Editors:
Prof. Photios Anninos, Democritus University of Thrace, GREECE
Prof. Marco Rossi, University of Pisa, ITALY
Prof. Tuan D. Pham, The University of New South Wales, AUSTRALIA
Prof. Carla Falugi, Universita di Genova, ITALY
Prof. Arndt Bussing, University Witten/Herdecke, GERMANY
Prof. Martha Koukkou, University of Zurich, SWITZERLAND

Advances in Biomedical Research

Advances in Biomedical Research

Proceedings of the 7th WSEAS International Conference on Mathematical Biology and Ecology (MABE '10)

Proceedings of the International Conference on Medical Physiology (PHYSIOLOGY '10)

Proceedings of the International Conference on Biochemistry and Medical Chemistry (BIOMEDCH '10)

University of Cambridge, UK, February 23-25, 2010

Recent Advances in Biology and Biomedicine
A Series of Reference Books and Textbooks

ISBN: 978-960-474-164-9
ISSN: 1790-5125

Published by WSEAS Press
www.wseas.org

ADVANCES IN BIOMEDICAL RESEARCH

Proceedings of the 7th WSEAS International Conference on MATHEMATICAL BIOLOGY and ECOLOGY (MABE '10)
Proceedings of the International Conference on MEDICAL PHYSIOLOGY (PHYSIOLOGY '10)
Proceedings of the International Conference on BIOCHEMISTRY and MEDICAL CHEMISTRY (BIOMEDCH '10)

University of Cambridge, UK
February 23-25, 2010

Recent Advances in Biology and Biomedicine
A Series of Reference Books and Textbooks

Published by WSEAS Press
www.wseas.org

ISSN: 1790-5125
ISBN: 978-960-474-164-9

ADVANCES IN BIOMEDICAL RESEARCH

Proceedings of the 7th WSEAS International Conference on MATHEMATICAL BIOLOGY and ECOLOGY (MABE '10)
Proceedings of the International Conference on MEDICAL PHYSIOLOGY (PHYSIOLOGY '10)
Proceedings of the International Conference on BIOCHEMISTRY and MEDICAL CHEMISTRY (BIOMEDCH '10)

University of Cambridge, UK
February 23-25, 2010

Recent Advances in Biology and Biomedicine
A Series of Reference Books and Textbooks

Published by WSEAS Press
www.wseas.org

Copyright © 2010, by WSEAS Press

All the copyright of the present book belongs to the World Scientific and Engineering Academy and Society Press. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without the prior written permission of the Editor of World Scientific and Engineering Academy and Society Press.

All papers of the present volume were peer reviewed by two independent reviewers. Acceptance was granted when both reviewers' recommendations were positive.
See also: http://www.worldses.org/review/index.html

ISSN: 1790-5125
ISBN: 978-960-474-164-9

World Scientific and Engineering Academy and Society

ADVANCES IN BIOMEDICAL RESEARCH

Proceedings of the 5th IASME / WSEAS International Conference on CONTINUUM MECHANICS (CM '10)
Proceedings of the 7th WSEAS International Conference on FLUID MECHANICS (FLUIDS '10)
Proceedings of the 7th WSEAS International Conference on HEAT and MASS TRANSFER (HMT '10)

University of Cambridge, UK
February 23-25, 2010

Editors:
Prof. Photios Anninos, Democritus University of Thrace, GREECE
Prof. Marco Rossi, University of Pisa, ITALY
Prof. Tuan D. Pham, The University of New South Wales, AUSTRALIA
Prof. Carla Falugi, Universita di Genova, ITALY
Prof. Arndt Bussing, University Witten/Herdecke, GERMANY
Prof. Martha Koukkou, University of Zurich, SWITZERLAND

International Program Committee Members:
Michiko N. Fukuda, USA
Ghassan S. Kassab, USA
Jeffrey Field, USA
Mohamed Labib Salem, USA
Emily A. Keshner, USA
Annet Te Lindert, THE NETHERLANDS
Yvette Mandi, HUNGARY
Allen Yeoh, SINGAPORE
Constantin Polychronakos, CANADA
David E. Featherstone, USA
Ann Walker, USA
Mahmoud H. El Kouni, USA
Markus Kraft, UK
Tzung K. Hsiai, USA
Kenji Izuhara, JAPAN
Jurgen Gailer, CANADA
Peter H. Roos, GERMANY
Natalija Koprivanac, CROATIA
Rand Wilcox, USA
Paula Gomes, PORTUGAL
Staffan Kjelleberg, AUSTRALIA
Thomas Dittmar, GERMANY
Coen Stehouwer, THE NETHERLANDS
Zelimir Kurtanjek, CROATIA
Beatriz Ruiz Diez, SPAIN
Leonard H. Robinson, USA
Aleksandra Fucic, CROATIA
Peter C. Doherty, USA
Vassilios Fanos, ITALY
Stephen Lord, USA
E.S. Kilpatrick, USA
Warren G. Darling, USA
Rada D. Ozrina, RUSSIA
Marwan Dwairy, ISRAEL
Elisabetta Di Giovanni, ITALY
Nikolai Grigorevich Khlebtsov, RUSSIA
Shmuel Einav, ISRAEL
Ken Kitajima, JAPAN
Zuhong Lu, CHINA
Seeroong Prichanont, THAILAND
Gertz I. Likhtenshtein, ISRAEL
Eddy Karnieli, ISRAEL
Marcela Kopacova, CZECH REPUBLIC
Xiaodan Jiang, CHINA
G. B. Arden, UK
Dhavendra Kumar, UK
Victor J. Hruby, USA
M. Pfreundschuh, GERMANY
Nobuo Inotsume, JAPAN
Draga Toncheva, BULGARIA
Alastair J Sloan, UK
K. Stephen Suh, USA
Geremia B. Bolli, ITALY
M. Wasif Saif, USA
Danny R. Welch, USA
Tony Lefebvre, FRANCE
Narihiko KONDO, JAPAN
Anna Maria Caccuri, ITALY
Kenneth K. Kidd, USA
Annamaria Lammel, FRANCE
Heloisa Sobreiro Selistre de Araujo, BRAZIL
Vassilios I Sikavitsas, USA
Leena Peltonen, UK
Adrian L. Harris, UK
Robert C Rees, UK
Karl-Ludwig Laugwitz, GERMANY
Kenneth B. Storey, CANADA
Brian . Carr, USA
J. . Geschwind, USA
Ashok K. Shetty, USA
Zelia M Correa, USA
Vinai Norasakkunkit, USA
A. . Hackney, USA
Marta Fulop, HUNGARY
Ignatia B. Van den Veyver, USA
J. Tinsley Oden, USA
Otto Horvath, HUNGARY
Jeb P. Owen, USA
Tjalf Ziemssen, GERMANY
Numa Dancause, USA
R. J. M. Klein Gebbink, THE NETHERLANDS
Michael Detamore, USA
Andrea Benucci, UK
Steven C. Elbein, USA
Polly A. Newcomb, USA
Rosalind Eeles, UK
Laurent Bosquet, FRANCE
Regina Hofmann-Lehmann, SWITZERLAND
Kevin D. Costa, USA
Bart Verkerke, THE NETHERLANDS
K. Muthumani, USA
Ulf Ziemann, GERMANY
James J. Feng, CANADA
Jeffrey A. Weiss, USA
Cheng Dong, USA
Muhammad H. Zaman, USA

Marwan Dwairy, ISRAEL
Karl Peltzer, SOUTH AFRICA
Yan-Ling He, USA
Tomas Palecek, CZECH REPUBLIC
Fabio Lang da Silveira, BRAZIL
David Mann, UK
Ian D. Hickson, UK
Jerzy Jochem, POLAND
Reiner A. Veitia, FRANCE
Andrzej Starek, POLAND
Csaba Soti, HUNGARY
Hector Escriva, FRANCE
C. Ratledge, UK
Aurel Popa-Wagner, GERMANY
Ulf Ziemann, GERMANY
Shulamith Kreitler, ISRAEL
Michael Evgenev, RUSSIA
Paul W Franks, USA
Tatyana Korolenko, RUSSIA
George G. Chen, HONG KONG
Joanna Zawacka-Pankau, POLAND
Katharina Paschinger, AUSTRIA
Lucio Sibilia, ITALY
Margo C. Honeyman, AUSTRALIA
Shosuke Kojo, JAPAN
Maurizio Bossola, ITALY
Warren G. Darling, USA
Johnny Ludvigsson, SWEDEN
Axel H. Schonthal, USA
Zan-Min Song, AUSTRALIA
Ima Nirwana Soelaiman, MALAYSIA
George Perry, USA
Miquel Sola, SPAIN
Curt Eckhert, USA
Alan Wells, USA
Emmanuel Katsanis, USA
Michael J. Lambert, USA
Roger Seymour, AUSTRALIA
Lucas Sanchez, SPAIN
Peter C. Doherty, USA
Greg Atkinson, UK
P. Gopalakrishnakone, SINGAPORE
Santosh Kumar, INDIA
Harvest F. Gu, SWEDEN
Rita Alevriadou, USA
Vladimir Jiranek, AUSTRALIA
Glen Atlas, USA
Bernardino Ghetti, USA
Ozgur Cogulu, TURKEY
Jaw-Lin Wang, USA
Harold A. Scheraga, USA
Ayten Yazgan-Karatas, TURKEY
Rudiger Wehner, SWITZERLAND
Julien Doyon, CANADA
A. Terrence Conlisk Jr., USA
C. Bolenz, GERMANY
Lakshmi Pendyala, USA
Vincent Launay-Vacher, FRANCE

Jerome Sanes, USA
Greg Tesch, AUSTRALIA
Edwin Wang, CANADA
Jose C. Florez, USA

Preface

This year the 7th WSEAS International Conference on MATHEMATICAL BIOLOGY and ECOLOGY (MABE '10), the International Conference on MEDICAL PHYSIOLOGY (PHYSIOLOGY '10) and the International Conference on BIOCHEMISTRY and MEDICAL CHEMISTRY (BIOMEDCH '10) were held at the University of Cambridge, UK, February 23-25, 2010. The conferences remain faithful to their original idea of providing a platform to discuss biophysics, bioengineering, biotechnology, biochemistry, cell physiology, endocrinology and metabolism, neurophysiology, clinical applications of physiology, medical chemistry, clinical chemistry, biochemistry and genetics etc. with participants from all over the world, both from academia and from industry.

Their success is reflected in the papers received, with participants coming from several countries, allowing a real multinational multicultural exchange of experiences and ideas.

The accepted papers of these conferences are published in this Book that will be indexed by ISI. Please, check it: www.worldses.org/indexes as well as in the CD-ROM Proceedings. They will be also available in the E-Library of the WSEAS. The best papers will be also promoted in many Journals for further evaluation.

Conferences such as these can only succeed as a team effort, so the Editors want to thank the International Scientific Committee and the Reviewers for their excellent work in reviewing the papers as well as their invaluable input and advice.

The Editors

Table of Contents

Plenary Lecture 2

Artificial Intelligence Applications in Health Care Systems

Professor Francklin Rivas-Echeverria
Universidad de Los Andes
Laboratorio de Sistemas Inteligentes
Merida, Venezuela
E-mail: rivas@ula.ve

Abstract: Artificial Intelligence (AI) techniques have been used in many applications. One scientific area where AI have proven to provide great benefits is in health area; because it evolves human lives, physical, psychological and social welfare, its contributions are invaluable.
This plenary will discuss artificial intelligence applications in areas such as rheumatoid disease, pregnancy-associated hypertension, obstructive sleep apnea, among other and will discuss the methodological frameworks for their use. It will also present possible areas of applications that can be explored.

Brief Biography of the Speaker:
Francklin Rivas-Echeverria Systems Engineer, MSc. in Control Engineering and Applied Science Doctor. Full professor in Control Systems Department, at Universidad de Los Andes, Venezuela. He has been invited professor in the Laboratoire d'Architecture et d'Analyse des Systemes (LAAS, Toulouse-France) and some Venezuelan and international Universities. He has also been technical advisor for “Venezuelan Oil Company” (PDVSA), “Aluminum Venezuelan Company” (VENALUM), “Steel Venezuelan Company” (SIDOR), Trolleybus System in Venezuela (TROLMERIDA). He has created and is the Director of the Intelligent Systems Laboratory and is the head of the University consulting unit (UAPIT-ULA). Over 180 publications in high level conferences and journals: the main topics of his papers are: Artificial Intelligence, Intelligent Control, Automation Systems and Industrial Applications. He has applied his results to many fields: Processes Control and Supervision, Oil production, Steel production processes, among others. Also, has developed several tools for automatic control teaching. He is coauthor of two books concerning Artificial Intelligence and Nonlinear Systems.

Plenary Lecture 3

The SQUID as Diagnostic Tool to Evaluate the Effect of Transcranial Magnetic Stimulation in Patients with CNS Disorders

Professor Photios Anninos
Co-Authors: Adam Adamopoulos, Athanasia Kotini, Nikolaos Tsagas
Laboratory of Medical Physics
Medical School
Democritus University of Thrace
Alexandroupolis, GREECE
E-mail: anninosf@otenet.gr

Abstract: Magnetoencephalograph (MEG) recordings of patients with CNS disorders were obtained using a whole-head 122-channel magnetometer SQUID and analyzed using Fourier statistical analysis. External transcranial magnetic stimulation in the order of pico Tesla (pTMS) was applied on the above patients with proper characteristics (magnetic field amplitude :1-7.5pT, frequency :the a-rhythm of the patient: 8-13 Hz) which were obtained with MEG recordings prior to pTMS. The MEG recordings after the application of pTMS shown a rapid attenuation of the high abnormal activity followed by an increase of the low frequency components toward the patients a-rhythm.

Brief Biography of the Speaker:
Prof. P.Anninos is Emeritus Prof. of Medical Physics in the Department of Medicine of Democritus University of Thrace, Alexandroupolis, Greece after serving there as a Professor of Medical Physics for many years. His research interests concern Theoretical neural models, experimental Neurophysiology with emphasis in MEG measurements using SQUID's and the use of pTMS(picoTesla Transcranial Magnetic Stimulation) in patients with CNS disorders.
He has published more than 200 scientific papers in reviewed journals and have written several books in his field. He is a scientific reviewer for several international Journals.

Plenary Lecture 4

The Central Histaminergic System - An Essential Part of Circulatory Homeostatic Mechanisms in Haemorrhagic Shock?

