Invited Conference Keynote Speakers

1. **From Terahertz to Telehealth Technologies**
   Dr. Emma Pickwell-MacPherson, The Chinese University of Hong Kong

2. **The MyHeart Project - How to Achieve a Paradigm Shift in Healthcare**
   Dr. Jorg Habetha, Philips Technologie GmbH Forschungslaboratorien

3. **The Wearable Revolution in Rehabilitation**
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4. **Wearable Cuff-less Blood Pressure Measuring Devices: From Principles to Standards**
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5. **Background to the Development of Terahertz Frequency Imaging & Sensing for Applications in Biology and Medicine**
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7. **THz Medical Applications: Perspectives and Promises**
   Dr. Peter H. Siegle, California Institute of Technology

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10. **Laser Techniques in Medicine**
    Dr. Mark Stringer, University of Leeds

11. **Terahertz Spectroscopy and Imaging for the Analysis of Quality of Medicines**
    Dr. Lynn F. Gladden, University of Cambridge

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    Dr. Ian Gregory, TeraView Ltd., UK

Invited Conference Keynote Speaker

From Terahertz to Telehealth Technologies

Presentation Time: 9:10 – 9:30, Aug. 20, Monday

Emma Pickwell-MacPherson

Department of Electronic Engineering, The Chinese University of Hong Kong, HK

Abstract:

Terahertz (10^{12} Hz) pulsed imaging is a relatively new non-destructive, non-ionising imaging modality which has emerged in the last five years as a potential new clinical tool for medical imaging. In order for terahertz technology to progress to being an established medical tool we need to overcome current size and cost limitations. Additionally we need to better understand the progression of medical research into medical devices. This presentation will discuss recent research in the medical applications, the development of terahertz technologies and how this event hopes to enlighten both terahertz scientists and medical scientists with ideas for future medical devices.

The optical excitation required for emission of terahertz radiation is derived from a femtosecond pulsed laser (commonly a Ti-Sapphire laser at 800nm). The relaxation of the photo-generated carriers produces pulses of electromagnetic radiation typically with a full-width half-maximum of 0.3 ps and an average power of 100 nW. The pulses are detected coherently using a photoconductive device and the Fourier-transformed pulse gives a usable frequency range of 0.1–3 THz. This broadband radiation is focused onto the sample of interest and then detected coherently in reflection geometry such that the measurement is non-invasive. There are strong water absorptions in the terahertz region of the electromagnetic spectrum which therefore means that imaging using terahertz radiation has the potential to be a useful tool to investigate soft tissues.

For example, there are potential biomedical applications in skin cancer, breast cancer, teeth, and pharmaceuticals - current terahertz research is continually progressing in these areas. In parallel to applications research, much work is also being done to investigate the use of alternative terahertz generation methods. The femtosecond pulsed laser required for TPI is expensive and bulky – these are significant drawbacks of the technology. An alternative method to generate terahertz radiation is by photo-mixing two detuned continuous wave (cw) lasers in a semiconductor. The beat frequency between the lasers can be adjusted to the required terahertz frequency. The radiation emitted in this case is not broadband but quasi-monochromatic. The cw lasers are much smaller than the femtosecond pulsed laser and are of the order of 1 cm in height; furthermore they are much less expensive. Thus, this terahertz technology has greater potential to be integrated into wearable or mobile devices than present established pulsed systems. Other terahertz technologies which are still developing include quantum cascade lasers and on chip devices.

The ultimate goal is to integrate terahertz technology into medical devices for use in a clinical environment. To this end, by learning more about the most cutting edge medical devices and biosensors in telehealthcare at this symposium, we can see how research ideas develop into medical devices and therefore learn how we should best develop terahertz technology in the future.

Short Biography:

Emma MacPherson (nee Pickwell) studied Natural Sciences at Cambridge University followed by an MSci in Physics where she specialised in Semiconductor Physics. After Cambridge, she worked on optical packet switching at BT labs, Martlesham, UK. In February 2002 she started working as a research assistant at TeraView Ltd, a company specialising in terahertz imaging which had spun out of Toshiba in 2001. She started her PhD with the Semiconductor Physics Group at Cambridge University and TeraView Ltd in October 2002. Her PhD thesis was entitled, "Biological applications of terahertz pulsed imaging and spectroscopy" – her PhD work focused on understanding contrast mechanisms in terahertz images of skin cancer. Having completed her thesis in 2005, she worked for TeraView Ltd as a Medical Scientist until moving to Hong Kong in 2006. Emma MacPherson joined the Department of Electronic Engineering in Sept 2006 as an assistant professor and here she is pursuing her research interests in Terahertz imaging with a view to establishing a terahertz group at CUHK.

Invited Conference Keynote Speaker

The MyHeart Project - How to Achieve a Paradigm Shift in Healthcare

Presentation Time: 9:30 – 10:15, Aug. 20, Monday

Jorg Habetha

Philips Technologie GmbH Forschungslaboratorien

Research Group 'Medical Signal Processing (MSP)'

Abstract:

MyHeart is a public research project funded by the European Commission in the 6th framework programme dealing with the prevention and early diagnosis of cardiovascular diseases. The idea behind MyHeart is to apply continuous or periodic monitoring of vital signs, in order to gain knowledge about a person's health status. The project is a major research initiative by Philips and more than 30 other industrial and academic partners, which started at the end of 2003 and will last until the end of 2008.

MyHeart integrates functional clothes with on-body sensors (textile and non-textile) and electronics into intelligent biomedical clothes. These are capable of acquiring, processing and evaluating physiological data. The results are sent via a wireless personal area network to a user device and from there to a hospital or any other professional care provider. Depending on the diagnosis, recommendations are given to the user. Such an approach towards integrated disease management has the potential to change the national healthcare systems dramatically.

The talk gives an overview of the project, the technical results and the four health-related applications that the project is addressing: activity coaching, healthy and preventative living, neurological rehabilitation and heart failure management.

Short Biography:

Dr. Joerg Habetha is with Philips Research Laboratories Aachen, where he first worked in the department for Connectivity Systems and is currently a Principal Scientist in the department for Medical Signal Processing.

He has led several internal as well as publicly funded research projects for Philips and participated in several EU projects. Since 2005 he is the coordinator of the European research project "MyHeart", which is developing personal healthcare solutions for the prevention and management of cardio-vascular diseases. With a budget of 35 M€ and 33 partners from 10 different countries the MyHeart project is one of the biggest research efforts in the field of eHealth. Dr. Habetha has a background in Electrical Engineering with a diploma degree of Ecole Centrale Paris and Aachen University of Technology. He also holds a diploma for Business Administration of Aachen University of Technology. He has received several awards, among them the Vodafone development prize for Mobile Communications 2003.

Invited Conference Keynote Speaker

The Wearable Revolution in Rehabilitation

Presentation Time: 10:15 – 11:00, Aug. 20, Monday

Paolo Bonato

Harvard Medical School and Harvard-MIT Division of Health Sciences and Technology, USA

Abstract:

Significant progress in computer technologies, solid-state micro sensors, and telecommunication has advanced the possibilities for individual health monitoring systems. A variety of compact, unobtrusive sensors are available today and it is expected that more will be available in the near future. This talk will discuss this rapidly evolving technology and how to use it in order to develop wearable systems to

monitor patients undergoing rehabilitation. System configurations consisting of wireless miniature sensors or a sensor suit that relies on e-textile solutions will be presented in the perspective of using such tools to measure motor functions and systemic responses during the accomplishment of motor activities. Measuring motor functions and associated systemic responses is key in physical medicine and rehabilitation to effectively plan and adapt clinical interventions as a function of the observed response on a patient-by-patient basis.

Data collection and storing are key elements of these systems. Wearable systems often rely on PDA's and similar data-logging devices, i.e. means to temporarily store physiological signals before uploading them to a server located in a clinical center. Data uploading may occur via a wireless local network (e.g. IEEE 802.11b or Bluetooth) installed in the inpatient unit or the patient's home, which allows communication with a clinical server via an access point. Alternatively, cell phone technology can be used when immediate access to the clinical data is an important consideration of the system design.

