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Recent Researches in Medicine, Biology & Bioscience

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Plenary Lecture 1

Discrete Event Models Applied in Bioengineering

Associate Professor Calin I. Ciufudean
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Abstract: Discrete event systems (DESs) represent an important chapter of artificial intelligence and have applications in several domains ranging from technical sciences to social sciences, environmental surveillance, bioengineering, and health care.
Biosignals are intensely analyzed using invasive and non invasive techniques. The significance of these measurements related to patient's pathology, as well as doctor's interpretation, are still on progress as emotion biosignals measurement is a hard task that may involve wired or wireless sensors that limit the patients' movement and stress them . Our work is focused on modeling and evaluating the links between physiology of human body and human emotional states using discrete evnt formalisms. We belive, based on some experiments realized in clinical evironment, that this new approach will help specialists to perform a correct diagnosis correlated to patient's expectations and emotional states, as we denoted here "the trust diagnose" (TD).

Brief Biography of the Speaker:
• Academic Positions: Assoc. Professor Ph.D. Eng., Dept. of Automatics and Computers, Faculty of Electrical Engineering and Computer Science, "Stefan cel Mare" University of Suceava, Romania.
• Fields of Scientific Activities: Discrete Event Systems, Complex Measurement Systems, Reliability and Diagnosis of Control Systems, Environmental Management.
• He published 11 books, 12 patents and over 160 scientific papers in conference proceedings and journals.
• Honor Member of the Romanian Society of Electrical & Control Engineering - Member of the Romanian Technical Experts Corp.
• Technical Expert of the Romanian Ministry of Justice.
• President of the Romanian Society of Electrical & Control Engineering, Suceava Branch.
• He is a member of the editorial boards of several international scientific journals and conferences of control systems and electric engineering science. He was designated chairmen at 21 international conferences.

Plenary Lecture 2

Second-Generation Artificial DNA Cutter for Analysis and Manipulation of Human Genome

Professor Makoto Komiyama
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Abstract: We recently developed a DNA cutting tool (Artificial Restriction DNA Cutter; ARCUT) which cuts double-stranded DNA at desired site with desired specificity. This tools is completely chemistry-based and is composed of (1) Ce(IV)/EDTA complex as molecular scissors to hydrolyze the targeted phosphodiester linkages and (2) two pseudo-complementary PNA strands. With the use of ARCUT, the whole genome of human beings (composed of 3 x 109 base-pairs) was cut at one target site. In this lecture, we present further applications of this new tool to various analytical and biological purposes. Typical examples are (1) clipping of the telomere from each of the 46 human chromosomes (choosing either p- or q-arm) and independent analysis of the telomere length of each chromosome, (2) promotion of targeted homologous recombination in human cells, and (3) clipping of a desired DNA fragment from human genome. The first-generation ARCUT thus described is further improved in terms of both the efficiency of site-selective scission and the site-specificity, through chemical modifications of the Ce(IV)/EDTA complex and/or pseudo-complementary PNA, extending the scope of the applications. Furthermore, a new type of ARCUT which selectively cuts the telomeric repeat of human beings (-GGGTTA-) will be 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 4 years at Northwestern University (Illinois, USA) as a postdoctoral fellow, he became an assistant professor of the University of Tokyo, and then an associate professor of University of Tsukuba. In 1991, he became a professor of the University of Tokyo. In 2012, he retired from the University of Tokyo and moved to Life Science Center of Tsukuba Advanced Research Alliance, University of Tsukuba. His main research area is bioorganic and bioinorganic chemistry, and the number of original papers is more than 500. 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, Award from Cyclodextrin Society of Japan, The Award of the Society of Polymer Science, The Chemical Society of Japan Award, and SPSJ Award for Outstanding Achievement in Polymer Science and Technology, and others.

