Engineering a better world:

BREAKTHROUGH TECHNOLOGIES FOR HEALTHCARE

CAETS 2022
PARIS - VERSAILLES • FRANCE

ACADÉMIE DES TECHNOLOGIES
POUR UN PROGRÈS RAISONNÉ CHOISI PARTAGÉ

NATIONAL ACADEMY OF TECHNOLOGIES OF FRANCE
SHARING A REASONED, CHOSEN PROGRESS

SUMMARY

About CAETS – International Council of Academies of Engineering and Technological Sciences

CAETS is an independent non-political, non-governmental, international organization of engineering and technological sciences academies, one member academy per country, that advances the following objectives:

- Provide an independent non-political and non-governmental international forum for enlightened dialog and communication of engineering and technological sciences;
- Contribute to advancing engineering and technological sciences in order to promote economic growth, sustainable development, and societal well-being throughout the world;
- Foster collaboration and the development of bi- and multilateral programs between the member academies;
- Prepare science-based proposals in order to advise governments and international organizations on policy issues related to engineering and technology development;
- Promote diversity and inclusion in the global engineering profession;
- Promote ethics in engineering education, research and practice;
- Contribute to continuous improvement and modernization of engineering education and practice internationally;
- Foster a balanced public understanding of the applications of engineering and technology; and
- Foster establishment of additional engineering academies in countries where none exist.

About the National Academy Technologies of France

The National Academy of Technologies of France (NATF) is a member of the CAETS, it's a national public administrative institution placed under the supervision of the Minister of High Education and Research and under the protection of the President of the Republic.

It has more than 300 elected members, from various backgrounds that reflect the diversity of technologies. Its organisation ensures the collegiality and relevance of its action in the exercise of its missions: opinions and reports, general orientations and action programmes are voted in plenary assembly. Four strong ideas govern the action of the Academy for an increasingly reasoned and collective appropriation of technologies: **progress, sense of general interest, listening, anticipation**.

Created at the beginning of the 21st century, the National Academy of Technologies of France is also heir to the age of Enlightenment. Its motto "*Sharing reasoned, chosen progress*" calls for technological development at the service of mankind, the environment and sustainable growth.

Denis RANQUE

Dear Participants,

Welcome to the 2022 CAETS Edition.

On behalf of all members of the National Academy of technologies of France, we are particularly pleased to host this edition, after these last two troubled years. Here we are, in person, in Versailles, gathered to listen, debate and network. And because technologies have mitigated the difficulties of Covid period, we are also able to welcome our digital guests live, from all around the world.

In accordance with CAETS baseline "Engineering a better world", the Committees have decided for this year to tackle a critical topic: **"Breakthrough technologies for healthcare"**.

It's no surprise, we all understand the importance of health issues for mankind in the years to come. During those two days of conference, we want to outline how technology and ethics have to be the two pillars of sustainable innovative development.

Our speakers are internationally renowned specialists. In their fields of expertise, they'll give us a broad vision of the main breakthrough we can expect in the upcoming years.

Gérard CREUZET

The programme is specially designed around six themes:

- Emerging technologies for innovative treatments and drug discovery
- Information and communication technologies for biology and health
- Disruptive technologies and global R&D trends
- Virtual Brain
- Technologies for repair – repairing the human body
- Ethics and societal impacts of technological breakthroughs

Our special thanks to our partner Dassault Systèmes and our sponsors, Air Liquide, Fondation Bettencourt Schueller, Fondation de l'Académie des technologies, Servier, European Institute for Creative Strategies & Innovation, and the Club de Paris des Directeurs de l'Innovation.

We wish you an excellent 2022 CAETS Edition and we look forward for very interesting presentations and rich debates.

Denis RANQUE,
Chairman of the National Academy of Technologies of France and Chairman of CAETS

Gérard CREUZET,
Chairman of the organizing and steering CAETS 2022 Committees

CAETS Committees

Organizing Committee

Gérard CREUZET
Chairman

Yves CARISTAN

Jean-Pierre CHEVALIER

Patrick LEDERMANN

Jacques LUKASIK

Bruno REVELLIN-FALCOZ

Steering Committee

Gérard CREUZET
Chairman

Yves BAMBERGER

Patrick COUVREUR

Erol GELENBE

Marc GIGET

Claudie HAIGNERÉ

Bruno JARRY

Patrick JOHNSON

Bruno REVELLIN-FALCOZ

Pascale SOURISSE

André SYROTA

Pascal VIGINIER

Gérard CREUZET, Chairman of Steering and Organizing committees, has a scientific background as a solid-state physicist. After graduating at École Normale Supérieure, he obtained a PhD thesis and a "Doctorat d'État" thesis at Orsay University. As a researcher in French CNRS, Gérard Creuzet is the author or co-author of 80 publications. Among other subjects, Gérard Creuzet is one of the co-author of the discovery of giant magnetoresistance in 1988, leading to the Nobel Prize of Albert Fert in 2007. In 1987, he moved to industry, beginning with various positions in R&D in Thales (professional electronics) and Valeo (automotive equipments) where he was Chief Technical Officer in 1996, and in 1999 General Manager of the Motors & Actuators Branch. In 2001, he moved to EDF as Senior VP for strategy and development, reaching the position of Chief Operating Officer in 2003. Since 2006, Gérard Creuzet is an independent consultant on strategy and management. He is currently working essentially as General Delegate of the "Groupe des Écoles Centrale" regrouping 5 engineering schools in France (Paris, Lyon, Nantes, Lille and Marseille) and 3 international locations (Beijing, Hyderabad, Casablanca). He is also Chairman of IPVF, a research Institute for photovoltaic compounds. Gérard Creuzet is a fellow of National Academy of Technologies of France, Delegate for foreign affairs.

Yves BAMBERGER was Head of Electricity de France R&D (2000 employees). Past positions include; CIO, Technical Director of the Generation and Transmission Division. Yves Bamberger began his career as research engineer in the French National Lab for Bridges and Roads. In parallel, he has been for 30 years Adjunct Professor at École Nationale des Ponts et Chaussées. Yves Bamberger is Vice President of the National Academy of Technologies of France.

Yves CARISTAN graduated from the École Normale Supérieure (ENS Ulm,1971), and has a PhD in Geophysics (MIT, USA,1981), and a PhD in Physics (University of Grenoble, 1984). Dr Caristan has been appointed to the following positions: Engineer at the French Atomic Energy Commission (CEA – 1981); Head of the Department of Monitoring of the Environment (DASE) at CEA (1996 – 1999); Director General of the French Geological Survey (Bureau de Recherche Géologiques et Minières, BRGM – 1999 – 2004); Director of the Physical Sciences Division (Direction des Sciences de la Matière, DSM) at CEA, and Director of the CEA/Saclay Research Center (2005 – 2012); Director for International Affairs at Université Paris-Saclay (2012 – 2015); ERC Counselor for Université Paris-Saclay ERC Candidates (Since 2015). Since 2013 he is a Fellow of the National Academy of Technology of France and Secretary General of Euro-CASE (the Network of Academies of Technologies in Europe) from 2017 to 2021. He received the Lamb Award from the French Academy of Sciences in 1999 and the CEA Applied Science Award in 1998. He is Knight of the Légion d'Honneur and Officer of the Ordre National du Mérite.

Jean-Pierre CHEVALIER trained as a physicist at Cambridge (M.A., Ph.D.) and is currently emeritus professor in the field of materials. He is a fellow of the NATF. He previously held the chair of industrial materials at the Conservatoire National des Arts et Métiers and was head of the engineering department of the Agence National de la Recherche.

Patrick COUVREUR, member of the Academy of Sciences, is an Emeritus Professor of Pharmacy at Paris-Saclay University. He is an internationally recognized scientist in nanomedicine. He co-founded three start-up companies (one of them entering the stock market) and developed an anticancer nanomedicine until end of phase III clinical trial. He is also member of the National Academy of Technologies of France, Medicine and Pharmacy in France and foreign member of two of the three US National Academies (Engineering and Medicine).

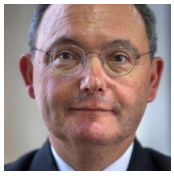
Erol GELENBE, BS (METU), PhD (NYU), DSc (Sorbonne) was Fulbright and NATO Science Fellow, and works on computer and network performance, and machine learning. Professor at the Polish Academy of Sciences and Fellow of several national Academies, he has held chairs at the Universities of Liege, Paris-Orsay, Paris-Descartes, Duke and Imperial College.

Marc GIGET is the Founder and President of the Euroconsult Group. Formal tenured professor of the Chair "Economics of Innovation" at CNAM Paris. President of the European Institute for Creative Strategies and Innovation and of the Paris Club of Chief Innovation Officers. Expert on Sciences & Technologies management for human progress.

Claudie HAIGNERÉ: MD rheumatologist (Hospital Cochin Paris 1984-90), PhD Neurosciences (CNRS (1986-1990)), Astronaut, Politician, CEO of a cultural public establishment. Astronaut with 2 space missions: Selected by CNES (French space agency) in 1985 as an astronaut candidate, training in Star City Russia from 1992, first space mission (16 days) on board Mir space station in 1996, became member of the European Astronaut Corps for ESA (European Space Agency) in 1999, second space mission (10 days) on board the ISS in 2001. Member of the French Government under the presidency of Jacques Chirac, as delegate Minister for research (2002-2004) and then delegate Minister for European Affairs (2004-2005). Advisor to ESA's DG for European space strategy (2005-2009). CEO of Universcience "science museum" (Palais de la Découverte + Cité des Sciences et de l'Industrie) (2009-2015). Senior advisor to ESA's DG (2015-2020) about Lunar exploration. Member of Foundations supporting STEM in education and innovation (Fondation L'Oréal, Fondation AIRBUS, Fondation CGenial). Grand Officier de la Légion d'Honneur. Docteur Honoris Causa (EPFL, Université de Mons, Université Catholique de Louvain), Beihang University (Beijing). Membre of the National Academy of Technologies of France, Académie des Sports, Académie des Sciences de l'Outre-Mer, Académie de l'Air et de l'Espace, International Academy of Astronautics, Membre of the Académie des Sciences de Belgique. Colonel (ADER network) in La Réserve Citoyenne de l'Armée de l'Air.

Bruno JARRY, PhD, has been a researcher in CNRS and Professor of Genetics in Strasbourg University. In 1986 he moved to industry as R&D Vice-president of ORSAN, the industrial biotechnology division of the Lafarge Group in which he also managed two business units, Sogetal in California and Ringdex, a joint-venture with the Japanese Group Mercian. He was also the cofounder of two biotech start-ups. Bruno was the R&D Director of the Belgian Group Amylum from 1994 to 2000 then Science Director of the British Group Tate & Lyle. From 2004 to 2008 he was a senior advisor to the President of Institut Curie, a French Foundation running a large medical research institute and a hospital, both devoted to cancer. He then served as a senior advisor for biofuels and green chemistry in the French Prime Minister cabinet from 2008 to 2012. An NATF elected fellow since 2003 he chaired its Biotechnology Commission for several years and served as Vice-president of the Academy in 2017 and as President in 2018. He sits at the board of several biotech-oriented companies.

Patrick JOHNSON is SrVP Research at 3DS, defining scientific bases and inventing disruptive technologies for the Industry Renaissance. After several R&D positions (head of AI, CATIA Brand), he took over Research, set up key public/private alliances and launched the Lifesciences strategic diversification (BIOVIA, MEDIDATA Brands). Member of the National Academy of Technologies of France and INRIA's Scientific Board.



