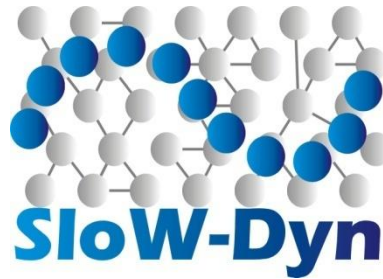




FLAG-ERA



Human Brain Project



Joint Transnational Call 2015

## **SloW-Dyn:** Slow Wave Dynamics: from experiments, analysis and models to rhythm restoration

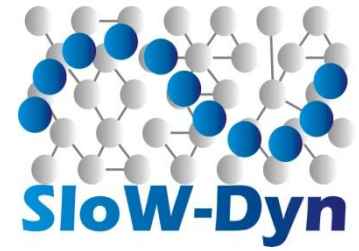
**Main area:** Theoretical and Mathematical Foundations of Neuroscience

**Keywords:** Slow oscillations; cortical models; Sleep restoration; non linear analysis; Up states; Up and Down states; Neuromorphic models; Slow waves; Pyramidal cells; Ageing; Slow wave sleep; Information theory; Causal analysis; Multiscale modeling

**Duration (months):** 36

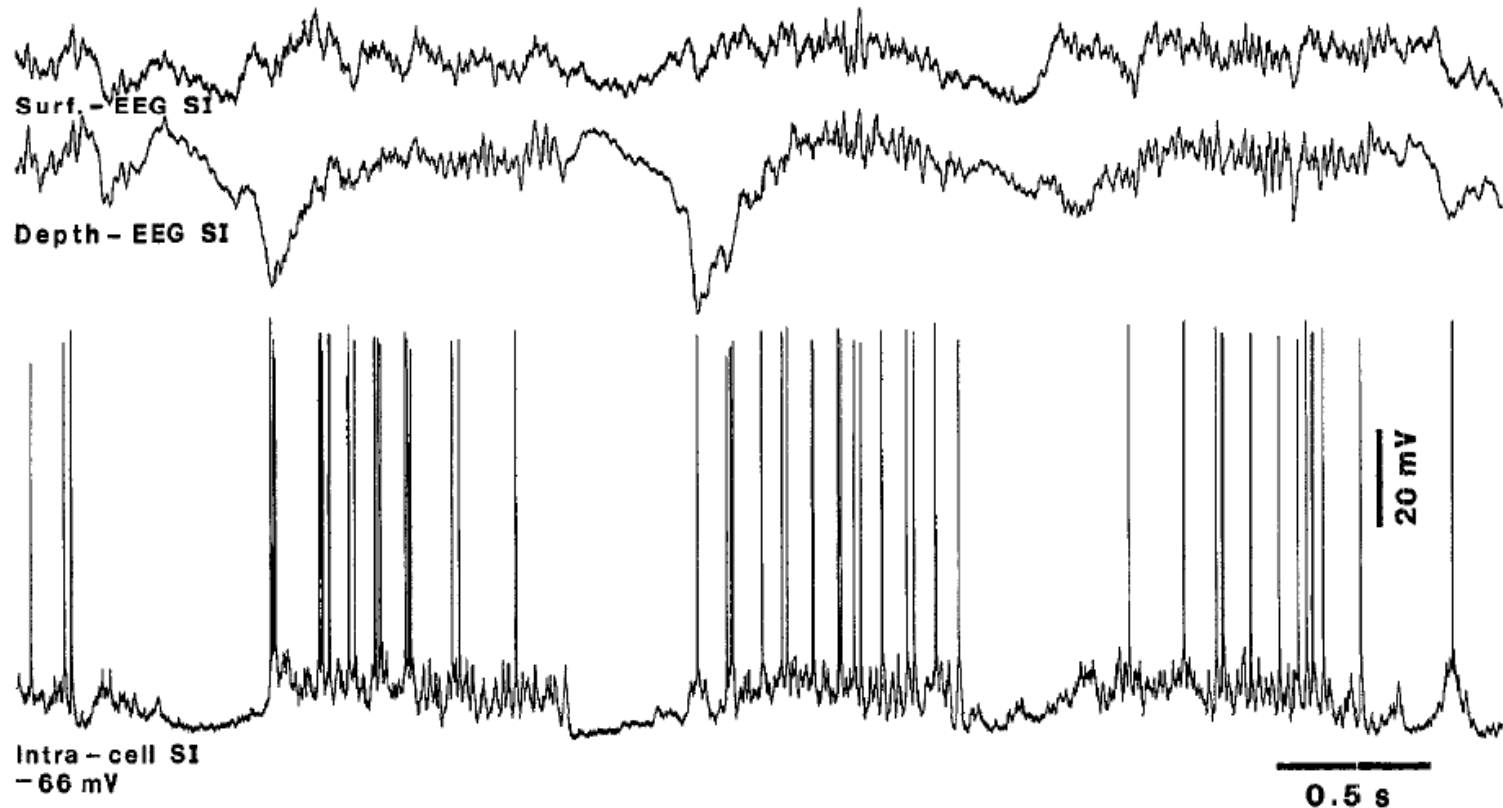
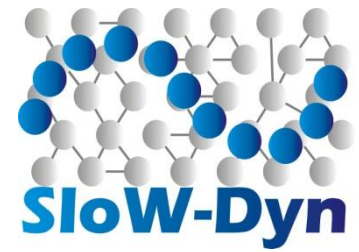
**Total project funding:** € 662 795