Plenary Lecture 3

Systems Molecular Medicine for Cancer Metastasis and Drug Discovery

Professor Hiroshi Tanaka
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Medical Research Institute
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Abstract: Epithelial-mesenchymal transition (EMT) is now widely recognized as the cause of cancer invasion and metastasis. From the dynamical systems view of the cellular molecular network, it is considered that each cell type represents the stable state of cellular molecular network which could be thought as a basin located in the epigenetic landscape, separated by “epigenetic barrier”. Thus, EMT could be considered as global “phase transition” of transcription network from the stable cellular network state of epithelial cell to that of mesenchymal cell. We developed a new method which can depict this epigenetic landscape quantitatively based on the statistics of fluctuation of the gene expression. To depict the EMT process on the epigenetic landscape, we conducted the experimental observation of temporal change of gene expression profile during EMT of retinal pigment epithelium cell line (ARPE-19) caused by TGF-beta and TNF-alpha. The ARACNe algorithm was used to infer structural change of gene regulatory network of about 4000 genes. The results showed that in the initial stage, keratin (KRT18) and e-cadherin (EDH1) are active, while TWIST1/2, ZEB1 and TCF3 start to globally regulate EMT process, and in final stage, messenchymal marker such as CD44 and COL1A are expressed. The global cooperative change of gene expression pattern was observed to suggest that the collective structural change of molecular network is taking place during EMT process which can be depicted on the quantitative epigenetic landscape.
Furthermore, the network hierarchical structure of protein interaction networks (PIN) and their relationship with lethal genes and possible drug targets was studied, so that the statistical likelihood of novel drug targets could be inferred. Our study revealed “three-layer structure” of PIN, and middle-layer nodes compose the backbone of PIN. Drug-target molecules are distributed with higher probability on middle degree layer. While the average degree of targets for cancer drugs was 7.82, the targets for non-cancerous diseases scored only 4.24 ($p = 0.01$). The reason is considered that, cancer is contracted mostly after reproduction period so that evolutional process has not eliminated cancer disease genes.

Brief Biography of the Speaker: Prof. Tanaka obtained a BS and MS degree from Mathematical Engineering, University of Tokyo (Japan), in 1974 and 1976, respectively. He got Dr. Med. from graduate school of medicine, University of Tokyo, in 1981 and Ph.D. in computer science from graduate school of engineering, University of Tokyo, in 1983. He was installed as an assistant professor of medicine, University of Tokyo in 1982. He was a visiting scientist at MIT laboratory of computer science during 1990. He was installed as a professor of bioinformatics, Medical Research Institute, Tokyo Medical and Dental University in 1991. He was the director of Information Center for Medicine in Tokyo Medical and Dental University from 1995-2010. He was Dean of School of Biomedical Science from 2006 to 2010. He worked as the president of Japan Association of Medical Informatics from 2003-2007. He is now chairman of Chem-Bioinformatics association and also that of the Japan association of Omics-based medicine, acting as one of the leaders of genomic medicine and translational bioinformatics in Japan.

Plenary Lecture 4

Oncoproteomics: Challenges, Techniques and Possibilities to Cancer Biomarker Discovery

Professor Shaden Muawia Hanafy
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Abstract: Proteomics is the large-scale study of the structure and function of proteins in complex biological sample. Such an approach has the potential value to reveal the complexity and heterogeneity of the human proteome. In addition, proteomics has been complemented by the analysis of posttranslational modifications and techniques for the quantitative comparison of different proteomes..Oncoproteomics is the study of proteins and their interactions in a cancer cell by proteomic technologies and parallels the related field of oncogenomics. There is an intense interest in applying proteomics to improve understanding of cancer pathogenesis, develop new tumor biomarkers for diagnosis, and early detection using proteomic portrait of samples. In pace with the successful completion of the Human Genome Project, the wave of proteomics has raised the curtain on the postgenome era. The study of oncoproteomics provides mankind with a better understanding of neoplasia. . It is now contributing to the development of personalized management of cancer. In recent years, substantial technological advances in proteomics have permitted the quantitative analysis and identification of protein changes associated with cancer. Tumor-associated biomarkers that can be determined via proteomic approaches represent a subset of possible cancer targets. To achieve this, several proteomic approaches including two-dimensional polyacrylamide gel electrophoresis, mass spectrometry and protein microarray have been developed and are being used in different combinations. This review provides an overview of the proteomic approaches available for cancer target identification and reviews recent analyses of protein expression in various cancers.

