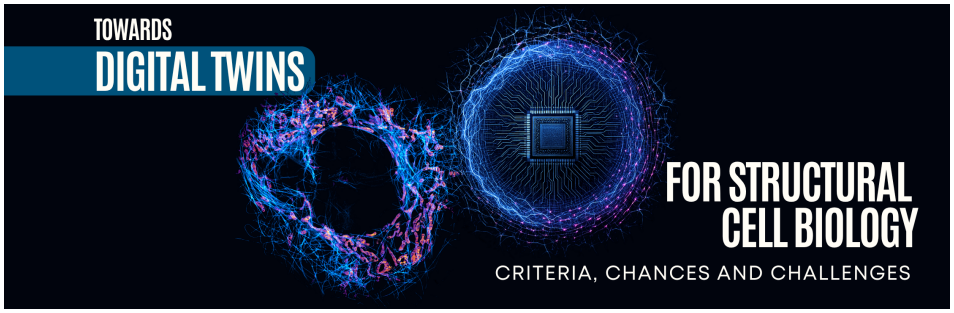
Giersch International Conference & SCALE Kick-Off

Monday, 2 March 2026 - Thursday, 5 March 2026

FIAS / OSZ



Book of Abstracts

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Invited Talks / 1

Using digital twins to probe the origins of intelligence

Author: Samantha Wood[1]

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The origins of perception and cognition have been debated for centuries, with ongoing disagreement about what knowledge and neural structure are hardwired at birth. A major obstacle to resolving this debate is that, until recently, it has been impossible to train formal computational models of intelligence on the same sensory experiences as developing animals. We address this limitation by building digital twins of newborn animals and their environments. We rear newborn animals and "newborn"artificial agents in the same environments, then test the animals and agents on the same tasks. This allows us to provide animals and models with matched learning contexts and test candidate brain models under identical constraints. Using this framework, we show that perceptual and cognitive capacities can emerge from coupling flexible, domain-general neural networks with structured, domain-optimized bodies. Ultimately, this digital-twin framework allows researchers to build formal models of the origins of intelligence, unifying insights across psychology, neuroscience, and artificial intelligence.

Invited Talks / 2

Digital Twins in biology and medicine: bridging experimental models, simulation, and health systems

Author: Liesbet Geris[1]

[1] *University of Liège, KU Leuven, VPH society*

In silico and in vitro technologies are complementary to traditional biological and biomedical tools, enabling the study of multifactorial processes under controlled conditions. In the first part of this talk, I will present examples from bone and joint degeneration and regeneration research, where we combine computer modeling and simulation with microphysiological systems to better understand pathophysiological processes and design regenerative strategies.
In the second part of the talk I will put this work into the context of ongoing work in the European Virtual Human Twins (VHT) initiative, which aims to facilitate the development, credibility assessment, and uptake of digital twins in all areas of health & care, including the basic biological and biomedical research. The recently concluded EDITH Coordination & Support Action brought together the entire VHT ecosystem (including academia, industry, patients, healthcare providers, regulators, payers, policy makers etc) to jointly create a roadmap towards the realization of the VHT. The roadmap (doi:10.5281/zenodo.14769224) provides the context and identified stakeholder needs, followed by a description of the required technology and infrastructure. It continues with a thorough discussion of the relevant standards, regulatory, health technology assessment, legal, ethical and social aspects, as well as the business elements and general incentives. It ends with 30 recommendations that have been formulated for all stakeholders to help advance this moonshot initiative and create a tangible impact on the life of patients.

Invited Talks / 3

If Machines Can Learn, Who Needs Scientists?

Author: Jeffery Hoch[1]

[1] *UConn Health*

Machine learning is impacting not just the natural sciences but also the social sciences, engineering, architecture, and the art world. In many fields an obstacle to the application of machine learning is the relative paucity of available training data. Other challenges
include the problem of interpreting the results of a machine learning algorithms, incorporating machine learning into hypothesis-driven research, and ethical and reproducible use. This perspective examines the potential of machine learning in NMR structural biology, the role of scientists, and speculates on possible approaches to the hurdles.

Invited Talks / 4

Toward Digital Twins of Development and Disease

Author: Dagmar Iber[1]

[1] *ETH Zürich*

Computational simulations have long been used to study emergent phenomena in biology. Data-driven in silico models of tissue behavior in development and disease now enable the creation of Digital Twins—virtual counterparts with applications in bioengineering and precision medicine. In this talk, I will present our simulation frameworks for high-resolution tissue modeling and parameter inference from imaging and experimental data. Finally, I will discuss our progress in constructing Digital Twins for epithelial tissues, morphogenesis, and medical treatments.

Invited Talks / 5

In-cell structural systems modeling

Author: Jan Kosinski[1]

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One of the central goals of computational biology is to build a realistic model of a cell –one that can simulate cellular processes, predict the effects of perturbations, and support rational drug design. This vision has gained new momentum through recent technological advances, for example, in single-cell omics, structural proteomics, and visual mapping of cells using in-cell cryo-electron tomography (cryo-ET) and volume electron microscopy. The emergence of AI-based methods such as AlphaFold and other AI-driven models of biological complexity further contributes to this renewed interest. Although the form of such a comprehensive cell model remains undefined, the recent technological advances now allow us to build components that were previously out of reach. In this context, I will present our contribution toward modeling a cell by leveraging some of these recent technological advances. I will show the computational tools we are developing as part of an effort to build a computational framework for in-cell structural systems biology, aimed at enabling spatial and systems-level mapping of the cellular environment. These will include methods for data-driven modeling macromolecular assemblies and interaction networks, as well as approaches for identifying and modeling molecules and membranes in cryo-ET data.

Invited Talks / 6

Teaching AI the Language of RNA: Foundation Models for Regulation and Therapeutic Design

Author: Annalisa Marsico[1]

[1] *Computational Health Center, Helmholtz Munich*

Computational analysis of high-resolution CLIP-seq data has enabled precise mapping of RBP binding sites and cis-regulatory elements underlying post-transcriptional RNA regulation. Recently, the field has shifted with the emergence of RNA foundation models—self-supervised models trained on vast unlabeled RNA sequences—that enable holistic modeling of RNA function and in silico hypothesis generation. Leveraging such models represents the next frontier, allowing prediction of multiple RNA regulatory processes, as well as in silico design of RNA-based therapeutics. Building on the premise that RNA function is encoded in its interaction partners, we developed Parnet, a multi-task model that densely represents the RNA interactome. Extending our earlier single-task model RBPNet, Parnet is trained end-to-end on raw CLIP-seq profiles from hundreds of RBPs to predict genome-wide binding profiles directly from sequence. In contrast to unsupervised RNA language models, Parnet learns embeddings that capture the combinatorial "RBP code"underlying post-transcriptional regulation. As a result, Parnet generalizes across downstream tasks—including splicing, intron retention, mRNA translation and degradation, and therapeutic design—often with minimal or no fine-tuning.