Patrick LEDERMANN is a member of the national academy of technologies of France, scientific advisor to the director of energies, CEA, and chairman of the nuclear development committee, OECD nuclear energy agency.

Jacques LUKASIK is a physicist, with a background in non-linear optics and lasers. He is a former Senior VP and Chief Scientific Officer of LAFARGE. A Fellow of the NATF he is also an Associate foreign member of the Civil Engineering Committee of the Polish Academy of Sciences. Between 2011 and 2016, he was appointed Secretary General of Euro-CASE.

Bruno REVELLIN-FALCOZ Graduated in 1964 from Supaero. Joined the Dassault Aviation Design Department in 1966. Focused his activities on new techniques and advanced military and civil programs, both on national and international level. Appointed Senior Vice President Research, Design and Engineering in 05/1982, he is in charge of all the technical programs (The family of business jets Falcon, Mirage 2000 and Rafale fighters). Vice Chairman in 2000. Leaves Dassault Aviation, after 45 years in the company. Member of the scientific advisory board of Office Parlementaire d'Etude des Choix Scientifiques et Technologiques (2010-2015). Member of the Air and Space Academy of France. Great Prize 2008 of "Ingenieurs de France". Corresponding member of the Swiss Academy of Engineering Sciences (SATW). Vice-Chairman of the European Institute of Innovation and Technologies (EIT) 2012-2018. President (2011/2012) of the National Academy of Technologies of France, then Honorary President and Delegate for Foreign Affairs (2013/2021). Member of the Euro-CASE Board (2013/2021).

Pascale SOURISSE is Senior Executive Vice President, International Development of Thales. She is a member of the Executive Committee. She graduated from École Polytechnique and Telecom ParisTech. She is an Officier of the French Légion d'honneur and is a Director of Renault, Vinci, École Polytechnique and a member of the National Academy of Technologies of France .

André SYROTA has been nominated Executive Director of the French National Institute of Health and Medical Research, Inserm, in October 2007. He previously was Director of the Life Sciences Division of the French Atomic Energy Commission (1993-2007) and Professor of Biophysics and Nuclear medicine (MD,PhD) at the University of Paris-Sud. He was also head of the Service hospitalier Frédéric Joliot (CEA, Orsay), one of the European leading nuclear medicine and medical imaging research institutes (1984-2007). André Syrota is the author of more than 200 articles and 40 book chapters in imaging with PET and NMR. He has been a member of various boards at national and European research institutions.

Pascal VIGINIER, chaired the French National Academy of Technology between 2019 and 2021. He is now honorary president. He is an engineer, as graduate of École Polytechnique and Telecom Paris, both now founders of the new Institut Polytechnique de Paris. His carreer is focused on telecommunications in Orange Group, where he was Group R&D EVP and then Group Chief Information Officer. He was appointed 5 years ago advisor to Orange CEO, leading customized high-level consulting. He is member of the scientific council of the French National Agency for Research (ANR) and chairman of Telecom Sud Paris, an engineer high school, member of Institut Polytechnique de Paris and Institut Mines Telecom.

1. Program

At a glance

TUESDAY 27 SEP. 2022	**WEDNESDAY** 28 SEP. 2022	**THURSDAY** 29 SEP. 2022
Registration and welcome coffee 08:00 - 09:00	Registration and welcome coffee 08:00 - 08:30	
Welcome introduction 09:00 - 09:15		
Government official speech 09:15 - 09:40	**SESSION 3** Disruptive technologies and global R&D trends 08:30 - 10:30	Science in the Age of Experience DASSAULT SYSTEMES
Introductory Keynotes address 09:40 - 10:30		
10:30 - 11:00 Coffee break	10:30 - 11:00 Coffee break	
SESSION 1 Emerging technologies for innovative treatments and drug discovery 11:00 - 13:00	**SESSION 4** Virtual brain 11:00 - 13:00	
13:00 - 14:30 Lunch break	13:00 - 14:30 Lunch break	
SESSION 2 The foundations of information and communication technologies (ict) for biology and health *(Part 1)* 14:30 - 15:45	**SESSION 5** Technologies for repair – repairing the human body 14:30 - 16:30	
15:45 - 16:15 Coffee break	16:30 - 17:00 Coffee break	
SESSION 2 The foundations of information and communication technologies (ict) for biology and health *(Part 2)* 16:15 - 17:25	**SESSION 6** Ethics and societal impacts of technological breakthroughs 17:00 - 18:30	
CAETS Communication Prizes – Awards Ceremony 17:25 - 18:00	Final address 18:30 - 18:55	
Dinner at Palais des Congrès 19:30 - 22:00	Gala Dinner at Château du Bois du Rocher 19:15 - 22:30	

Day 1 – 27 September 2022

OFFICIAL OPENING

9.00 - 9.05
Gérard CREUZET - Chairman of the organizing and steering CAETS 2022 Committees

9.05 - 9.15
Denis RANQUE - Chairman of the National Academy of Technologies of France and Chairman of CAETS

9.15 - 9.40
Sylvie RETAILLEAU - French Ministry for Higher Education and Research

KEYNOTES

9.40 - 10.05
Elias ZERHOUNI - Grand challenges in life sciences R&D

10.05 - 10.30
Christiane WOOPEN - Ethics by design in technologies for health

10.30 - 11.00 Coffee Break

SESSION 1

EMERGING TECHNOLOGIES FOR INNOVATIVE TREATMENTS AND DRUG DISCOVERY

Coordinator Patrick COUVREUR

11.00 - 11.25
Patrick COUVREUR - Advanced nanomedicines and drug delivery

11.25 - 11.50
Thomas CLOZEL - The medicine of tomorrow

11.50 - 12.15
Melissa J. MOORE - mRNA as Medicine

12.15 - 13.00 Q & A

13.00 - 14.30 Lunch

SESSION 2

THE FOUNDATIONS OF INFORMATION AND COMMUNICATION TECHNOLOGIES (ICT) FOR BIOLOGY AND HEALTH

Coordinator Erol GELENBE

14.30 - 14.55
Patrick JOHNSON - Virtual twins for Healthcare

14.55 - 15.20
Sushmita MITRA - Intelligent Analysis of Biomedical Images

15.20 - 15.45
Kristin LAUTER - Private AI for human health and genomic data

15.45 - 16.15 Coffee Break

16.15 - 16.40
Egidio d'ANGELO - Multiscale brain modelling for health and technology

16.40 - 17.25 Q & A

17.25 - 18.00
AWARD CEREMONY - CAETS COMMUNICATION PRIZES

18.00 - 19.30
NETWORKING

19.30 - 22.00
DINNER AT PALAIS DES CONGRÈS

Day 2 – 28 September 2022

SESSION 3

DISRUPTIVE TECHNOLOGIES AND GLOBAL R&D TRENDS

Coordinators Denis LE BIHAN and André SYROTA

8.30 - 8.55
Denis LE BIHAN - Science without instruments is the ruin of the soul: the MRI example

8.55 - 9.20
Mathias FINK - Ultrafast ultrasonic imaging: the future of ultrasound

9.20 - 9.45
Gondi Kondaiah ANANTHASURESH - Micromachinery for Mechano-diagnostics

9.45 - 10.10
Carrie HILLYARD - Turning health tech into better health outcomes: how ready are we to adopt disruptive healthcare technologies?

10.10 - 10.30 Q & A

10.30 - 11.00 Coffee Break

SESSION 4

VIRTUAL BRAIN

Coordinator André SYROTA

11.00 - 11.25
Viktor JIRSA - Personalized virtual brain technology for drug-resistant epilepsy and neurosurgery

11.25 - 11.50
Sridevi SARMA - A noninvasive EEG marker of the epileptic brain: how dynamic brain network properties reveal epileptogenicity during rest

11.50 - 12.15
Randy McINTOSH - Using The Virtual Brain to trace trajectories of brain health in ageing

12.15 - 13.00 Q & A

13.00 - 14.30 Lunch

SESSION 5

TECHNOLOGIES FOR REPAIR – REPAIRING THE HUMAN BODY

Coordinator Bruno JARRY

14.30 - 14.55
Zhongchao HAN - Stem cells based technologies

14.55 - 15.20
Stéphanie LACOUR - Neuroprosthetic medicine: innovation, interdisciplinarity and translation

15.20 - 15.45
Serge PICAUD - Restoring vision in blind patients: from prosthesis to optogenetic and sonogenetic therapy

15.45 - 16.30 Q & A

16.30 - 17.00 Coffee Break

SESSION 6

ETHICS AND SOCIETAL IMPACTS FO TECHNOLOGICAL BREAKTHROUGHS

Coordinators Claudie HAIGNERÉ, Christiane WOOPEN

17.00 - 18.30 **Panelists: Patrick COUVREUR, Virginia DIGNUM, Thierry MAGNIN, Alison NOBLE, Jeroen VAN DEN HOVEN**

18.30 - 18.40
SCIENCE IN THE AGE OF EXPERIENCE – Bernard CHARLES, vice Chairman of the Board, CEO Dassault Systèmes

18.40 - 18.50
FINAL ADDRESS – Denis RANQUE

18.50 - 18.55
PROGRAM FOLLOW UP – Gérard CREUZET

19.15 - 19.30
MEETING POINT IN THE LOBBY - TRANSFERT BY BUS

20.00 - 22.30
GALA DINNER AT CHÂTEAU DU BOIS DU ROCHER - Intervention by Thierry BRETON,
European Commissioner, Fellow of the National Academy of Technologies of France

Government Offical Speech

Sylvie RETAILLEAU

French Ministry for Higher Education
and Research

Credit : French Ministry for Higher Education and Research

Sylvie Retailleau graduated from ENS Cachan in 1988 and received her PhD in applied physics from the University of Paris-Sud in 1992. Her research in the Institut d'Electronique Fondamentale (IEF, Université Paris-Sud/CNRS) focused on the theoretical study of the physics of semiconductor components for advanced electronics.

She became a professor in 2001 at the Université Paris-Sud - renamed Université Paris-Saclay in 2020. She was then in charge of the IST Master's degree (Information, Systems, Technology) until 2008, and leaded a research operation on "Integrated Quantum Components for NanoElectronics" of the Institute of Fundamental Electronics until 2011.

Vice president of the physics department of the Faculty of Sciences of Orsay from 2007 to 2008, then Vice dean in charge of training from 2008 to 2011, she was Dean of the Faculty from September 2011 to May 2016. Sylvie Retailleau was then President of the Université Paris-Sud from May 2016 to December 2018. She then strongly involved in the creation of the Paris Saclay Idex project, working on the training plan and on the training-research structuring. She also participated in the preparatory work for the French research programming law.

She was elected President of the Université Paris-Saclay on March 2, 2020 exercised this mandate until her appointment as Minister of Higher Education and Research on 20 May 2022.

2. Speakers and abstracts

KEYNOTES

Elias ZERHOUNI

Emeritus Professor, Radiology and Biomedical Engineering, John Hopkins University - Fellow of the National Academy of Technologies of France and of the National Academy of Medicine

BIO

Elias Zerhouni, M.D., Professor Emeritus Radiology and Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland, USA. Dr. Zerhouni was most recently the President, Global Research & Development, and a member of the Executive Committee for Sanofi from January 2011 to July 2018.