# Aim of the project

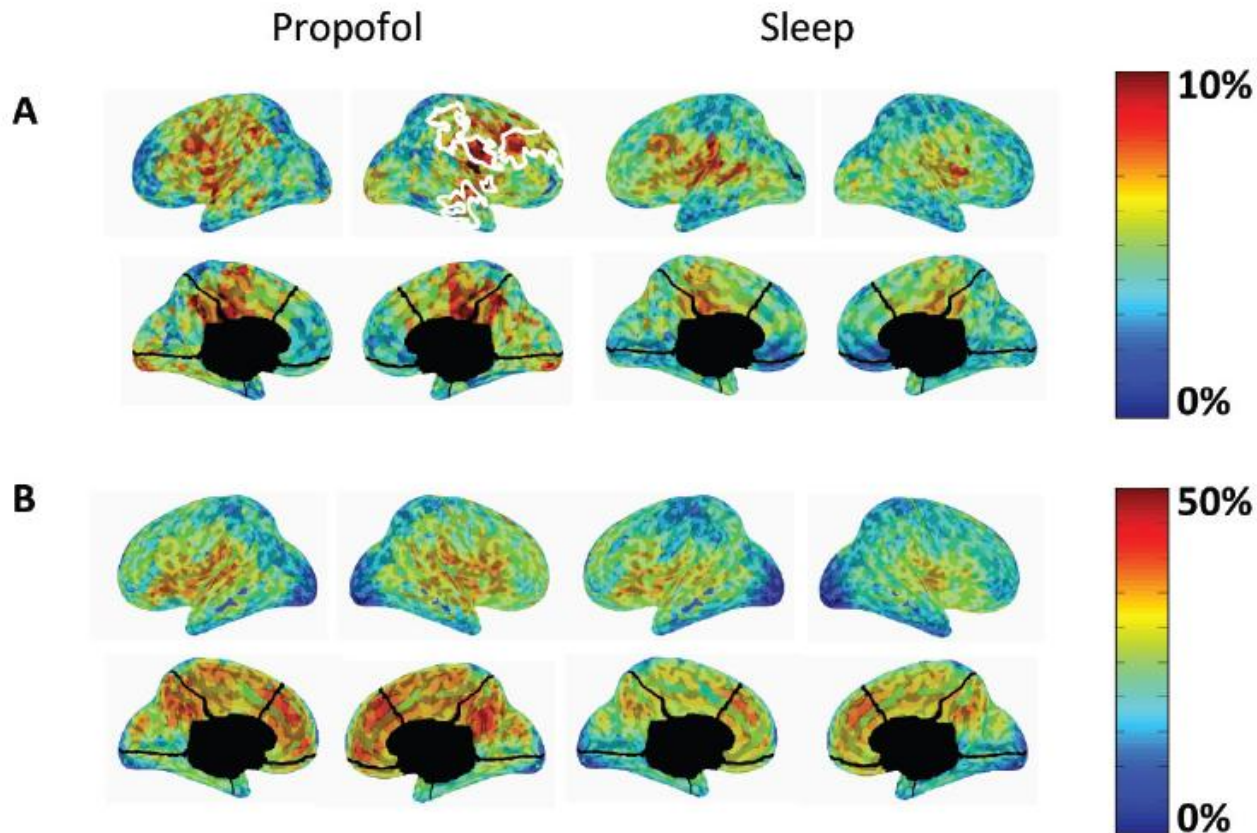


- **Data based model of Slow cortical oscillations**

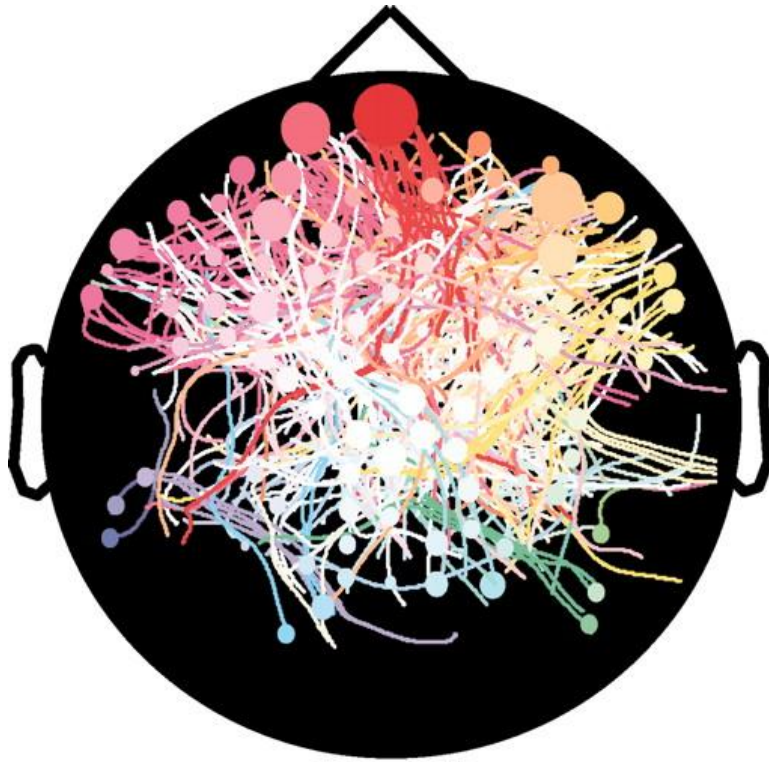
# Slow Wave activity-Background



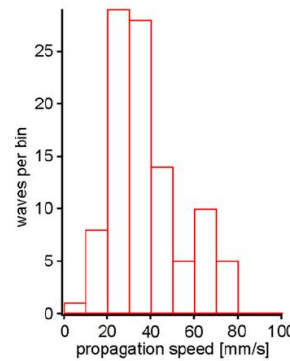
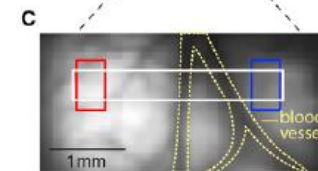
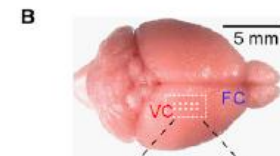