Invited Talks / 7

Bayesian metamodeling of early T-cell antigen receptor signaling accounts for its nanoscale activation patterns

Author: Barak Raveh[1]

[1] *The Hebrew University of Jerusalem*

T cells respond swiftly, specifically, sensitively, and robustly to cognate antigens presented on the surface of antigen presenting cells. Existing microscopic models capture various aspects of early T-cell antigen receptor (TCR) signaling at the molecular level. However, none of these models account for the totality of the data, impeding our understanding of early T-cell activation. Here, we study early TCR signaling using Bayesian metamodeling, an approach for systematically integrating multiple partial models into a metamodel of a complex system. We inform the partial models using multiple published super-resolution microscopy datasets. Collectively, these datasets describe the spatiotemporal organization, activity, interactions, and dynamics of TCR, CD45 and Lck signaling molecules in the early-forming immune synapse, and the concurrent membrane alterations. The resulting metamodel accounts for a distinct nanoscale dynamic pattern that could not be accounted for by any of the partial models on their own: a ring of phosphorylated TCR molecules, enriched at the periphery of early T cell contacts and confined by a proximal ring of CD45 molecules. The metamodel suggests this pattern results from limited activity range for the Lck molecules, acting as signaling messengers between kinetically-segregated TCR and CD45 molecules. We assessed the potential effect of Lck activity range on TCR phosphorylation and robust T cell activation for various pMHC:TCR association strengths, in the specific setting of an initial contact. We also inspected the impact of localized Lck inhibition via Csk recruitment to pTCRs, and that of splicing isoforms of CD45 on kinetic segregation. Due to the inherent scalability and adaptability of integrating independent partial models via Bayesian metamodeling, this approach can elucidate additional aspects of cell signaling and decision making.

Invited Talks / 8

From integrative structural biology to cell biology

Author: Andrej Sali[1]

[1] *UCSF*

Integrative modeling is an increasingly important tool in structural biology, providing structures by combining data from varied experimental methods and prior information. As a result, molecular architectures of large, heterogeneous, and dynamic systems, such as the ˜52 MDa Nuclear Pore Complex, can be mapped with useful accuracy, precision, and completeness. Key challenges in improving integrative modeling include expanding model representations, increasing the variety of input data and prior information, quantifying a match between input information and a model in a Bayesian fashion, inventing more efficient structural sampling, as well as developing better model assessment, analysis, and visualization. In addition, two community-level challenges in integrative modeling are being addressed under the auspices of the Worldwide Protein Data Bank (wwPDB). First, the impact of integrative structures is maximized by PDB-Dev, a prototype wwPDB repository for archiving, validating, visualizing, and disseminating integrative structures. Second, the scope of structural biology is expanded by linking the wwPDB resource for integrative structures with archives of data that have not been generally used for structure determination but are increasingly important for computing integrative structures, such as data from various types of mass spectrometry, spectroscopy, optical microscopy, proteomics, and genetics. To address the largest of modeling problems, a type of integrative modeling called metamodeling is being developed; metamodeling combines different types of input models as opposed to different types of data to compute an output model. Collectively, these developments will facilitate the structural biology mindset in cell biology and underpin spatiotemporal mapping of the entire cell.

Invited Talks / 9

Computational tools for building models of entire biological systems from light and electron microscopy

Author: Stephan Preibisch[1]

[1] *HHMI Janelia*

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Mining Molecular Data: from Single Cell Genomics to Cryo-E

Author: Judith Zaugg[1]

[1] *University of Basel*

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Insights into the mitochondrial collective

Author: Suliana Manley[1]

[1] *EPFL - Laboratory of Experimental Biophysics Lausanne*

Invited Talks / 13

Building a Virtual Embryo - A Single Cell At a Time.

Author: Loic Royer[1]

[1] *Biohub*

Imagine having an interactive digital twin of a developing embryo —one you could pause, rewind, or zoom into, exploring how every cell divides, moves, and differentiates. To make this vision real, we created Zebrahub, a dynamic atlas of zebrafish embryogenesis that combines cutting-edge microscopy, powerful computational lineage tracking (Ultrack), and precise molecular mapping into an interactive resource. Our journey begins with advanced multiview light-sheet microscopy, capturing millions of cells in living zebrafish embryos over days of continuous development (DaXi). Next, our uncertainty-aware cell tracker, Ultrack, transforms these enormous terabyte-scale datasets into coherent cellular histories, reconstructing precise lineages even in challenging imaging conditions. Combining these detailed lineages to single-cell transcriptomes, Zebrahub enables users not only to visualize developmental events in unprecedented detail but also to explore the molecular decisions underlying them.

Invited Talks / **14**

How cellular architecture modulates drug response

Author: Stefan Knapp[1]

[1] *Goethe University*

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Towards Digital Twins of Nuclear Pores

Author: Martin Beck[1]

[1] *Max Planck Institute of Biophysics*

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Biomolecular condensate architecture of an autophagic cargo at molecular resolution in situ

Biomolecular condensates organise cellular biochemistry, yet their molecular architecture in situ remains poorly understood. During selective autophagy, macromolecules frequently accumulate into biomolecular condensates, forming discrete entities for autophagic engulfment and degradation – ideal systems for structural analysis. We employed in situ cryo-electron tomography to determine the near-atomic resolution structure of Aminopeptidase 1 condensates within cells. These condensates form densely packed, spherical assemblies with amorphous organisation and liquid-like properties, elucidating the requirements of a selective autophagic cargo for exclusive targeting. Structural analysis and multiscale simulations reveal that the short, transient α-helical structures in the disordered N-terminus of Aminopeptidase 1 enable site-specific, coiled-coil-like interactions required for condensate formation and properties. A single point mutation that increases α-helical propensity directly modulates condensate viscosity and dynamics from a liquid-like to a glass-like state, while preserving local molecular packing. Our results demonstrate that disordered regions encode both specificity and material properties through transiently structured motifs, linking sequence specificity to phase behaviour in cells and expanding the molecular logic of phase separation in cells.

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Towards Digital Twins of the cerebral cortex

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Digital twins for modelling gene expression: applications to association studies and personalized drug recommendation

Modern applications of AI technologies have enabled to predict the expression of genes genome-wide in a cell-type specific way using DNA sequence or epigenetic information. In this talk I will explain how these methods can be used to build digital twins for modelling gene expression and introduce novel applications for associating genes with disease and suggest personalised drug treatments.

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Integrative Structural Biology in the era of Artificial Intelligence

Short Talk / 20

From in situ cryoET to digital twins of subcellular segments

High-confidence 3D template matching (hcTM) turns in situ cryoET tomograms into simulation-ready subcellular segments. Multiscale simulations then make predictions later confirmed experimentally. For example, how mutations or composition changes propagate to mesoscale organization and biological function. Examples include human chromatin organization, viral transport and mutation-driven condensate solidification.