Data processing and analysis will be discussed as a key issue to make progress toward the clinical application of wearable systems. Procedures can rely on advanced signal processing and data mining procedures to identify features of the recorded data that capture the desired clinical information. Development of data processing and analysis procedures will be discussed in the context of integrating laboratory and clinical assessments with data gathered in the field for the purpose of designing clinical interventions aimed at enhancing mobility in individuals with cardio-pulmonary, musculo-skeletal, and/or neurological conditions.

Through development of innovative, reliable, and unobtrusive means to monitor the health status of individuals in the home and community settings, researchers are expected to provide clinicians with information complementary to that typically gathered in clinical settings. This would enable clinicians to more precisely tailor their rehabilitative strategies to the daily lifestyle of the patient, and to remotely track and quantify the patient's progression toward recovery.

Short Biography:

Dr. Bonato is assistant professor in the department of Physical Medicine and Rehabilitation at Harvard Medical School and an affiliated faculty member at the Harvard-MIT Division Health Science and Technology. Dr. Bonato is senior member of the Institute of Electrical and Electronics Engineers (the "IEEE"), an elected member of the IEEE Engineering in Medicine and Biology Society Administrative Committee, and vice president of the International Society of Electrophysiology and Kinesiology. He is Editor-in-Chief of Journal of NeuroEngineering and Rehabilitation and Associate Editor of IEEE Transactions on Neural Systems and Rehabilitation Engineering and of IEEE Transactions on Information Technology in Biomedicine. Dr. Bonato is a member of the IEEE Engineering in Medicine and Biology Society technical committee on wearable biomedical sensors and systems. His research work is focused on wearable technology and its application in rehabilitation.

Invited Conference Keynote Speaker

Wearable Cuff-less Blood Pressure Measuring Devices: From Principles to Standards

Presentation Time: 11:15 – 12:15, Aug. 20, Monday

Abstract:

Increased blood pressure – the highly prevalent hypertension syndrome - is the most common risk factor of myocardial infarction, congestive heart failure, stroke, kidney failure and blindness. In the US 1 in 3 has hypertension and the total costs per year are $ 63.5 bln. State of the art devices for blood pressure monitoring are still mainly based on the sphygmo-manometric occlusive arm-cuff, which are clumsy, uncomfortable and allow only for intermittent measurements at intervals of several minutes. There is a strong demand for wearable comfortable solutions to estimate the blood pressure level and variation, which will give a more realistic representation of a patient's blood pressure in daily life situations.

The tutorial deals with technologies that enable cuff-less blood pressure measurements, possibly at heartbeat-to-heartbeat level and covers theoretical as well as practical issues. The basic underlying principles, effects of physiological and physical activities, experimental results together with some demonstrations and consequences for new blood pressure standards will be presented. The tutorial will be held jointly by Prof. Y.T. Zhang (The Chinese University Hong Kong) and Dr. J. Muehlsteff (Philips Research Europe), who are both active in this field.

Jens Muehlsteff

Philips Technologie GmbH Forschungslaboratorien
Research Group 'Medical Signal Processing (MSP)'

Jens Muehlsteff obtained a MSc degree of Physics in 1998 from the University of Jena (Germany) followed by a PhD in 2002 from the University of the Federal Armed Forces Germany at Munich. Main topic of his PhD research was to develop control strategies for large-scale production processes using online infrared-spectroscopy together with intelligent data interpretation techniques. The research was carried out at Siemens Corporate Technology Munich. In 2002 Dr. Muehlsteff joined Philips Research and has been working on biomedical sensors for monitoring solutions in personal health care applications since that time. His research interest is focused on wearable sensors and systems in order to enable 24/7 monitoring of vital body signs outside clinical settings. Since many years he has been investigating technologies for comfortable cuff-less blood pressure measurements, possibly at heartbeat-to-heartbeat level, which could give a more realistic representation of a patient's blood pressure in daily life situations. Presently, he is a Senior Scientist in the Medical Signal Processing group where he leads a project on novel biomedical sensor research.

Yuan-Ting Zhang

Division of Biomedical Engineering, The Chinese University of Hong Kong
Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences

Yuan-Ting Zhang received the Ph.D. from the University of New Brunswick, Fredericton, NB, Canada, in 1990. He is Director of the Joint Research Center for Biomedical Engineering and Head of the Division of Biomedical Engineering at the Chinese University of Hong Kong, Hong Kong. He also serves as the Chairman (Adjunct) of the Department of Biomedical Engineering at Sun Yat-Sen University, Guangzhou, China. He was a Research Associate and Adjunct Assistant Professor at the University of Calgary, Calgary, AB, Canada, from 1989 to 1994. He chaired the Biomedical Division of Hong Kong Institution of Engineers in 1996/97 and 2000/01. His research interests include neural engineering, wearable medical devices, and body sensor networks particularly for mobile health and telemedicine. He has published more than 300 scientific articles in the area of biomedical engineering.

Dr. Zhang has been very active in the IEEE Engineering in Medicine and Biology Society (EMBS). He was the Technical Program Chair of the 20th Annual Int'l Conference in 1998 and the General Conference Chair of the 27th Annual Int'l Conference in 2005. He served the TPC Chair of IEEE-EMBS Summer School and Symposium on Medical Devices and Biosensors (ISSS-MDBS) in 2006 and 2007. He was elected as an AdCom member in 1999 and served as Vice-President (Conferences) in 2000. He served as Associate Editor for IEEE Trans. on Biomedical Engineering and IEEE Trans. on Mobile Computing. He was also the Guest Editor of IEEE Communication Magazine and IEEE Trans. on Information Technology in Biomedicine. He has been selected as the Editor-in-Chief of IEEE Trans. on Information Technology in Biomedicine. He is currently on the Editorial Board of the Book Series of Biomedical Engineering published by the IEEE press, the IEEE-EMBS Technical Committee of Wearable Systems and Sensors, the editorial committee of China Medical Device Information, and Associate Editor of the Journal of Neuro-engineering and Rehabilitation. He is an honorary advisor of Hong Kong Medical and Healthcare Device Manufacture Association.

Invited Conference Keynote Speaker

Background to the Development of Terahertz Frequency Imaging & Sensing for Applications in Biology and Medicine

Presentation Time: 13:30 – 14:15, Aug. 20, Monday

John Chamberlain

Department of Physics, Durham University, UK

Abstract:

The Terahertz (THz) range lies in frequency between 300 GHz – 10 THz; in wavelength, 1000 µm – 30 µm; in energy, 1.25 meV – 37.5 meV; and, in temperature, 14K – 480 K. Until recently, this region of the spectrum has resisted

attempts to harness its potential for application, largely because of the difficulty in providing suitable radiation sources which were usually weak, bulky, expensive, and incoherent. This led to the expression 'Terahertz Gap' being used to describe the region between lower frequency, electronics-based (or 'radio') sources e.g. transistors and higher frequency, optics-based (or 'light') sources e.g. lasers. Some useful properties of this radiation are: (a)THz radiation is non-ionising, and intrinsically safe; (b)many visually opaque materials are transparent to THz; and (c)THz radiation provides a means of identification of specific materials, including materials of biomedical interest such as DNA or epithelial cell tumours. This is because molecular rotations, vibrations or librations occur in this frequency range.

As noted above, the principle interaction mechanism of interest in biological systems is with large groups of molecules. THz spectroscopy studies can elucidate their structure, dynamics and function and have led to the development of sensitive non-contact gene-mutation sensors. Since the THz energy scale corresponds approximately to the room temperature thermal energy, the excitation energies for many biological processes occur on the THz scale. Such processes include: proton tunnelling for enzyme active sites, the collective motion of DNA base pairs along the hydrogen-bonded backbone; protein conformational changes; the vibrational energy of cell membranes; or the nonlinear thermal fluctuations that may be responsible for the initiation of DNA transcription. On a larger length scale, THz radiation can distinguish the disease state of tissues and determine the extent of tumour; systematic investigations into the usefulness of THz imaging of epithelial cell cancers on the skin or within the mouth have been undertaken by a number of groups. Recently, the possibility of using a THz intra-operative probe for breast cancer investigation has also been reported. THz sensing may also be appropriate for the diagnosis of dental disorders, where the non-invasive nature of the radiation and the sensitivity to specific chemical signatures makes it appear attractive.