Dr. Zerhouni's academic career was spent at the Johns Hopkins University and Hospital where he was professor of Radiology and Biomedical engineering and senior adviser for Johns Hopkins Medicine. He served as Chair of the Russell H. Morgan Department of Radiology and Radiological Sciences, Vice Dean for Research and Executive Vice Dean of the School of Medicine from 1996 to 2002 before his appointment as Director of the National Institutes of Health from 2002 to 2008. In that position he oversaw the NIH's 27 Institutes and Centers with more than 18,000 employees and a budget of $29.5 billion (2008).

In November 2009, President Obama appointed Dr. Zerhouni as one of the first presidential U.S. science envoys. Dr. Zerhouni also served as senior fellow to the Bill and Melinda Gates foundation from 2009 to 2010 and senior advisor to the CEO of Sanofi.

Dr. Zerhouni has founded or co-founded five start-up companies, authored more than 200 publications and holds several patents. He has assumed positions on several Boards, including most recently, the board of the Lasker Foundation, Research! America and the NIH Foundation. He is also a member of the U.S. National Academy of Medicine and the U.S. National Academy of Engineering. He received the prestigious Legion of Honor medal from the French National Order in 2008, and was elected in 2010 as a member of the French Academy of Medicine and appointed as Chair of Innovation at the College de France in 2011.

ABSTRACT

"Grand challenges in life sciences R&D"

The core challenges facing the life sciences today are the enormous complexity of living systems and the need for more precise interventions. The nature of scientific inquiry in the life sciences is undergoing a profound transition driven by these two challenges. Over the past decades, most research was focused on discovering the basic molecular components of living systems. Based on the efforts of small focused teams, led by creative scientists, our knowledge of structures and functions of the core elements of living systems has progressed remarkably. This phase of discovery is comparable to what happened in the physical sciences a century before, with the characterization of chemical elements, atoms and particles and the basic forces linking them. As molecular discoveries such as that of DNA, RNA, enzymes, G-protein coupled receptors and many others, it became clear that integrating these discoveries into a coherent understanding of living systems would require novel approaches of a scale and scope beyond the capabilities of traditional mono-disciplinary teams. The emergence of larger multi-disciplinary R&D teams comprised of scientists and engineers trained in physical sciences, engineering, computing, data sciences and biology in a *convergence* of scientific fields is increasingly necessary to understand high complexity systems but presents challenges beyond those of more traditional reductionist approaches. These challenges in the life sciences can be divided into two distinct classes: 1: understanding of structure-function relationships at systems scale and 2: precisely modifying such structural and functional systems for defined benefits.

1-Key challenges in understanding biology: The successful development of many scientific technologies such as automated multiplexed experimental platforms and models, greater separation technologies such as microfluidics, higher temporal and spatial resolution imaging systems, high resolution mass spectroscopy, next generation sequencing and other basic technologies now generate a quantity and density of data several orders of magnitude greater than a few years ago. Laboratories today can create terabytes of data per experiment. Integration of these multidimensional data across multiple types of experiments greatly increases the difficulty of data acquisition, storage and analysis. This challenge is far from being overcome despite recent progress in data sciences and artificial intelligence. For example, the protein structure prediction program Alpha-Fold is a breakthrough made possible by years of well curated prior work accumulating precise coordinates of thousands of protein structural motifs available to provide learning sets to machine learning neural networks algorithms. Such well characterized data sets however do not yet exist for many other areas of research and need to be built in an integrated and standardized fashion: a major challenge not yet resolved. Understanding a complex system is rarely done in one step but requires full characterization of sub-modules such as the immune system or cancer pathways for example which can then be integrated at higher scale. Simultaneous analysis of multiple biomarkers to understand the behavior of such biologic modules has now become essential but remains challenging. The same is true for population level data acquisition and analysis of digital biomarkers and bio-sensors needed to better diagnose and manage chronic diseases such as diabetes, heart disease or Alzheimer disease.

2-Key challenges in modifying biology: The discovery of genetic modification tools has revolutionized the potential to harness biology for human benefit. The notion of genetically modifying organisms has been pursued for decades. The discovery 10 years ago of CRISPR mechanisms to edit the genome is revolutionizing the field but in vivo delivery of edited molecular constructs remains a fundamental challenge. Gene therapy is dependent on targeted viral vectors or nano-particles which require further innovation for generalization of these promising technologies. Less appreciated are the challenges inherent to the production of these biology modifying constructs. For example, the efficiency and quality of plasmids and cell lines transfection levels for complex proteins is still low. Downstream steps in the field of bioprocessing still rely on mammalian cell lines such as chinese hamster ovary (CHO) cells developed decades ago and multiple separation technologies such as proprietary media, Protein A, resins and chromatography. The yields achieved today of a few grams per litter of media can only economically support medical applications. Research in creating novel production cell lines with order of magnitude greater yields and improved manufacturing systems should be a priority despite all the understandable regulatory resistance to change. Batch processing in large expensive bioreactors should be replaced with more flexible, easily scalable modular systems such as continuous flow reactors. Ultimately, the costs and time of production have to be greatly reduced if the dream of making life sciences advances equitably accessible in combating the challenges such as pandemics, global warming and environmental degradation.

KEYNOTES

Christiane WOOPEN

Director of the Center for Life Ethics, University of Bonn; former Chair of the European Group on Ethics in Science and New Technologies, former member of IBC International Bioethics Committee UNESCO

BIO

She has been Heinrich Hertz Professor of Life Ethics at the University of Bonn and founding director of the Center for Life Ethics since October 2021. Previously, she was Professor of Ethics and Theory of Medicine at the University of Cologne, where she was Founding Director of the interfaculty Cologne Center for Ethics, Rights, Economics, and Social Sciences of Health (ceres). In addition to leading national and international research projects, she is involved in policy advocacy, including as Chair of the German Ethics Council (2012-2016), as President of the Global Summit of National Ethics Councils (2014-2016), as a member of the UNESCO International Bioethics Committee until 2017, as Co-Spokesperson of the German Government Data Ethics Council from 2018 – 2019, and as Chair of the European Group on Ethics in Science and New Technologies (EGE) from 2017 to 2021. Woopen is a member of several academies of sciences (NRW, BBAW, Academia Europaea) and was awarded the Federal Cross of Merit 1st Class.

ABSTRACT

"**Ethics by design in technologies for health**"
Technologies are increasingly shaping every area of our individual and societal life, including healthcare. They help to better understand, diagnose, treat, and prevent diseases and they can contribute to enhancing healthy functions. Especially digital technologies including algorithmic systems that are called artificial intelligence collect, store, and use tons of personal and nonpersonal data that can be used to develop precision medicine or the so called P4 medicine: a healthcare that is preventive, predictive, personalized and participatory. Eventually a learning healthcare system could emerge, where data from everyday healthcare can be used for research and the results from research are immediately introduced into everyday healthcare. Huge financial resources and technological skills are needed to develop and use these technologies, thus tech giants enter the stage and become increasingly powerful also in healthcare. "Values are baked into everything". There is no technology that doesn´t involve values. From the very idea what technologies are developed for to the way they are designed, deployed, and used values and ethically relevant aspects are touched upon. Furthermore, the system of organizations and institutions around the technologies and their mutual influence on each other impact ethical principles such as autonomy, privacy, justice and solidarity. Digital, social and political technologies shape how people can or cannot live healthy lives, not only within the healthcare system but also beyond. Not least they influence the understanding of underlying concepts such as health and disease, or body and mind. It is crucial to reflect ethical issues right from the beginning of technology development and to do so throughout the whole life cycle, including aspects of sustainability. Only then technologies will contribute to the good and flourishing lives that individuals and societies aspire to live.

SESSION 1

EMERGING TECHNOLOGIES FOR INNOVATIVE TREATMENTS AND DRUG DISCOVERY

Coordinator Patrick COUVREUR

SESSION ABSTRACT

Major advances in technology are transforming the way scientists conduct research on diseases prevention and treatment. Drug discovery and delivery, as well as vaccines are currently entering a period of significant changes, due to a better exposition to emerging and innovative technologies. This is illustrated by the clever mRNA modification and nano formulation, as a unique and disruptive platform for vaccination. Artificial intelligence and high-throughput screening for drug discovery, as well as the use of nanotechnologies for drug targeting are other examples improving the treatment or diagnosis of severe diseases.

Patrick COUVREUR

Fellow of the French Académie des Sciences, of the National Academy of Technologies of France, of the National Academy of Medicine and the French Academy of Pharmacy

BIO

Patrick Couvreur, member of the Academy of Sciences, is an Emeritus Professor of Pharmacy at Paris-Saclay University. He is an internationally recognized scientist in nanomedicine. He co-founded three start-up companies (one of them entering the stock market) and developed an anticancer nanomedicine until end of phase III clinical trial. He is also member of the Academies of Technologies, Medicine and Pharmacy in France and foreign member of two of the three US National Academies (Engineering and Medicine).

ABSTRACT

"**Advanced nanomedicines and drug delivery**"
The clinical use and efficacy of conventional chemotherapeutics is hampered by the following limitations: (i) drug resistance at the tissue level due to physiological barriers (non-cellular based mechanisms), (ii) drug resistance at the cellular level (cellular mechanisms), and (iii) non-specific distribution, biotransformation and rapid clearance of the drugs in the body. Nanomedicines (ie., drug loaded onto nanocarriers) may overcome some of these limitations. The presentation will show that before entering into clinical trials, the discovery of advanced nanomedicines rests on four scientific pillars: chemistry, physics, cellular and molecular biology as well as, experimental pharmacology. This will be illustrated by the following nanomedicine platforms with the demonstration that interdisciplinarity is the basis for scientific and technological successes:

- The design of biodegradable doxorubicin-loaded polyalkylcyanoacrylate nanoparticles for the treatment of the multidrug resistant hepatocarcinoma (a nanomedicine with phase III clinical trials ended).
- The construction of nanoparticles made of metal oxide frameworks (NanoMOFs), a highly hyperporous material obtained by the complexation of iron oxide clusters with diacids. The nanopores of this material may be finely tuned to the molecular dimension of the drug molecule to be encapsulated.
- The "squalenoylation", a technology that takes advantage of the squalene's dynamically folded molecular conformation, to link this natural and biocompatible lipid with anticancer drug molecules to achieve the spontaneous formation of nanoassemblies (100–300 nm) in water, without the aid of surfactants. Surprisingly, these squalene-based nanoparticles are using the circulating endogenous LDL as "indirect" carriers for targeting cancer cells with high expression of the LDL receptors. The application of the "squalenoylation" concept for the treatment of brain ischemia and spinal cord injury5 will be discussed, too. And it will be shown that the linkage of squalene to leu-enkephalin can confer to the targeted neuropeptide a significant anti-hyperalgesic effect, devoted of the morphine side effects (ie., addiction, tolerance and resiratory depression). The possibility to use other terpenes (natural or synthetic) than squalene to design nanoparticles for the treatment of cancer will be discussed, too.

The design of "multidrug" nanoparticles, combining in the same nanodevice chemotherapy and imaging properties (ie., "nanotheranostics") or various drugs with complementary biological targets will be also examined.

Finally, it will be shown that the construction of nanodevices sensitive to endogenous (ie., pH, ionic strength, enzymes etc.) or exogenous (ie., magnetic or electric field, light, ultrasounds etc.) stimuli may allow the spatio-temporal controlled delivery of drugs and overcome resistance to current treatments.

Thomas CLOZEL

Chief Executive Officer of Owkin

BIO

Thomas is the CEO and Co-Founder at Owkin, leading medical research and business intelligence. He is a former Assistant Professor of Clinical Onco-Hematology at Hopital Henri Mondor in Paris. Thomas is also a former member of Ari Melnick's lab at the Weill Cornell Medical College where he co-led several projects focused on prediction of resistance to chemotherapy in B-cell lymphoma.