Short Talk / 21

Control of the condensation of TDP-43 by enzymatic phosphorylation: a perspective from molecular dynamics simulations

Cellular processes are organized by the phase separation of proteins into biomolecular condensates. These condensates are regulated by post-translational modifications, most notably phosphorylation. Phosphorylation of proteins is catalysed by kinases which consumes the chemical fuel ATP. While the phosphorylation of TDP-43 is closely linked to neurodegenerative disease, how TDP-43 is phosphorylated remains poorly understood. It is not clear whether kinases interact directly with condensates or primarily with TDP-43 proteins within the dilute phase. Molecular dynamics simulations can potentially resolve these interactions, yet modelling fuel-driven, non-equilibrium dynamics remains a significant computational challenge. We show how to simulate chemical-driven enzymatic phosphorylation of proteins in coarse-grained molecular dynamics. Importantly, we demonstrate how to validate the thermodynamic consistency of these simulations by automatically constructing

Markov-state models from the resulting trajectories. Our results reveal that the kinase Casein kinase 1 delta binds preferentially to TDP-43 condensates over the dilute phase, thereby accelerating phosphorylation. While enzymes initially localise to the droplet surface, phosphorylation enables enzymes to interact with the condensate interior. Our simulations demonstrate that ultimately this localised enzymatic activity can trigger the complete dissolution of TDP-43 condensates.

Short Talk / **22**

Multiscale Modeling of Nuclear Membrane Sealing

During mitotic exit, the nuclear envelope seals spindle-microtubule holes in a process mediated via LEM2-ESCRT. Cryo-electron tomography (Cryo-ET) shows LEM2-ESCRT filament architecture but not the sealing mechanism. We built a digital twin by integrating Cryo-ET with multiscale molecular dynamics simulations of filaments in a 90 nm membrane hole, capturing conformational changes, showing how LEM2's disordered domain engages microtubules, and allowing in-silico tests of mechanical stress.

Short Talk / **23**

Deep-SegCLEM: unified segmentation and matching for correlative light–electron microscopy

Correlative light and electron microscopy (CLEM) links dynamic functional imaging with ultrastructural detail, yet automated correlation remains unresolved due to the difficulty of bridging two fundamentally different microscopy modalities. Current approaches either bypass segmentation or rely on generic models, leading to poor or inconsistent alignment. We present Deep-SegCLEM, a fully automated pipeline that leverages mitochondria-specific features to establish fiducial-free correspondence between LM and EM images. Deep-SegCLEM integrates two tailored segmentation networks—DSCLEM-LM for fluorescence microscopy and DSCLEM-EM for electron microscopy—with a multi-scale template-matching algorithm for cross-modal alignment. On fluorescence datasets spanning confocal, Airyscan, and SIM modalities, DSCLEM-LM achieved state-of-the-art performance (F1 = 0.98, IoU = 0.96), surpassing U-Net, U-Net++, DeepLabV3, FCNN, MitoSegNet (F1 = 0.93), and the µSAM foundation model (F1 = 0.73). DSCLEM-EM similarly outperformed classical CNN architectures and foundation models across multiple public EM benchmarks, including challenging conditions such as UroCell (F1 = 0.80 versus ≤0.57 for CNN baselines and ≤0.72 for µSAM). Failure-Driven Targeted Augmentation (FDTA) was essential for capturing rare morphologies and improving generalization. The correlation module achieves fully unsupervised LM–EM alignment in minutes, with over 80% matching accuracy and a mean centroid error of 2.0 µm relative to expert-generated STED–EM correspondence. Additional fluorescence channels are automatically co-registered with EM ultrastructure, enabling mechanistically meaningful mapping of molecular events. Using HALO-BAK and Drp1, Deep-SegCLEM associates apoptotic membrane discontinuities and mitochondrial fission sites with their ultrastructural counterparts, demonstrating biological relevance. Together, these advances deliver a scalable, end-to-end workflow for quantitative, fiducial-free correlative microscopy, enabling high-throughput mapping of molecular signals to ultrastructure during dynamic cellular processes.

Short Talk / **24**

rRNA expansion segments mediate the oligomerization of inac-

tive animal ribosomes

When stressed, all cells downregulate protein synthesis, to conserve energy and shift resources towards repair. Here, we show that in some mammalian cells, including neurons, stress also results in the formation of inactive ribosome-ribosome clusters (disomes). Using cryogenic electron tomography we visualized ribosomes in situ and observed that this dimerization is mediated by a homotypic interaction of rRNA expansion segment ES31Lb. ES31Lb interactions are both necessary and sufficient for disome formation and confer a growth advantage and stress-resistance to cells. ES31Lb is predicted to homo-dimerize in ˜20% of chordates, including both a chicken and human variants. Cryo-ET analysis of long-studied chicken tetrasomes revealed an interaction between ES31Lb and ES9La. Taken together, these data indicate a mechanism of translation regulation in animal cells that operates using a flexible component of the protein synthesis machinery - rRNA expansion segments.

Short Talk / 25

Area-specific signatures of time-irreversibility in spontaneous neural activity of the mouse brain

We study time-irreversibility in spontaneous neural activity as a multiscale dynamical phenomenon. Using large-scale Neuropixels recordings across mouse brain areas, we quantify temporal asymmetry from milliseconds to seconds (30–0.5 Hz) with complementary computational measures capturing population-level asymmetry, metastable state fluxes, and state-space divergence. This framework enables systematic analysis of time-irreversible dynamics across brain regions and timescales.

Short Talk / 26

In situ structure of a gap junction - stomatin complex.

Gap junctions (GJs) are intercellular channels that mediate electrical signals and transfer of small molecules. They are crucial for brain, heart, and other organ functions. While molecular structures of purified homomeric GJs are available, information of in situ structures is lacking. In vivo, GJs can form heteromers with different functionalities and may associate with other proteins. Here, we analyzed Caenorhabditis elegans GJs by cryo–electron tomography and subtomogram averaging. We observed hexagonal arrays of GJs at cellular junctions in primary embryonal cells that displayed distinct wide and narrow conformations. Moreover, we found a cap-like, cytosolic protein assembly enclosing the channel pore. We propose that the cap is formed by the stomatin UNC-1, known to interact with UNC-9 innexins. This is corroborated by matching AlphaFold3 models of UNC-1 multimers with our subtomogram average structure; by expressing GFP-tagged UNC-1, leading to cap structures with additional density; and by coarse-grained MD simulations. UNC-1/stomatin rings may affect GJ formation or functions, possibly beyond nematodes.

Short Talk / 27

Insights into the plasma membrane association of Extended Synaptotagmin 3

Membrane contact sites between the ER and the PM are site of non-vesicular lipid transport as

they harbor various lipid transfer proteins. They are established by protein tethers among which Extended Synaptotagmins (E-Syts) are the most abundant family in mammals. E-Syts are ER-resident and regulate ER-PM connectivity via reversible association of their C2 domains with lipids at the PM. Here, we study exact lipid binding properties of the individual C2 domains of E-Syt3 as well as of a large unstructured linker between the C2B and C2C domains. We use coarse-grained molecular dynamics simulations as well as live-cell confocal and TIRF imaging. We identify novel protein-lipid interactions like PI binding of the C2AB domains and PI4P binding of the C2C domain. Moreover, we show that the unstructured C2B-C2C linker associates with the PM via its aromatic residues. For the C2C domain, we identified two different PM association configurations with different lipid binding profiles.