Associate Professor Jerzy Jochem
Department of Basic Medical Sciences
Medical University of Silesia
Piekarska 18, 41-902 Bytom
Poland
E-mail: jjochem@poczta.onet.pl

Abstract: The histaminergic system consists of neurons concentrated in the tuberomammillary nucleus of the posterior hypothalamus and send innervation to almost all parts of the brain, including the cardiovascular complex. Recent hypotheses suggest that the system is implicated in the response to adverse or potentially dangerous stimuli, including dehydration, changes in blood pressure, nociceptive stimuli and other kinds of stress. In these conditions, there is an increase in the release or turnover of neuronal histamine leading to activation of compensatory mechanisms. The purpose of the study was to examine cardiovascular effects of endogenous central histamine in haemorrhage-shocked rats. Moreover, compensatory mechanisms activated by histamine were investigated. Studies were carried out in anaesthetized male Wistar rats subjected to a critical irreversible hypotension (mean arterial pressure [MAP] 20-25 mmHg). The protocol was approved by local ethics committee. Both histamine precursor L-histidine (intraperitoneally [ip]) and histamine N-methyltransferase (HNMT) inhibitors - SKF 91488 and metoprine (intracerebroventricularly [icv]) led to an increase in endogenous histamine concentrations in the cerebral cortex by 20-23%, hypothalamus by 25-27% and medulla oblongata by 23-29% in comparison to the control groups. L-histidine produced dose-dependent increases in MAP, heart rate (HR) and a survival rate of 2 h, whereas in normotensive animals it did not influence cardiovascular parameters. The effect was inhibited by (S)-a-fluoromethylhistidine, an irreversible inhibitor of L-histidine decarboxylase. SKF 91488 and metoprine evoked dose-dependent rises in MAP and HR, which were significantly higher than those in normotensive animals, and the improvement of survival rates at 2 h after treatment. The action was inhibited by H1 receptor antagonist chlorpheniramine (icv), while neither ranitidine (icv) nor thioperamide (icv), H2 and H3/H4 receptor blockers, respectively, influenced the effect. Metoprine-induced resuscitating action was accompanied by 2.7- and 1.7-fold higher plasma levels of noradrenaline and adrenaline, 2.5-fold higher concentration of arginine vasopressin (AVP), 2.9-fold higher level of angiotensin II, 3.3-fold higher level of ACTH and 1.7-fold higher level of a-MSH. In metoprine-treated animals, nicotinic cholinoceptor antagonist hexamethonium (intravenously [iv]) decreased MAP and HR changes, whereas muscarinic cholinoceptor blocker methylatropine (iv) inhibited only the pressor effect. Metoprine-induced MAP and regional haemodynamic effects were also reduced by a1- and a2-adrenoceptor antagonists prazosin (iv) and yohimbine (iv), while a-adrenoceptor blocker propranolol (iv) diminished only HR changes. V1a receptor antagonist [a-mercapto-a,a-cyclopentamethylenepropionyl1,O-me-Tyr2,Arg8]AVP (iv), but not V1b and V2 receptor blockers - SSR149415 (ip) and [adamantaneacetyl1,O-Et-D-Tyr2,Val4,aminobutyryl6,Arg8,9]AVP (iv), respectively, inhibited metoprine-induced haemodynamic effects, without influence on survival at 2 h. Moreover, angiotensin type 1 (AT1) receptor antagonist ZD 7155 (iv) and angiotensin-converting enzyme inhibitor captopril (iv) decreased regional vascular resistance and inhibited metoprine-induced increase in MAP, whereas AT2 receptor blocker PD 123319 (iv) had no effect. Finally, melanocortin type 4 (MC4) receptor antagonist HS014 (icv) inhibited metoprine-induced increase in MAP, which resulted from decreased regional vascular resistance; however, it did not affect HR and the survival at 2 h. In conclusion, an increase in endogenous central histamine concentrations after loading with L-histidine or inhibition of HNMT activity leads to rises in central histamine concentration and the reversal of haemorrhagic hypotension. The resuscitating action of central histamine results from H1 receptor activation. The study demonstrates an involvement of the sympathetic nervous system, AVP, the renin-angiotensin system and proopiomelanocortin-derived peptides in endogenous central histamine-induced resuscitating action. Present data confirm the hypothesis concerning the role of the histaminergic system in regulation of central homeostatic mechanisms in haemorrhagic shock.

Brief Biography of the Speaker:
Jerzy Jochem (MD, PhD) is an associate professor at Department of Basic Medical Sciences, Medical University of Silesia, Katowice, Poland, where he is also the Institutional Coordinator of the LLP-Erasmus Program. He is a specialist in internal medicine and cardiology. His main research interests concern cardiovascular physiology and

cardiology, especially the central and peripheral mechanisms involved in the cardiovascular regulation in hypotension. In these fields, he authored or co-authored over 70 scientific papers published in reviewed journals and over 80 communications presented at international conferences. Dr. Jochem has received Polish Prime Minister Habilitation Award (2006) and the National Education Committee Award (2007). Since 2005 he is a vice-president of the Polish Histamine Research Society.

Plenary Lecture 5

The Importance of Mathematical Physiology for the Future of Medical Physiology: Some Examples From the Study of Cardiac Mechanics

Professor Rachad M. Shoucri
Department of Mathematics and Computer Science
Royal Military College of Canada
Kingston, Ontario, Canada K7K 7B4
E-mail: shoucri-r@rmc.ca

Abstract: Mathematics have brought a fascinating contribution to medicine in many fields like signal analysis, statistical analysis of medical data, design of medical devices, medical imaging, study of blood flow and electrical activity of cells, laser and radiation therapy just to mention a few examples. It is becoming evident that mathematical physiology will have on the advancement of medical physiology the same impact that mathematical physics had on the advancement of experimental physics. This study will focus on some results obtained from the mathematical modeling of cardiac mechanics and the application of stress-strain analysis to the study of the contraction of the myocardium. New results have been derived that can be used for prognostic, diagnostic and prevention of left ventricular dysfunction. Possibility of implementation of those results in clinical routine work is discussed.

Brief Biography of the Speaker:
Rachad Mounir Shoucri was born in Alexandria, Egypt. He obtained a BSc in electrical engineering from Alexandria University in 1964, an MSc in chemistry from the Illinois Institute of technology (Chicago), and a PhD in theoretical physics from Laval University (Quebec) in 1975. He worked as an analyst at Hopital Laval, Quebec, from 1975-1981 where he became interested in mathematical physiology and cardiac dynamics. Since 1981 he is with the department of mathematics and computer science, Royal Military College of Canada, Kingston, Ontario. His current research interest is in mathematical physiology and cardiac dynamics, as well as in theoretical physics.

Plenary Lecture 6

Basic and Clinical Neurophysiology of Chronic Pain: From Localised Symptoms to Generalised and Widespread Pain

Professor Cesar Fernandez de las Penas
Departamento de Fisioterapia
Facultad de Ciencias de la Salud
Universidad Rey Juan Carlos
Avenida de Atenas s/n,
28922 Alcorcon, Madrid, SPAIN
E-mail: cesar.fernandez@urjc.es

Abstract: It has been reported that several local pain syndromes show both peripheral and central sensitization mechanisms. The existence of sensitization mechanisms in local pain syndromes suggests that prolonged peripheral noceceptive inputs driving to the central nervous system play a role in the initiation or maintenance of central sensitization mechanisms. This finding would explain the phenomenon seen by clinicians in which patients with local pain generally develop spreading of their symptoms with time. Some animal models where the phenomena of localized nociception cause the development of secondary, widespread hyperalgesia have been used. In addition, human experimental pain models are generally used as surrogate models simulating clinical conditions, particularly localised musculoskeletal pain conditions. Primary hyperalgesia in musculoskeletal tissues can be experimentally induced by infusion of different algogenic substances (nerve growth factor, or glutamate). Such experimental models can also be applied to patients with chronic musculoskeletal pain for mechanistic evaluation to investigate which aspects of the pain sensitisation process are modulated. Localised and experimentally induced muscle sensitisation can subsequently initiate central sensitisation which is manifested as sensitisation of adjacent structures and spread of pain. The temporal and spatial phenomena can be quantified. Finally, clinical evidence will concentrate on three local pain syndromes: chronic tension type headache (CTTH), lateral epicondylalgia (LE) and carpal tunnel syndrome (CTS) and how they can spread and cause generalized sensitization. Clinical evidence of central sensitization in these pain syndromes is the fact that both CTTH and LE have pressure pain hyperalgesia and larger referred pain areas elicited by active trigger points (TrPs). Further, CTTH is also characterized by the presence of multiple active TrPs in the same muscle (spatial summation) whereas unilateral LE is characterized by the presence of bilateral muscle TrPs. There is also clinical evidence of segmental and central sensitization mechanisms in other local pain syndromes, e.g. carpal tunnel syndrome, knee osteoarthritis, unilateral shoulder pain, myofascial temporomandibular disorders and low back pain. Finally, the presentation will also include the evidence for fibromialgia syndrome as pain condition representative of widespread pain sensitization and symptoms.

Brief Biography of the Speaker:
Cesar Fernandez-de-las-Penas is a Professor of Physical Therapy at Universidad Rey Juan Carlos, Madrid, Spain where he is the head division of a research group focused on clinical sciences related to pain. He has conducted his PhD in biomedical Sciences in the Center for Sensory Motor Interaction (SMI) in Aalborg University and a second PhD in Physical Therapy at the Universidad Rey Juan Carlos. His research activities are concentrated on biomedical sciences within neuroscience. The specific research areas have been on pain and assessment of pain in volunteers and chronic pain patients. The main focus is on human clinical chronic pain research. A substantial network of international collaborations with 5 different countries has been established with universities and hospitals. He has published around 100 publications and he is first author of approximately 85 of them. Most papers concentrate on clinical human pain research, drug screening and interaction between motor control and chronic pain. The most relevant topics of his research are focussed on neck pain, headache, carpal tunnel syndrome, lateral epicondylalgia and neuro-physiological effects of manual therapy. He has participated in 50 conferences with related published abstracts/ proceedings and he has given several lectures at Spanish and foreign universities and hospitals. He has given around 10 invited lectures at international meetings/workshops/seminars.

Plenary Lecture 7

Impact of Increased Intra-Abdominal Pressure on Venous Return in Positive Pressure Ventilated Pigs. An Echographic Study

Dr. Karim Bendjelid
Medecin Adjoint Agrege
Intensive Care Division
Geneva University Hospitals
CH-1211 Geneva 14
Switzerland
E-mail : karim.bendjelid@hcuge.ch

Abstract: Respiratory changes in the retrohepatic inferior vena cava size (DIVC) assessed by transthoracic echocardiography has been proposed to assess preload dependency. However, its relevance may be impaired by the occurrence of an increase in intra abdominal pressure (IAP). In an experimental model, we investigated the effects of a gradual IAP increase on the disappearance of respiratory IVC flow fluctuations and its related DIVC. In the present experimental study nine pigs were anesthetized, mechanically ventilated and instrumented. IAP was gradually increased from 0 to 30 mmHg by step of 15 mmHg during normovolemia and hypovolemia generated by blood withdrawal of 30% of total blood volume. At each step, cardiac output, IVC flow and area were assessed by flowmeters and transesophageal echocardiography, respectively. We found that at high IAP, neither DIVC nor modulations of IVC flow were observed whatever the volemic status. At normal IAP, even in presence of respiratory changes of IVC flows, no DIVC sizes were observed in the two groups of animals and the majority of animals exhibiting an expiratory IVC area less than 0.65 cm2 showed evidence of IAP greater than right atrial pressure (RAP) values. These results suggest that IVC flows are not associated to DIVC sizes in mechanically ventilated pigs regardless the volemic state or IAP value. However, IVC area less than 0.65 cm2 is associated with the presence of IAP values higher than RAP suggesting that IVC dimensions could anticipate this pathophysiologic state.

Brief Biography of the Speaker:
Karim Bendjelid, MD, PhD is a Cardiologist-Intensivist attending physician at the Geneva University Hospitals (Intensive Care Division) and a Privat Docent at Geneva Medical University. He has also a Master of Science (MSc) in Cardiovascular Pharmacology at University of Pierre-Marie Curie-Paris VI (France) and a PhD in Physiology at University of Claude Bernard-Lyon I (France). Dr Bendjelid succeeds to the Gold Decoration Competition ("Gold Medal awards") of the Lyon University Hospitals. His main research interests concern hemodynamic monitoring (macrocirculation-microcirculation) and reliability of static and dynamic markers to predict fluid responsiveness in critically ill patients. In these fields, he authored or co-authored over 60 scientific papers published in peer reviewed journals or presented at international conferences. He co-authored over 5 Review & Chapters papers books edited by Springer-Verlag, Distribuna Editorial and Elsevier. He was a chairman or keynote lecturer in a number of international conferences organized by different prestigious societies. He is a regular Member of The French Society of Cardiology (echocardiography), the French Cardio-Vasculaire Research Group, the European Society of Cardiology, the American Physiological Society and the European Society of Intensive Care. He is a technical reviewer for the following international journals: IEEE Transactions on Biomedical Engineering, Critical Care Medicine, Intensive Care Medicine, Anesthesia Analgesia, Circulation, Chest, Acta Anaesthesiologica Scandinavica, Anesthesiology, European Journal of Echocardiography, Pulmonary Pharmacology and Therapeutics, the American Journal of Respiratory Critical Care Medicine, Stroke, Critical Care, European Journal of clinical investigation, Journal of Surgical Research, and British medical journal. He is also, member of the editorial board of Current Drug Therapy, Annals of Thoracic Medicine and Open Critical Care Medicine Journal.

Plenary Lecture 8

Computational Cardiology: Can we Predict the Hemodynamics in the Human Heart?

Dr. Torsten Schenkel
Akademischer Rat
Institute of Fluid Mechanics
University of Karlsruhe
GERMANY
E-mail: torsten.schenkel@kit.edu

Abstract: Man's interest in the function of the body and it's organs is very old. The heart has played a special role in this as can be seen by the many non physiological functions that have been and still are attributed to it.
From the beginnings of physiology with Da Vinci's anatomical studies till today, the function of the heart has been most intriguing. The number of mathematical and physical models that have been developed to describe the heart function are countless. The range is from very simple models like the Laplace equation for ventricular pressure and stress or the windkessel models that can describe the circulatory system to complex multiscale models that describe the electrophysiology, myocardial- or hemodymics to name a few.
With the advent of modern computer technology it has become feasible to tackle the more complex models that cannot be solved in an analytical fashion and develop virtual models for specific areas of interest within the wide field of heart function.
I will give an overview over recent developments in "Computational Cardiology" and present ideas and first results for a multi-scale/multi-physics model of the human heart.

Brief Biography of the Speaker:
Dr.-Ing. Torsten Schenkel obtained his diploma (Dipl.-Ing.) in mechanical engineering at the University of Karlsruhe in 1998, and the doctorate in the field of convection flows and instrumentation of microgravity experiments in 2002 from the same university.
He is presently lecturer for fluid mechanics and mathematical methods for flow simulations at the faculty of mechanical engineering in Karlsruhe.
His research interest are in the field of biofluidmechanics, especially heart flow, numerical simulation of complex turbulent flows, aero acoustics and turbulent heat transfer.
He currently is head of a research group for development of a numerical model for patient specific simulation of intraventricular flow, the Karlsruhe Heart Model KaHMo.
He has published over 20 research papers in conferences and journals and has reviewed articles for a number of scientific journals including Zeitschrift fur Medizinische Physik, Microgravity Science and Technology, Journal of Hydraulic Research, International Journal for Numerical Methods in Fluids an Annals of Biomedical Engineering.

Plenary Lecture 9

Diagnostic Value of Multifocal-Electroretinogram in Retinal Diseases

Dr. Marilita M. Moschos
Department of Ophthalmology
University of Athens, Greece
E-mail: moschosmarilita@yahoo.fr

Abstract: Multifocal-Electroretinogram (mfERG) is a relatively new diagnostic method introduced by Sutter and Tran in 1922. This technique provides a topographic measurement of retinal activity and enables topographic mapping of retinal function in the central 40-50? of the retina.
In this presentation the authors summarize their experience from the clinical application of mfERG in the diagnosis and follow-up of hereditary macular diseases (eg Stargardt disease, Juvenile retinoschisis). The authors also support that the use of mfERG enables to diagnose and monitor the development of toxic retinopathy due to hydroxychloquine as also to follow-up objectively the efficacy of surgical or non-surgical treatment for retinal diseases, such as macular hole, epiretinal membrane, macular edema due to age-related macular degeneration (ARMD), diabetic retinopathy, central retinal vein occlusion (CRVO), or central serous chorioretinopathy (CSCR).