ABSTRACT

"**The medicine of tomorrow**"
Medicine today is booming in multiple fields. However, research is still slow on multiple fronts, many diseases are still unmet needs, precision medicine remains an exception, and pharmaceutical companies' efficiency is not building up at high pace. But the medicine of tomorrow is at our doors, fed by the progress of quantum computers and data science, breaking silos of research and competition, and energized by new flux of breakthroughs and data. What will the medicine of tomorrow look like in that regard? What can we hope for patients and caregivers?

Melissa MOORE

Chief Scientific Offier,
Platform Research, Moderna

BIO

Dr. Melissa J. Moore currently serves as Chief Scientific Officer, Scientific Affairs, at Moderna. She joined Moderna in 2016 from the University of Massachusetts Medical School (UMMS), where she served as Professor of Biochemistry & Molecular Pharmacology, Eleanor Eustis Farrington Chair in Cancer Research, and a long-time Investigator at the Howard Hughes Medical Institute (HHMI). Dr. Moore was also a founding Co-Director of the UMMS RNA Therapeutics Institute (RTI) and was instrumental in creating the Massachusetts Therapeutic and Entrepreneurship Realization initiative (MassTERi), a faculty-led program intended to facilitate the translation of UMMS discoveries into drugs, products, technologies and companies. Dr. Moore is an elected member of the National Academy of Sciences (2017), a Fellow of the American Academy of Arts and Sciences (2019), and recipient of the RNA Society Lifetime Achievement Award (2021). Other accolades include being named one of the 100 Fiercest Women in Biotech (2018) and to the PharmaVoice 100 (2019). She currently sits on the Board of Directors of Tessera Therapeutics, multiple Scientific Advisory Boards, and has co-founded two companies (Comanche Biopharma and Via Scientific) to further initiatives begun at UMMS.

Dr. Moore holds a B.S. in Chemistry and Biology from the College of William and Mary, and a Ph.D. in Biological Chemistry from MIT, where she specialized in enzymology under Prof. Christopher T. Walsh. She began working on RNA metabolism during her postdoctoral training with Phillip A. Sharp at MIT. During her 23 years as faculty member, first at Brandeis University (1994-2007) and then at UMMS (2007-2016), her research encompassed a broad array of topics related to the roles of RNA and RNA-protein (RNP) complexes in gene expression, and touched on many human diseases including cancer, neurodegeneration and preeclampsia. Her passions include educating the public about the coming age of nucleic acid medicines, increasing Diversity, Equality and Inclusion (DEI) at all levels of the Biotechnology workforce, and playing Texas Hold'em.

ABSTRACT

"**mRNA as Medicine**"
With synthetic mRNA now fully validated as a platform for the rapid creation and distribution of highly effective vaccines, the age of mRNA medicines is upon us. Because mRNAs can program the body to produce any desired protein (e.g., cytoplasmic, intraorganelle, membrane-bound, secreted) or set of proteins (e.g., multiprotein complexes) in their native state, possible applications are nearly infinite. In addition to a plethora of new vaccines (both prophylactic and therapeutic), experimental mRNA medicines already in the clinic include pro-inflammatory cytokines as anticancer agents, an angiogenic promoting blood vessel regrowth in damaged heart muscle, and protein replacement therapies for inborn metabolic diseases. I will discuss Moderna's overall process for production of mRNA medicines and our new "mRNA Access" initiative designed get Moderna's formulated mRNAs into the hands of academics interested in helping create the mRNA medicines of the future.

SESSION 2

THE FOUNDATIONS OF INFORMATION AND COMMUNICATION TECHNOLOGIES (ICT) FOR BIOLOGY AND HEALTH

Coordinator Erol GELENBE

SESSION ABSTRACT

Digital technologies are pervasive in all aspects of human health, and areas emerge where fundamental aspects join hands with urgent needs. This session focuses on key areas where the encounter between ICT and health can enable major improvements in health, including "Digital twins" that learn from reality to reproduce the behaviour of the "real twin", the ICT assisted enhancement of human capabilities in extreme environments such as underwater or outer space, the need to ensure the privacy and information security of the whole chain of health provisioning through ICT, and one of the greatest technological challenges being addressed to understand and emulate the cognitive capabilities of human and animal brains, by representing in-silico the emergence of thought and intelligence. Our four renowned speakers will take us into the revolution in computing and communications that supports and enhances health and well-being, ending with a panel discussion that will include questions from the audience.

Patrick JOHNSON

Fellow of the National Academy of Technologies of France, Senior Vice-President Corporate Research & Science Strategy of Dassault Systèmes

BIO

Mr Johnson is SrVP Research at 3DS, defining scientific bases and inventing disruptive technologies for the Industry Renaissance. After several R&D positions (head of AI, CATIA Brand), he took over Research, set up key public/private alliances and launched the Lifesciences strategic diversification (BIOVIA, MEDIDATA Brands). Member of the French Academy of Technology and INRIA's Scientific Board.

ABSTRACT

"**Virtual twins for Healthcare**"

What if we could invent new ways of representing life, specifically by creating the virtual twins of the human body.

Today's fragmentation of patient information, medical knowledge and know-how across disciplines and locations creates barriers in patient access to care and patient journey. These global health challenges require a transformative level of healthcare on multiple levels: patient-centric health systems & integrated care chains. Bringing this vision to life requires creating a digital medical Twin with a detailed view of each patient's condition, anatomy, biology and life exposure. This system must capture the vast amounts of data generated about each individual and connect that with knowledge from researchers and clinicians from around the globe. The system must also be available to a patient's entire care team. The unifying vision behind this is a virtual twin: an integrative reference of personal health information.

The virtual twin is created guided by science and known medical knowledge. It functions as a dynamic model, consistently fed by clinical data, medical history and environmental exposures. Because a virtual twin ambitions to provide multidiscipline and multi scale representations of a human body organs and systems, including all physiology, genetic code and fundamental biomarkers, it can act as a true enabler for new understandings and approaches to health diagnosis, prognosis, treatments and anticipation of future conditions. Medical practices, such as surgery will more and more exploit those 360° representations, also opening for a new level of know-how sharing and dissemination. The virtual twin enables playing 'What if' scenarios to compare different interventions on the same patients. It can help surgical planning, personalized implant design or surgical procedure guiding in the operating room. And as understanding of human biology, physiology, biomechanics and pharmacology improves, these virtual twins promise to become more precise, predictable and usable.

After decades-long support of helping manufacturing industries use virtual twins to innovative non-organic products, Dassault Systemes is now massively focusing to transform the organic world. You'll discover in the presentation examples of how we're doing this today, including patient's organs, hospitals and health systems' twins.

Sushmita MITRA

Full professor at the Machine Intelligence Unit (MIU), Indian Statistical Institute, Kolkata

BIO

Sushmita Mitra is Professor HAG at Indian Statistical Institute, Kolkata. She was in the RWTH Aachen, Germany as a DAAD Fellow (1992-1994). She received the National Talent Search Scholarship (1978-1983), University Gold Medal (1988), IEEE NNC Outstanding Paper Award (1994), CIMPA-INRIA-UNESCO Fellowship (1996) and Fulbright-Nehru Senior Research Fellowship (2018-2020). She is IEEE CIS Distinguished Lecturer, Chair IEEE Kolkata Section, INAE Chair Professor (and J. C. Bose National Fellow. She is the author of several books, serves in editorial boards of many journals and has more than 200 journal publications. According to the Stanford List, she is ranked among the top 2% scientists worldwide in the domain of Artificial Intelligence and Image Processing.

Dr. Mitra is a Fellow of the IEEE, The World Academy of Sciences (TWAS), Indian National Science Academy (INSA), International Association for Pattern Recognition (IAPR), and Fellow of the Indian National Academy of Engineering (INAE) and The National Academy of Sciences, India (NASI). She has visited more than 30 countries as a Plenary/Invited Speaker or an academic visitor.

ABSTRACT

"Intelligent Analysis of Biomedical Images"
The talk will focus on the role of Artificial Intelligence and Learning in the domain of healthcare. Topics like Genomics, Radiomics, Radiogenomics, and Personalized Medicine will be discussed.Some research applications made by our group in these domains will be described. These include detection, segmentation and survival prediction in brain tumors from MRI, screening of covid -19 from lung scans, and early detection of diabetic retinopathy from fundus images of the eye.

Kristin LAUTER

Director of West Coast AI Research, Meta

BIO

Kristin Lauter, Director of West Coast AI Research, Meta. Fellow of the American Association for the Advancement of Science, Fellow of the American Mathematical Society, Honorary Member of the Royal Mathematical Society of Spain, Fellow of the Society of Industrial and Applied Mathematics, Fellow and Past President of the Association for Women in Mathematics, Affiliate Professor University of Washington.

ABSTRACT

"**Private AI for human health and genomic data**"
Artificial Intelligence shows tremendous promise for improving human health, but the privacy risks inherent in collecting and handling human health data are many. Private AI is based on Homomorphic Encryption (HE), a new encryption paradigm which allows the cloud to operate on private data in encrypted form, without ever decrypting it, enabling private training and private prediction on health data. In 2016 the ICML CryptoNets paper showed for the first time that it was possible to evaluate neural nets on homomorphically encrypted data, and opened new research directions combining machine learning and cryptography. The security of Homomorphic Encryption is based on hard problems in mathematics involving lattices, a candidate for post-quantum cryptography. This talk will explain Homomorphic Encryption, Private AI, and show HE in action for protecting health and genomic data.

Egidio d'ANGELO

Full Professor of Department of brain and behavioural sciences, University of Pavia

BIO

Egidio d'Angelo is Full Professor of Physiology, co-chair of the Department of Brain and Behavioral Sciences and director of the Brain Connectivity Center of IRCCS Mondino. ED coordinates brain research at the international level, spanning from neurophysiology to neurotechnology and medicine, and has uninterruptedly coordinated 9 European projects and several National projects of the Italian Ministry of Health, of the Ministry of the University and Research and other institutions over the 1995-2022 period. In the last 10 years, ED has participated as core partner and co-director in the European Flagship Human Brain Project (HBP- 2020 Framework Program for Research and Innovation under the Framework Partnership Agreement No. 650003), aimed at bridging cellular-molecular research with integrative neuroscience through computational models and advanced ICT technologies. This HBP activity involves world-wide collaborations on neuronal and microcircuit modeling, MRI and BOLD signals, closed-loop robotic simulators, cellular recordings in vivo, neuronal modelling, Virtual Brain Modeling, Medical Informatics. ED is core partner of CEN (Cerebellum and Emotional Networks), a Marie Skłodowska-Curie ITN that will explore the brain circuits that underlie emotional behavior (Horizon 2020 research and innovation program- GA No 956414). ED published 234 peer reviewed papers (most as first or last author) including Nature, Science, Nature Neuroscience, Nature Communication, Nature Communications Biology, Cell, Neuron, TINS, J Neuroscience and presented his research at several meetings worldwide, often as invited speaker (recently UCL, CERN, Rimini, TEDex, CAETS). The main scientific interests are centered on the cellular and circuit functions of the cerebellum and its pathologies in the context of the whole-brain activity.