Short Talk / 28

Data Driven Modelling of Limb Bud Growth and Morphogenesis

Limb development is regulated by feedback between the tissue-scale mechanics and cellular decisions–migration, contraction, division, and death–implemented through gene-regulatory networks. The dynamically changing states of these cellular networks reflect the decisions being made. To integrate these interactions across 3 scales: genes, cells, and tissues, we develop a 3D cell-based model in which cellular decisions are spatially regulated by morphogen gradients. By constraining parameters with empirical data and optimizing against wild-type limb-bud shape, we obtain a model that links signal distributions to emergent mechanical behaviors. Multiple mechanisms have been proposed for limb-bud morphogenesis, including ectodermal mechanical constraints, proliferation gradients, oriented divisions, distally biased migration, motility gradients, and convergent extension. Yet which spatio-temporal combinations of these activities generate correct morphology remains unresolved. We use the model to test whether convergent extension alone is sufficient to reproduce limb-bud outgrowth and shaping. We compare 2 distinct modes of convergence: (1) orthogonal to an AER/FGF8-associated proximo-distal cue, and (2) parallel to a surface-to-core (radial) cue consistent with Wnt5a. For each mode, we quantify how the strength and timing of convergent extension affects predicted shape trajectories and whether either mode–or a combination of both–can match wild-type morphology.

Short Talk / 29

Initiative of Panoramic Digital Life Model Project

tba

Short Talk / 30

Multiscale Investigation of Membrane Remodeling during Selective ER-phagy

FAM134B drives selective ER-phagy to maintain ER homeostasis. Modeling, coarse-grained MD, and experiments capture RHD-driven curvature induction/sensing (isoform-specific), ubiquitination-triggered clustering, and IDR-amplified ER budding. These self-organizing principles inform a hierarchical digital twin of the ER–phagophore contact site linking membrane mechanics/curvature,

FAM134B–LC3B tethering, and ATG9-mediated lipid scrambling to predict nascent phagophore recruitment, growth, and maturation.

Short Talk / **31**

Molecular Digital Twins of Innate Immunity: Insights from Simulations of Human Guanylate-Binding Protein 1

This work explores digital twins for innate immunity, focusing on human guanylate-binding protein 1 (hGBP1) and its role in targeting intracellular pathogens. Using coarse-grained molecular dynamics simulations, we examine protein-membrane interfaces with realistic pathogen membranes. We find that hGBP1 interacts with various membrane types; negatively charged lipids enhance affinity, while lipopolysaccharides are crucial for effective interactions. Additionally, hGBP1 polymerization is essential for stable membrane binding required for pathogen clearance.

Short Talk / **32**

Nuclear speckle periphery organizes stable intron-retained RNAs into a distinct nuclear retention compartment

Intron retention (IR) is an important regulator of RNA fate, yet its spatial and temporal organization in human cells remains poorly understood. Here, we investigate the dynamics, localization, and regulation of intron-retained RNAs in pluripotent stem cells using compartment-resolved transcriptional shutdown, sequence-based modeling, and advanced RNA imaging. We focus on the relationship between IR, nuclear speckles, RNA stability, and cell-cycle–dependent RNA processing.

Short Talk / **33**

From Capability to Confidence: RNA Mass Spectrometry as a Criterion for Digital Twins

Digital twins in structural cell biology critically depend on experimental data quality and interpretability. RNA is a central molecular layer, yet its mass spectrometric analysis remains analytically fragile. I will discuss why RNA-MS cannot be treated as an extension of proteomics and how intrinsic ambiguity, redundancy, and modification complexity challenge confidence. I argue that explicit analytical control and RNA-aware validation criteria are essential for integrating RNA into mechanistically meaningful digital twins.

Short Talk / **34**

Molecular mechanism of membrane pore formation triggered by PI(4,5)P2- dependent FGF2 oligomerization

Fibroblast Growth Factor 2 (FGF2) is a key cell survival factor involved in tumor-induced angio-

genesis. Unlike most secreted proteins, FGF2 lacks a signal peptide and is exported via unconventional protein secretion (UPS), bypassing the ER/Golgi. It translocates directly across the plasma membrane (Type I UPS), a process initiated by PI(4,5)P_2- mediated recruitment to the inner leaflet. Subsequently, FGF2 forms membrane-spanning oligomers within toroidal membrane pores. The final stage of secretion involves heparan sulfate proteoglycans on the cell surface, which disassemble these oligomers at the outer membrane leaflet, ensuring FGF2 is released into the extracellular space to mediate autocrine and paracrine signaling. Using atomic force microscopy, biochemical reconstitution experiments, and multiscale molecular physics-based computer simulations, we show that FGF2 self-assembles into a ring-like structure, triggering PI(4,5)P_2 lipid sorting and membrane remodeling. When PI(4,5)P_2 reaches a critical threshold, its non-bilayer properties destabilize the membrane, forming a pore through which FGF2 translocate across the membrane. We propose that the geometry of FGF2 oligomers and their lipid sorting capacity are crucial for protein translocation, suggesting a shared mechanism with other pore-forming proteins that assemble into ring-like structures

Short Talk / 35

Learning Biomolecular Ensembles from Experimental Cryo-EM Data

Biomolecules are inherently flexible, continuously transitioning between conformations to carry out their cellular functions. Cryo–electron microscopy (cryo-EM) enables us to image individual biomolecules at near-atomic resolution. As a result, an image dataset can capture the entire biomolecular ensemble at once. By comparing cryo-EM images to structural hypotheses, one can identify the structure that best matches each image. In principle, this allows us to identify the structures in the images and infer the underlying ensemble. However, performing these exhaustive comparisons is computationally very expensive. To tackle this problem, we introduce simulation-based inference for Cryo-EM (CryoSBI), a novel method that utilizes simulation-based inference to infer biomolecular conformation from individual cryo-EM images. Our approach uses neural posterior estimation, a technique that directly approximates the Bayesian posterior using a simulator and a density estimator. Training is performed only once using simulated data generated with the simulator. Afterward, inference for each particle requires just a single forward pass through the neural network. This eliminates the need to estimate particle pose and imaging parameters for each observation, delivering substantial computational speedups compared to traditional explicit likelihood methods. We demonstrate this approach through experiments on real cryo-EM data, where cryoSBI successfully extracts molecular conformations with reliable confidence measures. In addition, we combine cryoSBI with established ensemble reweighting techniques to infer biomolecular ensembles directly from entire cryo-EM image datasets. This enables the recovery of population distributions over conformational states. We demonstrate this capability by reweighing p4p6-conformational ensembles using cryo-EM data collected under different environmental conditions, revealing how changes in the experimental environment modify the underlying ensemble.