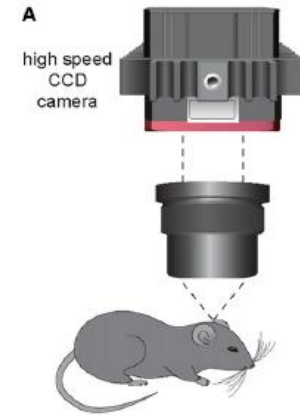
Steriade, Amzica, Contreras. J. Neurosci. 16:392, 1996



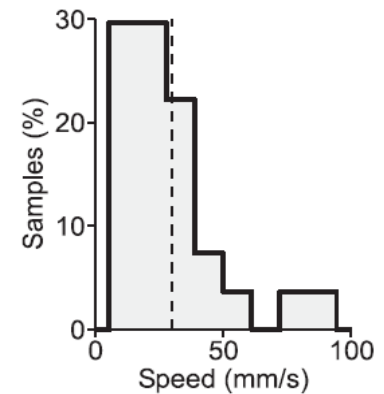
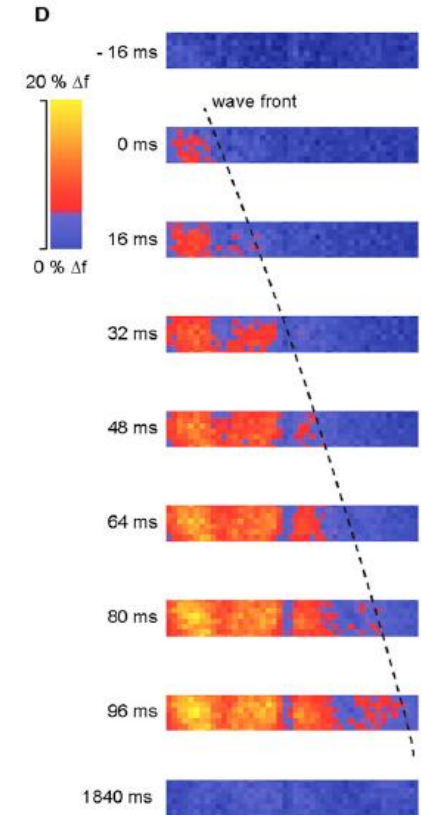
Murphy, M., et al (2011). Propofol anesthesia and sleep: a high-density EEG study. *Sleep*, 34(3), 283.



