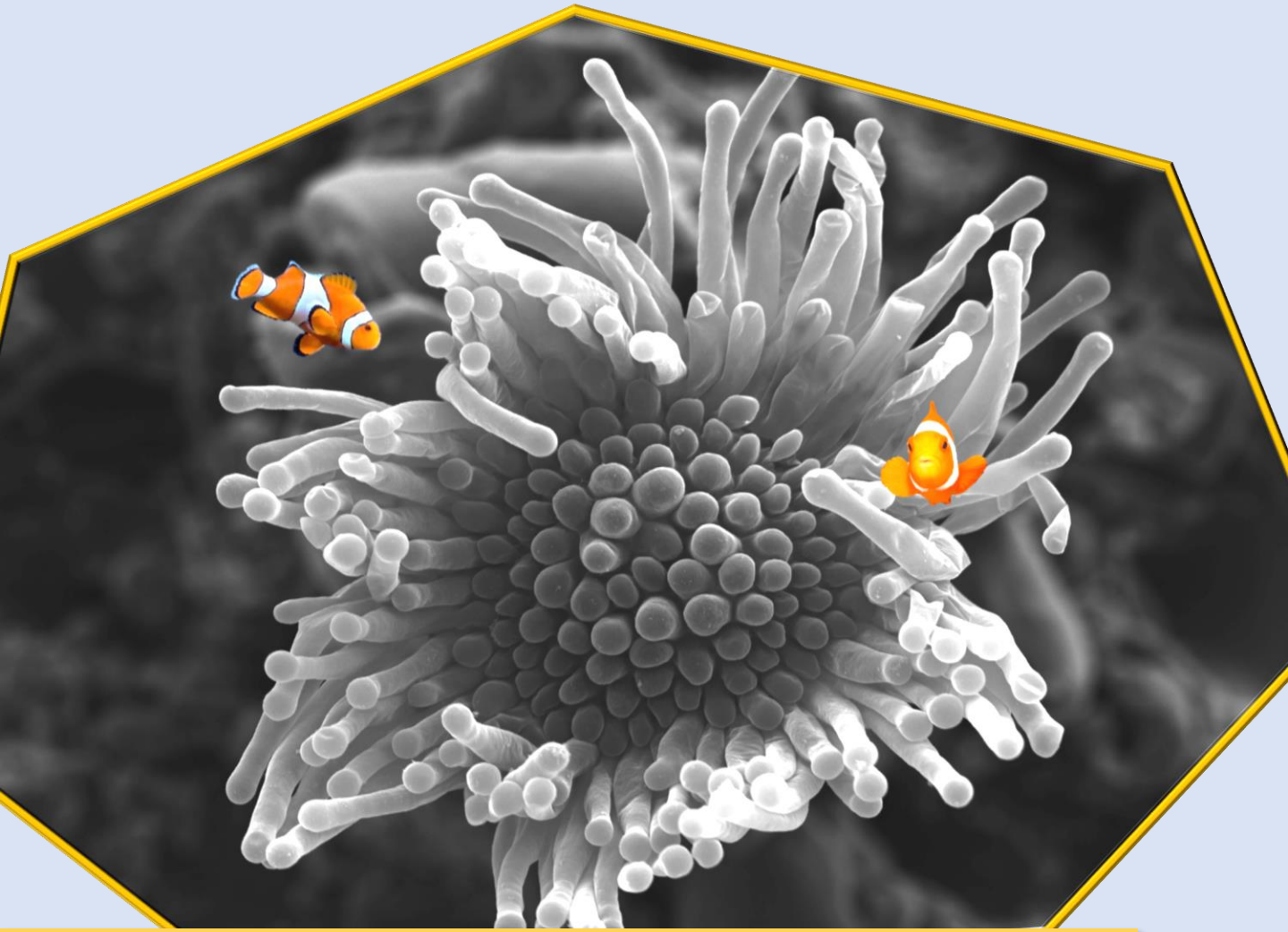
האוניברסיטה העברית בירושלים
THE HEBREW UNIVERSITY OF JERUSALEM

האגודה הישראלית למיקרוסקופיה
THE ISRAEL SOCIETY FOR MICROSCOPY

ISM2023

The 56th Annual Meeting of the Israel Society for Microscopy

May 23rd, 2023 | Binyanei Hauma - ICC, Jerusalem



Program & Abstracts

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Cover page micrograph:

"SEA ANEMONE AMBROSIA CONFERTIFLORA STAMINATE FLORET PISTILLODIUM"

Winning micrograph of the ISM2022 Micrographs Competition by Ilana Shtein & Einat Zelinger.

WELCOME LETTER

Dear Colleagues,

We are very happy to welcome you to the ISM annual meetings with ISM2023, the 56th Annual Meeting of the Israel Society for Microscopy.

A pre-meeting tutorial workshop on image processing in microscopy will be held on May 22nd at the Hebrew university faculty of Agriculture in Rehovot. During this workshop, recent advances, and practical aspects of image processing for microscopy will be addressed. This workshop reflects a growing interest and need within our community for deepening our knowledge and understanding of the different aspects of image processing to extract valuable and reliable information from experimental micrographs.

The main meeting will be on May 23rd in Jerusalem with talks presenting cutting edge research, which reflects the amazing advances made during recent years in many fields of microscopy in materials science as well as in life sciences.

The meeting is generously supported by 17 companies and academic institutes, and you are encouraged to visit their booths and learn about the latest technological innovations they present.

We hope that you will enjoy this meeting, find it fruitful and be inspired by the talks and posters and by meetings and discussions with experts and colleagues from Israel and from abroad.

On behalf of the ISM Board and the ISM2023 organizing committee,

Yaron Kauffmann	Zahava Barzilay	Alexander Upcher
Chair, ISM	Secretary, ISM	Treasurer, ISM

GENERAL INFORMATION

Meeting Venue

Binyanei Hauma - International Convention Center (ICC), Jerusalem
1 Shazar Blvd.
Jerusalem
Israel

Internet

Free WI-FI connection will be available at all meeting areas. To connect, use the **BiZon** network, password is not required.

Registration and Hospitality Desk

Diesenhaus-Unitours will operate the registration desk throughout the meeting.

Registration Envelope

Upon registration, you will receive your name badge and a voting slip for the Micrographs Competition. To vote, please insert your slip into the "Micrographs Voting" box until 14:00, the end of the lunch break.

Speakers and Session Chairpersons

Session chairs and speakers are requested to meet with each other 10 minutes prior to the commencement of their respective sessions, in the session hall. It is essential that the timetable be strictly adhered to, in order to enable participants to plan attendance at parallel sessions. The last few minutes of each talk should be reserved for questions and answers.

Data Projection

Please bring your presentation on a USB flash drive (disk-on-key) to the AV technician in your session hall, at least one hour before the start of your session. Your presentation will then be upload onto the Meeting computer. If you wish to use your own laptop, please coordinate it with the AV technician in advance. Presentations in the Sound Bites session have been uploaded on the Conference computer and the use of own laptops is not available in this session.

Instructions for Poster Presenters

Upon arrival at the meeting, please mount your poster on the final board number listed in this program as well as in the list posted in the posters area.
Set-up of posters: 08:30-09:30
Removal of posters: by 18:00 (after the last talk).

Meeting Secretariat

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Research and Academic Institutes

Workshop Program – May 22nd

"Image Processing in Microscopy"

The Hebrew University Faculty of Agriculture, Rehovot

09:00 – 09:30	***Get together & Coffee***
MORNING SESSION	
09:30 - 10:10	**Ehud Sivan** / Weizmann Institute ***Introduction to Deep Learning***
10:10 - 11:20	**Ofra Golani** / Weizmann Institute ***A Hitchhiker's Guide to The Universe Of Bioimage Analysis Software For Microscopy***
11:20 - 11:35	**Coffee Break**
11:35 - 12:25	**Ran Zalk** / Ben Gurion University ***3D Cryo-EM Reconstruction for Biological (And Other Soft) Materials***
12:30 - 13:10	**Lunch**

AFTERNOON SESSION - Parallel Hands-on Tutorials			
	Tutorial A	**Tutorial B**	**Tutorial C**
13:15 - 17:00	**Ofra Golani, Ehud Sivan, Dean Ranmar, Reinat Nevo** / Bioimage Analysts, MICC Cell Observatory, Weizmann Institute of Science ***Incorporating Machine Learning Tools into Image Analysis Workflows Using Fiji, Ilastik and StarDist***	**Sahar Hiram-Bab** / Core facility, faculty of Medicine, Tel-Aviv University ***Introduction To Dragonfly Software***	**Colin Ophus** / NCEM, Lawrence Berkeley National Laboratory, Berkley, USA ***Introduction To Phase Contrast Imaging and Crystal Orientation Mapping In 4D-STEM Using the Open Source py4DSTEM Toolkit***
17:00	**Departure**		

Workshop Organizing Committee:

Inna Popov, Hebrew University
Einat Zellinger, Hebrew University

Meeting Program – May 23rd

08:30 - 09:30	Registration & Light Refreshments / Vendors Exhibition & Posters Mounting		
OPENING SESSION - Hall A			
Session Chair:	**Yaron Kauffmann, ISM Chairperson**		
09:30 - 10:00	• Opening remarks • Presentation of the Lev Margulis & Yael Mutsafi Prizes		
PLENARY SESSION - Hall A			
Session Chairs:	**Michael Elbaum,** Weizmann Institute of Science **Thomas Schultheis,** Technion - Israel Institute of Technology		
10:00 - 10:45	Plenary Lecture: **Colin Ophus**, NCEM, Lawrence Berkeley National Laboratory, Berkley, USA ***CHARACTERIZING MATERIAL PROPERTIES FROM ATOMIC TO FUNCTIONAL LENGTH SCALES WITH COMPUTATIONAL IMAGING IN SCANNING TRANSMISSION ELECTRON MICROSCOPY***		
10:45 - 11:15	***Coffee Break & Vendors Exhibition***		
11:15 - 12:00	Plenary Lecture: **Lucy Collinson**, Francis Crick Institute, London, UK EXPLORING LIFE ACROSS SCALES WITH VOLUME CORRELATIVE LIGHT AND ELECTRON MICROSCOPY		
SOUND BITE SESSION - Hall A			
Session Chair:	**Ifat Kaplan-Ashiri,** Weizmann Institute of Science		
12:00 - 12:30	Posters Sound Bites		
LUNCH SESSION			
12:30 - 13:10	LIFE SCIENCES POSTERS MATERIALS SCIENCE POSTERS INSTRUMENTATION & METHODOLOGY POSTERS VENDORS EXHIBITION MICROGRAPH COMPETITION	**ISM GENERAL ASSEMBLY** (Nomination of new secretary and treasurer)	
12:30 - 14:00	***Lunch & Vendors Exhibition***		
PARALLEL SESSIONS			
14:00 - 15:35	**Life Sciences SESSION**	**Materials Science SESSION**	**Instrumentation & Methodology SESSION**
15:35 - 16:00	***Coffee Break & Vendors Exhibition***		
PARALLEL SESSIONS			
16:00 – 17:35	**Life Sciences SESSION**	**Materials Science SESSION**	
CLOSING SESSION - Hall A			
17:35 - 18:00	***Closing remarks + Best Poster & Best Micrograph nominations***		
18:00	***Departure***		

Afternoon Parallel Sessions – May 23rd

	Life Sciences	Materials Science	Instrumentation & Methodology
Hall name	**Hall B**	**Hall C**	**Hall A**
Session chair	**Natalie Elia,** Ben Gurion University	**Yuval Golan**, Ben Gurion University	**Amit Kohn**, Tel Aviv University
14:00 - 14:25	**Invited** **Gili Bisker**, Tel-Aviv University, Israel ***SINGLE-WALLED CARBON NANOTUBES FOR SENSING AND IMAGING IN THE NEAR-INFRARED***	**Invited** **Lucy Liberman Solomon,** Technion, Israel ***EXPOSING THE STRUCTURE OF METHYLCELLULOSE FIBRILLAR GELS WITH CRYO-TEM AND SAXS***	**Invited** **Alberto Bilenca,** Ben-Gurion University, Israel ***ALL-OPTICAL MECHANICAL IMAGING WITH STIMULATED BRILLOUIN MICROSCOPY***
14:25 – 14:40	**Mutsafi** **Jenny Capua Shenkar,** Weizmann Institute, Israel ***EXAMINING ATHEROSCLEROTIC LESIONS IN THREE DIMENSIONS AT THE NANOMETER SCALE WITH CATHODOLUMINESCENCE, CRYO-SEM AND CRYO-FIB/SEM***	**Margulis** **Avi Auslender,** Tel Aviv University, Israel ***THE MEAN INNER POTENTIAL OF HEMATITE α–Fe_2O_3 ACROSS THE MORIN TRANSITION***	**Tal Fishman,** Technion, Israel ***A LOSSLESS ELECTRON BEAM MONOCHROMATOR USING THZ NEARFIELD RADIATION FOR HIGH-RESOLUTION ELECTRON MICOSCOPY***
14:40 - 14:55	**Zvi Yaari,** The Hebrew University of Jerusalem, Israel ***AI-GUIDED OPTICAL SENSORS FOR THE EARLY DETECTION OF GYNECOLOGIC CANCERS***	**Shachar Keren,** Technion, Israel ***THE EFFECT OF WATER UPTAKE ON THE MECHANICAL BEHAVIOR OF HYBRID THIN FILMS FABRICATED BY SEQUENTIAL INFILTRATION SYNTHESIS***	**Shahar Seifer,** Weizmann Institute, Israel ***ELECTRON TOMOGRAPHY IN 4D-STEM***
14:55 - 15:10	**Rachael Deis,** Weizmann Institute, Israel ***PLATE-LIKE GUANINE BIOCRYSTALS FORM VIA TEMPLATED NUCLEATION OF CRYSTAL LEAFLETS ON PREASSEMBLED SCAFFOLDS***	**Melina Zysler,** Bar-Ilan University, Israel ***Pt-BASED NANOCATALYST MATERIAL: THE RELATIONSHIP BETWEEN STRUCTURE, PERFORMANCE, AND STABILITY***	**Adham Basha,** Tel Aviv University, Israel ***APPLICATION OF A DIRECT ELECTRON DETECTION CAMERA FOR SHORT-RANGE ORDER CHARACTERIZATION OF AMORPHOUS MATERIALS BY ELECTRON SCATTERING***
15:10 - 15:35	**Invited** **Michal Shoshkes-Carmel,** The Hebrew University of Jerusalem, Israel ***THE USE OF 3D IMAGING TO ANALYZE CELLULAR NETWORKS***	**Invited** **Hanna Bishara,** Tel Aviv University, Israel ***LOCAL ELECTRICAL PROPERTIES OF MICROSTRUCTURAL DEFECTS ASSESSED IN SCANNING ELECTRON MICROSCOPY***	**Invited** **Lothar Houben,** Weizmann Institute, Israel ***EELS SPECTROMETER WITH IMPROVED OPTICS AND ULTRA-HIGH SENSITIVITY ELECTRON DETECTOR FOR SHOT-NOISE LIMITED ENERGY-LOSS IMAGING AND SPECTROSCOPY***

Afternoon Parallel Sessions – May 23rd – cont.

	Life Sciences	Materials Science
Hall name	**Hall B**	**Hall C**
Session chair	**Dganit Danino,** Technion	**Doron Naveh,** Bar Ilan University
16:00 - 16:25	**Invited** **Shai Berlin**, Technion, Israel ***A NOVEL POLYCISTRONIC METHOD TAILORED FOR ENGINEERING SPLIT GECIS***	**Invited** **Assaf Ben-Moshe**, Bar-Ilan University, Israel ***TELLING LEFT FROM RIGHT USING ELECTRON MICROSCOPES***
16:25 – 16:40	**Leor Ariel Rose,** Ben-Gurion University, Israel ***QUANTITATIVE EVALUATION OF HUMAN GLIOMA NANOBIOPSY***	**Amram Azulay,** Technion, Israel ***CORRELATION BETWEEN CHARGE TRANSPORT AND LATTICE DYNAMICS IN La- AND Y-doped Ca_2MnO_4 PEROVSKITES***
16:40 - 16:55	**Nadav Scher,** Weizmann Institute, Israel ***DEVELOPMENT OF CORRELATIVE FIB-SEM TO STUDY MEMBRANE REMODELING***	**Avital Wagner,** Ben-Gurion University, Israel ***ELUCIDATING THE CONTROL MECHANISMS OF ORGANIC BIO-CRYSTALLIZATION***
16:55 - 17:10	**Levi A. Gheber,** Ben-Gurion University, Israel ***MACHINE-LEARNING AIDED QUANTIFICATION OF CELL CULTURES FROM PHASE-CONTRAST MICROSCOPY IMAGES***	**Daniel Khaykelson,** Weizmann Institute, Israel ***SCANNING ELECTRON NANOBEAM DIFFRACTION AT LOW DOSE FOR STRUCTURE MODELING OF NANO-OBJECTS***
17:10 - 17:35	**Invited** **Gilad Haran**, Weizmann Institute, Israel ***SINGLE-MOLECULE OPTICAL MICROSCOPY: FROM PROTEIN DYNAMICS TO T-CELL MEMBRANES***	**Invited** **Lioz Etgar**, Hebrew university, Israel ***DIMENSIONALITY IN PEROVSKITE - NANOSTRUCTURES AND SOLAR CELLS***

POSTERS – Life Sciences

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Belal Alhozeel, Keshet Shavit, Amir Sagi, Benjamin Palmer
Department of Chemistry, Ben-Gurion University of Negev, Rahat, Israel

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SPECTRAL IMAGING OF BREAST CANCER BIOPSIES FOR MULTIPLEX BIOMARKERS DETECTION

Maya Almagor, Yuval Garini, Roni Baron
Biomedical Engineering, Technion-Israel Institute of Technology, Haifa, Israel

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Mor Angel, Eden Fleshler, Mohammad Khaled Atrash, Noa Kinor, Yaron Shav-Tal
The Mina & Everard Godman Faculty of Life Sciences & Institute of Nanotechnology, Bar-Ilan University, Ramat-Gan, Israel

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VISUALIZING MEMBRANE INTERACTIONS USING IN-CELL CRYO-ELECTRON TOMOGRAPHY

Lior Aram[1], Diede de Haan[1], Neta Varsano[2], Katya Rechav[2], Eyal Shimoni[2], Nadav Elad[2], Assaf Gal[1]
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MIGRATING AND PROLIFERATING STUDIES OF MESENCHYMAL STEM CELLS USING MACHINE-LEARNING PROCESSING OF PHASE-CONTRAST IMAGES

Nambi Natchiyar Balakrishnan, Levi A Gheber
Biotechnology Engineering, Ben-Gurion University of the Negev, Beer-Sheva, Israel

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UNRAVELING THE MOLECULAR MECHANISM UNDERLYING URIC ACID CRYSTAL FORMATION IN MEDAKA LEUCOPHORE CELLS

Yuval Barzilay[1], Rachel Lynn-Deis[1], Zohar Eyal[1], Tali Lerer – Goldshtein[1], Anna Gorelick-ascetazi[1], Iddo Pinkas[2], Ziv Porat[3], Neta Versano[4], Smadar Zaidman[4], Nili Dezorella[4], Dvir Gur[1]
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CRYO-EM INVESTIGATIONS OF HOLOCOCCOLITH CALCITE INTRACELLULAR FORMATION

Oz Ben-Joseph[1], Lior Aram[1], Diede de Haan[1], Katya Rechav[2], Assaf Gal[1]
[1]*Department of Plant and Environmental Sciences, Weizmann Institute of Science, Rehovot, Israel*
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THE INTERPLAY BETWEEN pH and COLLAGEN ORGANIZATION IN THE TUMOR MICROENVIRONMENT: AN IN VITRO STUDY

Orit Bronner[1], Einat Nativ-Roth[2], Daniel Sevilla Sanchez[2], Michal Zaiden[1], Lior Cohen[1], Netta Vidavsky[1,2]
[1]*Chemical Engineering, Ben-Gurion University, Beer Sheva, Israel*
[2]*Ilse Katz Institute for Nanoscale Science & Technology, Ben-Gurion University, Beer Sheva, Israel*

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NATURAL EVOLUTION OF SILK HIERARCHICAL STRUCTURES: REVEALING THE MULTI-LENGTH SCALES ASSEMBLY BY COMBINATION OF MICROSCOPY TECHNIQUES

Ori Brookstein[1], Dror Eliaz[1], Eyal Shimoni[2], Ulyana Shimanovich[1]
[1]*Weizmann Institute of Science, Rehovot, Israel*
[1]*Molecular Chemistry and Material Science, Weizmann Institute of Science, Rehovot, Israel*
[2]*Chemical Research Support, Weizmann Institute of Science, Rehovot, Israel*

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MICROCALCIFICATIONS CAN TRIGGER OR SUPPRESS BREAST PRECANCER MALIGNANCY POTENTIAL AS A FUNCTION OF MINERAL TYPE IN A 3D TUMOR MODEL

Amit Cohen[1], Lotem Gotnayer[1], Dina Aranovich[1], Netta Vidavsky[1,2]
[1]*Chemical Engineering, Ben-Gurion University of the Negev, Beer Sheva, Israel*
[2]*Ilse Katz Institute for Nanoscale Science & Technology, Ben-Gurion University of the Negev, Beer Sheva, Israel*

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EXOCYTOSIS OF THE SILICIFIED CELL WALL OF DIATOMS INVOLVES EXTENSIVE MEMBRANE DISINTEGRATION

Diede de Haan[1], Lior Aram[1], Hadas Peled-Zehavi[2], Yoseph Addadi[3], Oz Ben-Joseph[1], Ron Rotkopf[3], Nadav Elad[4], Katya Rechav[4], Assaf Gal[1]
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ELUCIDATE THE ROLE OF VPS4 ISOFORMS IN CYTOKINETIC ABSCISSION

Inbar Dvilansky, Yarin Altaras, Dikla Nachmias, Natalie Elia
Life science, Ben Gurion University of the Negev, Beer Sheva, Israel

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Tamira Elul[1], Valerie Lew[1], Sukayneh Khetani[1], **William Woodward**[2]
[1]*College of Osteopathic Medicine, Touro University California, Vallejo, California, USA*
[2]*College of Osteopathic Medicine, Touro University Nevada, Henderson, Nevada, USA*

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STRUCTURAL AND ANTI-MICROBIAL STUDIES OF RIBOSOME-BINDING 16-MEMBER RING MACROLIDES AGAINST STAPHYLOCOCCUS AUREUS

Aliza Fedorenko[1], Andre Rivalta[1], Disha-Gajanan Hiregange[1], Anat Bashan[1], Jennifer J. Schmidt[2], David H. Sherman[2], Ada Yonath[1]

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SEM CHARACTERIZATION OF NON-CaP MINERAL PARTICLES FOR BREAST PRECANCER PROGNOSIS

Sahar Gal[1], Netta Vidavsky[1,2]

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MORPHOLOGICAL QUANTIFICATION OF LEISHMANIA PARASITE LIFE CYCLE STAGES USING IMAGING FLOW CYTOMETRY

Uzi Hadad[1], Nofar Baron[2], Michal Shapira[2]

[1]*Ilse Katz Institute for Nanoscale Science and Technology, Ben-Gurion University of the Negev, Beer Sheva, Israel*

[2]*Department of Life Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel*

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LABEL FREE IMAGING OF CHOLESTEROL CRYSTALS AND MACROPHAGES AS A MODEL SYSTEM FOR ATHEROSCLEROSIS

Antonia Kaestner[1,2], Yoseph Addadi[3], Neta Varsano[4], Ori Avinoam[2], Lia Addadi[1]

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DETERMINING THE COMPOSITION OF THE ESCRT-III FILAMENT IN CYTOKINESIS ABSCISSION OF MAMMALIAN CELLS

Nikita Kamenetsky, Natalie Elia

Life sciences, Ben-Gurion University of the Negev, Beer-Sheba, Israel

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SNAPSHOTS OF MITOCHONDRIAL FISSION THROUGH THE LENSE OF CRYO-SCANNING TRANSMISSION ELECTRON TOMOGRAPHY (CSTET)

Peter Kirchweger[1,2], Sharon Wolf[3], Deborah Fass[2], Michael Elbaum[1]

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ROBUSTNESS OF THE CANONICAL MITOCHONDRIAL FUSION MACHINERY PROMOTES NEBENKERN FORMATION IN DROSOPHILA SPERMATIDS.

Alina Kolpakova, Shmuel Pietrokovski, Eli Arama
Department of Molecular Genetics, Weizmann Institute of Science, Rehovot, Israel

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Zipora Lansky
Plant and Environmental Science, Weizmann Institute of Science, Rehovot, Israel

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Orlando Marin, Arina Dalaloyan, Michael Elbaum
Biological and Chemical Physics, Weizmann Institute of Science, Rehovot, Israel

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Asgard ESCRT-III and VPS4 reveal conserved chromatin binding properties of the ESCRT machinery

Dikla Nachmias[1], Melnikov Melnikov[1], Alvah Zorea[1], Maya Sharon[1], Reut Yemini[1], Yasmin De-picchoto[1], Ioannis Tsirkas[1], Amir Aharoni[1], Bela Frohn[2], Petra Schwille[2], Raz Zarivach[1], Itzhak Mizrahi[1], Natalie Elia[1]
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THE EFFECT OF LAMIN A ON THE COHERENT DYNAMICS OF THE CHROMATIN IN LIVING CELLS

Wajdi Nicola, Yuval Garini
Bio-medical Engineering, Technion-Israel Institute of Technology, Haifa, Israel

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STRUCTURAL STUDIES ON THE S. AUREUS ERMB METHYLTRANSFERASE MUTANT RIBOSOME IN COMPLEX WITH SOLITHROMYCIN

Andre' Rivalta[1], Aliza Fedorenko[1], Yehuda Halfon[1], Disha-Gajanan Hiregange[1], Ella Zimmerman[1], Anat Bashan[1], M.N. Frances Yap[2], Ada Yonath[1]
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THE EFFECT OF LOOP8 ON SPINDLE LOCALIZATION AND BI-DIRECTIONALITY OF S. CEREVISIAE KINESIN-5 CIN8

Mayan Sadan[1], Himanshu Pandey[1,2], Sudhir Kumar Singh[1], Mary Popov[1], Meenakshi Singh[1], Geula Davidov[3], Sayaka Inagaki[4], Jawdat Al-Bassam[5], Raz Zarivach[2,3], Steven S Rosenfeld[4], Larisa Gheber[1,2]
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BIOMINERAL FORMATION BY THE FRESHWATER GREEN ALGA PHACOTUS LENTICULARIS

Noy Shaked[1], Sophia Barinova[4], Sefi Addadi[2], Katya Rechav[3], Steve Weiner[1], Lia Addadi[1]
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IMPROVING CRYO-ELECTRON TOMOGRAPHY DATA QUALITY AND THROUGHPUT BY STREAMLINING THE WORKFLOW

Marit Smeets, Katherine Lau
Life Sciences, Delmic B.V., Delft, Zuid-Holland, Netherlands

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SPEC-NET: NUCLEAR SEGEMENTATION FROM H&E BIOPSY WITH SPECTRAL IMAGING SCREENING

Adam Soker, Yuval Garini
Bio-medical Engineering, Technion, Haifa, Israel, Israel

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THE ROLE OF THE NON-MOTOR N-TERMINAL REGION IN REGULATION OF FUNCTION OF THE BI-DIRECTIONAL KINESIN-5 CIN8

Neta Yanir, Himanshu Pandey, Sudhir Kumar Singh, Alina Goldstein-Levitin, Leah Gheber
Department of Chemistry, Ben-Gurion University of the Negev, Beer-Sheba, Israel

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MEASUREMENT-BASED CONTROL OF THE ELECTRON-PHOTON COUPLING COHERENCE

Hadar Aharon, Ofer Kfir
School of Electrical Engineering, Fleischman Faculty of Engineering, Tel Aviv University, Tel Aviv 69978, Israel

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IN-SITU INTERINSIC SELF-HEALING OF LOW-TOXIC Cs2ZnX4 (X= Cl, Br) METAL HALIDE NANOPARTICLES

Ben Aizenshtein, Lioz Etgar
Chemistry, Institute of Chemistry, The Center for Nanoscience and Nanotechnology, Casali Center for Applied Chemistry, The Hebrew University of Jerusalem, Jerusalem, Israel

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MODULATION OF BIOGENIC CRYSTAL MORPHOGENESIS IS ACHIEVED THROUGH TRANSITION FROM REACTION-LIMITED TO TRANSPORT-LIMITED GROWTH

Emanuel Avrahami
Department of Plant and Environmental Sciences, Weizmann Institute of Science, Rehovot, Israel

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SPATIALLY CONTROLLED ATOMIC LAYER DEPOSITION WITHIN POLYMER TEMPLATES FOR MULTI-MATERIAL NANORODS AND NANOWIRES FABRICATION

Rotem Azoulay, Tamar Segal Peretz
Chemical Engineering, Technion-Israel Institute of Technology, Haifa, Israel

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PROBING MAGNETIC PHASE TRANSITIONS VIA SPIN TORQUE DRIVEN SKYRMION RESONANCE

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[2]*Beijing National Laboratory for Condensed Matter Physics, Chinese Academy of Sciences, Beijing, China*

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EXPLORING SURFACE PHENOMENA WITH TEM AND STEM

Roei Broneschter[1], Yaron Kauffmann[1], Klaus Van Benthem[2], Wayne D. Kaplan[1]
[1]*Material Science and engineering, Technion, Haifa, Israel*
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ADVANCED TOOLS FOR DISCRIMINATING PHASES WITH SIMILAR CRYSTAL STRUCTURE BY EBSD

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[2]*Applications, Oxford Instruments America Inc., Pleasanton, California, USA*
[3]*Development, ST Development GmbH, Paderborn, Germany*

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CHIRAL GUIDED GROWTH OF CRYSTALS-ON-CRYSTALS: PREDICTABLE MORPHOLOGIES WITH LOCAL FUNCTIONALIZATION

Ofir Eisenberg[1], Qiang Wen[1], Maria Chiara di Gregorio[1], Linda J. W. Shimon[2], Lothar Houben[2], Ifat Kaplan-Ashiri[2], Tali Dadosh[2], Yoseph Addadi[3], Michal Lahav[1], Milko E. van der Boom[1]
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IN-SITU AND EX-SITU INVESTIGATION OF PHASE TRANSFORMATIONS IN THE Fe4Co2.1Ni2.1Cr0.8Al0.8Ti0.2 HIGH ENTROPY ALLOY

Ron Fishov[1], Guy Hillel[1], Susanna Syniakina[1], Yaniv Zriker[2], Ofer Omesi[2], Yoav Snir[2], Louisa Meshi[1]
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THE EFFECT OF ZN-CONTAINING MICROCALCIFICATIONS ON THE MALIGNANCY OF THYROID NODULES

Lotem Gotnayer[1], Dina Aranovich[1], Merav Fraenkel[2,3], Uri Yoel[2,3], Netta Vidavsky[1,4]
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SYSTEMATIC STUDY OF THE ANTI-PHASE BOUNDARIES FORMATION IN B2 FexAl1-x ALLOYS USING ex-situ AND in-situ TRANSMISSION ELECTRON MICROSCOPY

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[2]*NRCN, Beer-Sheva, Israel*

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TWO-STEP SINTERING OF MG-DOPED ALUMINA

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MICROSCOPE-INTEGRATED SPECTROSCOPIC ELLIPSOMETER FOR FAST AND IN-SITU OPTICAL INVESTIGATION OF MICRON-SCALE MATERIALS AND STRUCTURES

Ralfy Kenaz[1], Saptarshi Ghosh[1], Pradheesh Ramachandran[1], Kenji Watanabe[2], Takashi Taniguchi[3], Hadar Steinberg[1], Ronen Rapaport[1]
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[3]*International Center for Materials Nanoarchitectonics, National Institute for Materials Science, Tsukuba, Japan*

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BRILLIANT WHITENESS IN SHRIMP FROM ULTRA-THIN LAYERS OF BIREFRINGENT NANOSPHERES

Tali Lemcoff[1], Lotem Alus[2,3], Johannes S. Haataja[4,5], Avital Wagner[1], Gan Zhang[1,9], Mariela J. Pavan[6], Ventaka J. Yallapragada[7], Silvia Vignolini[4], Dan Oron[2], Lukas Schertel[4,8], Benjamin A. Palmer[1]
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[5]*Department of Applied Physics, Aalto University School of Science, Espoo, Finland*
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CATHODOLUMINESCENCE SEM OF CsPbBr3 PEROVSKITE NANOCRYSTAL SUPERLATTICES

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SIZE EFFECT ON STRENGTH OF EQUILIBRATED COPPER NANOPARTICLES FABRICATED BY SOLID-STATE DEWETTING

Zhao Liang[1], Nishchal Thapa Magar[2], Raj Koju[2], Yuri Mishin[2], Eugen Rabkin[1]
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REGULATING GRANULE STARCH HYDROLYSIS TO MAKE POROUS STARCH

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Cr/AlCoFeNi DIFFUSION COUPLE FOR MAPPING MICROSTRUCTURAL CHANGES

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MEASURING THE SOLUBILITY LIMIT OF DOPANTS BY FULLY STANDARDIZED WAVELENGTH DISPERSIVE SPECTROSCOPY

Rachel Marder, Wayne D. Kaplan
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CALCIUM AND ELONGATED GRAINS IN ALUMINA

Iman Naamneh, Rachel Marder, Wayne Kaplan
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THE INFLUENCE OF ADDITIVES ON THE CRYSTALLIZATION OF CALCIUM PHOSPHATE IN PHYSIOLOGICAL CONDITIONS

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DIRECTING THE MORPHOLOGY , PACKING, AND PROPERTIES OF CHIRAL METAL-ORGANIC FRAMEWORKS BY CATION EXCHANGE

Hadar Nasi[1], Maria Chiara di Gregorio[1], Qiang Wen[1], Linda J. W. Shimon[2], Ifat Kaplan-Ashiri[2], Tatyana Bendikov[2], Gregory Leitus[2], Miri Kazes[1], Dan Oron[1], Michal Lahav[1], Milko E. van der Boom[1]
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NANOSTRUCTUAL CHARACTERIZATION OF COMPLEXES OF DNA WITH A DIBLOCK-COPOLYMER OF POSITIVELY-CHARGED AND NEUTRAL BLOCKS, AND THEIR STABILITY IN THE PRESENCE OF BLOOD SERUM ALBUMIN

Sapir Rappoport[1], Varvara Chrysostomou[2], Stergios Pispas[2], Yeshayahu Talmon[1]
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OPTICAL CHARACTERIZATION OF LEAD HALIDE PEROVSKITES HETEROSTRUCTURE INTERFACE WITH CATHODOLUMINESCENCE SPECTROSCOPY

Betty Shamaev, Yehonadav Bekenstein
Materials Science and Engineering, Technion – Israel Institute of Technology, Haifa, Israel

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THE EFFECT OF SALTS ON THE NANOAGGREGATION OF SLES IN AQUEOUS SOLUTIONS OBSERVED BY CRYO-TEM

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A CATION EFFECT ON SELF-HEALING IN APbI3 PEROVSKITE THIN POLYCRYSTALLINE FILMS

Pallavi Singh[1], Yahel Soffer[1], Davide Raffaele Ceratti[2], Michael Elbaum[1], Dan Oron[1], Gary Hodes[1], David Cahen[1]
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CERAMIC–METAL INTERFACE: THE INFLUENCE OF TITANIUM ON THE MICROSTRUCTURE OF VACUUM BRAZED ALUMINA-ALUMINUM ALLOY

Stalin Sundara Dhas, Kalaichelvan K.
Department of Ceramic Technology, ACT campus, Anna University, Chennai, Tamil Nadu, India

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ON THE DEVELOPMENT AND ATOMIC STRUCTURE OF ZnO CRYSTALS GROWN IN POLYMERS FROM VAPOR PHASE PRECURSORS

Inbal Weisbord[1], Maya Barzilay[1], Alexei Kuzmin[2], Andris Anspoks[2], Edmund Welter[3], Tamar Segal-Peretz[1]
[1]*Chemical Engineering, Technion – Israel Institute of Technology, Haifa, Israel*
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[3]*Deutsches Elektronen-Synchrotron, (DESY), Hamburg, Germany*

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HIERARCHICAL SELF-ASSEMBLY INVOLVING CLASICAL AND NONCLASSICAL STEPS IN ORGANIC CRTYSTAL GROWTH

Idan Biran[1], Shaked Rosenne[1], **Haim Weissman**[1], Yael Tsarfati[1], Lothar Houben[2], Boris Rybtchinski[1]
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VISUALIZING THE EFFECT OF ELECTRIC FIELDS ON FOULING FORMATION USING CONFOCAL MICROSCOPY

Elina Yachnin[1], David Jassby[2], Tamar Segal-Peretz[3], Guy Z. Ramon[1]
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THE EFFECT OF CALCIUM OXALATE CRYSTAL PHASE, MORPHOLOGY, AND AGGREGATION ON PROTEIN ADSORPTION AND CANCER CELL ATTACHMENT

Gabriel Yazbek Grobman[1], Dina Aranovich1, Netta Vidavsky[1,2]
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P-72 (last minute submission)

RATIONAL DESIGN AND FABRICATION OF BLOCK COPOLYMER TEMPLATED HAFNIUM OXIDE NANOSTRUCTURE

Ruoke Cai, Tamar Segal-peretz
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POSTERS – Instrumentation & Methodology Development

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CRYOGENIC SCANNING ELECTRON MICROSCOPY AS AN EFFECTIVE TOOL FOR NANOSTRUCTURAL STUDY OF BIOLOGICAL SYSTEMS

Irina Davidovich[1], Ariel Koren[2], Carina Levin[2], Yeshayahu Talmon[1]
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COUNTING NANOPARTICLES IN GENERAL AND VIRUSES IN PARTICULAR ONE AT A TIME

Paz Drori[1], Odelia Mouhadeb[2], Gabriel Moya[3], Yair Razvag[1], Ron Alcalai[2], Philipp Klocke[3], Thorben Cordes[3], Eran Zahavy[2], Eitan Lerner[1]
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[3]*Physical and Synthetic Biology, Ludwig-Maximilians-Universität München, München, Germany*

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MOLECULAR MOTORS ON MICROTUBULE TRACKS CREATED WITH NANO FOUNTAIN PEN

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TIME-GATED FLUORESCENCE LIFETIME IMAGING IN THE NEAR INFRARED REGIME; A COMPREHENSIVE STUDY TOWARD IN VIVO IMAGING

Meital Harel, Uri Arbiv, Rinat Ankri
Physics, Ariel University, Ariel, Israel

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SCANNING NANO-STRUCTURE ELECTRON MICROSCOPY FOR DECODING THE STRUCTURAL EVOLUTION OF META-STABLE MATERIALS

Yevgeny Rakita[1,2,3], James L. Hart[3], Partha P. Das[4], Sina Shahrezaei[5], Daniel L. Foley[3], Suveen N. Mathaudhu[5], Stavros Nicolopoulos[4], Mitra L. Taheri[3], Simon J. L. Billinge[2]
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[5]*Department of Mechanical Engineering, University of California, Riverside, Riverside, CA, USA*

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FRET-SENSITIZED ACCEPTOR EMISSION LOCALIZATION (FRETsael) – NANOMETER ACCURACY LOCALIZATION OF BIOMOLECULAR INTERACTIONS USING FLIM-FRET LASER SCANNING CONFOCAL MICROSCOPY

Yair Razvag, Paz Drori, Eitan Lerner
Chemical Biology, The Hebrew University, Jerusalem, Israel

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SHAPING OF ELECTRON BEAMS USING SCULPTED THIN FILMS

Dolev Roitman, Ady Arie
Electrical Engineering, Tel Aviv University, Tel Aviv, Israel

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THE LABORATORY FOR SENSING NANOMATERIALS & CONTROLLED RELEASE TECHNOLOGIES

Gracia Safdie
Pharmacy, The Hebrew University of Jerusalem, Jerusalem, Israel

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DEEP THREE-PHOTON IMAGING OF AN ADULT ZEBRAFISH BRAIN

David Sinefeld[1,2], Dawnis M. Chow[3], Kristine E. Kolkman[3], Dimitre G. Ouzounov[2], Najva Akbari[2], Rose Tatarsky[3], Andrew Bass[3], Chris Xu[2], Joseph R. Fetcho[3]
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REAL-TIME STUDY OF SURFACE-GUIDED NANOWIRE GROWTH BY IN SITU SCANNING ELECTRON MICROSCOPY

XiaoMeng Sui[1], Amnon Rothman[2], Kristýna Bukvišová[3,4], Noya Ruth Itzhak[2], Ifat Kaplan-Ashiri[1], Anna Eden Kossoy[1], Libor Novák[5], Tomáš Šikola[3,4], Miroslav Kolíbal[3,4], Ernesto Joselevich[2]
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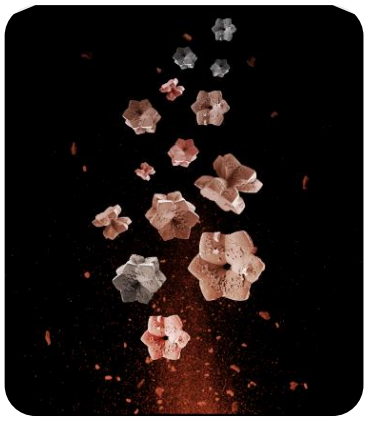
[3]*Institute of Physical Engineering, Brno University of Technology, Brno, Czech Republic*
[4]*CEITEC BUT, Brno University of Technology, Brno, Czech Republic*
[5]*Thermo Fisher Scientific, Brno, Czech Republic*

MICROGRAPH COMPETITION

1



STREAM OF FLOWERS

Hadar Nasi
Weizmann Institute of Science

Metal-organic frameworks (MOFs) based on a nickel(II) metal salt with a tetragonal pyridine-based ligand assemble under solvothermal conditions. Scanning Electron Microscopy image after 2 days reaction time, combining Photoshop editing. Graphic design: Neta Varsano.

