Physics in Biology and Medicine 2022

XXXVII Trobades Científiques de la Mediterrània - Josep Miquel Vidal

Maó, October 19-21, 2022

Program at a glance

Wednesday 19 October 2022	
11:00	Registration
11:45	Welcome
	SESSION 1: BIOPHYSICAL TOOLS & ANALYSIS
	Session chair: **Maria García-Parajo.** *ICREA & ICFO-Institut de Ciències Fotòniques.*
12:00	Superresolution microscopy for structural cell biology. **Jonas Ries**. *EMBL - European Molecular Biology Laboratory.*
12:40	Unraveling interactions between nucleic acids and proteins using single molecule force spectroscopy techniques. **Maria Mañosas.** *Universitat de Barcelona*.
13:20	Oral Sessions:
	Spatiotemporal Organization of Integrin Receptors and Adaptor Proteins inside Focal Adhesions. **Natalia Salvat**. *ICFO- Institut de Ciències Fotòniques.*
	A Python-based image analysis pipeline reveals the spatio-temporal dynamics of DNA damage during S-phase. **Christian Knapp**. *ICFO- Institut de Ciències Fotòniques*.
	Assessing how glucocerebrosidase defects alter receptor membrane nanoarchitecture to design improved nanomedicines. **Roger Pons.** *ICFO- Institut de Ciències Fotòniques.*
14:15	Lunch
	SESSION 2: SYSTEMS BIOLOGY (APPLIED)
	Session chair: **Blas Echebarria.** *Universitat Politècnica de Catalunya.*
16:00	Enabling precision medicine through multiscale modelling and simulation. **Blanca Rodríguez**. *University of Oxford*
16:40	Spatiotemporal characteristics of large scale human brain networks. **Roser Sala-Llonch**. *Universitat de Barcelona.*
17:20	Oral sessions:
	Relevance of CSF-blood flow coupling in the preclinical stage of Alzheimer's disease. Preliminary results. **Carles Falcon.** *BarcelonaBeta Brain Research Center.*
	Integration of functional diffuse correlation spectroscopy and electroencephalography for measuring task-triggered brain activation in infants. **Fen Zhang.** *ICFO-Institut de Ciències Fotòniques.*
18:00	Poster Session & Reception
20:30	Coffee Discussion at *Nou Bar*

Thursday 20 October 2022	
09:00	Institutional Welcome
	SESSION 3: MEDICAL DIAGNOSIS & TREATMENT
	Session chair: **Turgut Durduran**. *ICREA & ICFO-Institut de Ciències Fotòniques.*
09:15	Functional Imaging and Spectroscopy with Diffusing Light. **Arjun Yohd**. *University of Pennsylvania*.
09:55	A toolbox for personalized plasmonic photothermal cancer therapy. **Clara Vilches**. *ICFO-Institut de Ciències Fotòniques.*
10:35	Oral sessions:
	Hybrid diffuse optical device for the assessment of microvasculature health at the intensive care. **Marta Zanoletti**. *ICFO-Institut de Ciències Fotòniques.*
	BrainFocus: a computational toolbox to identify epileptic networks from intracranial EEG data. **Manel Vila-Vidal**. *Universitat Politècnica de Catalunya.*
	High density hybrid diffuse optical tomographic probe for infant neuromonitoring: a simulation study. **Anurag Behera.** *ICFO-Institut de Ciències Fotòniques.*
11:30	Coffee Break
	SESSION 4: ROLE OF PHYSICS IN MEDICINE & PUBLIC HEALTH
	Session chair: **Gerard Tobias.** *Institut de Ciencia de Materials de Barcelona.*
12:00	Photonics and advances in critical care. **Jaume Mesquida**. *Parc Taulí University Hospital.*
12:40	Computational modelling to inform public health decisions. **Clara Prats**. *Universitat Politècnica de Catalunya.*
13:20	Oral sessions:
	Bed-side evaluation of endothelial and microvascular impairments in severe COVID-19 patients through non-invasive near-infrared spectroscopy: the HEMOCOVID-19 trial. **Lorenzo Cortese**. *ICFO-Institut de Ciències Fotòniques.*
	Comparison of the severity of omicron and delta variants using hospitalization, and intensive care admissions rates in Catalonia. **Enrique Alvarez-Lacalle.** *Universitat Politècnica de Catalunya.*
	Thyroid cancer screening using ultrasound-guided hybrid diffuse optical techniques. **Pablo Fernandez Esteberena**. *Institut de Ciència de Materials de Barcelona.*
17:00	Excursion
20:30	Conference Dinner

Friday 21 October 2022	
	SESSION 5: PHYSICAL BIOLOGY
	Session chair: **Sarah Keary**. *ICFO-Institut de Ciències Fotòniques.*
09:15	Machine learning approaches to anomalous diffusion. **Gorka Muñoz-Gil**. *Universität Innsbruck*
09:55	Transducing - and shielding - mechanical signals from integrins to the nucleus. **Pere Roca-Cusachs**. *IBEC - Institute for Bioengineering of Catalonia, University of Barcelona*
10:35	Oral sessions:
	Inactivating SARS-CoV-2 with surfactants using computer simulations. **Marc Domingo**. *Institut de Ciència de Materials de Barcelona.*
	Actin buffers nuclear stress and maintains nuclear positioning during mechanotransduction. **Frederic Catala-Castro**. *ICFO-Institut de Ciències Fotòniques.*
	Stochastic particle unbinding modulates growth dynamics and size of transcription factor condensates in living cells. **Juan Torreño-Piña**. *ICFO-Institut de Ciències Fotòniques.*
11:30	Coffee Break
	SESSION 6: SYSTEMS BIOLOGY (FUNDAMENTAL)
	Session chair: *t.b.a.*
12:00	Epithelial mechanobiology from the bottom up. **Xavier Trepat**. *IBEC - Institute for Bioengineering of Catalonia.*
12:40	Tissue Remodeling: Elongation, Regeneration, and 3D Packing. **Javier Buceta**. *I^2SysBio - Instituto de Biología Integrativa de Sistemas.*
13:20	Oral sessions:
	An optogenetic and mechanical approach to control synthetic morphogenesis. **Miquel Bosch-Padrós**. *IBEC - Institute for Bioengineering of Catalonia.*
	Learning Synchronization Patterns with Neural Mass Model Networks. **Antonio Pons**. *Universitat Politècnica de Catalunya.*
	Detection of calcium sparks in cardiac cells using deep learning and biophysical models. **Jordi Condom i Tibau**. *Universitat Politècnica de Catalunya.*
14:15	Final remarks

POSTER SESSION	
	LIST OF POSTERS:
P01	Misery perfusion is often detected during hyperventilation therapy in traumatic brain injured patients: assessment by non-invasive hybrid diffuse optical methods. **Susanna Tagliabue**. *ICFO-Institut de Ciències Fotòniques.*
P02	Inferring the chemical step size of helicases from single molecule DNA unzipping data. **Victor Rodriguez**. *Universitat de Barcelona.*
P03	Mechanobiology of the secretory pathway: Golgi export responds to external mechanical cues. **Javier Vera Lillo**. *ICFO-Institut de Ciències Fotòniques.*
P04	A smart sensor board for improved laser-safety and data quality for diffuse correlation and near-infrared spectroscopy probes. **Muhammad Atif**.*ICFO-Institut de Ciències Fotòniques.*
P05	Statistical classifiers to predict "redo" in the treatment of atrial fibrillation (AF). **Leire Moriones**. *Universidad de Navarra.*
P06	Non-invasive assessment of cerebral autoregulation for the personalization of post-stroke physiotherapy. **Lisa Kobayashi-Frisk**. *ICFO-Institut de Ciències Fotòniques.*
P07	New tools for long-term super-resolution imaging of amyloid fibrils and cell surface proteins. **Joaquim Torra**. *ICFO-Institut de Ciències Fotòniques.*
P08	Fast in-vivo time-domain diffuse correlation spectroscopy: separating extra- and intra-cerebral signals. **Veronika Parfentyeva**. *ICFO-Institut de Ciències Fotòniques.*
P09	Evaluation of muscle performance, neuromuscular and oxidative dynamics in rock climbing. **Faruk Beslija**. *ICFO-Institut de Ciències Fotòniques.*
P10	Analysis of the epidemiological dynamics of monkeypox from May 15 to August 31, 2022. **Aida Perramon**. *Universitat Politècnica de Catalunya.*
P11	Multi-wavelength, multi-exposure time, and multi-distance laser speckle contrast simulations to infer microvascular blood flow and tissue optical properties. **Andrés Quiroga**. *ICFO-Institut de Ciències Fotòniques.*
P12	Pilot study: Continuous monitoring of cerebral and scalp blood flow of neonatal piglet during validation of different cardiologic procedures. **Osman Melih**. *ICFO-Institut de Ciències Fotòniques.*
P13	Epidemiological characteristics and modelling for short-term prediction of the Respiratory Syncytial Virus (RSV) and influenza spreading in Catalonia (Spain). **Aida Perramon**. *Universitat Politècnica de Catalunya.*
P14	Elucidating the role of shear forces in LFA-1 activation and dynamics by single particle tracking. **Lukas Lau**. *ICFO-Institut de Ciències Fotòniques.*
P15	Functional diffuse correlation spectroscopy measurements on cognitively healthy and mild cognitive impaired populations during single and dual motor tasks. **Stella Avtzi**. *ICFO-Institut de Ciències Fotòniques.*
P16	Spatiotemporal dynamics of secretory proteins in the Golgi apparatus. **Jessica Angulo-Capel**. *ICFO-Institut de Ciències Fotòniques.*
P17	Structural analysis of calcium waves in cardiomyocyte using a subcellular bidomain model. The role of the RyR release interaction with buffers. **David Conesa**. *Universitat Plotècnica de Catalunya.*
P18	Plasmonic antenna platforms for multicolor single-molecule studies with high-throughput. **Ediz Herkert**. *ICFO-Institut de Ciències Fotòniques.*
P19	Super-resolution microscopy reveals hierarchical organization of spatially segregated protein nano-clusters within focal adhesions. **Sarah Keary**. *ICFO-Institut de Ciències Fotòniques.*
P20	Exploring how force transmission to nuclear pore complexes affects nucleocytoplasmic transport. **Marc Molina Jordán**. *IBEC - Institute for Bioengineering of Catalonia.*