In this Talk, I shall trace the development of THz technologies from their earliest days in the late nineteenth century, when the pioneers of electromagnetism and quantum mechanics realised that there was something of significance in the 'Terahertz Gap' between 'radio and light'. I shall briefly describe some of the approaches that were taken to perform experimental spectroscopy measurements using tools from both the 'radio' and the 'light' traditions. Specifically, I shall concentrate on the most recent technological developments that have taken place within the last decade or so. Two main techniques are now emerging: in the first, streams of THz pulses with very broad frequency content are generated and detected coherently after they have interacted with the specimen or material of interest ; in the second, the principles of quantum mechanics are harnessed to make small semiconductor lasers which operate at frequencies down into the THz region. My talk will address the instrumentation aspects, and in particular, the problems of penetration depth and coping with the aqueous environment common to all biological and medical investigations in vivo. I shall also discuss the similarities between other imaging modalities, such as ultrasound, and comment on the opportunities for endoscopic techniques in tumour diagnosis. Finally, I shall make some predictions about the overall direction of the field and the strategic research that is urgently required to realise the potential of this unusual part of the spectrum.

Short Biography:

John Chamberlain holds a joint appointment as Professor of Applied Physics and Master of Grey College at Durham University in the UK. Until 2003 he was Director of the Institute of Microwaves & Photonics, and Professor of Engineering Physics at Leeds University. Previously he worked at Nottingham University, where he was Reader in Experimental Physics. His research group at Durham currently consists of seven persons, with funding from the EU, EPSRC, the Regional Development Agency and the UK Security Services. He has recently founded a company, Durham Photonics Ltd., to exploit his technical activities and is also the Chair of Durham University's Institute of Biophysical Science.

JMC is a semiconductor physicist by background, and has worked for many years on the technology and applicable science of the Terahertz (THz) frequency range. This concerns the (almost unexploited) part of the electromagnetic spectrum between radio and light. The applications are considerable: in medicine, security and surveillance, and in process control. Whilst at Leeds, JMC built up a large THz research group and ran a 2M€ European Research Consortium in this area (Teravision). A major part of that work involved the development of THz imaging as a tool for the detection of epithelial cell cancers, and the production of a catalogue of the THz frequency properties of human tissue. From September 1st 2004, JMC has been Scientific Coordinator of the 5 M€ EU Integrated Project TeraNova, of which he was the principal author. This activity brings together large and small industries, and academics, throughout Europe to further develop THz systems. JMC has a long-standing interest in the development of new tools and techniques for THz work, especially for biomedical applications.

His current work involves: the development of a THz frequency microscope; the design, fabrication and characterisation of artificial materials for use at THz frequencies; and fundamental studies of propagation and scattering phenomena of THz radiation in non-homogeneous materials such as human tissue.

Invited Conference Keynote Speaker

Terahertz Time Domain Spectroscopy: Present and Future Modalities

Presentation Time: 14:15 – 15:00, Aug. 20, Monday

John Cunningham

School of Electronic and Electrical Engineering,
The University of Leeds, UK

Abstract:

Terahertz time-domain spectroscopy (THz-TDS) has emerged, over the last decade, as a technique capable of determining the dielectric properties of an enormous range of materials. THz-TDS traditionally uses free-space propagating THz radiation to measure the (diffraction limited) local properties of samples. Sub-wavelength imaging in the THz frequency range is, however, relatively underdeveloped, although several methodologies have been proposed by groups worldwide. An important limitation of many potential techniques for THz microscopy is that they either require intense near infrared radiation to be focused onto the sample being studied, which makes them less suitable for observing several classes of light sensitive specimen such as biological substrates and semiconductor nanostructures. Alternatively, the techniques require the use of apertures, which can waste a large portion of the terahertz signal.

An alternative approach, which we are developing, is evanescent THz field microscopy using on-chip THz circuits. We fabricate on-chip terahertz devices with integrated terahertz emitters and detectors, and use the device as a scanned sensor of its local dielectric environment. In this modality, the pulsed evanescent THz electric field which extends about the device is used to probe specimens. The use of a lithographically-defined THz waveguide in the device, such as microstrip, restricts the electric field laterally, while the exponential decay of the field above the waveguide into free space controls the (sub-wavelength) penetration into specimens. I will present an overview of our on-chip devices and methodology, and show results on the interaction of pulsed 0.05-1.2 THz evanescent electric fields with dielectrics (optical photoresists, semiconductors, and DNA thin-films).

Short Biography:

John Cunningham obtained his BSc degree in Physics from University College London, and MSc from Imperial College London. In 2000, he was awarded a PhD in Physics at the Cavendish Laboratory, Cambridge, where he developed new ways to move single electrons around circuits at gigahertz frequencies. In 2002 he was elected Fellow and Director of Studies in Physics at Selwyn College Cambridge. Since 2003 he has worked at the University of Leeds in a faculty position, developing terahertz science and technology, holding first a Royal Academy of Engineering Fellowship, and now an EPSRC Advanced Fellowship. His present interests include terahertz spectroscopy and microscopy, surface acoustic wave devices, and the application of high frequency techniques to condensed matter physics.

Invited Conference Keynote Speaker

THz Medical Applications: Perspectives and Promises

Presentation Time: 15:45 – 16:00, Aug. 20, Monday

Peter H. Siegle

California Institute of Technology Jet Propulsion Laboratory, USA

Abstract:

Despite many early promises and substantial government and commercial interest, THz medical activities have yet to enter mainstream programs. Few proposed applications have received significant funding and it is still difficult to get articles accepted into conventional medical journals. In the US, only a handful of small grants have been given out by the National Institutes of Health despite a significant increase

in the amount of received proposals. It is interesting to examine more closely where these hurdles arise and what steps might be taken to surmount them. In this presentation the author hopes to relay some personal perspectives from the viewpoint of an engineer working across disciplinary boundaries. He will also present some examples of ongoing work that he believes hold promise for future THz medical applications, at least from his very particular perch. The article is necessarily written in a less formal style than a traditional scientific review in the context of stimulating discussion rather than communicating results.

Short Biography:

Peter H. Siegel (BS Colgate Univ., 1976, PhD Columbia Univ., 1983) has been involved in the analysis and development of millimeter-and submillimeter-wave sensors for over 30 years. He has worked on millimeter-wave component development at the Columbia Radiation Laboratory and the NASA Goddard Institute for Space Studies in New York City; submillimeter-wave low noise astronomical receivers for the Central Development Laboratory of the National Radio Astronomy Observatory in Charlottesville, Virginia; and THz semiconductor and superconductor devices, components and space instruments for the Jet Propulsion Laboratory in Pasadena, California. In 1993 he founded the JPL Submillimeter Wave Advanced Technology (SWAT) team, a group of some 25 engineers and scientists working on the development of submillimeter-wave technology for NASA's near and long term astrophysics, Earth remote sensing, and planetary mission applications. To date this group has delivered state-of-the-art submillimeter-wave instruments to four space flight missions, three of which have now successfully launched and deployed. The fourth is scheduled for launch in 2008. In 2002, Dr. Siegel joined the staff at Caltech as a Senior Scientist at the Beckman Institute, Division of Biology, where he began working on biomedical applications of THz technology. He recently added an appointment in the department of Electrical Engineering as a Faculty Associate and he continues to serve as Technical Group Supervisor for SWAT at JPL where he emphasizes space and defense applications of THz technology. Dr. Siegel has published more than 200 articles on millimeter and submillimeter wave technology and applications, has been PI or co-I on more than 60 programs totaling more than $55M and has received forty NASA certificates of recognition, eight NASA group achievement awards, a Space Act award, and he is a three time winner of JPL's highest award for technical excellence. Dr. Siegel is a member of AAAS, chair of IEEE MTT Committee 4 - Terahertz Technology, vice chair for the International Conference on Infrared and Millimeter Waves (IRMMW-THz) and an elected Fellow of the IEEE. He is also chair of the 33rd International Conference on Infrared and Millimeter Waves and THz Electronics (IRMMW-THz) to be held at Caltech in September 2008, and to which you are all invited!

I. Introduction

THz applications in the medical and biological fields span the gamut from sub-cellular level sensing and spectroscopy of DNA, amino acids and proteins to direct disease diagnostics (see many references in [1-4]). Although there has been widespread investment in THz technology development for such applications in Europe, more targeted investments in Asia (especially Japan and China), and interests spanning several decades in Russia and former Soviet Union countries, there is still little acknowledgment of any long term benefits in the medical communities themselves, especially in the United States. Some of this naturally comes from the lack of inexpensive equipment available for non-experts to use on problems of direct medical interest. However a combination of several less obvious factors may be playing a more dominant role. In the US this is certainly the case. The first half of this discussion will elucidate some of the elements that the author believes have contributed to this problem for THz researchers. The second half of the discussion focuses on specific topics the author is developing, and hoping will eventually make their entry into mainstream medical applications.