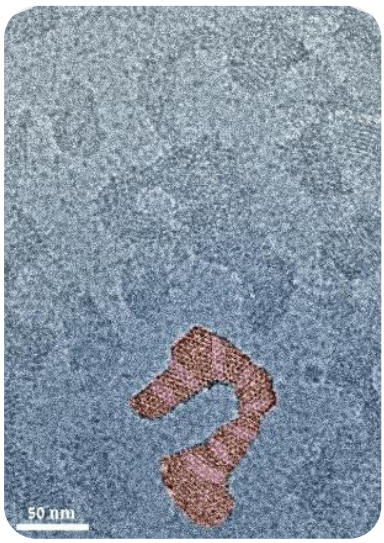
2

NATURAL MERCEDES

Olga Krichevsky, Natalia Litvak, Matan Oren, Keren Davidov, Shlomo Izhar
Ariel University

SRIATELLA UNIPUNCTATA
Tescan MAIA3.

3

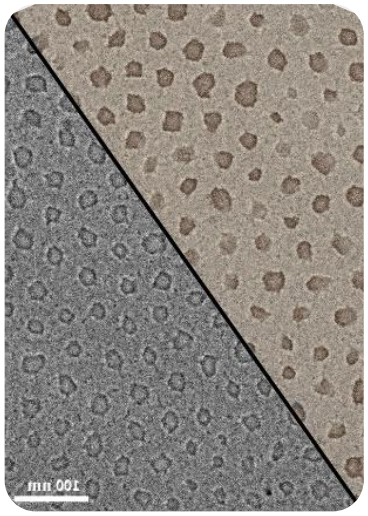


HEXAGONAL SEAHORSE

Sapir Rappoport
Technion – Israel Institute of Technology

The cryo-TEM micrograph shows a hexagonal structure complex of DNA and quaternized poly(2-(dimethylamino ethyl methacrylate)-b-poly(oligo(ethyleneglycol) methyl ether methacrylate) (QPDMAEMA-b-POEGMA). This is a diblock-copolymer with positively charged and neutral blocks. The charge ratio between the copolymer and the DNA is 4. This complex can be used as non-viral vector in gene therapy. The image was taken using cryogenic transmission electron microscopy with Volta phase plate for image contrast enhancement.

4

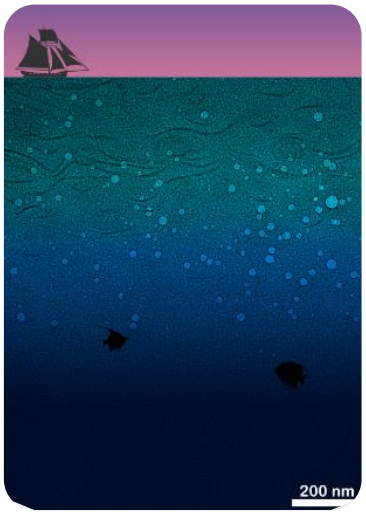


LEOPARD VESICLES

Sapir Rappoport
Technion – Israel Institute of Technology

The cryo-TEM micrograph shows vesicles of the two polyelectrolytes- quaternized poly(2-(dimethylamino ethyl methacrylate)-b-poly(oligo(ethyleneglycol) methyl ether methacrylate) (QPDMAEMA-b-POEGMA) and sodium poly(acrylic) acid (NaPAA). NaPAA is negatively charged, and QPDMAEMA-b-POEGMA is a diblock-copolymer with positively charged and neutral blocks. The charge ratio between the two polyelectrolytes is 1. The image was taken using cryogenic transmission electron microscopy with Volta phase plate for image contrast enhancement

5

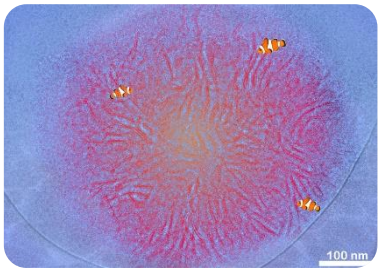


UNDER THE SEA

Sapir Lifshiz-Simon
Technion – Israel Institute of Technology

The cryo-TEM micrograph shows a “sea” environment in a specimen of sodium lauryl ether sulfate (SLES) with KCl at a salt-to-surfactant molar ratio of 4. The “waves” are elongated nano-aggregates of the surfactant in the presence of the salt, and the “bubbles” are radiation damage artifacts. The specimen was prepared in a controlled environment vitrification system and imaged using cryo-transmission electron microscopy with Volta phase-plate for image contrast enhancement.

6

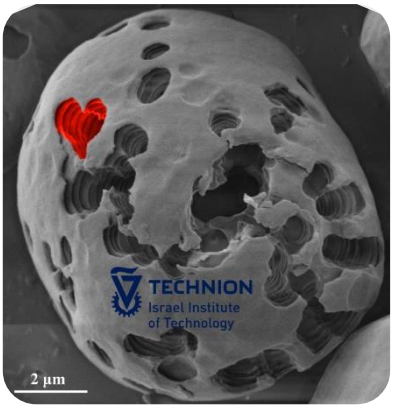


Sea anemone

Sapir Lifshiz-Simon
Technion – Israel Institute of Technology

The cryo-TEM micrograph shows a “sea anemone” nanostructure of sodium lauryl ether sulfate (SLES) with NaCl at a salt-to-surfactant molar ratio of 4. This shear-induced nanostructure was formed after an insufficient on-the-grid relaxation of 90 seconds. The specimen was prepared in a controlled environment vitrification system and imaged using cryo-transmission electron microscopy with Volta phase-plate for image contrast enhancement.

7



A HEART-SHAPED "TREE RING" STRUCTURE GROWS FROM THE POROUS STARCH

Hongxiang Liu, Inbal Ionita, Dganit Danino
Technion – Israel Institute of Technology

The image presented depicts a controlled hydrolysis starch granule with porous structures distributed from the surface to the core. Porous starch is a modified starch that serves as a non-toxic and cost-effective adsorbent, which is widely utilized in various applications such as food, pharmaceutical, and environmental industries. The internal multilayered pores exhibit an inner growth ring structure, revealing the alternating amorphous and crystalline layers that ensure the continuity of hydrolysis. The powder sample was affixed to a conductive tape with an Au/Pd coating and analyzed by a scanning electron microscope in room temperature mode. Both the InLens and SE2 detectors were employed, with the former providing details of the holes and the latter showing the surface features.

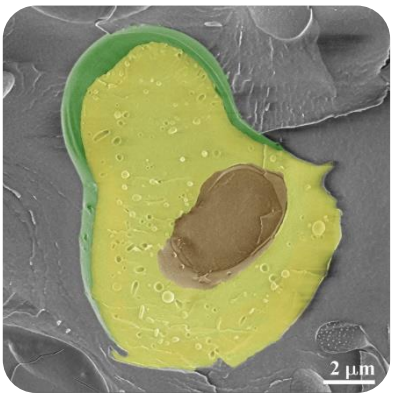
8

PHYTOSTEROLS SUNFLOWERS

Inbal Ionita
Technion – Israel Institute of Technology

Light Microscopy image of Phytosterols crystals, a plant sterol who spontaneously assembled into flower resemble structures, we therefore colored them inspired by the Van Gogh "sunflowers" famous painting.

9



LIFE. SCIENCE. AVOCADO

Irina Davidovich
Technion – Israel Institute of Technology

Cryo-SEM of the human leucocyte. The patient is suffers from hemoglobin S/beta-thalassemia disease and hypersplenism. The blood sample was incubated with sodium metabisulfite for 2 hours on the glass slide to provide hypoxia conditions. The specimen was prepared by high-pressure freezing (HPF) and imaged at cryogenic conditions by a Zeiss Ultra Plus HR-SEM equipped with a Schottky field-emission electron gun. We used the Everhart-Thornley (ET) detector and in-the-lens (InLens) detector to produce the mixed SE signal with 60% of ET signal. Acceleration voltage = 1.2 kV, working distance = 4 mm.

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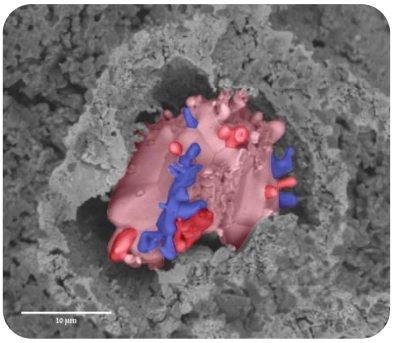
DIVE INTO DOLPHIN DREAMS

Irina Davidovich
Technion – Israel Institute of Technology

Cryo-SEM of a human sickled erythrocyte. The patient suffers from hemoglobin S/beta-thalassemia disease, which causes symptoms similar to those of sickle-cell disease. The blood sample was incubated with sodium metabisulfite overnight to stimulate cell sickling in hypoxia conditions. The specimen was prepared by high-pressure freezing (HPF), and imaged at cryogenic conditions by a Zeiss Ultra Plus HR-SEM equipped with a Schottky field-emission electron gun. We used the Everhart-Thornley (ET) detector to collect the SE signal. Acceleration voltage = 1.2 kV, working distance = 5 mm.

11



HEART OF CHROMIUM

Roei Broneschter
Technion – Israel Institute of Technology

Backscattered electron SEM micrograph of micro-metered sized Chromium particles dispersed in fine alumina powder after sintering in a microwave for 10 minutes.

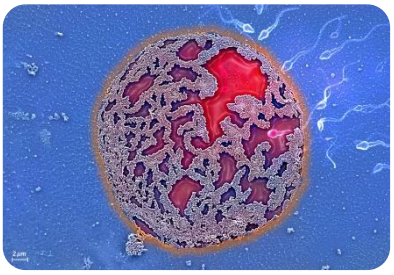
12

DREAM CITY

Shashanka Indri
Ben Gurion University of the Negev

SEM micrograph of Guanine crystals.

13



THE MIRACLE OF LIFE

Maria Koifman Khristosov
Technion – Israel Institute of Technology

$Cs_2AgInCl_6$ perovskite nanoplates on silicon wafer. Taken using Zeiss Ultra-Plus HR-SEM. Samples prepared by Sasha Khalfin, Prof. Yehonadav Bekenstein lab.
Photoshop by Victor Khristosov.

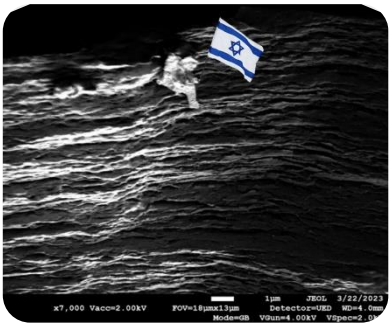
14

THE SECRET LIFE OF BIRDS

Maria Koifman Khristosov
Technion – Israel Institute of Technology

Crystals of Aspartic acid. Taken using Zeiss Ultra-Plus HR-SEM.
Photoshop by Victor Khristosov.

15

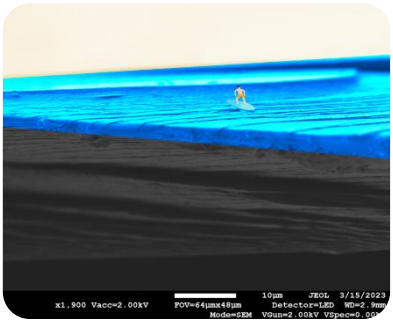


ISRAELI NANO-ASTRONAUT ON A CNC COMET

Einat Zelinger and Daniel Voignac
Hebrew University of Jerusalem

Cellulose Nano Crystals (CNC) self-assemble in highly organised nano-layers upon evaporation from an aqueous suspension. This micrograph is a cross-section image of such a self-assembled film. An anomaly which could be either a defect or a titanium carbide flake from the preparation sat on top of the film with a shape reminding of a suited astronaut in space. The image was taken by Dr. Einat Zelinger and Daniel Voignac at the Robert H. Smith faculty of agriculture, food and environment, Hebrew University of Jerusalem on a JEOL 7800 high resolution SEM. The cross-section was prepared by fracturing a 30µm film in liquid nitrogen. The Israeli flag was added in Microsoft Powerpoint.

16

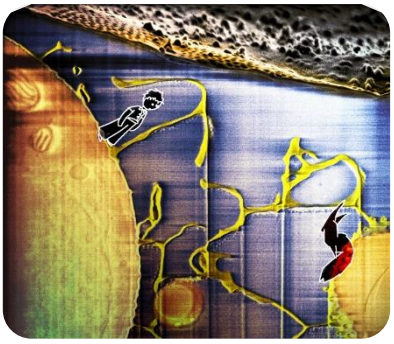


SURFING ON CNC

Daniel Voignac and Einat Zelinger
Hebrew University of Jerusalem

This image is a cross-section of a 30µm thin self-assembled Cellulose Nano Crystal film (CNC). CNC self-assembles in strong, flexible, transparent, degradable films. The cross-section was prepared by fracturing a 30µm film in liquid nitrogen. In this film, a straight fracture was not obtained, but the brittle, tilted aspect provided unique view points on the self-assembled layers reminding waves breaking on a shore.The image was taken by Dr. Einat Zelinger and Daniel Voignac at the Robert H. Smith faculty of agriculture, food and environment, Hebrew University of Jerusalem on a JEOL 7800 high resolution SEM. The image was then partially recolorised in FIJI and further edited on Microsoft Powerpoint.

17

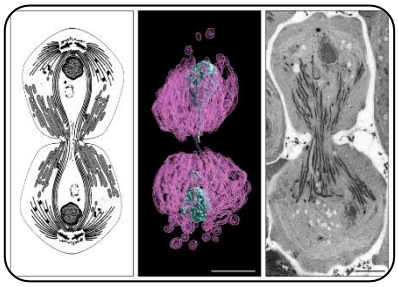


THE LITTLE PRINCE

Zipora Lansky
Weizmann Institute of Science

The sample contains Stephanopyxis turris diatoms that were cryo-preserved by plunge freezing. This SEM image was taken in a FIB-SEM microscope after milling the sample with the FIB to expose a cross section of the diatoms. The image was then colored in photoshop, and the little prince and the fox from the novel "The Little Prince" were added, each on its own diatom “planet” overgrown with its diatom cell wall “flora”.

18

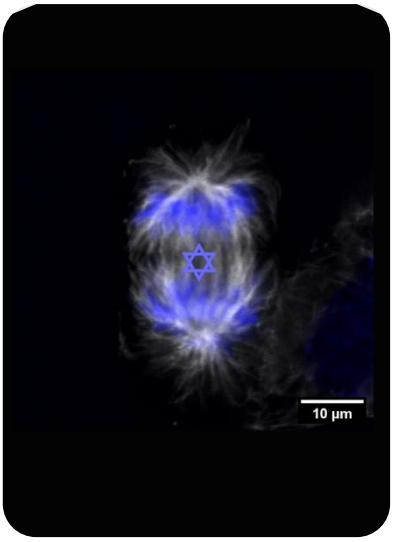


BREAKING EVEN

Alina Kolpakova
Weizmann Institute of Science

The image depicts two Drosophila male germ cells at the final stage of meiotic division. Immediately after meiosis all the mitochondria aggregate and fuse to a giant spherical mitochondrion called Nebenkern. We discovered that that the mechanism involves robust fusion of the mitochondria already during the second meiotic division. Left panel: schematic representation of a dividing spermatocyte. Middle panel: 3D reconstruction based on the image obtained using standard expansion microscopy method (mitochondria in magenta and nuclei in cyan). Right panel: cross section through the meiotic cells (pan-stained with NHS-Ester, Pan-Expansion microscopy method). The micrographs were taken using Dragonfly Spinning Disc microscope. Calibrated scale bar: 5 microns.

19

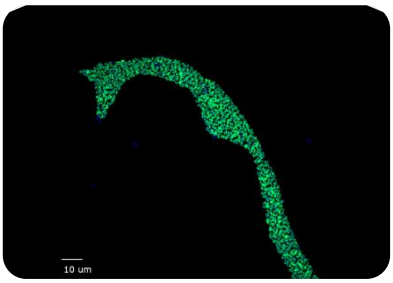


LEFT V/S RIGHT. NO MATTER THE CONTROVERSY, WE COME FROM THE SAME DNA. REFLECTIONS ON CELL DIVISION…

Sushmita Chatterjee
Tel Aviv University

Image represents a cancer cell showing cell division during metaphase and progressing towards anaphase. Cell was stained with anti-human mouse alpha tubulin primary antibody and anti-mouse Alexa 488 secondary antibody. Cell were further counterstained with DAPI. Image was captured with Zeiss 810 LSM confocal microscope at 60x magnification with 6x zoom.

20



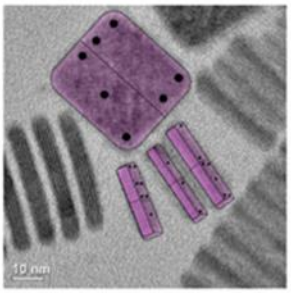
BACTERIAL SEAHORSE

Noa Mizrahi
Ben-Gurion University of the Negev

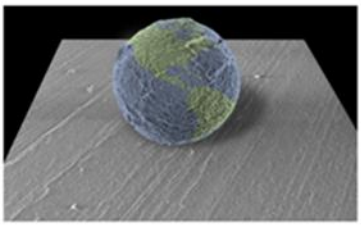
E. coli bacteria containing GFP proteins and DNA with hoechst staining. This was a control experiment, as part of a research project of Asgard ESCRTs in bactrial cells. The living bacteria were in a liquid solution on a flat surface, and the image was taken using confocal microscopy. It was the first time I got to see the margins of the liquid, and then noticed all kinds of special shpes it created. Here we can see a beautiful seahorse, filled with green and blue colors.

THE INTERNATIONAL ISM ART EXHIBITION, 2023

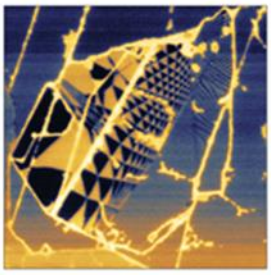
"Microscopy Meets Surrealism"



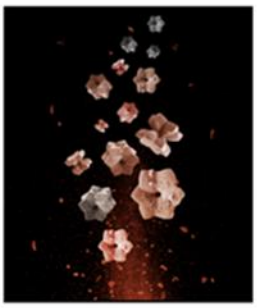
Sasha Khalfin / Technion
Domino Game / TEM micrograph



Noy Shaked / Weizmann Institute
It's a small world after all / SEM micrograph
Israel Society for Microscopy 2023



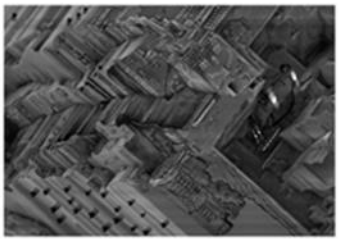
Maayan Vizner Stern / Tel Aviv university
Two atoms thick ferroelectric / AFM
Israel Society for Microscopy 2023



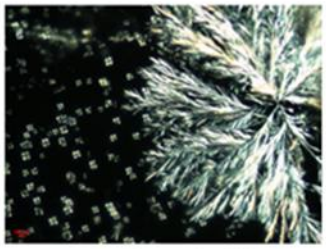
Hadar Nasi / Weizmann Institute
Stream of Flowers / SEM Micrograph
Israel Society for Microscopy 2023

Avi Auslender / Tel Aviv University
Graphene face / Light microscopy micrograph
Israel Society for Microscopy 2023

Zahava Barkay / Tel-Aviv University
Entanglement in Electron Microscopy / Painting
Israel Society for Microscopy 2023

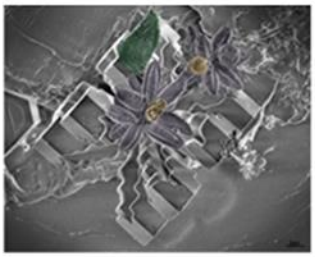


Shashanka Indri / Ben-Gurion University
City of Dreams / SEM micrograph
Israel Society for Microscopy 2023



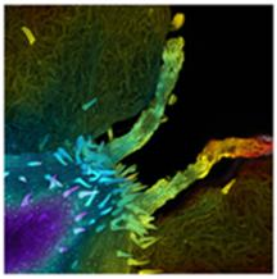
Lotem Alus / Weizmann Institute of Science
Microscopic Jungle / Optical microscope
Israel Society for Microscopy 2023

Nancy Fruchtman / Artist - Israel
Metamorphic Fish / Painting
Israel Society for Microscopy 2023

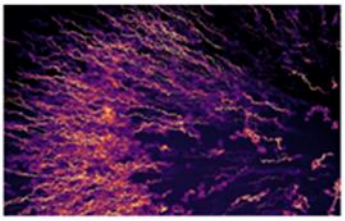


Jenny Capua Shenkar / Weizmann Institute
Flower-up the Cogwheels / SEM micrograph
Israel Society for Microscopy 2023

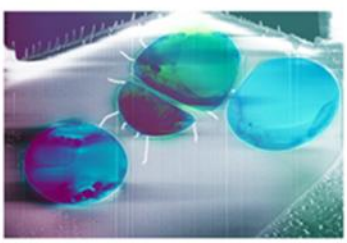
Helen Francis Sevitt/ Artist - Israel
Steps / Painting
Israel Society for Microscopy 2023



Alexandra Tsitrin / Ben-Gurion University
Gem seed / Light microscopy micrograph



Nadav Opatovski / Technion
Battle Inferno / Light microscopy micrograph
Israel Society for Microscopy 2023



Zipora Lansky / Weizmann Institute
Diatom beetle / SEM micrograph
Israel Society for Microscopy 2023

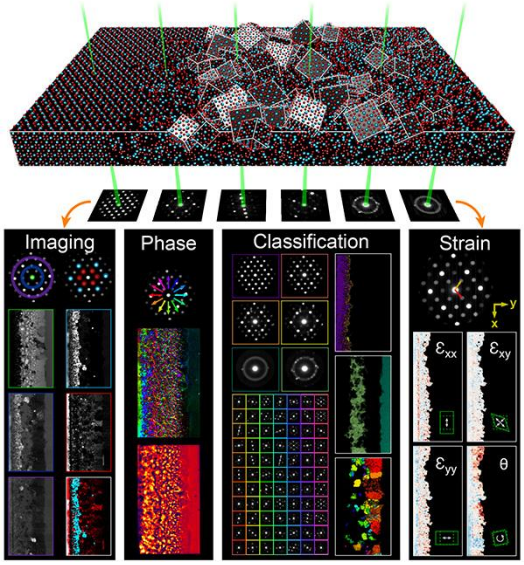
Fanfranco Finocchioli / Artist-Italy
Painting
Israel Society for Microscopy 2023

PLENARY

CHARACTERIZING MATERIAL PROPERTIES FROM ATOMIC TO FUNCTIONAL LENGTH SCALES WITH COMPUTATIONAL IMAGING IN SCANNING TRANSMISSION ELECTRON MICROSCOPY

Colin Ophus[1], Benjamin Savitzky[1], Stephanie Ribet[1], Steven Zeltmann[3], Philipp Pelz[4], Georgios Varnavides[2], Rakowski Alexander[1], Mary Scott[1,2]

[1]*National Center for Electron Microscopy, Molecular Foundry, Lawrence Berkeley National Laboratory, Berkeley, California, United States Minor Outlying Islands*
[2]*Materials Science and Engineering, University of California, Berkeley, Berkeley, CA, USA*
[3]*5PARADIM, Cornell University, Cornell, New York, USA*
[4]*Department of Materials Science and Engineering, Friedrich-Alexander Universität Erlangen-Nürnberg, Erlangen, Germany*



The past decade of development for transmission electron microscopy (TEM) and scanning TEM (STEM) has been enormously successful. In materials science, atomic-scale imaging, diffraction, and spectroscopy have become a routine part of nanoscale research. This development has been driven primarily by technological innovations: hardware aberration correction, better holders and microscope optics, direct electron detectors, and the transformation of S/TEM into a digital science with the rise of computational imaging. In this talk, I will show how advanced detectors and computational methods can improve signal-to-noise, resolution, and statistical power of property measurements in STEM materials science studies. The examples shown will include structural characterization of metallic alloys, complex ferroelectric oxides, 2D heterostructures, weakly-scattering soft matter samples, and materials for energy applications. I will also show examples of atomic electron tomography (AET) experiments, where the 3D position and species of every atom can be identified in nanoscale samples. I will emphasize the important role of developing open-source algorithms, codes, and simulation methods to promote robustness, reusability, and repeatability in materials science studies. Finally, I will also show how modern deep learning methods can remove one of the ultimate limits of STEM experiments, by inverting measurements in the presence of strong multiple scattering of the electron beam.

PLENARY

EXPLORING LIFE ACROSS SCALES WITH VOLUME CORRELATIVE LIGHT AND ELECTRON MICROSCOPY

Lucy Collinson[1]

Electron Microscopy Science Technology Platform, Francis Crick Institute, London, UK

Bioimaging holds the promise of identifying and mapping every molecule in a biological sample, unravelling their interactions and functions in health and disease. Volume Correlative Light and Electron Microscopy (vCLEM) is a powerful method for visualising molecules within the 3D context of cell and tissue structure. The molecule of interest, usually a protein, is labelled with a fluorescent tag and the sample is imaged sequentially by fluorescence microscopy (FM) and electron microscopy (EM). Imaging the same cell or region across both modalities reveals supramolecular complexes associated with underlying membranes and organelles. However, despite common misconceptions, there is no such thing as a single 'correlative microscope'. Correlative imaging is a workflow, requiring multiple optimised protocols, including probe labelling, sample preparation, multimodal imaging, and image processing, registration, overlay, reconstruction, quantification, and analysis. Many of these steps remain active fields of research that lack universal solutions. Here, we present developments aimed at both developing a high resolution vCLEM pipeline and democratizing the resulting technology. We are developing: new protocols that remove the requirement for expensive, complex sample preparation equipment; new semi-automated targeted ultramicrotomy solutions; low-cost, user-friendly STORM and SEM solutions in an array tomography format; and open source software solutions for data processing and analysis.

INVITED

SINGLE-WALLED CARBON NANOTUBES FOR SENSING AND IMAGING IN THE NEAR-INFRARED

Gili Bisker[1]

Biomedical Engineering Department, Faculty of Engineering, Tel Aviv University, Tel Aviv, Israel

Single-walled carbon nanotubes (SWCNTs) have unique optical and physical properties, and they benefit from the ease of surface functionalization and biocompatibility. Semiconducting SWCNTs fluoresce in the near-infrared (nIR) part of the spectrum, which overlaps with the transparency window of biological samples where absorption, scattering, and autofluorescence are reduced. Further, they do not photobleach or blink. Upon tailored surface functionalization, adsorption of target analytes onto the nanotube corona can result in spectral modulations manifested as either an intensity change or a shift in the peak emission wavelength. Hence, SWCNTs can be used as nIR optical probes for imaging and sensing in biological samples enabling real-time optical detection with both spatial and temporal resolution.
I will present recent advances from my lab, including *in vivo* imaging of fluorescent SWCNTs within *C. elegans* nematodes in the near-infrared window [1], monitoring the activity and inhibition of cholinesterase enzymes using SWCNTs fluorescent sensors [2], and super-resolution near-infrared fluorescence microscopy of SWCNTs using deep learning [3].

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MUTSAFI

EXAMINING ATHEROSCLEROTIC LESIONS IN THREE DIMENSIONS AT THE NANOMETER SCALE WITH CATHODOLUMINESCENCE, CRYO-SEM AND CRYO-FIB/SEM

Jenny Capua Shenkar[1], Neta Varsano[2], Noya-Ruth Itzhak[1], Ifat Kaplan-Ashiri[2], Katya Rechav[2], Vlad Brumfeld[2], Lia Addadi[1]

[1]*Department of Structural Biology, Weizmann Institute of Science, Rehovot, Israel*
[2]*Department of Chemical Research Support, Weizmann Institute of Science, Rehovot, Israel*

Cholesterol crystallization is central in atherogenesis. Cholesterol crystals lead to plaque instability and rupture, which can result in myocardial infarction and stroke. Cholesterol crystals are associated with intra-lesional macrophages, however, crystallization as well as plaque regression following cholesterol crystal dissolution are still obscure.

A specific workflow was developed to allow examination of human and rabbit atherosclerotic tissues from low-resolution-high-volume (cm scale), employing Micro CT (Figures A-C), to high-resolution-low-volume (nm scale) of regions of interest, using cryo-electron microscopy. Detection of cholesterol deposits is challenging by conventional techniques. Here it was accomplished in a correlative manner combining Cathodoluminescence (CL) (Figures E, insert in F and Figure H) with Cryo-SEM (Figures D, F, G, L) and cryo-FIB/SEM (Figures I, K, M, N). This allowed examination of both human and rabbit atherosclerotic lesions in two and three dimensions, with minimal sample processing, maintained in hydrated close to native state conditions, with a resolution of tens of nanometers (1).

In both rabbit and human tissues, early stages of crystalline cholesterol are associated with intra- or extracellular lipid droplets (Figures I and J) and the outer membrane of multi-lamellar bodies. However, in humans, regions containing mature crystals displayed intriguing foamy lysosome-like structures comprising seemingly disintegrating cholesterol crystals (Figures L, M, N). We interpret these phenomena as indicative of cholesterol crystal dissolution. Evidence for cholesterol crystal dissolution was detected only in the cellular regions of the lesions. Most of the lysosome-like structures, containing either cholesterol crystal fragments or cholesterol ester deposits could be linked to individual cells (Figure N). The foamy structures comprise vesicles with an aqueous content (the white vesicles in M and N), suitable environments for enzymatic activity. Based on these observations, we suggest that crystal dissolution occurs through cholesterol esterification and deposition of cholesteryl ester.

Combination of micro-CT, CL, cryo-SEM and Cryo-FIB/SEM allows direct, correlative high-resolution, three-dimensional examination of cholesterol deposits in atherosclerotic lesions. The developed workflow procedures could potentially benefit to diverse pathology-related fields of research.

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AI-GUIDED OPTICAL SENSORS FOR THE EARLY DETECTION OF GYNECOLOGIC CANCERS

Zvi Yaari[1]

School of Pharmacy, The Hebrew University of Jerusalem, Jerusalem, Israel

Gynecologic cancers are particularly difficult to diagnose. Patient prognosis and quality of life are affected substantially by this problem. We are developing new technologies to improve cancer detection using liquid biopsy and in vivo sensor approaches. With artificial intelligence algorithms, we harnessed the unique optical properties and sensitivity of single-walled carbon nanotubes to develop intelligent optical sensors. We developed platforms to detect multiple cancer biomarkers in both patient biofluids and within the uterine cavity as implantable devices. Applying machine learning algorithms to analyze the optical response of the sensors enabled the precise detection of multiplexed biomarkers. In addition, when implanted in human uteri, the sensors detected the biomarkers and successfully differentiated between benign and malignant cases. These technologies will significantly improve diagnostics and lead to robust, point-of-care technologies for early-stage diagnosis.

PLATE-LIKE GUANINE BIOCRYSTALS FORM VIA TEMPLATED NUCLEATION OF CRYSTAL LEAFLETS ON PREASSEMBLED SCAFFOLDS

Zohar Eyal[1], **Rachael Deis**[1], Neta Varsano[2], Nili Dezorella[2], Katya Rechav[2], Lothar Houben[2], Dvir Gur[1]

[1]*Department of Molecular Genetics, Weizmann Institute of Science, Rehovot, Israel*
[2]*Department of Chemical Research Support, Weizmann Institute of Science, Rehovot, Israel*

The nanoscale morphologies of crystalline materials determine their optical, electrical and mechanical properties and, thus, their potential applications1,2. However, producing crystals with particular shapes requires overriding their strong tendency to adopt thermodynamically stable structures3,4. Nevertheless, many organisms form crystals with distinct morphologies, such as the plate-like guanine crystals formed by a large variety of terrestrial and aquatic species for vision, camouflage, body temperature regulation, and kin recognition5-8. The control over crystal morphogenesis was hypothesized to involve physical growth restriction by the delimiting crystal chamber membrane, combined with fine-tuned interactions between organic molecules and the growing crystals9-11. Using cryo-electron tomography, we followed crystal formation in developing zebrafish larvae in three dimensions. We find that initially, crystals form in the lumen of the crystal forming organelle, with no contact with the delimiting membrane12. Only later in development, the elongating crystals reach the membrane and eventually push against it, deforming the organelle shape. We further show that crystals form via templated nucleation of multiple thin leaflets on preassembled, 20 nm thick, amyloid protein scaffolds. The initial thin leaflets then merge and coalesce into a single platelet crystal, with no obvious reminiscence of the initial leaflets. Our findings provide new insights into how organisms control the morphology and, thereby, optical properties of crystals, setting the stage for studying the interaction between proteins and molecular crystals.

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INVITED

THE USE OF 3D IMAGING TO ANALYZE CELLULAR NETWORKS

Michal Shoshkes Carmel[1], Marco Canella[1], Simcha Nalick[1], Noa Corem[1], Amal Gharbi[1], Ittai Ben-Porath[1]

Developmental Biology and Cancer Research, Hebrew University of Jerusalem Medical School, Jerusalem, Israel

One of the most fundamental questions in biology is how are individual cells acquire their fate and function during the formation of organs, and how do these functions provide the tissue with the ability to support homeostasis?