Marcello Massimini, Reto Huber,  
Fabio Ferrarelli, Sean Hill, and  
Giulio Tononi  
The Journal of  
Neuroscience, August 4, 2004,  
24(31):6862-6870;



av. speed:  $37 \pm 2$  mm/s

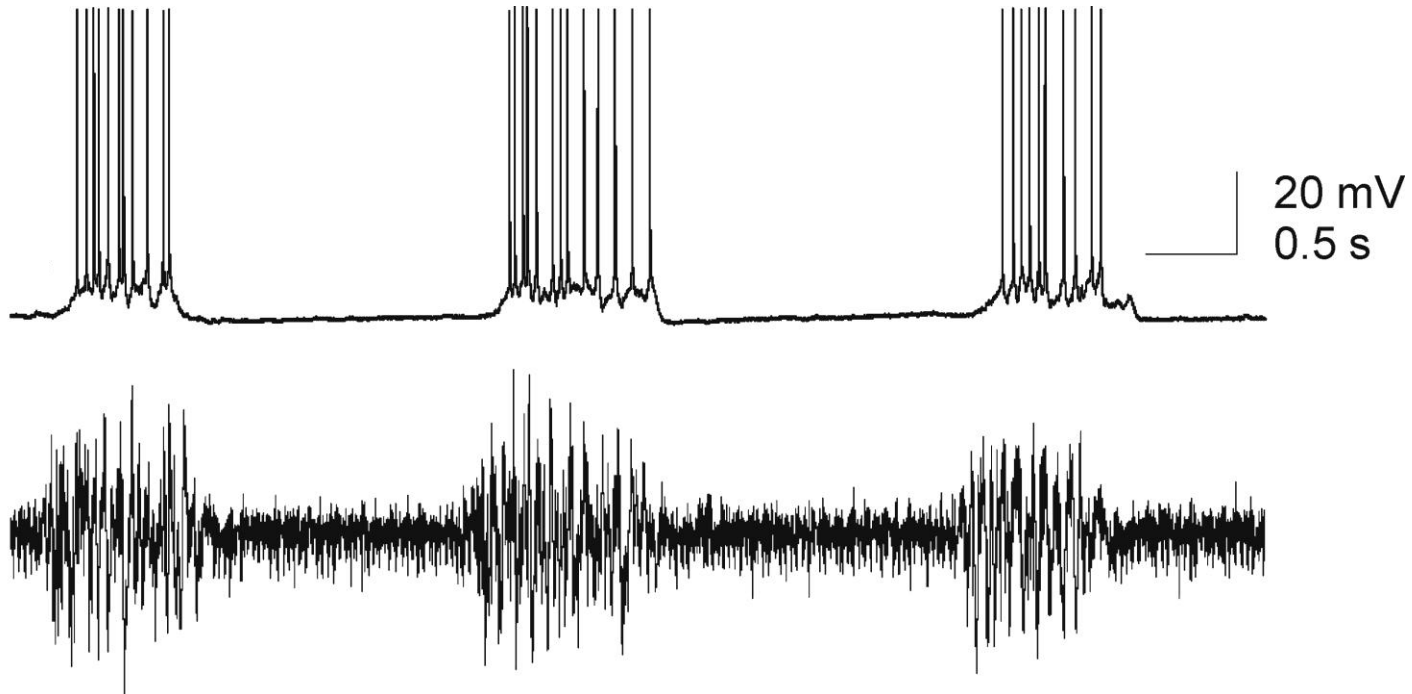
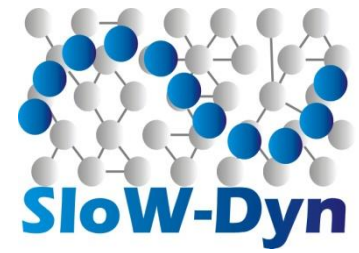
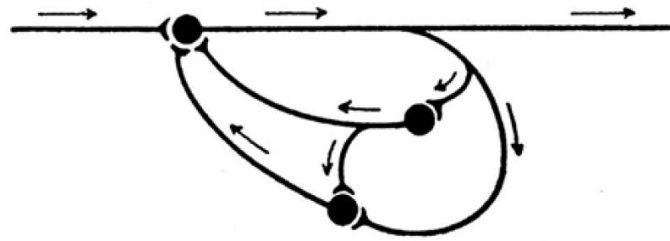


