NSF Summer Institute Short Course

Cancer Nanotechnology: analysis, imaging and treatment over multiple scales

Location: **Houston/TMHRI**
Dates: **7 – 9 June 2011**

Program and Lecturers

Instructors

1. Paolo Decuzzi (The Methodist Hospital Research Institute)
2. Mauro Ferrari (The Methodist Hospital Research Institute)
3. King Li (The Methodist Hospital Research Institute)
4. Wing Kam Liu (Northwestern University)
5. Stephen T.C. Wong (The Methodist Hospital Research Institute)
6. Jarek Wosik (University of Houston)

Course Organization

The integration of Nanotechnology with biomedical research and practice has already shown profound effects on the diagnosis, treatment and prevention of a variety of diseases, including cancer, generating a new scientific field known as Cancer Nanotechnology. Drug formulations based on injectable particulate systems are already used in the clinic for the treatment of breast and ovarian cancers, for hepatocellular carcinoma and leukemias; multifunctional nanoparticles incorporating both therapeutic and contrast agents for treatment and imaging are currently in clinical trials. Cancer Nanotechnology is the field where knowledge pertaining to chemistry, physics, mathematics and all the engineering sciences are fused with cancer biological and biomedical notions to solve truly multidisciplinary and complex problems with the guiding aim of being of true benefit to the humankind. Consequently, the course will provide first an overview of the main nanotechnological devices so far developed and under development for cancer treatment, imaging and analysis; second, a comprehensive description of nanoparticle systems available for the treatment and imaging of diseases including the fabrication/synthesis methodologies, the physico-chemical processes and laws governing their behavior and performances in vivo and the engineering criteria for their rational design and quality testing; followed, by the in silico and in vivo analysis of their transport mechanics within the vascular and extravascular compartment over multiple scales; and finally new therapeutic strategies on the electromagnetic and near-infra red thermal ablation of tumors. In each lecture, the nanotechnological devices will be described elucidating the biophysical and biochemical mechanisms governing their behaviors and performances and providing all the mathematical and engineering tools required for their analysis and optimal design.

The main objectives of the NSF Summer Institute on "*Cancer Nanotechnology: treatment, imaging and analysis over multiple scales*" are:

1 to present multiscale mathematical models for the analysis of blood flow in patient-specific vascular networks (both at the macro- and micro-circulation) and for the rational design of intravascular injectable nanoparticles;
2 to review the field of cancer nanotechnology, focusing in particular, on the rational design of nanoparticles for the treatment and imaging of tumor lesions;
3 to present the state of the art in cancer imaging over multiple spatial and temporal scales, with an emphasize on the development of new imaging techniques and on the combination of imaging and mathematical modeling;

4 to introduce the new field of particle-based hyperthermia, elucidating the physical mechanisms and the applications to tumor tissue ablation
5 to train future and practicing engineers, scientists and educators in the emerging areas of cancer nanotechnology.

DAY 1

8:00 – 9:00 *Cancer Nanotechnology*
Mauro Ferrari, PhD – TMHRI
9:00 – 11:30 *Rational Design of Nanoconstructs I - Basics*
Paolo Decuzzi, PhD – TMHRI

1:00 – 2:30 *Multiscale modeling and simulation of flow driven transport analysis of drug carriers and nanoparticle-enabled drug/gene delivery I*
Wing Kam Liu, PhD – Northwestern University
3:00 – 4:30 *Multiscale modeling and simulation of flow driven transport analysis of drug carriers and nanoparticle-enabled drug/gene delivery II*
Wing Kam Liu, PhD – Northwestern University

DAY 2

9:00 – 11:30 *Basics of imaging: Why do we need so many imaging modalities?*
King Li, MD, MBA – TMHRI
1:00 – 2:30 *Design of combined imaging and therapeutic nanocarriers: What are the key requirements for in vivo applications?*
King Li, MD, MBA – TMHRI

3:00 – 4:30 *Rational Design of Nanoconstructs II – An Integrated Approach*
Paolo Decuzzi, PhD – TMHRI