Invited Talks

Superresolution microscopy for structural cell biology

S1-I1
19 Oct
12:00h

Jonas Ries
EMBL- European Molecular Biology Laboratory

Superresolution microscopy, such as single-molecule localization microscopy (SMLM), is becoming a key technique for structural cell biology, ideally complementing electron microscopy. I will discuss projects in my group in which we push single-molecule localization microscopy towards nanometer resolution in 3D and multicolor with the aim to investigate the structure and dynamics of molecular machines in cells. I will show how these technologies allowed us to gain mechanistic insights into the machinery that drives endocytosis. Endocytosis is an essential cellular function by which cells take up molecules from the environment. We were able to reconstruct the dynamics of this process from thousands of snapshots taken in fixed cells. I will conclude with first results illustrating the potential of MINFLUX to image dynamic structural changes of protein machines in the living cell with nanometer resolution. Specifically, I will show how we resolved the precise stepping motion of the motor protein kinesin in living cells.

Unraveling interactions between nucleic acids and proteins using single molecule force spectroscopy techniques

S1-I2
19 Oct
12:40h

Maria Mañosas
Small Biosystems Lab. IN2UB - Institut de Nanociència i Nanotecnologia. Universitat de Barcelona

In this talk I will present single molecule experimental approaches used to study biophysical processes at the molecular level such as molecular folding, ligand binding and enzymatic reactions. I will also discuss physical tools we use to extract thermodynamic and kinetic information from experimental data. Finally, I will focus on a novel single-molecule method based on the application of fluctuation theorems to RNA force spectroscopy data, which is used to determine the non-specific and specific electrostatic contributions of magnesium binding to RNA.

Enabling precision medicine through multiscale modelling and simulation

S2-I1
19 Oct
16:00h

Blanca Rodríguez
Department of Computer Science. University of Oxford

Precision Medicine aims at providing the most accurate diagnosis and best treatments for each patient. Whereas this has primarily been genomic-centred so far, there is now a wide recognition of the need to consider a wide spectrum of lifestyle, environment, and biology conditions. Characterising such diversity of factors requires large quantity and quality of patients' datasets, and at the same time, innovative approaches for their analysis, drawing on the increasing power of computers and algorithms. New concepts are being proposed, such as the Digital Twin and In Silico Drug Trials. In this presentation, I will address this framework for cardiology and pharmacology, highlighting how combined computational approaches including image-based multiscale modelling and simulation can boost the capacity for diagnosis and prognosis, as well as future treatments.

Spatiotemporal characteristics of large scale human brain networks

S2-I2
19 Oct
16:40h

Roser Sala-Llonch
Institute of Neuroscience. Universitat de Barcelona

In human neuroscience, there has been a shift in paradigm towards integrative approaches of brain connectivity. While classical studies were based on region-function associations, there is evidence that human behavior is based on complex relationships between brain networks. Brain networks can be studied at the structural level -i.e., presence of white matter connections between regions- and at the functional level – i.e., temporal correlations between spontaneous activity across regions -. Network properties have been demonstrated across a wide range of spatial connections. In this context, functional and structural magnetic resonance imaging coupled with complex analytical tools applied at the systems level have been particularly impactful. In this talk, I will review some of the recent developments in the study of human brain connectivity, focusing on both the methodological choices and the impact of the findings for clinical and cognitive neuroscience.

Functional Imaging and Spectroscopy with Diffusing Light

S3-I1
20 Oct
09:15h

Arjun Yohd
Department of Physics and Astronomy. University of Pennsylvania

I will first review the basics of the transport of light and the transport of light correlations through tissue. I will explain how this optical information can be used to characterize tissue hemodynamics and tissue disease/injury states, including connections to oxygen metabolism and blood flow autoregulation. Finally, I will discuss recent clinical work from our group which utilizes these principles to elucidate tissue responses.

A toolbox for personalized plasmonic photothermal cancer therapy

S3-I2
20 Oct
09:55h

Clara Vilches
ICFO - Institut de Ciències Fotòniques

Plasmonic photothermal therapy (PPTT) is emerging as a complementary technique for the treatment of malignant solid tumours. It involves the use of gold nanoparticles that can be light-activated to locally and precisely shrink tumours via heat-induced cell death. However, and as most other cancer therapies, treatment outcome varies between individuals even under the same regime, compromising PPTT outcome and hindering its clinical translation. Thus, methods that allow for personalization of therapy based on individual's physiology are needed. In PPTT, the dose of gold nanoparticles injected and the amount of light delivered are parameters that can be adjusted to personalize the treatment and improve its efficacy. In this work, we show how diffuse optical techniques can be used to non-invasively gather physiological properties of the tumoral tissue and relate the optical and hemodynamic parameters to the crucial variables in PPTT. We have combined diffuse optical monitoring and PPTT in a preclinical mouse model of renal cancer, and the optical data has allowed us to measure gold nanoparticle accumulation in the tumour and to relate tumour physiology with nanoparticle concentration and treatment temperatures. Our results set the basis for a toolbox that would pave the way to PPTT personalization and bring this therapy closer to clinics.

Photonics and advances in critical care

S4-I1
20 Oct
12:00h

Jaume Mesquida
Hospital Universitari Parc Taulí

One of the main goals in critical care is maintaining the adequate oxygenation of the tissues, in order to ensure cellular respiration and thus, avoiding or improving organ failure, which can derive in the death of the individual. In addition, once global oxygenation is ensured, specific organ monitoring, support or therapies might also be required for improving patients' outcomes. Photonic technologies, and specially near-infrared spectroscopy (NIRS), have evolved towards non-invasive devices capable of monitoring the local oxygenation of the tissues. We will discuss the different applications in the field of intensive care where NIRS technologies have demonstrated their value, either in global body oxygenation evaluation and local organ-specific monitoring.

Computational modelling to inform public health decisions

S4-I2
20 Oct
12:40h

Clara Prats
Department of Physics. Universitat Politècnica de Catalunya

World Health Organization defines public health as the art and science of preventing disease, prolonging life and promoting health among the population as a whole through organized community efforts. This collective nature of both the tackled problems and the necessary measures entails that we are dealing with a complex system. As such, tools given by the physics and mathematics of complex systems can be a useful approach to public health Infectious diseases are a particular work area of public health, which was necessarily enhanced and fueled by the onset of the COVID-19 pandemic. In this field, computational models can be used to increase the understanding of the transmission dynamics and the main factors that can modulate it, to predict the incidence evolution for a certain period, and to analyse possible scenarios and evaluate intervention strategies, among others. The outcome of these modelling approaches provided essential information to help on the decision making during the pandemic, not only with regards to the prediction of the evolution of incidence and hospitalization to inform its management, but also to re-open schools in a more secure manner and to design the best massive vaccination strategy, among others.

Machine learning approaches to anomalous diffusion

S5-I1
21 Oct
09:15h

Gorka Muñoz-Gil
UIBK - University of Innsbruck

The analysis of trajectories arising from biophysical experiments is usually a challenging task. First, because the motion of these particles is usually random. Hence, characterizing the physical processes leading to their dynamics relies on statistical approaches, as for instance averages over a big sample of trajectories. Second, because experiments are usually very complex. As we often work beyond the diffraction limit, the tracked trajectories are heavily affected by different kinds of noises. Moreover, it is also hard to track a single particle for long times, thus having only access to very short trajectories. These two problems hinder the correct analysis of diffusion phenomena. Due to the recent improvement in experimental single particle techniques, there is now an increasing interest in developing robust analysis techniques. In this talk, I will present a promising approach: using state-of-the-art machine learning techniques. I will first show how these powerful models can be used to study stochastic data of different characteristics and their suitability in dealing with experimental trajectories. Then, I will present how, in collaboration with 14 research groups, we performed an objective comparison of the existing machine learning and statistical methods to characterize diffusion trajectories.

Transducing - and shielding - mechanical signals from integrins to the nucleus.

S5-I2
21 Oct
09:55h

Pere Roca-Cusachs
IBEC - Institute for Bioengineering of Catalonia & Universitat de Barcelona

Cell proliferation and differentiation, as well as key processes in development, tumorigenesis, and wound healing, are strongly determined by the properties of the extracellular matrix (ECM), including its mechanical rigidity and its composition. In this talk, I will discuss how mechanical force is transmitted from the ECM to the nucleus, and how this affects proteins in general, and transcription factors in particular, by controlling their shuttling between the cytoplasm and nucleus. Further, I will discuss how different matrix, integrin, and cytoskeletal proteins control whether the nucleus is exposed to, or shielded from, force transmission.

