Anaesthesia and sleep : recent experimental and theoretical aspects *

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Workshop Website: http://www.loria.fr/~huttaxel/cnsworkshop09.html

Duration: 1 day, Thursday, July 23

Abstract:

General anaesthesia (GA) has attracted much research attention in recent years since new experimental findings on the molecular action of anesthetic agents shed some more light on the underlying mechanisms. In addition several theoretical models have been developed in recent years which, for instance, reproduce the power spectrum changes in EEG during anesthesia. Interestingly sleep shows similarities to anesthesia, such as the loss of consciousness. Further the thalamus seems to play an important role both in GA and sleep. Hence it is assumed that both phenomena are based on similar neuronal mechanisms.
The workshop aims to present some recent aspects on the modeling and the experimental side of both phenomena and hence allows for an interaction of both research fields.

Invited speakers:

Victoria Booth, Assistant Professor, University of Michigan, USA
Title: "*A novel population model for sleep-wake regulation*"
Abstract:
In sleep/wake regulatory neuronal populations, microdialysis and microinjection experiments suggest that neurotransmitter dynamics play an important role in the initiation and maintenance of different behavioral states. However, traditional population firing-rate models include synaptic coupling terms without explicitly modeling the dynamics of neurotransmitter concentrations acting at these synapses. We have constructed a novel network modeling framework that describes both neuronal activity and concentrations of the neurotransmitters released by these nuclei. Using this novel framework, we investigate interactions among primary brainstem nuclei involved in rat sleep-wake regulation. In addition, the model framework allows realistic simulation of microinjection of GABA and GABA agonists/antagonists into several keysleepwake regulatory nuclei and analysis of the effects on sleep-wake patterning.

Aylin Cimenser, Harvard Medical School, USA
Title: "A new EEG correlate of general anesthesia-induced loss of consciousness"
Abstract:
The mechanism by which anesthetic drugs induce general anesthesia is not well understood. Even though distinct patterns in the electroencephalogram have been associated with general

anesthesia-induced loss of consciousness there remains a need to incorporate neurophysiological characterizations into the definition and understanding of anesthesia. Here we report results of multivariate frequency-domain characterizations of propofol induced changes in the scalp EEG of human subjects performing a behavioral task. We characterize the temporal dynamics of the EEG through analysis of the time and frequency dependent cross spectral matrix. Our findings suggest that the state of general anesthesia-induced unconsciousness as assessed from behavioral data is strongly correlated with the persistence of a single dominant mode in the high alpha low beta range concentrated in the frontal channels.

Falk von Dinklage, Charite, Humboldt University Berlin, Germany
Authors: B.Rehberg and F. von Dinklage
Title: "In-vivo electrophysiology of anesthetic action"
Abstract:
A broad clinical definition of anesthesia is non-responsiveness to stimuli. The depth of anesthesia is therefore determined by the applied stimulus, the observed response and the drug concentration at the site of action that blunts responsiveness. To create this state of nonresponsiveness, the hierarchical model defines the need of two components to create the anesthetic state: hypnosis and analgesia. Electrophysiological anesthesia experiments in humans help to investigate the interaction between these components in producing non-responsiveness to benign and noxious stimuli and bridge the gap between theoretical pharmacological models and clinical relevant endpoints.

Axel Hutt, Chargé de Recherche, INRIA Grand Est - Nancy, France
Authors: A.Hutt and A.Longtin
Title : "*The mathematical analysis of neural population dynamics subject to the anesthetic propofol*"
Abstract:
The neuronal mechanisms of general anesthesia are still poorly understood. Besides several characteristic features of anesthesia observed in experiments, a prominent effect is the bi-phasic change of power in the observed electroencephalogram. The work aims to derive analytical conditions for this bi-phasic spectral behavior by the study of a neural population model. This model describes mathematically the effective membrane potential and involves excitatory and inhibitory synapses, excitatory and inhibitory cells, nonlocal spatial interactions and a finite axonal conduction speed. The work derives conditions for synaptic time constants based on experimental results and gives conditions on the resting state stability. Further the power spectrum of EEG generated by the neural activity is derived analytically and allow for the detailed study of bi-spectral power changes. We find bi-phasic power changes both in monostable and bistable system states affirming the omnipresence of bi-spectral power changes in anesthesia. Further the work gives conditions for the strong increase of power in the deltafrequency band for large propofol concentrations as observed in experiments.

