#### **BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.** 

NAME Tononi, Giulio	POSITION TITLE Professor	
eRA COMMONS USER NAME (credential, e.g., agency login) gtononi		
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)		

INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Scuola Normale Superiore, Pisa, Italy	M.D.	1985	
Scuola Normale Superiore, Pisa, Italy	Ph.D.	1988	Neurobiology
University of Pisa Medical School, Italy	Specialist	1989	Psychiatry

#### A. Personal Statement

I have been working on sleep mechanisms and functions for more than 20 years, and my laboratory has extensive expertise in behavioral, electrophysiological, and EEG sleep measurements. My research group uses a combination of different approaches to try to understand what sleep is for, including analysis of cortical unit firing during sleep and wake, measurements of oxygen/lactate/glutamate release during the sleep/wake cycle, high density EEG in humans, and computer simulations. I will contribute at the theoretical level by developing software for evaluating information integration based on the anatomical connectivity, as well as complexity-based approximations of information integration that can be applied to both fMRI and EEG datasets. The analysis will allow Dr. McIntosh to quantify not only to what extent information integration is compromised after brain insults such as strokes, but also how brain networks are reconfigured and how this helps in functional recovery. He will also employ measured derived from information integration, such as matching and degeneracy, to track how well a patient's brain can distribute information about its inputs and outputs.

At the experimental level, I will employ a novel approach based on monitoring local changes in sleep spontaneous activity (slow waves and spindles) using high-density (hd)-EEG as markers of induced plasticity. This approach has proven to be a sensitive and topographically specific marker of cortical reorganization induced by therapeutic interventions, such as the IMITATE protocol, and can be used to follow and guide functional recovery in patients aphasic patients after a stroke. For NRG II, my team and I will expand our initial observations to a much larger sample of patients to extend these findings and to support the therapeutic rationale behind IMITATE. Also, they will enlarge the sleep hd-EEG dataset adding more time points during the course of the entire therapy. They will also investigate specific features of spontaneous sleep slow-wave, such as origin, propagation routes, and involvement, to further characterize changes in functional connectivity in brain-injured populations and during recovery. Finally, the same set of hd-EEG tools and techniques will be applied to newly available EEG datasets on epilepsy patients.

#### **B.** Positions and Honors

#### **Positions and Employment**

1985-1990	Fellow, Scuola Normale Superiore and Dept. Physiology, University of Pisa, Italy
1988	Fellow, Dept. Experimental Medicine, University of Lyon, France
1988	Medical Officer, Military Center for Applied Research, Pisa, Italy
1990-1993	Fellow in Theoretical Neurobiology, The Neurosciences Institute, New York
1993-2000	Senior Fellow in Theor. and Exp. Neurobiology, The Neurosciences Institute, San Diego
1999-2000	Associate Professor, The Scripps Research Institute, Department of Neurobiology
2001-	Professor, Department of Psychiatry, University of Wisconsin/Madison

## Honors and Awards

- 1992 Award for 'Best Young Scientist' of the Italian Physiological Society
- 2001 American Psychiatric Association Frontiers of Science Distinguished Psychiatrist Award
- 2005 NIH Director's Pioneer Award
- 2006 Distinguished Professor of Consciousness Science
- 2008 David P. White Chair in Sleep Medicine

## **Professional Societies**

- 1988 Member, European Sleep Research Society
- 1992 Member, Society for Neuroscience
- 1999 Member, Sleep Research Society
- 1993 Member, Editorial Board of Archives Italiennes de Biologie
- 1999 Member, Editorial Board of Consciousness and Cognition