II. Hurdles to Funding THz Medical Research

In the engineering and physical sciences, at least in the US these days, funding of a new idea or technology typically requires a proposal that clearly outlines the concept, emphasizes the societal benefits and/or specific applications, accurately summarizes the prior work, lays out the costs (with ever increasing detail it seems), identifies very specific and measurable milestones and often rigid schedules or timetables, and discusses the specific steps that must be taken to get from concept to successful program, where the definition of "success" is often harder to predict than the development path itself. The level of program risk can often be inferred from the detail (or lack of) present in the approach, as it is clearly harder to elucidate all the steps along a path that has not yet been traversed. In the author's own experience over the 30 years he has been continually writing such proposals, different sponsoring agencies have different definitions of risk, but most tend to spread their funds out in a more or less similar fashion – 10 to 15% on high risk (sometimes referred to in NASA circles as *Blue Sky*) proposals, 50-60% on medium risk and the remaining on low risk or *Slam Dunk*, (to use a dreaded sports euphemism) proposals. Within the medical funding agencies the author has been dealing with, this split seems to be weighted much more heavily on the medium and low risk categories, despite direct written testimony to the contrary [5]. Without direct poling statistics it is impossible to quantify this assertion, however it is a sentiment that has been expressed by almost all experienced NIH reviewers and many of the academicians the author has informally queried on this subject. One explanation that is often cited for this, perhaps unintended, emphasis on low risk development is the composition of the teams that make up most NIH review panels. These tend to have strong, if not dominant, representation from the clinical community. The parallel in the physical sciences might be to have review panels composed mainly of industry representatives, rather than program managers and academicians. The nearer term and perhaps more pragmatic approach to problem solving, or at least funds expenditures, that tend to be the driving force in industry, would certainly limit the number of Blue Sky proposals that might make it into the seemingly ever shrinking selection pools available to traditional funding agencies. Discretionary funding on the part of program managers in NASA and DoD agencies has helped, in the author's experience, to rebalance this sort of excessive weighting of lower-risk proposals when it occurs. Significant discretionary funding for this purpose does not appear to be equally exercised (or indeed available) within the NIH. What can we as a community do to mitigate this effect? Participation on NIH (and other medical agency) review committees is essential. Fortunately this is beginning to occur, but at a very low level and only after direct solicitation from "enlightened" program managers, who will often seek out expertise from outside the traditional biomedical community and bring (coerce) them into the review process.

A problem that does not really need to be mentioned in a community of researchers who are constantly competing for a normally decreasing pot of available government funding, is the greater emphasis on short term goals and accomplishments and the higher level of risk adverseness that naturally follows from this type of thinking. In the NIH there is a very nice mechanism that has been implemented for combating this very problem. Research proposals are distributed between two major categories, R21, shorter term, lower cost, higher risk efforts, and R01, slightly longer term, higher funded tasks. The proposer of a new THz technology application can start out with a small test program under the R21 and if successful, immediately proceed to the R01. In principle this should mitigate both the tendency to skew the risk to lower levels and at the same time relieve the often overly scrutinized program manager from blame for placing too much of their available resource into a lower percentage of program success stories. In practice however, both the R21 and the R01 (as well as every other variety of program offered by the NIH) are reviewed in the same panel session by the same cross section of the community. Again in the author's experience, this tends to blur the lines between the R21 and R01 categories to the extent that they both end up being scrutinized with more-or-less the same set of success oriented standards. It may in fact be more advantageous from a statistical point of view to submit a high risk proposal under the R01 mechanism simply because more R01's are funded than R21's. Certainly this is not the intended outcome. What can the THz community do in response? Over emphasize the exploratory nature of the work in the context of the R21, talk to program managers or study group leaders directly before the review process starts, recommend knowledgeable technical reviewers and suggest them as ad-hoc review group members on the cover sheet of the proposal. It seems unlikely this cultural barrier can readily be breached, but it may be thinned down a bit after repeated efforts.

Credibility is always an understated part of every review process, regardless of community or risk level. Crossing disciplinary borders raises this consideration to new heights. As a consequence a physicist or engineer spearheading a proposal with applications to the medical community without direct medical community involvement is an almost certain recipe for failure. This is usually understood and most new proposers to NIH do include medical community members on their inputs. What is frequently overlooked however, is that the same criteria that are applied within the physical sciences for judging the credibility of a proposal, extends equally to the medical community. That is, it may be insufficient to simply have a beginning career level medical doctor on an engineering style proposal, just as it might be insufficient to simply have a first year physicist on an NSF proposal. One would clearly want to understand the experience and credentials of any particular individual as judged by the community that will evaluate the proposal or the program. This might be difficult to ascertain without prior knowledge or association with the review community. The NIH makes it fairly easy to acquire useful preliminary data in this area. A few website clicks brings one into the CRISP database [6] with detailed information on past and current programs that have been funded within the agencies. Such information can help identify and hopefully allow one to coerce appropriately experienced and established investigators who might be willing to participate in some novel research task that stretches their own disciplinary boundaries!

Finally, writing a proposal or program plan, or even a paper, for a sponsor or reviewer that is used to a particular style and language without rigidly adhering to those long established expectations simply highlights the credibility issue and in consequence the funding risk. No matter how enlightened an academic you may be and how diverse your selection of reading materials, it is obvious that cross comparing and judging different proposal styles is as difficult as cross comparing and judging different categories of literature. Even if differences in style are forgiven, mistakes in emphasis, level of detail and simply vocabulary and terminology can only be detrimental. The remedies in this instance are fortunately within one's control. Either acquire the particular style, accompanying vocabulary and detailed reference base required and pay close attention to the expected level and categories of emphasis, or have someone who already understands these requirements read over and contribute where necessary to the proposal. This has been a particular thorn in the author's own side, as it seems, at least in his case, it requires also changing one's way of thinking and the approach to solving problems.

Keeping these considerations and limitations in mind the remainder of the paper is devoted to a summary of several tasks the author has been involved in that might yet lead to some longer term medical activities.

III. THz Medical Research Activities at Caltech

The benefits and limitations of THz spectral and imaging capabilities have been enumerated in many publications and texts [1-4,7-15]. The author's own involvement is predicated on his particular engineering background and emphasizes instrumentation and technology that stems from the radio frequency community. As such this has focused his past activities on those that can be realized through traditional frequency domain CW techniques [16,17]. Never-the-less the particular applications might benefit just as well (nay better) from pulsed optical or pulsed time domain techniques.

Tissue contrast was studied very early on by investigators in the terahertz pulse imaging (TPI) community [14,15] and found to be sufficiently different in loss tangent and index from optical and infrared imaging that some disease recognition was possible without the need for microtome sections or staining. The contrast between adipose tissue and muscle is particularly striking as is that between fluid filled tissue and bone or cartilage. However these distinctions are also observed optically, at least on a gross scale, and the capability to observe more subtle distinctions in fluid content or tissue type and disease state seem necessary if THz imaging is to find much use in the medical diagnostics areas. Taking a cue from the histology community the author has been pursuing the use of staining techniques to enhance THz absorption in gross tissue samples as a means towards establishing a quick and simple method for highlighting disease margins or involvement. The first step in this process is to identify those stains or dyes that both can be employed safely on in-vitro (or in-vivo) tissue and have a significant THz signature that can be easily observed macroscopically. After examining a number of common histology stains and embedding media we have found that one of the most common human tissue stains, hematoxylin [18], has a strongly enhanced THz absorption signature, whereas its often employed counterpart, eosin [19], has no observable THz absorption signature [Fig. 1]. Thus H&E staining may allow one to quickly contrast heavily loaded nucleic acid based tissue (a property of many cancers) from protein and intra or extracellular loaded samples.