Brief Biography of the Speaker:
Marilita M. Moschos graduated the Pharmacy School of the University of Patras and the Medical School of the University of Athens. She is actually working as a senior lecturer of Department of Ophthalmology of Athens University where she has the clinical and scientific co-responsibility of the Laboratory of Electrophysiology of Vision and the department of Glaucoma. She authored or co-authored over 45 scientific papers in pubmed reviewed journals and presented over 50 at international conferences, in some of them as invited speaker. She also wrote the chapter on 'Multifocal-Electroretinogram in retinal vascular diseases' in the annual edition of SFO (Societe Francaise d'Ophtalmologie). Finally she is a member of many international ophthalmological societies and reviewer in several ophthalmological journals, like, Clinical and Experimental Ophthalmology, Expert Review of Ophthalmology, Journal of Neuroscience Methods, Graefe's Archive for Clinical and Experimental Ophthalmology, BMC Ophthalmology, Clinical Ophthalmology, Indian Journal of Ophthalmology and others.

Plenary Lecture 10

Assessment of Collateral Function in 91 Patients with Chronic Total Coronary Occlusions by New Invasive Coronary Impedance and Conductance Parameters

Dr. Matthias Goernig
Clinic Internal Medicine
University Hospital of Jena
Bachstrasse 18, D-07740 Jena
Germany
E-mail: Matthias.Goernig@med.uni-jena.de

Abstract: Background: The evaluation of collateral pathways in coronary artery disease with total chronic occlusion require quantitative knowledge of the collateral function with respect to the morphologic characterization of collaterals.
Methods: In 91 patients (mean age 65 +/- 10 years, 69 male) with total chronic occlusion of a major coronary artery (duration > 2 weeks) collateral function was assessed invasive by Doppler flow and pressure recordings proximal and distal to the occlusion before recanalization. For collateral function form parameters of the Doppler flow profile (systolic, diastolic and combined flow), the constant part of the impedance (cIMP), the frequency dependant impedance, the average of time-resolved conductivity (aCON) and the total blood flow were calculated. Collateral morphology was assessed angiographically by the Rentrop grading, by Levin's anatomic location classification and by the grading of collateral connections according to Werner. On the basis of Receiver Operating Characteristics the frequency dependant parameters of collateral hemodynamics were validated with the simplified averages.
Results and Discussion: Receiver Operating Characteristics demonstrated no improvement using frequency dependant impedance compared to the constant part of the collateral impedance. The functional parameters aCon and cIMP were better than the total blood flow for the characterization of collateral function. The collateral function improved significantly during occlusion time (aCON in one= 0.20+/-0.17, two=0.22+/-0.25, three and more month= 0.28+/-0.18 cm*s-1*mmHg-1). A predominant systolic, diastolic or combined collateral flow profile was not correlated to the collateral function. Considering the anatomic location of Levin 17 patients had one, 15 two and 24 three different collateral pathways. In the majority of cases (63 of 91 patients) a septal pathway was included. In all patients the comparison of the Rentrop grading, the anatomic location classification and the collateral connection grading showed only for the latter an independent and significant relation with the collateral function. In patients with a single collateral pathway no correlation of the collateral function to the anatomic location could be observed. In reduced left ventricular function (EF<50) epicardial pathways (cIMP =3.3+/-1.0 mmHg*s*cm-1) compared to cases with inclusion of septal pathways (cIMP = 7.7+/-4.4 mmHg*s*cm-1) were associated with better collateral function. According to the Werner grading of collateral connections CC2 collaterals (cIMP =4.9+/-2.7 mmHg*s*cm-1) preserved regional left ventricular function better than did CC1 collaterals (cIMP =6.7+/-4.2 mmHg*s*cm-1). CC0 collaterals (cIMP =13.7+/-7.2 mmHg*s*cm-1) were predominantly observed in recent occlusions of 2 to 4 weeks duration, with the highest collateral impedance.
Conclusions: The simplified averages of collateral hemodynamics were sufficient enough for quantitative assessment of collateral function. The angiographic grading of collateral connections in total chronic occlusions could differentiate collaterals according to their functional capacity to preserve regional function and was closely associated with invasively determined parameters of collateral hemodynamics. Only in patients with reduced left ventricular function a correlation between the anatomical locations and the function of collateral pathways could be seen.

Brief Biography of the Speaker:
Dr. Matthias Goernig received a M.D. at the University of Hamburg, Germany, in 1993. From 1993 to 1994 he worked as an Internship at the Max von Pettenkofer Institute for Microbiology in Munich, Germany and at the National Cancer Institute in Bethesda, USA. From 1995 to 1998 he was working at the Clinic for Dermatology, University Hospital of Jena, Germany and in 1999 at the Dermatology Hospital of Leutenberg/Thuringia, Germany. Since 2000 he is at Clinic Internal Medicine (Dep. Cardiology), University Hospital of Jena, Germany. His research interests are in biological signal analysis and the clinical applications of bioelectric and biomagnetic fields.

Plenary Lecture 11

Non-Invasive Expressions of ipt in Whole Plants or Roots Indicate Cytokinins are Synthesized in Plant Aerial Parts, and Coordinate with Light Affect on the Phenotypes and the Formation of Anthocyanins, Lignins

Professor Jian-Chun Guo
Key Laboratory of Tropical Crops Biotechnology Agriculture Ministry
Institute of Tropical Bioscience and Biotechnology
Chinese Academy of Tropical Agricultural Sciences
571101 Haikou, China
E-mail: jianchunguoh@163.com

Abstract: To study the plant roots how in response to ipt gene activation, the transcriptional fusions of ipt-GUS and GUS-ipt were expressed in roots, or in whole plants of Arabidopsis under the control of a root-specific promoter TobRT7, or a CaMV35S promoter through pOp/LhG4 system in non-invasive conditions. The transgenic plants with constitutive expression of ipt-GUS or GUS-ipt showed 15-25 fold, or 1-2 fold increased cytokinin levels, respectively. ipt-GUS expressing Arabidopsis had severe root inhibition, serrated leaves, no or few sterile flowers, and an enlarged and retard phenotypes. The seedlings of enlarged phenotype had an enlarged shoot and shoot apical meristem. The ratio of the two phenotypes related with sucrose content in medium and light intensity. While, GUS-ipt expressing Arabidopsis grew faster, flowered early, and had more lateral shoots. However, when ipt-GUS and GUS-ipt were specially expressed in roots under the control of TobRT7, neither cytokinin content in roots or shoots, nor phenotypes were altered. In cytokinin over-producing ipt-GUS expressing Arabidopsis, light and aerial parts of plants played an important role for cytokinin synthesis and root inhibition, and ipt gene was vigorously expressed at the shoot apical parts. Meanwhile, calli were induced at the shoot apical parts of some cytokinin over-producing ipt-GUS expressing Arabidopsis. Increased cytokinins in ipt:::GUS activated Arabidopsis induced the syntheses of anthocyanins and lignins, while light speeded up the anthocyanin accumulation. The endogenous increased cytokinins and exogenous addition of sucrose in MS medium caused the similar effects on the formation of anthocyanins and lignins in shoot, especially in shoot apical meristem. Cytokinins induced CHS transcription in ipt:::GUS activated Arabidopsis seedlings in vigorous vegetative growth period, in which the transcription of CHS was low and photosynthesis was vigorous in wild type Columbia. Cytokinins were capable of influencing either the syntheses or distribution of chlorophylls, but did not alter cab and rbcS transcriptions in light-grown seedlings.

Brief Biography of the Speaker:
GUO Jianchun: Female, 1965, Chinese, Professor. Molecular Genetics PH.D of Masaryk University in Cezch. Supervisor of PH.D in the areas of Crop Genetic Breeding; Biochemistry and Molecular Biology; Plant Molecular Genetics. Deputy Secretary-General of Hainan Bioengineering Association in China. Works on Molecular Biology and Plant Engineering. Researches on Plant Physiology, the Mechanism of Plant Salt Tolerance, and the Engineering of Adversity Tolerance in Tropical Crops.

Plenary Lecture 12

Hand Reaching Adaptive and Online Motor Control Processes

Dr. Claude Prablanc
Directeur de Recherche at Unit 864 Espace et Action (INSERM-Bron)
France
E-mail: prablanc@free.fr

Abstract: Several sensori-motor processes are devoted to error reduction for the production of purposeful actions. When motor responses deviate from their goal, online corrections can be performed either under voluntary control with time consuming additional sub-movements or under fast automatic smooth control. When errors cannot be corrected online and are repeated over trials, subsequent responses can be improved iteratively through adaptation, a progressive adjustment of motor commands that acts to reduce the magnitude of error. The sources of these errors may result from an erroneous evaluation of the goal, from unexpected perturbations of the goal itself , or from a patient's inability to both plan and correct a movement after prefrontal, frontal, parietal, cerebellar or vestibular lesions from vascular or neurodegenerative origin.

Although long term natural sensorimotor recovery is not necessarily the same process as short term adaptation that can be studied experimentally, more knowledge about the latter helps improving the former, illustrated by the attentional and perceptual rehabilitation obtained through sensorimotor prism exposure in neglect patients.

As prism adaptation is rather complex, involving many sensorimotor loops along the eye head hand system connecting reciprocally the perception-action cycle, it is necessary to disentangle some of the major error signals acting upon adaptation.

It has been argued that reaching adaptation results essentially from a conflict between actual sensory feedback and expected sensory feedback. In order to show that such a mechanism is unlikely to be responsible for most of the adaptive process, we have developed two reaching paradigms that provide the subject with undistorted hand visual feedback. Both paradigms induce motor planning errors unknown to the subjects and allow an efficiency assessment of the many feedback loops through real time a control of the oculomotor and upper limb sensorimotor loops.

The first one yields continuous retinal and visuomotor feedback, allowing fast and complete automatic online corrections. It suggests that the same online corrective processes are carried out under natural conditions without awareness. In addition despite a reiterated motor planning error and an automatic online correction of the whole error, this paradigm shows a complete lack of adaptation.

The second paradigm allows an investigation of the role of terminal error feedback only, where all visual feedback is eliminated during movement execution.. In contrast to the first paradigm, it exhibits a robust and generalised adaptation, although devoid of limb inter-sensory mismatch. These results demonstrate independence between the induced motor adaptation and the automatic online correction, both characterized by the lack of any cognitive interference. A putative visuomotor cerebro-cerebellar network accounting for these results is proposed.

Brief Biography of the Speaker:

Claude Prablanc graduated from the Ecole Superieure de Marseille (Electrical Engineering) in 1966, and from the Ecole Nationale Superieure d'Electricite, d'Electronique, d'Informatique et d'Hydraulique de Toulouse in 1967. After a few years working as an engineer for the automated subway Network, he followed a training in neuropsychology and got a researcher position at the Institut National de la Sante et de la Recherche Medicale (INSERM) in 1973. He spent one year in 1981 at the Psychology Department in MIT, working on monkey motor control. His current position is Directeur de Recherche at Unit 864 Espace et Action (INSERM-Bron). His main research interests in Neuroscience are Motor Psychophysics of the eye-head-hand sensorimotor system and of its plasticity, in both normal subjects and neurological patients.

Plenary Lecture 13

Single Nucleotide Polymorphism: From Disease Susceptibility to Creativity

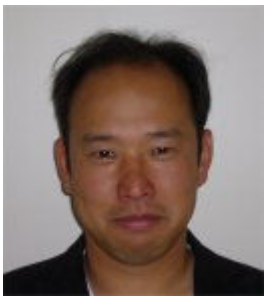
Dr. Victor Dosenko
Department of General and Molecular Pathophysiology
Bogomoletz Institute of Physiology
National Academy of Sciences of Ukraine
E-mail: dosenko@biph.kiev.ua

Abstract: Currently, it is well known that risk and clinical severity of cardiovascular diseases as well as majority of other chronic pathologies depend on patient's genotype that determines functionality of all enzymatic systems. Individualization of universal defense and self-damaging mechanisms is determined mainly by genetic variations of some genes, so called single nucleotide polymorphism (SNP). Large number of SNPs that make every human unique in genetic and phenotypic features are described recently. We studied frequency of more than 20 SNPs in patients with myocardial infarction (492 cases) and in children with essential hypertension (157 cases) in Ukrainian population. Association between SNPs in eNOS (-786T/C), ACE (I/D) genes and myocardial infarction was established. Risk of essential hypertension is increased in patients with SNPs in eNOS (-786T/C and exon 7 Glu298/Asp), LMP2 (Arg60/His), PSMA6 (-8C/G), alpha-2 macroglobulin (I/D) and BNP (T-381/C) genes. Functional genetic investigations with use of RT-PCR, real-time PCR, fluorescent spectroscopy and other methods demonstrated that -786C/C promoter of eNOS most significantly affects the gene expression and eNOS activity. LMP2 Arg60/His polymorphism influences on trypsin-like and chymotrypsin-like activities of proteasome, but does not affect level of LMP2 mRNA. Our pharmacogenetic observations indicate that thrombolytic and cholesterol-lowering medications are more effective in patients with eNOS -786T/T genotype. Study of SNPs in highly qualified sportsmen (candidates and members of Ukrainian Olympic team) indicated negative correlation between track records and exon 7 Glu298/Asp eNOS, ACE (I/D), ACNT (R/X) and positive link with PPARG (Pro12/Ala) polymorphisms. To test hypothesis about influence of human genetic variability on mental (creative and cognitive) functions we realized investigation on determination of 13 SNPs frequency in 11 genes (NOS3, ACE, AGT, AGTR1, LMP2, HIF1A, A2M, XRCC1, PPARG, PSMA6 and BNP) that have not direct relation to psychic processes. With use of special psychological tests the level of creative and cognitive indicators was estimated in 73 adolescents. Correlation analysis allows to establish significant interrelation between number of variant alleles and level of creativity ($r = 0.59$, $P < 0.05$). Thus, obtained data indicate important impact of SNPs totality on formation of individual creativity and partly explain progressive spreading in human population of altered, in some ways pathological, gene variants that increase risk of cardiovascular diseases.

Brief Biography of the Speaker:
Since 2005 - Group Leader of General and molecular pathophysiology department of Bogomoletz Institute of Physiology. In 1995 he has obtained Master Degree in Medicine and PhD program in Pathophysiology department of Bogomoletz Ukranian Medical University. His scientific interests concerning to genetic mechanisms of myocardial infarction, role of allelic gene polymorphisms, proteasomal proteolysis, programmed cell death, etc. He is a co-author of 4-th monographs and more than 90 articles published in reviewed journals or presented at international conferences.

Plenary Lecture 14

Effects of Exercise on Reaction Time to Peripheral Visual Stimuli



Dr. Soichi Ando
Post Doctoral Fellow
School of Nursing
Kyoto Prefectural University of Medicine
Japan
E-mail: sando@cmt.kpu-m.ac.jp

Abstract: Vision is one of the most important sensory modalities in humans. Visual reaction time (RT) is the time from the appearance of a visual stimulus to the onset of motor output, and it has been used to assess perceptual and cognitive abilities in athletes. Visual field is composed of central and peripheral components. The ability to respond to peripheral visual stimuli as quickly as possible may be relevant to ball sports in which capturing visual information from the periphery of the visual field plays a role in performance. The purpose of this study was to examine effects of acute exercise under normoxia, hypoxia, and hyperoxia on the ability to respond to peripheral visual stimuli. Results showed that: (1) under normoxia, premotor component of RT (Premotor time) to peripheral visual stimuli was vulnerable to exercise as compared with that to central visual stimuli; (2) under normoxia, RT to peripheral visual stimuli increased during exercise at high workloads above the ventilatory threshold (VT) relative to that at rest, while the RT was not affected by exercise at the VT and below the VT; (3) under hypoxia, Premotor time to peripheral visual stimuli increased during exercise at low, moderate, and high workloads, and the increase in Premotor time was accompanied with decrease in cerebral oxygenation; and (4) under hyperoxia, Premotor time to peripheral visual stimuli was not different between at rest and during exercise at high workloads. These findings suggest that exercise at high workloads has detrimental effects on the ability to respond to peripheral visual stimuli unless oxygen availability was increased. Cerebral oxygenation may play a key role in visual perceptual performance during exercise.