Brief Biography of the Speaker: Dr Sh. Muawia holds a BSc in Biochemistry from Faculty of Science- Alexandria University-Egypt. She holds a Master degree & a PhD in Biochemistry (1992, 2001 respectively) from the Faculty of Science- Alexandria University. She works as a Professor of Biochemistry and Molecular Biology in the Molecular Biology department in Genetic Engineering and Biotechnology research Institute (GEBRI) - Minofya University- Sadat City. Her research interests include: Apoptotic signalling pathway and apoptotic markers in different tumors (adult acute myeloid leukemia and in Hepatocellular Carcinoma) and in HCV patients. Single nucleotide polymorphism and gene expression of different genes in various diseases and tumors. Oxidative stress and antioxidant defence beside cytokine expression on the molecular and protein levels. She has 30 publications in highly rated ISI journals and attends 28 conferences.

Plenary Lecture 5

Adult T-Cell Lymphoma/Leukemia - Mysterious Disease

Associate Professor Kazuhiko Natori
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Abstract: The majority of malignant lymphoma and leukemia is unexplained. Adult T cell leukemia/lymphoma(ATLL) is a malignant tumor that develops virus-induced blood only from HTLV-I carrier. Over the world, the distribution of HTLV-I carriers are very unevenly distributed. Caribbean coast countries, South America, African central part, Papua New Guinea, etc. are known as the area where the ratio of the HTLV-I infectee is high. In Japan, the areas with a high proportion of infection HTLV-I. HTLV-I infection route is, breastfeeding, blood transfusions, and sexual intercourse may be mentioned. The rate of infection is high so that age is high. In Japan, the incidence of ATL lifetime is estimated to be 4-7% for men and 2-5% for women. Diagnosis of ATLL antibodies HTLV-I anti-positive, in peripheral blood, type lymphoma in the lymph nodes, admitted ATLL cells with a nucleus like clover, acute form into leukemia, chronic type, in the smoldering typical example diagnosis is easy. A prognosis is extremely poor in a hematopoietic malignancies Median period of all over survival appeared in acute type 6 month, lymphoma type10 month. As a result, there is a limit in the treatment strategy only for chemotherapies more. Future, the discovery of useful prognostic marker, it is necessary to develop a method for treating patients with low adverse event is aging.

Brief Biography of the Speaker: I entered Tokyo college of Pharmacy division of biochemical pharmacy at April 1983 and graduateted at March 1987. In 1989, I entered Toho university medical course and gradutated March 1995. I became a doctor. I selected Hematology for my special field. Now I engaged in Oncology. I also belong to Chemotherapy Center of Toho university Medical Center and I am central director. It is related to the chemotherapy now. The theme of the research is double cancer, therapy related leukemia/myelodysplastic syndrome, cancer family history and carcinogenesis. I want to amplify knowledge to the chemotherapy whole and to live in the future.

Plenary Lecture 6

Relationships Among the Hippocampus, Dentate Gyrus, Mammillary Body, Fornix, and Anterior Commissure from a Viewpoint of Elements

Professor Yoshiyuki Tohno
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Faculty of Medicine
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Abstract: To elucidate compositional changes of the brain with aging, the author previously investigated age-related changes of elements in the corpus callosum, anterior commissure, and fornix of the white matter and the pineal body, olfactory bulb and tract, mammillary body, hippocampus, dentate gyrus, basal ganglia, superior colliculus, and lateral geniculate body of the gray matter and found that the Ca content increased significantly in the mammillary body, hippocampus, and putamen with aging, and the Mg content increased significantly in the hippocampus, fornix, putamen, and globus pallidus. The elements changing significantly with aging were different among the various brain regions.