ABSTRACT

"**Multiscale brain modelling for health and technology**"

Addressing the multiscale brain organization is fundamental not only to understand its inherent mechanisms of function but also to answer neuropathological questions and promote the development of new technologies for AI and health. While relevant advances have been made on the experimental front - encompassing genetics, molecular biology, cell physiology and brain imaging – recent developments in informatics and big data have opened a new scenario, in which multiscale computational models can be used to simulate brain functions and to foster a range of technological applications. Multiscale brain modelling is an emerging technological sector. In principle, it should be possible to model neurons and synapses in detail and then connect them into large neuronal assemblies to explain the relationship between microscopic phenomena, large-scale brain functions, and behavior. More difficult is to infer neuronal functions from ensemble measurements like those currently obtained with MRI, EEG, MEG or PET. In this presentation, I will consider theories and strategies for combining bottom-up models, generated from principles of neuronal biophysics, with top-down models, based on ensemble representations of network activity and on functional principles. Modelling the relationship between microscopic phenomena and large-scale brain functions could allow to predict how a drug that binds specific receptors modifies local and distributed circuit activity or how genetic alterations of membrane ionic channels or receptors reverberate up to brain functions and dynamics. This, in turn, would allow to identify potential targets for pharmacological and physical therapy, e.g., through electrical or magnetic stimulation of specific circuits, or for precision surgery. Clearly, these applications open new perspectives toward personalized and precision medicine, for example generating brain digital twins. These can be intended as personalized copies of a subject's brain that can be used to simulate specific functionalities anticipating the consequences of, e.g., neurorehabilitation or surgical intervention. Multiscale brain modeling has also breakthrough potential in information technologies and AI. Spiking neural networks can be transformed in hardware to generate neuromorphic computers and be embedded inside closed-loop controllers to generate new computational architectures and autonomous robots. In conclusion, multiscale brain modelling is not just fundamental to understand brain functioning but also to promote digital technologies for society and health in ways that remain to be worked out and exploited in full.

SESSION 3

DISRUPTIVE TECHNOLOGIES AND GLOBAL R&D TRENDS

Coordinator Denis LE BIHAN

SESSION ABSTRACT

The past decade has seen several major "disruptive technologies" that refer to innovations that operate in a superior way to other products on the market, which leads to significant, usually positive change. This is mainly due to the evolution of new interdisciplinary research areas at the interface of biology, physics, mathematics and chemistry. Bioinformatics (with the development of Artificial Intelligence, Cognitive Computing, Machine Learning, Robotic Process Automation…), genomics, imaging, synthetic biology, systems biology, tissue engineering are examples. These new research areas have brought a revolution in medicine. Following an overview of R&D breakthroughs, two examples dealing with imagery are developed in more detail.

Denis LE BIHAN

Founding-Director, NeuroSpin, CEA, Saclay, France; Fellow of the French Academie des Sciences, of the National Academy of Technologies of France, of the National Academy of Medicine.

BIO

Denis Le Bihan, MD, PhD, is a widely cited physician and physicist (300+ articles with 70 000 citations including nearly 20 000 for the first top 5). He is especially recognized for pioneering diffusion MRI in the 1980s, setting up a complete technical and conceptual framework which has become a pillar of today's medical imaging. Over the last 35 years Denis Le Bihan has continuously improved diffusion MRI and extended its field of applications. Indeed, diffusion MRI has been the object of countless publications and meetings, allowing many scientists, technicians, engineers and clinicians in academia, hospitals and the medical imaging industry to work to further extend its potential in the clinical field for the benefit of patients. Denis Le Bihan is the Founding Director of NeuroSpin in Saclay, France, a leading institution dedicated to ultra-high field MRI where he set and led the Iseult project (11.7T whole-body MRI). He is an Honorary member of the American Society of Neuroradiology and the Japan Radiological Society. He was awarded the Gold Medal of the International Society of Magnetic Resonance in Medicine in 2001, as well as other prestigious international prizes, including the Lounsbery Award, Honda Prize, Louis D. Award and Louis-Jeantet Prize. Dr Le Bihan, an Officer of the French Order of Merit, is a full member of the French Academy of Sciences and of the Academy of Technologies, and an Associate Member of the National Academy of Pharmacy and a corresponding member of the National Academy of Medicine.

ABSTRACT

"**Science without instruments is the ruin of the soul: the MRI example**"

Innovation usually develops along two main lines. One is a cumulative process: Progressive, incremental changes in basic knowledge of certain concepts mature over a long time until suddenly a radical change occurs. This process applies well to classical radiology which led from the discovery of X-rays to radiography and then to the CT scanner. The other line is the discovery or development of a new concept initially without medical purpose. This is the case of MRI which came out of the blue from NMR which was an instrument used only for physics and chemistry. Another example is molecular diffusion, an ubiquitous physical phenomena occurring in the whole universe which, combined with MRI, provides exquisite information noninvasively on biological tissues at microscopic level, a kind of virtual biopsy. Regarding MRI recent advances have been made through technical progress is hardware (eg gradient systems, radiofrequency coils) and acquisition/processing methods (eg parallel imaging, sparse sampling or simultaneous multislice acquisitions), some already benefiting from Artificial Intelligence and Deep Learning approaches. Those advances have dramatically improved patient comfort and safety, mainly by shortening acquisition times, while providing a wider range of contrasts which can be manipulated and combined afterwards for diagnosis or disease monitoring purposes. Greatly benefiting from those hardware and software advances progress is now expected in magnet design here also

along two opposite lines: Designing of ultra-high field MRI magnets (eg 11.7T or higher), mainly for brain investigations at ultrahigh spatial resolution, as the understanding of the human brain is a major challenge of the 21st century, and making low field, cheap, helium free, open, portable magnets dedicated to one application (eg breast cancer screening). In the early 2000s the French Atomic Energy Commission launched the Iseult project, a program to build a "human brain explorer", the first whole-body MRI scanner operating at 11.7T. Since 2017 the outstanding magnet has been delivered and commissioned at NeuroSpin. The project aims, the system specifications, technological challenges and the solutions which have been chosen to overcome them are presented.

Mathias FINK

Fellow of the French Académie des Sciences and of the National Academy of Technologies of France, Professor at ESPCI Paris

BIO

Mathias Fink is the George Charpak Professor at the École Superieure de Physique et de Chimie Industrielles de la Ville de Paris where he founded In 1990 the Laboratory "Ondes et Acoustique" that became in 2009 the Langevin Institute. He is member of the French Academy of Science and of the National Academy of Technologies of France. In 2008, he was elected at the College de France on the Chair of Technological Innovation. Mathias Fink's area of research is concerned with the propagation of waves in complex media. His current research interests include medical ultrasonic imaging, telecommunications and wave control in complex media. With his colleagues, he pioneered different inventions in the field of medical imaging (ultrafast ultrasonic imaging, transient elastography, shear wave Elastography, supersonic shear imaging) and in telecommunications (Time-reversal processing and Large intelligent surfaces). 7 start-up companies with more than 500 employees have been created from his research (Echosens, Sensitive Object, Supersonic Imagine, Time Reversal Communications, CardiaWave and GreenerWave, Austral Diagnostic).

ABSTRACT

"**Ultrafast Ultrasonic Imaging: the future of ultrasound**"

Recent developments of ultrafast ultrasound imaging scanners open very exciting possibilities in the field of medical ultrasound. Thanks to a completely new approach based on the concept of "time-reversal mirrors", frame rates as large as 10.000 frames/s are reached today. Compared to classical ultrasound scanners that delivered some 50 frames/s these new possibilities represent a complete breakthrough and a new paradigm. We will describe various innovations that leverage ultrafast ultrasound imaging.

The first one is a new imaging mode that provides quantitative imaging of tissue elasticity by following the propagation mechanical shear waves with a spatial resolution and precision that were never obtained with classical techniques. This is the field of Shear Wave Elastography that shows many applications in cancer diagnostics, fibrosis evaluation as well as cardio-vascular applications.

A second innovation is a new way to perform Doppler flow imaging with ultrafast scanners. It gives ultrasound the ability to detect very subtle blood flow in very small vessels. In the brain, such ultrasensitive Doppler paves the way for fUltrasound (functional ultrasound imaging) of brain activity with unprecedented spatial and temporal resolution compared to fMRI. Examples will emphasize the potential of this new imaging modality.

A third recent innovation combines ultrafast imaging with the use of airborne low frequency ultrasound providing the first non-contact scanner of the body surface vibrations to diagnose and monitor both cardiac and pulmonary disease.

Gondi Kondaiah ANANTHASURESH

Professor of Mechanical Engineering
and the Dean of Mechanical Sciences
at the Indian Institute of Science, Bengaluru

BIO

G. K. Ananthasuresh, a professor of Mechanical Engineering and the Dean of Mechanical Sciences at the Indian Institute of Science-Bengaluru, earned his bachelor's degree from Indian Institute of Technology-Madras, master's from the University of Toledo, and PhD from the University of Michigan-Ann Arbor, all in mechanical engineering. His research interests are compliant mechanisms and topology optimization with applications in microelectromechanical systems, mechanics of biological cells, biomedical devices, and microrobotics. In addition to more than 300 journal and conference papers and 16 patents, his research group has spun off four startups. His work is recognized with 15 best paper awards, 10 design prizes, and NSF's (USA) Early Career Award, SAE's Ralph R. Teeter Educational Award as well as Swarnajayanthi Fellowship, Shanti Swarup Bhatnagar Prize, and Abdul Kalam Technology Innovation National Fellowship in India. He is a Fellow of the Indian National Academy of Engineers.

ABSTRACT

"**Micromachinery for Mechano-diagnostics**"
There is increasing evidence that mechanical response of biological cells changes when a cell is under disease conditions. Correlating the changed mechanical response to a specific disease condition might pave the way for mechano-diagnostics as much as it would help us understand a disease from the viewpoint of biomechanics.

The premise for mechano-diagnostics at the level of single cells harks back to early 20th century when researchers, including Francis Crick, investigated the physical properties of biological cells (Expt. Cell Res., 1(1), 1950, pp. 37-80). A biological cell, being a complex entity with passive and motile particles co-existing with filaments of varied sizes and shapes jostling about in a viscous fluid, gives different mechanical response depending on the composition and arrangement of organelle. It is akin to a heterogeneous solid made of a granular medium. Physics, mechanics in particular, contributes to a cell's response in addition to complex biochemical phenomena. Measuring the mechanical response needs tools and computational techniques. The cells must be kept alive when they are physically measured. And the tools should be portable, simple, and not expensive to be suitable for point-of-care diagnostics. Micromachined compliant tools rise to the occasion.

The field of microelectromechanical systems (MEMS), which began in the later part of 20th century, has revolutionized the field of sensors by miniaturizing them using photolithography-based microfabrication. Alongside, several miniature actuators and mechanisms were developed. Thus, researchers have access to a "micro workshop" to probe single biological cells from the viewpoint of mechanics. Even though early microsensors and microactuators were made of silicon, we now have several polymers available, for example, polydimethyl siloxane (PDMS) and SU-8, which we use. These materials have sufficiently low Young's modulus to design compliant tools with stiffness that matches that of biological cells. Compliant tools we have developed have stiffness as low as mN/m. These tools use compliant mechanisms, which are elastically deformable structures without any joints and designed to perform manipulation tasks such as grasping, rotating, stretching, peeling, etc. In this talk, we demonstrate a variety of such tools and describe how they can be used to manipulate single biological cells. The main idea is that we palpate cells with stiffness-matched tools the same way a physician would palpate abdomen to assess if something is abnormal. Microfluidic tools also exist for this purpose, which we will briefly describe for comparison.