DAY 3

8:00 – 10:30 *The Needle in a Haystack: Multi-scale imaging for target discovery and biomarker development in the molecular medicine era I*
Stephen Wong, PhD - TMHRI
11:00 – 12:30 *The Needle in a Haystack: Multi-scale imaging for target discovery and biomarker development in the molecular medicine era II*
Stephen Wong, PhD - TMHRI

2:00 – 3:30 *Alternating EM field in cancer thermal ablation*
Jarek Wosik, PhD – University of Houston

Cancer Nanotechnology

Speaker: Dr. Ferrari serves as President and CEO of The Methodist Hospital Research Institute, where he holds the Ernest Cockrell Jr. Distinguished Endowed Chair. He is also Professor of Internal Medicine at the Weill Cornell Medical College, Adjunct Professor of Experimental Therapeutics The University of Texas M.D. Anderson Cancer Center, Professor of Bioengineering at Rice University, Adjunct Professor of Biomedical Engineering at UT Austin, and President of The Alliance for NanoHealth in Houston. Dr. Ferrari is a founder of biomedical nano/micro-technology, especially in their applications to drug delivery, cell transplantation, implantable bioreactors, and other innovative therapeutic modalities. In these fields, he has published more than 200 peer-reviewed journal articles and 6 books. He is the inventor of more than 30 issued patents, with about thirty more pending in the US and internationally. His contributions have been recognized by a variety of accolades, including: the Presidential Young Investigator Award of the National Science Foundation; the Shannon Director's Award of the National Institutes of Health; the Wallace H. Coulter Award for Biomedical Innovation and Entrepreneurship; and the Italiani nel Mondo Award from the Italian Ministry of Foreign Affairs. His career research and development portfolio totals over $50 million, including support from the NCI, NIH, DoD, NASA, NSF, DARPA, DoE, the State of Texas, and the State of Ohio, The Ohio State University, and several private enterprises. He began his academic career at the University of California, Berkeley, where he tenured in Material Science, Civil Engineering, and Bioengineering. Upon recruitment to the Ohio State University, he served as the Edgar Hendrickson Professor of Biomedical Engineering, Professor of Internal Medicine, Mechanical Engineering, Materials Science and Associate Vice President, Health Sciences Technology and Commercialization, Associate Director of the Dorothy M. Davis Heart and Lung Research Institute and Director of the Biomedical Engineering Center. Upon recruitment to Houston, he served as Professor and Chair of the Department of Nanomedicine at the University of Texas Health Science Center. Dr. Ferrari also served as Special Expert on Nanotechnology at the National Cancer Institute in 2003-2005, providing leadership into the formulation, refinement, and approval of the NCI's Alliance for Nanotechnology in Cancer, currently the world's largest program in medical nanotechnology. Dr. Ferrari's degrees are in Mathematics (Padova, 1985, Italy), and Mechanical Engineering (U.C. Berkeley, M.S. 1987, & Ph.D. 1989). He attended medical school at the Ohio State University (2002-03). Dr. Ferrari is an academic-entrepreneur, with several companies that originated from his laboratory. He currently serves on the Board of Director three companies: Nanomedical Systems of Austin TX; Leonardo Biosystems of Houston TX, and NASDAQ-traded Arrowhead Research Corporation (NASDAQ:ARWR).

Rational Design of Nanoconstructs

Nanoconstructs are multifunctional particle-based devices for the ‘smart’ delivery of agents for biomedical imaging and thermal ablation therapy. The objective of this lecture is twofold: i) describe an integrated approach for the rational design of particle-based systems intended to target specifically and with high efficiency the diseased vasculature, whilst minimizing the non-specific uptake in organs of the reticulo-endothelial system; ii) present a new class of multifunctional nanoconstructs providing superior T1 contrast enhancement for MR imaging and thermal ablation capabilities under non invasive ElectroMagnetic fields. The rational design of nanoconstructs is based on an integrative approach where the mathematical modeling of the vascular transport and adhesion of blood-borne nanoparticles is combined with in-vitro assays in parallel plate flow chamber systems and in-vivo characterization in small animals. The multifunctional nanoconstructs are based on nanoporous silicon particles, exhibiting a variety of size and shape combinations, loaded with different families of Gd-based contrast agents, namely the commercially available Magnevist®; Gd-nanotubes and Gd-fullerenes. These nanoconstructs can also generate significant thermal toxicity inducing cell death and/or apoptosis in the presence of external alternating electrical and magnetic fields operated in different frequency regimes.