Brief Biography of the Speaker:
I received my MSc and Ph.D. degrees from Kyoto University, Kyoto, Japan in 2001 and 2004. I am currently a postdoctoral research fellow in Kyoto Prefectural University of Medicine. I have been working in the area related to human motor control and sports science. My current research interests focus on how exercise influences perceptual and cognitive performance.

Plenary Lecture 15

The Role of the Cerebellum in Associative Memory is Control of the Oculomotor Expression of the Memory but not its Storage

Professor I. Steele-Russell
Neuroscience & Experimental Therapeutics
College of Medicine
Texas A&M University System HSC
College Station, TX
USA
E-mail: Irussell@medicine.tamhsc.edu

Abstract: The eye-blink reflex in the rabbit is currently regarded as an ideal animal model to study the neural mechanisms of associative memory. This claim rests on three main assumptions, which are: (a) all the sensory inputs and motor outputs are under total experimental control, (b) the learning is completely isomorphic with the eye blink response, and (c) the memory storage of this learning is mediated by the cerebellar cortex. It will be argued that all of these assumptions are highly questionable.
(a) Input control: Recent research indicates that selective attention plays a major role in determining sensory processing in eye blink conditioning (Steele-Russell et al, 2006: Steele-Russell et al, 2007). Without control over the animal's selection of sensory channels it is not possible to restrict the learning to specific input pathways in the brain. For example, in visual Pavlovian conditioning, it is critical to control for albedo, regional flux, shift signals etc, during learning. Failure to do so can result in the activation of multiple pathways, i.e. pattern or brightness channels. In addition pathways including both auditory and tactile channels can be involved - all of which converge on the final common path of the oculomotor blink response. The failure to control for selective attention is the reason why the nature of the sensory inputs contributing to the learning remain unknown.
(b) Response invariance: Recent evidence has shown that the eye blink conditioning in the Pavlovian stock, when subsequently tested in a different free environment, is expressed by very different responses than a simple eye blink reflex (Castiglioni et al, 2009). These findings suggest that the conditioning does not involve simple reflex response learning. They indicate that the learning involves the acquisition of a new meaning to the sensory signal, which can produce different response patterns in different situations.
(c) Cerebellar memory storage: This position was tested by comparing eye blink conditioning in both normal and chiasma sectioned rabbits. Midline section of the optic chiasma results in disconnection of the direct retinal projections via the brainstem to the cerebellar oculomotor control system. Thus by comparing both normal and chiasma animals it is possible to determine the dependence/independence of conditioning on the motor expression of the eye blink response during training. Oculomotor tests showed a complete lack of eye-lid conditioning in chiasma sectioned rabbits. However the sensory tests of learning in these animals, revealed perfectly normal sensory recognition learning to the visual signal.
Conclusions: These findings establish that the critical element in conditioning is the cognitive learning of the change in the meaning of the sensory signal. Furthermore this learned information is totally independent of any cerebellar mechanisms.

Brief Biography of the Speaker:
Ian Steele-Russell is a full professor in the department of Psychiatry & Behavioral Science, the department of Neuroscience and experimental Therapeutics and the department of Veterinary Integrative Biomedical Sciences at Texas A & M University System Health Science center, USA. His areas of research are in visual neuroscience with a specific emphasis on cortical mechanisms of selective attention in visual perception and memory. He has authored or co/authored over 202 papers published in peer-reviewed journals or presented at scientific conferences. He contributed to the book The Structure and Function of the Cerebral Commissures edited by I Steele-Russell, MW van Hof, G. Berlucchi, 1979. He is the Founding Editor-in-Chief of the International Journal Behavioural Brain Research and has served on the editorial boards of several international journals in the neuroscience area, such as Physiology and Behavior, Brain Research Bulletin, Activitas Nervosa Superior, and Memory Research. He was a former President of the European Brain Behaviour Society from 1979-1982. He is currently head of the Visual Neuroscience Laboratory.

Plenary Lecture 16

Quiet Chaos in Psychophysiomatics

Professor Tuan D. Pham
ADFA School of Information Technology and Electrical Engineering
The University of New South Wales
Canberra, ACT 2600, Australia
E-mail: t.pham@adfa.edu.au

Abstract: We have recently coined the word "psychophysiomatics" to express our interest in this new direction of research. Advances in image and signal processing technologies play an increasingly important role in mental health research. Psychiatrists and psychologists rely on brain imaging and pulse wave data for the study of depression and cognitive functions to monitor mental health changes in patients. Physiologists apply biomedical images and electrical properties of biological cells and tissues to patients' therapy. Interestingly, such studies in computational psychiatry, psychology and physiology allow life-science researchers to investigate the causal relationships between social life style, depression, and pathophysiology. Our research group attempts to address issues and new directions in the applications of image and signal analysis to psychiatry, psychology and physiology. This talk presents novel computational and entropic models for studying the dynamic behaviors of the physiological, cardiac and neural signals: time series and images. These models can detect subtle patterns of disease and control; and hence a promising analytical tool for understanding life-science problems at systems level, early prediction, and biomedical hypothesis validation.

Brief Biography of the Speaker:
Tuan D. Pham received his PhD degree in 1995 from the University of New South Wales. His current research interests include image processing, molecular and medical image analysis, pattern recognition, bioinformatics, biomedical informatics, fuzzy-set algorithms, genetic algorithms, neural networks, geostatistics, signal processing, fractals and chaos. His research has been funded by the Australian Research Council, academic institutions, and industry. Dr. Pham is an editorial board member of several journals and book series including Pattern Recognition (Elsevier), Current Bioinformatics (Bentham), Recent Patents on Computer Science (Bentham), Proteomics Insights (open access journal, Libertas Academica Press), Book Series on Bioinformatics and Computational BioImaging (Artech House), invited Regional Editor of International Journal of Computer Aided Engineering and Technology (Inderscience Publishers), and invited Editor-in-Chief of WSEAS Transaction on Biology and Biomedicine. He has been serving as chair and technical committee member of more than 30 international conferences in the fields of image processing, pattern recognition, computational intelligence, and computational life sciences.

Plenary Lecture 17

Novel Respiratory Viruses: Epidemiology, Pathophysiology, and Optimized Strategies for Molecular Diagnosis

Dr. Oliver Schildgen
Senior Research Group Leader
Institute of Virology
University of Bonn Medical Centre
Sigmund-Freud-Str. 25
D-53105 Bonn
Germany
E-Mail: schildgen@virology-bonn.de

Abstract: Viral respiratory infections occur in all age groups and all over the year. Community strategies for detection of respiratory pathogens in general and respiratory viruses in particular depend on aberrant requirements and realities. Virologists intend to detect the disease causing virus or viruses, if more than one virus contributes to the illness. The treating physician has the intention to rapidly cure the patient but often makes use of antibiotic therapy without previous confirmation of a bacterial aetiology. Both, virologists and physicians "suffer" from limited budgets, making economic strategies essential. Since 2001, several viruses have been newly discovered by improved molecular techniques, i.e. the human metapneumovirus, human bocavirus, Melaka virus, human coronaviruses NL63 and SARS, and others. Most of them are clinically indistinguishable from each other and bear the risk of severe and sometimes fatal clinical courses, at least in high risk patient groups.

Community strategies for detection of viral pathogens are consequently influenced by a number of challenges. First, regional requirements have to be taken into account. Basic care hospitals usually have fewer capacities than maximum care hospitals and frequently have to outsource virological diagnostics. Therefore, they cannot cover the whole spectrum of viruses being responsible for respiratory infections, as maximum care hospitals can or at least should do. Second, the strategy for respiratory virus detection is dependent on the cohort of patients in the respective catchment area. Maximum care hospital tend to take care for more severe cases and patients with severe comorbidities and consists of specialized departments, whereas basic care hospitals are in general confronted with any kind of medical condition that sometimes need to be transferred to specialized hospitals. Third, despite of the catchment area and the patient cohorts care is taken for, any hospital and daily practitioner is confronted with an increasing number of pathogens. This increasing number of pathogen results from systematic virus discovery studies that newly identified "old" but so far unknown viruses and from new viruses that have emerged due to zoonotic transmissions, as e.g. the SARS coronavirus.

As a consequence of those challenges, the optimal strategy for detection of respiratory pathogens should make use of a stepwise process. In the first instance it is crucial to provide the treating physician with information that can be used for therapy decisions, thus those viruses that can directly be treated with approved drugs or that have been to be treatable by an off-label use of approved drugs should be tested. This will include obligate respiratory viruses such as influenza viruses, RSV, HMPV, and contingently rhinoviruses as well as obligate respiratory pathogens like the family of herpesviruses. As an important feature of the diagnostic process, virological investigation need to be complemented by microbiological diagnostics in order to identify typical and atypical bacteria and fungi, as those pathogens can be treated with antibiotics, or, in their absence, false use of antibiotics can be avoided.

In the second instance all other frequent pathogens should be tested that have been shown to cause respiratory infections but cannot be treated specifically so far (adenoviruses, parainfluenzaviruses, coronaviruses NL63/229E/OC43/HKU1, enteroviruses, parechoviruses, hantaviruses). Finally, rare pathogens and those with unclear clinical correlation (adenoviruses, bocavirus) should be investigated. In any case, this procedure should strongly take into account a detailed anamnesis including information on travel activity and animal contacts as those events may influence the diagnostic search.

Brief Biography of the Speaker:

Priv. Doz. Dr. rer. nat. Oliver Schildgen, married, born 23.07.1974 in Nuremberg, Germany, studied biology at the University of Cologne. His diploma thesis was on the pathogensis of the picornavirus ECHO9 in newborn mice and was performed in the Institute of Virology in Cologne under the guidance of Prof. Dr. H.J. Eggers and Priv.-Doz.in Dr.

B. Nelsen-Salz. Following his diploma thesis Oliver Schildgen worked at the University of Cologne's Institute for Genetics and the Max-Planck-Institute for Neurological Research in Cologne and studied the Baculovirus model before performing his PhD thesis on the woodchuck hepatitis virus in the lab of Prof. Dr. M. Roggendorf at the University of Essen. Since 2002 Dr. Schildgen works at the University of Bonn and meanwhile leads a small research group that focuses on the epidemiology of new respiratory pathogens. Since December 2006 he is "Privat-Dozent" (qualified lecturer) for Virology at the Bonn University. His major research interests are new or emerging respiratory viruses and the development of hepadnaviral resistance against antiviral drugs. Since January 2007 he is coordinator of the RespViruses EU funded project (LSHM-CT-2006-037276).

Plenary Lecture 18

Is Thermal Scanner Losing its Bite for Indoor Mass Blind Fever Screening of Pandemic Influenza at Ports of Entry and in the Community?

Associate Professor Eddie YK Ng
School of Mechanical and Aerospace Engineering
College of Engineering
Nanyang Technological University, 50 Nanyang Avenue, Singapore 639798
Also: Adjunct NUH Scientist
Office of Biomedical Research, National University Hospital of Singapore, Singapore
E-mail: mykng@ntu.edu.sg

Abstract: The outbreak of SARS-2003 and recent Influenza A (H1N1-2009) has ignited studies and research (and even the general public interests) in the field of infrared (IR) imaging system for blind mass human fever screening to control the spread of pandemic. The ideal device for blind mass fever screening should be speedy, non-invasive and be able to detect accurately those people with fever. IR thermography has been used to measure/indicate physiology variations, detect inflammatory abnormalities and has the potential to serve as a tool for mass screening of fever.
This talk reviews the IR fever screening systems, their effectiveness to detect subjects with elevated body temperature, followed by suggesting the performance and environmental requirements in characterizing thermography for possible fever screening due to pandemic under indoor controlled environmental conditions. The essential elements on performance requirements include display color scale, display temperature resolution, emissivity setting, screening temperature range, workable target plane, response time and selection of critical parameters such as uniformity, minimum detectable temperature difference, detector pixels and drift between auto-adjustment. It is critical for thermal imagers to be able to identify febrile from normal subjects accurately. Minimizing the number of false positive and false negative cases, improves the efficiency of the screening stations. False negative results should be avoided at all costs, as letting an infected person through the screening process may result in potentially catastrophic results. Various statistical methods such as linear regression, ROC analysis and neural networks based classification were used to analyze the temperature data collected from various sites on the face on both the frontal and side profiles. Two important conclusions were drawn from the analysis: the best region on the face to obtain temperature readings and the optimal pre-set threshold temperature for the thermal imager. Finally, the talk however does not preclude users from potential errors and misinterpretations of the data derived from thermal imagers.

Brief Biography of the Speaker:
Eddie received Ph.D. at Cambridge University with a Cambridge Commonwealth Scholarship. His main area of research is thermal imaging, human physiology, biomedical engineering; computational turbomachinery aerodynamics, microscale cooling problems, and CFD-CHT. He is an Associate Professor in NTU. He has published more than 285 papers in refereed international journals (170), international conference proceedings (70), textbook chapters (18), and others over the years. Currently he is an Editor for several journals such as JMMB, JBiSE, CMJ, CFDJ, IJRM, ONMJ, etc. He has co-edited 4 books on "Cardiac Pumping and Perfusion Engineering" by WSPC Press (2007), "Imaging and Modelling of Human Eye" by Artech House (2008), "Distributed Diagnosis and Home Healthcare" (ASP, 2009) and "Performance Evaluation in Breast Imaging, Tumor Detection and Analysis" by ASP (in-press). Co-authored a book: "Compressor Instability with Integral Methods" by Springer (2007). (see URL:http://www3.ntu.edu.sg/home/mykng).

Plenary Lecture 19

Nanomechanics and Nanomanipulation of Soft Biological Materials for Tissue Engineering/Growth

Professor Isaac Kuo-Kang Liu
Reader (Professor) in Nanotechnology and Microengineering
School of Engineering, University of Warwick
Coventry CV4 7AL, UK (from 1st Sept. 2009)
Reader in Biomedical Engineering
Institute of Science and Technology in Medicine
School of Medicine, Keele University
Stoke-on-Trent ST4 7QB, UK
E-mail: I.K.Liu@warwick.ac.uk

Abstract: It is generally believed that all living systems require certain forces for growth and maintenance of their physiological functions, and this is especially true for soft biological tissues. Although people normally tend to consider large forces which may affect their bodies, recently scientist found that very small (nanoscale) force may have profound influences on human tissue regeneration or deterioration and may consequently enhance their healing process. Hence, mechanical stimuli to enhance cell/tissue regeneration have become a new paradigm for the next-generation therapies such as tissue engineering, regenerative medicine and stem cell therapy. In an ageing population, common diseases such as osteodeterioration, cardiovascular and neurological problems often require tissue replacement/regeneration. Such new self-repairing therapies become increasingly demanding. In this talk, we will report state-of-the-art nanomechanical techniques for stimulating tissue growth and the corresponding physiological responses of the tissues. The applications of these new techniques which are essential for the advancement of the engineered-tissue based therapeutic products for the next-generation of healthcare will also be highlighted in the talk.