Palpation of cells necessitates not only miniature tools but also force sensors and computational techniques. Towards this, we have developed a micro-newton force sensor that works on a vision-based technique. We observe the amplified displacement of a miniature compliant mechanism and estimate the force. This is akin to a normal spring balance wherein the displacement of the spring multiplied by the spring constant gives the force. Here, we design Displacement-amplifying compliant mechanisms (DaCMs) to gently manipulate the cells and measure the forces applied on the cells or the forces applied by the cells.

Computational techniques we have developed for our miniature compliant tools come under the inverse problems in elasticity. The first inverse prob-

lem is to compute forces from the visually measured displacements of an elastic body undergoing geometrically nonlinear deformations. This is known as Cauchy's problem in elasticity. The elastic body here is the miniature compliant tool. This helps measure the force on cells minimally invasively. The second inverse problem is that of finding the Dirichlet to Neumann map of an elastic body. Here, we treat a biological cell an elastic body (which is an oversimplification for mathematical convenience) but made of a heterogeneous material. We estimate the elastic properties of the interior of a live cell from forces and displacements applied on the boundary. Here lies the question of uniqueness. So, we have arrived at a numerical technique to find the inhomogeneous elastic mapping of the cell so that we can determine specifically which parts of the cells have contributed to changed stiffness. After describing the mathematical modeling of inverse problems, a case study will be presented to illustrate how mechano-diagnostics helped in pinpointing proteins that play a role in Hepatitis C Virus-affected hepatocytes.

We present a study in which mechanical measurements showed that nuclear envelope of hepatocytes affected by HVC becomes more flexible while the cell membrane becomes stiffer than normal hepatocytes. We identified that Lamin-A,C proteins are downregulated while cortical actin is upregulated. Furthermore, we have developed a mechanical model that gives us the mechanical status of cell nuclei from simple morphological measurements of nuclear volume, surface area, and projected area as seen in confocal microscope images.

Taken together, the miniature compliant tools, mechanical manipulation capabilities, computational techniques, and mechanobiology experiments help us assess the state of a cell from the viewpoint of mechanical response with reasonable specificity. Much more work is needed to reach mechano-diagnostics.

Carrie HILLYARD

Fellow and Director, Australian Academy of Technology and Engineering,

Chair, Australian Pesticides and Veterinary Medicine Authority,

Chair, Fitgenes Ltd,

Chair, Mater Research Advisory Board.

BIO

Carrie Hillyard is an experienced director with a life sciences industry background. After a career spanning medical research in London to inventing and developing diagnostics in Brisbane, she co-founded venture capital firm, CM Capital and led its Life Sciences team, investing and taking an active rôle on the board of pharmaceutical, diagnostics and medical device companies. Carrie has also served on government, charity and university commercialisation company boards and is a Fellow of the Australian Institute of Company Directors. Passionate about assisting young people to achieve their life and career goals, she mentors those looking for industry connections or to redirect their careers into industry, most recently through ATSE's IMNIS program. She is involved in the start-up ecosystem and mentors founders and entrepreneurs developing their ideas.

In recognition of her contributions to biotechnology, she has received awards from AusBiotech and Women in Technology and a Centenary medal. Carrie was made a Member of the Order of Australia in 2019.

ABSTRACT

Turning health tech into better health outcomes: how ready are we to adopt disruptive healthcare technologies?

The aim of developing any health technology is to improve human health outcomes but the most innovative, efficacious technology in the world will not be effective if it is not adopted into practice. Sometimes the market just isn't ready, leading to missed opportunities for treating, diagnosing or preventing major health issues.

So how can we ensure that introduction of new technologies is as rapid and smooth as possible? A range of barriers can slow or prevent widespread adoption of new, disruptive health technologies by the target market which can include a range of end-users including clinicians, healthcare workers, patients and in some cases, the wider population. Assessing technology readiness can help overcome these barriers and quickly lead to widespread use and health impact.

In this presentation, Carrie will discuss a methodology for assessing tech readiness developed by the Australian Academy of Technological Sciences and Engineering (ATSE), which has been applied to the health sector in Australia. This approach aims to identify major barriers and prioritise actions needed to prepare for introduction of new technology. It is designed as a broadly applicable method that could be applied to other nations, sectors other than health and specific target groups or technologies.

When applied to the Australian health sector, ATSE's readiness analysis found that there were several barriers to adoption of new health technologies in Australia as we move towards a technology-enabled health system. Furthermore, these could be addressed through targeted action. The key findings and recommendations from the study were provided to the Australian Government and distributed widely across the sector.

To address the key barriers, Australia needs to:

- Transition to interoperable electronic health records - Australia has federal and state-based healthcare systems with limited interoperability across healthcare settings from hospitals to primary care (ie general practice), across both public and private healthcare. A switch to electronic health records for all healthcare providers would be a significant first step to addressing this barrier. This should be supported with clear communications about privacy and cybersecurity, which were the main concerns raised regarding widespread use of electronic records.
- Improve equity of access to healthcare through technology - Use of telehealth and AI-enabled devices must increase to support equitable outcomes for people living with disadvantage, to improve access and reduce financial burden.
- Support the existing and future healthcare workforce in the transition. The healthcare workforce – existing and future – must be equipped with the skills to adopt new technologies in daily practice. Supporting and empowering the national healthcare workforce to retrain, adapt and develop digital skills will be essential for introduction of new digital technologies in healthcare.
- Provide targeted support for a thriving health technology sector. Australian Governments must support investment in improving pathways to commercialisation for Australian-developed medical technology.

Carrie will also share examples of new disruptive health technologies developed in Australia, discuss barriers to their adoption and how the inventors are tackling these to increase likelihood of uptake in both Australian and global markets. These include Clinials, a digital, interactive platform for more efficient recruitment of participants in clinical trials and Fitgenes, which was one of the first companies globally to use genomics to assist with wellness and prevent chronic disease but struggled with uptake by medical practitioners.

While there is an appetite for new disruptive health technology across the globe, each nation likely faces different barriers to translation into widespread health practice. The methodology developed and published by ATSE and discussed in this presentation can be used to understand your country's technology readiness, what could slow down adoption of life saving health technology and how to put measures in place to accelerate uptake and improve health outcomes.

SESSION 4

VIRTUAL BRAIN

Coordinator André SYROTA

SESSION ABSTRACT

Digital twin models of human brains provide computational platforms for neuroscience research and increasingly find clinical translation in diagnostic and therapeutic applications. Virtual brains are data driven brain models derived from a patient's own brain imaging data. With further refinement through methods from machine learning and artificial intelligence, they provide personalized brain network models for clinical decision making, tailored to the individual patient's anatomy and pathology. Illustrative examples of virtual brain applications are found in epilepsy, neurosurgery and neurodegenerative diseases.

Viktor JIRSA

Director of the Systems Neuroscience Institute

BIO

Viktor Jirsa is Director of the Inserm Institut de Neurosciences des Systèmes at Aix-Marseille-Université and Director of Research at the Centre National de la Recherche Scientifique (CNRS) in Marseille, France. Dr. Jirsa received his PhD in 1996 in Theoretical Physics and has since then contributed to the field of Computational Neuroscience with a focus on networks and dynamics. His research has been foundational for network science in medicine, leading to novel technologies for personalized brain modeling and clinical translation in epilepsy. Dr. Jirsa is lead of the brain simulation platform The Virtual Brain (www.thevirtualbrain.org) and a lead scientist in the European flagship Human Brain Project (https://www.humanbrainproject.eu/). Dr. Jirsa has been awarded several international and national awards including the Human Brain Project Innovation Prize (2021) and Grand Prix Départemental de Recherche en Provence (2018). Dr. Jirsa serves on various Editorial and Scientific Advisory Boards and has published more than 160 scientific articles and book chapters, as well as co-edited several books including the Handbook of Brain Connectivity.

ABSTRACT

"**Personalized virtual brain technology for drug-resistant epilepsy and neurosurgery**"

The past two decades have seen enormous progress in the development of virtual brain technologies, primarily due to progress in brain imaging and high-performance computing.

Virtual brains integrate an individual's brain imaging data into a computational representation of a brain model and make it a personalized in-silico brain simulation platform. Since its initial proposal in 2002, virtual brains have been systematically built for the mouse, macaque and human and their individual predictive value has been established, regularly outperforming generic brain models. One reason for this success is the consideration of variability of individual connectivity in the brain model. A connectome is the set of all neuronal connections, which can be estimated using Diffusion Tensor weighted Imaging (DTI) obtained in Magnetic Resonance Imaging (MRI). Virtual brains are constructed around an individual's connectome, which characterizes the information transfer between even far distant brain areas. In case of injury or disease, such as stroke, neurodegeneration or epilepsy, the communication between brain areas is impaired and results in pathological brain activity. Virtual brains mimic the cause of such miscommunication and provide the capacity to simulate alternative treatments based on the individual's connectome.

A second source of predictive power is the inclusion of high-resolution data at spatial scales of up to 10μm. Such data exist only ex-vivo, which poses challenges to the integration with in-vivo data in a personalized brain modeling strategy. The two approaches can be integrated through application of latest techniques in Bayesian inference and Monte Carlo simulation, in which generic high-resolution brain templates are morphed to accommodate the patient's brain imaging data, leading to a maximum predictive power for a given individual.

We illustrate the virtual brain workflow along the example of drug resistant epilepsy, the so-called Virtual Epileptic Patient (VEP): we reconstruct the connectome of an epileptic patient using DTI and co-register other potential imaging data from the same individual (anatomical MRI, computer tomography (CT)). Each brain region is represented by neural population models, which are derived using mean field techniques from statistical physics

expressing ensemble activity via collective variables. Subsets of brain regions generating seizures in patients with refractory partial epilepsy are referred to as the epileptogenic zone (EZ). During a seizure, paroxysmal activity is not restricted to the EZ, but may recruit other healthy brain regions and propagate activity through large brain networks. The identification of the EZ is crucial for the success of neurosurgery and presents one of the historically difficult questions in clinical neuroscience. The application of Bayesian inference and model inversion, in particular Hamiltonian Monte Carlo, allows the estimation of the patient's EZ, including estimates of confidence and diagnostics of performance of the inference.

The example of epilepsy nicely illustrates the workflow of end-to-end modeling and the predictive value of personalized large-scale brain network models. Currently the VEP technology is validated in a large multisite clinical trial EPINOV with 400 prospective epilepsy patients. The Virtual Brain is the dedicated full brain simulator in the European digital neuroscience research infrastructure EBRAINS and enables neuroscientists worldwide to build and estimate personalized virtual brains.

Sridevi SARMA

Associate director of the Johns Hopkins Institute for Computational Medicine, and an associate professor in the Johns Hopkins Department of Biomedical Engineering

BIO

Sridevi Sarma received a B.S. in Electrical Engineering from Cornell University in 1994; and an M.S. and Ph.D. in Electrical Engineering and Computer Science from Massachusetts Institute of Technology (MIT) in 1997 and 2006. From 2000-2003 she took a leave to start a data analytics company. From 2006-2009, she was a Postdoctoral Fellow in the Brain and Cognitive Sciences Department at the MIT. She is now an Associate Professor in the Institute for Computational Medicine, Department of Biomedical Engineering, at Johns Hopkins University. Her research includes modeling, estimation and control of neural systems using electrical stimulation. She is a recipient of the the Burroughs Wellcome Fund Careers at the Scientific Interface Award, the Krishna Kumar New Investigator Award from the North American Neuromodulation Society, and a recipient of the Presidential Early Career Award for Scientists and Engineers and the Whiting School of Engineering Robert B. Pond Excellence in Teaching Award.