We study unique mesenchymal cells called telocytes characterized by extremely long cytoplasmic processes, which are separated from the epithelium by sub-micrometer distances.

In the intestine telocytes expressing the transcription factor Foxl1 form a continuous subepithelial three dimensional network which span the entire epithelium and provide the essential Wnt proteins required for stem cell function. Here, we made an attempt to test whether telocyte network exist in the skin and whether it is an important component for hair follicle stem cell function. We reveal a comprehensive network of telocytes within all hair follicle epithelial layers in contact with stem, progenitor and differentiated cells. Ablation of dermal telocytes or Wnt signals emanating from them abrogate hair follicle stem cell function demonstrating that telocytes constitute the hair follicle stem cell niche.

INVITED

EXPOSING THE STRUCTURE OF METHYLCELLULOSE FIBRILLAR GELS WITH CRYO-TEM AND SAXS

Lucy Liberman[1], Peter Schmidt[2], Mckenzie Coughlin[2], Asia Matatyaho Ya'akobi[1], Irina Davidovich[1], Jerrick Edmund[2], Yeshayahu Talmon[1], Frank Bates[2], Timothy Lodge[2]

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Methylcellulose (MC), a cellulose ether derivative, is a commercially important water-soluble polysaccharide, which thermoreversibly gels upon heating. Although MC has been studied and exploited in applications for many decades, it has only recently been discovered that the gelation occurs via self-assembly of the polymer chains into ca. 15 nm diameter fibrils, which percolate into a network. The network structure dictates the properties and mechanical behavior of the resulting hydrogel. The addition of salt to MC gels has been an area of academic and commercial interest. MC solutions containing salts exhibit an increase or decrease in the gelation temperature, generally following the Hofmeister series. We build upon those investigations and explore the effect of salt on MC fibril structure. We demonstrate how the addition of salt affects the gelation and dissolution temperatures using rheology and cloud point measurements. Small angle X-ray scattering (SAXS) and cryogenic transmission electron microscopy (cryo-TEM) provide us with information regarding the presence and structure of MC fibrils. Fitting the SAXS curves to a semiflexible cylinder model, we demonstrate that the fibril diameter decreases monotonically with increasing salt molarity. In agreement with SAXS, Volta phase-plate cryo-TEM shows the diameter reduction effect with salt molarity, and provides additional insight regarding the fibrillar internal structure.

MARGULIS

THE MEAN INNER POTENTIAL OF HEMATITE α–Fe_2O_3 ACROSS THE MORIN TRANSITION

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The mean inner potential (MIP) is defined as the volume averaged electrostatic (Coulomb) potential within a crystal with respect to vacuum [1]. It is a fundamental material property depending on composition, crystal structure and surfaces. We measured the MIP of crystals using off-axis electron holography (OAEH, see Fig. 1(a)) and transmission electron microscopy (TEM), e.g. Refs. [2-3].

The MIP is sensitive to the distribution of valence electrons, so we suggest its use as a chemical bonding parameter for solids:

Hematite, α-Fe_2O_3, is a test case to the sensitivity of the MIP as a proposed bonding parameter because of the Morin antiferromagnetic phase transition.

Below the Morin transition temperature (T_M, ~200K for thin films), magnetic moments are aligned along the principal c-axis of the hexagonal unit-cell, exactly antiparallel. Above TM, magnetic moments are aligned in the basal plane with a slight canting, resulting in a weak net moment. Furthermore, across T_M, no change in the corundum crystal structure can be distinguished, while a change in hybridized Fe-*3d* and O-*2p* states was reported, which affects ionic bonding and therefore magnetic alignment through super-exchange.

For a given crystallographic phase, the change in the MIP with temperature is minor, following thermal expansion. Indeed, we measured the temperature dependence of the MIP in corundum α-Al_2O_3(11-20) between 95K and 295K showing a constant value of 16.8 V within the measurement accuracy of 0.45V.

Therefore, the objectives of this work are:

· Measure the MIP of hematite as a function of temperature.

· Examine the sensitivity of the MIP as a bonding parameter for crystals.

OAEH measurements were undertaken in-situ, above and below T_M, applied to a wedge cross-sectional specimen of an antiferromagnetic hematite epitaxial layer film (~250 nm thick) grown on a c-plane (0001) sapphire substrate (see Fig.1 (b) and Fig.2). We note that reports on the temperature dependence of the MIP are scarce [4-5]. For α-Fe_2O_3(11-20), the measured MIP above the Morin transition are 17.85 ± 0.50 V, 17.93 ± 0.50 V, at temperatures of 295K, 230K, respectively. Below the Morin transition, at 95K, a significant reduction of approximately 1.3V is measured to 16.56 ± 0.46 V (see Fig.1(e)). By applying a range of TEM and Scannig TEM methods, e.g. geometric phase analysis, electron energy-dispersive X-ray spectroscopy, we show that the majority of the reduction of the MIP follows charge redistribution in the chemical bonding.

From our MIP measurements at 95K, the degree of ionicity is calculated at 86±14%, while at 295K, above the Morin transition, the degree of ionicity reduces significantly to 45±16%. These observations agree with previous reports that below the Morin transition, bonding in hematite is ionic. Above T_M, a covalent bonding is introduced by three membered oxygen ion rings connected via shared electrons [6].

Thus, we report for the first time the MIP of hematite as a function of temperature, and demonstrate the applicability of this parameter for quantifying chemical bonding in crystals.

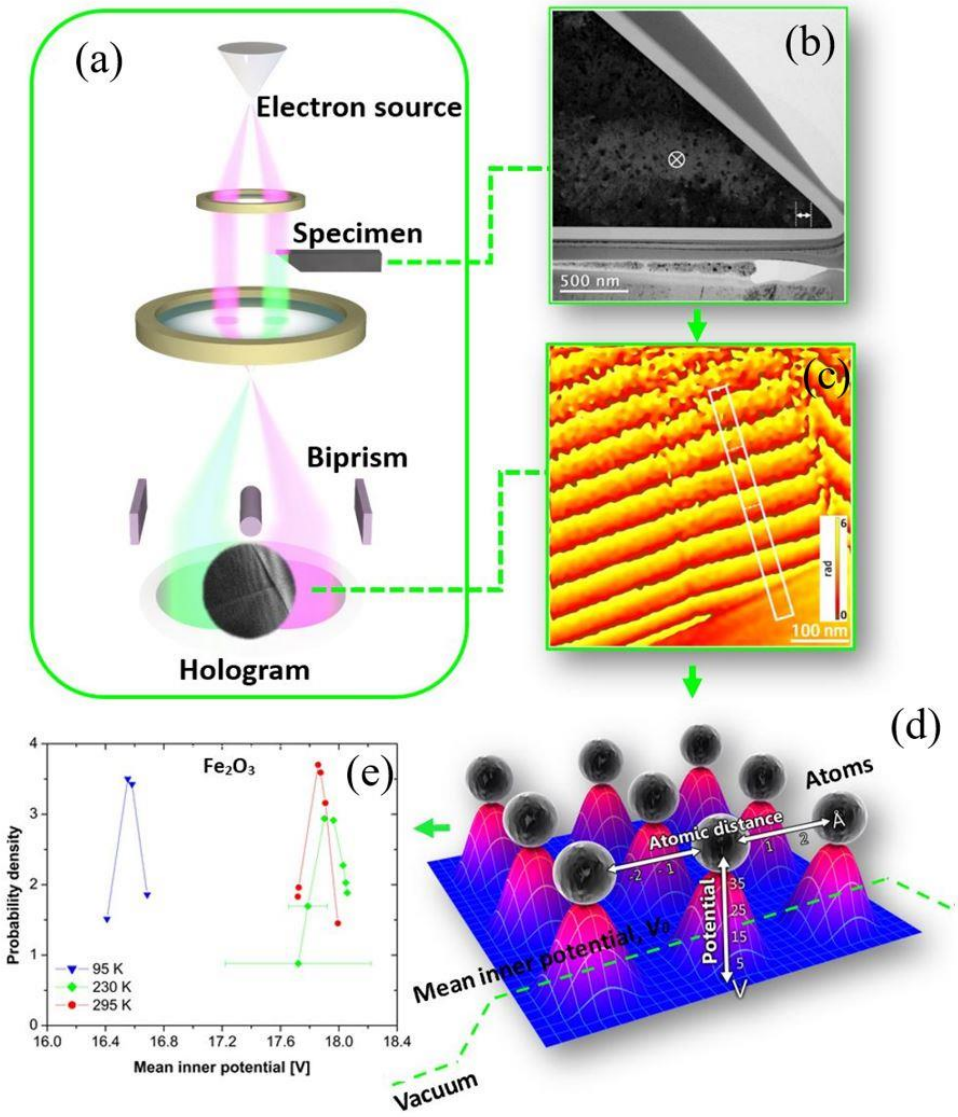

Fig. 1: (a) Schematic of the off-axis electron holography measurement. (b) Cross-sectional bright-field TEM micrograph of a hematite sample extracted from the TEM wedge sample following OAEH measurements. The arrows and dashed lines highlight the region from which phase gradients were measured. (c) Reconstructed electron phase map from the edge of the α-Fe_2O_3/Al_2O_3 wedge sample with the (11-20) plane at the base surface and nominal wedge angle of 40º (phase spacing: 2π) at a temperature of 95±1 K. (d) Illustration of the MIP related to the potential distribution of atoms in the crystal (e) Probability densities of normal distributions for the MIP measurements of a-Fe_2O_3 at temperatures of 95K, 230K and 295K. Examples of the standard deviation (0.133V) and estimated measurement error (0.5V) are presented for the 230K measurement.

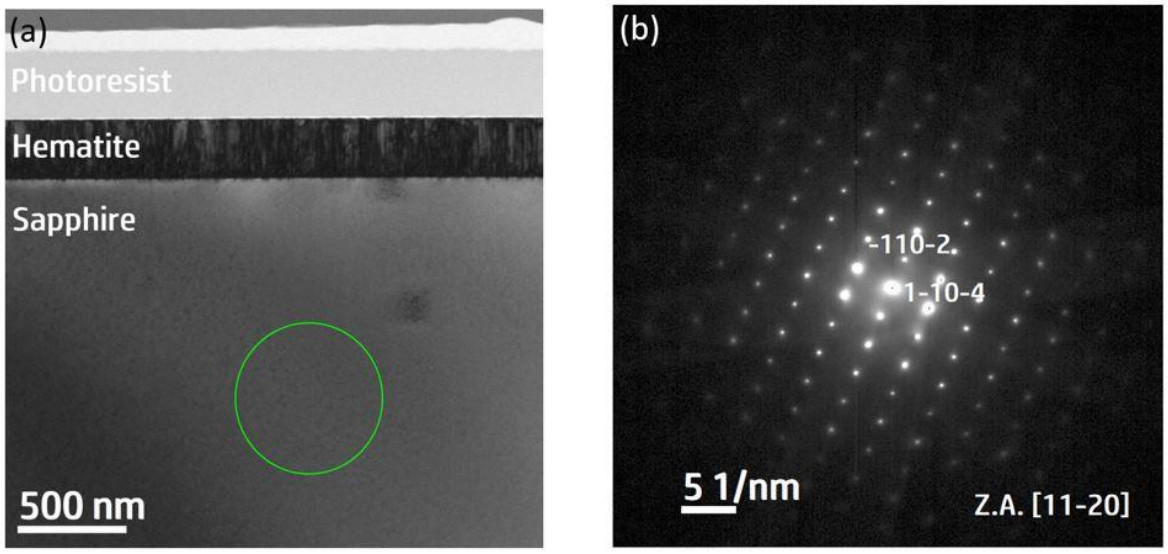

Fig. 2: (a) Cross-sectional Bright-field TEM micrograph showing the epitaxial α-Fe_2O_3 layer grown on the α-Al_2O_3 substrate, (b) SAED pattern from the region denoted schematically by the circle in (a) in the sapphire substrate demonstrating a single corundum crystal structure in a [11-20] zone-axis alignment.

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THE EFFECT OF WATER UPTAKE ON THE MECHANICAL BEHAVIOR OF HYBRID THIN FILMS FABRICATED BY SEQUENTIAL INFILTRATION SYNTHESIS

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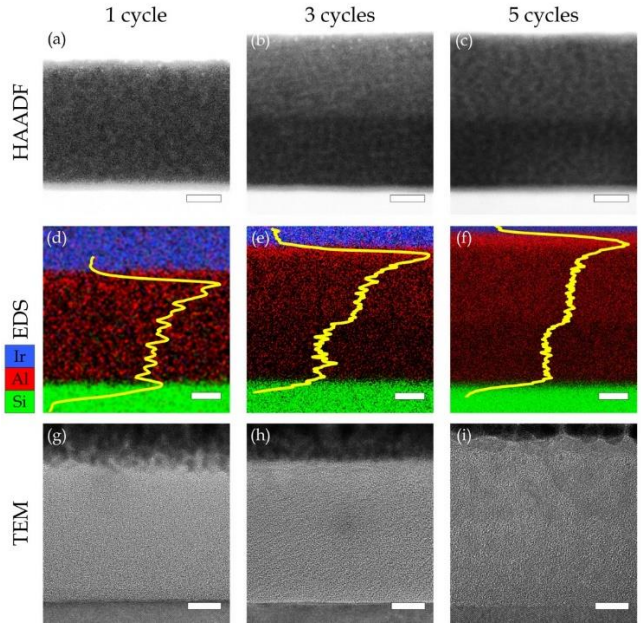
Hybrid organic-inorgnic materials are an exciting subclass of composites due to their unique structures and properties. Control over their mechanical properties is central to their implementation in various advanced applications. In recent years, sequential infiltration synthesis (SIS) has emerged as a promising new technique for fabricating hybrid materials with nanoscale precision. In SIS, inorganic materials are grown within polymers from vapor phase precursors using atomic layer deposition (ALD) chemistry. Several studies have demonstrated the potential of SIS to tune the mechanical properties of polymers. However, a full understanding of the nanostructure mechanical behavior is still an ongoing effort.

This research studies the mechanical response of SIS-based hybrid thin films and probes the effect of water uptake on their behavior. Hybrid thin films were fabricated by growing AlOx within PMMA films via SIS process, using trimethylaluminum and H2O as precursors. To reveal the hybrid films nano-scale structure, we used focus ion beam (FIB) milling to prepare cross-section samples from the hybrid films and characterized them via high-resolution transmission electron microscopy (HR-TEM), high angle annular dark field scanning TEM (HAADF-STEM), and elemental analysis with energy dispersive X-ray spectroscopy (EDS) (Figure 1). Via these techniques, we were able to directly probe the spatial distribution and morphology of the grown AlOx within the PMMA thin films, as well as volumetric changes. Tensile measurements of the thin films (~50 nm, supported by water surface) reveal counter-intuitive behavior with a softening effect despite the growth of AlOx clusters. Water uptake measurements carried out via in-situ microgravimetric measurements indicate that aluminum-oxide induces water uptake from the aqueous environment, implying a possible interaction between AlO-x and water.



Pt-BASED NANOCATALYST MATERIAL: THE RELATIONSHIP BETWEEN STRUCTURE, PERFORMANCE, AND STABILITY

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The increasing need for environmentally-friendly energy sources using hydrogen has led to the advancement of proton exchange membrane fuel cells with superior performance, which can transform hydrogen fuel into electricity. Nonetheless, the oxygen reduction reaction (ORR) on the cathode is hindered by slow kinetics and therefore necessitates a catalyst. Despite being the most commonly employed catalysts due to their high mass activity, Pt and its alloys have certain drawbacks, such as being costly and lacking stability over prolonged periods of operation.

There has been significant research into the relationship between the performance of nanoparticles (NPs) and their structural properties, particularly in the case of shape-controlled NPs used as catalysts for ORR. While Pt-based NPs have emerged as popular ORR catalysts, their low durability has limited their use in green energy technology. During use, these catalysts degrade due to various factors, such as acidic conditions leading to the leaching/dissolution of transition metals, particle detachment, coarsening, and dealloying.

This Ph.D. research focused on the relationship between structure, catalytic activity, and durability of the nanomaterial. The main goal is to produce a highly active Pt-based nanocatalyst with less precious material while high stability is achieved. Four first-author articles were published (and one more will be submitted soon), showing our achievements. Along the projects, nanocatalysts (Pt-Ni and Pt-Cu) were rationally designed and produced by reproducible, high-yield synthesis using a robust methodology.

Meticulous structural characterization was conducted, highlighting the transmission electron microscopy (TEM) technique. A concise summary of each published work`s achievements is described as follows. 1) Octahedral to cubo-octahedral morphology transition in 6 nm Pt-Ni nanocrystals was observed. The reason for this structural evolution is the oxygen pressure in the synthesis batch. The same precursors and experimental conditions (except the volume of the batch) resulted in an interesting 6-pointed star shape and particular electrochemical performance. In this system, Pt-skin was one of the targets to optimize the catalytic activity of the NP.

2) To study the NPs corrosion mechanism, a model that mimics the Ni-etching process was developed. Using a two-phase Ni-transfer treatment, it monitors the Ni leaching degradation from carbon-supported Pt-Ni NPs. For this purpose, six chelating agents were used. It correlated the chemical functional groups of the chelates to the degradation process.

3) Pt-Ni core-shell and core-bishell were rationally designed and synthesized in a two-step solvothermal synthesis. Core size and shell thickness were investigated by mixing two reducing agents. Bifunctional catalytic activity (ORR/OER) in alkaline medium was found for the Pt@Ni@Pt nanocatalyst. The outer Pt layer enhances the performance of the 1% weight Pt content catalyst.

4) High efficiency and durability were obtained from dealloyed PtCu octahedral nanocrystal. It was found that the synthesis duration and the capping agent used (CTAB) confer remarkable efficiency toward ORR in acidic medium. The TEM study shows the Pt-diffusion from the alloy core to the surface of the particle, generating a stable structure even if Cu leaches during electrochemical treatment. An interesting identical location TEM (IL-TEM) study was shown, analyzing the degradation mechanism of the catalyst due to electrochemical measurements.

All this work was possible and upgraded due to the TEM, HR-TEM, IL-TEM examination, and the collaboration with the INL (Portugal) that conducts the advanced microscopy techniques. Microscopy allows us to observe the Pt-skin, the lattice strain, the chemical composition segregation in the NPs, morphology transition, and hollowed or dealloyed NPs, among other features.

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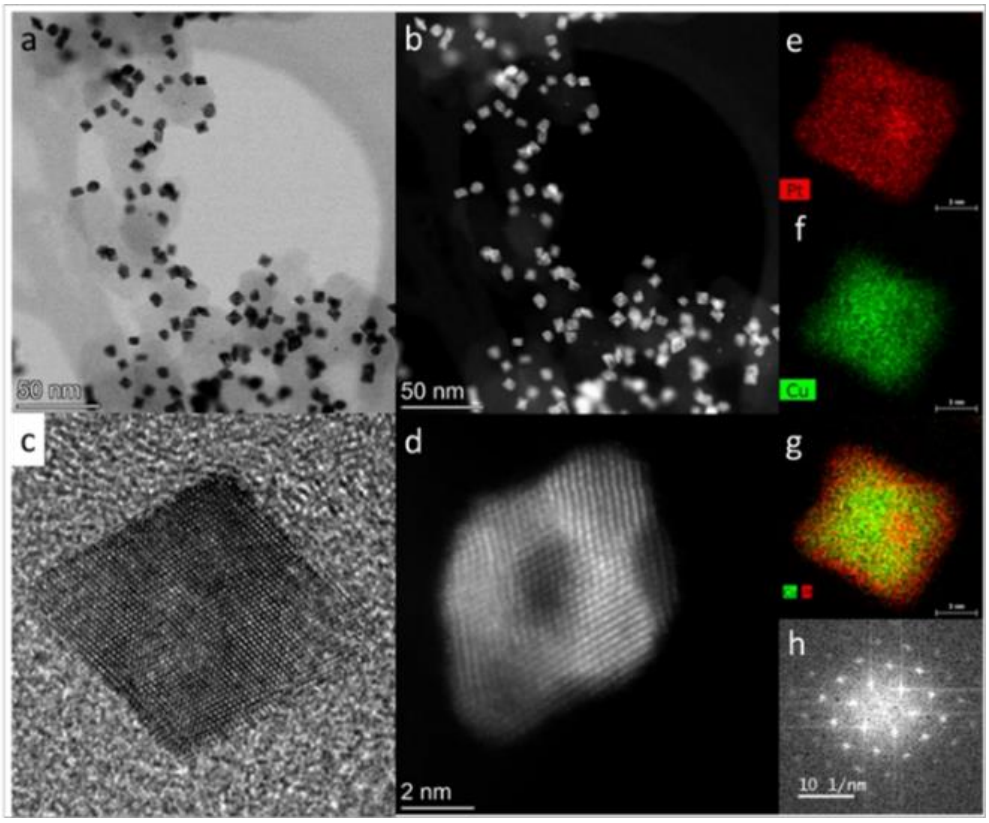

INVITED

LOCAL ELECTRICAL PROPERTIES OF MICROSTRUCTURAL DEFECTS ASSESSED IN SCANNING ELECTRON MICROSCOPY

Hanna Bishara[1]

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The impact of microstructural defects on the electrical properties of materials is generally captured as an accumulative effect of all the material's defects. Despite the different atomic and mesoscopic structures of defects (even within same defect sort e.g. grain boundaries - GBs), the impact of their structural characteristics on the resistivity is not yet understood. This limits the defect-engineering and hinders the development of alloys with excellent electrical conductivity.

This talk introduces a cutting-edge in-situ scanning electron microscope (SEM) methodology to measure the electrical resistivity of individual GB segments with high spatial resolution and high sensitivity. The local electrical measurements are employed to directly measure the resistivity of structurally well-defined GBs is bulk and thin film metallic materials. The resistivities of separated GB segments in pure and Fe-alloyed Cu are reported and correlated with the GB structural characteristics and its thermodynamic excess properties. In addition, the contribution of grain and phase boundaries to the resistivity/conductivity in functional alloys are discussed. The correlative electrical and microstructural studies contribute to a better understanding of the GB resistivity, which paves the way for knowledge-based multi-dimensional defect-engineering of conductors, functional materials, and internal interfaces.

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ALL-OPTICAL MECHANICAL IMAGING WITH STIMULATED BRILLOUIN MICROSCOPY

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Brillouin microscopy is an all-optical mechanical microscopy approach for imaging samples at the (sub)micrometer level with no contact or external mechanical stimulus. In this talk, I will present an emerging technique for all-optical mechanical imaging with high spectral, spatial, and temporal resolution based on stimulated Brillouin scattering (SBS). Our method uses continuous-wave, single-frequency lasers, and a phase sensitive detection scheme to provide a wealth of mechanical information about materials and living organisms and cells. SBS microscopy is likely to play an increasingly important role in material and biological imaging.

A LOSSLESS ELECTRON BEAM MONOCHROMATOR USING THZ NEARFIELD RADIATION FOR HIGH-RESOLUTION ELECTRON MICOSCOPY

Tal Fishman[1,2], Michael Yannai[1,2], Yuval Adiv[1,2], Raphael Dahan[1,2], Alexey Gorlach[1,2], Nicholas Rivera, Kangpeng Wang[1,2], Ido Kaminer[1,2]

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Electron energy loss spectroscopy (EELS)[1] is a primary technique in transmission electron microscopy (TEM), used routinely in the chemical and structural analysis of materials down to the atomic scale. A key parameter for determining the achievable spectral resolution in EELS is the energy spread of the incident electron beam which is associated with the chromatic aberration (CA) induced by the electron source and the electron optics inside the microscope column. The conventional approach for reducing CA in TEM is using slit-based energy-filtering monochromators[1]. These techniques come at the expense of incident electron flux (i.e., they are lossy), hindering the usage of monochromators in many applications, which become limited by the inherently low electron current. One example of such application is ultrafast transmission electron microscopy (UTEM)[2] that uses femtosecond light and electron pulses in a pump-probe configuration (Fig. 1a), thus allowing nanometer and femtosecond spatio-temporal resolution microscopy. Progress towards meV-scale electron energy resolution in UTEM could promote the study of a wide range of physical phenomena[3] such as exciton dynamics, phononic vibrational resonances, and nanometric charge transport effects. However standard slit-based monochromators can not be utilized in UTEM's due to their inherent low electron beam currents that severely limit their performance.

Here we present lossless monochromation of electron pulses, based on their interaction with a single-cycle THz nearfield. As the THz source we make use of the photo-Dember[4] effect in a laser-driven InAs crystal located near the electron path (Fig. 1a). At the optimal temporal overlap, the more energetic part of the electron pulse interacts with a decelerating THz field while the less energetic part interacts with an accelerating one, resulting in a compressed energy distribution (Fig. 1b). Comparing the electron energy spectra with and without compression shows a maximal compression of the electron energy spread by 2.8-fold for 80 keV electron primary energy (Fig. 2a). This result corresponds to a 0.28 eV electron energy spread (FWHM), which breaks the current record in UTEM. Furthermore, integrating over the spectra shows that the total electron count remains constant, proving that the proposed method is indeed lossless. Theoretical modeling of the monochromation effect is performed using the charge dynamics electron microscopy (CDEM) approach[3]. The theoretical results are in good agreement with the experimental data (Figs. 2b, c). A mapping of the monocromation effect across the lateral plane, i.e. perpendicular to the electron propagation direction (Fig. 2d), shows the robustness of our technique, as the interaction occurs uniformly over a relatively wide region. Our current investigations include developing methods to increase the overall electron current and energy compression efficiency. Looking forward, further engineering of the proposed monochromator can make it compatible with current state of the art high resolution TEMs (going beyond the application to UTEM demonstrated here), thereby simultaneously achieving both high resolution and high brightness.

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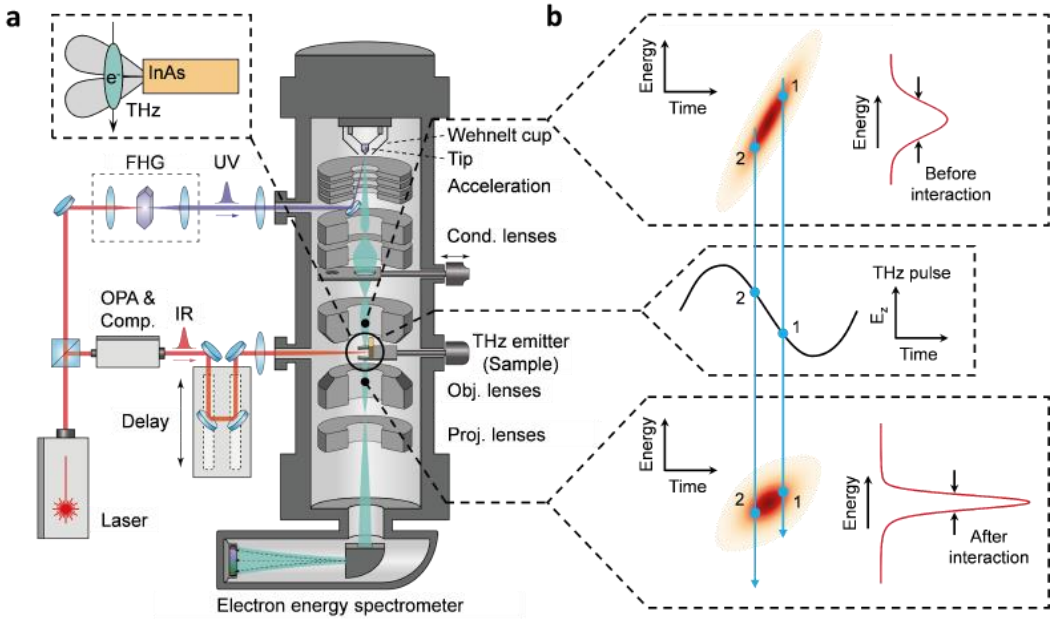

Fig. 1. Electron beam monochromator using nearfield THz radiation. (a) Illustration of an ultrafast transmission electron microscope (UTEM), depicting the UV and IR laser paths, and the TEM column. In our experiment, a 800 nm 50 femtosecond pulse (IR) irradiates an InAs crystal serving as a THz pulse emitter. A 200 fs UV pulse is guided to the TEM cathode, generating the electron pulses. The accelerated electrons travel down the TEM column, interacting with the emitted THz field (enlarged in the top-left inset). The electron energy spectrum after the interaction is analyzed using an electron energy spectrometer (EELS, bottom). **(b)** Illustration of the electron energy spectrum (right, red) and phase-space distribution (left) before and after the interaction with a time-synchronized THz pulse (center panel) conveying the lossless monochromation process.

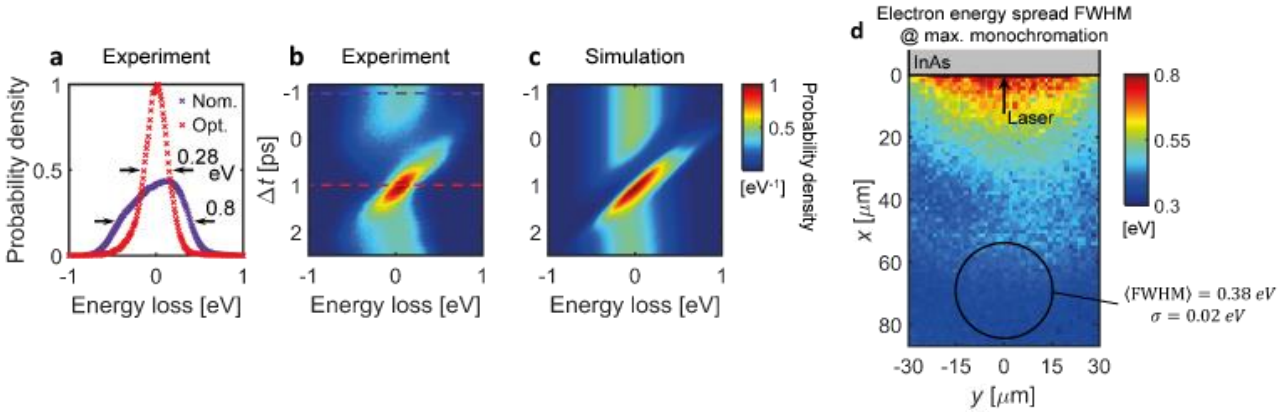

Fig. 2. Analyzing the lossless monochromator operation. (a) Electron energy spectra measured without THz interaction (purple), compared to optimal THz interaction (red). **(b)** Measured and **(c)** simulated electron energy spectra versus electron-THz relative time delay (Δt). The purple and red dashed lines in (b) correspond to the data in (a). **(d)** *x*-*y* plane map of the electron energy width. *x*=0 marks the sample face (gray box) and *x*0 is free space. The black circle illustrates a 30 μm aperture located 70 μm away from the emitter edge, inside which a high and homogeneous monochromation is achieved.

ELECTRON TOMOGRAPHY IN 4D-STEM

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Scanning transmission electron microscopy (STEM) is a popular method in materials science and an emerging technique in life science microscopy. For the latter it is often implemented in tomography, including cryo-tomography, where it can access thicker specimens than conventional wide-field imaging. The placement of one or more detectors in diffraction plane determines the type of contrast generated, e.g., bright field (BF), annular dark field (ADF) or differential phase contrast (DPC). Ideally, it should be possible to capture every scattered electron in the projected diffraction plane. This has become possible recently with the introduction of large area segmented detectors and fast pixelated cameras. We have developed a platform for driving the microscope scan and readout of two such systems under control of the open software framework SerialEM. Called SavvyScan, it appears to SerialEM as an ad hoc camera for smooth integration with the many facilities for grid navigation and automation of complex acquisition protocols, including tomography. The segmented diode (Opal, El Mul Technologies, Israel) is used in combination with conventional detectors to provide eight channels with MHz readout rates. The pixelated detector (ARINA, DECTRIS, Switzerland) provides a 96x96 pixel readout array at about 100 kHz frame rate. Using cryogenically-preserved samples of bacteriophage, we demonstrate the simultaneous generation of both angle-resolved scattering and phase contrast in tomographic reconstructions from single tilt series acquisitions. In comparison with conventional cryo-TEM imaging, the new methods are both dose-efficient and informative on materials composition.

APPLICATION OF A DIRECT ELECTRON DETECTION CAMERA FOR SHORT-RANGE ORDER CHARACTERIZATION OF AMORPHOUS MATERIALS BY ELECTRON SCATTERING

Adham Basha[1], Amit Kohn[1], George Levi[1], Lothar Houben[2], Tamir Amrani[1], Ilan Goldfarb[1]

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Direct electron detector cameras have revolutionized the field of transmission electron microscopy, especially for cryoTEM low-dose imaging of soft matter[1].

In comparison to traditional indirect electron detectors such as Charged-Coupled Devices (CCD), DEDs show an improved modulation transfer function (MTF) and detective quantum efficiency (DQE) across all spatial frequencies[2]–[4], e.g. Fig.1., as well as fast frame rates that enable single electron detection.

The benefits of these characteristics for imaging, spectroscopy and electron holography have been demonstrated previously[5], [6].

However, studies are lacking on the application of DEDs for localized characterization of short-range-order (SRO) in amorphous materials using electron scattering.

We evaluate a Monolithic Active Pixel Sensor DED (Gatan K2-summit) for the characterization of SRO in nanoscale volumes of amorphous materials, using SiO_2 and Ta_2O_5 thin films as test cases.

The performance of the detector is compared systematically to an indirect CCD detector (Gatan Ultrascan1000) using 200 keV electron scattering measurements at doses starting at ~ 500 e/Å² in order to extract the Radial Distribution Function (RDF). In addition, the effects of electron energy (80 keV), sample cooling and energy-filtering on the measured SRO of the oxides were investigated. In order to maintain parallel beam illumination and minimize multiple elastic scattering, we used nano-beam diffraction mode and samples were thinned to thicknesses lower than ~0.5 elastic mean free path (EMFP) for electron scattering [7].

We demonstrate that the advantages of the DED for RDF measurements are the improved SNR, approximately two-fold, at larger reciprocal wave-vector values (Fig.2a), which is attributed to the DQE, and fast acquisition rates (counting mode). Thus, using the DED can achieve a larger recorded maximal scattering vector,~16.5 1/Å compared to 15 1/Å for the CCD as shown in Fig.2b for the Ta_2O_5 case. Consequently, DED measurements enable to determine the coordination numbers of atomic bonds more accurately (Table 1).

Since the electron scattering data is comprised mostly of low-frequency oscillations, for which the MTF of the DED and CCD are comparable, no significant differences are observed in the extracted bond distances and angles of the amorphous oxides as shown in Fig.3.

Thus, we expect increased benefits of the DED for beam-sensitive amorphous materials for which the electron dose is limited to below ~ 50 e/Å² .

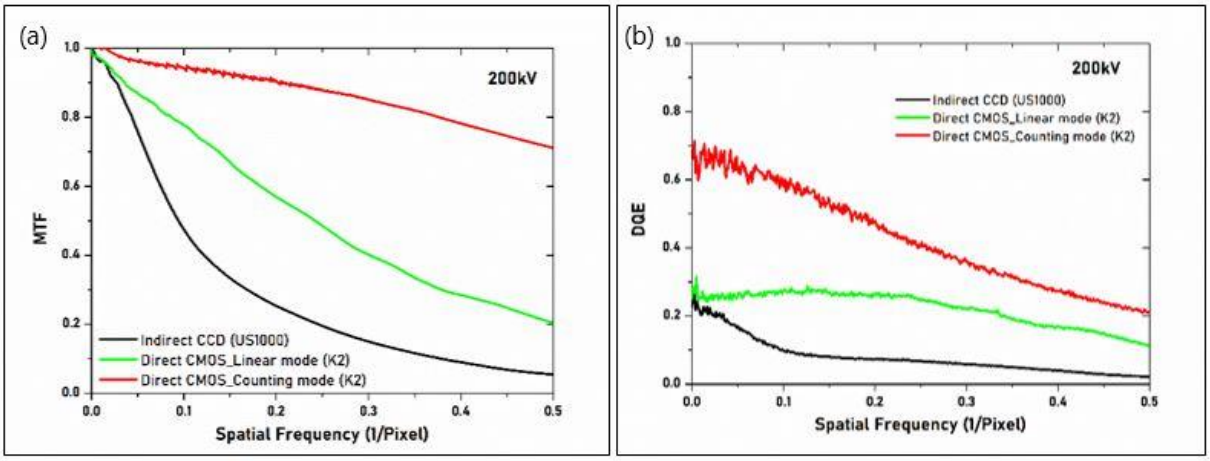

Figure 1. Measured (a) modulation transfer functions (MTF) and (b) detective quantum efficiencies (DQE) of an indirect CCD camera (Gatan US1000) and a direct MAPS detection camera (Gatan K2-summit) using acceleration voltages of 200 kV.