Brief Biography of the Speaker:
Dr. Isaac Kuo-Kang Liu is a Reader (Associate Professor) in Nanotechnology at School of Engineering, the University of Warwick, UK. Before joining Warwick in 2009, he was a Reader in Biomedical and Cell Engineering at the Institute of Science and Technology in Medicine, School of Medicine, Keele University, UK and an Associate Professor in the Mechanical and Production School of Nanyang Technological University (NTU), Singapore. He completed his PhD study at the Chemical Engineering Department of Imperial College London, UK in 1995. His research interests include Cellular Bioengineering, Biomechanics, Nanomedicine, Tissue Engineering, and Biomedical Devices. He is a fellow of the Royal Society of Medicine, a fellow of Nanotechnology Institute, and a senior member of American Institute of Chemical Engineers (AIChE). He is an editor of several prestigious journals (e.g. the Open J. Nanomedicine). He has published more than 40 high-impact journal papers in Bioengineering and Biophysical areas and 30 other publications, including 2 US patents.

Plenary Lecture 20

Suitable Methods of Dynamic System Identification in the Arterial Baroreceptor Reflex

Dr. Koji Kashihara
Researcher
Graduate School of Information Science
Nagoya University
Furo-cho, Chikusa-ku, Nagoya
464-8601, Japan
E-mail: kashihara@cog.human.nagoya-u.ac.jp

Abstract: Because of the stabilization of arterial pressure against external pressure disturbances, arterial baroreceptor reflex is an important negative feedback system. The assessment of the baroreflex function would require quantifying not only the dynamic but also static properties because the baroreflex sensitivity might be quickly changed during cardiovascular diseases. The time-domain analysis has evaluated the stable gains around the operating point, but might not accurately characterize the dynamic baroreflex properties with unstable hemodynamics and background noise. The FFT analysis in the frequency domain has identified dynamic properties under noisy conditions, requiring longer data segments to remove the noise and to evaluate the properties with low-frequency band. To evaluate the time-varying gain around the operating point, the spontaneous baroreflex method has adjusted the time window in the short-time FFT; however it might not be suitable for the evaluation of short-term changes in baroreflex properties, at multiple pressure points with noise. In contrast, a modified wavelet-based time-frequency analysis could identify the dynamic baroreflex property from the transient step pressure inputs, because of high temporal resolution.

Brief Biography of the Speaker:
Koji Kashihara received PhD (Eng.) degree in 2001 from Tokyo Institute of Technology. He belonged to National Cardiovascular Center Research Institute, RIKEN, University of Sydney, etc. He is currently a researcher at Nagoya University. His research interests are human brain activities and autonomic nervous system.

Plenary Lecture 21

The Influence of Musculoskeletal Properties and Neural Control on the Stability of Human Motion

Professor Heiko Wagner
University of Muenster
Motion Science
Horstmarer Landweg 62b
D-48149 Muenster
Germany
E-Mail: heiko.wagner@uni-muenster.de

Abstract: Several models have been developed to understand the motor control system of human and animal locomotion. Some of these models are based on psychological backgrounds and some are physiologically inspired. With the present talk a biomechanical model will be introduced which can be used to simulate some aspects of musculoskeletal motion. Especially the stability of such systems should be analyzed with the model.
Considering the large degree of freedom as well as the complexity of our locomotion system it seems to be hopeless to control bipedal walking. Internal and external disturbances increase these difficulties. One strategy to cope with disturbances is to change behavior, i.e. to change the motor program. But thinking about dynamic movements in sports one might imagine the enormous dataflow and the high demands on the accuracy, which are necessary to cope with all variations via the central nervous system.
Therefore it seems to be advantageous to use an 'intelligent' neuro-mechanical system which unburdens the central nervous system. The mechanical system itself should be stable with respect to small perturbations; this intrinsic property of musculoskeletal systems was named self-stability. On the other hand the properties of the neural network within the spinal column itself may support the stabilization of cyclic and acyclic motions.
To discuss stability in a mathematical sense we use the framework of dynamical systems and apply this to biological musculoskeletal systems. To investigate the self-stabilizing properties of single muscle contractions, quick-release contractions can be used as a simple perturbation test. As a next step, it is necessary to analyze the interaction between muscle properties and the geometry of a joint. Here, we are interested in the stabilizing properties of muscles and the skeleton in general.
To discuss the interaction of the neural network within the spinal column we introduce a simple model, which can describe the function of so called spinal pattern generators. These spinal pattern generators are able to generate complex muscular activation patterns, based on simple central commands and feedback from proprioceptive sensors.

Brief Biography of the Speaker:
Dr. Heiko Wagner, is a professor for Biomechanics and Motor Control, at the University of Muenster, Germany, since 2006. He took his PhD in physics at the University of Frankfurt, Department of Theoretical Physics, Germany on 2000, and his habilitation in motion science at the University of Jena, Department of Behavioural Sciences, Germany on 2004.
Since 1996 he worked as a academic assistant at the Institute of Sportscience, Science of Motion, Universtiy of Jena under supervision of Professor Reinhard Blickhan.
His current research interest is the biomechanical analysis of how humans and animals are able to perform highly accurate and stable motions. He developed musculoskeletal models based on biomechanical time-invariant properties, using experimental and analytical methods in biomechanics and nonlinear dynamics.
The focus of his work is to analyse the self-stabilising properties of the musculoskeletal system in human and animal locomotion. Self-stability is based on both the mechanical properties and the learned movement patterns of the humans and animals. Therefore, there is a deep connection between the motor control system, which includes reflexes and inter-muscular co-ordination, and the biomechanics of humans and animals. While trying to understand the biomechanics of motor control, it is necessary to bridge the gap between different scientific fields, i.e. mathematics, physics, biology, biomechanics, medicine and physiotherapy, psychology, robotic engineering and others. Furthermore, we are investigating the kinetics and motor control of patients with chronic back pain.

Plenary Lecture 22

Diagnostic Value of Skin Vasomotion Investigation in Vascular Diseases

Professor Marco Rossi
Department of Internal Medicine
University of Pisa, Italy
E-mail: mrossi@int.med.unipi.it

Abstract: Skin vasomotion is the rhythmic variation of skin microvessel diameter responsible for skin microcirculatory blood flow oscillation, the so called blood flowmotion. Experimental and clinical findings suggest that vasomotion depends on different mechanisms, such as the endothelial activity, the spontaneous myogenic activity of the microvascular wall and the sympathetic activity. Skin vasomotion can be indirectly investigated in humans by means of the spectral analysis of skin laser Doppler flowmetry tracing. A high number of studies have recently investigated skin vasomotion in patients with different vascular diseases, using this method. Findings obtained in these studies have contributed in understanding the pathophysiology of the microcirculatory impairment in the investigated pathological conditions. In my presentation, I'll summarize the method we can use for investigating skin vasomotion in patients and the diagnostic value of this investigation, as well as I'll report my centre experience in this diagnostic approach.

Brief Biography of the Speaker:
Marco Rossi is aggregate professor at the Internal Medicine Department of University of Pisa, Italy. He is responsible for vascular and microcirculatory investigation in the same Department. His main research fields are represented by the study of peripheral microcirculation and by the application of ultrasounds in vascular exploration. He has published more than 200 scientific papers, many in reviewed journals or presented at international conferences. He is a scientific reviewer for several international Journals. He is in the Editorial Board of 'The Open Microcirculation & Microvascular Journal'. He is vice-president of the 'Italian Society Clinical Hemorheology and Microcirculation' and national representative of this society in the 'European Society for Microcirculation'.

Plenary Lecture 23

Invasion of the Host Epithelium by the Microorganisms: Good or Bad News for the Host?

Dr. Nadia Nadejda Berkova
Senior Research Fellow, INRA
(French National Institute of Agriculture Research)
Laboratory of Mycoses, UMR 956, Jouy-en-Josas Research Centre
Maisons-Alfort, France
E-mail: nberkova@vet-alfort.fr

Abstract: The host epithelium has permanent contact with the environment and a multitude of diverse microorganisms, resulting in a network of the host's defense mechanisms. Pathogens use various strategies to invade epithelial barriers, to hijack eukaryotic host function to their own benefit and use the epithelium as a reservoir for dissemination throughout the host. Alteration of the host cell apoptosis, promotion of cell proliferation or conversely, inhibition of cell growth and modulation of the cell differentiation by blocking of cell cycle progression are some of them. The mechanisms all of the stratagems employed by the pathogens are not fully elucidated, but they can contribute to the virulence of those microorganisms. However, the latest investigation of the interaction between host epithelium and microorganisms suggest that the epithelium is not a simple mechanical barrier: epithelial cells recognize microorganisms and initiate appropriate signaling which contribute to the endocytosis of microorganisms. It appears that capture of microorganisms by the epithelial cells is selective and that the different endocytic mechanisms may be enhanced by proinflammatory cytokines. The specificity of the recognition is illustrated by the various studies, showing that the epithelial cells distinguish the different morphotypes of the microorganisms. Using the model of the infection of respiratory epithelium by opportunistic pathogen Aspergillus fumigatus, we have shown that the airway epithelial cells identify the most invasive fungal form that may be beneficial for the host defense. Moreover, host epithelium exposed to the microorganisms, express various cytokines and different protective substances, such as antimicrobial peptides, with direct microbicidal or chemotactic activities, which might contribute to the regulation of host adaptive immunity against microbial invasion. Autocrine mechanismes of antimicrobial peptides expression was shown with the epithelial cells exposed to Aspergillus fumigatus. Further study of the regulation of antimicrobial peptides expression might provide the new approaches that may enhance its expression for potential therapeutic use.
Nevertheless, despite permanent exposure to a considerable amount of the microorganisms present in the environment, epithelium possesses the enormous capacity to keep its integrity, suggesting that some microbial strategies link to the mechanisms, which control the structural integrity of the tissue. Recent evidence supports the role of microbial factors in the maintenance of the integrity of the epithelial tissue: it was shown that Staphylococcus aureus as well as other microbial products induce epithelial repair, survival and growth and that such compensatory epithelial responses are mediated by autonomous non-inflammatory pathway. Therefore the outcome of the interaction between the host epithelium and microorganisms depends on multiple features.

Brief Biography of the Speaker:
Research interest focuses on the molecular understanding of immunological pathways and analysis of gene expression in the context of immune deregulation of the organism.
1990- PhD thesis in the Institute of Bioorganic Chemistry, Moscow, Russian Federation and Max-Delbruck Cancer Centre, Berlin-Buch, Germany. The thesis was related to the structure-functional analysis of Tumor Necrosis Factor. Part of the work was linked to the establishment of the new approach for the development of anti-cancer drugs using bispecific monoclonal antibody.
1991-1993-Post-doctoral training in Cancerology laboratory of Laval University, Quebec. The topic of study was related to investigation of the mechanisms of TNF action on the cancer cells.
1993-1995-Wyeth-Ayerst fellow in human reproduction, laboratory of endocrinology, St-Francois d'Assise Hospital, Quebec. The work was focused on the investigation of the physiopathology of endometriosis, followed by the finding of the important role of the haptoglobin in infertile patients with endometriosis.
1995-1997- Associate Professor at the medical faculty, Laval University, Quebec and a FRSQ (Quebec Medical Research Fondation) fellowship. The investigation of the team was devoted to the study of the cytokine-cells interaction in acute inflammatory response.

1998-2002- Invited scientist in Genetic and Development Unit, CNRS (French National Centre for Scientific Research) at Rennes University. Scientific projects related to the study of the mechanisms of the regulation of protein synthesis as well as to the development of the new methods for gene mapping.
2002-present-Senior Research Fellow, INRA (French National Institute of Agriculture Research), Maisons-Alfort, UMR 956, Mycology laboratory, head of the team. The current scientific interest focussed on molecular understanding of immunological pathways, immunogenetics and analysis of gene expression in the context of fungi-induced host immune disturbances and the development of animal models of infection to enhance the knowledge of immune deregulation of infected host.
The results of the research were published in peer-reviewed journals, book chapters and granted numerous international patents.
Reviewer for journals related to the field of immunology, reproduction and cell biology (Biology of reproduction, Human reproduction, The European Journal of Obstetrics & Gynecology and Reproductive Biology, FEBS letter, Clinical Immunology), an editorial board member for " Dermatology" and some book series.
Invited speaker at numerous international meetings/workshops/seminars.

Plenary Lecture 24

Contribution of Nitric Oxide and Mitochondrial Permeability Transition to the Cardiovascular Control in Hypertension and Experimental Hyperglycemia

Professor Lyudmila N. Shapoval
Vice-head of the Circulation Department
Bogomolets Institute of Physiology
National Academy of Sciences of Ukraine, Kyiv
Ukraine
E-mail: shapoval@biph.kiev.ua

Abstract: Nitric oxide (NO) is an important transmitter in the CNS playing a crucial role in the control and coordination of the activities of different functional systems including cardiovascular system. We were the first to raise the possibility that NO influences mechanisms of neuronal vasomotor control realized by the neurons within ventrolateral medulla in cats via activation of guanylate cyclase. In my Plenary Speech, I will analyse changes in the renal nerve sympathetic activity and shifts in haemodynamics induced by modulations of the intensity of NO production in the neurons of both dorsomedial and ventrolateral medulla involved in the cardiovascular control as well as the peculiarities of NO participation in the cardiovascular control in rats with genetically determined hypertension and experimental hyperglycemia. The role of an important regulatory enzyme arginase, competing for L-arginine for its metabolism, the role of syperoxides, and interrelations between medullary NO and GABA systems in hypertension will be analyzed. In recent years it became evident, that cellular dysfunctions induced by different factors converge on the mitochondria and initiate a sudden increase in the permeability of their inner membrane and mitochondrial permeability transition pores (mPTPs) opening. We were the first to show that mitochondrial permeability is essential for medullary cardiovascular control. I will discuss effects of changes in mitochondrial permeability transition in the medullary cardiovascular control in hypertension and experimental hyperglycemia, and protective effects of both the inhibitor of mPTP opening melatonin and a substrate for endogenous NO synthesis L-arginine against mPTP opening in the medullary cardiovascular neurons.

Brief Biography of the Speaker:
Lyudmila Shapoval is a leading scientific researcher and vice-head of the Circulation department of the Bogomolets Institiute of Physiology, National Academy of Sciences of Ukraine. She has been a Doctor of Science (Biology) since 1993. In 1996, together with collaborators of the Circulation Department of the Bogomolets Institute of Physiology she was awarded State Prize of Ukraine in the field of science and technology for investigation titled ”Role of endothelium and biologically active substances of endothelial origin in the control of circulation and cardiac activity”. She is the secretary-general of the Ukrainian Physiological Society. The main scientific interests are focused on investigation of the mechanisms of medullary cardiovascular control by NO-synthesizing neurons and the role of changes in mitochondrial permeability transition in hypertension and diabetes mellitus.