ABSTRACT

"**A noninvasive EEG marker of the epileptic brain: how dynamic brain network properties reveal epileptogenicity during rest**"

We have developed and validated a noninvasive EEG marker of epileptogenicity. Patients will be more accurately diagnosed and more effectively treated immediately after their first seizure occurs.

Today millions of scalp EEGs are performed each year to aid in the diagnosis and treatment of epilepsy. Despite nearly 100 years of using this technique, clinicians still primarily evaluate scalp EEGs by visual inspection. They look for abnormalities in EEG waveforms called interictal (between seizure) epileptiform discharges (IEDs), which are known indicators of epilepsy. EEGs are typically captured for 20-30 minutes while the patient is not seizing or is "at rest", and thus abnormalities may not occur in such a brief window. Furthermore, during this monitoring period artifacts are prevalent, which can mask true IEDs. Overreliance on and misinterprÉtation of routine EEGs has been found to be a significant factor in the nearly 30% misdiagnosis rate of epilepsy, contributing to approximately $1 billion to $6.4 billion in annual costs in the US.

We have developed EPITrack-RS (RS stands for "resting state"), a novel EEG analytics software tool that improves the speed and accuracy of determining whether a patient is epileptic from EEG data captured while the patient is at rest (not seizing). EPITrack-RS constructs a dynamic network model of the patient's brain from EEG recordings and identifies pathological connections between network nodes (biomarker) in the network that are displayed as a heatmap for clinicians to interpret. EPITrack-RS produces heatmaps in minutes and has been evaluated on over 300 patients and has demonstrated 80% accuracy in distinguishing between PNES and epilepsy patients even when normal EEGs are normal (i.e., no IEDs present). This is significant as normal EEGs are otherwise unactionable by clinicians.

One may wonder how resting state EEG captured from epilepsy patients can reveal any abnormalities in the brain when they are not seizing? This is pre-

cisely the challenging question our study addresses. Current approaches view the epileptic marker discovery process as a signal processing or pattern recognition problem, concentrating on processing EEG observations to find events of interest on individual channels (e.g., IEDs). Instead, we seek to understand how the EEG observations are generated in the first place and how internal network properties can trigger seizures or prevent seizures. Conceptually, EPITrack-RS finds EEG patterns which are below the threshold of traditional visual interprÉtation. Dynamical network models derived from EEG data characterize the internal properties of the brain and are necessary to reveal the epileptic network connections and the underlying dynamics of seizure generation.

EPITrack-RS has the potential to change clinical practice, reducing social and economic costs associated with misdiagnosis. Early use of anti-seizure medications after accurate diagnosis of epilepsy has been associated with a decrease in seizure recurrence, and early access to psychotherapy after accurate diagnosis of PNESs has been associated with increasing a patient's quality of life - ultimately benefiting all individuals affected by epilepsy, their caregivers, and their families.

Randy McINTOSH

Director of the Institute for Neuroscience & Neurotechnology, Dept of Biomedical Physiology and Kinesiology, Simon Fraser University

BIO

Description introducing myself: I obtained my PhD in psychology and neuroscience, with a minor in statistics. This combination gave me an appreciation for the need to explore the brain from a strong theoretical foundation and have the quantitative methods to test these theories explicitly. The perspective drove my first research program at the Rotman Research Institute, Baycrest, Univ of Toronto, where it evolved to focus on aging and cognition. My program was further enhanced through an international collaboration that delivered TheVirtualBrain (thevirtualbrain.org) and integrates research efforts globally to accelerate research and translation. The ultimate goals of my program 1) to integrate the modeling platform into the standard workflow for clinical decision support, and 2) develop a cloud-based system where anyone can create brain models for research, clinical use, or education. I have recently moved to Simon Fraser University, where the research program will become a cornerstone for the new Institute for Neuroscience and Neurotechnology.

ABSTRACT

"**Using the Virtual Brain to trace trajectories of brain health in ageing**"

We introduced TheVirtualBrain (TVB) to the neuroscience community a decade ago. It was the first platform for creating large-scale simulations of human brain networks and has continued to evolve as a community project, extending to multiple basic and clinical applications and extensions to models of rodent and macaque brains. A singular feature of TVB is that the brain models can be constructed from an individual's neuroimaging data, giving a great degree of specificity. This is especially relevant in studies across the lifespan, where the biophysical parameters of the model have a direct neurophysiological interprÉtation (e.g., neural excitation/inhibition). This feature of TVB results in great prediction of cognitive function across age-groups, and by connecting potential trajectories between groups, may provide new information on paths that reflect good brain health. We can extend this to age-related dysfunction, such as dementia, opening a potential for early detection of problematic trajectories and developing mitigation strategies.

SESSION 5

TECHNOLOGIES FOR REPAIR – REPAIRING THE HUMAN BODY

Coordinator Bruno JARRY

SESSION ABSTRACT

Technologies for repairing the human body, at the organ, cellular or whole limb levels are making their way in medicine. It includes methods to regrow, repair or replace damaged or diseased cells, tissues, organs, and even neurological pathways.

Zhongchao HAN

Full Professor at the Institute of Hematology and Hospital of Blood Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College; Beijing Health-Biotech Group, Fellow of the National Academy of Technologies of France, of the National Academy of Medicine

BIO

Dr. Zhong Chao Han graduated from Jiangxi Medical College in 1982 and obtained a master's degree from Fujian Medical University in 1984 in China. In 1988, Dr. Han got his PhD from the Faculty of Medicine, University of Occidental Bretagne in France. He worked in the Institute of Vascular and Blood and University Paris VII from 1989 to1997 and the University of Lorraine, France, as an excellence visiting Professor from 2017 to 2021. He was elected corresponding member of the French National Academy of Medicine in 2004, and a full member of the French National Academy of Technologies in 2014.

From 1998 to 2007, Dr. Han was the president of the Blood Diseases Hospital (Institute of Hematology) of the Chinese Academy of Medical Sciences and Peking Union Medical College, distinguished Professor of the Changjiang Scholars Award Program of the Ministry of Education, National Outstanding Youth Fund recipient. Since 2007, he has become the Director of the National Stem Cell Engineering Technology Research Centre, Director of the National Engineering Research Centre for Cell Products, President and Chief Scientist of Beijing Health and Biotech (H&B) Group.

Dr. Han has been engaged in stem cell research for more than 30 years. He devoted his career to translating stem cell knowledge gained from laboratories to stem cell products and industrialization. He is the first system builder of the Tianjin model of stem cell translation, which represents a microcosm of stem cell research in China and offers rich experience for the development of translational medicine (STEM CELLS Transl Med. 2021;10:S4-S9). Han's team was the first to treat effectively several lower limb ischemia by transplantation of patient's own peripheral blood stem cells (Thromb Haemost,2004, 2007; Diabetes Care 2005), and to develop a P-MSCs bank for clinical uses in 2005 (Patent N.20051001542.2; Bull Acad Natl Med, 193:545,2009). Han and his colleagues demonstrated that P-MSCs are novel type of MSCs with hematopoiesis-supportive function and other potentials (Haematologica, 91:1017-26, 2006; Clinical Transplant, 2011).

Specially, Dr. Han's team was the first to treat successfully the refractory systemic sclerosis (Cell Research, 2008:s71), multiple sclerosis (Mult Scler,15:644-6, 2009) using umbilical cord MSCs, and type 2 diabetes using placental MSCs (Front Med, 5:94-100, 2011). Dr. Han identified from placenta a population of CD106-positive MSCs with increased proangiogenic activity and immunoregulatory function (Plos One, 2011). Moreover, Han's team developed for the first time a product of placental MSCs mixed with a biomaterial, which were prefabricated in syringe and frozen at -20°C before use. Besides, Han's team developed a series of standard platforms for cell products manufacturing and quality control. Based on these platforms, several stem cell products have obtained IND and are under clinical investigation (see STEM CELLS Transl Med. 2021;10:S18-S30). The dosage form of these cell drugs includes intravenous injection, local injection, external hydrogel and Eye drops.

As the principal founder, Dr. Han has established several biotech companies specialized in different cell therapy and regenerative medicine. Han's team has set up an international Cell Valley, a special science park combining the R&D center including several University Joint Lab, cell bank, CDMO platforms, regenerative medical center and industry cluster.

Dr. Han and his team have published more than 300 papers in English and 16 books on stem cells (cited > 13800 times) and obtained more than 30 local and national science and technology progress awards.

Therefore, Dr. Han has been considered as the pioneer of stem cell industry of China.

ABSTRACT

"**Stem cells based technologies**"
Thousands of clinical trials of stem cells have been registered in the past 20 years for a large panel of indications across the globe, which makes stem cell therapy one of the most intensely pursued and promising biotherapeutics. Analysis of clinical trials with first-generation mesenchymal stromal/stem cells (MSC) products has demonstrated safety, although clinical protocol still needs to be improved. A considerable amount of MSCs products have been completed the studies of chemistry manufacturing and control (CMC), and pre-clinical studies, and more than ten MSC products have been approved by the Medical Products Administration of several countries. Studies on other somatic stem cells as well as ESCs and iPSCs and ending on representatives with less potency—multi-, oligo- or unipotent cells have also made rapid progress for the use in regenerative medicine applications of injured or diseased tissues. Despite enthusiasm for stem cell therapy, the clinical and translational research of stem cells overall has been a slow and cumbersome process. In view of the diversity of types, sources and uses of stem cells, stem cell therapy could be a personalized replacement transplantation or a cells-as-drugs therapeutic approach. Therefore, the clinical translation and cell industry of stem cell technologies need to be explored by innovative ways.

Consistent with global development trends, recent years have witnessed the emphasis of translational research and the cell therapy industry in China. China's regulatory strategies for cell therapy are generally similar to but slower than those of other developed countries. Parallel to the "cells-as-drugs" approach for cell therapy, the National Medical Products Administration (NMPA) and the National Health Commission (NHC) of China issued regulations on stem cell clinical research in 2015 as an alternative and flexible approach. This allows investigators from the designated stem cell clinical research institutes to apply for stem cell clinical research. Once investigators gather sufficient scientific evidence and clinical benefits from these clinical studies, they can use these data to apply for clinical trials through the "cells-as-drugs" approach. Based on such regulations, we have first established a translational technological system of stem cells, called Tianjin model (Chen H. Stem cell translational medicine: The Tianjin model revisited. Stem Cells Transl Med. 2021;10:S4–S9). To accelerate the clinical application and industrial development of stem cell technologies using Tianjin model, we have subsequently built a Cell Valley, a special park with R&D center, CDMO platforms, medical center, clinical grade cell bank, and industry clusters. The Cell Valley builds a bridge between basic research, clinical research and industrial development and explores its full ability to offer new hope to the patients with life-threatening diseases. The central vision of Cell Valley is to promote the stem cell industry by uniting the forces of many parties in the stem cell field. To date, the Cell Valley has produced some good social and economic benefits. Where we store precious stem cells in cell bank, prepare stem cells products in GMP factory for pre-clinical research in GLP facility, and perform clinical translational researches in hospital. Some breakthrough progress has been made in the development of perinatal MSC products, including injection products and an external applicator of perinatal MSCs mixed with hydrogel. Five products of stem cells have been approved to enter clinical trials by NMPA of China, and one approved by ANSM (French National Agency of Medicinal and Health Products Security). The clinical indications of these stem cell products include the diabetic foot ulcer, graft versus host disease (GvHD), chronic (plus acute) liver failure, critical lower limb ischemia, and acute respiratory distress syndrome (ARDS). These cell products are expected to complete clinical trials within 3-5 years. Here, we report briefly some clinical research outcome related to our stem cell products.