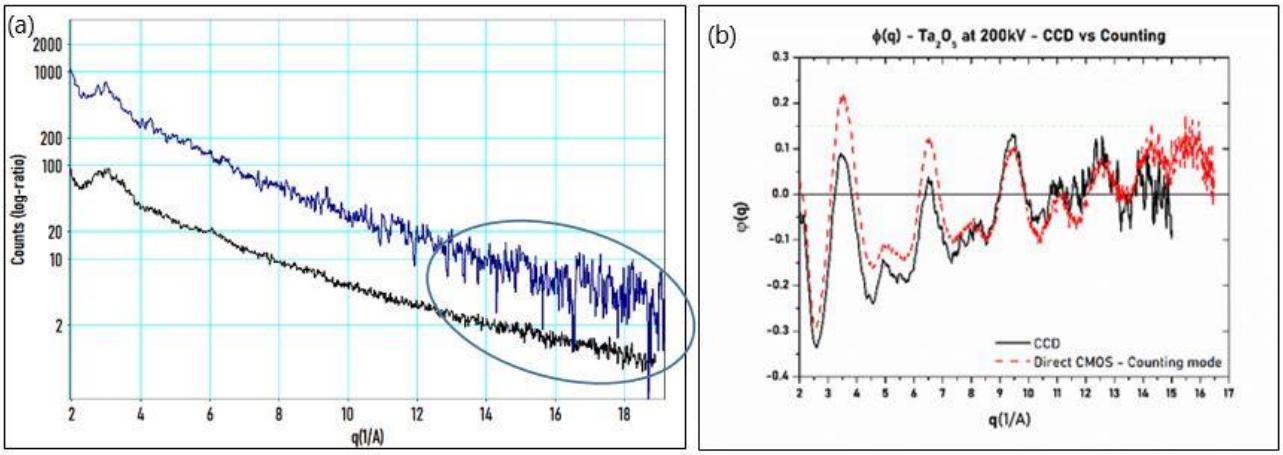

Figure 2. (a) Radial intensities at the high angle scattering range extracted from center to corner of the scattering pattern of Ta_2O_5, Showing higher noise levels in the CCD detector especially in q-range larger then $12\frac{1}{A}$. (b) Reduced intensity function $\varphi(q)$ of amorphous Ta_2O_5 acquired using 200 keV electrons and recorded with a CCD and a DED camera operated in counting mode.

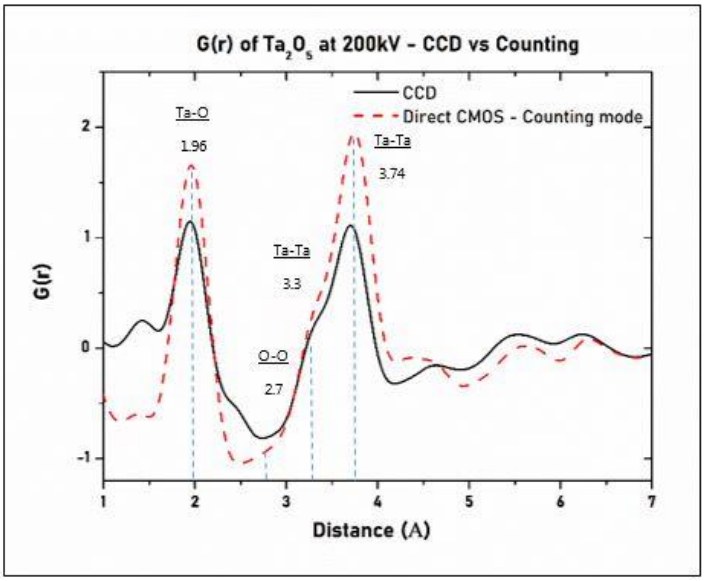

Figure 3. Reduced pair-distribution function, $G(r)$, reconstructed from 200 keV electron scattering patterns of amorphous Ta_2O_5 thin film recorded using an indirect CCD camera and a direct electron detection CMOS camera operated in counting mode.

Table 1. Measured average coordination numbers for amorphous Ta_2O_5 thin film

		C.N. (Ta-O)	C.N. (Ta-Ta)
200keV	DED	5 ± 0.7	19 ± 1
	CCD	4.6 ± 0.7	17 ± 1
80keV	DED	4.5 ± 0.7	17 ± 1

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INVITED

EELS SPECTROMETER WITH IMPROVED OPTICS AND ULTRA-HIGH SENSITIVITY ELECTRON DETECTOR FOR SHOT-NOISE LIMITED ENERGY-LOSS IMAGING AND SPECTROSCOPY

Lothar Houben

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The last two decades have seen the realization of aberration correctors for TEMs [1] and a new class of electron detectors having dramatically improved speeds and sensitivities that can approach the shot-noise limit [2]. These developments have opened the door for low-dose high-resolution electron imaging and diffraction while minimizing the radiation damage to materials, one of the biggest challenges remaining. For analytical imaging, EDS has benefitted from multi-detector setups with high-solid collection angle and frame averaging on fast detectors [3]. EELS spectrometers are transforming currently, pushing for better optics and detection capabilities. The recently launched CEOS CEFID spectrometer introduces spectroscopy with a remarkably low non-isochromaticity (NI), allowing for large collection apertures, and with long-term stability and reproducibility of optical alignments after switching between different modes of operation [4]. Flexibility over detector systems, control and scripting software, advanced user alignments, and data formats are ideal prerequisites for customized experimental setups in an academic environment. Specifically, integrating a DECTRIS ELA hybrid-pixel detector promises fast, single-electron sensitive data collection in EELS and 4D STEM at the highest dynamic range [5]. Flexible scan schemes, in combination with high detector frame rates and frame averaging without noise penalty, can circumvent traditional problems with radiation damage. Such a spectroscopy setup enables e.g. the detection of elements at low concentration even at high excitation edges in STEM EELS and energy-filtered imaging, the high SNR mapping of core-loss fine structures, the sparse diffraction mapping (4D STEM) filtered at energy loss, and the improved signal-to-background-noise ratio in low-loss EELS for bandstructure analysis or plasmonics, eventually in a momentum-resolved manner [5,6]. Here, I report on the installation of such a new EELS system on the double-corrected Titan Themis-Z at the Weizmann Institute of Science, and on initial results of energy-filtered scanning diffraction and low-loss spectroscopy.

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INVITED

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A NOVEL POLYCISTRONIC METHOD TAILORED FOR ENGINEERING SPLIT GECIs

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We assessed the feasibility of using stop-codons as means to obtain polycistronic expression in eukaryotic cells. We find robust expression of different open reading frames (ORFs), when these are cloned in-sequence and simply separated by stop codons (in- or out-of-frame), by heterologous expression systems and primary neurons. This method further supports polycistronic expression of three stop-codon-separated ORFs, which guided us to develop a technicolor Genetically-Encoded Functional Rainbow Indicators; GEFRIs for monitoring cellular morphology, neuronal firing and cellular stress, concomitantly. These findings further guided us to develop a new technique we denote SPLIT—Stop-codon mediated Polycistronic Induction in HeTerologous expression systems— for rapid and easy development of fragmented proteins by the simple introduction of stop codons within ORFs. We first validate the SPLIT method by generating several new split-GFP variants, then engineer a palette of functional split-GCaMP6 variants and, lastly, generate a split ca2+-probe localized at ER and mitochondria junctions. Together, we explore non-canonical translation mechanisms and show these to be highly prevalent in various cell types. We harness translation re-initiation to express multiple ORFs, to engineer rainbow indicators and to swiftly produce functional split-proteins and probes.

QUANTITATIVE EVALUATION OF HUMAN GLIOMA NANOBIOPSY

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Nanobiopsy is a platform for accurate, minimally invasive, label-free mapping of the molecular profile of a tumour tissue. Ordered arrays of conical-shaped porous silicon nano-needles are fabricated and pressed onto the tissue, to harvest molecules with little perturbation of cell activity and thus generating a molecular replica of the tissue. While we are able to generate a tissue replica, it is not clear whether and how much the molecular profile of the replica corresponds to that of the tissue. As a proof of principle, We used a dataset containing 27 matched mass spectrometry images of tissue and replica pairs of human glioma from 23 patients. We developed a multi step preprocessing pipeline to create a common and meaningful representation of a molecular signature across tissues and replicas. We found that the molecular signatures of matching tissue and replica were highly similar indicating that the replica can be used as a reliable model of its corresponding tissue. Finally, we demonstrated success in using these molecular signatures for machine learning prediction of the glioma grade. The classification performance of tissues and replica was comparable indicating the potential applicability of the nanobiopsy platform. These are the first steps toward future use of nanobiopsy in the clinic that will reduce invasiveness, and enable tumour-specific treatment based on longitudinal replica sampling from the same tissue under different treatments.

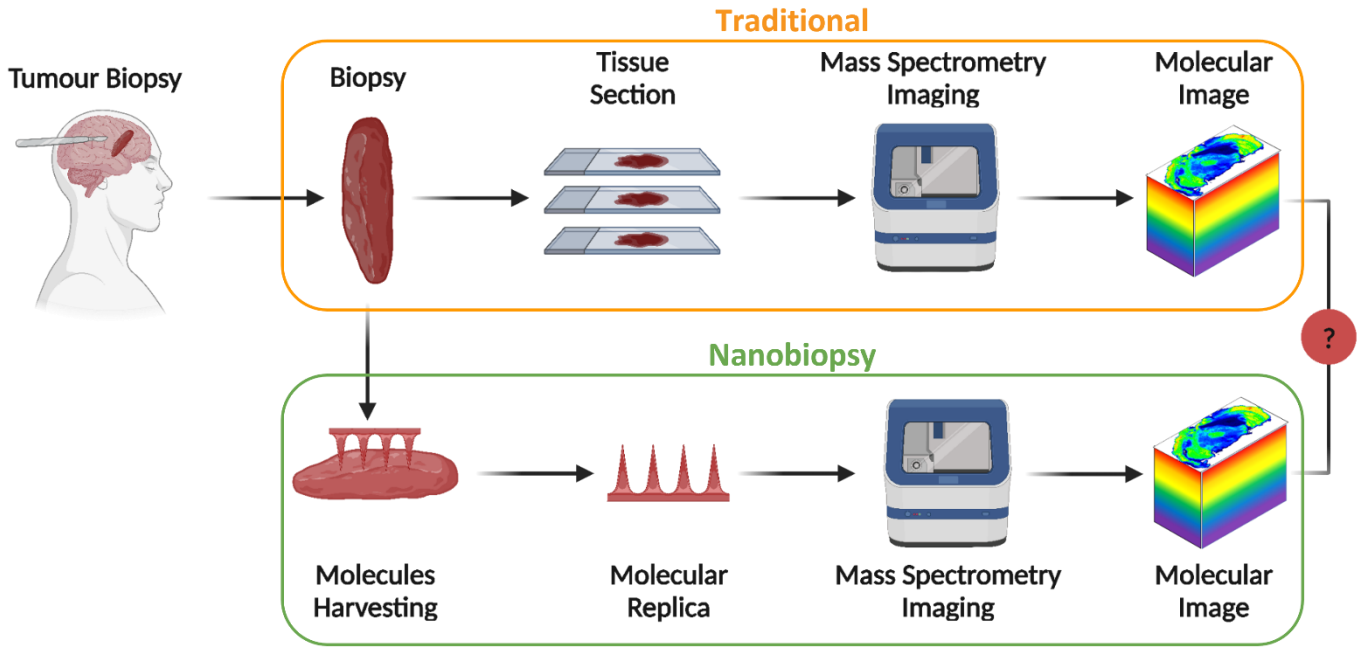

Figure 1: Comparison of the nanobiopsy pipeline with the traditional pathology pipeline. (Top) Traditional pathology pipeline that produces a molecular image of a tumour tissue. (Bottom) Nanobiopsy pipeline that produces a molecular image replica of a tumour nanobiopsy. Research question (Right): does the molecular profile of the replica correspond to that of the tissue?

DEVELOPMENT OF CORRELATIVE FIB-SEM TO STUDY MEMBRANE REMODELING

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Focused ion beam-scanning electron microscopy (FIB-SEM), provides ultrastructural information from large volumes with high resolution in 3D, delivering a holistic context to biological phenomena. Combining light and electron microscopy (LM; EM) to form correlative light and electron microscopy (CLEM) workflows utilizes the advantages of LM to target and follow rare and dynamic events with the ultrastructural information from EM. However, CLEM workflows combining FIB-SEM lag behind the development of TEM based workflows[1]. My research focuses on developing a CLEM pipeline that fits a verity of tissues and organisms, allows correlation of 3D LM and FIB-SEM datasets and works at room temperature and under cryogenic conditions.

To accomplish this goal, I had to overcome several challenges, including 3D image registration of two very different volumes and resolutions, introduction of fiducial markers to be able correlate datasets with high precision into the volume, and optimization of the sample preparation, milling and imaging conditions to preserve the fluorescent signals and obtain high contrast and reproducible imaging. Overcoming these challenges have allowed me to make several seminal contribution in general cell biology and specifically in the volume EM field. Using 3D CLEM we were able to target specific stages during exocrine secretion and unravel a new mechanism of secretion via membrane sequestration and membrane crumpling[2]. In parallel, I developed a cryo-3D-CLEM workflow that utilizes organelles as markers for cryo-FM and cryo-FIB-SEM correlation with sub-micron accuracy[3,4]. To my knowledge, this was the first demonstration of 3D image registration of cryo-fluorescence and cryo-FIB-SEM tomography data. I applied the same imaging, correlation and sample preparation principles to resin-embedded FIB-SEM samples, and expanded to various systems, such as the C.elegans nervous system (unpublished), human placenta (unpublished), and additional tissues in Drosophila. In the later, I used the secretory vesicles as fiducial markers for correlation, resulting in the discovery of BAR-domain protein that localizes to the actual site of vesicle fusion with the apical membrane (submitted manuscript; Figure 1).

A strong and unique aspect of my work is using FIB-SEM as a tool for quantitative biology, which is and inherent advantage of visualizing large volumes with higher throughput (originating from reproducible sample preparation and fluorescence-based targeting), yielding statistics from the ultrastructure. In my ongoing project, I utilize the 3D-CLEM pipeline I developed with image analysis tools to elucidate the function of vesicular pseudopodia in exocrine secretory vesicles. Owing to the increased throughput of the 3D-CLEM experiments, I gathered ultrastructural parameters from around 100 vesicles from 3-4 individuals and showed that that pseudopodia are polarized towards the apical membrane (Figure 2). My goal is to continue developing cutting-edge workflows using FIB-SEM as a primary tool, which has become my passion, and future career path.

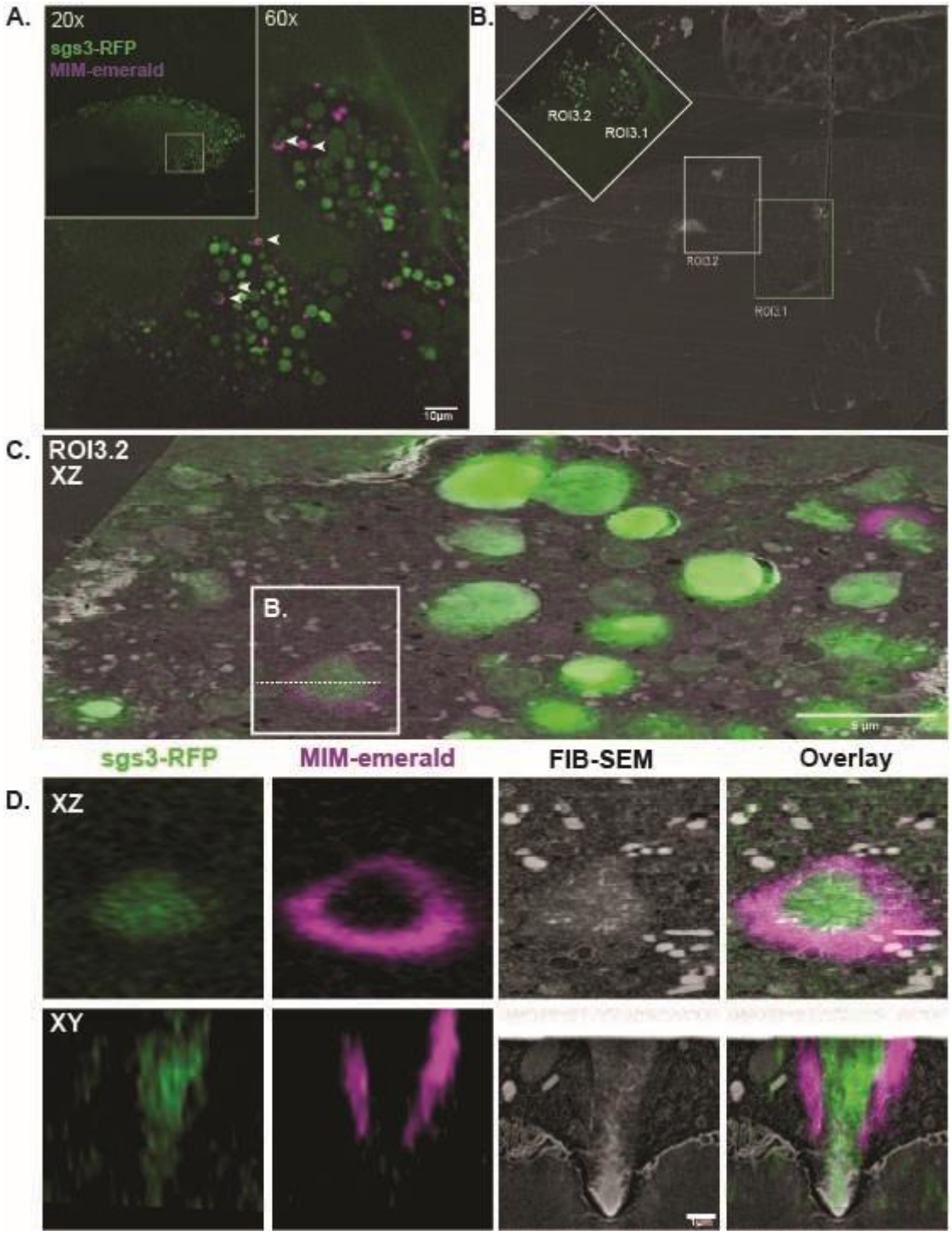

Figure 1: MIM-emerald localizes to nearly fusing vesicles.

Up-left: an overview of a gland after sample preparation for FIB-SEM. The main micrograph depicts a region of interest with two cells, in which MIM-emerald (magenta) form rings or semi-rings around secretory vesicles (white arrows; vesicle's labelled cargo: sgs3-RFP; green). B. SEM micrograph show the surface of the same sample, highlighting cells on interest (ROI3.1 and ROI3.2). Small box: 60x image from A. in the right orientation with respect to the SEM. C. Overlay of the XZ FIB-SEM plane with transformed MIM-emerald (magenta) and sgs3-GFP (green). The correlation was performed using affine transformation with 16 fiducial markers, yielding an error prediction ranging between 0.880-1.3 µm. D. Close-up micrograph showing MIM-ring localized to a vesicle that is poking the apical membrane from both XZ, and XY FIB-SEM planes.

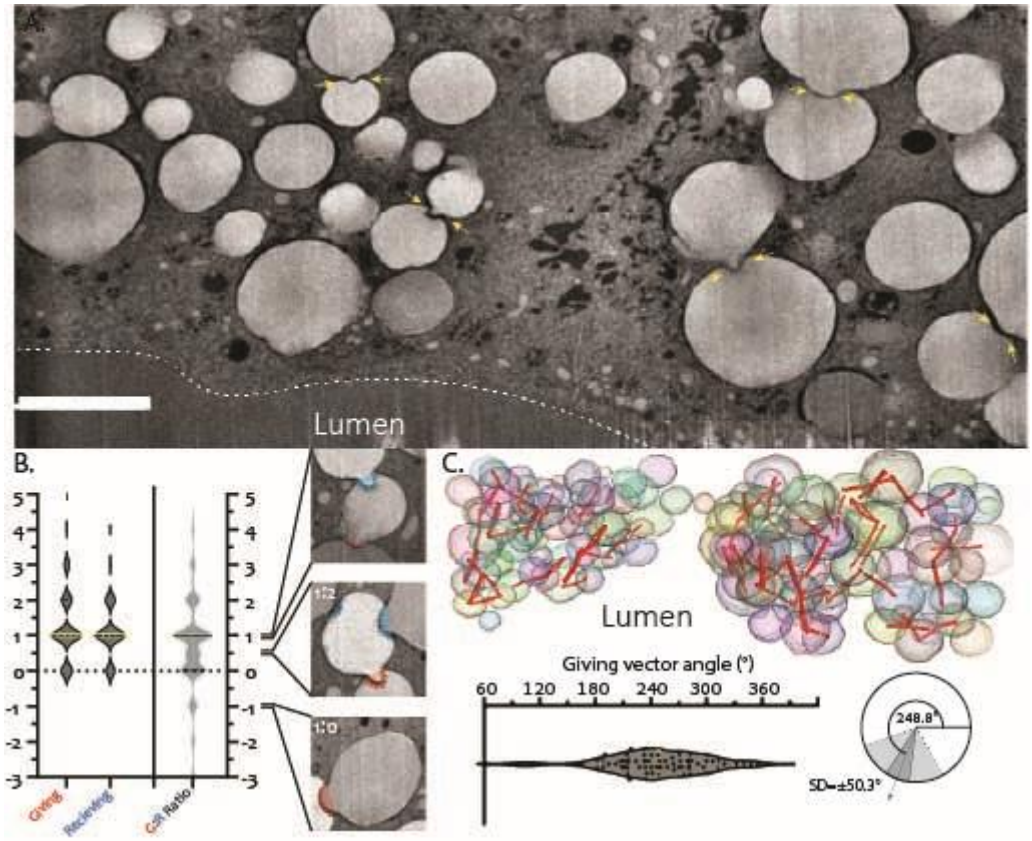

Figure 2: FIB-SEM used as a tool for statistically-significant ultrastructural analysis:

A. Cross-section form Drosophila larval salivary gland, showing the pseudopodia (yellow arrows) with respect to the apical surface (dashed line). B. Quantification of the number of interacting partners per secretory vesicle, showing that most vesicles have a 1:1 ratio between pseudopodia given and received (N=4, n=107). C. Polarity analysis in 3D showing the secretory vesicles in the whole volume in A. (assorted colours) and the interactions between them (red surfaces). Below – quantification of the giving pseudopodia vectors showing an average angle of 248.8º ± 50.3 º (SD: light grey in the angle plot; dark grey indicates the 95% confidence interval for the actual average) n=66.

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MACHINE-LEARNING AIDED QUANTIFICATION OF CELL CULTURES FROM PHASE-CONTRAST MICROSCOPY IMAGES

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The advances in machine learning (ML) software availability, efficiency, and friendliness, combined with the increase in the computation power of personal computers are harnessed to rapidly and (relatively) effortlessly analyze time-lapse image series of adherent cell cultures, taken with phase-contrast microscopy (PCM). Since PCM is arguably the most widely used technique to visualize adherent cells in a label-free, noninvasive, and nondisruptive manner, the ability to easily extract quantitative information on the area covered by cells, should provide a valuable tool for investigation.

We demonstrate two cases, in one we monitor the shrinking of cells in response to a toxicant, and in the second we measure the proliferation curve of mesenchymal stem cells (MSCs).

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INVITED

SINGLE-MOLECULE OPTICAL MICROSCOPY: FROM PROTEIN DYNAMICS TO T-CELL MEMBRANES

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Chemical and Biological Physics, Weizmann Institute of Science, Rehovot, Israel

The optical microscope has become an impressively versatile tool for studying biophysics at the single-molecule level. In this lecture we will discuss two exciting directions of research from our lab.

In the first project, we apply single-molecule microscopy to track the intramolecular dynamics of proteins with an exquisite time resolution. In particular, we are interested in protein machines, which process energy in order to perform a specific biological task. We have recently developed a novel method, which registers the arrival times of photons emitted from a protein and uses this information to trace conformational dynamics even on the microsecond time scale (1). We are using the new technique to study the dynamics of several protein machines and understand the relation of the ultrafast motions observed to the biological function (2, 3). Based on these studies, we propose a novel two-time-scale paradigm for the activity of protein machines: fast fluctuations take place on the microsecond-millisecond time scale, while on a slower time scale free energy is invested in order to push the system out of equilibrium and drive functional transitions.

The second project involves Microvillar Cartography (MC), a single-molecule microscopic method we developed in order to map proteins with respect to the topography of cellular membranes. The surfaces of many cells are not smooth, but are rather covered with various protrusions such as microvilli. These protrusions may play key roles in multiple cellular functions, due to their ability to control the distribution of specific protein assemblies on the cell surface. We used MC to study T cells and demonstrated that the important T-cell receptor and several of its proximal signaling proteins reside on microvilli, while other proteins are excluded from these projections (4, 5). These results have indicated that microvilli can function as key signaling hubs for the initiation of the immune response.

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INVITED

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TELLING LEFT FROM RIGHT USING ELECTRON MICROSCOPES

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Chemistry, Bar-Ilan University, Ramat Gan, Israel

In 1848 Louis Pasteur reported his findings on the separation of a racemic mixture of chiral molecules during their crystallization from the solution phase. Left and right molecules crystallized separately in crystals that exhibited left- and right-handedness at the macroscopic level as well, as portrayed by their overall chiral morphology. This monumental experiment is considered by many to have set the early foundations of modern stereochemistry.

Later, in the 20th century, a key question regarding determination of absolute configurations of molecules, and relations between microscopic and macroscopic handedness in chiral crystals became an ongoing challenge for chemists and crystallographers. This challenge is often addressed using chemical assays with chiral additives and x-ray crystallography.

More recently, the advent of electron microscopy led to many studies of crystal structures using powerful high-resolution techniques. Yet, the problem of handedness often remains untreated and elusive in these studies. In my talk I will describe our recent work on nanoscale systems that exhibit chirality at the atomic arrangement, as well as morphology, and simple approaches we take for resolution of absolute handedness using electron microscopy.

CORRELATION BETWEEN CHARGE TRANSPORT AND LATTICE DYNAMICS IN La- AND Y-doped Ca_2MnO_4 PEROVSKITES

Amram Azulay[1], Marwan Wahabi[1], Yuriy Natanzon[1], Yaron Kauffmann[1], Yaron Amouyal[1]

Materials Science and Engineering, Technion-Israel Institute of Technology, Haifa, Israel

Understanding the electrical conduction mechanisms of transition metal oxides is of prime technological importance due to their potential in next-generation electronic devices. Here, we investigate charge transport kinetics and elastic behavior of bulk polycrystalline $Ca_{2-x}R_xMnO_4$ oxides, where R = Y or La and $0.01 \leq x \leq 0.20$. Employing high resolution transmission electron microscopy (TEM) along with energy-dispersive x-ray spectroscopy (EDS), we show that both Y and La substitute for Ca sites. Using integrated differential phase contrast (iDPC), we are able to better resolve the atomic structure in terms of contrast; its advantage over the conventional high angle annular dark field (HAADF) signal, especially for light atoms such as oxygen, is evident. We analyze the temperature dependent electronic transport properties considering the small polaron hopping model in combination with first-principles calculations of elastic properties, indicating tight correlation between charge transport and lattice elasticity. Interestingly, the polaron hopping energies of Y- and La-doped compounds attain minimum values of 60 and 73 meV, respectively; this peculiar dependence is explained in terms of polaron-polaron separation and mutual electrostatic interactions across the Mn-O-Mn conduction path. Remarkably, we find that the lattice shear and Young moduli, Grüneisen parameters, Debye temperatures, and sound velocity also exhibit minimum values with respect to La and Y amount. A fundamental model for elastically isotropic materials indicates that the elastic energy induced by small polarons corresponds with the polaron hopping energies. Our study shows how charge carrier dynamics are strongly coupled with elastic properties, implying that the latter can be used to predict charge carrier mobility in oxide semiconductors.

ELUCIDATING THE CONTROL MECHANISMS OF ORGANIC BIO-CRYSTALLIZATION

Avital Wagner[1], Alexander Upcher[2], Raquel Maria[2], Benjamin Palmer[1]

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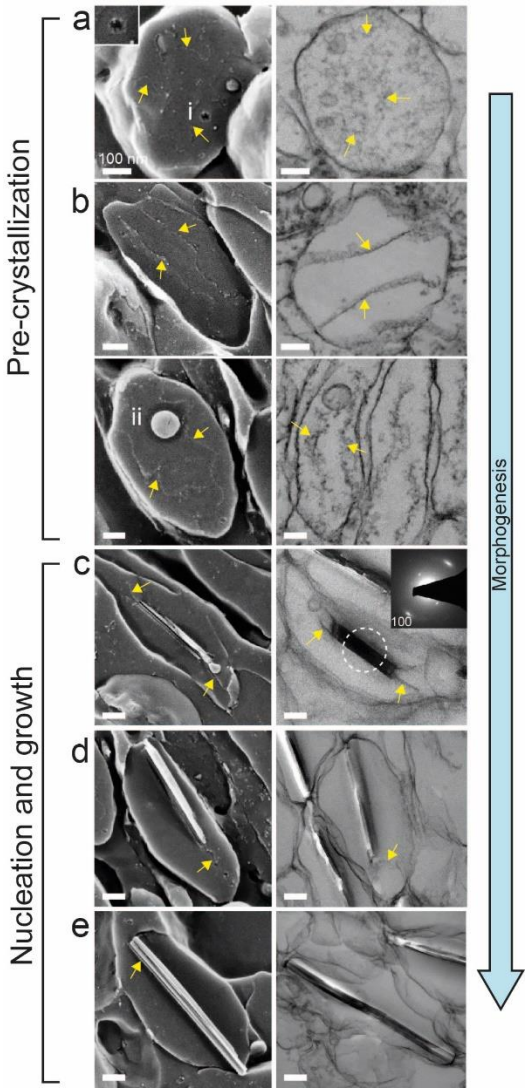
Many spectacular optical phenomena in animals are created by the interaction of light with crystals of small organic molecules. Examples include the silvery reflectance of fish scales, the brilliant iridescence of crustaceans, and the mirrored eyes of scallops. Guanine, best known as one of the DNA nucleobases, is also the most widespread molecular crystal in biology. The crystals are composed of π-stacked, hydrogen-bonded molecular layers, and their optical utility derives from their extreme in-plane refractive index (n = 1.83). Most biogenic guanine crystals are broad and thin, preferentially expressing the highly reflective face to maximize reflection. In contrast, guanine crystals grown in vitro from aqueous solutions grow preferentially along the π-stacking direction resulting in the expression of low-index (~1.45) crystal faces. Despite the well-understood optics of guanine-based systems, much remains unknown about how guanine crystals form, how their morphology is controlled, how complex photonic architectures are assembled, or the biochemical regulation underlying crystallization. We aim to answer these questions by following crystal formation in developing organisms using cryogenic scanning (cryo-SEM) and transmission electron microscopy (TEM).

Initially, we followed the morphological and structural evolution of guanine crystals in the integument of white widow spiderlings (Wagner et al. Adv. Mater. 2022, 2202242). This study revealed that, despite their final prismatic shape, these crystals grow by the formation of individual platelets which co-orient by a progressive relaxation of stacking faults and twinning defects. The final prismatic single crystals appeared to be composed of 25 nm crystal plates, preferentially expressing the highly reflective crystal face, interleaved with organic fibrils.

To understand the control mechanism used by organisms to form plate-like guanine crystal morphologies, we examined scallops that have hundreds of eyes, each containing a concave mirror made of tessellated layers of thin square guanine crystals. Guanine crystals form inside iridosome vesicles within chromatophore cells called iridophores. To investigate iridosomes prior to crystal formation we looked at juvenile scallop eyes by cryo-SEM and TEM, and found the mirror is composed of a variety of morphologically distinct spherical and ellipsoidal iridosomes (Wagner et al. Nat. Commun. 2023, 14, 589). Based on ultrastructure features, it was possible to derive the morphogenesis of iridosomes. We showed that two pre-assembled, intraluminal fibrils elongate the iridosomes so that their long axis is oriented perpendicular to the incident light and a small crystal nucleates between these fibrils. By in situ electron diffraction (ED) on ultra-thin tissue sections, the crystal was confirmed as β-guanine and its orientation was determined. The guanine crystal grows in the hydrogen-bonding direction along the fibrils, which become tightly bound to the (100) crystal faces.



To further investigate the nature and function of the intraluminal fibrils, we performed TEM tomography on tissue sections from juvenile scallop eyes. The three-dimensional tomographic reconstructions revealed that the two intraluminal "fibrils" are in fact 2D sheets that likely provide an interface for the planar face of the guanine molecules to nucleate. The macromolecular sheets define a volume within the iridosome in which the guanine crystals emerge. Moreover, they cap the highly reflective faces of immature guanine crystals, inhibiting growth along the π-stacking growth direction. Crystal growth then occurs preferentially along the sheets in the hydrogen-bonded direction to generate highly reflective plates.

In addition to templating guanine nucleation and growth, the sheets play a key role in controlling crystal orientation and organization. By mapping the orientation of sheets across different regions of the juvenile mirror, we determined that even before nucleation, the sheets closely align with the curvature of the mirror. Thus, the crystal orientation is "pre-programmed" into the early iridosomes.

In conclusion, iridosome morphogenesis from juvenile scallop eyes coupled with the internal plate-like structure of prismatic crystals found in spiders, show that fibrillar sheets provide an interface for nucleation, and direct the growth and orientation of the plate-like guanine crystals. Controlling the number, spacings, and length of these sheets may provide a means of controlling crystal morphology. These biological systems provide a testament to the effectiveness of macromolecular templates in molecular crystal growth, which we hope to harness to create novel molecular materials with desired properties.

SCANNING ELECTRON NANOBEAM DIFFRACTION AT LOW DOSE FOR STRUCTURE MODELING OF NANO-OBJECTS

Daniel Khaykelson[1], Eytan Balken[2], Yael Levi-Kalisman[3,4], Uri Raviv[2,3], Lothar Houben[5], Boris Rybtchinski[1]

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Recent advancements in electron detectors and aberration correction have significantly improved the capabilities of electron diffraction-based methods, such as nano/angstrom-beam diffraction and four-dimensional Scanning Transmission Electron Microscopy (4D-STEM). With single electron sensitivity, scanning diffraction with a finely focused beam is an ideal low-dose technique to record quantitative information of nanometer-sized objects in reciprocal space. However, the quantitative analysis of diffraction data from imperfect crystalline samples remains challenging, and accurate post-acquisition processing combined with forward simulation is required to extract structural information. In this contribution, we will demonstrate 4D-STEM results collected on an EMPAD detector (Electron Microscope Pixel Array Detector) with small convergence angle for high momentum resolution, spanning from the more traditional high-angle scattering towards the low angle scattering regime. Modeling of the diffraction data was achieved through forward calculation using a new simulation framework. This framework specifically handles aperiodic molecular arrangements, accurately assessing scattering intensities at the low-angle scattering regime. Exemplary results are shown for test cases of near-ideal graphene, twisted bilayer graphene, ordered Au144 clusters, and quasi-amorphous Au102 clusters. The twisted bilayer data cannot be modeled as two rotated graphene monolayers, as the modeling shows an additional distortion to the hexagonal phase that must be added. Au144 clusters are crystalline with FCC structure barely 2 nm in diameter. We tested and refined various structural models and showed their different orientations on the grid. Finally, we analyzed the assembly of quasi-amorphous Au102 clusters to study their interaction and organization in the small-angle regime (~1.2-0.3 nm^{-1}). Our results demonstrate that scanning nanobeam diffraction in combination with forward modeling into the low-angle scattering range is an extension to existing diffraction techniques for local order investigation on the nanometer scale.

INVITED

DIMENSIONALITY IN PEROVSKITE - NANOSTRUCTURES AND SOLAR CELLS

Lioz Etgar[1]

The Institute of Chemistry, Casali Center for Applied Chemistry, The Hebrew University of Jerusalem,, Jerusalem, Israel

Perovskite is a promising light harvester for use in photovoltaic solar cells. In recent years, the power conversion efficiency of perovskite solar cells has been dramatically increased, making them a competitive source of renewable energy. In this talk I will discuss new directions related to two-dimensional organic inorganic perovskite bulk and nanostructures and their applications.

In low dimensional systems, stability of excitons in quantum wells is greatly enhanced due to the confined effect and the coulomb interaction. The exciton binding energy of the typical 2D organic-inorganic perovskites is up to 300 meV and their self-assembled films exhibit bright photoluminescence at room temperature.

** In this work we will show the dimensionality in the perovskite structure. The 2D perovskite structure should provide stable perovskite structure compare to the 3D structure. The additional long organic cation, which is added to the perovskite structure (in the 2D structure), is expected to provide hydrophobicity, which will enhance the resistivity of the perovskite to humidity. Moreover we will demonstrate the use of 2D perovskite in high efficiency and high voltage solar cells.

** Hybrid perovskite is used mainly in its “bulk” form in the solar cell. Confined perovskite nanostructures could be a promising candidate for efficient optoelectronic devices, taking advantage of the superior bulk properties of organo-metal halide perovskite, as well as the nanoscale properties. In this work, we present facile low temperature synthesis of two-dimensional (2D) lead halide perovskite nanorods (NRs). In addition, by alternating the halide composition, we were able to tune the optical properties of the NRs. By varying the ligands ratio (e.g. octylammonium to oleic acid) in the synthesis, we were able to provide the formation mechanism of these novel 2D perovskite NRs.

** The quest for novel perovskite compositions in the nano-scale is significantly important. This work reports on a mixed-cation system of RbxCs1-xPbX3 (where X=Cl or Br) nanoparticles. The absorption of the nanoparticles is tunable in the near ultra-violet and visible regions between ~ 395-525 nm for RbxCs1-xPbX3 (x=0 to x=0.8 and X=Cl or Br). The photoluminescence quantum yields (PLQY) of the mixed Rb+/Cs+ nanoparticle systems are comparable to the PLQY of CsPbX3 nanoparticles. Interestingly the attempt to synthesize Cl- and Br-based nanoparticles with high Rb+ content succeeded, although possessing low tolerance factors. We conclude that these mixed Rb+/Cs+ nanoparticles are more adjustable to structural distortions caused by the cation substitutions than their bulk counterparts, what opens a way towards developing more advanced mixed-ion perovskite compositions in the nano-scale.