Epithelial mechanobiology from the bottom up

S6-I1
21 Oct
12:00h

Xavier Trepat
IBEC - Institute for Bioengineering of Catalonia

Epithelial sheets form specialized 3D structures suited to their physiological roles, such as branched alveoli in the lungs, tubes in the kidney, and villi in the intestine. To generate and maintain these structures, epithelia must undergo complex 3D deformations across length and time scales. How epithelial shape arises from active stresses, viscoelasticity and luminal pressure remains poorly understood. I will present different approaches to study the mechanobiology of epithelial shape from the bottom up. I will discuss new technologies to design epithelia of arbitrary size and geometry and to subject them to controlled mechanical deformations in 3D. I will show that monolayers exhibit superelastic behavior when stretch is applied and that they readily buckle when tension is released. We use this phenomenology and a 3D vertex model to rationally direct spontaneous pattern formation, and hence engineer tissue folding. I will also present our recent advances to understand the mechanobiology of intestinal organoids. We map the three-dimensional cell-ECM and cell-cell forces in mouse intestinal organoids grown on soft hydrogels. We show that these organoids exhibit a non-monotonic stress distribution that defines mechanical and functional compartments. From these experiments we conclude that the stem cell compartment folds through apical constriction and that cells are pulled out of the crypt along a gradient of increasing tension, rather than pushed by a compressive stress downstream of mitotic pressure as previously assumed. This experimental and theoretical work unveils how patterned forces enable folding and collective migration in the intestinal crypt.

Tissue Remodeling: Elongation, Regeneration, and 3D Packing

S6-I2
21 Oct
12:40h

Javier Buceta

I2SysBio - Institute for Integrative Systems Biology.

During development, the initial symmetry of the zygote undergoes complex changes in size and shape to form different tissues/organs and implement the body plan. In that context, axis elongation, tissue folding, and cellular packing are key morphogenetic geometric transformation that relies on the regulation of cellular activities due to the interplay between signaling and cell mechanical properties. Importantly, these processes also operate during tissue regeneration. In this talk I will review our recent contributions towards the understanding of these problems.

Oral sessions

Spatiotemporal Organization of Integrin Receptors and Adaptor Proteins inside Focal Adhesions

S1-O1
19 Oct
13:20h

N. Salvat [1], S. Keary[1], N. Mateos[1], C. Manzo[2], M. García-Parajo[1,3]

[1]ICFO - Institut de Ciències Fotòniques. [2]Facultat de Ciències i Tecnologia, Universitat de Vic-Universitat Central de Catalunya, Vic, Spain. [3] ICREA-Institució Catalana de Recerca i Estudis Avançats, Barcelona, Spain

Adhesion complexes are protein platforms found in the plasma membrane through which cells interact with the extracellular matrix (ECM) and sense external stimuli. Within these macromolecular structures, integrin proteins act as the main linkers between the ECM and the actin cytoskeleton of the cell through adaptors proteins that bind to the integrins cytoplasmatic tails. Integrins $\alpha5\beta1$ and $\alpha V\beta3$ are enriched within adhesion complexes but their specific role in converting mechanical cues into biochemical signals is still elusive. Integrins diffuse along the plasma membrane experiencing multiple arrestment cycles that correlate with their different activation states. Moreover, adaptor proteins are also constantly recruited and recycled underneath the plasma membrane. To quantify the dynamics of integrins $\alpha5\beta1$ and $\alpha V\beta3$, and detect possible synergistic effects and cross-talk, as well as transient interactions and recruitment of adaptor proteins we have implemented a multi-colour single particle tracking (SPT) strategy working under total internal reflection geometry. We will report on the labelling strategies used for extended and simultaneous SPT of both integrins, as well as labelling of the adaptor partners paxillin and vinculin, compatible with single molecule live cell imaging. We will show our analysis pipeline to detect transient interactions between different integrins inside focal adhesions and correlation of these interactions with potential changes in the activation state of both integrins. Finally, we will show preliminary single molecule data aiming at establishing the temporal scales involved in integrin activation and vinculin recruitment.

A Python-based image analysis pipeline reveals the spatio-temporal dynamics of DNA damage during S-phase

S1-O2
19 Oct
13:20h

C. Knapp [1], F. Campelo[1], M. García-Parajo[1,2]

[1] ICFO - Institut de Ciències Fotòniques. [2] ICREA-Institució Catalana de Recerca i Estudis Avançats, Barcelona, Spain

DNA damage and genomic instability are major hallmarks of aging and cancer. Replication stress can cause DNA damage in different subnuclear and genomic compartments, depending on the time of occurrence during S-phase, which can define the molecular response and pathological outcome. Fluorescence microscopy is a powerful tool to monitor DNA replication and DNA damage in space and time. However, the quantitative

analysis of high-content multi-channel live cell imaging data is still challenging. Here, I will present a flexible pipeline based on time-lapse live cell imaging and analysis, to correlate DNA damage with S-phase progression and additional reporters. Our method is based on high-resolution two-channel long-term fluorescence imaging of live cells expressing fluorescently-labeled markers for DNA damage and DNA replication, which can be easily extended with additional reporters. We developed an extensible image analysis pipeline implemented in the rich open-source Python ecosystem. We harnessed existing libraries for GPU-accelerated pre-processing and analysis together with machine-learning algorithms for segmentation and classification. We custom-trained the neural net YOLOv2 to detect S-phase by classifying typical patterns formed by the fluorescently-labeled replication reporter, PCNA. By using GPU-accelerated algorithms, we localized and quantified foci formed by fluorescently-labeled DNA repair proteins accumulating at sites of DNA damage. We demonstrated the versatility of this approach by treatment with different drugs and the additional quantification of a third fluorescence channel. In summary, our method allows to describe the spatio-temporal dynamics of DNA damage generation during S-phase under various conditions in combination with additional microscopy read-outs.

Assessing how glucocerebrosidase defects alter receptor membrane nanoarchitecture to design improved nanomedicines

S1-O3
19 Oct
13:20h

R. Pons[1], M. Loeck[2], E. Gutierrez[1], M. Solomon[3], M. Placci[2], A. Selvados[3], S. Muro[2], M. García-Parajo[1]

[1] ICFO - Institut de Ciències Fotòniques, Barcelona, Spain. [2] IBEC - Institute for Bioengineering of Catalonia, Barcelona, Spain [3] IBBR - Institute for Bioscience and Biotechnology Research, University of Maryland College Park, USA

A main current challenge in treating neurological diseases lies in the blood-brain barrier (BBB), a filter of endothelial cells which block the brain access of drugs. Thus, there is a need to investigate novel means of therapeutic strategies able to cross the BBB. In particular, we are interested in the specific case of a deficiency of the lysosomal enzyme glucocerebrosidase (GBA). The function of this enzyme is to break down cellular glycosphingolipids, and GBA defects are linked to both Parkinson's and Gaucher diseases. Increasing brain levels of GBA could offer a treatment option, but new tools are needed to allow brain delivery. A potential platform is loading therapeutical drugs into nanocarriers (NCs) that can be targeted to various receptors of brain endothelial cells and mobilize molecules across the interior via transcytosis. Within this context, we have focused on characterizing diseased brain endothelial cells, designing tailored NCs targeted to various entry routes and examining the resulting cell-NCs interactions. Using a combination of drug delivery nanotechnologies, multicolour super-resolution microscopy and single-molecule tracking on living cells, we show GBA deficiency affects receptor-mediated transcytosis across brain endothelial cells by influencing the spatiotemporal organization of plasma membrane lipids, receptors and associated cell machinery. While all NCs transcytosis rates are compromised, these effects however are different depending on the entry route. Notably, poly(lactic-co-glycolic acid) nanoparticles targeted to the membrane receptor ICAM-1 result in a less compromised transport. Altogether this study provides valuable information on BBB accessibility under these pathologies to guide the development of new therapeutic nanomedicines.

Relevance of CSF-blood flow coupling in the preclinical stage of Alzheimer's disease. Preliminary results

S2-O1
20 Oct
17:20h

C. Falcon[1,2,3], C. Mansilla[1], C. Morante[1], J. D. Gispert[1,2,3]

[1]BarcelonaBeta Brain Research Center, Pasqual Maragall Foundation. Barcelona, Spain [1] Centro de Investigación Biomédica en Red. CIBER-BBN. Madrid. Spain [1]IMIM. Parc Salut Mar, Barcelona. Spain

INTRODUCTION: Beta-amyloid and p-tau protein deposition in the brain appear several years before the clinical symptoms in Alzheimer's disease (AD), in the so-called preclinical AD. Given the role of cerebro-spinal fluid (CSF) in the clearance of brain metabolic waste, alterations in its circulation might be involved in the generation of such aggregates. CSF circulation is driven by intracranial blood dynamics. In this work, we studied the relationship of CSF and blood flow parameters and its association with AD CSF biomarkers. METHODS: The sample consisted in 253 subjects with AD CSF biomarkers available (age 60.8 ± 4.5, 81 males, 86 CSF beta-amyloid positives) submitted to MRI gated phase-encoded velocity sequences in carotids and foramen magnum. Volume per cycle (stroke volume), mean velocity, maximum velocity, area, velocity and area ranges were computed. We analyzed the relationship between blood and CSF flow parameters. We also looked for associations between CSF flow parameters with concentration of beta-amyloid and p-tau in CSF, correcting for age and sex ($p < 0.05$). RESULTS: CSF concentrations of beta-amyloid and p-tau were associated to CSF stroke volume. Blood flow in carotids shows several correlated characteristics to CSF flow through foramen magnum, as expected. Of note, CSF stroke volume and maximum velocity were associated to blood flow-velocity ranges. CONCLUSION: The joint analysis of blood and CSF flows in the brain are helpful to understand the contribution of metabolic waste clearance pathways in the buildup of proteins aggregates in the brain in relation with the circulatory system.

Integration of functional diffuse correlation spectroscopy and electroencephalography for measuring task-triggered brain activation in infants.

S2-O2
20 Oct
17:20h

F. Zhang[1], J. Ciarrusta Monzon[2], K. Zacharaki[2], A. Eken[1,3], C. Santolin[2], D. Senciales[1], M. Pagliazzi[1], M. Colomer[4], N. Sebastián Gallés[2], T. Durduran[1,5]

[1]ICFO-Institut de Ciències Fotòniques, The Barcelona Institute of Science and Technology, Spain [2]Center for Brain and Cognition, Universitat Pompeu Fabra, Spain [3]Biomedical Engineering Department, TOBB University of Economics and Technology, Ankara, Turkey [4]Department of Psychology, University of Chicago, USA [5]ICREA - Institució Catalana de Recerca i Estudis Avançats, Spain.

