENTIFIC REPORTS
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Estimating dyskinesia severity in Parkinson's disease by using a waist-worn sensor: concurrent validity study

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Alejandro Rodríguez-Molinero[1,2], Carlos Pérez-López[3,4], Albert Samà[3,4], Daniel Rodríguez-Martín[3,4], Sheila Alcaine[5], Berta Mestre[5], Paola Quispe[5], Benedetta Giuliani[6], Gabriel Vainstein[7], Patrick Browne[8,10,11], Dean Sweeney[2], Leo R. Quinlan[8], J. Manuel Moreno Arostegui[3,4], Àngels Bayes[5], Hadas Lewy[7], Alberto Costa[6,9], Roberta Annicchiarico[6], Timothy Counihan[8], Gearòid Ò. Laighin[2] & Joan Cabestany[3,4]

PD motor symptoms evaluation: some results

SYMPTOM	Sensitivity	Specificity
Bradykinesia	88%	89%
Dyskinesia	93%	95%
FoG	88,1%	80,1%
ON/OFF	90%	91%

Step detection accuracy = 97%

Sensitivity (also called the **true positive rate**) measures the proportion of actual positives that are correctly identified as such.

Specificity (also called the **true negative rate**) measures the proportion of actual negatives that are correctly identified as such

STAT-ON: clinical evaluation status

Activity	Character of the experience	Title of the experience	Main responsible	Funding scenario
1	Pilots for clinical validation of STAT-ON™	Comparison between classical visits and STAT-ON™ information	Consorci Sanitari Penedès-Garraf	MoMoPa-EC project. FIS project funded by ISCIII in Spain With the support of Abbvie
2		Clinical Use experience	UParkinson. Quirón Teknon and Hospital Moisès Brogi	Internal activity
3		Practical use and general opinion of neurologists	COPPADIS initiative	COPPADIS
4		Therapeutic medication adjustment by comparing different information	Hospital Germans Trias I Pujol	Internal, with the possible participation of Abbott
5		Therapy enhancement to prevent falls due to PD symptoms in PD patients	Hospital Universitario de Burgos	FIS project funded by ISCIII in Spain
6		User experience using STAT-ON™	Air-Liquide - Orkyn in France	Internal
7		Deep Brain Stimulation experience	Hospital Cruces - Bilbao (Spain) Osakidetza	Internal
8	Formal running projects	Integration into a large-scale system and analysis of data	Gatekeeper project (H2020 initiative) H2020-SC1-FA-DTS-2018-2020-85722	EU
9		Platform design to adapt information to hospital systems	REVEL-PARK action	ACTIVAGE project - EU
10	Independent actions	Other actions	A number of initiatives (private and corporative) including the free use of STAT-ON™ for a limited time	

Novembre de 2019 a Sevilla

Sociedad Española de Neurología
Fundada en 1949

Amazing performance at @TecnoSEN (Nov.2019) event from Dra. Bayès presenting results from 40 patients using STAT-ON.

Some conclusions from the study:

- Hauser diaries, is this the end?
- STAT-ON has more sensitivity to detect Motor Symptoms
- It has helped to view the general state of the patient.
- STAT-ON can detect the beginning of “wearing-off”.
- It detects patients with initial or mild dyskinesias.
- The system has very good usability
- It is useful to know when FoG episodes appear (ON, OFF or both states).
- With the analysis of the reports, it speeds up the visit of the patient at doctor’s office.
- The STAT-ON helps to improves QoL of the patient and helps to empower the patient.
- The sensor perceives less % OFF (the sensor cannot detect OFF when the patient is still).

Some additional conclusions:

- eHealth is a very challenging concept, opening the doors to very different view of the relationship between doctors and patients. **STAT-ON should be part of it**.

- **IoT** (Interner of Things), with the technological deployment, should be able to promote the use and diffusion of eHealth practices.

- AI is an embedded concept that can help in many aspects:
    - Big Data analysis
    - Recommend and suggest actions according personal needs
    - Stablish alarms to be launched in the presence of some circumstances
    - Suggest actions to the doctors (not to take automatic actions!!)

www.sense4care.com

Designed and made in Barcelona

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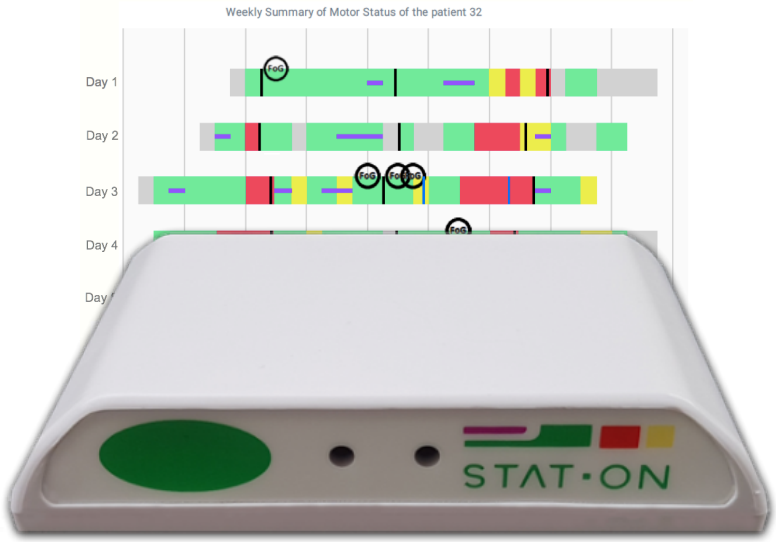

Questions?