$30.0 \pm 3.9$  mm/s

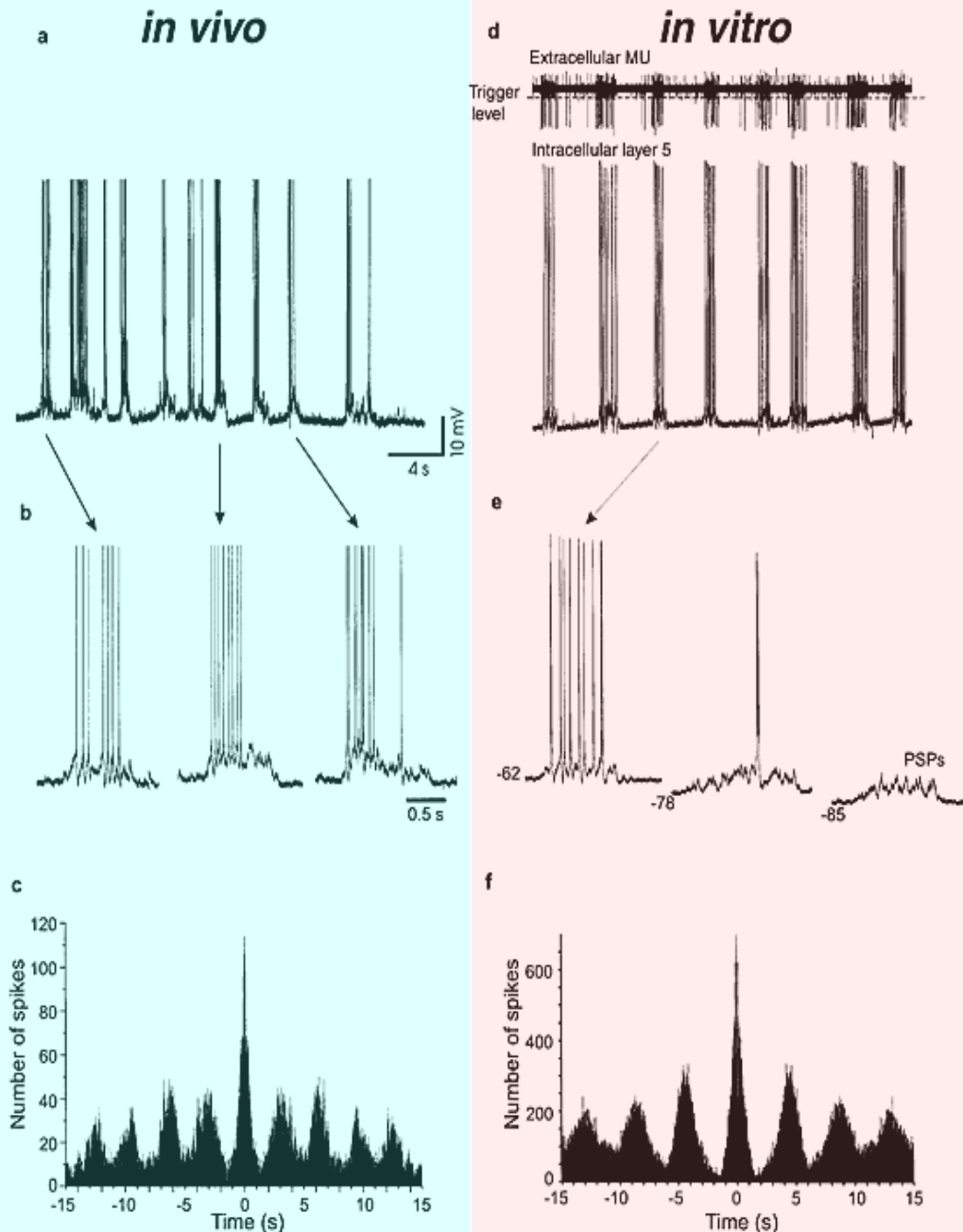
Stroh et al 2013

Ruiz-Mejias et al 2011





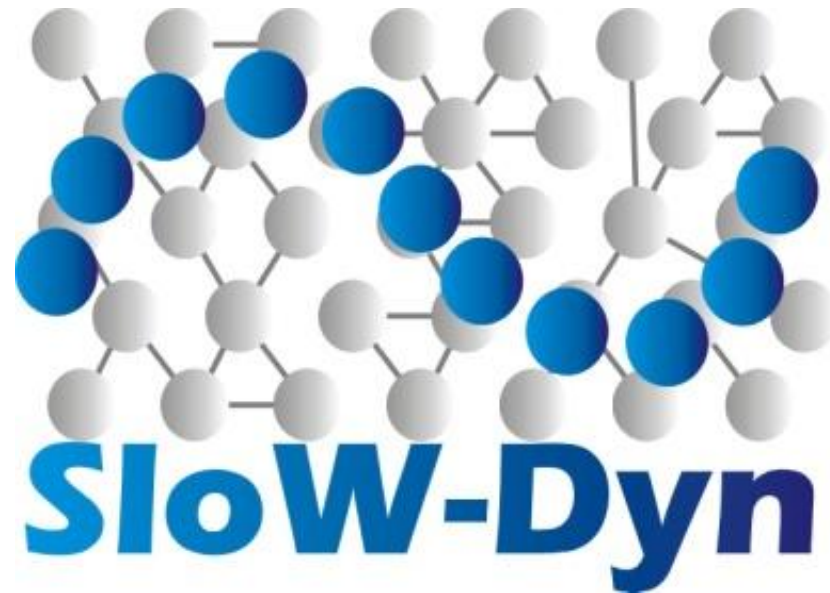




Slow wave activity has been proposed as the **default mode of the cerebral cortex**

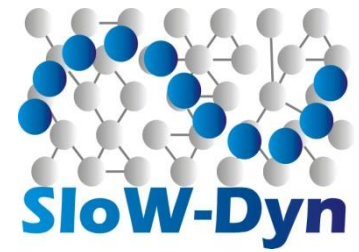
*Sanchez-Vives, M. V., & Mattia, M. (2014). Arch Ital Biol, 152, 147-155.*

Sanchez-Vives & McCormick  
Nat Neurosci 3: 1027, 2000





# Aim of the project



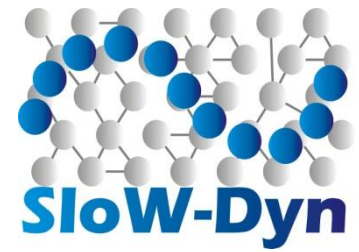
- **Data based model of Slow cortical oscillations**
- Understanding network mechanisms
- Multi-scale experimental data
- Study of transformation of Slow Wave Activity
  - Natural ageing in humans
  - Aging and associated neurodegenerative diseases (mouse models)

# Partners and participants involved in the realisation of the project



Partner	Country	Insitution/Department	Name of the Principal Investigator	Name of the co-Investigators
1 <i>Coordinator</i>	Spain	IDIBAPS	Maria V. Sanchez-Vives	
2	France	CNRS	Alain Destexhe	
3	Italy	IIT	Stefano Panzeri	Tommaso Fellin
4	Spain	UPF	Rubén Moreno-Bote	
5	USA	UChicago	Nicolas Brunel	
6	France	DREEM (SME)	Mathieu Galtier	

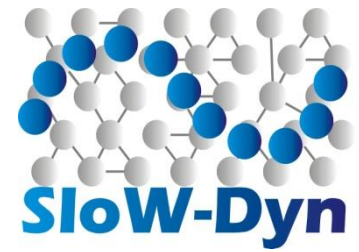
