Keynote Lectures

The Effects of Nicotine Exposure on the Complexity and the Genetic
Patterns of Dopamine Neurons in VTA

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Founding Chair, John S Dunn Endowed Chair Professor, Department of Biomedical Engineering, Cullen College of Engineering, University of Houston, Houston, TX, USA

From 6-Ps Medicine to Cardiovascular Health Informatics

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Computer-Aided Interpretation of Vascular Images towards Valid Diagnosis and Risk Stratification of Atherosclerosis

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From reading to writing (and rewriting) the code of life: the future of biology – scientific, ethical, legal, civil and social issues

Christos Ouzounis

Principal Investigator at the Centre for Research & Technology Hellas (CERTH), Thessalonica, Greece, and a visiting Professor at The Terrence Donnelly Centre for Cellular & Biomolecular Research (CCBR), University of Toronto, Canada

The Effects of Nicotine Exposure on the Complexity and the Genetic Patterns of Dopamine Neurons in VTA

Metin Akay

Founding Chair, John S Dunn Endowed Chair Professor, Department of Biomedical Engineering, Cullen College of Engineering, University of Houston, Houston, TX, USA

Abstract

Nicotine, the biologically active substance of tobacco, has been shown to increase the ventral tegmental area (VTA) dopaminergic (DA) neuron firing rate, bursting, and enhancement of dopamine release. The previous studies have shown that most of the VTA DA neurons recorded responded to acute nicotine injection immediately. Both firing rate and bursting were increased in these neurons. However, because of the complex neuronal networks in the VTA, the mechanism by which nicotine affects VTA DA neurons firing is still not clearly understood. We believe that the further studies at both the molecular and cellular levels with multi-scale modeling approach are necessary to shed lights on the nicotine addiction.

Our results have shown that the local field potentials corresponding to the neurons located in the PIF region of the VTA have ApEn values significantly higher ($p = 2 \times 10^{-4}$) in the maternal nicotine cases when compared to the saline. Therefore, we speculate that the dopamine neurons located in the PIF sub-region of the VAT are very likely involved with the nicotine addiction.

In our recent study, we attempted to explore the effects of cigarette smoking on the genetic patterns in the substantia nigra (SN) and the VTA. A few significant differentially expressed genes between the SN and the VTA from nicotine treated Sprague - Dawley (SD) male rats within three different age groups (3 months, 12 months, and 24 months) were analyzed with quantitative real-time polymerase chain reactions. Our data indicated that in both areas, nicotine promotes the expression of the PACAP gene in 3 month old rats. The lipoprotein lipase is up-regulated in the VTA, whereas it exhibits down-regulation in the SN upon nicotine treatment in 3 months old rats, but, nicotine up-regulated the GRP1 expression in both the SN and VTA in 24 months old rats. We speculated that PACAP and GRP1 gene up-regulations by nicotine in the SN may be responsible for reducing the risk of PD.

We are currently exploring the effect of maternal smoking during pregnancy by analyzing the mRNA expressions of a single cell analysis of the infant rats' dopamine neurons using patch-clamp electrophysiology and DNA microarrays. We are trying to identify nicotine-responsive mRNAs and nicotine-induced changes in gene expressions at the single cell level. By using microarray data, we will be able to construct a network of the significant genes to identify functional significance with respect to gene ontology, molecular networks, and canonical pathways.

Prof. Akay, received his B.S. and M.S. in Electrical Engineering from Bogazici University, Istanbul Turkey in 1981 and 1984, respectively and a Ph.D. degree from Rutgers University in 1990. He has played a key role in promoting the biomedical education in the world by writing several prestigious books and editing the Biomedical Engineering Book Series published by the Wiley and IEEE press. Prof. Akay is a recipient of the IEE EMBS Service Award, a IEEE Third Millennium Medal and the IEEE Engineering in Medicine and Biology Society Early Career Achievement Award in 1997, the Young Investigator Award of Sigma Xi Society, Northeast Region in 1998 and 2000, is a fellow of Institute of Physics and IEEE and serves on numerous editorial and advisory boards of several international journals.