Speaker: Paolo Decuzzi is a Senior Scientist/Professor of Biomedical and Mechanical Engineering at The Methodist Hospital Research Institute. Dr. Decuzzi earned his M.S. degree in Mechanical Engineering from the Politecnico of Bari (IT) in 1997 and his Ph.D. degree in Mechanical Engineering from the University of Naples – Federico II (IT) in 2000. He has been visiting fellow and faculty in several Academic and Research Institutions including The University of Michigan – Ann Arbor (MI); the Princeton Material Institute – Princeton (NJ); the Leibniz Institute for New Materials in Saarbrücken (D). Dr. Decuzzi has published more than 100 papers in international peer-reviewed journals, international conferences and book chapters; and holds 5 US Patent Office applications in the field of nanoparticle-based biotechnology. He chairs the NanoCouncil of the American Society for Mechanical Engineers (ASME) and his research activity is primarily supported through the NIH and DoD in USA, and the ESF in EU. PDecuzzi@tmhs.org

Imaging Considerations for Cancer Technology

There are tremendous variations in sensitivity, specificity, spatial resolution, temporal resolution, contrast resolution and tissue penetration in the different imaging techniques used for in vivo imaging. The major objectives of this part of the course are: (1) describe the various in vivo imaging techniques used for both pre-clinical and clinical applications; (2) compare the pros and cons of the various imaging techniques and illustrate why specific imaging techniques are more preferable than others in specific applications; (3) describe the principles in designing nanoparticle imaging agents; (4) describe the principles in designing combined nanoparticle imaging and therapeutic agents. A targetable polymerized and partially polymerized liposome system will be used to illustrate how to go from initial concept to successful in vivo imaging and therapeutic experiments.

Speaker: Dr. King Li is the M.D. Anderson Foundation Distinguished Chair in Radiology and Imaging Sciences, Professor of Radiology, Weill Cornell Medical College, Adjunct Professor of Bioengineering, Rice University and Chair of the Radiology Department, The Methodist Hospital. Dr. Li graduated from Faculty of Medicine, University of Toronto in 1981 and finished his residency in 1986 also at U. of T. Before joining the Methodist he was the Associate Director of the NIH Clinical Center and the Chief of Radiology and the Imaging Sciences Program. Dr. Li was on faculty in Stanford University School of Medicine for 10 years prior to joining the NIH. Dr. Li's main research interest is in molecular imaging, molecular image guided therapy, and integrating imaging with tissue analysis for studying systems biology. He has 9 issued and 6 pending patents, has won over ten different awards from four different professional organizations and has given numerous invited lectures. He has published over 100 scientific articles, 5 book chapters and 1 monograph and has received many grants from government, industry and private sources. Kli@tmhs.org

Multiscale modeling and simulation of flow driven transport analysis of drug carriers and nanoparticle-enabled drug/gene delivery

The lecture opens with an introduction on the development of a software system based on multiscale, multiphysis immersed electrokinetic finite element methods coupled with molecular dynamics for the analysis and design of nano-devices in bio-sensing and drug/gene transport. Multiscale uncertainty quantification techniques and validation experiments for the design of nanodevices in biotechnology and medicine will also be presented. The lecture will be followed by three illustrations of state of the art applications in nano-bio technology: (1) The coupling of the Navier-Stokes equations and cell-cell-particle interaction in the framework of the immersed molecular finite element method and meshfree method provides a unique tool to model complex blood flows with deformable cells and bio-molecules within micro- and capillary vessels in three dimensions; (2) flow driven transport analysis of drug/gene carriers and (3) the design of a nano-particle-enabled drug/gene delivery device for cancer therapy.