Since it is well known that THz absorption in all fluid filled tissue is extremely strong [15] the use of this frequency range for applications involving deep (or even modest) penetration in the body or in in-vitro tissue is extremely unlikely. One way to employ this spectral range for imaging or spectral applications within the body is to utilize catheter or endoscopic media for transmitting signals to and from the desired probing areas. The wavelength scale of THz radiation makes this a particularly appealing solution since both catheters and endoscopes have apertures that are on the order of a wavelength (mm scale) at the lower end of the submillimeter wave band. In the frequency domain this means that RF energy can be propagated down single mode pipes or waveguides with low dispersion if suitably low loss media can be found/assembled. Pure metal waveguides tend to have too much ohmic loss to accommodate the desired meter+ path lengths as do the most common dielectric based guide media. The author has been investigating the use of specially enhanced flexible low-loss ribbon waveguide [20] for such in-vivo applications. By confining the RF fields to a thin low-loss ribbon-like dielectric with lateral dimensions approaching one wavelength and vertical dimensions $<\lambda/10$ it is possible to propagate over large distances with almost no absorption loss. Fabricating and packaging such a medium however is not straightforward. Some recent success has come in the form of a new ribbon-waveguide package based on commercial technology used in the optical fiber and medical capillary tube industry [Fig. 2] where an encased ribbon guide is held inside a quartz tube that can be drawn in a simple glass extrusion process. Low loss, mode preserving RF launchers and capture transitions have also been developed for the cross-bar ribbon guide so as to allow simple coupling to rectangular or circular waveguides. Broadband pulse propagation (as used in TPI) requires somewhat different waveguide media characteristics, but is also being vigorously pursued [21,22].

Two other medical applications have been proposed

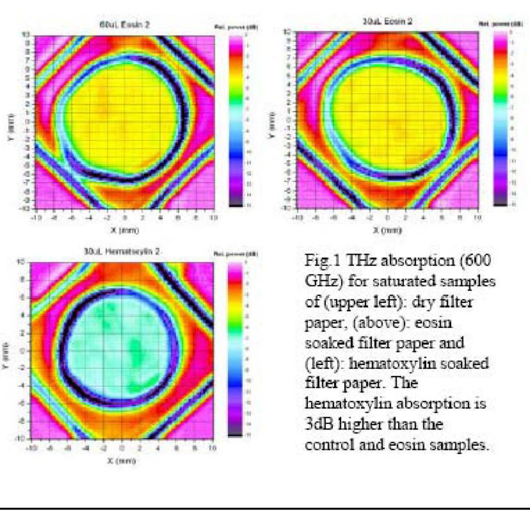

Fig.1 THz absorption (600 GHz) for saturated samples of (upper left): dry filter paper, (above): eosin soaked filter paper and (left): hematoxylin soaked filter paper. The hematoxylin absorption is 3dB higher than the control and eosin samples.

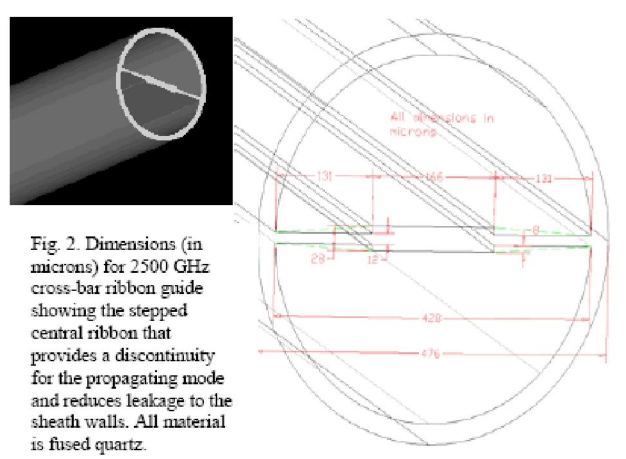

Fig. 2. Dimensions (in microns) for 2500 GHz cross-bar ribbon guide showing the stepped central ribbon that provides a discontinuity for the propagating mode and reduces leakage to the sheath walls. All material is fused quartz.

but remain unfunded at the author's facilities. The first involves the use of terahertz transmission measurements to quantify the degree of plaque loading in tissue samples macroscopically, i.e. without the need to use microtomed sections, staining and microscopy to identify tissue variations at the cellular scale [23]. The second involves the use of THz reflection spectroscopy to help distinguish tumor margins and quantify disease loading of tissue in-vivo for skin ailments [24,25]. In the plaque loading application the fact that terahertz wavelengths are somewhat less prone to scattering than infrared and optical signals and can propagate readily through paraffin perfused tissue samples means that local changes in average density can be observed macroscopically over large areas. The idea behind this application is that the degree of loading in tissue, specifically neuronal tissue, from build of beta-amyloid plaques, neurofibrillary tangles or Lewy body inclusions, as in Alzheimer's disease (AD), would show up quickly without resorting to microtome and staining procedures. If this change in absorption can be accurately correlated with disease state than perhaps a less costly and more globally applicable (i.e. extendable over the whole brain) procedure can be used to quantify AD staging. In the second, and in author's experience the most intriguing near term application for THz imaging in the medical community, the identification of tumor margin and disease loading in skin cancer is targeted. This application has been extensively pursued by Teraview and its associated university and medical partners in the UK [10,24]. The author has proposed to extend the UK study with additional disease morphology and clinical data (targeting both basal and squamous cell carcinomas) and with more penetration depth capability (using higher signal-to-noise frequency domain imaging), but so far without funding success [25].

SUMMARY

This paper gives some personal perspectives on THz cross-disciplinary work in the medical arena and some examples of programs and proposals being pursued in the author's laboratories. Despite near term hurdles, continued proposal pressure, new instrumentation and additional results keep this a fruitful area for development activities.

ACKNOWLEDGMENT

The author is forever indebted to the many individuals who have directly assisted him along his long and torturous path towards realizing a dream to work in a truly cross disciplinary manner. Chief among these are Dr. Richard Seligman, Director of Caltech's Office of Sponsored Research, Professor Scott Fraser, a developmental biologist at Caltech, Dr. Joe Waters an atmospheric scientist at JPL, Dr. Warren Grundfest a surgeon and Professor of Bioengineering at UCLA and Professor David Rutledge, Engineering and Science division chair at Caltech. Equally critical were Dr. Kathie Olsen (former Chief Scientist at NASA and currently Deputy Director, NSF), Dr. Donna Dean, former Director, National Institute of Bio Imaging and Bioengineering – NIH NIBIB). *Morituri te salutamus.*

The author is also grateful for extensive help and participation from the many past and current members of the JPL Submillimeter Wave Advanced Technology (SWAT) team with whom he has had the great pleasure of working over the past 15 years.

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Invited Conference Keynote Speaker

Clinical Applications of Terahertz Technology

Presentation Time: 16:00 – 16:45, Aug. 20, Monday

Vince Wallace

TeraView Ltd, Cambridge, UK

Abstract:

Medical physics is advancing rapidly, making use of many imaging/spectroscopic techniques across the electromagnetic spectrum. There are many cases where the demand for a medical imaging technique that is safe and non invasive has not been met. Terahertz could meet that need. Terahertz Pulsed Imaging (TPI) is a novel, non-invasive, imaging modality with current applications in pharmaceutical science, security and medicine. TPI uses pulses of electromagnetic radiation typically with a full width half maximum of 0.3 picoseconds and an average power of 100 nW. The pulses are detected coherently using a photoconductive device and the Fourier transformed pulse gives a usable frequency range of 0.1-4 THz. Terahertz radiation is non-ionising and power levels produced are well within safety guidelines. These frequencies typically interact with lattice vibrations of crystalline substances and hydrogen bonds in liquids thus making TPI extremely sensitive to water.

Early experiments by pioneers of THz imaging demonstrated that the technique could have a variety of applications, including medicine - terahertz images of bacon showed contrast between lean meat and fat. Another potential application of TPI is the diagnosis of dental caries. Changes in refractive index in the THz range caused by early stage tooth decay allow for the detection of small lesions not seen on X-ray. Work at TeraView Ltd, in Cambridge UK, has used THz imaging to reveal the contrast between regions of healthy skin and basal cell carcinoma (BCC) both in vitro and in vivo. More recent work at TeraView has been on excised breast carcinoma, again showing the THz can be used to differentiate between cancer and normal tissue.