# Multi scale approach - Micro



## Partner: IIT - Tommaso Fellin

- State of art techniques to identify the participation of genetically identified cell types in slow waves.
- Generation of highly valuable detailed information about local circuit contribution.

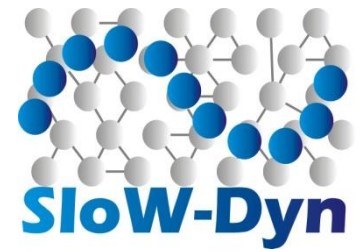
# Multi scale approach - Meso



**Partner: IDIBAPS – Maria V. Sanchez-Vives**

- Study of slow waves properties and 2D & 3D propagating waves mice at different ages, including 2 models of neurodegenerative diseases (SAMP-8 and APP-PS1)
- Preliminary evidence of transformation of slow oscillatory pattern in early ageing.

# Multi scale approach - Macro

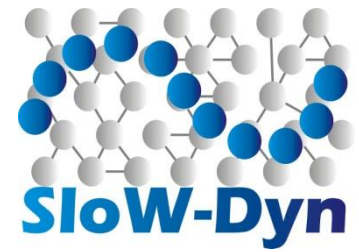


## Partner: DREEM

- Generation of largest sleep data base.
- EEG big data from slow wave sleep of (1000s) of individuals of different ages.
- Achieved through distribution of DREEM EEG head band.
- Valuable information about the transformation of slow waves during human ageing.



# Theoretical analysis



**Partner: IIT, UPF, CNRS, DREEM**

- Development of new and *ad hoc* analytical tools to explore multiscale correlations, information transfer and other aspects generated from multilevel data.



Slow oscillations, sleep, synchronization,  
correlations, cell types, biological signatures of disease,  
multilevel: from circuit to human.