INTRODUCTION: The integration of functional diffuse correlation spectroscopy (fDCS) and the electroencephalography (EEG) allows us to examine the metabolic and electrophysiological aspects of cortical activity. Here we have tested the feasibility of measuring task-triggered neuronal responses in infants using hybrid fDCS-EEG. METHOD: Forty-six healthy 4-month-old infants (mean age=4.44 ± 0.55 months, 23 females) were enrolled. A 16-channel fDCS device and 128-sensors Geodesic (EGI, USA) system were used simultaneously. Stimuli used include 12-Hz flickering checkerboard, attention getters (AT) with looming face/toy, and baseline stimuli of moving clouds. For fDCS, the baseline (T0) was defined as 4 seconds before the onset of the AT, while time-1 (T1) and time-2

(T2) were identified as the 2-6s and 8-12s post AT. Data processing and statistical analysis were performed in MATLAB. RESULTS: For fDCS, the ANOVA analysis revealed significant interactions between time windows and sessions ($F(1, 25) = 4.76$, $p = .04$) and significant main effect of time window ($F(1, 25) = 30.98$, $p < .001$). Significant increase of relative changes of cerebral blood flow (rCBF) was found in T2 compared to T1 during the CK session but not in the SH session. For EEG measurements, we also observed a significant increase of time-locked VEP between 200-600 ms towards checkerboard stimuli in the occipital regions ($p < .05$ after FDR correction). CONCLUSION: Infants at 4 months exhibit increased CBF and VEP in response to checkerboard stimuli in the occipital regions. fDCS is feasible to use, independently or hybridized with EEG, to investigate task-evoked responses and cognitive processing in healthy developing infants.

Hybrid diffuse optical device for the assessment of microvasculature health at the intensive care

S3-O1
20 Oct
10:35h

M. Zanoletti [1], C. Amendola[2], M. Buttafava[3], T. Carteano[4], D. Contini[2], L. Cortese[1], L. Demarteau[5], L. Frabasile[2], D. Sanoja Garcia[4], C. Nunzia Guadagno[6], T. Houtbeckers[5], U. Karadeniz[1], M. Lacerenza[2,3], J. Mesquida[7], M. Pagliazzi[1], S. Parsa[8], D. Senciales Sánchez[1], S. K. Venkata Sekar[6], J. Tomanik[5], A. Torricelli[2,9], A. Tosi[10], T. Wagenaar[5], U. M. Weigel[8], M. Atif Yaqub[1], T. Durduran[1,11].

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During the VASCOVID project, funded within the HORIZON2020 programme, we developed a compact and portable monitor which comprises of a hybrid diffuse optical technology alongside a pulse oximeter for assessing tissue metabolism at the bedside of critically ill patients (septic shock, acute respiratory distress syndrome and COVID-19, to name a few). The device is equipped with an automatized tourniquet to perform vascular occlusion tests, which combined with tissue oxygen saturation as derived from Near Infrared Spectroscopy signals, have been proven to hold prognostic meaningful information. The device performances have been evaluated through a rich set of tests that are internationally recognized by the scientific community, namely MEDPHOT (Pifferi, A. et al. 2014) and BIP (Wabnitz, H. et al. 2014). Finally, the device is under clinical validation at the Hospital Universitari Parc Tauli in Sabadell extrapolating important hemodynamic and VOT-derived parameters in septic and COVID-19 patients along with a control population recruited at the intensive care. Through VASCOVID we aim to impact clinical practice in: 1) stratification of patients according to their need in receiving endothelium targeting therapies, and 2) personalizing the management during prone positioning and predict readiness to wean from mechanical ventilation. Being a state-of-the-art hybrid diffuse optical technology, the platform is easily adaptable to neuromonitoring of cerebral blood flow and metabolism representing a valuable asset in the clinical management of brain injured patients.

BrainFocus: a computational toolbox to identify epileptic networks from intracranial EEG data

S3-O2
19 Oct
10:35h

M. Vila-Vidal[1], M. alKhawaja[2], M. Carreño[2,3], P. Roldán[4], J. Rumià[4], A. Donaire[2,3,5], A. Tauste Campo[1]

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The standard pre-surgical diagnostic procedure in drug-resistant epilepsy involves visual inspection of long intracranial electroencephalography (iEEG) recordings to identify epileptic regions. This is a very time-consuming procedure that might lead to inconclusive interpretations, resulting in mistakes and incomplete diagnosis. In this context, can computational tools unravel meaningful information that is invisible to the human eye?. To address this question, we have designed BrainFocus, a toolbox that is based on the combination of an own developed epileptogenic activity detection algorithm (Vila-Vidal et al. 2020) and frequency-dependent visualization maps of iEEG recordings (Vila-Vidal et al. 2017), which allow clinicians to exhaustively inspect the activity of the brain sites that compose the epileptic network during seizure and non-seizure periods. BrainFocus is now being validated in a heterogeneous cohort of drug-resistant epileptic patients from Hospital Clínic (Barcelona, Spain), including 60% of challenging cases associated with extra-temporal lobe epilepsies. This study is centered at analyzing the specificity (against the state-of-the-art diagnosis) of the epileptogenic activity detection algorithm as a means to assess the clinical relevance of brain sites that were not initially mapped by visual examination. Our preliminary results indicate that the mean specificity is of 0.80.1 over patients, and that clinicians uncover novel sites of clinical significance. BrainFocus is a computational toolbox aimed to assist clinicians in the diagnosis of epileptic patients with EEG, extracting epileptogenic relevant information that might be hidden to the human eye.

High-density hybrid diffuse optical tomographic probe for infant neuromonitoring: a simulation study

S3-O3
20 Oct
10:35h

A. Behera [1], M. Can[1], M. Camprubí[6], M. Domínguez[2], J. Sanchez de Toledo[6], T. Fontaine[2], C. N. Guadagno[5], C. Labbé[2], J. Larrouquere[2], M. Mahmoudzadeh[3], S. Parsa[4], M. Sanchez-Dominguez[2], S.K. Venakata Sekar[5], F. Wallois[3], U.M. Weigel[4], T. Durduran[1,7]

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Under the framework of the TinyBrains project, we aim to design a high-density multi modal probe to image infants heads. The probe combines diffuse correlation spectroscopy (DCS), functional near-infrared spectroscopy (fNIRS) and EEG probes in a tomographic manner to provide a complete picture of the neurovascular network in a developing head. An iterative approach was adapter to determine the optimal probe configuration. Various additional design considerations were considered. In order to achieve a dense

distribution of sources and detectors, a minimum of three nearest neighbors were chosen for both modalities. The simulations were performed using NIRFAST a medical image processing and analysis component built on 3DSLicer platform. Various versions of the probe were tested for following parameters: i) uniformity of the sensitivity profile ii) spatial localization error, iii) full-width at half-maximum of the reconstruction, iv) effective resolution and, v) signal-to-noise ratio. The results were compared to traditionally used grids for tomographic measurements. Finally, the probe configuration was employed on in infant head mesh. The simulations were performed for the above-mentioned parameters in a homogeneous case, with uniform optical properties for all brain regions and in homogeneous case, where different brain regions were simulated with their corresponding optical properties. In conclusion, various configurations were probe designs were simulated to determine the optimal probe configuration under given optical and mechanical constraints. The performance of this design was compared to traditionally used grids. This was then employed on an infant head mesh with homogeneous and realistic optical properties for different brain regions.

Bed-side evaluation of endothelial and microvascular impairments in severe COVID-19 patients through non-invasive near-infrared spectroscopy: the HEMOCOVID-19 trial.

S4-O1
20 Oct
13:20h

L. Cortese[1], L. Bacchin de Oliveira[2], L. E. Bernardes Delazari[2], E. M. Buckley[3], D.R. Busch[4], A. Caballer[5], V. Carbajal Robles[6], P. Castro[7], A.L. Cavallaro Barauna Lima[2], S. Cheruku[4], L. Chiscano[8], C. Choi[4], S. Dave[4], B. do Nascimento[2], L. dos Santos Roceto Ratti[2], A. L. Eiras Falcão[2], C. Espinal[5], S. Fernández[7], R. Ferrer[8], F. Font[9], R. M. Forti[10], M. Garcia de Acilu[8], G. Grasselli1[1], G. Gruartmoner[5], A. Guzzardella1[1], I. Jabeen[9], U. Karadeniz[1], P. Lahsaei[4], G. Lívio Emídio[2], J. Marin Corral[12], A. Matas[7], R. C. Mesquita[10], A. Mera[8], F.J. Monte De Oca Hernández[6], T. Myers[9], S. Nogales[5], D. Olson[4], M. Pagliazzi[1], M. Parada Guzmán[6], F. J. Parrilla-Gómez[12], A. Pérez Pacheco[6], P. Pérez Terán[12], L. Picazo Moreno[12], D. Pineda Vázquez[1,6], A. F. Quiroga Soto[10], R.M. Quispe Siccha[6], D. Romero[9], E. Santillán Aguayo[6], I. Serra[9], R. Serrano Loyola[6], A. Téllez[7], L. Utino Taniguchi[13], C. Vilà[12], M. Weinmann[3], A. Zanella1[11], M. Zanoletti[1], J. Mesquida[5], T. Durduran[1,14]

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The HEMOCOVID-19 international clinical trial (ClinicalTrials.gov NCT04689477) is carried out in ten hospitals and five countries with the objective of evaluating microvascular and endothelial impairments in severe COVID-19 patients admitted to the intensive care unit (ICU). Microcirculatory alterations are determined by measuring the local tissue oxygen saturation (StO2) through continuous-wave near-infrared spectroscopy (CW-NIRS) on a peripheral muscle (forearm muscle) continuously during a vascular occlusion test (VOT), consisting of a brief period of ischemia induced on the muscle by a cuff occlusion. StO2 derived parameters during VOT are indeed associated to tissue oxygen metabolism

(deoxygenation slope - DeO2 – during the ischemia period), and to endothelial and microvascular functions (reoxygenation slope – ReO2 – and hyperemic area – H_AUC after releasing the cuff). Here we report the results obtained on a group of 32 healthy controls and 130 COVID-19 patients. ICU-mortality was 14%. We found that severe COVID-19 subjects show impaired metabolism (slower DeO2) and impaired endothelial function (reduced H_AUC and ReO2) with respect to the healthy population. Impaired microcirculatory parameters furthermore correlate with the severity of the pulmonary disease (defined by the PF ratio) and, eventually, with the mortality. In addition, we found that patients previously treated with remdesivir antiviral show less pronounced microcirculatory alteration, associated with lower mortality. Finally, the level of respiratory support, use of sedative agents and vasopressors did not impact these metrics.