The high absorption of THz by water in this range (23 mm^{-1} at 1 THz) makes transmission imaging through a body impossible, but it is the difference in absorption due to water content which explains the contrast seen between muscle and adipose tissue and between tumour and normal tissue. Terahertz spectroscopic measurements of carcinoma show significant differences in the frequency dependent refractive index and absorption coefficient. Such contrast on the surface is often obvious at optical frequencies but it is the ability of THz to penetrate below the surface that provides the potential for medical imaging, in particular, of epithelial tissues (cancer with origins in tissue surfaces both external and internal), which includes skin, breast and colon cancer, accounts for 85% of all cancers.

To date in vivo measurements have been limited due to the restricted nature of imaging systems. Compact, mobile THz imaging systems are now being developed which allows for TPI measurements in a clinical setting.

Short Biography:

Vincent Wallace, PhD, MInstP, CPhys has over 12 years of experience in biomedical photonics. He graduated with a PhD in Medical Physics from the Institute of Cancer Research, University of London, in 1997. After 3 years at the Beckman Laser Institute and Medical Clinic, University of California, he joined Toshiba Research Europe in Cambridge, UK to look at potential medical applications of terahertz radiation. TeraView Ltd, also based in Cambridge, was spun-out of Toshiba Labs in April 2001 to commercialise Terahertz Technologies. At TeraView, Vince is head of a group developing THz technology for medical applications as well as supervising graduate students from Cambridge University.

Invited Conference Keynote Speaker

Body Sensor Networks

Presentation Time: 9:00 – 9:45, Aug. 21, Tuesday

Guang-Zhong Yang

Medical Imaging, Department of Computing, Imperial College, London, UK
Medical Image Computing, Imperial College London
Imaging and Robotics, Institute of Bioengineering, Imperial College London
Centre for Pervasive Sensing, Imperial College London
Royal Society/Wolfson Foundation Medical Image Computing Laboratory
Visual Information Processing, Department of Computing, Imperial College

Extended Summary

Shorter hospital stay and better community care are set to be the future trend of healthcare. Providing specialist service at a local level, however, is difficult, considering the relative infrequency with which a particular disease, or a combination of diseases, may be encountered by the typical general practitioner. Such schemes must be underpinned by a strong and intelligent information link between patients and specialist centres, which monitors the status of the patient through non-invasive or implanted sensory devices, and provides early warnings of potential problems. With demographic changes associated with the aging population and the increasing number of people living alone, such information exchange is crucial for maintaining the mobility and improving the quality of life for older people. This presentation outlines some of the major opportunities as well as technical challenges of pervasive healthcare based on body sensor networks (BSNs) [1]. It will also highlight some of the practical examples of using BSN to move from episodic patient management to pervasive healthcare strategies that allow the capturing of transient abnormalities.

The basic concept of BSN is to use a network of miniaturized, low cost and wireless wearable or implantable biosensor to provide continuous monitoring of the patient's physiological and contextual parameters. The key technical issues addressed by BSN research include:

- Biosensor design
- Biocompatibility and Sensor packaging
- Wireless Communication
- Low Power Design and Power Scavenging
- Autonomic Sensing
- Standards and Integration

1. Biosensor design

Recent advances in biological, chemical, electrical and mechanical sensor technologies have led to a wide range of wearable and implantable sensors suitable for continuous monitoring. In addition to sensor sensitivity, several factors have to be considered in the design of pervasive biosensors, such as reliability, ease of use, selectivity [2], sensor packaging, biocompatibility, and power consumption. Biosensors are often affected by noise due to bio-fouling, motion artefacts, and interference. To improve the sensor reliability, sensor arrays can be used. Sensor fusion techniques can then be applied to fuse information from these sensors. For example, source recovery can be employed to fuse the information from multiple sensors and infer the intrinsic signal characteristics [3]. Although by the introduction of additional sensors can improve the overall system performance, increasing the number of sensors can potentially increase the complexity of the system and affect its practical deployment. To circumvent this problem, a minimum number of sensors should be used for different application scenarios. In fact, selecting only relevant features or sensors not only simplifies the system configuration but also improves the classification accuracy [4]. In practice, feature selection techniques can be employed to identify relevant sensors and their optimum location.

2. Biocompatibility and Sensor packaging

As biosensors usually have direct contacts with the patients, biocompatibility is an important issues to consider, particularly for implantable sensors. Biocompatibility itself can also cause sensor failures due to biofouling, hermeticity of encapsulation, electrode passivation, and limited life-time of the immobilised enzymes [5, 6]. One approach to tackling sensor fouling and improving the reliability of the sensors is the use of micro-sensor arrays. The recent advances in micro-fabrication enable the fabrication of micro scale sensor arrays. This is advantageous in that given different causes of biofouling and sensor failure, it is unlikely that multiple sensors will fail at the same time. By fusing the readings from the sensors, more reliable measurement can be obtained [7].

3. Wireless Communication

Wireless communication constitutes the majority of the power utilisation in BSN. Thus far, several low power radio transceivers have been proposed for wireless sensors. The use of ultra wide band for wearable sensors has also been suggested [8]. The emerging ultra-wide band technology offers short-range wireless communication with a theoretical data rate up to 1Gbps but with a low power budget [9]. In addition to low power wireless transceivers, communication protocol is also an essential component for the development of energy efficient wireless sensors. Several industrially driven standards, such as ZigBee and Wibree, have also been launched to standardise the communication protocol for wireless sensor networks and BSN applications. Another issue to consider for BSN applications is antenna design. This is a determining factor for a reliable and energy efficient wireless communication link. Unlike typical wireless communication applications, to enable long term monitoring with miniaturised sensors for BSN applications, the power utilisation of the radio has to be kept to the minimum. To provide a reliable communication link, the antenna has to be optimised in order to maximise the throughput of the wireless link. The wireless data-path used to interrogate and communicate with the implants represents one of the most significant research challenges in overall system design due to its significant power consumption and complex characteristics within the human body. While wireless communication through the air has been extensively studied, communication from implanted devices through the human body is a new area of study. Current research is increasingly moving towards the use of imaging based subject-specific RF simulation environment for wearable and implantable BSNs.

4. Low Power Design and Power Scavenging

Although low power radio transceiver with energy aware protocol can greatly reduce the power consumption of a sensor node, to enable pervasive monitoring of a patient, sensor reading has to be transmitted continuously to a local processing unit for data processing, which can hinder the reduction in power consumption and sensor miniaturisation. The provision of processing on-node technology is therefore desirable both from the data reduction and user acceptance perspectives. In this way, the sensor data can be reduced at the node level to cut down radio transmission, and thus the overall power consumption. This can also avoid classification errors due to packet losses. In parallel to power reduction, perpetual energy supply with power scavenging can prolong the lifetime of the sensor and enable long term monitoring of the patient. A number of power scavenging sources have currently been proposed, which include motion, vibration, air flow, temperature difference, ambient electromagnetic fields, light and infra-red radiation.

5. Autonomic Sensing

As BSN systems become ubiquitous, managing and supporting the large number of micro scale sensors will be a challenging task. To this end, the concept of autonomic sensing has recently been proposed [10]. Autonomic sensing, which follows the concept of autonomic computing system, can be characterised with eight properties: self management, self configuration, self optimisation, self healing, self protection, self adaptation, self integration and self scaling [11]. In terms of self configuration, extensive research has been conducted in wireless sensor networks for automatic network formation and routing. Several distributed inferencing techniques have been proposed for wireless sensor networks, which enable the realisation of self healing of a sensing system. Due to the power and computational constraints of the miniaturised sensor node, developing a truly autonomic sensing system still remains an active research topic.

6. Standards and Integration

For BSN application development, ISM (Industrial, Scientific and Medical) bands are often used. In terms of the communication protocols, a few standards have been proposed, such as the IEEE 802.15.3 and 802.15.4, for low power short range communication. In addition, new initiatives have been established for standardising wireless sensing devices. To address the interoperability issues between health monitoring devices, a new industrial alliance called the Continua Health Alliance has recently been established. The objective of the alliance is to establish an ecosystem of interoperable personal health systems [12]. Through defining interfaces and establishing a certification programme, the alliance aims to resolve the interoperability and integration issues for personal healthcare systems. In addition to device level interoperability, integration with the healthcare information system is also crucial to assist and enhance patient management. The Health Level Seven (HL7) defines the specification for exchanging clinical and administrative information of the patients [13]. By integrating the pervasive sensing data with the patient's information, more accurate patient records can be implemented and long term trend analysis can be performed.