#### C. Selected Peer-reviewed Publications (selected from over100 peer-reviewed publications)

## Most relevant to the current application

- 1. Sarasso S, Santhanam P, Määtta S, Poryiazova R, Ferrarelli F, Tononi G, Small SL. (2010) Non-fluent aphasia and neural reorganization after speech therapy: insights from human sleep electrophysiology and functional magnetic resonance imaging. <u>Arch. Ital. Biol.</u> In press. NIHMSID: NIHMS237005.
- 2. Tononi G. (2010) Information integration: its relevance to brain function and consciousness. <u>Arch. Ital. Biol</u>. In press. Policy Exempt-not resulting from NIH funding.
- 3. Murphy M, Riedner BA, Huber R, Massimini M, Ferrarelli F, Tononi G. (2009) Source modeling sleep slow waves. <u>Proc Natl Acad Sci USA</u> 106:1608-1613. PMCID: PMC2635823.
- 4. Alkire MT, Hudetz AG, Tononi G. (2008) Consciousness and anesthesia. <u>Science</u> 322:876-880. PMCID: PMC2743249.
- Ferrarelli F, Peterson MJ, Sarasso S, Riedner BA, Murphy MJ, Benca RM, Bria P, Kalin NH, Tononi G. (2010) Thalamic dysfunction in Schizophrenia suggested by whole-night deficits in slow and fast spindles. <u>Am J Psychiatry</u> Sept. 15 Epub. NIHMSID: NIHMS237015.

# Additional recent publications of importance to the field

- 1. Tononi G. (2008) Consciousness as integrated information: a provisional manifesto. <u>Biologiacal Bulletin</u>, 215:216-242. Policy Exempt-not resulting from NIH funding.
- 2. Cirelli C, Tononi G. Is Sleep Essential? Plos Biology 6: e216. PMCID: PMC2525690.
- Vyazovskiy VV, Cirelli C, Pfister-Genskow M, Faraguna U, Tononi G. (2008) Molecular and electrophysiological evidence for net synaptic potentiation in wake and depression in sleep. <u>Nature</u> <u>Neuroscience</u> 11: 200-208. Accepted for publication prior to April 7, 2008.
- 4. Huber R, Ghilardi MG, Massimini M, Ferrarelli F, Riedner BA, Peterson MJ, Tononi G. (2006) Arm immobilization, cortical plasticity, and local sleep homeostasis. <u>Nature Neuroscience</u> 9:1169-1176.
- 5. Tononi G, Cirelli C. (2006) Sleep function and synaptic homeostasis. <u>Sleep Medicine Reviews</u> 10:49-62.
- 6. Massimini M, Ferrarelli F, Huber R, Esser SK, Singh H, Tononi G. (2005) Breakdown of cortical effective connectivity during sleep. <u>Science</u> 309:2228-2232.
- 7. Huber R, Ghilardi MF, Massimini M, Tononi G (2004) Local sleep and learning. <u>Nature</u> 430:78-81.

# D. Research Support

# Ongoing Research Support

P20 MH077967 NIH (NIMH)Tononi (Center Director)09/27/2007-06/30/2011Sleep Function and Synaptic Homeostasis:Linking Neurobiology and Mental Health

## Silvio O. Conte Centers to Develop Collaborative Neuroscience Research

Project II: Brain Plasticity and Local Sleep Homeostasis: An Electrophysiological Perspective (Tononi) This project will test two crucial predictions of the synaptic homeostasis hypothesis: that sleep slow waves i) are necessary for the renormalization of cortical circuits after learning; and ii) are necessary for the enhancement of performance after sleep. Role: Center Director and Project II PI

 R01 NS055185 (NIH/NINDS)
 Tononi (PI)
 04/01/2006-03/31/2011

 Local Sleep Regulation and Brain Plasticity
 The overall goal of this project is to determine the effects of implicit and explicit motor learning on sleep need in healthy subjects.