Comparison of the severity of omicron and delta variants using hospitalization, and intensive care admissions rates in Catalonia

S4-O2
20 Oct
13:20h

M. Català[1], E. Coma[2], S. Alonso[3], C. Andrés[4,5], I. Blanco[6], A. Antón[4,5], A.E. Bordoy[7], P. Cardona[7,8,9], F. Fina[2], E. Martró[7,10], M. Medina[2], N. Mora[2], V. Saludes[7,10], C. Prats[3], D. Prieto-Alhambra[1], E. Alvarez-Lacalle[3]

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We aim to explain our research on the severity of the infections by omicron and delta variant comparing its severity using hospitalization and ICU admission in Catalonia. We established two periods when delta and omicron were, respectively, dominant and performed a population-based cohort analysis to calculate the rates of hospital and intensive care unit (ICU) admissions in both periods. We complement this analysis with a substitution model that establishes the increase in transmissibility of omicron and the differential rate of hospital admissions. Both methods indicate an important decrease in severity for omicron relative to delta. The systematic reduction happens regardless of age. The severity is also reduced for non-vaccinated and vaccinated groups, but it remains always higher in the non-vaccinated population. The reduction is particularly large in the rate of ICU admission with omicron compared with delta. Most age groups and vaccination status groups have a reduction in hospitalization of 40–80% while for ICU admission it reaches 60–90%. Such a systematic reduction regardless of age and vaccination status suggests an overall reduction in severity which could be intrinsic to the omicron variant, and not due merely to the high level of immunization of the population.

Thyroid cancer screening using ultrasound-guided hybrid diffuse optical techniques

S4-O3
20 Oct
13:20h

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The standard diagnostic tools for thyroid cancer are ultrasound (US) screening and fine-needle aspiration biopsy, which lack in sensitivity and specificity, leading to large numbers of unnecessary surgeries. Thyroid cancer is the most common of the endocrine system, which means around 150000 thyroidectomies conducted a year could be avoided. A more effective technique to detect malignant nodules could then reduce economic and social costs significantly. In this project a multimodal platform combining US and diffuse optical techniques (the LUCA device) was used to non-invasively obtain hemodynamic information of thyroid nodules and try to classify them according to their malignancy status. The device uses both near-infrared time-resolved (at 8 different wavelengths) and diffuse correlation spectroscopies, and is capable of probing thyroid/nodule for microvascular tissue oxygen saturation (StO2), haemoglobin concentration, blood flow, metabolic rate of oxygen consumption and reduced scattering coefficient spectrum, using two different source-detector separations. We present the results of a clinical campaign (currently ongoing) including 48 patients with thyroid nodules and 18 healthy subjects. A standard ultrasound screening protocol was conducted on the subjects, followed by two rounds of measurement with the LUCA device in four positions of the neck (thyroid and externocleidomastoid muscle on each side). Linear mixed effects models showed a significant difference in StO2 between benign and malignant nodules (p=). In addition, logistic regression models showed that in the subgroup of 4A or 4B nodules in the Thyroid Imaging Reporting and Data System scale (20 benign, 7 malignant) StO2 was significant to classify them (AUC ROC=0.71).

Inactivating SARS-CoV-2 with surfactants using computer simulations

S5-O1
21 Oct
10:35h

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Surfactants are commonly used as disinfection agents in personal care products against bacteria and viruses, including SARS-CoV-2. However, there is a lack of understanding of the molecular mechanisms of the inactivation of viruses by surfactants. Here, we employ coarse grain (CG) molecular dynamics simulations to investigate the interaction between general families of surfactants and the SARS-CoV-2 virus. To this end, we considered a CG model of a full virion. Overall, we found that surfactants have only a small impact

over the virus envelope, being inserted into the envelope without dissolving it or generating pores, at the conditions considered here. However, we found that surfactants may induce a deep impact on the spike protein of the virus (responsible for its infectivity), easily covering it and inducing its collapse over the envelope surface of the virus. Our results suggest that the best strategy for the design of surfactants as virucidal agents will be to focus on those strongly interacting with the spike protein. In addition, we have also done molecular dynamics simulations using atomistic models of different parts of the SARS-CoV-2 virus. We have observed that the surfactants are able to insert themselves into the virus envelope and also to strongly interact with the spike protein.

Actin buffers nuclear stress and maintains nuclear positioning during mechanotransduction

S5-O2
21 Oct
10:35h

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Cells have spatially distinct mechanical properties and mechanotransduction pathways that allow them to respond to a plethora of mechanical cues during their life cycle. How forces are buffered or transmitted through different cell compartments is however poorly understood and needs further analysis to build a mechanistic picture of cellular mechanoresponses. Here, we used a dual optical trap assay to measure force propagation across the nucleus of isolated zebrafish progenitor stem cells. Through perturbations of cytoskeletal elements and genetic modifications, we identified the actin meshwork as the major element for mechanical stress buffering. Without a functional actin network, we found that force propagation through the nucleus was strongly enhanced. To decipher the role of the actin cytoskeleton on cytoplasmic and nuclear force propagation, we developed an active microrheology approach that allowed us to measure sub-nanometer deformations and sub-picoNewton forces directly inside living cells using a single, time-shared trapping laser. We found that the cytoplasmic shear modulus switched from an elastic response at low frequencies to a viscous-dominant behavior at a crossover frequency of 2 Hz. In contrast, the nucleus had an elastic response up to a 5-fold crossover frequency. Following actin depolymerization, the cytoskeleton showed a dramatic fluidization that resulted into nuclear positional drift upon mechanical indentation. This indicates that the actin cytoskeleton is key in mechanically stabilizing the nucleus and thereby allowing it to respond to mechanical stimulation through deformation.

Stochastic particle unbinding modulates growth dynamics and size of transcription factor condensates in living cells

S5-O3
21 Oct
10:35h

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Liquid-liquid phase separation (LLPS) is emerging as key physical principle for biological organization inside living cells, forming condensates that play important regulatory roles. Inside living nuclei, transcription factor (TF) condensates regulate transcriptional initiation and amplify transcriptional output of expressed genes. Yet, the biophysical parameters controlling TF condensation are still poorly understood. Here we applied a battery of single molecule imaging, theory and simulations to investigate the physical properties of TF condensates of the Progesterone Receptor (PR) in living cells. Analysis of individual PR trajectories at different ligand concentrations showed marked signatures of a ligand-tunable LLPS process. Using a machine learning architecture, we uncovered that receptor diffusion within condensates follows fractional Brownian motion resulting from viscoelastic interactions with chromatin. Interestingly, condensate growth dynamics at shorter times is dominated by Brownian motion coalescence (BMC), followed by a growth plateau at longer timescales that result in nanoscale condensate sizes. To rationalize these observations, we extended on the BMC model by including stochastic unbinding of particles within condensates. Our model reproduced the BMC behavior together with finite condensate sizes at the steady-state, fully recapitulating our experimental data. Overall, our results are consistent with condensate growth dynamics being regulated by the escaping probability of PR molecules from condensates. This phenomena must have implications for the biophysical regulation of other nuclear condensates and could also operate in multiple biological or non-biological scenarios.

An optogenetic and mechanical approach to control synthetic morphogenesis

S6-O1
21 Oct
13:20h

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A large number of processes that take place in developmental biology are currently being studied with a combined set of biological and physical tools, since morphogenesis is both controlled by physical forces and biochemical signaling. Gastrulation of embryos or organ formation are current examples of high interest in the field, involving reshaping of cell sheets and differentiation. Constriction of apical sides of cells is a known trigger of such events, but there is a knowledge gap concerning the role of cellular forces during them. By taking advantage of a novel optogenetic tool named OptoShroom3, we can spatiotemporally control apical constriction in human pluripotent stem cells and thus recapitulate stages of embryogenesis synthetically. Moreover, we report high resolution

force maps in three dimensions that depict and quantify apical contractility, proving that it generates crucial out-of-plane deformations as in many morphogenetic events. Since most of the state-of-the-art organoid technology relies on stem cells, the mechanical insights we obtain from controlling the forces of apical constriction are applicable to a wide variety of systems. We anticipate our study will establish a physical quantification of this cell shape change and determine its relevance in different embryo and organogenesis contexts.

Learning Synchronization Patterns with Neural Mass Model Networks

S6-O2
21 Oct
13:20h

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In this work we consider a realistic physiological model formed by a network of neural mass models which is feed with time traces which are synchronized in pairs. The network processes the input information following its natural dynamics and produces output signals, which eventually may drive others parts of the brain, that have different levels of synchronicity. These output synchronization patterns are used to classify the input signals. After training the network (changing the excitatory and inhibitory weights that couple the neural masses) using a Genetic Algorithm, we show that the resulting network is able to classify correctly arbitrary sets of input signals. We also show that the distribution of excitatory-inhibitory weights are organized in a nontrivial manner. Our results, taken as a whole, shed light to the problem of oscillatory processing at the mesoscale in the brain.