In summary, we have implemented a variety of initiatives to invent and develop the technological system, and have gathered momentum for its growth and consolidation. Our platforms met with a mass of interactions with an array of scientific, social, economic, and political variables and our experience may serve as a valuable and instructive reference for other institutions in stem cell translational medicine.

Stéphanie LACOUR

Full Professor, Foundation Bertarelli Chair
in Neuroprosthetic Technology (EPFL)

BIO

Stéphanie P. Lacour is full professor at the School of Engineering at the École Polytechnique Fédérale de Lausanne. She received her PhD in Electrical Engineering from INSA de Lyon, France, and completed postdoctoral research at Princeton University (USA) and the University of Cambridge (UK). She joined EPFL in 2011. She is a co-founding member and current director of EPFL Center for Neuroprosthetics, located at EPFL satellite – Campus Biotech in Geneva.

She is the recipient of the 2006 MIT TR35, the 2011 Zonta award, and she was selected as one of the 2015 WEF Young Global Leaders. She was awarded the ERC Starting Grant (2011), ERC POC Grants (2016 & 2018) and the SNSF Consolidator grant (2016).

ABSTRACT

"**Neuroprosthetic medicine:
innovation, interdisciplinarity and translation**"
Conditions affecting the health of the nervous system emerge throughout life in forms of traumatic injuries, neurological and psychiatric disorders. Neuroprosthetic medicine aims to offer therapeutical solutions that alleviate symptoms and restore impaired functions to patients suffering from such traumas and disorders.

The most successful neuroprosthetic device developed to date is the cochlear implant with more than 730'000 patients (adults and children with hearing impairment) implanted worldwide. Many other conditions such as paralysis, blindness or neurodegenerative diseases can benefit from innovative neurotechnologies. Their translation to clinical reality calls for interdisciplinary teams, deep understanding of biological processes, personalized and reliable manufacturing, stable performance and adoption by the clinicians for the patients' benefits. These enabling and integrated components of neuroprosthetic medicine will be illustrated with the recent demonstration of implantable neuroprosthetics to reverse paralysis.

Serge PICAUD

Director of the Paris Vision Institute

BIO

Serge PICAUD is the Director of the Paris Vision Institute since January 1st, 2021. After a PhD in Marseille (France), and studies in Frankfurt (Germany) and University of California Berkeley, He returned to Strasbourg and then to Paris to launch his own team on retinal information processing enlarging then the focus to neuroprotection. His team, for instance, revealed how an antiepileptic drug is leading to retinal degeneration. More recently, the team has moved to developing strategies for restoring vision in blind patients. The work involved novel materials for electrodes like Graphene and Diamond or event-based camera for visual information processing. His team has validated the photovoltaic and wireless retinal implants ex vivo and in vivo on the blind primate retina, paving the way for clinical trials by the company Pixium Vision. As an alternative to retinal implants, optogenetic therapy was evaluated on rodents and primate, opening the path toward clinical trials for the company Gensight biologics. The team is now moving toward visual restoration at the level of the visual cortex for patients with optic neuropathies.

ABSTRACT

"**Restoring vision in blind patients: from prosthesis to optogenetic and sonogenetic therapy**"
Following retinal degeneration, visual prostheses can restore some visual perception by stimulating residual neurons of the visual system but current devices fail to provide face recognition or autonomous motion in an unknown environment. We here tested the spatio-temporal resolutions of a novel photovoltaic prosthesis and of optogenetic therapy at the retinal level in addition to sonogenetic therapy at the cortical level.

Following their validation in non-human primates, the retinal prostheses, PRIMA, showed the best visual acuity for a prosthesis in patients affected by age-related macular degeneration. In parallel, we selected the best AAV viral vector coding for ChrimsonR-tdTomato, a microbial opsin, in living primates, and this vector was found to generate a partial recovery of vision in a patient affected by retinitis pigmentosa. Finally, we showed that expression of a mechanosensitive channel in rat cortical neurons can produce a sensitivity to ultrasound waves with a spatiotemporal resolution compatible for visual restoration.

These results demonstrated the functional efficacy of the PRIMA photovoltaic retinal prosthesis and of optogenetic therapy using ChrimsonR up to clinical trials. Following these strategies at the retinal level, sonogenetic therapy will likely offer a novel brain machine interface at the cortical level.

SESSION 6

ETHICS AND SOCIETAL IMPACTS FO TECHNOLOGICAL BREAKTHROUGHS

Panel session coordinated by Claudie HAIGNERÉ and Christiane WOOPEN

Patrick COUVREUR

Fellow of the French Académie des Sciences, of the National Academy of Technologies of France, of the National Academy of Medicine and the French Academy of Pharmacy

BIO

Patrick Couvreur, member of the Academy of Sciences, is an Emeritus Professor of Pharmacy at Paris-Saclay University. He is an internationally recognized scientist in nanomedicine. He co-founded three start-up companies (one of them entering the stock market) and developed an anticancer nanomedicine until end of phase III clinical trial. He is also member of the Academies of Technologies, Medicine and Pharmacy in France and foreign member of two of the three US National Academies (Engineering and Medicine).

Virginia DIGNUM

Professor at the Department of Computing Science at Umeå University

BIO

Virginia DIGNUM is Professor of Responsible Artificial Intelligence at Umeå University, Sweden and director of WASP-HS, the Wallenberg Program on Humanities and Society for AI, Autonomous Systems and Software, the largest Swedish national research program on fundamental multidisciplinary research on the societal and human impact of AI. She is a member of the Royal Swedish Academy of Engineering Sciences (IVA), and a Fellow of the European Artificial Intelligence Association (EURAI). She is member of the Global Partnership on AI (GPAI), World Economic Forum's Global Artificial Intelligence Council, Executive Committee of the IEEE Initiative on Ethically Aligned Design, of ALLAI, the Dutch AI Alliance, EU's High Level Expert Group on Artificial Intelligence, and leader of UNICEF's guidance for AI and children, member. She is author of "Responsible Artificial Intelligence: developing and using AI in a responsible way".

Thierry MAGNIN

Fellow of the National Academy of Technologies of France, author of numerous works, especially on science and theology

BIO

Thierry Magnin, born in 1953, co-president of UCL, responsible for Humanities at UCL, Professor, catholic priest, Doctor in physics and Doctor in theology, involved in solid state physics, science and faith, theology of creation, philosophy of sciences, bioethics, ethics of sciences and technologies. He is involved in research programmes on anthropology, particularly for the relation between the psychological and the spiritual dimension of humans.

He was member of the french national scientific reserach center (CNRS), received the Grand Prix of the Academy of Sciences (1991). He is member of the Academy of Technologies and of the Catholic Academy in France.

He was Rector of the Catholic University of Lyon, France.

He wrote more than 200 papers in the different domains and 13 books, among with 5 about anthropology at the time of sciences. He received the Price of christian humanities for his last book entitled "Penser l'humain au temps de l'homme augmenté" (Albin Michel, 2017).

Alison NOBLE

Technikos Professor of Biomedical Engineering at the University of Oxford, Fellow of the Royal Society and Fellow of the Royal Academy of Engineering

BIO

Professor Alison Noble FRS FREng is the Technikos Professor of Biomedical Engineering at the Institute of Biomedical Engineering (IBME), University of Oxford.

Professor Noble is a biomedical engineer, with academic research interests in biomedical image analysis. In recent years, her group is best known for its research on machine-learning applied to ultrasound image analysis and associated clinical applications in high income low-and-middle-income countries healthcare settings.

Prof. Noble received the Royal Society Gabor Medal for her inter-disciplinary research contributions in 2019, and the same year received the Medical Image Computing and Computer-Assisted Interventions (MICCAI) Society Enduring Impact award. She co-founded Intelligent Ultrasound Ltd to commercial research from her laboratory which was acquired by MedaPhor Group Plc in 2017 (now called Intelligent Ultrasound Group).

Professor Noble is a former president of the MICCAI Society, and her recent UK national roles include Chair of the EPSRC Healthcare Technologies Strategic Advisory Team, and a member of the UK REF 2021 Subpanel 12 (Engineering). She is an active Fellow of the Royal Academy of Engineering and of the Royal Society, an ELLIS Fellow, a Fellow of the MICCAI Society, and a former Trustee of the Institute of Engineering Technology (IET). Professor Noble chairs the Royal Society Privacy Enhancing Technologies (PETs) Policy Working Group which led to the Royal Society "Protecting privacy in practice" policy report in 2019 which will publish follow-on work in 2022. She received an OBE for services to science and engineering in the Queen's Birthday Honours list in June 2013.

Jeroen VAN DEN HOVEN

University professor and full professor of Ethics and Technology at Delft University of Technology

BIO

Jeroen van den Hoven is university professor and full professor of Ethics and Technology at Delft University of Technology. He is founding Editor in Chief of Ethics and Information Technology (Springer Nature).

He was the founding scientific director of 3TU. Centre for Ethics and Technology (2007-2013). In 2009, he won the World Technology Award for Ethics as well as the IFIP prize for ICT and Society for his work in Ethics and Information Technology. Jeroen van den Hoven was founder, and until 2016 Program Chair, of the Dutch Research Council Program on Responsible Innovation and advised the European Commission on Responsible Innovation in the Horizon2020 R&D Program. In 2017 he was appointed as a member of the European Group on Ethics (EGE) in Science and New Technologies to the president of the European Commission. In 2022 he was reappointed for 3 years.

He published widely on Ethics and Digital Technology and Ethics of Innovation, e.g. Information Technology and Moral Philosophy (Cambridge University Press, 2008), Designing in Ethics (eds. Van den Hoven, Miller, Pogge, Cambridge University Press, 2017), Evil Online (with Dean Cocking, Blackwell, 2018).

Gala Dinner – Official guest

Thierry BRETON

BIO

Thierry Breton is the EU Commissioner for Internal Market, in charge of industry, digital, space, defence, audiovisual and tourism. Engineer in computer science, he began his career as an entrepreneur in the IT sector. French business leader, he was CEO of Thomson electronics (1997-2002), France Telecom (2002-2005) and Atos (2009-2019). French Minister of Economy, Finance and Industry (2005-2007), he was a teacher at Harvard (2007) and authored a number of technology thrillers published in more than 40 languages.

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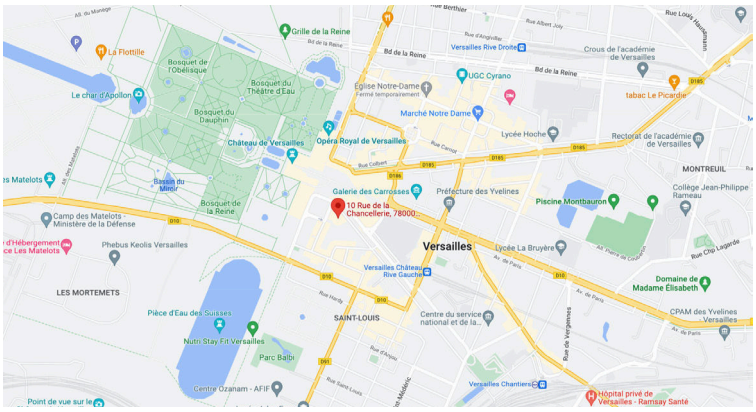

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10, rue de la Chancellerie - 78000 Versailles

Gala dinner
Château du Bois du Rocher
Route de Versailles - 78350 Jouy-en-Josas

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A transfer by bus will be organised between the Conference Centre and "Le Chateau du Bois du Rocher".

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