Plenary Lecture 25

Structure and Dynamics Elucidation of Biopolymers from Constrained QM/MM Calculations - From NMR Chemical Shifts to Structure and Dynamics

Professor Ulrich Sternberg
Karlsruhe Institute of Technology
POB 3640, D-76021 Karlsruhe
Germany
E-mail: Ulrich.Sternberg@ibg.fzk.de

Abstract: NMR is a major source of information on the structure and dynamics of bio-molecules. New computational methods are presented that use NMR data as target functions for structure elucidations. It can be shown that chemical shifts can be used for the 3D structure refinement of proteins and other biopolymers. Additionally the orientation and dynamics can be investigated from molecular dynamics (MD) simulations with orientational constraints. Prerequisites are a force field, an effective method for computing structure dependent atomic charges, and a very fast method for the computation of chemical shifts (bond polarization theory – BPT). Using the COSMOS-NMR hybrid force field with semi-empirical atomic charges and chemical shifts, the calculations can be performed in every step of an MD simulation or geometry optimization. To the energy, provided by the force field, pseudo energies are added. They depend on the differences between experimental and calculated chemical shifts. In addition to the energies pseudo forces have to be computed. This requires derivatives of the chemical shifts with respect to the coordinates. The pseudo forces are analytically derived from the integral expressions of the bond polarization theory (BPT).
In the case of liquid state NMR structure investigations of proteins, 13C and 15N chemical shift constraints can be added to obtain accurate structure data for the main chain and side chain carbons. This method was first applied to a zinc complex of a synthetic pseudo-peptide and to membrane active peptides. In the case of proteins chemical shifts can be used to find families of structures that represent best the conformer distribution in solution.
Chemical shifts constraints are beneficial especially in solid state structure investigations. In case of silk and cellulose, crystal structures have been computed that fulfil both the 13C-NMR chemical shift and the X-ray constraints. It was shown that for the newly refined structures the calculated chemical shift tensor elements match the experimental values very well. Since biopolymers like silk give poorly defined X-ray patterns, solid state NMR investigations can be used to obtain better resolved crystal structures.
Membrane and other solid state NMR investigations exploit the tensorial character of the NMR parameters. These tensors can be used in MD simulation as orientational constraints to produce a detailed picture of molecular motion and order.

Brief Biography of the Speaker:
20.11.1946: Born in Brandenburg/Havel, Germany.
1965-1970: Studies in chemistry at the Humboldt University Berlin.
1975: Thesis in Theoretical Chemistry on the calculation of magnetic susceptibilities and nuclear shieldings.
1975-1978: Development of the graphics for a computer system that predicts chemical reactions.
1976-1988: Research and lecturing at the physics department of the Fiedrich-Schiller University Jena. Development of the Bond Polarization Theory (BPT).
1988: Thesis B on BPT chemical shift calculations, facultas docendi and Dr. sc.
1991: Habilitation for applied physics.
Lectures for Physicists on „Atoms, Molecules and Quantum Theory“
1992: Privatdozent at the Physics Department of the Fiedrich-Schiller University Jena
1994: The software COSMOS (NMR Molecular Modelling) wins the “European Academic Software Award“.
2001: Group leader of the NMR facility at Physics Department.
2002: Development of computational methods at the Bio-NMR group of the Research Centre Karlsruhe

Plenary Lecture 26

New Insights into the Etiology of Human Disease by Probing the Bioinorganic Chemistry of the Bloodstream

Assistant Professor Jurgen Gailer
Department of Chemistry and
BSc Environmental Science Program
University of Calgary
2500 University Drive NW
Calgary, Alberta, T2N 1N4
Canada
E-mail: jgailer@ucalgary.ca

Abstract: Despite extensive research, the etiology and the biomolecular origin of many grievous human diseases, including Alzheimer's Disease, multiple sclerosis and Parkinson's disease, remains poorly understood and is regarded by many as one of biology's biggest challenges in the 21st century. In view of the fact that the human genome project has so far been rather insufficient in providing much needed insight into the origin of human diseases, we are left with 'environmental factors' as potential root causes. This proposition is quite relevant today since the industrial revolution, which started in ~1800, essentially transformed man into a global biogeochemical force. The massive consumption of fossil fuels, for instance, has already increased the CO2 concentration of the earth's atmosphere and thus perturbs the biogeochemical carbon-cycle on a global scale. What is generally much less appreciated – but nonetheless of considerable importance with regard to elucidating the origin of human diseases – is the notion that anthropogenic activities have also progressively increased the mobilization of toxic metals and metalloid compounds from the earth's crust into the global environment. The concomitant increased dietary exposure of certain human populations to these persistent pollutants and their subsequent absorption into the systemic blood circulation are therefore of increasing concern. Although the average concentrations of several toxic metals and metalloids in human blood are now firmly established, their interpretation with regard to their health relevance is exceedingly difficult. The aforementioned lack of understanding the etiology of human disease combined with the detection of several inorganic environmental pollutants in human blood suggests that a better understanding of the bioinorganic chemistry of toxic metals and metalloid compounds in the bloodstream may contribute to establish functional connections between the exposure to certain metals and specific human diseases. To this end, we have elucidated the erythrocyte-mediated bioinorganic basis for the antagonistic interaction between the environmentally abundant inorganic pollutants arsenite and mercuric mercury with the essential ultra trace element selenium in the bloodstream. After a brief discussion of the health relevance of these findings, a promising proteomic approach is introduced which is eminently suited to provide additional new insights into other disease-relevant bioinorganic chemistry processes in the mammalian bloodstream.

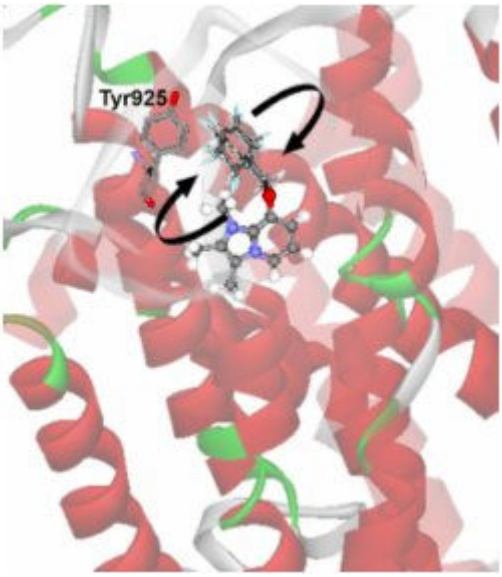
Brief Biography of the Speaker:
I received my PhD from the Institute for Analytical Chemistry of the Karl-Franzens University Graz, Austria in 1997. As an Erwin Schrodinger fellow, I subsequently joined the Department of Molecular and Cellular Biology of the University of Arizona (Tucson, AZ, USA) and thereafter worked as a research associate in the Department of Nutritional Sciences (University of Arizona). Between 2001 and 2002, I was an Alexander von Humboldt fellow at the GSF National Research Center for Environment and Health (Munich, Germany). In 2003, I joined Boehringer Ingelheim Austria, where I was the team leader for their downstream biopharmaceutical production plant in Vienna until 2004. I then started as an assistant professor in the Department of Chemistry of the University of Calgary in 2004.

Plenary Lecture 27

Resolving Nanoscale Details of Ligands at their Binding Sites of Membrane Targets

Professor Anthony Watts
Biomembrane Structure Unit
Biochemistry Department
Oxford University, Oxford
OX1 3QU, UK
E-mail: anthony.watts@bioch.ox.ac.uk

Abstract: It is now possible to resolve local dynamics within a membrane bound protein at near physiological conditions in natural membrane fragments or in reconstituted complexes, using solid state NMR approaches [1, 2]. This information is obtained by isotopically (2H, 13C, 19F, 15N, 17O) labeling selective parts of either a ligand or the protein understudy, and observing the nucleus in non-crystalline, macromolecular complexes [3,4].
Ligands with complex structure have differential mobility at their binding sites. Substituted imidazole pyridines, for example, which inhibit the H+/K+-ATPase and have therapeutic use, are constrained in the imidazole moiety, but shows significant flexibility at the pyridine group [5] (see figure). It is this group which has a direct interaction with an aromatic (phe198) residue, with the potential for ?-electron sharing [6]. Similarly, the steroid moiety of ouabain undergoes motions which are similar to those of the target protein, the Na+/K+-ATPase, but the rhamnose undergoes a high degree of flexibility at fast rates of motions whilst interacting with Tyr198 [7]. For acetyl choline when bound in the nicotinic acetyl choline receptor (nAChR), the quaternary ammonium group undergoes fast rotation at an aromatic binding site, which is driven by thermal fluctuations which may be functionally significant [8]. Our current focus is on GPCRs, specifically the brain neurotensin receptor (NTS1) for which the structure (by single molecule cryo-EM) and ligand binding interactions are being studied [9 - 14].



Plenary Lecture 28

NMR Spectroscopy of the Neuronal Tau Protein: Normal Function and Implication in Alzheimer's Disease

Professor Isabelle Landrieu
Co-authors: Laziza Amniai, Alain Sillen, Nathalie Sibille, Jean-Michel Wieruszeski, Arnaud Leroy, Caroline Smet, Guy Lippens
Charge de Recherche du CNRS
UMR8576-CNRS, Batiment C9
Universite des Sciences et Technologies de Lille
59655 Villeneuve d'Ascq
FRANCE
E-mail: isabelle.landrieu@univ-lille1.fr

Abstract: Tau, a natively unstructured protein, interacts with the microtubules (MTs) via its microtubule-binding (MTB) domain, located in the C-terminal half of the protein. The protein, when aggregated in Paired Helical Filaments (PHF) in Alzheimer's disease (AD)-affected neurons, is invariably hyperphosphorylated and potentially phosphorylated on sites unique to the disease. Nuclear magnetic Resonance (NMR) Spectroscopy was used to explore the different aspects of the Tau normal and pathological functions but proved challenging, because the protein contains 441 amino acids and has poor signal dispersion. The interaction of Tau with taxol-stabilized microtubules was first studied using NMR experiments to obtain a per residue information. Tau can be forced to form AD like aggregates through the addition of poly-anions such as heparin. High Resolution Magic Angle Spinning NMR and solution NMR were used to further characterize these fibers. We next ask how the heparin can promote the fiber formation. The interaction with Tau was studied by using small heparin fragments of well-defined size, at 20 0C, in conditions where no aggregation occur. Still, the relevance of heparin as the intracellular aggregating agent is far from clear. We have set out to dissect the phosphorylation pattern of Tau in order to understand better its role in the aggregation process and the microtubule binding. Our current knowledge on the functional consequences of specific phosphorylation patterns is still limited, mainly because producing and assessing quantitatively phosphorylated Tau samples is far from straightforward. We have applied NMR spectroscopy to identify and quantify in a single experiment the phosphorylation pattern of Tau, after in vitro phosphorylation, for example with the PKA kinase. Once the pattern of phosphorylation is characterized by NMR, the phosphorylated Tau can be use for functional assays like aggregation or microtubules interaction.We present here our results on Tau samples that have been in vitro phosphorylated by the Cyclin dependent kinase 2 (CDK2)/Cyclin A3 (CycA3) kinase complex. The impact of these phosphorylations on the local structuration of Tau was also analyzed. Finally, NMR was use to explore other aspects of the regulation of Tau function by phosphorylation. This includes characterisation of its interaction with phospho-dependent protein partners, such as the prolyl cis/trans isomerase PIN1 and dephosphorylation by the PP2A phosphatase.

Brief Biography of the Speaker:
As a PhD student, I spent 2 years in the European Molecular Biology Laboratory (EMBL), Grenoble Outstation in France, learning about Protein Biochemistry. I received my PhD in Agronomy and Biological Engineering from the Agronomical Faculty of Gembloux (FUSAGx) in Belgium in 1997. As Belgium National Foundation Fellow, I next joined the Department of Plant System Biology in Gent University/ Vlaams Institute for Biotechnology in Belgium, in the lab of Prof D. Inze and Prof. M. Van Montagu. During this time, I studied cell cycle regulatory proteins from Arabidopsis thaliana. I did functional characterizations but also worked on their structural characterization using NMR spectroscopy. In 2001, I joined the French National Science Center (CNRS) and started to work in the NMR group directed by Prof. G. Lippens in Lille, France. I obtained my habilitation in 2003 from the Science and Technology University in Lille, France. My main interest is ever since the regulation of Tau function by phosphorylation and the recognition of these phosphorylated sites by protein partners and various enzymes.

Plenary Lecture 29

Regulatory Networks, Chemical Oscillations, Biological Switches, and Intrinsic Noise in Cells. Why and What for?

Professor Eduardo S. Zeron
Department of Mathematics
Research and Advanced Studies Centre (Cinvestav)
Mexico City, Mexico
E-mail: moises.santillan@me.com

Abstract: The cellular communications that regulates cell fate must be precisely controlled to avoid dangerous errors. How is this achieved? Recent work has highlighted the importance of positive and negative feedback networks in the dynamic regulation of signalling. These feedback interactions can impart precision, robustness, noise rejection and versatility to cellular signals. They can also produce interesting emergent dynamical properties like biological switches and chemical oscillators, whose properties and purpose must be explained.

Brief Biography of the Speaker:
Eduardo S. Zeron is a Tenure Professor in the Department of Mathematics of the Research and Advanced Studies Centre (Cinvestav) in Mexico City. He was born in 1971 and obtained his Doctor degree in Mathematics (Cinvestav) in 1996 under the supervision of Professor Adalberto Garcia Maynez from UNAM (Mexico City). He is a member of the Mexican Academy of Science since 2008 and he has been Postdoctoral and Sabbatical Fellow in York University (Canada), University of Toronto, Universite de Montreal, and Universitaet Konstanz. He has graduated two Doctoral Students and two Master Students. Finally he has published almost 30 scientific papers in the fields of Systems Biology and Several Complex Variables. 20 of these papers has been published in Journals enlisted in the ISI Web of Science. He has also been the coauthor of a special chapter in Systems Biology published by Nova Science.

Plenary Lecture 30

Studies on a Promising Anticancer Molecule of Marine Origin. Results of an Interdisciplinary Study

Professor Carla Falugi
Universita di Genova - Dipartimento di Biologia
Laboratory of Experimental Embryology and Cytotoxicology
Viale Benedetto XV, N°5 - I-16132 Genova, Italy
E-mail: falugi@unige.it

Abstract: Since the first '80s, we found that some tumour types present over expression of cholinesterase activities, and in particular of acetylcholinesterase (AChE, E.C: 3.1.17).
AChE is an enzyme associated to the cholinergic signal system, whose classic role is to remove acetylcholine (ACh) from the receptors. Nevertheless, the protein is also involved in cell-to-cell communication driving embryonic development, by mechanisms yet largely unknown, possibly related to the intracellular dynamics evoked by ACh signalling, and in morphogenetic cell movements, related to AChE function as a cell-substrate adhesion molecule (SAM), through the affinity for laminin. Moreover, this molecule is affected by a number of natural and synthetic inhibitors, including environmental contaminants. For this reason, the activity of AChE was found to be a good biomarker for environmental toxicity, related to the role played by ACh in inflammation.
During studies on environmental toxicants, such as organophosphate pesticides, we found that a low AChE inhibition promotes apoptosis in human cultured cells, and decreases cell movements, causing embryonic anomalies such as cardia bifida in chick embryos. Apoptosis is one of the good cell responses against tumour, and preventing cells migration is a bad feature for embryonic development, but a good feature for metastasis spreading prevention.
In particular, Non Small Cell Lung Cancer (NSCLC) biopsies and cultured cell lines present enhanced AChE activity, and possess a complete set of molecules related to cholinergic signal system, including vesicular ACh transporter, ACh biosynthetic enzyme, and receptors. Thus, our hypothesis was that down-regulation of this signalling system, in a natural-like and non-toxic way would help in enhancing anti-cancer cell features.
A natural anti-AChE complex compound, belonging to the class of polymeric alkylpyridinium salts (poly-APS), is produced by the Mediterranean sponge, Reinera sarai, to avoid infestation from other marine organisms. Poly-APS were found to be a mixture of two of 3-octylpyridinium polymers, including 29 and 99 monomeric units, and were demonstrated to exert strong AChE-inhibitory activity in vitro. Colleagues of the CNR-ISMAR demonstrated the neurotransmitter/neuromodulator role of AChE in living organisms and the non toxic and reversible activity of poly-APS. This confirmed the requested features of the compound, that was used on NSCLC cells for a preliminary battery of tests, in order to check selective apoptosis among NSCLC and healthy cells.
On exposure to low poly-APS doses, a high percentage of the cancer cells underwent apoptosis, in a significant amount vs normal lymphocytes, used as a healthy control ($P<0.05$). Then, a complex series of experiments was begun, both in vitro and in vivo, in cooperation with the Institute for the Study of cancer (IST), who supplied cells and operated on mice for pre-clinical experiments. In living mice, the low toxicity of poly-APS on normal cells was confirmed by injection in the caudal vein. No overt effects on health parameters, such as weight gain and physical behaviour, were observed, and histological analysis of major organs did not reveal differences between the treated animals as compared to controls. A series of synthetic homologs of poly-APS molecules were performed and tested, in order to choose the more promising substances to be used for further pre-clinical experiments. The results of this work are the object of this presentation.