David Liley, Associate Professor, Swinburne University, Australia
Title: "*Modeling the electrocortical effects of anaesthetic agents*"
Abstract:
Despite many decades of research into the mechanisms underlying general anaesthesia there are surprisingly few integrated theories attempting to explain this remarkable phenomenon. This has

been largely due to the fact that there has been no real agreement on what macroscopic observable or observables of anesthetic action are to be modeled that quantitatively reflect the hypnotic (unconsciousness) state. However the recent development of a number of successful clinical depth-of-anaesthesia monitoring approaches clearly indicate that the macroscopic consequences of general anaesthesia correlate well with electroencephalographic (EEG) activity. Here we outline an integrated theory of general anaesthetic (GA) action based on a physiologically motivated continuum theory of cortical electrorhythmogenesis. This theory establishes a mesoscopic link between the well characterised effects of GAs on the subcellular and molecular machinery of inter-neuronal communication with the GA induced electroencephalographic changes, as well as explaining a number of paradoxical phenomena associated with anaesthetic action: the low dose acceleration of the EEG and the anomalous generation of ictal (epileptiform) activity. We will conclude this presentation by discussing how this mean-field model of anaesthetic action may potentially aid efforts to better understand the genesis and functional relevance of awake EEG.

Behnam Molaee Ardekani, Postdoctoral Fellow, University of Rennes, France
Title: "*Mean-field models and slow mechanisms in general anesthesia*"
Abstract:
Over the past decades, two complementary modeling approaches have been developed in order to analyze the activity generated by networks of neurons. In the first approach, referred to as 'detailed', single neurons are accurately modeled regarding their structural components (dendrites, soma and axons), synaptic and ionic activities. These models are proper to study electrical activities of small cortical patches (in a few millimeters) in details, but due to high computation costs and large number of free parameters they are not so convenient to study whole brain electrical activities. In the second approach, referred to as 'macroscopic' or 'lumped', similar single neurons in small regions of the brain are considered as single entities and their synaptic interactions are expressed by the means of mean firing rate and mean membrane potentials. In this approach, ionic properties and action potentials of single neurons are not represented explicitly. Instead, a sigmoidal function is usually employed to relate mean firing rate and mean membrane potential of a neuronal population. According to literatures, in general anesthesia and sleep some slow ionic currents can play major rolls in neuronal activities. The aim is to explore overall characteristic of this type of ionic channels, and to suggest a way for considering the effects of these ionic currents in macroscopic models.

Jamie Sleigh, University of Auckland, New Zealand
Authors: J.W. Sleigh, M.T. Wilson, L.Voss, D.A. Steyn-Ross, M.L. Steyn-Ross, X.Li
Title : "*The transition from slow-wave sleep to REM sleep: experiment and theory*."
Abstract:
The transition from slow-wave sleep to REM sleep is one of the most dramatic changes seen in the EEG. It is not clear how the sequence of abrupt changes (occurring over time scales of seconds) which are observed in the cortical dynamics (as measured by the electrocorticogram); could result from the more gradual change in sub-cortical cholinergic input (occurring over time scales of minutes), as reported in previous studies. Here we present a continuum model of cortical neuronal dynamics that is quantitatively consistent with our experimentally-derived rat electrocorticogram data; showing discontinuous changes in state from slow-wave sleep (0.5-2Hz) to REM sleep (8Hz), via an intermediate stage, in which both modes are present. The

model provides a natural basis to explain neuromodulator-induced changes in cortical activity; and emphasizes the importance of the cortical response to alterations in brain-stem activity in various states of sleep.

Aneta Stefanovska, Reader, University of Lancaster, UK
Title: "*Brain and cardiovascular interactions in anaesthesia*"
Abstract:
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Schedule

When : July 23 2009, 9:00-18:00 , see detailed schedule below
Where: Berlin Gendarmenmarkt, Hilton Hotel, room #Hil1

9:00 – 9:10 Axel Hutt *Introduction*

9:00 – 9:50 Jamie Sleigh *The transition from slow-wave sleep to REM sleep: experiment and theory*

9:50 – 10:30 Nikolai Axmacher *Intracranial EEG evidence for sleep-related memory consolidation*

10:30 – 11:00 Coffee break

11:00 – 11:40 Victoria Booth *A novel population model for sleep-wake regulation*

11:40 – 12:20 David Liley *Modeling the electrocortical effects of anaesthetic agents*

14:00 – 14:40 Behnam Molaee-Ardekani *Mean-field models and slow mechanisms in general anesthesia*

14:40 – 15:20 Falk von Dinklage *In-vivo electrophysiology of anesthetic action*

15:20 – 15:50 Coffee break

15:50 – 16:30 Aneta Stefanovska *Brain and cardiovascular interactions in anesthesia*

16:30 – 17:20 Aylin Cimenser *A new EEG correlate of general anesthesia induced loss of consciousness*

17:20 – 18:00 Axel Hutt *The mathematical analysis of neural population dynamics subject to the anesthetic propofol*