Detection of calcium sparks in cardiac cells using deep learning and biophysical models

S6-O3
21 Oct
13:20h

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We have developed a deep learning (DL) model in order to automatically detect spontaneous calcium release events in cardiac cells from sequences of life fluorescent microscopy images. Deep learning has consolidated as the leading approach to automatically recognise complex patterns in digital images. However, although DL models typically provide higher accuracy than traditional machine learning approaches using tailored features, they require a large dataset and the resulting procedure is difficult to interpret by experts in the field. The aim of this study is twofold: On one side, to explore the possibility of training the DL using realistic simulations instead of using experimental data. On the other, an encoder-decoder architecture of the convolutional neural network has been chosen to provide further interpretability in terms of localisation of relevant patterns. The model has been trained using a large dataset of simulations obtained from

a realistic biophysical model under a wide range of signal-to-noise conditions. The detection performance in unseen synthetic data has been favourably compared against a spark detection system using space-frequency wavelet features.

Posters

P1. Misery perfusion is often detected during hyperventilation therapy in traumatic brain injured patients: assessment by non-invasive hybrid diffuse optical methods

POSTER SESSION

S. Tagliabue[1], M. Kacprzak[1,2], I. Serra[3], F. Maruccia[1,4], J. Fischer[1,5], M. Riveiro-Vilaboa[6], A. Rey-Perez[6], L. Expósito[6], C. Lindner[1], M. Báguena[6], T. Durduran[1,7], M.A. Poca[3,8,9]

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Hyperventilation (HV) can be used to decrease raised intracranial pressure (ICP) as therapy to avoid secondary injuries, like ischemia, in traumatic brain injury (TBI) patients. Misery perfusion (MP) is a symptom of a precondition that warns if the brain is at risk of ischemia, occurring when a decrease in the cerebral blood flow (CBF) is simultaneous with an increase in oxygen extraction fraction (OEF). Non-invasive hybrid diffuse optics (HDO) was hypothesized to be able of detecting MP during HV and characterize its incidence (i.e. duration, magnitude). Continuous bi-frontal HDO and invasive sensors multi-monitoring on TBI patients during a protocol including 30 minutes of HV were synchronized. Advanced methods of statistical analysis were employed to evaluate MP risk both at group, single-measurement and over time level. Linear mixed effect models were used to check associations between clinical variables and MP. A total of twenty-seven measurement sessions were performed on eighteen TBI patients. The response was heterogeneous at the group level, without showing MP ($p>0.05$). As for the single-measurement and over time analyses, twenty-two measurement sessions showed at least one MP risk event (minimum duration of 30 seconds), with a total of 89 events. No significant associations were found between clinical variables and the presence of MP ($p>0.05$). MP risk during HV is high and HDO can safely convey this information for personalized therapy administration.

P2. Inferring the chemical step size of helicases from single molecule DNA unzipping data.

POSTER SESSION

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Helicases are molecular motors that convert the chemical energy of ATP hydrolysis into mechanical work to move along one strand of DNA and unzip the double helix. Using magnetic tweezers we follow the activity of a single helicase unzipping a DNA hairpin. From these experiments we can characterize the enzyme motion (e.g. velocity and diffusion) but the ATP hydrolysis reaction is not directly measured. Here we investigate whether we can infer information about the helicase chemical cycle from our helicase displacement data by using non-equilibrium relations such as the thermodynamic uncertainty relation (TUR) and the fluctuation theorem (FT) for entropy production. We propose a simple framework to obtain an analytical expression for the FT and compare with experimental results.

P3. Mechanobiology of the secretory pathway: Golgi export responds to external mechanical cues

POSTER SESSION

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Cells interact with their environment through integrin-mediated adhesion complexes, molecular platforms that bridge the extracellular matrix (ECM) and the cytoplasm. These adhesion complexes serve as mechanosensors of ECM rigidity, and act as initiators of different signaling cascades that regulate cellular processes such as differentiation, proliferation and adhesion. Importantly, cell surface availability of integrins is a key factor determining how cells adapt to the mechanical properties of the environment. Besides the fast recycling of integrins from the endosomal system, the trafficking of newly synthesized integrins from the Golgi apparatus to the cell surface can also contribute to modulate surface expression of these receptors. However, whether or how Golgi-to-plasma membrane trafficking of integrins is modulated by extracellular mechanical cues remains unknown. Recent studies have shown that mechanical cues modulate the levels of components involved in Golgi lipid homeostasis and transport carrier formation, revealing a role of the Golgi apparatus in mechanotransduction. Importantly, the molecular identity of the carriers trafficking cargoes to focal adhesions overlaps with that of CARTS, a specific class of Golgi-derived transport carriers that contain the transmembrane protein TGN46. Interestingly, TGN46 escorts the integrin $\beta 1$ during its export. Altogether, these data let us hypothesize a role for CARTS in integrin delivery from the Golgi to focal adhesions. Here, I will present our results studying integrin incorporation in CARTS and whether these carriers are formed in a mechanically-regulated manner to control the levels of mechanosensors at the plasma membrane. Ultimately, our data will help us

understand the mechanisms governing the communication between the Golgi and the extracellular milieu.

P4. A smart sensor board for improved laser-safety and data quality for diffuse correlation and near-infrared spectroscopy probes

POSTER SESSION

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The usage of lasers requires an efficient and rapid interlock system to confirm quality contact with the tissue (IEC 60601-2-22:2020 standard). Furthermore, in an experiment, wobbly scalp-probe coupling, ambient light, subject movements, and probe displacement can introduce noise in the acquired signal. Moreover, the reproducibility is affected by the pressure exerted by the probe on the tissue. We have designed a miniaturized sensor board to address these issues. The sensor board combines a capacitive touch sensor, a polymer thick film based load sensor, a 3-axis accelerometer, and a surface mount phototransistor based ambient light sensor. It can provide feedback in real-time for probe adjustment and record data for offline analysis. The tiny sensor board was verified through benchtop experiments assessing the stability, timing, accuracy, and linearity of the respective parameters. It has been assessed in vivo on the forehead and the forearm to mimic human study protocols. This sensor board extends the efforts described by the BabyLux project. The probe detachment was detected in 15 ± 1 ms that is much less than 100 ms limit set by the IEC standard for switching off the laser. The load sensor showed a linear behavior when with increasing and decreasing weight on top of it. The light sensor sensed all the changes in light and the accelerometer detected all the movements. The results show the possibility of using the developed miniaturized sensor board for device safety and detecting noises to improve the fidelity of the analyzed data.

P5. Statistical classifiers to predict "redo" in the treatment of atrial fibrillation (AF)

POSTER SESSION

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Aims: High-resolution voltage maps (HRVM) are used as a predictor tool of the post-ablation recurrence of AF. This study aims to assess the statistical power of electrical biomarkers extracted from the HRVM. This paper is a follow-up from a previous analysis, with the number of patients in the cohort augmented from 98 to 122. These patients are treated for AF. We observe that Atrial fibrillation Recurrence (AFR) is related to lower mean voltage of the patient's left atrium. Methods: With the same catheter used in the ablation procedure, an acquisition of HRVM was performed on the left atrium (Rhythmia, Boston Scientific). Bipolar voltage maps were evaluated with two electrical biomarkers and one geometrical characteristic (Area). Supervised classifier (from Matlab Machine Learning Toolbox) is used, specifically, the logistic regression and the coarse tree classifiers. Results: AUC, accuracy and confusion matrices were compared between the two

classifiers. For the cohort of 98 patients, logistic regression classifier accuracy's is 76.5%; ACU=0.74 and coarse tree's accuracy is 70.4%; ACU=0.63. The cohort of 122 patients gives a logistic classification accuracy of 77.0%; AUC=0.74 and coarse tree's accuracy is 77.0%; AUC=0.57. Conclusions: Slight improvement in classification is reported when increasing the sample size (n=122 and before n=98). This minor improvement is presumably due to the fact that the HRVMs are not enough to predict redo with very high accuracy. More comprehensive classifiers with combination of clinical, demographical and comorbidities should somewhat improve the prediction of future redo procedure for a given patient.

P6. Non-invasive assessment of cerebral autoregulation for the personalization of post-stroke physiotherapy

POSTER SESSION

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INTRODUCTION: Mortality in stroke has decreased, however morbidity is significant in survivors. Literature suggests that early mobilization (EM) protocols may reduce morbidity but have shown a heterogeneous response making the clinical decision to carry out EM difficult. Impaired cerebral autoregulation (CAR) plays a defining role here. We hypothesized that non-invasive assessment of CAR during mobilization can be used to personalize physiotherapy to be safe and effective. METHOD: Diffuse correlation spectroscopy (DCS) was used to non-invasively monitor cerebral blood flow (CBF). Physiological parameters including continuous blood pressure (BP) were also monitored. Using non-invasive CBF and BP data, a cerebral autoregulation index (DCSx) was measured. Patients were monitored continuously during first mobilization. After monitoring, patients were randomly allocated to a standard or intensive physiotherapy group. Efficacy of physiotherapy was measured by PASS scores (Postural Assessment Scale for Stroke). Safety was measured by neurological deterioration defined by changes in NIHSS score (National Institutes of Health Stroke Scale). RESULTS: 106 patients were included in the analysis. A linear regression model suggested a significant relationship between efficacy and the interaction between DCSx and physiotherapy dose ($b = -0.02, p < 0.05$). Logistic regression analysis suggested that a higher DCSx (impaired CAR) is predictive of neurological deterioration ($OR > 1$, $p < 0.05$). CONCLUSION: The results suggest that higher doses of physiotherapy benefits patients with intact CAR. However, patients with impaired CAR had a greater probability of deteriorating. A threshold value for impaired CAR was estimated for DCSx > 0.25 and lies around DCSx = 0.58.