Technological developments in sensing and monitoring devices are reshaping the general practice in clinical medicine. Although extensive measurement of biomechanical and biochemical information is available in almost all major hospitals, the diagnostic and monitoring utility is generally limited to the brief time points and perhaps unrepresentative physiological states such as supine and sedated, or artificially introduced exercise tests. With the emergence of miniaturised mechanical, electrical, biochemical and genetic sensors, there is likely to be a rapid expansion of biosensor use over the next ten years with corresponding reduction in size and cost. This will facilitate continuous wireless monitoring, initially of at-risk patients but eventually screening an increasing proportion of the population for abnormal conditions.

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Short Biography:

Guang-Zhong Yang received Ph.D. in Computer Science from Imperial College London and has served as a senior and then principal scientist of the Cardiovascular Magnetic Resonance Unit of the Royal Brompton Hospital prior to assuming his current full-time academic post. He is Director and Founder of the Royal Society/Wolfson Medical Image Computing Laboratory at Imperial, co-founder of the Wolfson Surgical Technology Laboratory at Imperial, and Chairman of the Imperial College Imaging Sciences Centre (ISC). He is an associate editor of IEEE Transactions on Medical Imaging, Series Editor of Artech House Bioinformatics and Biomedical Imaging, and a referee for a large number of international medical imaging journals. Professor Yang received several major international awards including the I.I. Rabi Award from the International Society for Magnetic Resonance in Medicine (ISMRM). He is widely regarded as the founder of Body Sensor Networks (BSN), which is attracting increasingly significant international focus. He has attracted significant funding from the EPSRC, the Royal Society, the Wolfson Foundation, the British Heart Foundation, UK Department of Trade and Industry, and various industrial partners. He is holder of the Royal Society Research Merit Award in Medical Image Computing and has published over 200 original research articles including over 100 peer reviewed academic journal papers.

Invited Conference Keynote Speaker

Laser Techniques in Medicine

Presentation Time: 9:45 – 10:30, Aug. 21, Tuesday

Mark Stringer

Institute of Microwaves and Photonics
School of Electronic and Electrical Engineering, University of Leeds, UK

Abstract:

Since the first demonstration of laser action, in 1960, a wide range of devices and systems, generating coherent light over an extensive breadth of parameters, have been developed. Consequently, lasers have found myriad applications within numerous disciplines, including industrial machining processes, entertainment (artistic displays), and digital read/write devices (bar-codes and compact discs) as well as in fundamental research. Medical practitioners quickly recognised the destructive power of a high-intensity laser beam as a potential means of targeting diseased tissue, and the notion of a laser eliminating some undesirable presence within the human body is now well established. However, the acceptance of the laser within the clinic has only been possible through an understanding of the light-tissue interaction. Since a laser demonstrates output characteristics that are different from those of a conventional light source, this interaction is dependant not just upon the wavelength of the incident beam, but also on the spatial and temporal parameters. By taking advantage of the precise control that can be imposed upon this interaction, a wide range of surgical and medical techniques have been made possible. This presentation will highlight the different categories of physical interaction between laser light and tissue, the consequent biological effects, and show examples of how these have become established laser therapies.

In addition to therapeutic interventions, a number of laser-based techniques have been used as methods for monitoring physiological status. Also, a range of spectroscopic modalities are currently under investigation as potential methods of cancer diagnosis. The onset of the disease is accompanied by changes in the relative amounts of natural tissue components, as well as by changes in morphology. The remitted signal induced by interrogating the target area with light of an appropriate wavelength may contain characteristic information that allows discrimination between diseased and healthy tissue. Such a method is non-invasive, and the results are obtained much more rapidly and at lower cost than by complex histopathological examination of an excised sample. The principles of a selection of these so-called “optical biopsies” will be described, representing diagnostic laser techniques spanning a wide range of the electro-magnetic spectrum.

Short Biography:

Dr Mark Stringer is a Senior Research Fellow in the Institute of Microwaves and Photonics, at the University of Leeds. He has a wide range of experience in the use of lasers for spectroscopic analysis, investigating diverse samples ranging from meteorites to the human body. His principal research interest is in the use of non-ionising radiation for the identification of tissue abnormality and physiological imbalance, and is currently involved in the development and application of Terahertz technologies. He is a member of the executive committee of the British Medical Laser Association, and sits upon the editorial board of the journal *Photodiagnosis and Photodynamic Therapy*.

Invited Conference Keynote Speaker

Terahertz Spectroscopy and Imaging for the Analysis of Quality of Medicines

Presentation Time: 13:00 – 13:45, Aug. 21, Tuesday

Presented by Dr. Alex Zeitler

Lynn F. Gladden
Department of Chemical Engineering, University of Cambridge, UK

Abstract:

Over the past decades research and development activities in the pharmaceutical industry have lead to the discovery of thousands of new molecules and chemical structure motifs that would have the potential be used in the treatment of human diseases, yet only a small proportion of these lead candidates have made it to the market. The major reason for the rejection of most potential drug molecules during the development process is originating in the toxicological properties of the compounds. However, increasingly low solubility and complex polymorphism of lead candidates limits the suitability for those molecules to make it to the market. It is only through a thorough understanding of their physico-chemical properties that it is possible to develop such drug molecules into a stable pharmaceutical dosage form such as a tablet.

Terahertz radiation is an ideal probe for the characterisation of pharmaceutical solids. It is non-destructive and interacts with vibrational modes that extend across large domains of the lattice in organic molecular crystals. The ability to directly probe the lattice dynamics which represents vibrations of the whole molecule, rather than just the vibrations of single functional moieties within molecules as is the case in infrared spectroscopy, makes terahertz spectroscopy a very powerful tool for the analysis of complex solid-state materials properties.

Besides the need for enhanced solubility of new drug compounds a further challenge in pharmaceutics is associated with the growing number of medications that patients have to take simultaneously. More sophisticated tablets are being developed that combine two or more drugs into one tablet and allow the drug to be released in a highly controlled way. A number of different concepts have been developed: multiple layers tablets; semi-permeable membranes incorporated into a tablet, or polymeric coatings that control the release of the drug. With such tablets it is possible to target the release of the drug from the tablet to specific areas of the human body. This leads to a significant decrease in side effects and a reduced amount of tablets that a patient has to take on a daily basis. However, the manufacture of such advanced tablets is much more difficult than conventional ones. Even though highly promising concepts have been demonstrated, again very few of them have made it to the market. This is due to the difficulties in quality control because, as yet, no tool has been developed that can be used for a quick and non-destructive test of the product after manufacture.

Terahertz imaging is a very important, novel, technique with the potential to fundamentally change the way the pharmaceutical industry performs its quality control. Terahertz light can be used to scan through a tablet and exhibit its internal structure. Most of the excipients that make up the bulk of a tablet are transparent to terahertz light, whereas the drug and interfaces from different coating layers or substructures within the tablet lead to a contrast in the images.

This presentation will summarise state-of-the-art applications of terahertz spectroscopy and imaging in these applications, and highlight future prospects in this field.

Short Biography:

Lynn is currently Shell Professor of Chemical Engineering in the Department of Chemical Engineering at the University of Cambridge. Since 1990, her research interests have been focused on the development and application of magnetic resonance spectroscopy and imaging techniques in chemical engineering, with a particular interest in applied catalysis and the characterisation of pharmaceutical delivery systems. More recently, she has been interested in exploring the combined use of magnetic resonance and THz techniques to characterize the structure and performance of materials, with a particular interest in pharmaceutical systems.

Amongst many other activities both inside and outside Cambridge, Lynn is a member of the Royal Society/Royal Academy of Engineering Advisory Group to the National Physical Laboratory and the International Advisory Board of the MacDiarmid Institute for Advanced Materials and Nanotechnology, New Zealand.

Invited Conference Keynote Speaker

Future Terahertz Devices

Presentation Time: 13:45 – 14:30, Aug. 21, Tuesday

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Abstract:

The ongoing development of pulsed photoconductive terahertz generation and detection has already yielded a range of successful products, and further research into both applications and complementary terahertz technologies promises much more. In medical imaging, terahertz shows promise in both diagnosis roles and as a real-time surgical tool. The demonstration of performance and functionality is an important first step in a product development process, which must then also address commercial and physical constraints. Continuous-wave terahertz systems and components based on photomixer technology are attracting increasing interest, and appear to fulfil many of the required criteria.