From 6-Ps Medicine to Cardiovascular Health Informatics

Yuan-Ting Zhang
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Abstract

Cardiovascular diseases continue to be the leading cause of death worldwide. A cost-effective solution to control cardiovascular diseases is to commence monitoring and modifying risk factors and other possible causes leading to the development of the diseases before noticeable symptoms of illnesses have developed. In essence, future healthcare systems should encourage the Participation of all nations for the Prevention of illnesses and the early Prediction of diseases such that Preemptive treatment is delivered to realize Pervasive and Personalized healthcare, i.e., the paradigm of the 6-Ps medicine [1]. Health informatics plays an important role in implementing the 6-Ps medicine and improving the human health. Advancing health informatics has been identified as one of 14 grand challenges in engineering in the 21st century [2]. This talk will present the concept and challenges of cardiovascular health informatics together with the progress of our project on "Myocardial Infraction and Stroke Screening and Intervention among Nations (MISSIoN 2020)". The enabling technologies such as cardiovascular sensing, imaging, informatics, and intervention (CS3I) that are used in the MISSIoN 2020 project will be discussed in the presentation. Using the MISSIoN 2020 project as an example, we will illustrate that these approaches should allow the practice of 6-Ps medicine that is pervasive, predictive, preventive, personalized, participatory, and preemptive [3,4].

References:
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[4] Y.T. Zhang, "Challenges in Cardiovascular Health Informatics", IEEE Life Sciences Grand Challenges at National Academy of Sciences, USA, (http://www.ieee-lifesci-gc.org/), Oct., 2012.

BIOGRAPHICAL SKETCH

Dr. Yuan-Ting Zhang serves currently the Director of Joint Research Center for Biomedical Engineering and Professor of Department of Electronic Engineering at the Chinese University of Hong Kong (CUHK), Hong Kong, China; and the Director of the Key Lab for Health Informatics of the Chinese Academy of Sciences (HICAS) at SIAT, Shenzhen, China. He became the founding Head of Biomedical Engineering Division at the CUHK in Hong Kong and the founding Director of the CAS-SIAT Institute of Biomedical and Health Engineering in Shenzhen in 2007.

His research spans several fields including wearable medical devices, body sensor networks, bio-THz technologies, bio-modeling, neural engineering, cardiovascular health informatics, and e-p-m-Heath and telemedicine technologies, and is closely tied up to his teaching and publishing activities. He has authored/co-authored over 400 scientific publications and 11 book chapters, and filed 31 patents. His research work has won him and his team a number of Awards including the outstanding conference paper awards, the best journal paper awards for their papers published on IEEE Transactions, the outstanding service award from IEEE-EMBS, and the Asia Pacific ICTA e-Health Grand Award.

Dr. Zhang provided extensively professional services of significant value to the local industries and global academic communities. He served as Associate Editor of IEEE Transactions on Biomedical Engineering, founding Associate Editor of IEEE Transactions on Mobile Computing, Guest Editor for IEEE Transactions on Information Technology in Biomedicine, and Guest Editor for IEEE Communication Magazine. He was previously AdCom member and the Vice-President of the IEEE-EMBS. He served as the Technical Program Chair and the General Conference Chair of the 20th and 27th IEEE-EMBS Annual International Conferences in 1998 and 2005, respectively. He was a member of IEEE Fellow Elevation Committee and the Award Committee for IEEE Medal on Innovations in Healthcare Technology.

Dr. Zhang serves currently on IAMBE Fellow Membership Committee, HK-ITC Projects Assessment Panel, Editorial Board Member for the Book Series of Biomedical Engineering published by IEEE Press and Willey, Chair of the working group for developing an IEEE standard, and Editor-in-Chief of IEEE Transactions on Information Technology in Biomedicine (which will be renamed as IEEE Journal of Biomedical and Health Informatics (J-BHI) starting from Jan. 2013).

Dr. Zhang holds the fellowships from the International Academy of Medical and Biological Engineering (IAMBE), Institute of Electrical and Electronics Engineers (IEEE), and the American Institute of Medical and Biological Engineering (AIMBE) in recognition of his outstanding contributions to the development of wearable medical devices and mHealth technologies.

Dr. Zhang completed his undergraduate and Master Degree studies in 1976 and 1981, respectively, in telecommunication from Department of Electronics of Shandong University and was conferred a Ph.D. in the area of Biomedical Engineering from the Department of Electrical Engineering at the University of New Brunswick in 1990.