Short Talk / 36

The role of SAM domain in ΔNp63α

he p53 family member p63 exhibits multiple isoforms and functional domains, with ΔNp63α serving as a critical transcriptional regulator implicated in epithelial-mesenchymal transition. While the various domains of ΔNp63α have been extensively characterized, the precise function of its Sterile Alpha Motif (SAM) domain stays elusive. Mutations within the SAM domain are associated with Ankyloblepharon-Ectodermal Defects-Cleft Lip/Palate (AEC) syndrome and Rapp-Hodgkin syndrome (RHS), primarily due to SAM domain destabilization. These conditions are characterized by severe

skin erosions, underscoring the domain's significance in maintaining epithelial integrity. SAM domains are ubiquitous in eukaryotic proteins and are renowned for their propensity to oligomerize through diverse mechanisms. However, the p63 SAM domain has not previously demonstrated such oligomerization tendencies. Intriguingly, the presence of a putative zinc-binding motif within the SAM domain prompted our investigation into zinc-mediated effects using Nuclear Magnetic Resonance (NMR) spectroscopy. In this study, we present evidence of zinc-induced dimerization of the p63 SAM domain and elucidate its dimeric structure. Additionally, we explore the potential implications this dimerization might have on the full protein.

Short Talk / **37**

Parameterization of Molecular Photoswitches for Martini 3 and their Application in Photopharmacology

Molecular photoswitches are light-responsive compounds that undergo reversible conformational changes upon irradiation. We present Martini 3 coarse-grained models for seven photoswitches, parameterized using semi-empirical reference data and experimental water–octanol partitioning. These models enable the development of digital twins for light-controlled biological systems including membrane modulation, peptide conformational control, and ion channel regulation to study photopharmacology at system sizes and time scales inaccessible to atomistic simulations.

Panel discussion: Digital twins - Criteria, Chances and Challenges / **38**

Digital Twins –Criteria, Chances and Challenges

Panelists: Stefan Knapp, Jan Kosinski,
Loic Royer, Stephan Preibisch,
Liesbet Geris and Sacha van Albada

POSTER SESSION / **39**

HTP screening of SAR–hATG8 interactions in selective autophagy

We developed an integrative pipeline that combines multi-omics data, structural screening, AlphaFold2 modeling, and all-atom molecular dynamics to identify and characterize selective autophagy receptors (SARs). The framework enables rapid screening of canonical LIR-LDS interactions by scoring motif-based residue contacts and pocket occlusion across experimental structures, AF2 models, and MD trajectories. Our analysis reveals family-specific LIR-LDS and UIM-UDS binding patterns and shows how UDS mutations and post-translational modifications modulate SAR-hATG8 engagement.

POSTER SESSION / **40**

Contact dynamics in the phase-separated MUT-16 condensate us-

ing cascade computing

Molecular dynamics (MD) simulations have been proven essential for elucidating the hierarchical interplay of molecular interaction patterns on different time and length scales. To study the material properties of biomolecular condensates and ultimately their biological function, simulations of large systems require a vast amount of computational resources. Gaining insight into minute details such as the transient dynamics of IDPs requires excessive contact analysis on the atomistic level - a present bottleneck in both storage and processing of large trajectory datasets. Meeting the growing demand for machine-learning analysis for revealing complex contact patterns and property prediction such datasets must be consistent, accessible, and reproducible. We present a cascade computing framework designed as a FAIR-compliant workflow to leverage full pairwise contact information from MD trajectories. Designed for high-performance computing (HPC) clusters, it facilitates the calculation of pairwise contact data through a high degree of parallelization into a contact record that feeds individual consecutive downstream tasks. We apply this framework to investigate the molecular drivers of liquid–liquid phase separation (LLPS) in the foci-forming region (FFR) of MUT-16. Analyzing an aggregate of 10 μs of atomistic simulations—generated via backmapping from Martini 3 coarse-grained models—we utilized the cascade computing package to systematically quantify residue-resolved contact frequencies alongside interaction persistence times. This dual approach enabled a direct comparison between the prevalence of interactions and their lifetimes. We specifically characterized the relative contributions of hydrogen bonding, π–π stacking, cation–π interactions, and salt bridges. Our results reveal that condensate dynamics are governed by specific cation–π interactions and salt bridges rather than non-specific forces. Additionally, the analysis highlighted the critical role of the solvent environment, demonstrating how Na^+ ions and bulk water modulate stability through ion-mediated bridging. These findings provide deep atomistic insight into the physicochemical principles of MUT-16 condensates and validate the cascade framework as a robust tool for the high-throughput analysis of large-scale protein simulations.

POSTER SESSION / 41

Nuclear speckle periphery organizes stable intron-retained RNAs into a distinct nuclear retention compartment

Intron retention (IR) is an important regulator of RNA fate, yet its spatial and temporal organization in human cells remains poorly understood. Here, we investigate the dynamics, localization, and regulation of intron-retained RNAs in pluripotent stem cells using compartment-resolved transcriptional shutdown, sequence-based modeling, and advanced RNA imaging. We focus on the relationship between IR, nuclear speckles, RNA stability, and cell-cycle–dependent RNA processing.

POSTER SESSION / 42

TRIM28 prevents the export of retrotransposons

After completion of processing in the nucleus eukaryotic mRNAs are bound by the nuclear export factor NXF1 and are exported to the cytoplasm. For binding to mRNAs, NXF1 requires adapter proteins that recruit NXF1 to newly transcribed pre-mRNAs in a non-sequence-specific manner. To identify novel NXF1 adapter proteins for the selective export of specific transcript classes we developed a screen, which is based on their known characteristics: I) they bind in close proximity to NXF1 on the same RNA and II) the interaction is stabilized by the bound RNA. Our screen confirmed all known NXF1 adapter proteins, but also identified several chromatin-regulating proteins (CRPs) that were not known as NXF1 adapters or RNA binders. Interestingly, a lot of them are involved in retrotransposon silencing. We then focused on TRIM28 and tested whether it affects the export of retrotransposons via NXF1. TRIM28 is known to silence retrotransposons at the DNA level by interacting

with KRAB zinc-finger proteins and recruiting the silencing machinery leading to heterochromatin formation. We confirmed that TRIM28 binds to RNA and iCLIP of NXF1 and TRIM28 showed that both proteins co-bind within retrotransposons (LTRs & non-LTRs), but also within protein coding transcripts and pseudogenes. Investigating whether TRIM28 acts as a novel NXF1 adapter for the export of mRNA we found that the depletion of TRIM28 does not affect the export of polyadenylated mRNA and it does not shuttle between nucleus and cytoplasm. Co-immunoprecipitations confirmed that NXF1 interacts with TRIM28 and with other proteins of the silencing machinery. Interestingly, TRIM28 also interacts with NXF1 but not with mRNA processing factors such as SRSF7 or PABPN1. This implies that NXF1 is present in different subcomplexes, either for bulk mRNA export or for retrotransposon silencing. A comparison of export targets derived from FRAC-Seq data after depletion of NXF1 and TRIM28 suggest that NXF1 binding is important for the export of retrotransposon and other foreign transcripts to the cytoplasm for translation and that TRIM28 normally prevents their export. This would represent a new layer of RNA-based mechanism for genome surveillance.