To elucidate the relationships among the brain regions belonging to the limbic system, the author investigated the relationships among the hippocampus, dentate gyrus, mammillary body, and fornix, using the anterior commissure as a control, from a viewpoint of elements. After ordinary dissections at Nara Medical University were finished, the hippocampi, dentate gyri, mammillary bodies, fornices, and anterior commissures were removed from identical cerebra of Japanese subjects. The subjects consisted of 23 men and 23 women, ranging in age from 70 to 101 years (average age=83.5±7.5 years). After incinerating with nitric acid and perchloric acid, element contents were determined by inductively coupled plasma-atomic emission spectrometry. With regard to seven elements of Ca, P, S, Mg, Zn, Fe, and Na, it was examined whether there were significant correlations among the hippocampus, dentate gyrus, mammillary body, fornix, and anterior commissure. It was found that there were extremely or very significant direct correlations among all of the five brain regions of the hippocampus, dentate gyrus, mammillary body, fornix, and anterior commissure in the P content. Likewise, with regard to the Fe content, there were significant direct correlations among the four brain regions belonging to the limbic system, except for the anterior commissure. In both the Ca and Zn contents, there were extremely or very significant direct correlations among the hippocampus, dentate gyrus, and mammillary body of the gray matter. Assuming that the P content indicates metabolically active cell density, namely, the number of active cells per volume, there may be significant direct correlations among active cell densities of the hippocampus, dentate gyrus, fornix, mammillary body, and anterior commissure. In other words, the cerebrum with a high active cell density in one brain region also has high active cell densities in the other brain regions.

Brief Biography of the Speaker: Yoshiyuki Tohno was born in Osaka, Japan, in 1944. He graduated from Nara Medical University, Japan, in 1969. He received Medical Doctor Degree from Nara Medical University, Japan, in 1984. From 1984 to 1996, he was an Associate Professor at the Department of Anatomy, Nara Medical University, Japan. From 1996 to 2009, he was a Professor at the Department of Anatomy, Nara Medical University, Japan. In 2009, the title of Professor emeritus was bestowed upon him from Nara Medical University. Since 2004, he has been a Visiting Professor of Fujian Medical University, P. R. China. From 2009 to the present, he has been a Visiting Professor at the Department of Anatomy, Faculty of Medicine, Chiang Mai University, Thailand. He is mainly interested in compositional changes of human tissues, such as the arteries, cardiac valves, sino-atrial node, myocardium, brain, cartilages, bones, ligaments, and tendons with development and aging. He is an active member of New York Academy of Sciences, a member of International Association of Bioinorganic Scientists, a member of Fuzhou Giant Panda Research Center, P. R. China, a member of Primate Research Institute of Kyoto University, and on the Editorial Boards of Nephrology: Advances and Applications and ISRN Vascular Medicine.

Plenary Lecture 7

Advances, Challenges and Shortcomings of Epilepsy Drug Treatment

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Abstract: Epilepsy is the group name for convulsion symptom arising from neural organized function deficits originated within or outside the brain. Since considerable number (around 50million people) of the World population of all ages is affected, it is one of health care problems worldwide. Many drugs have been used in the past to relive symptoms by inducing changes in permeability to specific ions thus to stabilize membranes and interfering with release of neurotransmitters or other mechanisms. Nowadays, there are more drugs, but no one is developed for causal therapy as classification of epilepsy itself is very complex despite advanced technology utilization for diagnostic strategies. Although there is continuous emergence of new agents, pharmacoresistant symptom and adverse reactions including drug-drug interactions continue to challenge. Hardly preventable adverse effects (gastrointestinal, mental, or behavioural, neurologic or less commonly dermatological, haematological, hepatological) by some agents may lead to reduction of quality of life, whereas some agents are known teratogens. In spite of significant all developments in the field, no drug is considered as causal therapy for epilepsy to date. Thus the aim of antiepileptic drug prescription after management of emergency situation like status epilepticus is prophylactic rather than therapeutic. The purpose of this paper is to emphasize practical challenges and shortcomings associated with old and new antiepileptic drugs (AEDs).The paper also discusses the importance of therapeutic drug monitoring with very qualified interpretation and close interdisciplinary work of clinician and laboratories determining the drug plasma levels. Some case studies are purposely included in the paper as useful demonstration, how therapeutic drug monitoring is of vital importance in very challenging situations of epilepsy management.