P-01

THE MOLECULAR BASIS OF CRYSTALLIZATION OF ISOXANTHOPTERIN CRYSTALS

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Highly reflective molecular crystals are used in many animal coloration and visual systems. Organisms exquisitely control the shape and assembly of these crystals to generate a large variety of different optical effects. However, almost nothing is known about the genes and proteins which control crystallization. Crystals of isoxanthopterin are found in reflective structures in the eyes of decapod crustaceans [1, 2]. Recent studies have shown that such crystals grow inside specialized cells called iridophores, inside a special organelle [3] [2]. We seek to elucidate the biological control mechanisms underlying crystallization. To do so, we performed a combined transcriptomic/proteomic study on a model species of freshwater prawn Machrobrachium rosenbergii .

In M. rosenbergii, we perform genetic mining of RNAseq libraries constructed at specific time points during embryo development that correlate with the emergence of crystals during ontogeny formation (Fig. 1). Crystals (indicated by the presence of birefringence in polarized micrographs), emerge after 10 days of embryognesis in the iridophore cells (Fig. 1). In the larval organism, these crystals are used as a camouflage reflector to conceal the animal from view [2]. Candidate transcripts that are upregulated during crystal formation will then be silenced by CRISPR in early-stage embryos to ascertain the function of the related genes to the crystallization process. This strategy utilizes a recent proof-of-concept CRISPR protocol published on M. rosenbergii embryos [4]. Resulting phenotypic changes in the crystal morphology will be elucidated by cryo-SEM imaging in comparison with wild-type developing animals. This transcriptomic approach is supported by extraction of structural proteins directly from the mature crystal-forming organelles. This proteomic approach will further resolve the list of possible gene candidates utilized for CRISPR editing. Preliminary results show a 13 possible of proteins candidates within the crystal organelle that are intrinsically associated with the crystal. We are currently using the CRISPR system and ds-RNA injections to examine the role of those proteins and other selected genes to the crystal formation.

Fig. 1. Optical micrographs of M. rosenbergii embryos during development 6 distinct time points were investigated viaRNA extraction in correlation with crystal emergence starting from day 9 post-fertillization (No eye) to day 16 (fully developed eyeshine) post-fertilization.

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P-02

SPECTRAL IMAGING OF BREAST CANCER BIOPSIES FOR MULTIPLEX BIOMARKERS DETECTION

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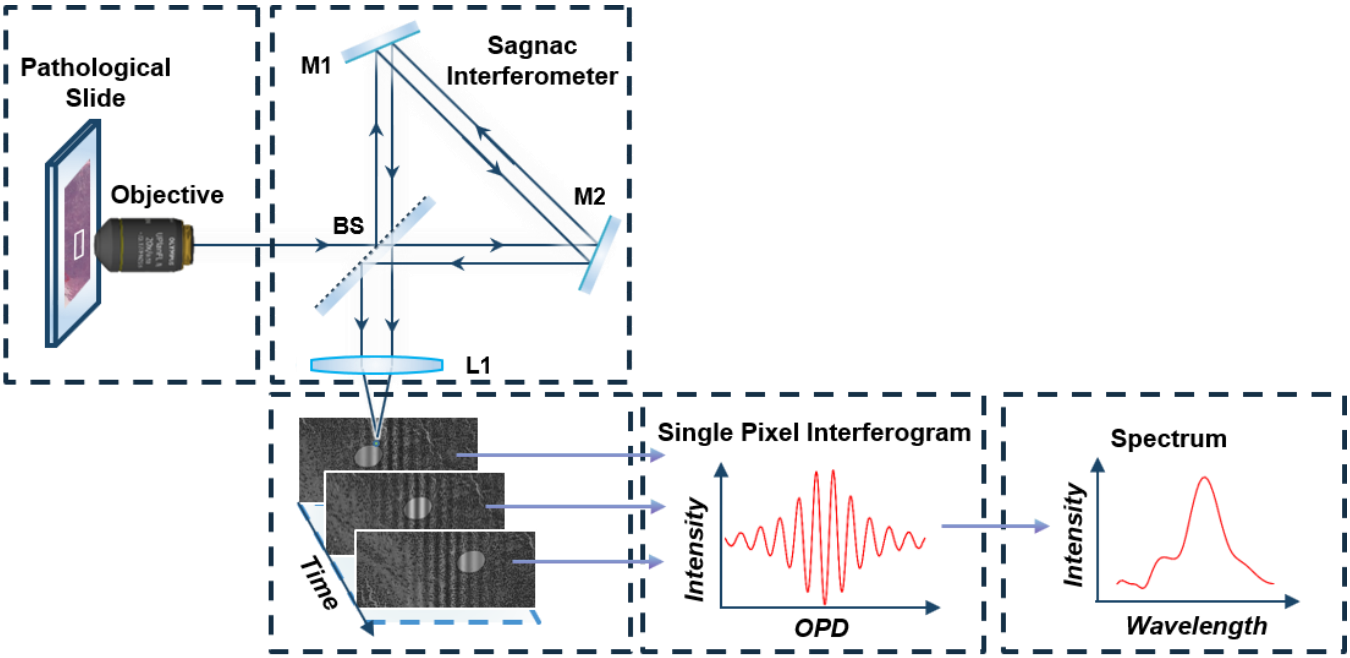
Precision medicine has revolutionized modern approaches to cancer treatment. Personalized drugs are effective only for a fraction of patients, which requires screening of biopsies so that the appropriate drugs can be prescribed to patients. One of the most common approaches for the characterization of biopsies utilizes the labeling of biomarkers by fluorescent molecules that are then imaged under a microscope. The accuracy of the clinical diagnosis increases as more data is collected, emphasizing the need for an efficient and practical method to detect multiple biomarkers. Due to optical and biological limitations, labeling and imaging of multiplex samples presents a challenge. Current methods measure fluorochromes sequentially, often leading to time-consuming and noisy measurements.

Here we present a novel method for efficient identification of multiple biomarkers by using a novel spectral imaging optical system on breast cancer biopsies. Imaging was performed using a Fourier spectroscopy system which is based on a Sagnac interferometer creating an optical path difference (OPD) between beams that merge and interfere on the detector, generating an interferogram. The signal collected is Fourier-transformed allowing the retrieval of a spectrum for each pixel scanned.

We performed an immunohistochemistry protocol for staining and detecting multiple protein-based biomarkers. The stained biopsies were then spectrally imaged, using an optimized optical filter. This allowed for the generation of a spectral signature of the sample which provided the basis for the calculation of molecular profiles for each cell in the imaged tissue. These results can be used as a clinical tool by providing pathologists with the cancer profiles so that the most suitable medicine can be assigned for treatment. While we studied breast cancer biomarkers, our approach can be adapted to other types of solid tumor cancers.



P-03

RNA RELATED NUCLEAR PROCESSES MODULATE THE ASSEMBLY OF CYTOPLASMIC RNA GRANULES

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Stress granules (SGs) are cytoplasmic assemblies, formed under various stress conditions as a consequence of translation arrest. SGs contain RNA binding proteins, ribosomal subunits and mRNAs. It is well known that mRNAs contribute to SG formation, however, the connection between SG assembly and nuclear processes which involve mRNAs is not well established. Here, we examine the effects of transcription, splicing and nuclear export inhibition on the assembly of SGs. Specifically, we demonstrate that inhibiting splicing by targeting SF3B1, or using specific splicing inhibitors reduces the formation of canonical SGs. We also find that the splicing inhibitor madrasin promotes the assembly of RNA granules, and that splicing inhibitors have an effect not only on SGs, but also on other RNA granules such as P bodies (PBs). Strikingly, inhibiting mRNA export from the nucleus to the cytoplasm suppresses SG assembly, yet does not affect PB formation. We further investigated the effect of adding synthetic mRNAs to the cytoplasm, and found that an abundance of cytoplasmic mRNA, without applying additional stress, can directly lead to SG formation. We show that the assembly of these granules requires the activation of stress-associated protein synthesis pathways. Finally, we demonstrate that adding an excess of mRNA to cells that do not have active splicing, promotes SG formation under stress conditions, emphasizing the importance of the abundance of newly transcribed mRNA in the assembly of SGs.

P-04

VISUALIZING MEMBRANE INTERACTIONS USING IN-CELL CRYO-ELECTRON TOMOGRAPHY

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The silica cell wall formation in diatoms, a widespread group of unicellular microalgae, is a spectacular example of biological control over mineral formation. Diatom silicification occurs intracellularly in a membrane-bound organelle responsible for silica precipitation and morphogenesis. Despite many years of research, the inorganic-organic interactions that drive silica formation inside this organelle are unclear. This is due mainly to the limitations of traditional TEM techniques in elucidating the structural motifs of this organelle. Here we collected cryo-electron tomography datasets of cryo-FIB milled lamellae from diatom cells at various stages during cell wall formation. We visualize the mineral formation process in-situ with nanometer-scale resolution and reconstruct a timeline of mineral formation inside the cell. Our observations show that the silicification occurs in a highly confined lumen, bordered by the organelle membranes, which are in very close proximity to the plasma membrane. The plasma and organelle membranes interact via membrane contact sites, possibly facilitating continuous transport of lipids from the plasma membrane to the growing organelle, and building blocks for mineralization. These membrane-membrane interactions are manifested in the curvature of the distal organelle membrane, which molds the silica. Our findings reveal a new mechanism that regulates silica growth and shaping through membrane crosstalk.

P-05

MIGRATING AND PROLIFERATING STUDIES OF MESENCHYMAL STEM CELLS USING MACHINE-LEARNING PROCESSING OF PHASE-CONTRAST IMAGES

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Mesenchymal stem cells (MSCs) are multipotent cells with the ability to self-renew and differentiate into a number of cell types. Since the precise cues leading to MSCs' differentiation into various lineages are not well understood, following the cells' dynamics in a non-invasive and non-disrupting manner is imperative. Thus, we are following MSCs in their native form using Phase-Contrast microscopy. Subsequently, using Machine Learning, we are extracting quantitative proliferation (density) curves. Additionally, using movies of crawling MSCs, we are using Optic Flow approaches to extract velocities and angles of locomotion of the cells. The velocities as a function of cell density curves are universal for non-differentiating cells, however, may change along a differentiation pathway that the cells may take. This may aid in identification of the differentiation onset, in a continuous and non-invasive way.

P-06

UNRAVELING THE MOLECULAR MECHANISM UNDERLYING URIC ACID CRYSTAL FORMATION IN MEDAKA LEUCOPHORE CELLS

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In nature, colors can arise through the absorption of light by pigment molecules or the interaction of light with nanoscale crystalline materials, known as structural colors. Structural colors are prevalent in the animal kingdom from unicellular to multicellular organisms, serving a diverse range of optical functions such as vision, camouflage, and astonishing coloration in marine animals and chameleons. Leucophores are specialized cells containing uric acid (UA) crystals that can synthesize, transport, and accumulate large amounts of insoluble UA within organelles called leucosomes. Although these crystal-forming cells have been identified for some time, their underlying intracellular molecular processes during crystal formation remain poorly understood. Pathological UA crystallization can lead to severe illnesses such as gout and kidney stones. In this study, we used a combination of cutting-edge microscopy and spectroscopy techniques to investigate leucosome morphogenesis and molecular identity. We employed fluorescence-activated single-cell sorting (FACS) to isolate leucophores based on their unique optical properties and utilized various microscopy approaches to image leucosomes during different developmental stages. Micro-Raman spectroscopy was used to analyze the molecular content of the leucosomes, revealing them to be composed of anhydrous UA crystals. Our findings shed new light on the molecular mechanisms governing the controlled formation of molecular crystals and may contribute to the development of new biomaterials while enhancing our understanding of uncontrolled pathological UA crystallization in human diseases.

P-07

CRYO-EM INVESTIGATIONS OF HOLOCOCCOLITH CALCITE INTRACELLULAR FORMATION

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Organisms can execute tight control over crystal morphology using a cellular toolkit that is not well understood. A prominent example of biological control over crystal morphology is the calcite crystals of coccolith scales covering the cell surface of marine algae. Interestingly, crystal morphology fundamentally differs in coccoliths produced by the same species` diploid and haploid life-cycle phases, called heterococcoliths and holococcoliths. While calcite crystals of heterococcoliths are highly complex and species-specific, holococcolith crystals are simple rhombohedra, the most common morphology of calcite. In this study, we focus on the growth environment of the simple holococcolith crystals utilizing cryo electron-tomography of FIB-SEM lamella. However, preparing lamellae that contain the vesicle of interest is challenging due to the small ratio of vesicle to cell volume. To overcome this challenge, thin cell layers are sequentially removed by the FIB and the exposed surface is imaged using the SEM. Once the crystal-forming vesicle is identified at the exposed cell surface, a lamella containing the region of interest is prepared. Our results indicate that rhombohedral crystals nucleate and grow intracellularly within voluminous vesicles while experiencing an unconfined, isotropic environment. In addition, solution chemistry parameters within the vesicle are evaluated. Comparing these findings with the known heterococcolith formation environment suggests that confinement of the crystallization process is a critical factor in shaping biomineral morphology.

P-08

THE INTERPLAY BETWEEN pH and COLLAGEN ORGANIZATION IN THE TUMOR MICROENVIRONMENT: AN *IN VITRO* STUDY

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Dynamic abnormal extracellular matrix (ECM) processes are a hallmark of many diseases, including cancer. These processes can manifest as altered physical and biomechanical properties of the ECM, shifts in its composition, and changes in the spatial arrangement. Studies have shown that specific ECM properties are closely linked to the malignancy of cancerous tumors and cell migration. One fundamental property associated with cancer progression is the organization of collagen fibers. Linear, rigid collagen fibers can enhance cell migration, while curly and anisotropic fibers inhibit it. However, the relationship between ECM and cancer is complex, and it is challenging to determine whether specific ECM properties trigger cancer or whether the disease leads to abnormal ECM dynamics. The collagen structure in the tumor microenvironment can be linked to pre-malignant processes induced by cancer cells. A prominent process that characterizes a tumor microenvironment is a decrease in pH due to the anaerobic metabolism of the cancer cells. Since collagen contains ionizable residues, changes in pH can affect electrostatic interactions between collagen fibers and alter the fibers` organization. In this study, we investigate the influence of pH on the organization of collagen fibers *in vitro*. As a model for the tumor microenvironment, we use type I collagen hydrogel matrices with and without breast precancer multicellular spheroids. Initially, the collagen has a neutral pH, which changes with time due to incubation with buffer solutions or cellular activity. We characterized pH changes in the matrix over time using a pH microelectrode and confocal microscopy imaging of a fluorescent pH indicator. We show that the collagen matrix`s exposure to pH resembling those of the tumor microenvironment leads to changes in structural and rheological parameters. Using Cryo Scanning Electron Microscopy (Cryo-SEM) of high-pressure frozen and freeze fractured collagen hydrogels, we observe that decreasing the collagen matrix pH to values detected in cancer resulted in shorter and disorganized fibrils. Conversely, the fibrils were longer, helical, and organized spatially when the pH increased. We employed advanced image processing to support these findings quantitatively. Switching the acidic buffer to a basic buffer resulted in long and linear fibers, indicating that the collagen structure could be restored. The structure reversibility observed in neutral collagen that became acidic and neutral again can potentially be tailored to promote healing. Additionally, rheological measurements demonstrate that the collagen`s mechanical properties change under altered pH conditions. However, using Fourier Transform InfraRed Spectroscopy (FTIR), we found that the collagen secondary structure remained unaffected by pH changes, providing insights into pathological conditions. By comparing these results with Cryo-SEM imaging of the spheroids and collagen model, we evaluate the impact of acidity on collagen fibers` organization in proximity to the solid tumors and contribute to a better understanding of the ECM`s complex dynamics and structural changes during cancer.

P-09

NATURAL EVOLUTION OF SILK HIERARCHICAL STRUCTURES: REVEALING THE MULTI-LENGTH SCALES ASSEMBLY BY COMBINATION OF MICROSCOPY TECHNIQUES

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Silk fibers are a natural brilliant material design, having a highly-ordered hierarchical structure which gives it its extraordinary mechanical properties, combining high strength, extensibility, and toughness. Although it have been extensively studied, the self-assembly and structural transition stages that take place during the natural formation of silk multi-scale structure are still poorly understood. Generally, silk fibrillation is accompanied by the protein`s transition from a soluble Random-coil state into a solidified Beta-sheet-rich conformation under acting shear forces, elongational flow, changes in metal ions composition, and pH. However, silk natural formation involves more complex and dynamic events that allow the highly unstable silk feedstock to be kept as the fluid inside the silk gland and upon the need to adopt the ordered structure of the final fiber.

Our research combines different advanced microscopy techniques to reveal the key events, at different length scale, of the silk protein`s self-assembly and fiber`s formation inside the silk gland. The results shed light on the multi-step process of silk protein transition in-vivo. The evolution process starts from the protein`s colloidal "storage" state. It continues through the assembly of several macromolecular structures, phase separations, and transition events, which end up as bundles of nano-fibrils that form the final fiber.

P-10

MICROCALCIFICATIONS CAN TRIGGER OR SUPPRESS BREAST PRECANCER MALIGNANCY POTENTIAL AS A FUNCTION OF MINERAL TYPE IN A 3D TUMOR MODEL

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Most early breast precancer lesions contain microcalcifications (MCs), calcium-containing pathological minerals that form in the breast and appear in more than 90% of precancer cases. The most common type of MCs is calcium phosphate crystals, mainly carbonated apatite, associated with either benign or malignant lesions. A less common type of MCs is calcium oxalate dihydrate (COD), which is almost always found in benign lesions. *In vitro* studies show that the crystal properties of apatite MCs can affect breast cancer progression. We developed a 3D tumor model of multicellular spheroids of human precancer cells containing synthetic MC analogs to link the crystal phase and properties of MCs with the progression of breast precancer to invasive cancer. Our methodology includes imaging techniques such as micro-computerized tomography, Scanning Electron Microscopy (SEM), and light microscopy to characterize the sizes, morphology, and distribution of mineral particles embedded within the multicellular spheroids. We show that apatite crystals induce precancer cell proliferation and human epidermal growth factor receptor 2 (Her2) overexpression. This tumor-triggering effect increases when the carbonate fraction in the MCs decreases. COD crystals, in contrast, reduce Her2 expression compared to control spheroids with no added MC analogs. This finding suggests that COD is not randomly located only in benign lesions but may be actively contributing to suppressing precancer progression in its surroundings. Our model provides an easy-to-manipulate platform to better understand the interactions between breast precancer cells and MCs that will potentially provide new directions for precancer prognosis and treatment.

P-11

EXOCYTOSIS OF THE SILICIFIED CELL WALL OF DIATOMS INVOLVES EXTENSIVE MEMBRANE DISINTEGRATION

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Exocytosis is a fundamental process for cellular metabolism, communication, and growth. During exocytosis, a vesicle fuses with the plasma membrane to deliver its contents to the extracellular space. In classical exocytosis, where the secretory vesicles are much smaller than the cell, membrane homeostasis is maintained by recycling excess membrane back into the cell. An extreme case of exocytosis is the extrusion of silica cell wall elements by eukaryotic microalgae called diatoms. After formation in a membrane-bound silica deposition vesicle (SDV), the large and rigid silica element is exocytosed. During this process, the cell needs to deal with a nominal doubling of its plasma membrane. We studied membrane dynamics during cell wall exocytosis in two diatom species, using live-cell confocal microscopy, transmission electron microscopy and cryo-electron tomography. Our results show that silica is precipitated in a highly confined lumen bound by the SDV membrane, which is tethered to the plasma membrane via membrane contact sites. During exocytosis, the distal SDV membrane and the plasma membrane gradually detach from the mineral and disintegrate in the extracellular space, without any noticeable endocytic retrieval or extracellular repurposing. Within the cell, there is no evidence for the formation of a new plasma membrane, thus the proximal SDV membrane becomes the new barrier between the cell and its environment and assumes the role of a new plasma membrane. Our findings reveal a unique exocytosis mechanism used by these organisms to cope with the geometrical and physical challenges of exocytosis.[1]

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P-12

ELUCIDATE THE ROLE OF VPS4 ISOFORMS IN CYTOKINETIC ABSCISSION

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The AAA-ATPase, VPS4, is part of the ESCRT machinery that drives membrane constriction and fission in numerous processes in cells. The ESCRT complex is comprised of over 20 proteins in mammalian cells that are divided into 5 sub-families, ESCRT 0-III and VPS4. VPS4 is the most evolutionary conserved and is indispensable for the fission reaction. Notably, mammalian cells encode for two VPS4 isoforms – VPS4A and VPS4B, but the role of each isoform is unknown. Here, we set to characterize the role of VPS4 isoforms in ESCRT mediated membrane fission, employing the well documented ESCRT mediated cytokinetic abscission as a model.

To this end, we generated CRISPR/cas9 knock out cell lines of VPS4A, VPS4B and VTA1, a cofactor that stabilizes the hexameric, active form of VPS4. Our results show that depletion of VPS4A causes a considerably more severe delay in abscission compared to VPS4B depletion. STORM imaging revealed that lack of VPS4A leads to over-accumulation of the ESCRT-III protein IST1, at early abscission stages, suggesting a role for VPS4A in early abscission stages that precedes the fission reaction itself. Unexpectedly, a VPS4A mutant locked in the monomeric, inactive, state was able to partially rescue the abscission delay in VPS4A KO cells, and interacted with known abscission checkpoint proteins. Moreover, depletion of VTA1, shifted endogenous VPS4A proteins to their monomeric resulting in accelerated abscission. Collectively, our data highlight a role for monomeric VPS4A in regulating the abscission checkpoint, which is independent from its ATP hydrolysis activity.

P-13

FRACTAL DIMENSION AND FRACTIONAL CONCAVITY MEASUREMENTS OF GROWTH CONE CONTOURS OF OPTIC AXONS IN SITU

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Establishment of neuronal connectivity during development requires that axons extend along specific paths to reach their target tissues in the developing fetal brain. Growth cones located at the tips of axons are responsible for much of the extension and navigation of these growing axons. Non muscle Myosin IIB is one essential cellular factor that can modify the shape and motility of growth cones through modulating actin cytoskeletal dynamics. In this study, we used morphometrics to determine whether two novel shape parameters not previously applied to growth cone contours (fractal dimension and fractional concavity) could differentiate between GFP-expressing control and Myosin II inhibitor (Blebbistatin) exposed growth cones of optic axons in the optic tract of whole mount brains from Xenopus laevis tadpoles. Our results show that fractal dimension mean was not while fractional concavity mean were significantly different between control and experimental growth cones. However, variability in fractal dimension did differentiate between control and experimental growth cones. These results advance our understanding of growth cone morphology and introduce new morphometric parameters that can potentially assess the impacts of specific perturbations on growth cone contour complexity.

P-14

STRUCTURAL AND ANTI-MICROBIAL STUDIES OF RIBOSOME-BINDING 16-MEMBER RING MACROLIDES AGAINST STAPHYLOCOCCUS AUREUS

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The increasing emergence of bacterial resistance to antibiotics, and a dwindling pipeline for new antibiotic discovery, threaten a regression to the pre-antibiotic era. One way to combat this problem is to perform chemical derivatization to the current drugs by rational drug design, which requires deep structural knowledge of the target in complex with proposed next-generation compounds. The antimicrobial activity of the 16-member ring macrolides M-4365 G2, Juvenimicin A3, and 5-O-desosaminyl-tylonolide, originally discovered in the 70's and 80's, showed promise but have remained underexplored. To expand rational design efforts, we determined the cryo-EM structures of three promising 16-member ring macrolides in complex with the ribosome of *Staphylococcus aureus*, an aggressive Gram-positive pathogen. We determined the IC_{50} values of these compounds with *S. aureus* and compared their activity and structure to other macrolides currently in clinical use. Our structural results indicate that the differences in activity between the three derivatives do not result from differences in binding, as first hypothesized, but may result from differences in the interactions between the antibiotics and the nascent peptide chain. Other observed differences in activity between these compounds and the clinically relevant drugs, such as erythromycin and tylosin, can be attributed to structural elements other than the derivatizations, such as a specific covalent bond between the antibiotic and the ribosome, or the lack of additional sugar groups. These provide insights for directed antibiotic engineering.

P-15

SEM CHARACTERIZATION OF NON-CaP MINERAL PARTICLES FOR BREAST PRECANCER PROGNOSIS

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Ductal Carcinoma in Situ (DCIS) is a non-invasive precancer stage of breast cancer, and only ~35% of DCIS cases develop into invasive cancer[1]. However, it is currently impossible to predict the progression of DCIS, possibly leading to unnecessary treatments. Microcalcifications (MCs) are calcium deposits in the breast, a common finding in DCIS mammography[2]. MCs are either calcium phosphate (CaP) or, less commonly, non-CaP crystals, such as calcium oxalates and calcite. The MC crystal phase is correlated with malignancy, and while CaP crystals are associated with either benign or malignant lesions, non-CaP MCs are commonly found in benign lesions[1,2]. Hence, the crystal properties of CaP MCs were the focus of many studies, which show that the CaP crystal morphology, particle size, structure, and chemical composition correlate with malignancy and may have a diagnostic or prognostic value[2]. Recent in vitro work from our group shows that non-CaP MCs consisting of calcium oxalate dihydrate (COD) might suppress precancer cell malignancy potential, suggesting that COD presence in precancer lesions may be correlated with better DCIS prognosis.

Here, we report on a retrospective study of clinical samples collected from DCIS patients more than five years ago, for which the overall clinical state, including illness progression, is known. We study breast MCs embedded within tissue sections using microscopy and vibrational spectroscopy, focusing on non-CaP crystals. To investigate links between the MC crystal properties and precancer prognosis, we use SEM and EDS to obtain the MC morphologies, particle sizes, and elemental composition, Raman mapping to determine the MC phases, and light microscopy for a histopathological overview of the sections.

We analyzed 81 individual MCs obtained from three patients with different illness outcomes. Individual MCs can be either from tumorous or normal tissue regions for the same patient. The non-CaP MCs varied in particle sizes, ranging from hundreds of nanometers to tens of micrometers. We identified morphologies such as punctulate, faceted, spherical, and spongy particles. Furthermore, some MCs were in the form of aggregates with either homogenous or heterogeneous sub-morphologies. In the developed DCIS cases, we mostly identified small homogeneous aggregates, less than 10 µm in diameter, consisting of spherical sub-morphologies. In both tumorous and benign regions for all illness outcomes, Raman spectroscopy showed calcite, which is currently not correlated with prognosis.

Because individual non-CaP MCs are often smaller than one micrometer and are dispersed in the tissue, in future work, we will locate them in the tissue using XRF mapping and measure their Ca K-edge µ-XANES to detect their structures to be correlated with DCIS prognosis. By retrospectively integrating medical information with the MC features, this study will potentially shed light on the role of the less common breast microcalcifications non-CaP crystals and provide a better insight into the DCIS prognosis based on their features.

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P-16

MORPHOLOGICAL QUANTIFICATION OF LEISHMANIA PARASITE LIFE CYCLE STAGES USING IMAGING FLOW CYTOMETRY

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Leishmaniasis is a parasitic disease that is found in parts of the tropics, subtropics, and southern Europe. Leishmaniasis is caused by infection with Leishmania parasites that are transmitted to humans by the bite of phlebotomine sand flies. The parasites cycle between sand-fly vectors and mammalian hosts adapting to different environments. These life cycle events are accompanied by distinct morphological changes that involve differences in size and dimensions including the flagellum length.

Imaging flow cytometry (IFC) is a high thruput widefield microscopy-based method that capture fluorescence and brightfield images of particles (e.g. cells) in suspension, providing the morphological information. We developed an IFC method to analyze changes in shape and flagellum length of Leishmania parasites. We used this method to provide information on the changes that Leishmania cells are presenting following CRISPR-Cas9 mediated hemizygous deletion in the Eukaryotic translation initiation factor 4E2 (LeishIF4E2). We found that cells that lack one copy of LeishIF4E2 (LeishIF4E2 +/-) are smaller, round, and equipped with a very short flagellum.

Our quantitative method can be expanded to other parasites thus providing researchers with an efficient and simple tool to analyze morphological changes, without the need to label the cells.

P-17

LABEL FREE IMAGING OF CHOLESTEROL CRYSTALS AND MACROPHAGES AS A MODEL SYSTEM FOR ATHEROSCLEROSIS

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Atherosclerosis is a pathology characterized by the build-up of plaques from an accumulation of cholesterol-rich lipoproteins and later cholesterol crystals inside the arterial walls, and is the cause of most cardiovascular diseases. A key player in the atherosclerotic lesions are macrophages. The macrophage tasks in the body include the identification, uptake and disposal of harmful bodies. Within the plaques, their recruitment is triggered by the excess presence of cholesterol-rich lipoproteins. There is however also evidence that crystalline cholesterol is a target for the macrophages [1].

Understanding the cholesterol crystal interaction with other plaque components is important due to their activation of an inflammatory immune response, the possible crystal-induced rupture of cell membranes and plaque rupture, which may cause obstruction of arteries [1].

Previous research showed that macrophages have the capacity for uptake of cholesterol crystals [1], and mainly focused on understanding the immune response triggered by the cholesterol crystals. Meanwhile, our focus is to observe the crystal phagocytosis events, possibly followed by crystal dissolution. To gain a better understanding of the mechanism of crystal uptake and subsequent processing, we incubate macrophages of the J774A.1 cell line with synthetic cholesterol crystals. We utilize three label free imaging techniques: confocal reflection microscopy, a refraction-based microscopy technique (NanoLive) and scanning electron microscopy under cryogenic conditions (cryo-SEM). Labeling the crystals is undesirable because it may alter the recognition, uptake and dissolution of the crystals by the macrophages. Imaging in the NanoLive allowed live 3D observation of the uptake process. Starting at around 45min after co-incubating cells and cholesterol crystals, phagocytosis events of clusters of crystals occur. Each uptake process takes around 10 to 15 minutes, and some cells will phagocytose multiple sets of crystals. The cholesterol crystals can be identified extra- and intracellularly both visually and based on the NanoLive detection of differences in the refractive index of the crystals (~ 1.6), relative to the cytoplasm (~1.3-1.4). Using confocal reflection microscopy with a 488 or 514nm laser, cholesterol crystals can also be confirmed both inside and outside the cells.

Cryo-SEM images performed on freeze-fractured surfaces show abundant intracellular cholesterol crystals. Unambiguously identifying instances of dissolution is difficult, although the increased presence of what appear to be lipid droplets near or directly attached to clusters of cholesterol crystals, may be a good indication of crystal processing by the macrophages.

Combining the information collected with the different imaging technologies provides a detailed observation of the process in space and time with high fidelity and minimal influence on the biological process.

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P-18

DETERMINING THE COMPOSITION OF THE ESCRT-III FILAMENT IN CYTOKINESIS ABSCISSION OF MAMMALIAN CELLS

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The ESCRT machinery (ESCRT 0, I, II, III and the AAA ATPase VPS4) participates in membrane constriction and fission in a variety of processes in cells. Cytosolic ESCRT-III proteins and VPS4, the driving force for membrane fission, assemble into cortical filaments to induce membrane constriction and severing. One of the ESCRT mediated processes is abscission of the intercellular bridge connecting two daughter cells at the end of cytokinesis, which constitutes the last step of cell division.

Over 10 different ESCRT-III proteins were identified in the mammalian genome (named CHMP 1-7 and IST1), but the specific role of ESCRT-III subunits in constriction and fission have not been defined. In vitro studies suggest that the ESCRT-III components CHMP2A was designated as one of the components required for the final fission event. To test the effect of CHMP2A on ESCRT mediated membrane remodeling in cells, we generated CHMP2A knock-out HeLa cells. Live-cell imaging experiments performed in CHMP2A KO cells revealed that abscission is severely delayed in the absence of CHMP2A. Surprisingly, in contrast to other essential abscission components, all the cells eventually completed abscission suggesting that CHMP2A is not essential for the final fission event. SIM imaging of the core ESCRT-III components CHMP4B and IST1 revealed defected in the spatiotemporal organization of the filament during the process. Surprisingly, labeling both proteins in the same cell revealed that while these proteins co-localize in normal cells, their organization pattern is spatially separated in CHMP2A KO cells, suggesting that the polymerization process itself is affected by CHMP2A depletion. Together, these results suggest a role for CHMP2A in filament polymerization rather than in the final fission process itself.

P-19

SNAPSHOTS OF MITOCHONDRIAL FISSION THROUGH THE LENSE OF CRYO-SCANNING TRANSMISSION ELECTRON TOMOGRAPHY (CSTET)

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Cryo-Scanning Transmission Electron Tomography (CSTET) allows imaging of areas in a cell up to 1 µm in thickness (Wolf, Houben, and Elbaum 2014; Wolf et al. 2017), values unreached by cryo-ET. Thus, CSTET enables the visualization of intact mitochondria and their surrounding environment in native cells without sectioning or milling.

We developed deconvolved dual-axis CSTET(ddCSTET, Waugh et al. 2020; Kirchweger et al. 2022). Deconvolution successfully removes the "salt-and-pepper" noise, and by combining dual-axis tomography with deconvolution, the missing wedge is reduced and accounted for, which results in near-isotropic resolution. s

We applied ddCSTET to image stalled fission intermediates of mitochondria. A set of proteins play a significant role in fission. These include the mitochondrial fission factor (Mff), an outer mitochondrial membrane (OMM) protein that recruits dynamin-related protein 1 (Drp1), a cytosolic GTPase, which performs the final fission step. Cells lacking Mff (Mff-/-) generate mitochondrial constrictions under fission-inducing conditions, but, as expected, successful fission is reduced. We first image Mff-/- cells under normal and fission-inducing conditions by fluorescence microscopy. While the diameter of the WT mitochondria appears to be more equal, the MFF-/- mutant displays different morphologies. These include "beads-on-the-string" and mitochondria with increased thickness, up to several µm in diameter. We then characterized them by ddCSTET. DdCSTET of those different mitochondrial morphologies displays different health states of the mitochondria, as judged by the appearance of the cristae. We show 3D CSTET volumes of the "beads-on-the-string" morphology, of a "garbage can", i.e., a mitochondrial blob with several µm in diameter, and a 3D volume of a 10 µm long mitochondria. This shows that the cell tries to segregate the healthy section of a mitochondria from the unhealthy section. Additionally, we show contacts between mitochondria and their surrounding organelles and the cytoskeleton participating in the fission process.

As a summary, ddCSTET provides insight into the whole "cellular theater".

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P-20

ROBUSTNESS OF THE CANONICAL MITOCHONDRIAL FUSION MACHINERY PROMOTES NEBENKERN FORMATION IN DROSOPHILA SPERMATIDS.

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Mitochondria are the bioenergetics powerhouses and biosynthetic centers of the cell. The mitochondria are constantly changing shape and subcellular distribution according to function, energy and metabolic demands of the cell. Mitochondrial morphology usually ranges from small spheres and short tubules to elongated tubules and reticular networks. These changes are mainly controlled by the balance between two opposing mechanisms of membrane dynamics, fusion and fission, which when perturbed, can lead to severe pathologies.

Perhaps the most dramatic morphological changes and structural organizations of the mitochondria occur during spermatogenesis. In *Drosophila* spermatids, individual mitochondria aggregate near the newly formed haploid nucleus and subsequently coalesce and fuse into a giant sphere called Nebenkern. The Nebenkern is composed of two giant mitochondria wrapped around each other and arranged in an onion-like spherical segments of layers upon layers. During subsequent spermatid elongation stages, the Nebenkern is transformed from a 6.7 µm sphere to two, 1.8 mm long, cylindrical mitochondrial derivatives extending alongside the axoneme. Although detailed ultrastructural description of Nebenkern formation was already reported five decades ago, the molecular mechanisms underlying the formation of this extraordinary organelle remains largely obscure.

To further characterize the genetic components, involved in Nebenkern formation, we utilized several advanced microscopy techniques such as live imaging, electron microscopy and expansion microscopy. We show that already during the second meiosis division, mitochondria start fusing to elongated tubular organelles, which continue fusing and collapsing to form the spherical Nebenkern, achieved by the robust and lasting action of the canonical fusion machinery. We demonstrate that the testis-specific mitochondrial fusion protein, Fzo, and the more generally expressed mitochondrial fusion protein, Marf, function similarly in promoting spherical mitochondrial fusion.

Finally, using a candidate screen through a compiled list of mitochondrial and cytoskeletal genes, we identified additional components involved in Nebenkern formation.

P-21

FIB-SEM IMAGING REVEALS IN-SITU FORMATION OF THE SILICA CELL WALL OF ALGAE

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The intricate geometrical patterns in the silica cell wall of unicellular algae have long sparked curiosity as to their process of formation. These cells take up silicic acid from the ocean and precipitate it in a controlled manner to form a cell wall patterned with pores and ridges that are species specific. Here we visualize in 3D the in-situ cell wall formation of the diatom Stephanopyxis turris. We imaged whole cells using a slice-and-view approach with a focused ion beam SEM (FIB-SEM), both in fixed cells and at cryo conditions. Our data reveal that the hexagonal pore pattern of the mature valve is created by silica precipitating into radial rods which are then connected by bridges to form pores. These results of radial rods being the initial step of silica cell wall formation was observed in studies of very different diatom species, and may suggest an underlying principle of silica precipitation in diatoms.