POSTER SESSION / 43

Nuclear speckle periphery organizes stable intron-retained RNAs into a distinct nuclear retention compartment

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POSTER SESSION / 44

Lipid highways: Mechanistic insights into ATG2-mediated lipid transport

Autophagy requires lipid transfer from the ER to growing phagophores. Using structural predictions, molecular dynamics simulations, and in vitro lipid transfer assays, we investigated how the lipid transfer protein ATG2A mediates this process. We identified a novel gating mechanism driven by conformational rearrangements of N-terminal amphipathic helices. Guided by this insight, we designed an ATG2A mutant that transfers lipids threefold faster than the wild type in vitro.

POSTER SESSION / 45

Multi-scale classification decodes the complexity of the human E3 ligome

E3 ubiquitin ligases define the ubiquitin code, regulating protein degradation and non-degradative processes such as DNA repair, signaling, and immunity. We present a comprehensive classification of the human E3 ligome by integrating sequence, structural, functional, and expression data using a weakly supervised metric-learning framework. This approach captures relationships across E3 families, extends canonical classes, and maps E3s to substrates and therapeutic opportunities.

POSTER SESSION / 46

iCLIP3: A streamlined, non-radioactive protocol for mapping protein-RNA interactions in cellular transcripts at single-nucleotide resolution

UV-C crosslinking and immunoprecipitation (CLIP)–based methods are the gold standard for identifying direct RNA binding protein (RBP) interaction sites on cellular RNA in vivo. Here, we describe individual nucleotide resolution CLIP version 3 (iCLIP3), an optimized protocol for generating transcriptome-wide maps of RBP-RNA interaction sites at single-nucleotide resolution from low-input material. iCLIP3 introduces several key improvements over previous iCLIP variants, including rapid and safe infrared-based visualization of RBP–RNA complexes, silica column–based RNA isolation, and the incorporation of TruSeq adapter sequences with unique dual indexing. These modifications streamline library preparation, facilitate multiplexing, and enable concurrent sequencing of iCLIP3 libraries alongside unrelated RNA-seq libraries. In addition, we provide a detailed bioinformatics workflow for identifying RBP crosslinking events and defining RBP binding sites.

POSTER SESSION / 47

Functional imaging in plants: deciphering molecular regulators of stem cell niche maintenance

In plant biology, functional imaging enables the visualization and quantitative analysis of molecular activities in living cells with high spatiotemporal resolution. It involves fluorescent protein (FP) tagging combined with advanced fluorescence microscopy techniques, such as laser-scanning confocal imaging, super-resolution Airyscan detection, Förster Resonance Energy Transfer (FRET) and Fluorescence Lifetime Imaging Microscopy (FLIM). In our study, we combined these techniques to investigate the transcription factors (TFs) regulating the stem cell niche (SCN) maintenance in Arabidopsis thaliana. First, we analyzed their subcellular localization and temporal behavior within the root meristem. Then, we quantified their protein-protein interactions within protein complexes using FRET-FLIM. Furthermore, we simulated and predicted their regulatory dynamics in the SCN via computational modeling. This integrative approach revealed how different assemblies of TFs regulate SCN maintenance and cell-fate determination.

POSTER SESSION / 48

Nuclear speckle periphery organizes stable intron-retained RNAs into a distinct nuclear retention compartment that resolves during mitosis

Intron retention (IR) is an important regulator of RNA fate, yet its spatial and temporal organization in human cells remains poorly understood. Here, we investigate the dynamics, localization, and regulation of intron-retained RNAs in pluripotent stem cells using compartment-resolved transcriptional shutdown, sequence-based modeling, and advanced RNA imaging. We focus on the relationship between IR, nuclear architecture, RNA stability, and cell-cycle–dependent RNA processing.

POSTER SESSION / 49

Functional imaging in plants: deciphering molecular regulators of stem cell niche maintenance

In plant biology, functional imaging enables the visualization and quantitative analysis of molecular activities in living cells with high spatiotemporal resolution. It involves fluorescent protein (FP) tagging combined with advanced fluorescence microscopy techniques, such as laser-scanning confocal imaging, super-resolution Airyscan detection, Förster Resonance Energy Transfer (FRET) and Fluorescence Lifetime Imaging Microscopy (FLIM). In our study, we combined these techniques to investigate the transcription factors (TFs) regulating the stem cell niche (SCN) maintenance in Arabidopsis thaliana. First, we analyzed their subcellular localization and temporal behavior within the root meristem. Then, we quantified their protein-protein interactions within protein complexes using FRET-FLIM. Furthermore, we simulated and predicted their regulatory dynamics in the SCN via computational modeling. This integrative approach revealed how different assemblies of TFs regulate SCN maintenance and cell-fate determination.

POSTER SESSION / 50

Combining experiments and molecular simulations

We combine experiments with molecular simulations to learn more about a biomolecular system than we could from the individual methods alone. Ensemble and force-field refinement provide consistent, reproducible, and robust ways to do so. Biophysical experiments like SAXS, FRET, NMR, PELDOR/DEER provide ensemble averaged information. Although valuable by themselves, such information can be of low structural resolution and/or sparse and insufficient to reconstruct high-resolution structural biomolecular ensembles. Understanding of the structural ensemble gives mechanistic insight related to their functions. Molecular dynamics simulations can provide such high-resolution structural ensembles. Balancing force field inaccuracies and sampling errors limits their predictive power, though. We thus combine information from experiments and simulations in two ways. We refine the predicted structural ensembles directly or we refine the underlying force field by learning (atomistic) interactions. Both approaches are valuable tools for learning from experiments, simulations, or any machine learning method providing structural ensembles.

POSTER SESSION / 51

Phylogeny of Reticulon and Reticulon-like Protein Families

Membrane remodeling underlies many eukaryotic processes and is presumed to have co-evolved with the ER. We characterize six protein families that contain the Reticulon and Reticulon-like domains across all sequenced genomes. We present a new sequence-based subfamily classification. Despite poor sequence conservation across various phyla, this classification correlates with distinct changes in membrane-shaping elements (TM hairpins and AH segments) and their physico-chemical properties.

POSTER SESSION / 52

Single-cell perturbations reveal adaptive, stimulus-dependent recurrence in visual cortex

Cortical circuits are proposed to amplify weak sensory inputs but transition to feature competition during strong drive. However, the evidence for this is scarce in cortices with a functional, modular organization, such as in primates and carnivores, where neighboring excitatory and inhibitory cells share feature selectivity. Here, we demonstrate that networks in ferret primary visual cortex switch

between amplification and competition depending on sensory input. Combining cellular perturbations and statistical modeling, we uncovered broad suppressive influence modulated by visual contrast. At low contrast, functionally-coupled cells exhibited mutual amplification, switching to suppression at high contrast. This reversal emerged in recurrent network models in a Cross-Dominant regime, where inhibitory-excitatory coupling exceeds excitatory-excitatory coupling. These models predicted strong suppression from inhibitory cells, confirmed with cell-type-specific perturbations. Our results provide direct evidence that cortical recurrence with functional, modular organization toggles between amplification and suppression, supporting long-standing predictions from predictions from theory and models of visual cortex.