Brief Biography of the Speaker: The author is MD, and PhD graduate of the Charles University, in Prague. Trained as Paediatrician and later as Clinical Pharmacologist, holds Board Certificate from the Institute for Postgraduate Education in Medicine. His present position is consultant in clinical pharmacology at the faculty hospital. The main interest and consultancy area of the author is in particular therapeutic drug monitoring in needy patients including, paediatric and geriatric populations given their pharmacokinetic/pharmacodynamic differences and vulnerability. The author participated in bioequivalence studies and clinical trials including as principal investigator and co-investigator. He is also dedicated to aid dosage adjustment for transplantation patients, oncology patients and others in intensive care including those with renal failure. The author participates in pregraduate and post graduate education both as a faculty member and as invited speaker in the field of clinical pharmacology dedicated for safe and better use of medicines for human wellbeing.

Plenary Lecture 8

Recent Achievement of Research in a Neuron and Its Group in Brain

Professor Atsushi Fukasawa
Institute of Statistical Mathematics
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Abstract: He will present recent results of studies in a neuron and its group as a system in brain. A brain seems like a space with huge number of neurons with variety of functions related to activities of life and intelligence. To find the substance of brain, both of individual and group of neurons must be known exactly. He focused the study first to know the principle of operation of a neuron, and found that it is a three port electrolyte device capable of pulse generation or signal amplification.
He focused the study secondly to know how a group of neurons are gathered to realize a function as a system. By introducing the concept of recurrent connection and mutual pulse injection among neurons, a synchronous neural system is given clearly. Now this neural system operates as an actual system to treat values in physical measures of time, space, and motion defined by events. This capability provides topographical mapping function in brain with basis of knowledge.
He will present a new viewpoint to summarize result of studies achieved by the author and the colleague, and he will present a concept to develop neurology later on.

Brief Biography of the Speaker: Atsushi Fukasawa received the B.S. degree in Electrical Engineering from Chiba University in 1962, the Master of Arts degree in Electrical communication and the Ph.D. degree from Waseda University in 1967 and 1983.
He joined Graduate School of Science and Technology, Chiba University as a professor in 1997.
He received the Award of the Ministry of Science and Technology, Japan in 1967, and received the Ohm Science and Technology Prize from Ohmsha in 1994 respectively. He received also the Prize on Telecommunication System Technology from the Foundation of Telecommunication Association, Japan in 2004. He is a senior member of the IEEE.

Plenary Lecture 9

Methotrexate-Induced Intestinal Barrier Dysfunction

Professor Toshiharu Horie
Biopharmaceutics and Molecular Toxicology Unit
Faculty of Pharmaceutical Sciences
Teikyo Heisei University
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Abstract: Methotrexate (MTX), a folate antagonist and inhibitor of the dihydrofolate reductase, has been used for the treatment of acute leukemia, rheumatoid arthritis, and intraosseous sarcoma. MTX is known to induce gastrointestinal toxicity such as abdominal pain, diarrhea and nausea. We found production of reactive oxygen species, change of intestinal permeability, change of Zonula Occludens-1 which forms tight junction, and neutrophil infiltration in the small intestine of MTX-treated rats. Intending to investigate the mechanism of MTX-induced intestinal barrier dysfunction, we measured the release of IL-8 (neutrophil chemotactic factor) into cultured medium of T84 (human colonic carcinoma cell) exposed to MTX for 72 hr (conditioned medium). Neutrophil transmigration across T84 monolayer was assessed in a transwell migration study. The results showed that there was significant elevation of IL-8 production and release into cultured medium on exposure to MTX for 72 hr. In the transmigration assay, significant neutrophil migration across the T84 monolayer was observed on the addition of the conditioned medium. This increase of transmigration was inhibited by the addition of neutralizing antibody to IL-8. From these results, MTX-induced release of neutrophil chemotactic factor (IL-8) resulted in the intestinal neutrophil migration which may possibly lead to exacerbation of inflammation.