P7. New tools for long-term super-resolution imaging of amyloid fibrils and cell surface proteins.

POSTER SESSION

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Super-resolution fluorescence microscopy techniques such as STimulated Emission Depletion microscopy (STED) or Single Molecule Localization Microscopy (SMLM) enable nanoscale imaging and have provided fundamental insights with unprecedented levels of spatial and temporal detail. Each method offers particular advantages and/or limitations over the other for a given application, yet photobleaching of the fluorescent probes remains a common limiting factor for long acquisition times and is particularly severe in STED microscopy. Here, I will present novel strategies that overcome this limitation, allowing sub-diffraction imaging over long acquisition times. The first approach is based on exchangeable fluorophores that reversibly bind to amyloid fibrils involved in neurodegenerative diseases and fluoresce only when bound. Such fluorogenic properties together with their transient binding favor both the rapid exchange of photobleached labels, enabling prolonged STED imaging as well as the generation of blinking events required for SMLM. I will show that this method can achieve a spatial resolution of 45-55 nm in both super-resolution techniques, very low background signal and increased photostability. In addition, I will explore the potential of TauSTED imaging for studying the nanoscale organization of cell surface proteins. TauSTED combines the STED optical signals and the photophysical information from the fluorescence lifetime, providing higher resolution and reduced background signal using very low STED laser powers, thus prolonging the performance of the fluorophores.

P8. Fast in-vivo time-domain diffuse correlation spectroscopy: separating extra- and intra-cerebral signals

POSTER SESSION

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Diffuse correlation spectroscopy (DCS) uses laser speckle intensity fluctuations to calculate blood flow index (BFI) which has been shown to be correlated with the absolute blood flow. It allows to non-invasively measure changes in cerebral blood flow (CBF) and has a potential for continuous bedside monitoring. Additionally, recent developments allow to use DCS with higher rates (up to 40Hz), thus it is possible to resolve pulsatile behaviour of BFI and study new pulsatility related parameters. However, typical continuous wave DCS (CW-DCS) does not allow photon pathlength discrimination, thus cannot readily distinguish extra- and intra-cerebral signals. There have been few attempts to

decrease extracerebral contamination of DCS signal by applying external pressure on optical probe or by using multi-layered models. Another promising way of separating extra and intra-cerebral signals is the use of time-domain DCS (TD-DCS). TD-DCS implies using of pulsed, yet sufficiently coherent laser, which gives an opportunity to discriminate photons by pathlength. Moreover, TD-DCS allows to extract optical properties of the tissue which is necessary for correct estimation of BFI. On the other hand, this technique suffers from a low number of photons per correlation curve (due to temporal gating) resulting in a poor signal-to-noise ratio (SNR). To overcome this issue, an advanced detection system like superconducting nanowire single-photon detector (SNSPD) could be used. In this work, we use TD-DCS system with SNSPD for in-vivo measurements in order to look at the pulsatile blood flow and its response to Valsalva maneuver exercise at early and late time gates.

P9. Evaluation of muscle performance, neuromuscular and oxidative dynamics in rock climbing

POSTER SESSION

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Sports climbing is one of the fastest growing sports worldwide in the recent years. Flexor digitorum profundus (FDP), the muscle that generates the flexion between the distal phalanges of the fingers, in considered responsible for the climbing-specific fingertips grip. In this study, we wanted to test the relation between the muscular adaptations and the climbing performance of the FDP muscle in static and dynamic conditions, in order to help explaining the physiological adaptations and the development of the fatigue during climbing. Thirty-eight healthy subjects with no injury in the upper limb were recruited, out of which 22 advanced climbers and 16 non-climbers. For the static experiment, a vascular occlusion test (VOT) was performed on the subject's self-reported dominant arm, and the dynamics of the blood flow and the oxygenation were assessed during and after the arm cuff release. For the dynamic test, subjects performed an all-out fatigue test on a climbing-mimicking platform. For this test, along with the oxygenation, the force and the electromyography (EMG) were recorded. VOT test did not show significant difference between the two groups, indicating that the metabolism may not be primarily related to a single muscle performance. Fatigue test has shown that it is possible to track the fatigue onset not only from the force profile, but also the EMG frequency profile. Preliminary results of oxygenation profiles show similar trends to the force and the EMG profiles. Further data analysis is pending.

P10. Analysis of the epidemiological dynamics of monkeypox from May 15 to August 31, 2022

POSTER SESSION

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While the COVID-19 pandemic is still ongoing, the monkeypox (MPX) has spread through several non-endemic countries and forced the declaration of a new Public Health Emergency of International Concern by the World Health Organization on 23 July 2022. At the end of August 2022, the total number of diagnosed cases was above 1000 in 9 countries, between 100 and 1000 in 18 countries and less than 100 in 55 countries. We used the public data available in Our World in Data to study the MPX outbreak in those countries with more than 1000 reported cases. We used an empirical approach to model the epidemiological dynamics from May 15 to August 31. We proved that the Gompertz growth equation describes correctly the dynamics in these countries. Given that the collection of data presents many temporal irregularities, the Gompertz model allowed for estimating the order of magnitude of the number of new cases per day in each country. The model's capacity to provide short-term reliable predictions was also proved, while it does not allow to predict what the long-term epidemiological behaviour will be. Both the processed data and the short-term predictions show that in most of the studied countries the situation is improving or will soon improve. The first countries to report cases had the highest number of daily cases in early July (UK) or mid-July (Spain). Globally, the maximum number of daily cases was reached at the end of August.

P11. Multi-wavelength, multi-exposure time, and multi-distance laser speckle contrast simulations to infer microvascular blood flow and tissue optical properties

POSTER SESSION

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Speckle contrast optical spectroscopy (SCOS) is a diffuse optical method that uses the laser speckle phenomena and statistics to infer the microvascular blood flow (BF). However, currently is not possible to measure BF without providing simultaneous information about tissue optical properties, this implies that SCOS should be combined with another optical technique such as near-infrared spectroscopy (NIRS), increasing its cost. We present simulation findings for evaluating a speckle contrast optical spectroscopy approach that employs speckle patterns from multi-wavelength, multi-distance, and multi-exposure time to simultaneously infer microvascular blood flow and tissue optical properties. This novel approach offers improvements to SCOS and provides additional information about oxyhemoglobin and deoxyhemoglobin concentration and tissue oxygen saturation. Additionally, will be an independent technique that simultaneously infers microvascular blood flow and tissue optical properties. We demonstrated the applicability of this approach based on simulating realistic speckle contrast from in tissue for three wavelengths (690, 785, and 830 nm), four source-detector distances (1.2, 1.5, 2.0, and 2.5 cm,) and four exposure times (0.5, 1.0, 3.0 and 5 ms). Simulation findings are used to determine the relationship between these parameters on precision and accuracy.

P12. Pilot study: Continuous monitoring of cerebral and scalp blood flow of neonatal piglet during validation of different cardiologic procedures

POSTER SESSION

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Newborns diagnosed with severe congenital heart defects (CHD) have been rescued with cardiac surgeries over the years. However, studies have shown that the surviving patients develop neurodevelopmental problems. Although CHD infants are highly susceptible to hypoxia and ischemia, additional injuries may occur during cardiopulmonary bypass (CBP) and cardiac arrest. The main interest of this study to investigate the effect of different surgical procedures on cerebral blood flow non-invasively and continuously. This study presents the results of a pilot study of a neonatal piglet model. In this pilot study, two piglets were used: CBP and 30 minutes of cardiac arrest were applied to each piglet, while hypothermia is induced on one piglet and the other remained in normothermia. 16-channel diffuse correlation spectroscopy device was used in monitoring of cerebral and scalp blood flow index (CBFi and SBFi) by using two source-detector-separation distances (1.5 cm and 0.75 cm). The probe (5 cm – 2 cm) was placed only on one hemisphere. 8 channels are used for CBFi and SBFi measurements. Recording of the flow data was started before the cardiac arrest, while the piglets were anesthetized and intubated. Stages of decreased correlation were observed between CBFi and SBFi after resuscitation in the one piglet induced neuroprotective hypothermia.

P13.Epidemiological characteristics and modelling for short-term prediction of the Respiratory Syncytial Virus (RSV) and influenza spreading in Catalonia (Spain)

POSTER SESSION

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Respiratory Syncytial Virus (RSV) has been the most prevalent cause of viral respiratory infection in children until the outbreak of the SARS-CoV-2 pandemic. Besides, influenza used to play a similar role among adults every year, generating a seasonal excess in mortality among most vulnerable population. The seasonality of both infectious diseases has been altered with the appearance of SARS-CoV-2, the agent that causes COVID-19. Our aim was to characterize the RSV and influenza epidemics in Catalonia using a model-based approach in order to analyse the changes in the observed patterns caused by the SARS-CoV-2 pandemic. Additionally, we tested the model for short- and mid-term predictive purposes, as well as the influence of meteorological factors. We used data from public databases such as DIAGNOSTICAT and SIVIC, combined with ad-hoc data obtained in the context of a multicentric project that includes paediatricians from tertiary hospitals and primary care settings (COPEDI-CAT). As for the mathematical modelling, we combined an empirical approach using a Gompertz with a mechanistic approach using SEIR-like models. We also incorporated the effect of meteorological factors in a so-called meteomodel. We characterized the pre-pandemic and pandemic RSV and influenza outbreaks using the Gompertz approach, in order to detect changes in the patterns. These changes could be caused either by viral interference or by the

non-pharmaceutical interventions. We explored the prediction capacity of the different models with the design of successive fittings with incremental data for each season and infectious disease.