Computer-Aided Interpretation of Vascular Images towards Valid Diagnosis and Risk Stratification of Atherosclerosis

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Abstract

Atherosclerosis is a syndrome that affects arterial blood vessels, in which deposits of various substances, such as cholesterol, build up in the inner wall of an artery. This process may begin as early as childhood, its progression is chronic, slow, and cumulative and it finally leads to the formation of atherosclerotic plaques. Although atherosclerotic lesions may remain "silent" for decades, they constitute a usual cause of poor blood circulation, transient ischemic events, heart attacks, and strokes, thereby being strictly associated with cardiovascular disease (CVD). Considering that CVD is the leading cause of death in US and accounts for 41% of deaths in EU, valid detection and risk stratification of atherosclerosis represent a crucial public health challenge.

The degree of stenosis has traditionally been approved as a key point laboratory measurement for the therapeutic decision making (revascularization surgery or medication with statins) of atherosclerosis. However, several studies have proved that most cardiovascular disorders are associated with less severe stenosis, while high stenosis often remain asymptomatic. Given the substantial socio-economic cost of the disease and the risk to patient safety related to the limitations of the current clinical practice, there is an undoubted need for new diagnostic tools that will enhance validity in recognizing vulnerable plaques. To this end, advanced diagnostic procedures are being developed to identify novel risk markers which are related to geometry, morphology and mechanical properties of the arterial wall.

This talk will elucidate the contribution of computerized vascular image processing and analysis in the identification of sophisticated risk markers, including the intima-media thickness, wall shear strains, changes in arterial wall distensibility and the material distribution (fibers, blood, lipids) in atherosclerotic plaques, expressed in terms of texture properties. Advanced methodologies for segmentation, motion estimation and texture analysis of vascular images, as well as measurements derived by applying them to normal and diseased subjects will be presented. A modular software system incorporating these methodologies within a user-friendly environment to facilitate the management and processing of large amounts of imaging data in clinical practice will be illustrated, while the potential of semantic technology in vascular image annotation and retrieval will be discussed.

BIOGRAPHICAL SKETCH

Konstantina S. Nikita received the Diploma in Electrical Engineering, and the Ph.D. degree in Biomedical Engineering both from the National Technical University of Athens (NTUA). She then received her M.D. degree from the Medical School, University of Athens. In 1996, she joined the

Faculty of Electrical Engineering at the NTUA, where she is currently Professor and Deputy Head. Her current research interests include biomedical signal and image processing and analysis, biomedical informatics, biological effects and medical applications of radiofrequency electromagnetic fields, and simulation of physiological systems. Dr. Nikita has authored or edited 8 books and authored or co-authored 160 journal papers and book chapters, and over 300 papers in international conference proceedings. She holds two patents. She has been the technical manager of several European and National Research and Development projects in the field of biomedical engineering. She is member of the Editorial Board of the IEEE Transactions on Biomedical Engineering and guest editor of several international journals. She has been the advisor of twenty completed Ph.D. theses, several of which have received various awards. Dr. Nikita has been the recipient of various honors/awards, among which, the Bodossakis Foundation Academic Prize for exceptional achievements in "Theory and Applications of Information Technology in Medicine" (2003). Dr. Nikita is a member of the Technical Chamber of Greece and the Athens Medical Association. She is also the Founding Chair and Ambassador of the IEEE EMBS Greece chapter, Vice Chair of the IEEE Greece Section, and member of the IEEE EMBS Education Committee. She is also a Fellow of the European Alliance for Medical and Biological Engineering and Science (EAMBES).

Turning data into predictions of gene and protein function

Miguel Andrade

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Affiliate investigator at the Ottawa Hospital Research Institute,
Canada*

Abstract

We are developing methods to use data on gene expression, protein-DNA interactions, protein-protein interactions, protein sequence features and bibliographic data, to produce predictions of the functions of genes and proteins. We have a focus on human disease; I will introduce applications to the search for factors influencing induction of human pluripotent stem cells, and to research on proteins related to neurodegeneration.

BIOGRAPHICAL SKETCH

Miguel Andrade received his Ph.D. in Biochemistry at the Universidad Complutense de Madrid in 1994. He trained at the post-doctoral level at the European Molecular Biology Laboratory in Heidelberg and Cambridge with Chris Sander and Peer Bork. His post-doctoral studies involved the development and application of computational methods for the analysis of gene and protein function and structure. From 2003 to 2007, he was Assistant Professor in the Department of Medicine of the University of Ottawa and Scientist and Head of the Bioinformatics Group of the Ottawa Health Research Instuitute in Ottawa, Canada, where he was promoted to Senior Scientist in 2006. In September 2007 Miguel moved to the Max Delbrück Center for Molecular Medicine in Berlin to start the Computational Biology and Data Mining group. His group (http://cbdm.mdc--berlin.de/) focuses on the development and application of computational methods that are used to research the molecular and gene components of human disease.