Speaker: Wing Kam Liu is Walter P. Murphy Professor of Mechanical Engineering at Northwestern University and Founding Chair of the ASME NanoEngineering Council. He received his B.S. from the University of Illinois at Chicago; his M.S. and Ph.D. both from Caltech. He is a world leader in multiscale simulation-based engineering and science and has applied a spectrum of atomistic, quantum, and continuum strategies towards the understanding of nanomaterial function and biological processes. He was the first to develop concurrent multiscale methods for materials design. These methods have been used to design new alloys and nano-composites. Recently, he has developed the 3D immersed electrokinetic molecular finite element method for modeling the microfluidic electrokinetic assembly of nano wires and filaments and bio-molecules. This transformative bio-nanotechnology has the potential to revolutionalize drug delivery system to achieve the desired therapeutic effects. Selected honors include the 2009 Dedicated Service Award, the Robert Henry Thurston Lecture Award, the Gustus L. Larson Memorial Award, the Pi Tau Sigma Gold Medal and the Melville Medal, (all from ASME); the John von Neumann Medal from US Association of Computational Mechanics (USACM); and the Computational Mechanics Awards of the International Association of Computational Mechanics (IACM) and the Japanese Society of Mechanical Engineers. Liu chaired the ASME Applied Mechanics Division and is past president of USACM. He is listed by the Institute for Scientific Information as one of the most highly cited researchers in engineering. He is the editor of two International Journals and honorary editor of two journals and has been a consultant for more than 20 organizations. Liu has written three books, the Finite element book becomes a classical in the field and the Nano Mechanics and Materials book received a very favorable review by Nanotoday (Nov, 2006). w-liu@northwestern.edu

The Needle in a Haystack: Multi-scale imaging for target discovery and biomarker development in the molecular medicine era

Imaging has long lagged the throughput and visibility of other biological modalities in the era of molecular medicine, but recent improvements are putting it back on the radar screen as a systems-scale tool to view and interrogate cells, tissues, or even whole organisms over time and space. Scientists are beginning to ask genome- or proteome-scale questions using high throughput imaging modalities, whereas combining imaging with other biotechnologies promises to bring molecular medicine into a new and exciting level with the potential of translating scientific discovery from lab bench to healthcare delivery at patient bedside, and back. In this lecture, I will describe representative biological questions being investigated and associated clinical developments in our group. The corresponding imaging acquisition devices being investigated ranging from high resolution fluorescence microscopy and automated multi-well in vitro bioassays to in vivo MRI/PET and molecular image-guided interventions. I will present systematic integration of image phenotype information with multiple levels of biological information to better understand the mechanism of diseases and provide potential targets and biomarkers for drug development, disease prediction, diagnosis, therapeutic intervention, and monitoring. The multi-scale imaging requires not just the development of new computational algorithms and modeling approaches, but also may demand a new kind of mathematics to make sense of complex, voluminous, heterogeneous life science signals and data at the abstract-theoretical level.

Speaker Stephen TC Wong, PhD, MSc (EECS, Lehigh University '91 '89), BE (EE Hons, U. Western Austrialia '83), PE (EE '90), is John S Dunn

Distinguished Endowed Chair in Biomedical Engineering, Professor of Radiology, Neuroscience, Pathology & Laboratory Medicine and Chief of Medical Physics, The Methodist Hospital; Director of Bioinformatics & Bioengineering Program and Chief Research Information Officer, The Methodist Hospital Research Institute, Weill Cornell Medical College. Dr. Wong published over 300 peer-reviewed papers, 4 books, and holds 8 patents. Before joining Methodist, he founded HCNR Center for Bioinformatics, Harvard Medical School and Functional and Molecular Imaging Center, Brigham and Women's Hospital where he implemented Cyclotron and molecular imaging core facilities. Dr. Wong has over two decades of R&D experience in academic medicine and private industry, and headed research labs and product divisions at HP, AT&T Bell Labs, ICOT-Japanese Fifth Generation Computer Systems Project, Philips Medical Systems - Royal Philips Electronics, Charles Schwab, and Harvard Medical School. He has made pioneering contributions to picture archiving and communication systems, optical time domain reflectometer, VLSI automation, and neuroinformatics. His current research focuses on systems medicine and molecular image-guided interventions. Dr. Wong received his senior executive education from Stanford University Graduate School of Business, Columbia University GSB, and MIT Sloan School of Management. STWong@tmhs.org