P14. Elucidating the role of shear forces in LFA-1 activation and dynamics by single particle tracking

POSTER SESSION

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Upon seeking a site of infection, circulating leukocytes undergo the process of extravasation, in which they leave the blood stream through the vessel endothelium. The β2 integrin Lymphocyte function-associated antigen 1 (LFA-1) is a transmembrane receptor expressed on most leukocytes. It plays a crucial role in extravasation, as it facilitates the required firm adhesion between leukocytes and endothelial cells. More recently, LFA-1 has proven to be more than a passive anchor, but a force-sensitive transducer and adhesion regulator. LFA-1 binding is mechano-sensitive, its ligand affinity regulated by force-dependent inside-out and outside-in signaling. However, in the native environment of leukocytes, blood flow is an abiding mechanical stimulus. It produces forces acting on the cell, consequently resulting in forces on the cell's molecular interactions. While commonly omitted, understanding the effect of these forces is required for a full understanding of LFA-1 function in extravasation. We will show data giving insight to the role of forces in LFA-1 interactions using Single Particle Tracking (SPT) in a shear flow environment. In resting conditions, the majority of LFA-1 is laterally diffusing within the cell membrane. Upon either intracellular or extracellular interaction, LFA-1 stalls. Consequently, the mobility accessible via SPT encloses information about its interactions. We employ SPT on live-cells in the presence and absence of shear flow and under different chemical stimuli and thereby show their respective effect on lateral LFA-1 mobility.

P15. Functional diffuse correlation spectroscopy measurements on cognitively healthy and mild cognitive impaired populations during single and dual motor tasks

POSTER SESSION

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Alterations in the normal function of the prefrontal cortex could be caused due to either cerebrovascular lesions or neurodegeneration resulting in disorders of cognition and mobility, which are considered risk factors for developing dementia. The current study is focused on using diffuse correlation spectroscopy measurements alongside with physiological and accelerometer data, during functional tasks to use cerebral blood flow (CBF) as a potential biomarker of cognitive decline. To do so, a cohort of 69 subjects constitute

the population of this study, of cognitively healthy (n = 33) and mild cognitive impaired (n = 36) subjects. Our protocol included two types of single motor tasks (ST) and three dual tasks (DT), where the motor task was performed in combination with an additional cognitive task. In order to reveal the brain hemodynamic activity evoked from the stimulation tasks, we used General Linear Model (GLM) to regress out systemic contamination or motion artefacts on individual basis. Linear mixed effects model (LME) was used for the group analysis. Results show increased activation during the more demanding DT statistically different from our control test with a p-value ¡ 0.001 for both cases, but this was not observed for a less demanding DT. However, no statistical difference was observed between cognitively healthy and aMCI subjects during the tests (p = 0.36). Our main findings show significantly different response on the CBF depending on the cognitive demand of the task, meaning thus that CBF could be used as a potential biomarker for functional studies in realistic environments.

P16. Spatiotemporal dynamics of secretory proteins in the Golgi apparatus

POSTER SESSION

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Single particle tracking (SPT) is a fluorescence microscopy technique that allows to monitor the dynamics of individual molecules in living cells with a very high spatiotemporal resolution (10s nm and 10s ms, respectively) [1]. Although SPT has been widely used to investigate protein diffusion at the cell surface, its application to the study of intracellular processes has been limited due to a number of technical challenges. Here, I will present our SPT-PALM-based experimental and computational pipeline, and how we use it to monitor the intracellular dynamics of single secretory proteins along the secretory pathway. Interestingly, the formation at the Golgi of transport carriers destined for secretion has been recently shown to require the establishment of functional and dynamic interactions between Endoplasmic Reticulum (ER) and Golgi membranes: the so-called ER-Golgi membrane contact sites (MCS) [2,3]. However, the mechanism for this still remains unclear. Aiming at understanding how ER-Golgi MCS regulate protein sorting and carrier formation for secretion, we used intracellular SPT-PALM to monitor the spatiotemporal dynamics of secretory proteins with respect to MCS. I will present our results on the dynamics of secretory cargoes in the Golgi, and how that depends on the existence of functional ER-Golgi MCS.

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P17. Structural analysis of calcium waves in cardiomyocyte using a subcellular bidomain model. The role of the RyR release interaction with buffers.

POSTER SESSION

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Normal heart beating requires that the electric signal propagating in each cardiomyocyte triggers a transient increase in the level of calcium ions in the cytosol. During this transient, the contraction machinery in the cell is activated thanks to the secondary messenger nature of calcium ions. This is heavily regulated by different proteins which control the flux of calcium ions in an out of the cell and, more important, in and out of the Sarcoplasmic Reticulum, regulated by the RyR. Also, by other proteins (buffers) that attach to calcium ions and regulate the peak levels of the transient. A key feature of some cardiac malfunction is the appearance of spontaneous calcium waves that propagate inside the cell not triggered by an electric signal. The appearance of these calcium waves can generate spontaneous electrical activity due to associate currents that appear when this extra calcium is exchanged outside of the cell. This entails two problems. First, there must be technical feasibility of releasing calcium locally and by a fire-diffuse-fire process generate a wave. Second, the homeostatic conditions of the cell must let this process be sustained. In this analysis, we focus on the first. We generate a detailed model of the cell with two domains, cytosol and SR, and with the proper structural disposition of channels and buffers that regulate calcium fluxes. We show that, under very general conditions, calcium waves do not appear and the release properties of RyR and buffer activity are key to sustain the possibility of calcium waves.

P18. Plasmonic antenna platforms for multicolor single-molecule studies with high-throughput

POSTER SESSION

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Antenna-in-box platforms are a type of nanostructure arrays that can be integrated onto conventional microscopy cover slides and have demonstrated their capability to resolve dynamic processes in living cells with unprecedented spatiotemporal resolution. This has been recently achieved through the strong localized electromagnetic fields and background suppression provided by the Gold-based nanostructures. However, these nanoantenna platforms cannot be exploited for multicolor experiments due to material intrinsic limitations of Gold. In this work, we aim to establish a second generation of Aluminum-based antenna-in-box platforms that enables multicolor and multiplexed read-out and therefore provides much greater flexibility and faster data acquisition than demonstrated with previously designed nanostructures. This requires not only profound changes in the platform design and fabrication but also modifications of the optical setup to accomplish parallelized fluorescence detection. We show that embedding plasmonic antennas in apertures not only reduces the fluorescence background but also increases the intensity enhancement provided by the antennas improving the more modest response of Aluminum antennas as compared to Gold antennas. Furthermore, we present an electron-beam lithography overlay process to fabricate large arrays of Aluminum-based antenna-

in-box platforms with ultrathin passivation layers suppressing undesired interactions between the antennas and their biological environment. With the new platforms we aim to demonstrate the multicolor and multiplexing capabilities using different dyes and integrating a camera closely matched to the demanding experimental conditions. This ultimately promises to enable the in-vivo detection of plasma membrane-bound receptor-ligand interactions on a single molecule level even at physiologically relevant concentrations providing a large amount of statistics due to the camera-based multiplexed and multicolor capabilities.

P19. Super-resolution microscopy reveals hierarchical organization of spatially segregated protein nano-clusters within focal adhesions

POSTER SESSION

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Focal Adhesions (FA) are mechanosensitive complexes that connect the extracellular matrix (ECM) with the actin cytoskeleton. This is achieved through clustered integrins, their ligands in the ECM, and an internal dynamic protein complex linking the cytosolic domain of integrins with the actin cytoskeleton. In contrast to the established view that FAs are homogenous micron-scale protein assemblies, recent super-resolution imaging and single molecule dynamic approaches are challenging this view. These studies suggest that FA molecular components are highly organized in the axial direction establishing segregated layers of functional activity. Recent data also indicate that similar type of nanoscale modularity might exist in the horizontal plane of FAs. Here, we present a set of experiments aimed at dissecting the lateral nanoscale organisation of different adhesion proteins inside FAs. Using dual-colour STORM nanoscopy and novel analytical techniques we revealed that key FA proteins, i.e. $\alpha 5\,\beta 1$, $\alpha v\,\beta 3$, paxillin, talin and vinculin, are organised into segregated nanoclusters, around 50nm in size. Moreover, nanoclusters of the same proteins exhibited a lateral segregation at 55nm and were enriched at distances of 100-200nm. Intriguingly, we found that one of the two main FA integrins, $\alpha 5\beta 1$, localized at the edge of FAs. In this peripheral ring, we show that clusters of the adaptors paxillin and talin are preferentially found in close proximity to $\alpha 5\beta 1$ clusters, indicating a functional organisation of these protein nanoclusters. As a whole, our data indicate a highly complex spatiotemporal organisation laterally within FAs with different proteins forming functional nanohubs of activity.

P20. Exploring how force transmission to nuclear pore complexes affects nucleocytoplasmic transport

POSTER SESSION

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Transport of molecules between the nucleus and the cytoplasm is one of the most tightly controlled processes in cells. Recently, the application of mechanical force to the nucleus has been shown to regulate nuclear transport. Nuclear pore complexes (NPCs), as the gateways to the nucleus, stand at the center of this process. However, the mechano-molecular link of force transmission to the NPC remains unclear. Through super-resolution imaging, we show that nuclei submitted to force have NPCs with increased diameters. Further, knocking down two key structural NPC proteins, nucleoporins 153 (NUP153) and 155 (NUP155), results in a decrease in nuclear accumulation of the transcriptional regulator (TR) YAP/TAZ, which is known to be regulated by nucleocytoplasmic transport. This evidence suggests that these proteins may regulate the structural integrity of NPCs under force, or even be involved in the transmission of force to the NPC. To further explore this hypothesis, we are carrying out experiments to measure diffusion across NPCs in the different conditions, and to perturb force transmission between nuclei and the cytoskeleton.