POSTER SESSION / 53

Quantifying membrane perturbation induced by membrane-remodeling proteins

Large-scale membrane remodeling events, such as budding, fusion, fission, and pore formation, help maintain cellular homeostasis. Integral and peripheral membrane proteins play crucial roles in these remodeling events. By using coarse-grained molecular dynamics simulations, we quantify the protein-induced membrane perturbation fields. By employing the continuum Helfrich model and incorporating a protein-induced distance-dependent spontaneous curvature tensor, we capture the intrinsic curvature properties of remodeling proteins and associated emergent effects at the mesoscale.

POSTER SESSION / 54

An architectural checkpoint for the licensing of spliced mRNAs for mRNA export.

Harsh Vinodkumar Oza, *Marius Wegener*, Timur Makarov*, Jonas Busam, Kathi Zarnack# & Michaela Müller-McNicoll# A critical quality control step in gene expression is the coupling of pre-mRNA splicing to nuclear export, ensuring that only fully processed transcripts reach the cytoplasm. How splicing fidelity is monitored and translated into export competence, however, remains poorly understood. Here we show that the splicing factor SRSF3 establishes an architectural checkpoint that licenses spliced messenger ribonucleoprotein complexes (mRNPs) for nuclear export. Using mild splicing inhibition by isoginkgetin in pluripotent mouse P19 cells, we induce selective intron retention in otherwise normally processed, polyadenylated transcripts. These intron-containing mRNAs fail to be exported and accumulate transiently and reversibly in enlarged nuclear speckles. Within these structures, mRNPs adopt a striking spatial organization, with coding regions buried in the core and retained introns and poly(A) tails exposed at the periphery, forming a characteristic donut-like pattern. Mechanistically, we find that splicing inhibition stabilizes SRSF3 in a hyperphosphorylated state. Hyperphosphorylated SRSF3 remains bound to RNA but fails to recruit the nuclear export receptor NXF1 and the poly(A)-binding protein ZC3H14. ZC3H14 is identified as a splicing-sensitive SRSF3 interactor whose recruitment to mRNA depends on SRSF3 dephosphorylation. iCLIP analysis reveals that ZC3H14 binds CA-rich regions near transcript 3′ ends in spliced mRNAs, while upon splicing inhibition it binds almost exclusively to poly(A) tails. Consistently, splicing inhibition selectively impairs nucleo-cytoplasmic shuttling of ZC3H14. Together, our findings identify an export-competency checkpoint that operates at the level of mRNP architecture. We propose that SRSF3-dependent recruitment of ZC3H14 enables poly(A)-tail internalization and mRNP compaction, allowing release from nuclear speckles and export, whereas failure of this process traps mis-spliced mRNPs in a reversible, pre-export state.

POSTER SESSION / 55

Follow the MEP: Scalable Neural Representations for Minimum-Energy Path Discovery in Molecular Systems

Characterizing conformational transitions in physical systems remains a fundamental challenge, as traditional sampling methods struggle with the high-dimensional nature of molecular systems and high-energy barriers between stable states. These rare events often represent the most biologically significant processes, yet may require months of continuous simulation to observe. One way to understand the function and mechanics of such systems is through the minimum energy path (MEP), which represents the most probable transition pathway between stable states in the high-friction, low-temperature limit. We present a method that reformulates MEP discovery as a fast and scalable neural optimization problem. By representing paths as implicit neural representations and training with differentiable molecular force fields, our method discovers transition pathways without expensive sampling. Our approach scales to large biomolecular systems through a simple loss function derived from the path's likelihood via the Onsager-Machlup action and a scalable new architecture, AdaPath. We demonstrate this approach using four proteins, including an explicitly hydrated BPTI system with over 3,500 atoms. Our method identifies a MEP that captures the same conformational change observed in a millisecond-scale molecular dynamics (MD) simulation, obtaining this pathway in minutes on a standard GPU, rather than the weeks required on a specialized cluster.

POSTER SESSION / 56

In Situ and In Silico Structure and Dynamics of a C. elegans Stomatin–Gap Junction Complex

Here, we investigate Caenorhabditis elegans gap junctions (GJs) using an integrative approach combining electron cryo-tomography and molecular dynamics (MD) simulations. Cryo-tomographic analysis of primary embryonic cells revealed hexagonally packed arrays of GJs at cell–cell junctions. Notably, we identified a previously uncharacterized cap-like cytosolic density occluding the channel pore. We propose that this density corresponds to a multimeric assembly of the stomatin protein UNC-1, which is known to interact with the innexin UNC-9. To test this hypothesis, we generated AlphaFold 3 models of multimeric UNC-1 and compared them with experimentally observed GFP-tagged UNC-1 assemblies. Coarse-grained MD simulations were used to probe the stability, conformational dynamics, and lipid interactions of the proposed UNC-1 cap complex. In addition, atomistic MD simulations of palmitoylated UNC-1 dimers demonstrate a stabilizing role for palmitoyl anchors in mediating membrane association and positioning relative to the gap junction pore. Together, our results suggest a structural and dynamic basis for stomatin-mediated regulation of gap junctions and illustrate how the integration of in situ structural data with multiscale simulations can elucidate complex regulatory mechanisms in membrane protein assemblies.

POSTER SESSION / 57

Millimeter-scale selective amplification in the developing visual cortex

The highly recurrent networks of the cerebral cortex are thought to profoundly shape neural responses, amplifying certain patterns of activity over others. However, whether such selective amplification organizes network activity at the level of the millimeter-scale networks which underlie perception and behavior remains unknown. Here, we combine patterned optogenetic stimulation informed by a computational model with in vivo calcium imaging in immature ferret visual cor-

tex to show that cortical networks are preferentially activated by inputs aligned to endogenous recurrent subnetworks. Motivated by our model indicating that spontaneous activity can provide a proxy for the millimeter-scale dominant functional subnetworks within recurrent cortical circuits, we found that the reliability and specificity of responses to input activity patterns was determined by the degree of overlap with the dominant modes of spontaneous activity. Inputs well matched to endogenous networks evoked reliable and specific responses that showed greater spatiotemporal stability than random misaligned input patterns, demonstrating the selective amplification of millimeter scale activity within cortical networks. This preferential amplification suggests that early cortical networks act as tuned filters, leveraging endogenous dynamics to stabilize and refine the precise sensory representations that emerge throughout development.