P-22

MAPPING OF PHASE SEPARATION OF SUPRAMOLECULAR PROTEIN ASSEMBLIES BY LIVE CELL HOLOTOMOGRAPHY MICROSCOPY

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Protein condensation, phase separation, and self-assembly are different aspects of very similar phenomena. Weak but multivalent intermolecular interactions drive the growth of supramolecular protein assemblies much larger than the size of the protein unit. The physical state of such condensates may be crystalline, amorphous solid, gel, or liquid. Ferritin proves to be an ideal scaffold on which to study self-assembly. Mammalian ferritin contains 24 polypeptide subunits in a nearly-spherical shell with octagonal symmetry. The N termini are disordered and point to the exterior. Exogenous expression in cells of a hybrid ferritin with dimerizing fluorescent proteins such as Citrine resulted in self-assembly of fluorescent protein bodies1. Mutation of the hydrophobic dimerizing patch to one containing cysteine led to oxidation-sensitive self-assembly2. Addition to ferritin of intrinsically disordered domains with light-sensitive coupling, named Corelets, has helped to map phase separation within cellular compartments by means of protein condensation3. In this work we revisit these systems using a new holographic microscopy tool to map refractive index in 3D, avoiding dependence on fluorescence imaging and setting the stage for correlative electron tomography of the protein assemblies in solid or liquid phase.

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P-23

ASGARD ESCRT-III AND VPS4 REVEAL CONSERVED CHROMATIN BINDING PROPERTIES OF THE ESCRT MACHINERY

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The archaeal Asgard superphylum currently stands as the most promising prokaryotic candidate, from which eukaryotic cells emerged. This unique superphylum encodes for eukaryotic signature proteins (ESP) that could shed light on the origin of eukaryotes, but the properties and function of these proteins is largely unresolved. Here, we set to understand the function of an Asgard archaeal protein family, namely the ESCRT machinery, that is conserved across all domains of life and executes basic cellular eukaryotic functions, including membrane constriction during cell division. We find that ESCRT proteins encoded in Loki archaea, express in mammalian and yeast cells, and that the Loki ESCRT-III protein, CHMP4-7, resides in the eukaryotic nucleus in both organisms. Moreover, Loki ESCRT-III proteins associated with chromatin, recruited their AAA-ATPase VPS4 counterpart to organize in discrete foci in the mammalian nucleus, and directly bind DNA. The human ESCRT-III protein, CHMP1B, exhibited similar nuclear properties and recruited both human and Asgard VPS4s to nuclear foci, indicating interspecies interactions. Mutation analysis revealed a role for the N terminal region of ESCRT-III in mediating these phenotypes in both human and Asgard ESCRTs. These findings suggest that ESCRT proteins hold chromatin binding properties that were highly preserved through the billion years of evolution separating Asgard archaea and humans. The conserved chromatin binding properties of the ESCRT membrane remodeling machinery, reported here, may have important implications for the origin of eukaryogenesis.

P-24

THE EFFECT OF LAMIN A ON THE COHERENT DYNAMICS OF THE CHROMATIN IN LIVING CELLS

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During the last decade, extensive studies highlighted the complex structure of the chromatin inside the cell nucleus. The chromatin is packed inside the small volume of the cell nucleus in an organized yet dynamic manner. The organization and dynamics of the chromatin within the nucleus of eukaryotic cells are closely related to cellular functions, such as gene regulation and mitosis. The mechanism of genome organization has been studied through various models and the identification of the nuclear structural proteins.

Recent experiments have shown that lamin A contributes significantly to reducing chromatin dynamics and directly affects the mechanical properties of the nucleus. These studies were based on tracking specific chromosome loci and single particle tracking methods. However, further experiments are needed to understand the inner life of the nucleus. In this research, we aim to study the chromatin as a bulk material and the role of lamin A in the large-scale dynamics of the chromatin.

Our measurements include mapping the whole chromatin dynamics in living cells using H2B-GFP tagged histones. We used displacement correlation spectroscopy methods, based on particle image velocimetry (PIV) techniques, in order to map the whole chromatin across the entire nuclear volume. We measured cells with modified levels of the protein lamin A to quantify the role of the protein in governing the dynamics of the chromatin at large length and time scales.

In our research we use various techniques, such as confocal microscopy and PIV analysis, to develop a theoretical model that describes the biophysical function of the proteins and the mechanisms involved in chromatin organization. Our research will contribute to better understanding of genome organization as well as the dynamic properties of the chromatin in eukaryotic cells.

P-25

STRUCTURAL STUDIES ON THE S. AUREUS ERMB METHYLTRANSFERASE MUTANT RIBOSOME IN COMPLEX WITH SOLITHROMYCIN

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About 40% of clinically used antibiotics target ribosomes, the complex nano-machines that translate the genetic code to proteins in all living cells. However, we are witnessing an increasing number of drug-resistant pathogens, coupled with the underwhelming development of new antibiotics. Additional structural studies on antibiotic-resistant strains may provide insights onto mode of action and improve our odds in fighting against bacterial infections. A prime example of resistance mechanisms is the methylation of adenosine 2058 of the 23S ribosomal RNA by an Erm–methyltransferase, which confers resistance to several drugs, including macrolides. Here we show the cryo-EM structure of a methylated A2058 ribosome from *Staphylococcus aureus* (SA), a life-threatening Gram-positive bacterium, that forms a complex with a macrolide despite the presence of methylation.

P-26

THE EFFECT OF LOOP8 ON SPINDLE LOCALIZATION AND BI-DIRECTIONALITY OF S. CEREVISIAE KINESIN-5 CIN8

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Precise segregation of chromosomes during mitosis is essential for maintaining genetic stability and preventing mutations that can lead to genetic diseases and cancer. Chromosome segregation is mediated by the mitotic spindle, a microtubule based bipolar structure. In each mitotic cycle, the mitotic spindle undergoes a well-defined set of morphological changes that are temporally and spatially regulated. Thus, the elucidation of unknown mechanisms and regulatory pathways will enable the identification of potential new targets for treating and preventing cancer. We use a genetically traceable eukaryote, *S. cerevisiae*, as a model to answer basic unresolved questions regarding the mechanisms and regulation of mitosis.

Kinesin-5 motor proteins are highly conserved from yeast to humans and play central roles in establishing and maintaining the mitotic spindle during cell division. These motors are homotetramers with two pairs of catalytic domains located at the opposite sides of the active complex. This architecture enables kinesin-5s to crosslink and slide apart antiparallel microtubules (MTs) of the mitotic spindle. Recent studies have demonstrated that some kinesin-5 motors, including the *Saccharomyces cerevisiae* Cin8 move bi-directionally along microtubules, switching directionality under different conditions. Cin8 carries a uniquely large insert in loop8 in its motor domain, compared to other Kinesin-5 homologues. The role of loop 8 in regulating the motile properties of Cin8 is still unknown.

P-27

BIOMINERAL FORMATION BY THE FRESHWATER GREEN ALGA PHACOTUS LENTICULARIS

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Many unicellular algae produce $CaCO_3$ minerals in marine and freshwater ecosystems, and some of them are known to also form guanine crystals. One freshwater species, *Phacotus lenticularis*, is abundant in lakes and ponds. *P. lenticularis* produces a complex shell composed of aligned crystal plates of calcite. These shells constitutes a significant fraction of basin sediments especially during the bloom period.

We investigate the mechanism of shell formation, and the pathway of ion transport and mineral deposition, using multimodal microscopy techniques. We enriched natural *P. lenticularis* cells and followed the different stages of shell formation using in-vivo fluorescence microscopy assays combined with cryo-SEM, which enable observation of the shell and the associated cells under fully hydrated conditions. We observed calcium trafficking into the cell, intracellular crystallization and developmental changes in the hierarchy and morphology of the shell crystals.

P. lenticularis in our cell cultures does not calcify, and we investigate the signals that trigger calcification both in the cell cultures and in natural environments at the onset of the bloom period.

We also observed that cell cultures grown under phosphate stress conditions, produce birefringent crystals that were identified as beta guanine. The crystals were observed inside specific vacuoles using cryo-SEM and cryo-FIB-SEM. Localization and distribution of the crystals was obtained using cryo-Soft-X-ray tomography and near edge spectroscopy.

Investigation of the two biomineralization pathways and determining if any connections between the two exist, may provide insight into the guanine and calcite crystals' function and evolutionary development in *P. lenticularis* and other unicellular organisms.

P-28

IMPROVING CRYO-ELECTRON TOMOGRAPHY DATA QUALITY AND THROUGHPUT BY STREAMLINING THE WORKFLOW

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Cryo-electron tomography (cryo-ET) is a very powerful technique that allows researchers to obtain high resolution information about macromolecular complexes in their native cellular environment. Recently the technique has gained popularity and an increasing number of researchers are implementing it in their lab.

The power of cryo-ET is undisputed but the fact that the workflow is very error-prone has limited the data output1. In the workflow, there are two main challenges: keeping the sample ice contamination-free and targeting the region of interest (ROI).

At Delmic we developed two workflow solutions called CERES and METEOR to solve these problems. The CERES Ice Defence System is based on the tools developed by Tacke et al2. and consists of multiple innovative tools that are tailored to minimize ice contamination during sample handling (Clean Station), transfer (Vitri-Lock) and FIB milling (Ice Shield). METEOR is an integrated fluorescence light microscope (FLM) that greatly enhances the ROI targeting inside the cryo-FIB/SEM while reducing the number of handling steps required3.

We show that combining these innovative tools can lead to improved cryo-ET data quality and throughput.

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P-29

SPEC-NET: NUCLEAR SEGEMENTATION FROM H&E BIOPSY WITH SPECTRAL IMAGING SCREENING

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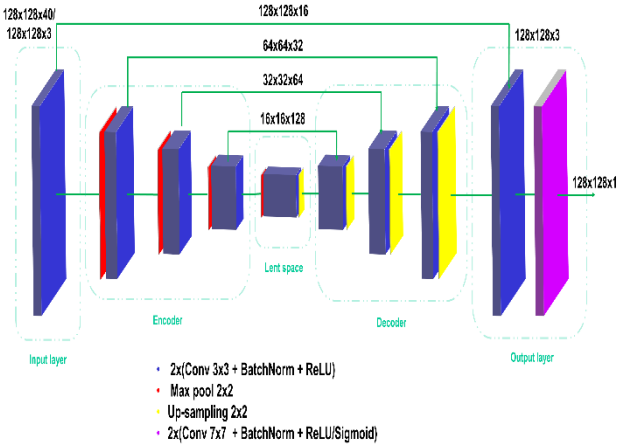
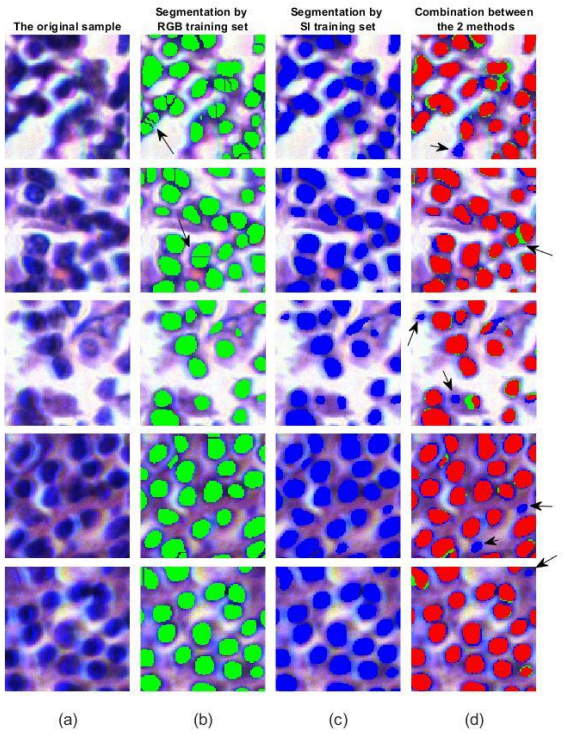
Biopsy diagnostics is a common method for analyzing cancer and other fatal diseases. In recent years, digital tools like digital imaging and Whole-Slide Imaging (WSI) have become more popular for biopsy analyzing, which allows the use of image processing and artificial intelligence (AI). One of the main tasks for these technologies is nuclei segmentation from Hematoxylin and Eosin stain (H&E). While AI has shown some success in this area, it is still not widely used in the medical community due to concerns about accuracy. In this paper, we present a novel approach for analyzing H&E stains using Spectral Imaging (SI) screening, which provides multiple intensity values for each pixel, compared to just three values for each pixel with RGB imaging. Our application is based on a U-net model with an adjusted input layer for SI size and was compared to Performance of model that was train on RGB images. Despite limitations with the quality of the data labeling, the models showed improved performance when measured by F1-score and Aggregated Jaccard Index (AJI). The study also showed by logistic regression model, that SI images had an advantage in pixel-level classification compared to RGB images.





P-30

THE ROLE OF THE NON-MOTOR N-TERMINAL REGION IN REGULATION OF FUNCTION OF THE BI-DIRECTIONAL KINESIN-5 CIN8

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During mitosis, the bipolar kinesin-5 motor proteins perform central functions in mitotic spindle dynamics by crosslinking and sliding antiparallel microtubules (MTs) apart. Recent studies have indicated that the *Saccharomyces cerevisiae* kinesin-5 Cin8 moves bi-directionally along MTs, in minus-end and plus-end directions. The mechanism of this bi-directional motility remains unknown. In this study we examined the roles of sequences in the non-motor N-terminal region in regulating the function of bi-directional Cin8. For this purpose, we generated N-terminal deletion variants of GFP-tagged Cin8 and examined their intracellular localization. We found that in *S. cerevisiae* cells containing Cin8 variant, in which aa 39-69 were deleted (Cin8Δ39-69), close to 30% of the cells were monopolar with no Cin8-GFP signal, compared to wt Cin8 that exhibited only 7% of this phenotype, suggesting that the deletion of aa 39-69 within Cin8 generated less stable Cin8 variant. In addition, in monopolar cells, Cin8Δ39-69 and Δ70-75, exhibited mis localization in the nucleus and/or on nuclear MTs, compared to wt Cin8 that concentrated mainly at the poles, indicating that these variants are either defective in minus-end directed motility or exhibit reduced affinity to MTs. Consistently, these two variants exhibited lower percentage of cells with short bipolar spindles compared to wt Cin8, indicating that these variants are defective in bipolar spindle assembly. According to these results we suggest that sequences in the nonmotor N-terminal region of Cin8 regulate the intracellular localization of this motor, mainly prior to spindle assembly, which affects the functionality of Cin8 in cells.

P-31

MEASUREMENT-BASED CONTROL OF THE ELECTRON-PHOTON COUPLING COHERENCE

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Electron microscopes allow for nanometric resolution for material science, microelectronics, and research of light fields well below the wavelength of visible light. The electron-photon coupling induced by the electron beam can be used to generate a high-resolution image of samples by producing various types of emissions, thus helpful in studying the properties of materials and their interactions with electromagnetic radiation. Where the properties of luminescence from the passage of a localized electron beam are readily derived by assuming a point-particle electron, the expansion to higher dimensions depends on its quantum aspects. A pioneering experiment by Remez et al. on Smith-Purcell radiation [1], found that its wave-function is extended spatially the electron still behaves as a point-like particle, passing along one path at a time. Here we derive an interaction model allowing for entanglement between the electron and the cathodoluminescent photons, and suggest an approach to control the quantumness of the coupling. Our model shows that the distinguishability of the electron paths in experiments thus far suppressed quantum interference, leading to radiation distribution compatible with a point-particle electron. As an experimentally viable approach for observing the quantum coupling features we suggest:(i) the use of long-lived optical modes within micro-sphere resonators, characterized by full spatial coherence, and (ii), manipulate the electron`s final state such that the measurement lacks "which-path" information. This work extends the fundamental concept of electron-photon entanglement to two dimensions, thereby solving a standing question in the coupling of basic particles. This proposal and the experiment suggested here open a path to implications in the fields of quantum physics while deepen our understanding of the fundamental principles that govern the behavior of matter and energy.

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P-32

IN-SITU INTERINSIC SELF-HEALING OF LOW-TOXIC Cs_2ZnX_4 (X= Cl, Br) METAL HALIDE NANOPARTICLES

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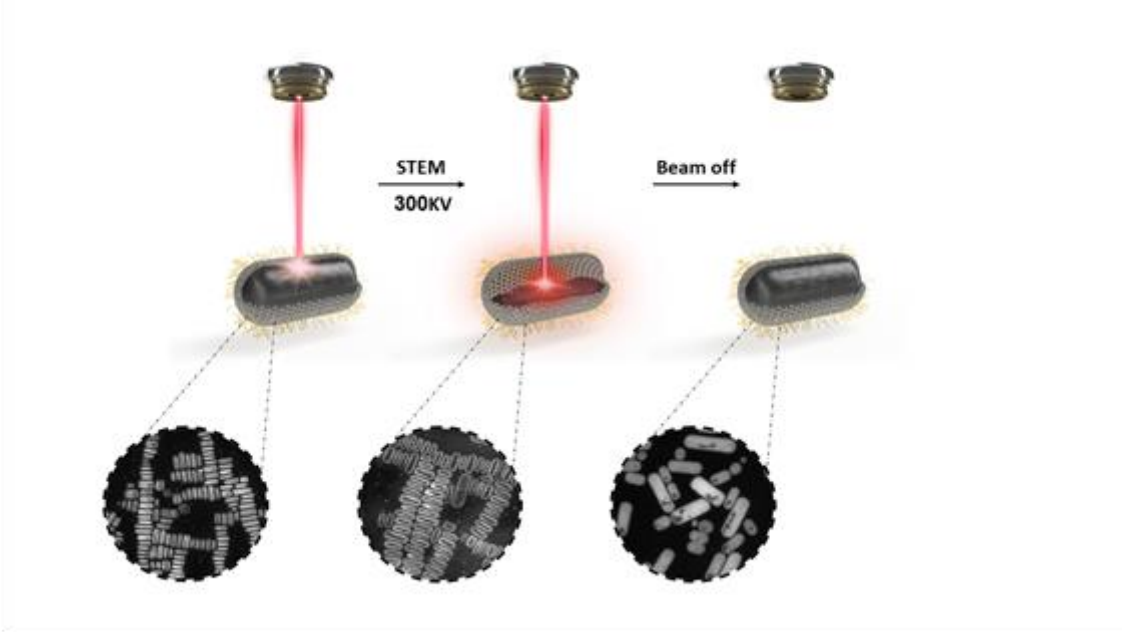
This study presents research on metal halide nanoparticles with the composition Cs_2ZnX_4 (X=Cl, Br) and their unique ability for self-healing under a wide range of damages in a fast time scale of seconds without the intervention of an external additive of material. The phenomenon is divided into several parts, including the ability to create nanoshells from the original nanoparticles by an electron beam in STEM mode. The resulting nanoshells preserve the original morphology of the nanoparticles and can be obtained in different morphologies depending on the shape of the nanoparticles from which they started. These nanoshells exhibit extensive self-healing, and by closing the electron beam for a short time, it is possible to observe the complete healing of the nanoshells back to the original complete intact particles. The research also revealed another form of self-healing that manifests as dynamic and continuous self-healing where damage created in the particle in the TEM mode by the beam moves from side to side within the frame of the particle, while the areas where the damage occurred crystallize back to the original phase, structure, and composition of the particle before the damage.

We used EDS and FFT analyzes to prove that after healing, the particles return to the original structure and phase like the particles before the creation of the nanoshells. High-resolution images taken as well as EDS analyzes show that in all the different states of damage, there remains a thin crystalline layer that remains as a shell around the entire particle both in the state of local damage by the TEM and in the state of the nanoshells formed in the STEM. As a result of the electron beam hitting the particles, many inelastic interactions are created, which create local heat that stimulates atomic vibrations in the material resulting in the displacement of atoms and their diffusion within the particle. The mobilized atomic fraction inside the particle is kept throughout all the state of damage inside the particle and cannot come out because of the thin crystalline layer that remains as a container and shell that keeps the damaged material inside.

We conducted an extensive and comprehensive research in different irradiation conditions, including variation of the dose and the acceleration voltage (80,200,300 KV) to examine the effect of different irradiation intensities on the damage created and the healing processes prevented. For each defined irradiation condition, we took high-resolution videos from which we extracted trends and analytical values such as the damage growth rate for a given acceleration voltage and dose, the healing velocity, and linear adjustments between the size of the damage and the irradiation time.

In order to support the theory and make sure that the damage and healing processes are not created only as a result of an electron beam, the researchers carried out a unique experiment that included the use of an in-situ TEM heating stage holder that allows the particles to be heated while they are being eluted in EM. Minimizing the beam to a necessary minimum made it possible to isolate the effect of heating in the 50-250 ^{O}C range and to observe damage and heating processes that are identical to those observed by the re the electron beam.



This work concludes that these nanoparticles, which exhibit extensive healing capabilities at the atomic level, can be used for a wide variety of optoelectronic applications that require stability and healing capabilities over time.

P-33

MODULATION OF BIOGENIC CRYSTAL MORPHOGENESIS IS ACHIEVED THROUGH TRANSITION FROM REACTION-LIMITED TO TRANSPORT-LIMITED GROWTH

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Biogenic crystals exhibit a wide range of intricate morphologies that are formed with precision that is unmatched by synthetic means. Coccoliths, which are calcite multi-crystal arrays created by unicellular marine algae, form complex shapes using only stable rhombohedral facets. However, it is currently unclear how through seemingly simple crystallography species-specific architectures are constructed. To investigate this, we utilized various advanced electron microscopy techniques to observe crystal growth both in and out of the cellular environment. Our findings suggest that crystal growth can switch between space-filling and branched growth, similar to forming of snowflakes, albeit in a reproducible manner. During this process, the crystals elongate via their stable crystallographic facets and corners, but the final shape is determined by growth arrest due to transport limitation. Directional membrane-mediated fluxes are believed to control this process, regulating the switch between reaction-limited and transport-limited growth regimes. This study demonstrates how precise control over crystal morphology can be achieved by coupling crystallographic growth with a well-controlled environment.

P-34

SPATIALLY CONTROLLED ATOMIC LAYER DEPOSITION WITHIN POLYMER TEMPLATES FOR MULTI-MATERIAL NANORODS AND NANOWIRES FABRICATION

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Today's nanofabrication techniques require multistep and costly processes in order to fabricate complex, multi-materials nanostructures. Performing atomic layer deposition (ALD) within polymeric templates can offer a simple solution for nanostructure fabrication. In this process, named sequential infiltration synthesis (SIS), high partial pressures and long exposures times lead to inorganic materials growth within polymers. Sequential polymer removal results in polymer-templated inorganic nanostructure. While SIS shows great potential in fabricating large variety of structures, it is currently limited to a single material growth process.

In this research, we demonstrated, for the first time, multi-material SIS process with control over the spatial location of each material and fabricate heterostructure nanorods and nanowires. We studied SIS within self-assembled block copolymer (BCP) films and electrospun polymer fibers and developed multi-material SIS, where two metal oxides are grown together in a single process, with precise control over their location within the polymer template. We used cylinder forming poly (styrene-block-methyl methacrylate) (PS-b-PMMA) films and electrospun PMMA as the polymeric template and DEZ (diethyl zinc), TMA (trimethyl aluminum) as the organometallic precursors. We achieved control over the growth location of each metal oxide by tuning the organometallic precursors diffusion time, forming heterostructures after polymer removal. A short exposure of the first precursor resulted in a limited growth only at the outer part of the polymer, while a long exposure of the second precursor enabled it to reach the full depth of the polymer besides the section which was already occupied by the first precursor. An exposure to water completed the cycle. We demonstrated this process on BCP films to achieve AlOx-ZnO nanorods arrays, and on polymer fibers to achieve AlOx-ZnO fibers. We performed structural characterization using scanning and transmission electron microscopy (SEM and TEM, respectively) to characterize the nanowires and nanorods as well as three-dimensional characterization scanning TEM (STEM) tomography and energy-dispersive X-ray spectroscopy (EDS) STEM tomography in order to probe the structure and the chemical composition in 3D. This research opens new pathways for multi-materials nano scale structure fabrication through ALD-based growth within polymers.

P-35

PROBING MAGNETIC PHASE TRANSITIONS VIA SPIN TORQUE DRIVEN SKYRMION RESONANCE

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Magnetic Skyrmions are attractive for ultra-dense data storage applications such as the racetrack memory (RM) [1-3]. Recently, frustration in ferromagnetic (FM) crystals was predicted of being capable of providing the topological protection of the Skyrmion [4] without relying on the DMI and the effect was immediately discovered in Fe3Sn2 bulk crystals [5,6]. Surprisingly, these Skyrmions survive even at room temperature and are controllable by electrical current. These advances illustrate the exceptional technological potential of the Fe_3Sn_2 system. In this work, we study the dynamics of a bulk Fe_3Sn_2 crystal through an optically probed spin torque driven ferromagnetic resonance (OSTFMR) technique. We excite the magnetic system by passing RF current through the crystal where the charge current converts into spin-polarized current through the spin Hall effect. From the dynamical response we identify the rotational (clock-wise or counter-clock-wise) and the translational (breathing) modes and reconstruct the phase transitions of the magnetic skyrmion texture. Using this technique, we follow the evolution of the two modes as a function of the externally applied magnetic field and map the magnetic phase transitions of the Fe_3Sn_2 crystal. A complementary numberical micromagnetic simulations confirms our results.

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P-36

EXPLORING SURFACE PHENOMENA WITH TEM AND STEM

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The surfaces of a material are planar defects with excess energy and the 2-D structure may differ from that of the bulk. Surface conducting materials can be characterized by scanning tunneling microscopy (STM) which is challenging or impossible for insulators such as most ceramic materials. To characterize ceramic surfaces, electron microscopy in a direction parallel to the surface can be used.

In this work, the atomic structure of the thermally annealed {111} surface of yttria stabilized zirconia (YSZ) was characterized by three different electron microscopy techniques implemented together. Both high resolution transmission electron microscopy (HRTEM) and scanning transmission electron microscopy (STEM) micrographs of the same region were acquired and subsequently analyzed to determine the atomic structure of the {111} surface and a reconstructed {101} surface of YSZ.

In STEM mode, micrographs of the sample were acquired using both high angle annular dark field (HAADF) and integrated differential phase contrast (iDPC) techniques. iDPC complements HAADF imaging by providing information on the position of light atoms, in this case oxygen anions. In HRTEM mode, micrographs were acquired through focal series image acquisition to ensure imaging conditions with a negative spherical aberration coefficient (Cs). Multislice image simulations and automatic matching software were used to determine objective lens defocus and relative sample thickness. This approach allows for an assessment of the accuracy of the surface characterization by TEM. The combined TEM and STEM data provided information on the 2-D structure of the {101} and {111} surfaces of YSZ.

P-37

ADVANCED TOOLS FOR DISCRIMINATING PHASES WITH SIMILAR CRYSTAL STRUCTURE BY EBSD

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Electron Back Scatter Diffraction (EBSD) is a very effective technique for discriminating between phases with different crystallographic characteristics, but is less sensitive to the subtle changes in diffraction patterns from phases with similar structures. For example, EBSD can easily separate ferrite (body centered cubic Fe, space group 229) from austenite (face centered cubic Fe, space group 225) but will struggle to separate Cu from Ni (both face centered cubic, space group 225).

The use of compositional information from energy dispersive X-ray spectrometry (EDS) can be used to assist phase discrimination. However, the X-ray signal typically comes from a much larger source volume than the EBSD pattern, making effective discrimination between small features (e.g 5 µm) and across phase boundaries very challenging. In addition, some EBSD systems are not equipped with an integrated EDS capability, or there may exist geometrical limitations that prevent effective combined EBSD and EDS analyses.

Here we highlight two developments that enable more effective discrimination between phases with similar crystal structures, by EBSD alone.

1. Using Kikuchi band widths

Firstly, the width of individual Kikuchi bands can be used to differentiate between structures that have different sized unit cells. We outline an iterative approach that, when activated for selected phases, determines accurately the Kikuchi band widths and then applies a voting scheme to select the best fitting structure. This approach is fast (with little impact on the maximum analysis speed) and is very effective on structures that have significant (e.g. 10%) differences between their respective unit cell dimensions.

2. Pattern Matching

The second approach is to use newly developed pattern matching techniques. Here, the experimental EBSD pattern is indexed using standard Hough-based techniques, but the pattern is saved and is subsequently compared to simulated patterns for candidate phases using the previously determined crystallographic orientation. The phase that gives the highest cross correlation coefficient between the experimental and simulated patterns is then selected for each point. This approach allows for discrimination between structures with very similar unit cell dimensions. For both approaches, we will examine the limits of the respective techniques to separate close structures, and we will investigate the role of the EBSD pattern resolution and quality, providing examples from a range of different application fields.

P-38

CHIRAL GUIDED GROWTH OF CRYSTALS-ON-CRYSTALS: PREDICTABLE MORPHOLOGIES WITH LOCAL FUNCTIONALIZATION

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Metal-organic frameworks (MOFs) are a promising class of porous, crystalline materials with diverse potential applications. Their properties depend on their structures, including both their compositions and architectures. The intensive research of MOFs has led to an emerging family of hybrid crystals constructed by the conjugation of two or more different MOF units. Such hybrid crystals mainly consist of a core-shell structure, in which a guest MOFs is grown on a pre-synthesized host MOF, isotropically. We designed a unique co-MOF by combining two known crystal structures resulting in a dumbbell-shaped morphology. The dumbbell "weights" have been formed by epitaxial growth on the bases of the dumbbell's "bar", due to a common (001) facet. These unique crystals maintain their original morphologies and crystal structures in the co-MOF and their chiral nanosized channels are perfectly aligned along their long axis. Moreover, single crystal X-Ray analysis and modelling confirmed that there is chirality transfer from the "bar" to the "weights". The two crystal structures have channel walls with different chemical properties. We were able to utilize this difference and selectively confine different chromophores to the "bar" and "weight" regions resulting in selective optical functionalization of these micro-scale objects.

P-39

IN-SITU AND EX-SITU INVESTIGATION OF PHASE TRANSFORMATIONS IN THE $Fe_4Co_{2.1}Ni_{2.1}Cr_{0.8}Al_{0.8}Ti_{0.2}$ HIGH ENTROPY ALLOY

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Fe-Ni-Co-Cr-Al-Ti system is part of the wide family of Face-Centered Cubic (FCC)-based High Entropy Alloys (HEAs) with outstanding mechanical properties [1-2, and references therein]. Although FCC-HEAs exhibit high ductility, their strength is not sufficient for many industrial applications. One of the possible ways to enhance this property is by precipitation-strengthening mechanism. In this system, either precipitates of the $Ni_3(Al,Ti)$-type (γ') with $L1_2$ structure (ordered FCC) or NiAl-type B2 (ordered Body Centered Cubic (BCC)) phase can form as a function of thermo-mechanical history and composition. One of the most important factors influencing the precipitation sequence and type is total (Al+Ti) amount and/or specific Al/Ti ratio [2-5]. Depending on the precipitates` type and their size - mechanical properties of the alloys vary dramatically. Therefore, precise characterization of the precipitates which form during the phase transformation and precipitation sequence is of primarily importance for future industrial implementation.

In the Fe-Ni-Co-Cr-Al-Ti system, most researchers have focused on Ni-rich alloys [4]. In our work we have concentrated on Fe-rich composition, namely $Fe_4Co_{2.1}Ni_{2.1}Cr_{0.8}Al_{0.8}Ti_{0.2}$. Following recrystallization and cold rolling, ex-situ heat treatments at 600-800°C (for four hours) were performed studying the phase transitions and microstructural changes. Characterization was carried out using Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM). Precipitation sequence was studied by in-situ TEM, heating the sample up to 900°C. The effect of phase transformations on mechanical properties was evaluated by hardness test. Upon aging, coherent $L1_2$-$Ni_3(Al,Ti)$ - type particles have formed. As a function of temperature, they dissolved and instead B2-NiAl - type flake-like particles precipitated. Although both precipitates` types could contribute to strengthening, the $L1_2$ particles influenced the hardness more effectively probably due to their smaller size and more coherent interfaces with the matrix (as compared to B2).

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P-40

THE EFFECT OF ZN-CONTAINING MICROCALCIFICATIONS ON THE MALIGNANCY OF THYROID NODULES

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Thyroid nodules (TNs) are common neck ultrasonography (US) findings, yet only 5-10% of these nodules harbor thyroid cancer. Fine needle aspiration for cytology (FNAC) is performed when US characteristics indicate an intermediate or high suspicion of TN malignancy. Up to 30% of FNAC results can be indeterminate, necessitating repeated tests, expensive molecular testing, or diagnostic partial thyroid resection. TN diagnostic algorithms should thus be further refined without exposing patients to additional invasive procedures. As calcifications detected during thyroid US are considered a high-risk feature for malignancy, we used the remaining material following routine thyroid FNAC to isolate microcalcifications (MCs). Our subsequent analysis of these MCs revealed differences between benign and malignant TN regarding their elemental composition, morphology, and crystal phases. Specifically, we use SEM-EDS and FTIR to show that thyroid MCs are calcium phosphate crystals containing varying magnesium, sodium, iron, and zinc levels. The MCs obtained from malignant TNs were composed of sub-micrometer spherical particles, while those from benign TNs were faceted. Zinc was largely absent from MCs from benign TNs, whereas samples from malignant TNs contained zinc (7% vs. 91%, respectively, p0.001). Thus, zinc in MCs obtained from TN during routine FNAC can serve as a biomarker of TN malignancy.

P-41

SYSTEMATIC STUDY OF THE ANTI-PHASE BOUNDARIES FORMATION IN B2 FexAl1-x ALLOYS USING ex-situ AND in-situ TRANSMISSION ELECTRON MICROSCOPY

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Anti-Phase Boundary (APB) is a planar crystalline defect which might appear in ordered superlattice structures, such as the B2 (ordered Body Centered Cubic (BCC)). APBs are classified into two types, based on their morphology and the way they are formed [1]: thermal (appearing due to order/disorder transformation) and shear (formed in B2 by the dissociation of super-dislocations into partials separated by APB). It was proposed that increase in density of the APBs in B2 might improve its poor ductility [2]. Having this idea in mind, major goal of this research was to engineer the material so that APBs density will be substantially high, improving the ductility without reduction in strength. Current work presents first milestone towards achieving this goal. Here, understanding of the APB formation mechanism in B2 structure was attained. To perform this task – Fe_xAl_{1-x} B2 alloys were chosen following [3] as a model of B2 matrix of the AlCoCrFeNi High Entropy Alloys (which have a potential to become new structural materials). These alloys exhibited improved properties following the appearance of APBs [4,5]. In the past, Fe_xAl_{1-x} B2 alloys were studied with regard APBs formation experimentally [6,7] and using computational methods [8] presenting nonsystematic, contradicting results.

In current research, systematic study was performed on a series of Fe_xAl_{1-x} (x = 0.5-0.73) alloys which were cast and investigated using transmission electron microscopy (TEM). As can be seen in Figure $1a_1$-a_5, no APBs have formed in alloys with x=0.5-0.67. Instead, varying density of dislocations was detected. Applying 2 beam conditions and trace analyses [9], two different slip systems – (001)[100] and (011)[111] were revealed. Identification of a presence of type dislocations is of high importance, since as stated earlier, they can dissociate into partials which bound APBs. APBs themselves were found only in samples having x≥0.68. Increasing the Fe content, over 68 at %Fe and up to 70 at %Fe elevated the density of the APBs. Yet, these boundaries have not formed cells of domains but appeared as ribbons. Furthermore, in these samples along with an increase in the number of APBs, small highly dense DO_3 phase (identified by means of electron diffraction) has formed [10]. Increasing the content of Fe to 73 at % has altered the APBs morphology to more orthodox cellular structure. The density of the APBs has dramatically increased, and they were commonly found in the B2 grains. Amount of DO3 phase has increased with the Fe content. The presence of DO_3 raises a question of "an egg and the chicken": the APBs are formed in B2 regardless DO_3 or formation of APBs is correlated to the B2-DO_3 phase transformation. Numerous quenching from high temperature has not eliminated the DO_3 formation. To evaluate the necessity of DO_3 for APB formation, *in-situ* heating in TEM was done.

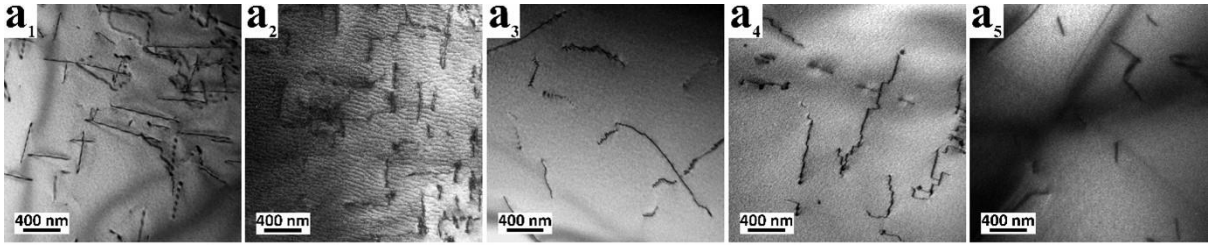

Figure 1: TEM images of the (a_1) 50at%Fe, (a_2) 55at%Fe, (a_3) 59at%Fe, (a_4) 62at%Fe, (a_5) 64at%Fe samples

For this purpose, 70 at% Fe sample was heated *in-situ* in TEM from room temperature (RT) to temperature above the B2-DO_3 transition to a single-phase B2, i.e., above 1073K (the hold was 30 min) and then cooled down (at rate of 1°C/ms) back to RT. Figure 2a_1 shows APBs in the B2 matrix at RT, prior heating. The changes that accrued during the *in-situ* heating process are presented in Fig. 2a_2-a_5. DO_3 phase was found to be stable up to ~1063K, and no change in morphology of the APBs was observed until that point, see Fig. 2a_2. At 1073K, decomposition of the DO_3 phase was documented by electron diffraction. At this temperature, growth of the existing at RT APB and formation of additional APBs was observed, see Fig. 2a_3-a_4. Furthermore, APBs maintained their cellular morphology during cooling, as shown in Fig. 2a_5. Following this experiment, it can be concluded that APBs formation does not relate to the B2-DO_3 phase transition. Furthermore, taking into account that the value at which APBs have started to form was x=0.68, we estimated, using [11], the long-range order parameter at this composition as 0.53. Knowing this value – other means to achieve required degree of disorder can be proposed (such as alloying) to engineer the material. Density Functional Theory calculations performed by group of Prof. Fuks yielded results which fully agree with our observations.