**WP1  
MICRO**

Local circuit level; healthy mouse  
Experimental data and Data Analysis



**WP2  
MESO**

Multielectrode, multiarea LFP  
Healthy mouse, ageing and related  
diseases  
Experimental data and Data Analysis



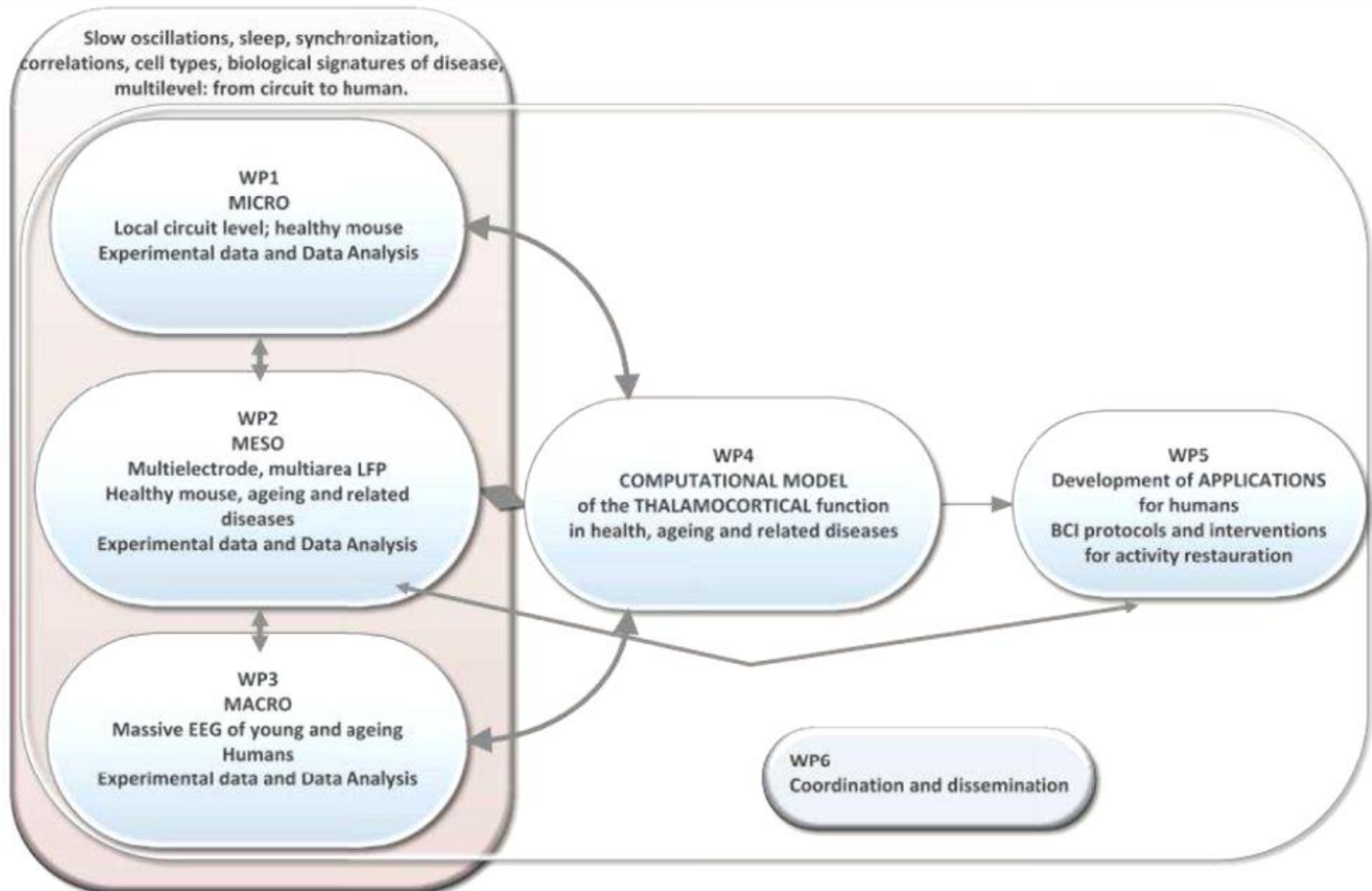
**WP3  
MACRO**

Massive EEG of young and ageing  
Humans  
Experimental data and Data Analysis

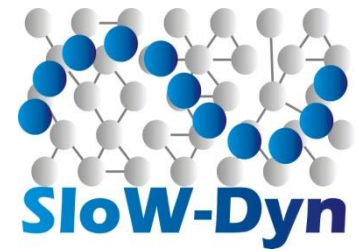
**WP4  
COMPUTATIONAL MODEL**  
of the THALAMOCORTICAL function  
in health, ageing and related diseases