From reading to writing (and rewriting) the code of life: the future of biology – scientific, ethical, legal, civil and social issues

Christos Ouzounis

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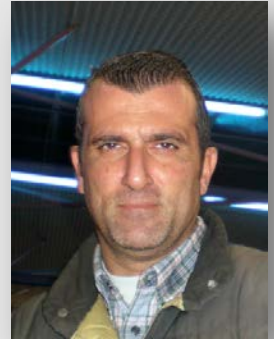
Abstract

The rapid progress in DNA sequencing technology is poised to transform the management of human health and disease. The findings of the human genome sequence have expanded from genetics into human variation, pharmacogenomics and clinical practice. These overarching implications have revealed certain ethical, legal and social issues that will need to be addressed by society at large.

We review basic ideas in large-scale biology, the deciphering of our own genome, examples of mini-breakthroughs in medicine, and the vast quantities of data that have emerged from sequencing. We are now at a point where instead of addressing therapies, we are uncovering genetic variations less prone to disease.

The management of human health and well-being is impacted by the genomic revolution. Human genome equivalent quantities are of the order of thousands and probably soon millions. This wealth of information can transform patient management from general practice to personalized medicine and personal genomics. Patient and citizen participation in this endevour becomes essential.

Thus, as modern medicine concentrates on the p4 concept – predictive, preventive, personalized and participatory – it will require a totally different approach from traditional practice. Precision and effectiveness will become key. Differential and early diagnosis are within reach, with low cost and high accuracy.

Patients and citizens will not only request access rights to data but will probably demand right of exchange of genetic information. We will thus be moving from a 'subject' to a 'consumer' role, with significant implications for clinical genetics.

References:
[1] Ouzounis CA (2012) Rise and demise of bioinformatics? Promise and progress. PLoS Comput. Biol. 8(4), e1002487.
[2] Valeyev NV, Hundhausen C, Umezawa Y, Kotov NV, Williams G, Clop A, Ainali C, Ouzounis C, Tsoka S, Nestle FO (2010) A systems model for immune cell interactions unravels the mechanism of inflammation in human skin. PLoS Comput. Biol. 6(12), e1001024.
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Christos A. Ouzounis is a Principal Investigator at the Centre for Research & Technology Hellas (CERTH), Thessalonica, Greece, and a visiting Professor at The Terrence Donnelly Centre for Cellular & Biomolecular Research (CCBR), University of Toronto, Canada. He received his PhD from the University of York, United Kingdom, for research carried out at EMBL (-1993), and was a Human Frontiers Science Program (HFSP) postdoctoral fellow at the AI Center, SRI International in Menlo Park, CA (-1996). He later led the Computational Genomics Group at EMBL's European Bioinformatics Institute (Cambridge, United Kingdom) (-2005), the Computational Genomics Unit at CERTH (-2007), and the Centre for Bioinformatics at King's College London (-2010). He is an Associate Editor for PLoS Computational Biology, PLoS ONE, and BioSystems, has been an Associate Editor for Bioinformatics, and an editorial board member of a number of journals and the Faculty of 1000. He is a founding officer of the International Society for Computational Biology (ISCB), the Mikrobiokosmos initiative (Greece), and the Hellenic Society for Computational Biology and Bioinformatics (HSCBB). His scientific interests revolve around genome structure, function and evolution, biological sequence comparison, knowledge representation for genomics, synthetic biology, exobiology, personalized biomedicine, and science communication. He has published over 170 scientific reports, which received over 9,500 citations over 20 years, with an h-index of 54. Some of his best known contributions in the field of computational genomics include automated sequence annotation, the discovery of genomic context methods, the inference of metabolic pathways from genome sequences, the development of methods for large-scale clustering of sequence similarities, the definition of the Last Universal Common Ancestor (LUCA), and the quantification of horizontal gene transfer patterns across the "net of life". He also maintains a strong interest in the development of computational biology as an exemplary paradigm in the history of contemporary science.