Short Biography:

Ian S. Gregory, PhD, AMInstP, joined TeraView as an industrial student in 2001, and has held a full-time Research and Development role since 2004. He graduated with a PhD in Physics from the Semiconductor Physics Group, University of Cambridge, in 2005. He is presently working in the 'Core Technology' group within TeraView, characterising semiconductors and photoconductive antenna structures for improved terahertz sources and detectors. He specialises in the development of continuous-wave terahertz systems, components and spectrometers based on photomixing using diode lasers, and has demonstrated their application in both security and medical fields.

Imaging at frequencies in the terahertz (THz) region of the electromagnetic spectrum (0.1-10 THz) has rapidly progressed in recent years, owing to the provision of suitable THz sources and detectors [1]. In particular, the development of coherent, phase sensitive detection schemes [2] has allowed a multitude of information to be acquired at each image pixel, utilising both the time and frequency domain data available. THz imaging is therefore more versatile than many other imaging modalities.

Many established THz imaging systems rely on the production of single-cycle pulses, using a femtosecond laser to excite a photoconductive antenna. Such lasers are, however, relatively costly and bulky, which limits their use in some applications. In contrast, continuous-wave (cw) THz radiation can be produced by photomixing two detuned cw lasers in a semiconductor [3]. The beat frequency between the lasers is adjusted to the required THz frequency, and quasi-monochromatic cw-THz radiation is emitted from the photomixer.

We have previously demonstrated all-optoelectronic, cw-THz spectroscopy and imaging systems based on compact and cost-efficient temperature-tunable DFB diode lasers (see figure 1). Time-domain waveforms are acquired for each pixel, and the use of multiple frequencies enables spectroscopic image display modes. When using a homodyne detection scheme with our photomixers, both amplitude and phase information may be utilised.

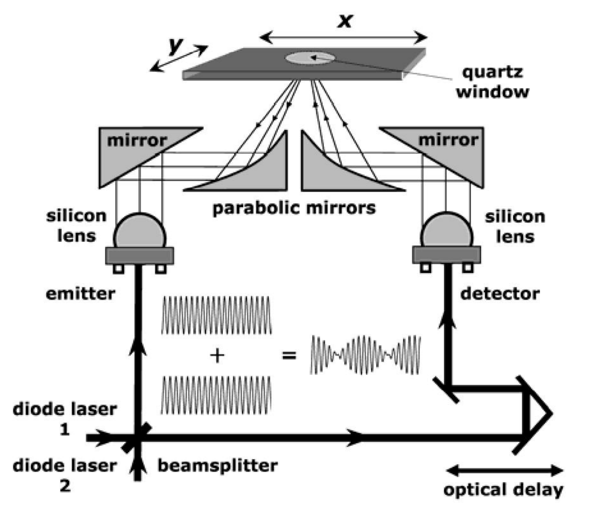

Fig. 1. *Cw-THz schematic diagram to show the traditional layout comprising the combining beamsplitter, optical delay line and imaging mirrors. The resulting beat pattern is inset schematically.*

Previous work has focused upon the pulsed terahertz study of basal cell carcinoma, both *in vivo* and *ex vivo* [4], and has suggested that contrast exists that may enable the cancer to be diagnosed and the extent to be assessed.

More recent studies have been since made to explore the use of THz technology to examine excised breast tissue for malignant tissue during surgical procedures [5].

For cw-THz techniques, it is more convenient to interpret data in the frequency domain, rather than using waveform analysis. Figure 2 shows the spectral response of healthy and diseased tissue. Inset are images of one excised sample used in the study. (A) shows a visible photograph of the sample, with a dotted curve overlaid to delineate the cancerous (light) and healthy (dark) regions. The dotted curve is overlaid onto the THz image, (B), taken at a single frequency of 0.5 THz using the cw photomixer system. Closer inspection reveals that the diseased area extends beyond the visible boundary in the THz image (white arrow), indicating the increased sub-surface lateral extent of the tumour. The cw-THz system is able to obtain monochromatic images at frequencies in the continuous range 0.1-1 THz.

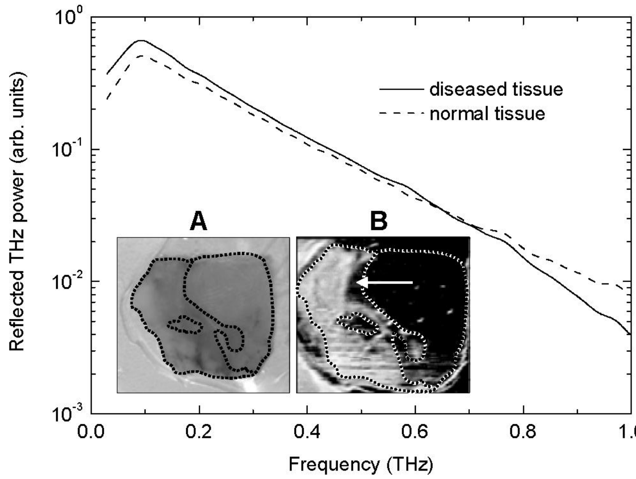

Fig. 2. *The reflected THz power as a function of frequency, for both diseased (solid curve) and normal (dashed curve) tissue. Inset is an example of a tissue image: (A) is a visible photograph of the excised tissue, and (B) is a cw THz image taken at 0.5 THz.*

The use of free space laser beams and optics allows an experiment to be rapidly built for proof-of-concept purposes. From a commercial and engineering viewpoint, the preferred approach is the adoption of fibre optic coupling, as shown in figure 3. In comparison to the free-space arrangement, the optical beams are transmitted by a single mode fibre 'end-to-end' from the diodes to the semiconductor devices. Each laser beam is independently aligned to a fibre-port integrated onto the laser base-plate. The beams are combined and then split 50:50 in a fused fibre 2×2 coupler, with the outputs phase-modulated using a piezoelectric fibre modulator system. This arrangement is substantially more elegant than the experimental system shown in figure 1.

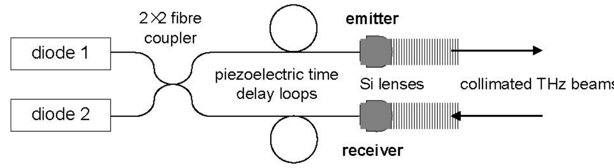

Fig. 3.

Top: the fibre-coupled optical excitation system.

Left: the photomixer cartridge prototype.

The ability to use standard connectors to join fibers underlines the modular approach, allowing ease of interchange of devices. This extends to the semiconductor emitter and receiver devices (photomixers), which are sealed in hermetic packages. The termination of the fibre is integrated into the device 'cartridge' that allows the output optical mode to be precisely matched to the device active area. The accurate alignment of the internal lenses is factory-locked. The enclosed device is more robust with respect to handling and static discharge, is light-weight (<10 g), compact, and requires no translation stages to maintain alignment of the optical beam.

Intensive product development of this technique could yield 'real-world' systems in relative short timescales, since no significant commercial barriers exist. For this concept, no large ancillary equipment: high voltage, high magnetic field, cryogens, or other significant environmental requirements are present. Although the photomixing process is relatively inefficient (< 1%), the output power is derived from the dc bias circuit and not the incident laser power. Similarly, the power output is relatively low (10 μW), but this is largely mitigated by the high detector sensitivity. Therefore the technology should be assessed as an emitter-receiver system (and not isolated as sources) in these respects.

A key challenge traditionally presented by this technology is the improvement of semiconductor responsivity for higher signal-to-noise ratio. The continuing development of semiconductor materials and fabrication techniques will allow more power (emitters) and higher sensitivity (receivers), lower noise levels and increased robustness to high applied bias and high optical powers. This will be necessary since present limits are device failure through heating and electrical breakdown.

TeraView's existing pulsed technology offers complete systems and solutions, and provides a research platform with which to evaluate applications, and there are many high value applications in which pulsed technology is a long term solution. Therefore the cw system complements the existing technology. The modular approach to the component engineering will allow component supply on a 'plug and play' basis, facilitating development work with both partners and customers. Further development of both hardware and software will allow increased sophistication for the requirements of operational systems.

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References -

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