Nonlinear Dynamics of Anæsthesia

1. **Title** – Nonlinear dynamics of anæsthesia.

2. **Authors** –

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3. **Types of institutions involved** –

- Public or private organizations: Public.
- Size of organizations: Typically 2000 employees.
- Areas of activity: Education & research.
- Institutions involved:

Partic. Role	Partic. no.	Participant name	Participant short name	Country	Date enter project	Date leave project
CO	1	Lancaster University, Department of Physics/Nonlinear Group	UNILANCS	UK	month 1	month 45
CR	2	Univerza v Ljubljani, Medical Faculty, Institute of Pathophysiology, Physiological Laboratory	ULFM	Slovenia	month 1	month 45
CR	3	Morecambe Bay Hospitals NHS Trust, Royal Lancaster Infirmary, Department of Anæsthesia	MBHT	UK	month 1	month 45
CR	4	Ecole Polytechnique Federale de Lausanne, School of Computer and Communication Sciences, Laboratory of Nonlinear Systems	EPFL	Switzerland	month 1	month 45
CR	5	Ullevael University Hospital, Medical Faculty at the University of Oslo, Department of Anæsthesiology	UOUH	Norway	month 1	month 45
CR	6	Universitaet Potsdam, Institute fuer Physik	UP	Germany	month 1	month 45
CR	7	Ustav Informatiky AVCR, Institute of Computer Science	ICSASCR	Czech Republic	month 1	month 45

4. **Identification of the problem/aim of the application** –

- Aims of the project: The work was carried out by the FP6-supported BRACCIA consortium, with the aim of has investigating the complex interactions between brain waves (especially delta and gamma) and cardio-respiratory oscillations that occur during anæsthesia. Preliminary investigations had shown that marked changes occur in the inter-oscillator interactions during anæsthesia. It was hypothesised that these could perhaps form a new basis for measurement of depth of anæsthesia, and the aim of BRACCIA was to perform the basic research needed to explore this possibility.

- Persons involved: The project was run by the organisations listed in the table and involved academic staff, consultant anæsthetists, research staff, nursing staff, PhD students, and healthy subjects who volunteered to be monitored in both their awake and anaesthetised states.
- Actual and potential beneficiaries: The immediate beneficiaries are within the academic community, including scientists and engineers interested in the physiology of anæsthesia, coupled oscillators and their interactions, and the stochastic dynamics of nonlinear systems. In the medium term, the results will be of benefit to instrument engineers designing better types of monitor for assessing depth of anaesthesia. So they should help clinicians to optimise their services to the general public.

5. **Approach, techniques and tools that were used** –

   The work involved making measurements on rats and humans undergoing anæsthesia, and complementary developments in the theory of coupled oscillators. The specific objectives were

   - To develop the methodology needed to test for causal relationships between interacting complex systems, both generally, and specifically for physiological signals
   - To set up measurement systems for acquisition of high quality physiological data in Ljubljana, Lancaster and Oslo; the data are to be suitable for analysis of their *dynamical* characteristics.
   - To collect cardiac, respiratory, and cortical time series data from human subjects, in the waking state and under anæsthesia, for spontaneous, controlled and paced respiration.
   - To collect cardiac, respiratory, and cortical, time series data from anæsthetised rats.
   - To analyse the data by use of the methodology developed under Objective 1.
   - To seek neurological, physiological and clinical interpretations of the results of the analyses.
   - To model interactions within the cardiovascular system, considered as a five coupled oscillators.
   - To model brain waves by use of a ensemble of coupled oscillators.
   - To model interactions between the cortical, cardiac and respiratory oscillators, on both the microscopic and macroscopic levels.
   - To consider the potential of the phenomena investigated to provide the basis of a new kind of anæsthetic monitor and, if merited, to prepare the protocol for a large-scale multi-centre study.
   - To disseminate the results of the research to scientists, clinicians, and the general public.

6. **Where and when was the application created and applied?** –

   - Institutions, teams, researchers: See table on page 1.
   - Number of people involved and their qualifications: There were about 27 researchers in total (mostly with PhD or working towards PhD) , plus the 61 anæsthetized subjects, plus assistance from many other persons in relation to particular problems.
   - Start and end date: 01/06/2005 – 28/02/2009
   - When the research, creation of methodology and implementation applied? The methodology was developed for BRACCIA based on earlier research. Instruments and data collection systems were designed, constructed and delivered to partners in the early stages of BRACCIA, and a central database system was set up to receive data from the clinical centres. The data was then accessed and processed by the analysis centres. Several new methods of time series analysis were developed during BRACCIA.

     Is it still being applied? Yes, although the BRACCIA programme has formally ended, it leaves behind a huge volume of high quality clinical anæsthetic data which will be analysed and re-analysed in the years to come, as new methods become available.

7. **Funding of the project** –

- Total amount – EUR 1,417,200.00.
- Funding sources – FP6 NEST grant under "Tackling Complexity in Science" to support *Brain, Respiration and Cardiac Causalities in Anæsthesia* (BRACCIA).

8. **What are the quantitative and qualitative measures of success?**

   The short/medium-term success of BRACCIA is best gauged from the considerable improvements in the understanding of the physiology of anæsthesia, and in the enhanced methods of time series data analysis developed to support BRACCIA as the the programme evolved. Quantitative measures include the numbers of papers published (?? to date), the number of citations (?? to date) they receive from other scientists, and the numbers of invited conference papers (?? to date) given by BRACCIA members. Apart from BRACCIA's scientific impact, there is also the possibility of an enhanced anæsthetic monitor designed in part on the basis of BRACCIA-derived physiological understanding, but that lies in the future.

9. **Conclusion and final remarks** –

   What can be learned from this story? That the analysis of complex systems can link quite large interdisciplinary, geographically-distributed, multi-centre research programmes focused on a common theme: BRACCIA has paved the way to important applications of complexity analysis in clinical medicine.

10. **Resources** –

    - Web links: `http://www.lancs.ac.uk/depts/physics/braccia/default.htm`
    - Bibliographic references: See listing on above URL for a partial listing up to the end of 2008. Papers will continue to appear for years into the future. In addition, a book is under contract with Springer for publication in 2011: *Nonlinear Dynamics of Anæsthesia: From Theory to Clinical Application*, edited by A Stefanovska, P V E McClintock, J Ræder and A F Smith (eds.).