Brief Biography of the Speaker:
Carla Falugi, born in Seggiano (GR) 12/10 1943, is full professor since 1999; graduated in Natural Science, the 21st November 1968, with thesis evaluation 110/110, performed didactic and research tasks since 1970 (MPI grant for didactic and scientific training up to 1972; MPI research contract up to 1976; assistant professor since 1977; professor with didactic charge of Comparative Anatomy from 1977 to 1983)
After 1983, she was teacher of Cytology and Histology; Experimental Embryology and Morphology, Developmental Biology. At present she teaches 4 courses: Developmental Biology (since 1990); Cytotoxicology; Environemntal Toxicology and Biomarkers of environmental damage.
Her research, since 1970, regards the functions of signal molecules, belonging to the cholinergic neurotransmitter system, and their receptors in regulation of cell-to-cell and cell-environment communication promoting differentiation

(induction, ion flux, membrane depolarisation etc.)during early developmental stages, from fertilisation. The model mainly used for this basic study has been represented by marine invertebrates, and in particular embryonic and larval development of sea urchin up to metamorphosis and juvenile stages. This model has been found very sensitive to environment interaction. In the latest years, the interst on neurogenesis and neural functioning was carried out by the use of two human in vitro models: the NTERA2 cells (classic and well known neurogenic model) able to differentiate towards cholinergic neurons and olygodendrocyte co-culture, and preadipocyte from lipoaspirate primary cultures, appropriately differentiated towards hMADS (human Multipotent Adipose-Derived Stem cells). These two models offer a tool system to investigate cell differentiation/functioning in a manner pertinent to embryogenesis, that also retain interactions between glial cells and neurons.

Based on this experience. Since 1987 she has undergone a study on the effects of xenobiotics, able to interact in the correct reception of signal molecules, in order to establish the effects of these substances on correct embryonic development and cell differentiation and at the same time to select alternative models, to use for obtaining biomarkers of environmental state. In this context, she is member of the Italian Platform for Alternative Models (IPAM).

Plenary Lecture 31

Artificial Restriction DNA Cutter for Manipulation of Huge DNA

Professor Makoto Komiyama
Research Center for Advanced Science and Technology
University of Tokyo, Tokyo
153-8904 Japan
E-mail: komiyama@mkomi.rcast.u-tokyo.ac.jp

Abstract: Current molecular biology is based on site-selective scission of DNA by restriction enzymes. However, site-specificity of naturally occurring restriction enzymes is too low to manipulate huge DNA. In order to solve this problem, we developed man-made tools which cut double-stranded DNA at desired site (artificial restriction DNA cutter; ARCUT).1) These tools are composed of (1) Ce(IV)/EDTA complex as molecular scissors and (2) two pseudo-complementary PNAs (blue lines in Fig. 1). By changing the sequences and the lengths of PNA strands, the scission-site and site-specificity are freely chosen.

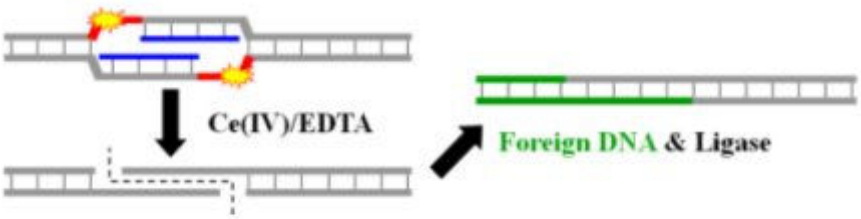


Fig. 1. Site-selective scission of double-stranded DNA by ARCUT and ligation of the scission fragment with foreign DNA.

With the use of ARCUT, even huge DNAs (e.g., the whole genome of human beings) were selectively cut at target site. The resultant scission fragments were ligated with foreign DNAs (green lines in Fig. 1) and expressed in mammalian cells. Applications of ARCUT for promotion of homologous recombination in human cells are also presented.

Brief Biography of the Speaker:
Makoto Komiyama graduated from the University of Tokyo in 1970, and got his Ph.D. from the same University in 1975. After spending four years at Northwestern University (USA) as a postdoctoral fellow, he became an assistant professor at the University of Tokyo, and then an associate professor at University of Tsukuba. From 1991, he has been a professor of the University of Tokyo. His main research area is bioorganic and bioinorganic chemistry. He received Awards for Young Scientist from the Chemical Society of Japan, Japan IBM Science Award, Award from the Rare Earth Society of Japan, Inoue Prize for Science, The Award of the Society of Polymer Science, Japan, Award from Cyclodextrin Society of Japan, and others.

Plenary Lecture 32

Butantan Pulmonary Surfactant Development (Not a Merely Me-Too)

Professor Flavia Saldanha Kubrusly
Biotechnology Center, Instituto Butantan
Av. Vital Brasil, 1500
05503-900- Brazil
E-mail: kubruslyfs@butantan.gov.br

Abstract: The public mission of Instituto Butantan (Brazil) engages undoubtedly the reduction of infant mortality rate by being responsible for 80% childhood immunization. One main cause of postnatal mortality is associated with respiratory distress syndrome (RDS) caused by pulmonary surfactant deficiency. Synthetic or biologically derived surfactants has been developed to improve lung function and to decrease the mortality associated with RDS. In 1998 Butantan has begun to develop a porcine pulmonary surfactant (Butantan surfactant). Butantan idea was to offer an alternative surfactant replacement therapy mainly for developing countries, focus on low cost but same efficacy and safety. The Butantan preparation was obtained from ground porcine lungs by organic extraction coupled with adsorption on a cellulose derivative. The lungs were kindly donated by a major Brazilian food producer (Sadia). The key advantages of this preparation are to avoid at any volume high-speed centrifugation or extra steps of liquid-gel chromatography. The in vivo evaluation of Butantan surfactant compared to other commercially available surfactants using the preterm rabbit model showed similar pulmonary effects, improving pulmonary functions as assessed by the decrease of the ventilatory pressure and the increase of the dynamic compliance. After having completed all of the pre-clinical test phases, the validation of the medicine was initiated, covering 19 institutions throughout Brazil. The clinical trial (Phases II and III) showed that both the imported and the Butantan surfactant are equally efficient. "The quantity of the product necessary for the survival of the children is also the same" commemorates Prof. Isaias Raw, the coordinator of the project and its main incentive". Currently, investments to make the surfactant plant production as safe as possible to the environment, and also sustainable still concern, since the hot points of the industrial plant besides the surfactant yield, are the completely recovery of the solvents and the cellulose derivative to mitigate costs. The search of promissory therapeutic molecules on porcine pulmonary extract usually rejected during surfactant production is another possibility to aggregate extra biotechnological value to the process. Purification of surfactant proteins and purification of protease inhibitors are examples of this virtuous circle. In a near future to join these proteins to the surfactant preparation will open new frontiers to the surfactant replacement therapy or other not straight related to surfactant. Butantan surfactant is by definition a me-too (drugs that apparently do not offer any distinction from existing therapy) but this experience is also a good example of the Brazilian governmental initiatives to stimulate the research and development of the biopharmaceutical sector in Brazil.

Supported by: Fundacao Butantan, FAPESP, CNPq, MS.

Brief Biography of the Speaker:
Flavia Saldanha Kubrusly has studied Biology and received her master degree from Universidade Estadual de Campinas (UNICAMP) in 1984 and got her PhD from Universidade de Sao Paulo (USP) in 1992. Both universities are located in Sao Paulo, Brazil. Since 1987, she has a permanent R&D position at the Instituto Butantan, Sao Paulo, Brazil. Most of her career is dedicated to vaccine production and control (measles, hepatitis B, rabies). In the last ten years, she is also dedicated to the purification and production of medical drugs derived by direct extraction from native biological source (pulmonary surfactant, aprotinin, vaccine adjuvant) under coordination of Prof. Dr. Isaias Raw, her former post doctoral supervisor (1994) and the Head of the Butantan Foundation. She has authored more than 70 publications (20 original scientific papers, one book chapter, one scientific prize, four patents and more than 50 presentations in conferences). Since 2000, she supervises graduates on the Biotechnology Graduate Interunit Program (USP), concluding at the present, three masters and one PhD.

Plenary Lecture 33

Disintegrins as Prototypes for Drug Design Targeting Adhesion Receptors for Anti-Metastatic Therapy

Professor Heloisa Sobreiro Selistre de Araujo
UFSCar, Sao Carlos
SP, Brazil
E-mail: hsaraujo@ufscar.br

Abstract: Metastasis is a key characteristic of malignant cells, which must reach the bloodstream to colonize distant target organs. Once in the circulation, tumor cells must attach to vascular endothelial cells, platelets or components of the vessel wall and invade through them until reach the target organs. Most of these steps are mediated by specific adhesive functions of tumor cell receptors such as the integrins. Disintegrins are small integrin-ligand molecules that specifically inhibit cell adhesion to natural substrates found in the extracellular matrix. Disintegrin structural variations result in the specificity of integrin recognition. Most disintegrins have an RGD motif that is relevant for a3 (aIIba3, platelet fibrinogen receptor, and ava3, vitronectin receptor) and a1 integrin binding (a5a1, fibronectin receptor). DisBa-01, a recombinant RGD-disintegrin derived from the venom glands of Bothrops alternatus inhibited the adhesion of ?v?3-expressing human microvascular endothelial cell line-1 (HMEC-1) and murine melanoma cell line B16F10 to vitronectin (IC50 = 555 nM and 225 nM, respectively), but it did not affect the binding of a human breast cancer-derived cell line (MDA-MB-231) not expressing ava3. In vivo, DisBa-01 dose-dependently decreased bFGF-induced angiogenesis in a matrigel plug assay in athymic nude mice (IC50 = 83 nM). When injected intravenously to C57BL/6 mice together with B16F10 melanoma cells, DisBa-01 time- and dose-dependently inhibited lung metastasis monitored by bioluminescent imaging. DisBa-01 also inhibited chemotactic migration of 4T1BM2 cell migration towards serum or vitronectin. Molecular modelling of the interaction between DisBa-01 and the ?v?3 integrin showed that the N-terminal region of the disintegrin was not involved in receptor binding. Deletion of the first 36 residues of the N-terminal region of DisBa-01 did not affect significantly the cell adhesion properties of the molecule. On the other hand, ADAM9D, a recombinant disintegrin domain from a human homologue, was able to support tumor cell adhesion through binding to the ?1 integrin subunit. In a dynamic flow assay ADAM9D inhibited about 60% and 55% of MDA-MB-231 tumor cells and platelet adhesion to collagen, respectively. In conclusion, disintegrins are useful tools for the design of selective inhibitors against the adhesion and extravasation of cancer cells.

Support: FAPESP, CAPES e CNPq (Brazil).

Brief Biography of the Speaker:
I received my PhD in Biochemistry from the University of Sao Paulo, in Ribeirao Preto, SP, Brazil in 1988. I subsequently joined the Department of Physiological Sciences at Federal University of Sao Carlos (UFSCar), in Sao Carlos, SP, Brazil, as Professor of Biochemistry and Biophysics. Between 1993 and 1995, I was a visiting scientist fellow at the Venom Research Group at the Department of Physiological Sciences of the College of Veterinary Medicine of the Oklahoma State University, Ok, USA, collaborating with Dr. Charlotte L. Ownby. Back to the Federal University of Sao Carlos in 1995, I started the research group in integrin binding proteins from snake venoms and their applications in prevention of metastasis. Currently, I am the team leader of the Biochemistry and Molecular Biology Laboratory at UFSCar, which focus on integrin-dependent cell adhesion and migration, extracellular matrix interactions and intracellular signaling of metastatic cells.

Plenary Lecture 34

Cross-Talk of Hypoxic and Map Kinase-Dependent Signalling Pathways in Toll-Like Receptor (TLR)-Mediated Inflammatory Reactions

Dr. Vadim Sumbayev
Medway School of Pharmacy
University of Kent
Anson Building, Central Avenue
Chatham Maritime, Kent ME4 4TB
United Kingdom
E-mail: V.Sumbayev@kent.ac.uk

Abstract: TLRs are the key pattern recognition receptors that lie at the core of resistance to disease, initiating most of the phenomena that occur in the course of innate immune reactions. In our studies we found that ligand-induced TLR4 (cell membrane-associated receptor which recognises LPS of Gram-negative bacteria) signalling triggers cross-talk of ASK1 downstream pathway and HIF-1alpha in THP-1 human myeloid cells. Both pathways were activated via redox-dependent mechanism associated with tyrosine kinase/phospholipase C-1gamma-mediated activation of protein kinase C alpha/beta. The latter activated NADPH oxidase and, therefore, the production of ROS which up-regulate both HIF-1alpha and ASK1. ASK1 contributes to the stabilisation of HIF-1alpha protein via activation of p38 MAP kinase which directly phosphorylates HIF-1alpha. Knockdown of HIF-1alpha in THP-1 cells with siRNA suggested that this protein supports TLR4-dependent production of pro-inflammatory cytokines by protecting the cells against depletion of ATP and therefore against death. Ligand-induced activation of TLR7/8 (endosomal receptors which recognise viral ssRNA) leads to the accumulation of HIF-1alpha protein in THP-1 human myeloid macrophages via redox- and reactive nitrogen species-dependent mechanisms. ASK1 and its downstream MAP kinases as well as PI3-kinase are not involved in TLR7/8-mediated HIF-1alpha accumulation. Experiments with HIF-1alpha knockdown THP-1 cells have clearly demonstrated that this protein is?important for the protection of these cells against TLR7/8-induced depletion of ATP and for production of the pro-inflammatory cytokines. Therefore membrane-associated and endosomal TLRs use differential mechanisms of activation of HIF-1alpha but the function of the protein is similar in both cases.

Brief Biography of the Speaker:
I achieved my PhD degree in 1999 from the Palladin Institute of Biochemistry, National Academy of Science of the Ukraine. After graduating, I worked as Assistant, then Associate, Professor at the Department of Biochemistry, Mechnikov Odessa National University in the Ukraine. Then I moved to Germany where I received an Alexander von Humboldt research fellowship and worked as a Humboldt fellow in the Institute for Cell Biology, University of Kaiserslautern. Upon complete of my fellowship, I spent three years in Denmark at the University of Aarhus, working as Assistant Professor at the Department of Molecular Biology at the Interdisciplinary Nanoscience Centre. In December 2006, I joined the Medway School of Pharmacy, University of Kent as a Lecturer in Biochemistry where I have established my research group.