Radio-frequency electromagnetic fields for cancer thermal treatment

The role of electromagnetic fields (EMF) that influence biological tissue gains increasingly strong recognition both in medical diagnostics and therapeutics. Due to the nature of cellular and subcellular structures, different operation modes of EMF, such as dc *vs.* ac, low *vs.* high fields, low *vs*. high frequencies find different bio-applications. In this lecture we will discuss basics mechanisms of interactions between EMF and cells using physics and engineering approaches. Understanding of these processes will let us focus on cancer therapy based on EMF. Options related to thermal and nonthermal interaction of EMF with tissues will be presented as methods to selectively kill cancer cells. We will talk about radio-frequency (*rf*) hyperthermia (*HPT*) and *rf* ablation (*RFA*) procedures, for which cell temperatures are increased to 41-46 °C and above 56 °C, respectively. These are well recognized and important modalities for treatment of malignant tumors, which have already gained clinical acceptance. No other thermal energy technology, including laser, cryotherapy, or focused ultrasound, can achieve results comparable to *rf*- and microwave-based methods. This is primarily due to the limited penetration depths of these competing modalities while *rf* electromagnetic waves show excellent tissue penetration. *Rf* procedures can be non-invasive, if combined with nanoparticles (NP's) for heating enhancement, and can be also cell-selective if proper functionalization is used. We will elucidate physical mechanisms of radio frequency (*rf)* heating of nanoparticles (NP) in both in-vitro and in a physiological environment and we will discuss parameters for optimized *rf*-induced NP enhanced hyperthermia as well as NP-based drug delivery *in-vivo*.

Speaker: Jarek Wosik is a Research Professor of Electrical and Computer Engineering at University of Houston and Director of High Frequency Bioengineering Laboratory at the Texas Center for Superconductivity. He is an expert in high frequency characterization of both solid state and biological samples. He has a world-recognized track record of accomplished research on fundamental properties and applications of magnetic, dielectric, metallic and superconducting materials at microwave and radio frequencies. His current activities in this area focus on characterization of nanoparticles for implementation in thermal cancer treatment as well as characterization of carbon nanotubes and magnetic nanoparticles for applications as MRI contrast agents. Jarek Wosik's extensive experience in designing high frequency resonators has led to a pioneer work on cryogenic MRI coils and coil arrays of superior sensitivity and resolution. He holds 6 US patents and applications in the area of high frequency bioengineering. Jarek.Wosik@mail.uh.edu

Registration Fee

Status	Registration Fee	Deadline
Fellowship Application	Covered by NSF	March 31, 2011
Early Registration	$1600	April 15, 2011
Registration after April 15, 2010	$2,000	

Location

The course will be held at the Methodist Hospital Research Institute**,** 6670 Bertner Ave, Houston, Texas 77030 – USA.

Accommodations

A block of rooms will be reserved at the Hilton Houston Plaza/Medical Center, 6633 Travis Street, Houston, TX 77030-1308.

Registration

Please register through the NSF Summer Institute website: www.tam.northwestern.edu/summerinstitute

Fellowships

U.S. professors, post-doctoral researchers and graduate students can apply for fellowship support through the website noted above. Fellowship applications are due March 31, 2011. Each fellowship award covers the following:

1) Full course registration
2) Up to three-night stay at the Hilton based upon double occupancy
3) Lunches will be provided.

Contact

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