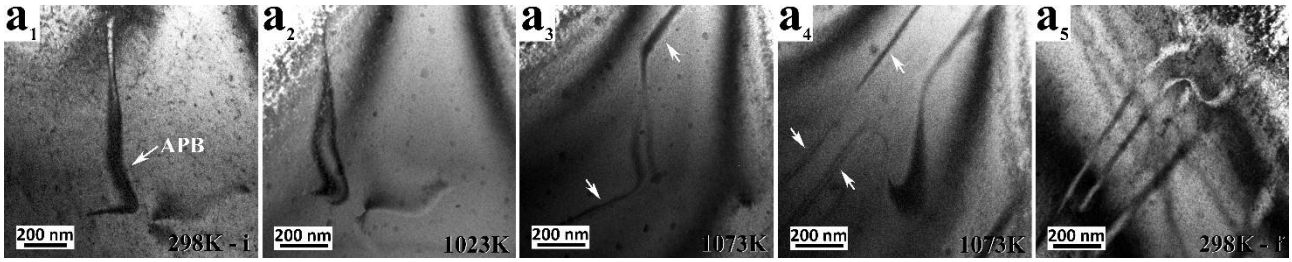

Figure 2: *in-situ* heating of the 70% at Fe sample from (a_1) initial room temperature (RT) to (a_2) 1023K. Image prior the decomposition of DO3 phase. (a_3) 1073K. APBs grow in the B2 phase, as marked by arrows. (a_4) After a hold at 1073K. Density of the APBs increased. (a_5) Final RT state.

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P-42

TWO-STEP SINTERING OF Mg-DOPED ALUMINA

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This work verifies the applicability of two-step sintering as a means of suppressing grain growth while preparing high-density alumina samples made by uniaxially pressing RTP (ready-to-press) powder prior to CIP (cold isostatic pressing). The first step of the process should be short at a relatively high temperature of 1500°C in order to achieve a high initial densification without significant grain growth. The second step is carried out at a lower temperature of 1250°C over an extended period of time to facilitate further densification with little to no additional grain growth. The density of the sintered samples was measured by Archimedes' method. The microstructure was observed using secondary electron scanning electron microscopy of fracture surfaces and polished cross-sections. Alumina with a relative (to the theoretical) density of 98.1% and a mean grain size of 1.4 ± 0.7 μm was prepared by two-step sintering. A conventional sintering process at 1500°C for 2 hours yielded a higher relative density of 99.6% and a mean grain size of 3.0 ± 1.5 μm.

P-43

MICROSCOPE-INTEGRATED SPECTROSCOPIC ELLIPSOMETER FOR FAST AND IN-SITU OPTICAL INVESTIGATION OF MICRON-SCALE MATERIALS AND STRUCTURES

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Spectroscopic ellipsometry (SE) is a widely used optical technique in both industry and research for determining the optical properties and thicknesses of thin films. The technique is based on analyzing the change in light polarization upon oblique-angle reflection from a sample. SE is well-established, non-invasive, highly accurate and sensitive; for example, capable of measuring the thicknesses of thin films with atomic-level precision. However, the effective use of SE on micro-structures is limited by low lateral resolution down to tens-of-microns only, or very slow data acquisition. As micron-scale structures are crucial and abundant in today's technology and research, these limitations significantly hinder the utilization of the powerful SE technique for future technologies.

In this work, we introduce our patented [1] Spectroscopic Micro-Ellipsometer (SME), which is a microscope-integrated ellipsometer with a lateral resolution down to 2 microns, capable of recording spectrally resolved ellipsometric data simultaneously at multiple angles of incidence in a single measurement of a few seconds, *by utilizing Fourier-plane imaging for ellipsometry* [2]. This makes SME the fastest in ellipsometric data acquisition, three orders-of-magnitude faster than the state-of-the-art high-resolution commercial ellipsometers. Most importantly, the SME can be easily integrated into generic optical microscopes as an add-on unit without disturbing their capabilities (Figs. 1a and 1b), by addition of a few standard components. *This allows transforming an imaging microscope into a sophisticated optical characterization instrument*.

In order to address a current scientific challenge in material sciences and demonstrate the unique combined accuracy and high lateral resolution of the SME, we have shown characterization of the optical properties and thicknesses of exfoliated two-dimensional material flakes which only have a few microns of lateral dimensions. As performance of van der Waals heterostructure devices is governed by the nanoscale thicknesses and homogeneity of their constituent mono- to few-layer flakes, accurate mapping of these properties with high lateral resolution becomes imperative. The SME can perform angstrom-level accurate and consistent thickness mapping on mono-, bi- and trilayers of graphene, hexagonal boron nitride (hBN) and transition metal dichalcogenide (MoS_2, WS_2, MoS_2, WSe_2) flakes [3]. Our highly sensitive system can successfully identify near-transparent monolayer hBN, a challenging proposition for other characterization tools. The optical microscope integrated ellipsometer can also map minute thickness variations over a micron-scale flake, revealing its lateral inhomogeneity (Figs. 1c-1e). *The prospect of adding standard optical elements to augment generic optical microscopes with accurate in-situ ellipsometric mapping capability presents new opportunities for investigation of exfoliated 2D materials, as well as many other micron-scale systems such as meta-materials and biological structures which previously were not conveniently addressable by spectroscopic ellipsometry.*

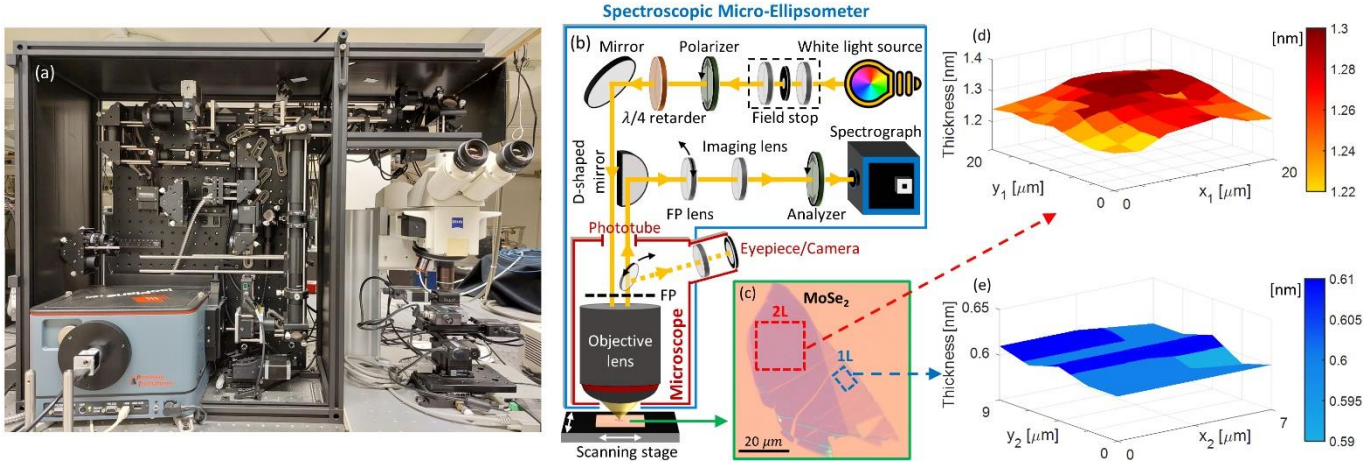

Figure 1 – (a) Current version of the Spectroscopic Micro-Ellipsometer (SME), integrated into a commercial optical microscope. (b) Schematic of the SME; FP: Fourier Plane. (c) Exfoliated $MoSe_2$ monolayer (1L) and bilayer (2L) flake with marked areas for thickness mapping by the SME. (d) Thickness map of $MoSe_2$ bilayer over an area of 20 x 20 μm^2. (e) Thickness map of $MoSe_2$ monolayer over an area of 7 x 9 μm^2. The SME spot size for these measurements is 5 μm.

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P-44

BRILLIANT WHITENESS IN SHRIMP FROM ULTRA-THIN LAYERS OF BIREFRINGENT NANOSPHERES

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White colors are produced by diffuse light propagation in disordered media. To generate whiteness, photons of all wavelengths must be scattered multiple times and lose their directional information to produce broadband, angular independent reflectance. While this is easily achieved with thick samples, it is difficult to obtain with thin layers of material. For typical nanoparticle-based scatterers, reflectance decreases above filling fractions of ~30% due to near-field coupling of adjacent scatterers. Here we show how cleaner shrimp generate one of the most efficient white colors in nature, by tuning both single particle and ensemble scattering properties(1). We used cryo-scanning electron microscopy, STEM, TEM, selected-area-electron-diffraction and Raman spectroscopy to discover the nature of the impressive white color, which provides effective signaling in an aqueous habitat. The whiteness arises from white chromatophore cells containing densely packed nanospheres composed of isoxanthopterin. The nanospheres are composed of 1-dimensionally ordered, stacked assemblies of isoxanthopterin which project radially outwards from the center of the sphere (i.e., a spherulite). Strikingly, numerical simulations reveal that extreme birefringence, which originates from the spherulitic arrangement of isoxanthopterin molecules, diminishes optical crowding effects, enabling intense scattering up to the maximal packing achievable for random spheres (~65% filling fraction). Overall, the combination of the high refractive index ($n \approx 2.0$), extreme birefringence (~ 30%), and polydispersity of the nanospheres enables intense scattering from an ultra-thin layer. These results inspire the design of biologically benign replacements for artificial scatterers like titanium dioxide and highlight the importance of birefringence as a structural handle to enhance the performance of such materials.

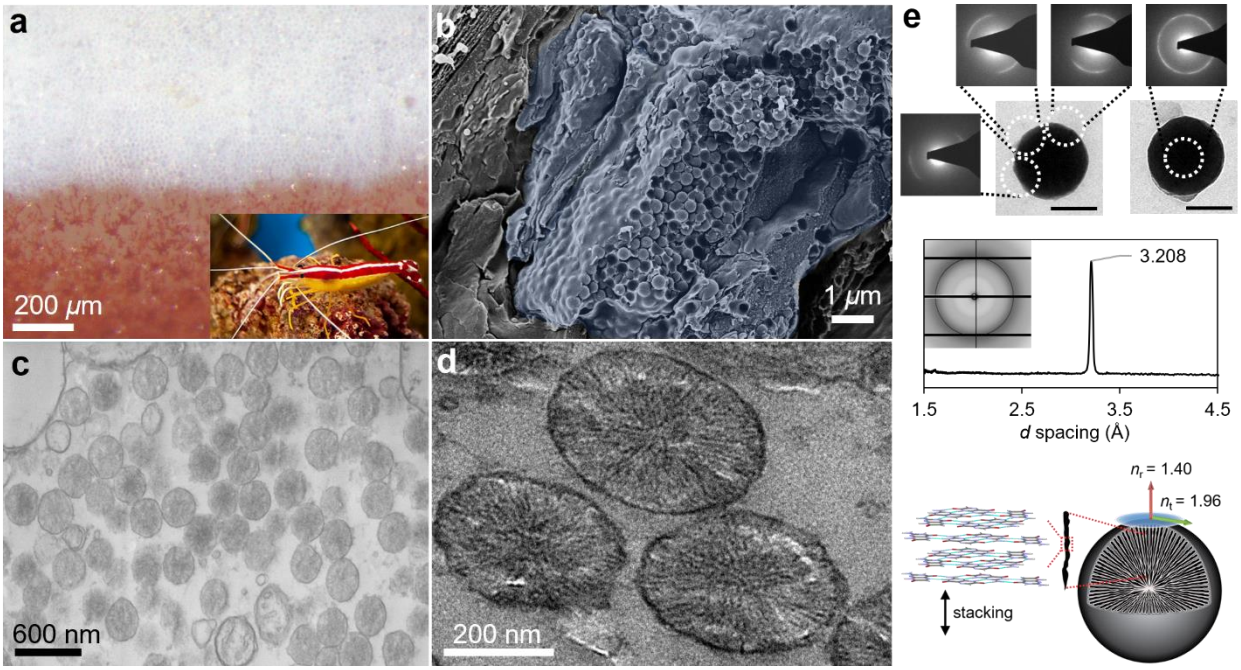

Figure 1. a) Optical image of the white stripe on the cleaner shrimp's back exhibiting the dense and dendritic white chromatophores. Insert: Image of the Pacific Cleaner Shrimp (Lysmata amboienesis). b) Cryo-SEM image of a white chromatophore cell under the transparent chitin cuticle. c) STEM micrograph of nanospheres within a cell in an ultrathin tissue section (~100 nm). d) TEM micrograph of the nanospheres in an ultrathin tissue section exhibiting the spoke-like, spherulitic structure. e) Top: TEM images and corresponding selected area electron diffraction of two particles with d spacing ~3.2 Å. The reflection angle changes when moving along the dihedral angles of the particle indicating that the stacking axis projects away from the center of the sphere. Scale bar: 200 nm. Middle: In situ μ-spot wide-angle X-ray scattering (WAXS) diffraction pattern from the maxilliped (obtained by radial integration of the 2D scattering pattern (inset)). Bottom: Schematic of a nanosphere showing the spherulitic arrangement of stacked isoxanthopterin molecules. Radial (nr) and tangential (nt) refractive index vectors on the nanosphere surface illustrate the birefringence produced from the spherulitic arrangement.

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P-45

CATHODOLUMINESCENCE SEM OF $CsPbBr_3$ PEROVSKITE NANOCRYSTAL SUPERLATTICES

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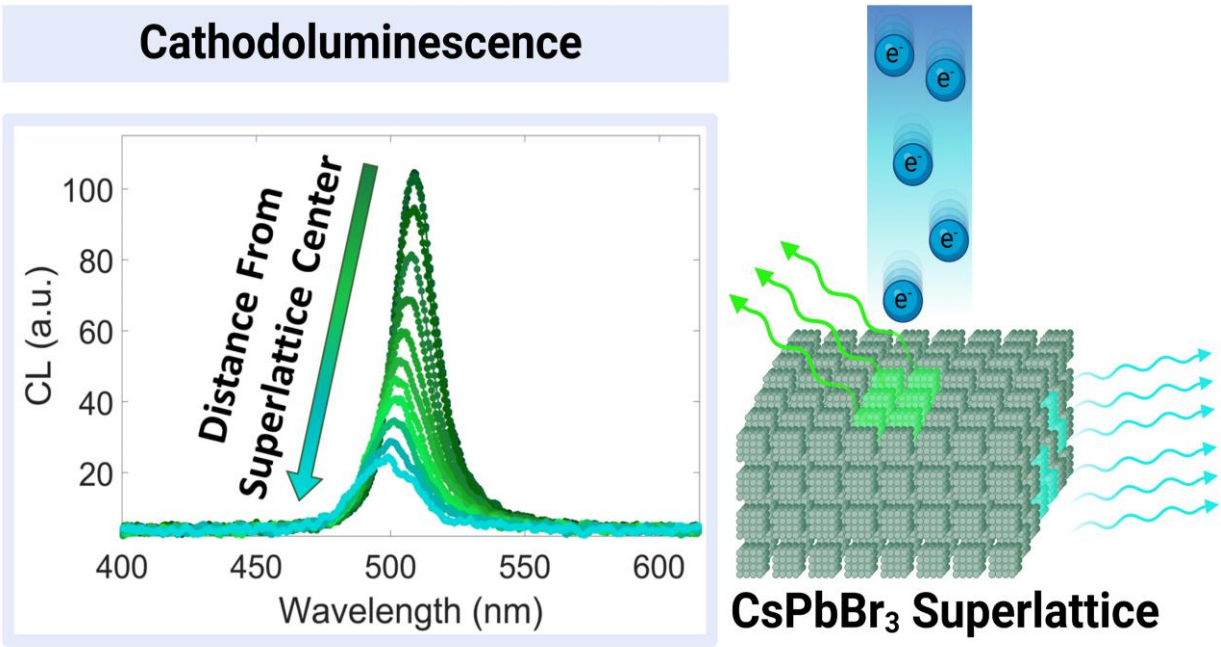
Perovskite nanocrystal superlattices (NC SLs) display optoelectronic properties which differ from individual crystals, and give rise to new ensemble collective phenomena. Structural and optical heterogeneities in the SLs lead to a reduced coupled emission, and change the collective ensemble properties. Free electrons in scanning electron microscopy (SEM) are used to probe the cathodoluminescence (CL) properties of $CsPbBr_3$ SLs with high spatial resolution. Combined CL-SEM measurements allow simultaneous characterization of structural and optical heterogeneities of the SLs. Hyperspectral CL mapping shows multipole emissive domains within a single SL. Additionally, light emission from the edges of the SLs is blue shifted by up to 65meV relative to their center. This CL shift is dependent both on the sizes of the SL and NC building blocks. Residual uniaxial compressive strains accompanying SL formation are contributors to this emission shifts.



P-46

SIZE EFFECT ON STRENGTH OF EQUILIBRATED COPPER NANOPARTICLES FABRICATED BY SOLID-STATE DEWETTING

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It is now well established that mechanical properties of metal samples of nanometric dimensions are very different from those of their bulk counterparts. Strong size effect in mechanical strength has been reported for many face centered cubic (FCC) metals and alloys, yet the dislocation nucleation-controlled plasticity mechanisms are still poorly understood. In the present work, solid state dewetting technique was employed to produce defect-scarce copper nano- and microparticles of various sizes exhibiting equilibrium crystal shape. The results of in-situ microcompression tests revealed two clear size-related regimes, where large copper particles exhibit a strong size effect in strength with size exponent comparable to other FCC metals, while their smaller counterparts show weak size dependence of strength, which saturates at about 10 GPa. Our experimental results were in good quantitative agreement with the results of atomistic molecular dynamic simulations of Cu nanoparticles compression. We related the two different size effect regimes to the high probability of dislocation nucleation event at the corner of the particle facets, and increasing probability of finding crystal structure defects inside the particles with increasing particle size.

P-47

REGULATING GRANULE STARCH HYDROLYSIS TO MAKE POROUS STARCH

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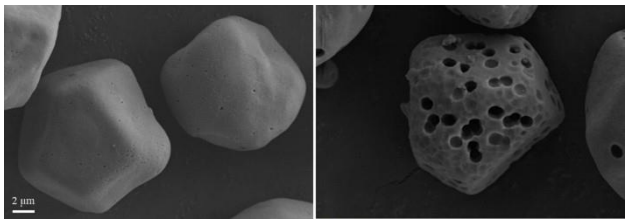
Starch is the second most abundant biological polymer, after cellulose, produced on earth. Native starch exists in the form of granules of different sizes and shapes, that depend on the botanical source. Porous starch is a modified starch that is non-toxic and economical adsorbent extensively used in food, pharmaceutical and environmental applications. It consists of abundant pores that are distributed on the granule surface and extend towards the central cavities, without changing the granular structure. Enzymolysis of raw starch granule at sub-gelatinization temperature is a good way to make porous starch. The alternating structure of amorphous and crystalline layers of starch guarantees the continuity of this hydrolysis.

In this work, we make porous starch from different botanical sources by hydrolysis with amylase. We study the structure and morphology using advanced electron microscopy methods, and additionally defined the concept of GSHU (Granule Starch Hydrolysis Units) and prove it is a useful tool to regulate double-amylase hydrolysis treated with UHP (Ultra high-pressure processing). GSHU reflects the difficulty of how granular starches are attacked by enzyme and it can be a good way to unify the degree of hydrolysis of granule starch. With UHP treatment, lower amount of enzyme (or shorter processing) is needed to reach the same porosity compared to untreated samples. The GSHU parameter can guide the selection of catalysts to achieve similar porosity.



P-48

Cr/AlCoFeNi DIFFUSION COUPLE FOR MAPPING MICROSTRUCTURAL CHANGES

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Novel metallurgical approach of High Entropy Alloys (HEAs) suggests using multiple elements at approximately equiatomic composition to achieve solid solutions which exhibit unique physical properties [1]. One of the most studied HEAs is AlCoCrFeNi. This system might form: Cr-Fe rich Body Centered Cubic (BCC), Al-Ni rich B2 (ordered BCC) and Fe-Co-Cr rich Face Centered Cubic (FCC) phases as a function of thermo-mechanical treatments and composition [2, for example]. To understand the effect of composition, influence of specific elements on quinary Al-Co-Cr-Fe-Ni system was studied [3-7]. It was concluded in [7] that Cr influences dramatically the microstructure and, thus, the mechanical properties of the $(AlCoFeNi)_{1-x}Cr_x$ alloys. However, all investigations of the effect of elements on this system were performed non-linearly, i.e. by casting specific compositions. Therefore, the knowledge gathered in this way is not complete. In current research, diffusion couple approach was used to study the effect of Cr on $(AlCoFeNi)_{1-x}Cr_x$ alloys in details. To the best of our knowledge, this approach was not used before on any HEAs. The Cr/AlCoFeNi diffusion couple was prepared using arc-melting. Microstructural study was carried out by High Resolution Scanning Electron Microscopy (HRSEM) and Transmission Electron Microscopy (TEM). Focused Ion Beam (FIB) was used to extract TEM lamellae at specific compositions. This allowed mapping the microstructure, crystallographic structures and composition of different phases forming as a function of Cr content.

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P-49

MEASURING THE SOLUBILITY LIMIT OF DOPANTS BY FULLY STANDARDIZED WAVELENGTH DISPERSIVE SPECTROSCOPY

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The development and implementation of polycrystalline ceramic materials strongly depends on the ability to control the microstructure of the sintered material. Many studies have focused on the mechanism that governs and influences the evolving microstructure during densification and how such changes in the microstructure affect the properties. Specifically in alumina, the influence of impurities and dopants has been extensively studied. Changes in the grain boundary mobility were observed at impurity levels below the solubility limit, without the presence of a secondary phase or liquid phase, due to solute-drag or solute-acceleration caused by an adsorbate. To understand the role of key dopants in alumina and their influence on the microstructure, it is important to know their solubility.

In our group, a technique was developed to measure the solubility limit of dopants in a ceramic matrix using fully standardized wavelength dispersive spectroscopy (WDS). Due to the low concentration of many key dopants in fully saturated alumina, WDS is an ideal technique to measure the solubility limit, which can be as low as a few ppms. The solubility limits of key dopants, such as Mg, Ca, Si, Fe, and C in alumina at 1600°C were measured by WDS using fully saturated alumina samples quenched from 1600°C [1-6]. The technique will be presented and the results will be discussed.

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P-50

CALCIUM AND ELONGATED GRAINS IN ALUMINA

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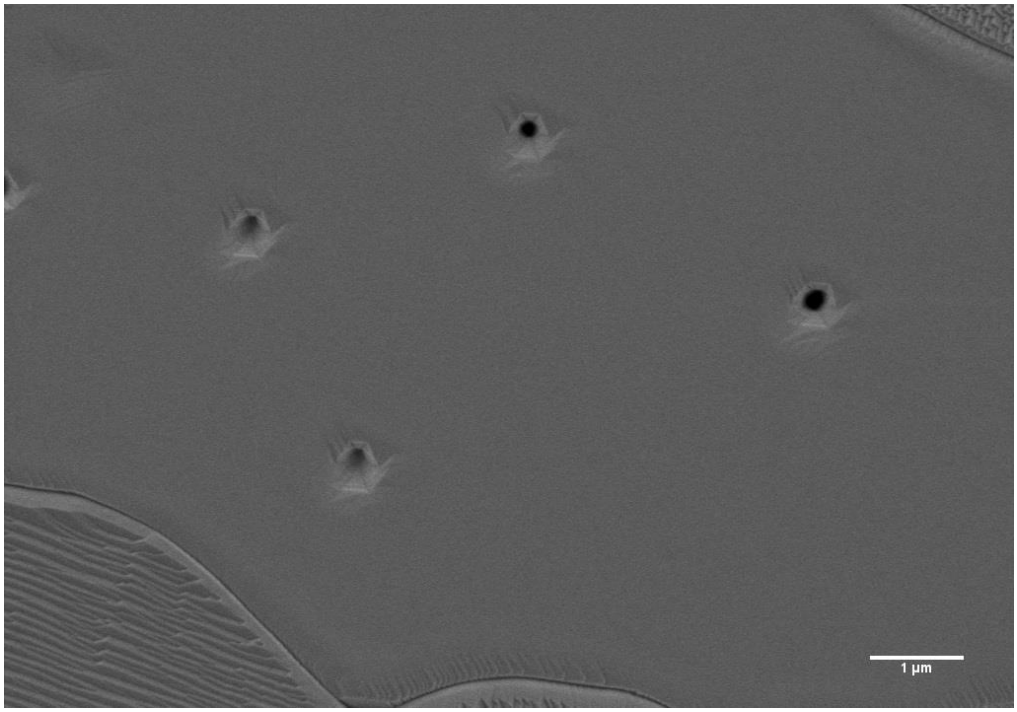
Grain growth is an important process which occurs together with densification during sintering of polycrystalline ceramic materials. The shape of grains can influence the properties of a sintered material, and thus it is important to understand the reasons behind morphological changes during thermal processing of ceramics.

α-alumina is one of the most studied ceramics, in part due to its optical and mechanical properties, and thus it is often used as a model system for fundamental studies. Previous studies have clearly demonstrated that doping alumina with calcium (Ca) below the solubility limit results in accelerated and anisotropic grain growth, and as a result changes the crystal shape, where elongated plate-like alumina grains form. It is not clear if the elongated shape is due to the system approaching equilibrium, i.e. the equilibrium crystal shape of alumina due to adsorbed Ca to some crystallographic surfaces, or if this is a kinetic shape where Ca results in anisotropic grain boundary mobility.

In on-going this study, undoped and Ca-doped alumina was sintered to obtain a dense microstructure. Combined electron microscopy techniques were used to correlate the crystallographic shape of elongated grains in Ca-doped alumina, compared to the shape of equilibrated pores occluded in the alumina grains.



P-51

THE INFLUENCE OF ADDITIVES ON THE CRYSTALLIZATION OF CALCIUM PHOSPHATE IN PHYSIOLOGICAL CONDITIONS

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Hydroxyapatite (HA) crystals are the inorganic component of physiological minerals such as bones and teeth. They are a significant component of pathological calcifications, mineral deposits that form in soft tissues. HA crystals can form in renal and cardiovascular disorders, inflammation, and cancer. In breast and thyroid cancers, microscopic HA particles called microcalcifications (MCs) are associated with higher malignancy and poorer prognosis. While physiological mineralization is a highly regulated process yielding crystals with consistent characteristics, pathological minerals are often heterogeneous in composition, crystal phase, and morphology. Most studies report that in tumors, HA crystallization occurs in the extracellular environment. Blood plasma is such extracellular fluid that is supersaturated with respect to HA. Hence, a solution mimicking the blood plasma can serve as a platform to manipulate and inhibit HA crystallization in the context of cancer. We utilize a simulated body fluid (SBF) solution specifically modified to resemble the inorganic ion concentrations, pH, ionic strength, and temperature of blood plasma. We use anionic additives rich in carboxyl acid groups, such as polyacrylic acid (PAA) and polyaspartic acid (PAsp), to inhibit HA precipitation in SBF. We were able to inhibit more than 88% of HA crystallization using PAA, depending on its concentration (100; 200 mg/mL) and molecular weight (8000; 100,000 g/mol), with inhibition increasing with molecular weight and concentration. We show that PAsp can inhibit and promote HA formation in a concentration-dependent manner, as high PAsp concentration inhibits HA formation while low concentration promotes it. Those additives not only inhibit the formation of HA but also affect the resulting crystal phase by stabilizing amorphous calcium phosphate (ACP), an unstable precursor for HA formation. Furthermore, significant HA inhibition (40%) occurs through the stabilization of ACP. The effects of various additives on the crystallization process and behavior within the SBF solution are investigated using optical microscopy, while the morphological influence of the additives is analyzed using scanning electron microscopy. In the future, we will explore these additives in an in vitro 3D tumor model for their ability to inhibit MC formation and potentially suppress malignancy. We aim to contribute to developing new approaches for inhibiting pathological mineralization and ultimately improving patient outcomes in breast and other cancers.

P-52

DIRECTING THE MORPHOLOGY , PACKING, AND PROPERTIES OF CHIRAL METAL-ORGANIC FRAMEWORKS BY CATION EXCHANGE

Hadar Nasi[1], Maria Chiara di Gregorio[1], Qiang Wen[1], Linda J. W. Shimon[2], Ifat Kaplan-Ashiri[2], Tatyana Bendikov[2], Gregory Leitus[2], Miri Kazes[1], Dan Oron[1], Michal Lahav[1], Milko E. van der Boom[1]

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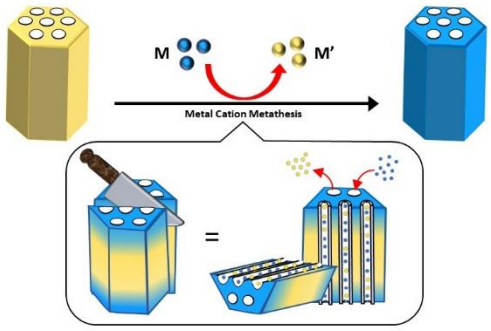
Predicting crystal morphology, packing and composition is with great interest in material science. Metal-organic frameworks (MOFs) are well studied and explore materials due to their use for many applications.[1-3] Here we show that metal–organic frameworks, based on tetrahedral pyridyl ligands, can be used as a morphological and structural template to form a series of isostructural crystals having different metal cations and properties. The primary manganese-based crystals are characterized by an uncommon space group (*P*622). The packing includes two different chiral channels that can mediate the cation exchange, as indicated by energy-dispersive X-ray spectroscopy on microtome-sectioned crystals. The observed cation exchange is in excellent agreement with the Irving–Williams series [4] associated with the relative stability of the resulting coordination nodes (MnFeCoNiCuZn). The crystals maintain their morphology, allowing a quantitative comparison of their optical and magnetic properties at both the ensemble and single-crystal level.



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P-53

NANOSTRUCTUAL CHARACTERIZATION OF COMPLEXES OF DNA WITH A DIBLOCK-COPOLYMER OF POSITIVELY-CHARGED AND NEUTRAL BLOCKS, AND THEIR STABILITY IN THE PRESENCE OF BLOOD SERUM ALBUMIN

Sapir Rappoport[1], Varvara Chrysostomou[2], Stergios Pispas[2], Yeshayahu Talmon[1]

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Quaternized poly(2-(dimethylamino ethyl methacrylate)-b-poly(oligo(ethyleneglycol) methyl ether methacrylate) (QPDMAEMA-b-POEGMA) is a copolymer of a positively charged block and a non-ionic hydrophilic block. The positively charged block, QPDMAEMA, can electrostatically interact with oppositely charged polymers such as DNA, to form complexes, also known as polyplexes. These complexes are stable in aqueous solution due to the hydrophilic block, POEGMA, which provides colloidal stability and biocompatibility. Polyplexes can be used as non-viral vectors in gene therapy. The polyplexes are essential for delivering genetic material into cells because they protect the genetic material from degradation before reaching the target cells, thus increasing the transfection efficiency. In-vitro study of these polyplexes at charge ratio of 2 and 4, showed transfection efficiency of almost 50%. However, currently used polyplexes show a low transfection efficiency in-vivo, probably because the polyplexes are exposed to blood proteins, such as serum albumin, which cause their dissociation.

We used cryogenic transmission electron microscopy (cryo-TEM) and small-angle x-ray scattering (SAXS) to study the inner structure of QPDMAEMA-b-POEGMA and DNA complexes at different charge ratios. The results show that lamellar and hexagonal structures are formed depending on the charge ratio. Studies showed that hexagonal complexes have higher transfection efficiency than lamellar complexes. Such hexagonal complexes are shown in Figure 1. The complexes were also examined after exposing them to bovine serum albumin (BSA). We found that BSA does not affect the complexes for seven days. That stability is essential for better design and formulation of vectors for gene therapy.

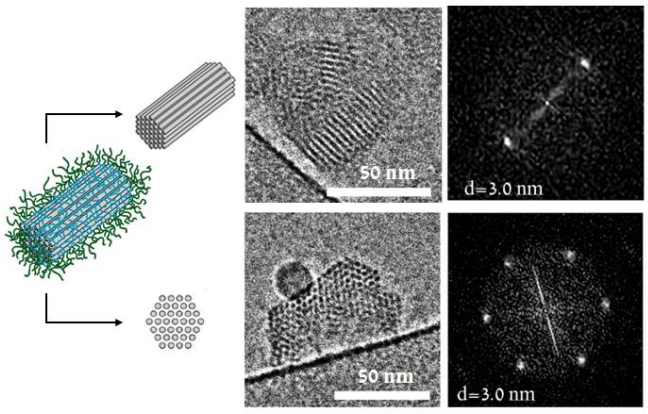

Figure 1. Different projections of a hexagonal structure of QPDMAEMA-b-POEGMA and DNA complexes at CR of 10 in cryo-TEM micrographs (left). The spacing is 3 nm, as shown in the Fourier transforms on the right.

P-54

OPTICAL CHARACTERIZATION OF LEAD HALIDE PEROVSKITES HETEROSTRUCTURE INTERFACE WITH CATHODOLUMINESCENCE SPECTROSCOPY

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Heterostructures and interfaces are crucial in determining the local electronic material properties in semiconducting devices. Halide perovskites are less explored semiconductors that have raised interest due to their unique optoelectronic properties with promising suitability for photovoltaics, lasing, and detection applications.

In this work, we explore the interfaces of CsPbBr3 with competing phases - Cs4PbBr6 and CsPb2Br5 grown from the vapor phase on Si substrate.

Although these phases are similar in composition, they vary in microstructures and electronic properties. Cathodoluminescence spectroscopy (CL) and time-resolved cathodoluminescence (TRCL) are high-energy electron microscopy techniques that provide a powerful way to characterize optical properties. This research used a CL DELMIC SPARC installed in SEM (FEI Quanta 650) with an ultra-fast beam blanker, providing a few nm spatial resolution and around 50ps time resolution. These properties enable distinguishing between such phases, mapping the material interface, and correlating microstructure with dynamic properties of the emitted light.

Using those methods, we detect an enhancement of CL emission at the perovskite interface. In a similar setup, we detect defects and analyze their effects on optical properties, enabling an advanced understanding of material properties and engineering. Our vision is to develop and engineer perovskite heterostructures with controlled properties for ultra-fast light emission.

P-55

THE EFFECT OF SALTS ON THE NANOAGGREGATION OF SLES IN AQUEOUS SOLUTIONS OBSERVED BY CRYO-TEM

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Sodium lauryl ether sulfate (SLES) is an amphiphilic molecule widely used as an anionic surfactant in soaps, personal care, and cosmetic products. Minor components, like salts or fragrance molecules, are usually added to the industrial formulations of SLES-based products, and significantly affect their nanostructure and properties. SLES in aqueous solutions, with the addition of minor components, self-assemble into different nanoaggregates, such as nanometric spheroidal micelles, threadlike micelles, branched networks, and vesicles (Figure 1), depending on the concentrations of SLES and the additive. Direct imaging of SLES with commonly used salt additives can explain the nanostructural modifications affecting the macroscopic properties of the solution. This could serve as a basis for optimized formulation design of SLES-based products.

We use cryogenic transmission electron microscopy (cryo-TEM) direct imaging to study the effect of different salts on the nanostructure of SLES aqueous solutions, at different salt-to-surfactant molar ratios (X). We conduct rheological measurements to predict nanostructural changes, as the viscosity is strongly affected by the self-aggregated nanostructure of the system. In our study, we show the correlation between the rheological properties and the nanostructural changes of SLES with varying salt concentrations. Moreover, we present the formation of different nanostructures when different types of salts (LiCl, NaCl, KCl, and CsCl). We also demonstrate how the specimen preparation process affects the imaged nanostructures through artifact formation.

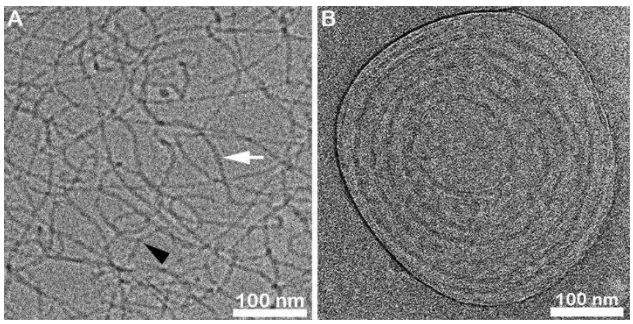

Figure 1. Cryo-TEM micrographs demonstrating the different nanostructures of 5 wt.% SLES with a salt-to-surfactant molar ratio, X, that gives the maximum zero-shear viscosity, with NaCl and KCl; (A) With NaCl, at X=10, showing networks of elongated threadlike micelles (white arrow) with several branching points (black arrowhead). (B) with KCl, at X=3.5, showing concentric multi-layered vesicle-like structures.