 Role: PI
 DP 10D579 (NDPA)
 Tononi (PI)
 09/30/2005-07/31/2011

 NIH Director's Pioneer Award
 Tononi (PI)
 09/30/2005-07/31/2011

This program is meant to complement NIH's traditional, investigator-initiated grant programs by supporting individual scientists of exceptional creativity who propose pioneering approaches to major contemporary challenges in biomedical research. Role: PI

Tononi (PI)

Philips Healthcare

Slow Wave Induction

The major goal of this project is to identify ideal stimulation parameters for slow wave induction in sleep. Role: PI

James S. McDonnell Foundation

Tononi (PI)

02/01/2007-01/31/2011

05/01/2009-04/30/2011

Brain Work and Plasticity

This project employs EEG, MRI and PET to directly test the synaptic homeostasis hypothesis; examining the metabolic correlates of learning a simple motor task in healthy subjects. Role: PI

City University of New York (NIH) Ghilardi (PI) 02/15/2007-01/31/2012 Subcontract Tononi (PI) *Consolidation of Motor Skills and Sleep Homeostasis in Parkinson's Disease* This proposal characterizes the relationship between sleep and motor learning in Parkinson's Disease. Role: Subcontract PI

University of Toronto/McDonnell Foundation Macintosh (PI) 12/01/2005-11/15/2010 Network Mechanisms Underlying Cognition and Recovery of Function in the Human Brain This project focuses on studies of effective connectivity utilizing transcranial magnetic stimulation (TMS) and high-density electroencehalography (hd-EEG). Role: Subcontract PI

P01AT004952 (NIH/NCCAM)Davidson (PI)09/30/2008-05/31/2013Wisconsin Center for the Neuroscience and Psychophysiology of Meditation; Project 3Effects of Meditation on Spontaneous and Evoked Brain Activity

This project aims at establishing whether meditation training produces lasting consequences on the brain by testing two hypotheses: 1) meditation training produces lasting effects on spontaneous brain activity and 2) meditation training produces lasting changes in brain function as revealed by direct stimulation, so as to avoid confounding factors such as the subject's cognitive state. Role: Project 3 PI

# DARPA-08-28-SyNAPSE-FP-010 (DOD/DARA) Modha (PI)

Cognitive Computing via Synaptronics and Supercomputing (C2S2) Subcontract (Tononi) *Neuromorphic Design: Theory and Implementation* 

This project will apply the integrated information theory of consciousness, in conjunction with techniques adapted from machine learning, to implement a flexible architecture based on STDP (spike-timing dependent plasticity) in a neuro-anatomically informed distributed computer architecture.

R01MH091326 Tononi (PI) 09/01/2010-05/31//2015 Synapses and Sleep in Neurodevelopment: A Critical Interaction at a Critical Time This project seeks to establish whether the slow waves that can be recorded using EEG during sleep in children and adolescents can be used as a sensitive, well-tolerated indicator of the number and strength of synapses. Moreover, this project will establish whether sleep can affect synaptic pruning during development. Role: PI

# **Completed Research Support**

MERC UW SOMPH / Wisconsin Partnership Benca (PI) A Comprehensive Approach to Insomnia

This project uses hdEEG, TMS and Molecular techniques to probe and better understand the underlying neurobiology of insomnia, with the intent to improve diagnostic and treatment approaches; increase awareness of the public health consequences of insomnia and educational efforts for healthcare providers and the public. Role: Faculty

Dana Foundation

Anatomical and Functional Connectivity in Schizophrenia

This project is covered under the Brain and Immuno-Imaging Program and is intended to facilitate the testing of innovative, experimental hypotheses that have the potential to advance human health. Role: Faculty

Alexander (PI)

DAAD19-02-1-0036 Phase II Tononi (PI) 04/01/2004-03/31/2007 From 24/7 Flies and Birds to 24/7 Humans – The UW Continuous Performance Project Phase II resulted from the combination of two independent projects in Phase I (now completed): *Rapid Discovery of Continuous Performance and Power-Nap Compounds Through Large-Scale Mutagenesis in Drosophila* and *Avian Models of Sustained Wakefulness*. The overall goals for Phase II were to characterize the mechanisms for these models and determine how to switch them on safely in humans. Role: Overall Phase II PI and Project III PI

10/24/2008-01/23/2011

01/01/2005-12/3120/07

09/01/2007-08/31/2010