Brief Biography of the Speaker: Toshiharu Horie graduated from the University of Tokyo, Faculty of Pharmaceutical Sciences in 1972. After he graduated from its Graduate School of Pharmaceutical Sciences, he got a position of an assistant professor in Tokyo University of Pharmacy and Life Sciences, and then, became an associate professor in 1992. He moved to Chiba University, Faculty of Pharmaceutical Sciences as a professor in 1994 and became a professor of Chiba University, Graduate School of Pharmaceutical Sciences in 2001. He became a professor emeritus of Chiba University in 2013 and is a professor of Teikyo Heisei University, Faculty of Pharmaceutical Sciences, from 2013. His research area is biopharmaceutics and drug toxicity.

Plenary Lecture 10

Calcineurin Inhibitor in Autoimmune Enteropathy Management

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Abstract: Autoimmune enteropathy (AIE) is an entity reported primarily in infancy, resulting in intractable diarrhoea and associated with small bowel villous atrophy and the presence of circulating anti-enterocyte antibodies. It is a multisystem disorder with a response, in many cases, to immunosuppressive therapy. However, small bowel enteropathies that are associated with an autoimmune process are often resistant to initial treatment. Cyclosporine is a well known calcineurin inhibitor and potent immunosuppressive drug mostly used in organ transplantation. Since the mid-1980s, this drug is also being used to treat patients with inflammatory bowel diseases. At this time, cyclosporine is most useful in severely ill patients with ulcerative colitis, who have not responded to corticosteroid therapy. In such patients, intravenously administered cyclosporine may be highly effective for rapid disease control, thus changing a risky emergency situation into a less urgent procedure. However, cyclosporine is lipid-bound and may be associated with an increased risk of seizures when it is administered to acutely ill, severely malnourished patients with mal lipid absorption. The drug has a significant side effect profile that includes renal insufficiency and hypertension in some individuals. Therefore, therapeutic drug monitoring (TDM) is required for dosing of the drug to optimize immunosuppressive efficacy, while minimizing its side effects. Some data also indicate a correlation between trough concentrations and area under the curve (AUC), whereas others recommend 2 hours post dose (C2) drug concentration monitoring. The objective of the present paper is to demonstrate case model of effective outcomes of autoimmune entreopathy after therapeutic drug-monitoring guided calcineurin inhibitor, cyclosporine-A (CSA) therapy in a paediatric patient. The paper also discusses the new insights on mechanisms of action of calcineuin to control autoimmune diseases in general and autoimmune bowel diseases in particular.

Brief Biography of the Speaker: The author is MD, and PhD graduate of the Charles University, in Prague. Trained as Paediatrician and later as Clinical Pharmacologist, holds Board Certificate from the Institute for Postgraduate Education in Medicine. His present position is consultant in clinical pharmacology at the faculty hospital. The main interest and consultancy area of the author is in particular therapeutic drug monitoring in needy patients including, paediatric and geriatric populations given their pharmacokinetic/pharmacodynamic differences and vulnerability. The author participated in bioequivalence studies and clinical trials including as principal investigator and co-investigator. He is also dedicated to aid dosage adjustment for transplantation patients, oncology patients and others in intensive care including those with renal failure. The author participates in pregraduate and post graduate education both as a faculty member and as invited speaker in the field of clinical pharmacology dedicated for safe and better use of medicines for human wellbeing.