P-56

A CATION EFFECT ON SELF-HEALING IN APbI3 PEROVSKITE THIN POLYCRYSTALLINE FILMS

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In terms of sustainable use, Halide Perovskite (HaP) semiconductors have a strong advantage over other classes of (opto)electronic materials, as they can self-heal from damage autonomously.[1-4] Using "1-Photon fluorescence recovery after photobleaching" (FRAP) technique, we show for the first time self-healing (SH) in encapsulated Pb iodide perovskite ($APbI_3$) polycrystalline thin films (the form used in devices for PV, LED, radiation detection). We showed the electronically inactive A cation significantly affects the kinetics of SH. We excite and damage the material with 488 nm supra-bandgap laser pulses of different power densities to inflict different extents of damage and measure the PL to compare SH in 4 types of photoactive $APbI_3$ encapsulated perovskite thin films, viz., 1. Tetragonal $MAPbI_3$; 2. Tetragonal 20% Guanidinium-substituted $MAPbI_3$; 3. High-temperature cubic α-$FAPbI_3$ and 4. Low-temperature orthorhombic γ-$CsPbI_3$. We compared the healing kinetics and extent of healing of numerous spots that were damaged by the laser pulses, over given periods of time. Among them, γ-$CsPbI_3$ healed fastest and completely from close to 100% damage, in less than 1.5 hrs, followed by complete healing of the HT photoactive α-$FAPbI_3$ phase in 3 hrs; 20% Guanidinium substituted $MAPbI_3$ took 6 hrs, whereas, $MAPbI_3$ showed the slowest healing kinetics and only 30% PL recovery occurs from >95% photo-damage after 9 hrs. Compared to $MAPbI_3$, all other perovskite films, substituted with either bulkier organic cations with lower dipole moments (and with additional options for H-bonds) or smaller inorganic cations, can be viewed as strained due to monovalent cation size mismatch (as per tolerance factor). Remarkably all these recovered completely in a period equivalent to one night cycle, i.e., highly relevant for solar cells. This study will help in the selection of better functional materials for autonomously sustainable optoelectronics. The more reversible the photo-damage (without external intervention), the more sustainable is the material, and, with it, the device that is based on its function.

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P-57

CERAMIC–METAL INTERFACE: THE INFLUENCE OF TITANIUM ON THE MICROSTRUCTURE OF VACUUM BRAZED ALUMINA-ALUMINUM ALLOY

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The influence of titanium (Ti) active metal element on grain growth in enhancing the wetting behaviour and adhesion of the alumina (Al_2O_3) substrate and its effect on the aid of residual stress in vacuum brazed Al_2O_3/Aluminum alloy joints were evaluated. Physical vapour deposition (PVD) of the titanium of 5 µm thickness coated over the surface of Al_2O_3 as additive manufacturing (AM) vacuum brazed with aluminum alloy at 630 °C holding for 5 minutes using eutectic Al4047 filler alloy in a vacuum condition ranging from 10^{-3} to 10^{-5} torr. The effect of titanium on interfacial joint microstructure with respect to the brazing temperature and brazing time was investigated by scanning electron microscopy with energy dispersive spectrometry and the X-ray diffraction technique was used to identify the reaction compound formation, and also to measure the relief of residual stress at the interface. The typical interfacial structure of ceramic-metal joint: ceramic Al_2O_3/(Ti-O-Al)/Ti/(Ti-Al-Cu-Fe)/(Al-Si-Fe) intermetallic/(Al-Si-Cu-Fe)/Aluminum alloy substrate. The interfacial characterization of titanium-doped alumina exhibits titanium adsorption to the grain surface. The titanium-rich reaction phase adjoining Al_2O_3 becomes gradually discontinuous from continuity as the brazing time extends. The brazed interface response to residual stress was assessed by measuring the d-spacings using the X-ray diffraction method. The evaluated tensile residual stress on the interface is -3.4 MPa. The brazed Al_2O_3 with titanium coating resulted in a significant increase in relieving the residual stress formed due to the thermal expansion coefficient mismatch. Achieving a highly reliable metal-ceramic joint is dependent on both enhancing the wettability of the Al_2O_3 faying surface through the titanium-rich intermetallic compound formation in a controlled atmosphere and also by the relief of residual stress at the interface.

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P-58

ON THE DEVELOPMENT AND ATOMIC STRUCTURE OF ZnO CRYSTALS GROWN IN POLYMERS FROM VAPOR PHASE PRECURSORS

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Sequential infiltration synthesis (SIS), an ALD-derived method for growth of inorganic materials inside polymeric structures, is an emerging technique for hybrid materials and inorganic nanostructure fabrication which can be utilized in a wide array of applications. In this work, we study the development of ZnO crystalline particles within SU-8, polymethacrolein (PMCHO), and polymethyl methacrylate (PMMA) at the atomic scale. We probe the growth throughout diethyl zinc (DEZ)/H_2O SIS cycles, as well as after polymer removal. The crystalline ZnO structure is deciphered by combining two powerful methods: extended x-ray absorption fine structure (EXAFS) and high-resolution scanning transmission electron microscopy (HR-STEM). Synchrotron-based EXAFS provides large-scale statistical information on the crystals' long-range order and predicts their Wurtzite structure. HR-STEM of the hybrid polymer-ZnO films corroborates the predicted structure and allows for precise analysis of crystal size, orientation, and existing defects, as well as the dispersion of the particles inside each polymer. Significantly, the polymer matrix allows us to probe the growth, cycle-by-cycle, providing insights to ZnO atomic growth mechanism inside different polymers and extending our understanding of SIS. In addition, the methodology developed for such high-resolution imaging of hybrid films will allow future studies of additional hybrid systems.

P-59

HIERARCHICAL SELF-ASSEMBLY INVOLVING CLASICAL AND NONCLASSICAL STEPS IN ORGANIC CRTYSTAL GROWTH

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Organic crystal nucleation and growth are complex processes that often do not fit into the scope of the existing crystallization theories. We investigated a crystal growth mechanism of an organic dye, perylene diimide, using high-resolution cryogenic transmission electron microscopy and optical spectroscopy. We were able to demonstrate that the evolution of order in our system had a high level of complexity and involved both classical and nonclassical steps. The crystallization mechanism included a series of supramolecular transformations, where each step defined the next one. The crystal growth started from a molecular self-assembly into π-stacks that eventually underwent intermolecular ordering that optimized interactions within the stacks. The latter transformed at the larger scale, by stack interactions, which formed crystalline domains. Finally, the formed faceted crystals gradually grew through oriented attachment of other crystal, and attachment of residual monomeric molecules from solution (Figure 1).

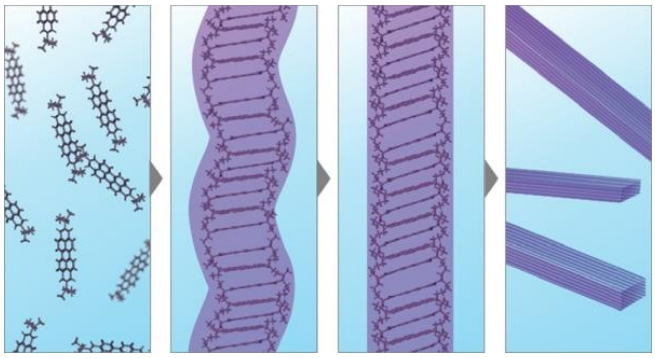

Fig.1 An illustration of order evolution during the crystallization of perylene diimide.

Our findings present a detailed insight into organic crystal growth and reveal that both classical and nonclassical mechanisms can operate within a crystallization process.[1] However, classical/nonclassical dichotomy provides only a partial insight into the crystallization mechanism, which may be described as a sequence of supramolecular events, traversing a vast size scale from the optimization of intermolecular interactions to the oriented attachment of crystals. In summary, our work revealed the inherent nature of supramolecular transformations occurring in organic crystallization, thus advancing conceptually our understanding of order evolution in organic matter.

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P-60

VISUALIZING THE EFFECT OF ELECTRIC FIELDS ON FOULING FORMATION USING CONFOCAL MICROSCOPY

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The accumulation of organic and inorganic substances on functional equipment, often reffered to as fouling, is a common and severe problem in various processes, such as water treatment membranes and heat exchangers. The formation of a fouled layer leads to reduced performance, increased energy consumption, increased chemical waste, and increased operational costs. Fouling mitigation using electric fields is a promising method[1,2]; however, an understanding of the exact dynamics and scalant-surface interactions is still lacking. It is hypothesized that electric fields mitigate heterogeneous scaling formation through the disruption of the ion stoichiometry required for nucleation, via counter-ion repulsion within the electric double layer (EDL) formed near a charged surface. This study aims to understand the effect of electric field application on fouling formation and removal using in-situ direct observation confocal microscopy. For that purpose, a designated flow cell was designed. The novelty of this flow cell is that it enables to preform microscopic process experiments, such as water filtration through a membrane or heat exchange process, under applied electric field. The flow cell was mounted on a confocal microscope, and the spatial and temporal accumulation of deposit on the functional surface was monitored during the experiment. Dyes and microparticles with fluorescent labels were used as model foulants, simulating salts and colloids forming foulants found in water, used for membrane filtration and heat exchange processes. Copper foil and electrically conductive membranes were used as model surfaces. As electric field was applied, the foulant distribution at the surface and at different distances from it was imaged (Fig. 1); higher concentration of foulant near a surface will result in increased fouling. Analysis of these images showed that electric field affects the dye distribution near the surface in agreement with the charge of the dye and surface polarity, leading to potential use of electric field as foulant removing method. For the microparticles, a tradeoff between the applied electric field and process parameters was observed. This led to irreversible deposition at the tested conditions.

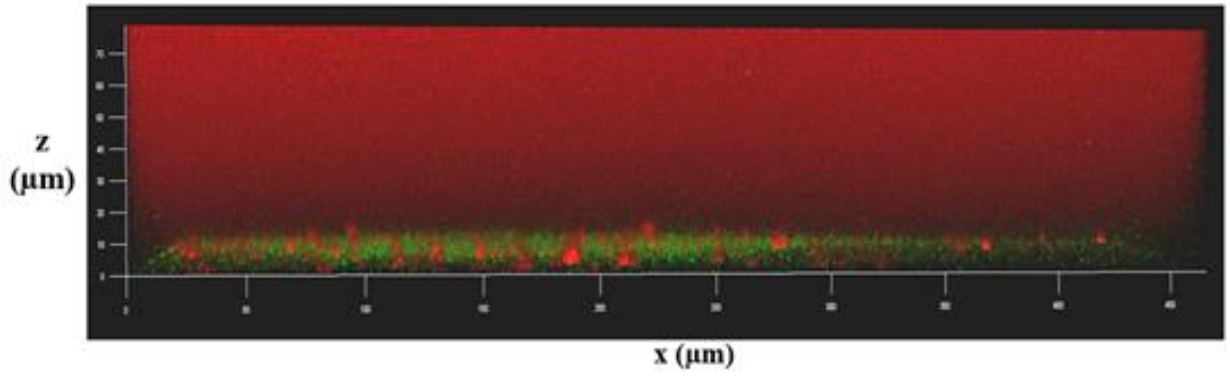

Fig. 1: Confocal image of a positively charged fluorescent dye (red) near a negatively charged surface (green)

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P-61

THE EFFECT OF CALCIUM OXALATE CRYSTAL PHASE, MORPHOLOGY, AND AGGREGATION ON PROTEIN ADSORPTION AND CANCER CELL ATTACHMENT

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Calcium oxalates (CaOx) are pathological biominerals observed in kidney stones and breast and thyroid cancer. In breast cancer microcalcifications, CaOx crystals are exclusively associated with benign lesions. However, calcium phosphates are found in both malignant and benign lesions and trigger cancerous behavior in breast epithelial cells in vitro according to their crystal properties. Based on recent results from our lab showing that calcium oxalate dihydrate (COD) crystals can suppress breast cancer progression *in vitro*, we hypothesize that this positive effect will also vary as a function of COD crystal properties.

Here, we focus on the two physiologically relevant calcium oxalate hydrates, COD and calcium oxalate monohydrate (COM). We study the influence of COD and COM with different crystal properties, including morphology, particle size, and surface area on crystal aggregation, protein adsorption, and crystal-cell interactions. We synthesized five different COD morphologies: Thin-bipyramid, thick-bipyramid, dumbbell-like, rod-like, and spherical, by crystallization from solutions, varying the supersaturation, stirring speed, modifier addition, and time of crystallization. The crystal phases were characterized by Fourier transform infrared spectroscopy (FTIR) and X-ray diffraction (XRD), and the crystal morphology and particle sizes by scanning electron microscopy (SEM). Furthermore, we used light microscopy to monitor crystal aggregation. The crystal aggregation rate of COD with all five morphologies was more significant in a biological-like environment (cell culture media) than in phosphate buffer saline (PBS), most likely due to the presence of biological macromolecules that adsorb to the crystal surfaces. Additionally, the thick-bipyramid morphology is prone to form bigger aggregates than the other four COD morphologies, while dumbbell-like morphology forms the greatest number of aggregates. Our ongoing work includes an assessment of model protein adsorption and cell attachment to COD and COM crystals, normalized to their surface area, to determine the role of the CaOx hydration state and morphology on the crystal interactions with biological materials.

P-72 (last minute submission)

RATIONAL DESIGN AND FABRICATION OF BLOCK COPOLYMER TEMPLATED HAFNIUM OXIDE NANOSTRUCTURE

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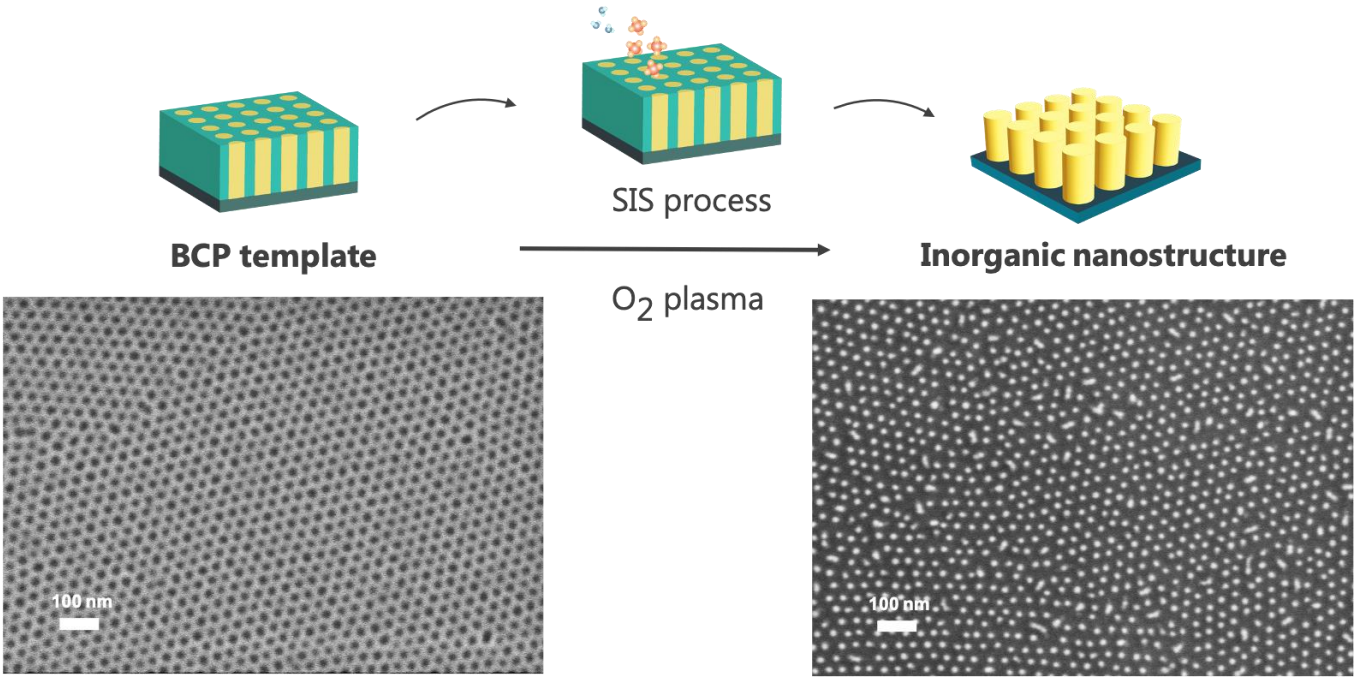
Hafnium oxide (HfO_2) is an attractive material for optoelectronic applications and high-κ dielectrics in semiconductor devices due to its advantageous properties- high dielectric constant, wide band gap, and high stability. However, hafnium oxide nanostructure fabrication currently relies on complex nanofabrication processes. Sequential infiltration synthesis (SIS)- a method derived from atomic layer deposition (ALD), in which vapor phase precursors diffuse into polymers and react with them to form hybrid material, can provide a simple and cost-effective alternative for these processes.

In this study, we demonstrate the formation of hafnium oxide nanostructures within block copolymers (BCPs) templates. BCP were self-assembled into highly ordered and periodic nanostructures. In SIS, selective interactions between the hafnium organometallic precursor and the polar block of the BCP resulted in selective growth within the polar block domains. Following the growth, the BCP template was removed to yield hafnium nanostructures templated by the BCP morphology. We explored the precursor-polymer interactions in various homopolymers using quartz crystal microbalance (QCM) microgravimetric measurements. This knowledge was further applied in finding a suitable BCP for templating HfO2 inorganic nanostructure.



P-62

CRYOGENIC SCANNING ELECTRON MICROSCOPY AS AN EFFECTIVE TOOL FOR NANOSTRUCTURAL STUDY OF BIOLOGICAL SYSTEMS

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Diseases resulting from blood cell dysfunction, like cardiovascular diseases, account for most of the mortality in modern society. Recent developments in microbiology lead to a greater understanding of cell function and structure. Techniques such as PCR, FACS, gel electrophoresis, and macromolecule blotting promote investigation of biochemical processes. However, all these techniques give numerical input, which can be interpreted by several models. It is necessary to use high-resolution (HR) imaging techniques to fully understand molecular organization within the cell and its connection to cell function and communication with its environment.

Cryo-SEM allows direct imaging of biological systems without modifying their nanostructure. The technique applicability ranges from studying the morphology of different subpopulations that may coexist in a sample, to understanding physiological processes by imaging the system at varying stages. Cryofixation with high-pressure freezing allows for maximum morphological preservation, becuase it captures nano-aggregates within cells at near-native conditions, while cryogenic electron microscopy provides an opportunity to study cells at high resolution as close to their native state as possible.

Here, I present an application of the cryo-SEM to analyze human blood cells. It is focused on optimization of specimen preparation procedure, and working parameters for better characterization of cell morphology, ultrastructure, and cell-cell interactions.

P-63

COUNTING NANOPARTICLES IN GENERAL AND VIRUSES IN PARTICULAR ONE AT A TIME

Paz Drori[1], Odelia Mouhadeb[2], Gabriel Moya[3], Yair Razvag[1], Ron Alcalai[2], Philipp Klocke[3], Thorben Cordes[3], Eran Zahavy[2], Eitan Lerner[1]

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The SARS-CoV-2 pandemic underlined the necessity for accurate, sensitive and rapid viral diagnostics, three aspects that are commonly thought of trading off. We demonstrate the detection of single specific nanoparticles based on their correlated fluorescence signals indicating both their volumes and specific antigens. This detection scheme is achieved by probing microfluidic laminar flow of a sample of nanoparticles immersed in free dyes and with specifically dye-labeled antibodies with a dual-color 3D-printed confocal setup. First, we demonstrate the detection capabilities using nanometer-sized beads and then on two different viruses expressing the Spike protein from SARS-CoV-2: (i) rVSV-ΔG-spike, and (ii) neutralized SARS-CoV-2. Additionally, employing this detection scheme together with microfluidic hydrodynamic focusing, we count single bio-nanoparticles rapidly for viral load as low as 104 viruses/mL, which covers the a wide range of the biomedically-relevant load for viruses in general, and for SARS-CoV-2 in particular. Overall, viruses can now be counted one at a time with the presented simple to use and affordable optofluidic technology rapidly, without giving up on specificity and sensitivity, and this capability will further expand to other important bio-nanoparticles in the near future.

P-64

MOLECULAR MOTORS ON MICROTUBULE TRACKS CREATED WITH NANO FOUNTAIN PEN

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[2]*Department of Chemistry, Ben-Gurion University, Beer-Sheva, Israel*

We are exploring an approach for transport of biological cargo using motor proteins (kinesin cin-8) on their natural tracks, microtubules, between predefined stations. Using Nano Fountain Pen (NFP), we attempt to lay down microtubules between the point of origin and destination, to serve as directional tracks on which kinesin molecules will carry biological cargo.

To this end, we are patterning lines of avidin, to which biotinylated MTs are adhered. The functionality of thus immobilized MTs is demonstrated by observation of single kinesin molecules walking on the MTs. We also demonstrate alignment of MTs is via hydrodynamic drag.

Together with future refinement of alignment and polarization approaches, this method has the potential to serve as the conveyor network in miniaturized lab-on-a-chip(s).

P-65

TIME-GATED FLUORESCENCE LIFETIME IMAGING IN THE NEAR INFRARED REGIME; A COMPREHENSIVE STUDY TOWARD IN VIVO IMAGING

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Fluorescence lifetime imaging (FLI) is increasingly recognized as a powerful tool for biochemical and cellular investigations, including in vivo applications. Fluorescence lifetime is an intrinsic characteristic of any fluorescent dye which, to a large extent, does not depend on excitation intensity and signal level. In particular, it allows distinguishing dyes with similar emission spectra, offering additional multiplexing capabilities. However, in vivo FLI in the visible range is complicated by the contamination by (i) tissue autofluorescence, which decreases contrast, and by (ii) light scattering and absorption in tissues, which significantly reduce fluorescence intensity and modify the temporal profile of the signal. Therefore, in order to enable deeper tissue imaging, we use the near infrared (NIR) regime, in which the tissue's scattering and autofluorescence are significantly lower. We present a time-saving Monte Carlo (MC) simulation of fluorescent photons scattering within a turbid medium, followed by phasor analyses which enabled the simple multiplexing of different targets in one frame. We then demonstrate that using the most advanced time-gated single-photon avalanche diode (SPAD) array camera, SPAD512S, provide a simple and fast method for in vivo lifetime imaging. In particular, we show how phasor dispersion increases with increasing depth, but by using an appropriate background correction, simple "cut off" method and averaging analyses we are able to multiplex two targets in one frame, from 10 mm deep within the tissue. These results showcase the possibility to perform FLI in challenging conditions, using standard, NIR fluorophores.

P-66

SCANNING NANO-STRUCTURE ELECTRON MICROSCOPY FOR DECODING THE STRUCTURAL EVOLUTION OF META-STABLE MATERIALS

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In recent years, Electron Diffraction, and especially the 4D-STEM [1] is growingly becoming a routine part of structural characterizations of materials at the nano-scale. Its un-matched spatial resolution (down to sub-nm) enables the exploration of local variations within a sample, which alternatively is averaged over the entire irradiated sampled area, when explored, for example, by x-rays. As often shown in electron microscope, samples are often heterogeneous, and consequently their local properties, which then reflect on the average behaviour of the material, composite, or device. Besides morphology and composition, the local structural order can vary, especially in meta-stable systems which continuously evolve. In this study, we explore how far we can take electron diffraction when the interest is in the evolution of meta-stable materials.

We challenge ourselves with mapping the local structure in a composite of crystalline Ni and amorphous Zr-Cu-Ni-Al Bulk Metallic Glass (BMG) that was fused into a composite via hot-rolling [2]. Using a fast camera looking through the fluorescence screen, we captured diffraction patterns in a 4D-STEM modality, where we captured diffraction patterns coupled with beam precession with 3 nm step size in a Ni/BMG/Ni cross-section sample that was cut from the composite - in total 131x289 diffraction patterns (see FIGURE). Using the collected diffraction patterns and tailoring automated data reduction and analysis pipelines, such as auto-masking, azimuthal-integration, Fourier-transformation to get the electron Pair Distribution Function (ePDF) and various fittings of the PDF, we were efficiently deriving a large set of physically meaningful scalars, which we generalize as Quantities of Interest, or QoI of a Scanning Nano-structure Electron Microscopy (SNEM). [3]

By generating different QoI maps – each containing different structural information – we see in the Figure that one can extract very rich and unique structural information about the sample. For example, we see that chemical clustering may be a predeceasing (or following) step to the nucleation of nano-crystalline inclusions within the BMG. This example demonstrates the richness SNEM-based experiments can reveal, and with the assistance of automated analysis and feature detection pipelines can trace the evolution of disordered and meta-stable systems.

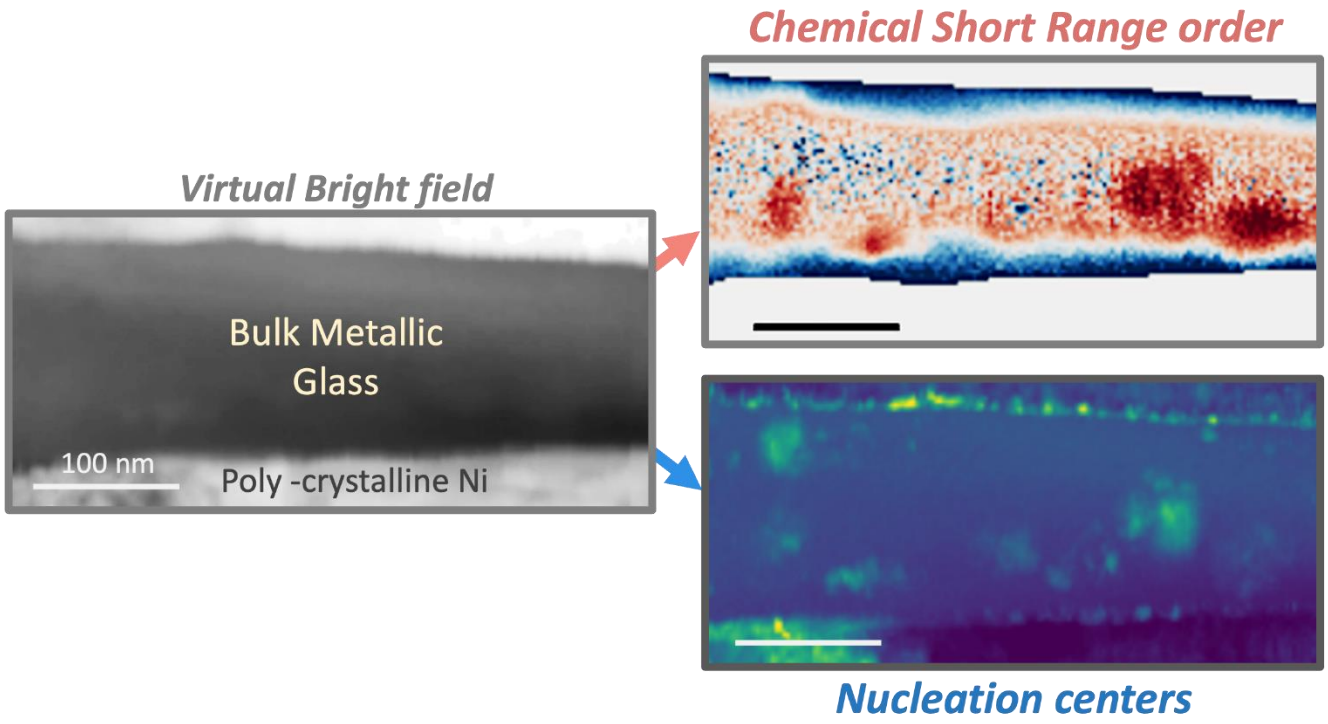

Figure Caption: QoI SNEM maps of the Ni/BMG/Ni structure showing: (left) a regular bright field image that emphasizes the amorphous region; (top-right) a chemical short-range order showing regions where there is a chemical ordering change (blue = ordering – increase in A-B-A-B; red = clustering – increase in A-A-A, or B-B-B clustering); (top-right) virtual dark-field mapping from a selected area of the diffraction patterns, showing (yellow-green intensity) location of nano-crystalline nucleai presence in the BMG. The scale bare in all maps is 100 nm.

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P-67

FRET-SENSITIZED ACCEPTOR EMISSION LOCALIZATION (FRETsael) – NANOMETER ACCURACY LOCALIZATION OF BIOMOLECULAR INTERACTIONS USING FLIM-FRET LASER SCANNING CONFOCAL MICROSCOPY

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Super-resolution light microscopy techniques shifted the diffraction-limited microscopy into nanoscopy, in which it is finally possible to observe the nanometer-scale biomolecules in the cell. Attaining the super-resolved information requires either using fluorescent dyes flickering between bright and dark states, immediate depletion of a well-defined region of dye excited states or using the knowledge of the illumination profile to track single biomolecules. We developed a technique dubbed FRET-sensitized acceptor emission localization (FRETsael), in which we gain nanometer localization accuracy of biomolecular interactions in FRET-FLIM. This is achieved by few nanometer laser scanning steps remembering the confocal illumination profile is spatially non-uniform illumination, and by finding the local extrema of parameters that report on the contribution of excitation to FRET. Using simulations, we show that no the localization accuracy is 20-30 nm for all true-positive detections no matter what are the underlying experimental conditions. We also report the dynamic range in which the false discovery rate is minimal, and the true positive rate is maximal. Furthermore, we show the performance of the algorithm on a more realistic simulations of Actin-Vinculin and ER-Ribosomes pairs of interactions. Finally, we explore the performance of the FRETsael approach on cells with the nuclear pore protein Nup96 tagged with a donor GFP and with Alexa Fluor 647-labeled antibodies against GFP, as acceptors. The FRETsael imaging approach paves the way towards studying biomolecular interactions with improved spatial resolution from alternating laser excitation scanned frames in confocal microscopy without the use of blinking dyes or special optics.

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SHAPING OF ELECTRON BEAMS USING SCULPTED THIN FILMS

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Electron-matter interactions and the wave nature of electrons allow for electron beam shaping by sculpted thin films. It can be used to develop technological applications in transmission electron microscopy (TEM) that offer increased resolution in different imaging modes and thus to improve measurement techniques. In this poster, we present preliminary results of two such applications. First, we show spherical aberration correction of field-free STEM mode in FEI Titan G2 Holo microscope by eliminating the spherical wavefront of the electron beam focused by the C3 lens. Such an application may lead to spherical aberration corrected Lorentz STEM, used for measurements of magnetic materials, which, nowadays, is impossible in many systems because even if a multipole aberration corrector is installed in them, their condenser lenses aren't strong enough to focus the beam onto it. Second, and towards the correction of chromatic aberration of STEM, we use thin film diffractive electron lenses to chromatically manipulate a focusing electron beam wavefront. Practically, we fabricated diffractive lenses which their focal lengths are dependent on the electron beam energy, changing the total focus of a TEM beam at Low Angle Diffraction (LAD) mode when they are placed at the sample holder. Due to fabrication limitations chromatic aberration correction may be impractical in the present, but this work may be a proof of concept and pave the way towards such achievements in the future.

P-69

THE LABORATORY FOR SENSING NANOMATERIALS & CONTROLLED RELEASE TECHNOLOGIES

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Real-time sensing of biological processes in diseases is critical for many fields. Optical sensors enable fast, reliable, and highly sensitive detection of various states. Among many materials, the physical and optical properties of single-walled carbon nanotubes (SWCNTs) set them apart as indispensable sensors and offer unique applications in biology and medicine. Our lab is interested in engineering nanosensors for detecting diseases and monitoring biological processes. Specifically, we synthesized, characterized, and implemented the nanosensors composed of SWCNTs for in vitro and in vivo purposes. Among the various sensors, we engineered a novel sensor that tracks a specific enzymatic suicide inactivation pathway that leads to irreversible enzyme inactivation and can be further used to screen novel molecules to identify enzyme inhibitors (Yaari et al. Nano Letters, 2020). Additionally, we developed a novel platform based on an array of DNA-wrapped SWCNTs nanosensors and machine learning technology to detect multiple ovarian cancer biomarkers without using a specific binding moiety (Yaari et al., Science Advances, 2021). We are fabricating a clinical nanosensor comprising a particular antibody of biomarker conjugated to DNA-wrapped SWCNTs (Ab-SWCNTs) for early ovarian cancer detection. The nanosensors detect the three ovarian cancer biomarkers and will be tested in patients shortly. These nanosensors strengthen the utility and diversity of nanomaterial formulations in medicine.

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DEEP THREE-PHOTON IMAGING OF AN ADULT ZEBRAFISH BRAIN

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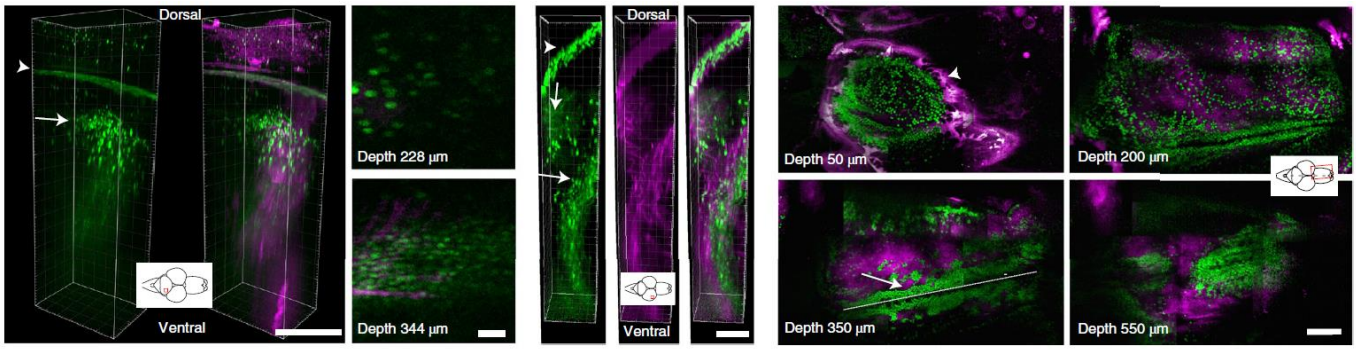
Multiphoton fluorescence microscopy (MPM) is a well-established technique for deep-tissue imaging with subcellular resolution. In fact, 2-photon laser scanning microscopy (2PM) is currently one of the main optical tools in in vivo animal brain imaging, which allows the visualization of a single neuron and neuronal processes in a living brain. In the last couple of years it was shown that higher order nonlinear microscopy, e.g. 3-photon fluorescence microscopy (3PM), when combined with long wavelength excitation, allows to achieve deeper imaging than 2PM [1]. This method was found to be particularly useful for volumetric animal brain imaging, because out-of-focus background generation can be further reduced due to the higher order nonlinear excitation.

The zebrafish model allowed for the first non-invasive calcium imaging in a vertebrate with both synthetic and genetically encoded calcium indicator lines, setting the stage for the burgeoning use of transparent larval fish for imaging of neurons throughout the brain of a behaving vertebrate. In contrast, opaque adult zebrafish, like other vertebrates, have proven less tractable for deep noninvasive approaches.

Here we demonstrate non-invasive long wavelength 3P imaging in adult zebrafish and reveal its power to image structure and function through the entire telencephalon, as well as deep into the optic tectum and cerebellum of intact adult fish. Large portions of the brain of an established vertebrate model are thus visible for non-invasive structural and functional studies from embryo to adult.

All zebrafish experiments were performed on adult fish, 3 to 7 months old. We used a custom made three photon (3P) imaging system that combines a femto-second pulsed laser with a repetition rate of 500K Hz at 1300 and 1700 nm, together with dispersion compensation, and scanning system and a high NA objective for imaging and collection. The collected fluorescence signal was divided to two spectral regions for florescence and third harmonic generation (THG). Most of the imaging was performed at 1300 nm with GCaMP6s indicators to assess both structural resolution as well as perform functional imaging. In addition, we imaged structural features at 1700 nm with glutamatergic neurons labeled with DSRed to image red light emitting fluorophores as well.

We imaged genetically labeled neurons through the zebrafish head in the cerebellum, optic tectum, and telencephalon. Our results show deep 3P non-invasive imaging of structure and/or function in major brain regions of mature adult zebrafish. In the figure below 3P imaging of the cerebellum (left) and the optic tectum of an intact zebrafish are shown [2]. In the cross section images to the right is possible to see the 3P fluorescence signal from the neurons (in green) and the THG from the tissue structure (in purple).



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P-71

REAL-TIME STUDY OF SURFACE-GUIDED NANOWIRE GROWTH BY IN SITU SCANNING ELECTRON MICROSCOPY

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Surface-guided growth has proven to be an efficient approach for the production of nanowire arrays with controlled orientations and their large-scale integration into electronic and optoelectronic devices. There are intensive studies on different mechanisms of guided nanowire growth. Yet, many aspects of the surface-guided growth process remain unclear due to a lack of observation in real-time. In this work, we adopt two heating systems under different environmental scanning electron microscopes (ESEMs, Quattro S and Quattro, Thermo Fisher Scientific) to observe and record the *in situ* growth of ZnSe surface-guided nanowires grow. Parameters were carefully tuned to avoid nonselective growth on the exposed substrate surfaces and other artifacts.

ZnSe surface-guided nanowires growing on periodically faceted substrates of annealed M-plane sapphire clearly show how the nanowires elongate along the substrate nano-grooves while pushing the catalytic Au nanodroplet forward at the tip of the nanowire. The *in situ* experiments allow us to study the growth mechanism in great detail, for example, to compare competing processes, and to reveal the effect of topographic discontinuities of the substrate on the growth direction. A decrease in precursor concentration as it is consumed after a long reaction time causes the nanowires to shrink back instead of grow, thus indicating that the process is reversible and takes place near equilibrium. This real-time study of surface-guided growth, enabled by *in situ* ESEM, enables a better understanding of the formation of nanostructures on surfaces.

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