POSTER SESSION / 58

Molecular basis of specificity in alternative splicing regulation through splicing regulator SRSF6

The human serine-arginine rich splicing factor 6 (SRSF6) is part of the SR-protein family consisting of 12 members and as such is involved in (alternative-) splicing regulation. It is composed of an N-terminal RRM domain, followed by a pseudo RRM and a C-terminal serine-arginine rich disordered domain. With SRSF6 being an integral part of the splicing machinery, all three domains have been implicated in interacting with RNA and/or proteins, but individual interactions mediating SRSF6 specificity remain poorly understood. Therefore, our goal was to structurally and biochemically analyse single domains and their combinations to decipher their RNA interaction sites as well as their sequence requirements. To this end, we used RNA Bind-n-Seq to obtain RNA consensus motifs for the single and tandem RRMs. We then used nuclear magnetic resonance (NMR) spectroscopy combined with electrophoretic mobility shift assay, fluorescent polarization, spectral shift assay and X-ray crystallography, applied to recombinant SRSF6 variants and the derived RNA motifs. We found the two single RRMs to have significantly different binding affinities and sequence requirements towards RNA: RRM1 binds to cytosine- and adenine-rich RNAs in a canonical way, whereas RRM2 prefers purine-rich sequences in a non-canonical mode of interaction. To understand the latter on an atomistic level, we solved the NMR-structure of RRM1 alone to verify the canonical binding mode. For RRM2, we solved the crystal structure both in the apo- and RNA-bound forms and confirm the NMR derived non-canonical RNA-binding mode mediated by RRM2's α-helix 1. Additionally, we found the linker between RRMs to play an important part in increasing affinity towards RNA in concert with RRM2. Furthermore, by combining NMR relaxation data with SAXS-based modelling, we were able to shed light on the arrangement of the two RRMs with respect to each other and the role of the linker. Finally, we confirmed our data from E. coli produced protein by a comparison with protein produced in the human cell line HEK293, which allows examining the role of the SR region, not accessible with bacterial protein. Altogether, our data provide a strong structural basis for understanding the functions and target specificity of SRSF6 as opposed to the other 11 members of the SR protein family on a molecular level.

POSTER SESSION / 59

Progressive Development of Complex Synthetic Cells via Inverted Emulsion

Synthetic cells are vital for modeling cellular complexity. We present a progressive inverted emulsion method that transitions from robust on-chip vesicle production to engineering complex bilayers with ˜95% asymmetry. By integrating lateral phase-separation (L_o/L_d domains) and domain-specific protein binding , we induce spontaneous curvature leading to autonomous budding and fission. These biomimetic models provide essential experimental benchmarks for digital twins in structural

cell biology.

POSTER SESSION / 60

A paradigm change for cardiolipin remodeling in mitochondria

Cardiolipin (CL) is the signature phospholipid of mitochondria. CL is essential for cristae formation and the functionality of the enzyme complexes involved in biological energy conversion. The mitochondrial transacylase Tafazzin catalyses the obligatory remodeling of CL, a process in which the composition of the four CL acyl chains is altered. Tafazzin dysfunction causes Barth syndrome, a severe multisystem disorder. We combined biochemistry, structure determination, and molecular simulations to identify the mechanism of tafazzin action. Our finding that Coenzyme A is a co-factor set up for direct acyl-chain transfer challenges established views. Moreover, our work provides clues as to how pathogenic mutations impact the function of Tafazzin and thus enables a molecular understanding of Barth syndrome.

POSTER SESSION / 61

Consistent Protein Intrinsic Curvature Estimation from Buckled Membrane Simulations

Membrane buckling simulations are routinely analysed using Fourier fits to estimate protein intrinsic curvature. We show that such fits introduce systematic artifacts, despite accurate height profiles. Fitting the analytical Helfrich buckle shape yields consistent curvature distributions and intrinsic curvatures. Applying this approach to Martini 3 simulations, we extract the intrinsic curvature preference of the tetraspanin CD63 in agreement with experimental values for homologs.

POSTER SESSION / 62

Understanding STIM1 by combining advanced simulations and experiments

We used the AI for Molecular Mechanism Discovery to simulate and understand the activation cascade of the Ca(2+)-sensing stromal interaction molecule 1 (STIM1) dimer. The detailed atomistic insight into the dimerization pathways enabled us to shed light on the experimentally observed changes in dimerization propensities for four different mutants and to reconcile previous experimental results. This work highlights the potential of combining advanced simulations with experimental measurements to further our understanding of biomolecular processes.

POSTER SESSION / 63

Investigating Executive Networks in Language Comprehension: A Foundation for Digital Twin Applications in Cognitive Neuroscience

Our sham-controlled TMS study causally investigated the Angular Gyrus (AG) and DLPFC's roles in language comprehension and particularly examines how their contributions change under varying cognitive loads via dual-task reading/n-back. This detailed empirical data could serve as a valuable foundation for cognitive Digital Twins in the future, enabling simulation of individual responses and prediction of brain stimulation effects for personalized interventions.

POSTER SESSION / 64

Digital Models for Electric Field Dosimetry in Non-Invasive Brain Stimulation

Accurate evaluation of the delivered electric dose is a key challenge in therapeutic brain stimulation based on physical stimulation, as clinical effects depend on the spatial distribution of brain induced electric fields. Numerical simulations were developed to describe electric field distributions in the heads of patients using two modelling approaches: one simulating transcranial magnetic stimulation treatments and one addressing time-interfering electric field paradigms for deep brain stimulation with surface electrodes. MRI-based personalized head models were used to predict electric field distributions as a function of electrode or coil placement, signal amplitude and duration, and anatomical and morphological variability. These digital models provide key information for therapy dosing and for defining safe and effective stimulation protocols.

POSTER SESSION / 65

Digital twin to support the design and manufacture of functional nanoparticles with applications in biomedicine

We are standing at a unique crossroads in the fabrication of nanoparticles in-house [1-6] and AI algorithms. A decade from now, we have seen computational power explode, giving us the tools to dream up new biocompatible materials as novel drugs and treatments, designed faster than ever before. However, in the high-stakes world of nanomedicine, simply having a 'black-box answer' from AI isn't enough, it must be understandable. We don't just need algorithms that predict; we need algorithms that are interpretable. Our project mission is to bridge the gap between complex Deep Learning [7] and human understanding with the help of computer molecular simulations. In this poster, I will present the various experimental, as well as computational efforts performed by two groups at the material science's institute of Barcelona. Both synergetically working in three different project stages to achieve this ambitious objective which motivates us, namely, (i) the establishment of a 'global'database infrastructure for the systematic storage of experimental results; (ii) creation of complementary data from molecular dynamics simulation models to be used together with experimental data to improve the predictive power of AI models; and (iii) the development of statistical and artificial intelligence models capable of extracting properties and physico-chemical characteristics from our dataset of macromolecular structures. References [1] I. Cabrera et al., Nano Lett. 13(8), 3766–3774 (2013) [2] J. Tomsen et al., ACS Appl. Mater. Interfaces 13 (7), 7825–7838 (2021) [3] L. Ferrer-Tasies et al., Adv. Therapeutics 4(6) 2000260 (2021) [4] M. Martínez-Miguel et al., ACS Appl. Mater. Interfaces 14(42), 48179–48193 (2022) [5] J. Morlà et al., Chem. Mater. 34 (19), 8517–8527 (2022) [6] A. Boloix et al., Small 18(3) 2101959 (2022)] [7] U. Pratiush, ⋯, H.V. Guzman, et al.,S.V. Kalinin, Mic-hackathon 2024: Hackathon on Machine Learning for Electron and Scanning Probe Microscopy, Mach. Learn.: Sci. Technol. 2025, 6, 040701