**WP5  
Development of APPLICATIONS**  
for humans  
BCI protocols and interventions  
for activity restauration

**WP6  
Coordination and dissemination**



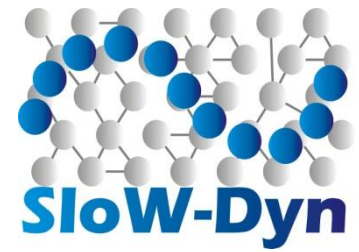
# Model development



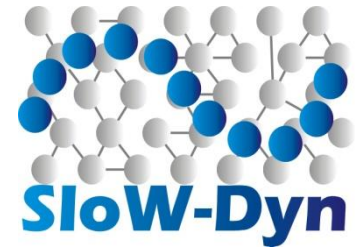
## Partners: CNRS, IIT, UChicago, DREEM

- Creation of a biophysically realistic model of thalamocortical function in health, ageing and related diseases.
- Model of adaptive exponential (AdEx) integrate-and-fire (IF) cells which is fully compatible with existing neuromorphic implementations in HBP.
- Beyond state-of-art by fitting not only 1st, but also 2nd order structure of spatio-temporal properties of slow-wave oscillations in young and ageing subjects.

# Aim of the project



- **Data based model of Slow cortical oscillations**
- Understanding network mechanisms
  - Natural ageing in humans
  - Aging and associated neurodegenerative diseases (mouse models)
- Multi-scale experimental data
- **Restoration of young sleep**



## LETTERS

## Boosting slow oscillations during sleep potentiates memory

Lisa Marshall<sup>1</sup>, Halla Helgadóttir<sup>1</sup>, Matthias Mölle<sup>1</sup> & Jan Born<sup>1</sup>

*J. Sleep Res.* (2013) 22, 22–31

Induction of slow oscillations

### Induction of slow oscillations by rhythmic acoustic stimulation

HONG-VIET V. NGO<sup>1,2</sup>, JENS C. CLAUSSEN<sup>1</sup>, JAN BORN<sup>3,4</sup>  
AND MATTHIAS MÖLLE<sup>3,4</sup>

<sup>1</sup>Institute for Neuro- and Bioinformatics, University of Lübeck, Germany, <sup>2</sup>Graduate School for Computing in Medicine and Life Sciences, University of Lübeck, Germany, <sup>3</sup>Department of Neuroendocrinology, University of Lübeck, Germany and <sup>4</sup>Department of Medical Psychology and Behavioral Neurobiology, University of Tübingen, Germany

Neuron  
Article

## Auditory Closed-Loop Stimulation of the Sleep Slow Oscillation Enhances Memory

Hong-Viet V. Ngo,<sup>1,2,3</sup> Thomas Martinetz,<sup>2</sup> Jan Born,<sup>1,4,\*</sup> and Matthias Mölle<sup>1,4</sup>

<sup>1</sup>Institute of Medical Psychology and Behavioral Neurobiology, and Center for Integrative Neuroscience, University of Tübingen, 72076 Tübingen, Germany

<sup>2</sup>Institute for Neuro- and Bioinformatics

<sup>3</sup>Graduate School for Computing in Medicine and Life Sciences

<sup>4</sup>Department of Neuroendocrinology

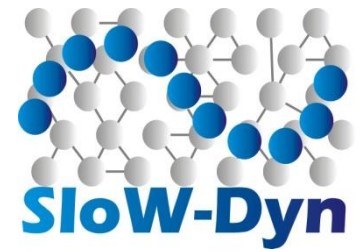
University of Lübeck, 23538 Lübeck, Germany

\*Correspondence: [jan.born@uni-tuebingen.de](mailto:jan.born@uni-tuebingen.de)

<http://dx.doi.org/10.1016/j.neuron.2013.03.006>



# Restoration of young sleep



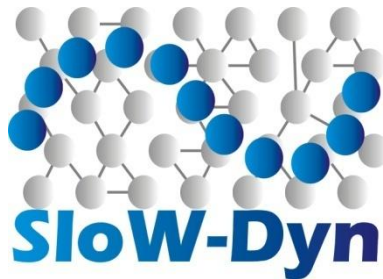
## Partners: DREEM, IDIBAPS, UPF

- Model the role of external stimulation (auditory clicks) to predict impact of „pattern-modulation stimulation“ protocols in diseased subjects.
- Refinement and optimization of stimulation protocols to restore young sleep in ageing individuals.
- Development of application for humans accessible to society through DREEM.

# THANK YOU!



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