Plenary Lecture 35

Short Cationic Host Defense Peptides – Determination of Sequence Requirements for Killing Pseudomonas Aeruginosa

Dr. Kai Hilpert
Team Leader "Bioactive Peptides"
Institute of Biological Interfaces 2
Karlsruhe Institute of Technology (KIT)
Karlsruhe, Germany
E-mail: kai.hilpert@web.de

Abstract: Host defense peptides are part of innate immunity, often possessing the potential to kill both Gram-negative and Gram-positive microorganisms, rapidly and directly, and modulate other parts of host innate immunity. Today, more than 700 cationic peptides have been identified, originating from bacteria, fungi, insects, tunicates, amphibians, crustaceans, birds, fish and mammals, including humans. These peptides all have certain conserved physical features, including a net positive charge, approximately 50% hydrophobic amino acid content, and sizes that range from 12 to 50 amino acids; however, from these physical features, virtually any type of secondary structure can arise, including alpha-helix, beta-sheet and loop structures of beta-turn and extended loops. The multitude of cationic peptide sources, structures and spectra of activities is matched by a number of complex and controversial models that attempt to describe and explain the mode of action.
Little is known about the sequence requirements of short host defense peptides. With the help of our novel technique, using an artificially created, luminescence-producing Gram-negative bacterium and peptide synthesis on cellulose, we investigated the sequence requirements of these peptides. Hundreds of peptides were tested for their ability to kill Pseudomonas aeruginosa. Complete substitutional analysis of different indolicidin variants, as well as a semi-random peptide library with about 3000 members were studied. The complete substitutional analysis gave us information about the importance of each single position within a peptide sequence, whereas the peptide library provided broader information concerning the composition of amino acids, resulting in an active antimicrobial peptide. The data were analyzed using a quantitative structure-activity relationship approach (QSAR) to identify sequence patterns that discriminated among superior activity, equivalent activity and inactive peptide sequences. This information provides us with mechanistic cues to better understand the mode of action of the short antimicrobial peptides. The results of these measurements and analyses will be discussed in detail.

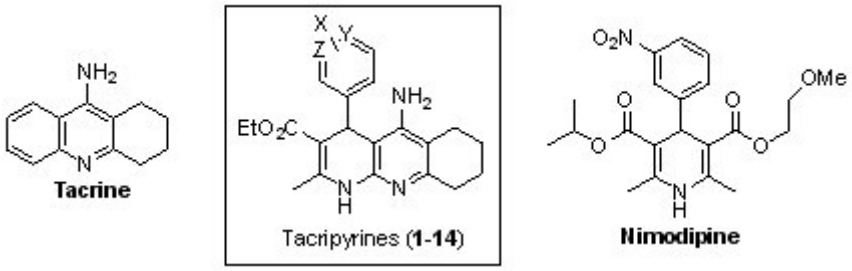
Brief Biography of the Speaker:
Kai Hilpert is a team leader of the research team "Bioactive Peptides" at the Karlsruhe Institute of Technology (KIT) in Germany. He is a member of the new “BioInterfaces” program, within the Helmholtz Association. He studied biochemistry at Humboldt University in Germany. Kai Hilpert had the opportunity to be a postdoctoral fellow with the Canadian Institutes of Health Research (CIHR) program at the University of British Columbia, Canada. For 15 years, he has used the peptide SPOT synthesis method to study various protein/protein or peptide/protein interactions. In the past 5 years, his research interests have focused on host defense peptides. Currently, he is investigating sequence requirements of short cationic host defense peptides with activity against Pseudomonas aeruginosa. He has authored or co-authored over 25 peer-reviewed scientific papers, which have been published in journals that include Nature Biotechnology, Nature Protocols and Chemistry & Biology. Further information can be found at www.kaihilpert.de.

Plenary Lecture 36

Tacripyrines, the First Tacrine-Dihydropyridine Hybrids, as Multitarget-Directed Ligands for the Treatment of Alzheimer's Disease

Associate Professor Maria do Carmo Carreiras
Co-authors: J. Marco-Contelles, F. Javier Luque, R. Leon, A. Samadi
iMed.UL, Research Institute for Medicines and Pharmaceutical Sciences
Faculty of Pharmacy, University of Lisbon
Av. Forcas Armadas, 1600-083 Lisbon
Portugal
E-mail: mcdamaso@ff.ul.pt

Abstract: Tacripyrines (1-14) have been designed by combining an AChE inhibitor (tacrine) with a calcium antagonist such as nimodipine and are aimed to develop a multitarget therapeutic strategy to confront Alzheimer's disease (AD). Tacripyrines are selective and potent AChE inhibitors in the nanomolar range. The mixed type inhibition of hAChE activity of compound 11 (IC50 105 ± 15 nM) is associated to a 30.7 ± 8.6% inhibition of the proaggregating action of AChE on the Aa and a moderate inhibition of Aa self-aggregation (34.9 ± 5.4%). Molecular modelling indicates that binding of compound 11 to the AChE PAS mainly involves the (R)-11 enantiomer, which also agrees with the noncompetitive inhibition mechanism exhibited by p-methoxytacripyrine 11.



Tacripyrines are neuroprotective agents, show moderate Ca2+ channel blocking effect, and cross the BBB, emerging as lead candidates for treating AD.

Brief Biography of the Speaker:
Maria do Carmo Carreiras received her degree in Pharmacy from University of Lisbon in 1977, her Master Sci. in Organic chemistry from University Nova of Lisbon in 1987, and her Ph.D. in Pharmaceutical chemistry from University of Lisbon in 1989 (with honours). In 1985 she was a fellow at the Institut de Chimie des Substances Naturelles (CNRS), Gif-sur-Yvette, France, working under the direction of Prof. Henry-Philippe Husson. From 1986 to 1988 she was a Ph D student at Instituto de Quimica Organica General (IQOG), Consejo Superior de Investigaciones Cientificas of Madrid, working under direction of Prof. Benjamin Rodriguez.
From 1989 to 2006 she was Assistant Professor at the Faculty of Pharmacy, University of Lisbon. In 2006 she was appointed Associate Professor. She has been involved in teaching organic chemistry, heterocyclic chemistry and medicinal chemistry at the graduate and post-graduate level. From 1997 to 2004, in different periods, she was Visiting Professor at the IQOG, in Madrid, working under direction of Prof. Marco-Contelles. In 2005 she was Invited Professor at the Faculty of Sciences, University of Picardie Jules Verne, Amiens, France.
She is a member of the COST D34 Action in the frame of the project Molecular Targeting and Drug Design in Neurological and Bacteriological Diseases.
Her research interests involve the rational design of cholinesterase inhibitors as well as multitarget compounds for Alzheimer's disease.

Plenary Lecture 37

Liposomes in Tuberculosis Diagnosis

Professor P. S. Bisen
Co-authors: Anish Zachariya, R. P. Tiwari
Bisen Biotech & Biopharma Pvt. Ltd.
M-7 Laxmipuram, Transport Nagar
Gwalior, India
E-mail: psbisen@bisenbiotech.com

Abstract: The tuberculosis which is responsible for several millions of deaths in the tropical world can be addressed very effectively if diagnosed at an early stage. The diagnosis of tuberculosis continues to pose serious problems, mainly because of difficulties in differentiating between patients with active tuberculosis and those with healed lesions, normal mycobacterium boris BCG (Bacillus Calmette Guerin) vaccinated individuals, and unvaccinated Manteux positives. The present study explores the potential utility of liposomes in serodiagnosis (antibody as well as antigen based) of tuberculosis in humans. A cock tail of Glycolipid antigens from Mycobacterium tuberculosis H37 Rv were extracted purified and characterized by analytical techniques. The glycolipid antigens were either inserted in to liposomes or injected into rabbits for raising specific polyclonal antibodies. Affinity purified rabbit anti-glycolipid antibodies (IgG) were coupled to liposome particles (0.2-0.4 μm) in presence of 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride and N-hydroxysuccinamide. Antibody-conjugated liposomes were employed by agglutination test for detection specific antigens. A visible dark blue agglutination within 4 minutes is seen if M. tuberculosis antigens are present in the diagnostic specimen. Hundreds of sera samples from subjects with pulmonary tuberculosis and extra-pulmonary tuberculosis were screened for detection of M. tuberculosis specific antigens as well as antibodies by liposomal agglutination tests and the results were compared with conventional tests and those commercially available diagnostic tests. The liposomal agglutination tests were shown to be effective in diagnosing patients with active tuberculosis with high sensitivity and specificity and the prototype kits developed were compared with those commercially available kits in terms not only of sensitivity and specificity but also of rapidity and cost effectiveness. The technology has been evaluated in well known research institutions, hospitals, medical colleges and pathology centers among various parts of our country for it's sensitivity and specificity. The kit worked consistently well at every Institute / hospital where validation studies had taken place. The sensitivity, specificity, simplicity, cost effective ness have been established with clarity. The liposomal agglutination tests demands neither technical expertise nor expensive equipment for reading the result. The result can be read with naked eye and without any ambiguity with in 5 minutes. Another innovative feature of the technology developed is it's longevity even at ambient temperature. The liposomal kits do not require refrigeration either during transport or during storage. Thus the liposome based diagnostic technology is superior to existing ones, cost effective and is first of it's kind in the world.

Brief Biography of the Speaker:
Worked at University of Illinois at Chicago and at University of California, Davis, U.S.A. during 1986-87, Marie Curie Fellow of European Union in 1994,1996 and worked at Lancaster University, Lancaster, UK, DAAD Fellow in Bonn University, Germany in 1997 and 1998, UNDP Fellow at Biological Research Centre, Hungarian Academy of Sciences, Szeged, (1978-1979) and 1982 and WHO Fellow at the Institute of Microbiology, Czechoslovakia Academy of Sciences, Praha, Czecholovakia in 1983. He has served as Professor of Microbiology and Biotechnology, Barkatullah University, Bhopal (1985 - 2001), Vice-Chancellor Jiwaji University, Gwalior (1994 to 1996), Dean, Academic, Planning and Development, Bundelkhand University, JHANSI, (U.P.) June 2004 to July 2005. Director, Madhav Institute of Technology and Science, Gwalior, (2001 - June 2004). Since 2007, Professor Bisen is an Honorary Professor of Biotechnology at Jiwaji University, Gwalior, India.
Presently, Professor Bisen is the Chairman of Bisen Biotech and Biopharma (P) Ltd. - a private equity venture which focuses on diagnostic solutions for widespread diseases. Professor Bisen is also the Chairman of the Vikrant Group, which focuses on advancing technical education through technical institutes at Gwalior and Indore, India.

Plenary Lecture 38

A Simple Surface Plasmon Resonance Biosensor for Detection and Quantification of Recombinant Human Epidermal Growth Factor (rhEGF) in Escherichia Coli Crude Extract

Associate Professor Tau Chuan Ling
Department of Process and Food Engineering
Faculty of Engineering
Universiti Putra Malaysia
43400 UPM, Serdang, Malaysia
E-mail: ltc555@eng.upm.edu.my

Abstract: A reliable detection and quantification assay is important in order to monitor the performance of recombinant human epidermal growth factor (rhEGF) recovery process. Knowing the benefits offered by the surface plasmon resonance (SPR) biosensor, a rhEGF analysis method employing the commercially available BIAcore 3000 equipment was developed by using polyclonal anti-EGF antibody as the capture ligand. The linearity of the assay (determined using the authentic human epidermal growth factor) was found to be in the range of 25 - 250 ng/mL. The performance of the developed assay was further evaluated in terms of accuracy, precision (intra and inter-assay), detection and quantification limit. The practical applicability of the assay was justified as a high accuracy (within 10% recovery of the target) and precision (less than 3.4% CV) were obtained for Escherichia coli crude extract samples. The assay was highly reproducible given that the intra- and inter-assay precision obtained were less than 20 % CV. A considerably high sensitivity was also achieved with 8.0 ng/mL of quantification limit.

Brief Biography of the Speaker:
Ling Tau Chuan obtained his PhD (specialized in the biochemical engineering) from the University of Birmingham, UK in 2002. He then joined Universiti Putra Malaysia as a lecturer and has been serving the Department of Process and Food Engineering, Faculty of Engineering. He is the research coordinator in the department. He has published more than 60 papers in leading scientific journals and conference proceedings. He is an Editorial Board Member to the scientific journal namely, The Open Biotechnology Journal since 2007. He is appointed as a visiting professor at Yuan Ze University, Taiwan from 20 November 2007 to 20 December 2007.

Plenary Lecture 39

Platinum Drugs, Still Essential in our Fight Against Cancer

Associate Professor Janice Aldrich-Wright
Nanoscale Organisation and Dynamics Group
School of Biomedical and Health Sciences
College of Health & Science
University of Western Sydney
Locked Bag 1797, Penrith South DC
N.S.W. 1797 Australia
E-mail: J.Aldrich-Wright@uws.edu.au

Abstract: Introduction
In order to overcome the toxic side-effects of cisplatin and its analogues and the acquired resistance many cancers develop to platinum treatment1 my group has been developing two new families of platinum based anticancer agents, as well as new drug delivery vehicles (DDVs).
Metallointercalators
We have developed a family of over 70 structurally related metallointercalators based on phenanthroline and phenanthroline-derivatives and chiral ancillary ligands which display cytotoxicity at levels up 10-fold lower than cisplatin in many different cancer cells lines which are sensitive or resistance to cisplatin.2-5 In in vivo trials the maximum tolerated dose was found to be around 16 mg/Kg compared to cisplatin (6 mg/kg). We are currently conducting further in vitro and in vivo trials which include efficacy trials in rats with HCT8 colon cancer and nude mice with human breast, lung and colon tumour xenographs.
Sequence Selective Agents
We have been developing a range of platinum-based drugs which include ligands that are capable of binding to specific DNA sequences.6-7 These agents bind to their target sequences with greater affinity than other sequences, are able to prevent RNA synthesis in vitro and unwind DNA helices by up to 13o. We are currently synthesising more soluble forms of these cationic complexes that we hope will have sufficient sequence specificity to selectively bind to telomere regions or mutant p53 genes of DNA.
Drug Delivery Vehicles (DDV)
Cationic lipids have been widely studied for their ability to deliver genes and DNA vaccines for therapeutic purposes. These lipids provide a DNA delivery vehicle into the cell and protect DNA from extracellular degradation. In the 1990's, CSIRO developed a platform drug and gene delivery technology by using a very common buffer, 2-amino-2-hydroxymethyl-propane-1,3-diol (Tris).8-10 It was recognised that Tris could provide a straightforward yet novel method for attaching one, two or three fatty acids to amino acids or peptides to alter their physicochemical properties. Tris cationic lipids (DDV) offer chemical flexibility, readily allowing generation of a range of conjugates with one, two or three different fatty acyl substituents, which can then be tailored, for different functions. Although there has been a lot of interest in the application of cationic lipids for gene delivery, their usage for delivery of anticancer drugs has remained relatively unexplored.

Brief Biography of the Speaker:
Associate Professor Janice Aldrich-Wright; (B.App.Sc., University of Technology Sydney; Ph.D, Macquarie University) is currently based at the University of Western Sydney. She is a Royal Australian Chemical Institute Fellow and her research has been the subject of patent application and more than sixty peer reviewed publications. Over the past 20 years she has established a research group at UWS that focuses on metal complex-DNA interactions with numerous local and international collaborations. Importantly, she has established anticancer compounds which operate under a mode of action different to current clinical alternatives. Innovative bioinorganic molecular design, elegant synthesis and the biophysical and biological testing of these compounds are at the heart of her research drive.

Authors Index